

# **Post-transcriptional Gene Silencing in Neuronal Differentiation, Development and Schizophrenia**

**Natalie Jane Beveridge  
B.Sc (Biotech) (Hons)**

**Doctor of Philosophy (Experimental Pharmacology)  
University of Newcastle, Australia**

**March 2011**



---

## **DECLARATION**

*This thesis contains no material which has been accepted for the award of any other Degree or Diploma in any University or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. I give consent to this copy of my thesis, when deposited in the University Library, being made available for loan and photocopying subject to the provisions of the Copyright Act 1968.*

*I hereby certify that this thesis is in the form of a series of published papers of which I am a joint author. I have included as part of the thesis a written statement from each co-author, endorsed by the Deputy Head of Faculty (Research and Research Training), attesting to my contribution to the joint publications.*

---

**NATALIE J. BEVERIDGE**

**March, 2011**

---

## **ACKNOWLEDGEMENTS**

It is a pleasure to thank the many people who made this thesis possible. Foremost, I would like to thank my supervisors, Dr Murray Cairns and Dr Paul Tooney, for giving me a very interesting and challenging project to study and for their guidance and support; not only during my PhD, but throughout the many years I have been associated with this lab. Thank you also for all the travel opportunities you have given me over the years, they have been invaluable experiences, for which I am ever grateful.

I wish to acknowledge funding support from the University of Newcastle and the Schizophrenia Research Institute. Also, I would like to thank each of my collaborators who have contributed their knowledge, resources and expertise to our studies.

It is also a pleasure to thank Michelle Manhood, for without her guidance and encouragement over many years, I would perhaps never have pursued this scientific career path.

I would have never got to this stage of my career without the support from my family. Thank you for bearing with me through the stressful times and supporting me whilst I've travelled. Finally, I would like to thank my partner, Daniel. You have been a fantastic travel buddy when I have attended conferences far and wide overseas. Thank you for your continued support, encouragement and interest in my work, and most importantly, keeping a smile on my face. We made it!! 😊

---

## **TABLE OF CONTENTS**

<b>DECLARATION.....</b>	<b>I</b>
<b>ACKNOWLEDGEMENTS .....</b>	<b>II</b>
<b>ABSTRACT .....</b>	<b>1</b>
<b>LIST OF ABBREVIATIONS .....</b>	<b>2</b>
<b>CHAPTER 1: LITERATURE REVIEW.....</b>	<b>4</b>
THE REGULATION OF GENE EXPRESSION .....	4
MIRNA EXPRESSION AND PROCESSING.....	6
THE CELLULAR FUNCTION OF MIRNA.....	6
<i>Inhibition of Translation Initiation.....</i>	<i>6</i>
<i>Post-initiation Inhibition .....</i>	<i>8</i>
<i>miRNA-mediated mRNA decay .....</i>	<i>8</i>
MIRNA IN BRAIN DEVELOPMENT AND DISEASE .....	8
MIRNA IN SCHIZOPHRENIA.....	11
SCHIZOPHRENIA: A BIOLOGICAL DISORDER OF THE BRAIN .....	12
<i>Alterations in Brain Structure and Function.....</i>	<i>13</i>
HERITABILITY IN SCHIZOPHRENIA.....	14
<i>Genetic Linkage Studies.....</i>	<i>15</i>
<i>Copy Number Variation .....</i>	<i>16</i>
<i>Genome-wide Association Studies .....</i>	<i>16</i>
<b>RATIONALE.....</b>	<b>18</b>
<b>AIMS &amp; HYPOTHESES.....</b>	<b>19</b>
<b>MANUSCRIPTS .....</b>	<b>20</b>
<b>CHAPTER 2 : DOWN-REGULATION OF MIR-17 FAMILY EXPRESSION IN RESPONSE TO RETINOIC ACID INDUCED NEURONAL DIFFERENTIATION .....</b>	<b>22</b>
STATEMENT I: AUTHOR CONTRIBUTION TO CHAPTER 2 MANUSCRIPT .....	22



---

<b>CHAPTER 3 : MATURATION OF THE HUMAN DORSOLATERAL PREFRONTAL CORTEX COINCIDES WITH A DYNAMIC SHIFT IN MICRORNA EXPRESSION.....</b>	<b>33</b>
STATEMENT II: AUTHOR CONTRIBUTION TO CHAPTER 3 MANUSCRIPT .....	33
<b>CHAPTER 4: DYSREGULATION OF MIRNA 181B IN THE TEMPORAL CORTEX IN SCHIZOPHRENIA.....</b>	<b>43</b>
STATEMENT III: AUTHOR CONTRIBUTION TO CHAPTER 4 MANUSCRIPT .....	43
<b>CHAPTER 5: SCHIZOPHRENIA IS ASSOCIATED WITH AN INCREASE IN CORTICAL MICRORNA BIOGENESIS .....</b>	<b>59</b>
STATEMENT IV: AUTHOR CONTRIBUTION TO CHAPTER 5 MANUSCRIPT .....	59
<b>CHAPTER 6: UPREGULATION OF DICER AND MICRORNA EXPRESSION IN THE DORSOLATERAL PREFRONTAL CORTEX BRODMANN'S AREA 46 IN SCHIZOPHRENIA.....</b>	<b>75</b>
STATEMENT V: AUTHOR CONTRIBUTION TO CHAPTER 6 MANUSCRIPT.....	75
<b>CHAPTER 7: GENERAL DISCUSSION .....</b>	<b>85</b>
NEURONAL DIFFERENTIATION .....	85
NORMAL DEVELOPMENT OF THE HUMAN BRAIN .....	86
SCHIZOPHRENIA .....	87
FUTURE RECOMMENDATIONS.....	89
<b>REFERENCES .....</b>	<b>91</b>
<b>APPENDIX I: SUPPLEMENTARY DATA FOR CHAPTER 2.....</b>	<b>99</b>
SUPPLEMENTARY TABLE 1: GENE LISTS OF UP-REGULATED miR-17 TARGETS AND DOWN-REGULATED BRAIN-ENRICHED miRNA TARGETS.....	99
SUPPLEMENTARY TABLE 2: MICROARRAY AND QPCR DATA FOR UP- AND DOWN-REGULATED MICRORNA.....	111
SUPPLEMENTARY TABLE 3: POTENTIAL GENE TARGETS OF miR-17 FAMILY IDENTIFIED USING TARGETCOMBO PREDICTION ALGORITHM.....	112

---

---

SUPPLEMENTARY TABLE 4: GENES SHOWING ALTERED EXPRESSION DUE TO DIFFERENTIATION BY ILLUMINA MICROARRAY ANALYSIS.....	145
SUPPLEMENTARY TABLE 5: GENE LISTS OF UP-REGULATED miR-17 TARGETS AND DOWN-REGULATED BRAIN-ENRICHED miRNA TARGETS.....	179
 <b>APPENDIX II: SUPPLEMENTARY DATA FOR CHAPTER 3 .....</b>	<b>191</b>
SUPPLEMENTARY TABLE 1: DETAILED DEMOGRAPHIC INFORMATION FOR 97 POSTMORTEM DLPFC SAMPLES.....	191
SUPPLEMENTARY TABLE 2: OLIGONUCLEOTIDE SEQUENCES.....	193
SUPPLEMENTARY TABLE 3: SPEARMAN CORRELATIONS OF miRNA EXPRESSION AND DEMOGRAPHIC VARIABLES.....	194
SUPPLEMENTARY TABLE 4: miRNA DISPLAYING EXPRESSION CHANGES ACROSS THE LIFESPAN. ...	206
SUPPLEMENTARY TABLE 5: TARGET GENE PATHWAY ANALYSIS.....	208
SUPPLEMENTARY FIGURE 1: miRNA MICROARRAY QUANTITATIVE REAL-TIME PCR VALIDATION. ....	210
SUPPLEMENTARY FIGURE 2: THE AXON GUIDANCE PATHWAY IS HEAVILY REGULATED BY AGE-RELATED miRNA. ....	211
 <b>APPENDIX III: SUPPLEMENTARY DATA FOR CHAPTER 4.....</b>	<b>212</b>
SUPPLEMENTARY TABLE 1: miRNA EXPRESSED IN STG USING DNA MICROARRAYS .....	212
SUPPLEMENTARY TABLE 2A: miR-181B TARGETS - miRANDA ALGORITHM (WEB VERSION) .....	214
SUPPLEMENTARY TABLE 2B: miR-181B TARGETS - TARGETCOMBO (UNION) - DIANA-MICROT, PicTar, TARGETSCANS, miRANDA .....	220
SUPPLEMENTARY TABLE 2C: FUNCTIONAL ANNOTATION CLUSTERING OF miR-181B GENE TARGETS – .....	237
SUPPLEMENTARY TABLE 2D: KEGG PATHWAY ANALYSIS OF miR-181B GENE TARGETS.....	238
SUPPLEMENTARY TABLE 2E: miR-181B TARGETS - DOWN REGULATED IN THE STG (BOWDEN ET AL., 2007) .....	239

---

---

<b>APPENDIX IV: SUPPLEMENTARY DATA FOR CHAPTER 5.....</b>	<b>240</b>
SUPPLEMENTARY TABLE 1: DEMOGRAPHIC INFORMATION FOR STG AND DLPFC POSTMORTEM TISSUE. .....	240
SUPPLEMENTARY TABLE 2: DIFFERENTIALLY EXPRESSED miRNA BY MICROARRAY AS DETERMINED .....	242
SUPPLEMENTARY TABLE 3: TOTAL RNA ANALYSIS .....	244
SUPPLEMENTARY TABLE 4: OVER-REPRESENTED KEGG PATHWAYS PREDICTED TO BE REGULATED BY .....	245
SUPPLEMENTARY TABLE 5: INVESTIGATING miRNA/TARGET GENE RELATIONSHIPS BY LUCIFERASE REPORTER GENE ASSAY. ....	246
 <b>APPENDIX V: SUPPLEMENTARY DATA FOR CHAPTER 6 .....</b>	 <b>247</b>
SUPPLEMENTARY TABLE 1: BA46 SCHIZOPHRENIA AND NON-PSYCHIATRIC CONTROL COHORT DEMOGRAPHICS AND TISSUE CHARACTERISATION.....	247
SUPPLEMENTARY TABLE 2: miRNA AND BIOGENESIS GENE EXPRESSION CORRELATION MATRIX. BLUE SHADED CELLS REPRESENT SIGNIFICANT CORRELATIONS.....	249
SUPPLEMENT 3: SCHIZOPHRENIA-RELEVANT KEGG PATHWAYS PREDICTED TO BE REGULATED BY UP- REGULATED MICRORNA IN BA46. ....	250
SUPPLEMENT 4: OVER-REPRESENTED KEGG PATHWAYS PREDICTED TO BE REGULATED BY UP- REGULATED MICRORNA IN BA46: .....	252

---

---

## **ABSTRACT**

Efforts to understand the underlying mechanisms driving changes in gene expression have focused predominantly on genetic and epigenetic influences on transcription mediated by alterations in signal transduction pathways, their transcription factors, or gene promoter elements and associated chromatin structure. However, recent studies have emerged that also highlight the impact of post-transcriptional regulation of gene expression. Post-transcriptional influences mediated by microRNA (miRNA) play a major role in coordinating the regulation of gene expression during the differentiation and development of the brain. This study has established the specific patterns miRNA expression throughout neuronal differentiation, normal human brain development and schizophrenia.

Using a custom microarray, miRNA expression was examined in differentiating neuroblasts *in vitro*. This revealed that the entire miR-17 family of miRNA displayed reduced expression in response to the differentiation process and was shown to target several known neuronal markers. This result suggested that the miR-17 family might be working co-operatively to fine tune the gene expression changes taking place in the neuronal differentiation process. miRNA expression was also examined in human neurodevelopment. These results demonstrated that a large proportion of miRNA displayed distinct expression changes with age and are likely to be responsible for many of the gene expression changes observed during brain maturation and throughout aging. Perhaps even more significantly, miRNA expression profiling of postmortem brain in the superior temporal gyrus and dorsolateral prefrontal cortex revealed an increase in miRNA expression and biogenesis that suggested a role for miRNA expression in the neuropathology of schizophrenia.

The findings presented in this thesis support mounting evidence that miRNA play a crucial role in the regulation of gene expression in normal neurodevelopment and alterations to miRNA expression contributes to the pathogenesis of schizophrenia.

---

## **LIST OF ABBREVIATIONS**

<b>3'-UTR</b>	3' untranslated region
<b>Ago</b>	Argonaute
<b>BDNF</b>	brain-derived neurotrophic factor
<b><i>C. elegans</i></b>	<i>Caenorhabditis elegans</i>
<b>CAMK2<math>\gamma</math></b>	Calcium/calmodulin-dependent protein kinase type II gamma
<b>CLOCK</b>	Circadian Locomotor Output Cycles Kaput
<b>CNV</b>	copy number variant
<b>CREB</b>	cAMP response element-binding
<b>DGCR8</b>	DiGeorge critical region 8
<b>DISC1</b>	Disrupted in schizophrenia 1
<b>DLPFC</b>	dorsolateral prefrontal cortex
<b>DNA</b>	deoxyribonucleic acid
<b>ERBB4</b>	Receptor tyrosine-protein kinase erbB-4
<b>FEZ1</b>	Fasciculation and elongation protein zeta-1
<b>FMR1</b>	fragile X mental retardation 1
<b>FMRP</b>	fragile X mental retardation protein
<b>GABA</b>	$\gamma$ -Aminobutyric acid
<b>GWAS</b>	genome-wide association study
<b>IRES</b>	internal ribosome entry site
<b>LIMK1</b>	Lim-domain-containing protein kinase 1
<b>MECP2</b>	methyl CpG binding protein 2 (Rett syndrome)
<b>miRNA</b>	microRNA
<b>mRNA</b>	messenger RNA
<b>NDEL1</b>	Nuclear distribution protein nudE-like 1
<b>NMDA</b>	N-Methyl-D-aspartic acid
<b>NRG1</b>	neuregulin-1
<b>P bodies</b>	processing bodies
<b>PABP</b>	polyA binding protein
<b>PDE4B</b>	cAMP-specific 3',5'-cyclic phosphodiesterase 4B
<b>pre-miRNA</b>	precursor miRNA
<b>pri-miRNA</b>	primary miRNA
<b>PTBP1</b>	Polypyrimidine tract-binding protein 1
<b>REST</b>	RE1-Silencing Transcription factor
<b>RISC</b>	RNA induced silencing complex
<b>RNA</b>	ribonucleic acid
<b>RNAi</b>	RNA interference
<b>rRNA</b>	ribosomal RNA
<b>siRNA</b>	short-interfering RNA
<b>SLITRK1</b>	SLIT and NTRK-like family, member 1
<b>SNP</b>	single nucleotide polymorphism
<b>STG</b>	superior temporal gyrus
<b>tRNA</b>	transfer RNA

---

---

# CHAPTER 1

## *Introduction*

---

---

## **CHAPTER 1: LITERATURE REVIEW**

### **The Regulation of Gene Expression**

---

It has been generally understood that genes and proteins are synonymous, except those that code for ribosomal RNA (rRNA), spliceosomal RNA or transfer RNA (tRNA) that are indirectly or directly required for mRNA processing and translation <sup>1</sup>. The idea that genes code for proteins using an mRNA intermediate is derived from the central dogma, which states that DNA codes for RNA which then codes for protein. This essentially holds true for prokaryotes, whose genomes are almost entirely composed of tightly packed protein-coding sequences, along with some non-coding RNA genes and those encoding rRNAs and tRNAs. However, this is not simply the case for higher organisms, where coding sequences only occupy a small fraction of the genome <sup>2, 1, 3</sup>. The fact that intronic RNA constitutes approximately 95% of primary protein coding transcripts <sup>4</sup>, coupled with the thought that non-coding RNA transcripts without extensive open reading frames may correspond to at least half of all transcripts, has led to the estimate that a large proportion of the transcriptional output of the human genome is non-coding RNA <sup>1</sup>. Non-coding RNA can be derived from their own genes or introns of protein-coding genes and many are also antisense to, or overlapping protein-coding genes <sup>2, 1, 5, 6, 3</sup>. They produce transcripts that function directly as structural or regulatory RNA instead of expressing mRNA that encode proteins <sup>7</sup>.

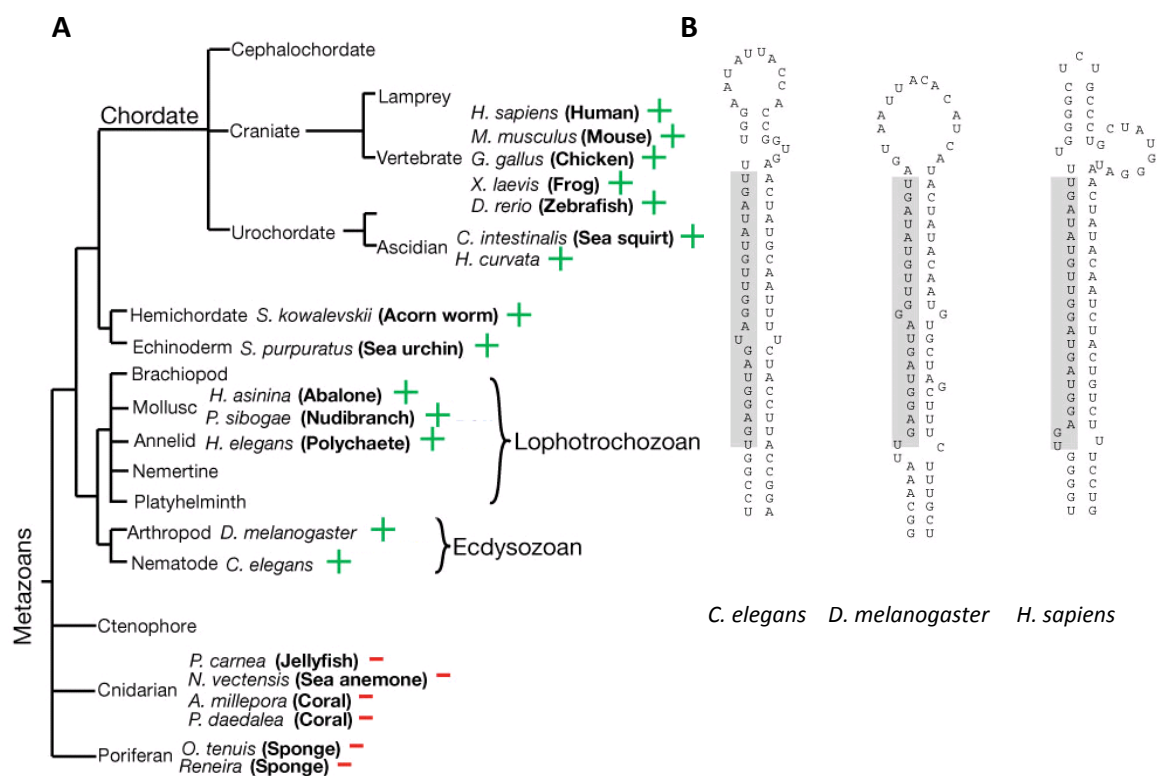
Research has shown that two main groups of small non-coding RNA have been

identified as sequence-specific post-transcriptional regulators of gene expression; the microRNA (miRNA) and the small-interfering RNA (siRNA) <sup>8</sup>. The mechanisms whereby miRNA and siRNA act to regulate gene expression are highly overlapping, though the miRNA pathway that exists in animals ultimately leads to mRNA destabilisation and translation inhibition, while siRNA (primarily in plants) act through the RNA interference (RNAi) pathway to cleave and destroy the target mRNA sequence <sup>9</sup>. The production and subsequent function of the small non-coding RNA requires the presence of certain types of proteins: double-stranded RNA-specific endonucleases and small RNA-binding proteins called Argonaute (Ago) proteins. Together, the small RNA and their associated proteins collectively act in distinct RNA silencing pathways such as RNAi or the miRNA pathway to regulate transcription, genome integrity, chromatin structure and mRNA stability <sup>10-12</sup>.

miRNA are expressed in a developmental and tissue-specific manner and are thought to regulate the majority of all human genes <sup>13, 14</sup>. These small RNA are 18 to 26 nucleotides long and inhibit transcription and translation through the sequence-specific base pairing of nucleotides 2 to 8 (seed region) with the 3'-UTR of specifically targeted mRNA <sup>15, 13, 16</sup>. Although the first published account of a miRNA appeared almost two decades ago <sup>17</sup>, it is only in more recent years that the diversity of these small regulatory RNA has been acknowledged. The first miRNA, *lin-4*, was discovered in *Caenorhabditis elegans* (*C. elegans*) where it was

found to be necessary for the temporal control of many developmental events after embryogenesis. Interestingly, the *lin-4* RNA was found to lack an open reading frame and was shown to have sequence complementarity with the 3'-UTR of the *lin-14* mRNA via an antisense RNA-RNA interaction. At the first stage of larval development, the level of the *lin-14* protein was shown to decrease and as such, it was suggested that the *lin-4* miRNA was able to negatively regulate the level of the *lin-14* protein<sup>17</sup>. The discovery of this miRNA was thought to be a unique case until the discovery of *let-7* in the year 2000, which was

later shown to be conserved throughout almost all metazoans (Fig. 1)<sup>18, 19</sup>. Thousands of miRNA have by now been identified in species such as *Drosophila*, *C. elegans*, and *Arabidopsis thaliana* as well as viruses, mammals and other plant species by using molecular cloning and bioinformatics prediction techniques<sup>19-23</sup>. In higher eukaryotes, hundreds of miRNA genes are predicted to be present<sup>24</sup>. A variety of bioinformatics approaches have estimated that any given miRNA could have up to 800 target genes, suggesting there may be numerous regulatory roles played by miRNA<sup>25, 26, 13, 14, 12</sup>.



**Figure 1: Phylogenetic tree showing species expressing *let-7* miRNA and its conservation among species.** The majority of metazoans express the miRNA, *let-7*. Species denoting (+) express *let-7* and those denoting (-) do not. The *let-7* miRNA is highly conserved throughout *Caenorhabditis elegans*, *Drosophila melanogaster* and *Homo sapiens*. The conserved region of each stem-loop structure is shown shaded in grey. (Adapted from Pasquinelli *et al.*<sup>18</sup> and Reinhart *et al.*<sup>19</sup>)



---

## miRNA Expression and Processing

---

The expression, excision and activation of the single-stranded miRNA from precursor transcripts occur through a multi-step process (Fig. 2). miRNA are initially expressed as part of RNA transcripts termed primary miRNA (pri-miRNA) which are usually transcribed by RNA Polymerase II, and include 5' caps and 3' poly(A) tails<sup>27</sup>. The miRNA portion of the pri-miRNA transcript forms a hairpin accompanied with signals for nuclease cleavage. The microprocessor complex (consisting of the double-stranded RNA-specific ribonuclease III, Drosha and DGCR8) then digests the pri-miRNA in the nucleus in order to release the hairpin precursor miRNA (pre-miRNA). Pre-miRNA are approximately 70 nucleotides long and have 3' overhangs between one and four nucleotides long, 25 to 30 base pair stems, and relatively small loops (Fig. 2)<sup>28, 9</sup>. The nuclear export receptor, Exportin-5 has been shown to bind specifically to correctly processed pre-miRNA and appears to be responsible for export of pre-miRNA from the nucleus to the cytoplasm<sup>29</sup>. Once in the cytoplasm, another member of the ribonuclease III superfamily; Dicer, cleaves the pre-miRNA approximately 19 bases from the microprocessor cut site, resulting in a double-stranded RNA (Fig. 2)<sup>28, 30, 9</sup>. After the strands become separated, the strand with the weakest base pairing at the 5' end of the duplex will preferentially associate with the RNA induced silencing complex (RISC). This strand becomes the active miRNA which guides the RISC to its mRNA target while the other strand is often degraded. However, there is evidence that in many cases both strands continue to form

mature miRNA (e.g. miR-9 and miR-9\*, miR-17 and miR-17\*)<sup>31, 9</sup>, though the miRNA\* species are less abundant than their partners<sup>32</sup>.

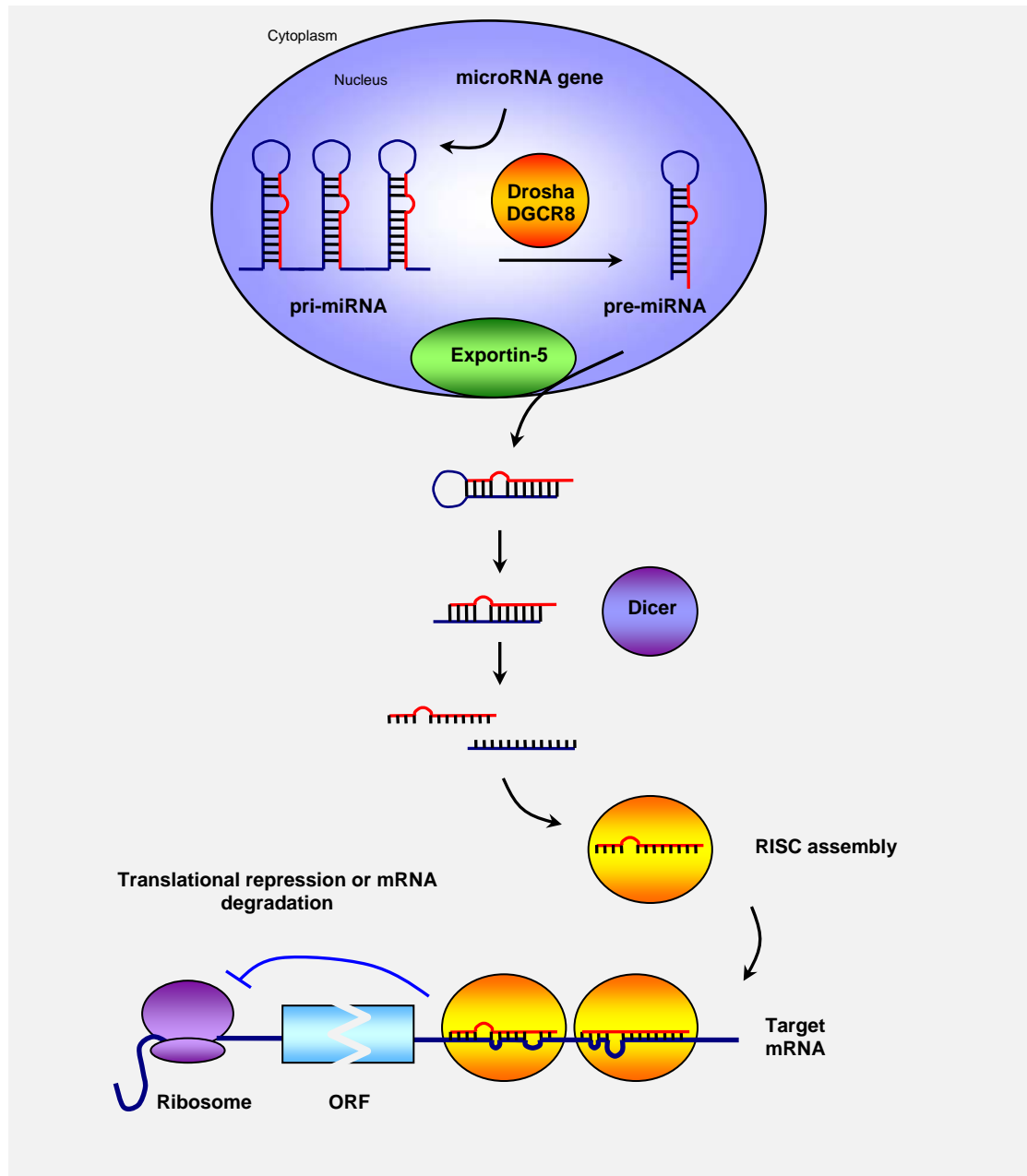
## The Cellular Function of miRNA

---

The precise mechanisms of miRNA-mediated repression remain elusive despite numerous models and hypotheses. However, in recent years, there has been substantial progress in understanding miRNA functions and mechanisms.

### *Inhibition of Translation Initiation*

Differing views exist on how miRNA might inhibit the initiation of translation. Firstly, miRNA may block initiation by interfering with the competent ribosome assembly (Fig. 3). Drosophila studies have shown that miRNA can repress the 48S translational complex which precedes the addition of the 60S ribosomal unit to create the competent ribosome<sup>33</sup>. Secondly, the active RISC might repress the formation of initiation complexes, since miRNA regulation requires the presence of a cap structure<sup>34</sup>. It is thought that Ago2 competes with the translational machinery for the cap binding site and represses the formation of the initiation complex when it is recruited to the 3'-UTR of the target mRNA<sup>35</sup>. Lastly, miRNA may block the PolyA Binding Protein (PABP) binding site on the mRNA. Also, by inducing de-adenylation and shortening the polyA tail, PABP is prevented from associating with the mRNA<sup>36, 37</sup>.



**Figure 2: An animal-centric view of miRNA processing.** Inside the nucleus, the microprocessor complex (Drosha and DGCR8) processes the primary miRNA transcripts into 70-nucleotide pre-miRNA. Exportin-5 then transports pre-miRNA into the cytoplasm where it is then processed into RNA duplexes by Dicer. One strand of RNA duplex is assembled into the RNA-induced silencing complex (RISC) which consequently acts on its target to reduce mRNA and/or protein levels. (Adapted from He & Hannon <sup>38</sup>)

---

### *Post-initiation Inhibition*

The model for repression occurring after the initiation step is supported by findings where mRNA targets have been shown to associate with actively translating polysomes<sup>39</sup> and miRNA can repress cap-independent translation initiated by an internal ribosome entry site (IRES). The post-initiation inhibition could also result from the degradation of the nascent polypeptide encoded by the target mRNA or an increased rate of ribosome drop off, creating incomplete protein products that are rapidly degraded<sup>40</sup> (Fig. 3).

### *miRNA-mediated mRNA decay*

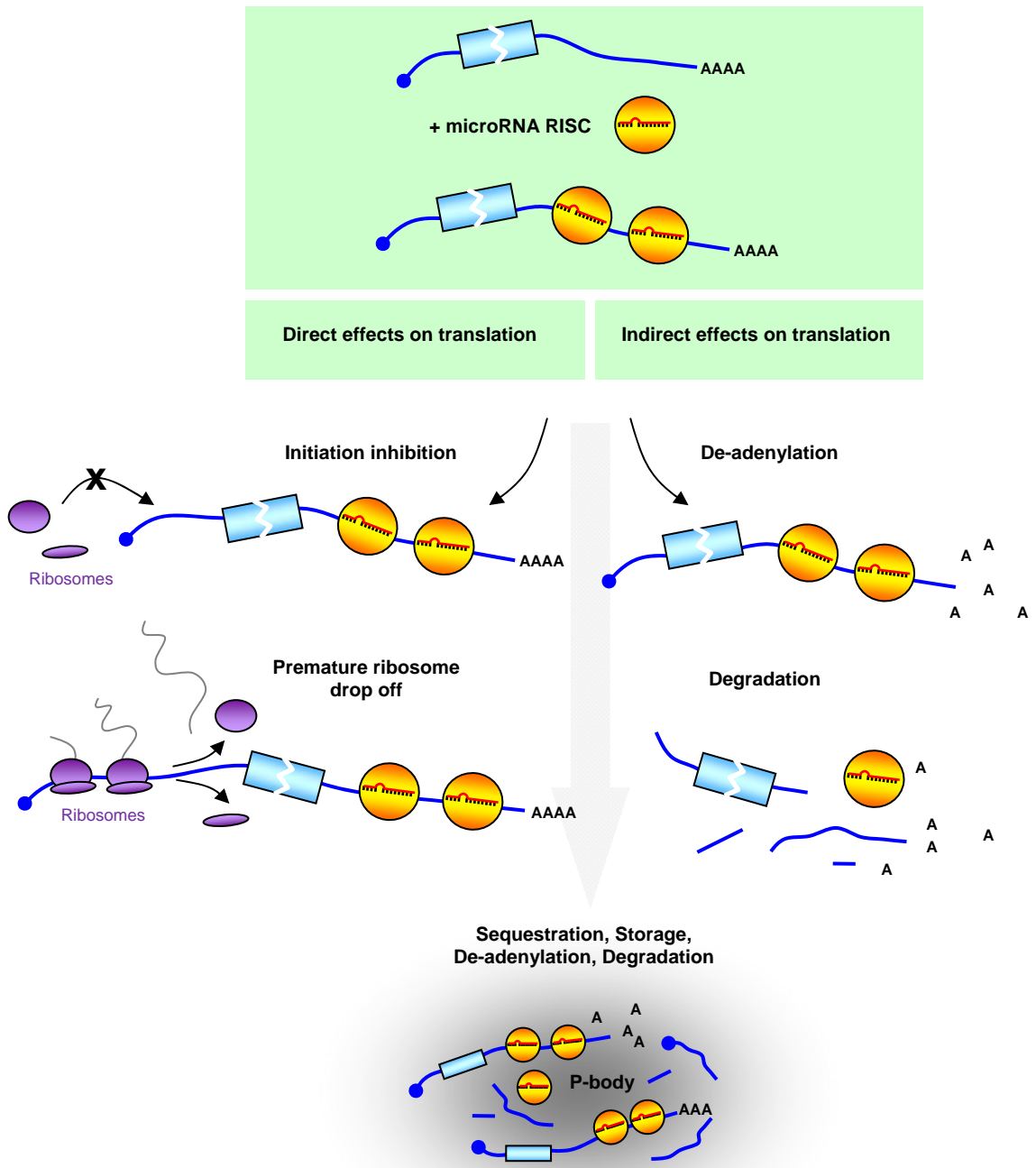
miRNA can downregulate the levels of mRNA that contain imperfectly complementary binding sites within their 3'-UTR. This has been demonstrated during zebrafish embryogenesis, where miR-430 controls the turnover of maternal mRNA<sup>41</sup>. Components of the RISC machinery (such as Ago proteins) have consistently been shown to localise to sites of mRNA degradation known as processing bodies (P bodies)<sup>42</sup>. These contain the enzymes required for mRNA degradation such as deadenylase, decapase and exonuclease. The co-localisation of RISC complexes and P body enzymes supports the model of miRNA-mediated mRNA decay. In addition, various Ago proteins are capable of interfering with translation or degrading mRNA<sup>43</sup>. Altogether, these data reveal that miRNA can mediate mRNA degradation in a direct or indirect fashion.

---

### **miRNA in Brain Development and Disease**

Several groups have provided evidence that miRNA act as key regulators of processes as diverse as cell proliferation, differentiation, development, apoptosis and metabolism<sup>19, 25, 44-47</sup>. In addition to regulating important growth and developmental processes, miRNA have been shown to be involved in the pathogenesis of disease. For instance, abnormalities in miRNA expression have been implicated numerous cancers, heart disease, viral infection as well as various neurological disorders<sup>48-54, 46, 55-60</sup>.

A large proportion of human miRNA display a brain specific or brain enriched expression pattern<sup>61</sup>. Within the nervous system, miR-124a and miR-9 regulate glial versus neuronal patterns of gene expression and alternative splicing<sup>62</sup>. The expression of miR-124 is restricted to differentiating and mature neurons by the transcriptional repressor, REST. In the absence of REST, miR-124 inhibits a large number of non-neuronal genes, including the splicing factor PTBP1, the absence of which leads to the establishment of alternative splicing patterns specific to neurons<sup>63, 64</sup>. miRNA have also been shown to play a crucial role in neural development and patterning. In zebrafish studies, the disruption of Dicer during development has resulted in an ablation of the miRNA pathway. Precursor miRNA could not be processed into mature miRNA and as such, the development of the zebrafish; particularly the brain and nervous system were severely affected<sup>46</sup> (Fig. 4).



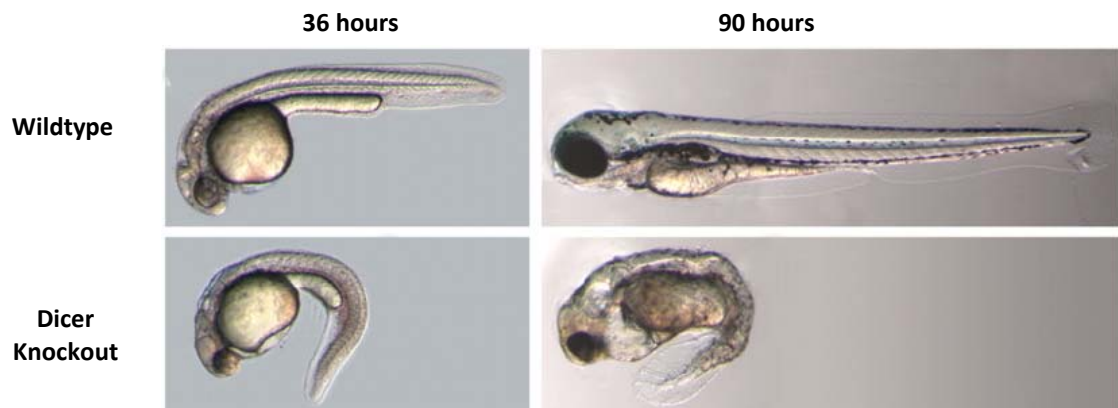
**Figure 3: Mechanisms for miRNA function in animal cells.** The interaction of miRNA/RISC complexes with mRNA can elicit direct and indirect effects on translation. Direct effects (left side) occur through the inhibition of initiation of translation, which prevents ribosome association with the mRNA, or through inhibition of translation post-initiation, such as ribosome drop off. Indirect effects (right side) include promoting de-adenylation and degradation most likely take place in P bodies. In addition, the targeted mRNA could be sequestered from the translational machinery and degraded or stored for subsequent use. (Adapted from Nilsen <sup>65</sup>)

---

In *C. elegans*, neuronal left-right asymmetry is established by two miRNA, *lsy-6* and *miR-273*. On the left, the transcription factor *die-1* induces expression of *lsy-6*, which represses the homeobox gene *cog-1*; on the right, *miR-273* targets *die-1* for inhibition, effectively repressing *lsy-6* expression<sup>66, 57</sup>. miRNA continue to play a major role in nervous system function during adulthood. A number of studies have linked miRNA to processes such as synaptic plasticity and circadian regulation, as well as neurological disease. *miR-134* has been shown to negatively regulate the size of dendritic spines in the rat hippocampus<sup>59</sup>. It was suggested that *miR-134* could regulate the expression of the synaptic Lim-domain-containing protein kinase 1 (*LIMK1*), thus controlling dendritic spine size. The brain-enriched *miR-132* also regulates dendritic outgrowth via interactions with Rho family GTPase-activating protein *p250GAP*. *miR-132* transcription is induced by CREB signalling, resulting in translational inhibition of *p250GAP*, de-inhibition of Rac family GTPases, and a subsequent increase in dendritic size and branching<sup>67</sup>. *miR-132* also plays a role in circadian rhythm, along with the brain-enriched *miR-219*. *miR-219* is induced by the circadian proteins *CLOCK* and *BMAL* and regulates phase length, whereas *miR-132* transcription is induced by light-dependent activation of CREB and regulates light-induced phase-shifting. In addition, *miR-132* regulates neuronal excitability by potentiating the depolarizing effects of glutamate and NMDA, while *miR-219* has the opposite effect<sup>68</sup>. These data suggest that these miRNA may be working in concert to regulate neuronal activity<sup>69, 68</sup>.

The widespread expression and activity of miRNA in the brain support the

idea they may be implicated in numerous neurological disorders. Studies have shown that the global reduction of Dicer in the brain (thus reducing miRNA biogenesis) is associated with dopaminergic behaviours and Parkinson's-like symptoms. Depletion of Dicer in dopamine neurons results in the progressive loss of these neurons and an increase in Parkinson's-like behaviours (such as reduced locomotion and increased immobility, behavioural changes and other neuronal defects)<sup>70, 71</sup>. *miR-133b* has also been shown to be decreased in the midbrain of Parkinson's patients, suggesting that miRNA dysregulation could contribute to some aspects of this disease<sup>70</sup>. miRNA are thought to play a role in several other neurological disorders. In Fragile X mental retardation, the gene responsible for the disorder, *FMR1*, encodes the protein *FMRP*, which is present in synapses and is part of the RISC complex. Loss of *FMRP* impairs the function of RISC-mediated gene silencing, resulting in altered neural development and synaptogenesis, ultimately impairing brain function<sup>48</sup>. In Tourette's syndrome, mutations in the *miR-189* binding site in the 3'-UTR of *SLITRK1*, a protein involved in neurite outgrowth, have been associated with the disorder<sup>51</sup>. Additionally, multiple studies have also suggested a link between miRNA dysregulation and Alzheimer's disease (including *miR-29a/b*, *miR-106a/b*, *miR-107* and *miR-9*), although the specific molecular mechanisms remain unknown<sup>72-74</sup>.



**Figure 4: Dicer knockouts in zebrafish show miRNA are crucial to brain development.** The wildtype (top two panels) display a normal developmental progression and healthy CNS. In the knockout (Bottom two panels), the absence of the Dicer prevents the formation of mature miRNA, and as such the development of the brain and nervous system of zebrafish is greatly disrupted. Left panels depict embryos at 36 hours post fertilisation, right panels; 90 hours post fertilisation. (Adapted from Giraldez *et al.* <sup>46</sup>)

---

### miRNA in Schizophrenia

---

The fact that miRNA can elicit a broad effect on gene expression and function, has important implications for psychiatric disorders. Disorders such as schizophrenia have been characterised by a dysregulation of multiple signalling pathways (schizophrenia is reviewed in more detail later in this chapter). The involvement of multiple signalling pathways in psychiatric disease complicates both the investigation of the underlying biological causes and efforts to develop effective therapies. It is also likely that drugs that target only a single receptor or signalling pathway will be unsuccessful.

Focusing on the role of miRNA in psychiatric disease may explain dysregulation of multiple pathways as well as offer a path to novel therapies that can target entire gene networks. Studies are emerging which have directly looked at miRNA dysregulation in schizophrenia. A recent study by Perkins *et al.*

examined miRNA expression in the prefrontal cortex (Brodmann's area 9) and identified a number of miRNA with altered expression (including miR-26b, miR-30b, miR-29b, and miR-106b) <sup>75</sup>. Deletions at the 22q11.2 locus in humans result in deficits in attention, learning and executive function <sup>76</sup>. A number of schizophrenia-like phenotypes were also observed in a mouse model that was hemizygous for a deletion of a 1.3 Mb region syntenic to 22q11.2. Also within the 22q11.2 region and the deleted murine locus is DGCR8 (a component of the microprocessor complex). The absence of DGCR8 results in a bottleneck in the processing of precursor miRNA to mature miRNA and was also sufficient to produce a number of schizophrenia-like behaviours in mice <sup>77</sup>.

Studies of single nucleotide polymorphisms (SNPs) and copy-number variants (CNVs) are beginning to find significant associations with schizophrenia. This is exemplified by dysregulation of minor

---

allele frequencies<sup>78</sup> and increases in ultra-rare mutations in primary, precursor and mature miRNA<sup>79</sup>. Additionally, several miRNA are located within the 8p21–23 locus; a CNV hot-spot that has been linked to schizophrenia and autism<sup>80</sup>.

The specific molecular mechanisms through which altered miRNA activity may cause psychiatric phenotypes are still poorly understood. Recently, miR-219 was found to mediate the behavioural effects of MK-801 treatment in mice<sup>81</sup>. Acute MK-801 treatment decreased levels of miR-219 in the prefrontal cortex, and inhibition of miR-219 prevented MK-801-induced hyperlocomotion and stereotypies (repetitive movements). One of mRNA targets of miR-219 is CAMK2 $\gamma$ , a member of the calcium/calmodulin-dependent protein kinase family involved in NMDA signalling. When combined with data showing that miR-219 attenuates NMDA-induced neuronal depolarization<sup>68</sup>, these results indicate that miR-219 could inhibit NMDA signalling at the level of both the receptor and second messenger signalling.

Brain-derived neurotrophic factor (BDNF) is also highly implicated in schizophrenia and other neurological disorders such as bipolar disorder, and depression. There is growing evidence that BDNF is the target of several miRNA. miR-30a and miR-195, that are expressed in human prefrontal cortex, have been shown to target the BDNF 3'-UTR, and reduce BDNF expression<sup>82</sup>. BDNF is also indirectly regulated by miR-132, as CREB-induced transcription of this miRNA results in a decrease of MECP2 (the protein involved in Rett syndrome) and a subsequent decrease in BDNF due to de-repression of REST<sup>83</sup>. CREB

expression has been shown to be reduced in schizophrenia, and this suggests that miR-132 expression could also be reduced<sup>84</sup>.

---

### **Schizophrenia: A Biological Disorder of the Brain**

---

The term schizophrenia comes from the two Greek words schizo (split or divide) and phrenos (mind) and refers to one of the most debilitating mental illnesses known. The lifetime risk for the general population is approximately 1% of the population and incurs a high social and economic burden on society. Despite years of research, there have only been incremental advancements in the diagnosis, treatment and epidemiology of schizophrenia, and the aetiology of the disorder remains largely unknown. The modern perception of schizophrenia has been based on early studies by Emil Kraepelin<sup>85</sup> and Eugen Bleuler<sup>86</sup> describing the symptoms and course of the illness. Although characterised by a specific set of symptoms, the severity of schizophrenia varies among individuals, and may even change over time with any particular patient. The three broad types of symptoms include positive symptoms, negative symptoms, and cognitive impairment<sup>87</sup>. Positive symptoms are displayed as a gain of function that is represented by a loss of contact with reality and include delusions and hallucinations. While auditory hallucinations are the most common in schizophrenia, there are numerous types which occur and include visual, olfactory and tactile hallucinations<sup>88</sup>. The negative symptoms of schizophrenia involve a loss of function where simple behavioural and emotional processes are greatly diminished<sup>89</sup>. Common negative

---

symptoms include monotonous voice tone, lack of pleasure, immobile facial expressions and the diminished ability to initiate and follow through on plans. The cognitive impairment observed in schizophrenia includes problems in learning and memory, concentration and attention and problem solving. A decline in cognitive abilities is observed in the majority of patients with schizophrenia, however cognitive functioning after onset of the illness usually remains relatively stable <sup>89</sup>. Schizophrenia usually develops between the ages of 16 and 30, rarely before adolescence or after 45 years of age, and persists for the lifetime of the affected individual <sup>89</sup>. Approximately 10% of those diagnosed with schizophrenia will attempt suicide; with the rate even higher than this in the first few years of illness <sup>90</sup>. The incidence is slightly higher in males (approx. 3:2), although a later age of onset has been observed in females, which is more often followed by less severe course of illness resulting in fewer hospital admissions and better social functioning <sup>90</sup>.

An exact cause of schizophrenia remains unknown, though studies have shown that environmental factors coupled with a genetic predisposition can increase the risk of schizophrenia. One of the most highly favoured hypotheses for the development of schizophrenia is the neurodevelopmental hypothesis. This states that schizophrenia arises as a consequence of underlying genetic determinants which when acted upon by environmental influences impact on the development of the brain, leading to abnormal communication between important brain regions such as the temporal and prefrontal cortices, midbrain, thalamus and nucleus accumbens <sup>91-93</sup>. It is thought that

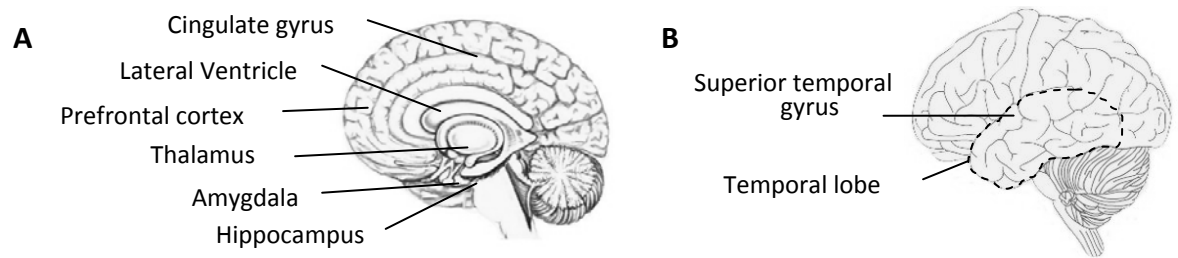
developmental processes which take place during adolescence such as myelination, synaptogenesis, apoptosis and synaptic pruning, as well as neural circuit refinement in early adulthood, can lead to the onset of full psychosis when coupled with any adverse biochemical or psychological factors <sup>91</sup>.

#### *Alterations in Brain Structure and Function*

The pathophysiology of schizophrenia varies widely, though much research has focused on differences in structure or function in certain brain areas. Early evidence for differences in the neural structure came from the discovery of ventricular enlargement in people diagnosed with schizophrenia <sup>94</sup>. Neuropsychological testing and brain scanning technologies such as positron emission tomography and functional magnetic resonance imaging have been used to examine functional differences in brain activity, and have shown that differences most commonly occur in the hippocampus and the frontal and temporal lobes. These differences are profoundly linked to the neurocognitive deficits which often occur with schizophrenia, particularly in areas of attention, memory, problem solving and social cognition <sup>95-101</sup>.

Studies have shown that the brain regions showing the greatest reduction in volume in patients with schizophrenia when compared to healthy controls are the dorsolateral prefrontal cortex (DLPFC), amygdala, hippocampus, thalamus, cingulate gyrus (Fig. 5A), medial temporal lobe, and superior temporal gyrus (STG) (Fig. 5B) <sup>95, 102, 96-98, 103, 99, 104-106, 100, 101</sup>. In relation to this body of work, two regions of interest are the STG (Brodmann's area 22)





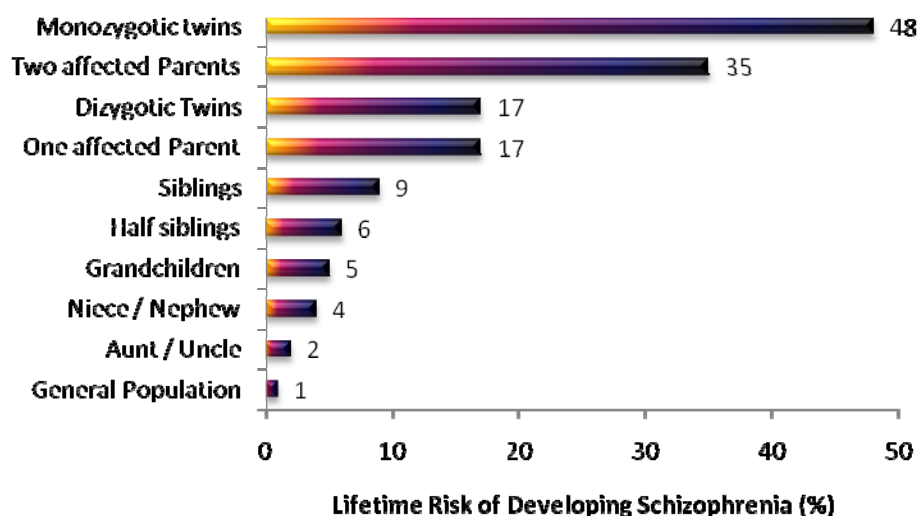
**Figure 5: Regions of the Brain implicated in Schizophrenia.** Brain regions with altered volume in schizophrenia patients include (A) the lateral ventricle, thalamus, prefrontal cortex, cingulate gyrus, amygdala, hippocampus and (B) the superior temporal gyrus and the temporal lobe. (Adapted from McKenzie Illustrations <sup>107</sup>)

and the DLPFC (Brodmann's area 9, 46). The STG is the primary cortical area for auditory input and is believed to be heavily involved in speech, language and communication <sup>108</sup>. Significant evidence suggests the STG plays an important role in the pathophysiology of some symptoms of schizophrenia with its connections to the hippocampus and amygdala and neocortical association areas in the DLPFC and the thalamus <sup>102, 103, 109, 110</sup>. The interest in the DLPFC in schizophrenia stems from its involvement in the processing of cognitive tasks such as working memory, which is known to be deficient in schizophrenia <sup>111-113</sup>. In addition to alterations in brain structure, alterations to several important neurotransmitter systems have been reported in schizophrenia. The brain regions shown to have structural changes in schizophrenia (Fig. 5) are directly linked by neurotransmitter systems, and the most studied are the dopamine, serotonin, gamma-aminobutyric acid (GABA) and glutamate systems <sup>93</sup>. Indeed, the current drugs used to treat schizophrenia (termed antipsychotics) predominately act as dopamine receptor antagonists, therefore implicating this neurotransmitter. Alterations involving the

reception or release of these neurotransmitters are thought to play a large part in the disruption of the cognitive and sensory processing in the brains of those with schizophrenia <sup>114, 115</sup>.

### Heritability in Schizophrenia

Rates of schizophrenia are known to be higher among relatives of affected individuals than in the general population <sup>116</sup>. Those with a second degree relative such as aunt/uncle, niece/nephew or grandparent, have a several fold higher risk of developing schizophrenia than the general population; and first degree relatives such as parents, siblings and dizygotic twins, have a lifetime risk of schizophrenia up to seventeen times that of the general population. Those with two affected parents or an identical twin with schizophrenia face almost a 50% chance of developing the illness in their lifetime <sup>117, 118</sup> (Fig. 6). These findings coupled with adoption and twin studies have shown that there is a genetic component associated with the risk of developing schizophrenia; however the inheritance does not follow simple Mendelian



**Figure 6: Lifetime Risk of Developing Schizophrenia.** The more closely you are related to a person with schizophrenia, the higher the risk of developing the disorder. (Adapted from Gottesman <sup>119</sup>)

single-gene inheritance patterns, and there is also evidence that environmental factors play a role in its development.

#### Genetic Linkage Studies

For decades, countless genetic linkage studies have been performed in an attempt to identify susceptibility genes for schizophrenia. Unfortunately, simple forms of Mendelian inheritance never materialised, with many studies not meeting genome-wide levels of significance <sup>120</sup>. Traditional genetic approaches have linked more than 7000 genetic polymorphisms to schizophrenia <sup>121</sup>, but the majority of these studies have not been replicated in separate populations, or have produced loci that are too large for candidate gene identification. The loci that have been most clearly linked to psychiatric disorders including 1q21, 8p, and 13q, have yet to yield candidate genes that have been definitively associated with schizophrenia <sup>122-</sup>

<sup>124</sup>. Candidate gene analysis has also had limited success. There is clear molecular evidence supporting altered glutamate and dopamine signalling in schizophrenia, but genetic studies have often failed to associate mutations in key genes in these pathways with disease risk <sup>125</sup>.

The biggest advances in the understanding of the genetics of schizophrenia have resulted from small family-based studies that include schizophrenia or psychosis as a phenotype. The Disrupted-in-Schizophrenia-1 (DISC1) locus was originally identified in a Scottish pedigree with a high rate of schizophrenia, bipolar disorder, and psychosis <sup>126</sup>. The Scottish family carries a balanced translocation that results in the truncation of the DISC1 gene. Further studies have shown that DISC1 plays a major role in human hippocampal structure and function, cerebral cortex development, and foetal and adult

---

neurogenesis<sup>127, 128</sup>. Although DISC1 mutations are highly penetrant in only a subset of patients, it may provide important insight into the neurobiology of schizophrenia. While the full length mRNA transcript of DISC1 does not appear to be altered in schizophrenia, numerous alternatively spliced transcripts have been identified. Many of these transcripts display increased expression in the hippocampus of schizophrenic subjects and are associated with schizophrenia risk polymorphisms<sup>129</sup>. This suggests a molecular mechanism of genetic risk associated with DISC1 involving specific alterations in gene processing. Binding partners of DISC1 (such as NDEL1, FEZ1 and PDE4B) have also been shown to be altered in some schizophrenic patients, suggesting that the DISC1 pathway may play a central role in schizophrenia in at least a subset of the population<sup>130, 131</sup>.

#### *Copy Number Variation*

Genome-wide analysis of CNV has also linked a number of psychiatric diseases to CNV burden<sup>132-135</sup>, and it is thought that schizophrenia-associated CNVs preferentially disrupt genes that may be involved in nervous system function<sup>136, 137</sup>. Although the increased CNV burden in schizophrenia has been replicated in multiple populations, CNVs are believed to account for only a small minority of cases. Additionally, many of the CNVs represent very rare genomic rearrangements, and therefore cannot account for the significant heritability of schizophrenia<sup>138</sup>.

#### *Genome-wide Association Studies*

It is estimated that approximately 10% of psychiatric disorders are caused by

rare highly penetrant genes such as DISC1, or by mutations resulting in copy number variation, suggesting that the majority of cases are the result of the interaction of many genes, each with a small effect<sup>138, 139</sup>. Genome-wide associations studies (GWAS), which use high-density SNP genotyping to link phenotypes to underlying haplotypes, have been successfully applied to complex polygenic disorders such as breast cancer, but have had limited success when applied to psychiatric disorders. To date, approximately 10 GWAS studies have been directed at schizophrenia and although several of these studies are of sufficient power to detect loci carrying a relative risk of approximately 1%, few genes have been linked to schizophrenia at a significant level<sup>140-143, 134, 139</sup>. Statistical analysis of the most recent GWAS results suggests that schizophrenia is highly polygenic, with thousands of common SNPs contributing to a large percentage of disease burden<sup>139</sup>.

Ultimately, there are a number of issues which might limit the success of genetic studies, including genetic and phenotypic heterogeneity, epistatic gene interactions, and the role that the environment plays in the development of psychiatric illness<sup>144</sup>. The recent associations between genomic variants with schizophrenia, bipolar disorder, and autism indicate that there may be many biological pathways that, when disrupted, lead to affective and cognitive disorders. To this end, schizophrenia and bipolar disorder may not be individual diseases, but rather phenotypes of altered neuronal development<sup>145</sup>.

This idea is supported by a number of lines of evidence, particularly for schizophrenia: (1) The genes that have been

---

most clearly associated with schizophrenia are genes involved in neuronal development. DISC1 and its binding partners regulate hippocampal grey matter volume, neurite outgrowth, dendritic arborization, and neuronal migration and maturation <sup>146, 147</sup>. Two other genes associated with schizophrenia; NRG1 and ERBB4, interact to regulate neuronal migration, axon myelination, and synapse formation <sup>148, 149</sup>. (2) The symptoms of psychiatric illness have a developmental trajectory that parallels the maturation of the brain. The timing of peak disease risk for all psychiatric disorders overlaps with the substantial cortical dendritic pruning that occurs during adolescence <sup>150</sup> and although there are clear prodromal signs for some disorders, outright symptoms such as psychosis are rare during childhood <sup>151</sup>. (3) A number of studies have found significant structural differences between schizophrenic and control brains, including decreased cortical neuron spine density, enlarged lateral ventricle size, and decreased hippocampal and cortical volume <sup>152</sup>.

The association of CNVs and genes involved in neurodevelopment with schizophrenia also has important implications for therapeutic treatments. If there are multiple biological pathways that can lead to psychiatric disease, with any single cause being relatively rare in the population, useful therapies must have a broad effect. Currently available antipsychotics reduce psychosis via activity at the dopamine D2 receptor, but also

act non-specifically on almost all the catecholaminergic and monoaminergic systems of the brain <sup>153</sup>. These drugs not only have poor efficacy and serious side effects, but also fail to address what may be the underlying genetic and molecular causes of psychiatric disease <sup>154</sup>. Alternatively, drugs that have the ability to regulate a large network of protein coding targets such as miRNA or miRNA-mimics may prove to be a much a more promising therapeutic strategy.

---

## **RATIONALE**

Typically, the purpose of identifying genes implicated in disease is to enhance the understanding of its pathogenesis. Whilst researchers have managed to highlight hundreds of genes with altered expression, it is also crucial to understand the downstream effects of altering these genes as well as identifying the mechanisms whereby these genes are regulated or altered by outside influences. Based on the number of publications in recent years, mechanisms of gene regulation such as gene silencing pathways have been one of the fastest growing fields in research. Further investigation into this phenomenon may help increase the understanding of how genes in the context of neural differentiation and development are regulated and consequently how they may contribute to neurological disorders such as schizophrenia.

Several brain regions including the STG and DLPFC have been observed to have altered structure and function in schizophrenia. A number of approaches have been used to identify the genes that underlie these brain changes in schizophrenia. Although putative schizophrenia susceptibility genes are being identified, it is important to remember that the inheritance of schizophrenia does not follow normal Mendelian inheritance patterns. Twin studies have shown that there is only approximately 50% concordance with the disease in monozygotic twins; individuals who share identical DNA profiles. It has primarily been this observation which highlights epigenetic and environmental phenomena as an attractive mechanism whereby the abnormal regulation of gene expression could lead to schizophrenia. An important component of this system is the post-transcriptional regulation by non-coding RNA, specifically the miRNA pathway. Investigation of miRNA profiles and their potential silencing effect on schizophrenia candidate genes may provide a mechanism for their dysregulation in schizophrenia. This will hopefully lead to a better understanding of the pathogenesis of schizophrenia which is an important step in the development of better treatments for the disorder.

---

## **AIMS & HYPOTHESES**

The studies within this thesis test the hypotheses that specific patterns of miRNA expression and RNA-mediated gene silencing are involved in human neural differentiation and development and are potentially associated with schizophrenia. The following aims test these hypotheses:

- ❖ To determine how miRNA expression changes during neuronal development by monitoring miRNA expression during the differentiation of SH-SY5Y neuroblasts.
- ❖ To observe the specific patterns of miRNA expression in the developing prefrontal cortex of normal individuals aged from 1 month to 78 years.
- ❖ To investigate whether mature miRNA expression is altered in schizophrenia by comparing the expression of known miRNA in cortical brain regions in subjects with schizophrenia and non-psychiatric controls.
- ❖ To investigate what effect altered miRNA expression in the brain may have on schizophrenia-associated gene expression by using bioinformatics to identify genes which could be targeted by specific miRNA.

---

## MANUSCRIPTS

The work described in this thesis has examined the specific patterns miRNA expression throughout neuronal differentiation, normal human brain development and schizophrenia.

This thesis is subdivided into five manuscripts:

- ❖ **Beveridge, N.J.**, Carroll, A.P., Tooney, P.A., Cairns, M.J. (2009) Down-regulation of miR-17 family expression in response to retinoic acid induced neuronal differentiation. *Cellular Signalling* 21, 1837-1845.
- ❖ **Beveridge, N.J.**, Santarelli, D.M, Tooney, P.A., Webster, M., Weickert, C.S., Cairns, M.J. Maturation of the human dorsolateral prefrontal cortex coincides with a dynamic shift in microRNA expression (2011) *Submitted to Molecular Psychiatry*
- ❖ **Beveridge, N.J.**, Tooney, P.A., Carroll, A.P., Gardiner, E., Bowden, N., Scott, R.J., Tran, N., Dedova, I., Cairns, M.J. (2008) Dysregulation of miRNA 181b in the temporal cortex in schizophrenia. *Human Molecular Genetics*. 17, 1156-1168.
- ❖ **Beveridge, N.J.**, Gardiner, E., Tooney, P.A., Carroll, A.P., Cairns, M.J. (2009) Schizophrenia is associated with an increase in cortical microRNA biogenesis. *Molecular Psychiatry*. 15, 1176-1189
- ❖ Santarelli, D.M, **Beveridge, N.J.**, Tooney, P.A., Cairns, M.J. (2011) Upregulation of Dicer and MicroRNA Expression in the Dorsolateral Prefrontal Cortex Brodmann's Area 46 in Schizophrenia. *Biological Psychiatry*. 69, 180-187

---

## CHAPTER 2

*Down-regulation of miR-17 family  
expression in response to retinoic acid  
induced neuronal differentiation*

---



---

**CHAPTER 2 : Down-regulation of miR-17 family expression in response to  
retinoic acid induced neuronal differentiation**

**Natalie J. Beveridge**, Paul A. Tooney, Adam P. Carroll, Nham Tran  
and Murray J. Cairns

**Cellular Signalling (2009) Vol. 21, pp 1837-1845**  
2009 Journal Impact Factor: 4.237

**Statement I: Author contribution to Chapter 2 manuscript**

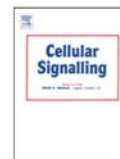
Author	Description of Contribution to Article	Signature
Natalie J. Beveridge	Designed and executed the study. Provided significant insight into the interpretation of the data. Wrote the manuscript.	
Paul A. Tooney	Aided in data interpretation and manuscript compilation.	
Adam P. Carroll	Provided some technical assistance.	
Nham Tran	Aided in establishing the methodology.	
Murray J. Cairns	Designed the study, provided the concept and corrected the manuscript.	

4<sup>th</sup> November, 2010

---

**PROFESSOR JOHN ROSTAS**  
Deputy Head of Faculty (Research and Research Training)

---



## Down-regulation of miR-17 family expression in response to retinoic acid induced neuronal differentiation

Natalie J. Beveridge<sup>a,b,c</sup>, Paul A. Tooney<sup>a,b,c</sup>, Adam P. Carroll<sup>a,b,c</sup>, Nham Tran<sup>d,e</sup>, Murray J. Cairns<sup>a,b,c,\*</sup>

<sup>a</sup> Schizophrenia Research Institute, Sydney, NSW 2006, Australia

<sup>b</sup> School of Biomedical Sciences, Faculty of Health, The University of Newcastle, University Drive, Callaghan, NSW 2308, Australia

<sup>c</sup> Hunter Medical Research Institute, John Hunter Hospital, Lookout Road, New Lambton, NSW 2305, Australia

<sup>d</sup> The Centenary Institute, Royal Prince Alfred Hospital, Sydney, NSW 2006, Australia

<sup>e</sup> University of Sydney, Sydney, NSW 2006, Australia

### ARTICLE INFO

#### Article history:

Received 24 March 2009

Received in revised form 9 July 2009

Accepted 30 July 2009

Available online 8 August 2009

#### Keywords:

MicroRNA

miR-17

miR-17-92

Differentiation

Gene expression

Cancer

### ABSTRACT

Whole-genome microRNA and gene expression analyses were used to monitor changes during retinoic acid induced differentiation of neuroblasts *in vitro*. Interestingly, the entire miR-17 family was over-represented among the down-regulated miRNA. The implications of these changes are considerable, as target gene prediction suggests that the miR-17 family is involved in the regulation of the mitogen-activated protein kinase (MAPK) signaling pathway, synaptic plasticity and other markers of neuronal differentiation. Significantly, many of the target responses predicted by changes in miRNA expression were supported by the observed changes in gene expression. As expected, markers of neuronal differentiation such as anti-apoptotic protein B-cell lymphoma 2 (*BCL2*), myocyte enhancer factor-2D (*MEF2D*) and zipper protein kinase (*MAP3K12*; aka *ZPK/MUK/DLK*) were each up-regulated in response to differentiation. The expression of these genes was also reduced in response to miR-17 and miR-20a transfection, and more specifically they were also shown to contain functional miRNA recognition elements for members of the miR-17 family by reporter gene assay. This suggests that the miR-17 family have an integral role in fine-tuning the pathways involved in the regulation of neuronal differentiation.

© 2009 Elsevier Inc. All rights reserved.

### 1. Introduction

In the past few years there has been an enormous increase in the discovery of small non-coding RNA (ncRNA), including small nucleolar RNA (snoRNA), short-interfering RNA (siRNA), miRNA and the slightly longer piwi-interacting RNA (piRNA). While these all appear to be vital for normal growth and development, miRNA are particularly interesting as each one has the ability to influence the expression of hundreds of genes and collectively are predicted to regulate at least a third of all human genes [1,2]. This is especially important throughout development, during which these molecules have been shown to display a stage and tissue-specific pattern of expression [3–5].

miRNA are 18 to 26 nucleotides long and inhibit translation and mediate mRNA decay through sequence-specific base pairing with the 3'-untranslated region of specific target mRNAs [1,6,7]. Mature

miRNA are initially expressed as long transcripts called primary miRNA (pri-miRNA) which are digested by Drosha (ribonuclease III) to form hairpin precursor miRNA (pre-miRNA). Pre-miRNA are exported into the cytoplasm by Exportin-5 where another ribonuclease III, Dicer, cleaves the pre-miRNA resulting in a double stranded RNA [8–10]. The strand with the weakest base pairing at the 5' end of the duplex preferentially associates with the RNA-induced silencing complex (RISC) and this strand becomes the active miRNA which then guides the RISC to its mRNA target [10,11]. In higher eukaryotes, hundreds of miRNA genes are predicted to exist [12] and currently 475 pre-miRNA are known to be transcribed in humans producing 564 unique mature miRNA (miRBase version 10.1) [13]. A variety of bioinformatics approaches have estimated that any given miRNA could have from one to more than 800 target genes, suggesting there may be numerous regulatory roles played by miRNA [1,2,14,15].

Several research groups have provided evidence that miRNA act as key regulators of processes diverse as cell proliferation and differentiation, development, apoptosis and metabolism [14,16–20]. In addition to regulating these important growth and developmental processes, miRNA have been found to be involved in the pathogenesis of disease [21–26]. Expression profiling experiments have shown that a large proportion of mammalian miRNA are enriched or specific to the brain, where many miRNA appear to influence the development of

\* Corresponding author. School of Biomedical Sciences, The University of Newcastle, University Drive, Callaghan, NSW 2308, Australia. Tel.: +61 2 4921 8670; fax: +61 2 4921 7903.

E-mail addresses: [natalie.beveridge@newcastle.edu.au](mailto:natalie.beveridge@newcastle.edu.au) (N.J. Beveridge), [paul.tooney@newcastle.edu.au](mailto:paul.tooney@newcastle.edu.au) (P.A. Tooney), [adam.carroll@newcastle.edu.au](mailto:adam.carroll@newcastle.edu.au) (A.P. Carroll), [murray.cairns@newcastle.edu.au](mailto:murray.cairns@newcastle.edu.au) (M.J. Cairns).

or LNA-modified anti-miRs with recombinant firefly luciferase reporter gene constructs containing 3'-UTR sequences substituted from the target gene. Oligonucleotides encoding target gene miRNA recognition elements (or mutant controls) were annealed to form *SpeI* and *HindIII* restricted overhangs of a ligatable cassette compatible with *SpeI* and *HindIII* digested pMIR-REPORT vector (Ambion). Reporter gene silencing was monitored with respect to a spiked-in control plasmid expressing renilla luciferase using the dual luciferase reporter assay (Promega). To control for non-specific effects associated with miRNA/anti-miR transfection, the controls were co-transfected with miRNA-9\* or anti-miR-9\* as it is predicted to have little or no activity against the fusion transcripts tested here.

### 3. Results

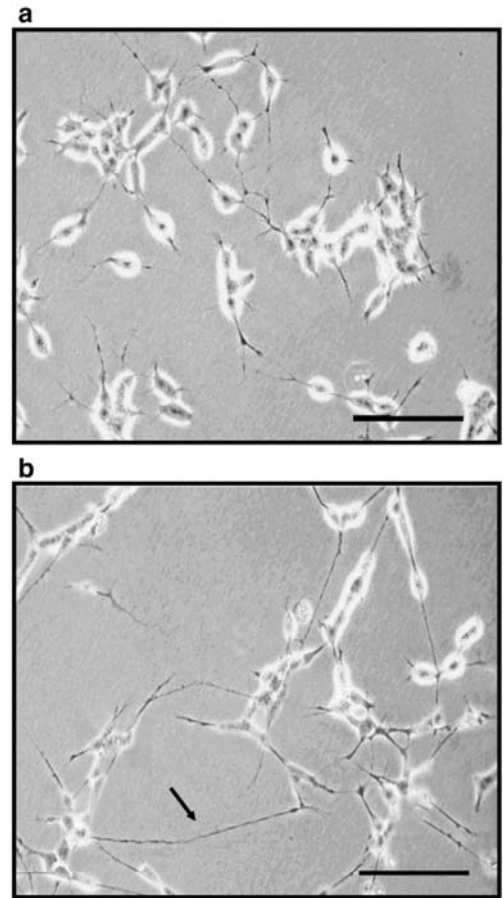
#### 3.1. miRNA expression in SH-SY5Y cells

The SH-SY5Y cell line is a widely used model system for studying neuronal properties *in vitro*. These cells express neuronal markers such as proteins MAP2, tau, neurofilament and NSE, and their morphology and growth characteristics can be easily manipulated by the addition of differentiation agents such as brain-derived neurotrophic factor (BDNF) and RA [35,36]. After treatment with RA, these cells stop proliferating and produce extensive neurite outgrowths consistent with a more neuronal phenotype (Fig. 1) [37]. In order to examine mature miRNA expression in cultured SH-SY5Y neuroblast cell culture, a custom array platform was established using LNA modified capture probes [38]. Analysis indicated that 174 miRNA were expressed in undifferentiated SH-SY5Y cells. These included miRNA known to be highly expressed in the brain (e.g. let-7 group, miR-29a, -29b, -30b, -30c) as well as brain-enriched miRNA (e.g. miR-9, -124a, -125b, -138) (Supplementary Table 1). After RA induced differentiation, this number decreased slightly to 171 miRNA, however, the relative proportions of miRNA expression changed quite significantly.

#### 3.2. miRNA expression in differentiated SH-SY5Y cells

To identify the effect of neuronal differentiation on miRNA expression, a two-class unpaired analysis was performed using U6 snRNA normalized fluorescence values and SAM software (version 2.23). This analysis identified 43 miRNA with altered expression (false discovery rate = 4.67%,  $\Delta = 0.94$ , 120 permutations) in SH-SY5Y cells following RA treatment with 32 miRNA displaying significantly decreased expression and 11 miRNA showing significantly increased expression as a result of RA-induced differentiation (Supplementary Table 2). Five of the miRNA showing increased expression (miR-9, miR-124a, -128a, -208, -210 and -423) are known to be brain-specific or brain-enriched miRNA and are thought to be important for brain development, neuronal maturation, and neuronal differentiation [39,40].

The most striking observation from the microarray analysis was the down-regulation of the entire miR-17 family as a result of RA-induced differentiation. The human miR-17 cluster contains six pre-miRNA (yielding 7 mature miRNA, miR-17-3p (aka miR-17\*), -17-5p (aka miR-17), -18, -19a, -19b, -20 and -92 (aka miR-92a)) within about 1 kb on chromosome 13. Paralogs also exist on the X-chromosome (miR-106a, -19b, -363 and -92) and chromosome 7 (miR-106b, -93 and -25) [41]. A total of 14 mature miRNA are associated with the miR-17 family and remarkably, all of these were observed to be down-regulated in this study (Table 2, Fig. 2). To validate the microarray expression data, several miRNA shown to be altered by differentiation were analyzed using a custom quantitative real-time RT-PCR method [22]. Expression data obtained by microarray was confirmed for miR-128a, -10a and 124a (up-regulated) and miR-301, -20a, -106a, -19a, -29b, -134 and -15b (down-regulated).



**Fig. 1.** Differentiation of SH-SY5Y neuronal cells. (a) Undifferentiated SH-SY5Y cells at 20x magnification. Cell bodies displayed a rounded shape with short neuritic processes. (b) SH-SY5Y cells at 20x magnification after differentiation with RA and BDNF. Upon differentiation, SH-SY5Y neuronal cells changed shape to form long spindly neurites (as indicated by the arrow) and displayed a more neuronal phenotype. Cell bodies were elongated and neurites extended from both poles of the cell body. Bar represents 100  $\mu$ m.

**Table 2**  
Neuronal differentiation with RA causes down-regulation of the miR-17 family.

miR-17 family member	Fold change	p value	Genome context
hsa-miR-19a	-2.42	0.003	13q31.3
hsa-miR-18a	-1.93	0.002	13q31.3
hsa-miR-17-5p <sup>a</sup>	-2.58	0.108	13q31.3
hsa-miR-17-3p <sup>a</sup>	-1.60	0.115	13q31.3
hsa-miR-20a	-1.78	0.041	13q31.3
hsa-miR-19b	-1.62	0.002	13q31.3, Xq26.2
hsa-miR-92 <sup>a</sup>	-1.47	0.042	13q31.3, Xq26.2
hsa-miR-106a	-1.85	0.025	Xq26.2
hsa-miR-18b	-1.11	0.443	Xq26.2
hsa-miR-20b	-1.72	0.002	Xq26.2
hsa-miR-363	-1.38	0.198	Xq26.2
hsa-miR-25	-1.71	0.021	7q22.1
hsa-miR-106b	-1.56	0.028	7q22.1
hsa-miR-93	-1.46	0.009	7q22.1

<sup>a</sup> In accordance with miRBase hsa-miR-92 has been renamed hsa-miR-92a; hsa-miR-17-5p has been renamed hsa-miR-17; hsa-miR-17-3p has been renamed hsa-miR-17\*.

**Table 1**  
Oligonucleotide sequences.

Type	Name	Sequence	Target
Primers <sup>a</sup>	U6_probe	GCCATGCTAATCTTCTGTATC	U6 snRNA
	U6_F339	CGGCAGCATATATACTAAATTTGG	U6 snRNA
	GUSB-F	GCCAAATGAACAGGTATCCC	GUSB
	GUSB-R	GCTCAAGTAAACAGGCTGTTTCC	GUSB
	HMBS-F	GAGAGTGATTGCGCTGGTA	HMBS
	HMBS-R	CAGGGTACGAGGCTTTCAAT	HMBS
	106a-F	AAAAGTGCTTACAGTG	miR-106a
	106a-R	GTAACGACGGCCAGTGCTACCTG	miR-106a
	10a-F	TACCTGTGATCCG	miR-10a
	10a-R	GTAACGACGGCCAGTCACAAAAT	miR-10a
	124a-F	TTAAGGACGGG	miR-124a
	124a-R	GTAACGACGGCCAGTTGGCATTAC	miR-124a
	128a-F	TCACAGTGAACCG	miR-128a
	128a-R	GTAACGACGGCCAGTAAAGAGAC	miR-128a
	134-F	TGTGACTGGTTGAC	miR-134
	134-R	GTAACGACGGCCAGTCCCTCTG	miR-134
	15b-F	TAGCAGCATCAT	miR-15b
	15b-R	GTAACGACGGCCAGTTGTAACC	miR-15b
	19a-F	TGTGCAATCTATGC	miR-19a
	19a-R	GTAACGACGGCCAGTTCACTTTT	miR-19a
	20a-LNA-F <sup>b</sup>	T+AA+AGTGCTTATAGT	miR-20a
	20a-R	GTAACGACGGCCAGTTCTACCTG	miR-20a
	29b-LNA-F	T+AG+CACCATTTGAA	miR-29b
	29b-R	GTAACGACGGCCAGTAACTAGT	miR-29b
	301-F	CAGTGCAATAGTATTG	miR-301
	301-R	GTAACGACGGCCAGTCTTTGA	miR-301
	9-F	TCTTTGTTATCTAG	miR-9
	9-R	GTAACGACGGCCAGTTCATACA	miR-9
Cassettes <sup>c</sup>	BC12-wt-T	CTAGAGTTGGCCACATTAGCTATAATGGCACTTTGTTGTG	BC12
	BC12-wt-B	AGCTCACAACAAAGTGCATTATAGCTAATGGTGGCCAACT	BC12
	BC12-mut-T	CTAGAGTTGGCCACATTAGCTATAATGGCAGTCTGTTGTG	Mutant
	BC12-mut-B	AGCTCACAACAGACTGCCATTATAGCTAATGGTGGCCAACT	Mutant
	MEF2D-wt-T	CTAGGTATGCTGATTGACGGGTGCTACTTTGTATT	MEF2D
	MEF2D-wt-B	AGCTAATACAAAAGTACACCGTGCAATCAGACATAC	MEF2D
	MEF2D-mut-T	CTAGGTATGCTGATTGACGGGTGCTACTTTGTATT	Mutant
	MEF2D-mut-B	AGCTAATACATATGTACACCGTGCAATCAGACATAC	Mutant
	MAP3K12-wt-T	CTAGCAGGAGAGAAAACCACTTAGACTGCACCTTTCTGTTCCGTTTACTCTGTTTACACATTTGCACTTGGGAGG	MAP3K12
	MAP3K12-wt-B	AGCTCTCCCAAGTGCAAAATGTGTAACAGAGTAAACGGAACAGAAAGTGCAGTCTAAGTGTTTCTCTCTCTG	MAP3K12
	MAP3K12-mut-T	CTAGCAGGAGAGAAAACCACTTAGACTGCAGTATTCTGTTCCGTTTACTCTGTTTACACATTTGGACATGGGAGG	Mutant
	MAP3K12-mut-B	AGCTCTCCCATGTCCAAATGTGTAACAGAGTAAACGGAACAGAACTACTGCAGTCTAAGTGTTTCTCTCTCTG	Mutant
siRNA <sup>d</sup>	si-17+	CAAAGUGCUUACAGUGCAGGUAG	miR-17
	si-17−	ACCUGACUGUAAGCACUUUGUU	miR-17
	si-20a+	UAAAGUGCUUACAGUGCAGGUAG	miR-20a
	si-20a−	ACCUGACUGUAAGCACUUUUAU	miR-20a
	si-9*+	UAAAGUCUAGUAACCGAAAGU	miR-9*
	si-9*−	UUUCGCUUUAUCUAGCUUUCUU	miR-9*
	si-EGFP+	CGGCAAGCUGACCCUGAAGUU	Control
	si-EGFP−	CUUCAGGUGCAGCUUGCCGUU	Control
Antisense <sup>e</sup>	as-17	CTA+CCT+GCA+CTG+TAA+GCA+CTT+TG	miR-17
	as-20a	CTA+CCT+GCA+CTA+TAA+GCA+CTT+TA	miR-20a
	as-9*	A+CTT+TCG+GTT+ATC+TAG+CCT+TA	miR-9*

<sup>a</sup> The direction of primers with respect to the target sequence was denoted in the name as either F or R for forward and reverse respectively. Underlined sequence is not gene specific and was used to increase the amplicon size and primer recognition sequence.

<sup>b</sup> The positions of LNA modified bases are preceded by a "+" symbol.

<sup>c</sup> SpeI/HindIII cassettes containing putative target recognition elements were used to generate recombinant luciferase reporter gene constructs. "T" indicates top strand and "B" indicates bottom strand.

<sup>d</sup> siRNA are used to over-express microRNA. "+" indicates top strand and "−" indicates bottom strand.

<sup>e</sup> Antisense are used to suppress endogenous microRNA.

## 2.6. Enrichment and analysis of miRNA co-transfected SH-SY5Y cells

SH-SY5Y cultures were maintained as described above and seeded into 24-well plates before transfection 24 h later (~90% confluency) using Lipofectamine 2000 according to the manufacturer's instructions (Invitrogen). To enrich the population for miRNA/EGFP co-transfected cells (50 pmol miRNA; 500 ng pEGFP-n1), EGFP labeled cells were sorted 24 h post-transfection and collected using the FACSCalibur flow cytometer according to the manufacturer's instructions (BD Biosciences). Cells were pelleted by centrifugation and washed once with PBS prior to RNA extraction as described above (Section 2.1). The expression of the predicted target genes was measured by real-time RT-PCR as described in Section 2.4 (using

random primers for reverse transcription). Relative gene expression was determined by the difference between their individual Ct value and that produced in the same sample for the geometric mean of the constitutively expressed  $\beta$ -glucuronidase (GUSB) and hydroxymethylbilane synthase (HMBS/PBGD) genes. To control for non-specific effects associated with miRNA transfection, the controls were co-transfected with siRNA targeting the EGFP (si-EGFP).

## 2.7. Target gene reporter assay

HEK-293 cultures were maintained as described for SH-SY5Y cells (Section 2.6). Validation of predicted miR-17 family target genes was accomplished by co-transfecting HEK-293 cells with synthetic miRNA



the brain and nervous system, neurite outgrowth, dendritic spine morphology and synaptic plasticity [20,27–30].

To gain further insight into the role of miRNA expression in the process of neuronal differentiation, a custom miRNA microarray and whole-genome array was used to monitor changes in mature miRNA and mRNA expression following retinoic acid induced differentiation of a human (SH-SY5Y) neuroblast culture. This analysis revealed a large number of miRNA and mRNA expression changes including both up- and down-regulation. Of particular significance was the remarkable decrease of the miR-17 family of miRNA. Reporter gene assays suggest that there is a functional biological relationship between the miR-17 family of miRNA and genes involved in neuronal differentiation; in particular, *BCL2*, *MEF2D* and *MAP3K12*.

## 2. Materials and methods

### 2.1. Cell culture and RNA extraction

The SH-SY5Y cell line was obtained from the American Tissue Culture Collection and propagated in DMEM (supplemented with 10% fetal calf serum, 2 mM L-glutamine, 20 mM HEPES and 0.15% bicarbonate of soda; Gibco-BRL). In three independent experiments, approximately  $1 \times 10^7$  cells were seeded into 10 cm Petri dishes (Greiner Bio-One) and differentiated in low serum DMEM (supplemented with 1% fetal calf serum, 2 mM L-glutamine, 20 mM HEPES and 0.15% bicarbonate of soda) containing 10  $\mu$ M *all-trans* retinoic acid (Sigma) and 50 ng/ml brain-derived neurotrophic factor (BDNF) (Sigma). The differentiated cells were maintained in this media for a total of 6 days, with the media being replenished after 72 h.

To extract total RNA, 2 ml of Trizol (Invitrogen) was added directly to each dish and the cells were removed using a disposable cell scraper (Greiner Bio-One). The RNA was then prepared from each lysate according to the manufacturer's instructions. The RNA concentration and integrity was determined using an Experion microcapillary electrophoresis apparatus (Bio-Rad).

### 2.2. miRNA expression analysis

miRNA were labeled directly using a ligation approach developed by Igloi [31] and applied to miRNA by Thomson et al., 2005. These reactions typically contained 3  $\mu$ g of total RNA, in 50 mM HEPES pH 7.8, 3.5 mM DTT, 20 mM MgCl<sub>2</sub>, 0.1 mM ATP, 10  $\mu$ g/ml BSA, 10% DMSO, 500 ng 5'-phosphate-cytidyl-uridyl-Cy3-3' (Dharmacon) and 20 units T4 RNA ligase (Fermentas). The labeling reaction was allowed to proceed on ice for 2 h before the labeled RNA was precipitated with 0.3 M sodium acetate, 2 volumes 100% ethanol and 20  $\mu$ g glycogen at  $-20^\circ\text{C}$  overnight. A synthetic reference library consisting of DNA oligonucleotide (representing the entirety of miRBase version 7.1) was labeled with AlexaFluor 647 (equivalent to Cy5) for detection in the control channel, using the Ulysis labeling kit according to the manufacturer's instructions (Invitrogen). Unconjugated label was removed by gel filtration through a Sephadex G-25 spin column (GE Healthcare). The labeled reference library was used at a 1/700 dilution, alongside the Cy3 labeled miRNA, in each array hybridization.

Microarrays were prepared using miRCURY™ Locked Nucleic Acid (LNA) modified anti-sense probes corresponding to the miRBase Version 7.1 (Exiqon) containing 319 human miRNA sequences. The oligonucleotide probes were printed in quadruplicate onto GAPS-2 glass slides (Corning). The slides were then prepared and hybridized with the labeled miRNA and synthetic controls using the method of Thompson et al. [32]. Briefly, slides were pre-hybridized in  $3 \times$  SSC, 0.1% SDS and 0.2% BSA for 1 h at  $65^\circ\text{C}$  and washed 4 times with RNase-free water, once with 100% ethanol, and dried by centrifugation at  $150 \times g$  for 5 min. Hybridization chambers were created around each array using 17 mm  $\times$  28 mm disposable frame seals and cover slides (Bio-Rad). The labeled RNA sample was added to 100  $\mu$ l

hybridization buffer (400 mM Na<sub>2</sub>HPO<sub>4</sub> pH 7.0, 0.8% BSA, 5% SDS, 12% formamide) and heated for 4 min at  $95^\circ\text{C}$  (in the dark). The mixture was injected into the chamber and hybridized for 2 h at  $55^\circ\text{C}$  in a rotary hybridization oven. The coverslips and frames were removed and the slides were washed once in  $2 \times$  SSC, 0.025% SDS at room temperature, 3 times in  $0.8 \times$  SSC at room temperature and 3 times in ice cold  $0.4 \times$  SSC. Each slide was then dried by centrifugation at  $60 \times g$  for 10 min. Microarrays were then scanned with a Genepix 4000B Scanner (Axon Instruments) and raw pixel intensities extracted with Genepix Pro 3.0 software (Axon Instruments).

### 2.3. Computational methods and statistical analysis

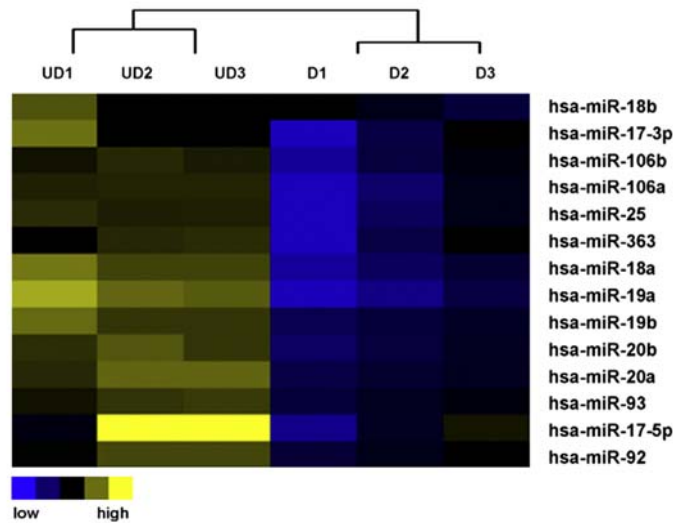
A miRNA was considered expressed if its raw Cy3 pixel intensity was at least 150% above background. Raw Cy3 median pixel intensity values were background subtracted and normalized with respect to the mean values of U6 small-nuclear RNA (U6 snRNA) probes on the array. Differential miRNA expression was analyzed using Significance Analysis of Microarrays (SAM) version 2.23 (Stanford University) [33] (available from <http://www-stat.stanford.edu/~tibs/SAM/>). The threshold for significance was set at 5% and a two-class comparison was performed using 120 permutations of the data. A list of significantly altered miRNA was compiled (false-discovery rate (FDR) < 5%). Unpaired *t*-tests ( $p < 0.05$ ) were also performed on the average fluorescence data to confirm the altered miRNA expression.

### 2.4. Quantitative real-time RT-PCR

Multiplex reverse transcription was performed on 500 ng of DNaseI treated total RNA using a combination of reverse primers specific for the mature miRNA of interest and U6 snRNA, to a final concentration of 40 nM each (for primer sequences see Table 1). Reactions were performed using Superscript II reverse transcriptase in  $1 \times$  first strand buffer according to the manufacturer's instructions (Invitrogen). Real-time PCR was performed essentially as previously described [22], in triplicate on diluted cDNA combined with Power SybrGreen master mix (Applied Biosystems) with 1  $\mu$ M of the appropriate forward and reverse primers (Table 1), in a final volume of 12.5  $\mu$ l using an ABI prism 7500 sequence detection system (Applied Biosystems). Relative miRNA expression was determined by the difference between their individual cycle threshold (Ct) value and that produced in the same sample for the U6 snRNA ( $\Delta\text{Ct}$ ). Differential expression of a given miRNA was determined by the difference between the mean  $\Delta\text{Ct}$  for the differentiated and undifferentiated cohorts ( $\Delta\Delta\text{Ct}$ ) expressed as a ratio ( $2^{-\Delta\Delta\text{Ct}}$ ) [34].

### 2.5. Illumina microarray procedure

Total RNA was purified using the RNeasy MiniElute Cleanup Kit (Qiagen). The concentration of the purified total RNA samples was measured using a Quant-It RiboGreen RNA Assay Kit (Invitrogen, USA) and a fluorometer (Qubit, Invitrogen). To synthesize first and second strand cDNA and amplify biotinylated cRNA from the total RNA, an Illumina Totalprep RNA Amplification Kit was used as per manufacturer's instructions. The purified cRNA samples were quantified to determine the volume required for the BeadChip hybridization step using the Quant-It RiboGreen RNA Assay Kit. Hybridization to the Illumina HumanRef-8-V2 BeadChip was performed according to the manufacturer's instructions without modification. The HumanRef-8-V2 BeadChips were read using an Illumina Bead array reader (San Diego, CA, USA). Analysis and normalization of expression data from the 21,000 transcripts was carried out using BeadStudio 3.0 (Illumina, San Diego, CA, USA). The *t*-test error model and cubic spline normalization was used for all samples. A differential analysis was applied to the samples using the Illumina custom test of significance, utilizing the undifferentiated samples as the reference group.



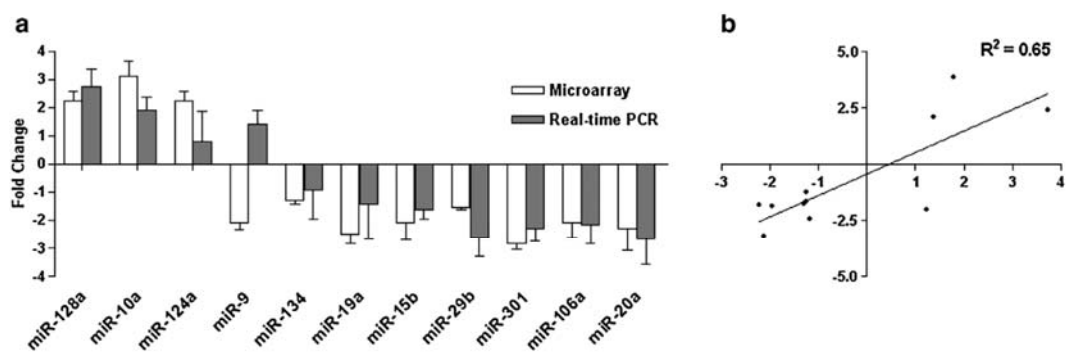
**Fig. 2.** Expression profiles of the miR-17 family show decreased expression after neuronal differentiation in SH-SY5Y cells. Heat map comparing miRNA expression in undifferentiated SH-SY5Y cells and SH-SY5Y cells differentiated with RA and BDNF over three biological replicates. Samples U1, U2, and U3 are undifferentiated SH-SY5Y cells; samples D1, D2, and D3 are differentiated SH-SY5Y cells. Arrays were median-centered using Gene Cluster 2.0 and average linkage clustering was performed by using uncentered correlation metric. The colour bar indicates relative miRNA expression; blue indicates low expression and yellow indicates high expression. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

The only discordance in expression was miR-9 which was shown to be down-regulated by microarray analysis but up-regulated by RT-PCR upon differentiation (Fig. 3a). The correlation between the two methods was substantial, displaying an  $r$ -squared correlation coefficient of 0.65 ( $p = 0.002$ ) (increasing to 0.81 without the discordant miR-9 data) (Fig. 3b).

### 3.3. miRNA target prediction and gene expression analysis

Alteration to the expression of a single miRNA has the capacity to affect the expression of hundreds of genes, making the regulatory roles for miRNA numerous. Potential miRNA target genes may be identified depending on the degree of complementarity a miRNA has to the 3'UTR of the target gene. The identification of miRNA targets on a large scale is difficult at present, however a number of algorithms have been developed to computationally predict miRNA binding sites

on mRNA transcripts [1,42–48]. TargetCombo [<http://www.diana.pcbi.upenn.edu/cgi-bin/TargetCombo.cgi>] is a program which combines other leading homology search algorithms such as DIANA-micro T, PicTar, TargetScanS, and miRanda [49]. TargetCombo identified approximately 1800 genes as potential targets of the miRNA showing up-regulation with known brain-enrichment (miR-124a, -128a, -9 and -10a) and approximately 2700 genes were identified as potential targets of the down-regulated miR-17 family of miRNA (Supplementary Table 3). To further understand the potential of these changes, the predicted gene lists were subjected to functional annotation clustering and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis using the Database for Annotation, Visualization and Integrated Discovery (DAVID) Bioinformatics Database [DAVID; <http://david.abcc.ncifcrf.gov>] [50]. The Gene Ontology (GO) annotation provided by DAVID highlighted processes such as system development, cell differentiation and cell morphogenesis as likely to



**Fig. 3.** Real-time PCR validation of miRNA microarrays. (a) miRNA expression as a result of RA-induced differentiation of SH-SY5Y cells. Data is expressed as a ratio of differentiated to undifferentiated samples. miRNA expression as determined by microarray appear as white bars and RT-PCR results appear as gray bars. For RT-PCR, relative miRNA expression was determined by the difference between their individual cycle threshold (Ct) value and that produced in the same sample for the U6 snRNA ( $\Delta Ct$ ). Microarray and RT-PCR data arose from three biological replicates. Bars are mean  $\pm$  SEM. (b) Microarray data was validated by RT-PCR with a correlation coefficient of 0.65 ( $p = 0.002$ ).



be targeted by the brain-enriched group of miRNA. Similarly, processes such as metabolism, signal transduction, nervous system development and neuron differentiation were likely to be regulated by the down-regulated miR-17 family of miRNA. The KEGG pathways were charted and the most significant terms for both lists included: long-term potentiation (LTP), mitogen-activated protein kinase (MAPK)/Wnt signaling pathways, focal adhesion and axon guidance; with additional pathways including regulation of the actin cytoskeleton and the Notch signaling pathway specific to the up-regulated group of miRNA.

While miRNA target prediction algorithms provide a useful starting point for understanding the function of particular miRNA, they are also prone to a degree of over prediction leading to false positives [46,51]. In order to examine the altered miRNA expression in the context of differentiation-associated changes, whole-genome expression analysis was carried out using Illumina whole-genome microarrays. The data indicated that approximately 18,000 genes were expressed in SH-SY5Y neuroblasts, and upon differentiation nearly a third of these displayed significantly altered expression (Supplementary Table 4). The list of putative targets for the brain-enriched group (up-regulated) was cross-matched with genes shown to be down-regulated; and the list of putative targets for miR-17 family (down-regulated) was cross-matched with genes shown to be up-regulated by whole-genome array (Supplementary Table 4). Of the 1800 genes predicted to be targets of the brain-enriched group, approximately 350 (~20%) of these showed a significant down-regulation by the whole-genome analysis (Supplementary Table 5). While this is still a substantial gene list, it carries with it more biological validity than computationally predicted targets alone. The functional annotation tools offered by the DAVID were used to identify over-represented pathways and provide some biological meaning to this list of 350 genes. The GO annotation for these down-regulated genes highlighted numerous processes involved in the cell cycle, cell organization and biogenesis and cell proliferation however the KEGG pathway analysis failed to highlight any over-represented pathways involving communication or signaling cascades as predicted. With respect to the 2700 genes predicted to be targets of the miR-17 family (down-regulated), approximately 700 (~26%) of these showed a significant up-regulation by the whole-genome analysis (Supplementary Table 5). The functional analyses highlighted numerous processes involved in intracellular signaling cascades, signal transduction and cell communication and the over-represented KEGG pathways highlighted MAPK/Wnt signaling pathways, LTP, focal adhesion and axon guidance; similar to what was proposed from the predicted gene target list.

### 3.4. Regulation of differentiation by miRNA

Consistent with expectation, expression analysis revealed that some markers of neuronal differentiation such as *BCL2*, *MEF2D* and *MAP3K12* each displayed a significant increase in expression in response to the RA and BDNF treatment. *BCL2* displayed a 1.73-fold up-regulation ( $p = 0.022$ ), *MEF2D* 1.61-fold ( $p = 0.035$ ) and *MAP3K12* 2.03-fold ( $p = 0.034$ ) (Fig. 4). Computational analysis by TargetCombo indicated that each of these genes was indeed potential gene targets of the miR-17 family of miRNA, and reciprocal expression of the genes and miRNA highlight the miR-17 family as potential regulators of these genes involved in the differentiation process. To gain further biological insight into the miR-17 family target genes, SH-SY5Y cultures were transfected with synthetic miR-17 and miR-20a. An EGFP expression construct was also co-transfected with each miRNA to facilitate the selection of transfected cells by flow cytometry. Expression of all three target genes by quantitative RT-PCR responded as expected with suppression of between 50 and 80% in response to elevated miR-17 or miR-20a (Fig. 5).

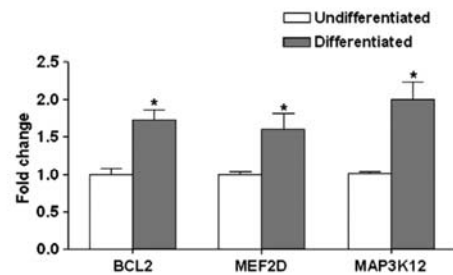


Fig. 4. Markers of neuronal differentiation display elevated expression following retinoic acid and BDNF treatment. *BCL2*, *MEF2D* and *MAP3K12* each displayed an up-regulation in SH-SY5Y cells following neuronal differentiation with RA and BDNF. *BCL2* was elevated by 1.73-fold ( $p = 0.022$ ), *MEF2D* 1.61-fold ( $p = 0.035$ ) and *MAP3K12* 2.03-fold ( $p = 0.034$ ). Undifferentiated samples are shown as white bars and differentiated samples are shown as gray bars. Error bars are  $\pm$  SD.

To further examine the potential of a functional relationship between the miRNA and these differentiation-associated target genes, reporter gene assays were established. For this purpose, miRNA recognition elements (MRE) from each of the target genes predicted to bind members of the miR-17 family (miR-17 and -20a) were cloned into the 3'UTR of the firefly luciferase gene of the pMIR-REPORT vector (Fig. 6a). Mutant versions of these MREs created by introducing polymorphisms in the seed-pairing region were also cloned into the pMIR-REPORT vector (Fig. 6b,c). Each of these reporter constructs and the control plasmid (pRLN-TK) encoding renilla luciferase, were co-transfected with synthetic miR-17, miR-20a or a combination of the two. LNA modified anti-miRs were also transfected into HEK-293 cells and their relative luciferase activity was measured. In accordance with expectation, luciferase expression from reporter constructs derived from *BCL2* was significantly suppressed by synthetic miRNA and increased by anti-miR transfections (mutant constructs were unresponsive). The *MEF2D* wildtype constructs produced significant suppression by each miRNA and anti-miR transfection also resulted in a significant increase in luciferase expression. The *MEF2D* wildtype construct was not responsive to the miR-17/20a combined transfection for the miRNA or anti-miR. The *MEF2D* mutant MREs were generally unresponsive, however anti-miR miR-17 displayed a significant increase in luciferase expression (though the wildtype

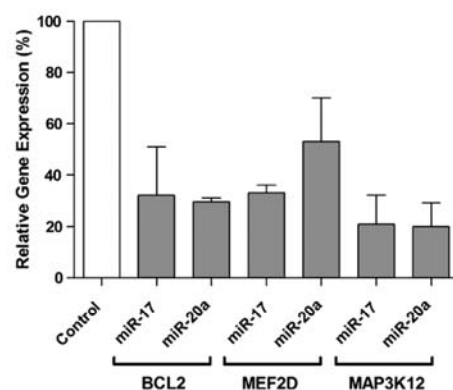
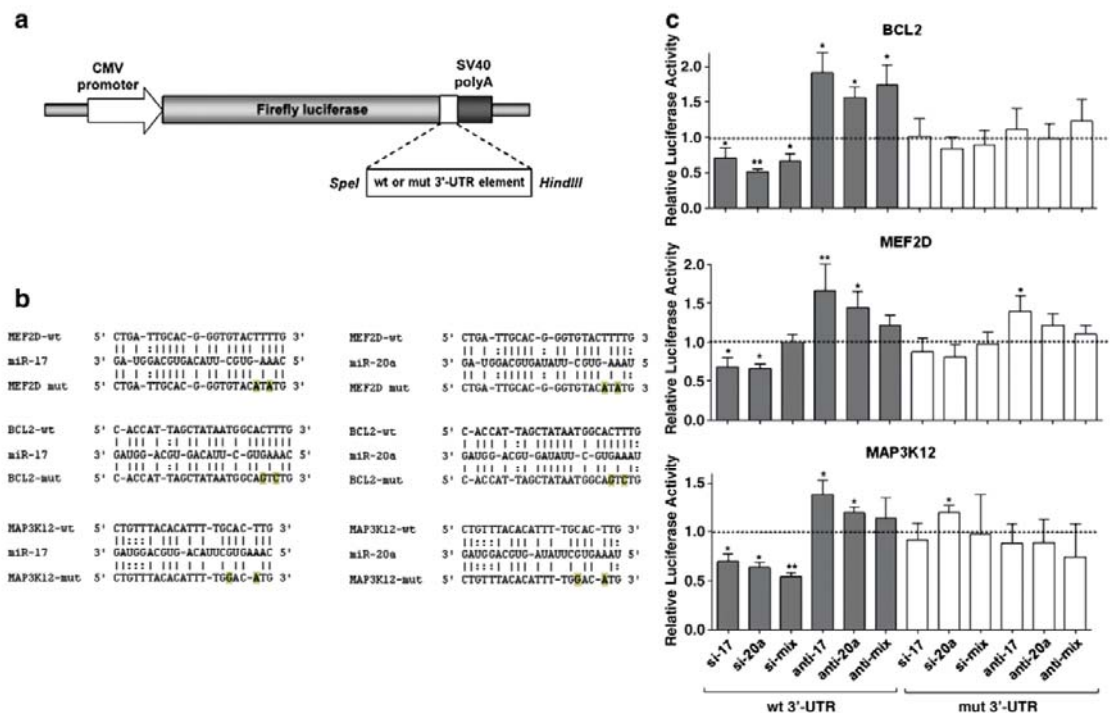


Fig. 5. Relative expression of target genes in response to miR-17 and -20a transfection. A synthetic miR-17/20a/eGFP transfection system was established to monitor the expression of *BCL2*, *MEF2D* and *MAP3K12* in response to changes in miRNA concentration *in vitro*. Relative expression was determined by real-time RT-PCR. Decreased expression of all three target genes corresponded to elevated miR-17 or miR-20a levels. Bars represent mean  $\pm$  SEM.



**Fig. 6.** Regulation of differentiation-associated reporter gene constructs by miRNA. (a) The pMIR-REPORT<sup>TM</sup> miRNA expression reporter system contains a firefly luciferase gene under the control of CMV promoter. The putative miR-17/miR-20a MRE for *BCL2*, *MEF2D* or *MAP3K12* was inserted into the multiple cloning site in the 3' UTR of the luciferase gene. (b) Mutant versions of each MRE were also prepared such that base changes (indicated by highlighted bases) were introduced to the miRNA seed pairing region. (c) Luciferase expression was measured in response to synthetic miRNA (to increase miRNA concentration) and anti-miR transfections (to suppress endogenous miRNA). Wildtype constructs are shown as gray bars, and mutant constructs as white bars. Luciferase expression in response to transfection was analyzed for miR-17 and miR-20a individually as well as the two combined. Using the wildtype MRE derived from *BCL2*, luciferase expression was significantly suppressed by synthetic miRNA and increased by anti-miR transfections. In all cases, the mutant constructs were unresponsive. The *MEF2D* wildtype construct produced significant suppression by miR-17 and miR-20a and anti-miR transfection also resulted in a significant increase in luciferase expression. The *MEF2D* wildtype construct was not responsive to the miR-17/20a combined transfection for the miRNA or anti-miR. The *MEF2D* mutant MREs were generally unresponsive, however anti-miR-17 displayed a significant increase in luciferase expression though the wildtype construct displayed a greater anti-miR response. Using the wildtype MREs derived from *MAP3K12*, luciferase expression was significantly suppressed by synthetic miRNA and increased by anti-miR transfections (with the exception of the combined anti-miR). Mutant MREs were all unresponsive except miR-20a, which displayed an increase in luciferase expression (the wildtype showed a significant decrease, as expected). Bars represent mean  $\pm$  SD.

construct displayed a greater anti-miR response). In a similar manner, the wildtype *MAP3K12* MREs displayed significant luciferase suppression by the synthetic miRNA and was increased by anti-miR transfections (with the exception of the combined anti-miR). Mutant MREs were all unresponsive except miR-20a, which displayed an increase in luciferase expression however the wildtype showed a significant decrease, as expected. These reporter gene assays show that *BCL2*, *MEF2D* and *MAP3K12* are each able to be bi-directionally modulated by synthetic miRNA and anti-miR transfections by miR-17 and miR-20a, and suggest that each of the MREs tested are indeed functional.

#### 4. Discussion

To investigate the role of miRNA during the neuronal differentiation process, a custom miRNA microarray was used along with whole-genome analysis and reporter gene assays to observe miRNA and mRNA changes during the RA-induced differentiation of SH-SY5Y neuroblasts. This study identified 43 miRNA with altered expression following RA treatment; with 32 miRNA displaying significantly decreased expression and 11 miRNA showing significantly increased expression as a result of differentiation. Changes in miRNA expression

post-differentiation have been reported previously in a number of cell lines, primary cells and developing tissues *in vivo*. A number of these changes are consistent with our observations. For example miR-9, -124a [52], -128a, -208, -210 and -423 were also found to be up-regulated in response to RA in NT2/D1 (human testicular embryonal carcinoma) cells and P19 (mouse embryonal carcinoma) cells [52,53]. This increase in expression observed in SH-SY5Y neuroblasts is in agreement with those studies and most likely corresponds with the maturation from neural progenitors towards committed cells [40]. Contrary to expectation, however, none of the up-regulated mature miRNA in this study corresponds to pre-miRNA transcripts reported to be up-regulated in SH-SY5Y cells differentiated with the phorbol ester, TPA [54]. This discordance could be a reflection of the differences between retinoic acid and TPA induced differentiation, however they are perhaps due to differences between pre-miRNA and mature miRNA expression; as the base line expression of pre-miRNA in undifferentiated cells is discordant with mature miRNA expression [55]. It is also possible that the TPA study missed some of these changes as it only considered 180 transcripts compared with the 319 mature miRNA in this current study.

Some of the miRNA showing up-regulation; miR-9, -124a, -128a and -10a are known to be brain-enriched; and may serve an



important role in neuronal development [20,27–29]. *In silico* analysis generated a list of potential gene targets of these miRNA which was correlated with those that were up-regulated by whole-genome array, generating a list of approximately 350 genes. The GO annotation for this gene list cited processes involved with cell cycle and cell proliferation, consistent with the neuronal differentiation process. Genes with known importance to cell cycle arrest were histone deacetylase 9 (*HDAC9*), phosphatase and tensin homolog (*PTEN*), cyclin J (*CCNJ*), cyclin G1 (*CCNG1*), mitogen-activated protein kinase 4 (*MAPK4*) and discs, large homolog 5 (*DLG5*). Each of these genes was shown to be down-regulated due to differentiation and all contain at least one binding site in their 3'UTR for the brain-enriched/up-regulated group of miRNA, suggesting that these miRNA may play a role in regulating the expression of these genes. A miRNA showing down-regulation; miR-134, is also of particular interest as it was recently shown to negatively regulate the size of dendritic spines in the rat hippocampus [28]. It was suggested that miR-134 could regulate the expression of the synaptic Lim-domain-containing protein kinase 1 (*LIMK1*), thereby controlling dendritic spine size. Therefore, the coordinate reduction of miR-134 and up-regulation of *LIMK1* observed in this study (data not shown) may facilitate the increase in dendritic spine size observed throughout neuroblast differentiation.

Numerous miRNA were identified with significantly decreased expression, however the down-regulation of the entire miR-17 family of miRNA was striking. A total of 14 mature miRNA are associated with the miR-17 family and remarkably, all of these were found to be down-regulated in this study (Table 2, Fig. 2). The miR-17 family (the miR-17-92 cluster more specifically) is heavily implicated in numerous cancers, with increased expression in B-cell lymphoma [26,56], T-cell leukemia [57], lung cancer, colorectal cancer and various solid tumors [26,58–60], where the increased expression may play a role in maintaining the undifferentiated phenotype of cancerous cells. This cluster has also been shown to be pro-angiogenic *in vivo* [61]; however an explicit role in the differentiation process has yet to be identified. Some members of the miR-17 family (miR-20a, -106a and -17) have recently been identified to show decreased expression upon the RA-induced differentiation of NT2/D1 cells [52] and other miRNA have been shown to be down-regulated in RA-induced differentiated HL-60 (human myeloid) cells [53]. Surprisingly, there was no overlap between the down-regulated miRNA in the HL-60 study and those observed here in RA-differentiated SH-SY5Y neuroblasts; which could be a reflection of the differences in miRNA expression profiles between myeloid and neuronal cell lineages.

Additional *in silico* analysis indicated that approximately 700 genes were up-regulated due to differentiation which were potentially targeted by the miR-17 family of miRNA. Subjecting this list to KEGG pathway analysis highlighted the MAPK signaling pathway as the pathway containing the greatest number of genes from this list. MAPK pathways are integral to neuronal differentiation as they are able to switch their function from that mediating proliferation, to inducing cellular differentiation [62–64]. Activated MAPKs have also been shown to be important in inducing neurite outgrowths and the expression of neuronal markers such as the anti-apoptotic protein B-cell CLL/lymphoma 2 (*BCL2*) and growth associated protein 43 (*Gap-43*). Differentiated neuronal cells also express other neuronal markers such as tau, myocyte enhancer factor-2 (*MEF2*), neurofilaments and neuron-specific enolase (*NSE*) [35]. In accordance with expectation, this study identified a significant up-regulation of many markers of neuronal differentiation (e.g. *BCL2*, *MEF2D*, tau (*MAPT*) and *NSE* (*ENO2*)). *BCL2* is known to influence the axonal growth of sensory neurons [65] and has been previously shown to be up-regulated following differentiation of SH-SY5Y cells [66–69]. Furthermore, the expression of *MEF2D* has recently been shown to positively correlate with the length of neurite projections [70]. The *MEF2* family of calcium-regulated transcription factors regulates neuronal develop-

ment by controlling synapse formation and supporting the survival of newly formed neurons. It is thought that *MEF2* proteins could also influence early aspects of neuronal differentiation such as neuronal fate specification and their subsequent morphological and functional maturation [70]. Specifically, this study identified that the neuronal markers *BCL2* and *MEF2D* were up-regulated by 1.73-fold and 1.61-fold respectively. In addition, the mixed-lineage kinase, *MAP3K12* also displayed an increase in expression of 2.03-fold in response to RA and BDNF induced differentiation (Fig. 4). *MAP3K12* is known to be essential to the JNK/SAPK signaling pathway (a major MAPK pathway) [71,72]. It was initially identified by displaying increased expression upon the RA induced differentiation of NT2 cells [73] and its expression is enriched in the developing brain [74].

Interestingly, the 3'UTR of *MEF2D* contains binding sites for each of the miR-17 family members; some with multiple sites. *BCL2* also contains at least one binding site for each member of the miR-17 family (with the exception of miR-19a and -19b) and *MAP3K12* contains putative binding sites for 10 of the 14 miR-17 family members. Due to the reciprocal expression of these genes and the miR-17 family, it is suggested that the down-regulation of this family may have an integral role in regulating the expression of *BCL2*, *MEF2D* and *MAP3K12* during the differentiation process. To further support the plausibility of a relationship between *BCL2*, *MEF2D* and *MAP3K12* expression and miR-17 family, we established a synthetic miR-17/20a transfection system and monitored the expression of these genes in response to changes in miRNA concentration *in vitro*. The expression of each of these genes responded in accordance with expectation by showing a substantial drop in expression after the addition of the miRNA (Fig. 5). This supports the hypothesis that the three differentiation-associated target genes are repressed in the presence of miR-17 family miRNA in undifferentiated cells. However, in order to directly characterize the influence of miR-17 family miRNA on these targets, a reporter gene assay was established.

To substantiate a link between these differentiation-associated target genes and altered expression in this group of miRNA, the respective miRNA recognition elements (MRE) from *BCL2*, *MEF2D* and *MAP3K12* (or mutant controls) were cloned into the 3'UTR of a luciferase reporter gene construct and co-transfected into a recipient cell line with miRNA (miR-17 and -20a) or anti-miRs (miRNA antagonists). The extent of reporter gene activity and the influence of miRNA were then determined by measuring the relative luciferase activity (Fig. 6). Many of these constructs behaved in accordance with expectation and were significantly repressed in the presence of synthetic miRNA, and significantly de-repressed (increased luciferase) in the presence of the corresponding anti-miR (Fig. 6d). The most responsive target was derived from the 3'UTR of *BCL2*. Transfection with miR-17 and -20a caused a suppression of luciferase activity and anti-miRs caused a significant increase. The same trend was observed when a combination of both miR-17 and -20a was used, suggesting that a synergistic relationship may exist between the two family members. In a similar manner, the *MEF2D* and *MAP3K12* constructs also displayed suppression by the miRNA and increased activity in response to the anti-miRs; however the synergistic relationship between miR-17 and -20a was not observed as for the *BCL2* constructs. Together, these data suggest that the miR-17 family may be working co-operatively to fine tune the expression of differentiation-related targets. This is surely not limited to *BCL2*, *MEF2D* and *MAP3K12* and may have numerous regulatory roles during differentiation.

Data continues to emerge in support of the miRNA pathway being crucial in the development of the brain and the nervous system, predominantly in relation to neuronal development and plasticity. The heavily reported cancer-related phenomenon of increased miR-17 family expression could serve as an interesting anti-parallel for the neuronal differentiation process. Many gene changes observed in this study of neuronal differentiation are in accordance with previous research, though in addition, many miRNA have been identified that

may function collectively to fine-tune the regulation of the many genes involved with neuronal differentiation. While this is clearly important during development and aging, understanding the consequences of miRNA dysfunction may also shed important light on the pathophysiology of neurodevelopmental disorders.

### Acknowledgments

This study was supported by the Schizophrenia Research Institute, utilizing funding from NSW Health and the Henderson Foundation. Further support was also received from the National Alliance for Research on Schizophrenia and Depression (NARSAD). Murray Cairns is supported by the M.C. Ainsworth Fellowship in Schizophrenia Research.

### Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.cellsig.2009.07.019](https://doi.org/10.1016/j.cellsig.2009.07.019).

### References

- [1] B.P. Lewis, C.B. Burge, D.P. Bartel, *Cell* 120 (1) (2005) 15.
- [2] X. Xie, J. Lu, E.J. Kulbokas, T.R. Golub, V. Mootha, K. Lindblad-Toh, E.S. Lander, M. Kellis, *Nature* 434 (7031) (2005) 338.
- [3] M. Lagos-Quintana, R. Rauhut, A. Yalcin, J. Meyer, W. Lendeckel, T. Tuschl, *Curr. Biol.* 12 (9) (2002) 735.
- [4] R.C. Lee, V. Ambros, *Science* 294 (5543) (2001) 862.
- [5] L.F. Sempere, S. Freemantle, I. Pitha-Rowe, E. Moss, E. Dmitrovsky, V. Ambros, *Genome Biol.* 5 (3) (2004) R13.
- [6] R.S. Pillai, S.N. Bhattacharyya, C.G. Artus, T. Zoller, N. Cougot, E. Basyuk, E. Bertrand, W. Filipowicz, *Science* 309 (5740) (2005) 1573.
- [7] F. Gebauer, M.W. Hentze, *Nat. Rev. Mol. Cell Biol.* 5 (10) (2004) 827.
- [8] R. Yi, Y. Qin, L.G. Macara, B.R. Cullen, *Genes Dev.* 17 (24) (2003) 3011.
- [9] Y. Lee, C. Ahn, J. Han, H. Choi, J. Kim, J. Yim, J. Lee, P. Provost, O. Radmark, S. Kim, V.N. Kim, *Nature* 425 (6956) (2003) 415.
- [10] G. Tang, *Trends Biochem. Sci.* 30 (2) (2005) 106.
- [11] D.S. Schwarz, G. Hutvagner, T. Du, Z. Xu, N. Aronin, P.D. Zamore, *Cell* 115 (2) (2003) 199.
- [12] L.P. Lim, M.E. Glasner, S. Yekta, C.B. Burge, D.P. Bartel, *Science* 299 (5612) (2003) 1540.
- [13] S. Griffiths-Jones, *Methods Mol. Biol.* 342 (2006) 129.
- [14] J. Brennecke, D.R. Hipfner, A. Stark, R.B. Russell, S.M. Cohen, *Cell* 113 (1) (2003) 25.
- [15] B. John, A.J. Enright, A. Aravin, T. Tuschl, C. Sander, D.S. Marks, *PLoS Biol.* 2 (11) (2004) e363.
- [16] B.J. Reinhart, F.J. Slack, M. Basson, A.E. Pasquinelli, J.C. Bettinger, A.E. Rougvie, H.R. Horvitz, G. Ruvkun, *Nature* 403 (6772) (2000) 901.
- [17] J. Dostie, Z. Mourelatos, M. Yang, A. Sharma, G. Dreyfuss, *Rna* 9 (2) (2003) 180.
- [18] P. Xu, S.Y. Vernooij, M. Guo, B.A. Hay, *Curr. Biol.* 13 (9) (2003) 790.
- [19] I. Naguibneva, M. Ameyar-Zazoua, A. Poleskaya, S. Ait-Si-Ali, R. Groisman, M. Soudi, S. Cuvelier, A. Harel-Bellan, *Nat. Cell Biol.* 8 (3) (2006) 278.
- [20] A.J. Giraldez, R.M. Cinalli, M.E. Glasner, A.J. Enright, J.M. Thomson, S. Baskerville, S.M. Hammond, D.P. Bartel, A.F. Schier, *Science* 308 (5723) (2005) 833.
- [21] J.F. Abelson, K.Y. Kwan, B.J. O'Roak, D.Y. Baek, A.A. Stillman, T.M. Morgan, C.A. Mathews, D.L. Pauls, M.R. Rasin, M. Gunel, N.R. Davis, A.G. Ercan-Sencicek, D.H. Guez, J.A. Spertus, J.F. Leckman, L.St. Dure, R. Kurlan, H.S. Singer, D.L. Gilbert, A. Farhi, A. Louvi, R.P. Lifton, N. Sestan, M.W. State, *Science* 310 (5746) (2005) 317.
- [22] N.J. Beveridge, P.A. Tooney, A.P. Carroll, E. Gardiner, N. Bowden, R.J. Scott, N. Tran, I. Dedova, M.J. Cairns, *Hum. Mol. Genet.* (2008).
- [23] P. Jin, R.S. Alisch, S.T. Warren, *Nat. Cell Biol.* 6 (11) (2004) 1048.
- [24] M. Landthaler, A. Yalcin, T. Tuschl, *Curr. Biol.* 14 (23) (2004) 2162.
- [25] D.O. Perkins, C.D. Jeffries, L.F. Jarskog, J.M. Thomson, K. Woods, M.A. Newman, J.S. Parker, J. Jin, S.M. Hammond, *Genome Biol.* 8 (2) (2007) R27.
- [26] H. Tagawa, K. Karube, S. Tsuzuki, K. Ohshima, M. Seto, *Cancer Sci.* 98 (9) (2007) 1482.
- [27] L. Sempere, S. Freemantle, I. Pitha-Rowe, E. Moss, E. Dmitrovsky, V. Ambros, *Genome Biol.* 5 (3) (2004) R13.
- [28] G.M. Schratt, F. Tuebing, E.A. Nigh, C.G. Kane, M.E. Sabatini, M. Kiebler, M.E. Greenberg, *Nature* 439 (7074) (2006) 283.
- [29] A.M. Krichevsky, K.S. King, C.P. Donahue, K. Khrapko, K.S. Kosik, *Rna* 9 (10) (2003) 1274.
- [30] S.I. Ashraf, A.L. McLoon, S.M. Scarsic, S. Kunes, *Cell* 124 (1) (2006) 191.
- [31] G.L. Igloi, *Anal. Biochem.* 233 (1) (1996) 124.
- [32] J.M. Thomson, J. Parker, C.M. Perou, S.M. Hammond, *Nat. Methods* 1 (1) (2004) 47.
- [33] V.G. Tusher, R. Tibshirani, G. Chu, *Proc. Natl. Acad. Sci. U. S. A.* 98 (9) (2001) 5116.
- [34] K.J. Livak, T.D. Schmittgen, *Methods* 25 (4) (2001) 402.
- [35] M. Encinas, M. Iglesias, Y. Liu, H. Wang, A. Muhaisen, V. Cena, C. Gallego, J.X. Comella, *J. Neurochem.* 75 (3) (2000) 991.
- [36] M. Encinas, M. Iglesias, N. Llecha, J.X. Comella, *J. Neurochem.* 73 (4) (1999) 1409.
- [37] Y.M. Yu, P.L. Han, J.K. Lee, *Neuroreport* 14 (7) (2003) 941.
- [38] M. Castoldi, S. Schmidt, V. Benes, M. Noerholm, A.E. Kulozik, M.W. Hentze, M.U. Muckenthaler, *Rna* 12 (5) (2006) 913.
- [39] A.M. Krichevsky, K.C. Sonntag, O. Isacson, K.S. Kosik, *Stem Cells* 24 (4) (2006) 857.
- [40] L. Smirnova, A. Grafe, A. Seiler, S. Schumacher, R. Nitsch, F.G. Wulczyn, *Eur. J. Neurosci.* 21 (6) (2005) 1469.
- [41] A. Tanzer, P.F. Stadler, *J. Mol. Biol.* 339 (2) (2004) 327.
- [42] M. Rehmsmeier, *Methods Mol. Biol.* 342 (2006) 87.
- [43] B. John, C. Sander, D.S. Marks, *Methods Mol. Biol.* 342 (2006) 101.
- [44] M. Rehmsmeier, P. Steffen, M. Hochsmann, R. Giegerich, *Rna* 10 (10) (2004) 1507.
- [45] A.J. Enright, B. John, U. Gaul, T. Tuschl, C. Sander, D.S. Marks, *Genome Biol.* 5 (1) (2003) R1.
- [46] B.P. Lewis, I.H. Shih, M.W. Jones-Rhoades, D.P. Bartel, C.B. Burge, *Cell* 115 (7) (2003) 787.
- [47] A. Stark, J. Brennecke, R.B. Russell, S.M. Cohen, *PLoS Biol.* 1 (3) (2003) E60.
- [48] S. Griffiths-Jones, R.J. Grocock, S. van Dongen, A. Bateman, A.J. Enright, *Nucleic Acids Res.* 34 (Database issue) (2006) D140.
- [49] P. Sethupathy, M. Megraw, A.G. Hatzigeorgiou, *Nat. Methods* 3 (11) (2006) 881.
- [50] G. Dennis Jr., B.T. Sherman, D.A. Hosack, J. Yang, W. Gao, H.C. Lane, R.A. Lempicki, *Genome Biol.* 4 (5) (2003) P3.
- [51] M. Yousef, M. Nebozhyn, H. Shatkey, S. Kanterakis, L.C. Showe, M.K. Showe, *Bioinformatics* 22 (11) (2006) 1325.
- [52] H. Hohjoh, T. Fukushima, *Biochem. Biophys. Res. Commun.* 362 (2) (2007) 360.
- [53] K. Kasashima, Y. Nakamura, T. Kozu, *Biochem. Biophys. Res. Commun.* 322 (2) (2004) 403.
- [54] Y. Fukuda, H. Kawasaki, K. Taira, *Nucleic Acids Symp. Ser. (Oxf.)* 49 (2005) 341.
- [55] J.M. Thomson, M. Newman, J.S. Parker, E.M. Morin-Kensicki, T. Wright, S.M. Hammond, *Genes Dev.* 20 (16) (2006) 2202.
- [56] L. He, J.M. Thomson, M.T. Hemann, E. Hernandez-Monge, D. Mu, S. Goodson, S. Powers, C. Cordon-Cardo, S.W. Lowe, G.J. Hannon, S.M. Hammond, *Nature* 435 (7043) (2005) 828.
- [57] S. Landais, S. Landry, P. Legault, E. Rassart, *Cancer Res.* 67 (12) (2007) 5699.
- [58] Y. Hayashita, H. Osada, Y. Tatematsu, H. Yamada, K. Yanagisawa, S. Tomida, Y. Yatabe, K. Kawahara, Y. Sekido, T. Takahashi, *Cancer Res.* 65 (21) (2005) 9628.
- [59] G. Lanza, M. Ferracin, R. Gafa, A. Veronese, R. Spizzo, F. Pichiorri, C.G. Liu, G.A. Calin, C.M. Croce, M. Negrini, *Mol. Cancer* 6 (2007) 54.
- [60] S. Volinia, G.A. Calin, C.G. Liu, S. Ambs, A. Cimmino, F. Petrocca, R. Visone, M. Iorio, C. Roldo, M. Ferracin, R.L. Prueitt, N. Yanaihara, G. Lanza, A. Scarpa, A. Vecchione, M. Negrini, C.C. Harris, C.M. Croce, *Proc. Natl. Acad. Sci. U. S. A.* 103 (7) (2006) 2257.
- [61] M. Dewes, A. Homayouni, D. Yu, D. Murphy, C. Seignani, E. Wentzel, E.E. Furth, W.M. Lee, G.H. Enders, J.T. Mendell, A. Thomas-Tikhonenko, *Nat. Genet.* 38 (9) (2006) 1060.
- [62] A.K. Olsson, E. Nanberg, *Exp. Cell Res.* 265 (1) (2001) 21.
- [63] T. Morooka, E. Nishida, *J. Biol. Chem.* 273 (38) (1998) 24285.
- [64] T.K. Monaghan, C.J. Mackenzie, R. Plevin, E.M. Lutz, *J. Neurochem.* 104 (1) (2008) 74.
- [65] D.A. Hilton, S. Love, R. Barber, *Neuropathol. Appl. Neurobiol.* 23 (6) (1997) 507.
- [66] Z. Feng, A.G. Porter, *J. Biol. Chem.* 274 (43) (1999) 30341.
- [67] A. Lasorella, A. Iavarone, M.A. Israel, *Cancer Res.* 55 (20) (1995) 4711.
- [68] M. Hanada, S. Krajewski, S. Tanaka, D. Cazals-Hatem, B.A. Spengler, R.A. Ross, J.L. Biedler, J.C. Reed, *Cancer Res.* 53 (20) (1993) 4978.
- [69] G. Raguenet, L. Desire, V. Lantrua, Y. Courtois, *Biochem. Biophys. Res. Commun.* 258 (3) (1999) 745.
- [70] B.Y. Lam, S. Chawla, *Neurosci. Lett.* 427 (3) (2007) 153.
- [71] G. Fan, S.E. Merritt, M. Kortjenann, P.E. Shaw, L.B. Holzman, *J. Biol. Chem.* 271 (40) (1996) 24788.
- [72] S. Hirai, M. Katoh, M. Terada, J.M. Kyriakis, L.I. Zon, A. Rana, J. Avruch, S. Ohno, *J. Biol. Chem.* 272 (24) (1997) 15167.
- [73] U.R. Reddy, D. Pleasure, *Biochem. Biophys. Res. Commun.* 205 (2) (1994) 1494.
- [74] A. Nadeau, G. Grondin, R. Blouin, *J. Histochem. Cytochem.* 45 (1) (1997) 107.

---

## CHAPTER 3

*Maturation of the human dorsolateral  
prefrontal cortex coincides with a dynamic  
shift in microRNA expression*

---

---

**CHAPTER 3 : Maturation of the human dorsolateral prefrontal cortex  
coincides with a dynamic shift in microRNA expression**

**Natalie J. Beveridge**, Danielle M. Santarelli, Paul A. Tooney, Maree Webster,  
Cynthia S. Weickert and Murray J. Cairns

**Submitted to Molecular Psychiatry: Under Review**

**Statement II: Author contribution to Chapter 3 manuscript**

Author	Description of Contribution to Article	Signature
Natalie J. Beveridge	Designed and executed the study. Provided significant insight into the interpretation of the data. Wrote the manuscript.	
Danielle M. Santarelli	Executed the study. Provided insight into the interpretation of the data.	
Paul A. Tooney	Aided in data interpretation and corrected the manuscript.	
Maree Webster	Established the sample cohort	
Cynthia Shannon Weickert	Established the sample cohort and corrected the manuscript	
Murray J. Cairns	Designed the study, provided the concept and corrected the manuscript.	

4<sup>th</sup> November, 2010

---

**PROFESSOR JOHN ROSTAS**  
Deputy Head of Faculty (Research and Research Training)

---

---

# Maturation of the human dorsolateral prefrontal cortex coincides with a dynamic shift in microRNA expression

Natalie J. Beveridge<sup>1,2</sup>, Danielle M. Santarelli<sup>1,2</sup>, Paul A. Tooney<sup>1,2</sup>, Maree J. Webster<sup>3</sup>, Cynthia Shannon Weickert<sup>1,4,5</sup> and Murray J. Cairns<sup>1,2\*</sup>

## \* Corresponding Author:

Dr Murray J. Cairns, School of Biomedical Sciences & Pharmacy, The University of Newcastle, University Drive, Callaghan, NSW 2308, Australia.

Phone: +61-2-4921-8670 Fax: +61-2-4921-7903

Email: murray.cairns@newcastle.edu.au

<sup>1</sup> Schizophrenia Research Institute, Sydney NSW, Australia

<sup>2</sup> School of Biomedical Sciences & Pharmacy, and Hunter Medical Research Institute, University of Newcastle, Callaghan NSW, Australia

<sup>3</sup> The Stanley Medical Research Institute, Rockville, MD, USA

<sup>4</sup> Neuroscience Research Australia, Randwick NSW, Australia

<sup>5</sup> School of Psychiatry, Faculty of Medicine, University of New South Wales, Sydney NSW, Australia

---

## KEYWORDS

miRNA  
neurodevelopment  
development  
aging  
prefrontal cortex  
DGCR8

## ABSTRACT

Expression profiling and functional genomics studies have shown that a large number of miRNA are involved in the function and development of the mammalian nervous system. To further study the role of miRNA in human cerebral cortex development, we investigated postmortem miRNA expression and biogenesis in a cohort of 97 normal human samples from the dorsolateral prefrontal cortex (DLPFC) ranging from 1 month to 78 years of age using a commercial microarray platform (Illumina). The results validated by quantitative RT-PCR demonstrate that a large proportion of miRNA display distinct expression changes with age illustrated by a dramatic inflection point at approximately 20 years of age. As mature miRNA expression is largely post-transcriptionally regulated, we also examined the expression of genes involved in the miRNA biogenesis pathway including DGCR8, Drosha, Dicer and Exportin-5. Interestingly, the overall pattern of DGCR8 expression was consistent with global miRNA expression. Further investigation of the function of these neurodevelopmentally regulated miRNA will not only improve our understanding of how genes are regulated during the normal development of the human brain, but also give insight to how dysregulation of these transcripts could underlie many of the molecular changes observed in neurodevelopmental and neuropsychiatric disorders.

---

## INTRODUCTION

Efforts to understand the underlying mechanisms driving gene expression have focused predominantly on genetic and epigenetic influences on transcription, mediated by alterations in signal transduction pathways, their transcription factors, or gene promoter elements and associated chromatin structure. However, recent studies have emerged that highlight the impact of post-transcriptional regulation of gene expression. Post-transcriptional influences mediated by miRNA play a major role in coordinating the regulation of gene expression during the differentiation and development of the brain<sup>1</sup>. Indeed, a large proportion of human miRNA display a brain-enriched pattern of expression<sup>2</sup>. Considering that each miRNA can potentially manipulate

the expression of hundreds of target genes, the clinical implications of a disturbance to this system are substantial, particularly if such abnormality occurs during critical developmental periods. The human prefrontal cortex (PFC) is one of the last cortical regions to mature structurally and functionally, and continues to develop into young adulthood<sup>3</sup>. The PFC is one of the most functionally advanced regions of the brain, mediating working memory, attention, decision making and executive function<sup>4,5</sup>. It is suggested that any disruption in the development of the PFC may result in abnormalities in function that could increase vulnerability to psychiatric illness<sup>6-8</sup>. Abnormalities in miRNA-mediated regulation have already been identified for numerous neurological disorders including schizophrenia<sup>9-13</sup>, bipolar disorder<sup>12</sup>, autism<sup>14</sup>, fragile X mental retardation<sup>15</sup> as well as Rett<sup>16</sup>, Tourette's<sup>17</sup> and DiGeorge

<sup>18</sup> syndromes. In this study, we sought to identify miRNA that were significantly associated with aging or displayed significant expression changes in the DLPFC during neurodevelopmentally sensitive stages. As mature miRNA expression is largely post-transcriptionally regulated, we also examined the expression of genes involved in the miRNA biogenesis pathway. This was accomplished using whole genome miRNA microarrays on postmortem tissue from non-psychiatric individuals ranging from one month to 78 years of age. This revealed significant age-associated changes with a prominent adjustment of miRNA expression at approximately 20 years of age that may coincide with cortical maturation.

## MATERIALS & METHODS

### Postmortem brain tissue

Fresh frozen postmortem prefrontal cortex tissue (Brodmann's area 46) of 60 individuals was obtained from the National Institute of Child Health and Human Development Brain and Tissue Bank for Developmental Disorders (UMBB; NICHD contract# NO1-HD8-3283) and of 37 individuals from the NSW Tissue Resource Centre (University of Sydney). Use of these tissue cohorts was approved by the Institutional Review Board (University of Maryland, Baltimore, USA) and the Human Research Ethics Committee (University of Newcastle, Australia). Consent was obtained from the next of kin. All individuals were free of neurological and psychiatric symptoms at the time of death, and toxicological analyses showed them to be free of drug use. Detailed cohort characteristics are outlined in Supp. Table 1. For analysis samples were subdivided into 8 age groups: neonate, infant, toddler, school age, teenage, young adult, adult and elderly. Demographic variables

pH ( $p=0.49$ ), PMI ( $p=0.23$ ) and RIN ( $p=0.81$ ) do not differ between age groups (ANOVA).

### RNA Extraction

Cortical grey matter tissue was carefully dissected from postmortem brain slices of the crown of the middle frontal gyrus, anterior to the genu of the corpus callosum using a dental drill <sup>19</sup>. While still frozen, tissue was immediately homogenized and total RNA extracted using TRIzol reagent (Invitrogen, Life Technologies) according to the manufacturer's instructions. RNA concentration and integrity was determined using the Bioanalyzer 2100 electrophoresis system (Agilent Technologies). Mean RNA integrity number (RIN) was 6.85.

### miRNA microarray

Profiling of miRNA expression was achieved using a high throughput commercial bead based miRNA microarray platform (Illumina). Each Sentrix array matrix contains 1,536 unique oligonucleotide sequence probes for 470 annotated miRNA sequences as well as 265 recently identified miRNA sequences corresponding to miRBase version 9.1. Total RNA (1µg) was amplified and labeled within a 96-well plate format for hybridization to the miRNA beadarray matrix according to the manufacturer's instructions (Illumina Inc.). Microarray data were compiled and background subtracted within the BeadStudio software (Illumina, version 3.0) and normalized with respect to the geometric mean of U66 and U49 snoRNA expression. Of the three small RNA probe sets present on the microarray, geNorm <sup>20</sup> identified U66 and U49 to be the most stable across the cohort. The effect of individual demographic variables on miRNA expression revealed that a large proportion of miRNA were regulated by age (40%) and PMI (7%). Other variables such as pH and RIN affected  $\leq 1\%$  miRNA in this analysis.

**Table 1: Summary of demographic information for postmortem prefrontal cortex tissue from 97 individuals used in microarray analysis.**

Age group	n	Age range	Gender (M:F)	Race (C:AA)	pH	PMI	RIN
Neonate	7	0.1-0.2	5:2	5:2	6.5 (0.24)	21 (5.6)	6.0 (2.0)
Infant	13	0.3-0.9	8:5	2:11	6.6 (0.20)	17 (6.5)	6.9 (1.2)
Toddler	8	0.6-4.9	5:3	4:4	6.7 (0.26)	20 (4.7)	6.4 (1.2)
School Age	9	5.4-13.0	5:4	7:2	6.6 (0.27)	15 (4.7)	6.7 (1.1)
Teenage	9	15.0-18.0	7:2	7:2	6.8 (0.08)	19 (6.6)	6.4 (0.9)
Young Adult	10	20.0-24.9	7:3	7:3	6.7 (0.23)	19 (14.0)	6.9 (0.8)
Adult	30	33.0-49.2	24:6	26:4	6.7 (0.27)	21 (9.3)	7.2 (0.6)
Elderly	11	50.0-78.0	9:2	11:0	6.5 (0.29)	24 (13.4)	7.2 (0.6)

C: Caucasian; AA: African-American; PMI: postmortem interval (hours); RIN: RNA integrity number. Values for pH, PMI and RIN are shown as group mean (standard deviation).



---

#### *Hierarchical cluster analysis*

Hierarchical clustering was performed on miRNA displaying significant correlations with age. Expression values were log2-transformed, median-centered and uncentered correlation (average linkage) by genes was carried out using Gene Cluster v3.0 (Stanford University). Clustering was displayed by heatmap and was constructed using Java Treeview v1.1.1 21.

#### *Quantitative real-time reverse transcription PCR*

Microarray validation was performed by quantitative real-time RT-PCR (qPCR) on a cohort of 60 subjects (Supp. Table 1) as described previously 22. Briefly, RNA was treated with DNaseI (Invitrogen) and multiplex reverse transcription performed with Superscript II reverse transcriptase (Invitrogen, Life Technologies) and a mix of miRNA sequence specific primers along with primers for U6, U44 and U49 (for sequences, see Supp. Table 2). Triplicate reactions were set up in a 96-well format using the epMotion 5070 automated pipetting system (Eppendorf) and carried out using the Applied Biosystems 7500 real-time PCR machine. Cycling conditions were 1 cycle for 2 min at 50°C, 1 cycle for 10 min at 95°C, 40 cycles of 15 sec at 95°C and 1 min at 50°C (followed by standard dissociation curve analysis). qPCR was analyzed using the relative quantitation method with efficiency correction. cDNA was produced from human prefrontal cortex RNA samples and serial dilutions were used as standards. Relative miRNA expression was calculated as the ratio of the miRNA and the geometric mean of controls U6 and U49 (the most stable of the 3 controls as determined by geNorm). Expression data was Pearson correlated (1-tailed) with that obtained by microarray to determine the validity of the qPCR (PASW Statistics 18, SPSS Inc., IBM). To examine relative mRNA expression of miRNA biogenesis genes, cDNA synthesis was carried out as described above using random primers. Cycling conditions were 1 cycle for 2 min at 50°C, 1 cycle for 10 min at 95°C, 40 cycles of 15 sec at 95°C and 1 min at 60°C (followed by standard dissociation curve analysis). Relative mRNA expression was calculated as the ratio of the gene and the geometric mean of controls hydroxymethylbilane synthase (HMBS) and beta-glucuronidase (GUSB). For sequences, see Supp. Table 2.

#### *Analyzing the effect of age on miRNA expression*

To examine the influence of demographic variables (age, PMI, pH and RIN) on miRNA, data was tested for normality and Spearman correlations were performed. As expected, a large proportion of miRNA expression significantly correlated with age ( $p < 0.001$  was set as a threshold). The second-most influential factor affecting miRNA expression was PMI (approximately 9% of probes) and was therefore included as a covariate in further analyses. miRNA displaying differential expression throughout aging were identified by

multivariate analysis of covariance (ANCOVA) using PMI as a covariate with a threshold for significance of  $p < 0.05$  (PASW Statistics 18, SPSS Inc., IBM).

#### *Target gene and pathway analysis*

For those miRNA identified with expression changes with age, target gene predictions were performed using the miRanda algorithm 23. For an extra level of stringency, putative target genes were included for subsequent analysis only if they contained 3 or more putative miRNA binding sites. This arises from a miRNA having 3 sites within the one 3'-UTR, or 3 separate miRNA predicted to target that 3'-UTR. In order to relate the altered miRNA activity in the context of age-associated changes in the DLPFC, the list of putative targets was cross-matched with genes already shown in microarray experiments to be altered in the same tissue 24. Pathway analysis of the predicted gene lists was achieved as previously described 24 using the functional annotation tools on the Database for Annotation, Visualization and Integrated Discovery (DAVID) (version 6.7; <http://david.abcc.ncifcrf.gov/>) 25.

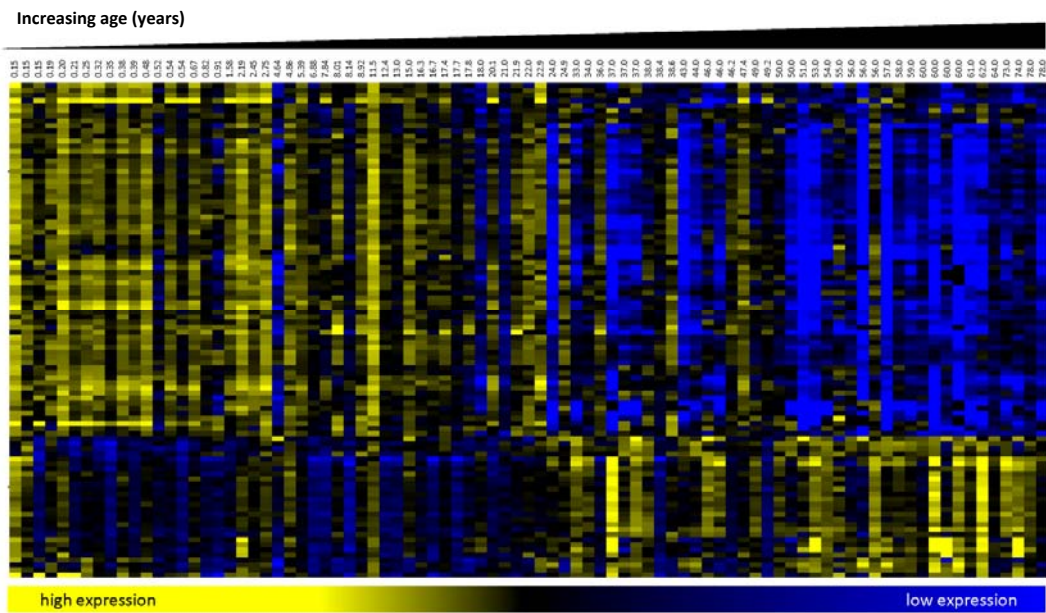
## **RESULTS**

---

#### *miRNA associated with age*

The expression of 470 miRNA was analyzed in the DLPFC (BA46) of 97 postmortem samples (Table 1). Of the 470 miRNA probes present on the microarray, 381 were expressed in this tissue. Quantitative real-time PCR array validation was performed on a selection of miRNA including miR-16, miR-17-5p, miR-107, miR-181b, miR-195 and miR-219. Correlation of expression data obtained by microarray and qPCR indicated that the two methods were comparable; miR-17-5p ( $r = 0.456$ ,  $p = 0.001$ ), miR-219 ( $r = 0.421$ ,  $p = 0.009$ ) and miR-195 ( $r = 0.355$ ,  $p = 0.010$ ) were most significant, followed by miR-181b ( $r = 0.209$ ,  $p = 0.051$ ), miR-107 ( $r = 0.191$ ,  $p = 0.071$ ) and miR-16 ( $r = 0.171$ ,  $p = 0.091$ ). Additionally, when the cohort was separated into 3 age groups (0-14 years, 15-24 years and 25-50 years), expression patterns and ranges between the groups were similar for each of the miRNA tested (Supp. Fig. 1).

Individual variable analysis revealed that age was the most influential factor affecting miRNA expression. At a threshold of  $p < 0.001$ , 191 (~40%) miRNA significantly correlated with age (Supp. Table 3). Interestingly, the majority of miRNA decreased with age (154 miRNA; ~80%) compared with only 37 increasing with age (~20%). As PMI was the second-most influential variable, it was used as a covariate in subsequent analysis. Utilizing the miRNA that significantly correlated with age, ANCOVA revealed that 102 miRNA remained significantly associated with age; 74 miRNA decreasing with age and 28 miRNA increasing with age (Fig. 1; Supp. Table 4).



**Figure 1: Cluster analysis of 102 miRNA displaying age-related expression changes in the human prefrontal cortex.** A total of 74 miRNA displayed a decrease in expression and 28 miRNA displayed an increase in expression throughout aging. Yellow shading in this heat map indicates high expression and blue shading indicates low expression.

#### *Cluster analysis of miRNA displaying age-associated changes in expression*

Unsupervised cluster analysis was performed on the expression data for miRNA displaying significant correlations with age. With yellow and blue indicative of high and low expression levels respectively, the 74 miRNA decreasing with age and the 28 miRNA increasing with age are displayed clearly. In both groups, a distinct change in expression is apparent at approximately 20 years of age (Fig. 1).

#### *The expression of miRNA and biogenesis genes across the lifespan*

Global miRNA expression displayed a distinct profile, displaying troughs in expression in toddlers (approx. 3 years) and young adults (early twenties), with a rise in expression of the school age (5-12 years) and adult groups (>25 years) (Fig. 2). The overall pattern of DGCR8 mRNA expression was consistent with global miRNA expression; also displaying troughs in expression at the toddler and young adult time points (Fig. 2a). Drosha mRNA expression was similar to that of global miRNA expression, only from the school age time point onwards. It shows an increase in early life which is maintained until school age, then decreasing until adulthood (Fig. 2b). Interestingly, neither Dicer nor Exportin-5 mRNA expression corresponded with global miRNA expression levels, though both displayed apparent age-related changes. Dicer has very low expression in the neonate,

continuously increasing until adulthood. Conversely, Exportin-5 begins with moderately high expression in the neonate, which continuously decreases throughout aging (Fig. 2c,d). Spearman correlations were performed on qPCR expression data to identify any age-related changes within the miRNA biogenesis genes. DGCR8 ( $r=0.059$ ,  $p=0.656$ ) and Drosha ( $r=-0.170$ ,  $p=0.194$ ) did not significantly correlate with age. Dicer was observed to significantly increase with age ( $r=0.274$ ,  $p=0.034$ ) and Exportin-5 to significantly decrease with age ( $r=-0.511$ ,  $p<0.001$ ) (Fig. 3)

#### *Target gene and pathway analysis*

To gain some appreciation of the biological implications of changes in miRNA expression with aging, we examined predicted miRNA targets and their associated pathways to see whether any patterns emerged. The more miRNA binding sites a gene has within its 3'-UTR, the more likely it is to be post-transcriptionally regulated. The target prediction algorithm miRanda, is capable of identifying those miRNA which bind multiple times within the one 3'-UTR. As such, this information was used to predict target genes that were most likely to be heavily regulated by age-associated miRNA. Due to a high degree of false positives, the list of target genes was filtered to only include those genes that were targeted by three or more miRNA, or contained three or more binding sites for a particular miRNA within its 3'-UTR. This target analyses process was performed on the top ten most significant miRNA that increased expression with



age and the top ten that decreased with age (Table 2). Genes identified through this process were then collectively subjected to pathway analysis using the functional annotation tools on DAVID (version 6.7). This revealed a number of significantly enriched pathways with relevance to neural connectivity and synaptic plasticity including axon guidance, long term potentiation, focal adhesion, neurotrophin and MAPK signaling (Supp. Table 5). These gene lists were then filtered further with respect to genes already known to be quantitatively correlated with age, in this same tissue cohort <sup>155</sup>. In this step, miRNA decreasing with age were cross-referenced with genes that increase with age (219 genes remaining); and the target list for miRNA which increase with age was cross-referenced with genes known to decrease with age (247 genes remaining). Using this directional approach, functional annotation was repeated. In regards to both lists, the enriched KEGG pathway of most interest was axon guidance (Supp. Table 5). Interestingly, 'psych' was identified as a significant genetic association class for both lists ( $p \leq 0.007$ , 2-fold enrichment,  $FDR \leq 4.7\%$ ). This is represented visually in a KEGG pathway diagram (Supp. Fig. 2) which further demonstrates that a substantial number of genes in the axon guidance pathway were targeted by age-related miRNA and also displayed expression changes in the predicted direction. Each gene in the pathway was color-coded to denote the frequency of putative age-associated miRNA targeting. This provides additional information about the relative significance of age-associated miRNA in the regulation of individual genes in this pathway.

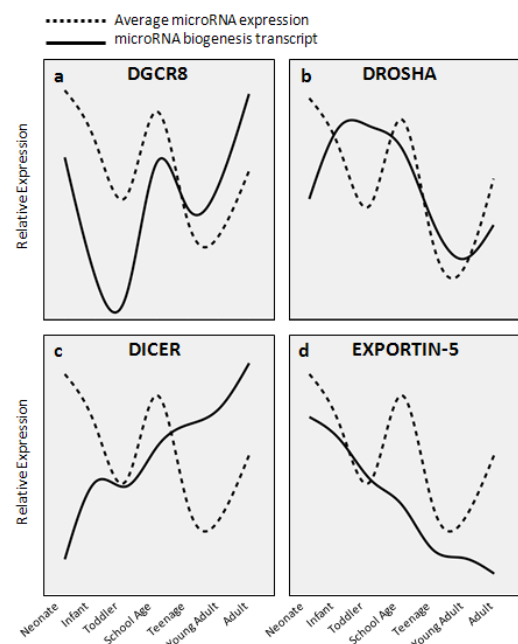
## DISCUSSION

Genome-wide expression studies in postmortem brain have shown that many genes display age-related changes throughout development and ageing <sup>156-160, 155, 161</sup>. Efforts to understand the underlying mechanisms driving changes in gene expression have focused predominantly on genetic influences on transcription; however recent studies have emerged suggesting that there are also substantial post-transcriptional influences on gene expression. Post-transcriptional regulation mediated by miRNA in particular, has been shown to play a major role in coordinating gene expression during the differentiation and development of the brain <sup>1, 32-34</sup>.

In this study, whole-genome miRNA microarrays were used to examine miRNA expression throughout the postnatal development of the dorsolateral prefrontal cortex. This cohort consisting of 97 samples, spanning 1 month to 78 years of age, is the most comprehensive study of human neurodevelopmental miRNA expression to date. Approximately 40% of the 381 miRNA expressed in this tissue, displayed a significant correlation with age, and remarkably, a large majority (80%) of these molecules were observed to decreased with age (Supp. Table 3). This significant age-dependent change in miRNA

expression is supported by a study in the human superior frontal gyrus where 31% of expressed miRNA were shown to be associated with age <sup>35</sup>. This decrease is also consistent with the age-associated changes observed in the mouse cerebral cortex; exemplified by decreases in miR-124a, -125a/b, -9, -199a and -301 across the postnatal lifespan <sup>36</sup>.

From the cluster analysis of age-associated miRNA expression it is clear that early adulthood (~20 years) is characterized by a dramatic inflection point for a switch in both the low to high and high to low expressing miRNA molecules, suggesting that this period important for cortical maturation also involves a significant reorganization of the prevailing post-transcriptional regulatory environment. This suggestion that the neurodevelopmental influence of miRNA can be divided into two separate stages is supported by previous work in the human and macaque brain <sup>35</sup>. As these molecules are potentially influencing thousands of target genes,



**Figure 2: Dynamic changes of global miRNA expression miRNA biogenesis genes across the lifespan by qPCR.** In each panel, global miRNA expression is denoted by the dotted line. (a) The overall pattern of DGCR8 expression was consistent with global miRNA expression. (b) Droscha expression was similar to that of global miRNA expression, only from school age onwards. (c-d) Dicer and Exportin-5 expression did not correspond with miRNA expression levels. Data is displayed as a spline interpolation line through the mean expression values for each age group. The series of dashed lines denotes global miRNA expression; the solid lines denote expression of the respective biogenesis genes.

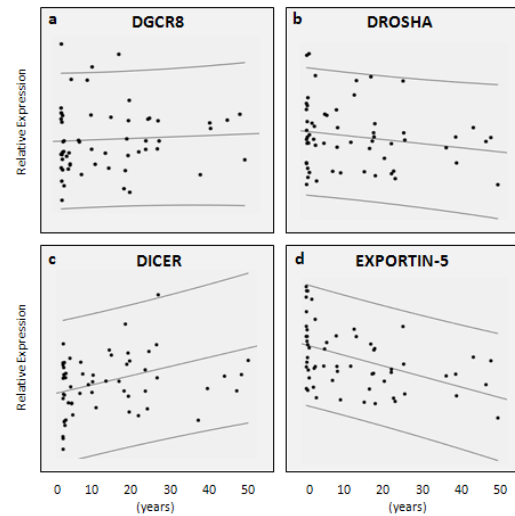
**Table 2: miRNA displaying the most significant age-related changes**

miRNA increasing with age	miRNA decreasing with age
miR-133a	miR-130b
miR-135b	miR-148a
miR-302b	miR-15b
miR-31	miR-17-5p
miR-507	miR-19a
miR-512-3p	miR-368
miR-518a	miR-424
miR-519b	miR-450
miR-548a	miR-503
miR-571	miR-542-5p

The top 10 most significant miRNA displaying age-related changes as determined by ANCOVA (PMI as covariate).

disruptions to this program may also have implications for neurodevelopmental disorders, such as schizophrenia, that are known to emerge at this stage of development. It is therefore significant that a number of laboratories, including our own, have recently identified schizophrenia-associated alteration of cortical miRNA expression in postmortem samples<sup>9-11, 13</sup>. Our investigation of miRNA expression in the DLPFC from subjects with schizophrenia were characterized by an increase in miRNA including let-7d/e, miR-107, miR-15 family, miR-17-5p, miR-219, miR-328 and miR-7 which not only display an age-associated expression pattern in normal development, were also all downregulated in contrast to their alteration in schizophrenia<sup>22, 13</sup>. It is plausible that in schizophrenia, these neurodevelopment-associated miRNA that are expressed at higher levels before adulthood and while normally undergo the transition to a lower in expression during brain maturation, in schizophrenia they remain elevated and enforce inappropriate levels of gene silencing.

Other interesting age-associated transitions in cortical miRNA expression were observed in the toddler (~3yrs) and young adult (~20yrs) segments of the cohort. These time intervals were both characterised by rapid changes in global miRNA expression that collectively appear as troughs in the expression profile. These expression patterns do not appear to be unique to humans, as a parallel study conducted in macaques, not only showed that miRNA expression highly correlates between the two species, but these same transition points identified in this study are highly conserved at the equivalent developmental periods<sup>35</sup>. In accordance with our miRNA study, this data suggests that age-related gene expression first begins changing direction around 4 years of age, coinciding with key events in neural development such as the peak in synaptic density<sup>35, 37</sup>. The second change in expression occurring in young adulthood could correspond to a shift between exuberant growth and



**Figure 3: Age-associated changes of genes involved in miRNA biogenesis. (a-b)** DGCR8 and Drosha did not correlate with age. **(c-d)** Both Dicer and Exportin-5 transcripts significantly correlated with age. Dicer expression increased (Spearman  $r=0.274$ ,  $p=0.034$ ) and Exportin-5 expression decreased (Spearman  $r=-0.511$ ,  $p<0.001$ ) across the lifespan. Each dot on the scatter-plot represents one subject, the central line is a linear line of fit and the outermost lines represent 95% confidence intervals.

normal age-related decline in developmental processes<sup>38</sup>.

miRNA and their biogenesis genes are considered to be largely post-transcriptionally regulated, and to this end, we sought to examine the expression profiles of these genes. Remarkably, components of the microprocessor complex; DGCR8 and Drosha displayed expression trajectories similar to that of global miRNA expression, especially DGCR8. Whilst DGCR8 is considered to be post-transcriptionally regulated, it is unlikely to be due to the actions of miRNA, as the DGCR8 3'-UTR is almost devoid of any miRNA binding sites. Recent data suggests that DGCR8 is post-transcriptionally self-regulated by its own microprocessor complex and the mechanism is instead related to the presence of primary miRNA-like hairpin structures in the DGCR8 mRNA, which are themselves substrates for cleavage by the microprocessor<sup>39</sup>. In a cohort of postmortem schizophrenia subjects, increases in DGCR8 and Drosha expression in the prefrontal cortex have been shown to correspond with a global increase in mature miRNA expression<sup>22</sup>, highlighting the possibility that components of the microprocessor complex may be acting as rate-limiting steps of miRNA biogenesis. Furthermore, the membrane-bound Exportin-5 and cytoplasmic Dicer displayed significant correlations with age; Exportin-5 decreasing and Dicer increasing in expression across the lifespan. In a differing manner to the microprocessor complex, these molecules could very likely be heavily post-transcriptionally regulated, exemplified by their long 3'-

---

UTRs of >1kb (Exportin-5) and >4kb (Dicer) containing many putative miRNA binding sites <sup>20</sup>.

As miRNA can regulate the expression of hundreds of target genes this large age-associated alteration of gene expression will have significant functional implications. Target genes hosting a multiplicity of miRNA binding sites for differentially expressed miRNA, have a higher probability of being post-transcriptionally regulated and to a greater extent because of the cooperative or synergistic interactions between multiple RISCs on a single target's 3'-UTR <sup>38</sup>. In view of this, the list of genes identified as targets of age-related miRNA in this study were filtered to only include those genes with multiple miRNA recognition elements within their 3'-UTR. Functional annotation of these predicted targets indicated that a number of pathways relevant to neural function were enriched, such as axon guidance, long term potentiation, focal adhesion and neurotrophin and MAPK signaling (Supp. Table 4). These target genes were also cross-referenced with published genome-wide gene expression data from the same cohort <sup>155</sup>. Target genes whose expression were reciprocally regulated by corresponding miRNA displaying age-related changes were identified and subjected to pathway analysis. This revealed that axon guidance was retained as the most heavily regulated pathway by these altered miRNA (Supp. Fig. 2).

There are numerous molecular and cellular changes that occur throughout the normal development of the prefrontal cortex <sup>160, 155</sup> and there is accumulating evidence that showcases the importance of post-transcriptional gene regulation during nervous system development. This study has provided support for the role of miRNA in the regulation of gene expression throughout the lifespan and also highlights that disturbances to this regulatory system at critical time points in development could be an additional insult conferring increased vulnerability to psychiatric illness later in life.

#### ACKNOWLEDGEMENTS

This work was supported by the Schizophrenia Research Institute utilizing infrastructure funding from NSW Health. Tissue was received from the Australian Brain Donor Programs NSW Tissue Resource Centre, which is supported by The University of Sydney, National Health and Medical Research Council of Australia, Schizophrenia Research Institute, National Institute of Alcohol Abuse and Alcoholism, National Institutes of Health, and the NSW Department of Health. Tissue was also received from the University of Maryland Brain Bank. MC is supported by a NARSAD Young Investigator Award, the Hunter Medical Research Institute; the Neurobehavioural Genetics Unit and NSW

Department of Health project grant and an M.C. Ainsworth Research Fellowship in Epigenetics.

#### CONFLICT OF INTEREST

The authors declare no conflict of interest.

#### REFERENCES

1. Giraldez, A.J., et al., (2005). MiRNAs regulate brain morphogenesis in zebrafish. *Science*, 308(5723): p. 833-8.
2. Sempere, L., et al., (2004). Expression profiling of mammalian miRNAs uncovers a subset of brain-expressed miRNAs with possible roles in murine and human neuronal differentiation. *Genome Biol.*, 5(3): p. R13.
3. Gogtay, N., et al., (2004). Dynamic mapping of human cortical development during childhood through early adulthood. *Proc Natl Acad Sci U S A*, 101(21): p. 8174-9.
4. Fuster, J.M., (2002). Frontal lobe and cognitive development. *J Neurocytol*, 31(3-5): p. 373-85.
5. Goldman-Rakic, P.S., (1987). Development of cortical circuitry and cognitive function. *Child Dev*, 58(3): p. 601-22.
6. Lewis, D.A., et al., (2004). Postnatal development of prefrontal inhibitory circuits and the pathophysiology of cognitive dysfunction in schizophrenia. *Ann N Y Acad Sci*, 1021: p. 64-76.
7. Weickert, C.S. and D.R. Weinberger, (1998). A candidate molecule approach to defining developmental pathology in schizophrenia. *Schizophr Bull*, 24(2): p. 303-16.
8. Weinberger, D.R., (1987). Implications of normal brain development for the pathogenesis of schizophrenia. *Arch Gen Psychiatry*, 44(7): p. 660-9.
9. Beveridge, N.J., et al., (2009). Schizophrenia is associated with an increase in cortical miRNA biogenesis. *Mol Psychiatry*.
10. Beveridge, N.J., et al., (2008). Dysregulation of miRNA 181b in the temporal cortex in schizophrenia. *Hum Mol Genet*.

- 
11. Kim, A.H., et al., MiRNA expression profiling in the prefrontal cortex of individuals affected with schizophrenia and bipolar disorders. *Schizophr Res.*
  12. Perkins, D.O., et al., (2007). miRNA expression in the prefrontal cortex of individuals with schizophrenia and schizoaffective disorder. *Genome Biol*, 8(2): p. R27.
  13. Sarachana, T., et al., Investigation of post-transcriptional gene regulatory networks associated with autism spectrum disorders by miRNA expression profiling of lymphoblastoid cell lines. *Genome Med*, 2(4): p. 23.
  14. Jin, P., R.S. Alisch, and S.T. Warren, (2004). RNA and miRNAs in fragile X mental retardation. *Nat Cell Biol*, 6(11): p. 1048-53.
  15. Nomura, T., et al., (2008). MeCP2-dependent repression of an imprinted miR-184 released by depolarization. *Hum Mol Genet*, 17(8): p. 1192-9.
  16. Abelson, J.F., et al., (2005). Sequence variants in SLITRK1 are associated with Tourette's syndrome. *Science*, 310(5746): p. 317-20.
  17. Gregory, R.I., et al., (2004). The Microprocessor complex mediates the genesis of miRNAs. *Nature*, 432(7014): p. 235-40.
  18. Vandesompele, J., et al., (2002). Accurate normalization of real-time quantitative RT-PCR data by geometric averaging of multiple internal control genes. *Genome Biol*, 3(7): p. RESEARCH0034.
  19. Saldanha, A.J., (2004). Java Treeview--extensible visualization of microarray data. *Bioinformatics*, 20(17): p. 3246-8.
  20. John, B., et al., (2004). Human MiRNA targets. *PLoS Biol*, 2(11): p. e363.
  21. Choi, K.H., et al., (2009). Expression profiles of schizophrenia susceptibility genes during human prefrontal cortical development. *J Psychiatry Neurosci*, 34(6): p. 450-8.
  22. Dennis, G., Jr., et al., (2003). DAVID: Database for Annotation, Visualization, and Integrated Discovery. *Genome Biol*, 4(5): p. P3.
  23. Somel, M., et al., MiRNA, mRNA, and protein expression link development and aging in human and macaque brain. *Genome Res.*
  24. Lu, T., et al., (2004). Gene regulation and DNA damage in the ageing human brain. *Nature*, 429(6994): p. 883-91.
  25. Somel, M., et al., (2009). Transcriptional neoteny in the human brain. *Proc Natl Acad Sci U S A*, 106(14): p. 5743-8.
  26. Polleux, F., G. Ince-Dunn, and A. Ghosh, (2007). Transcriptional regulation of vertebrate axon guidance and synapse formation. *Nat Rev Neurosci*, 8(5): p. 331-40.
  27. Schratt, G., (2009). miRNAs at the synapse. *Nat Rev Neurosci*, 10(12): p. 842-9.
  28. Schratt, G.M., et al., (2006). A brain-specific miRNA regulates dendritic spine development. *Nature*, 439(7074): p. 283-9.
  29. Dogini, D.B., et al., (2008). MiRNA expression profile in murine central nervous system development. *J Mol Neurosci*, 35(3): p. 331-7.
  30. Santarelli, D., et al., (Under Review). Upregulation of Dicer and MiRNA Expression in the Dorsolateral Prefrontal Cortex Brodmann's Area 46 in Schizophrenia.
  31. Huttenlocher, P.R. and A.S. Dabholkar, (1997). Regional differences in synaptogenesis in human cerebral cortex. *J Comp Neurol*, 387(2): p. 167-78.
  32. de Magalhaes, J.P., J. Curado, and G.M. Church, (2009). Meta-analysis of age-related gene expression profiles identifies common signatures of aging. *Bioinformatics*, 25(7): p. 875-81.
  33. Han, J., et al., (2004). The Drosha-DGCR8 complex in primary miRNA processing. *Genes Dev*, 18(24): p. 3016-27.
  34. He, L. and G.J. Hannon, (2004). MiRNAs: small RNAs with a big role in gene regulation. *Nat Rev Genet*, 5(7): p. 522-31.
-

---

## CHAPTER 4

### *Dysregulation of miRNA 181b in the temporal cortex in schizophrenia*

---

---

**CHAPTER 4: Dysregulation of miRNA 181b in the temporal cortex**  
**in schizophrenia**

**Natalie J. Beveridge**, Paul A. Tooney, Adam P. Carroll, Erin Gardiner,  
Nikola A. Bowden, Rodney J. Scott, Nham Tran, Irina Dedova and  
Murray J. Cairns

**Human Molecular Genetics (2008) Vol. 17, No. 8, pp 1156-1168**  
2009 Journal Impact factor: 7.349

**Statement III: Author contribution to Chapter 4 manuscript**

Author	Description of Contribution to Article	Signature
Natalie J. Beveridge	Designed and executed the study. Provided significant insight into the interpretation of the data. Wrote the manuscript.	
Paul A. Tooney	Aided in data interpretation and manuscript compilation.	
Adam P. Carroll	Provided some technical assistance.	
Erin Gardiner	Provided some technical assistance.	
Nikola A. Bowden	Provided some technical assistance.	
Rodney J. Scott	Provided equipment and some technical assistance.	
Nham Tran	Aided in establishing the methodology.	

(CONT.)

---

**Statement III: Author contribution to Chapter 4 manuscript (cont.)**

Irina Dedova	Aided in establishing the sample cohort	
Murray J. Cairns	Designed the study, provided the concept and corrected the manuscript.	

4<sup>th</sup> November, 2010

---

**PROFESSOR JOHN ROSTAS**

Deputy Head of Faculty (Research and Research Training)

## Dysregulation of miRNA 181b in the temporal cortex in schizophrenia

Natalie J. Beveridge<sup>1,2</sup>, Paul A. Tooney<sup>1,2</sup>, Adam P. Carroll<sup>1,2</sup>, Erin Gardiner<sup>1,2</sup>, Nikola Bowden<sup>1,2</sup>, Rodney J. Scott<sup>1,2</sup>, Nham Tran<sup>3</sup>, Irina Dedova<sup>1,4</sup> and Murray J. Cairns<sup>1,2,\*</sup>

<sup>1</sup>Schizophrenia Research Institute, Sydney, NSW 2006, Australia, <sup>2</sup>School of Biomedical Sciences, Faculty of Health, and Hunter Medical Research Institute, The University of Newcastle, University Drive, Callaghan, NSW 2308, Australia, <sup>3</sup>Department of Infectious Diseases and Immunology and <sup>4</sup>Department of Pathology, The University of Sydney, Blackburn Building Level 6, Sydney, NSW 2006, Australia

Received November 1, 2007; Revised and Accepted January 4, 2008

**Analysis of global microRNA (miRNA) expression in postmortem cortical grey matter from the superior temporal gyrus, revealed significant up-regulation of miR-181b expression in schizophrenia. This finding was supported by quantitative real-time RT-PCR analysis of miRNA expression in a cohort of 21 matched pairs of schizophrenia and non-psychiatric controls. The implications of this finding are substantial, as this miRNA is predicted to regulate many target genes with potential significance to the development of schizophrenia. They include the calcium sensor gene visinin-like 1 (VSINL1) and the ionotropic AMPA glutamate receptor subunit (GRIA2), which were found to be down-regulated in the same cortical tissue from the schizophrenia group. Both of these genes were also suppressed in miR-181b transfected cells and shown to contain functional miR-181b miRNA recognition elements by reporter gene assay. This study suggests altered miRNA levels could be a significant factor in the dysregulation of cortical gene expression in schizophrenia.**

### INTRODUCTION

Schizophrenia is a severely debilitating psychiatric disorder characterized by a diverse range of symptoms. While extensive research has not determined the definitive cause(s), it is generally accepted that a number of influences including genetic, environmental and developmental factors are involved. Genetics in particular has been known for many years to play a key role in the development of schizophrenia. The pattern of inheritance, however, is far from clear with a complex array of associated loci and putative candidate genes each with a relatively small effect, disbursed across the entire genome (1–3). This picture is further complicated by environmental and epigenetic influences evident by the relatively low rate of concordance in monozygotic twins (~50%) (4,5).

Recent research from a variety of quarters has lent support to the neurodevelopmental hypothesis, which suggests that genetic and environmental influences affect neurodevelopmental processes that cause abnormalities in brain plasticity and connectivity leading to schizophrenia in early adulthood. In this model, regulatory factors that control the stage and

tissue expression of molecules involved in neurodevelopmental processes will be particularly important. While transcription factors and protein based signal transduction pathways are usually considered in this context, a new class of gene expression modulators consisting entirely of RNA is also emerging as a significant regulatory factor. These small non-coding RNA molecules known as microRNAs (miRNA) function as guide sequences for the cellular gene silencing pathway to bring about target gene suppression through a process known as post-transcriptional gene silencing (PTGS) (6). These riboregulators are now believed to play a major role in coordinating the regulation of gene expression during the differentiation and development of the brain (7). Indeed, a large proportion of human miRNAs display a brain-specific or brain-enriched expression pattern (8). There is even evidence to suggest they are involved in brain function and neural plasticity via the regulation of molecules involved in long-term potentiation (LTP) (9,10) and in the establishment and maintenance of dendrites (11).

\*To whom correspondence should be addressed. Tel: +61 249218670; Fax: +61 249217903; Email: murray.cairns@newcastle.edu.au



Considering that each miRNA is potentially manipulating the expression of hundreds of target genes, the clinical implications of an abnormality or disturbance of this system are substantial, particularly if such abnormality occurs during development of the central nervous system. Neurological manifestations of abnormalities in miRNA-mediated regulation have in fact already been identified for fragile X mental retardation (9) and Tourette's syndrome (12). The miRNA pathway is also implicated in DiGeorge syndrome as one of the deleted genes, DGCR8 is associated with the microprocessor complex with Drosha and is essential for processing of the primary miRNA transcript (13). Interestingly, 25% of patients with DiGeorge syndrome also develop schizophrenia (14). In view of these findings, it is reasonable to suspect that alteration in miRNA gene silencing pathways may also be involved in the development of complex psychiatric disorders such as schizophrenia. This is supported by a recent study of miRNA expression in the prefrontal cortex, which identified a number of altered miRNAs (15). In the study reported here, we examined miRNA expression in cortical grey matter from the superior temporal gyrus (STG). The STG contains the primary and secondary auditory cortex thought to be involved in the generation of auditory hallucinations and appears to have reduced volume in schizophrenia (16,17). This analysis revealed significant up-regulation of miR-181b, which was found to correlate inversely with expression of schizophrenia-associated miR-181b target genes GRIA2 and visinin-like 1 (VSNL1) in STG from the same schizophrenia cohort.

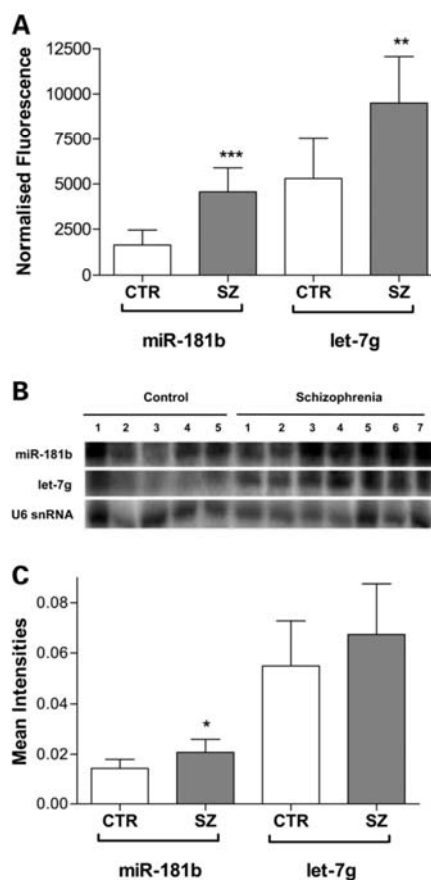
## RESULTS

### miRNA expression in the temporal cortex

High throughput miRNA expression analysis in postmortem cortical grey matter from the STG was accomplished using a custom DNA microarray platform (18). Fluorescence signals observed in duplicate array features at a level 2-fold that of background were considered to be indicative of miRNA expression. This expression profile consisted of 76 miRNAs out of a total of 262 probes corresponding to miRBase version 7.0. Many of these miRNAs have previously been identified as either brain-specific, brain-enriched or constitutively expressed (Supplementary Material, Table S1). This is exemplified by strong expression of miR-125a/b, miR-124a, miR-9/9\*, miR-128a/b as well as miR-138, miR-219 and miR-338 which are brain-specific or brain-enriched. The constitutively expressed let-7 group of miRNAs were also well represented.

### Differential miRNA expression in schizophrenia

Differential expression of miRNA in postmortem STG from the schizophrenia cohort compared with their matched non-psychiatric controls was determined through two-class unpaired analysis using statistical analysis of microarrays software (Significance Analysis of Microarrays, SAM, version 2.23) (19). This analysis revealed significant up-regulation of two miRNAs, hsa-let-7g and hsa-miR-181b in the schizophrenia group, to levels 1.8-fold ( $P = 0.008$ ) and 2.8-fold ( $P = 0.001$ ), respectively (Fig. 1A).



**Figure 1.** Expression analysis of miR-181b and let-7g by microarray and northern blot. (A) Mean normalized microarray fluorescence values for miR-181b (2.8-fold,  $P < 0.001$ ) and let-7g (1.8-fold,  $P = 0.008$ ) in the STG from 7 matched pairs of subjects with schizophrenia and non-psychiatric controls (SZ and CTR 1–7). (B) Northern blot analysis of STG RNA comparing schizophrenia samples (SZ 1–7) and non-psychiatric controls (CTR1–5). Each panel consists of phosphorimages of bands probed for miR-181b, let-7g and U6 snRNA, respectively. The intensity of bands corresponding to each miRNA species was then determined using ImageQuant v5.2 and normalized with respect to U6 snRNA. (C) Mean normalized intensity for miR-181b and hsa-let-7g miRNAs in the STG of schizophrenia non-psychiatric controls determined by northern blot hybridization. Bars represent mean  $\pm$  SD; \* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ .

To confirm the differential expression status of mature let-7g and miR-181b observed by the microarray analysis, RNA from the same tissue was subjected to northern blot analysis with  $^{32}$ P-labelled locked nucleic acid (LNA)-modified probes. As miR-181b expression in the STG was in the low to mid range compared with the entire profile and below that of the constitutively expressed let-7g, the naïve membrane was hybridized first with the miR-181b probe. After stripping, the membrane was re-probed for let-7g and then the U6 snRNA loading control, respectively, with the latter being

used to normalize the expression value of each miRNA (Fig. 1B). Quantitative analysis with normalization to the U6 band intensity confirmed a significantly higher expression of miR-181b in the schizophrenia samples with an average increase of 1.5-fold ( $P = 0.041$ ) compared with the controls. In contrast, the difference in let-7g expression between the two groups was not significant ( $P = 0.12$ ; Fig. 1C).

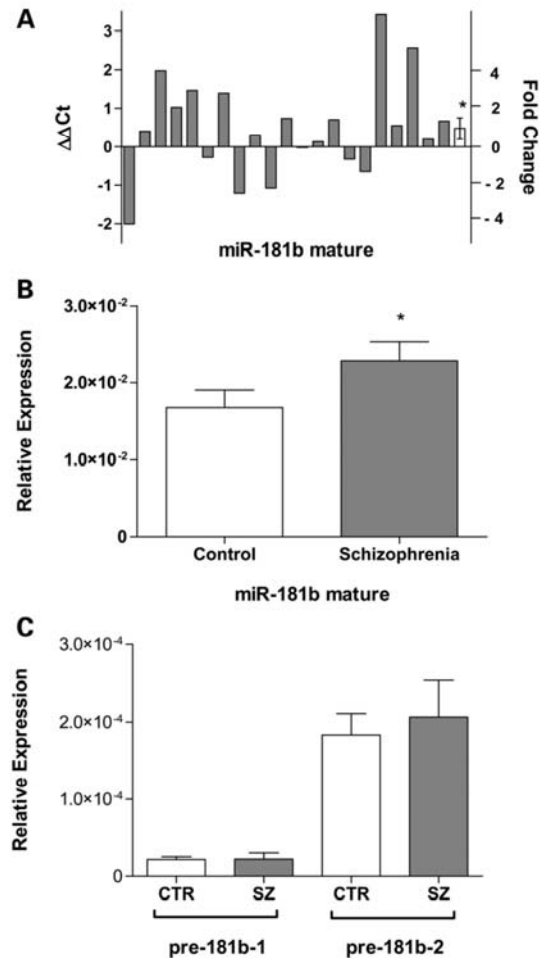
#### Validation of miR-181b over-expression in schizophrenia

To further validate the apparent association between altered miR-181b expression in the STG and schizophrenia, tissue from an additional 14 matched pairs was obtained and the RNA extracted to generate a substantially larger cohort (schizophrenia  $n = 21$ , controls  $n = 21$ ). As less tissue was available from these new cases yielding lower quantities of total RNA, a highly sensitive and specific quantitative real-time RT-PCR-based approach to determining miR-181b expression was established. This method utilized a miR-181b reverse primer consisting of a 9-nucleotide target-specific 3' segment and an adjoining 9-nucleotide arbitrary tag sequence at the 5' terminus. While the sequence-specific 9-mer component primed low-temperature cDNA extension on the miRNA target, the adjacent 9-mer tag provided the additional length required for primer recognition during the higher temperature PCR analysis phase. The relative expression of miR-181b from this RT-PCR analysis was consistent with the northern blot analysis confirming a significant up-regulation of this miRNA in the schizophrenia group, with an average increase of 1.24-fold ( $P = 0.049$ ) that was observed in 14 out of 21 matched pairs. However, removal of one control sample, CTR1, that had a higher expression of miR-181b (differed by more than 2.7 SD units from the control mean), elevated the average fold change in miR-181b expression in schizophrenia across the remaining 20 pairs to 1.39-fold ( $P = 0.029$ ).

To determine if the differential expression observed in miR-181b was due to alteration in 181b precursor RNA transcription, primers specific to the pre-181b-1 (transcribed from 1q31.3) and pre-181b-2 (transcribed from 9q33.3) were used for quantitative real-time RT-PCR. These were both normalized against U6 snRNA expression as described for the mature miRNA expression. The results of this analysis (Fig. 2C) indicated that the pre-181b-2 transcript is in much greater abundance in the STG than the pre-181b-1 transcript, with >10-fold higher relative expression. When the expression levels of these precursor miRNA transcripts in the schizophrenia samples were compared with the controls, there was no significant difference (Fig. 2C).

#### MiR-181b target prediction and pathway analysis

In order to gather some clues about the functional implication of elevated miR-181b concentrations in the cerebral cortex, an extensive list of putative target genes was assembled from a variety of publicly available miRNA data bases using the online TargetCombo web service (<http://www.diana.pcbi.upenn.edu/cgi-bin/TargetCombo.cgi>) (20). This provides the option of combining target predictions from the leading homology search algorithms miRanda, PicTar, TargetScanS and



**Figure 2.** Expression analysis of mature and precursor 181b molecules by quantitative RT-PCR. (A) Real-time PCR verification of altered miR-181b expression in the STG. For each sample, the change in cycle threshold ( $\Delta\Delta Ct$ ) was obtained by subtracting the  $Ct$  of U6 snRNA from the  $Ct$  of miR-181b. For each pair, the  $\Delta\Delta Ct$  was obtained by subtracting the  $\Delta Ct$  of each schizophrenia subject from the  $\Delta Ct$  of its corresponding control subject. The pair-wise expression changes are represented for each of the 21 matched pairs (grey bars) and the mean ( $\pm$  SEM) is shown to the far right (white bar). (B) Relative expression of miR-181b by RT-PCR in 21 matched pairs of postmortem STG. miR-181b was up-regulated 1.24-fold in the schizophrenia cohort ( $P = 0.049$ ; paired  $t$ -test). (C) Relative expression of precursor 181b molecules. CTR, control samples; SZ, schizophrenia samples. Bars represent mean  $\pm$  SEM (bar graphs); \* $P < 0.05$ .

DIANA-microT (21–24). Each of these programmes screen for motifs with various miRNA homology attributes in the phylogenetically conserved segments of 3' UTR sequences taken from the genome database. Collectively, these searches identified >800 putative target genes (Supplementary Material, Table S2). A number of these genes are known to play an important role in human brain function and development, and could



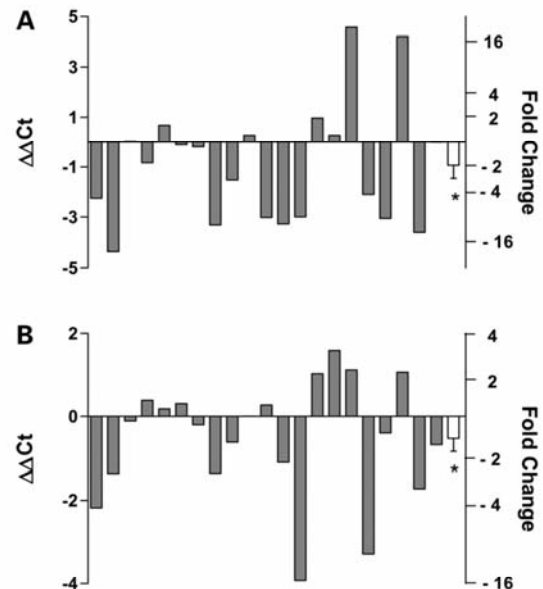
conceivably be involved in schizophrenia. This was exemplified by genes involved in synaptic transmission, including gamma amino butyric acid A receptor (GABRA1), glutamate receptors (GRM5, GRM7, GRIK2, GRID and GRIA2), serotonin receptors (HTR1B and HTR2C) and the cannabinoid receptor (CNR1). Some predicted target genes are also thought to be involved in brain development and neurodevelopmental disorders, for example ataxin 1 (ATXN1), zic family member 1 (ZIC1), SLIT and NTRK-like family, member 1 (SLTRK1) and fragile X mental retardation 1 (FMR1). The latter two involved in Tourette's syndrome and fragile X mental retardation, respectively, are already known to be associated with miRNA-related dysfunction.

To further understand the potential of miR-181b regulation, the predicted gene lists were subjected to functional annotation clustering and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis using the sdatabase for annotation, visualization, and integrated discovery (DAVID; <http://david.abcc.ncifcrf.gov>) (25). Interestingly, of the 144 conserved target genes predicted by the online version of the miRanda algorithm at the Memorial Sloan-Kettering Cancer Center Computational biology web site (<http://www.micro-ma.org>) (21), the most highly enriched gene ontology cluster related to development, nervous system development, neurogenesis and differentiation (Supplementary Material, Table S2). This was followed by a cluster of terms relating more broadly to signalling, signal transduction and transcription. When the combination gene list, consisting of 789 miR-181b target genes was submitted, a similar picture emerged except the ranking of the top two clusters was reversed. The KEGG pathways were also charted and ranked according to their *P*-value. The top five most significant terms for the large list included: LTP, MAPK signalling pathway, axon guidance and neurodegenerative disorders. In the smaller miRanda list developmentally related GO terms again featured highly with the top five consisting of development, neural development, cell differentiation, system development and organ development.

While miRNA target prediction algorithms provide a useful starting point for understanding the function of particular miRNA, they are also prone to a degree of over prediction leading to false positives (23,26). In order to relate the increased miR-181b activity in the context of schizophrenia-associated changes in the STG, the list of putative targets for this miRNA was cross matched with genes already shown in microarray experiments to be down regulated in the same tissue (Supplementary Material, Table S2; Bowden *et al.*, manuscript in preparation). This revealed a number of interesting target genes potentially regulated by miR-181b in the same tissue including the ionotropic glutamate receptor (GRIA2), fragile X-related 2 and VSNL1. Alteration of GRIA2 and VSNL1 expression in the dorsolateral prefrontal cortex and in the hippocampus, respectively, have also been shown to be associated with schizophrenia (27,28).

#### Validation of schizophrenia associated changes in VSNL1 and GRIA2 expression

To confirm the schizophrenia-associated down-regulation of VSNL1 and GRIA2 from the microarray analysis (Bowden



**Figure 3.** Relative expression of VSNL1 and GRIA2 in the superior temporal gyrus. (A) Relative expression of VSNL1 determined by quantitative real-time RT-PCR in 21 matched pairs of STG samples. VSNL1 showed a 1.91-fold down-regulation in the schizophrenia cohort ( $P = 0.037$  one-tailed paired *t*-test). (B) Relative expression of GRIA2 determined by quantitative real-time RT-PCR in 21 matched pairs of STG samples. GRIA2 showed a 1.44-fold down-regulation in the schizophrenia cohort ( $P = 0.047$  one-tailed paired *t*-test). Data is presented as previously described in Figure 2A. Analysis of changes in VSNL1 and GRIA2 expression using unpaired *t*-tests gave *P*-values of 0.027 and 0.073, respectively.

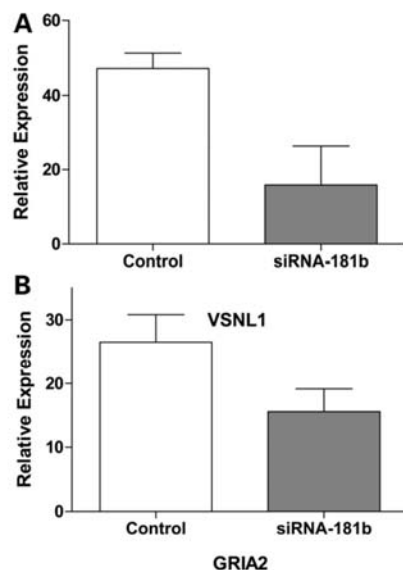
*et al.*, manuscript in preparation), STG RNAs (21 matched pairs) were subjected to quantitative real-time RT-PCR (Fig. 3). In the case of VSNL1, a significant decrease in expression was observed in the schizophrenia group averaging 1.91-fold with respect to the control cohort ( $P = 0.037$ ) (Fig. 3A). Similarly, GRIA2 was also decreased by an average of 1.44-fold ( $P = 0.047$ ) in the schizophrenia cohort (Fig. 3B).

#### Repression of miR-181b target genes *in vitro*

To gain further biological insight into the miRNA 181b target genes, *in vitro* cell cultures were transfected with synthetic miR-181b (siRNA-181b) and the mRNA expression analyzed using genome-wide Sentrix bead chip arrays (Illumina) (29). Interestingly, both VSNL1 and GRIA2 expression was suppressed by 67 and 41%, respectively, in response to elevated miR-181b in HEK293 cells and SH-SY5Y cells, respectively (Fig. 4).

#### Biological activity of miR-181b elements in VSNL1 and GRIA2

While circumstantial evidence supported an association between miR-181b expression and the repression of predicted



**Figure 4.** Relative expression of VSNT1 and GRIA2 in response to miRNA 181b transfection. (A) Relative VSNT1 expression in untransfected HEK293 cells (control) and HEK293 cells transfected with synthetic miR-181b. (B) Relative expression of GRIA2 in untransfected SH-SY5Y cells and those transfected with synthetic miR-181b. Expression was determined in each case using Illumina Sentrix bead arrays. Decreased expression of both VSNT1 and GRIA2 in both cases corresponded to elevated miR-181b levels *in vitro*. Bars represent mean  $\pm$  SEM.

target genes VSNT1 and GRIA2, both in the STG in schizophrenia and *in vitro*, a reporter gene assay was established to further investigate the biological validity of this link. For this purpose, miRNA recognition elements (MRE) from each of the target genes predicted to bind miR-181b were cloned into the 3'UTR of the firefly luciferase gene of the pMIR-REPORT vector (Fig. 5A). Mutant versions of these MREs containing single nucleotide polymorphisms in the seed-pairing region were also cloned into the pMIR-REPORT vector (Fig. 5B and C). Each of these reporter constructs and the control plasmid (pRNL-TK) encoding renilla luciferase were co-transfected (10 and 2.5 ng, respectively) with either siRNA-181b or LNA-modified antisense 181b (250 ng), into HEK-293 cells and their relative luciferase activity measured. In accordance with expectation, relative luciferase expression from reporter constructs containing the VSNT1-1 MRE was found to be significantly reduced with respect to the control (average  $-20\%$ ,  $P = 0.007$ ) when co-transfected with si181b, while being significantly increased in the presence of antisense 181b (average  $28\%$ ,  $P = 0.012$ ) (Fig. 5D). The constructs containing the mutant VSNT1 MRE displayed a smaller response to transfection, with suppression of  $8\%$  after co-transfection with si181b ( $P = 0.033$ ), whereas it did not show a significant change in response to antisense 181b (Fig. 5D). The GRIA2 reporter gene displayed a similar response to siRNA-181b transfection, with an average suppression of  $21\%$  ( $P = 0.006$ ), whereas

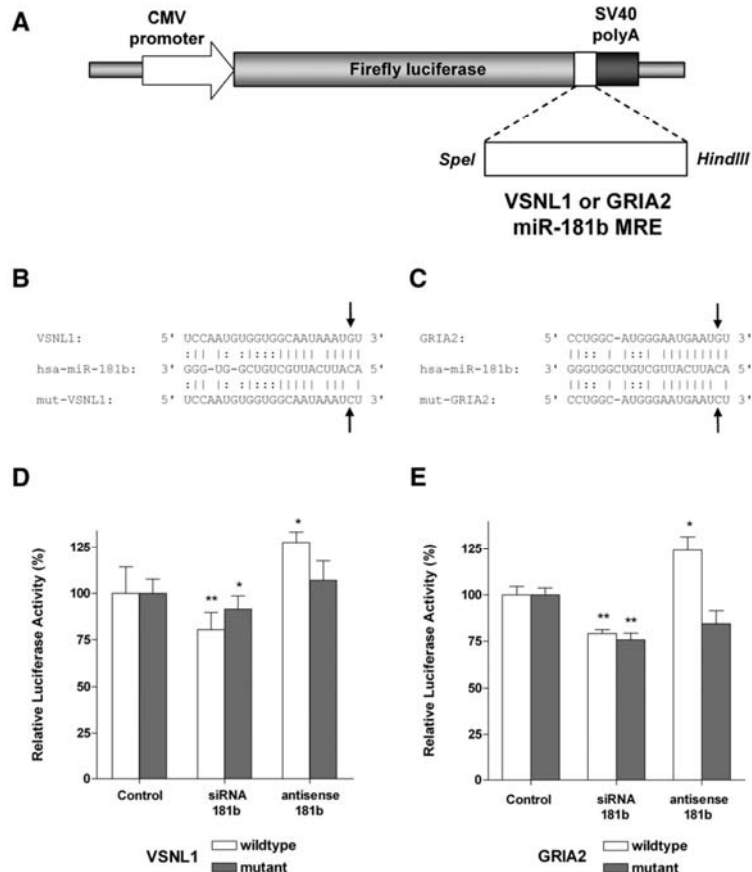
antisense 181b transfection increased its expression  $24\%$  ( $P = 0.038$ ). Surprisingly, luciferase activity from the construct containing the mutant GRIA2 MRE was also suppressed by si181b transfection (down  $24\%$ ,  $P = 0.003$ ), though the antisense 181b did not induce a significant change in its expression (Fig. 5E).

## DISCUSSION

### STG, miRNA expression and schizophrenia

In recent years, a number of genome-wide expression studies in schizophrenia including those from our own laboratory, have shown alterations in large numbers of genes (30,31). In view of the breadth of changes in the neural genomes activity in schizophrenia, it is reasonable to speculate that these could at least in part be due to changes in post-transcriptional gene silencing. To test this hypothesis, we initiated an investigation of miRNA expression patterns in the normal human cerebral cortex and in a matched cohort of tissue derived from subjects with schizophrenia. Postmortem grey matter from the STG of both normal and schizophrenia groups were dissected and the RNA extracted and subjected to high throughput analysis on custom miRNA-specific microarrays (18). While many post-mortem expression studies of schizophrenia have focused on the prefrontal cortex, there is evidence to suggest the STG is also a participant in the pathophysiology of schizophrenia. Genome-wide analysis of schizophrenia-associated gene expression in the STG recently reported a large number of altered genes (Bowden *et al.*, manuscript in preparation). In this study, we used the exact same tissue to enable a direct comparison between the schizophrenia-associated changes in gene and miRNA expression. The microarray analysis revealed up-regulation of let-7g and miR-181b, and this was also supported for miR-181b by northern blot hybridization and further validated by quantitative real-time RT-PCR in a larger cohort of 21 matched pairs.

miRNA 181b is encoded at two genomic loci, which give rise to primary transcripts for pre-miRNAs 181b-1 (MIRN181B1; 1q31.3) and pre-miRNA 181b-2 (MIRN181B2; 9q33.3). As the 181b-1 locus resides in the vicinity of a schizophrenia linkage region (1q23.3-1q31.1) (32) and the schizophrenia-associated genes for interleukin 10 (IL10; 1q31-32) and plexin A2 (PLXNA2; 1q32.2) (33-35), it is conceivable that its transcription could have been affected by schizophrenia-associated genetic alterations present in this region. To determine the relative contributions of each 181b transcript in the context of schizophrenia, we performed precursor-specific quantitative real-time RT-PCR. This analysis showed that the MIRN181B2 locus on chromosome 9 was actually far more active ( $\sim 10$ -fold) than its counterpart on chromosome 1. While there was some increase in the average pre-miR-181b-2 expression in the schizophrenia group, this was not statistically significant. One interpretation of this finding is that the up-regulation of mature miR-181b expression was not due to changes at the level of transcription, but rather changes that affected its processing or maturation. This would be consistent with the hypothesis developed to explain miRNA expression changes observed in the dorsolateral prefrontal cortex (DLPFC) in



**Figure 5.** VSNL1 and GRIA2 MRE reporter assay. (A) The pMIR-REPORT<sup>™</sup> miRNA expression reporter system contains a firefly luciferase gene under the control of CMV promoter. The putative miR-181b MRE for VSNL1 or GRIA2 were inserted into the multiple cloning site in the 3'-UTR of the luciferase gene. (B and C) Mutant versions of each MRE were also prepared such that a single base change (indicated by arrows) was introduced to the miRNA seed pairing region. (D) Using the wild-type MRE derived from VSNL1, expression was suppressed 20% by siRNA 181b ( $P = 0.007$ ) and increased 28% by antisense 181b ( $P = 0.012$ ). Whereas the mutant version was suppressed 8% by siRNA 181b ( $P = 0.033$ ), and not significantly altered by antisense 181b. (E) The wild-type MRE from GRIA2 was suppressed 21% by siRNA 181b ( $P = 0.006$ ) and increased 24% by antisense 181b ( $P = 0.038$ ). The GRIA2 mutant MRE was suppressed 24% by siRNA 181b ( $P = 0.003$ ), but was not significantly altered by antisense 181b. Bars represent mean  $\pm$  SD.

schizophrenia (15). In this study, a subset of down-regulated miRNAs (which incidentally did not include miR-181b) shared an upstream consensus sequence, which was suggestive of a role in miRNA maturation. This concept is also supported by the loss of the DiGeorge critical region 8 (DGCR8; an accessory for the primary miRNA processing protein Drosha) (13) in the 21q11 micro deletion responsible for DiGeorge or Velo Cardio Facial syndrome, which is known to be the highest risk factor for schizophrenia (~25%) (14) apart from having a monozygotic twin with the disorder (~50%). However, a more specific effect could be operating in respect to the changes in miR-181b expression, observed here, perhaps through changes to pre-miRNA sequence

elements involved in maturation of the miRNA. More general deficits in pri-miRNA processing suggested for the DLPFC were not supported here as pre-miR-181b was not altered in the STG and it does not contain the consensus sequence reported for miRNA altered in the DLPFC (15).

#### miR-181b target genes

The implications of even a small increase in miR-181b expression in the cerebral cortex could be profound, particularly during development as it is capable of extending a repressive influence over hundreds of different target genes. While miRNA 181b is known to be expressed in a variety of



mammalian tissues, a number of studies have shown brain enrichment (8,36,37) with expression in both neurons and neuroglia (38,39). It is also highly expressed in the thymus and lungs, and has been shown to be directly associated with B-cell lineage differentiation of hematopoietic progenitor cells (40). miR-181b was also found to be up-regulated in acute promyelocytic leukaemia cells in response to retinoic acid-induced differentiation (41). It was also up in thyroid papillary carcinoma cells compared with those from normal thyroid tissue (42). Conversely, miR-181b was observed to be down-regulated in glioblastoma cells (39). Most of these findings, however, are consistent with a role for miR-181b in differentiation and development. This is broadly supported by miR-181b target gene predictions, which implicate an apparent bias towards genes involved in development, brain development and brain function.

While it is interesting to consider the potential of genome wide interactions, we were able to examine miRNA targets specifically in the context of genes shown previously to be down-regulated in schizophrenia and in the same tissue from the same cohort of controls and schizophrenia subjects (Supplementary Material, Table S2c; Bowden *et al.*, manuscript in preparation). Among the 23 genes in this category, two targets including GluR2, the ionotropic glutamate/AMPA receptor gene (GRIA2) and the calcium sensor/trkB mRNA binding protein known as VSNL1 were particularly interesting in the context of schizophrenia. GRIA2 is a major ionotropic glutamate receptor subunit involved in fast excitatory neurotransmission. It has been shown to have an important function in the development of synaptic plasticity because of its involvement with NMDA receptors in the establishment of LTP, long-term depression (43) and by directly stimulating increased growth and density of dendritic spines (44). GRIA2 has also shown a consistent association with schizophrenia and is compatible with the glutamate hypofunction hypothesis, with an observed decrease in both mRNA and protein levels in postmortem samples from a number of brain regions including the medial temporal lobe, hippocampus and dorsolateral prefrontal cortex (27,45,46). The calcium sensor protein VSNL1 has also been shown to be differentially expressed in schizophrenia (28). Specific changes in VSNL1 expression have been reported in the rat brain in phencyclidine (PCP) and ketamine models of schizophrenia (47,48). VSNL1 is thought to be a calcium sensitive signal transduction molecule. Its location within hippocampal neurons has also been shown to be altered in response to stimulation by glutamate (49). Interestingly, VSNL1 is also a calcium-dependent double-stranded RNA-binding protein, that may provide activity-dependent trafficking of certain neuronal mRNAs to the dendrites and more specifically is known to bind the 3' UTR of mRNA for the neurotrophin receptor (trkB) (50).

To further support the plausibility of a relationship between GRIA2 and VSNL1 expression in the STG and miR-181b, we established a synthetic miRNA 181b transfection system and monitored the expression of these genes in response to changes in miRNA 181b concentration *in vitro*. The expression of both of these genes responded in accordance with expectation by showing a substantial drop in expression after the addition of the miRNA (Fig. 4). However, in order

to directly characterize the miR-181b target status of GRIA2 and VSNL1, the putative MRE from their respective 3' UTR were cloned downstream of the firefly luciferase gene to measure their response to miR-181b *in vitro*. The presence of either of these MRE and si181b was observed to significantly reduce expression of luciferase expression compared with the control siRNA. In both cases reporter gene expression was also elevated in response to antisense 181b transfection, presumably as a result of depleting the bioavailability of endogenous miR-181b. In most cases, these responses were absent or diminished substantially in the mutant MRE constructs, which contained point mutations in the miRNA seed regions. The one exception to this was the reporter gene carrying the mutant version of the GRIA2 MRE, which was also silenced significantly by si181b. This was not surprising as the mutant was predicted to be a viable miR-181b target gene (albeit a weaker one) and thus capable of responding to saturating levels of the cognate miRNA. In contrast, at lower endogenous concentrations it did not display any signs of the silencing observed with the wild-type reporter gene, evident by the absence of response to the antisense miR-181b. From these experiments, we were able to conclude that both VSNL1 and GRIA2 3'UTR segments are sufficient to support PTGS by miR-181b *in vitro*, enhancing their status as functioning targets of this miRNA.

In summary, we have considered the possibility that alteration of miRNA-mediated PTGS is associated with the pathophysiology of schizophrenia. In support of this hypothesis, miR-181b was shown to be up-regulated in grey matter from the STG. In a similar approach, miRNA expression was also shown to be altered in the DLPFC in schizophrenia, although changes in miRNA 181b expression was not reported in this tissue (15). Genetic analysis of polymorphisms in the vicinity of brain expressed miRNA genes hsa-miR-206 and hsa-miR-198, was recently determined to be weakly associated with schizophrenia (51). There has also been some interest in the analysis of hsa-miR-103b in the context of schizophrenia due to its location in the 22q11 locus, however, no association was observed (52). Time will tell if schizophrenia-associated changes in miRNA expression are due to direct genetic influence or some other upstream regulatory, epigenetic or mechanistic factors affecting miRNA maturation. In either case it has important implications for understanding the neurodevelopmental origins of the schizophrenia, particularly as changes in a given miRNA can affect the expression of hundreds of target genes. In the case of miR-181b there are up to 800 conserved targets predicted in the human genome that have the potential to interact with the miRNA. The true extent of its influence, however, will depend on the biological context and other so far unidentified factors. In respect to schizophrenia and changes in the STG, we have identified two important candidate target genes for miR-181b (GRIA2 and VSNL1) that are suppressed in the same tissue, and may be responding to changes in the local miRNA environment. If these specific effects are a manifestation of the observed changes in miRNA expression, they probably represent the 'tip of the iceberg' in terms of their global regulatory influence. The full impact of this and other changes in miRNA expression will no doubt take some time to unravel and appreciate fully.

## MATERIALS AND METHODS

### Tissue collection

Fresh frozen postmortem STG grey matter tissue from 21 subjects with schizophrenia and 21 non-psychiatric controls was obtained through the NSW Tissue Resource Centre, The University of Sydney, Australia. The grey matter tissue was taken from the outer edge of blocks of STG tissue from the most caudal coronal brain slice containing the STG (Brodmann's Area 22). In all cases, a diagnosis of schizophrenia in accordance with DSM-IV criteria was confirmed by medical file review using the Item Group Checklist of the Schedules for Clinical Assessment in Neuropsychiatry and the Diagnostic Instrument for Brain Studies. Consent was obtained from the next of kin and subjects with a significant history of drug or alcohol abuse, or other condition or gross neuropathology that might have influenced agonal state were excluded. In addition, control subjects were excluded if there was a history of alcoholism or suicide. All subjects were of Caucasian descent. Subjects with schizophrenia were matched for gender, age, brain hemisphere, postmortem interval and pH (Table 1). This cohort of tissue contained 13 matched pairs that were previously analyzed for mRNA expression using microarray analysis (Bowden *et al.*, manuscript in preparation).

### Tissue dissection and RNA extraction

Postmortem cortical grey matter was dissected from the outer edge of frozen coronal sections (1 cm) using a fine diameter hole punch and scalpel. In each case, ~50–60 mg grey matter was removed and immediately homogenized in 1 ml of Trizol reagent and the total RNA extracted according to the manufacturer's instructions (Invitrogen). The RNA concentration and integrity was determined using an Experion bioanalyser (BioRad).

### miRNA expression arrays

miRNAs were labelled directly using a ligation approach consisting of 9 µg of total RNA, in 50 mM HEPES, pH 7.8, 3.5 mM DTT, 20 mM MgCl<sub>2</sub>, 0.1 mM ATP, 10 µg/ml BSA, 10% DMSO, 500 ng 5'-phosphate-cytidyl-uridyl-Cy3-3' (Dharmacon) and 20 units T4 RNA ligase (Fermentas) (18,53). After incubating for 2 h on ice the labelled RNA was precipitated with 0.3 M sodium acetate, 2 volumes 100% ethanol and 20 µg glycogen at –20°C overnight. A synthetic reference library consisting of DNA oligonucleotides (representing the entirety of miRBase version 7.0) was labelled with Ulysis platinum conjugated AlexaFluor 647 (equivalent to Cy5) for detection in the control channel, using the labelling kit, according to the manufacturer's instructions (Invitrogen). Unconjugated label was then removed by gel filtration through a Sephadex G-25 spin column (GE Healthcare). The labelled reference library was used at a 1/700 dilution, along side the Cy3 labelled miRNAs, in each array hybridization.

Microarrays were prepared using anti-sense DNA oligonucleotides corresponding to the miRBase Version 7.0 (Sanger Institute, UK) containing 261 human miRNAs sequences.

The oligonucleotide probes were printed in duplicate onto GAPS-2 glass slides (Corning). The slides were then prepared and hybridized with the labelled miRNA and synthetic controls as described previously (18). Briefly, slides were pre-hybridized in 3 × SSC, 0.1% SDS and 0.2% BSA for 1 h at 65°C and washed four times with RNase-free water, once with 100% ethanol, and dried by centrifugation at 150g for 5 min. Hybridization chambers were created around each array using 17 mm × 28 mm disposable frame seals and cover slides (Bio-Rad). The labelled RNA sample was added to 100 µl hybridization buffer (400 mM Na<sub>2</sub>HPO<sub>4</sub>, pH 7.0, 0.8% BSA, 5% SDS, 12% formamide) and heated for 4 min at 95°C (in the dark). The mixture was injected into the chamber and hybridized for 2 h at 37°C in a rotary hybridization oven. The coverslips and frames were removed and the slides washed once in 2 × SSC, 0.025% SDS at room temperature, three times in 0.8 × SSC at room temperature and three times in ice-cold 0.4 × SSC. Each slide was then dried by centrifugation for 10 min at 60g. Arrays were then scanned with a Genepix 4000B Scanner (Axon Instruments) and raw pixel intensities extracted with Genepix Pro 3.0 software (Axon Instruments).

A miRNA was considered expressed if its raw Cy3 pixel intensity was at least 200% above background. Raw Cy3 median pixel intensity values were background subtracted and normalized by median centring with respect to arrays using Cluster version 2.2 (Stanford University). Differential miRNA expression was analyzed using Significance Analysis of Microarrays SAM version 2.23 (Stanford University) (19) (available from <http://www-stat.stanford.edu/~tibs/SAM/>). The threshold for significance was set at 5% and a two-class comparison was performed using 5000 permutations of the data. A list of significantly altered miRNAs was compiled (false-discovery rate <5%).

### Northern hybridization

Total RNA from each case (30 µg) was combined with equal volumes of loading dye (0.01% bromophenol blue, 10 mM EDTA and formamide), pre-heated at 95°C for 5 min then electrophoresed on a 16% denaturing (8.3 M urea) polyacrylamide sequencing gel. The RNA was then electro-transferred in a semi-dry blotter at 400 mA for 1 h to GeneScreen Plus nylon membrane (Perkin Elmer NEN) and immobilized by UV-cross linking, followed by baking at 80°C for 1 h. The membrane was then pre-hybridized and hybridized in PerfectHyb Plus hybridization buffer (Sigma) for 3 and 16h, respectively. The later was carried out with the addition of 50 pmol of <sup>32</sup>P-labelled unmodified or LNA-modified anti-sense oligonucleotide prepared earlier using [ $\gamma$ -<sup>32</sup>P] ATP (Perkin Elmer) and polynucleotide kinase (Fermentas) as described by previously (54). After low and high stringency washes, the radiolabelled membranes were imaged using a typhoon phosphorimager (Amersham) and analyzed using ImageQuant software (Amersham). The sequences of anti-sense probes for the detection of miR-181b, let-7g and U6 snRNA are presented in Table 2. Statistical analysis, consisting of a one-tailed *t*-test, was performed on the normalized intensity values to determine the significance of observed differences in average expression.

Table 1. Demographic data for schizophrenia and non-psychiatric control subjects

Pair	Diagnosis	Sex	Age	Height	PMI	pH	COD	Toxicology	DOI	CPI <sup>1</sup>
1	CPS	M	51	L	21	6.02	IHD <sup>a,c,g</sup>	Thioridazine 2.2 mg/l (fatal), Mesoridazine 2.4 mg/l (toxic/fatal)	24	100–700
2	CPS	M	57	L	33	6.40	Coronary artery thrombosis <sup>a,e</sup>	Thioridazine 0.6 mg/l, Sertraline <0.1 mg/l	26	100–400
3	CPS	M	52	R	8	6.10	IHD <sup>a,f</sup>	Tenazepam <0.1 mg/l	31	260–600
4	CUS	M	44	L	35	6.55	Hanging suicide <sup>a</sup>	Urine THC detected	17	500–1000
5	CPS	M	30	L	24	6.60	CO poisoning <sup>a,b</sup>	Carbon Monoxide 74% saturation, Clozapine 0.7 mg/l	3.5	130–975
6	CDS	M	52	L	25	6.24	Hanging suicide <sup>a</sup>	N/A	13	780
7	CPS	M	51	R	18	6.62	IHD <sup>a,f</sup>	N/A	30	300–1300
8	CPS	F	51	L	12	5.40	Emphysema <sup>a</sup>	Lithium 20 mg/l (fatal), Midazolam 0.02 mg/l	16	112–1000
9	CDS	F	67	R	27	6.20	IHD <sup>a,f</sup>	Benzotripine, Mesoridazine, Thioridazine and Paracetamol detected	46	150–1100
10	CPS	M	75	L	36	6.40	IHD <sup>a,f</sup>	Olanzapine - 0.2 mg/l, Fluvoxamine - 0.7 mg/l	44	200–1200
11	CPS	M	54	R	27	6.20	Coronary artery thrombosis <sup>a,i</sup>	Chlorpromazine: 0.7 mg/l, Diazepam: <0.1 mg/l, Nordiazepam: 0.1 mg/l, Insulin: 2 uU/ml	35	50–600
12	CPS	F	61	R	49	6.70	Ischaemic heart disease <sup>c,f</sup>	Clozapine 1.1 mg/l; Diazepam 0.2 mg/l; Laudanosine 0.4 mg/l; Nordiazepam 0.4 mg/l; Olanzapine 0.2 mg/l	42	800–1500
13	CUS	M	67	R	5	6.40	Cardiovascular disease <sup>e,g</sup>	Negative	41	200–2400
14	CPS	M	57	R	48	6.70	ASCVD <sup>a,e</sup>	Carbamazepine 10 mg/l, Citalopram 0.2 mg/l, Quetiapine <0.1 mg/l	17	225–975
15	CPS	M	40	R	21.5	6.20	Dihydrocodeine toxicity and obstructive sleep apnoea <sup>a</sup>	Valproic acid 20 mg/l, Dihydrocodeine 0.7 mg/l, Quetiapine 0.3 mg/l, Sertraline 0.3 mg/l	23	225–1800
16	CPS	F	66	R	12.5	6.30	Facetoid peritonitis <sup>a,i</sup>	Negative	30	1200–2500
17	CPS	F	61	R	39	6.60	Undetermined <sup>a,c</sup>	Thioridazine and Mesoridazine detected	32	100–600
18	CPS	F	61	L	19	6.10	Sepsis and chronic renal failure <sup>a</sup>	Morphine: 0.06 mg/l, Codeine: 0.05 mg/l, Carbamazepine: 7 mg/l, Peritidine: 0.1 mg/l, Paracetamol: 6 mg/l, Metoclopramide 0.1 mg/l, Diazepam: <0.1 mg/l	39	300–400
19	CPS	M	33	L	48	6.70	Hanging suicide <sup>a</sup>	Doxylamine: 0.9 mg/l, Olanzapine: 0.2 mg/l, Paracetamol: 3 mg/l	10	222
20	CUS	M	52	R	46	6.40	Cardiomegaly <sup>a,i</sup>	N/A	32	17–1165
21	CPS	F	54	R	29	6.50	Asthma <sup>a,d</sup>	Citalopram 0.6 mg/l	35	15–600
Mean (SD)			52.7 (11.7)		28.9 (13.4)	6.4 (0.3)				
1	CON	M	50	L	19	6.26	IHD <sup>c</sup>	Negative		
2	CON	M	58	L	38	6.50	IHD <sup>c</sup>	N/A		
3	CON	M	59	R	20	6.56	Coronary thrombosis <sup>f</sup>	Negative		
4	CON	M	43	L	13	6.43	Thrombotic coronary artery occlusion <sup>i</sup>	Negative		
5	CON	M	34	L	20.5	6.73	Asthma <sup>e</sup>	N/A		
6	CON	M	38	L	13.5	6.00	ASCVD <sup>c</sup>	Negative		
7	CON	M	46	R	25	6.70	Cardiac arrest	Negative		
8	CON	F	52	L	9.5	5.80	IHD	N/A		
9	CON	F	70	R	30	6.80	IHD <sup>g</sup>	Blood EtOH: 0.251 g per 100 mL, Paracetamol <3mg/L		
10	CON	M	73	L	10	6.20	Cardiac arrest	N/A		
11	CON	M	56	R	37	6.80	Pulmonary thromboembolus	N/A		
12	CON	F	56	R	23	6.70	Pulmonary thromboembolus <sup>e</sup>	N/A		
13	CON	M	69	R	16	6.60	Cardiac atheroma <sup>f,g</sup>	Paracetamol 23 mg/l, 1% blood saturation of CO (low)		
14	CON	M	56	R	24	6.50	Coronary artery atheroma <sup>i</sup>	N/A		
15	CON	M	37	L	21	6.60	IHD	Negative		
16	CON	F	71	L	16	6.20	Adenocarcinoma of the pancreas <sup>c</sup>	N/A		
17	CON	F	52	L	11	6.20	Ischaemic heart disease <sup>i</sup>	N/A		
18	CON	M	46	L	29	6.70	Pulmonary thromboembolus <sup>e</sup>	N/A		
19	CON	M	46	L	29	6.10	M <sup>h</sup>	N/A		

Continued



Table 1. Continued

Pair	Diagnosis	Sex	Age	Hemi	PMI	pH	COD	Toxicology	DOI	CPE <sup>†</sup>
20	CON	M	53	R	27	6.60	MI	N/A		
21	CON	F	49	R	15	6.90	Arrhythmogenic right ventricular dysplasia	Chloride ions 118 mmol/l		
Mean (SD)			53.2 (11.4)		21.4 (8.5)	6.5 (0.3)				

CRS, chronic residual schizophrenia; CPS, chronic paranoid schizophrenia; CUS, chronic undifferentiated schizophrenia; CDS, chronic disorganized schizophrenia; CON, control subject; Hemi, brain hemisphere; PMI, postmortem interval (h); COD, cause of death; DOI, duration of illness (years); CPE, chlorpromazine equivalent (mg/day); IHD, ischaemic heart disease; MI, myocardial infarction; ASCVD, atherosclerotic cardiovascular disease.

<sup>a</sup>Schizophrenia subjects medicated with predominantly typical antipsychotics over their lifetime.

<sup>b</sup>Medicated with predominantly atypical antipsychotics over their lifetime.

<sup>c</sup>Medicated with only typical antipsychotics over their lifetime.

<sup>d</sup>Medicated equally with typical and atypical antipsychotics over their lifetime.

<sup>e</sup>Moderate nicotine consumption.

<sup>f</sup>Heavy nicotine consumption.

<sup>g</sup>Moderate alcohol consumption.

<sup>h</sup>Heavy alcohol consumption.

<sup>†</sup>Calculated using the mean CPE dosage for each subject. All toxicology results are from blood unless otherwise stated (e.g. urine). All subjects are of Caucasian descent. Mean PMI is higher (6.5 h) in the schizophrenia cohort.

### Quantitative real-time RT-PCR

Multiplex reverse transcription was performed on 500 ng of DNaseI-treated total RNA using either random hexamers (mRNA analysis), or a combination of reverse primers (miRNA analysis) specific for mature hsa-miR-181b, the U6 snRNA and  $\beta$ -actin, to a final concentration of 40 nM each (for sequences see Table 2). Reactions were performed using Superscript II reverse transcriptase in 1  $\times$  first-strand buffer according to the manufacturer's instructions (Invitrogen). Real-time PCR was performed essentially as previously described (31), in triplicate on diluted cDNA combined with Power SybrGreen master mix (Applied Biosystems) with 1  $\mu$ M of the appropriate forward and reverse primers (Table 2), in a final volume of 25  $\mu$ l using an ABI prism 7500 sequence detection system (PE Applied Biosystems). Relative miRNA expression was determined by the difference between their individual cycle threshold (Ct) value and that produced in the same sample for the U6 snRNA ( $\Delta$ Ct). Similarly, relative mRNA expression ratio was normalized with respect to the geometric mean of  $\beta$ -actin and U6 snRNA expression. Differential expression of a given miRNA or mRNA was determined by the difference between the mean  $\Delta$ Ct for the schizophrenia and control cohorts ( $\Delta\Delta$ Ct) expressed as a ratio ( $2^{-\Delta\Delta$ Ct}) (55). To determine the significance of any difference in average expression in a given direction between the two cohorts, a paired one-tailed *t*-test was applied. No significant differences in the expression of normalizing genes ( $\beta$ -actin and U6 snRNA) were observed with respect to each other, between the schizophrenia and control cohorts.

### Cell culture and siRNA transfection

HEK-293 and SH-SY5Y cell cultures were maintained as confluent monolayers at 37°C with 5% CO<sub>2</sub> and 90% humidity in DMEM with 10% (vol/vol) fetal calf serum, 20 mM HEPES, 0.15% (wt/vol) sodium bicarbonate and 2 mM L-glutamine. HEK-293 cells were seeded into 10 cm petri dishes and transfected 24 h later using Lipofectamine 2000 (Invitrogen). SH-SY5Y cells were harvested and electroporated using the Nucleofector Kit V (Amaxa), before being seeded into 6-well plates at  $1 \times 10^5$  cells/well. In each case transfections were performed according to manufacturer's instructions with 100 nM siRNA (si181b) oligonucleotide (Table 2).

### Target gene expression profiling

RNA was extracted directly from plates 24 h post-transfection using 2 ml of Trizol and a disposable cell scraper (Greiner Bio-One). miR-181b expression levels in transfected cells were analyzed using real-time PCR as described above. RNA was purified further using an RNeasy MinElute kit (Qiagen) before amplification-labelling with a TotalPrep amplification kit (Ambion) and hybridization on HumanRef-8 whole-genome expression arrays (Illumina) according to the manufacturer's instructions. Data were normalized and analyzed using Illumina Beadstudio 3.0 and GeneSpringGX 7.3.1 (Agilent Technologies, USA).

**Table 2.** Oligonucleotide sequences

Type	Name	Sequence	Target
Antisense <sup>a</sup>	181b_antisense	C+CCA+CCG+ACA+GCA+ATG+AAI+GI	miRNA 181b
	let7g_antisense	ACTGTACAACTACTACCTCA	miRNA let-7g
Primers <sup>b</sup>	U6_antisense	GCCATGCTAACTCTCTCTGATC	U6 snRNA
	ActinB-1F	TGTGGCATCCACGAACTACC	$\beta$ -actin
	ActinB-1R	ACATCTGCTGGGAAGGTGGACA	$\beta$ -actin
	U6_F339	CGGCAGCATATATACTAAAATTGG	U6 snRNA
	VSNL1_F1	AAACAACCTGCCACAATGTGATATG	VSNL1
	VSNL1_R2	ATAGTATTTTACAGGAGGGTAGTGA	VSNL1
	GRIA2_F	GTCCCTTACGTGAGTCCTG	GRIA2
	GRIA2_R	TAAACACACAAGAAAACCAT	GRIA2
	181b_1F5	TGCAGAGATTATTTTAAAAAGG	pre-181b-1
	181b_1R60	TGAGCTTGTCCACACAGTTC	pre-181b-1
	181b_2F1	CTGATGGCTGCACCTCAACAT	pre-181b-2
	181b_2R42	TGATCAGTGAGTTGATTCAGACT	pre-181b-2
	181b_F	TTTCTAACAATTCATTGCT	miRNA 181b
	181b_R	CAACCTTCTCCACCGAC	miRNA 181b
Cassettes <sup>c</sup>	VSNL1_181bT	CTAGAAGGCTTCCAAATGTGGTGGCAATAAATGTCCAAAT	VSNL1
	VSNL1_181bB	AGCTATTTGGGACATTTATTGCCACACATTGGAAGCCTT	VSNL1
	VSNL1_181bmT	CTAGAAGGCTTCCAAATGTGGTGGCAATAAATCTCCCAAT	mutant
	VSNL1_181bmB	AGCTATTTGGGAGATTTATTGCCACACATTGGAAGCCTT	mutant
	GRIA2_181bT	CTAGCTTACGTGAGTCTTGGCATGGGAAATGAATGTCACTGT	GRIA2
	GRIA2_181bB	AGCTACACTGACATTCATCCCATGCCAGGACTCACGTAAG	GRIA2
	GRIA2_181bmT	CTAGCTTACGTGAGTCTTGGCATGGGAAATGAATCTCACTGT	mutant
	GRIA2_181bmB	AGCTACACTGAGATTCATTCCTATGCCAGGACTCACGTAAG	mutant
siRNA <sup>d</sup>	siEGFP+	CGGCAAGCUGACCCUGAAGUU	EGFP
	siEGFP-	GACUCCAGUGGUAAUCUACUU	EGFP
	si9*+	UAAAGCUAGAUAAACCGAAAGU	miR-9*
	si9*-	UUUCGGUUAUCUAGCUUUUCUU	miR-9*
	si181b+	AACAUCUACUUGUCUGGUGGG	miR-181b
	si181b-	CACCGACAGCAAUGAUGUUUU	miR-181b

<sup>a</sup>The positions of LNA modified bases are preceded by a '+' symbol. U6 antisense was used as a probe for northern hybridization and as a reverse primer for quantitative RT-PCR.

<sup>b</sup>The direction of primers with respect to the target sequence was denoted in the name as either F or R for forward and reverse respectively. Underlined sequence is not gene specific and was used to increase the amplicons size and primer recognition sequence.

<sup>c</sup>SpeI/HindIII cassettes containing putative target MRE were used to generate recombinant luciferase reporter gene constructs.

<sup>d</sup>siRNA was used to over express miRNA.

### Target gene reporter assay

Validation of predicted miR-181b target genes VSNL1 and GRIA2 was accomplished by co-transfecting HEK293 cells with synthetic si181b or an LNA-modified antisense inhibitor and recombinant firefly luciferase reporter gene constructs containing 3' UTR sequences substituted from the target gene. Oligonucleotides encoding target gene MRE (or mutant controls) were annealed to form *SpeI* and *HindIII* restricted overhangs of a ligatable cassette compatible with *SpeI* and *HindIII* digested pMIR-REPORT vector (Ambion). Reporter gene silencing in response to miRNA co-transfection was monitored with respect to a 'spiked-in' control plasmid expressing renilla luciferase using the dual luciferase reporter assay (Promega). To control for non-specific effects associated with siRNA transfection, the controls were co-transfected with siEGFP or miR-9\* siRNA predicted to have little or no activity against the fusion transcripts tested here. HEK293 cells were cultured and transfected as described above (except in 24-well plates) using Lipofectamine2000 (Invitrogen).

### SUPPLEMENTARY MATERIAL

Supplementary Material is available at HMG Online.

### ACKNOWLEDGEMENTS

Tissues were received from the Australian Brain Donor Programs NSW Tissue Resource Centre, which is supported by The University of Sydney, National Health and Medical Research Council of Australia, Schizophrenia Research Institute, National Institute of Alcohol Abuse and Alcoholism and NSW Department of Health. The authors would like to thank Professor Vaughan Carr for critical reading of the manuscript.

*Conflict of Interest statement.* None declared.

### FUNDING

This study was supported by the Schizophrenia Research Institute, utilizing funding from NSW Health and the Henderson Foundation; a NARSAD Young Investigator Award (M.C.); a University of Newcastle pilot grant; and the M.C. Ainsworth Research Fellowship in Epigenetics (M.C.). Funding for the open access publication charge was provided by the Schizophrenia Research Institute.

## REFERENCES

- Badner, J.A. and Gershon, E.S. (2002) Meta-analysis of whole-genome linkage scans of bipolar disorder and schizophrenia. *Mol. Psychiatry*, **7**, 405–411.
- Lewis, C.M., Levinson, D.F., Wise, L.H., DeLisi, L.E., Straub, R.E., Hovatta, I., Williams, N.M., Schwab, S.G., Pulver, A.E., Faraone, S.V. *et al.* (2003) Genome scan meta-analysis of schizophrenia and bipolar disorder, part II: Schizophrenia. *Am. J. Hum. Genet.*, **73**, 34–48. Epub June 11, 2003.
- Harrison, P.J. and Weinberger, D.R. (2005) Schizophrenia genes, gene expression, and neuropathology: on the matter of their convergence. *Mol. Psychiatry*, **10**, 40–68 (image 5).
- Tsuang, M. (2000) Schizophrenia: genes and environment. *Biol. Psychiatry*, **47**, 210–220.
- Petronis, A. (2004) The origin of schizophrenia: genetic thesis, epigenetic antithesis, and resolving synthesis. *Biol. Psychiatry*, **55**, 965–970.
- He, L. and Hannon, G.J. (2004) MicroRNAs: small RNAs with a big role in gene regulation. *Nat. Rev. Genet.*, **5**, 522–531.
- Giraldez, A.J., Cinalli, R.M., Glasner, M.E., Enright, A.J., Thomson, J.M., Baskerville, S., Hammond, S.M., Bartel, D.P. and Schier, A.F. (2005) MicroRNAs regulate brain morphogenesis in zebrafish. *Science*, **308**, 833–838. Epub March 17, 2005.
- Sempere, L.F., Freemantle, S., Pitha-Rowe, I., Moss, E., Dmitrovsky, E. and Ambros, V. (2004) Expression profiling of mammalian microRNAs uncovers a subset of brain-expressed microRNAs with possible roles in murine and human neuronal differentiation. *Genome Biol.*, **5**, R13. Epub February 16, 2004.
- Jin, P., Zarnescu, D.C., Ceman, S., Nakamoto, M., Mowrey, J., Jongens, T.A., Nelson, D.L., Moses, K. and Warren, S.T. (2004) Biochemical and genetic interaction between the fragile X mental retardation protein and the microRNA pathway. *Nat. Neurosci.*, **7**, 113–117. Epub January 4, 2004.
- Ashraf, S.I., McLeon, A.L., Sclarsic, S.M. and Kunes, S. (2006) Synaptic protein synthesis associated with memory is regulated by the RISC pathway in *Drosophila*. *Cell*, **124**, 191–205.
- Schratt, G.M., Tuebing, F., Night, E.A., Kane, C.G., Sabatini, M.E., Kiebler, M. and Greenberg, M.E. (2006) A brain-specific microRNA regulates dendritic spine development. *Nature*, **439**, 283–289.
- Abelson, J.F., Kwan, K.Y., O'Roak, B.J., Baek, D.Y., Stillman, A.A., Morgan, T.M., Mathews, C.A., Pauls, D.L., Rasin, M.R., Gunel, M. *et al.* (2005) Sequence variants in *SLITRK1* are associated with Tourette's syndrome. *Science*, **310**, 317–320.
- Gregory, R.I., Yan, K.P., Amuthan, G., Chendrimada, T., Doratotaj, B., Cooch, N. and Shiekhattar, R. (2004) The Microprocessor complex mediates the genesis of microRNAs. *Nature*, **432**, 235–240. Epub November 7, 2004.
- Murphy, K.C., Jones, L.A. and Owen, M.J. (1999) High rates of schizophrenia in adults with velo-cardio-facial syndrome. *Arch. Gen. Psychiatry*, **56**, 940–945.
- Perkins, D.O., Jeffries, C.D., Jarskog, L.F., Thomson, J.M., Woods, K., Newman, M.A., Parker, J.S., Jin, J. and Hammond, S.M. (2007) microRNA expression in the prefrontal cortex of individuals with schizophrenia and schizoaffective disorder. *Genome Biol.*, **8**, R27.
- Rajarethinam, R.P., DeQuardo, J.R., Nalepa, R. and Tandon, R. (2000) Superior temporal gyrus in schizophrenia: a volumetric magnetic resonance imaging study. *Schizophr. Res.*, **41**, 303–312.
- Honea, R., Crow, T.J., Passingham, D. and Mackay, C.E. (2005) Regional deficits in brain volume in schizophrenia: a meta-analysis of voxel-based morphometry studies. *Am. J. Psychiatry*, **162**, 2233–2245.
- Thomson, J.M., Parker, J., Perou, C.M. and Hammond, S.M. (2004) A custom microarray platform for analysis of microRNA gene expression. *Nat. Methods*, **1**, 47–53. Epub September 29, 2004.
- Tusher, V.G., Tibshirani, R. and Chu, G. (2001) Significance analysis of microarrays applied to the ionizing radiation response. *Proc. Natl. Acad. Sci. USA*, **98**, 5116–5121. Epub April 17, 2001.
- Schupath, P., McGraw, M. and Hatzigeorgiou, A.G. (2006) A guide through present computational approaches for the identification of mammalian microRNA targets. *Nat. Methods*, **3**, 881–886.
- John, B., Enright, A.J., Aravin, A., Tuschl, T., Sander, C. and Marks, D.S. (2004) Human MicroRNA targets. *PLoS Biol.*, **2**, e363. Epub October 5, 2004.
- Krek, A., Grun, D., Poy, M.N., Wolf, R., Rosenberg, L., Epstein, E.J., MacMenamin, P., da Piedade, I., Gunsalus, K.C., Stoffel, M. *et al.* (2005) Combinatorial microRNA target predictions. *Nat. Genet.*, **37**, 495–500. Epub April 3, 2005.
- Lewis, B.P., Shih, I.H., Jones-Rhoades, M.W., Bartel, D.P. and Burge, C.B. (2003) Prediction of mammalian microRNA targets. *Cell*, **115**, 787–798.
- Kiriakidou, M., Nelson, P.T., Kouranov, A., Fitziev, P., Bouyioukos, C., Mourelatos, Z. and Hatzigeorgiou, A. (2004) A combined computational-experimental approach predicts human microRNA targets. *Genes Dev.*, **18**, 1165–1178. Epub May 6, 2004.
- Dennis, G. Jr, Sherman, B.T., Hosack, D.A., Yang, J., Gao, W., Lane, H.C. and Lempicki, R.A. (2003) DAVID: database for annotation, visualization, and integrated discovery. *Genome Biol.*, **4**, 3. Epub April 3, 2003.
- Yousef, M., Nebozhyn, M., Shatkey, H., Kanterakis, S., Showe, L.C. and Showe, M.K. (2006) Combining multi-species genomic data for microRNA identification using a Naive Bayes classifier. *Bioinformatics*, **22**, 1325–1334. Epub March 16, 2006.
- Vawter, M.P., Crook, J.M., Hyde, T.M., Kleinman, J.E., Weinberger, D.R., Becker, K.G. and Freed, W.J. (2002) Microarray analysis of gene expression in the prefrontal cortex in schizophrenia: a preliminary study. *Schizophr. Res.*, **58**, 11–20.
- Bernstein, H.G., Brauneis, K.H., Spilker, C., Danos, P., Baumann, B., Funke, S., Diekmann, S., Gundelfinger, E.D. and Bogerts, B. (2002) Hippocampal expression of the calcium sensor protein visinin-like protein-1 in schizophrenia. *Neuroreport*, **13**, 393–396.
- Kuhn, K., Baker, S.C., Chudin, E., Lieu, M.H., Oeser, S., Bennett, H., Rigault, P., Barker, D., McDaniel, T.K. and Chee, M.S. (2004) A novel, high-performance random array platform for quantitative gene expression profiling. *Genome Res.*, **14**, 2347–2356.
- Mirmics, K., Middleton, F.A., Marquez, A., Lewis, D.A. and Levitt, P. (2000) Molecular characterization of schizophrenia viewed by microarray analysis of gene expression in prefrontal cortex. *Neuron*, **28**, 53–67.
- Weidenhofer, J., Bowden, N.A., Scott, R.J. and Tooney, P.A. (2006) Altered gene expression in the amygdala in schizophrenia: up-regulation of genes located in the cytomatrix active zone. *Mol. Cell. Neurosci.*, **31**, 243–250. Epub October 19, 2005.
- Schwab, S.G., Hallmayer, J., Albus, M., Lerer, B., Eckstein, G.N., Bormann, M., Segman, R.H., Hanses, C., Freymann, J., Yakir, A. *et al.* (2000) A genome-wide autosomal screen for schizophrenia susceptibility loci in 71 families with affected siblings: support for loci on chromosome 10p and 6. *Mol. Psychiatry*, **5**, 638–649.
- Yu, L., Yang, M.S., Zhao, J., Shi, Y.Y., Zhao, X.Z., Yang, J.D., Liu, Z.J., Gu, N.F., Feng, G.Y. and He, L. (2004) An association between polymorphisms of the interleukin-10 gene promoter and schizophrenia in the Chinese population. *Schizophr. Res.*, **71**, 179–183.
- He, G., Zhang, J., Li, X.W., Chen, W.Y., Pan, Y.X., Yang, F.P., Gu, N.F., Feng, G.Y., Yang, S.L., He, J.Y. *et al.* (2006) Interleukin-10 -1082 promoter polymorphism is associated with schizophrenia in a Han Chinese sib-pair study. *Neurosci. Lett.*, **394**, 1–4. Epub December 27, 2005.
- Mah, S., Nelson, M.R., Delisi, L.E., Reneland, R.H., Markward, N., James, M.R., Nyholt, D.R., Hayward, N., Handoko, H., Mowry, B. *et al.* (2006) Identification of the semaphorin receptor PLXNA2 as a candidate for susceptibility to schizophrenia. *Mol. Psychiatry*, **11**, 471–478.
- Krichevsky, A.M., King, K.S., Donahue, C.P., Khrapko, K. and Kosik, K.S. (2003) A microRNA array reveals extensive regulation of microRNAs during brain development. *RNA*, **9**, 1274–1281.
- Kim, J., Krichevsky, A., Grad, Y., Hayes, G.D., Kosik, K.S., Church, G.M. and Ruvkun, G. (2004) Identification of many microRNAs that copurify with polyribosomes in mammalian neurons. *Proc. Natl. Acad. Sci. USA*, **101**, 360–365. Epub December 22, 2003.
- Dostie, J., Mourelatos, Z., Yang, M., Sharma, A. and Dreyfuss, G. (2003) Numerous microRNPs in neuronal cells containing novel microRNAs. *RNA*, **9**, 180–186.
- Ciafre, S.A., Galardi, S., Mangiola, A., Ferracin, M., Liu, C.G., Sabatino, G., Negrini, M., Maira, G., Croce, C.M. and Farace, M.G. (2005) Extensive modulation of a set of microRNAs in primary glioblastoma. *Biochem. Biophys. Res. Commun.*, **334**, 1351–1358.
- Chen, C.Z., Li, L., Lodish, H.F. and Bartel, D.P. (2004) MicroRNAs modulate hematopoietic lineage differentiation. *Science*, **303**, 83–86. Epub December 4, 2003.

41. Garzon, R., Pichiotti, F., Palumbo, T., Visentini, M., Aqeilan, R., Ciminino, A., Wang, H., Sun, H., Volinia, S., Alder, H. *et al.* (2007) MicroRNA gene expression during retinoic acid-induced differentiation of human acute promyelocytic leukemia. *Oncogene*, **26**, 4148–4157. Epub January 29, 2007.
42. Pallante, P., Visone, R., Ferracin, M., Ferraro, A., Berlingieri, M.T., Troncone, G., Chiappetta, G., Liu, C.G., Santoro, M., Negrini, M. *et al.* (2006) MicroRNA deregulation in human thyroid papillary carcinomas. *Endocr. Relat. Cancer*, **13**, 497–508.
43. Carroll, R.C., Beattie, F.C., von Zastrow, M. and Malenka, R.C. (2001) Role of AMPA receptor endocytosis in synaptic plasticity. *Nat. Rev. Neurosci.*, **2**, 315–324.
44. Passafium, M., Nakagawa, T., Sala, C. and Sheng, M. (2003) Induction of dendritic spines by an extracellular domain of AMPA receptor subunit GluR2. *Nature*, **424**, 677–681.
45. Eastwood, S.L., McDonald, B., Burnet, P.W., Beckwith, J.P., Kerwin, R.W. and Harrison, P.J. (1995) Decreased expression of mRNAs encoding non-NMDA glutamate receptors GluR1 and GluR2 in medial temporal lobe neurons in schizophrenia. *Brain Res. Mol. Brain Res.*, **29**, 211–223.
46. Eastwood, S.L., Kerwin, R.W. and Harrison, P.J. (1997) Immunohistochemical evidence for a loss of alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionate-preferring non-N-methyl-D-aspartate glutamate receptors within the medial temporal lobe in schizophrenia. *Biol. Psychiatry*, **41**, 636–643.
47. Kajimoto, Y., Shirakawa, O., Kuno, T., Nishino, N. and Nakai, H. (1995) Delayed changes in neural visinin-like calcium-binding protein gene expression caused by acute phencyclidine administration. *J. Neural Transm. Gen. Sect.*, **100**, 257–262.
48. Bernstein, H.G., Becker, A., Keilhoff, G., Spilker, C., Gorczyca, W.A., Braunewell, K.H. and Grecksch, G. (2003) Brain region-specific changes in the expression of calcium sensor proteins after repeated applications of ketamine to rats. *Neurosci. Lett.*, **339**, 95–98.
49. Spilker, C., Dresbach, T. and Braunewell, K.H. (2002) Reversible translocation and activity-dependent localization of the calcium-myristoyl switch protein VII-IP-1 to different membrane compartments in living hippocampal neurons. *J. Neurosci.*, **22**, 7331–7339.
50. Mathisen, P.M., Johnson, J.M., Kawczak, J.A. and Tuohy, V.K. (1999) Visinin-like protein (VII-IP) is a neuron-specific calcium-dependent double-stranded RNA-binding protein. *J. Biol. Chem.*, **274**, 31571–31576.
51. Hansen, T., Olsen, L., Lindow, M., Jakobsen, K.D., Ullum, H., Jonsson, E., Andreassen, O.A., Djurovic, S., Melle, L., Agartz, I. *et al.* (2007) Brain expressed micromas implicated in schizophrenia etiology. *PLoS ONE*, **2**, e873.
52. Burmistrova, O.A., Goltsov, A.Y., Abramova, I.I., Kaloda, V.G., Orlova, V.A. and Rogaev, E.I. (2007) MicroRNA in schizophrenia: genetic and expression analysis of miR-130b (22q11). *Biochemistry (Moscow)*, **72**, 578–582.
53. Igloi, G.L. (1996) Nonradioactive labeling of RNA. *Anal. Biochem.*, **233**, 124–129.
54. Valoczi, A., Hornyik, C., Varga, N., Burgyan, J., Kauppinen, S. and Havelda, Z. (2004) Sensitive and specific detection of microRNAs by northern blot analysis using LNA-modified oligonucleotide probes. *Nucleic Acids Res.*, **32**, e175.
55. Livak, K.J. and Schmittgen, T.D. (2001) Analysis of relative gene expression data using real-time quantitative PCR and the 2(-Delta Delta C(T)) Method. *Methods*, **25**, 402–408.

---

## CHAPTER 5

*Schizophrenia is associated with an  
increase in cortical microRNA biogenesis*

---

---

**CHAPTER 5: Schizophrenia is associated with an increase in cortical  
microRNA biogenesis**

**Natalie J. Beveridge**, Erin Gardiner, Adam P. Carroll, Paul A. Tooney  
and Murray J. Cairns

**Molecular Psychiatry (2009) pp 1-14**  
2009 Journal Impact Factor: 15.039

**Statement IV: Author contribution to Chapter 5 manuscript**

Author	Description of Contribution to Article	Signature
Natalie J. Beveridge	Designed and executed the study. Provided significant insight into the interpretation of the data. Wrote the manuscript.	
Erin Gardiner	Provided some technical assistance.	
Adam P. Carroll	Provided some technical assistance.	
Paul A. Tooney	Aided in establishing the methodology.	
Murray J. Cairns	Designed the study, provided the concept and corrected the manuscript.	

4<sup>th</sup> November, 2010

---

**PROFESSOR JOHN ROSTAS**  
Deputy Head of Faculty (Research and Research Training)

---

## ORIGINAL ARTICLE

## Schizophrenia is associated with an increase in cortical microRNA biogenesis

NJ Beveridge<sup>1,2</sup>, E Gardiner<sup>1,2</sup>, AP Carroll<sup>1,2</sup>, PA Tooney<sup>1,2</sup> and MJ Cairns<sup>1,2</sup><sup>1</sup>Schizophrenia Research Institute, Sydney, NSW, Australia and <sup>2</sup>School of Biomedical Sciences, Faculty of Health, and Hunter Medical Research Institute, The University of Newcastle, University Drive, Callaghan, NSW, Australia

MicroRNA expression profiling and quantitative reverse transcription-PCR analysis of the superior temporal gyrus and the dorsolateral prefrontal cortex revealed a significant schizophrenia-associated increase in global microRNA expression. This change was associated with an elevation of primary microRNA processing and corresponded with an increase in the microprocessor component *DGCR8*. The biological implications for this extensive increase in gene silencing are profound, and were exemplified by members of the miR-15 family and other related microRNA, which were significantly upregulated in both brain regions. This functionally convergent influence is overrepresented in pathways involved in synaptic plasticity and includes many genes and pathways associated with schizophrenia, some of which were substantiated *in vitro* by reporter gene assay. Given the magnitude of microRNA changes and their wide sphere of influence, this phenomenon could represent an important dimension in the pathogenesis of schizophrenia.

Molecular Psychiatry advance online publication, 1 September 2009; doi:10.1038/mp.2009.84

**Keywords:** schizophrenia; microRNA; miRNA; DGCR8; dicer

## Introduction

Schizophrenia is a debilitating neuropsychiatric disorder characterized by a diverse range of symptoms and neurocognitive impairments. Although its exact pathogenesis remains obscure, there is a broad consensus that schizophrenia is of neurodevelopmental origin, arising through the complex interplay of numerous genetic and environmental factors.<sup>1</sup> Some insight into the molecular interactions within this matrix has been provided by high-throughput gene expression analyses of post-mortem brain tissues.<sup>2–6</sup> These investigations have consistently shown that numerous genes are affected in schizophrenia. Although some of these changes reflect alterations in known candidate genes and their downstream influences, most are inexplicable and their origins may lie well beyond the reach of these well-known mechanisms. Despite the perplexing array of findings, there are patterns in schizophrenia-associated gene expression that are indicative of systematic regulatory dysfunction. In contexts where these coincide with functional pathways, for example, in neurotransmitter systems and neural development, they support plausible hypotheses that correspond with our

limited understanding of schizophrenia pathophysiology. Efforts to understand the underlying mechanisms driving these changes in gene expression have focused predominantly on genetic and epigenetic influences on transcription, mediated by alterations in signal-transduction pathways, their transcription factors, or gene promoter elements and associated chromatin structure. However, some recent studies have emerged showing that post-transcriptional influences on gene expression mediated by changes in non-coding microRNA (miRNA) expression are also associated with schizophrenia.<sup>7</sup> We identified an increase in miR-181b expression in the superior temporal gyrus in schizophrenia and analyzed its activity with respect to candidate genes suppressed in the same tissue.<sup>8</sup> We now present evidence suggesting that this represented a mere fraction of the overall scale of schizophrenia-associated alteration in miRNA expression. This striking deviation in global miRNA expression was observed in post-mortem tissue from both the superior temporal gyrus (STG) and the dorsolateral prefrontal cortex (DLPFC) and seemed to involve an increase in miRNA biogenesis.

## Materials and methods

## Tissue collection and dissection

Fresh frozen post-mortem STG gray matter tissue from 21 subjects with schizophrenia and 21 non-psychiatric controls and DLPFC gray matter from 15 subjects with schizophrenia and non-psychiatric controls was obtained through the NSW Tissue Resource Centre,

Correspondence: Dr MJ Cairns, School of Biomedical Sciences, Faculty of Health, and Hunter Medical Research Institute, The University of Newcastle, University Drive, Callaghan, NSW 2308, Australia.  
E-mail: murray.cairns@newcastle.edu.au  
Received 11 December 2008; revised 7 July 2009; accepted 20 July 2009

The University of Sydney, Australia. The gray matter tissue was taken from the outer edge of blocks of STG tissue that was obtained from the most caudal coronal brain slice containing the STG (Brodmann's Area 22) or DLPFC (Brodmann's Area 9). Dissections were performed blind on coded tissue blocks such that disease status was not identifiable during this procedure. In all cases, a diagnosis of schizophrenia in accordance with DSM-IV criteria was confirmed by medical file review using the Item Group Checklist of the Schedules for Clinical Assessment in Neuropsychiatry and the Diagnostic Instrument for Brain Studies. Consent was obtained from the next of kin, and subjects with a significant history of drug or alcohol abuse, or other condition or gross neuropathology that might have influenced the agonal state were excluded. In addition, control subjects were excluded if there was a history of alcoholism or suicide. All subjects were of Caucasian descent. Subjects with schizophrenia were matched for gender, age, brain hemisphere, postmortem interval (PMI) and pH (Supplementary Table 1). The tissue was dissected and RNA extracted as described earlier.<sup>8</sup>

#### MicroRNA expression profiling

The microarray procedure was carried out as described earlier,<sup>9</sup> with some alterations.<sup>8</sup> miRNAs were labeled directly by a ligation approach using 3 µg total RNA. A synthetic reference library consisting of oligonucleotides (representing the entirety of miR-Base version 7.1) was labeled with Ulysis platinum-conjugated AlexaFluor 647 (equivalent to Cy5) for detection in the control channel, according to the manufacturer's instructions (Invitrogen, Carlsbad, CA). The unconjugated label was then removed by gel filtration through a Sephadex G-25 spin column (GE Healthcare, Piscataway, NJ). The labeled reference library was used at 1/700 dilution, alongside the Cy3-labeled miRNAs in each array hybridization. Microarrays were prepared using anti-sense Locked Nucleic Acid (LNA) oligonucleotides (Exiqon, Vedbaek, Denmark) corresponding to the miRBase Version 7.1, containing 322 human miRNA sequences. The oligonucleotide probes were printed in quadruplicate onto GAPS-2 glass slides (Corning, Lowell, MA) by the Australian Genome Research Facility. Feature deposition consistency was analyzed before hybridization by examining spot autofluorescence and after hybridization by comparing the reference intensity (AlexaFluor 647) from probe replicates. Single- and double-mismatch probes for a number of miRNAs were also printed in quadruplicate to assess the hybridization specificity. The slides were prepared as described earlier<sup>8</sup> and hybridized for 2 h at 55 °C in a rotary hybridization oven. Arrays were then scanned and raw image extracted with a Genepix 4000B Scanner and Genepix Pro 3.0 software (Axon Instruments, Sunnyvale, CA). Features with a median Cy3 pixel intensity value more than 200% background had the background subtracted and were normalized with respect to U6 small nuclear RNA

(snRNA) expression. Differential miRNA expression was analyzed using Significance Analysis of Microarrays (SAM) version 2.23 (Stanford University)<sup>10</sup> (available from <http://www-stat.stanford.edu/~tibs/SAM/>). SAM uses permutations of the data to determine whether multiple differences are significantly related to the disorder. The threshold for significance was determined with respect to the false-discovery rate. Any miRNA showing a false-discovery rate <5% was considered as significantly altered. The SAM analysis parameters were: two-class unpaired analysis, *t*-test statistic and 5000 permutations of the data.

#### Total RNA analysis

Total RNA from the STG was quantified using a RNA Quant-it assay according to the manufacturer's instructions (Invitrogen). Individual and pooled RNA samples (schizophrenia and control groups) (100 ng µl<sup>-1</sup>) were dephosphorylated in 1 × SAP buffer and 1 unit of shrimp alkaline phosphatase (Fermentas, Vilnius, Lithuania) at 37 °C for 30 min. After heat inactivation, the dephosphorylated RNA was then rephosphorylated in the presence of [<sup>32</sup>P-γ] adenosine triphosphate in 1 × polynucleotide kinase forward reaction buffer and 1 unit of polynucleotide kinase (Fermentas). Labeled RNA was then combined with an equal volume of formamide/bromophenol blue/25 mM EDTA loading dye and denatured at 95 °C before electrophoresis on a 16% denaturing (TBE/Urea) sequencing gel. Images were generated and analyzed from the radiolabeled gel using a Typhoon phosphorimager and ImageQuant software (GE Bioscience, Piscataway, NJ).

#### Quantitative reverse transcription-PCR (Q-PCR)

Reverse transcription and Q-PCR was conducted as described earlier<sup>8</sup> with some adaption. Reactions were carried out in a final volume of 12.5 µl using a 7500 Real Time PCR system (Applied Biosystems, Foster City, CA). For miRNA expression, the delta Ct was calculated by subtracting the Ct of the endogenous controls (geometric mean of U6 snRNA, U44 small nucleolar RNA (snoRNA) and U49 snoRNA) from the Ct of the miRNA. For mRNA expression, the delta Ct was calculated by subtracting the Ct of the endogenous controls (geometric mean of β-glucuronidase and hydroxymethylbilane synthase) from the Ct of the mRNA. Primary miRNA (pri-miRNA) transcripts and processed precursor miRNA (pre-miRNA) hairpins were reverse transcribed using random primers as described for mRNA.<sup>8</sup> Primers specific for the pri-miRNAs were designed to amplify a segment of the primary transcript upstream of the precursor sequence. The pre-miRNA primers were designed to hybridize to partially single-stranded segments within the precursor hairpin in both the precursor miRNA and the primary miRNA transcript. A dissociation curve analysis was performed for every Q-PCR reaction. A single peak was observed for all reactions to confirm the specificity of the reaction. In



some cases, further confirmation was achieved by gel electrophoresis, in which products of the correct size were observed on the gel.

#### Statistical analyses

The demographic characteristics for each cohort were compared using Student's *t*-tests to verify matching for age, PMI and tissue pH. PMI was higher in the DLPFC schizophrenia group ( $29.9 \pm 11.0$  h) when compared with the control group ( $21.9 \pm 9.9$  h;  $P = 0.045$ ). The Kolmogorov–Smirnov test for normality was used to determine whether each data set was normally distributed to satisfy the conditions for parametric statistics (Prism 4.00, GraphPad Software, Inc., La Jolla, CA). To determine the significance of differential miRNA expression between the two cohorts, an un-paired one-tailed *t*-test was applied. Differential gene expression (mRNA) was determined by un-paired two-tailed Student's *t*-tests, in which significance was considered as  $P < 0.05$ . In addition, Pearson's product moment correlations were performed for miRNA/mRNA expression levels and the demographic variables (age, PMI and pH) using control data. Where expression showed correlation, the significance was further tested for analysis of covariance (ANCOVA) using the demographic variable as a covariate (SPSS Statistics 17.0, SPSS Inc., Chicago, IL).

#### Target gene and pathway analyses

Putative target genes were identified using the publically available database, TargetCombo (which combines information gathered from multiple databases such as Diana-microT, PicTar, TargetScanS and miRanda; available at <http://www.diana.pcbi.upenn.edu/cgi-bin/TargetCombo.cgi>). Pathway analyses of the target gene lists were carried out using the Database for Annotation, Visualization, and Integrated Discovery bioinformatics resource (available at <http://david.abcc.ncifcrf.gov/>).

**Cell culture, transfection and target gene reporter assay**  
Human embryonic kidney cells (HEK)-293 cell cultures were maintained as confluent monolayers at  $37^\circ\text{C}$  with 5%  $\text{CO}_2$  and 90% humidity in Dulbecco's modified Eagles's medium (DMEM) with 10% (vol/vol) fetal calf serum, 20 mM HEPES (4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid), 0.15% (wt/vol $^{-1}$ ) sodium bicarbonate and 2 mM L-glutamine. Cells were seeded into 24-well plates and transfected 24 h later using Lipofectamine 2000 (Invitrogen). In each case transfections were performed according to the manufacturer's instructions, with 100 nM synthetic miRNA or anti-miR oligonucleotide (Table 1). Validation of predicted target genes was accomplished by co-transfecting HEK293 cells with synthetic miRNA or an LNA-modified antisense inhibitor and recombinant firefly luciferase reporter gene constructs containing 3'-UTR sequences substituted from the target gene. Oligonucleotides encoding target gene miRNA recognition elements were annealed to

form *SpeI* and *HindIII* restricted overhangs of a ligatable cassette compatible with *SpeI* and *HindIII* digested pMIR-REPORT vector (Ambion, Austin, TX) (Table 1). Reporter gene silencing in response to miRNA co-transfection was monitored with respect to a control plasmid expressing renilla luciferase using the dual-luciferase reporter assay (Promega, Madison, WI). To control for the nonspecific effects associated with siRNA transfection, the controls were co-transfected with mutant miRNAs or mutant anti-miRs. The miR-15 family miRNAs (that share an identical seed pairing region) were all controlled with a mutant form of miR-16 containing a scrambled seed-pairing region. Transfection of miR-107 was controlled by a mutant control version of miR-107 containing a scrambled seed pairing sequence. Although these reporter gene constructs, consisting of the miRNA recognition elements (MREs) and a small amount of 3'-UTR (Table 1), are useful for evaluating target-miRNA interactions, the reporter genes' mRNA secondary structure will be different from that of the native transcript and could positively or negatively influence the extent of gene silencing observed.

## Results

#### Elevation of miRNA expression in the STG in schizophrenia

Changes in miRNA expression have broad implications for disease, as each miRNA molecule is capable of influencing the expression of hundreds of target genes. The expression of miRNA has been shown to be important during development, particularly in the mammalian brain;<sup>11</sup> therefore, it is plausible that these molecules have great significance in neurodevelopmental disorders such as schizophrenia. In this study, we analyzed miRNA expression in the STG (Brodmann's Area 22, 17 matched pairs of schizophrenia and non-psychiatric controls) and the DLPFC (Brodmann's Area 9, 15 matched pairs), using a microarray printed with LNA-modified capture probes corresponding to miRBase version 7.1 (Exiqon).<sup>9</sup> In contrast to our earlier study, which identified two differentially expressed miRNAs in a relatively small cohort of STG tissue normalized by global miRNA expression,<sup>8</sup> these arrays were also furnished with two probes specific for different sites in the U6 snRNA that enabled external or miRNA-independent normalization of miRNA expression between samples. In this new analysis, miR-181b (earlier found to be upregulated in the STG) represented only one of many significantly elevated miRNAs in the schizophrenia group. This observation, apparent in scatter plots of the average expression between schizophrenia and controls for each miRNA (Figure 1a), implied there was a schizophrenia-associated global elevation of miRNA expression in the STG. The significance of these changes was supported by SAM analysis, which reported that 59 miRNAs (or 21% of the miRNAs expressed in the STG) were upregulated (Supplementary Table 2).

**Table 1** Oligonucleotide sequences

Type	Name	Sequence	Target
Primers <sup>a</sup>	U6-probe	5'-GCCATGCTAATCTTCTCTGTATC-3'	U6 snRNA
	U6-F339	5'-CGGCAGCACATATACTAAAATTGG-3'	U6 snRNA
	U49-F	5'-ATCACTAATAGGAAGTCCGTC-3'	U49 snoRNA
	U49-R	5'-ACAGGAGTAGTCTTCGTCACT-3'	U49 snoRNA
	U44-F	5'-TGATAGCAAATGCTGACTGA-3'	U44 snoRNA
	U44-R	5'-CAGTTAGAGCTAATTAAGACC-3'	U44 snoRNA
	107-F	5'-AGCAGCATTGTACAG-3'	miR-107
	107-R	5'-GTAAAACGACGGCCAGTTGATAGCC-3'	miR-107
	15a-F <sup>b</sup>	5'-T + AG + CAGCACATAA-3'	miR-15a
	15a-R	5'-GTAAAACGACGGCCAGTCACAAACCA-3'	miR-15a
	15b-F	5'-TAGCAGCACATCAT-3'	miR-15b
	15b-R	5'-GTAAAACGACGGCCAGTTGTAAACC-3'	miR-15b
	16-F	5'-TAGCAGCACATCAT-3'	miR-16
	16-R	5'-GTAAAACGACGGCCAGTTGTAAACC-3'	miR-16
	128a-F	5'-TCACAGTGAACCCG-3'	miR-128a
	128a-R	5'-GTAAAACGACGGCCAGTAAAGAGAC-3'	miR-128a
	181a-F	5'-AACATTCAACGCTG-3'	miR-181a
	181a-R	5'-GTAAAACGACGGCCAGTACTCACCAG-3'	miR-181a
	181b-F	5'-TTTCTAACATTTCATTGCT-3'	miR-181b
	181b-R	5'-CAACCTTCTCCACCCGAC-3'	miR-181b
	195-F	5'-T + AGCAGCACAGA-3'	miR-195
	195-R	5'-GTAAAACGACGGCCAGTGCCAATATT-3'	miR-195
	19a-F	5'-TGTGCAAAATCTATGC-3'	miR-19a
	19a-R	5'-GTAAAACGACGGCCAGTTCAGTTT-3'	miR-19a
	20a-F	5'-T + AA + AGTGCTTATAGTG-3'	miR-20a
	20a-R	5'-GTAAAACGACGGCCAGTCTACCTG-3'	miR-20a
	219-F	5'-T + GAT + TGTCCAAAC-3'	miR-219
	219-R	5'-GTAAAACGACGGCCAGTAGAATTGC-3'	miR-219
	26b-F	5'-TT + CA + AGTAATTCAGG-3'	miR-26b
	26b-R	5'-GTAAAACGACGGCCAGTAACCTAT-3'	miR-26b
	27a-F	5'-TT + CACAGTGGCTA-3'	miR-27a
	27a-R	5'-GTAAAACGACGGCCAGTGCAGAACT-3'	miR-27a
	29b-F	5'-T + AG + CACCATTGAA-3'	miR-29c
	29c-R	5'-GTAAAACGACGGCCAGTTAACCGAT-3'	miR-29c
	338-F	5'-AA + CAATATCCTGGT-3'	miR-338
	338-R	5'-GTAAAACGACGGCCAGTCACTCAGC-3'	miR-338
	7-F	5'-T + GGAAGACTAGTGA-3'	miR-7
	7-R	5'-GTAAAACGACGGCCAGTACAACAAAA-3'	miR-7
	let-7d-F	5'-AGA + GGTAGTAGGT-3'	let-7d
	let-7d-R	5'-GTAAAACGACGGCCAGTAACATGTC-3'	let-7d
	let-7e-F	5'-TG + AGGTAGGAGT-3'	let-7e
	let-7e-R	5'-GTAAAACGACGGCCAGTACTATACA-3'	let-7e
	M13-F	5'-GTAAAACGACGGCCAGT-3'	Rev primer for miRNA Q-PCR
	GUSB-F	5'-GCCAATGAAACAGGTATCCC-3'	GUSB
	GUSB-R	5'-GCTCAAGTAAACAGGCTGTTTCC-3'	GUSB
	HMBS-F	5'-GAGAGTGATTCCGCTGGGTA-3'	HMBS
	HMBS-R	5'-CAGGGTACGAGGCTTTCAAT-3'	HMBS
	FXR2-F	5'-ACCGCCAGCCAGTCACTGTG-3'	FXR2
	FXR2-R	5'-AGTCACCCCTCTGTCTGAAA-3'	FXR2
	DICER1-F	5'-CACATCAATAGATACTGTGCT-3'	DICER
	DICER-R	5'-TTGGTGGACCAACAATGGAGG-3'	DICER
	DGCR8-F	5'-GCTGAGGAAAGGGAGGAG-3'	DGCR8
	DGCR8-R	5'-ACGTCCACGGTGCACAG-3'	DGCR8
	DROSHA-F	5'-AAGCGTTAATAGGAGCTGTTTACT-3'	DROSHA
	DROSHA-R	5'-CGTCCAAATAACTGCTTGGCT-3'	DROSHA
	XPO5-F	5'-ATATATGAGGCACTGCGCC-3'	EXP-5
	XPO5-R	5'-AAACTGGTCCAGTGAGTCCCT-3'	EXP-5
	DDX26-F2	5'-AGATCCGAAAGCCAGGAAGAAAA-3'	DDX26
	DDX26-R2	5'-TTTGTAACCTGCCTTGACATGC-3'	DDX26
	DDX5-F	5'-AAGGATGAAAAACTTATTCGT-3'	DDX5
	DDX5-R	5'-TTTTCATGTTTGAATTCATT-3'	DDX5
	DDX17-F	5'-GTGAAAAAGACCACAAGTTGA-3'	DDX17
	DDX17-R	5'-TACACATAGCTGGCCACCAT-3'	DDX17
	FXR2-F	5'-ACGGCCAGCCAGTCACTGTG-3'	FXR2
	FXR2-R	5'-AGTCACCCCTCTGTCTGAAA-3'	FXR2
	pri-181b-2-F1	5'-AAGAAGAGCCAGGAGTCAGC-3'	pri-181b-2
	pri-181b-2-R1	5'-TCAGTTGGTGGGTTGCCTT-3'	pri-181b-2
	pre-181b-2-F	5'-CTGATGGCTGCACTCAACAT-3'	pre-181b

Table 1 Continued

Type	Name	Sequence	Target
Cassettes <sup>a</sup>	pre-181b-2-R	5'-TGATCAGTGAGTTGATTCAGACT-3'	pre-181b
	pri-26b-F	5'-CCGTGCTGTCTCCCT-3'	pri-26b
	pri-26b-R	5'-CGAGCCAAGTAATGGAGAACAG-3'	pri-26b
	pre-26b-F	5'-GACCCAGTTCAAGTAATTCAGGA-3'	pre-26b
	pre-26b-R	5'-CGAGCCAAGTAATGGAGAACAG-3'	pre-26b
	VSNL1-107-T	5'-CTAGTTCTCCGAAAGCCTGGGCAGAAATGTGCTGCAAA-3'	VSNL1
	VSNL1-107-B	5'-AGCTTTTGACAGCACATTTCTGCCAGGCTTTGGAGGAA-3'	VSNL1
	RELN-107-T	5'-CTAGTTTACTTGTATGTTGTAATATTTTGGCTGCTGAATT-3'	RELN
	RELN-107-B	5'-AGCTAAATTCAGCAGCAAAATATTACAACATAACAAGTAA-3'	RELN
	HTR2A-107-T	5'-CTAGCTATTTTCAAGTGGAAACCTTGCTGCTATGCTGTTCA-3'	HTR2A
	HTR2A-107-B	5'-AGCTTGAACAGCATAGCAGCAAGGTTTCCACTTGAAATAG-3'	HTR2A
	GRIN3A-107-T	5'-CTAGGCACAAACCTATCAAGAGCTGCTGCTTCCCT-3'	GRIN3A
	GRIN3A-107-B	5'-AGCTAGGGAAGCAGCAGCTCTTGATAGGGTTTGTGC-3'	GRIN3A
	PLEXNA2-107-T	5'-CTAGGACAGTTCTGCTCTGTGACTGCTGCTTTGCTATG-3'	PLEXNA2
	PLEXNA2-107-B	5'-AGCTCATGCAAAAGCAGCAGTCACAGAGGCAGAACTGTC-3'	PLEXNA2
	DLG4-107-T	5'-CTAGGTCGGGAGCCAGGGAAGACTGGAATGCTGCCG-3'	DLG4
	DLG4-107-B	5'-AGCTCGGCAGCATTTCCAGTCTTCCCTGGCTCCGGAC-3'	DLG4
	DRD1-107-T	5'-CTAGCAATTTACGATCTTAGGTGGTAATGAAAGTATGCTGCTT-3'	DRD1
	DRD1-107-B	5'-AGCTCAAAAGCAGCATATCTTTTCAATACCACTAAGATCGTAAAT-3'	DRD1
	GRM7-107-T	5'-CTAGGTTTGTAAATAGTACTTTCTGTTAATCTTGCTGCTTATGTG-3'	GRM7
	GRM7-107-B	5'-AGCTCACATAAGCAGCAAGATTAACGAAAGTACTTATTACAAC-3'	GRM7
miRNA <sup>d</sup>	RGS4-107-T	5'-AATGCACTAGTCCACATTGTAGCCTAATATTCATGCTGCCTGCCA TGAAGCTTAATGC-3'	RGS4
	RGS4-107-B	5'-GCATTAAAGCTTCATGGCAGGCAGCATGAATATTAGGCTACAATGTGA CTAGTGCATT-3'	RGS4
	miR-107 +	5'-AGCAGCAUUGUACAGGGCUAUA-3'	miR-107
	miR-107 -	5'-AUAGCCUGUACAAUGGUGUAUU-3'	miR-107
	miR-15a +	5'-UAGCAGCACAUAUUGGUUGUG-3'	miR-15a
	miR-15a -	5'-CAAACCAUUAUGUGCUGUUAUU-3'	miR-15a
	miR-15b +	5'-UAGCAGCACAUAUUGGUUAUA-3'	miR-15b
	miR-15b -	5'-UAAACCAUGAUGUGCUGUUAUU-3'	miR-15b
	miR-16 +	5'-UAGCAGCAGCUAAUAUUGGCG-3'	miR-16
	miR-16 -	5'-CCAAUAUUUACGUGCUGUUAUU-3'	miR-16
Anti-miRs <sup>e</sup>	miR-195 +	5'-UAGCAGCAGCAAAUAUUGGCG-3'	miR-195
	miR-195 -	5'-CAUAUUUUCUGUGCUGUUAUU-3'	miR-195
	control-miRNA-1 +	5'-AUCCACCACGUAUAUUGGCG-3'	miR-15 family
	control-miRNA-1 -	5'-CCAAUAUUUACGUGGUGGAUCG-3'	miR-15 family
	control-miRNA-2 +	5'-UCCACCAUUGUACAGGGCUAUA-3'	miR-107
	control-miRNA-2 -	5'-AUAGCCUGUACAUUGGUGAAUU-3'	miR-107
	Anti-miR-107	5'-T + GAT + AGC + CCT + GTA + CAA + TGC + TG-3'	miR-107
	Anti-miR-15a	5'-C + ACA + AAC + CAT + TAT + GTG + CTG + CTA-3'	miR-15a
	Anti-miR-15b	5'-T + GTA + AAC + CAT + GAT + GTG + CTG + CTA-3'	miR-15b
	Anti-miR-16	5'-C + GCC + AAT + ATT + TAC + GTG + CTG + CTA-3'	miR-16
Control anti-miR-1	Anti-miR-195	5'-G + CCA + ATA + TTT + CTG + TGC + TGC + TA-3'	miR-195
	Control anti-miR-1	5'-C + GCC + AAT + ATT + TAC + GTG + GTG + GAT-3'	miR-15 family
	Control anti-miR-2	5'-T + GAT + AGC + CCT + GTA + CAT + TGG + TG-3'	miR-107

<sup>a</sup>The direction of primers with respect to the target sequence was denoted as either F or R for forward and reverse, respectively. The underlined sequence is not gene specific and was used to provide a primer recognition sequence. For miRNA Q-PCR, the Rev primer is used for reverse transcription, and the For primer is used in the Q-PCR with M13-F as the reverse primer.

<sup>b</sup>The positions of LNA-modified bases are preceded by a '+' symbol.

<sup>c</sup>*SpeI/HindIII* cassettes containing putative target recognition elements were used to generate recombinant luciferase reporter gene constructs. 'T' indicates top strand and 'B' indicates bottom strand.

<sup>d</sup>Synthetic miRNAs are used to over-express microRNA. '+' indicates top strand and '-' indicates bottom strand.

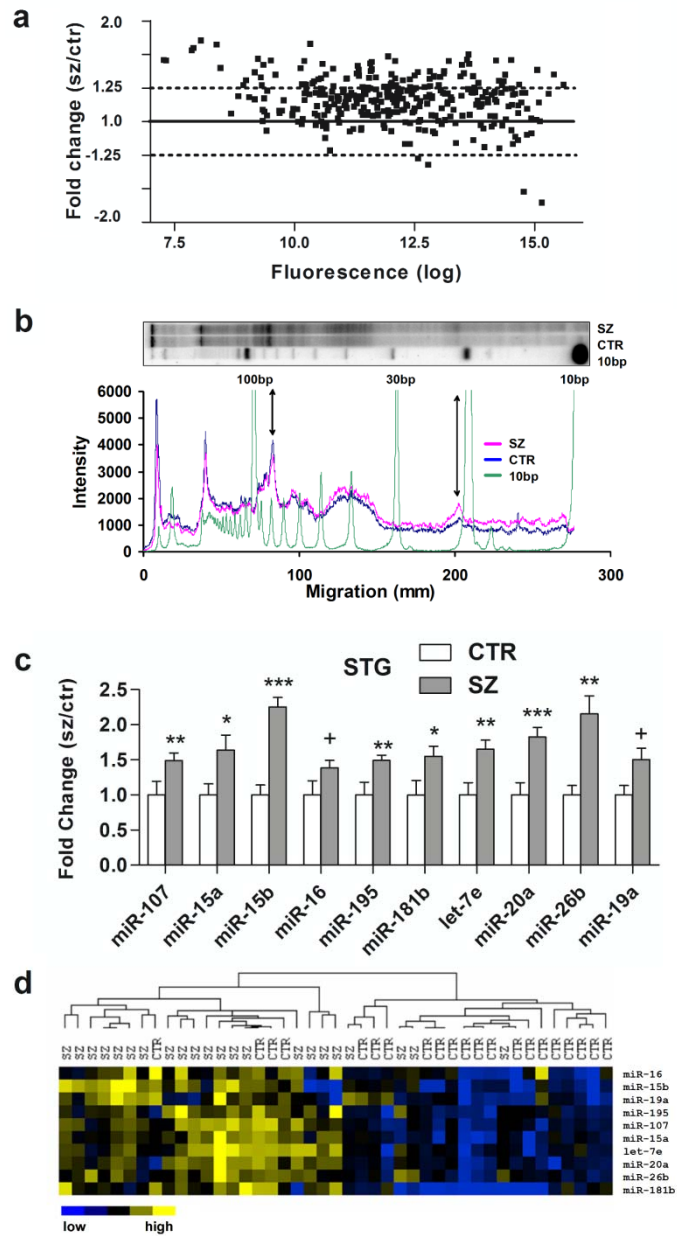
<sup>e</sup>Anti-miRs are used to suppress endogenous microRNA.

With the apparent scope of this alteration in small RNA expression, we considered that it might be possible to directly visualize this in the small RNA fraction of <sup>32</sup>P-labeled total RNA separated on a sequencing gel. On pooled samples this experiment

revealed that the ~22-nt band (corresponding to the miRNAs) was 1.5 times more intense for the schizophrenia sample than that of the controls (normalized to the ~75-nt tRNA band) (Figure 1b). In individual samples, the schizophrenia-associated increase in the

22/75-mer ratio was 1.26-fold ( $P < 0.05$ ), indicative of a general increase in small RNA expression in schizophrenia (Supplementary Table 3).

For more specific evidence of this phenomenon, Q-PCR assays for 10 miRNAs shown to be among the most significantly upregulated by microarray analysis



were established. The relative expression values for each miRNA across an extended cohort, consisting of 21 schizophrenia samples and 21 matched controls of post-mortem cortical gray matter from the STG, were normalized with respect to the geometric mean of three constitutively expressed small RNAs (including U6 snRNA, U44 and U49 snoRNA) (Figure 1c). In each case the level of concordance with the microarray and Q-PCR was very high, and in many cases the average schizophrenia-associated increase was even greater by Q-PCR than that observed by microarray. This trend was also highly visible in individual samples clustered by expression and visualized by heat map (Figure 1d). Unsupervised clustering of these differentially expressed miRNAs was characterized by a high degree of segregation between the schizophrenia and control groups. Prominent among this group of miRNAs associated with schizophrenia was the apparent upregulation of the miR-15 family miRNAs such as miR-15a, miR-15b and miR-195, all of which share the same functionally important seed-pairing region and consequently a large proportion of target genes. In addition, miR-107 was among the most significantly upregulated miRNA in the STG and also shared a high degree of seed region homology with the miR-15 family (Figure 1c). Collectively they are predicted to target a wide array of target genes, with many of them implicated in schizophrenia, such as brain *BDNF*, *NRG1*, *RELN*, *DRD1*, *HTR4*, *GABR1*, *GRIN1*, *GRM7*, *CHRM1* and *ATXN2*.

#### Elevation of miRNA expression in the DLPFC in schizophrenia

In view of the possibility that these changes in miRNA expression were merely STG-related phenomena, we initiated a similar investigation of the DLPFC (BA9), a region most frequently identified in the neuropathology of schizophrenia. Total RNA from post-mortem gray matter from a cohort of 15 cases with a history of schizophrenia and 15 matched controls with no record of psychiatric illness was extracted and subjected to microarray analysis as described for the STG. The miRNA expression profile in this tissue was similar to that in the STG, with 274 expressed miRNAs (compared with 280 in the STG). Importantly, the DLPFC showed a schizophrenia-associated global increase in miRNA expression that

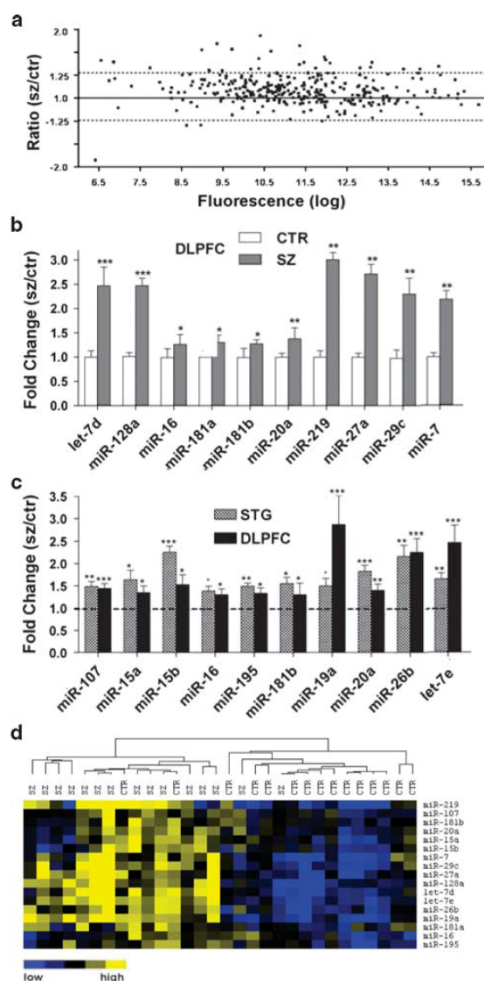
was broadly consistent with the observations in the STG (Figure 2a). According to SAM analysis, 26 (9.5%) of the miRNAs expressed in the DLPFC were significantly upregulated, such as miR-181b, miR-16 and miR-20a, which were also increased in the STG.

Again, to validate the microarray results, Q-PCR assays were performed on a subset of 10 differentially expressed miRNAs as described for the STG, using the expression of three constitutively expressed small RNAs as a reference. This analysis supported the array findings and in some cases exceeded the expectation by showing an even stronger schizophrenia-associated upregulation in miRNAs (Figure 2b). To determine whether the differentially expressed miRNAs in common extended beyond the scope identified by SAM analysis of the DLPFC microarray experiment, the DLPFC samples were also examined for the remaining schizophrenia-associated miRNAs validated for the STG cohort. These miRNAs, including let-7e, miR-19a, miR-26b, miR-107 and the remaining members of the miR-15 family, were all found to be significantly upregulated in the DLPFC by Q-PCR (Figure 2c). In a manner similar to the STG cohort, unsupervised hierarchical clustering of miRNA expression in individual DLPFC samples also produced very good segregation between the schizophrenia and control groups (Figure 2d).

#### Altered miRNA biogenesis in the STG and DLPFC

The scope and consistency of the schizophrenia-associated increase in miRNA expression led us to consider both miRNA processing and the activity of genes in the miRNA biogenesis pathway in this context. For this purpose, we analyzed the relative expression of pri-miRNA and pre-miRNA in addition to the mature miRNA transcripts for miR-181b and miR-26b. Interestingly, although there was a significant increase in pre-miRNA species (consistent with the mature miR-181b and miR-26b), there was no difference in transcription of the pri-miRNA, or the host gene mRNA (*CDTSP1*) for the intronic miR-26b (Figure 3b). This supported the hypothesis that there was a schizophrenia-associated increase in miRNA biogenesis rather than any change at the level of miRNA transcription. To further support this assertion, we examined the expression of the microprocessor constituents *Drosha* and *DGCR8* involved in

**Figure 1** Schizophrenia-associated miRNA expression in the superior temporal gyrus (STG). (a) Average fold change of miRNA expression (schizophrenia to control) was plotted against log<sub>2</sub>-transformed fluorescence values ( $n=17$  matched pairs). A global increase in miRNA expression in the STG in schizophrenia is indicated by the majority of miRNA showing a ratio  $>1.0$ . (b) Electrophoresis of dephosphorylated total RNA (pooled samples) labeled with polynucleotide kinase (PNK). Whole lane densitometry of the phosphor image indicated an increase in small RNA in the schizophrenia cohort (pink trace) compared with the controls (blue trace), particularly in the small RNA fraction (20–24 nt) region corresponding to most miRNAs (indicated by long arrow). Densitometry was normalized to the ~75-nt band in each lane (indicated by short arrow). (c) Increased miRNA expression in the STG was validated using quantitative real-time reverse transcription-PCR (Q-PCR) ( $n=21$  matched pairs). Level of expression for controls was set at 1. Bars are mean  $\pm$  s.e.m. \* $P<0.05$ ; \*\* $P<0.01$ ; \*\*\* $P<0.001$ ; + miR-16 and miR-19a were significant by  $t$ -test but were found to correlate with pH ( $r=-0.459$  and  $-0.443$ , respectively) and fell short of significance by analysis of covariance. (d) Q-PCR expression data hierarchically clustered (correlation uncentered, average linkage; Cluster 3.0). Blue indicates low expression and yellow indicates high expression (Java Treeview; <http://www.sourceforge.net/projects/jtreeview/files>).



**Figure 2** Schizophrenia-associated miRNA expression in the dorsolateral prefrontal cortex (DLPFC). **(a)** miRNA expression in the DLPFC in schizophrenia was characterized by the global upregulation illustrated in this scatter plot (see Figure 1a for description), with the majority of individual miRNAs showing a ratio >1.0. **(b)** Increased miRNA expression in the DLPFC was validated using quantitative real-time reverse transcription-PCR (Q-PCR) ( $n = 15$  matched pairs). Level of expression for controls was set at 1. **(c)** Further Q-PCR expression analysis indicated that 11 miRNAs with altered expression showed an upregulation in both the superior temporal gyrus and DLPFC. Bars indicate mean fold change + s.e.m. \* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ . **(d)** Q-PCR expression data were subjected to hierarchical clustering and heat map, shown as described in Figure 1d.

primary miRNA processing.<sup>12</sup> The mRNA for both of these microprocessor components was found to be significantly upregulated in the DLPFC, and *DGCR8* was also upregulated in the STG (Figure 3c). Importantly, *DGCR8* was shown to be upregulated in 13 of the 15 matched pairs of DLPFC tissue, and in 16 of the 21 matched pairs of STG when analyzed as matched pairs rather than by their cohort-wide average (Figure 3d). These microprocessor components are thought to be rate limiting in the miRNA biogenesis pathway,<sup>13</sup> and, as a consequence, their elevation in schizophrenia represents a highly plausible explanation for the corresponding increase in both pre-miRNA and mature miRNA expression. The expression of additional genes implicated in primary miRNA processing, such as the deadbox helicases *DDX5* and *DDX17*, were also examined. Neither of these genes, however, was significantly altered in either part of the cerebral cortex. The difference in magnitude observed in differential miRNA and pre-miRNA expression (Figure 3b) was possibly due to some dilution of the pre-miRNA by pri-miRNA template as the pre-miRNA primer set has the capacity to amplify both of these sequences. However, it is also conceivable that other influences downstream of the microprocessor could further elevate mature miRNA expression and contribute to this difference. In this regard, we examined the expression of *Exportin-5*, *Dicer* and *FXR2* by Q-PCR and found that *Dicer* was also significantly upregulated in schizophrenia in the DLPFC (Figure 3c). *Dicer* remained significant after ANCOVA using brain pH as a covariate, despite showing some correlation with pH in the DLPFC ( $r = -0.553$ ;  $F = 4.26$ ; d.f. = 1, 27;  $P = 0.048$ ).

#### Target genes and pathways associated with miR-107 and miR-15 family microRNAs

To gain some appreciation of the biological implications of changes in miRNA expression observed in schizophrenia, we examined predicted miRNA targets and their associated pathways to see whether any patterns emerged. A conspicuous aspect of miRNA expression analyses in the STG and DLPFC was the prominence of all members of the miR-15 family and miR-107, all of which share a similar seed region (Figure 4a). To ascertain an overall perspective of this influence, a collection of predicted target genes derived using a range of search algorithms (collated on the TargetCombo web service <http://www.diana.pcbi.upenn.edu/cgi-bin/TargetCombo.cgi>)<sup>14</sup> was subjected to pathway analysis using the Database for Annotation, Visualization, and Integrated Discovery bioinformatics resource (<http://david.abcc.ncifcrf.gov/tools.jsp>)<sup>15</sup> Predicted target genes common to the miR-15 family and miR-107 were highly enriched in pathways involved in neural connectivity and synaptic plasticity, such as axon guidance, long-term potentiation, Wingless/int (Wnt), epidermal growth factor receptor family (ErbB) and Mitogen-activated protein (MAP) kinase signaling (Supplementary Table 4). These processes are repeatedly



implicated in the pathophysiology of schizophrenia and a number of individual genes have been shown to be associated with schizophrenia.

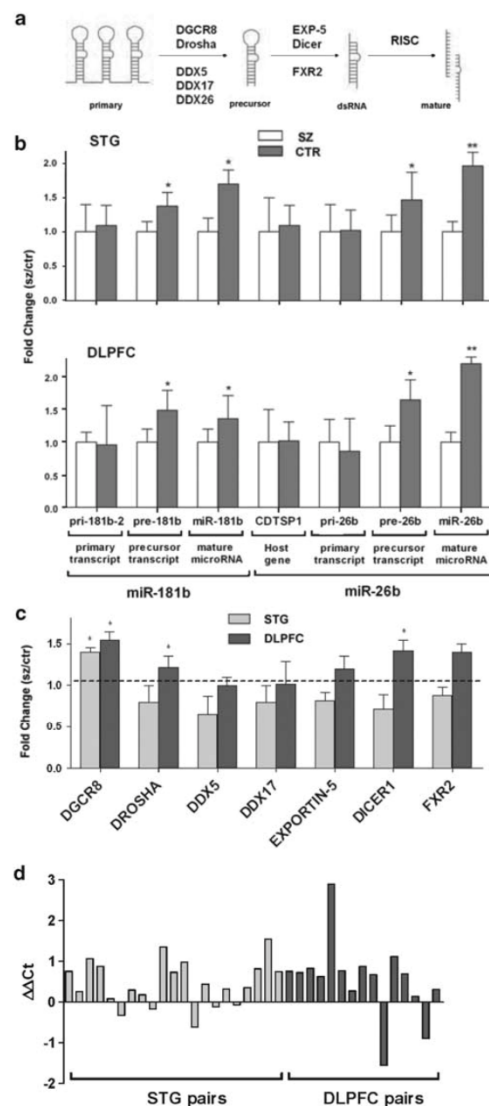
#### Target gene silencing in vitro

To substantiate a link between these schizophrenia-associated target genes and altered expression in this group of miRNAs, the respective MREs from nine target genes, such as *RGS4*, *GRM7*, *GRIN3A*, *HTR2A*, *RELN*, *VSNL1*, *DLG4*, *DRD1* and *PLXNA2*, were

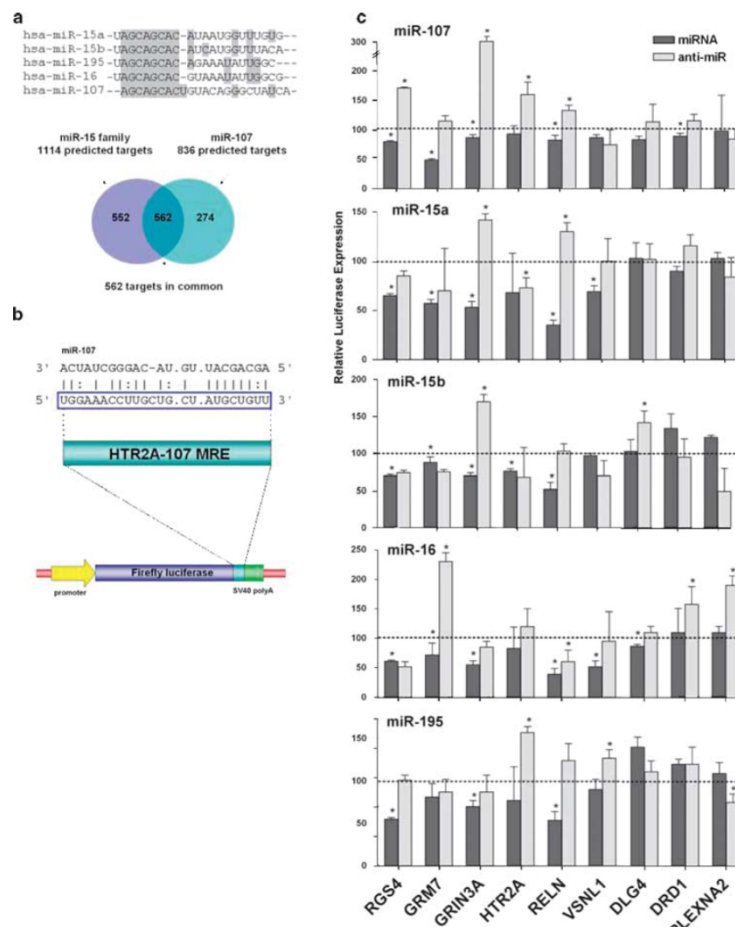
cloned into the 3'-UTR region of a luciferase reporter gene construct and co-transfected into a recipient cell line with miRNA or anti-miRs (miRNA antagonists). The extent of reporter gene activity and the influence of miRNAs were then determined by measuring the relative luciferase activity (Figure 4c).<sup>16</sup> Many of these constructs behaved in accordance with the expectation and were significantly repressed in the presence of synthetic miRNA, and significantly de-repressed (increased luciferase) in the presence of the corresponding anti-miR (Figure 4c, Supplementary Table 5). The most consistently responsive targets were derived from the 3'-UTR of *RGS4*, *GRM7*, *GRIN3A* and *RELN*, whereas the least responsive was *PLXNA2*. With respect to the miRNA, miR-107 appeared to have the greatest overall effect, whereas miR-195 had the least effect on these target gene constructs. Collectively, these reporter assays showed a potential relationship between genes reported to be associated with schizophrenia and a large functionally related group of upregulated miRNAs.

#### Discussion

Analysis of the post-mortem brain tissue from two regions of the cerebral cortex in schizophrenia revealed a substantial alteration of the post-transcriptional regulatory environment, characterized by a global increase in miRNA expression. This change could have profound implications for the development and ongoing pathophysiology of the disorder, as each miRNA has the capacity to regulate the expres-



**Figure 3** Alterations in miRNA processing in schizophrenia. **(a)** Simplified schematic of miRNA biogenesis showing genes involved in key enzymatic steps. **(b)** Primary, precursor and mature transcripts for miR-181b were analyzed by Q-PCR in the superior temporal gyrus (STG). The primary transcript was not altered in schizophrenia; however, the precursor and mature transcripts were both upregulated 1.4-fold ( $P=0.048$ ) and 1.7-fold ( $P=0.039$ ), respectively. The host gene of miR-26b (*CDTSP1*) and primary transcript were not altered. The precursor and mature miR-26b transcript were both upregulated in schizophrenia (1.5-fold ( $P=0.023$ ) and 1.9-fold ( $P=0.001$ ), respectively). In the dorsolateral prefrontal cortex (DLPFC), a similar trend followed. Host gene and primary transcripts were not altered in schizophrenia. For miR-181b, the precursor and mature were upregulated 1.5-fold ( $P=0.043$ ) and 1.4-fold ( $P=0.039$ ), respectively. For miR-26b, the precursor and mature were upregulated 1.6-fold ( $P=0.046$ ) and 2.2-fold ( $P=0.001$ ), respectively. **(c)** Expression of miRNA biogenesis genes was analyzed in the STG ( $n=21$  matched pairs) and the DLPFC ( $n=15$  matched pairs). *DGCR8* was significantly upregulated in the STG and DLPFC, whereas *Drosha* and *Dicer* were significantly upregulated in the DLPFC only. Bars indicate mean fold change (schizophrenia to control)  $\pm$  s.e.m. \* $P<0.05$ ; \*\* $P<0.01$  unpaired Student's *t*-test. **(d)** *DGCR8* expression was determined by Q-PCR in matched paired samples (SZ vs CTR). *DGCR8* was upregulated in 16 out of 21 matched pairs of STG tissue and in 13 out of 15 matched pairs of DLPFC tissue.



**Figure 4** Regulation of schizophrenia-associated reporter gene constructs by miRNA. **(a)** Sequence alignment showing miR-107 and the miR-15 family seed region homology (gray highlight). Together, the two groups were predicted to have many target genes in common (Venn diagram). **(b)** The pMIR-REPORT miRNA expression reporter system contains a firefly luciferase gene under the control of the cytomegalovirus (CMV) promoter. Putative miRNA recognition elements for various schizophrenia candidate genes were inserted into the multiple cloning site in the 3'-UTR of the firefly luciferase gene (*HTR2A* shown as an example). **(c)** A matrix chart showing the relative activity of reporter gene constructs (x-axis) in response to co-transfected miRNA (dark bars) or their cognate anti-miR (light bars). Relative luciferase activity for each reporter/miRNA/anti-miR combination was expressed as a percentage of the response to scrambled controls ( $\pm$ s.d.;  $*P < 0.05$ ).

sion of hundreds of target genes. Studies in model systems have highlighted the significance of miRNA expression in brain development and a host of more specific neurobiological functions, such as regulation of the left-right asymmetry, long-term potentiation and establishment or maintenance of dendrites.<sup>17–21</sup> In this work, we focused on the implications of miRNAs in the miR-15 family and closely related miR-107 as these functionally convergent

miRNAs were consistently upregulated in both regions of the cerebral cortex in schizophrenia, and could collectively contribute a significant biological influence.

The miR-15 family of miRNAs has already been shown to have an important role in chronic lymphocytic leukemia, with a well-characterized association between a reduction of miR-15a/miR-16 concentration and increased expression of the anti-apoptosis



gene *BCL2*.<sup>22</sup> The relationship between miR-15 family expression and this gene may also have the opposite implications in schizophrenia, which has been associated with a downregulation of *BCL2* expression. Reduced *BCL2* expression in schizophrenia, perhaps in response to increased miR-15 family expression, is thought to contribute to elevated cortical apoptosis, cerebral atrophy and even a reduction in the risk of some forms of cancer.<sup>23–25</sup>

Pathway analysis of predicted target genes suggested that there are probably many other ways of influence of this group of miRNAs that are of significance to schizophrenia, such as axon guidance, long-term potentiation, WNT, ErbB and MAP kinase signaling (Supplementary Table 4). Many of these predicted target genes, such as *RGS4*, *GRM7*, *GRIN3A*, *HTR2A*, *RELN*, *VSNL1*, *DLG4*, *DRD1* and *PLXNA2*, have been shown to be associated with schizophrenia.<sup>26–33</sup> In relation to the current study, *RGS4* and *VSNL1* were reported to be downregulated in the same STG tissue;<sup>8,34</sup> however, the expression of these and other candidate genes has not been analyzed at the protein level in these cohorts. To further examine the potential for a functional relationship between MREs in these candidate genes and the miR-15-related miRNAs, we established luciferase reporter constructs and measured the degree of silencing from individual miRNA. Regulation of 3'-UTR elements from the metabotropic glutamate receptor *GRM7* and the N-methyl-D-aspartic acid (NMDA) receptor subunit *GRIN3A* was particularly strong and, along with *DLG4* (PSD95; scaffold protein that supports these and other receptors in the post-synaptic density), provides a post-transcriptional mechanism that could underlie the many accounts of schizophrenia-associated glutamatergic hypofunction.<sup>35</sup> It may also explain the apparent conflict between the schizophrenia-associated reduction of region-specific protein expression in the absence of change or even paradoxical increase in corresponding mRNA.<sup>36</sup> Another target gene element that showed a consistent response to miR-107 and the miR-15 family miRNAs was one derived from the Reelin (*RELN*) 3'-UTR. *RELN* is a secreted glycoprotein involved in neuronal migration and synaptogenesis during development. It is also important for the establishment of long-term memory in the adult brain because of its role in the modulation of synaptic activity and dendritic spine development.<sup>37</sup> *RELN* is a highly plausible candidate gene and its expression has been shown to be altered in schizophrenia.<sup>30,38</sup> Although this alteration has been associated with epigenetic regulation through promoter hypermethylation,<sup>39,40</sup> it is now conceivable that post-transcriptional gene silencing is also contributing to *RELN* dysregulation in schizophrenia.

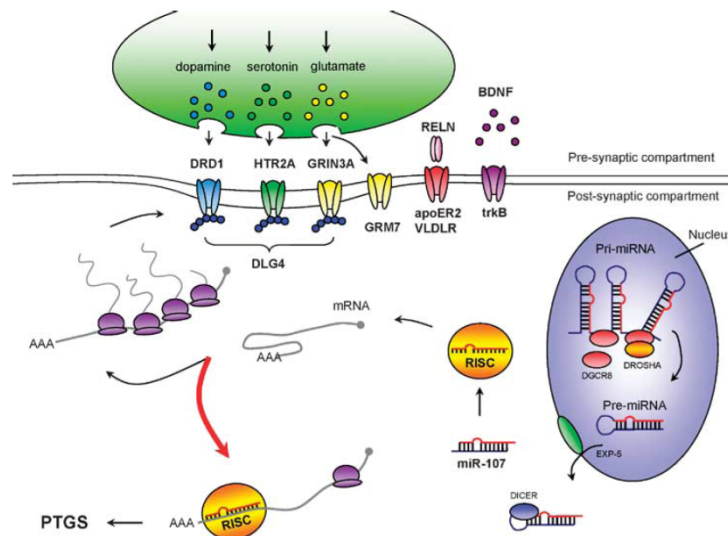
Collectively, these experiments were broadly supportive of a role for this group of miRNAs in the regulation of schizophrenia-associated target genes; however, the response was quite variable for the individual miRNAs, with miR-107 showing the most consistent activity, whereas miR-195 appeared to

have the least activity against the elements tested here. In contrast, a recent study has found that miR-195 (among others) was capable of regulating *BDNF* expression *in vitro*.<sup>41</sup> The temporal and spatial expression pattern of this miR-15 family member in the DLPFC was inversely correlated with *BDNF* and may be important for the developmental regulation of this schizophrenia candidate gene.

Experiments in animal systems may also provide important insight into the behavioral consequences of altered cortical miRNA expression. In a recent study, mice treated with the NMDA receptor antagonist MK801 and hypomorphic *GRIN1* (NR1) mutants showed a marked decrease in miR-219 expression.<sup>42</sup> *CaMKII $\gamma$* , a predicted target gene for this miRNA involved in NMDA signaling, was shown to be sensitive to miR-219 concentration *in vitro*. Moreover, suppression of miR-219 expression via intraventricular delivery of the corresponding LNA-modified anti-miR restored MK801 induced neurobehavioral dysfunction back to levels approaching that of the controls.<sup>42</sup> Interestingly, in our study miR-219 was the most highly upregulated miRNA in the DLPFC and, in addition to the miR-15 family-related miRNA, could also be mediating a schizophrenia-associated reduction in NMDA signaling. These observations add support to the idea that these altered miRNAs are influential in the regulation of schizophrenia-associated genes and provide the basis of a model for the influence of disease-related miRNAs on genes involved in synaptic structure and function (Figure 5).

Although the examples of gene-miRNA interactions mentioned above and modeled in Figure 5 provide a conceptual framework for the mechanisms that may take place in the context of cortical miRNA dysregulation, they may only touch the surface of the broader ramifications for gene regulation in this altered environment. In this regard, it is worth noting that gene expression profiles in the same STG cohort (albeit smaller than the one examined in this study) showed more than twice as many downregulated genes in schizophrenia compared with those upregulated.<sup>5</sup> This observation at the mRNA level has been observed in other studies as well,<sup>4,43,44</sup> and may be reflective of an elevation in global gene silencing mediated by increased miRNA expression in these tissues.

The question of why such an extensive and consistent change in cortical miRNA expression was seen in the schizophrenia group led to the consideration of key components of the miRNA biogenesis pathway. Significantly, we identified a corresponding upregulation of the microprocessor component *DGCR8* mRNA in both the STG and DLPFC. This alteration was consistent with an increase of both mature miRNA and precursor forms of miR-181b and miR-26b in the absence of a change in their level of transcription. Although the mechanism behind this apparent increase in *DGCR8* expression at the mRNA level is currently unknown, the gene is situated



**Figure 5** Model for miRNA-associated dysregulation of synaptic structure and function in schizophrenia. The microprocessor activity is elevated in cortical nuclei as a consequence of a schizophrenia-associated increase in *DGCR8* expression. The increase in pri-miRNA processing results in an increase in pre-miRNAs, which are exported from the nucleus and processed without delay by Exportin-5 (*XPO5*) and Dicer, respectively. Mature miRNAs are recruited into the RNA-induced silencing complex (RISC) and associate with the 3'-UTR of their target transcripts encoding synaptic components (among other proteins), such as neurotrophins/ligands (*BDNF*, *Reelin*), neurotransmitter receptors (*GRM7*, *GRIN3A*, *HTR2A*, *DRD1*) and structural components of the post-synaptic density (*DLG4*). This association reduces the stability of the transcript and reduces its ability to undergo translation. Inappropriate levels of mature miRNA and gene silencing (red arrow) result in the reduction of synaptic proteins and consequently a loss of synaptic structure and function.

within a region of the genome that is prone to spontaneous structural variation associated with schizophrenia and other neurodevelopmental disorders.<sup>45–47</sup> Microdeletion at this locus (22q11.2) is responsible for the DiGeorge/Velocardiofacial syndrome, which is also strongly associated with schizophrenia.<sup>48</sup> In a neurodevelopmental model, mice with a specific deficiency in *DGCR8* and miRNA biogenesis showed similar behavioral deficits to the larger hemizygous deletion of a larger region of chromosome 16 syntenic to that of the 22q11 locus in humans.<sup>49</sup> Although the deletion model and human syndrome, involving haploinsufficiency, does not accord with the increased *DGCR8* activity observed in this study, the low copy repeats that give rise to deletion can also induce microduplication. Interestingly, the syndrome associated with duplication at this locus also appears to be associated with behavioral abnormalities and cognitive deficits akin to those seen in the deletion syndrome, but, like schizophrenia, shows fewer dysmorphic features.<sup>50</sup> As a consequence of this more subtle phenotype, the frequency of this poorly characterized syndrome may be underrepresented through misdiagnosis.<sup>50</sup> Microduplications are also more difficult to identify by classical cytogenetic approaches than microdeletions, which may have

historically masked their relative abundance. In theory, however, they are just as abundant as microdeletions, a view supported in a recent molecular analysis of copy number variation, which found that microduplications outnumbered microdeletions and were more highly associated with schizophrenia.<sup>47</sup> In view of these observations, it is possible that changes in *DGCR8* expression in some individuals could be due to increased gene dosage through chromosomal microduplication.

Alternatively, the increase in *DGCR8* may be due to transcriptional or post-transcriptional dysregulation. A recent study has shown that *DGCR8* is post-transcriptionally autoregulated by its own microprocessor complex.<sup>51</sup> Contrary to expectation, this is probably not miRNA-mediated as the 3'-UTR for *DGCR8* mRNA is almost devoid of predicted MREs, an exception being an MRE for the microprocessor-independent miRNA-intron or mirtron hsa-miR-1227.<sup>52</sup> The mechanism is instead related to the presence of primary miRNA-like hairpin structures in the *DGCR8* mRNA, which are themselves substrates for cleavage by the microprocessor. Cleavage results in destabilization of the mRNA and reduction in *DGCR8* expression.<sup>51</sup> Polymorphisms with a capacity to destabilize these secondary structures in the

mRNA could hinder feedback inhibition and result in *DGCR8* elevation.

In conclusion, our data suggest that schizophrenia is associated with a global increase in miRNA biogenesis and expression in the cerebral cortex. This could have profound neurodevelopmental and broader neurological implications in the context of schizophrenia by influencing genes involved in cortical structure and neural plasticity. It also has significance for our understanding of the mechanism underlying patterns of cortical gene expression associated with the disorder.

### Conflict of interest

The authors declare no conflict of interest.

### Acknowledgments

This study was supported by the Schizophrenia Research Institute, using funding from NSW Health and the Henderson Foundation; a NARSAD Young Investigator Award (MC); a University of Newcastle pilot grant; a Hunter Medical Research Institute project grant; and the MC Ainsworth Research Fellowship in Epigenetics (MC). Tissues were received from the Australian Brain Donor Program's NSW Tissue Resource Centre, which is supported by The University of Sydney, National Health and Medical Research Council of Australia, Schizophrenia Research Institute, National Institute of Alcohol Abuse and Alcoholism, Neurobehavioural Genetics Unit and NSW Department of Health. We thank Professor Vaughan Carr for his critical reading of the paper.

### References

- Harrison PJ. Schizophrenia: a disorder of neurodevelopment? *Curr Opin Neurobiol* 1997; **7**: 285–289.
- Mirnes K, Middleton FA, Marquez A, Lewis DA, Levitt P. Molecular characterization of schizophrenia viewed by microarray analysis of gene expression in prefrontal cortex. *Neuron* 2000; **28**: 53–67.
- Hakak Y, Walker JR, Li C, Wong WH, Davis KL, Buxbaum JD et al. Genome-wide expression analysis reveals dysregulation of myelination-related genes in chronic schizophrenia. *Proc Natl Acad Sci USA* 2001; **98**: 4746–4751.
- Weidenhofer J, Bowden NA, Scott RJ, Tooney PA. Altered gene expression in the amygdala in schizophrenia: up-regulation of genes located in the cytomatrix active zone. *Mol Cell Neurosci* 2006; **31**: 243–250.
- Bowden NA, Scott RJ, Tooney PA. Altered gene expression in the superior temporal gyrus in schizophrenia. *BMC Genomics* 2008; **9**: 199.
- Kim S, Webster MJ. Correlation analysis between genome-wide expression profiles and cytoarchitectural abnormalities in the prefrontal cortex of psychiatric disorders. *Mol Psychiatry* 2008 (E-pub ahead of print).
- Perkins DO, Jeffries CD, Jarskog LF, Thomson JM, Woods K, Newman MA et al. microRNA expression in the prefrontal cortex of individuals with schizophrenia and schizoaffective disorder. *Genome Biol* 2007; **8**: R27.
- Beveridge NJ, Tooney PA, Carroll AP, Gardiner E, Bowden N, Scott RJ et al. Dysregulation of miRNA 181b in the temporal cortex in schizophrenia. *Hum Mol Genet* 2008; **17**: 1156–1168.
- Thomson JM, Parker J, Perou CM, Hammond SM. A custom microarray platform for analysis of microRNA gene expression. *Nat Methods* 2004; **1**: 47–53.
- Tusher VG, Tibshirani R, Chu G. Significance analysis of microarrays applied to the ionizing radiation response. *Proc Natl Acad Sci USA* 2001; **98**: 5116–5121.
- Sempere LF, Freemantle S, Pitha-Rowe I, Moss E, Dmitrovsky E, Ambros V. Expression profiling of mammalian microRNAs uncovers a subset of brain-expressed microRNAs with possible roles in murine and human neuronal differentiation. *Genome Biol* 2004; **5**: R13.
- Gregory RJ, Yan KP, Amuthan G, Chendrimada T, Doratotaj B, Cooch N et al. The microprocessor complex mediates the genesis of microRNAs. *Nature* 2004; **432**: 235–240.
- Thomson JM, Newman M, Parker JS, Morin-Kensicki EM, Wright T, Hammond SM. Extensive post-transcriptional regulation of microRNAs and its implications for cancer. *Genes Dev* 2006; **20**: 2202–2207.
- Sethupathy P, Megraw M, Hatzigeorgiou AG. A guide through present computational approaches for the identification of mammalian microRNA targets. *Nat Methods* 2006; **3**: 881–886.
- Dennis Jr G, Sherman BT, Hosack DA, Yang J, Gao W, Lane HC et al. DAVID: Database for Annotation, Visualization, and Integrated Discovery. *Genome Biol* 2003; **4**: P3.
- Lewis BP, Shih IH, Jones-Rhoades MW, Bartel DP, Burge CB. Prediction of mammalian microRNA targets. *Cell* 2003; **115**: 787–798.
- Giraldez AJ, Cinalli RM, Glasner ME, Enright AJ, Thomson JM, Baskerville S et al. MicroRNAs regulate brain morphogenesis in zebrafish. *Science* 2005; **308**: 833–838.
- Johnston RJ, Hobert O. A microRNA controlling left/right neuronal asymmetry in *Caenorhabditis elegans*. *Nature* 2003; **426**: 845–849.
- Jin P, Zarnescu DC, Ceman S, Nakamoto M, Mowrey J, Jongens TA et al. Biochemical and genetic interaction between the fragile X mental retardation protein and the microRNA pathway. *Nat Neurosci* 2004; **7**: 113–117.
- Ashraf SI, McLoon AL, Sclarsic SM, Kunes S. Synaptic protein synthesis associated with memory is regulated by the RISC pathway in *Drosophila*. *Cell* 2006; **124**: 191–205.
- Schratt GM, Tuebing F, Nigh EA, Kane CG, Sabatini ME, Kiebler M et al. A brain-specific microRNA regulates dendritic spine development. *Nature* 2006; **439**: 283–289.
- Cimmino A, Calin GA, Fabbri M, Iorio MV, Ferracin M, Shimizu M et al. miR-15 and miR-16 induce apoptosis by targeting BCL2. *Proc Natl Acad Sci USA* 2005; **102**: 13944–13949.
- Jarskog LF, Gilmore JH, Selinger ES, Lieberman JA. Cortical bcl-2 protein expression and apoptotic regulation in schizophrenia. *Biol Psychiatry* 2000; **48**: 641–650.
- Jarskog LF, Selinger ES, Lieberman JA, Gilmore JH. Apoptotic proteins in the temporal cortex in schizophrenia: high Bax/Bcl-2 ratio without caspase-3 activation. *Am J Psychiatry* 2004; **161**: 109–115.
- Catts VS, Catts SV. Apoptosis and schizophrenia: is the tumour suppressor gene, p53, a candidate susceptibility gene? *Schizophr Res* 2000; **41**: 405–415.
- Mirnes K, Middleton FA, Stanwood GD, Lewis DA, Levitt P. Disease-specific changes in regulator of G-protein signaling 4 (RGS4) expression in schizophrenia. *Mol Psychiatry* 2001; **6**: 293–301.
- Ohtsuki T, Koga M, Ishiguro H, Horiuchi Y, Arai M, Niizato K et al. A polymorphism of the metabotropic glutamate receptor mGluR7 (GRM7) gene is associated with schizophrenia. *Schizophr Res* 2008; **101**: 9–16.
- Mueller HT, Meador-Woodruff JH. NR3A NMDA receptor subunit mRNA expression in schizophrenia, depression and bipolar disorder. *Schizophr Res* 2004; **71**: 361–370.
- Burnet PW, Eastwood SL, Harrison PJ. 5-HT1A and 5-HT2A receptor mRNAs and binding site densities are differentially altered in schizophrenia. *Neuropsychopharmacology* 1996; **15**: 442–455.
- Impagnatiello F, Guidotti AR, Pesold C, Dwivedi Y, Caruncho H, Pisu MG et al. A decrease of reelin expression as a putative

- vulnerability factor in schizophrenia. *Proc Natl Acad Sci USA* 1998; **95**: 15718–15723.
- 31 Ohnuma T, Kato H, Arai H, Faull RL, McKenna PJ, Emson PC. Gene expression of PSD95 in prefrontal cortex and hippocampus in schizophrenia. *Neuroreport* 2000; **11**: 3133–3137.
  - 32 Okubo Y, Suhara T, Suzuki K, Kobayashi K, Inoue O, Terasaki O *et al*. Decreased prefrontal dopamine D1 receptors in schizophrenia revealed by PET [see comments]. *Nature* 1997; **385**: 634–636.
  - 33 Mah S, Nelson MR, Delisi LE, Reneland RH, Markward N, James MR *et al*. Identification of the semaphorin receptor PLXNA2 as a candidate for susceptibility to schizophrenia. *Mol Psychiatry* 2006; **11**: 471–478.
  - 34 Bowden NA, Scott RJ, Tooney PA. Altered expression of regulator of G-protein signalling 4 (RGS4) mRNA in the superior temporal gyrus in schizophrenia. *Schizophr Res* 2007; **89**: 165–168.
  - 35 Kristiansen LV, Huerta I, Beneyto M, Meador-Woodruff JH. NMDA receptors and schizophrenia. *Curr Opin Pharmacol* 2007; **7**: 48–55.
  - 36 Kristiansen LV, Beneyto M, Haroutunian V, Meador-Woodruff JH. Changes in NMDA receptor subunits and interacting PSD proteins in dorsolateral prefrontal and anterior cingulate cortex indicate abnormal regional expression in schizophrenia. *Mol Psychiatry* 2006; **11**: 737–747.
  - 37 Fatemi SH. Reelin glycoprotein: structure, biology and roles in health and disease. *Mol Psychiatry* 2005; **10**: 251–257.
  - 38 Guidotti A, Auta J, Davis JM, Di-Giorgi-Gerevini V, Dwivedi Y, Grayson DR *et al*. Decrease in reelin and glutamic acid decarboxylase67 (GAD67) expression in schizophrenia and bipolar disorder: a postmortem brain study. *Arch Gen Psychiatry* 2000; **57**: 1061–1069.
  - 39 Grayson DR, Jia X, Chen Y, Sharma RP, Mitchell CP, Guidotti A *et al*. Reelin promoter hypermethylation in schizophrenia. *Proc Natl Acad Sci USA* 2005; **102**: 9341–9346.
  - 40 Abdolmaleky HM, Cheng KH, Russo A, Smith CL, Faraone SV, Wilcox M *et al*. Hypermethylation of the reelin (RELN) promoter in the brain of schizophrenic patients: a preliminary report. *Am J Med Genet B Neuropsychiatr Genet* 2005; **134**: 60–66.
  - 41 Mellios N, Huang HS, Grigorenko A, Rogaev E, Akbarian S. A set of differentially expressed miRNAs, including miR-30a-5p, act as post-transcriptional inhibitors of BDNF in prefrontal cortex. *Hum Mol Genet* 2008; **17**: 3030–3042.
  - 42 Kocerha J, Faghihi MA, Lopez-Toledano MA, Huang J, Ramsey AJ, Caron MG *et al*. MicroRNA-219 modulates NMDA receptor-mediated neurobehavioral dysfunction. *Proc Natl Acad Sci USA* 2009; **106**: 3507–3512.
  - 43 Vawter MP, Crook JM, Hyde TM, Kleinman JE, Weinberger DR, Becker KG *et al*. Microarray analysis of gene expression in the prefrontal cortex in schizophrenia: a preliminary study. *Schizophr Res* 2002; **58**: 11–20.
  - 44 Katsel P, Davis KL, Gorman JM, Haroutunian V. Variations in differential gene expression patterns across multiple brain regions in schizophrenia. *Schizophr Res* 2005; **77**: 241–252.
  - 45 Xu B, Roos JL, Levy S, van Rensburg EJ, Cogos JA, Karayiorgou M. Strong association of *de novo* copy number mutations with sporadic schizophrenia. *Nat Genet* 2008; **40**: 880–885.
  - 46 Stefansson H, Rujescu D, Cichon S, Pietiläinen OP, Ingason A, Steinberg S *et al*. Large recurrent microdeletions associated with schizophrenia. *Nature* 2008; **455**: 232–236.
  - 47 Consortium IS. Rare chromosomal deletions and duplications increase risk of schizophrenia. *Nature* 2008; **455**: 237–241.
  - 48 Murphy KC, Jones LA, Owen MJ. High rates of schizophrenia in adults with velo-cardio-facial syndrome. *Arch Gen Psychiatry* 1999; **56**: 940–945.
  - 49 Stark KL, Xu B, Bagchi A, Lai WS, Liu H, Hsu R *et al*. Altered brain microRNA biogenesis contributes to phenotypic deficits in a 22q11-deletion mouse model. *Nat Genet* 2008; **40**: 751–760.
  - 50 Yobb TM, Somerville MJ, Willatt L, Firth HV, Harrison K, MacKenzie J *et al*. Microduplication and triplication of 22q11.2 a highly variable syndrome. *Am J Hum Genet* 2005; **76**: 865–876.
  - 51 Han J, Pedersen JS, Kwon SC, Belair CD, Kim YK, Yeom KH *et al*. Posttranscriptional crossregulation between Drosha and DGCR8. *Cell* 2009; **136**: 75–84.
  - 52 Berezikov E, Chung WJ, Willis J, Cuppen E, Lai EC. Mammalian mirtron genes. *Mol Cell* 2007; **28**: 328–336.



This work is licensed under the Creative Commons Attribution-NonCommercial-No Derivative Works 3.0 License. To view a copy of this license, visit <http://creativecommons.org/licenses/by-nc-nd/3.0/>

Supplementary Information accompanies the paper on the Molecular Psychiatry website (<http://www.nature.com/mp>)

---

## CHAPTER 6

*Upregulation of Dicer and microRNA  
expression in the dorsolateral prefrontal  
cortex in schizophrenia*

---

---

**CHAPTER 6: Upregulation of Dicer and MicroRNA Expression in the  
Dorsolateral Prefrontal Cortex Brodmann's Area 46 in Schizophrenia**

Danielle M. Santarelli, **Natalie J. Beveridge**, Paul A. Tooney, Murray J. Cairns

**Biological Psychiatry (2011) Vol 69, pp 180-187**  
2009 Journal Impact Factor: 8.369

**Statement V: Author contribution to Chapter 6 manuscript**

Author	Description of Contribution to Article	Signature
Danielle M. Santarelli	Designed and executed the study. Provided significant insight into the interpretation of the data. Wrote the manuscript.	
Natalie J. Beveridge	Designed and executed the study. Provided significant insight into the interpretation of the data. Corrected the manuscript.	
Paul A. Tooney	Aided in data interpretation and manuscript compilation.	
Murray J. Cairns	Designed the study, provided the concept and corrected the manuscript.	

4<sup>th</sup> November, 2010

---

**PROFESSOR JOHN ROSTAS**  
Deputy Head of Faculty (Research and Research Training)

---

---

## ARCHIVAL REPORTS

# Upregulation of Dicer and MicroRNA Expression in the Dorsolateral Prefrontal Cortex Brodmann Area 46 in Schizophrenia

Danielle M. Santarelli, Natalie J. Beveridge, Paul A. Tooney, and Murray J. Cairns

**Background:** MicroRNA (miRNA) are capable of regulating multitudes of target genes and are essential factors in mediating healthy neurodevelopment. We hypothesize that abnormal miRNA levels contribute to the complex global changes in gene expression that underlie the pathophysiology of schizophrenia.

**Methods:** With a commercial bead array platform, we investigated miRNA expression in 74 samples of postmortem dorsolateral prefrontal cortex (Brodmann Area 46) ( $n = 37$  matched pairs schizophrenia/schizoaffective disorder and control subjects). A subset of differentially expressed miRNA and genes in the miRNA biogenesis pathway was also analyzed with quantitative reverse transcription-polymerase chain reaction. Gene targets of miRNAs demonstrating significantly altered expression were predicted, and pathways analysis was performed.

**Results:** After correction for multiple testing, microarray analysis identified differential expression of 28 miRNA in the schizophrenia group. Significantly, 89% of these molecules were elevated in accordance with earlier work in other brain regions that showed a broad increase in miRNA expression in schizophrenia. These observations were supported by quantitative reverse transcription-polymerase chain reaction, for miR-328, miR-17-5p, miR-134, miR-652, miR-382, and miR-107 and were consistent with a schizophrenia-associated increase in miRNA processing through elevated Dicer expression. Target and pathways analysis provided insight into the potential cellular effects, with particular enrichment of miRNA targets in axon guidance and long-term potentiation.

**Conclusions:** These results suggest that schizophrenia is associated with altered miRNA biogenesis and expression, which might have important implications in the complex pathophysiology of the disorder.

**Key Words:** BA46, dicer, gene silencing, microRNA, neuropathology, schizophrenia

Schizophrenia is a complex neuropsychiatric disorder thought to arise during development, because of multiple genetic and environmental risk factors (1,2). Although the precise genetic changes that give rise to the pathology are not clear, numerous genetic loci have been associated with the disorder, and dozens of schizophrenia candidate genes have been reported (3–5). Unfortunately, the effect size of these genes is often small and, alone, not sufficient to support the heritability of schizophrenia. Genome-wide investigation of gene activity in postmortem brain tissue has identified changes in gene expression in postmortem brain of schizophrenia (6–10). These analyses provide a biological dimension to the study of genes in schizophrenia that sometimes intersects with the genetics. In many more cases, however, a functional relationship remains elusive. One trend seen often among many gene expression studies has been the bias toward downregulation of gene activity (8,9,11). These observations give rise to the possibility of an abnormality in gene regulation in schizophrenia. In this event, over-representation of gene repression would implicate a loss of function in mechanisms that promote or elevate gene expression or a gain of function in mechanisms capable of driving a

systematic reduction of gene expression. In this study we explored this latter possibility by examining gene silencing and the influence of miRNA biogenesis in schizophrenia.

The discovery of endogenous regulatory noncoding RNA, known as microRNA (miRNA), has led to wide spread interest because of the implication to several human diseases, including schizophrenia (12–14). miRNA are short (approximately 22 nt) RNA sequences with the capacity to target hundreds of genes via sequence complementarity to the 3' untranslated region of the target messenger RNA (mRNA) (15,16). The consequence of this is predominantly a silencing of gene and/or protein expression. miRNA have already been identified as essential factors in mediating healthy neurodevelopment (17). It is hence plausible to suggest that abnormalities at the miRNA levels might contribute to the complex differences in gene expression and disruptions in neurodevelopmental processes that are apparent in the pathophysiology of schizophrenia.

In the investigation presented here, miRNA expression profiling was performed on postmortem brain tissue of the dorsolateral prefrontal cortex (DLPFC) Brodmann area 46 (BA46), from a cohort of 37 matched pairs of schizophrenia and nonpsychiatric control subjects, with a recently developed commercial miRNA microarray platform (Illumina, Sunnyvale, California). The BA46 is a region of the DLPFC adjacent to BA9, BA10, and the mid-ventrolateral region. Disturbances to BA46 result in a reduced ability to analyze information and make choices on the basis of short-term memory, a cognitive function that is particularly known to be impaired in schizophrenia termed "monitoring of working memory" (reviewed in [18]). Overactivation of BA46 during working memory tasks has been reported in first-degree relatives of schizophrenia (19), further highlighting the anatomical specificity of this region in the disorder. To our knowledge, this is the first miRNA study to be performed in BA46 for schizophrenia and the largest cohort to be used for any miRNA expres-

---

From the Schizophrenia Research Institute (DMS, NJB, PAT, MJC), Sydney; School of Biomedical Sciences and Pharmacy (DMS, NJB, PAT, MJC), Faculty of Health, The University of Newcastle, Callaghan; and the Hunter Medical Research Institute (DMS, NJB, PAT, MJC), New Lambton, New South Wales, Australia.

Address correspondence to Murray J Cairns, Ph.D., School of Biomedical Sciences and Pharmacy, The University of Newcastle, University Drive, Callaghan, New South Wales 2308, Australia; E-mail: [murray.cairns@newcastle.edu.au](mailto:murray.cairns@newcastle.edu.au).

Received Mar 6, 2010; revised Sep 15, 2010; accepted Sep 18, 2010.

0006-3223/\$36.00  
doi:10.1016/j.biopsych.2010.09.030

BIOL PSYCHIATRY 2011;69:180–187  
© 2011 Society of Biological Psychiatry



sion profiling across all previous brain regions studied in schizophrenia (12–14).

## Methods and Materials

### Tissue Sample Cohort

Postmortem brain tissue samples were collected by the NSW Tissue Resource Centre (University of Sydney). Use of this tissue was approved by the University of Newcastle Human Research Ethics Committee, and consent was obtained from the next of kin. All cases had been diagnosed with schizophrenia or schizoaffective disorder according to the DSM-IV criteria and were confirmed by medical file review with the Item Group Checklist of the Schedules for Clinical Assessment in Neuropsychiatry. The class “schizoaffective” refers to patients that experience a combination of schizophrenia and affective disorder, particularly depressive forms of psychosis (20). Subjects with a significant history of drug or alcohol abuse, neurological disorder or medical illness that might have influenced agonal state, any abnormality on neuropathological examination, or head injury were excluded. Control subjects were excluded if there was a history of alcoholism or suicide. All subjects were of Caucasian descent. The cohort comprised 37 matched pairs of postmortem brain tissue from BA46 of the DLPFC on the middle frontal gyrus, from subjects with schizophrenia or schizoaffective disorder and nonpsychiatric control subjects. Samples were matched according to donor age, gender, brain pH, brain hemisphere, and duration of illness, among other characteristics. Full cohort description, matching, and analysis is detailed in Weickert *et al.* (21) and summarized in Table S1 in Supplement 1. Demographic variables age ( $p = .95$ ), pH ( $p = .49$ ), postmortem interval ( $p = .23$ ), and RNA integrity number (RIN) ( $p = .81$ ) do not differ between schizophrenia and control cohorts (two-tailed Student *t* test).

### RNA Extraction

Cortical gray matter tissue was carefully dissected from postmortem brain slices of the crown of the middle frontal gyrus, anterior to the genu of the corpus callosum with a dental drill (21). The tissue was immediately homogenized, and total RNA was extracted with TRIzol reagent (Invitrogen, Carlsbad, California) according to manufacturer instructions. The RNA concentration and integrity was determined with a bioanalyzer (Agilent, Palo Alto, California). Mean RIN was 7.3.

### miRNA Microarray

Profiling of miRNA expression was achieved with the commercial miRNA microarray platform developed by Illumina. Each array matrix on the Illumina microarray platform holds 96 sample arrays, and each array houses 1536 unique oligonucleotide sequence probes for 470 annotated miRNA sequences as well as 265 recently identified miRNA sequences corresponding to miRBase version 9.1 (22). Total RNA (1  $\mu$ g) was amplified and labeled within a 96-well plate format for hybridization to the miRNA bead array matrix according to the manufacturer instructions (Illumina).

### Microarray Data Normalization and Analysis

In this study, schizophrenia-associated miRNA expression was investigated in the DLPFC (BA46) with a commercial bead-based microarray platform (Illumina) (22). Expression data were background subtracted and normalized to the geometric mean of U66 and U49 small nucleolar RNA (snoRNA) expression with BeadStudio software (Illumina, version 3.0), because these had the most stable expression across the control cohort according to geNorm analysis (23). miRNA were considered expressed if fluorescence intensity was at least twice the level of background fluorescence. Differential expres-

sion analysis was performed on normalized data with the Significance Analysis of Microarrays (SAM) statistical analysis program (full academic version 2.23) (24) (<http://www-stat.stanford.edu/~tibs/SAM/>). This program reports the validity of genes that it identifies as being significantly differentially expressed according to a *q*-value, an adaptation of the *p* value that is appropriate for multiple hypothesis testing, and denotes the lowest possible false discovery rate that might occur before a reported gene is not to be considered significantly differentially expressed (25). The SAM differential expression analysis was performed with a two-class unpaired Wilcoxon test of unlogged data and 5000 permutations. Significantly different miRNA were identified as those with a *q*-value  $< 5$  (false discovery rate  $< 5\%$ ).

### Quantitative Real-Time Reverse Transcription Polymerase Chain Reaction (Q-PCR)

Validation of differentially expressed miRNA was performed by Q-PCR on the entire cohort, similarly to that described previously (12). Briefly, 500 ng of sample RNA was treated with DNase-I (Invitrogen), and multiplex reverse transcription was performed with Superscript II reverse transcriptase (Invitrogen), a 3 nmol/L mix of miRNA sequence specific primers and primers for U6 small nuclear RNA and U49 snoRNA. For mRNA Q-PCR, random-primed reverse transcription was performed. For Q-PCR, triplicate reactions were set up in a 96-well format with the epMotion 5070 automated pipetting system (Eppendorf, Hamburg, Germany) and carried out with the Applied Biosystems (Foster City, California) 7500 real-time PCR machine. Serial dilutions of DLPFC complementary DNA were used as standards, and data were analyzed with the relative quantitation method with efficiency correction. Relative miRNA expression was calculated as the ratio of the miRNA and the geometric mean of controls U6 and U49 (the most stable of the three controls as determined by geNorm). Relative mRNA (biogenesis gene) expression was calculated as the ratio of the gene and the geometric mean of controls hydroxymethylbilane synthase (HMBS) and  $\beta$ -glucuronidase (GUSB). Outliers were identified as values  $\pm 3$  SD outside of the mean and were removed. Statistical significance of differential miRNA and mRNA expression between schizophrenia and control samples was assessed by multivariate analysis of variance. To examine the influence of demographic variables (age, postmortem interval, and pH) on miRNA and mRNA expression, data were tested for normality, and Spearman Product Moment correlations were performed on the entire cohort. If the expression of any miRNA or gene significantly correlated with any demographic variable, an analysis of covariance was performed to reassess its significance. The expression of the miRNA biogenesis genes was also examined in a pair-wise fashion. The expression for each schizophrenia sample was compared with the corresponding matched control sample and expressed as a ratio (schizophrenia/control) (e.g., schizophrenia #1 is matched to control #1). Pearson correlations (two-tailed) were also performed on expression data of validated miRNA and the biogenesis genes to identify any similarities in expression.

### Target Gene and Pathway Analysis

miRNA target predictions determined with a variety of algorithms including DIANA-microT, miRanda, PicTar, and TargetScanS were collected for the validated miRNA with the miRGen database (version 4.0) (26) (<http://www.diana.pcbi.upenn.edu/miRGen.html>). Multi-hit miRNA target analysis was also performed with miRanda alone (<http://www.microRNA.org>) to enrich for target genes with three or more target sites for the validated schizophrenia-associated miRNA (27). The frequency of miRNA targeting for any given target gene was determined for the pooled gene list of validated

miRNA with PASW Statistics 18, (SPSS, Chicago, Illinois; IBM, Armonk, New York). In the multi-hit analysis, target genes with more putative miRNA binding sites were assumed to have more potential for post-transcriptional regulation and greater intensity than those with only one or two (28). Pathway analysis of these lists was achieved with the functional annotation tools on the Database for Annotation, Visualization and Integrated Discovery (DAVID; <http://david.abcc.ncifcrf.gov/>) (29,30).

## Results

### Upregulation of miRNA Expression in BA46 in Schizophrenia

High-throughput miRNA expression analysis of 470 annotated miRNA (from miRBase 9.1) revealed that 281 miRNAs (60%) were expressed in BA46. A scatterplot of the average fold change in expression of each expressed miRNA against its log<sub>2</sub>-transformed fluorescence intensity indicated a large upregulation of miRNA in BA46 (Figure 1A), following the trend for global miRNA upregulation observed in BA22 and BA9 tissue. Differential expression analysis by SAM revealed 25 miRNA to be significantly upregulated in schizophrenia and three miRNA to be significantly downregulated (false discovery rate <5%) (Figure 1B). Of the upregulated miRNA, 10 have also been shown to be significantly increased in BA22 (superior temporal gyrus [STG]) and two in BA9 (DLPFC). Unsupervised clustering of the expression data for these miRNA reveals a moderate split between predominantly schizophrenia samples with high miRNA expression (Figure 1B, right) and control subjects with lower miRNA expression (Figure 1B, left).

Validation of 10 differentially expressed miRNA was performed by Q-PCR similarly to that described previously (12). Although not reaching the threshold for significance by array, miR-107 was also included in the Q-PCR analysis, because it has been previously shown to be differentially expressed in BA9 and BA22 (14). Relative miRNA expression was determined with respect to the geometric mean of U6 and U49 snoRNA expression. Significant changes in expression were confirmed for miR-328 (1.32-fold increase,  $p = .005$  covaried for age), miR-17-5p (1.18-fold increase,  $p = .029$ ), miR-134 (1.16-fold increase,  $p = .037$ ), miR-652 (1.15-fold increase,  $p = .032$ ), miR-382 (1.26-fold increase,  $p = .042$ ), and miR-107 (1.34-fold increase,  $p = .042$ ) (Figure 1C).

### Upregulation of miRNA Biogenesis in BA46

The microprocessor component genes DiGeorge syndrome critical region 8 (DGCR8) and Drosha and the type III ribonuclease responsible for cleavage of the pre-miRNA hairpin structure to form the mature miRNA, Dicer, have been shown to have increased expression in BA9 in schizophrenia (14). Alterations in microprocessor component genes might also be influential in the elevation of miRNA expression observed in this microarray analysis of the BA46 cohort. To this end, we examined the expression of these three miRNA biogenesis genes in the context of schizophrenia with Q-PCR. Analysis of covariance was used to assess the significance of gene expression changes in the miRNA biogenesis genes. Dicer displayed a 1.23-fold increase in expression in schizophrenia ( $p = .025$ ; covaried for postmortem interval). The DGCR8 and Drosha both displayed a robust 1.5-fold increase in the schizophrenia cohort but fell below the threshold of statistical significance, due to greater variance within the samples (Drosha  $p = .06$  covaried for age; DGCR8  $p = .16$  covaried for age, pH and RIN). These data support previous observations of increased miRNA biogenesis in schizophrenia. The DGCR8 was considered significantly increased ( $p = .049$ ), when exploring the pair-wise expression of these genes individually, although Drosha ( $p = .096$ ) and Dicer ( $p = .087$ ) fell

below the threshold for significance. Interestingly, when examining the group as a whole, it was revealed that 33 of the 37 matched pairs (89%) display schizophrenia-related upregulation in at least one of these miRNA biogenesis genes (Figures 2B–2D).

Furthermore, correlation analysis indicated a significant relationship between the expression of Dicer with miR-17-5p ( $p = .002$ ) and miR-382 ( $p = .014$ ) and also between the expression of DGCR8 with miR-382 ( $p = .009$ ). There were also numerous significant correlations between the expression of various miRNA and a significant correlation between Dicer and Drosha expression ( $p = .04$ ) (refer to Table S2 in Supplement 1 for the complete correlation matrix).

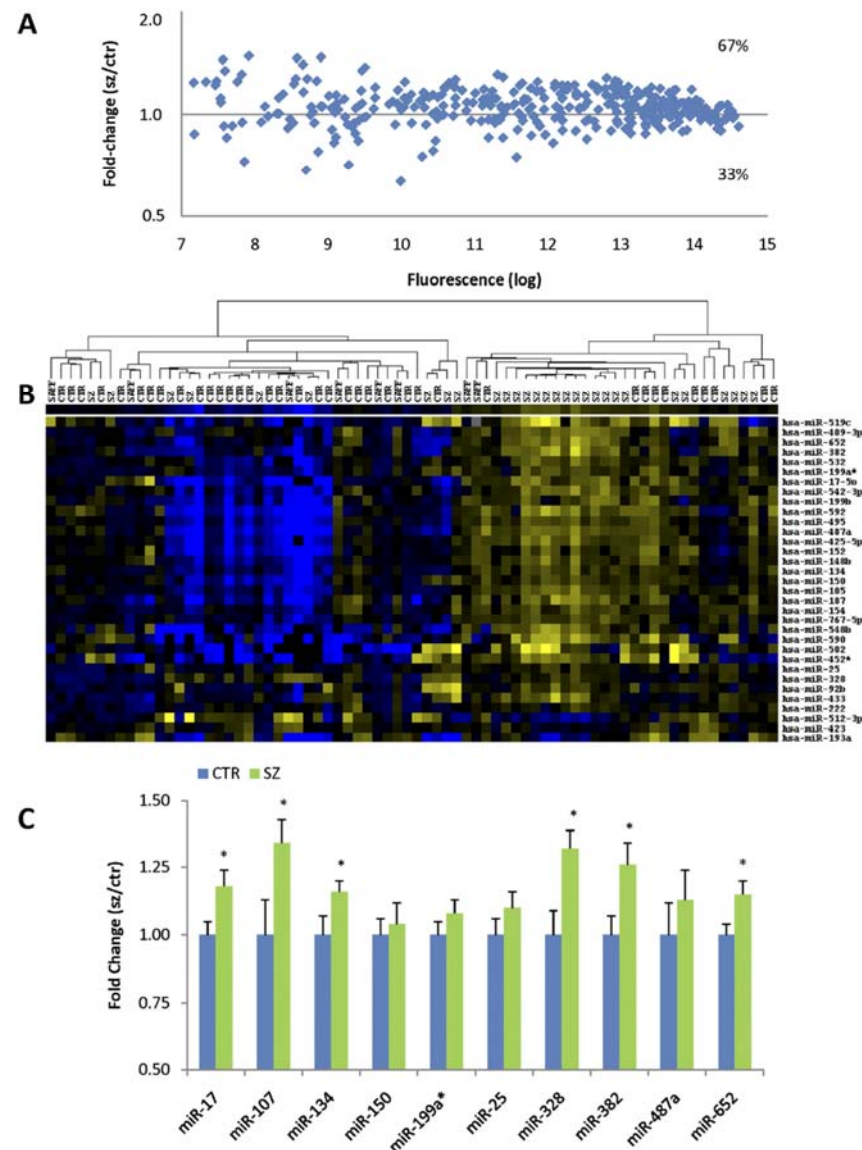
### Functional Significance of Upregulated miRNA

To explore the biological implications of validated miRNA altered in schizophrenia, predicted target genes from multiple algorithms were collated with the miRGen database. This identified several schizophrenia candidate genes, including nine glutamate receptors, five serotonin receptors, two  $\gamma$ -aminobutyric acid receptors, neuregulin 1 and two, and brain-derived neurotrophic factor. Pathway analysis performed on these genes also revealed the enrichment of a number of pathways with significance to schizophrenia, including axon guidance (modified Fisher exact test = .017) and long-term potentiation (modified Fisher exact test = .039) (Table 1). Maps of these Kyoto Encyclopedia of Genes and Genomes pathways were obtained via DAVID, allowing visualization of the involvement of target genes within these pathways (Figure S1 in Supplement 1). To provide an extra level of stringency in the pathway analysis, pooled target gene lists generated by miRanda—for the validated miRNA—were filtered on the basis of their target site content, such that only genes with three or more conserved binding sites were included. Target genes hosting a multiplicity of miRNA binding sites for differentially expressed miRNA have a higher probability of being post-transcriptionally regulated and to a greater extent, because of the cooperative or synergistic interactions between multiple RNA-induced silencing complexes on a single target 3' untranslated region (28). Significantly, many of the pathways enriched in this multi-hit target gene analysis retained relevance in the context of schizophrenia and included the axon guidance pathway and long-term potentiation (Table S3 in Supplement 1). Gene ontology analysis of these genes also indicated the enrichment of biological processes with relevance to schizophrenia, including nervous system development, neurogenesis, generation of neurons, and neuron differentiation (Table 2).

## Discussion

We investigated miRNA expression in BA46 of the DLPFC with commercial bead array technology. After background subtraction, normalization, and correction for multiple testing with SAM, we were able to identify 28 miRNA that were differentially expressed in schizophrenia. Significantly, 25 of these miRNA were upregulated with respect to the control subjects, 10 of these in a manner consistent with previous investigation of the STG (BA22), and 2 consistent with investigations in BA9 (14). Many of these altered miRNA, such as miR-17-5p, miR-134, miR-148b, miR-150, miR-222, miR-328, miR-382, and miR-425-5p, have been shown to be brain-enriched, particularly in the cortex (31); and many also display neuron-specific expression (32,33). Consistent with the array and displaying significant upregulation in schizophrenia across the entire cohort were miR-328, miR-17-5p, miR-134, miR-652, and miR-382. Also analyzed by Q-PCR and shown to be significantly upregulated was miR-107, a miRNA displaying consistent elevation in studies of BA9 and STG. This support for an elevation of miRNA expression in schizophrenia



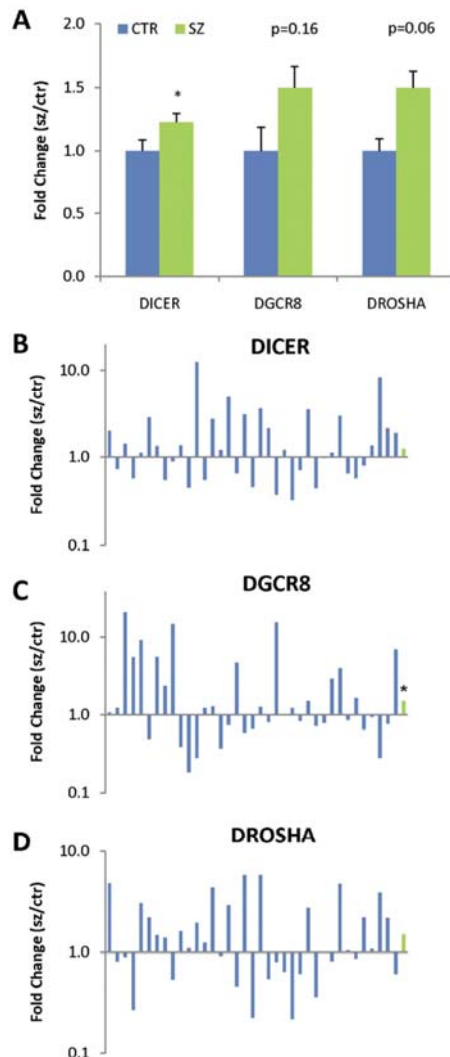


**Figure 1.** Schizophrenia (SZ)-associated microRNA (miRNA) expression in the dorsolateral prefrontal cortex (Brodmann area [BA46]). (A) Scatterplot of the average fold change in expression of each miRNA and  $\log_2$  transformed fluorescence intensity (y axis log scale). (B) Hierarchical clustering of significant upregulated miRNA microarray expression data (uncentered correlation, average linkage; Cluster 3.0). Blue, low expression; yellow, high expression. Produced with Java Treeview 1.1.1 (58) (<http://treeview.sourceforge.net>). (C) Significantly increased miRNA in SZ (BA46) validated by quantitative real-time reverse transcription polymerase chain reaction. Bars represent mean fold change in expression (SZ vs. control subjects [CTR];  $n = 37$  matched pairs) + SEM; \* $p$  value  $< .05$  (analysis of variance/analysis of covariance).

and similarity to previous work led us to again consider the influence of the miRNA biogenesis pathway. In this regard we observed a significant increase in Dicer mRNA expression in BA46 tissue in schizophrenia compared with control subjects. This increase in Dicer expression in BA46 was consistent with a previously reported increase in Dicer in BA9 (14). Interestingly, although the trend to-

ward increases in Drosha and DGCR8 expression (significant in paired analysis) was supportive of elevated miRNA biogenesis in the entire cohort, on an individual matched paired basis, at least one biogenesis gene was found to be upregulated in a large majority (33 of 37; 89%) of pairs. Moreover, there was also significant correlation between the differentially expressed miRNA and be-

[www.sobp.org/journal](http://www.sobp.org/journal)



**Figure 2.** Upregulation of miRNA biogenesis genes in SZ (BA46). (A) Quantitative real-time reverse transcription polymerase chain reaction analysis of miRNA biogenesis genes in SZ versus CTR ( $n = 37$  matched pairs). Bars represent fold change in expression  $\pm$  SEM. (B–D) Pair-wise expression of miRNA biogenesis genes. (B) Dicer expression was upregulated in 21 of the 37 matched pairs. The green bar furthest to the right indicates the overall fold increase. (C) DGCR8 expression was upregulated in 19 of the 37 matched pairs. (D) Drosha expression was upregulated in 20 of the 37 matched pairs. Abbreviations as in Figure 1.

tween various miRNA and the miRNA biogenesis genes. These findings were significant, because each of these genes has the potential to influence the level of cortical miRNA maturation in schizophrenia. Dicer in particular has been shown to play an important role in normal central nervous system development and function. In a zebrafish knockout model, Dicer deficiency was shown to induce failure of brain morphogenesis (17). In a Purkinje cell model system,

www.sobp.org/journal

Dicer inactivation results in cell degeneration and eventually neurodegeneration, due to a significant loss of neuron-specific miRNA (34). Moreover, Dicer has been shown to be enriched in the postsynaptic densities of neurons and activated by calpain in response to synaptic excitation (35). Increased Dicer expression is also associated with differentiation and maintenance of mature neural lineages during development (36,37). In cortical neurons, Dicer has also been shown to localize in the dendrites (36). Upregulation of Dicer and consequential upregulation of global miRNA has also been reported in various tumor cells, such as adenocarcinomas (38). Dicer elevation in the DLPFC in schizophrenia could have important implications for structural and functional plasticity of the synapse and might hence contribute to the pathophysiology of the disorder.

The phenotypic implications of elevated miRNA biogenesis in the context of schizophrenia are very broad and difficult to predict, even when considering individual miRNA. In the case of miR-328, upregulation has been observed in response to prion-induced neurodegeneration in mouse brain, leading to speculation that this might involve the targeting of the transcriptional co-repressor methyl CpG-binding protein 2 (MeCP2) (39). Mutations in MeCP2 are known to be linked to the neurodevelopmental disorder Rett syndrome. The MeCP2 has also been shown to modulate brain-derived neurotrophic factor, a schizophrenia candidate gene involved in the coordination of dendrite/axon development in neurons, thus promoting dendritic spine growth (40,41). By contrast, miR-134 is a brain-specific miRNA localized within dendrites that has been well-characterized as a negative regulator of dendrite development and synaptic maturation, particularly by inhibition of *Limk1* mRNA; however, this inhibition might be relieved by brain-derived neurotrophic factor (33,42). More recently, miR-134 elevation in response to stress has been linked to alternative splicing of acetylcholinesterase, which is known to have downstream neurodegenerative effects (43). Also stress-responsive are miR-382 and miR-17-5p (43). Our group has previously shown expression of the miR-17 family, especially miR-17-5p, to be a feature of undifferentiated SH-SY5Y neuronal cells (44). In that study, miR-17-5p was demonstrated to inhibit the expression of differentiated neuronal cell markers B-cell CLL/lymphoma 2 and myocyte enhancer factor 2D as well as the mitogen-activated protein kinase 12; mitogen-activated protein kinases play important roles in neurite outgrowth. Interestingly, miR-107 was also shown to be significantly upregulated by Q-PCR, having previously shown to be significantly upregulated in

**Table 1.** Enriched KEGG Pathways Involving Target Genes of miRNA Significantly Upregulated in BA46 in Schizophrenia

KEGG ID	Term	N	EASE
hsa04916	Melanogenesis	12	.0063
hsa04010	MAPK signaling pathway	23	.0067
hsa04660	T cell receptor signaling pathway	12	.012
hsa04360	Axon guidance <sup>a</sup>	13	.017
hsa04020	Calcium signaling pathway	15	.036
hsa04720	Long-term potentiation <sup>a</sup>	8	.039
hsa05410	Hypertrophic cardiomyopathy	9	.045

Enriched Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways identified with the Database for Annotation, Visualization and Integrated Discovery functional annotation table tool. Some degree of overprediction of target genes is likely, because multiple prediction algorithms were used in miRecords to ascertain microRNA (miRNA) targets.

BA, Brodmann area; N, number of input genes in pathway; EASE, modified Fisher exact test  $p$  value (probability of enrichment); MAPK, mitogen-activated protein kinase.

<sup>a</sup>Terms of particular interest to the pathophysiology of schizophrenia.

**Table 2.** Pathways Enriched with miRNA Target Genes Containing  $\geq 3$  Binding Sites for Schizophrenia-Associated miRNA

GO ID	Term	N	EASE	FDR
GO:0007399	Nervous system development	198	4.30E-18	7.92E-15
GO:0032502	Developmental process	422	1.35E-12	2.49E-09
GO:0022008	Neurogenesis	111	1.38E-10	2.54E-07
GO:0048699	Generation of neurons	101	3.52E-09	6.49E-06
GO:0030182	Neuron differentiation	80	1.11E-07	2.05E-04
GO:0048666	Neuron development	64	7.65E-07	.001410
GO:0007417	Central nervous system development	75	1.16E-06	.002140
GO:0048812	Neuron projection morphogenesis	44	5.05E-06	.009295
GO:0007420	Brain development	54	8.47E-06	.015597
GO:0031175	Neuron projection development	49	1.21E-05	.022363
GO:0007409	Axonogenesis	39	3.15E-05	.058061
GO:0016337	Cell–cell adhesion	50	4.40E-05	.080955
GO:0050793	Regulation of developmental process	99	7.35E-05	.135319
GO:0030900	Forebrain development	32	8.28E-05	.152382
GO:0019226	Transmission of nerve impulse	58	1.33E-04	.243955
GO:0045664	Regulation of neuron differentiation	28	2.51E-04	.461107
GO:0048041	Focal adhesion formation	8	4.90E-04	.898106
GO:0050767	Regulation of neurogenesis	31	9.30E-04	1.698497
GO:0030031	Cell projection assembly	19	.001164	2.123024
GO:0051960	Regulation of nervous system development	34	.001300	2.366951
GO:0009790	Embryonic development	80	.001360	2.476111
GO:0007268	Synaptic transmission	47	.001779	3.226482
GO:0030099	Myeloid cell differentiation	20	.001818	3.297068
GO:0050773	Regulation of dendrite development	7	.002197	3.971032
GO:0007155	Cell adhesion	94	.002296	4.145431
GO:0009966	Regulation of signal transduction	114	.002393	4.317135

Enriched Gene Ontology (GO) terms identified with the Database for Annotation, Visualization and Integrated Discovery functional annotation table tool. N, number of input genes in the cellular process; FDR, false discovery rate; other abbreviations as in Table 1.

the STG and DLPFC (BA9) of schizophrenia brain (14). Positive results were reported for a reporter gene assay investigating the interaction of miR-107 and a predicted target gene Reelin (RELN). RELN is a notable schizophrenia candidate gene with roles in regulating synaptic activity in the adult brain and, once again, dendritic spine growth (45). Numerous studies have reported reductions in RELN in schizophrenia and other neurological disorders (46–48), supporting the notion that increases in miRNA expression might be the cause of changes in neurological gene expression relevant to the pathophysiology of schizophrenia.

Prediction of potential target genes of the altered miRNA collectively revealed 299 schizophrenia candidate genes. Present within this list were nine glutamate receptors, including GRIN1, GRIN2, and GRIN3 N-methyl-D-aspartate receptors—all potential targets of miR-328—and of which impaired transmission of has been linked to observations of decreased dendrite length and density in cortical neurons in schizophrenia (49) (reviewed in [50–52]). Also on the target list was the early growth response transcription factor EGR3, a schizophrenia candidate gene upregulated at times of high neuronal activity that is critical in numerous synaptic plasticity processes (53) and also reported to be downregulated in schizophrenia (54). According to our target predictions, all the increased miRNA validated by Q-PCR in this study might potentially target EGR3. Furthermore, EGR3 regulates various schizophrenia candidate genes as well as miRNA genes that target additional schizophrenia candidate genes. According to Guo *et al.* (55), this might be an important feedback loop for which disturbances would be highly relevant to schizophrenia.

Pathway analysis of the target list further highlighted the relevance of these upregulated miRNA to the pathophysiology of schizophrenia, with processes involved in nervous system development and synaptic transmission—among numerous

other relevant processes—being highly enriched with target genes. Many of the differentially expressed miRNA share potential target genes and might affect the same biological pathways/processes. Hence, various combinations of miRNA changes of small effect, especially those with roles in schizophrenia-related biological processes, might very well produce a similar outcome in terms of biological abnormalities and ultimately schizophrenia symptoms.

Many of the miRNA reported here to be upregulated in BA46 are either now known or thought to play a part in directing dendritic development. From the collection of information about these miRNA, it is possible that miR-17-5p, miR-134, miR-107, and possibly miR-328 might be involved in intricate modulation of neuron differentiation regulatory processes. Furthermore, target predictions identified numerous neurotransmitter receptors to be potential miRNA targets. Pathway analysis of potential target genes further highlighted processes involved in synaptic transmission as major effect points of these upregulated miRNA. These observations are all consistent with the disconnection hypothesis, which suggests that schizophrenia is a phenomenon of abnormal synaptic plasticity because of inefficient or inappropriate wiring of neural networks (56). This hypothesis has also been supported by neuropathology with reports of dendrite length and density reductions in schizophrenia cortex (49,57).

This study provides further support for a role of altered miRNA expression in the neuropathology of schizophrenia and suggests that disturbances to miRNA biogenesis could be the underlying mechanism. Ultimately, the consequence of this change in regulatory environment is the alteration of gene expression and biological processes that might play a significant role in the pathogenesis and pathophysiology of schizophrenia.



This study was supported by the Schizophrenia Research Institute, with funding from New South Wales (NSW) Health and an M.C. Ainsworth Research Fellowship in Epigenetics (MC); a National Alliance for Research on Schizophrenia and Depression Young Investigator Award; a Hunter Medical Research Institute project grant; an National Health and Medical Research Council project grant 631057; the Neurobehavioral Genetics Unit; and NSW Department of Health. Tissue was dissected and extracted in the Schizophrenia Research Laboratory at the Prince of Wales Medical Research Institute under the supervision of Professor Cynthia Shannon Weickert on behalf of the Australian Brain Donor Program's NSW Tissue Resource Centre. The Tissue Resource Centre is supported by The University of Sydney, National Health and Medical Research Council of Australia, Schizophrenia Research Institute, and the National Institute of Alcohol Abuse and Alcoholism. All authors report no biomedical financial interests or potential conflicts of interest.

Supplementary material cited in this article is available online.

- Harrison PJ (1997): Schizophrenia: A disorder of neurodevelopment? *Curr Opin Neurobiol* 7:285–289.
- Roth TL, Lubin FD, Sodhi M, Kleinman JE (2009): Epigenetic mechanisms in schizophrenia. *Biochim Biophys Acta* 1790:869–877.
- O'Donovan MC, Williams NM, Owen MJ (2003): Recent advances in the genetics of schizophrenia. *Hum Mol Genet* 12:R125–R133.
- Tsuang M (2000): Schizophrenia: Genes and environment. *Biol Psychiatry* 47:210–220.
- Waddington JL, Corvin AP, Donohoe G, O'Tuathaigh CM, Mitchell KJ, Gill M (2007): Functional genomics and schizophrenia: Endophenotypes and mutant models. *Psychiatr Clin North Am* 30:365–399.
- Dean B, Keriakous D, Scarr E, Thomas EA (2007): Gene expression profiling in Brodmann's area 46 from subjects with schizophrenia. *Aust N Z J Psychiatry* 41:308–320.
- Mirnics K, Middleton FA, Lewis DA, Levitt P (2001): Analysis of complex brain disorders with gene expression microarrays: Schizophrenia as a disease of the synapse. *Trends Neurosci* 24:479–486.
- Weidenhofer J, Bowden NA, Scott RJ, Tooney PA (2006): Altered gene expression in the amygdala in schizophrenia: Up-regulation of genes located in the cytomatrix active zone. *Mol Cell Neurosci* 31:243–250.
- Bowden NA, Scott RJ, Tooney PA (2008): Altered gene expression in the superior temporal gyrus in schizophrenia. *BMC Genomics* 9:199.
- Kim S, Webster MJ (2010): Correlation analysis between genome-wide expression profiles and cytoarchitectural abnormalities in the prefrontal cortex of psychiatric disorders. *Mol Psychiatry* 15:326–336.
- Katsel P, Davis KL, Gorman JM, Haroutunian V (2005): Variations in differential gene expression patterns across multiple brain regions in schizophrenia. *Schizophr Res* 77:241–252.
- Beveridge NJ, Tooney PA, Carroll AP, Gardiner E, Bowden N, Scott RJ, et al. (2008): Dysregulation of miRNA 181b in the temporal cortex in schizophrenia. *Hum Mol Genet* 17:1156–1168.
- Perkins DO, Jeffries CD, Jarskog LF, Thomson JM, Woods K, Newman MA, et al. (2007): microRNA expression in the prefrontal cortex of individuals with schizophrenia and schizoaffective disorder. *Genome Biol* 8:R27.
- Beveridge NJ, Gardiner E, Carroll AP, Tooney PA, Cairns MJ (2009): Schizophrenia is associated with an increase in cortical microRNA biogenesis. *Mol Psychiatry*.
- Lau NC, Lim LP, Weinstein EG, Bartel DP (2001): An abundant class of tiny RNAs with probable regulatory roles in *Caenorhabditis elegans*. *Science* 294:858–862.
- Murchison EP, Hannon GJ (2004): miRNAs on the move: miRNA biogenesis and the RNAi machinery. *Curr Opin Cell Biol* 16:223–229.
- Giraldez AJ, Cinalli RM, Glasner ME, Enright AJ, Thomson JM, Baskerville S, et al. (2005): MicroRNAs regulate brain morphogenesis in zebrafish. *Science* 308:833–838.
- Petrides M (2005): Lateral prefrontal cortex: Architectonic and functional organization. *Philos Trans R Soc Lond B Biol Sci* 360:781–795.
- Seidman LJ, Thermenos HW, Poldrack RA, Peace NK, Koch JK, Faraone SV, et al. (2006): Altered brain activation in dorsolateral prefrontal cortex in adolescents and young adults at genetic risk for schizophrenia: an fMRI study of working memory. *Schizophr Res* 85:58–72.
- Tsuang MT, Simpson JC (1984): Schizoaffective disorder: Concept and reality. *Schizophr Bull* 10:14–25.
- Weickert CS, Sheedy D, Rothmond DA, Dedova I, Fung S, Garrick T, et al. (2010): Selection of reference gene expression in a schizophrenia brain cohort. *Aust N Z J Psychiatry* 44:59–70.
- Chen J, Lozach J, Garcia EW, Barnes B, Luo S, Mikoulitch I, et al. (2008): Highly sensitive and specific microRNA expression profiling using BeadArray technology. *Nucleic Acids Res* 36:e87.
- Vandesompele J, De Preter K, Pattyn F, Poppe B, Van RN, De Paepe A, et al. (2002): Accurate normalization of real-time quantitative RT-PCR data by geometric averaging of multiple internal control genes. *Genome Biol* 3:RESEARCH0034.
- Tusher VG, Tibshirani R, Chu G (2001): Significance analysis of microarrays applied to the ionizing radiation response. *Proc Natl Acad Sci U S A* 98:5116–5121.
- Storey JD (2002): A direct approach to false discovery rates. *J R Stat Soc B Stat Methodol* 64:479–498.
- Megraw M, Sethupathy P, Corda B, Hatzigeorgiou AG (2007): miRGen: A database for the study of animal microRNA genomic organization and function. *Nucleic Acids Res* 35:D149–D155.
- John B, Enright AJ, Aravin A, Tuschl T, Sander C, Marks DS (2004): Human MicroRNA targets. *PLoS Biol* 2:e363.
- Hon LS, Zhang Z (2007): The roles of binding site arrangement and combinatorial targeting in microRNA repression of gene expression. *Genome Biol* 8:R166.
- Dennis G Jr, Sherman BT, Hosack DA, Yang J, Gao W, Lane HC, et al. (2003): DAVID: Database for annotation, visualization, and integrated Discovery. *Genome Biol* 4:3.
- Huang da W, Sherman BT, Lempicki RA (2009): Systematic and integrative analysis of large gene lists using DAVID bioinformatics resources. *Nat Protoc* 4:44–57.
- Baskerville S, Bartel DP (2005): Microarray profiling of microRNAs reveals frequent coexpression with neighboring miRNAs and host genes. *RNA* 11:241–247.
- Kim J, Krichevsky A, Grad Y, Hayes GD, Kosik KS, Church GM, et al. (2004): Identification of many microRNAs that copurify with polyribosomes in mammalian neurons. *Proc Natl Acad Sci U S A* 101:360–365.
- Schratt GM, Tuebing F, Nigh EA, Kane CG, Sabatini ME, Kiebler M, et al. (2006): A brain-specific microRNA regulates dendritic spine development. *Nature* 439:283–289.
- Schaefer A, O'Carroll D, Tan CL, Hillman D, Sugimori M, Linas R, et al. (2007): Cerebellar neurodegeneration in the absence of microRNAs. *J Exp Med* 204:1553–1558.
- Lugli G, Larson J, Martone ME, Jones Y, Smalheiser NR (2005): Dicer and eIF2c are enriched at postsynaptic densities in adult mouse brain and are modified by neuronal activity in a calpain-dependent manner. *J Neurochem* 94:896–905.
- Barbato C, Ciotti MT, Serafino A, Calissano P, Cogoni C (2007): Dicer expression and localization in post-mitotic neurons. *Brain Res* 1175:17–27.
- Potenza N, Papa U, Russo A (2009): Differential expression of Dicer and Argonaute genes during the differentiation of human neuroblastoma cells. *Cell Biol Int* 33:734–738.
- Chiose S, Jelezcova E, Chandran U, Acquafondata M, McHale T, Sobol RW, et al. (2006): Up-regulation of dicer, a component of the microRNA machinery, in prostate adenocarcinoma. *Am J Pathol* 169:1812–1820.
- Saba R, Goodman CD, Huzarewicz RL, Robertson C, Booth SA (2008): A miRNA signature of prion induced neurodegeneration. *PLoS One* 3:e3652.
- Manadas B, Santos AR, Szabadfi K, Gomes JR, Garbis SD, Fountoulakis M, et al. (2009): BDNF-induced changes in the expression of the translation machinery in hippocampal neurons: Protein levels and dendritic mRNA. *J Proteome Res* 8:4536–4552.
- Cohen-Cory S, Fraser SE (1995): Effects of brain-derived neurotrophic factor on optic axon branching and remodelling in vivo. *Nature* 378:192–196.
- Ji Y, Pang PT, Feng L, Lu B (2005): Cyclic AMP controls BDNF-induced TrkB phosphorylation and dendritic spine formation in mature hippocampal neurons. *Nat Neurosci* 8:164–172.
- Meerson A, Cacheaux L, Goossens KA, Sapolsky RM, Soreq H, Kaufer D (2010): Changes in brain MicroRNAs contribute to cholinergic stress reactions. *J Mol Neurosci* 40:47–55.
- Beveridge NJ, Tooney PA, Carroll AP, Tran N, Cairns MJ (2009): Down-regulation of miR-17 family expression in response to retinoic acid induced neuronal differentiation. *Cell Signal* 21:1837–1845.

www.sobp.org/journal

45. Fatemi SH (2005): Reelin glycoprotein: Structure, biology and roles in health and disease. *Mol Psychiatry* 10:251–257.
46. Costa E, Davis J, Grayson DR, Guidotti A, Pappas GD, Pesold C (2001): Dendritic spine hypoplasticity and downregulation of reelin and GABAergic tone in schizophrenia vulnerability. *Neurobiol Dis* 8:723–742.
47. Fatemi SH, Earle JA, McMenomy T (2000): Reduction in Reelin immunoreactivity in hippocampus of subjects with schizophrenia, bipolar disorder and major depression. *Mol Psychiatry* 5:654–663:571.
48. Guidotti A, Auta J, Davis JM, Di-Giorgi-Gerevini V, Dwivedi Y, Grayson DR, *et al.* (2000): Decrease in reelin and glutamic acid decarboxylase67 (GAD67) expression in schizophrenia and bipolar disorder: A postmortem brain study. *Arch Gen Psychiatry* 57:1061–1069.
49. Glantz LA, Lewis DA (2000): Decreased dendritic spine density on prefrontal cortical pyramidal neurons in schizophrenia. *Arch Gen Psychiatry* 57:65–73.
50. Goto Y, Yang CR, Otani S (2010): Functional and dysfunctional synaptic plasticity in prefrontal cortex: Roles in psychiatric disorders. *Biol Psychiatry* 67:199–207.
51. Rajan I, Cline HT (1998): Glutamate receptor activity is required for normal development of tectal cell dendrites in vivo. *J Neurosci* 18:7836–7846.
52. Sin WC, Haas K, Ruthazer ES, Cline HT (2002): Dendrite growth increased by visual activity requires NMDA receptor and Rho GTPases. *Nature* 419:475–480.
53. Hansen T, Olsen L, Lindow M, Jakobsen KD, Ullum H, Jonsson E, *et al.* (2007): Brain expressed microRNAs implicated in schizophrenia etiology. *PLoS One* 2:e873.
54. Yamada K, Gerber DJ, Iwayama Y, Ohnishi T, Ohba H, Toyota T, *et al.* (2007): Genetic analysis of the calcineurin pathway identifies members of the EGR gene family, specifically EGR3, as potential susceptibility candidates in schizophrenia. *Proc Natl Acad Sci U S A* 104:2815–2820.
55. Guo AY, Sun J, Jia P, Zhao Z (2010): A novel microRNA and transcription factor mediated regulatory network in schizophrenia. *BMC Syst Biol* 4:10.
56. Friston KJ (1998): The disconnection hypothesis. *Schizophr Res* 30:115–125.
57. Garey LJ, Ong WY, Patel TS, Kanani M, Davis A, Mortimer AM, *et al.* (1998): Reduced dendritic spine density on cerebral cortical pyramidal neurons in schizophrenia. *J Neurol Neurosurg Psychiatry* 65:446–453.
58. Saldanha AJ (2004): Java Treeview—extensible visualization of microarray data. *Bioinformatics* 20:3246–3248.



---

## CHAPTER 7

### *General Discussion*

---

---

## **CHAPTER 7: GENERAL DISCUSSION**

Several brain regions including the temporal and prefrontal cortices have been observed to have altered structure and function in schizophrenia, and a number of approaches have been used to identify the genes that underlie these brain changes. Although putative schizophrenia susceptibility genes are being identified, it is important to remember that the inheritance of schizophrenia does not follow normal Mendelian inheritance patterns. Twin studies have shown that there is only approximately 50% concordance with the disease in monozygotic twins; individuals who share identical DNA profiles. It has primarily been this observation which highlights epigenetic and environmental events as attractive mechanisms whereby the abnormal regulation of gene expression could produce the schizophrenia phenotype. Based on the number of studies in recent years, mechanisms of gene regulation such as post-transcriptional gene silencing by microRNA has been one of the fastest growing fields in research. microRNA have been shown to be associated with several human diseases, including schizophrenia, and have already been identified as essential factors in mediating healthy neurodevelopment. It is plausible to suggest that abnormalities at the microRNA level may contribute to the complex differences in gene expression and disruptions in neurodevelopmental processes that are apparent in the pathophysiology of schizophrenia.

For the study presented herein, specific patterns of microRNA expression were examined throughout normal brain development and schizophrenia. An improved understanding of this phenomenon not only in disease, but in the healthy brain, will hopefully lead to a better understanding of the pathogenesis of schizophrenia which is an important step in the development of better treatments for the disorder.

This thesis has explored post-transcriptional gene silencing by microRNA covering three themes:

- ❖ Neuronal Differentiation
- ❖ Normal Development of the human brain
- ❖ Schizophrenia

### **Neuronal Differentiation**

---

The first study of this thesis, described in Chapter 2, examined the role of microRNA expression in the process of neuronal differentiation. The results of this study revealed a large number of microRNA and gene expression changes and of particular significance was the remarkable decrease of the entire miR-17 family of microRNA.

A total of 14 mature microRNA are associated with the miR-17 family and remarkably, all of these were found to be down-regulated in this study. The miR-17

---

family (the miR-17-92 cluster more specifically) is heavily implicated in numerous cancers <sup>48-54, 46, 55-60</sup>, where the increased expression is thought play a role in maintaining the undifferentiated phenotype of cancerous cells. This heavily reported cancer-related phenomenon of increased miR-17 family expression serves as an interesting anti-parallel, and novel finding for the neuronal differentiation process.

Furthermore, this study combined *in silico* analysis with gene expression data to identify potential gene targets of miR-17. In accordance with expectation, the differentiated neuroblasts were shown to have elevated levels of neuronal markers such as BCL2 and tau, as well as other genes important for inducing neurite outgrowths such as MAP3K12. In a reciprocal manner, upon transfection with miR-17, the expression of these genes were significantly reduced.

Reporter gene assays were established to substantiate a link between miR-17 (and other family members) and these differentiation-related genes, and as such, each were shown to contain functional miR-17 binding sites within their 3'-UTR. These findings suggest that the miR-17 family might be working co-operatively to fine tune the expression of the neuronal differentiation process.

This study provided more evidence in support of the miRNA pathway being crucial in the development of the brain and the nervous system, predominantly in relation to neuronal development and plasticity.

---

## Normal Development of the human brain

---

The human prefrontal cortex is one of the last cortical regions to mature structurally and functionally, and continues to develop into young adulthood <sup>162</sup>. It is one of the most functionally advanced regions of the brain, mediating working memory, attention, decision making and executive function <sup>163, 164</sup>. Gene expression studies have shown that numerous genes undergo expression changes with age, though what drives these changes is not fully understood.

In Chapter 4, microRNA expression and biogenesis was examined in a developmental cohort of normal human brain samples ranging from 1 month to 78 years of age. With a cohort of 97 samples, this is the largest study of its kind to date. Findings from this study revealed that a large proportion of microRNA are significantly correlated with age and display a switch in expression in young adulthood at approximately 20 years of age. This period is of particular interest to psychiatry research, as this time window corresponds to the age of onset of major neuropsychiatric disorders.

It was also revealed that global microRNA expression displays a distinct pattern with age. In accordance with the only other study of this kind <sup>165</sup>, microRNA expression was shown to display two remarkable changes in expression at the toddler and young adult time points. These changes in expression were mimicked in a reciprocal manner at the gene expression level and is thought to coincide with a peak in

---

synaptic density and later, the onset of aging

<sup>165</sup>.

As mature microRNA expression is largely post-transcriptionally regulated, the expression of genes involved in the microRNA biogenesis pathway were also examined. Novel findings indicated that components of the microprocessor complex; DGCR8 and Drosha displayed expression trajectories similar to that of global microRNA expression, while the cytoplasmic components of the pathway displayed distinct correlations with age. This presents additional evidence that components of the microprocessor complex may be acting as rate-limiting steps of microRNA biogenesis <sup>166</sup>, whilst Dicer and Exportin-5 are likely to be heavily post-transcriptionally regulated.

It is likely that age-related gene expression changes are directly influenced by microRNA, as they have been shown to be more negatively correlated with their putative target genes <sup>165</sup>. The potential target gene information from this study was combined with gene expression data from this same cohort <sup>155</sup> and functional pathway analysis revealed that axon guidance was the most heavily regulated pathway throughout aging. The standalone gene expression data indicated that genes within the axon guidance pathway undergo distinct changes with aging; however this is the first report to suggest a role for a certain group of microRNA regulating this pathway.

---

## Schizophrenia

---

Schizophrenia is one of the most debilitating mental illnesses known. The lifetime risk for the general population is approximately 1% of the population and incurs a high social and economic burden on society. Despite years of research, there have only been incremental advancements in the diagnosis, treatment and epidemiology of schizophrenia, and the aetiology of the disorder remains largely unknown. Efforts to understand the underlying mechanisms that confer disease vulnerability have focused predominantly on genetic influences. Recently, the post-transcriptional effects of microRNA have been shown to play a major role in coordinating the regulation of gene expression during the differentiation and development of the brain. Any disruption to gene expression in the developing brain could predispose these individuals to schizophrenia. To this end, this study examined microRNA expression in the temporal and prefrontal cortices of schizophrenia subjects alongside non-psychiatric controls.

Chapters 4 and 5 presented novel findings in respect to microRNA expression in the STG, as there are no previous studies of microRNA expression in this region. A significant schizophrenia-associated increase in microRNA expression was revealed, exemplified by the miR-15 family and other related microRNA. Chapter 4 highlighted that miR-181b displayed an increase in expression in schizophrenia and importantly this finding was replicated in the larger cohort represented in Chapter 5. The miR-15 family of microRNA has already been shown to have

---

an important role in some forms of cancer, with a well-characterized association between a reduction of miR-15a/miR-16 concentration and increased expression of the anti-apoptosis gene BCL2<sup>54</sup>. The relationship between miR-15 family expression and this gene could have the opposite implications in schizophrenia, which has been associated with a downregulation of BCL2 expression. Reduced BCL2 expression in schizophrenia, perhaps in response to increased miR-15 family expression, is thought to contribute to elevated cortical apoptosis, cerebral atrophy and even a reduction in the risk of some forms of cancer<sup>167, 168</sup>.

Remarkably, these findings were replicated in the DLPFC/BA9, as detailed in Chapter 5. The biological implications for this extensive increase in gene silencing are profound and represent a new mechanism for the dysregulation of gene expression observed in schizophrenia. Pathway analysis of potential miR-15 family gene targets suggested schizophrenia-relevant processes such as axon guidance and long-term potentiation are likely to be influenced by these microRNA. This relationship was substantiated at the individual gene level by reporter gene assay validating a biological relationship between miR-15 family members and schizophrenia candidate genes such as GRM7, GRIN3A, DLG4 and RELN.

The scope and consistency of the schizophrenia-associated increase in microRNA expression led to the consideration of both microRNA processing and the activity of genes in the miRNA biogenesis pathway. To this end, the relative expression of various primary and precursor microRNA transcripts

were examined. Interestingly, while there was a significant increase in precursor species, there was no difference in transcription of the primary transcript or host gene. This represented a novel finding that there was a schizophrenia-associated increase in microRNA biogenesis rather a change in the levels of microRNA transcription. Furthermore, DGCR8 mRNA was found to be significantly upregulated in both the STG and the DLPFC; and in addition, Drosha was also significantly upregulated in the DLPFC. These components are thought to be rate limiting in the microRNA biogenesis pathway<sup>166</sup> and therefore their elevation in schizophrenia represents a highly plausible explanation for the corresponding increase in both precursor and mature microRNA expression.

This study was extended to the DLPFC/BA46, as examined in Chapter 6. To date, this is the only study of microRNA expression in this region, and consists of the largest sample cohort to be used for any microRNA study across all previous brain regions studied in schizophrenia. In accordance with the results presented in Chapters 4 and 5, numerous microRNA displayed a significant upregulation in this tissue, with substantial overlap in microRNA species altered in the STG and DLPFC/BA9. Consistent with the findings detailed in previous Chapters, components of the biogenesis pathway, Dicer and DGCR8 displayed increased expression; potentially influencing the levels of cortical microRNA expression.

Interestingly, there was less overlap in altered miRNA species between the STG/BA9 and BA46. This could be a result of

---

differing cytoarchitecture between the different brain regions; however other external influences can contribute to these inconsistencies. Inherently, there are limitations in interpreting findings based on human postmortem tissue, as confounding variables such as age, gender, postmortem interval and brain pH all can all affect gene expression and often introduce difficulties in interpreting the data. In addition to these variables, changes in methodology can also be a source of variation. Studies presented in this thesis were conducted over the course of many years, and with massive advances in microarray technology, the use of varying platforms was unavoidable. The impact of such changes was assessed in these studies by assaying a number of samples over the multiple platforms to ensure similar expression profiles were obtained, regardless of the method used.

Altogether, this study provides further support for a role of altered miRNA expression in the neuropathology of schizophrenia, and suggests that disturbances to microRNA biogenesis could be the underlying mechanism. Ultimately, the consequence of this change in regulatory environment is the alteration of gene expression and biological processes that may play a significant role in the pathogenesis and pathophysiology of schizophrenia.

### **Future Recommendations**

---

Based on the findings discussed throughout this thesis, there are several avenues of further investigation to undertake,

such as investigating the molecular basis of schizophrenia-associated abnormalities in microRNA biogenesis. A logical progression of these studies would involve investigation of genetic variation in these genes; including copy-number variation and single nucleotide polymorphisms associated with elevated expression. Epigenetic changes such as promoter methylation or transcription factor expression should also be examined.

In addition, further investigation is needed into the molecular and cellular consequences of elevated microRNA expression. Whilst this body of work provides evidence of altered microRNA expression in cortical grey matter in schizophrenia, the cortical cytoarchitecture of this change is yet to be characterised. To address this, *in situ* hybridisation and other techniques can be used to quantify and identify the anatomical distribution of the differentially expressed microRNA discussed in this thesis. Furthermore, *in vitro* modulation of microRNA expression can facilitate the identification and validation of microRNA target genes and is less susceptible to false-positives than homology-based prediction algorithms.

Ultimately it is important to determine if the schizophrenia-associated change in cortical miRNA biogenesis can alter neurobehavioural parameters *in vivo*. The consequences of microRNA or biogenesis gene over-production can be studied in the mouse, searching for any changes in locomotion, behaviour and various other traits. These additional studies will provide greater understanding of the role of gene silencing in the pathophysiology of

---

schizophrenia, which could have important clinical implications for the development of new treatments that can leverage changes on a genome wide scale. A better understanding of this important neurodevelopmental parameter may also have implications for the development of psychosocial intervention strategies.

---

**The End**



---

## REFERENCES

1. Mattick, J.S., (2003). Challenging the dogma: the hidden layer of non-protein-coding RNAs in complex organisms. *Bioessays*, 25(10): p. 930-9.
2. Mattick, J.S., (2001). Non-coding RNAs: the architects of eukaryotic complexity. *EMBO Rep*, 2(11): p. 986-91.
3. Mattick, J.S. and I.V. Makunin, (2005). Small regulatory RNAs in mammals. *Hum Mol Genet*, 14 Spec No 1: p. R121-32.
4. Venter, J., (2001). The sequence of the human genome. *Science*, 291: p. 1304-1351.
5. Cawley, S., et al., (2004). Unbiased mapping of transcription factor binding sites along human chromosomes 21 and 22 points to widespread regulation of noncoding RNAs. *Cell*, 116(4): p. 499-509.
6. Mattick, J.S., (2004). RNA regulation: a new genetics? *Nat Rev Genet*, 5(4): p. 316-23.
7. Erdmann, V.A., et al., (2001). Regulatory RNAs. *Cell Mol Life Sci*, 58(7): p. 960-77.
8. Zamore, P.D. and B. Haley, (2005). Ribo-gnome: the big world of small RNAs. *Science*, 309(5740): p. 1519-24.
9. Tang, G., (2005). siRNA and miRNA: an insight into RISCs. *Trends Biochem Sci*, 30(2): p. 106-14.
10. Gregory, R.I., et al., (2005). Human RISC couples microRNA biogenesis and posttranscriptional gene silencing. *Cell*, 123(4): p. 631-40.
11. Rossi, J.J., (2005). RNAi and the P-body connection. *Nat Cell Biol*, 7(7): p. 643-4.
12. Zhao, S. and M.F. Liu, (2009). Mechanisms of microRNA-mediated gene regulation. *Sci China C Life Sci*, 52(12): p. 1111-6.
13. Lewis, B.P., C.B. Burge, and D.P. Bartel, (2005). Conserved seed pairing, often flanked by adenosines, indicates that thousands of human genes are microRNA targets. *Cell*, 120(1): p. 15-20.
14. Xie, X., et al., (2005). Systematic discovery of regulatory motifs in human promoters and 3' UTRs by comparison of several mammals. *Nature*, 434(7031): p. 338-45.
15. Gebauer, F. and M.W. Hentze, (2004). Molecular mechanisms of translational control. *Nat Rev Mol Cell Biol*, 5(10): p. 827-35.
16. Pillai, R.S., et al., (2005). Inhibition of translational initiation by let-7 microRNA in human cells. *Science (In Press)*.
17. Lee, R.C., R.L. Feinbaum, and V. Ambros, (1993). The *C. elegans* heterochronic gene *lin-4* encodes small RNAs with antisense complementarity to *lin-14*. *Cell*, 75(5): p. 843-54.
18. Pasquinelli, A.E., et al., (2000). Conservation of the sequence and temporal expression of let-7 heterochronic regulatory RNA. *Nature*, 408(6808): p. 86-9.
19. Reinhart, B.J., et al., (2000). The 21-nucleotide let-7 RNA regulates developmental timing in *Caenorhabditis elegans*. *Nature*, 403(6772): p. 901-6.
20. Lau, N.C., et al., (2001). An abundant class of tiny RNAs with probable regulatory roles in *Caenorhabditis elegans*. *Science*, 294(5543): p. 858-62.
21. Lee, R.C. and V. Ambros, (2001). An extensive class of small RNAs in *Caenorhabditis elegans*. *Science*, 294(5543): p. 862-4.
22. Lagos-Quintana, M., et al., (2003). New microRNAs from mouse and human. *Rna*, 9(2): p. 175-9.
23. Lim, L.P., et al., (2003). The microRNAs of *Caenorhabditis elegans*. *Genes Dev*, 17(8): p. 991-1008.
24. Lim, L.P., et al., (2003). Vertebrate microRNA genes. *Science*, 299(5612): p. 1540.
25. Brennecke, J., et al., (2003). *bantam* encodes a developmentally regulated microRNA that controls cell proliferation and regulates the

- 
- proapoptotic gene hid in *Drosophila*. *Cell*, 113(1): p. 25-36.
26. John, B., et al., (2004). Human MicroRNA targets. *PLoS Biol*, 2(11): p. e363.
27. Cai, X., C.H. Hagedorn, and B.R. Cullen, (2004). Human microRNAs are processed from capped, polyadenylated transcripts that can also function as mRNAs. *Rna*, 10(12): p. 1957-66.
28. Lee, Y., et al., (2003). The nuclear RNase III Drosha initiates microRNA processing. *Nature*, 425(6956): p. 415-9.
29. Lund, E., et al., (2004). Nuclear export of microRNA precursors. *Science*, 303(5654): p. 95-8.
30. Yi, R., et al., (2003). Exportin-5 mediates the nuclear export of pre-microRNAs and short hairpin RNAs. *Genes Dev*, 17(24): p. 3011-6.
31. Schwarz, D.S., et al., (2003). Asymmetry in the assembly of the RNAi enzyme complex. *Cell*, 115(2): p. 199-208.
32. Okamura, K., et al., (2008). The regulatory activity of microRNA\* species has substantial influence on microRNA and 3' UTR evolution. *Nat Struct Mol Biol*, 15(4): p. 354-63.
33. Thermann, R. and M.W. Hentze, (2007). *Drosophila* miR2 induces pseudo-polysomes and inhibits translation initiation. *Nature*, 447(7146): p. 875-8.
34. Pillai, R.S., (2005). MicroRNA function: multiple mechanisms for a tiny RNA? *RNA*, 11(12): p. 1753-61.
35. Kiriakidou, M., et al., (2007). An mRNA m7G cap binding-like motif within human Ago2 represses translation. *Cell*, 129(6): p. 1141-51.
36. Wakiyama, M., et al., (2007). Let-7 microRNA-mediated mRNA deadenylation and translational repression in a mammalian cell-free system. *Genes Dev*, 21(15): p. 1857-62.
37. Beilharz, T.H., et al., (2009). microRNA-mediated messenger RNA deadenylation contributes to translational repression in mammalian cells. *PLoS One*, 4(8): p. e6783.
38. He, L. and G.J. Hannon, (2004). MicroRNAs: small RNAs with a big role in gene regulation. *Nat Rev Genet*, 5(7): p. 522-31.
39. Nottrott, S., M.J. Simard, and J.D. Richter, (2006). Human let-7a miRNA blocks protein production on actively translating polyribosomes. *Nat Struct Mol Biol*, 13(12): p. 1108-14.
40. Petersen, C.P., et al., (2006). Short RNAs repress translation after initiation in mammalian cells. *Mol Cell*, 21(4): p. 533-42.
41. Wu, L. and J.G. Belasco, (2008). Let me count the ways: mechanisms of gene regulation by miRNAs and siRNAs. *Mol Cell*, 29(1): p. 1-7.
42. Liu, J., et al., (2005). MicroRNA-dependent localization of targeted mRNAs to mammalian P-bodies. *Nat Cell Biol*, 7(7): p. 719-23.
43. Filipowicz, W., S.N. Bhattacharyya, and N. Sonenberg, (2008). Mechanisms of post-transcriptional regulation by microRNAs: are the answers in sight? *Nat Rev Genet*, 9(2): p. 102-14.
44. Dostie, J., et al., (2003). Numerous microRNPs in neuronal cells containing novel microRNAs. *Rna*, 9(2): p. 180-6.
45. Xu, P., et al., (2003). The *Drosophila* microRNA Mir-14 suppresses cell death and is required for normal fat metabolism. *Curr Biol*, 13(9): p. 790-5.
46. Giraldez, A.J., et al., (2005). MicroRNAs regulate brain morphogenesis in zebrafish. *Science*, 308(5723): p. 833-8.
47. Naguibneva, I., et al., (2006). The microRNA miR-181 targets the homeobox protein Hox-A11 during mammalian myoblast differentiation. *Nat Cell Biol*, 8(3): p. 278-84.
48. Jin, P., R.S. Alisch, and S.T. Warren, (2004). RNA and microRNAs in fragile X mental retardation. *Nat Cell Biol*, 6(11): p. 1048-53.
49. Metzler, M., et al., (2004). High expression of precursor microRNA-155/BIC RNA in children with Burkitt lymphoma. *Genes Chromosomes Cancer*, 39(2): p. 167-9.
50. Veneri, M., F. Zalfa, and C. Bagni, (2004). FMRP and its target RNAs: fishing for the specificity. *Neuroreport*, 15(16): p. 2447-50.
51. Abelson, J.F., et al., (2005). Sequence variants in SLITRK1 are associated with Tourette's syndrome. *Science*, 310(5746): p. 317-20.
-

- 
52. Alvarez-Garcia, I. and E.A. Miska, (2005). MicroRNA functions in animal development and human disease. *Development*, 132(21): p. 4653-62.
53. Calin, G.A., et al., (2005). A MicroRNA signature associated with prognosis and progression in chronic lymphocytic leukemia. *N Engl J Med*, 353(17): p. 1793-801.
54. Cimmino, A., et al., (2005). miR-15 and miR-16 induce apoptosis by targeting BCL2. *Proc Natl Acad Sci U S A*, 102(39): p. 13944-9.
55. He, H., et al., (2005). The role of microRNA genes in papillary thyroid carcinoma. *Proc Natl Acad Sci U S A*, 102(52): p. 19075-80.
56. Iorio, M.V., et al., (2005). MicroRNA gene expression deregulation in human breast cancer. *Cancer Res*, 65(16): p. 7065-70.
57. Johnston, R.J., Jr., et al., (2005). MicroRNAs acting in a double-negative feedback loop to control a neuronal cell fate decision. *Proc Natl Acad Sci U S A*, 102(35): p. 12449-54.
58. Pfeffer, S., et al., (2005). Identification of microRNAs of the herpesvirus family. *Nat Methods*, 2(4): p. 269-76.
59. Schratt, G.M., et al., (2006). A brain-specific microRNA regulates dendritic spine development. *Nature*, 439(7074): p. 283-9.
60. Volinia, S., et al., (2006). A microRNA expression signature of human solid tumors defines cancer gene targets. *Proc Natl Acad Sci U S A*, 103(7): p. 2257-61.
61. Sempere, L.F., et al., (2004). Expression profiling of mammalian microRNAs uncovers a subset of brain-expressed microRNAs with possible roles in murine and human neuronal differentiation. *Genome Biol*, 5(3): p. R13.
62. Krichevsky, A.M., et al., (2006). Specific microRNAs modulate embryonic stem cell-derived neurogenesis. *Stem Cells*, 24(4): p. 857-64.
63. Conaco, C., et al., (2006). Reciprocal actions of REST and a microRNA promote neuronal identity. *Proc Natl Acad Sci U S A*, 103(7): p. 2422-7.
64. Makeyev, E.V., et al., (2007). The MicroRNA miR-124 promotes neuronal differentiation by triggering brain-specific alternative pre-mRNA splicing. *Mol Cell*, 27(3): p. 435-48.
65. Nilsen, T.W., (2007). Mechanisms of microRNA-mediated gene regulation in animal cells. *Trends Genet*, 23(5): p. 243-9.
66. Chang, S., et al., (2004). MicroRNAs act sequentially and asymmetrically to control chemosensory laterality in the nematode. *Nature*, 430(7001): p. 785-9.
67. Wayman, G.A., et al., (2008). An activity-regulated microRNA controls dendritic plasticity by down-regulating p250GAP. *Proc Natl Acad Sci U S A*, 105(26): p. 9093-8.
68. Cheng, H.Y., et al., (2007). microRNA modulation of circadian-clock period and entrainment. *Neuron*, 54(5): p. 813-29.
69. Cheng, H.Y. and K. Obrietan, (2007). Revealing a role of microRNAs in the regulation of the biological clock. *Cell Cycle*, 6(24): p. 3034-5.
70. Kim, J., et al., (2007). A MicroRNA feedback circuit in midbrain dopamine neurons. *Science*, 317(5842): p. 1220-4.
71. Cuellar, T.L., et al., (2008). Dicer loss in striatal neurons produces behavioral and neuroanatomical phenotypes in the absence of neurodegeneration. *Proc Natl Acad Sci U S A*, 105(14): p. 5614-9.
72. Nelson, P.T. and W.X. Wang, MiR-107 is Reduced in Alzheimer's Disease Brain Neocortex: Validation Study. *J Alzheimers Dis*.
73. Wang, W.X., et al., MiR-107 Regulates Granulin/Progranulin with Implications for Traumatic Brain Injury and Neurodegenerative Disease. *Am J Pathol*.
74. Hebert, S.S. and B. De Strooper, (2009). Alterations of the microRNA network cause neurodegenerative disease. *Trends Neurosci*, 32(4): p. 199-206.
75. Perkins, D.O., et al., (2007). microRNA expression in the prefrontal cortex of individuals with schizophrenia and schizoaffective disorder. *Genome Biol*, 8(2): p. R27.
76. Karayiorgou, M., et al., (1995). Schizophrenia susceptibility associated with interstitial
-

- 
- deletions of chromosome 22q11. *Proc Natl Acad Sci U S A*, 92(17): p. 7612-6.
77. Stark, K.L., et al., (2008). Altered brain microRNA biogenesis contributes to phenotypic deficits in a 22q11-deletion mouse model. *Nat Genet*, 40(6): p. 751-60.
  78. Hansen, T., et al., (2007). Brain expressed microRNAs implicated in schizophrenia etiology. *PLoS One*, 2(9): p. e873.
  79. Feng, J., et al., (2009). Evidence for X-chromosomal schizophrenia associated with microRNA alterations. *PLoS One*, 4(7): p. e6121.
  80. Tabares-Seisdedos, R. and J.L. Rubenstein, (2009). Chromosome 8p as a potential hub for developmental neuropsychiatric disorders: implications for schizophrenia, autism and cancer. *Mol Psychiatry*, 14(6): p. 563-89.
  81. Kocerha, J., et al., (2009). MicroRNA-219 modulates NMDA receptor-mediated neurobehavioral dysfunction. *Proc Natl Acad Sci U S A*, 106(9): p. 3507-12.
  82. Mellios, N., et al., (2008). A set of differentially expressed miRNAs, including miR-30a-5p, act as post-transcriptional inhibitors of BDNF in prefrontal cortex. *Hum Mol Genet*, 17(19): p. 3030-42.
  83. Abuhatzira, L., et al., (2007). MeCP2 deficiency in the brain decreases BDNF levels by REST/CoREST-mediated repression and increases TRKB production. *Epigenetics*, 2(4): p. 214-22.
  84. Yuan, P., et al., Altered levels of extracellular signal-regulated kinase signaling proteins in postmortem frontal cortex of individuals with mood disorders and schizophrenia. *J Affect Disord*, 124(1-2): p. 164-9.
  85. Kraepelin, E., *Dementia praecox and paraphrenia*. 1971, New York: Krieger.
  86. Bleuler, E., *Dementia praecox or the group of schizophrenias*. 1950, New York: International Universities Press.
  87. Liddle, P.F., (2000). Cognitive impairment in schizophrenia: its impact on social functioning. *Acta Psychiatr Scand Suppl*, 400: p. 11-6.
  88. Fenton, W.S. and T.H. McGlashan, (1991). Natural history of schizophrenia subtypes. II. Positive and negative symptoms and long-term course. *Arch Gen Psychiatry*, 48(11): p. 978-86.
  89. Mueser, K.T. and S.R. McGurk, (2004). Schizophrenia. *The Lancet*, 363: p. 2063-2072.
  90. Inskip, H.M., E.C. Harris, and B. Barraclough, (1998). Lifetime risk of suicide for affective disorder, alcoholism and schizophrenia. *Br J Psychiatry*, 172: p. 35-7.
  91. Sivagnansundaram, S., et al., (2003). Genetics of schizophrenia: current strategies. *Clinical Neuroscience Research*, 3(1-2): p. 5-16.
  92. Rapoport, J.L., et al., (2005). The neurodevelopmental model of schizophrenia: update 2005. *Mol Psychiatry*, 10(5): p. 434-49.
  93. Rehn, A.E. and S.M. Rees, (2005). Investigating the neurodevelopmental hypothesis of schizophrenia. *Clin Exp Pharmacol Physiol*, 32(9): p. 687-96.
  94. Johnstone, E., et al., (1976). Cerebral ventricular size and cognitive impairment in chronic schizophrenia. *The Lancet*, 2(1): p. 924-926.
  95. Swayze, V.W., 2nd, et al., (1990). Developmental abnormalities of the corpus callosum in schizophrenia. *Arch Neurol*, 47(7): p. 805-8.
  96. Andreasen, N., et al., (1994). Regional brain abnormalities in schizophrenia measured with magnetic resonance imaging. *JAMA*, 272(1): p. 1763-1769.
  97. Jaskiw, G.E., et al., (1994). Cerebral ventricular enlargement in schizophreniform disorder does not progress. A seven year follow-up study. *Schizophr Res*, 14(1): p. 23-8.
  98. DeLisi, L.E., et al., (1995). A prospective follow-up study of brain morphology and cognition in first-episode schizophrenic patients: preliminary findings. *Biol Psychiatry*, 38(6): p. 349-60.
  99. Lawrie, S. and S. Abukmeil, (1998). Brain abnormality in schizophrenia: a systematic and quantitative review of volumetric magnetic resonance imaging studies. *British Journal of Psychiatry*, 172(1): p. 110-120.
  100. Gaser, C., et al., (2004). Ventricular enlargement in schizophrenia related to volume
-

- 
- reduction of the thalamus, striatum, and superior temporal cortex. *Am J Psychiatry*, 161(1): p. 154-6.
101. Gaser, C., et al., (2004). Neuroanatomy of "hearing voices": a frontotemporal brain structural abnormality associated with auditory hallucinations in schizophrenia. *Cereb Cortex*, 14(1): p. 91-6.
102. McCarley, R., et al., (1993). Auditory P300 abnormalities and left posterior superior temporal gyrus volume reduction in schizophrenia. *Arch Gen Psychiatry*, 50(3): p. 190-197.
103. Tune, L., et al., (1996). striatal dopamine D2 receptor quantification and superior temporal gyrus: volume determination in 14 chronic schizophrenic subjects. *Psychiatry Research*, 67(2): p. 155-158.
104. Wright, I.C., et al., (2000). Meta-analysis of regional brain volumes in schizophrenia. *Am J Psychiatry*, 157(1): p. 16-25.
105. Narr, K., et al., (2001). Three-dimensional mapping of temporo-limbic regions and the lateral ventricles in schizophrenia: gender effects. *Biol Psychiatry*, 15(2): p. 84-97.
106. Byne, W., et al., (2002). Postmortem assessment of thalamic nuclear volumes in subjects with schizophrenia. *Am J Psychiatry*, 159(1): p. 159-165.
107. McKenzie Illustrations, (1998). Brain Map. *Brain Injury Resource Program*.
108. Rajarethinam, R., et al., (2000). Superior temporal gyrus in schizophrenia: a volumetric magnetic resonance imaging study. *Schizophr Res*, 41: p. 303-312.
109. Taylor, J.L., et al., (2005). Superior temporal gyrus differences in childhood-onset schizophrenia. *Schizophr Res*, 73(2-3): p. 235-41.
110. Deng, C. and X.F. Huang, (2006). Increased density of GABA(A) receptors in the superior temporal gyrus in schizophrenia. *Exp Brain Res*, 168(4): p. 587-90.
111. Weinberger, D.R., K.F. Berman, and R.F. Zec, (1986). Physiologic dysfunction of dorsolateral prefrontal cortex in schizophrenia. *Archives of General Psychiatry*, 43: p. 114-124.
112. Goldman-Rakic, P.S., (1994). Working memory dysfunction in schizophrenia. *Journal of Neuropsychiatry*, 6: p. 348-357.
113. Taylor, S.F., (1996). Cerebral blood flow activation and functional lesions in schizophrenia. *Schizophrenia Research*, 19: p. 129-140.
114. Keltner, N.L., (2005). Genomic influences on schizophrenia-related neurotransmitter systems. *J Nurs Scholarsh*, 37(4): p. 322-8.
115. Neale, J.H., et al., (2005). The neurotransmitter N-acetylaspartylglutamate in models of pain, ALS, diabetic neuropathy, CNS injury and schizophrenia. *Trends Pharmacol Sci*, 26(9): p. 477-84.
116. Cardno, A., E. Marshall, and B. Coid, (1999). Heritability estimates for psychotic disorders: the Maudsley twin psychosis series. *Arch Gen Psychiatry*, 56(1): p. 162-168.
117. Lichtermann, D., E. Karbe, and W. Maier, (2000). The genetic epidemiology of schizophrenia and of schizophrenia spectrum disorders. *Eur Arch Psychiatry Clin Neurosci*, 250(6): p. 304-10.
118. Tsuang, M., (2000). Schizophrenia: genes and environment. *Biol Psychiatry*, 47(3): p. 210-20.
119. Gottesman, I., *Schizophrenia Genesis: The Origins of madness*. 1991, New York: WH Freeman & Co.
120. Owen, M.J., N. Craddock, and M.C. O'Donovan, (2005). Schizophrenia: genes at last? *Trends Genet*, 21(9): p. 518-25.
121. Allen, N.C., et al., (2008). Systematic meta-analyses and field synopsis of genetic association studies in schizophrenia: the SzGene database. *Nat Genet*, 40(7): p. 827-34.
122. Craddock, N., M.C. O'Donovan, and M.J. Owen, (2005). The genetics of schizophrenia and bipolar disorder: dissecting psychosis. *J Med Genet*, 42(3): p. 193-204.
123. Bertram, L., (2008). Genetic research in schizophrenia: new tools and future perspectives. *Schizophr Bull*, 34(5): p. 806-12.
124. Porteous, D., (2008). Genetic causality in schizophrenia and bipolar disorder: out with the
-

- 
- old and in with the new. *Curr Opin Genet Dev*, 18(3): p. 229-34.
125. Owen, M.J., N.M. Williams, and M.C. O'Donovan, (2004). The molecular genetics of schizophrenia: new findings promise new insights. *Mol Psychiatry*, 9(1): p. 14-27.
126. St Clair, D., et al., (1990). Association within a family of a balanced autosomal translocation with major mental illness. *Lancet*, 336(8706): p. 13-6.
127. Kamiya, A., et al., (2005). A schizophrenia-associated mutation of DISC1 perturbs cerebral cortex development. *Nat Cell Biol*, 7(12): p. 1067-78.
128. Duan, X., et al., (2007). Disrupted-In-Schizophrenia 1 regulates integration of newly generated neurons in the adult brain. *Cell*, 130(6): p. 1146-58.
129. Nakata, K., et al., (2009). DISC1 splice variants are upregulated in schizophrenia and associated with risk polymorphisms. *Proc Natl Acad Sci U S A*, 106(37): p. 15873-8.
130. Lipska, B.K., et al., (2006). Expression of DISC1 binding partners is reduced in schizophrenia and associated with DISC1 SNPs. *Hum Mol Genet*, 15(8): p. 1245-58.
131. Tomppa, L., et al., (2009). Association between genes of Disrupted in schizophrenia 1 (DISC1) interactors and schizophrenia supports the role of the DISC1 pathway in the etiology of major mental illnesses. *Biol Psychiatry*, 65(12): p. 1055-62.
132. (2008). Rare chromosomal deletions and duplications increase risk of schizophrenia. *Nature*, 455(7210): p. 237-41.
133. Xu, B., et al., (2008). Strong association of de novo copy number mutations with sporadic schizophrenia. *Nat Genet*, 40(7): p. 880-5.
134. Need, A.C., et al., (2009). A genome-wide investigation of SNPs and CNVs in schizophrenia. *PLoS Genet*, 5(2): p. e1000373.
135. Zhang, D., et al., (2009). Singleton deletions throughout the genome increase risk of bipolar disorder. *Mol Psychiatry*, 14(4): p. 376-80.
136. Wilson, G.M., et al., (2006). DNA copy-number analysis in bipolar disorder and schizophrenia reveals aberrations in genes involved in glutamate signaling. *Hum Mol Genet*, 15(5): p. 743-9.
137. Walsh, T., et al., (2008). Rare structural variants disrupt multiple genes in neurodevelopmental pathways in schizophrenia. *Science*, 320(5875): p. 539-43.
138. Conrad, D.F., et al., (2008). Origins and functional impact of copy number variation in the human genome. *Nature*, 464(7289): p. 704-12.
139. Purcell, S.M., et al., (2009). Common polygenic variation contributes to risk of schizophrenia and bipolar disorder. *Nature*, 460(7256): p. 748-52.
140. O'Donovan, M.C., et al., (2008). Identification of loci associated with schizophrenia by genome-wide association and follow-up. *Nat Genet*, 40(9): p. 1053-5.
141. Shifman, S., et al., (2008). Genome-wide association identifies a common variant in the reelin gene that increases the risk of schizophrenia only in women. *PLoS Genet*, 4(2): p. e28.
142. Sullivan, P.F., et al., (2008). Genomewide association for schizophrenia in the CATIE study: results of stage 1. *Mol Psychiatry*, 13(6): p. 570-84.
143. Kirov, G., et al., (2009). A genome-wide association study in 574 schizophrenia trios using DNA pooling. *Mol Psychiatry*, 14(8): p. 796-803.
144. Burmeister, M., M.G. McInnis, and S. Zollner, (2008). Psychiatric genetics: progress amid controversy. *Nat Rev Genet*, 9(7): p. 527-40.
145. Guilmatre, A., et al., (2009). Recurrent rearrangements in synaptic and neurodevelopmental genes and shared biologic pathways in schizophrenia, autism, and mental retardation. *Arch Gen Psychiatry*, 66(9): p. 947-56.
146. Callicott, J.H., et al., (2005). Variation in DISC1 affects hippocampal structure and function and increases risk for schizophrenia. *Proc Natl Acad Sci U S A*, 102(24): p. 8627-32.
-

- 
147. Millar, J.K., et al., (2007). Disrupted in schizophrenia 1 and phosphodiesterase 4B: towards an understanding of psychiatric illness. *J Physiol*, 584(Pt 2): p. 401-5.
148. Buonanno, A., et al., (2008). Neuregulins and neuronal plasticity: possible relevance in schizophrenia. *Novartis Found Symp*, 289: p. 165-77; discussion 177-9, 193-5.
149. Mei, L. and W.C. Xiong, (2008). Neuregulin 1 in neural development, synaptic plasticity and schizophrenia. *Nat Rev Neurosci*, 9(6): p. 437-52.
150. Kessler, R.C., et al., (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*, 62(6): p. 593-602.
151. Paus, T., M. Keshavan, and J.N. Giedd, (2008). Why do many psychiatric disorders emerge during adolescence? *Nat Rev Neurosci*, 9(12): p. 947-57.
152. Fatemi, S.H. and T.D. Folsom, (2009). The neurodevelopmental hypothesis of schizophrenia, revisited. *Schizophr Bull*, 35(3): p. 528-48.
153. Carpenter, W.T. and J.I. Koenig, (2008). The evolution of drug development in schizophrenia: past issues and future opportunities. *Neuropsychopharmacology*, 33(9): p. 2061-79.
154. Gogos, J.A., (2007). Schizophrenia susceptibility genes: in search of a molecular logic and novel drug targets for a devastating disorder. *Int Rev Neurobiol*, 78: p. 397-422.
155. Choi, K.H., et al., (2009). Expression profiles of schizophrenia susceptibility genes during human prefrontal cortical development. *J Psychiatry Neurosci*, 34(6): p. 450-8.
156. Fillman, S.G., et al., Developmental co-regulation of the beta and gamma GABAA receptor subunits with distinct alpha subunits in the human dorsolateral prefrontal cortex. *Int J Dev Neurosci*, 28(6): p. 513-9.
157. Fung, S.J., et al., Expression of interneuron markers in the dorsolateral prefrontal cortex of the developing human and in schizophrenia. *Am J Psychiatry*, 167(12): p. 1479-88.
158. Sinclair, D., et al., Dynamic molecular and anatomical changes in the glucocorticoid receptor in human cortical development. *Mol Psychiatry*.
159. Webster, M.J., M. Elashoff, and C.S. Weickert, Molecular evidence that cortical synaptic growth predominates during the first decade of life in humans. *Int J Dev Neurosci*.
160. Lu, T., et al., (2004). Gene regulation and DNA damage in the ageing human brain. *Nature*, 429(6994): p. 883-91.
161. Somel, M., et al., (2009). Transcriptional neoteny in the human brain. *Proc Natl Acad Sci U S A*, 106(14): p. 5743-8.
162. Gogtay, N., et al., (2004). Dynamic mapping of human cortical development during childhood through early adulthood. *Proc Natl Acad Sci U S A*, 101(21): p. 8174-9.
163. Goldman-Rakic, P.S., (1987). Development of cortical circuitry and cognitive function. *Child Dev*, 58(3): p. 601-22.
164. Fuster, J.M., (2002). Frontal lobe and cognitive development. *J Neurocytol*, 31(3-5): p. 373-85.
165. Somel, M., et al., MicroRNA, mRNA, and protein expression link development and aging in human and macaque brain. *Genome Res*.
166. Gregory, R.I., et al., (2004). The Microprocessor complex mediates the genesis of microRNAs. *Nature*, 432(7014): p. 235-40.
167. Jarskog, L.F., et al., (2000). Cortical bcl-2 protein expression and apoptotic regulation in schizophrenia. *Biol Psychiatry*, 48(7): p. 641-50.
168. Jarskog, L.F., et al., (2005). Apoptotic mechanisms in the pathophysiology of schizophrenia. *Prog Neuropsychopharmacol Biol Psychiatry*, 29(5): p. 846-58.
-



---

## APPENDICES

---

## APPENDIX I: SUPPLEMENTARY DATA FOR CHAPTER 2

**Supplementary Table 1: Gene Lists of up-regulated miR-17 targets and down-regulated brain-enriched miRNA targets**

### miR-17 family targets which were up-regulated during differentiation

Gene Symbol	Gene Name
ABCA1	atp-binding cassette, sub-family a (abc1), member 1
ABCC5	atp-binding cassette, sub-family c (cfltr/mrp), member 5
ABCC4	atp-binding cassette, sub-family g (white), member 4
ABHD3	abhydrolase domain containing 3
ABI3BP	abi gene family, member 3 (nesh) binding protein
ABR	active bcr-related gene
ACCN2	amiloride-sensitive cation channel 2, neuronal
ACTN1	actinin, alpha 1
ACTR1A	arp1 actin-related protein 1 homolog a, centractin alpha (yeast)
ACVR1B	activin a receptor, type ib
ADAM19	adam metalloproteinase domain 19 (meltrin beta)
ADCY6	adenylate cyclase 6
ADD3	adducin 3 (gamma)
AFTIPHILIN	aftiphilin protein
AK3	adenylate kinase 3
AKAP13	lymphoid blast crisis oncogene
ALS2	amyotrophic lateral sclerosis 2 (juvenile)
AMFR	autocrine motility factor receptor
ANK2	ankyrin 2, neuronal
ANKFY1	ankyrin repeat and fyve domain containing 1
ANKRD12	ankyrin repeat domain 12
AP2M1	adaptor-related protein complex 2, mu 1 subunit
APEG1	aortic preferentially expressed gene 1
APPL	adaptor protein containing ph domain, pth domain and leucine zipper motif 1
APRIN	androgen-induced proliferation inhibitor
ARHGAP1	rho gtpase activating protein 1
ARHGAP12	hypothetical protein flj10971
ARHGAP20	rho gtpase activating protein 20
ARHGAP21	rho gtpase activating protein 21
ARHGEF11	rho guanine nucleotide exchange factor (gef) 11
ARHGEF18	rho/rac guanine nucleotide exchange factor (gef) 18
ARHGEF3	rho guanine nucleotide exchange factor (gef) 3
ARIH2	ariadne homolog 2 (drosophila)
ARL4C	adp-ribosylation factor-like 4c
ARL8B	adp-ribosylation factor-like 8b
ARPP-21	cyclic amp-regulated phosphoprotein, 21 kd
ARRDC4	arrestin domain containing 4
ASXL2	additional sex combs like 2 (drosophila)
ATP1B1	atpase, na+/k+ transporting, beta 1 polypeptide
ATP2A2	atpase, ca++ transporting, cardiac muscle, slow twitch 2
ATP6V1B2	atpase, h+ transporting, lysosomal 56/58kda, v1 subunit b2
ATXN1	ataxin 1
ATXN2	ataxin 2
AUTS2	autism susceptibility candidate 2
AXIN2	axin 2 (conductin, axil)
B4GALT5	udp-gal:betaglcnaac beta 1,4- galactosyltransferase, polypeptide 5
BACH2	btb and cnc homology 1, basic leucine zipper transcription factor 2
BAI3	brain-specific angiogenesis inhibitor 3
BAZZB	dkfzp434h071 protein
BCAP29	b-cell receptor-associated protein 29
BCL2L1	bcl2-like 1
BCL2L2	bcl2-like 2
BCL9L	b-cell cl/lymphoma 9-like
BDNF	brain-derived neurotrophic factor
BIRC6	baculoviral iap repeat-containing 6 (apollon)
Bles03	basophilic leukemia expressed protein bles03
BM88	bm88 antigen
BNC2	basonuclin 2
BRPF3	bromodomain and phd finger containing, 3
BRUNOL6	bruno-like 6, rna binding protein (drosophila)
BSCL2	bernardinelli-seip congenital lipodystrophy 2 (seipin)
BSDC1	bsd domain containing 1
BSN	bassoon (presynaptic cytomatrix protein)
BTBD10	btb (poz) domain containing 10
BTG1	b-cell translocation gene 1, anti-proliferative
BTG2	btg family, member 2
BTG3	btg family, member 3
BZRAP1	benzodiazepine receptor (peripheral) associated protein 1
C10orf6	chromosome 10 open reading frame 6
C14orf147	chromosome 14 open reading frame 147
C15orf17	chromosome 15 open reading frame 17
C16orf28	chromosome 16 open reading frame 28
C16orf7	chromosome 16 open reading frame 7

---

C16orf9	chromosome 16 open reading frame 9
C1orf21	chromosome 1 open reading frame 21
C1QDC1	c1q domain containing 1
C20orf35	chromosome 20 open reading frame 35
C20orf46	chromosome 20 open reading frame 46
C5orf13	chromosome 5 open reading frame 13
C5orf5	chromosome 5 open reading frame 5
C6orf134	chromosome 6 open reading frame 134
C9orf5	chromosome 9 open reading frame 5
CA10	carbonic anhydrase x
CACNA1C	calcium channel, voltage-dependent, 1 type, alpha 1c subunit
CALM1	calmodulin 1 (phosphorylase kinase, delta)
CAMK2G	calcium/calmodulin-dependent protein kinase (cam kinase) ii gamma
CAMK2N1	calcium/calmodulin-dependent protein kinase ii inhibitor 1
CAMSAP1L1	calmodulin regulated spectrin-associated protein 1-like 1
CAMTA1	calmodulin binding transcription activator 1
CBX4	chromobox homolog 4 (pc class homolog, drosophila)
CBX7	chromobox homolog 7
CCDC24	coiled-coil domain containing 24
CCM2	cerebral cavernous malformation 2
CCND1	cyclin d1
CCPG1	cell cycle progression 1
CDC2L5	cell division cycle 2-like 5 (cholinesterase-related cell division controller)
CDC2L6	cell division cycle 2-like 6 (cdk8-like)
CDC42EP2	cdc42 effector protein (rho gtpase binding) 2
CDH2	cadherin 2, type 1, n-cadherin (neuronal)
CDK6	cyclin-dependent kinase 6
CDKN1C	cyclin-dependent kinase inhibitor 1c (p57, kip2)
CEP350	centrosomal protein 350kda
CEP70	centrosomal protein 70kda
CETN2	centrin, ef-hand protein, 2
CGGBP1	egg triplet repeat binding protein 1
CGI-38	cgi-38 protein
CHD5	chromodomain helicase dna binding protein 5
CHD5	coronary heart disease, susceptibility to, 5
CHD9	hypothetical protein bc022889
CHRNB1	cholinergic receptor, nicotinic, beta 1 (muscle)
CHST1	carbohydrate (keratan sulfate gal-6) sulfotransferase 1
CHST7	carbohydrate (n-acetylglucosamine 6-o) sulfotransferase 7
CIC	capicua homolog (drosophila)
CLASP2	cytoplasmic linker associated protein 2
CLCF1	cardiotrophin-like cytokine factor 1
CLDN12	claudin 12
CLIPR-59	clip-170-related protein
CNIH2	cornichon homolog 2 (drosophila)
CNOT4	ccr4-not transcription complex, subunit 4
CNR1	cannabinoid receptor 1 (brain)
CNTRF	ciliary neurotrophic factor receptor
CNTNAP1	contactin associated protein 1
COL17A1	collagen, type xvii, alpha 1
COL23A1	collagen, type xxiii, alpha 1
COP57A	cop9 constitutive photomorphogenic homolog subunit 7a (arabidopsis)
COX7A2L	cytochrome c oxidase subunit viia polypeptide 2 like
CPEB1	cytoplasmic polyadenylation element binding protein 1
CPEB3	cytoplasmic polyadenylation element binding protein 3
CREB5	camp responsive element binding protein 5
CREBBP	creb binding protein (rubinstein-taybi syndrome)
CRMP1	collapsin response mediator protein 1
CRTC2	creb regulated transcription coactivator 2
CSMD2	cub and sushi multiple domains 2
CSNK2A2	casein kinase 2, alpha prime polypeptide
CSPG3	chondroitin sulfate proteoglycan 3 (neurocan)
CTNNBIP1	catenin, beta interacting protein 1
CUL5	cullin 5
CXorf45	chromosome x open reading frame 45
CXXC5	cxxc finger 5
CYLD	cyllindromatosis (turban tumor syndrome)
CYP26B1	cytochrome p450, family 26, subfamily b, polypeptide 1
DAAM1	dishevelled associated activator of morphogenesis 1
DACH1	dachshund homolog 1 (drosophila)
DAG1	dystroglycan 1 (dystrophin-associated glycoprotein 1)
DAZAP2	daz associated protein 2
DCAMKL2	doublecortin and cam kinase-like 2
DCBLD2	discoidin, cub and lcl domain containing 2
DCX	doublecortin; lissencephaly, x-linked (doublecortin)
DDEF2	development and differentiation enhancing factor 2
DDR1	discoidin domain receptor family, member 1
DDX26	dkfzp434b105 protein
DDX42	dead (asp-glu-ala-asp) box polypeptide 42
DHDDS	dehydrodolichyl diphosphate synthase
DIRA52	diras family, gtp-binding ras-like 2
DKFZp761I2123	hypothetical protein dkfzp761I2123
DKK1	dickkopf homolog 1 (xenopus laevis)
DKK2	dickkopf homolog 2 (xenopus laevis)
DKK3	dickkopf homolog 3 (xenopus laevis)
DL1L1	delta-like 1 (drosophila)
DLST	dihydroliipoamide s-succinyltransferase (e2 component of 2-oxo-glutarate complex)
DMTF1	cyclin d binding myb-like transcription factor 1
DNAJB1	dnaj (hsp40) homolog, subfamily b, member 1
DNAJB5	dnaj (hsp40) homolog, subfamily b, member 5
DNAJB6	dnaj (hsp40) homolog, subfamily b, member 6

---

---

DNAJB9	dnaj (hsp40) homolog, subfamily b, member 9
DNAJC14	cytokine induced protein 29 kda
DNAL4	dynein, axonemal, light polypeptide 4
DOCK9	dedicator of cytokinesis 9
DPYSL2	dihydropyrimidinase-like 2
DUSP10	dual specificity phosphatase 10
DUSP16	dual specificity phosphatase 16
DUSP6	dual specificity phosphatase 6
DUSP8	dual specificity phosphatase 8
DYNC1I2	dynein, cytoplasmic 1, intermediate chain 2
DYNC1L12	dynein, cytoplasmic 1, light intermediate chain 2
DYNLT3	dynein, light chain, tctex-type 3
DYRK1A	dual-specificity tyrosine-(y)-phosphorylation regulated kinase 1a
EDEM1	er degradation enhancer, mannosidase alpha-like 1
EGR1	early growth response 1
EIF1B	eukaryotic translation initiation factor 1b
EIF4A2	eukaryotic translation initiation factor 4a, isoform 2
EIF5A2	eukaryotic translation initiation factor 5a2
ELOVL4	elongation of very long chain fatty acids (fen1/elo2, sur4/elo3, yeast)-like 4
EP300	e1a binding protein p300
EPAS1	endothelial pas domain protein 1
EPB41L1	erythrocyte membrane protein band 4.1-like 1
EPC1	enhancer of polycomb homolog 1 (drosophila)
ETV5	ets variant gene 5 (ets-related molecule)
EVI5L	ecotropic viral integration site 5-like
EXTL3	exostosins (multiple)-like 3
EYA1	eyes absent homolog 1 (drosophila)
FALZ	fetal alzheimer antigen
FAM38A	family with sequence similarity 38, member a
FAM43A	family with sequence similarity 43, member a
FAM45A	family with sequence similarity 45, member a
FAM57A	family with sequence similarity 57, member a
FAM8A1	family with sequence similarity 8, member a1
FBXL2	f-box and leucine-rich repeat protein 2
FBXL20	f-box and leucine-rich repeat protein 20
FBXL5	f-box and leucine-rich repeat protein 5
FBXO11	f-box only protein 11
FBXO21	f-box protein 21
FBXO34	f-box protein 34
FGF11	fibroblast growth factor 11
FHL2	four and a half lim domains 2
FLJ10154	hypothetical protein flj10154
FLJ14503	hypothetical protein flj14503
FLJ20558	hypothetical protein flj20558
FLJ31818	hypothetical protein flj31818
FLJ31951	hypothetical protein flj31951
FLJ37266	hypothetical protein loc283225
FLJ38101	hypothetical protein flj38101
FLJ40142	flj40142 protein
FLJ45187	flj45187 protein
FLNC	filamin c, gamma (actin binding protein 280)
FLOT2	flotillin 2
FMN2	formin 2
FNBP1	formin binding protein 1
FNBP4	formin binding protein 4
FOXC1	forkhead box c1
FOXJ2	forkhead box j2
FOXJ3	forkhead box j3
FRMD4A	ferm domain containing 4a
FSTL1	follicle-stimulating-like 1
FTS	fused toes homolog (mouse)
FVT1	follicular lymphoma variant translocation 1
FZD7	frizzled homolog 7 (drosophila)
GAB2	grb2-associated binding protein 2
GAS1	growth arrest-specific 1
GATAD2B	gata zinc finger domain containing 2b
GFPT2	glutamine-fructose-6-phosphate transaminase 2
GLRB	glycine receptor, beta
GNAI2	guanine nucleotide binding protein (g protein), alpha inhibiting activity polypeptide 2
GNAO1	guanine nucleotide binding protein (g protein), alpha activating activity polypeptide o
GNAQ	guanine nucleotide binding protein (g protein), q polypeptide
GOLGA1	golgi autoantigen, golgin subfamily a, 1
GOLGA3	golgi autoantigen, golgin subfamily a, 3
GRIK2	glutamate receptor, ionotropic, kainate 2
GRIK4	glutamate receptor, ionotropic, kainate 4
GTPBP2	gtp binding protein 2
GULP1	gulp, engulfment adaptor pth domain containing 1
H3F3B	h3 histone, family 3a
HAND1	heart and neural crest derivatives expressed 1
HARSL	histidyl-trna synthetase-like
HBP1	hmg-box transcription factor 1
HCN3	hyperpolarization activated cyclic nucleotide-gated potassium channel 3
HDAC4	histone deacetylase 4
HDHC3	hd domain containing 3
HELZ	helicase with zinc finger
HIC1	hypermethylated in cancer 1
HIF1AN	hypoxia-inducible factor 1, alpha subunit inhibitor
HIVEP1	human immunodeficiency virus type i enhancer binding protein 1
HIVEP2	human immunodeficiency virus type i enhancer binding protein 2
HNRPU	heterogeneous nuclear ribonucleoprotein u (scaffold attachment factor a)
HOXC8	homeobox c8

---

---

HRIHFB2122	
IGF2R	insulin-like growth factor 2 receptor
IGSF4	immunoglobulin superfamily, member 4
IGSF4B	immunoglobulin superfamily, member 4b
IGSF4C	immunoglobulin superfamily, member 4c
IGSF4D	immunoglobulin superfamily, member 4d
IL17RD	interleukin 17 receptor d
ILF3	interleukin enhancer binding factor 3, 90kda
IQWD1	iq motif and wd repeats 1
IRF1	interferon regulatory factor 1
IRS2	insulin receptor substrate 2
ITGB1	integrin, beta 1 (fibronectin receptor, beta polypeptide, antigen cd29 includes mdf2, msk12)
ITM2C	integral membrane protein 2c
IXL	intersex-like (drosophila)
JAG1	jagged 1 (alagille syndrome)
JARID1B	jumonji, at rich interactive domain 1b (rbp2-like)
JOSD1	josephin domain containing 1
JUN	v-jun sarcoma virus 17 oncogene homolog (avian)
KBTD2	kelch repeat and btb (poz) domain containing 2
KCND1	potassium voltage-gated channel, shal-related subfamily, member 1
KCNJ2	potassium inwardly-rectifying channel, subfamily j, member 2
KCNQ2	potassium voltage-gated channel, kqt-like subfamily, member 2
KIAA0240	kiaa0240
KIAA0323	kiaa0323
KIAA0350	kiaa0350 protein
KIAA0376	kiaa0376 protein
KIAA0494	kiaa0494
KIAA0513	kiaa0513
KIAA0828	kiaa0828 protein
KIAA0831	kiaa0831
KIAA1128	kiaa1128
KIAA1267	dkfzp727c091 protein
KIAA1370	kiaa1370
KIAA1522	kiaa1522
KIAA1598	kiaa1598
KIAA1600	kiaa1600
KIAA1961	kiaa1961 gene
KIF1B	kinesin family member 1b
KIF3B	kinesin family member 3b
KIF3C	kinesin family member 3c
KIT	v-kit hardy-zuckerman 4 feline sarcoma viral oncogene homolog
KLC2	kinesin light chain 2
KLF10	kruppel-like factor 10
KLF11	kruppel-like factor 11
KLF12	kruppel-like factor 12
KLF13	kruppel-like factor 13
KLHL13	kelch-like 13 (drosophila)
KLHL3	kelch-like 3 (drosophila)
LASS6	lag1 longevity assurance homolog 6 (s. cerevisiae)
LEFTY1	left-right determination factor 1
LEMD3	lem domain containing 3
LJFR	leukemia inhibitory factor receptor
LIMK1	lim domain kinase 1
LKAP	limkain b1
LMAN2L	lectin, mannose-binding 2-like
LOC129285	smooth muscle myosin heavy chain 11 isoform sm1-like
LOC153222	adult retina protein
LONRF1	lon peptidase n-terminal domain and ring finger 1
LONRF2	lon peptidase n-terminal domain and ring finger 2
LPHN2	latrophilin 2
LPP	lim domain containing preferred translocation partner in lipoma
LRIG1	leucine-rich repeats and immunoglobulin-like domains 1
LRRFIP2	leucine rich repeat (in flin) interacting protein 2
LZTFL1	leucine zipper transcription factor-like 1
MAFG	v-maf musculoaponeurotic fibrosarcoma oncogene homolog g (avian)
MAGI2	membrane associated guanylate kinase, ww and pdz domain containing 2
MAP2K4	mitogen-activated protein kinase kinase 4
MAP3K12	mitogen-activated protein kinase kinase kinase 12
MAP3K4	mitogen-activated protein kinase kinase kinase 4
MAP3K5	mitogen-activated protein kinase kinase kinase 5
MAP3K8	mitogen-activated protein kinase kinase kinase 8
MAP3K9	mitogen-activated protein kinase kinase kinase 9
MAP4	microtubule-associated protein 4
MAP4K1	mitogen-activated protein kinase kinase kinase kinase 1
MAP4K5	mitogen-activated protein kinase kinase kinase kinase 5
MAPK3	mitogen-activated protein kinase 3
MAPK6	mitogen-activated protein kinase 6
MAPK8IP3	mitogen-activated protein kinase 8 interacting protein 3
MAPK9	mitogen-activated protein kinase 9
MAPRE3	microtubule-associated protein, rp/eb family, member 3
MBTPS1	membrane-bound transcription factor peptidase, site 1
MECP2	methyl cpq binding protein 2 (rett syndrome)
MEF2C	mads box transcription enhancer factor 2, polypeptide c (myocyte enhancer factor 2c)
MEF2D	mads box transcription enhancer factor 2, polypeptide d (myocyte enhancer factor 2d)
MEIS1	meis1, myeloid ecotropic viral integration site 1 homolog (mouse)
MGC3123	hypothetical protein mgc3123
MGC33486	hypothetical protein mgc33486
MGC40405	hypothetical protein mgc40405
MGEA5	meningioma expressed antigen 5 (hyaluronidase)
MIDIIP1	mid1 interacting protein 1 (gastrulation specific g12-like (zebrafish))
MKRN1	makorin, ring finger protein, 1

---

---

MLL	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, drosophila)
MLL5	hypothetical protein flj10078
MLR2	ligand-dependent corepressor
MMD	monocyte to macrophage differentiation-associated
MNT	max binding protein
MOAP1	modulator of apoptosis 1
MON2	mon2 homolog (yeast)
MPPED2	metallophosphoesterase domain containing 2
MTF1	metal-regulatory transcription factor 1
MTMR3	myotubularin related protein 3
MXI1	max interactor 1
MYST4	myst histone acetyltransferase (monocytic leukemia) 4
NAGK	n-acetylglucosamine kinase
NANOS1	nanos homolog 1 (drosophila)
NAPB	neuritis with brachial predilection
NAPB	n-ethylmaleimide-sensitive factor attachment protein, beta
NAV1	hypothetical protein mgc14961
NBEA	neurobeachin
NCOA1	nuclear receptor coactivator 1
NCOA3	nuclear receptor coactivator 3
NCOA7	nuclear receptor coactivator 7
NCSTN	nicastin
NDEL1	nude nuclear distribution gene e homolog like 1 (a. nidulans)
NDRG4	ndrg family member 4
NEBL	nebulin
NEDD4L	neural precursor cell expressed, developmentally down-regulated 4-like
NEDD9	neural precursor cell expressed, developmentally down-regulated 9
NEUROG2	neurogenin 2
NFAT5	nuclear factor of activated t-cells 5, tonicity-responsive
NFIA	nuclear factor i/a
NFIB	nuclear factor i/b
NIP30	nefa-interacting nuclear protein nip30
NKIRAS1	nfkb inhibitor interacting ras-like 1
NLGN1	neuroligin 1
NLGN2	neuroligin 2
NPC1	niemann-pick disease, type c1
NPC1	nasopharyngeal carcinoma 1
NPEPL1	aminopeptidase-like 1
NR2F2	nuclear receptor subfamily 2, group f, member 2
NRBP1	nuclear receptor binding protein 1
NTE	neuropathy target esterase
NXP1	neurexophilin 1
OACT2	o-acyltransferase (membrane bound) domain containing 2
OACT5	o-acyltransferase (membrane bound) domain containing 5
OCRL	oculocerebrorenal syndrome of lowe
OLFM3	olfactomedin 3
OSBPL5	kiaa1534 protein
OSTM1	osteopetrosis associated transmembrane protein 1
OTUD4	kiaa1046 protein
P2RX4	purinergic receptor p2x, ligand-gated ion channel, 4
PAFAH1B1	platelet-activating factor acetylhydrolase, isoform ib, alpha subunit 45kda
PALLD	palladin, cytoskeletal associated protein
PAM	peptidylglycine alpha-amidating monooxygenase
PANX2	pannexin 2
PAPPA	pregnancy-associated plasma protein a, pappalysin 1
PBX3	pre-b-cell leukemia transcription factor 3
PCDHA4	protocadherin alpha 4
PCGF2	polycomb group ring finger 2
PCGF4	polycomb group ring finger 4
PCNP	pest-containing nuclear protein
PDAF1	pdgfa associated protein 1
PDGFRA	platelet-derived growth factor receptor, alpha polypeptide
PDPR	pyruvate dehydrogenase phosphatase regulatory subunit
PGM2L1	phosphoglucomutase 2-like 1
PHC1	polyhomeotic-like 1 (drosophila)
PHF1	phd finger protein 1
PHF12	phd finger protein 12
PHF13	phd finger protein 13
PHF15	phd finger protein 15
PHF2	phd finger protein 2
PIAS3	protein inhibitor of activated stat, 3
PIB5PA	inositol polyphosphate 5-phosphatase
PIK3R1	phosphoinositide-3-kinase, regulatory subunit 1 (p85 alpha)
PIP5K1C	phosphatidylinositol-4-phosphate 5-kinase, type i, gamma
PIP5K2C	phosphatidylinositol-4-phosphate 5-kinase, type ii, gamma
PLSD	phosphatidylserine decarboxylase
PKD1	polycystic kidney disease 1 (autosomal dominant)
PLCB1	phospholipase c, beta 1 (phosphoinositide-specific)
PLCC1	phospholipase c, gamma 1
PLEKHA1	pleckstrin homology domain containing, family a (phosphoinositide binding specific) member 1
PLEKHA6	pleckstrin homology domain containing, family a member 6
PLEKHH1	pleckstrin homology domain containing, family h (with myth4 domain) member 1
PLEKHM1	pleckstrin homology domain containing, family m (with run domain) member 1
POGZ	pogo transposable element with znf domain
POLQ	polymerase (dna directed), theta
PPCS	phosphopantothienoylcysteine synthetase
PPF1A3	protein tyrosine phosphatase, receptor type, f polypeptide (ptprf), interacting protein (liprin), alpha 3
PPP2R2C	protein phosphatase 2 (formerly 2a), regulatory subunit b (pr 52), gamma isoform
PPP3CB	protein phosphatase 3 (formerly 2b), catalytic subunit, beta isoform (calcineurin a beta)
PPP3R1	protein phosphatase 3 (formerly 2b), regulatory subunit b, 19kda, alpha isoform (calcineurin b, type i)
PRDM4	pr domain containing 4

---

---

PRKCE	protein kinase c, epsilon
PRO0149	pro0149 protein
PSAP	prosaposin (variant gaucher disease and variant metachromatic leukodystrophy)
PSD2	pleckstrin and sec7 domain containing 2
PTCH	patched homolog (drosophila)
PTPRA	protein tyrosine phosphatase, receptor type, a
PTPRM	protein tyrosine phosphatase, receptor type, m
PUM2	pumilio homolog 2 (drosophila)
PURA	purine-rich element binding protein a
PURB	purine-rich element binding protein b
PVRL2	poliovirus receptor-related 2 (herpesvirus entry mediator b)
RAB10	rab10, member ras oncogene family
RAB11FIP2	rab11 family interacting protein 2 (class i)
RAB22A	rab22a, member ras oncogene family
RAB23	rab23, member ras oncogene family
RAB2B	rab2b, member ras oncogene family
RAB4B	rab4b, member ras oncogene family
RAB5B	rab5b, member ras oncogene family
RAB6B	rab6b, member ras oncogene family
RAB7	rab7, member ras oncogene family
RABGAP1	rab gtpase activating protein 1
RAD23A	rad23 homolog a (s. cerevisiae)
RAD9A	rad9 homolog a (s. pombe)
RAI17	retinoic acid induced 17
RAI2	retinoic acid induced 2
RALGDS	ral guanine nucleotide dissociation stimulator
RALGPS1	ral gef with ph domain and sh3 binding motif 1
RAP2C	rap2c, member of ras oncogene family
RAPGEFL1	rap guanine nucleotide exchange factor (gef)-like 1
RARB	retinoic acid receptor, beta
RB1CC1	rb1-inducible coiled-coil 1
RBJ	ras-associated protein rap1
RBL2	retinoblastoma-like 2 (p130)
RBM9	rna binding motif protein 9
RBMS1	rna binding motif, single stranded interacting protein 1
RCE1	rce1 homolog, prenyl protein peptidase (s. cerevisiae)
RCOR3	rest corepressor 3
RECK	reversion-inducing-cysteine-rich protein with kazal motifs
RET	ret proto-oncogene (multiple endocrine neoplasia and medullary thyroid carcinoma 1, hirschsprung disease)
REV1L	rev1-like (yeast)
REV3L	rev3-like, catalytic subunit of dna polymerase zeta (yeast)
RFX1	regulatory factor x, 1 (influences hla class ii expression)
RGL1	ral guanine nucleotide dissociation stimulator-like 1
RG517	regulator of g-protein signalling 17
RHOC	ras homolog gene family, member c
RHPN2	rhophilin, rho gtpase binding protein 2
RIMS3	regulating synaptic membrane exocytosis 3
RIN2	ras and rab interactor 2
RNF103	ring finger protein 103
RNF144	ring finger protein 144
RNF167	ring finger protein 167
RNF38	hypothetical protein flj21343
RNF41	ring finger protein 41
RNF44	ring finger protein 44
RNH1	ribonuclease/angiogenin inhibitor 1
RPS6KA2	ribosomal protein s6 kinase, 90kda, polypeptide 2
RPS6KA4	ribosomal protein s6 kinase, 90kda, polypeptide 4
RPS6KA5	ribosomal protein s6 kinase, 90kda, polypeptide 5
RRAGB	ras-related gtp binding b
RSBN1	round spermatid basic protein 1
RSPRY1	ring finger and spry domain containing 1
RTN1	reticulin 1
RTN2	reticulin 2
RTN3	reticulin 3
RUNX1	runt-related transcription factor 1 (acute myeloid leukemia 1; aml1 oncogene)
RUNX1T1	runt-related transcription factor 1; translocated to, 1 (cyclin d-related)
RYBP	ring1 and yy1 binding protein
SARI1B	sar1 gene homolog b (s. cerevisiae)
SCAMP5	secretory carrier membrane protein 5
SCARB2	scavenger receptor class b, member 2
SCHIP1	schwannomin interacting protein 1
SCOC	short coiled-coil protein
SCRN1	secernin 1
SEMA4B	sema domain, immunoglobulin domain (ig), transmembrane domain (tm) and short cytoplasmic domain, (semaphorin) 4b
SEMA6A	ht018 protein
SERTAD3	serta domain containing 3
SFRS5	splicing factor, arginine/serine-rich 5
SGIP1	sh3-domain grb2-like (endophilin) interacting protein 1
SH3BGRL2	sh3 domain binding glutamic acid-rich protein like 2
SH3BP4	sh3-domain binding protein 4
SHANK2	sh3 and multiple ankyrin repeat domains 2
SHC4	shc (src homology 2 domain containing) family, member 4
SIGIRR	single immunoglobulin and toll-interleukin 1 receptor (tir) domain
SIP1IL2	signal-induced proliferation-associated 1 like 2
SIRT7	pyrroline-5-carboxylate reductase 1
SLC1A2	solute carrier family 1 (glial high affinity glutamate transporter), member 2
SLC25A1	solute carrier family 25 (mitochondrial carrier; citrate transporter), member 1
SLC25A27	solute carrier family 25, member 27
SLC2A4RG	slc2a4 regulator
SLC30A3	solute carrier family 30 (zinc transporter), member 3
SLC30A7	solute carrier family 30 (zinc transporter), member 7

---



---

SLC31A2	solute carrier family 31 (copper transporters), member 2
SLC36A1	lysosomal amino acid transporter 1
SLC39A1	solute carrier family 39 (zinc transporter), member 1
SLC6A17	hypothetical protein loc284462
SLC9A6	solute carrier family 9 (sodium/hydrogen exchanger), member 6
SLIT2	slit homolog 2 (drosophila)
SMAD5	smad, mothers against dpp homolog 5 (drosophila)
SMOC1	sparc related modular calcium binding 1
SNIP1	smad nuclear interacting protein 1
SNN	stannin
SNRK	snf related kinase
SNX16	sorting nexin 16
SNX27	sorting nexin family member 27
SOC55	suppressor of cytokine signaling 5
SORCS1	sortilin-related vps10 domain containing receptor 1
SORL1	sortilin-related receptor, l(dlr class) a repeats-containing
SOX4	sry (sex determining region y)-box 4
SOX9	sry (sex determining region y)-box 9 (campomelic dysplasia, autosomal sex-reversal)
SPEN	spen homolog, transcriptional regulator (drosophila)
SPHK2	sphingosine kinase 2
SPIRE1	spire homolog 1 (drosophila)
SPRYD3	spry domain containing 3
SPTBN4	spectrin, beta, non-erythrocytic 4
SQSTM1	sequestosome 1
SREBF1	sterol regulatory element binding transcription factor 1
SRGAP3	slit-robo rho gtpase activating protein 3
SRR	serine racemase
SRRM2	serine/arginine repetitive matrix 2
SSI1L1	synovial sarcoma translocation gene on chromosome 18-like 1
STAT3	signal transducer and activator of transcription 3 (acute-phase response factor)
STK11IP	serine/threonine kinase 11 interacting protein
STK19	serine/threonine kinase 19
STMN4	stathmin-like 4
STX1A	syntaxin 1a (brain)
STX3A	syntaxin 3a
STXBP1	syntaxin binding protein 1
SURF4	surfeit 4
SUZ12	suppressor of zeste 12 homolog (drosophila)
SYDE1	synapse defective 1, rho gtpase, homolog 1 (c. elegans)
SYN1	synapsin i
SYN2	synapsin ii
SYNGR1	synaptogyrin 1
SYT1	synaptotagmin i
SYT11	synaptotagmin xi
SYT13	synaptotagmin xiii
TACC2	transforming, acidic coiled-coil containing protein 2
TANC1	tetratricopeptide repeat, ankyrin repeat and coiled-coil containing 1
TAOK1	tao kinase 1
TARDBP	tar dna binding protein
TAX1BP1	tax1 (human t-cell leukemia virus type i) binding protein 1
TBC1D20	tbc1 domain family, member 20
TCERG1L	transcription elongation regulator 1-like
TCF4	transcription factor 4
TGOLN2	trans-golgi network protein 2
TIA1	tia1 cytotoxic granule-associated rna binding protein
TJP1	tight junction protein 1 (zona occludens 1)
TLX3	t-cell leukemia homeobox 3
TMEM15	transmembrane protein 15
TMEM16C	transmembrane protein 16c
TMEM16F	transmembrane protein 16f
TMEM32	transmembrane protein 32
TMEM55B	transmembrane protein 55b
TMEM87A	transmembrane protein 87a
TMEPA1	transmembrane, prostate androgen induced rna
TNFAIP1	tumor necrosis factor, alpha-induced protein 1 (endothelial)
TNFRSF12A	tumor necrosis factor receptor superfamily, member 12a
TNRC6A	trinucleotide repeat containing 6a
TP53INP1	tumor protein p53 inducible nuclear protein 1
TP53INP2	tumor protein p53 inducible nuclear protein 2
TPP1	tripeptidyl peptidase i
TRAK2	trafficking protein, kinesin binding 2
TRIB2	tribbles homolog 2 (drosophila)
TRIM2	tripartite motif-containing 2
TSC1	tuberous sclerosis 1
TSC22D2	tsc22 domain family, member 2
TSC22D3	tsc22 domain family, member 3
TSGA14	testis specific, 14
TSPYL2	tspy-like 2
TUBB2B	tubulin, beta 2b
TULP4	tubby like protein 4
TUSC2	tumor suppressor candidate 2
TXNDC12	thioredoxin domain containing 12 (endoplasmic reticulum)
TXNIP	thioredoxin interacting protein
UBE2D2	ubiquitin-conjugating enzyme e2d 2 (ubc4/5 homolog, yeast)
UBE2H	ubiquitin-conjugating enzyme e2h (ubc8 homolog, yeast)
UBE2J1	ubiquitin-conjugating enzyme e2, j1 (ubc6 homolog, yeast)
UBE2Q2	ubiquitin-conjugating enzyme e2q (putative) 2
UBE2W	ubiquitin-conjugating enzyme e2w (putative)
UBE2Z	ubiquitin-conjugating enzyme e2z (putative)
UBL3	ubiquitin-like 3
UBLCP1	ubiquitin-like domain containing ctd phosphatase 1

---

---

UBTD1	ubiquitin domain containing 1
UCP3	uncoupling protein 3 (mitochondrial, proton carrier)
UNC84A	unc-84 homolog a (c. elegans)
USF2	upstream transcription factor 2, c-fos interacting
USP32	ubiquitin specific peptidase 32
USP34	ubiquitin specific peptidase 34
UTX	ubiquitously transcribed tetratricopeptide repeat, x chromosome
VAMP1	vesicle-associated membrane protein 1 (synaptobrevin 1)
VAMP2	vesicle-associated membrane protein 2 (synaptobrevin 2)
VAMP3	vesicle-associated membrane protein 3 (cellubrevin)
VAT1	vesicle amine transport protein 1 homolog (t. californica)
VCL	vinculin
VGLL4	vestigial like 4 (drosophila)
VPS4B	vacuolar protein sorting 4b (yeast)
WAC	ww domain containing adaptor with coiled-coil
WASL	wiskott-aldrich syndrome-like
WBP2	ww domain binding protein 2
WBSCR18	williams beuren syndrome chromosome region 18
WDR22	wd repeat domain 22
WDR26	wd repeat domain 26
WDR42A	wd repeat domain 42a
WDR44	wd repeat domain 44
WNT3	wingless-type mmtv integration site family, member 3
WSB1	wd repeat and socs box-containing 1
YPEL4	yippee-like 4 (drosophila)
YPEL5	yippee-like 5 (drosophila)
ZAK	sterile alpha motif and leucine zipper containing kinase ask
ZBTB4	zinc finger and btb domain containing 4
ZBTB7A	zinc finger and btb domain containing 7a
ZDHHC1	zinc finger, dhhc-type containing 1
ZDHHC17	zinc finger, dhhc-type containing 17
ZDHHC7	zinc finger, dhhc-type containing 7
ZFAND3	zinc finger, an1-type domain 3
ZFHX4	zinc finger homeodomain 4
ZFP91	zinc finger protein 91 homolog (mouse)
ZFYVE21	zinc finger, fyve domain containing 21
ZFYVE26	zinc finger, fyve domain containing 26
ZHX2	zinc fingers and homeoboxes 2
ZKSCAN1	zinc finger with krab and scan domains 1
ZMYND11	zinc finger, mynd domain containing 11
ZNFI61	zinc finger protein 161
ZNIF238	zinc finger protein 238
ZNIF289	zinc finger protein 289, id1 regulated
ZNIF3	zinc finger protein 3 (a8-51)
ZNIF319	zinc finger protein 319
ZNIF436	zinc finger protein 436
ZNIF518	zinc finger protein 518
ZNIF608	dkfzp434m098 protein
ZYG11BL	zyg-11 homolog b (c. elegans)-like
ZYX	zyxin

## "Brain-enriched" group of targets which were down-regulated during differentiation

Gene Symbol	Gene Name
ABCC4	atp-binding cassette, sub-family c (cftr/mrp), member 4
ABCG1	atp-binding cassette, sub-family g (white), member 1
ABHD5	abhydrolase domain containing 5
ACSL1	fatty-acid-coenzyme a ligase, long-chain 1
ACTB, ACTG1	actin, beta
ACTR3	arp3 actin-related protein 3 homolog (yeast)
ADCY1	adenylate cyclase 1 (brain)
ADCY9	adenylate cyclase 9
ADORA2B	adenosine a2b receptor
AK2	adenylate kinase 2
AKT1S1	akt1 substrate 1 (proline-rich)
ALDH9A1	aldehyde dehydrogenase 9 family, member a1
ANF32B	acidic (leucine-rich) nuclear phosphoprotein 32 family, member b
ANXA11	annexin a11
ANXA5	annexin a5
ARG2	arginase, type ii
ASAM	adipocyte-specific adhesion molecule
ASCC2	hypothetical protein dkfzp586o0223
ASF1A	asf1 anti-silencing function 1 homolog a (s. cerevisiae)
ATG4C	atg4 autophagy related 4 homolog c (s. cerevisiae)
ATP1A1	atpase, na+/k+ transporting, alpha 1 polypeptide
ATP6V0A2	atpase, h+ transporting, lysosomal v0 subunit a2
BCAT2	branched chain aminotransferase 2, mitochondrial
BCKDHA	branched chain keto acid dehydrogenase e1, alpha polypeptide
BCL11A	b-cell cll/lymphoma 11a (zinc finger protein)
BRP44L	brain protein 44-like
C10orf42	hypothetical protein flj21463
C14orf130	chromosome 14 open reading frame 130
C1GALT1	core 1 synthase, glycoprotein-n-acetylgalactosamine 3-beta-galactosyltransferase, 1
C9orf72	hypothetical protein flj11109

---

---

C9orf88	chromosome 9 open reading frame 88
CAMKK2	calcium/calmodulin-dependent protein kinase kinase 2, beta
CAPN2	calpain 2, (m/ii) large subunit
CAPZA1	capping protein (actin filament) muscle z-line, alpha 1
CASC3	cancer susceptibility candidate 3
CAST	calpastatin
CBLN2	cerebellin 2 precursor
CBX1	chromobox homolog 1 (hp1 beta homolog drosophila )
CCDC43	coiled-coil domain containing 43
CCDC6	coiled-coil domain containing 6
CCDC71	coiled-coil domain containing 71
CCNG1	cyclin g1
CCNJ	cyclin j
CDCA4	cell division cycle associated 4
CDH11	cadherin 11, type 2, ob-cadherin (osteoblast)
CECR6	cat eye syndrome chromosome region, candidate 6
CHSY1	carbohydrate (chondroitin) synthase 1
CNOT7	ccr4-not transcription complex, subunit 7
CNTN1	contactin 1
COL4A1	collagen, type iv, alpha 1
CSTF3	cleavage stimulation factor, 3' pre-rna, subunit 3, 77kda
CTDSP1	ctd (carboxy-terminal domain, rna polymerase ii, polypeptide a) small phosphatase 1
CTDSP2	ctd (carboxy-terminal domain, rna polymerase ii, polypeptide a) small phosphatase 2
CUL4A	cullin 4a
CXCR4	chemokine (c-x-c motif) receptor 4
DAZAP1	daz associated protein 1
DCP2	dcp2 decapping enzyme homolog (s. cerevisiae)
DHCR24	24-dehydrocholesterol reductase
DKFZP564J0863	dkfzp564j0863 protein
DLG5	discs, large homolog 5 (drosophila)
DLX5	distal-less homeobox 5
DOLPP1	dolichyl pyrophosphate phosphatase 1
DRD2	dopamine receptor d2
DSCR1	down syndrome critical region gene 1
DTNA	dystrobrevin, alpha
DYNCL11	dynein, cytoplasmic 1, intermediate chain 1
E2F5	e2f transcription factor 5, p130-binding
E2F7	e2f transcription factor 7
EEFSEC	eukaryotic elongation factor, selenocysteine-trna-specific
EGLN3	hypothetical protein flj21620
EHD4	eh-domain containing 4
EIF1AX	eukaryotic translation initiation factor 1a, x-linked
EIF3S1	eukaryotic translation initiation factor 3, subunit 1 alpha, 35kda
EIF4EBP2	eukaryotic translation initiation factor 4e binding protein 2
ELMO1	engulfment and cell motility 1
ELOVL1	cgi-88 protein
ELOVL5	elovl family member 5, elongation of long chain fatty acids (fen1/elo2, sur4/elo3-like, yeast)
ELOVL6	elovl family member 6, elongation of long chain fatty acids (fen1/elo2, sur4/elo3-like, yeast)
EPHA2	eph receptor a2
ERF	ets2 repressor factor
ESRRG	estrogen-related receptor gamma
ETF1	eukaryotic translation termination factor 1
ETS1	v-ets erythroblastosis virus e26 oncogene homolog 1 (avian)
EXOSC9	exosome component 9
EZH2	enhancer of zeste homolog 2 (drosophila)
FAM35A	family with sequence similarity 35, member a
FAM53B	family with sequence similarity 53, member b
FBXL11	f-box and leucine-rich repeat protein 11
FCHSD2	fch and double sh3 domains 2
FGFR1OP	fgfr1 oncogene partner
FKBP1A	fk506 binding protein 1a, 12kda
FLJ14768	hypothetical protein flj14768
FLJ20152	hypothetical protein flj20152
FLJ22222	hypothetical protein flj22222
FLRT3	fibronectin leucine rich transmembrane protein 3
FMNL2	formin-like 2
FN5	fn5 protein
FOXP1	forkhead box p1
FXR1	fragile x mental retardation, autosomal homolog 1
G3BP	ras-gtpase-activating protein sh3-domain-binding protein
GABPB2	ga binding protein transcription factor, beta subunit 1, 53kda
GALNT1	udp-n-acetyl-alpha-d-galactosamine:polypeptide n-acetylgalactosaminyltransferase 1 (galnac-t1)
GLTP	glycolipid transfer protein
GNA13	guanine nucleotide binding protein (g protein), alpha inhibiting activity polypeptide 3
GNG12	guanine nucleotide binding protein (g protein), gamma 12
GNPNAT1	glucosamine-phosphate n-acetyltransferase 1
GPAM	glycerol-3-phosphate acyltransferase, mitochondrial
GPM6B	glycoprotein m6b
GRIA3	glutamate receptor, ionotropic, ampa 3
GRIN1	glutamate receptor, ionotropic, n-methyl d-aspartate 1
GRSF1	g-rich rna sequence binding factor 1

---

---

GTF2I	general transcription factor ii, i
GYS1	glycogen synthase 1 (muscle)
HADHA	hydroxyacyl-coenzyme a dehydrogenase/3-ketoacyl-coenzyme a thiolase/enoyl-coenzyme a hydratase (trifunctional protein), alpha subunit
HADHSC	l-3-hydroxyacyl-coenzyme a dehydrogenase, short chain
HDAC9	histone deacetylase 9
HIC2	hypermethylated in cancer 2
HIP1	huntingtin interacting protein 1
HIST1H4K	h4 histone, family 2
HNRPF	heterogeneous nuclear ribonucleoprotein f
HNRPK	heterogeneous nuclear ribonucleoprotein k
HNRPLL	heterogeneous nuclear ribonucleoprotein l-like
IARS2	isoleucine-trna synthetase 2, mitochondrial
IGF2BP3	insulin-like growth factor 2 mrna binding protein 3
IPO11	importin 11
IPO7	importin 7
IQGAP1	iq motif containing gtpase activating protein 1
ITSN1	intersectin 1 (sh3 domain protein)
JAZF1	juxtaposed with another zinc finger gene 1
KATNA1	katanin p60 (atpase-containing) subunit a 1
KCNQ2	potassium voltage-gated channel, kqt-like subfamily, member 2
KCTD12	potassium channel tetramerisation domain containing 12
KIAA0963	kiaa0963
KIAA1576	kiaa1576 protein
KIAA1967	kiaa1967
KIF1C	kinesin family member 1c
KIF2	kinesin heavy chain member 2
KLHL18	kelch-like 18 (drosophila)
LDB2	lim domain binding 2
LGTN	ligatin
LHFP	lipoma hmgic fusion partner
LIN28B	lin-28 homolog b (c. elegans)
LITAF	lipopolysaccharide-induced tnfr factor
LMNA	lamin a/c
LMNB1	lamin b1
LMO3	lim domain only 3 (rhombotin-like 2)
LMO4	lim domain only 4
LOC133619	hypothetical protein mgc12103
LOC144097	hypothetical protein bc007540
LOC153364	similar to metallo-beta-lactamase superfamily protein
LOC400451	hypothetical gene supported by ak075564; bc060873
LSM12	lsm12 homolog (s. cerevisiae)
LUC7L2	cgi-59 protein
M6PRBP1	mannose-6-phosphate receptor binding protein 1
MAML1	mastermind-like 1 (drosophila)
MAP1A	microtubule-associated protein 1a
MAP3K7	mitogen-activated protein kinase kinase kinase 7
MAPK4	mitogen-activated protein kinase 4
MARCKS	myristoylated alanine-rich protein kinase c substrate
MED8	mediator of rna polymerase ii transcription, subunit 8 homolog (yeast)
MESDC1	mesoderm development candidate 1
MORC4	morc family cw-type zinc finger 4
MPZL1	myelin protein zero-like 1
MRPS7	mitochondrial ribosomal protein s7
MTDH	metadherin
MTHFD2	methylenetetrahydrofolate dehydrogenase (nadp+ dependent) 2, methenyltetrahydrofolate cyclohydrolase
MTMR12	myotubularin related protein 12
MYLIP	myosin regulatory light chain interacting protein
MYO10	myosin x
MYOHD1	myosin head domain containing 1
NAGPA	n-acetylglucosamine-1-phosphodiester alpha-n-acetylglucosaminidase
NARG1	nmda receptor regulated 1
NCK2	nck adaptor protein 2
NCOA4	nuclear receptor coactivator 4
NDUFS4	nadh dehydrogenase (ubiquinone) fe-s protein 4, 18kda (nadh-coenzyme q reductase)
NEF3	neurofilament 3 (150kda medium)
NEK2	nima (never in mitosis gene a)-related kinase 2
NFIX	nuclear factor i/x (ccat-binding transcription factor)
NFKB1	nuclear factor of kappa light polypeptide gene enhancer in b-cells 1 (p105)
NKAP	nf-kappab activating protein
NME4	non-metastatic cells 4, protein expressed in
NMT1	n-myristoyltransferase 1
NRCAM	neuronal cell adhesion molecule
NSMAF	neutral sphingomyelinase (n-smase) activation associated factor
NSUN2	nol1/nop2/sun domain family, member 2
NUDCD2	nudc domain containing 2
NUMA1	nuclear mitotic apparatus protein 1
NUTF2	nuclear transport factor 2
NXN	nucleoredoxin
NXT2	nuclear transport factor 2-like export factor 2
OPRS1	opioid receptor, sigma 1
ORC5L	origin recognition complex, subunit 5-like (yeast)

---

---

OXSR1	oxidative-stress responsive 1
P15RS	hypothetical protein flj10656
P4HA1	procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide i
PAK7	p21(cdkn1a)-activated kinase 7
PANK1	pantothenate kinase 1
PAQR8	progesterone and adiponectin receptor family member viii
PARP1	poly (adp-ribose) polymerase family, member 1
PBEF1	pre-b-cell colony enhancing factor 1
PCAF	p300/cbp-associated factor
PDE2A	phosphodiesterase 2a, cgmp-stimulated
PDE7B	phosphodiesterase 7b
PDIA5	protein disulfide isomerase family a, member 5
PFN2	profilin 2
PGM1	phosphoglucomutase 1
PHF16	phd finger protein 16
PHF19	phd finger protein 19
PHF20L1	phd finger protein 20-like 1
PHTF2	putative homeodomain transcription factor 2
PI4K2B	phosphatidylinositol 4-kinase type 2 beta
PLACL2	pleiomorphic adenoma gene-like 2
PLEKHC1	pleckstrin homology domain containing, family c (with ferm domain) member 1
PLOD3	procollagen-lysine, 2-oxoglutarate 5-dioxygenase 3
PLP2	proteolipid protein 2 (colonic epithelium-enriched)
PMP22	peripheral myelin protein 22
PODXL	podocalyxin-like
POU3F2	pou domain, class 3, transcription factor 2
PPM1F	protein phosphatase 1f (pp2c domain containing)
PPP1CC	protein phosphatase 1, catalytic subunit, gamma isoform
PPP2R5D	protein phosphatase 2, regulatory subunit b (b56), delta isoform
PRNP	prion protein interacting protein
PRPS1	phosphoribosyl pyrophosphate synthetase 1
PSME3	proteasome (prosome, macropain) activator subunit 3 (pa28 gamma; ki)
PTEN	phosphatase and tensin homolog (mutated in multiple advanced cancers 1)
PTGFRN	prostaglandin f2 receptor negative regulator
RAB1B	rab1b, member ras oncogene family
RAB6A	rab6a, member ras oncogene family
RAF1	v-raf-1 murine leukemia viral oncogene homolog 1
RAI14	retinoic acid induced 14
RALBP1	rala binding protein 1
RANBP5	ran binding protein 5
REEP4	receptor accessory protein 4
RHBDF2	rhomboid 5 homolog 2 (drosophila)
RHOG	ras homolog gene family, member g (rho g)
RHOT1	ras homolog gene family, member t1
RIMS4	regulating synaptic membrane exocytosis 4
RNF130	ring finger protein 130
ROR2	receptor tyrosine kinase-like orphan receptor 2
RORB	rar-related orphan receptor b
RPIA	ribose 5-phosphate isomerase a (ribose 5-phosphate epimerase)
RPS6KA2	ribosomal protein s6 kinase, 90kda, polypeptide 2
RQCD1	rcd1 required for cell differentiation1 homolog (s. pombe)
RWDD4A	rwd domain containing 4a
RXRA	retinoid x receptor, alpha
SDC1	syndecan 1
SDC2	syndecan 2 (heparan sulfate proteoglycan 1, cell surface-associated, fibroglycan)
SDF2L1	stromal cell-derived factor 2-like 1
SEC13L1	sec13-like 1 (s. cerevisiae)
SEC61A1	sec61 alpha 1 subunit (s. cerevisiae)
SELI	selenoprotein i
SERP1	stress-associated endoplasmic reticulum protein 1
SERTAD4	serta domain containing 4
SFRS1	splicing factor, arginine/serine-rich 1 (splicing factor 2, alternate splicing factor)
SFRS10	splicing factor, arginine/serine-rich 10 (transformer 2 homolog, drosophila)
SFXN2	sideroflexin 2
SGK	serum/glucocorticoid regulated kinase
SKP2	s-phase kinase-associated protein 2 (p45)
SLC29A1	solute carrier family 29 (nucleoside transporters), member 1
SLC35A4	solute carrier family 35, member a4
SMAD7	smad, mothers against dpp homolog 7 (drosophila)
SOX13	sry (sex determining region y)-box 13
SP1	sp1 transcription factor
SPPL2A	signal peptide peptidase-like 2a
SPRY2	sprouty homolog 2 (drosophila)
SPT2D1	spt2, suppressor of ty, domain containing 1 (s. cerevisiae)
ST6GALNAC3	st6 (alpha-n-acetyl-neuraminyl-2,3-beta-galactosyl-1,3)-n-acetylgalactosaminide alpha-2,6-sialyltransferase 3
STARD7	start domain containing 7
STK39	serine threonine kinase 39 (ste20/sps1 homolog, yeast)
STMN1	stathmin 1/oncoprotein 18
STRN3	striatin, calmodulin binding protein 3
SUCLG2	succinate-coa ligase, gdp-forming, beta subunit
SUGT1	sgt1, suppressor of g2 allele of skp1 (s. cerevisiae)

---

---

SUV39H1	suppressor of variegation 3-9 homolog 1 (drosophila)
SYAP1	hypothetical protein flj14495
SYPL1	synaptophysin-like 1
TBC1D22A	tbc1 domain family, member 22a
TCF12	transcription factor 12 (htf4, helix-loop-helix transcription factors 4)
TCF3	transcription factor 3 (e2a immunoglobulin enhancer binding factors e12/e47)
TEX261	testis expressed sequence 261
TFAP4	transcription factor ap-4 (activating enhancer binding protein 4)
TFDP2	transcription factor dp-2 (e2f dimerization partner 2)
TIPRL	tip41, tor signalling pathway regulator-like (s. cerevisiae)
TJP2	tight junction protein 2 (zona occludens 2)
TLK1	tousled-like kinase 1
TLK2	tousled-like kinase 2
TMEM109	transmembrane protein 109
TOE1	hypothetical protein flj13949
TOM1L1	target of myb1-like 1 (chicken)
TOMM34	translocase of outer mitochondrial membrane 34
TPCN2	two pore segment channel 2
TPP2	tripeptidyl peptidase ii
TPST2	tyrosylprotein sulfotransferase 2
TRIM9	tripartite motif-containing 9
TUBG1	tubulin, gamma 1
TXNDC	thioredoxin domain containing
TXNDC5	thioredoxin domain containing 5
TYSD1	trypsin domain containing 1
UBE2H	ubiquitin-conjugating enzyme e2h (ubc8 homolog, yeast)
UBE2V2	ubiquitin-conjugating enzyme e2 variant 2
UBE4A	ubiquitination factor e4a (ufd2 homolog, yeast)
UHRF1	ubiquitin-like, containing phd and ring finger domains, 1
USF2	upstream transcription factor 2, c-fos interacting
USP14	ubiquitin specific peptidase 14 (trna-guanine transglycosylase)
USP38	ubiquitin specific peptidase 38
USP46	ubiquitin specific peptidase 46
USP48	hypothetical protein flj11328
VDAC3	voltage-dependent anion channel 3
VIM	vimentin
VPS37B	vacuolar protein sorting 37b (yeast)
WASF1	was protein family, member 1
WDR20	wd repeat domain 20
WEE1	wee1 homolog (s. pombe)
XPO4	exportin 4
XPO5	exportin 5
YME1L1	yme1-like 1 (s. cerevisiae)
YOD1	yod1 otu deubiquinating enzyme 1 homolog ( yeast)
ZCCHC3	zinc finger, cchc domain containing 3
ZDHHC23	zinc finger, dhhc-type containing 23
ZFX1B	zinc finger homeobox 1b
ZMPSTE24	zinc metallopeptidase (ste24 homolog, yeast)
ZNF313	zinc finger protein 313
ZNF503	zinc finger protein 503

**Supplementary Table 2: Microarray and qPCR data for up- and down-regulated microRNA**

miRNA	Fold change microarray	p value	Fold change qPCR	Genomic Context
<i>Up-regulated</i>				
hsa-miR-10a	3.98	1.84E-05	1.79	17q21.32
hsa-miR-128a	2.39	0.004	3.73	2q21.3 <sup>a</sup>
hsa-miR-331	2.17	0.035		12q22
hsa-miR-124a	2.05	0.007	1.37	8p23.1, 8p12.3, 20q13.33 <sup>a</sup>
hsa-miR-409-5p	1.78	0.008		14q32.31
hsa-miR-210	1.65	0.03		11p15.5
hsa-miR-149	1.61	0.049		2q37.3
hsa-miR-9	-2.53	0.008	1.23	1q23.1, 5q14.3, 15q26.1 <sup>a</sup>
hsa-miR-423	1.43	0.004		17q11.2
hsa-miR-483	1.22	0.043		11p15.5
hsa-miR-208	1.08	0.046		14q11.2
hsa-miR-184	1.07	0.046		15q25.1
<i>Down-regulated</i>				
hsa-miR-301	-3.26	0.004	-2.13	17q23.2
hsa-miR-19a	-2.42	0.003	-1.18	13q31.3 <sup>#</sup>
hsa-miR-520d*	-2.08	0.006		19q13.42 <sup>#</sup>
hsa-miR-18a	-1.93	0.002		13q31.3 <sup>a, #</sup>
hsa-miR-106a	-1.85	0.025	-1.96	Xq26.2 <sup>#</sup>
hsa-miR-218	-1.81	0.031		4p15.31, 5q34
hsa-miR-20a	-1.78	0.04	-2.22	13q31.3 <sup>#</sup>
hsa-miR-137	-1.76	0.035		1p21.3
hsa-miR-15b	-1.73	0.034	-1.3	3q25.33
hsa-miR-20b	-1.72	0.002		Xq26.2 <sup>#</sup>
hsa-miR-25	-1.71	0.021		7q22.1 <sup>#</sup>
hsa-miR-130a	-1.66	0.021		11q12.1
hsa-miR-29b	-1.65	0.023	-1.25	7q32.3, 1q32.2 <sup>a</sup>
hsa-miR-19b	-1.62	0.002		13q31.3 <sup>#</sup> , Xq26.2 <sup>#</sup>
hsa-miR-34a	-1.62	0.01		1p36.22
hsa-let-7a	-1.58	0.036		9q22.32, 11q24.1, 22q13.31
hsa-miR-195	-1.57	0.042		17q13.1
hsa-miR-106b	-1.56	0.028		7q22.1 <sup>#</sup>
hsa-miR-199a*	-1.53	0.028		19p13.2, 1q24.3
hsa-miR-92	-1.47	0.042		13q31.3 <sup>#</sup> , Xq26.2 <sup>#</sup>
hsa-miR-138	-1.46	0.039		3p21.33, 16q13 <sup>a</sup>
hsa-miR-93	-1.46	0.009		7q22.1 <sup>#</sup>
hsa-miR-432*	-1.4	0.006		14q32.31
hsa-miR-519e*	-1.37	0.025		19q13.42
hsa-miR-101	-1.36	0.016		1p31.3, 9p24.1
hsa-miR-518*-526a	-1.35	0.006		19q13.42
hsa-miR-21	-1.33	0.004		17q23.2
hsa-miR-134	-1.25	0.02	-1.25	14q32.31
hsa-miR-98	-1.22	0.027		Xp11.22
hsa-miR-370	-1.13	0.004		14q32.31
hsa-miR-525	-1.07	0.039		19q13.42
hsa-miR-91 (aka miR-17-5p)	-2.58	0.108		13q31.3 <sup>#</sup>

**Abbreviations:** a: Brain-specific miRNA; #/shaded: Located within the mir-17 miRNA cluster on chromosome 13 or paralogous regions on chromosomes X and 7.



**Supplementary Table 3: Potential gene targets of miR-17 family identified using TargetCombo prediction algorithm**

Gene Symbol	Gene Name
AATK	apoptosis-associated tyrosine kinase
ABCA1	atp-binding cassette, sub-family a (abc1), member 1
ABCB7	atp-binding cassette, sub-family b (mdr/tap), member 7
ABCC5	atp-binding cassette, sub-family c (cfr/mrp), member 5
ABCC8	atp-binding cassette, sub-family c (cfr/mrp), member 8
ABCG4	atp-binding cassette, sub-family g (white), member 4
ABHD10	abhydrolase domain containing 10
ABHD13	chromosome 13 open reading frame 6
ABHD2	abhydrolase domain containing 2
ABHD3	abhydrolase domain containing 3
ABHD5	abhydrolase domain containing 5
ABI3BP	abi gene family, member 3 (nesh) binding protein
ABR	active bcr-related gene
ACAD9	acyl-coenzyme a dehydrogenase family, member 9
ACBD3	acyl-coenzyme a binding domain containing 3
ACBD5	acyl-coenzyme a binding domain containing 5
ACCN2	amiloride-sensitive cation channel 2, neuronal
ACCN4	amiloride-sensitive cation channel 4, pituitary
ACIN1	apoptotic chromatin condensation inducer 1
ACOX1	acyl-coenzyme a oxidase 1, palmitoyl
ACSBG1	acyl-coa synthetase bubblegum family member 1
ACSL1	fatty-acid-coenzyme a ligase, long-chain 1
ACSL4	acyl-coa synthetase long-chain family member 4
ACTC	actin, alpha, cardiac muscle
ACTL6A	actin-like 6a
ACTN1	actinin, alpha 1
ACTR1A	arp1 actin-related protein 1 homolog a, centractin alpha (yeast)
ACTR2	arp2 actin-related protein 2 homolog (yeast)
ACVR1	activin a receptor, type i
ACVR1B	activin a receptor, type ib
ACVR2A	activin a receptor, type iia
ADAM10	adam metallopeptidase domain 10
ADAM12	adam metallopeptidase domain 12 (meltrin alpha)
ADAM19	adam metallopeptidase domain 19 (meltrin beta)
ADAM23	adam metallopeptidase domain 23
ADAM9	adam metallopeptidase domain 9 (meltrin gamma)
ADAMTS18	adam metallopeptidase with thrombospondin type 1 motif, 18
ADAMTS3	adam metallopeptidase with thrombospondin type 1 motif, 3
ADAMTS5	adam metallopeptidase with thrombospondin type 1 motif, 5 (aggrecanase-2)
ADAMTSL3	adamts-like 3
ADCY1	adenylate cyclase 1 (brain)
ADCY2	adenylate cyclase 2 (brain)
ADCY3	adenylate cyclase 3
ADCY6	adenylate cyclase 6
ADCY9	adenylate cyclase 9
ADD3	adducin 3 (gamma)
ADIPOR2	adiponectin receptor 2
ADM	adrenomedullin
ADNP	activity-dependent neuroprotector
ADRB2	adrenergic, beta-2-, receptor, surface
ADSS	adenylosuccinate synthase
AEBP2	ae binding protein 2
AFF1	af4/tmr2 family, member 1
AFTIPHILIN	aftiphilin protein
AGGF1	fetal hypothetical protein
AGTR2	angiotensin ii receptor, type 2
AHCTF1	at hook containing transcription factor 1
AK2	adenylate kinase 2
AK3	adenylate kinase 3
AK3L1, AK3L2	adenylate kinase 3-like 1
AKAP1	a kinase (prka) anchor protein 1
AKAP11	a kinase (prka) anchor protein 11
AKAP13	lymphoid blast crisis oncogene
AKR1D1	aldo-keto reductase family 1, member d1 (delta 4-3-ketosteroid-5-beta-reductase)
AKT3	v-akt murine thymoma viral oncogene homolog 3 (protein kinase b, gamma)
ALKBH5	alkb, alkylation repair homolog 5 (e. coli)
ALPK3	alpha-kinase 3
ALS2	amyotrophic lateral sclerosis 2 (juvenile)
ALX4	aristaless-like homeobox 4
AMFR	autocrine motility factor receptor
AMIGO3	adhesion molecule with ig-like domain 3
AMPD3	adenosine monophosphate deaminase (isoform e)
AMPH	amphiphysin (stiff-man syndrome with breast cancer 128kda autoantigen)
ANGEL1	angel homolog 1 (drosophila)
ANGPTL2	angiopoietin-like 2
ANK2	ankyrin 2, neuronal
ANKFY1	ankyrin repeat and fyve domain containing 1
ANKRD12	ankyrin repeat domain 12
ANKRD13C	ankyrin repeat domain 13c
ANKRD15	ankyrin repeat domain 15
ANKRD27	ankyrin repeat domain 27 (vps9 domain)
ANKRD9	ankyrin repeat domain 9
ANP32E	acidic (leucine-rich) nuclear phosphoprotein 32 family, member e
ANUBL1	an1, ubiquitin-like, homolog (xenopus laevis)

---

ANXA7	annexin a7
AOF1	amine oxidase (flavin containing) domain 1
AP1G1	adaptor-related protein complex 1, gamma 1 subunit
AP1GBP1	ap1 gamma subunit binding protein 1
AP2A1	adaptor-related protein complex 2, alpha 1 subunit
AP2M1	adaptor-related protein complex 2, mu 1 subunit
AP3D1	adaptor-related protein complex 3, delta 1 subunit
APBB2	amyloid beta (a4) precursor protein-binding, family b, member 2 (fe65-like)
APEG1	aortic preferentially expressed gene 1
APG16L	
APP	amyloid beta (a4) precursor protein (peptidase nexin-ii, alzheimer disease)
APPL	adaptor protein containing ph domain, pth domain and leucine zipper motif 1
APRN	androgen-induced proliferation inhibitor
ARC	activity-regulated cytoskeleton-associated protein
ARCN1	archain 1
ARF1	adp-ribosylation factor 1
ARF4	adp-ribosylation factor 4
ARF6	adp-ribosylation factor 6
ARFGEF1	adp-ribosylation factor guanine nucleotide-exchange factor 1(brefeldin a-inhibited)
ARHGAP1	rho gtpase activating protein 1
ARHGAP12	hypothetical protein flj10971
ARHGAP20	rho gtpase activating protein 20
ARHGAP21	rho gtpase activating protein 21
ARHGAP24	rho gtpase activating protein 24
ARHGDI1A	rho gdp dissociation inhibitor (gdi) alpha
ARHGEF10	rho guanine nucleotide exchange factor (gef) 10
ARHGEF11	rho guanine nucleotide exchange factor (gef) 11
ARHGEF12	rho guanine nucleotide exchange factor (gef) 12
ARHGEF17	rho guanine nucleotide exchange factor (gef) 17
ARHGEF18	rho/rac guanine nucleotide exchange factor (gef) 18
ARHGEF3	rho guanine nucleotide exchange factor (gef) 3
ARHGEF5	rho guanine nucleotide exchange factor (gef) 5
ARHGEF9	cdc42 guanine nucleotide exchange factor (gef) 9
ARID1A	at rich interactive domain 1a (swi- like)
ARID1B	dan15 protein
ARID2	kiaa1557 protein
ARID4A	at rich interactive domain 4a (rbp1-like)
ARID4B	at rich interactive domain 4b (rbp1- like)
ARID5B	at rich interactive domain 5b (mrf1-like)
ARIH2	ariadne homolog 2 (drosophila)
ARL10A	
ARL10C	
ARL2	adp-ribosylation factor-like 2
ARL4A	adp-ribosylation factor-like 4a
ARL4C	adp-ribosylation factor-like 4c
ARL6IP2	adp-ribosylation factor-like 6 interacting protein 2
ARL6IP4	adp-ribosylation-like factor 6 interacting protein 4
ARL7	
ARL8B	adp-ribosylation factor-like 8b
ARMC1	armadillo repeat containing 1
ARMC8	armadillo repeat containing 8
ARMCX2	armadillo repeat containing, x-linked 2
ARPC2	actin related protein 2/3 complex, subunit 2, 34kda
ARPP-19	cyclic amp phosphoprotein, 19 kd
ARPP-21	cyclic amp-regulated phosphoprotein, 21 kd
ARRDC3	arrestin domain containing 3
ARRDC4	arrestin domain containing 4
ASB7	hypothetical protein flj22551
ASF1A	asf1 anti-silencing function 1 homolog a (s. cerevisiae)
ASNA1	arsa arsenite transporter, atp-binding, homolog 1 (bacterial)
ASPH	aspartate beta-hydroxylase
ASXL2	additional sex combs like 2 (drosophila)
ATAD2	atpase family, aaa domain containing 2
ATF7IP2	activating transcription factor 7 interacting protein 2
ATG16L1	atg16 autophagy related 16-like 1 (s. cerevisiae)
ATP11A	atpase, class vi, type 11a
ATP11C	atpase, class vi, type 11c
ATP1A1	atpase, na+/k+ transporting, alpha 1 polypeptide
ATP1A2	atpase, na+/k+ transporting, alpha 2 (+) polypeptide
ATP1B1	atpase, na+/k+ transporting, beta 1 polypeptide
ATP2A2	atpase, ca++ transporting, cardiac muscle, slow twitch 2
ATP2B2	atpase, ca++ transporting, plasma membrane 2
ATP2C1	atpase, ca++ transporting, type 2c, member 1
ATP6V1B2	atpase, h+ transporting, lysosomal 56/58kda, v1 subunit b2
ATP6V1F	atpase, h+ transporting, lysosomal 14kda, v1 subunit f
ATRX	alpha thalassemia/mental retardation syndrome x-linked (rad54 homolog, s. cerevisiae)
ATXN1	ataxin 1
ATXN2	ataxin 2
ATXN2L	ataxin 2-like
ATXN3	ataxin 3
ATXN7L1	ataxin 7-like 1
ATXN7L3	ataxin 7-like 3
AUH	au rna binding protein/enoyl-coenzyme a hydratase
AUTS2	autism susceptibility candidate 2
AVEN	apoptosis, caspase activation inhibitor
AXIN2	axin 2 (conductin, axil)
AXL	axl receptor tyrosine kinase
B3GALNT2	udp-galnac:betaglcnac beta 1,3-galactosaminyltransferase, polypeptide 2
B3GALT2	udp-gal:betaglcnac beta 1,3-galactosyltransferase, polypeptide 2
B3GAT1	beta-1,3-glucuronyltransferase 1 (glucuronosyltransferase p)
B4GALT1	udp-gal:betaglcnac beta 1,4- galactosyltransferase, polypeptide 1

---

---

B4GALT2	udp-gal:betaglcnac beta 1,4- galactosyltransferase, polypeptide 2
B4GALT5	udp-gal:betaglcnac beta 1,4- galactosyltransferase, polypeptide 5
BAAT	bile acid coenzyme a: amino acid n-acyltransferase (glycine n-choloyltransferase)
BACE1	beta-site app-cleaving enzyme 1
BACH1	btb and cnc homology 1, basic leucine zipper transcription factor 1
BACH2	btb and cnc homology 1, basic leucine zipper transcription factor 2
BAG5	bcl2-associated athanogene 5
BAHD1	bromo adjacent homology domain containing 1
BAI1	brain-specific angiogenesis inhibitor 1
BAI2	brain-specific angiogenesis inhibitor 2
BAI3	brain-specific angiogenesis inhibitor 3
BAIAP1	
BAMBI	bmp and activin membrane-bound inhibitor homolog (xenopus laevis)
BARX2	barh-like homeobox 2
BAZZA	bromodomain adjacent to zinc finger domain, 2a
BAZZB	dkfzp434h071 protein
BCAP29	b-cell receptor-associated protein 29
BCAT2	branched chain aminotransferase 2, mitochondrial
BCL11A	b-cell cl/lymphoma 11a (zinc finger protein)
BCL11B	b-cell cl/lymphoma 11b (zinc finger protein)
BCL2	b-cell cl/lymphoma 2
BCL2L1	bcl2-like 1
BCL2L11	bcl2-like 11 (apoptosis facilitator)
BCL2L2	bcl2-like 2
BCL3	b-cell cl/lymphoma 3
BCL6	b-cell cl/lymphoma 6 (zinc finger protein 51)
BCL9	b-cell cl/lymphoma 9
BCL9L	b-cell cl/lymphoma 9-like
BCLAF1	bcl2-associated transcription factor 1
BCR	breakpoint cluster region
BDNF	brain-derived neurotrophic factor
BFAR	bifunctional apoptosis regulator
BHLHB3	basic helix-loop-helix domain containing, class b, 3
BHLHB5	basic helix-loop-helix domain containing, class b, 5
BICD2	bicaudal d homolog 2 (drosophila)
BIRC4	baculoviral iap repeat-containing 4
BIRC6	baculoviral iap repeat-containing 6 (apollon)
BLCAP	bladder cancer associated protein
Bles03	basophilic leukemia expressed protein bles03
BLMH	bleomycin hydrolase
BM88	bm88 antigen
BMPER	bmp binding endothelial regulator
BMPRI1A	bone morphogenetic protein receptor, type ia
BMPRI2	bone morphogenetic protein receptor, type ii (serine/threonine kinase)
BMX	bmj non-receptor tyrosine kinase
BNC2	basonuclin 2
BNIP2	bcl2/adenovirus e1b 19kda interacting protein 2
BRP44L	brain protein 44-like
BRPF3	bromodomain and phd finger containing, 3
BRUNOL6	bruno-like 6, rna binding protein (drosophila)
BRWD3	bromodomain and wd repeat domain containing 3
BSC1	bernardinelli-seip congenital lipodystrophy 2 (seipin)
BSDC1	bsd domain containing 1
BSN	bassoon (presynaptic cytomatrix protein)
BTA1	btaf1 rna polymerase ii, b-tfiiid transcription factor-associated, 170kda (mot1 homolog, s. cerevisiae)
BTBD10	btb (poz) domain containing 10
BTBD12	btb (poz) domain containing 12
BTBD14B	btb (poz) domain containing 14b
BTBD15	btb (poz) domain containing 15
BTBD3	btb (poz) domain containing 3
BTBD7	btb (poz) domain containing 7
BTG1	b-cell translocation gene 1, anti-proliferative
BTG2	btg family, member 2
BTG3	btg family, member 3
BTRC	beta-transducin repeat containing
BZRAP1	benzodiazapine receptor (peripheral) associated protein 1
C10orf104	chromosome 10 open reading frame 104
C10orf118	chromosome 10 open reading frame 118
C10orf12	chromosome 10 open reading frame 12
C10orf46	chromosome 10 open reading frame 46
C10orf6	chromosome 10 open reading frame 6
C10orf74	
C11orf11	chromosome 11 open reading frame 11
C11orf23	
C11orf24	chromosome 11 open reading frame 24
C11orf30	chromosome 11 open reading frame 30
C11orf9	chromosome 11 open reading frame 9
C12orf14	
C13orf25	chromosome 13 open reading frame 25
C13orf6	
C14orf129	chromosome 14 open reading frame 129
C14orf147	chromosome 14 open reading frame 147
C14orf168	chromosome 14 open reading frame 168
C14orf32	chromosome 14 open reading frame 32
C14orf35	
C14orf4	chromosome 14 open reading frame 4
C15orf17	chromosome 15 open reading frame 17
C16orf28	chromosome 16 open reading frame 28
C16orf7	chromosome 16 open reading frame 7
C16orf9	chromosome 16 open reading frame 9
C17orf39	chromosome 17 open reading frame 39

---

---

C18orf1	chromosome 18 open reading frame 1
C18orf23, RNF165	chromosome 18 open reading frame 23
C18orf25	chromosome 18 open reading frame 25
C18orf4	hypothetical protein flj11787
C19orf2	chromosome 19 open reading frame 2
C1orf21	chromosome 1 open reading frame 21
C1orf22	dkfzp434n126 protein
C1orf9	chromosome 1 open reading frame 9
C1QDC1	c1q domain containing 1
C1QL3	complement component 1, q subcomponent-like 3
C20orf111	chromosome 20 open reading frame 111
C20orf161	chromosome 20 open reading frame 161
C20orf178	
C20orf23	chromosome 20 open reading frame 23
C20orf35	chromosome 20 open reading frame 35
C20orf39	chromosome 20 open reading frame 39
C20orf46	chromosome 20 open reading frame 46
C21orf25	chromosome 21 open reading frame 25
C21orf4	
C2orf10	chromosome 2 open reading frame 10
C2orf26	chromosome 2 open reading frame 26
C2orf4	chromosome 2 open reading frame 4
C5orf13	chromosome 5 open reading frame 13
C5orf5	chromosome 5 open reading frame 5
C6orf110	
C6orf134	chromosome 6 open reading frame 134
C6orf62	chromosome 6 open reading frame 62
C6orf85	ion transporter protein
C9orf12	
C9orf150	chromosome 9 open reading frame 150
C9orf42	chromosome 9 open reading frame 42
C9orf5	chromosome 9 open reading frame 5
C9orf54	
C9orf60	
C9orf88	chromosome 9 open reading frame 88
CA10	carbonic anhydrase x
CA2	carbonic anhydrase ii
CA8	carbonic anhydrase viii
CAB39	calcium binding protein 39
CACNA1C	calcium channel, voltage-dependent, 1 type, alpha 1c subunit
CACNA1H	calcium channel, voltage-dependent, alpha 1h subunit
CACNA1I	calcium channel, voltage-dependent, alpha 1i subunit
CACNB1	calcium channel, voltage-dependent, beta 1 subunit
CALCRL	calcitonin receptor-like
CALD1	caldesmon 1
CALM1	calmodulin 1 (phosphorylase kinase, delta)
CALN1	calneuron 1
CALU	calumenin
CAMK2G	calcium/calmodulin-dependent protein kinase (cam kinase) ii gamma
CAMK2N1	calcium/calmodulin-dependent protein kinase ii inhibitor 1
CAMKK1	calcium/calmodulin-dependent protein kinase kinase 1, alpha
CAMKK2	calcium/calmodulin-dependent protein kinase kinase 2, beta
CAMKV	cam kinase-like vesicle-associated
CAMSAP1	calmodulin regulated spectrin-associated protein 1
CAMSAP1L1	calmodulin regulated spectrin-associated protein 1-like 1
CAMTA1	calmodulin binding transcription activator 1
CAMTA2	calmodulin binding transcription activator 2
CAPN6	calpain 6
CAPZA1	capping protein (actin filament) muscle z-line, alpha 1
CAPZA2	capping protein (actin filament) muscle z-line, alpha 2
CAPZB	capping protein (actin filament) muscle z-line, beta
CARD10	caspase recruitment domain family, member 10
CASKIN1	cask interacting protein 1
CASP14	caspase 14, apoptosis-related cysteine peptidase
CASR	calcium-sensing receptor (hypocalciuric hypercalcemia 1, severe neonatal hyperparathyroidism)
CAST	calpastatin
CAV1	caveolin 1, caveolae protein, 22kda
CBFA2T3	core-binding factor, runt domain, alpha subunit 2; translocated to, 3
CBFB	core-binding factor, beta subunit
CBL	cas-br-m (murine) ecotropic retroviral transforming sequence
CBLN2	cerebellin 2 precursor
CBLN4	cerebellin 4 precursor
CBX1	chromobox homolog 1 (hp1 beta homolog drosophila )
CBX4	chromobox homolog 4 (pc class homolog, drosophila)
CBX7	chromobox homolog 7
CC2D1A	coiled-coil and c2 domain containing 1a
CCDC19	coiled-coil domain containing 19
CCDC24	coiled-coil domain containing 24
CCDC28A	coiled-coil domain containing 28a
CCDC47	coiled-coil domain containing 47
CCDC6	coiled-coil domain containing 6
CCM2	cerebral cavernous malformation 2
CCNC	cyclin c
CCND1	cyclin d1
CCND2	cyclin d2
CCNE1	cyclin e1
CCNE2	cyclin e2
CCNG2	cyclin g2
CCNJ	cyclin j
CCNT2	cyclin t2
CCPG1	cell cycle progression 1

---

---

CCRN4L	ccr4 carbon catabolite repression 4-like (s. cerevisiae)
CD164	cd164 antigen, sialomucin
CD24	cd24 antigen (small cell lung carcinoma cluster 4 antigen)
CD28	cd28 antigen (tp44)
CD2AP	cd2-associated protein
CD320	cd320 antigen
CD44	cd44 antigen (indian blood group)
CD69	cd69 antigen (p60, early t-cell activation antigen)
CD9	cd9 antigen (p24)
CD96	cd96 antigen
CDC25A	cell division cycle 25a
CDC27	cell division cycle 27
CDC2L5	cell division cycle 2-like 5 (cholinesterase-related cell division controller)
CDC2L6	cell division cycle 2-like 6 (cdk8-like)
CDC37L1	cdc37 cell division cycle 37 homolog (s. cerevisiae)-like 1
CDC42	cell division cycle 42 (gtp binding protein, 25kda)
CDC42EP2	cdc42 effector protein (rho gtpase binding) 2
CDC44	cell division cycle associated 4
CDC47	cell division cycle associated 7
CDC47L	cell division cycle associated 7-like
CDH10	cadherin 10, type 2 (t2-cadherin)
CDH11	cadherin 11, type 2, ob-cadherin (osteoblast)
CDH2	cadherin 2, type 1, n-cadherin (neuronal)
CDH23	cadherin-like 23
CDH8	cadherin 8, type 2
CDK2	cyclin-dependent kinase 2
CDK5R1	cyclin-dependent kinase 5, regulatory subunit 1 (p35)
CDK6	cyclin-dependent kinase 6
CDK8	cyclin-dependent kinase 8
CDKN1A	cyclin-dependent kinase inhibitor 1a (p21, cip1)
CDKN1C	cyclin-dependent kinase inhibitor 1c (p57, kip2)
CDV3	cdv3 homolog (mouse)
CDX2	caudal type homeobox transcription factor 2
CEBPA	caat/enhancer binding protein (c/ebp), alpha
CECR6	cat eye syndrome chromosome region, candidate 6
CELSR2	cadherin, egl lag seven-pass g-type receptor 2 (flamingo homolog, drosophila)
CENPB	centromere protein b, 80kda
CENTG1	phosphoinositide 3-kinase enhancer
CEP170	centrosomal protein 170kda
CEP192	centrosomal protein 192kda
CEP350	centrosomal protein 350kda
CEP57	centrosomal protein 57kda
CEP70	centrosomal protein 70kda
CEPT1	choline/ethanolamine phosphotransferase 1
CETN2	centrin, ef-hand protein, 2
CFL2	cofilin 2 (muscle)
CGGBP1	cgg triplet repeat binding protein 1
CGI-38	cgi-38 protein
CGN	cingulin
CHD1	chromodomain helicase dna binding protein 1
CHD5	coronary heart disease, susceptibility to, 5
CHD5	chromodomain helicase dna binding protein 5
CHD9	hypothetical protein bc022889
CHEK1	chk1 checkpoint homolog (s. pombe)
CHES1	checkpoint suppressor 1
CHGA	chromogranin a (parathyroid secretory protein 1)
CHMP4B	chromatin modifying protein 4b
CHMP7	chmp family, member 7
CHORDC1	cysteine and histidine-rich domain (chord)-containing 1
CHRM2	cholinergic receptor, muscarinic 2
CHRNB1	cholinergic receptor, nicotinic, beta 1 (muscle)
CHRNE	cholinergic receptor, nicotinic, epsilon
CHST1	carbohydrate (keratan sulfate gal-6) sulfotransferase 1
CHST7	carbohydrate (n-acetylglucosamine 6-o) sulfotransferase 7
CHST8	carbohydrate (n-acetylgalactosamine 4-0) sulfotransferase 8
CIC	capicua homolog (drosophila)
CIT	citron (rho-interacting, serine/threonine kinase 21)
CITED2	cbp/p300-interacting transactivator, with glu/asp-rich carboxy-terminal domain, 2
CKLFSF5	
CLASP2	cytoplasmic linker associated protein 2
CLCF1	cardiotrophin-like cytokine factor 1
CLCN2	chloride channel 2
CLCN5	chloride channel 5 (nephrolithiasis 2, x-linked, dent disease)
CLDN11	claudin 11 (oligodendrocyte transmembrane protein)
CLDN12	claudin 12
CLDN2	claudin 2
CLEC2D	c-type lectin domain family 2, member d
CLIPR-59	clip-170-related protein
CLK3	cdc-like kinase 3
CLOCK	clock homolog (mouse)
CLTC	clathrin, heavy polypeptide (hc)
CMIP	c-maf-inducing protein
CMPK	cytidylate kinase
CMTM4	cklf-like marvel transmembrane domain containing 4
CNIH	cornichon homolog (drosophila)
CNIH2	cornichon homolog 2 (drosophila)
CNN1	calponin 1, basic, smooth muscle
CNNM4	cyclin m4
CNOT2	ccr4-not transcription complex, subunit 2
CNOT4	ccr4-not transcription complex, subunit 4
CNOT6	ccr4-not transcription complex, subunit 6

---

---

CNOT7	ccr4-not transcription complex, subunit 7
CNR1	cannabinoid receptor 1 (brain)
CNTRF	ciliary neurotrophic factor receptor
CNTN4	contactin 4
CNTNAP1	contactin associated protein 1
CNTNAP2	contactin associated protein-like 2
COBLL1	cobl-like 1
COL1	collin
COL12A1	collagen, type xii, alpha 1
COL17A1	collagen, type xvii, alpha 1
COL19A1	collagen, type xix, alpha 1
COL1A1	collagen, type i, alpha 1
COL1A2	collagen, type i, alpha 2
COL23A1	collagen, type xxiii, alpha 1
COL24A1	collagen, type xxiv, alpha 1
COL4A3	collagen, type iv, alpha 3 (goodpasture antigen)
COLECI10	collectin sub-family member 10 (c-type lectin)
COP52	cop9 constitutive photomorphogenic homolog subunit 2 (arabidopsis)
COP54	cop9 constitutive photomorphogenic homolog subunit 4 (arabidopsis)
COP57A	cop9 constitutive photomorphogenic homolog subunit 7a (arabidopsis)
COP57B	cop9 constitutive photomorphogenic homolog subunit 7b (arabidopsis)
CORO1C	coronin, actin binding protein, 1c
CORO2B	coronin, actin binding protein, 2b
COX7A2L	cytochrome c oxidase subunit viia polypeptide 2 like
CPD	carboxypeptidase d
CPEB1	cytoplasmic polyadenylation element binding protein 1
CPEB2	cytoplasmic polyadenylation element binding protein 2
CPEB3	cytoplasmic polyadenylation element binding protein 3
CPEB4	cytoplasmic polyadenylation element binding protein 4
CPNE2	copine ii
CPNE8	copine viii
CPSF6	cleavage and polyadenylation specific factor 6, 68kda
CREB1	camp responsive element binding protein 1
CREB3L2	camp responsive element binding protein 3-like 2
CREB5	camp responsive element binding protein 5
CREBBP	creb binding protein (rubinstein-taybi syndrome)
CREBL1	camp responsive element binding protein-like 1
CREBL2	camp responsive element binding protein-like 2
CREM	camp responsive element modulator
CRH	corticotropin releasing hormone
CRIM1	cysteine rich transmembrane bmp regulator 1 (chordin-like)
CRK	v-crk sarcoma virus ct10 oncogene homolog (avian)
CRKL	v-crk sarcoma virus ct10 oncogene homolog (avian)-like
CRMP1	collapsin response mediator protein 1
CRSP6	cofactor required for sp1 transcriptional activation, subunit 6, 77kda
CRSP7	cofactor required for sp1 transcriptional activation, subunit 7, 70kda
CRTC2	creb regulated transcription coactivator 2
CRY2	cryptochrome 2 (photolyase-like)
CS	citrate synthase
CSF1	colony stimulating factor 1 (macrophage)
CSK	c-src tyrosine kinase
CSMD1	cub and sushi multiple domains 1
CSMD2	cub and sushi multiple domains 2
CSMD3	cub and sushi multiple domains 3
CSNK1G1	casein kinase 1, gamma 1
CSNK2A2	casein kinase 2, alpha prime polypeptide
CSPG3	chondroitin sulfate proteoglycan 3 (neurocan)
CTCF	ccctc-binding factor (zinc finger protein)
CTDSP1	ctd (carboxy-terminal domain, rna polymerase ii, polypeptide a) small phosphatase 1
CTDSPL	ctd (carboxy-terminal domain, rna polymerase ii, polypeptide a) small phosphatase-like
CTDSP12	hypothetical protein hspc058
CTGF	connective tissue growth factor
CTNBP1	catenin, beta interacting protein 1
CTNND2	catenin (cadherin-associated protein), delta 2 (neural plakophilin-related arm-repeat protein)
CTTNBP2	cortactin binding protein 2
CUGBP2	cug triplet repeat, rna binding protein 2
CUL2	cullin 2
CUL3	cullin 3
CUL4A	cullin 4a
CUL5	cullin 5
CX3CL1	chemokine (c-x3-c motif) ligand 1
CXCL5	chemokine (c-x-c motif) ligand 5
CXCR4	chemokine (c-x-c motif) receptor 4
CXorf15	chromosome x open reading frame 15
CXorf32	
CXorf45	chromosome x open reading frame 45
CXXC5	cxcc finger 5
CXXC6	cxcc finger 6
CYB561D1	cytochrome b-561 domain containing 1
CYLD	cylindromatosis (turban tumor syndrome)
CYorf15B	chromosome y open reading frame 15b
CYP26B1	cytochrome p450, family 26, subfamily b, polypeptide 1
CYP26C1	cytochrome p450, family 26, subfamily c, polypeptide 1
CYP2C19	cytochrome p450, family 2, subfamily c, polypeptide 19
D4S234E	dna segment on chromosome 4 (unique) 234 expressed sequence
DAAM1	dishevelled associated activator of morphogenesis 1
DAB2IP	ngap-like protein
DACH1	dactshund homolog 1 (drosophila)
DAG1	dystroglycan 1 (dystrophin-associated glycoprotein 1)
DAZAP1	daz associated protein 1
DAZAP2	daz associated protein 2

---

DBCCR1L	
DBN1	drebrin 1
DCAMKL1	doublecortin and cam kinase-like 1
DCAMKL2	doublecortin and cam kinase-like 2
DCBLD2	discoidin, cub and lccl domain containing 2
DC-UbP	dendritic cell-derived ubiquitin-like protein
DCUN1D1	dcn1, defective in cullin neddylation 1, domain containing 1 (s. cerevisiae)
DCUN1D4	dcn1, defective in cullin neddylation 1, domain containing 4 (s. cerevisiae)
DCUN1D5	dcn1, defective in cullin neddylation 1, domain containing 5 (s. cerevisiae)
DCX	doublecortex; lissencephaly, x-linked (doublecortin)
DDEF2	development and differentiation enhancing factor 2
DDHD1	ddhd domain containing 1
DDIT4	dna-damage-inducible transcript 4
DDR1	discoidin domain receptor family, member 1
DDX26	dkfzp434b105 protein
DDX3X	dead (asp-glu-ala-asp) box polypeptide 3, x-linked
DDX3Y	dead (asp-glu-ala-asp) box polypeptide 3, y-linked
DDX42	dead (asp-glu-ala-asp) box polypeptide 42
DDX5	dead (asp-glu-ala-asp) box polypeptide 5
DDX6	dead (asp-glu-ala-asp) box polypeptide 6
DEDD	death effector domain containing
DERL2	der1-like domain family, member 2
DHDDS	dehydrodolichyl diphosphate synthase
DHX40	deah (asp-glu-ala-his) box polypeptide 40
DHX57	deah (asp-glu-ala-asp/his) box polypeptide 57
DHX8	deah (asp-glu-ala-his) box polypeptide 8
DIP2A	dip2 disco-interacting protein 2 homolog a (drosophila)
DIRAS1	diras family, gtp-binding ras-like 1
DIRAS2	diras family, gtp-binding ras-like 2
DIXDC1	dix domain containing 1
DKFZp313N0621	
DKFZP434C212	
DKFZp434H2215	
DKFZp547D2210	
DKFZP564G2022	
DKFZP564J0863	dkfzp564j0863 protein
DKFZP564O0823	dkfzp564o0823 protein
DKFZP566D1346	
DKFZP566E144	
DKFZP566M1046	
DKFZp667B0210	
DKFZp686L1814	hypothetical protein dkfzp686l1814
DKFZp761I12123	hypothetical protein dkfzp761i2123
DKFZp762C1112	
DKFZp762K222	
DKFZp762O076	
DKK1	dickkopf homolog 1 (xenopus laevis)
DKK2	dickkopf homolog 2 (xenopus laevis)
DKK3	dickkopf homolog 3 (xenopus laevis)
DLAT	dihydroliipoamide s-acetyltransferase (e2 component of pyruvate dehydrogenase complex)
DLC1	deleted in liver cancer 1
DLEU7	deleted in lymphocytic leukemia, 7
DLG5	discs, large homolog 5 (drosophila)
DLGAP2	discs, large (drosophila) homolog-associated protein 2
DLL1	delta-like 1 (drosophila)
DLL4	delta-like 4 (drosophila)
DLST	dihydroliipoamide s-succinyltransferase (e2 component of 2-oxo-glutarate complex)
DLSTP	dihydroliipoamide s-succinyltransferase pseudogene (e2 component of 2-oxo-glutarate complex)
DLX1	distal-less homeobox 1
DLX3	distal-less homeobox 3
DLX5	distal-less homeobox 5
DMRT3	doublesex and mab-3 related transcription factor 3
DMTF1	cyclin d binding myb-like transcription factor 1
DMXL1	dmx-like 1
DMXL2	dmx-like 2
DNAJA2	dnaj (hsp40) homolog, subfamily a, member 2
DNAJB1	dnaj (hsp40) homolog, subfamily b, member 1
DNAJB12	dnaj (hsp40) homolog, subfamily b, member 12
DNAJB5	dnaj (hsp40) homolog, subfamily b, member 5
DNAJB6	dnaj (hsp40) homolog, subfamily b, member 6
DNAJB9	dnaj (hsp40) homolog, subfamily b, member 9
DNAJC1	dnaj (hsp40) homolog, subfamily c, member 1
DNAJC13	dnaj (hsp40) homolog, subfamily c, member 13
DNAJC14	cytokine induced protein 29 kda
DNAJC16	dnaj (hsp40) homolog, subfamily c, member 16
DNAJC3	dnaj (hsp40) homolog, subfamily c, member 3
DNAL4	dynein, axonemal, light polypeptide 4
DNM2	dynamain 2
DNMT3A	dna (cytosine-5-)-methyltransferase 3 alpha
DOC1	downregulated in ovarian cancer 1
DOCK10	kiaa0694 gene product
DOCK11	dedicator of cytokinesis 11
DOCK3	dedicator of cytokinesis 3
DOCK5	dedicator of cytokinesis 5
DOCK9	dedicator of cytokinesis 9
DOLPP1	dolichyl pyrophosphate phosphatase 1
DPH1	dph1 homolog (s. cerevisiae)
DPP10	dipeptidyl-peptidase 10
DPYSL2	dihydropyrimidinase-like 2
DPYSL5	dihydropyrimidinase-like 5
DRD1	dopamine receptor d1

---

DSC2	desmocollin 2
DSCAML1	down syndrome cell adhesion molecule like 1
DTNA	dystrobrevin, alpha
DTX2	kiaa1528 protein
DUS2L	dihydrouridine synthase 2-like, smm1 homolog (s. cerevisiae)
DUSP10	dual specificity phosphatase 10
DUSP16	dual specificity phosphatase 16
DUSP2	dual specificity phosphatase 2
DUSP5	dual specificity phosphatase 5
DUSP6	dual specificity phosphatase 6
DUSP8	dual specificity phosphatase 8
DVL1	dishevelled, dsh homolog 1 (drosophila)
DVL1L1	dishevelled, dsh homolog 1 (drosophila)-like 1
DYNC1I1	dynein, cytoplasmic 1, intermediate chain 1
DYNC1I2	dynein, cytoplasmic 1, intermediate chain 2
DYNC1LI1	dynein, cytoplasmic 1, light intermediate chain 1
DYNC1LI2	dynein, cytoplasmic 1, light intermediate chain 2
DYNLL2	dynein, light chain, lc8-type 2
DYNLT3	dynein, light chain, tc8-type 3
DYRK1A	dual-specificity tyrosine-(y)-phosphorylation regulated kinase 1a
DYRK2	dual-specificity tyrosine-(y)-phosphorylation regulated kinase 2
DYRK4	dual-specificity tyrosine-(y)-phosphorylation regulated kinase 4
E2F1	e2f transcription factor 1
E2F3	e2f transcription factor 3
E2F5	e2f transcription factor 5, p130-binding
E2F7	e2f transcription factor 7
E2F8	e2f transcription factor 8
EBAG9	estrogen receptor binding site associated, antigen, 9
EBF2	early b-cell factor 2
ECT2	epithelial cell transforming sequence 2 oncogene
EDA	ectodysplasin a
EDARADD	edar-associated death domain
EDD1	e3 ubiquitin protein ligase, hect domain containing, 1
EDEM1	er degradation enhancer, mannosidase alpha-like 1
EDG1	endothelial differentiation, sphingolipid g-protein-coupled receptor, 1
EDNRB	endothelin receptor type b
EEA1	early endosome antigen 1, 162kd
EEF1A1	eukaryotic translation elongation factor 1 alpha 1
EEIG1	
EFNA3	ephrin-a3
EFNB1	ephrin-b1
EFNB2	ephrin-b2
EGLN2	hypothetical protein dkfzp434e026
EGLN3	hypothetical protein flj21620
EGR1	early growth response 1
EGR2	early growth response 2 (krox-20 homolog, drosophila)
EGR3	early growth response 3
EHMT1	euchromatic histone-lysine n-methyltransferase 1
EI24	etoposide induced 2.4 mrna
EIF1B	eukaryotic translation initiation factor 1b
EIF2C1	eukaryotic translation initiation factor 2c, 1
EIF2C2	eukaryotic translation initiation factor 2c, 2
EIF2C4	argonaute 4
EIF3S1	eukaryotic translation initiation factor 3, subunit 1 alpha, 35kda
EIF3S10	eukaryotic translation initiation factor 3, subunit 10 theta, 150/170kda
EIF4A2	eukaryotic translation initiation factor 4a, isoform 2
EIF4B	eukaryotic translation initiation factor 4b
EIF4E	eukaryotic translation initiation factor 4e
EIF4G2	eukaryotic translation initiation factor 4 gamma, 2
EIF4G3	eukaryotic translation initiation factor 4 gamma, 3
EIF5	eukaryotic translation initiation factor 5
EIF5A2	eukaryotic translation initiation factor 5a2
EIF5B	eukaryotic translation initiation factor 5b
ELAVL1	elav (embryonic lethal, abnormal vision, drosophila)-like 1 (hu antigen r)
ELAVL2	elav (embryonic lethal, abnormal vision, drosophila)-like 2 (hu antigen b)
ELK3	elk3, ets-domain protein (srf accessory protein 2)
ELL	elongation factor ma polymerase ii
ELL2	elongation factor, ma polymerase ii, 2
ELMO1	engulfment and cell motility 1
ELMO2	engulfment and cell motility 2
ELMOD2	elmo/ced-12 domain containing 2
ELOVL4	elongation of very long chain fatty acids (fen1/elo2, sur4/elo3, yeast)-like 4
ELOVL5	elovl family member 5, elongation of long chain fatty acids (fen1/elo2, sur4/elo3-like, yeast)
ELOVL7	elovl family member 7, elongation of long chain fatty acids (yeast)
EMG1	emg1 nucleolar protein homolog (s. cerevisiae)
EMX1	empty spiracles homolog 1 (drosophila)
EMX2	empty spiracles homolog 2 (drosophila)
EN1	engrailed homolog 1
EN2	engrailed homolog 2
ENPP5	ectonucleotide pyrophosphatase/phosphodiesterase 5 (putative function)
ENSA	endosulfine alpha
EOMES	eomesodermin homolog (xenopus laevis)
EP300	e1a binding protein p300
EPAS1	endothelial pas domain protein 1
EPB41L1	erythrocyte membrane protein band 4.1-like 1
EPB41L4B	erythrocyte membrane protein band 4.1 like 4b
EPB49	erythrocyte membrane protein band 4.9 (dematin)
EPC1	enhancer of polycomb homolog 1 (drosophila)
EPC2	enhancer of polycomb homolog 2 (drosophila)
EPHA1	eph receptor a1
EPHA2	eph receptor a2

---



---

EPHA4	eph receptor a4
EPHA5	eph receptor a5
EPHA7	eph receptor a7
EPHA8	eph receptor a8
EPHB3	eph receptor b3
EPN2	epsin 2
EPS15	epidermal growth factor receptor pathway substrate 15
EPS8	epidermal growth factor receptor pathway substrate 8
ERBB2IP	erb2 interacting protein
ERBB4	v-erb-a erythroblastic leukemia viral oncogene homolog 4 (avian)
ERCC6	excision repair cross-complementing rodent repair deficiency, complementation group 6
EREG	epiregulin
ESR1	estrogen receptor 1
ESRRA	estrogen-related receptor alpha
ESRRG	estrogen-related receptor gamma
ETF1	eukaryotic translation termination factor 1
ETV1	ets variant gene 1
ETV3	ets variant gene 3
ETV5	ets variant gene 5 (ets-related molecule)
ETV6	ets variant gene 6 (tel oncogene)
EVA1	epithelial v-like antigen 1
EVJ5L	ecotropic viral integration site 5-like
EVX2	eve, even-skipped homeobox homolog 2 (drosophila)
EXOC5	exocyst complex component 5
EXOSC8	exosome component 8
EXOSC9	exosome component 9
EXTL3	exostosins (multiple)-like 3
EYA1	eyes absent homolog 1 (drosophila)
EZH1	enhancer of zeste homolog 1 (drosophila)
EZH2	enhancer of zeste homolog 2 (drosophila)
F3	coagulation factor iii (thromboplastin, tissue factor)
FALZ	fetal alzheimer antigen
FAM102A	family with sequence similarity 102, member a
FAM104A	family with sequence similarity 104, member a
FAM13C1	family with sequence similarity 13, member c1
FAM19A1	family with sequence similarity 19 (chemokine (c-c motif)-like), member a1
FAM20B	family with sequence similarity 20, member b
FAM38A	family with sequence similarity 38, member a
FAM38B	family with sequence similarity 38, member b
FAM40B	family with sequence similarity 40, member b
FAM43A	family with sequence similarity 43, member a
FAM45A	family with sequence similarity 45, member a
FAM45B	family with sequence similarity 45, member b
FAM46B	family with sequence similarity 46, member b
FAM46C	family with sequence similarity 46, member c
FAM53A	family with sequence similarity 53, member a
FAM57A	family with sequence similarity 57, member a
FAM59A	family with sequence similarity 59, member a
FAM5B	family with sequence similarity 5, member b
FAM60A	family with sequence similarity 60, member a
FAM69A	family with sequence similarity 69, member a
FAM70A	family with sequence similarity 70, member a
FAM73B	family with sequence similarity 73, member b
FAM80A	family with sequence similarity 80, member a
FAM81A	family with sequence similarity 81, member a
FAM84B	family with sequence similarity 84, member b
FAM8A1	family with sequence similarity 8, member a1
FAM98A	family with sequence similarity 98, member a
FASLG	fas ligand (tnf superfamily, member 6)
FASN	fatty acid synthase
FASTK	fas-activated serine/threonine kinase
FAT	fat tumor suppressor homolog 1 (drosophila)
FAT2	fat tumor suppressor homolog 2 (drosophila)
FBLN1	fibrulin 1
FBN1	fibrillin 1 (marfan syndrome)
FBN2	fibrillin 2 (congenital contractural arachnodactyly)
FBXL11	f-box and leucine-rich repeat protein 11
FBXL2	f-box and leucine-rich repeat protein 2
FBXL20	f-box and leucine-rich repeat protein 20
FBXL3	f-box and leucine-rich repeat protein 3
FBXL4	f-box and leucine-rich repeat protein 4
FBXL5	f-box and leucine-rich repeat protein 5
FBXO11	f-box only protein 11
FBXO21	f-box protein 21
FBXO28	f-box protein 28
FBXO33	f-box protein 33
FBXO34	f-box protein 34
FBXW11	f-box and wd-40 domain protein 11
FBXW7	f-box and wd-40 domain protein 7 (archipelago homolog, drosophila)
FCHO2	fch domain only 2
FCHSD1	fch and double sh3 domains 1
FCHSD2	fch and double sh3 domains 2
FEM1B	fem-1 homolog b (c. elegans)
FEM1C	fem-1 homolog c (c. elegans)
FGD1	fyve, rhogef and ph domain containing 1 (faciogenital dysplasia)
FGD5	fyve, rhogef and ph domain containing 5
FGF10	fibroblast growth factor 10
FGF11	fibroblast growth factor 11
FGF12	fibroblast growth factor 12
FGF13	fibroblast growth factor 13
FGF2	fibroblast growth factor 2 (basic)

---

---

FGF7	fibroblast growth factor 7 (keratinocyte growth factor)
FGF9	fibroblast growth factor 9 (glia-activating factor)
FGFR2	fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, crouzon syndrome, pfeiffer syndrome, jackson-weiss syndrome)
FCR	gardner-rasheed feline sarcoma viral (v-fgr) oncogene homolog
FHL1	four and a half lim domains 1
FHL2	four and a half lim domains 2
FHL3	four and a half lim domains 3
FHOD3	formin homology 2 domain containing 3
FIGN	fidgetin
FJX1	four jointed box 1 (drosophila)
FKBP1A	fk506 binding protein 1a, 12kda
FKBP1C	fk506 binding protein 1c
FLI1	friend leukemia virus integration 1
FLJ10099	hypothetical protein flj10099
FLJ10154	hypothetical protein flj10154
FLJ10350	
FLJ10597	
FLJ10748	
FLJ10925	hypothetical protein flj10925
FLJ10980	
FLJ11011	
FLJ11021	similar to splicing factor, arginine/serine-rich 4
FLJ11783	hypothetical protein flj11783
FLJ11838	
FLJ12443	
FLJ12529	pre-mrna cleavage factor i, 59 kda subunit
FLJ12666	
FLJ12750	
FLJ13089	
FLJ13448	
FLJ13576	hypothetical protein flj13576
FLJ13855	
FLJ14213	hypothetical protein flj14213
FLJ14503	
FLJ14668	hypothetical protein flj14668
FLJ14775	
FLJ14800	
FLJ20160	flj20160 protein
FLJ20186	hypothetical protein flj20186
FLJ20241	
FLJ20257	
FLJ20273	rna-binding protein
FLJ20298	
FLJ20308	
FLJ20315	
FLJ20366	hypothetical protein flj20366
FLJ20399	
FLJ20489	hypothetical protein flj20489
FLJ20558	hypothetical protein flj20558
FLJ20701	hypothetical protein flj20701
FLJ20716	
FLJ21168	
FLJ21616	
FLJ21918	
FLJ21945	hypothetical protein flj21945
FLJ22104	
FLJ22313	hypothetical protein flj22313
FLJ22833	
FLJ23191	hypothetical protein flj23191
FLJ23311	
FLJ23749	
FLJ25476	flj25476 protein
FLJ25555	
FLJ30046	hypothetical protein flj30046
FLJ30435	
FLJ31818	hypothetical protein flj31818
FLJ31951	hypothetical protein flj31951
FLJ32356	
FLJ32642	
FLJ33674	
FLJ34969	hypothetical protein flj34969
FLJ35954	
FLJ36070	hypothetical protein flj36070
FLJ36090	hypothetical protein flj36090
FLJ36874	flj36874 protein
FLJ37266	hypothetical protein loc283225
FLJ37357	hypothetical protein flj37357
FLJ37478	hypothetical protein loc339983
FLJ38101	hypothetical protein flj38101
FLJ39441	
FLJ40142	flj40142 protein
FLJ40432	hypothetical protein flj40432
FLJ40773	
FLJ40873	
FLJ45187	flj45187 protein
FLJ45455	flj45455 protein
FLJ45686	
FLJ46347	hypothetical loc389064
FLJ90579	hypothetical protein flj90579
FLNC	filamin c, gamma (actin binding protein 280)

---

---

FLOT2	flotillin 2
FLRT2	fibronectin leucine rich transmembrane protein 2
FLRT3	fibronectin leucine rich transmembrane protein 3
FLT1	fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor)
FMN2	formin 2
FMNL2	formin-like 2
FMR1	fragile x mental retardation 1
FMR2	
FNBP1	formin binding protein 1
FNBP4	formin binding protein 4
FNDC3A	fibronectin type iii domain containing 3a
FNDC3B	fibronectin type iii domain containing 3b
FNDC8	fibronectin type iii domain containing 8
FOSL1	fos-like antigen 1
FOXA1	forkhead box a1
FOXC1	forkhead box c1
FOXF1	forkhead box f1
FOXF2	forkhead box f2
FOXG1B	forkhead box glb
FOXG1C	forkhead box glc
FOXJ2	forkhead box j2
FOXJ3	forkhead box j3
FOXJ2	forkhead box j2
FOXN1	forkhead box n1
FOXO1A	forkhead box o1a (rhabdomyosarcoma)
FOXP1	forkhead box p1
FREQ	frequenin homolog (drosophila)
FRK	fyn-related kinase
FRMD4A	ferm domain containing 4a
FRMPD1	ferm and pdz domain containing 1
FRS2	fibroblast growth factor receptor substrate 2
FRY	furry homolog (drosophila)
FSD1	fibronectin type iii and spry domain containing 1
FSTL1	folliculin-like 1
FTS	fused toes homolog (mouse)
FUBP3	far upstream element (fuse) binding protein 3
FUNDC1	fun14 domain containing 1
FURIN	furin (paired basic amino acid cleaving enzyme)
FUSIP1	fus interacting protein (serine/arginine-rich) 1
FVT1	follicular lymphoma variant translocation 1
FZD1	frizzled homolog 1 (drosophila)
FZD10	frizzled homolog 10 (drosophila)
FZD4	frizzled homolog 4 (drosophila)
FZD7	frizzled homolog 7 (drosophila)
FZD8	frizzled homolog 8 (drosophila)
G0S2	g0/g1switch 2
G3BP2	ras-gtpase activating protein sh3 domain-binding protein 2
GAB1	grb2-associated binding protein 1
GAB2	grb2-associated binding protein 2
GABBR2	gamma-aminobutyric acid (gaba) b receptor, 2
GABPB2	ga binding protein transcription factor, beta subunit 1, 53kda
GABRA1	gamma-aminobutyric acid (gaba) a receptor, alpha 1
GABRB3	gamma-aminobutyric acid (gaba) a receptor, beta 3
GAD1	glutamate decarboxylase 1 (brain, 67kda)
GALNT1	udp-n-acetyl-alpha-d-galactosamine:polypeptide n-acetylgalactosaminyltransferase 1 (galnac-t1)
GALNT2	udp-n-acetyl-alpha-d-galactosamine:polypeptide n-acetylgalactosaminyltransferase 2 (galnac-t2)
GALNT3	udp-n-acetyl-alpha-d-galactosamine:polypeptide n-acetylgalactosaminyltransferase 3 (galnac-t3)
GALNT7	udp-n-acetyl-alpha-d-galactosamine:polypeptide n-acetylgalactosaminyltransferase 7 (galnac-t7)
GAN	giant axonal neuropathy (gigaxonin)
GAP43	growth associated protein 43
GAS1	growth arrest-specific 1
GATA2	gata binding protein 2
GATA6	gata binding protein 6
GATAD2B	gata zinc finger domain containing 2b
GBF1	golgi-specific brefeldin a resistance factor 1
GCLC	glutamate-cysteine ligase, catalytic subunit
GDA	guanine deaminase
GDF11	growth differentiation factor 11
GDF6	growth differentiation factor 6
GDF8	growth differentiation factor 8
GDNF	glial cell derived neurotrophic factor
GFP72	glutamine-fructose-6-phosphate transaminase 2
GGA3	golgi associated, gamma adaptin ear containing, arf binding protein 3
GHR	growth hormone receptor
GIT2	g protein-coupled receptor kinase interactor 2
GJA1	gap junction protein, alpha 1, 43kda (connexin 43)
GJA7	gap junction protein, alpha 7, 45kda (connexin 45)
GK001	
GLCC11	islet cell autoantigen 1, 69kda
GLCE	glucuronyl c5-epimerase
GLRB	glycine receptor, beta
GLUD1, GLUD2	glutamate dehydrogenase 1
GM632	kiaa1196 protein
GMEB2	glucocorticoid modulatory element binding protein 2
GMRP-1	
GNAI1	guanine nucleotide binding protein (g protein), alpha inhibiting activity polypeptide 1
GNAI2	guanine nucleotide binding protein (g protein), alpha inhibiting activity polypeptide 2
GNAI3	guanine nucleotide binding protein (g protein), alpha inhibiting activity polypeptide 3
GNAO1	guanine nucleotide binding protein (g protein), alpha activating activity polypeptide o
GNAQ	guanine nucleotide binding protein (g protein), q polypeptide
GNB1	guanine nucleotide binding protein (g protein), beta polypeptide 1

---

---

GNB5	guanine nucleotide binding protein (g protein), beta 5
GNG12	guanine nucleotide binding protein (g protein), gamma 12
GNPDA2	glucosamine-6-phosphate deaminase 2
GOLGA1	golgi autoantigen, golgin subfamily a, 1
GOLGA3	golgi autoantigen, golgin subfamily a, 3
GOLGA4	golgi autoantigen, golgin subfamily a, 4
GOLGA7	golgi autoantigen, golgin subfamily a, 7
GOLGIN-67	
GOLPH3	golgi phosphoprotein 3 (coat-protein)
GOLT1B	golgi transport 1 homolog b (s. cerevisiae)
GORASP2	golgi reassembly stacking protein 2, 55kda
GOSR1	golgi snap receptor complex member 1
GOT1	glutamic-oxaloacetic transaminase 1, soluble (aspartate aminotransferase 1)
GPAM	glycerol-3-phosphate acyltransferase, mitochondrial
GFPB1L1	gc-rich promoter binding protein 1-like 1
GPM6A	glycoprotein m6a
GPR124	g protein-coupled receptor 124
GPR137B	g protein-coupled receptor 137b
GPR157	g protein-coupled receptor 157
GPR6	g protein-coupled receptor 6
GPR63	g protein-coupled receptor 63
GPR85	g protein-coupled receptor 85
GPR88	g protein-coupled receptor 88
GRAMD1B	gram domain containing 1b
GRAMD3	gram domain containing 3
GRB10	growth factor receptor-bound protein 10
GRHL1	grainyhead-like 1 (drosophila)
GRHL2	grainyhead-like 2 (drosophila)
GRIA2	glutamate receptor, ionotropic, ampa 2
GRIA3	glutamate receptor, ionotropic, ampa 3
GRIA4	glutamate receptor, ionotropic, ampa 4
GRIK2	glutamate receptor, ionotropic, kainate 2
GRIK3	glutamate receptor, ionotropic, kainate 3
GRIK4	glutamate receptor, ionotropic, kainate 4
GRIN1	glutamate receptor, ionotropic, n-methyl d-aspartate 1
GRIN2A	glutamate receptor, ionotropic, n-methyl d-aspartate 2a
GRIP2	glutamate receptor interacting protein 2
GRK5	g protein-coupled receptor kinase 5
GRK6	g protein-coupled receptor kinase 6
GRLF1	glucocorticoid receptor dna binding factor 1
GRM1	glutamate receptor, metabotropic 1
GRM2	glutamate receptor, metabotropic 2
GRM4	glutamate receptor, metabotropic 4
GRM7	glutamate receptor, metabotropic 7
GRM8	glutamate receptor, metabotropic 8
GRSF1	g-rich ma sequence binding factor 1
CSC	goosecoid
GTF2H1	general transcription factor iih, polypeptide 1, 62kda
GTPBP2	gtp binding protein 2
GUCY1A2	guanylate cyclase 1, soluble, alpha 2
GULP1	gulp, engulfment adaptor ptb domain containing 1
H2AFZ	h2a histone family, member z
H3F3A, H3F3B	h3 histone, family 3a
HABP4	hyaluronan binding protein 4
HAN11	
HAND1	heart and neural crest derivatives expressed 1
HAND2	heart and neural crest derivatives expressed 2
HAPLN1	hyaluronan and proteoglycan link protein 1
HARSL	histidyl-trna synthetase-like
HAS2	hyaluronan synthase 2
HAS3	hyaluronan synthase 3
HBP1	hmg-box transcription factor 1
HCFC1	host cell factor c1 (vp16-accessory protein)
HCN2	hyperpolarization activated cyclic nucleotide-gated potassium channel 2
HCN3	hyperpolarization activated cyclic nucleotide-gated potassium channel 3
HCN4	hyperpolarization activated cyclic nucleotide-gated potassium channel 4
HDAC4	histone deacetylase 4
HDDC3	hd domain containing 3
HDFG	hepatoma-derived growth factor (high-mobility group protein 1-like)
HDHD2	haloacid dehalogenase-like hydrolase domain containing 2
HDLBP	high density lipoprotein binding protein (vigilin)
HECA	headcase homolog (drosophila)
HECTD1	hect domain containing 1
HECW1	hect, c2 and ww domain containing e3 ubiquitin protein ligase 1
HECW2	hect, c2 and ww domain containing e3 ubiquitin protein ligase 2
HELZ	helicase with zinc finger
HERC2	hect domain and rld 2
HEY2	hairy/enhancer-of-split related with yrpw motif 2
HEYL	hairy/enhancer-of-split related with yrpw motif-like
HHIP	hedgehog interacting protein
HIAT1	hippocampus abundant transcript 1
HIC1	hypermethylated in cancer 1
HIC2	hypermethylated in cancer 2
HIF1A	hypoxia-inducible factor 1, alpha subunit (basic helix-loop-helix transcription factor)
HIF1AN	hypoxia-inducible factor 1, alpha subunit inhibitor
HIP1	huntingtin interacting protein 1
HIPK1	kiaa0630 protein
HIRA	hir histone cell cycle regulation defective homolog a (s. cerevisiae)
HIVEP1	human immunodeficiency virus type i enhancer binding protein 1
HIVEP2	human immunodeficiency virus type i enhancer binding protein 2
HLF	hepatic leukemia factor

---

---

HMBOX1	homeobox containing 1
HMG20A	high-mobility group 20a
HMG2L1	partial transcript encompassing thc211630 gene
HMG2	high mobility group at-hook 2
HMG1	high-mobility group box 1
HMG3	high-mobility group box 3
HMGCS1	3-hydroxy-3-methylglutaryl-coenzyme a synthase 1 (soluble)
HMOX1	heme oxygenase (decycling) 1
HN1	hematological and neurological expressed 1
HNRPA0	heterogeneous nuclear ribonucleoprotein a0
HNRPA1	heterogeneous nuclear ribonucleoprotein a1
HNRPF	heterogeneous nuclear ribonucleoprotein f
HNRPH3	heterogeneous nuclear ribonucleoprotein h3 (2h9)
HNRPL	heterogeneous nuclear ribonucleoprotein l
HNRPM	heterogeneous nuclear ribonucleoprotein m
HNRPR	heterogeneous nuclear ribonucleoprotein r
HNRPU	heterogeneous nuclear ribonucleoprotein u (scaffold attachment factor a)
HNRPU1	heterogeneous nuclear ribonucleoprotein u-like 1
HOOK3	hook homolog 3 (drosophila)
HOXA1	homeobox a1
HOXA10	homeobox a10
HOXA13	homeobox a13
HOXA3	homeobox a3
HOXA5	homeobox a5
HOXA9	homeobox a9
HOXB3	homeobox b3
HOXB4	homeobox b4
HOXB8	homeobox b8
HOXC10	homeobox c10
HOXC11	homeobox c11
HOXC5	homeobox c5
HOXC8	homeobox c8
HOXD10	homeobox d10
HPCA	hippocalcin
HPR	haptoglobin-related protein
HP55	hermansky-pudlak syndrome 5
HP56	hermansky-pudlak syndrome 6
HRB	hiv-1 rev binding protein
HRBL	hiv-1 rev binding protein-like
HRHFB2122	
HS3ST2	heparan sulfate (glucosamine) 3-o-sulfotransferase 2
HS3ST3B1	heparan sulfate (glucosamine) 3-o-sulfotransferase 3b1
HS3ST4	heparan sulfate (glucosamine) 3-o-sulfotransferase 4
HS3ST5	heparan sulfate (glucosamine) 3-o-sulfotransferase 5
HSF2	heat shock transcription factor 2
HSIN1	
HSPA4L	heat shock 70kda protein 4-like
HSPA9B	heat shock 70kda protein 9b (mortalin-2)
HSPC129	
HSPG2	heparan sulfate proteoglycan 2 (perlecan)
hSyn	
HT008	
HTLF	human t-cell leukemia virus enhancer factor
HTR1B	5-hydroxytryptamine (serotonin) receptor 1b
HTR2C	5-hydroxytryptamine (serotonin) receptor 2c
HTR4	5-hydroxytryptamine (serotonin) receptor 4
HTR7	5-hydroxytryptamine (serotonin) receptor 7 (adenylate cyclase-coupled)
IARS2	isoleucine-trna synthetase 2, mitochondrial
IBRDC1	ibr domain containing 1
IBRDC2	ibr domain containing 2
IBRDC3	ibr domain containing 3
IBTK	inhibitor of bruton agammaglobulinemia tyrosine kinase
ICK	intestinal cell (mak-like) kinase
ID4	inhibitor of dna binding 4, dominant negative helix-loop-helix protein
IDH3G	isocitrate dehydrogenase 3 (nad+) gamma
IFRD2	interferon-related developmental regulator 2
IGF1	insulin-like growth factor 1 (somatomedin c)
IGF1R	insulin-like growth factor 1 receptor
IGF2R	insulin-like growth factor 2 receptor
IGFBP3	insulin-like growth factor binding protein 3
IGSF10	immunoglobulin superfamily, member 10
IGSF3	immunoglobulin superfamily, member 3
IGSF4	immunoglobulin superfamily, member 4
IGSF4B	immunoglobulin superfamily, member 4b
IGSF4C	immunoglobulin superfamily, member 4c
IGSF4D	immunoglobulin superfamily, member 4d
IGSF9B	immunoglobulin superfamily, member 9b
IHPK1	inositol hexaphosphate kinase 1
IL17E	interleukin 17e
IL17RD	interleukin 17 receptor d
IL1RAPL1	interleukin 1 receptor accessory protein-like 1
ILF3	interleukin enhancer binding factor 3, 90kda
IMPA3	
IMPDH1	imp (inosine monophosphate) dehydrogenase 1
INC2	inhibitor of growth family, member 2
INHBA	inhibin, beta a (activin a, activin ab alpha polypeptide)
INHBB	inhibin, beta b (activin ab beta polypeptide)
INOC1	ino80 complex homolog 1 (s. cerevisiae)
INSIG1	insulin induced gene 1
IPP	intracisternal a particle-promoted polypeptide
IQGA2	iq motif containing gtpase activating protein 2

---

---

IQSEC1	iq motif and sec7 domain 1
IQWD1	iq motif and wd repeats 1
IRAK2	interleukin-1 receptor-associated kinase 2
IRF1	interferon regulatory factor 1
IRF2	interferon regulatory factor 2
IRF2BP1	interferon regulatory factor 2 binding protein 1
IRS2	insulin receptor substrate 2
IRS4	insulin receptor substrate 4
IRXL1	iroquois homeobox protein-like 1
ISL1	isl1 transcription factor, lim/homeodomain, (islet-1)
ISOC2	isochorismatase domain containing 2
ITCH	atrophin-1 interacting protein 4
ITGA2	integrin, alpha 2 (cd49b, alpha 2 subunit of vla-2 receptor)
ITGA5	integrin, alpha 5 (fibronectin receptor, alpha polypeptide)
ITGA6	integrin, alpha 6
ITGA9	integrin, alpha 9
ITGAV	integrin, alpha v (vitronectin receptor, alpha polypeptide, antigen cd51)
ITGB1	integrin, beta 1 (fibronectin receptor, beta polypeptide, antigen cd29 includes mdf2, msk12)
ITGB4	integrin, beta 4
ITGB6	integrin, beta 6
ITGB7	integrin, beta 7
ITGB8	integrin, beta 8
ITM2C	integral membrane protein 2c
ITPKB	inositol 1,4,5-trisphosphate 3-kinase b
ITR	intimal thickness-related receptor
ITSN1	intersectin 1 (sh3 domain protein)
IVNS1ABP	influenza virus ns1a binding protein
IXL	intersex-like (drosophila)
JAG1	jagged 1 (alagille syndrome)
JAKMIP1	janus kinase and microtubule interacting protein 1
JARID1B	jumonji, at rich interactive domain 1b (rbp2-like)
JAZF1	juxtaposed with another zinc finger gene 1
JDP2	jun dimerization protein 2
JMJD1A	jumonji domain containing 1a
JMJD3	jumonji domain containing 3
JOSD1	josephin domain containing 1
JRKL	jerky homolog-like (mouse)
JUB	jub, ajuba homolog (xenopus laevis)
JUN	v-jun sarcoma virus 17 oncogene homolog (avian)
K6IRS2	keratin protein k6irs
KALRN	kalirin, rhogef kinase
KBTBD2	kelch repeat and btb (poz) domain containing 2
KBTBD8	kelch repeat and btb (poz) domain containing 8
KBTBD9	hypothetical protein flj14106
KCMF1	potassium channel modulatory factor 1
KCNA1	potassium voltage-gated channel, shaker-related subfamily, member 1 (episodic ataxia with myokymia)
KCNA3	potassium voltage-gated channel, shaker-related subfamily, member 3
KCNA4	potassium voltage-gated channel, shaker-related subfamily, member 4
KCNA5	potassium voltage-gated channel, shaker-related subfamily, member 5
KCNAB1	potassium voltage-gated channel, shaker-related subfamily, beta member 1
KCNC4	potassium voltage-gated channel, shaw-related subfamily, member 4
KCND1	potassium voltage-gated channel, shal-related subfamily, member 1
KCND2	potassium voltage-gated channel, shal-related subfamily, member 2
KCND3	potassium voltage-gated channel, shal-related subfamily, member 3
KCNH3	potassium voltage-gated channel, subfamily h (eag-related), member 3
KCNH4	potassium voltage-gated channel, subfamily h (eag-related), member 4
KCNH5	potassium voltage-gated channel, subfamily h (eag-related), member 5
KCNH8	potassium voltage-gated channel, subfamily h (eag-related), member 8
KCNIP3	kv channel interacting protein 3, calsenilin
KCNJ10	potassium inwardly-rectifying channel, subfamily j, member 10
KCNJ2	potassium inwardly-rectifying channel, subfamily j, member 2
KCNJ3	potassium inwardly-rectifying channel, subfamily j, member 3
KCNK10	potassium channel, subfamily k, member 10
KCNMA1	potassium large conductance calcium-activated channel, subfamily m, alpha member 1
KCNN2	potassium intermediate/small conductance calcium-activated channel, subfamily n, member 2
KCNN4	potassium intermediate/small conductance calcium-activated channel, subfamily n, member 4
KCNQ2	potassium voltage-gated channel, kqt-like subfamily, member 2
KCNQ5	potassium voltage-gated channel, kqt-like subfamily, member 5
KCNS2	potassium voltage-gated channel, delayed-rectifier, subfamily s, member 2
KCTD1	potassium channel tetramerisation domain containing 1
KCTD16	potassium channel tetramerisation domain containing 16
KCTD8	potassium channel tetramerisation domain containing 8
KCTD9	potassium channel tetramerisation domain containing 9
KDELRL1	kdel (lys-asp-glu-leu) endoplasmic reticulum protein retention receptor 1
KHDRBS1	kh domain containing, rna binding, signal transduction associated 1
KHDRBS2	kh domain containing, rna binding, signal transduction associated 2
KIAA0152	kiaa0152
KIAA0157	kiaa0157
KIAA0182	kiaa0182
KIAA0217	
KIAA0240	kiaa0240
KIAA0241	kiaa0241
KIAA0252	
KIAA0258	kiaa0258
KIAA0261	kiaa0261
KIAA0276	
KIAA0280	kiaa0280
KIAA0318	
KIAA0323	kiaa0323
KIAA0329	kiaa0329
KIAA0350	kiaa0350 protein

---

---

KIAA0376	kiaa0376 protein
KIAA0423	kiaa0423
KIAA0494	kiaa0494
KIAA0513	kiaa0513
KIAA0553	kiaa0553
KIAA0649	kiaa0649
KIAA0664	kiaa0664
KIAA0674	kiaa0674
KIAA0685	
KIAA0828	kiaa0828 protein
KIAA0831	kiaa0831
KIAA0882	
KIAA0907	kiaa0907
KIAA0922	kiaa0922
KIAA0931	
KIAA0934	
KIAA0992	
KIAA1002	
KIAA1024	kiaa1024 protein
KIAA1040	
KIAA1078	
KIAA1086	kiaa1086
KIAA1102	
KIAA1115	
KIAA1128	kiaa1128
KIAA1189	kiaa1189
KIAA1193	kiaa1193
KIAA1212	hypothetical protein loc55580
KIAA1217	kiaa1217
KIAA1267	dkfzp727c091 protein
KIAA1333	kiaa1333
KIAA1370	kiaa1370
KIAA1404	
KIAA1409	kiaa1409
KIAA1411	kiaa1411
KIAA1468	kiaa1468
KIAA1522	kiaa1522
KIAA1533	
KIAA1598	kiaa1598
KIAA1600	kiaa1600
KIAA1623	
KIAA1729	kiaa1729 protein
KIAA1787	kiaa1787 protein
KIAA1904	kiaa1904 protein
KIAA1946	kiaa1946
KIAA1961	kiaa1961 gene
KIAA2010	kiaa2010
KIAA2022	
KIF1B	kinesin family member 1b
KIF1C	kinesin family member 1c
KIF21A	kinesin family member 21a
KIF21B	kinesin family member 21b
KIF23	kinesin family member 23
KIF3B	kinesin family member 3b
KIF3C	kinesin family member 3c
KIF5A	kinesin family member 5a
KIF5B	kinesin family member 5b
KIT	v-kit hardy-zuckerman 4 feline sarcoma viral oncogene homolog
KLC2	kinesin light chain 2
KLF10	kruppel-like factor 10
KLF11	kruppel-like factor 11
KLF12	kruppel-like factor 12
KLF13	kruppel-like factor 13
KLF15	kruppel-like factor 15
KLF2	kruppel-like factor 2 (lung)
KLF3	kruppel-like factor 3 (basic)
KLF4	kruppel-like factor 4 (gut)
KLF9	kruppel-like factor 9
KLHDC2	kelch domain containing 2
KLHDC5	kelch domain containing 5
KLHL13	kelch-like 13 (drosophila)
KLHL14	kelch-like 14 (drosophila)
KLHL15	kelch-like 15 (drosophila)
KLHL18	kelch-like 18 (drosophila)
KLHL2	kelch-like 2, mayven (drosophila)
KLHL20	kelch-like 20 (drosophila)
KLHL26	kelch-like 26 (drosophila)
KLHL3	kelch-like 3 (drosophila)
KLHL4	kelch (drosophila)-like 4
KNG1	kininogen 1
KPNA1	karyopherin alpha 1 (importin alpha 5)
KPNA2	karyopherin alpha 2 (rag cohort 1, importin alpha 1)
KPNA3	karyopherin alpha 3 (importin alpha 4)
KPNA4	karyopherin alpha 4 (importin alpha 3)
KPNB1	karyopherin (importin) beta 1
KRAS	v-ha-ras harvey rat sarcoma viral oncogene homolog
KRT1	keratin 1 (epidermolytic hyperkeratosis)
KRTAP11-1	keratin associated protein 11-1
KRTAP4-4	keratin associated protein 4-4
KTN1	kinectin 1 (kinesin receptor)
Kua-UEV, UBE2V1	ubiquitin-conjugating enzyme e2 variant 1

---

---

L3MBTL3	l(3)mbt-like 3 (drosophila)
LACE1	lactation elevated-1
LAMC1	laminin, gamma 1 (formerly lamb2)
LAMP2	lysosomal-associated membrane protein 2
LAPTM4A	lysosomal-associated protein transmembrane 4 alpha
LASP1	lim and sh3 protein 1
LASS6	lag1 longevity assurance homolog 6 (s. cerevisiae)
LAT1-3TM	slc7a5 pseudogene
LATS2	lats, large tumor suppressor, homolog 2 (drosophila)
LBH	hypothetical protein dkfzp566j091
LBX1	ladybird homeobox homolog 1 (drosophila)
LDLRAP1	low density lipoprotein receptor adaptor protein 1
LEF1	lymphoid enhancer-binding factor 1
LEFTY1	left-right determination factor 1
LEMD3	lem domain containing 3
LGALS3	lectin, galactoside-binding, soluble, 3 (galectin 3)
LGR4	leucine-rich repeat-containing g protein-coupled receptor 4
LHFP	lipoma hmgic fusion partner
LHFPL2	lipoma hmgic fusion partner-like 2
LHX1	lim homeobox 1
LHX6	lim homeobox 6
LHX8	lim homeobox 8
LIF	leukemia inhibitory factor (cholinergic differentiation factor)
LIFR	leukemia inhibitory factor receptor
LIMA1	lim domain and actin binding 1
LIMD2	lim domain containing 2
LIMK1	lim domain kinase 1
LIMR	
LIN10, Lin10	lin-10 homolog (c. elegans)
LIN28	lin-28 homolog (c. elegans)
LIN9	lin-9 homolog (c. elegans)
LKAP	limkain b1
LMAN2L	lectin, mannose-binding 2-like
LMO3	lim domain only 3 (rhombotin-like 2)
LMO7	lim domain 7
LNPEP	leucyl/cystinyl aminopeptidase
LOC113251	
LOC129138	hypothetical protein bc014641
LOC129285	smooth muscle myosin heavy chain 11 isoform sm1-like
LOC144363	hypothetical protein loc144363
LOC144983	
LOC146174	
LOC147991	
LOC153222	adult retina protein
LOC153364	similar to metallo-beta-lactamase superfamily protein
LOC155435	
LOC162427	hypothetical protein loc162427
LOC168850	hypothetical protein loc168850
LOC205251	loc205251
LOC220594	tl132 protein
LOC221442	hypothetical protein loc221442
LOC222171	hypothetical protein loc222171
LOC283377	
LOC283768	
LOC284058	
LOC284296	hypothetical protein loc284296
LOC339745	hypothetical protein loc339745
LOC340156	
LOC387646	hypothetical loc387646
LOC390535	
LOC399947	similar to expressed sequence ai593442
LOC493861	
LOC51334	mesenchymal stem cell protein dsc54
LOC56181	
LOC64744	
LOC81558	c/ebp-induced protein
LOC84661	dpy-30-like protein
LOC90355	hypothetical gene supported by af038182; bc009203
LOC92689	hypothetical protein bc001096
LOC92912	
LONRF1	lon peptidase n-terminal domain and ring finger 1
LONRF2	lon peptidase n-terminal domain and ring finger 2
LOXL3	lysyl oxidase-like 3
LPGAT1	lysophosphatidylglycerol acyltransferase 1
LPHN1	latrophilin 1
LPHN2	latrophilin 2
LPHN3	latrophilin 3
LPIN2	lipin 2
LPP	lim domain containing preferred translocation partner in lipoma
LPPR4	plasticity related gene 1
LRCH1	leucine-rich repeats and calponin homology (ch) domain containing 1
LRCH2	leucine-rich repeats and calponin homology (ch) domain containing 2
LRFN5	leucine rich repeat and fibronectin type iii domain containing 5
LRIG1	leucine-rich repeats and immunoglobulin-like domains 1
LRIG2	leucine-rich repeats and immunoglobulin-like domains 2
LRP12	low density lipoprotein-related protein 12
LRP1B	low density lipoprotein-related protein 1b (deleted in tumors)
LRP2	low density lipoprotein-related protein 2
LRP4	low density lipoprotein receptor-related protein 4
LRP6	low density lipoprotein receptor-related protein 6
LRRC16	leucine rich repeat containing 16

---



---

LRRC20	leucine rich repeat containing 20
LRRC4	leucine rich repeat containing 4
LRRC41	leucine rich repeat containing 41
LRRC55	leucine rich repeat containing 55
LRRC7	leucine rich repeat containing 7
LRRFIP2	leucine rich repeat (in flil) interacting protein 2
LRRIQ2	leucine-rich repeats and iq motif containing 2
LRRK1	leucine-rich repeat kinase 1
LRRN1	leucine rich repeat neuronal 1
LRRN3	leucine rich repeat neuronal 3
LRRTM2	leucine rich repeat transmembrane neuronal 2
LRTM1	leucine-rich repeats and transmembrane domains 1
LUC7L2	cgi-59 protein
LUZP1	leucine zipper protein 1
LY6E	lymphocyte antigen 6 complex, locus e
LYCAT	lysocardiolipin acyltransferase
LYPLA2	lysophospholipase ii
LYRIC	
LYST	lysosomal trafficking regulator
LZTFL1	leucine zipper transcription factor-like 1
M6PR	mannose-6-phosphate receptor (cation dependent)
MAB21L2	mab-21-like 2 (c. elegans)
MACF1	microtubule-actin crosslinking factor 1
MAD2L1BP	mad2l1 binding protein
MAF1	maf1 homolog (s. cerevisiae)
MAFG	v-maf musculoaponeurotic fibrosarcoma oncogene homolog g (avian)
MAGI2	membrane associated guanylate kinase, ww and pdz domain containing 2
MAK3	mak3 homolog (s. cerevisiae)
MAMDC1	mam domain containing 1
MAML1	mastermind-like 1 (drosophila)
MAN1A2	mannosidase, alpha, class 1a, member 2
MAN2A1	mannosidase, alpha, class 2a, member 1
MAP1A	microtubule-associated protein 1a
MAP1B	microtubule-associated protein 1b
MAP2K1	mitogen-activated protein kinase kinase 1
MAP2K3	mitogen-activated protein kinase kinase 3
MAP2K4	mitogen-activated protein kinase kinase 4
MAP3K1	mitogen-activated protein kinase kinase kinase 1
MAP3K11	mitogen-activated protein kinase kinase kinase 11
MAP3K12	mitogen-activated protein kinase kinase kinase 12
MAP3K14	mitogen-activated protein kinase kinase kinase 14
MAP3K2	mitogen-activated protein kinase kinase kinase 2
MAP3K3	mitogen-activated protein kinase kinase kinase 3
MAP3K4	mitogen-activated protein kinase kinase kinase 4
MAP3K5	mitogen-activated protein kinase kinase kinase 5
MAP3K8	mitogen-activated protein kinase kinase kinase 8
MAP3K9	mitogen-activated protein kinase kinase kinase 9
MAP4	microtubule-associated protein 4
MAP4K1	mitogen-activated protein kinase kinase kinase kinase 1
MAP4K5	mitogen-activated protein kinase kinase kinase kinase 5
MAP7	microtubule-associated protein 7
MAPK14	mitogen-activated protein kinase 14
MAPK3	mitogen-activated protein kinase 3
MAPK4	mitogen-activated protein kinase 4
MAPK6	mitogen-activated protein kinase 6
MAPK8IP3	mitogen-activated protein kinase 8 interacting protein 3
MAPK9	mitogen-activated protein kinase 9
MAPRE1	microtubule-associated protein, rp/eb family, member 1
MAPRE3	microtubule-associated protein, rp/eb family, member 3
MARCKS	myristoylated alanine-rich protein kinase c substrate
MARK1	map/microtubule affinity-regulating kinase 1
MARK2	map/microtubule affinity-regulating kinase 2
MARK4	map/microtubule affinity-regulating kinase 4
MARVELD1	marvel domain containing 1
MAST4	microtubule associated serine/threonine kinase family member 4
MASTL	microtubule associated serine/threonine kinase-like
MAT2A	methionine adenosyltransferase ii, alpha
MAT2B	ddtp-4-keto-6-deoxy-d-glucose 4-reductase
MBD5	methyl-cpg binding domain protein 5
MBD6	methyl-cpg binding domain protein 6
MBIP	map3k12 binding inhibitory protein 1
MBNL1	muscleblind-like (drosophila)
MBNL2	muscleblind-like 2 (drosophila)
MBTPS1	membrane-bound transcription factor peptidase, site 1
MBTPS2	membrane-bound transcription factor peptidase, site 2
MCCD1	mitochondrial coiled-coil domain 1
MCL1	myeloid cell leukemia sequence 1 (bcd2-related)
MCM3	mcm3 minichromosome maintenance deficient 3 (s. cerevisiae)
MDFIC	myod family inhibitor domain containing
MDGA1	mam domain containing glycosylphosphatidylinositol anchor 1
MEA1	male-enhanced antigen 1
MECP2	methyl cpg binding protein 2 (rett syndrome)
MED12L	kiaa1635 protein
MEF2C	mads box transcription enhancer factor 2, polypeptide c (myocyte enhancer factor 2c)
MEF2D	mads box transcription enhancer factor 2, polypeptide d (myocyte enhancer factor 2d)
MEIS1	meis1, myeloid ecotropic viral integration site 1 homolog (mouse)
MESP1	mesoderm posterior 1 homolog (mouse)
MFAP3L	microfibrillar-associated protein 3-like
MGC11061	
MGC11266	hypothetical protein mgc11266
MGC20470	hypothetical protein mgc20470

---

---

MGC23908	
MGC26690	
MGC29816	
MGC3101	hypothetical protein mgc3101
MGC3123	hypothetical protein mgc3123
MGC32065	
MGC33371	
MGC33486	hypothetical protein mgc33486
MGC33630	
MGC33926	hypothetical protein mgc33926
MGC39325	
MGC39518	hypothetical protein mgc39518
MGC40405	hypothetical protein mgc40405
MGC4504	
MGC45441	
MGC47816	
MGC48972	
MGC61598	similar to ankyrin-repeat protein nrarp
MGC61716	
MGEA5	meningioma expressed antigen 5 (hyaluronidase)
MGLL	monoglyceride lipase
MIDIIP1	mid1 interacting protein 1 (gastrulation specific g12-like (zebrafish))
MI-ER1	
MINA	myc induced nuclear antigen
MINK1	missshapen-like kinase 1 (zebrafish)
MIPOL1	mirror-image polydactyly 1
MITF	microphthalmia-associated transcription factor
MKNK1	map kinase interacting serine/threonine kinase 1
MKNK2	map kinase interacting serine/threonine kinase 2
MKRN1	makorin, ring finger protein, 1
MLL	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, drosophila)
MLL3	myeloid/lymphoid or mixed-lineage leukemia 3
MLL4	myeloid/lymphoid or mixed-lineage leukemia 4
MLL5	hypothetical protein flj10078
MLLT2	
MLLT6	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, drosophila); translocated to, 6
MLR1	transcription factor mlr1
MLR2	ligand-dependent corepressor
MMD	monocyte to macrophage differentiation-associated
MMP16	matrix metalloproteinase 16 (membrane-inserted)
MMP2	matrix metalloproteinase 2 (gelatinase a, 72kda gelatinase, 72kda type iv collagenase)
MMP24	matrix metalloproteinase 24 (membrane-inserted)
MN1	meningioma (disrupted in balanced translocation) 1
MNT	max binding protein
MOAP1	modulator of apoptosis 1
MOBK1A	mob1, mps one binder kinase activator-like 1a (yeast)
MOBK1B	mob1, mps one binder kinase activator-like 2b (yeast)
MON2	mon2 homolog (yeast)
MORC3	morc family cw-type zinc finger 3
MORF4	mortality factor 4
MORF4L1	mortality factor 4 like 1
MOSPD1	motile sperm domain containing 1
MPDU1	mannose-6-phosphate utilization defect 1
MPHOSPH9	m-phase phosphoprotein 9
MPPED2	metallophosphoesterase domain containing 2
MRA5	muscle ras oncogene homolog
MRI25	mitochondrial ribosomal protein s25
MSH5	mutS homolog 5 (e. coli)
MSL2L1	male-specific lethal 2-like 1 (drosophila)
MTERFD2	mtorf domain containing 2
MTF1	metal-regulatory transcription factor 1
MTMR3	myotubularin related protein 3
MTMR4	myotubularin related protein 4
MTSS1	metastasis suppressor 1
MTUS1	mitochondrial tumor suppressor 1
MUTED	muted homolog (mouse)
MXI1	max interactor 1
MYBL1	v-myc myeloblastosis viral oncogene homolog (avian)-like 1
MYCBP2	myc binding protein 2
MYCL1	v-myc myelocytomatosis viral oncogene homolog 1, lung carcinoma derived (avian)
MYCN	v-myc myelocytomatosis viral related oncogene, neuroblastoma derived (avian)
MYF5	myogenic factor 5
MYH9	myosin, heavy polypeptide 9, non-muscle
MYLIP	myosin regulatory light chain interacting protein
MYLK	myosin, light polypeptide kinase
MYO10	myosin x
MYO1B	myosin ib
MYO1D	myosin id
MYO1E	myosin ie
MYO5A	myosin va (heavy polypeptide 12, myosin)
MYST3	myst histone acetyltransferase (monocytic leukemia) 3
MYST4	myst histone acetyltransferase (monocytic leukemia) 4
MYT1	myelin transcription factor 1
MYTIL	myelin transcription factor 1-like
N4BP1	nedd4 binding protein 1
NAB2	ngfi-a binding protein 2 (egr1 binding protein 2)
NAGK	n-acetylglucosamine kinase
NANOS1	nanos homolog 1 (drosophila)
NAPB	neuritis with brachial plexopathy
NAPB	n-ethylmaleimide-sensitive factor attachment protein, beta
NARG1	nmda receptor regulated 1

---

---

NAV1	hypothetical protein mgc14961
NAV3	neuron navigator 3
NBEA	neurobeachin
NBL1	neuroblastoma, suppression of tumorigenicity 1
NCALD	neurocalcin delta
NCK2	nck adaptor protein 2
NCKIPSD	nck interacting protein with sh3 domain
NCOA1	nuclear receptor coactivator 1
NCOA2	nuclear receptor coactivator 2
NCOA3	nuclear receptor coactivator 3
NCOA5	nuclear receptor coactivator 5
NCOA7	nuclear receptor coactivator 7
NCSTN	nicastrin
NDEL1	nude nuclear distribution gene e homolog like 1 (a. nidulans)
NDFIP2	nedd4 family interacting protein 2
NDRG4	ndrg family member 4
NDUFA1	nadh dehydrogenase (ubiquinone) 1 alpha subcomplex, 1, 7.5kda
NEBL	nebulin
NECAP1	neap endocytosis associated 1
NEDD4	neural precursor cell expressed, developmentally down-regulated 4
NEDD4L	neural precursor cell expressed, developmentally down-regulated 4-like
NEDD9	neural precursor cell expressed, developmentally down-regulated 9
NEF3	neurofilament 3 (150kda medium)
NEFH	neurofilament, heavy polypeptide 200kda
NEGR1	neuronal growth regulator 1
NEK9	nima (never in mitosis gene a)- related kinase 9
NELF	nasal embryonic lhrh factor
NEO1	neogenin homolog 1 (chicken)
NETO1	neuropilin (nrp) and tolloid (tll)-like 1
NETO2	hypothetical protein flj10430
NEUROD1	neurogenic differentiation 1
NEUROD6	neurogenic differentiation 6
NEUROG1	neurogenin 1
NEUROG2	neurogenin 2
NFAT5	nuclear factor of activated t-cells 5, tonicity-responsive
NFATC3	nuclear factor of activated t-cells, cytoplasmic, calcineurin-dependent 3
NFE2L1	nuclear factor (erythroid-derived 2)-like 1
NFIA	nuclear factor i/a
NFIB	nuclear factor i/b
NFIX	nuclear factor i/x (ccat-binding transcription factor)
NFKBIA	nuclear factor of kappa light polypeptide gene enhancer in b-cells inhibitor, alpha
NFYA	nuclear transcription factor y, alpha
NFYB	nuclear transcription factor y, beta
NFYC	nuclear transcription factor y, gamma
NHLH1	nescent helix loop helix 1
NHLH2	nescent helix loop helix 2
NHS	nance-horan syndrome (congenital cataracts and dental anomalies)
NHSL1	nhs-like 1
NIP30	nfa-interacting nuclear protein nip30
NIPA1	non imprinted in prader-willi/angelman syndrome 1
NIPBL	nipped-b homolog (drosophila)
NKD1	naked cuticle homolog 1 (drosophila)
NKIRAS1	nfkb inhibitor interacting ras-like 1
NKX2-2	nk2 transcription factor related, locus 2 (drosophila)
NKX2-3	nk2 transcription factor homolog c (drosophila)
NKX6-1	nk6 transcription factor related, locus 1 (drosophila)
NLGN1	neuroligin 1
NLGN2	neuroligin 2
NLK	nemo-like kinase
NME7	non-metastatic cells 7, protein expressed in (nucleoside-diphosphate kinase)
NMT2	n-myristoyltransferase 2
NOG	noggin
NOL7	nucleolar protein 7, 27kda
NOL9	nucleolar protein 9
NOMO1	nodal modulator 1
NOMO2	nodal modulator 2
NOMO3	nodal modulator 3
NOTCH1	notch homolog 1, translocation-associated (drosophila)
NOVA1	neuro-oncological ventral antigen 1
NOVA2	neuro-oncological ventral antigen 2
NOX4	nadh oxidase 4
N-PAC	uncharacterized bone marrow protein bm045
NPAS2	neuronal pas domain protein 2
NPAS3	neuronal pas domain protein 3
NPAT	nuclear protein, ataxia-telangiectasia locus
NPC1	niemann-pick disease, type c1
NPC1	nasopharyngeal carcinoma 1
NPD014	
NPEPL1	aminopeptidase-like 1
NPLOC4	nuclear protein localization 4 homolog (s. cerevisiae)
NPM1	nucleophosmin (nucleolar phosphoprotein b23, numatrin)
NPPC	natriuretic peptide precursor c
NPTN	neuropilin
NPTX1	neuronal pentraxin i
NR1D2	nuclear receptor subfamily 1, group d, member 2
NR1H2	nuclear receptor subfamily 1, group h, member 2
NR2F2	nuclear receptor subfamily 2, group f, member 2
NR3C1	nuclear receptor subfamily 3, group c, member 1 (glucocorticoid receptor)
NR3C2	nuclear receptor subfamily 3, group c, member 2
NR4A2	nuclear receptor subfamily 4, group a, member 2
NR4A3	nuclear receptor subfamily 4, group a, member 3

---

---

NRBF2	nuclear receptor binding factor 2
NRBP1	nuclear receptor binding protein 1
NRF1	nuclear respiratory factor 1
NRG1	neuregulin 1
NRIP1	nuclear receptor interacting protein 1
NRK	nik related kinase
NRP1	neuropilin 1
NRP2	neuropilin 2
NRXN3	neurexin 3
NS3TP2	
NSE2	
NSF	n-ethylmaleimide-sensitive factor
NSMAF	neutral sphingomyelinase (n-smase) activation associated factor
NT5C1A	5'-nucleotidase, cytosolic ia
NTE	neuropathy target esterase
NTN4	netrin 4
NTRK3	neurotrophic tyrosine kinase, receptor, type 3
NUAK1	nuak family, snf1-like kinase, 1
NUMB	numb homolog (drosophila)
NUP153	nucleoporin 153kda
NUP35	nucleoporin 35kda
NXPH1	neurexophilin 1
NXT2	nuclear transport factor 2-like export factor 2
NYX	nyctalopin
OACT2	o-acyltransferase (membrane bound) domain containing 2
OACT5	o-acyltransferase (membrane bound) domain containing 5
OAZ3	ornithine decarboxylase antizyme 3
OBFC2A	oligonucleotide/oligosaccharide-binding fold containing 2a
OCRL	oculocerebrorenal syndrome of lowe
OFD1	oral-facial-digital syndrome 1
OGT	o-linked n-acetylglucosamine (glcnac) transferase (udp-n-acetylglucosamine:polypeptide-n-acetylglucosaminyl transferase)
OLFM1	olfactomedin 1
OLFM3	olfactomedin 3
OLFML2B	olfactomedin-like 2b
OMG	oligodendrocyte myelin glycoprotein
OPCML	opioid binding protein/cell adhesion molecule-like
OR10Q1	olfactory receptor, family 10, subfamily q, member 1
OR2V2	olfactory receptor, family 2, subfamily v, member 2
OR9G1	olfactory receptor, family 9, subfamily g, member 1
ORCL5	origin recognition complex, subunit 5-like (yeast)
ORMDL3	hypothetical protein loc51242
OSBPL11	hypothetical protein flj13164
OSBPL5	kiaa1534 protein
OSBPL8	oxysterol binding protein-like 8
OSR1	odd-skipped related 1 (drosophila)
OSTM1	osteopetrosis associated transmembrane protein 1
OTP	orthopedia homolog (drosophila)
OTUB1	otu domain, ubiquitin aldehyde binding 1
OTUD1	otu domain containing 1
OTUD4	kiaa1046 protein
OTX1	orthodenticle homolog 1 (drosophila)
OXSR1	oxidative-stress responsive 1
P2RX4	purinergic receptor p2x, ligand-gated ion channel, 4
P2RY13	purinergic receptor p2y, g-protein coupled, 13
P66beta	
PA2G4	proliferation-associated 2g4, 38kda
PABPN1	poly(a) binding protein, nuclear 1
PACSLN1	protein kinase c and casein kinase substrate in neurons 1
PAFAH1B1	platelet-activating factor acetylhydrolase, isoform ib, alpha subunit 45kda
PAFAH1B2	platelet-activating factor acetylhydrolase, isoform ib, beta subunit 30kda
PAIP1	poly(a) binding protein interacting protein 1
PAI-RBP1	
PAK6	p21(cdkn1a)-activated kinase 6
PAK7	p21(cdkn1a)-activated kinase 7
PALLD	palladin, cytoskeletal associated protein
PALMD	palmdelphin
PAM	peptidylglycine alpha-amidating monooxygenase
PANX2	pannexin 2
PAPD4	pap associated domain containing 4
PAPOLA	poly(a) polymerase alpha
PAPOLB	poly(a) polymerase beta (testis specific)
PAPOLG	poly(a) polymerase gamma
PAPPA	pregnancy-associated plasma protein a, pappalysin 1
PARD6B	par-6 partitioning defective 6 homolog beta (c. elegans)
PARG1	
PARP8	poly (adp-ribose) polymerase family, member 8
PAX2	paired box gene 2
PAX3	paired box gene 3 (waardenburg syndrome 1)
PBEF1	pre-b-cell colony enhancing factor 1
PBX2	pre-b-cell leukemia transcription factor 2
PBX3	pre-b-cell leukemia transcription factor 3
PCAF	p300/cbp-associated factor
PCANAP6	
PCBP1	poly(rc) binding protein 1
PCBP2	poly(rc) binding protein 2
PCBP4	poly(rc) binding protein 4
PCDH10	protocadherin 10
PCDH11X, PCDH11Y	protocadherin 11 x-linked
PCDH17	protocadherin 17
PCDH8	protocadherin 8
PCDH9	protocadherin 9

---

---

PCDHA1	protocadherin alpha 1
PCDHA10	protocadherin alpha 10
PCDHA11	protocadherin alpha 11
PCDHA12	protocadherin alpha 12
PCDHA13	protocadherin alpha 13
PCDHA2	protocadherin alpha 2
PCDHA3	protocadherin alpha 3
PCDHA4	protocadherin alpha 4
PCDHA5	protocadherin alpha 5
PCDHA6	protocadherin alpha 6
PCDHA7	protocadherin alpha 7
PCDHA8	protocadherin alpha 8
PCDHA9	protocadherin alpha 9
PCDHAC1	protocadherin alpha subfamily c, 1
PCDHAC2	protocadherin alpha subfamily c, 2
PCGF2	polycomb group ring finger 2
PCGF3	polycomb group ring finger 3
PCGF4	polycomb group ring finger 4
PCGF5	polycomb group ring finger 5
PCMT1	protein-l-isoaspartate (d-aspartate) o-methyltransferase
PCNP	pest-containing nuclear protein
PCNX	pecanex homolog (drosophila)
PCTK1	pctaire protein kinase 1
PCTK2	pctaire protein kinase 2
PCYOX1	prenylcysteine oxidase 1
PDAP1	pdgfa associated protein 1
PDCD10	programmed cell death 10
PDCD4	programmed cell death 4 (neoplastic transformation inhibitor)
PDE3B	phosphodiesterase 3b, cgmp-inhibited
PDE4D	phosphodiesterase 4d, camp-specific (phosphodiesterase e3 dunce homolog, drosophila)
PDE5A	phosphodiesterase 5a, cgmp-specific
PDE7B	phosphodiesterase 7b
PDGFR4	platelet-derived growth factor receptor, alpha polypeptide
PDHA1	pyruvate dehydrogenase (lipoamide) alpha 1
PDIA6	protein disulfide isomerase family a, member 6
PDIK1L	pdlim1 interacting kinase 1 like
PDK4	pyruvate dehydrogenase kinase, isozyme 4
PDLIM5	pdz and lim domain 5
PDPR	pyruvate dehydrogenase phosphatase regulatory subunit
PDZD2	pdz domain containing 2
PDZK10	
PDZK4	
PEA15	phosphoprotein enriched in astrocytes 15
PEL12	pellino homolog 2 (drosophila)
PER1	period homolog 1 (drosophila)
PER2	period homolog 2 (drosophila)
PERQ1	perq amino acid rich, with gyf domain 1
PEX13	peroxisome biogenesis factor 13
PEX5L	peroxisomal biogenesis factor 5-like
PFA5	phosphoribosylformylglycinamide synthase (fgar amidotransferase)
PFKFB3	6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 3
PFKP	phosphofructokinase, platelet
PFN1	profilin 1
PFN2	profilin 2
PGAM1	phosphoglycerate mutase 1 (brain)
PGBD5	piggybac transposable element derived 5
PGM2L1	phosphoglucomutase 2-like 1
PHACTR2	phosphatase and actin regulator 2
PHC1	polyhomeotic-like 1 (drosophila)
PHF1	phd finger protein 1
PHF10	phd finger protein 10
PHF12	phd finger protein 12
PHF13	phd finger protein 13
PHF15	phd finger protein 15
PHF16	phd finger protein 16
PHF17	phd finger protein 17
PHF19	phd finger protein 19
PHF2	phd finger protein 2
PHF20	phd finger protein 20
PHF20L1	phd finger protein 20-like 1
PHF21B	phd finger protein 21b
PHF3	kiaa0244 protein
PHF6	phd finger protein 6
PHIP	pleckstrin homology domain interacting protein
PHLDA3	pleckstrin homology-like domain, family a, member 3
PHTF2	putative homeodomain transcription factor 2
PHYHIP	phytanoyl-coa 2-hydroxylase interacting protein
PHYHIPL	phytanoyl-coa 2-hydroxylase interacting protein-like
PI4KII	phosphatidylinositol 4-kinase type ii
PIAS1	protein inhibitor of activated stat, 1
PIAS3	protein inhibitor of activated stat, 3
PIB5PA	inositol polyphosphate 5-phosphatase
PIG8	
PIK3CA	phosphoinositide-3-kinase, catalytic, alpha polypeptide
PIK3R1	phosphoinositide-3-kinase, regulatory subunit 1 (p85 alpha)
PIK3R3	phosphoinositide-3-kinase, regulatory subunit 3 (p55, gamma)
PIK4CB	phosphatidylinositol 4-kinase, catalytic, beta polypeptide
PIM1	pim-1 oncogene
PIP5K1C	phosphatidylinositol-4-phosphate 5-kinase, type i, gamma
PIP5K2C	phosphatidylinositol-4-phosphate 5-kinase, type ii, gamma
PISD	phosphatidylserine decarboxylase

---

PITPNA	phosphatidylinositol transfer protein, alpha
PITPNC1	phosphatidylinositol transfer protein, cytoplasmic 1
PITPNM2	phosphatidylinositol transfer protein, membrane-associated 2
PITX1	paired-like homeodomain transcription factor 1
PKD1	polycystic kidney disease 1 (autosomal dominant)
PKD2	polycystic kidney disease 2 (autosomal dominant)
PKD2L2	polycystic kidney disease 2-like 2
PKIA	protein kinase (camp-dependent, catalytic) inhibitor alpha
PKNOX1	pbx/knotted 1 homeobox 1
PKP4	plakophilin 4
PLAA	phospholipase a2-activating protein
PLAG1	pleiomorphic adenoma gene 1
PLAGL1	pleiomorphic adenoma gene-like 1
PLAGL2	pleiomorphic adenoma gene-like 2
PLCB1	phospholipase c, beta 1 (phosphoinositide-specific)
PLCG1	phospholipase c, gamma 1
PLEKHA1	pleckstrin homology domain containing, family a (phosphoinositide binding specific) member 1
PLEKHA3	hypothetical protein flj20067
PLEKHA6	pleckstrin homology domain containing, family a member 6
PLEKHA7	pleckstrin homology domain containing, family a member 7
PLEKHC1	pleckstrin homology domain containing, family c (with ferm domain) member 1
PLEKHH1	pleckstrin homology domain containing, family h (with myth4 domain) member 1
PLEKHM1	pleckstrin homology domain containing, family m (with run domain) member 1
PLEKHQ1	pleckstrin homology domain containing, family q member 1
PLK1	polo-like kinase 1 (drosophila)
PLS1	plastin 1 (i isoform)
PLS3	plastin 3 (t isoform)
PLXNA1	plexin a1
PLXNA2	plexin a2
PLXNC1	plexin c1
PNN	pinin, desmosome associated protein
PNRC1	proline-rich nuclear receptor coactivator 1
PODN	podocan
PODXL	podocalyxin-like
POFUT1	protein o-fucosyltransferase 1
POGZ	pogo transposable element with znf domain
POLD3	polymerase (dna-directed), delta 3, accessory subunit
POLG	polymerase (dna directed), gamma
POLK	polymerase (dna directed) kappa
POLQ	polymerase (dna directed), theta
POLR2C	polymerase (rna) ii (dna directed) polypeptide c, 33kda
POLR3F	polymerase (rna) iii (dna directed) polypeptide f, 39 kda
POLRMT	polymerase (rna) mitochondrial (dna directed)
POLS	polymerase (dna directed) sigma
POM121	pom121 membrane glycoprotein (rat)
POU2F1	pou domain, class 2, transcription factor 1
POU3F2	pou domain, class 3, transcription factor 2
POU4F1	pou domain, class 4, transcription factor 1
POU4F2	pou domain, class 4, transcription factor 2
PPARA	peroxisome proliferative activated receptor, alpha
PPCS	phosphopantothencysteine synthetase
PPFIA3	protein tyrosine phosphatase, receptor type, f polypeptide (ptprf), interacting protein (liprin), alpha 3
PTIG	peptidylprolyl isomerase g (cyclophilin g)
PPM1A	protein phosphatase 1a (formerly 2c), magnesium-dependent, alpha isoform
PPM1D	protein phosphatase 1d magnesium-dependent, delta isoform
PPM1E	protein phosphatase 1e (pp2c domain containing)
PPM1G	protein phosphatase 1g (formerly 2c), magnesium-dependent, gamma isoform
PPME1	protein phosphatase methylesterase 1
PPP1CB	protein phosphatase 1, catalytic subunit, beta isoform
PPP1CC	protein phosphatase 1, catalytic subunit, gamma isoform
PPP1R10	protein phosphatase 1, regulatory subunit 10
PPP1R11	protein phosphatase 1, regulatory (inhibitor) subunit 11
PPP1R12A	protein phosphatase 1, regulatory (inhibitor) subunit 12a
PPP1R12C	protein phosphatase 1, regulatory (inhibitor) subunit 12c
PPP1R15B	protein phosphatase 1, regulatory (inhibitor) subunit 15b
PPP1R2P9	protein phosphatase 1, regulatory (inhibitor) subunit 2 pseudogene 9
PPP1R3A	protein phosphatase 1, regulatory (inhibitor) subunit 3a (glycogen and sarcoplasmic reticulum binding subunit, skeletal muscle)
PPP1R3C	protein phosphatase 1, regulatory (inhibitor) subunit 3c
PPP1R9B	protein phosphatase 1, regulatory subunit 9b, spinophilin
PPP2CA	protein phosphatase 2 (formerly 2a), catalytic subunit, alpha isoform
PPP2R1A	protein phosphatase 2 (formerly 2a), regulatory subunit a (pr 65), alpha isoform
PPP2R2A	protein phosphatase 2 (formerly 2a), regulatory subunit b (pr 52), alpha isoform
PPP2R2C	protein phosphatase 2 (formerly 2a), regulatory subunit b (pr 52), gamma isoform
PPP2R4	protein phosphatase 2a, regulatory subunit b' (pr 53)
PPP2R5C	protein phosphatase 2, regulatory subunit b (b56), gamma isoform
PPP2R5E	protein phosphatase 2, regulatory subunit b (b56), epsilon isoform
PPP3CA	protein phosphatase 3 (formerly 2b), catalytic subunit, alpha isoform (calcineurin a alpha)
PPP3CB	protein phosphatase 3 (formerly 2b), catalytic subunit, beta isoform (calcineurin a beta)
PPP3R1	protein phosphatase 3 (formerly 2b), regulatory subunit b, 19kda, alpha isoform (calcineurin b, type i)
PPP4R1	protein phosphatase 4, regulatory subunit 1
PPP6C	protein phosphatase 6, catalytic subunit
PPRC1	peroxisome proliferative activated receptor, gamma, coactivator-related 1
PPTC7	ptc7 protein phosphatase homolog (s. cerevisiae)
PRC1	protein regulator of cytokinesis 1
PRDM1	pr domain containing 1, with znf domain
PRDM12	pr domain containing 12
PRDM13	pr domain containing 13
PRDM2	pr domain containing 2, with znf domain
PRDM4	pr domain containing 4
PRDM8	pr domain containing 8
PRDX5	peroxiredoxin 5

---

PREI3	preimplantation protein 3
PREX1	phosphatidylinositol 3,4,5-trisphosphate-dependent rac exchanger 1
PRG-3	
PRICKLE2	prickle-like 2 (drosophila)
PRKAA1	protein kinase, amp-activated, alpha 1 catalytic subunit
PRKAB2	protein kinase, amp-activated, beta 2 non-catalytic subunit
PRKACB	protein kinase, camp-dependent, catalytic, beta
PRKAR2A	protein kinase, camp-dependent, regulatory, type ii, alpha
PRKAR2B	protein kinase, camp-dependent, regulatory, type ii, beta
PRKCA	protein kinase c, alpha
PRKCE	protein kinase c, epsilon
PRKD1	protein kinase d1
PRKG1	protein kinase, cgmp-dependent, type i
PRLR	prolactin receptor
PRNPIP	prion protein interacting protein
PRO0149	pro0149 protein
PROKR2	prokineticin receptor 2
PRPF38B	prp38 pre-mrna processing factor 38 (yeast) domain containing b
PRPF4B	prp4 pre-mrna processing factor 4 homolog b (yeast)
PRRG1	proline rich gla (g-carboxyglutamic acid) 1
PRRX1	paired related homeobox 1
PSAP	prosaposin (variant gaucher disease and variant metachromatic leukodystrophy)
PSD	pleckstrin and sec7 domain containing
PSD2	pleckstrin and sec7 domain containing 2
PSD3	pleckstrin and sec7 domain containing 3
PSKH1	protein serine kinase h1
PSMC6	proteasome (prosome, macropain) 26s subunit, atpase, 6
PSME3	proteasome (prosome, macropain) activator subunit 3 (pa28 gamma; ki)
PSMF1	proteasome (prosome, macropain) inhibitor subunit 1 (pi31)
PTCD1	pentatricopeptide repeat domain 1
PTCH	patched homolog (drosophila)
PTCHD1	patched domain containing 1
PTCHD3	patched domain containing 3
PTEN	phosphatase and tensin homolog (mutated in multiple advanced cancers 1)
PTGER4	prostaglandin e receptor 4 (subtype ep4)
PTGES3	prostaglandin e synthase 3 (cytosolic)
PTGERN	prostaglandin f2 receptor negative regulator
PTH	parathyroid hormone
PTH1H	parathyroid hormone-like hormone
PTK2	ptk2 protein tyrosine kinase 2
PTK2B	ptk2b protein tyrosine kinase 2 beta
PTK9	ptk9 protein tyrosine kinase 9
PTP4A1	protein tyrosine phosphatase type iva, member 1
PTP4A2	protein tyrosine phosphatase type iva, member 2
PTPN2	protein tyrosine phosphatase, non-receptor type 2
PTPN21	protein tyrosine phosphatase, non-receptor type 21
PTPN3	protein tyrosine phosphatase, non-receptor type 3
PTPN4	protein tyrosine phosphatase, non-receptor type 4 (megakaryocyte)
PTPN9	protein tyrosine phosphatase, non-receptor type 9
PTPRA	protein tyrosine phosphatase, receptor type, a
PTPRG	protein tyrosine phosphatase, receptor type, g
PTPRM	protein tyrosine phosphatase, receptor type, m
PTPRO	protein tyrosine phosphatase, receptor type, o
PTPRR	protein tyrosine phosphatase, receptor type, r
PUM1	pumilio homolog 1 (drosophila)
PUM2	pumilio homolog 2 (drosophila)
PURA	purine-rich element binding protein a
PURB	purine-rich element binding protein b
PVRL2	poliovirus receptor-related 2 (herpesvirus entry mediator b)
PVRL3	poliovirus receptor-related 3
PXDN	peroxidasin homolog (drosophila)
PXN	paxillin
QKI	quaking homolog, kh domain rna binding (mouse)
R3HDM1	r3h domain containing 1
R3HDM2	r3h domain containing 2
RAB10	rab10, member ras oncogene family
RAB11A	rab11a, member ras oncogene family
RAB11FIP1	rab11 family interacting protein 1 (class i)
RAB11FIP2	rab11 family interacting protein 2 (class i)
RAB14	rab14, member ras oncogene family
RAB18	rab18, member ras oncogene family
RAB1A	rab1a, member ras oncogene family
RAB21	rab21, member ras oncogene family
RAB22A	rab22a, member ras oncogene family
RAB23	rab23, member ras oncogene family
RAB2B	rab2b, member ras oncogene family
RAB30	rab30, member ras oncogene family
RAB33B	rab33b, member ras oncogene family
RAB34	rab34, member ras oncogene family
RAB35	rab35, member ras oncogene family
RAB4B	rab4b, member ras oncogene family
RAB5B	rab5b, member ras oncogene family
RAB5C	rab5c, member ras oncogene family
RAB6A	rab6a, member ras oncogene family
RAB6B	rab6b, member ras oncogene family
RAB6C	rab6c, member ras oncogene family
RAB7	rab7, member ras oncogene family
RAB8A	rab8a, member ras oncogene family
RAB8B	rab8b, member ras oncogene family
RAB9B	rab9b, member ras oncogene family
RABEP1	rabaptin, rab gtpase binding effector protein 1

---

---

RABGAP1	rab gtpase activating protein 1
RAD21	rad21 homolog (s. pombe)
RAD23A	rad23 homolog a (s. cerevisiae)
RAD23B	rad23 homolog b (s. cerevisiae)
RAD9A	rad9 homolog a (s. pombe)
RAF1	v-raf-1 murine leukemia viral oncogene homolog 1
RAI17	retinoic acid induced 17
RAI2	retinoic acid induced 2
RALGDS	ral guanine nucleotide dissociation stimulator
RALGPS1	ral gef with ph domain and sh3 binding motif 1
RaLP	
RANBP2	ran binding protein 2
RANBP3	ran binding protein 3
RANBP9	ran binding protein 9
RAP1A	rap1a, member of ras oncogene family
RAP1B	rap1b, member of ras oncogene family
RAP1GA1	rap1, gtpase activating protein 1
RAP2A	rap2a, member of ras oncogene family
RAP2C	rap2c, member of ras oncogene family
RAPGEF2	rap guanine nucleotide exchange factor (gef) 2
RAPGEF4	rap guanine nucleotide exchange factor (gef) 4
RAPGEFL1	rap guanine nucleotide exchange factor (gef)-like 1
RAPH1	ras association (ralgds/af-6) and pleckstrin homology domains 1
RAPSN	receptor-associated protein of the synapse, 43kd
RARB	retinoic acid receptor, beta
RARG	retinoic acid receptor, gamma
RASD1	ras, dexamethasone-induced 1
RASGEF1A	rasgef domain family, member 1a
RASGEF1B	rasgef domain family, member 1b
RASL11B	ras-like, family 11, member b
RASL12	ras-like, family 12
RASSF2	ras association (ralgds/af-6) domain family 2
RASSF5	ras association (ralgds/af-6) domain family 5
RB1	retinoblastoma 1 (including osteosarcoma)
RB1CC1	rb1-inducible coiled-coil 1
RBBP6	retinoblastoma binding protein 6
RBBP7	retinoblastoma binding protein 7
RBBP8	retinoblastoma binding protein 8
RBJ	ras-associated protein rap1
RBL1	retinoblastoma-like 1 (p107)
RBL2	retinoblastoma-like 2 (p130)
RBM15	rna binding motif protein 15
RBM15B	rna binding motif protein 15b
RBM21	rna binding motif protein 21
RBM27	rna binding motif protein 27
RBM35A	rna binding motif protein 35a
RBM35B	rna binding motif protein 35b
RBM6	rna binding motif protein 6
RBM9	rna binding motif protein 9
RBM51	rna binding motif, single stranded interacting protein 1
RBM53	rna binding motif, single stranded interacting protein
RBMX	rna binding motif protein, x-linked
RC3H1	ring finger and cch-type zinc finger domains 1
RCBTB1	regulator of chromosome condensation (rcl) and btb (poz) domain containing protein 1
RCE1	rce1 homolog, prenyl protein peptidase (s. cerevisiae)
RCOR3	rest corepressor 3
RDBP	rd rna binding protein
RECK	reversion-inducing-cysteine-rich protein with kazal motifs
REEP3	receptor accessory protein 3
RELN	reelin
RET	ret proto-oncogene (multiple endocrine neoplasia and medullary thyroid carcinoma 1, hirschsprung disease)
REV1L	rev1-like (yeast)
REV3L	rev3-like, catalytic subunit of dna polymerase zeta (yeast)
RFC4	replication factor c (activator 1) 4, 37kda
RFP	ret finger protein
RFX1	regulatory factor x, 1 (influences hla class ii expression)
RFX4	regulatory factor x, 4 (influences hla class ii expression)
RFXDC2	regulatory factor x domain containing 2
RGL1	ral guanine nucleotide dissociation stimulator-like 1
RGMA	rgm domain family, member a
RGS17	regulator of g-protein signalling 17
RGS3	regulator of g-protein signalling 3
RHBDP2	rhomboid 5 homolog 2 (drosophila)
RHEBL1	ras homolog enriched in brain like 1
RHOB	ras homolog gene family, member b
RHOC	ras homolog gene family, member c
RHOV	ras homolog gene family, member v
RHPN2	rhophilin, rho gtpase binding protein 2
RIC8B	resistance to inhibitors of cholinesterase 8 homolog b (c. elegans)
RIMS1	regulating synaptic membrane exocytosis 1
RIMS3	regulating synaptic membrane exocytosis 3
RIMS4	regulating synaptic membrane exocytosis 4
RIN2	ras and rab interactor 2
RKHD1	ring finger and kh domain containing 1
RKHD2	ring finger and kh domain containing 2
RNF103	ring finger protein 103
RNF11	ring finger protein 11
RNF111	ring finger protein 111
RNF12	ring finger protein 12
RNF125	ring finger protein 125
RNF128	ring finger protein 128

---



---

RNF13	ring finger protein 13
RNF138	ring finger protein 138
RNF139	ring finger protein 139
RNF144	ring finger protein 144
RNF149	ring finger protein 149
RNF167	ring finger protein 167
RNF184	
RNF2	ring finger protein 2
RNF38	hypothetical protein flj21343
RNF4	ring finger protein 4
RNF41	ring finger protein 41
RNF44	ring finger protein 44
RNF6	ring finger protein (c3h2c3 type) 6
RNH1	ribonuclease/angiogenin inhibitor 1
ROBO1	roundabout, axon guidance receptor, homolog 1 (drosophila)
ROCK1	rho-associated, coiled-coil containing protein kinase 1
ROPN1	ropporin, rhophilin associated protein 1
RORB	rar-related orphan receptor b
RP2	retinitis pigmentosa 2 (x-linked recessive)
RP42	
RPA2	replication protein a2, 32kda
RPS6KA1	ribosomal protein s6 kinase, 90kda, polypeptide 1
RPS6KA2	ribosomal protein s6 kinase, 90kda, polypeptide 2
RPS6KA3	ribosomal protein s6 kinase, 90kda, polypeptide 3
RPS6KA4	ribosomal protein s6 kinase, 90kda, polypeptide 4
RPS6KA5	ribosomal protein s6 kinase, 90kda, polypeptide 5
RPS6KB1	ribosomal protein s6 kinase, 70kda, polypeptide 1
RRAGB	ras-related gtp binding b
RRAGD	ras-related gtp binding d
RRAS2	related ras viral (r-ras) oncogene homolog 2
KRM2	ribonucleotide reductase m2 polypeptide
RSBN1	round spermatid basic protein 1
RSBN1L	round spermatid basic protein 1-like
RSN	restin (reed-steinberg cell-expressed intermediate filament-associated protein)
RSNL2	restin-like 2
RSP02	r-spondin 2 homolog (xenopus laevis)
RSPRY1	ring finger and spry domain containing 1
RTN1	reticulin 1
RTN2	reticulin 2
RTN3	reticulin 3
RTN4RL1	reticulin 4 receptor-like 1
RUNX1	runt-related transcription factor 1 (acute myeloid leukemia 1; aml1 oncogene)
RUNX1T1	runt-related transcription factor 1; translocated to, 1 (cyclin d-related)
RUNX3	runt-related transcription factor 3
RXRA	retinoid x receptor, alpha
RYBP	ring1 and yy1 binding protein
RYS3	ryanodine receptor 3
SACS	spastic ataxia of charlevoix-saguenay (sacsin)
SALL1	sal-like 1 (drosophila)
SALL3	sal-like 3 (drosophila)
SAR1A	sar1 gene homolog a (s. cerevisiae)
SAR1B	sar1 gene homolog b (s. cerevisiae)
SASH1	sam and sh3 domain containing 1
SATB1	special at-rich sequence binding protein 1 (binds to nuclear matrix/scaffold-associating dna's)
SATB2	satb family member 2
SBF2	set binding factor 2
SCAMP2	secretory carrier membrane protein 2
SCAMP5	secretory carrier membrane protein 5
SCARB2	scavenger receptor class b, member 2
SCARF1	scavenger receptor class f, member 1
SCC-112	scc-112 protein
SCHIP1	schwannomin interacting protein 1
SCML2	sex comb on midleg-like 2 (drosophila)
SCN1A	sodium channel, voltage-gated, type i, alpha
SCN3A	sodium channel, voltage-gated, type iii, alpha
SCN4B	sodium channel, voltage-gated, type iv, beta
SCN8A	sodium channel, voltage gated, type viii, alpha
SCOC	short coiled-coil protein
SCRN1	secernin 1
SCRT2	scratch homolog 2, zinc finger protein (drosophila)
SCUBE3	signal peptide, cub domain, egf-like 3
SDC1	syndecan 1
SDC2	syndecan 2 (heparan sulfate proteoglycan 1, cell surface-associated, fibroglycan)
SDCBP	syndecan binding protein (syntenin)
SEC11L1	sec11-like 1 (s. cerevisiae)
SEC14L1	sec14-like 1 (s. cerevisiae)
SEC22L1	sec22 vesicle trafficking protein-like 1 (s. cerevisiae)
SEC22L2	sec22 vesicle trafficking protein-like 2 (s. cerevisiae)
SEC24C	sec24 related gene family, member c (s. cerevisiae)
SEC31L2	sec31-like 2 (s. cerevisiae)
SEC61A1	sec61 alpha 1 subunit (s. cerevisiae)
SEH1L	seh1-like (s. cerevisiae)
SELI	selenoprotein i
SEMA3A	sema domain, immunoglobulin domain (ig), short basic domain, secreted, (semaphorin) 3a
SEMA3C	sema domain, immunoglobulin domain (ig), short basic domain, secreted, (semaphorin) 3c
SEMA3D	sema domain, immunoglobulin domain (ig), short basic domain, secreted, (semaphorin) 3d
SEMA4B	sema domain, immunoglobulin domain (ig), transmembrane domain (tm) and short cytoplasmic domain, (semaphorin) 4b
SEMA4C	sema domain, immunoglobulin domain (ig), transmembrane domain (tm) and short cytoplasmic domain, (semaphorin) 4c
SEMA4G	sema domain, immunoglobulin domain (ig), transmembrane domain (tm) and short cytoplasmic domain, (semaphorin) 4g
SEMA6A	ht018 protein
SEMA6D	kiaa1479 protein

---

---

SEN1	sumo1/sentrin specific peptidase 1
SEN2	sumo1/sentrin/smt3 specific peptidase 2
SEN5	sumo1/sentrin specific peptidase 5
SERBP1	serpine1 mrna binding protein 1
SERINC4	serine incorporator 4
SERP1	stress-associated endoplasmic reticulum protein 1
SERTAD2	serta domain containing 2
SERTAD3	serta domain containing 3
SESN1	sestrin 1
SESN3	sestrin 3
SET	set translocation (myeloid leukemia-associated)
SETD3	set domain containing 3
SF3B3	kiaa0017 gene product
SFMBT1	dkfzp434l243 protein
SFPQ	splicing factor proline/glutamine-rich (polypyrimidine tract binding protein associated)
SFRS1	splicing factor, arginine/serine-rich 1 (splicing factor 2, alternate splicing factor)
SFRS10	splicing factor, arginine/serine-rich 10 (transformer 2 homolog, drosophila)
SFRS11	splicing factor, arginine/serine-rich 11
SFRS12	splicing factor, arginine/serine-rich 12
SFRS16	splicing factor, arginine/serine-rich 16 (suppressor-of-white-apricot homolog, drosophila)
SFRS2	splicing factor, arginine/serine-rich 2
SFRS5	splicing factor, arginine/serine-rich 5
SFRS6	splicing factor, arginine/serine-rich 6
SFRS7	splicing factor, arginine/serine-rich 7, 35kda
SFXN1	likely ortholog of mouse sideroflexin 1
SFXN5	sideroflexin 5
SGCD	sarcoglycan, delta (35kda dystrophin-associated glycoprotein)
SGCZ	sarcoglycan zeta
SGIP1	sh3-domain grb2-like (endophilin) interacting protein 1
SGK	serum/glucocorticoid regulated kinase
SGPP1	sphingosine-1-phosphate phosphatase 1
SH2D2A	sh2 domain protein 2a
SH3BGR12	sh3 domain binding glutamic acid-rich protein like 2
SH3BP4	sh3-domain binding protein 4
SH3BP5	sh3-domain binding protein 5 (btk-associated)
SH3GL2	sh3-domain grb2-like 2
SH3KBP1	sh3-domain kinase binding protein 1
SH3PX3	sh3 and px domain containing 3
SHANK2	sh3 and multiple ankyrin repeat domains 2
SHANK3	sh3 and multiple ankyrin repeat domains 3
SHC4	shc (src homology 2 domain containing) family, member 4
SHOX2	short stature homeobox 2
SIAH1	seven in absentia homolog 1 (drosophila)
SIAH2	seven in absentia homolog 2 (drosophila)
SIDT1	sid1 transmembrane family, member 1
SIGIRR	single immunoglobulin and toll-interleukin 1 receptor (tir) domain
SIM2	single-minded homolog 2 (drosophila)
SIP1IL2	signal-induced proliferation-associated 1 like 2
SIP1IL3	signal-induced proliferation-associated 1 like 3
SIRT1	sirtuin (silent mating type information regulation 2 homolog) 1 (s. cerevisiae)
SIRT7	pyrroline-5-carboxylate reductase 1
SIX3	sine oculis homeobox homolog 3 (drosophila)
SIX4	sine oculis homeobox homolog 4 (drosophila)
SKI	v-ski sarcoma viral oncogene homolog (avian)
SLC11A2	solute carrier family 11 (proton-coupled divalent metal ion transporters), member 2
SLC12A2	solute carrier family 12 (sodium/potassium/chloride transporters), member 2
SLC12A5	solute carrier family 12, (potassium-chloride transporter) member 5
SLC13A3	solute carrier family 13 (sodium-dependent dicarboxylate transporter), member 3
SLC16A2	solute carrier family 16 (monocarboxylic acid transporters), member 2
SLC17A6	solute carrier family 17 (sodium-dependent inorganic phosphate cotransporter), member 6
SLC17A7	solute carrier family 17 (sodium-dependent inorganic phosphate cotransporter), member 7
SLC1A2	solute carrier family 1 (glial high affinity glutamate transporter), member 2
SLC20A2	solute carrier family 20 (phosphate transporter), member 2
SLC23A2	solute carrier family 23 (nucleobase transporters), member 2
SLC24A3	solute carrier family 24 (sodium/potassium/calcium exchanger), member 3
SLC24A4	solute carrier family 24 (sodium/potassium/calcium exchanger), member 4
SLC24A5	solute carrier family 24, member 5
SLC25A1	solute carrier family 25 (mitochondrial carrier; citrate transporter), member 1
SLC25A25	solute carrier family 25 (mitochondrial carrier; phosphate carrier), member 25
SLC25A27	solute carrier family 25, member 27
SLC25A31	solute carrier family 25 (mitochondrial carrier; adenine nucleotide translocator), member 31
SLC25A35	solute carrier family 25, member 35
SLC26A7	solute carrier family 26, member 7
SLC2A14	solute carrier family 2 (facilitated glucose transporter), member 14
SLC2A3	solute carrier family 2 (facilitated glucose transporter), member 3
SLC2A4	solute carrier family 2 (facilitated glucose transporter), member 4
SLC2A4RG	slc2a4 regulator
SLC30A1	solute carrier family 30 (zinc transporter), member 1
SLC30A3	solute carrier family 30 (zinc transporter), member 3
SLC30A4	solute carrier family 30 (zinc transporter), member 4
SLC30A7	solute carrier family 30 (zinc transporter), member 7
SLC31A2	solute carrier family 31 (copper transporters), member 2
SLC32A1	solute carrier family 32 (gaba vesicular transporter), member 1
SLC35E2	solute carrier family 35, member e2
SLC35F3	solute carrier family 35, member f3
SLC36A1	lysosomal amino acid transporter 1
SLC38A2	solute carrier family 38, member 2
SLC39A1	solute carrier family 39 (zinc transporter), member 1
SLC39A10	solute carrier family 39 (zinc transporter), member 10
SLC39A9	solute carrier family 39 (zinc transporter), member 9
SLC40A1	solute carrier family 40 (iron-regulated transporter), member 1

---

---

SLC44A1	solute carrier family 44, member 1
SLC45A3	solute carrier family 45, member 3
SLC4A4	solute carrier family 4, sodium bicarbonate cotransporter, member 4
SLC4A7	solute carrier family 4, sodium bicarbonate cotransporter, member 7
SLC6A1	solute carrier family 6 (neurotransmitter transporter, gaba), member 1
SLC6A15	solute carrier family 6, member 15
SLC6A17	hypothetical protein loc284462
SLC6A4	solute carrier family 6 (neurotransmitter transporter, serotonin), member 4
SLC6A6	solute carrier family 6 (neurotransmitter transporter, taurine), member 6
SLC6A8	solute carrier family 6 (neurotransmitter transporter, creatine), member 8
SLC7A6	solute carrier family 7 (cationic amino acid transporter, y+ system), member 6
SLC9A1	solute carrier family 9 (sodium/hydrogen exchanger), member 1 (antiporter, na+/h+, amiloride sensitive)
SLC9A2	solute carrier family 9 (sodium/hydrogen exchanger), member 2
SLC9A3R2	solute carrier family 9 (sodium/hydrogen exchanger), member 3 regulator 2
SLC9A6	solute carrier family 9 (sodium/hydrogen exchanger), member 6
SLC05A1	solute carrier organic anion transporter family, member 5a1
SLIT2	slit homolog 2 (drosophila)
SLITRK1	slit and ntrk-like family, member 1
SLITRK3	slit and ntrk-like family, member 3
SLITRK6	slit and ntrk-like family, member 6
SLK	ste20-like kinase (yeast)
SLMAP	sarcolemma associated protein
SMAD2	smad, mothers against dpp homolog 2 (drosophila)
SMAD5	smad, mothers against dpp homolog 5 (drosophila)
SMAD6	smad, mothers against dpp homolog 6 (drosophila)
SMAD7	smad, mothers against dpp homolog 7 (drosophila)
SMARCA2	swi/snf related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 2
SMARCC1	swi/snf related, matrix associated, actin dependent regulator of chromatin, subfamily c, member 1
SMARCD1	swi/snf related, matrix associated, actin dependent regulator of chromatin, subfamily d, member 1
SMARCD2	swi/snf related, matrix associated, actin dependent regulator of chromatin, subfamily d, member 2
SMBP	sm-11044 binding protein
SMCX	smcy homolog, x-linked (mouse)
SMOC1	sparc related modular calcium binding 1
SMOC2	sparc related modular calcium binding 2
SMOX	spermine oxidase
SMPD3	sphingomyelin phosphodiesterase 3, neutral membrane (neutral sphingomyelinase ii)
SMURF1	smad specific e3 ubiquitin protein ligase 1
SMURF2	smad specific e3 ubiquitin protein ligase 2
SMYD5	smyd family member 5
SNAP91	synaptosomal-associated protein, 91kda homolog (mouse)
SNAPC1	small nuclear rna activating complex, polypeptide 1, 43kda
SNCB	synuclein, beta
SNF1LK	snf1-like kinase
SNF1LK2	snf1-like kinase 2
SNIP1	smad nuclear interacting protein 1
SNN	stannin
SNPH	syntaphilin
SNRK	snf related kinase
SNRPD1	small nuclear ribonucleoprotein d1 polypeptide 16kda
SNX16	sorting nexin 16
SNX17	sorting nexin 17
SNX2	sorting nexin 2
SNX25	sorting nexin 25
SNX27	sorting nexin family member 27
SNX4	sorting nexin 4
SOC51	suppressor of cytokine signaling 1
SOC53	suppressor of cytokine signaling 3
SOC55	suppressor of cytokine signaling 5
SOC56	suppressor of cytokine signaling 6
SOC57	suppressor of cytokine signaling 7
SOLH	small optic lobes homolog (drosophila)
SON	son dna binding protein
SORBS1	sorbin and sh3 domain containing 1
SORCS1	sortilin-related vps10 domain containing receptor 1
SORL1	sortilin-related receptor, l(dlr class) a repeats-containing
SOS2	son of sevenless homolog 2 (drosophila)
SOST	sclerosteosis
SOX11	sry (sex determining region y)-box 11
SOX21	sry (sex determining region y)-box 21
SOX3	sry (sex determining region y)-box 3
SOX4	sry (sex determining region y)-box 4
SOX5	sry (sex determining region y)-box 5
SOX9	sry (sex determining region y)-box 9 (campomelic dysplasia, autosomal sex-reversal)
SP1	sp1 transcription factor
SP192	
SP3	sp3 transcription factor
SP7	sp7 transcription factor
SP8	sp8 transcription factor
SPATA2	spermatogenesis associated 2
SPEN	spen homolog, transcriptional regulator (drosophila)
SPFH2	spfh domain family, member 2
SPG20	spastic paraplegia 20, spartin (troyer syndrome)
SPHK2	sphingosine kinase 2
SPIB	spi-b transcription factor (spi-1/pu.1 related)
SPIRE1	spire homolog 1 (drosophila)
SPN	sialophorin (gpl115, leukosialin, cd43)
SPOP	speckle-type poz protein
SPRED1	sprouty-related, evh1 domain containing 1
SPRED2	sprouty-related, evh1 domain containing 2
SPRY3	sprouty homolog 3 (drosophila)
SPRY4	sprouty homolog 4 (drosophila)

---

---

SPRYD3	spry domain containing 3
SPRYD4	spry domain containing 4
SPTBN2	spectrin, beta, non-erythrocytic 2
SPTBN4	spectrin, beta, non-erythrocytic 4
SPTLC1	serine palmitoyltransferase, long chain base subunit 1
SPTY2D1	spt2, suppressor of ty, domain containing 1 (s. cerevisiae)
SQSTM1	sequestosome 1
SREBF1	sterol regulatory element binding transcription factor 1
SRF	serum response factor (c-fos serum response element-binding transcription factor)
SRGAP3	slit-robo rho gtpase activating protein 3
SRP72	signal recognition particle 72kda
SRPK1	sfrs protein kinase 1
SRPK2	sfrs protein kinase 2
SRPR	signal recognition particle receptor ('docking protein')
SRR	serine racemase
SRRM1	serine/arginine repetitive matrix 1
SRRM2	serine/arginine repetitive matrix 2
SSI1L1	synovial sarcoma translocation gene on chromosome 18-like 1
SSBP3	single stranded dna binding protein 3
SSFA2	sperm specific antigen 2
SSH2	slingshot homolog 2 (drosophila)
SSR1	signal sequence receptor, alpha (translocon-associated protein alpha)
SSR3	signal sequence receptor, gamma (translocon-associated protein gamma)
SSTR1	somatostatin receptor 1
SSX2IP	kiaa0923 protein
ST3GAL5	st3 beta-galactoside alpha-2,3-sialyltransferase 5
ST3GAL6	st3 beta-galactoside alpha-2,3-sialyltransferase 6
ST6GALNAC3	st6 (alpha-n-acetyl-neuraminyl-2,3-beta-galactosyl-1,3)-n-acetylgalactosaminide alpha-2,6-sialyltransferase 3
ST8SIA2	st8 alpha-n-acetyl-neuraminide alpha-2,8-sialyltransferase 2
ST8SIA3	st8 alpha-n-acetyl-neuraminide alpha-2,8-sialyltransferase 3
ST8SIA4	st8 alpha-n-acetyl-neuraminide alpha-2,8-sialyltransferase 4
STAG2	stromal antigen 2
STAMBP1	stam binding protein-like 1
STAT3	signal transducer and activator of transcription 3 (acute-phase response factor)
STC1	stanniocalcin 1
STIM2	stromal interaction molecule 2
STK11IP	serine/threonine kinase 11 interacting protein
STK19	serine/threonine kinase 19
STK33	serine/threonine kinase 33
STK35	serine/threonine kinase 35
STK38	serine/threonine kinase 38
STK39	serine threonine kinase 39 (ste20/sps1 homolog, yeast)
STK4	serine/threonine kinase 4
STMN4	stathmin-like 4
STRN	striatin, calmodulin binding protein
STRN3	striatin, calmodulin binding protein 3
STX1A	syntaxin 1a (brain)
STX3A	syntaxin 3a
STX6	syntaxin 6
STXBP1	syntaxin binding protein 1
STXBP3	syntaxin binding protein 3
STYX	serine/threonine/tyrosine interacting protein
SUHW4	suppressor of hairy wing homolog 4 (drosophila)
SULF1	sulfatase 1
SUMF1	sulfatase modifying factor 1
SUMO4	smt3 suppressor of mif two 3 homolog 4 (yeast)
SUPT16H	suppressor of ty 16 homolog (s. cerevisiae)
SURF4	surfeit 4
SUV39H1	suppressor of variegation 3-9 homolog 1 (drosophila)
SUV420H1	suppressor of variegation 4-20 homolog 1 (drosophila)
SUZ12	suppressor of zeste 12 homolog (drosophila)
SV2A	synaptic vesicle glycoprotein 2a
SYAP1	hypothetical protein flj14495
SYBL1	synaptobrevin-like 1
SYDE1	synapse defective 1, rho gtpase, homolog 1 (c. elegans)
SYN1	synapsin i
SYN2	synapsin ii
SYNC1	syncoilin, intermediate filament 1
SYNE1	spectrin repeat containing, nuclear envelope 1
SYNGAP1	synaptic ras gtpase activating protein 1 homolog (rat)
SYNGR1	synaptogyrin 1
SYNJ1	synaptojanin 1
SYPL1	synaptophysin-like 1
SYPL2	synaptophysin-like 2
SYT1	synaptotagmin i
SYT11	synaptotagmin xi
SYT13	synaptotagmin xiii
SYT3	synaptotagmin iii
SYT7	synaptotagmin vii
SYT8	synaptotagmin viii
TAAR5	trace amine associated receptor 5
TAB3	tak1-binding protein 3
TAC1	tachykinin, precursor 1 (substance k, substance p, neurokinin 1, neurokinin 2, neuromedin 1, neurokinin alpha, neuropeptide k, neuropeptide gamma)
TACC2	transforming, acidic coiled-coil containing protein 2
TACSTD2	tumor-associated calcium signal transducer 2
TADA2L	transcriptional adaptor 2 (ada2 homolog, yeast)-like
TAI15	taf15 rna polymerase ii, tata box binding protein (tbp)-associated factor, 68kda
TAF4	taf4 rna polymerase ii, tata box binding protein (tbp)-associated factor, 135kda
TAF5	taf5 rna polymerase ii, tata box binding protein (tbp)-associated factor, 100kda
TAIP-2	tgf-beta induced apoptosis protein 2
TA-KRP	

---

---

TAL1	t-cell acute lymphocytic leukemia 1
TANC1	tetratricopeptide repeat, ankyrin repeat and coiled-coil containing 1
TAOK1	tao kinase 1
TAOK2	tao kinase 2
TAOK3	tao kinase 3
TA-PP2C	
TARDBP	tar dna binding protein
TAX1BP1	tax1 (human t-cell leukemia virus type i) binding protein 1
TBC1D10B	tbc1 domain family, member 10b
TBC1D15	tbc1 domain family, member 15
TBC1D20	tbc1 domain family, member 20
TBC1D8	tbc1 domain family, member 8 (with gram domain)
TBK1	tank-binding kinase 1
TBL1X	transducin (beta)-like 1x-linked
TBL1XR1	transducin (beta)-like 1x-linked receptor 1
TBP	tata box binding protein
TBPL1	tbpl-like 1
TBX15	t-box 15
TBX2	t-box 2
TBX3	t-box 3 (ulnar mammary syndrome)
TCEAL8	transcription elongation factor a (sii)-like 8
TCEB3	transcription elongation factor b (siii), polypeptide 3 (110kda, elongin a)
TCERG1	transcription elongation regulator 1
TCERGL1	transcription elongation regulator 1-like
TCF2	transcription factor 2, hepatic; lf-b3; variant hepatic nuclear factor
TCF20	transcription factor 20 (ar1)
TCF21	transcription factor 21
TCF4	transcription factor 4
TCFL5	transcription factor-like 5 (basic helix-loop-helix)
TCTEXID1	tcex1 domain containing 1
TEAD1	tea domain family member 1 (sv40 transcriptional enhancer factor)
TEF	thyrotrophic embryonic factor
TERF2	telomeric repeat binding factor 2
Term of Service   Contact Us   Site Map	
TESK2	testis-specific kinase 2
TEX14	testis expressed sequence 14
TFAP2D	transcription factor ap-2 delta (activating enhancer binding protein 2 delta)
TFAP4	transcription factor ap-4 (activating enhancer binding protein 4)
TFCP2L2	
TFCP2L3	
TFDP2	transcription factor dp-2 (e2f dimerization partner 2)
TFE3	transcription factor binding to ighm enhancer 3
TGFBR3	transforming growth factor, beta receptor iii (betaglycan, 300kda)
TGIF	tgfb-induced factor (tale family homeobox)
TGIF2	hypothetical protein loc57163
TGM3	transglutaminase 3 (e polypeptide, protein-glutamine-gamma-glutamyltransferase)
TCOLN2	trans-golgi network protein 2
THBS3	thrombospondin 3
THOC4	tho complex 4
THRA	thyroid hormone receptor, alpha (erythroblastic leukemia viral (v-erb-a) oncogene homolog, avian)
THRAP2	thyroid hormone receptor associated protein 2
THSD2	
THTPA	thiamine triphosphatase
TIA1	tia1 cytotoxic granule-associated rna binding protein
TIAF1	tgfb1-induced anti-apoptotic factor 1
TIAL1	tia1 cytotoxic granule-associated rna binding protein-like 1
TIAM1	t-cell lymphoma invasion and metastasis 1
TIMP2	timp metalloproteinase inhibitor 2
TIMP3	timp metalloproteinase inhibitor 3 (sorsby fundus dystrophy, pseudoinflammatory)
TIPARP	tcdd-inducible poly(adp-ribose) polymerase
TJP1	tight junction protein 1 (zona occludens 1)
TLE4	transducin-like enhancer of split 4 (esp1) homolog, drosophila)
TLK1	tousled-like kinase 1
TLL1	tolloid-like 1
TLN2	talin 2
TLX3	t-cell leukemia homeobox 3
TM4SF10	
TM6SF1	transmembrane 6 superfamily member 1
TM7SF1	
TMCC1	transmembrane and coiled-coil domain family 1
TMCC3	transmembrane and coiled-coil domain family 3
TMED10	transmembrane emp24-like trafficking protein 10 (yeast)
TMED8	transmembrane emp24 protein transport domain containing 8
TMEM127	transmembrane protein 127
TMEM131	transmembrane protein 131
TMEM15	transmembrane protein 15
TMEM16A	transmembrane protein 16a
TMEM16C	transmembrane protein 16c
TMEM16D	transmembrane protein 16d
TMEM16F	transmembrane protein 16f
TMEM23	transmembrane protein 23
TMEM25	transmembrane protein 25
TMEM28	transmembrane protein 28
TMEM32	transmembrane protein 32
TMEM33	transmembrane protein 33
TMEM47	transmembrane protein 47
TMEM49	transmembrane protein 49
TMEM50B	transmembrane protein 50b
TMEM55A	transmembrane protein 55a
TMEM55B	transmembrane protein 55b
TMEM56	transmembrane protein 56

---

---

TMEM64	transmembrane protein 64
TMEM68	transmembrane protein 68
TMEM87A	transmembrane protein 87a
TMEM87B	transmembrane protein 87b
TMEPA1	transmembrane, prostate androgen induced rna
TMTC2	transmembrane and tetra-trico-peptide repeat containing 2
TNFAIP1	tumor necrosis factor, alpha-induced protein 1 (endothelial)
TNFAIP3	tumor necrosis factor, alpha-induced protein 3
TNFAIP8L3	tumor necrosis factor, alpha-induced protein 8-like 3
TNFRSF12A	tumor necrosis factor receptor superfamily, member 12a
TNFRSF21	tumor necrosis factor receptor superfamily, member 21
TNFSF11	tumor necrosis factor (ligand) superfamily, member 11
TNFSF7	tumor necrosis factor (ligand) superfamily, member 7
TNIP1	tnfaip3 interacting protein 1
TNKS1BP1	tankyrase 1 binding protein 1, 182kda
TNKS2	tankyrase, trf1-interacting ankyrin-related adp-ribose polymerase 2
TNPO2	transportin 2 (importin 3, karyopherin beta 2b)
TNRC6A	trinucleotide repeat containing 6a
TNRC6C	hypothetical protein flj20015
TNRC9	trinucleotide repeat containing 9
TOB1	transducer of erbb2, 1
TOB2	transducer of erbb2, 2
TOE1	hypothetical protein flj13949
TOP1	topoisomerase (dna) i
TOPORS	topoisomerase i binding, arginine/serine-rich
TOR1B	torsin family 1, member b (torsin b)
TOX	thymus high mobility group box protein tox
TP53INP1	tumor protein p53 inducible nuclear protein 1
TP53INP2	tumor protein p53 inducible nuclear protein 2
TP73L	tumor protein p73-like
TPCN1	two pore segment channel 1
TPP1	tripeptidyl peptidase i
TRAF3	tnf receptor-associated factor 3
TRAF7	tnf receptor-associated factor 7
TRAK2	trafficking protein, kinesin binding 2
TRAM1	translocation associated membrane protein 1
TRAM2	translocation associated membrane protein 2
TRHDE	thyrotropin-releasing hormone degrading enzyme
TRIB2	tribbles homolog 2 (drosophila)
TRIM2	tripartite motif-containing 2
TRIM3	tripartite motif-containing 3
TRIM33	kiaa1113 protein
TRIM36	tripartite motif-containing 36
TRIM9	tripartite motif-containing 9
TRIO	triple functional domain (pltrf interacting)
TRIP10	thyroid hormone receptor interactor 10
TRIP11	thyroid hormone receptor interactor 11
TRPS1	trichorhinophalangeal syndrome i
TRPV6	alu-binding protein with zinc finger domain
TSC1	tuberous sclerosis 1
TSC22D1	tsc22 domain family, member 1
TSC22D2	tsc22 domain family, member 2
TSC22D3	tsc22 domain family, member 3
TSG101	tumor susceptibility gene 101
TSGA14	testis specific, 14
TPAN12	tetraspanin 12
TPAN13	tetraspanin 13
TSPYL2	tspy-like 2
TSSK2	testis-specific serine kinase 2
TSSK6	testis-specific serine kinase 6
TTC13	tetratricopeptide repeat domain 13
TTC21B	tetratricopeptide repeat domain 21b
TTN	titin
TTYH3	tweetie homolog 3 (drosophila)
TUB	tubby homolog (mouse)
TUBA1	tubulin, alpha 1 (testis specific)
TUBA3	tubulin, alpha 3
TUBB2B	tubulin, beta 2b
TULP4	tubby like protein 4
TUSC2	tumor suppressor candidate 2
TWIST1	twist homolog 1 (acrocephalosyndactyly 3; saethre-hotzen syndrome) (drosophila)
TXNDC	thioredoxin domain containing
TXNDC12	thioredoxin domain containing 12 (endoplasmic reticulum)
TXNIP	thioredoxin interacting protein
U2AF1L2	u2(rnu2) small nuclear rna auxiliary factor 1-like 2
U2AF2	u2 (rnu2) small nuclear rna auxiliary factor 2
UBE2A	ubiquitin-conjugating enzyme e2a (rad6 homolog)
UBE2B	ubiquitin-conjugating enzyme e2b (rad6 homolog)
UBE2D1	ubiquitin-conjugating enzyme e2d 1 (ubc4/5 homolog, yeast)
UBE2D2	ubiquitin-conjugating enzyme e2d 2 (ubc4/5 homolog, yeast)
UBE2D3	ubiquitin-conjugating enzyme e2d 3 (ubc4/5 homolog, yeast)
UBE2E2	ubiquitin-conjugating enzyme e2e 2 (ubc4/5 homolog, yeast)
UBE2E3	ubiquitin-conjugating enzyme e2e 3 (ubc4/5 homolog, yeast)
UBE2F	ubiquitin-conjugating enzyme e2f (putative)
UBE2G1	ubiquitin-conjugating enzyme e2g 1 (ubc7 homolog, yeast)
UBE2H	ubiquitin-conjugating enzyme e2h (ubc8 homolog, yeast)
UBE2J1	ubiquitin-conjugating enzyme e2, j1 (ubc6 homolog, yeast)
UBE2O	ubiquitin-conjugating enzyme e2o
UBE2Q2	ubiquitin-conjugating enzyme e2q (putative) 2
UBE2R2	ubiquitin-conjugating enzyme e2r 2
UBE2V2	ubiquitin-conjugating enzyme e2 variant 2

---

---

UBE2W	ubiquitin-conjugating enzyme e2w (putative)
UBE2Z	ubiquitin-conjugating enzyme e2z (putative)
UBE3A	ubiquitin protein ligase e3a (human papilloma virus e6-associated protein, angelman syndrome)
UBE3C	ubiquitin protein ligase e3c
UBE4B	ubiquitination factor e4b (ufd2 homolog, yeast)
UBL3	ubiquitin-like 3
UBLCP1	ubiquitin-like domain containing ctd phosphatase 1
UBPH	ubiquitin-binding protein homolog
UBQLN2	ubiquilin 2
UBTD1	ubiquitin domain containing 1
UBXD3	ubx domain containing 3
UBXD7	ubx domain containing 7
UCN3	urocortin 3 (stresscopin)
UCP3	uncoupling protein 3 (mitochondrial, proton carrier)
UGCGL1	udp-glucose ceramide glucosyltransferase-like 1
UGP2	udp-glucose pyrophosphorylase 2
UHMK1	u2af homology motif (uhm) kinase 1
UHRF2	ubiquitin-like, containing phd and ring finger domains, 2
ULK1	unc-51-like kinase 1 (c. elegans)
ULK3	unc-51-like kinase 3 (c. elegans)
UMP-CMPK	
UNC13C	unc-13 homolog c (c. elegans)
UNC84A	unc-84 homolog a (c. elegans)
USF2	upstream transcription factor 2, c-fos interacting
USP14	ubiquitin specific peptidase 14 (trna-guanine transglycosylase)
USP15	ubiquitin specific peptidase 15
USP2	ubiquitin specific peptidase 2
USP21	ubiquitin specific peptidase 21
USP25	ubiquitin specific peptidase 25
USP28	ubiquitin specific peptidase 28
USP3	ubiquitin specific peptidase 3
USP31	ubiquitin specific peptidase 31
USP32	ubiquitin specific peptidase 32
USP33	ubiquitin specific peptidase 33
USP34	ubiquitin specific peptidase 34
USP44	ubiquitin specific peptidase 44
USP46	ubiquitin specific peptidase 46
USP6	hyperpolymorphic gene 1
UTX	ubiquitously transcribed tetratricopeptide repeat, x chromosome
UTY	ubiquitously transcribed tetratricopeptide repeat gene, y-linked
VAMP1	vesicle-associated membrane protein 1 (synaptobrevin 1)
VAMP2	vesicle-associated membrane protein 2 (synaptobrevin 2)
VAMP3	vesicle-associated membrane protein 3 (cellubrevin)
VAMP8	vesicle-associated membrane protein 8 (endobrevin)
VANGL1	hypothetical protein mgc5338
VASP	vasodilator-stimulated phosphoprotein
VAT1	vesicle amine transport protein 1 homolog (t. californica)
VAV2	vav 2 oncogene
VAV3	vav 3 oncogene
VCL	vinculin
VCPIP1	valosin containing protein (p97)/p47 complex interacting protein 1
VGLL4	vestigial like 4 (drosophila)
VLDLR	very low density lipoprotein receptor
VPS26A	vacuolar protein sorting 26 homolog a (yeast)
VPS37A	vacuolar protein sorting 37a (yeast)
VPS37B	vacuolar protein sorting 37b (yeast)
VPS37C	vacuolar protein sorting 37c (yeast)
VPS4A	vacuolar protein sorting 4a (yeast)
VPS4B	vacuolar protein sorting 4b (yeast)
VPS54	vacuolar protein sorting 54 (yeast)
VSNL1	visinin-like 1
VSN1	visual system homeobox 1 homolog, chx10-like (zebrafish)
VTIB	vesicle transport through interaction with t-snares homolog 1b (yeast)
WAC	ww domain containing adaptor with coiled-coil
WASL	wiskott-aldrich syndrome-like
WBP11	ww domain binding protein 11
WBP2	ww domain binding protein 2
WBSCR1	williams-beuren syndrome chromosome region 1
WBSCR18	williams beuren syndrome chromosome region 18
WDFY3	wd repeat and fyve domain containing 3
WDR1	wd repeat domain 1
WDR20	wd repeat domain 20
WDR22	wd repeat domain 22
WDR26	wd repeat domain 26
WDR37	wd repeat domain 37
WDR42A	wd repeat domain 42a
WDR43	wd repeat domain 43
WDR44	wd repeat domain 44
WDR45L	wdr45-like
WDR47	wd repeat domain 47
WDR48	wd repeat domain 48
WDR9	
WDTC1	wd and tetratricopeptide repeats 1
WEE1	wee1 homolog (s. pombe)
WIBG	within bgcn homolog (drosophila)
WIF1	wnt inhibitory factor 1
WIPI-2	
WIRE	wire protein
WISP1	wnt1 inducible signaling pathway protein 1
WNK3	kiaa1566 protein
WNT2B	wingless-type mmtv integration site family, member 2b

---

---

WNT3	wingless-type mmtv integration site family, member 3
WNT3A	wingless-type mmtv integration site family, member 3a
WNT5A	wingless-type mmtv integration site family, member 5a
WNT7A	wingless-type mmtv integration site family, member 7a
WRNIP1	werner helicase interacting protein 1
WSB1	wd repeat and socs box-containing 1
WT1	wilms tumor 1
WWC1	ww, c2 and coiled-coil domain containing 1
WWP1	ww domain containing e3 ubiquitin protein ligase 1
WWP2	ww domain containing e3 ubiquitin protein ligase 2
XAB1	xpa binding protein 1, gtpase
XPO4	exportin 4
XPRI	xenotropic and polytropic retrovirus receptor
XRN1	5'-3' exoribonuclease 1
XRN2	5'-3' exoribonuclease 2
XTP7	protein 7 transactivated by hepatitis b virus x antigen (hbxag)
XYLT2	xylosyltransferase ii
YEATS4	yeats domain containing 4
YES1	v-yes-1 yamaguchi sarcoma viral oncogene homolog 1
YIPF4	yip1 domain family, member 4
YPEL4	yippee-like 4 (drosophila)
YPEL5	yippee-like 5 (drosophila)
YTHDF2	yth domain family, member 2
YTHDF3	yth domain family, member 3
YWHA8	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, beta polypeptide
YWHA8	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon polypeptide
YWHAH	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, eta polypeptide
YWHAQ	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, theta polypeptide
YWHAZ	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, zeta polypeptide
YY1	yy1 transcription factor
ZA20D2	zinc finger, a20 domain containing 2
ZA20D3	zinc finger, a20 domain containing 3
ZAK	sterile alpha motif and leucine zipper containing kinase azk
ZBTB10	zinc finger and btb domain containing 10
ZBTB11	zinc finger and btb domain containing 11
ZBTB4	zinc finger and btb domain containing 4
ZBTB7A	zinc finger and btb domain containing 7a
ZBTB9	zinc finger and btb domain containing 9
ZC3H12C	zinc finger cchc-type containing 12c
ZC3H5	zinc finger cchc-type containing 5
ZC3HDC1	
ZC3HDC6	
ZCCHC2	zinc finger, cchc domain containing 2
ZCCHC3	zinc finger, cchc domain containing 3
ZCCHC5	zinc finger, cchc domain containing 5
ZDHC1	zinc finger, dhhc-type containing 1
ZDHC17	zinc finger, dhhc-type containing 17
ZDHC18	zinc finger, dhhc-type containing 18
ZDHC2	zinc finger, dhhc-type containing 2
ZDHC21	zinc finger, dhhc-type containing 21
ZDHC23	zinc finger, dhhc-type containing 23
ZDHC3	zinc finger, dhhc-type containing 3
ZDHC5	zinc finger, dhhc-type containing 5
ZDHC7	zinc finger, dhhc-type containing 7
ZDHC9	zinc finger, dhhc-type containing 9
ZF	hcf-binding transcription factor zhangfei
ZFAND3	zinc finger, an1-type domain 3
ZFHX1B	zinc finger homeobox 1b
ZFHX4	zinc finger homeodomain 4
ZFP36L1	zinc finger protein 36, c3h type-like 1
ZFP36L2	zinc finger protein 36, c3h type-like 2
ZFP91	zinc finger protein 91 homolog (mouse)
ZFPM2	zinc finger protein, multitype 2
ZFYVE21	zinc finger, fyve domain containing 21
ZFYVE26	zinc finger, fyve domain containing 26
ZFYVE9	zinc finger, fyve domain containing 9
ZHX1	zinc fingers and homeoboxes 1
ZHX2	zinc fingers and homeoboxes 2
ZHX3	zinc fingers and homeoboxes 3
ZIC1	zic family member 1 (odd-paired homolog, drosophila)
ZIC4	zic family member 4
ZIC5	zic family member 5 (odd-paired homolog, drosophila)
ZKSCAN1	zinc finger with krab and scan domains 1
ZMYND11	zinc finger, mynd domain containing 11
ZNF148	zinc finger protein 148 (phz-52)
ZNF161	zinc finger protein 161
ZNF198	zinc finger protein 198
ZNF217	zinc finger protein 217
ZNF236	zinc finger protein 236
ZNF238	zinc finger protein 238
ZNF265	zinc finger protein 265
ZNF275	zinc finger protein 275
ZNF287	zinc finger protein 287
ZNF289	zinc finger protein 289, id1 regulated
ZNF3	zinc finger protein 3 (a8-51)
ZNF318	zinc finger protein 318
ZNF319	zinc finger protein 319
ZNF367	zinc finger protein 367
ZNF385	zinc finger protein 385
ZNF423	zinc finger protein 423
ZNF436	zinc finger protein 436

---



---

ZNF482	zinc finger protein 482
ZNF516	zinc finger protein 516
ZNF518	zinc finger protein 518
ZNF532	zinc finger protein 532
ZNF533	zinc finger protein 533
ZNF597	zinc finger protein 597
ZNF608	dkfzp434m098 protein
ZNF622	zinc finger protein 622
ZNF644	hypothetical protein bm-005
ZNF650	zinc finger protein 650
ZNF651	zinc finger protein 651
ZNF652	zinc finger protein 652
ZNF654	zinc finger protein 654
ZNF9	zinc finger protein 9 (a cellular retroviral nucleic acid binding protein)
ZNFN1A1	zinc finger protein, subfamily 1a, 1 (ikaros)
ZNFN1A2	zinc finger protein, subfamily 1a, 2 (helios)
ZNFN1A4	zinc finger protein, subfamily 1a, 4 (eos)
ZNFX1	zinc finger, nfx1-type containing 1
ZSWIM3	zinc finger, swim-type containing 3
ZSWIM6	zinc finger, swim-type containing 6
ZYG11BL	zyg-11 homolog b (c. elegans)-like
ZYX	zyxin
ZZZ3	zinc finger, zz-type containing 3

**Supplementary Table 4: Genes showing altered expression due to differentiation by Illumina microarray analysis**

Gene Symbol	Gene Name
15E1.2	hypothetical protein loc283459
2'-PDE	2'-phosphodiesterase
AACS	acetoacetyl-coa synthetase
AAMP	angio-associated, migratory cell protein
AARSD1	alanyl-trna synthetase domain containing 1
AASDHPPT	dkfzp566e2346 protein
AATF	apoptosis antagonizing transcription factor
ABAT	4-aminobutyrate aminotransferase
ABCA3	atp-binding cassette, sub-family a (abc1), member 3
ABCB7	atp-binding cassette, sub-family b (mdr/tap), member 7
ABCC1	atp-binding cassette, sub-family c (cfr/mrp), member 1
ABCC5	atp-binding cassette, sub-family c (cfr/mrp), member 5
ABCD3	atp-binding cassette, sub-family d (ald), member 3
ABCE1	atp-binding cassette, sub-family e (oabp), member 1
ABCF2	atp-binding cassette, sub-family f (gc20), member 2
ABCG1	atp-binding cassette, sub-family g (white), member 1
ABHD10	abhydrolase domain containing 10
ABHD14B	abhydrolase domain containing 14b
ABHD5	abhydrolase domain containing 5
ABI2	abl interactor 2
ABLIM1	actin binding lim protein 1
ACAA2	acetyl-coenzyme a acyltransferase 2 (mitochondrial 3-oxoacyl-coenzyme a thiolase)
ACAD9	acyl-coenzyme a dehydrogenase family, member 9
ACAT1	acetyl-coenzyme a acetyltransferase 1 (acetoacetyl coenzyme a thiolase)
ACAT2	acetyl-coenzyme a acetyltransferase 2 (acetoacetyl coenzyme a thiolase)
ACBD6	acyl-coenzyme a binding domain containing 6
ACN9	acn9 homolog (s. cerevisiae)
ACO2	aconitase 2, mitochondrial
ACOT11	acyl-coa thioesterase 11
ACOT2	acyl-coa thioesterase 2
ACOT9	acyl-coa thioesterase 9
ACOX1	acyl-coenzyme a oxidase 1, palmitoyl
ACPI	acid phosphatase 1, soluble
ACP6	acid phosphatase 6, lysophosphatidic
ACSL1	fatty-acid-coenzyme a ligase, long-chain 1
ACTA2, ACTG2	actin, alpha 2, smooth muscle, aorta
ACTB, ACTG1	actin, beta
ACTL6A	actin-like 6a
ACTR3	arp3 actin-related protein 3 homolog (yeast)
ACTR3B	arp3 actin-related protein 3 homolog b (yeast)
ACTR5	arp5 actin-related protein 5 homolog (yeast)
ACVR1	activin a receptor, type i
ACY1	aminoacylase 1
ADA	adenosine deaminase
ADAM12	adam metalloproteinase domain 12 (meltrin alpha)
ADAM22	mdc2
ADAM23	adam metalloproteinase domain 23
ADAMTS3	adam metalloproteinase with thrombospondin type 1 motif, 3
ADAMTS4	adam metalloproteinase with thrombospondin type 1 motif, 4
ADAMTSL2	adamts-like 2
ADCY1	adenylate cyclase 1 (brain)
ADCY9	adenylate cyclase 9
ADFP	adipose differentiation-related protein
ADI1	acireductone dioxygenase 1
ADK	adenosine kinase
ADM	adrenomedullin
ADORA2B	adenosine a2b receptor
ADPRHL1	adp-ribosylhydrolase like 1
ADSL	adenylosuccinate lyase
ADSS	adenylosuccinate synthase
AFAP	actin filament associated protein
AFG3L2	afg3 atpase family gene 3-like 2 (yeast)
AFMID	arylfornamidase
AGPAT2	1-acylglycerol-3-phosphate o-acyltransferase 2 (lysophosphatidic acid acyltransferase, beta)
AGPAT3	1-acylglycerol-3-phosphate o-acyltransferase 3
AGPS	alkylglycerone phosphate synthase
AGTR1	angiotensin ii receptor, type 1
AGTRAP	angiotensin ii receptor-associated protein
AHCY	s-adenosylhomocysteine hydrolase
AHSA1	aha1, activator of heat shock 90kda protein atpase homolog 1 (yeast)
AK1	adenylate kinase 1
AK2	adenylate kinase 2
AK5	adenylate kinase 5
AKAP1	a kinase (prka) anchor protein 1
AKAP12	a kinase (prka) anchor protein (gravin) 12
AKNA	at-hook transcription factor
AKR1B1	aldo-keto reductase family 1, member b1 (aldose reductase)
AKR1C3	aldo-keto reductase family 1, member c3 (3-alpha hydroxysteroid dehydrogenase, type ii)
AKR7A2	aldo-keto reductase family 7, member a2 (aflatoxin aldehyde reductase)
AKT1S1	akt1 substrate 1 (proline-rich)
ALDH1A3	aldehyde dehydrogenase 1 family, member a3
ALDH1B1	aldehyde dehydrogenase 1 family, member b1
ALDH4A1	aldehyde dehydrogenase 4 family, member a1
ALDH9A1	aldehyde dehydrogenase 9 family, member a1

ALDOA	aldolase a, fructose-bisphosphate
ALDOC	aldolase c, fructose-bisphosphate
ALG1	asparagine-linked glycosylation 1 homolog (yeast, beta-1,4-mannosyltransferase)
ALG14	asparagine-linked glycosylation 14 homolog (yeast)
ALG3	asparagine-linked glycosylation 3 homolog (yeast, alpha-1,3-mannosyltransferase)
ALG5	asparagine-linked glycosylation 5 homolog (yeast, dolichyl-phosphate beta-glucosyltransferase)
ALG8	asparagine-linked glycosylation 8 homolog (yeast, alpha-1,3-glucosyltransferase)
ALG9	asparagine-linked glycosylation 9 homolog (yeast, alpha-1,2-mannosyltransferase)
ALKBH2	alkb, alkylation repair homolog 2 (e. coli)
ALKBH3	alkb, alkylation repair homolog 3 (e. coli)
ALPL	alkaline phosphatase, liver/bone/kidney
ALS2CR2	amyotrophic lateral sclerosis 2 (juvenile) chromosome region, candidate 2
ALS2CR4	amyotrophic lateral sclerosis 2 (juvenile) chromosome region, candidate 4
AMD1	adenosylmethionine decarboxylase 1
AMMECR1	alport syndrome, mental retardation, midface hypoplasia and elliptocytosis chromosomal region, gene 1
AMY1B, AMY1C	amylase, alpha 1a; salivary
ANAPC1	anaphase promoting complex subunit 1
ANAPC11	apc11 anaphase promoting complex subunit 11 homolog (yeast)
ANAPC5	anaphase promoting complex subunit 5
ANAPC7	anaphase promoting complex subunit 7
ANGPTL2	angiopoietin-like 2
ANKRD13B	ankyrin repeat domain 13b
ANKRD16	ankyrin repeat domain 16
ANKRD39	ankyrin repeat domain 39
ANKRD40	ankyrin repeat domain 40
ANKRD41	ankyrin repeat domain 41
ANLN	anillin, actin binding protein (scraps homolog, drosophila)
ANP32A	acidic (leucine-rich) nuclear phosphoprotein 32 family, member a
ANP32B	acidic (leucine-rich) nuclear phosphoprotein 32 family, member b
ANP32C	acidic (leucine-rich) nuclear phosphoprotein 32 family, member c
ANTXR1	hypothetical protein flj10601
ANXA11	annexin a11
ANXA5	annexin a5
AOF1	amine oxidase (flavin containing) domain 1
AOF2	amine oxidase (flavin containing) domain 2
API51	adaptor-related protein complex 1, sigma 1 subunit
AP4B1	adaptor-related protein complex 4, beta 1 subunit
APEX2	apex nuclease (apurinic/apyrimidinic endonuclease) 2
APITD1	cortistatin
APP	amyloid beta (a4) precursor protein (peptidase nexin-ii, alzheimer disease)
APPBP1	amyloid beta precursor protein binding protein 1
APRT	adenine phosphoribosyltransferase
APS	adaptor protein with pleckstrin homology and src homology 2 domains
ARAF	v-raf murine sarcoma 3611 viral oncogene homolog
ARC	activity-regulated cytoskeleton-associated protein
ARFIP1	adp-ribosylation factor interacting protein 1 (arfaptin 1)
ARG2	arginase, type ii
ARHGAP11A	rho gtpase activating protein 11a
ARHGAP19	rho gtpase activating protein 19
ARHGAP22	rho gtpase activating protein 22
ARHGEF1	rho guanine nucleotide exchange factor (gef) 1
ARID5B	at rich interactive domain 5b (mrfl-like)
ARL5B	adp-ribosylation factor-like 5b
ARL6	adp-ribosylation factor-like 6
ARL6IP2	adp-ribosylation factor-like 6 interacting protein 2
ARL6IP4	adp-ribosylation-like factor 6 interacting protein 4
ARMC6	armadillo repeat containing 6
ARMCX5	armadillo repeat containing, x-linked 5
ARNTL	aryl hydrocarbon receptor nuclear translocator-like
ARRB1	arrestin, beta 1
ARSB	arylsulfatase b
AS3MT, C10orf32	arsenic (+3 oxidation state) methyltransferase
ASAM	adipocyte-specific adhesion molecule
ASB3	ankyrin repeat and socs box-containing 3
ASB9	dkfzp564l0862 protein
ASCC2	hypothetical protein dkfzp586o0223
ASCC3	activating signal cointegrator 1 complex subunit 3
ASCL1	achaete-scute complex-like 1 (drosophila)
ASF1A	asf1 anti-silencing function 1 homolog a (s. cerevisiae)
ASF1B	asf1 anti-silencing function 1 homolog b (s. cerevisiae)
ASNSD1	asparagine synthetase domain containing 1
ASTN2	astrotactin 2
ATAD2	atpase family, aaa domain containing 2
ATAD3A	atpase family, aaa domain containing 3a
ATF1	activating transcription factor 1
ATF6	activating transcription factor 6
ATG3	atg3 autophagy related 3 homolog (s. cerevisiae)
ATG4C	atg4 autophagy related 4 homolog c (s. cerevisiae)
ATG7	atg7 autophagy related 7 homolog (s. cerevisiae)
ATIC	5-aminoimidazole-4-carboxamide ribonucleotide formyltransferase/imp cyclohydrolase
ATP11C	atpase, class vi, type 11c
ATP1A1	atpase, na+/k+ transporting, alpha 1 polypeptide
ATP1A3	atpase, na+/k+ transporting, alpha 3 polypeptide
ATP1B3	atpase, na+/k+ transporting, beta 3 polypeptide
ATP2A2	atpase, ca++ transporting, cardiac muscle, slow twitch 2
ATP5C1	atp synthase, h+ transporting, mitochondrial f1 complex, gamma polypeptide 1
ATP5F1	atp synthase, h+ transporting, mitochondrial f0 complex, subunit b1
ATP5G1	atp synthase, h+ transporting, mitochondrial f0 complex, subunit c1 (subunit 9)
ATP5G2	atp synthase, h+ transporting, mitochondrial f0 complex, subunit c2 (subunit 9)
ATP5G3	atp synthase, h+ transporting, mitochondrial f0 complex, subunit c3 (subunit 9)
ATP5J	atp synthase, h+ transporting, mitochondrial f0 complex, subunit f6

---

ATP5J2	atp synthase, h <sup>+</sup> transporting, mitochondrial f0 complex, subunit f2
ATP5S	atp synthase, h <sup>+</sup> transporting, mitochondrial f0 complex, subunit s (factor b)
ATP6V0A2	atpase, h <sup>+</sup> transporting, lysosomal v0 subunit a2
ATP6V1F	atpase, h <sup>+</sup> transporting, lysosomal 14kda, v1 subunit f
ATPAF2	atp synthase mitochondrial f1 complex assembly factor 2
ATPIF1	atpase inhibitor precursor
ATXN7L2	ataxin 7-like 2
AURKAIP1	aurora kinase a interacting protein 1
AURKB	aurora kinase b
AVEN	apoptosis, caspase activation inhibitor
B3GALNT2	udp-galnac:betaglcnac beta 1,3-galactosaminyltransferase, polypeptide 2
B3GAT1	beta-1,3-glucuronyltransferase 1 (glucuronosyltransferase p)
B3GNTL1	udp-glcnac:betagal beta-1,3-n-acetylglucosaminyltransferase-like 1
BAG3	bcl2-associated athanogene 3
BAIAP2	bai1-associated protein 2
BAIAP2L1	bai1-associated protein 2-like 1
BAK1	bcl2-antagonist/killer 1
BAMBI	bmp and activin membrane-bound inhibitor homolog (xenopus laevis)
BANF1	barrier to autointegration factor 1
BAT4	hla-b associated transcript 4
BAX	bcl2-associated x protein
BAZ1A	bromodomain adjacent to zinc finger domain, 1a
BCAT2	branched chain aminotransferase 2, mitochondrial
BCCIP	cdk inhibitor p21 binding protein
BCDIN3	bin3, bicoid-interacting 3, homolog (drosophila)
BCKDHA	branched chain keto acid dehydrogenase e1, alpha polypeptide
BCKDHB	branched chain keto acid dehydrogenase e1, beta polypeptide (maple syrup urine disease)
BCL11A	b-cell cl/lymphoma 11a (zinc finger protein)
BCL2	b-cell cl/lymphoma 2
BCL2L12	bcl2-like 12 (proline rich)
BCL2L13	bcl2-like 13 (apoptosis facilitator)
BCL9	b-cell cl/lymphoma 9
BCR	breakpoint cluster region
BCS1L	bcs1-like (yeast)
BET1	bet1 homolog (s. cerevisiae)
BID	bh3 interacting domain death agonist
BIRC5	baculoviral iap repeat-containing 5 (survivin)
BLCAP	bladder cancer associated protein
BLM	bloom syndrome
BLVRA	biliverdin reductase a
BMP2	bone morphogenetic protein 2
BMP2K	bmp2 inducible kinase
BNIP1	bcl2/adenovirus e1b 19kda interacting protein 1
BNIP2	bcl2/adenovirus e1b 19kda interacting protein 2
BOC	boc homolog (mouse)
BOLA1	bola-like 1 (e. coli)
BOLA2	bola-like 2 (e. coli)
BOLA3	bola-like 3 (e. coli)
BOP1	block of proliferation 1
BPNT1	3'(2'), 5'-bisphosphate nucleotidase 1
BRE	brain and reproductive organ-expressed (tnfrsf1a modulator)
BRMS1	breast cancer metastasis suppressor 1
BRP44L	brain protein 44-like
BSG	basigin (ok blood group)
BTBD1	btb (poz) domain containing 1
BTBD15	btb (poz) domain containing 15
BTBD6	btb (poz) domain containing 6
BTF3	basic transcription factor 3
BTN3A2	butyrophilin, subfamily 3, member a2
BUB1	bub1 budding uninhibited by benzimidazoles 1 homolog (yeast)
BUB1B	bub1 budding uninhibited by benzimidazoles 1 homolog beta (yeast)
BUB3	bub3 budding uninhibited by benzimidazoles 3 homolog (yeast)
BXDC1	brix domain containing 1
BXDC2	brix domain containing 2
BXDC5	brix domain containing 5
BYSL	bystin-like
BZRP	benzodiazapine receptor (peripheral)
BZW2	basic leucine zipper and w2 domains 2
C10orf114	chromosome 10 open reading frame 114
C10orf119	chromosome 10 open reading frame 119
C10orf125	chromosome 10 open reading frame 125
C10orf42	hypothetical protein flj21463
C10orf57	chromosome 10 open reading frame 57
C10orf59	chromosome 10 open reading frame 59
C10orf7	chromosome 10 open reading frame 7
C10orf70	chromosome 10 open reading frame 70
C10orf78	chromosome 10 open reading frame 78
C11orf31	chromosome 11 open reading frame 31
C11orf51	chromosome 11 open reading frame 51
C12orf10	chromosome 12 open reading frame 10
C12orf11	hypothetical protein flj10630
C12orf24	chromosome 12 open reading frame 24
C12orf29	chromosome 12 open reading frame 29
C12orf30	chromosome 12 open reading frame 30
C12orf31	chromosome 12 open reading frame 31
C12orf32	chromosome 12 open reading frame 32
C12orf34	chromosome 12 open reading frame 34
C12orf41	chromosome 12 open reading frame 41
C12orf43	chromosome 12 open reading frame 43
C12orf44	chromosome 12 open reading frame 44
C12orf45	chromosome 12 open reading frame 45

---

---

C12orf48	chromosome 12 open reading frame 48
C12orf5	chromosome 12 open reading frame 5
C12orf52	chromosome 12 open reading frame 52
C13orf12	chromosome 13 open reading frame 12
C13orf3	chromosome 13 open reading frame 3
C13orf8	kiaa1802 protein
C14orf10	chromosome 14 open reading frame 10
C14orf104	chromosome 14 open reading frame 104
C14orf112	chromosome 14 open reading frame 112
C14orf122	chromosome 14 open reading frame 122
C14orf126	chromosome 14 open reading frame 126
C14orf130	chromosome 14 open reading frame 130
C14orf151	chromosome 14 open reading frame 151
C14orf156	chromosome 14 open reading frame 156
C14orf166	chromosome 14 open reading frame 166
C14orf169	chromosome 14 open reading frame 169
C14orf172	chromosome 14 open reading frame 172
C14orf173	chromosome 14 open reading frame 173
C14orf174	chromosome 14 open reading frame 174
C14orf2	chromosome 14 open reading frame 2
C14orf80	chromosome 14 open reading frame 80
C14orf93	chromosome 14 open reading frame 93
C15orf21	chromosome 15 open reading frame 21
C15orf23	chromosome 15 open reading frame 23
C15orf42	chromosome 15 open reading frame 42
C16orf33	chromosome 16 open reading frame 33
C16orf34	hypothetical protein similar to mouse hn1 (hematological and neurological expressed sequence 1)
C16orf60	chromosome 16 open reading frame 60
C17orf25	chromosome 17 open reading frame 25
C17orf48	chromosome 17 open reading frame 48
C17orf58	chromosome 17 open reading frame 58
C17orf59	chromosome 17 open reading frame 59
C17orf71	chromosome 17 open reading frame 71
C18orf10	chromosome 18 open reading frame 10
C18orf17	chromosome 18 open reading frame 17
C18orf21	chromosome 18 open reading frame 21
C18orf24	chromosome 18 open reading frame 24
C18orf37	chromosome 18 open reading frame 37
C18orf45	chromosome 18 open reading frame 45
C19orf10	chromosome 19 open reading frame 10
C19orf2	chromosome 19 open reading frame 2
C19orf24	chromosome 19 open reading frame 24
C19orf28	hypothetical protein pp3501
C1GALT1	core 1 synthase, glycoprotein-n-acetylgalactosamine 3-beta-galactosyltransferase, 1
C1orf102	chromosome 1 open reading frame 102
C1orf106	chromosome 1 open reading frame 106
C1orf112	chromosome 1 open reading frame 112
C1orf121	chromosome 1 open reading frame 121
C1orf131	chromosome 1 open reading frame 131
C1orf144	chromosome 1 open reading frame 144
C1orf149	chromosome 1 open reading frame 149
C1orf155	chromosome 1 open reading frame 155
C1orf156	chromosome 1 open reading frame 156
C1orf163	chromosome 1 open reading frame 163
C1orf164	hypothetical protein loc51261
C1orf165	chromosome 1 open reading frame 165
C1orf171	chromosome 1 open reading frame 171
C1orf173	chromosome 1 open reading frame 173
C1orf19	chromosome 1 open reading frame 19
C1orf25	chromosome 1 open reading frame 25
C1orf31	chromosome 1 open reading frame 31
C1orf33	chromosome 1 open reading frame 33
C1orf36	chromosome 1 open reading frame 36
C1orf37	chromosome 1 open reading frame 37
C1orf41	chromosome 1 open reading frame 41
C1orf48	chromosome 1 open reading frame 48
C1orf50	chromosome 1 open reading frame 50
C1orf51	chromosome 1 open reading frame 51
C1orf59	chromosome 1 open reading frame 59
C1orf61	chromosome 1 open reading frame 61
C1orf69	chromosome 1 open reading frame 69
C1orf73	chromosome 1 open reading frame 73
C1orf77	chromosome 1 open reading frame 77
C1orf83	chromosome 1 open reading frame 83
C1orf97	chromosome 1 open reading frame 97
C1QBP	complement component 1, q subcomponent binding protein
C1QL1	complement component 1, q subcomponent-like 1
C20orf108	chromosome 20 open reading frame 108
C20orf129	chromosome 20 open reading frame 129
C20orf155	chromosome 20 open reading frame 155
C20orf172	chromosome 20 open reading frame 172
C20orf177	chromosome 20 open reading frame 177
C20orf19	chromosome 20 open reading frame 19
C20orf20	chromosome 20 open reading frame 20
C20orf24	chromosome 20 open reading frame 24
C20orf27	chromosome 20 open reading frame 27
C20orf29	chromosome 20 open reading frame 29
C20orf55	chromosome 20 open reading frame 55
C20orf7	chromosome 20 open reading frame 7
C21orf45	chromosome 21 open reading frame 45
C21orf56	chromosome 21 open reading frame 56

---

---

C21orf59	hypothetical protein flj20467
C21orf70	chromosome 21 open reading frame 70
C22orf16	chromosome 22 open reading frame 16
C22orf18	chromosome 22 open reading frame 18
C22orf8	chromosome 22 open reading frame 8
C2orf10	chromosome 2 open reading frame 10
C2orf25	chromosome 2 open reading frame 25
C2orf29	chromosome 2 open reading frame 29
C2orf32	chromosome 2 open reading frame 32
C2orf34	chromosome 2 open reading frame 34
C2orf7	chromosome 2 open reading frame 7
C3orf14	chromosome 3 open reading frame 14
C3orf23	chromosome 3 open reading frame 23
C3orf26	chromosome 3 open reading frame 26
C3orf28	chromosome 3 open reading frame 28
C3orf31	chromosome 3 open reading frame 31
C3orf32	chromosome 3 open reading frame 32
C3orf54	chromosome 3 open reading frame 54
C4orf14	chromosome 4 open reading frame 14
C4orf16	chromosome 4 open reading frame 16
C4orf9	chromosome 4 open reading frame 9
C6orf108	chromosome 6 open reading frame 108
C6orf117	chromosome 6 open reading frame 117
C6orf125	chromosome 6 open reading frame 125
C6orf129	chromosome 6 open reading frame 129
C6orf149	chromosome 6 open reading frame 149
C6orf153	chromosome 6 open reading frame 153
C6orf173	chromosome 6 open reading frame 173
C6orf203	chromosome 6 open reading frame 203
C6orf49	chromosome 6 open reading frame 49
C6orf51	chromosome 6 open reading frame 51
C6orf54	chromosome 6 open reading frame 54
C6orf57	chromosome 6 open reading frame 57
C6orf66	chromosome 6 open reading frame 66
C6orf75	chromosome 6 open reading frame 75
C6orf96	chromosome 6 open reading frame 96
C7	complement component 7
C7orf10	chromosome 7 open reading frame 10
C7orf11	chromosome 7 open reading frame 11
C7orf20	chromosome 7 open reading frame 20
C7orf23	chromosome 7 open reading frame 23
C7orf24	chromosome 7 open reading frame 24
C7orf29	chromosome 7 open reading frame 29
C7orf30	chromosome 7 open reading frame 30
C7orf36	chromosome 7 open reading frame 36
C8orf13	chromosome 8 open reading frame 13
C8orf30A	chromosome 8 open reading frame 30a
C8orf36	chromosome 8 open reading frame 36
C8orf38	chromosome 8 open reading frame 38
C8orf41	chromosome 8 open reading frame 41
C8orf52	chromosome 8 open reading frame 52
C8orf72	chromosome 8 open reading frame 72
C9orf10	chromosome 9 open reading frame 10
C9orf100	chromosome 9 open reading frame 100
C9orf100S	chromosome 9 open reading frame 10 opposite strand
C9orf114	chromosome 9 open reading frame 114
C9orf140	chromosome 9 open reading frame 140
C9orf30	chromosome 9 open reading frame 30
C9orf40	chromosome 9 open reading frame 40
C9orf46	chromosome 9 open reading frame 46
C9orf58	chromosome 9 open reading frame 58
C9orf6	chromosome 9 open reading frame 6
C9orf72	hypothetical protein flj11109
C9orf74	chromosome 9 open reading frame 74
C9orf80	chromosome 9 open reading frame 80
C9orf85	chromosome 9 open reading frame 85
C9orf86	chromosome 9 open reading frame 86
C9orf88	chromosome 9 open reading frame 88
C9orf91	chromosome 9 open reading frame 91
CAB39L	calcium binding protein 39-like
CABC1	chaperone, abc1 activity of bc1 complex like (s. pombe)
CABLES1	cdk5 and abl enzyme substrate 1
CACHD1	cache domain containing 1
CACNA1G	calcium channel, voltage-dependent, alpha 1g subunit
CACYBP	calcyclin binding protein
CALCB	calcitonin-related polypeptide, beta
CALD1	caldesmon 1
CAMK1D	calcium/calmodulin-dependent protein kinase id
CAMKK2	calcium/calmodulin-dependent protein kinase kinase 2, beta
CAMKV	cam kinase-like vesicle-associated
CAND1	cullin-associated and neddylation-dissociated 1
CANX	calnexin
CAPN2	calpain 2, (m/ii) large subunit
CAPZA1	capping protein (actin filament) muscle z-line, alpha 1
CAPZB	capping protein (actin filament) muscle z-line, beta
CARD9	caspase recruitment domain family, member 9
CARHSP1	calcium regulated heat stable protein 1, 24kda
CART1	cartilage paired-class homeoprotein 1
CASC3	cancer susceptibility candidate 3
CASK	calcium/calmodulin-dependent serine protein kinase (maguk family)
CASP6	caspase 6, apoptosis-related cysteine peptidase

---

---

CAST	calpastatin
CASZ1	castor homolog 1, zinc finger (drosophila)
CBLN1	cerebellin 1 precursor
CBLN2	cerebellin 2 precursor
CBR1	carbonyl reductase 1
CBS	cystathionine-beta-synthase
CBX1	chromobox homolog 1 (hp1 beta homolog drosophila )
CBX3	chromobox homolog 3 (hp1 gamma homolog, drosophila)
CCDC12	coiled-coil domain containing 12
CCDC16	coiled-coil domain containing 16
CCDC25	coiled-coil domain containing 25
CCDC3	coiled-coil domain containing 3
CCDC32	coiled-coil domain containing 32
CCDC34	hypothetical protein af301222
CCDC4	coiled-coil domain containing 4
CCDC41	coiled-coil domain containing 41
CCDC43	coiled-coil domain containing 43
CCDC44	coiled-coil domain containing 44
CCDC5	coiled-coil domain containing 5 (spindle associated)
CCDC51	coiled-coil domain containing 51
CCDC58	coiled-coil domain containing 58
CCDC59	coiled-coil domain containing 59
CCDC6	coiled-coil domain containing 6
CCDC71	coiled-coil domain containing 71
CCDC74A	coiled-coil domain containing 74a
CCDC74B	coiled-coil domain containing 74b
CCNA2	cyclin a2
CCNB1	cyclin b1
CCNB2	cyclin b2
CCNC	cyclin c
CCND3	cyclin d3
CCNF	cyclin f
CCNG1	cyclin g1
CCNH	cyclin h
CCNJ	cyclin j
CCNK	cyclin k
CCRN4L	ccr4 carbon catabolite repression 4-like (s. cerevisiae)
CCT2	chaperonin containing tcp1, subunit 2 (beta)
CCT3	chaperonin containing tcp1, subunit 3 (gamma)
CCT4	chaperonin containing tcp1, subunit 4 (delta)
CCT5	chaperonin containing tcp1, subunit 5 (epsilon)
CCT6A	chaperonin containing tcp1, subunit 6a (zeta 1)
CCT7	chaperonin containing tcp1, subunit 7 (eta)
CCT8	chaperonin containing tcp1, subunit 8 (theta)
CD24	cd24 antigen (small cell lung carcinoma cluster 4 antigen)
CD320	cd320 antigen
CD44	cd44 antigen (indian blood group)
CD58	cd58 antigen, (lymphocyte function-associated antigen 3)
CD9	cd9 antigen (p24)
CD97	cd97 antigen
CD99	cd99 antigen
CDC2	cell division cycle 2, g1 to s and g2 to m
CDC20	cdc20 cell division cycle 20 homolog (s. cerevisiae)
CDC25A	cell division cycle 25a
CDC25B	cell division cycle 25b
CDC25C	cell division cycle 25c
CDC26	cell division cycle 26
CDC34	cell division cycle 34
CDC42	cell division cycle 42 (gtp binding protein, 25kda)
CDC45L	cdc45 cell division cycle 45-like (s. cerevisiae)
CDC5L	cdc5 cell division cycle 5-like (s. pombe)
CDCA1	cell division cycle associated 1
CDCA2	cell division cycle associated 2
CDCA3	cell division cycle associated 3
CDCA4	cell division cycle associated 4
CDCA7	cell division cycle associated 7
CDCA7L	cell division cycle associated 7-like
CDCA8	cell division cycle associated 8
CDGAP	cdc42 gtpase-activating protein
CDH11	cadherin 11, type 2, ob-cadherin (osteoblast)
CDK2	cyclin-dependent kinase 2
CDK4	cyclin-dependent kinase 4
CDK5	cyclin-dependent kinase 5
CDK5RAP2	cdk5 regulatory subunit associated protein 2
CDK8	cyclin-dependent kinase 8
CDKAL1	cdk5 regulatory subunit associated protein 1-like 1
CDKN3	cyclin-dependent kinase inhibitor 3 (cdk2-associated dual specificity phosphatase)
CDR2	cerebellar degeneration-related protein 2, 62kda
CDYL	chromodomain protein, y-like
CECR6	cat eye syndrome chromosome region, candidate 6
CENPB	centromere protein b, 80kda
CENPH	centromere protein h
CENTG2	centaurin, gamma 2
CEP55	centrosomal protein 55kda
CEP76	centrosomal protein 76kda
CFL1	cofilin 1 (non-muscle)
CGI-09	cgi-09 protein
CGI-115	cgi-115 protein
CGNL1	cingulin-like 1
CHAC2	chac, cation transport regulator-like 2 (e. coli)
CHAF1A	chromatin assembly factor 1, subunit a (p150)

---

---

CHCHD3	coiled-coil-helix-coiled-coil-helix domain containing 3
CHCHD4	coiled-coil-helix-coiled-coil-helix domain containing 4
CHCHD5	coiled-coil-helix-coiled-coil-helix domain containing 5
CHCHD6	coiled-coil-helix-coiled-coil-helix domain containing 6
CHCHD8	coiled-coil-helix-coiled-coil-helix domain containing 8
CHEK1	chk1 checkpoint homolog (s. pombe)
CHERP	calcium homeostasis endoplasmic reticulum protein
CHID1	chitinase domain containing 1
CHORDC1	cysteine and histidine-rich domain (chord)-containing 1
CHPT1	choline phosphotransferase 1
CHRM1	cholinergic receptor, muscarinic 1
CHRNA5	cholinergic receptor, nicotinic, alpha 5
CHST13	carbohydrate (chondroitin 4) sulfotransferase 13
CHST3	carbohydrate (chondroitin 6) sulfotransferase 3
CHST8	carbohydrate (n-acetylgalactosamine 4-0) sulfotransferase 8
CHSY1	carbohydrate (chondroitin) synthase 1
CIAPIN1	cytokine induced apoptosis inhibitor 1
CIB2	calcium and integrin binding family member 2
CINP	cyclin-dependent kinase 2-interacting protein
CIRH1A	cirrhosis, autosomal recessive 1a (cirhin)
CITED1	cbp/p300-interacting transactivator, with glu/asp-rich carboxy-terminal domain, 1
CKAP2	cytoskeleton associated protein 2
CKLF	chemokine-like factor
CKMT1A, CKMT1B	creatine kinase, mitochondrial 1b
CKS1B	cdc28 protein kinase regulatory subunit 1b
CKS2	cdc28 protein kinase regulatory subunit 2
CLEC2D	c-type lectin domain family 2, member d
CLN6	ceroid-lipofuscinosis, neuronal 6, late infantile, variant
CLNS1A	chloride channel, nucleotide-sensitive, 1a
CLPP	clpp caseinolytic peptidase, atp-dependent, proteolytic subunit homolog (e. coli)
CLPX	clpx caseinolytic peptidase x homolog (e. coli)
CLTC	clathrin, heavy polypeptide (hc)
CLYBL	citrate lyase beta like
CMA5	cytidine monophosphate n-acetylneuraminic acid synthetase
CMIP	c-maf-inducing protein
CMPK	cytidylate kinase
CMTM7	cklf-like marvel transmembrane domain containing 7
CNAP1	chromosome condensation-related smc-associated protein 1
CNIH	cornichon homolog (drosophila)
CNIH4	cornichon homolog 4 (drosophila)
CNNM1	cyclin m1
CNO	cappuccino homolog (mouse)
CNOT7	ccr4-not transcription complex, subunit 7
CNOT8	ccr4-not transcription complex, subunit 8
CNTN1	contactin 1
CNTN4	contactin 4
CNTNAP2	contactin associated protein-like 2
COASY	coenzyme a synthase
COBLL1	cobl-like 1
COG2	component of oligomeric golgi complex 2
COIL	coilin
COL1A1	collagen, type i, alpha 1
COL4A1	collagen, type iv, alpha 1
COL4A2	collagen, type iv, alpha 2
COL8A2	collagen, type viii, alpha 2
COMMMD1	copper metabolism (murr1) domain containing 1
COMMMD10	comm domain containing 10
COMMMD2	comm domain containing 2
COMMMD7	chromosome 20 open reading frame 92
COMMMD9	comm domain containing 9
COMTD1	catechol-o-methyltransferase domain containing 1
COPB2	coatomer protein complex, subunit beta 2 (beta prime)
COP53	cop9 constitutive photomorphogenic homolog subunit 3 (arabidopsis)
COP54	cop9 constitutive photomorphogenic homolog subunit 4 (arabidopsis)
COP55	cop9 constitutive photomorphogenic homolog subunit 5 (arabidopsis)
COP56	cop9 constitutive photomorphogenic homolog subunit 6 (arabidopsis)
COPZ1	coatomer protein complex, subunit zeta 1
COQ2	coenzyme q2 homolog, prenyltransferase (yeast)
COQ3	coenzyme q3 homolog, methyltransferase (yeast)
COQ9	coenzyme q9 homolog (yeast)
CORO1C	coronin, actin binding protein, 1c
COX10	cox10 homolog, cytochrome c oxidase assembly protein, heme a: farnesyltransferase (yeast)
COX15	cox15 homolog, cytochrome c oxidase assembly protein (yeast)
COX17	cox17 homolog, cytochrome c oxidase assembly protein (yeast)
COX4I2	cytochrome c oxidase subunit iv isoform 2 (lung)
COX4NB	cox4 neighbor
COX5A	cytochrome c oxidase subunit va
COX6A1	cytochrome c oxidase subunit via polypeptide 1
COX6B1	cytochrome c oxidase subunit vib polypeptide 1 (ubiquitous)
COX7B	cytochrome c oxidase subunit viib
COX8A	cytochrome c oxidase subunit 8a (ubiquitous)
CPLX1	complexin 1
CPLX2	complexin 2
CPSF2	cleavage and polyadenylation specific factor 2, 100kda
CPSF6	cleavage and polyadenylation specific factor 6, 68kda
CRABP1	cellular retinoic acid binding protein 1
CRADD	casp2 and ripk1 domain containing adaptor with death domain
CREB3L2	camp responsive element binding protein 3-like 2
CR11	crebbp/ep300 inhibitor 1
CRIPT	postsynaptic protein cript
CRKRS	cdc2-related kinase, arginine/serine-rich

---



---

CRLF3	cytokine receptor-like factor 3
CRNKL1	crn, crooked neck-like 1 (drosophila)
CRSP8	cofactor required for sp1 transcriptional activation, subunit 8, 34kda
CRTAC1	cartilage acidic protein 1
CRTAP	cartilage associated protein
CRTC1	creb regulated transcription coactivator 1
CRYBB2	crystallin, beta b2
CRYZ	crystallin, zeta (quinone reductase)
CS	citrate synthase
CSE1L	cse1 chromosome segregation 1-like (yeast)
CSK	c-src tyrosine kinase
CSNK1D	casein kinase 1, delta
CSNK2A1	casein kinase 2, alpha 1 polypeptide
CSRP2	cysteine and glycine-rich protein 2
CSRP2BP	csp2 binding protein
CST3	cystatin c (amyloid angiopathy and cerebral hemorrhage)
CSTF2	cleavage stimulation factor, 3' pre-rna, subunit 2, 64kda
CSTF3	cleavage stimulation factor, 3' pre-rna, subunit 3, 77kda
CTDSP1	ctd (carboxy-terminal domain, rna polymerase ii, polypeptide a) small phosphatase 1
CTDSP2	ctd (carboxy-terminal domain, rna polymerase ii, polypeptide a) small phosphatase 2
CTH	cystathionase (cystathionine gamma-lyase)
CTNNA1	catenin (cadherin-associated protein), alpha-like 1
CTNNA1	catenin (cadherin-associated protein), alpha-like 1
CTNNA1	catenin (cadherin-associated protein), beta 1, 88kda
CTNNA1	catenin, beta like 1
CTPS	ctp synthase
CTSC	cathepsin c
CTSL2	cathepsin l2
CUL1	cullin 1
CUL4A	cullin 4a
CUTC	cutc copper transporter homolog (e. coli)
CUTL2	cut-like 2 (drosophila)
CWF19L1	cwf19-like 1, cell cycle control (s. pombe)
CX3CL1	chemokine (c-x3-c motif) ligand 1
CXCR4	chemokine (c-x-c motif) receptor 4
CXorf26	chromosome x open reading frame 26
CXorf33	chromosome x open reading frame 33
CXorf39	chromosome x open reading frame 39
CYB5A	cytochrome b5 type a (microsomal)
CYB5R4	cytochrome b5 reductase 4
CYC1	cytochrome c-1
CYTL1	cytokine-like 1
D15Wsu75e	dna segment, chr 15, wayne state university 75, expressed
D4S234E	dna segment on chromosome 4 (unique) 234 expressed sequence
DAB2IP	ngap-like protein
DAK	dihydroxyacetone kinase 2 homolog (yeast)
DAP3	death associated protein 3
DAPK1	death-associated protein kinase 1
DARS	aspartyl-trna synthetase
DARS2	aspartyl-trna synthetase 2 (mitochondrial)
DAZAP1	daz associated protein 1
DBH	dopamine beta-hydroxylase (dopamine beta-monooxygenase)
DBN1	drebrin 1
DC2	dc2 protein
DCC1	defective in sister chromatid cohesion homolog 1 (s. cerevisiae)
DCLRE1A	dna cross-link repair 1a (psa2 homolog, s. cerevisiae)
DCN	decorin
DCP2	dcp2 decapping enzyme homolog (s. cerevisiae)
DCPS	decapping enzyme, scavenger
DCTN5	dynactin 5 (p25)
DCTN6	dynactin 6
DCUN1D5	dcn1, defective in cullin neddylation 1, domain containing 5 (s. cerevisiae)
DCXR	dicarbonyl/l-xylulose reductase
DDHD2	ddhd domain containing 2
DDIT4	dna-damage-inducible transcript 4
DDOST	dolichyl-diphosphooligosaccharide-protein glycosyltransferase
DDR2	discoidin domain receptor family, member 2
DDT	d-dopachrome tautomerase
DDX10	dead (asp-glu-ala-asp) box polypeptide 10
DDX18	dead (asp-glu-ala-asp) box polypeptide 18
DDX19A	dead (asp-glu-ala-asp) box polypeptide 19b
DDX21	dead (asp-glu-ala-asp) box polypeptide 21
DDX23	dead (asp-glu-ala-asp) box polypeptide 23
DDX24	dead (asp-glu-ala-asp) box polypeptide 24
DDX27	dead (asp-glu-ala-asp) box polypeptide 27
DDX28	dead (asp-glu-ala-asp) box polypeptide 28
DDX31	dead (asp-glu-ala-asp) box polypeptide 31
DDX39	dead (asp-glu-ala-asp) box polypeptide 39
DDX47	dead (asp-glu-ala-asp) box polypeptide 47
DDX48	dead (asp-glu-ala-asp) box polypeptide 48
DDX49	dead (asp-glu-ala-asp) box polypeptide 49
DDX50	dead (asp-glu-ala-asp) box polypeptide 50
DDX51	dead (asp-glu-ala-asp) box polypeptide 51
DDX54	dead (asp-glu-ala-asp) box polypeptide 54
DDX55	dead (asp-glu-ala-asp) box polypeptide 55
DEAF1	deformed epidermal autoregulatory factor 1 (drosophila)
DECRI	2,4-dienoyl coa reductase 1, mitochondrial
DEDD	death effector domain containing
DENND1A	denn/madd domain containing 1a
DEPDC1	dep domain containing 1
DEPDC1B	dep domain containing 1b
DERA	2-deoxyribose-5-phosphate aldolase homolog (c. elegans)

---

---

DERL2	der1-like domain family, member 2
DFFB	dna fragmentation factor, 40kda, beta polypeptide (caspase-activated dnase)
DGCR6	digeorge syndrome critical region gene 6
DGCR6L	digeorge syndrome critical region gene 6-like
DGKI	diacylglycerol kinase, iota
DGUOK	deoxyguanosine kinase
DHCR24	24-dehydrocholesterol reductase
DHFR	dihydrofolate reductase
DHODH	dihydroorotate dehydrogenase
DHRS4L2	dehydrogenase/reductase (sdr family) member 4 like 2
DHX32	hypothetical protein flj10694
DHX34	deah (asp-glu-ala-his) box polypeptide 34
DHX38	deah (asp-glu-ala-his) box polypeptide 38
DHX9	deah (asp-glu-ala-his) box polypeptide 9
DIAPH3	diaphanous homolog 3 (drosophila)
DIP2A	dip2 disco-interacting protein 2 homolog a (drosophila)
DIP2B	dip2 disco-interacting protein 2 homolog b (drosophila)
DIPA	hepatitis delta antigen-interacting protein a
DISP2	dispatched homolog 2 (drosophila)
DKC1	dyskeratosis congenita 1, dyskerin
DKFZP564J0863	dkfzp564j0863 protein
DKFZP564O0523	hypothetical protein dkfzp564o0523
DKFZP686A01247	hypothetical protein
DKFZp686O24166	hypothetical protein dkfzp686o24166
DKFZp762E1312	hypothetical protein dkfzp762e1312
DKFZP779L1558	hypothetical protein
DLAT	dihydrolipoamide s-acetyltransferase (e2 component of pyruvate dehydrogenase complex)
DLG5	discs, large homolog 5 (drosophila)
DLG7	discs, large homolog 7 (drosophila)
DLX5	distal-less homeobox 5
DMN	desmuslin
DNAJA2	dnaj (hsp40) homolog, subfamily a, member 2
DNAJA3	dnaj (hsp40) homolog, subfamily a, member 3
DNAJC11	dnaj (hsp40) homolog, subfamily c, member 11
DNAJC12	dnaj (hsp40) homolog, subfamily c, member 12
DNAJC17	dnaj (hsp40) homolog, subfamily c, member 17
DNAJC7	dnaj (hsp40) homolog, subfamily c, member 7
DNM1L	dynamitin 1-like
DNMT3B	dna (cytosine-5-)-methyltransferase 3 beta
DNPEP	aspartyl aminopeptidase
DOCK1	dedicator of cytokinesis 1
DOCK10	kiaa0694 gene product
DOCK7	dedicator of cytokinesis 7
DOK4	docking protein 4
DOK6	docking protein 6
DOLPP1	dolichyl pyrophosphate phosphatase 1
DPAGT1	dolichyl-phosphate (udp-n-acetylglucosamine) n-acetylglucosaminephosphotransferase 1 (glcnac-1-p transferase)
DPF1	d4, zinc and double phd fingers family 1
DPH2	dph2 homolog (s. cerevisiae)
DPM2	dolichyl-phosphate mannosyltransferase polypeptide 2, regulatory subunit
DPP6	dipeptidyl-peptidase 6
DRB1	developmentally regulated rna-binding protein 1
DRD2	dopamine receptor d2
DRG1	developmentally regulated gtp binding protein 1
DRG2	developmentally regulated gtp binding protein 2
DSCR1	down syndrome critical region gene 1
DSCR1L2	down syndrome critical region gene 1-like 2
DSCR2	down syndrome critical region gene 2
DSTN	destrin (actin depolymerizing factor)
DTNA	dystrobrevin, alpha
DTWD1	dtw domain containing 1
DTYMK	deoxythymidylate kinase (thymidylate kinase)
DUS3L	dihydrouridine synthase 3-like (s. cerevisiae)
DUSP11	dual specificity phosphatase 11 (rna/rnp complex 1-interacting)
DUSP14	dual specificity phosphatase 14
DUSP2	dual specificity phosphatase 2
DUSP26	dual specificity phosphatase 26 (putative)
DUSP4	dual specificity phosphatase 4
DYM	dymecilin
DYNC1I1	dynein, cytoplasmic 1, intermediate chain 1
DYNLL2	dynein, light chain, lc8-type 2
DYRK2	dual-specificity tyrosine-(y)-phosphorylation regulated kinase 2
DYRK3	dual-specificity tyrosine-(y)-phosphorylation regulated kinase 3
DYRK4	dual-specificity tyrosine-(y)-phosphorylation regulated kinase 4
DZIP1	daz interacting protein 1
E2F2	e2f transcription factor 2
E2F5	e2f transcription factor 5, p130-binding
E2F7	e2f transcription factor 7
E2F8	e2f transcription factor 8
EAF2	ell associated factor 2
EBNA1BP2	ebna1 binding protein 2
EBP	emopamil binding protein (sterol isomerase)
EBPL	emopamil binding protein-like
ECD	ecdysoneless homolog (drosophila)
ECHDC2	enoyl coenzyme a hydratase domain containing 2
ECHDC3	enoyl coenzyme a hydratase domain containing 3
ECHS1	enoyl coenzyme a hydratase, short chain, 1, mitochondrial
EDG3	endothelial differentiation, sphingolipid g-protein-coupled receptor, 3
EDNRA	endothelin receptor type a
EEF1B2	eukaryotic translation elongation factor 1 beta 2
EEF1D	eukaryotic translation elongation factor 1 delta (guanine nucleotide exchange protein)

---

---

EEF1E1	eukaryotic translation elongation factor 1 epsilon 1
EEF2K	eukaryotic elongation factor-2 kinase
EEFSEC	eukaryotic elongation factor, selenocysteine-trna-specific
EFHB	ef-hand domain family, member b
EFNA4	ephrin-a4
EFTUD2	elongation factor tu gtp binding domain containing 2
EGFR	epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian)
EGLN3	hypothetical protein flj21620
EHD1	eh-domain containing 1
EHD4	eh-domain containing 4
EIF1AX	eukaryotic translation initiation factor 1a, x-linked
eIF2A	eukaryotic translation initiation factor 2a, 65kda
EIF2AK1	eukaryotic translation initiation factor 2-alpha kinase 1
EIF2B1	eukaryotic translation initiation factor 2b, subunit 1 alpha, 26kda
EIF2B2	eukaryotic translation initiation factor 2b, subunit 2 beta, 39kda
EIF2B3	eukaryotic translation initiation factor 2b, subunit 3 gamma, 58kda
EIF2B5	eukaryotic translation initiation factor 2b, subunit 5 epsilon, 82kda
EIF2S1	eukaryotic translation initiation factor 2, subunit 1 alpha, 35kda
EIF3S1	eukaryotic translation initiation factor 3, subunit 1 alpha, 35kda
EIF3S10	eukaryotic translation initiation factor 3, subunit 10 theta, 150/170kda
EIF3S12	eukaryotic translation initiation factor 3, subunit 12
EIF3S2	eukaryotic translation initiation factor 3, subunit 2 beta, 36kda
EIF3S3	eukaryotic translation initiation factor 3, subunit 3 gamma, 40kda
EIF3S5	eukaryotic translation initiation factor 3, subunit 5 epsilon, 47kda
EIF3S6	eukaryotic translation initiation factor 3, subunit 6 48kda
EIF3S7	eukaryotic translation initiation factor 3, subunit 7 zeta, 66/67kda
EIF3S8	eukaryotic translation initiation factor 3, subunit 8, 110kda
EIF3S9	eukaryotic translation initiation factor 3, subunit 9 eta, 116kda
EIF4E2	eukaryotic translation initiation factor 4e member 2
EIF4EBP1	eukaryotic translation initiation factor 4e binding protein 1
EIF4EBP2	eukaryotic translation initiation factor 4e binding protein 2
EIF5A	eukaryotic translation initiation factor 5a
ELAC2	hypothetical protein flj10530
ELF3	e74-like factor 3 (ets domain transcription factor, epithelial-specific)
ELF4	e74-like factor 4 (ets domain transcription factor)
ELMO1	engulfment and cell motility 1
ELOF1	elongation factor 1 homolog (s. cerevisiae)
ELOVL1	cgi-88 protein
ELOVL5	elovl family member 5, elongation of long chain fatty acids (fen1/elo2, sur4/elo3-like, yeast)
ELOVL6	elovl family member 6, elongation of long chain fatty acids (fen1/elo2, sur4/elo3-like, yeast)
ELP4	elongation protein 4 homolog (s. cerevisiae)
EMG1	emg1 nucleolar protein homolog (s. cerevisiae)
EMILIN1	elastin microfibril interfacer 1
EML1	echinoderm microtubule associated protein like 1
EML4	echinoderm microtubule associated protein like 4
ENDOG	endonuclease g
ENG	endoglin (osler-rendu-weber syndrome 1)
ENO1	enolase 1, (alpha)
ENOSF1	enolase superfamily member 1
ENSA	endosulfine alpha
ENY2	enhancer of yellow 2 homolog (drosophila)
EPB49	erythrocyte membrane protein band 4.9 (dematin)
EPDR1	ependymin related protein 1 (zebrafish)
EPHA2	eph receptor a2
EPHB2	eph receptor b2
EPRS	glutamyl-prolyl-trna synthetase
ERAL1	gtpase, human homolog of e. coli essential cell cycle protein era
ERCC1	excision repair cross-complementing rodent repair deficiency, complementation group 1 (includes overlapping antisense sequence)
ERCC8	excision repair cross-complementing rodent repair deficiency, complementation group 8
ERF	ets2 repressor factor
ERGIC1	endoplasmic reticulum-golgi intermediate compartment (ergic) 1
ERGIC2	ergic and golgi 2
ERH	enhancer of rudimentary homolog (drosophila)
ERO1L	ero1-like (s. cerevisiae)
ESCO2	establishment of cohesion 1 homolog 2 (s. cerevisiae)
ESD	esterase d/formylglutathione hydrolase
ESPL1	extra spindle poles like 1 (s. cerevisiae)
ESRRA	estrogen-related receptor alpha
ESRRG	estrogen-related receptor gamma
ETF1	eukaryotic translation termination factor 1
ETFA	electron-transfer-flavoprotein, alpha polypeptide (glutaric aciduria ii)
ETFB	electron-transfer-flavoprotein, beta polypeptide
ETNK1	ethanolamine kinase 1
ETS1	v-ets erythroblastosis virus e26 oncogene homolog 1 (avian)
EWSR1	ewing sarcoma breakpoint region 1
EXO1	exonuclease 1
EXOSC2	exosome component 2
EXOSC3	exosome component 3
EXOSC4	exosome component 4
EXOSC5	exosome component 5
EXOSC6	exosome component 6
EXOSC7	exosome component 7
EXOSC8	exosome component 8
EXOSC9	exosome component 9
EZH2	enhancer of zeste homolog 2 (drosophila)
F2R	coagulation factor ii (thrombin) receptor
FABP5	fatty acid binding protein 5 (psoriasis-associated)
FADD	fas (tnfrsf6)-associated via death domain
FAF1	fas (tnfrsf6) associated factor 1
FAH	fumarylacetoacetate hydrolase (fumarylacetoacetase)
FAHD1	fumarylacetoacetate hydrolase domain containing 1

---

---

FAIM	fas apoptotic inhibitory molecule
FAIM3	fas apoptotic inhibitory molecule 3
FAM100B	family with sequence similarity 100, member b
FAM105A	family with sequence similarity 105, member a
FAM105B	family with sequence similarity 105, member b
FAM107B	family with sequence similarity 107, member b
FAM109A	family with sequence similarity 109, member a
FAM112B	family with sequence similarity 112, member b
FAM24B	family with sequence similarity 24, member b
FAM33A	family with sequence similarity 33, member a
FAM35A	family with sequence similarity 35, member a
FAM49B	family with sequence similarity 49, member b
FAM50B	family with sequence similarity 50, member b
FAM51A1	family with sequence similarity 51, member a1
FAM53A	family with sequence similarity 53, member a
FAM53B	family with sequence similarity 53, member b
FAM54A	family with sequence similarity 54, member a
FAM59A	family with sequence similarity 59, member a
FAM60A	family with sequence similarity 60, member a
FAM64A	family with sequence similarity 64, member a
FAM69B	family with sequence similarity 69, member b
FAM72A	family with sequence similarity 72, member a
FAM77C	family with sequence similarity 77, member c
FAM80A	family with sequence similarity 80, member a
FAM82B	family with sequence similarity 82, member b
FAM86A	family with sequence similarity 86, member a
FAM86B1	family with sequence similarity 86, member b1
FAM89A	family with sequence similarity 89, member a
FAM98A	family with sequence similarity 98, member a
FANCB	fanconi anemia, complementation group b
FANCE	fanconi anemia, complementation group e
FARS2	phenylalanine-trna synthetase 2 (mitochondrial)
FARSLA	phenylalanine-trna synthetase-like, alpha subunit
FASN	fatty acid synthase
FAT	fat tumor suppressor homolog 1 (drosophila)
FBL	fibrillarlin
FBLN1	fibulin 1
FBXL10	f-box and leucine-rich repeat protein 10
FBXL11	f-box and leucine-rich repeat protein 11
FBXO22	f-box protein 22
FBXO28	f-box protein 28
FBXO5	f-box protein 5
FBXO8	f-box protein 8
FCHSD2	fch and double sh3 domains 2
FDFT1	farnesyl-diphosphate farnesyltransferase 1
FDPS	farnesyl diphosphate synthase (farnesyl pyrophosphate synthetase, dimethylallyltranstransferase, geranyltranstransferase)
FEN1	flap structure-specific endonuclease 1
FER	fer (fps/fes related) tyrosine kinase (phosphoprotein ncp94)
FEV	fev (ets oncogene family)
FEZ1	fasciculation and elongation protein zeta 1 (zygin i)
FGFR1OP	fgfr1 oncogene partner
FH	fumarate hydratase
FHIT	fragile histidine triad gene
FHOD1	formin homology 2 domain containing 1
FHOD3	formin homology 2 domain containing 3
FJX1	four jointed box 1 (drosophila)
FKBP14	fk506 binding protein 14, 22 kda
FKBP1A	fk506 binding protein 1a, 12kda
FKBP4	fk506 binding protein 4, 59kda
FKBP5	fk506 binding protein 5
FKSG14	leucine zipper protein fks14
FKSG30	actin-like protein
FLAD1	fad1, flavin adenine dinucleotide synthetase, homolog (yeast)
FLJ10006	hypothetical protein loc55677
FLJ10099	hypothetical protein flj10099
FLJ10374	hypothetical protein flj10374
FLJ10379	hypothetical protein flj10379
FLJ10661	similar to cg7889-pa
FLJ10847	hypothetical protein flj10847
FLJ11184	hypothetical protein flj11184
FLJ11200	hypothetical protein flj11200
FLJ11712	deleted in leukemia 8 protein
FLJ11806	nuclear protein ukp68
FLJ12886	hypothetical protein flj12886
FLJ13149	hypothetical protein flj13149
FLJ13912	hypothetical protein flj13912
FLJ14001	hypothetical protein flj14001
FLJ14668	hypothetical protein flj14668
FLJ14768	hypothetical protein flj14768
FLJ20105	flj20105 protein
FLJ20125	hypothetical protein flj20125
FLJ20152	hypothetical protein flj20152
FLJ20186	hypothetical protein flj20186
FLJ20272	hypothetical protein flj20272
FLJ20323	hypothetical protein flj20323
FLJ20364	hypothetical protein flj20364
FLJ20366	hypothetical protein flj20366
FLJ20397	hypothetical protein flj20397
FLJ20422	hypothetical protein flj20422
FLJ20516	timeless-interacting protein
FLJ20534	hypothetical protein flj20534

---

---

FLJ20628	hypothetical protein flj20628
FLJ20647	hypothetical protein flj20647
FLJ20718	hypothetical protein flj20718
FLJ21820	hypothetical protein flj21820
FLJ21945	hypothetical protein flj21945
FLJ22222	hypothetical protein flj22222
FLJ22313	hypothetical protein flj22313
FLJ22374	hypothetical protein flj22374
FLJ22555	hypothetical protein flj22555
FLJ22624	flj22624 protein
FLJ22688	hypothetical protein flj22688
FLJ25416	hypothetical protein flj13936
FLJ32745	hypothetical protein flj32745
FLJ36888	hypothetical protein flj36888
FLJ38451	flj38451 protein
FLJ38663	hypothetical protein flj38663
FLJ39155	hypothetical protein flj39155
FLJ40432	hypothetical protein flj40432
FLJ40629	hypothetical protein flj40629
FLNA	filamin a, alpha (actin binding protein 280)
FLRT3	fibronectin leucine rich transmembrane protein 3
FLVCR	feline leukemia virus subgroup c cellular receptor
FN5	fn5 protein
FOXM1	forkhead box m1
FOXP1	forkhead box p1
FOXR2	forkhead box r2
FRAG1	fgf receptor activating protein 1
FRAS1	kiaa1500 protein
FRAT2	frequently rearranged in advanced t-cell lymphomas 2
FREQ	frequenin homolog (drosophila)
FRG1	fshd region gene 1
FRZB	frizzled-related protein
FSHPRH1	fsh primary response (lrpr1 homolog, rat) 1
FTSJ1	ftsj homolog 1 (e. coli)
FTSJ2	ftsj homolog 2 (e. coli)
FUBP1	far upstream element (fuse) binding protein 1
FUCA2	fucosidase, alpha-l- 2, plasma
FUNDC1	fun14 domain containing 1
FUSIP1	fus interacting protein (serine/arginine-rich) 1
FUT8	fucosyltransferase 8 (alpha (1,6) fucosyltransferase)
FXR1	fragile x mental retardation, autosomal homolog 1
G3BP	ras-gtpase-activating protein sh3-domain-binding protein
G6PD	glucose-6-phosphate dehydrogenase
GABPB2	ga binding protein transcription factor, beta subunit 1, 53kda
GADD45A	growth arrest and dna-damage-inducible, alpha
GADD45GIP1	growth arrest and dna-damage-inducible, gamma interacting protein 1
GALK1	galactokinase 1
GALM	galactose mutarotase (aldose 1-epimerase)
GALNAC4S-6ST	kiaa0598 gene product
GALNT1	udp-n-acetyl-alpha-d-galactosamine:polypeptide n-acetylgalactosaminyltransferase 1 (galnac-t1)
GALNT13	udp-n-acetyl-alpha-d-galactosamine:polypeptide n-acetylgalactosaminyltransferase 13 (galnac-t13)
GAMT	guanidinoacetate n-methyltransferase
GAPDH	glyceraldehyde-3-phosphate dehydrogenase
GARS	glycyl-trna synthetase
GATA2	gata binding protein 2
GATA3	gata binding protein 3
GATAD2A	gata zinc finger domain containing 2a
GBAS	glioblastoma amplified sequence
GBE1	glucan (1,4-alpha-), branching enzyme 1 (glycogen branching enzyme, andersen disease, glycogen storage disease type iv)
GCAT	glycine c-acetyltransferase (2-amino-3-ketobutyrate coenzyme a ligase)
GCDH	glutaryl-coenzyme a dehydrogenase
GCLC	glutamate-cysteine ligase, catalytic subunit
GCLM	glutamate-cysteine ligase, modifier subunit
GCN1L1	gcn1 general control of amino-acid synthesis 1-like 1 (yeast)
GCNT2	glucosaminyl (n-acetyl) transferase 2, i-branching enzyme (i blood group)
GDI2	gdp dissociation inhibitor 2
GEMIN4	dkfzp434b131 protein
GEMIN5	gem (nuclear organelle) associated protein 5
GEMIN6	gem (nuclear organelle) associated protein 6
GFM1	hypothetical protein flj12662
GFRA2	gdnf family receptor alpha 2
GGCX	gamma-glutamyl carboxylase
GIPC1	gipc pdz domain containing family, member 1
GIYD1, GIYD2	giy-yig domain containing 2
GK	glycerol kinase
GLDC	glycine dehydrogenase (decarboxylating; glycine decarboxylase, glycine cleavage system protein p)
GLE1L	gle1 rna export mediator-like (yeast)
GLI2	gli-kruppel family member gli2
GLMN	glomulin, fkbp associated protein
GLO1	glyoxalase i
GLOXD1	glyoxalase domain containing 1
GLRX5	glutaredoxin 5 homolog (s. cerevisiae)
GLT25D2	glycosyltransferase 25 domain containing 2
GLT28D1	glycosyltransferase 28 domain containing 1
GLTP	glycolipid transfer protein
GLYCTK	cg9886-like
GMCL1	germ cell-less homolog 1 (drosophila)
GMD5	gdp-mannose 4,6-dehydratase
GMIP	gem interacting protein
GMNN	geminin, dna replication inhibitor
GMPPA	gdp-mannose pyrophosphorylase a

---

---

GMPS	guanine monphosphate synthetase
GNAI3	guanine nucleotide binding protein (g protein), alpha inhibiting activity polypeptide 3
GNAO1	guanine nucleotide binding protein (g protein), alpha activating activity polypeptide o
GNB1L	guanine nucleotide binding protein (g protein), beta polypeptide 1-like
GNCI1	guanine nucleotide binding protein (g protein), gamma 11
GNG12	guanine nucleotide binding protein (g protein), gamma 12
GNG4	guanine nucleotide binding protein (g protein), gamma 4
GNG5	guanine nucleotide binding protein (g protein), gamma 5
GNL2	guanine nucleotide binding protein-like 2 (nucleolar)
GNL3	guanine nucleotide binding protein-like 3 (nucleolar)
GNL3L	guanine nucleotide binding protein-like 3 (nucleolar)-like
GNPNAT1	glucosamine-phosphate n-acetyltransferase 1
GNPTAB	hypothetical protein dkfzp762b226
GOLPH4	golgi phosphoprotein 4
GOSR2	golgi snap receptor complex member 2
GOT2	glutamic-oxaloacetic transaminase 2, mitochondrial (aspartate aminotransferase 2)
GPAM	glycerol-3-phosphate acyltransferase, mitochondrial
GPATC4	g patch domain containing 4
GPC6	glypican 6
GPD1L	glycerol-3-phosphate dehydrogenase 1-like
GPHN	gephyrin
GPI	glucose phosphate isomerase
GPM6B	glycoprotein m6b
GPR124	g protein-coupled receptor 124
GPR30	g protein-coupled receptor 30
GPR63	g protein-coupled receptor 63
GPX1	glutathione peroxidase 1
GPX7	glutathione peroxidase 7
GREB1	greb1 protein
GRIA3	glutamate receptor, ionotropic, ampa 3
GRIN1	glutamate receptor, ionotropic, n-methyl d-aspartate 1
GRK6	g protein-coupled receptor kinase 6
GRM2	glutamate receptor, metabotropic 2
GRM7	glutamate receptor, metabotropic 7
GRM8	glutamate receptor, metabotropic 8
GRPEL1	grpe-like 1, mitochondrial (e. coli)
GRSF1	g-rich rna sequence binding factor 1
GRWD1	glutamate-rich wd repeat containing 1
GSG2	germ cell associated 2 (haspin)
GSK3B	glycogen synthase kinase 3 beta
GSP1T	g1 to s phase transition 1
GSP1T2	g1 to s phase transition 2
GSR	glutathione reductase
GSS	glutathione synthetase
GSTA4	glutathione s-transferase a4
GSTO1	glutathione s-transferase omega 1
GSTP1	glutathione s-transferase pi
GTF2E2	general transcription factor iie, polypeptide 2, beta 34kda
GTF2F2	general transcription factor iif, polypeptide 2, 30kda
GTF2H2	general transcription factor iih, polypeptide 2, 44kda
GTF2H3	general transcription factor iih, polypeptide 3, 34kda
GTF2I	general transcription factor ii, i
GTF2IRD2, GTF2IRD2B	gtf2i repeat domain containing 2
GTF3A	general transcription factor iiaa
GTF3C3	general transcription factor iiaa, polypeptide 3, 102kda
GTF3C5	general transcription factor iiaa, polypeptide 5, 63kda
GTPBP3	gtp binding protein 3 (mitochondrial)
GTPBP4	gtp binding protein 4
GTPBP8	gtp-binding protein 8 (putative)
GTSE1	g-2 and s-phase expressed 1
GUF1	guf1 gtpase homolog (s. cerevisiae)
GUSBL2	glucuronidase, beta-like 2
H2AFX	h2a histone family, member x
H2AFY2	h2a histone family, member y2
H2BFS	h2b histone family, member s
HADH2	hydroxyacyl-coenzyme a dehydrogenase, type ii
HADHA	hydroxyacyl-coenzyme a dehydrogenase/3-ketoacyl-coenzyme a thiolase/enoyl-coenzyme a hydratase (trifunctional protein), alpha subunit
HADHSC	l-3-hydroxyacyl-coenzyme a dehydrogenase, short chain
HARS2	histidyl-trna synthetase 2
HAT1	histone acetyltransferase 1
hCAP-D3	kiaa0056 protein
hCAP-G	chromosome condensation protein g
HDAC1	histone deacetylase 1
HDAC9	histone deacetylase 9
HDHC2	hd domain containing 2
HDGF	hepatoma-derived growth factor (high-mobility group protein 1-like)
HDHD1A	haloacid dehalogenase-like hydrolase domain containing 1a
HDHD2	haloacid dehalogenase-like hydrolase domain containing 2
HEATR1	heat repeat containing 1
HECW2	hect, c2 and ww domain containing e3 ubiquitin protein ligase 2
HELLS	helicase, lymphoid-specific
hfl-B5	dendritic cell protein
HIATL2	hippocampus abundant gene transcript-like 2
HIBCH	3-hydroxyisobutyryl-coenzyme a hydrolase
HIC2	hypermethylated in cancer 2
HIF1A	hypoxia-inducible factor 1, alpha subunit (basic helix-loop-helix transcription factor)
HIG2	hypoxia-inducible protein 2
HINT3	histidine triad nucleotide binding protein 3
HIP1	huntingtin interacting protein 1
HIRIP3	hira interacting protein 3
HIST1H1C	histone 1, h1c

---

---

HIST1H2AM	histone 1, h2ai
HIST1H2BC, HIST1H2BD,	histone 1, h2bd
HIST1H2BG	
HIST1H2BH	histone 1, h2bh
HIST1H2BJ	histone 1, h2bj
HIST1H2BK	histone 1, h2bk
HIST1H3C, HIST1H3G,	
HIST1H3F, HIST1H3D	histone 1, h3a
HIST1H4K	h4 histone, family 2
HIST2H2AC	histone 2, h2ac
HK1	hexokinase 1
HK2	hexokinase 2
HLRC1	heat-like (pbs lyase) repeat containing 1
HM13	histocompatibility (minor) 13
HMB5	hydroxymethylbilane synthase
HMG1L1	high-mobility group (nonhistone chromosomal) protein 1-like 1
HMG1	high-mobility group box 1
HMG2	high-mobility group box 2
HMG3	high-mobility group box 3
HMG3	high mobility group nucleosomal binding domain 3
HMMR	hyaluronan-mediated motility receptor (rhamm)
HMP19	hmp19 protein
HMX1	homeobox (h6 family) 1
HNRPA1	heterogeneous nuclear ribonucleoprotein a1
HNRPA2B1	heterogeneous nuclear ribonucleoprotein a2/b1
HNRPA3	heterogeneous nuclear ribonucleoprotein a3
HNRPA4	heterogeneous nuclear ribonucleoprotein a/b
HNRPC	heterogeneous nuclear ribonucleoprotein c (c1/c2)
HNRPD	heterogeneous nuclear ribonucleoprotein d (au-rich element rna binding protein 1, 37kda)
HNRPF	heterogeneous nuclear ribonucleoprotein f
HNRPH1	heterogeneous nuclear ribonucleoprotein h1 (h)
HNRPK	heterogeneous nuclear ribonucleoprotein k
HNRPL	heterogeneous nuclear ribonucleoprotein l
HNRPL1	heterogeneous nuclear ribonucleoprotein l-like
HNRPM	heterogeneous nuclear ribonucleoprotein m
HOMER1	homer homolog 1 (drosophila)
HPRT1	hypoxanthine phosphoribosyltransferase 1 (lesch-nyhan syndrome)
HPS3	hermansky-pudlak syndrome 3
HR	hairless homolog (mouse)
HRAS	v-ha-ras harvey rat sarcoma viral oncogene homolog
HRASL5	hras-like suppressor
HRH3	histamine receptor h3
HRSP12	heat-responsive protein 12
HS2ST1	heparan sulfate 2-o-sulfotransferase 1
HSA9761	dimethyladenosine transferase
HSCARG	hscarg protein
HSF1	heat shock transcription factor 1
HSP90AA1	heat shock protein 90kda alpha (cytosolic), class a member 1
HSP90B1	heat shock protein 90kda beta (grp94), member 1
HSPA14	heat shock 70kda protein 14
HSPA4	heat shock 70kda protein 4
HSPA4L	heat shock 70kda protein 4-like
HSPBP1	hsp70-interacting protein
HSPC23	hspc23 protein
HSPC111	hypothetical protein hspc111
HSPC117	similar to c. elegans hypothetical 55.2 kd protein fl6a11.2
HSPC159	hspc159 protein
HSPC176	hematopoietic stem/progenitor cells 176
HSPC196	hypothetical protein hspc196
HSPC268	hypothetical protein hspc268
HSPD1	heat shock 60kda protein 1 (chaperonin)
HSPF1	heat shock 10kda protein 1 (chaperonin 10)
HTATSF1	hiv-1 tat specific factor 1
HTLF	human t-cell leukemia virus enhancer factor
HTR1E	5-hydroxytryptamine (serotonin) receptor 1e
HTRA1	htra serine peptidase 1
IARS2	isoleucine-trna synthetase 2, mitochondrial
IBTK	inhibitor of bruton agammaglobulinemia tyrosine kinase
ICAM3	intercellular adhesion molecule 3
ICT1	immature colon carcinoma transcript 1
ID1	inhibitor of dna binding 1, dominant negative helix-loop-helix protein
ID2	inhibitor of dna binding 2, dominant negative helix-loop-helix protein
ID3	inhibitor of dna binding 3, dominant negative helix-loop-helix protein
ID4	insulin-degrading enzyme
IDH2	isocitrate dehydrogenase 2 (nadp+), mitochondrial
IDH3B	isocitrate dehydrogenase 3 (nad+) beta
IDS	iduronate 2-sulfatase (hunter syndrome)
IER3IP1	immediate early response 3 interacting protein 1
IFP38	ifp38
IFRD2	interferon-related developmental regulator 2
IGF2BP3	insulin-like growth factor 2 mrna binding protein 3
IGFBP2	insulin-like growth factor binding protein 2, 36kda
IGFBP3	insulin-like growth factor binding protein 3
IGFBP4	insulin-like growth factor binding protein 4
IGFBP5	insulin-like growth factor binding protein 5
IKIP	ikk interacting protein
ILF2	interleukin enhancer binding factor 2, 45kda
ILF3	interleukin enhancer binding factor 3, 90kda
ILVBL	ilvb (bacterial acetolactate synthase)-like
IMMP1L	imp1 inner mitochondrial membrane peptidase-like (s. cerevisiae)
IMMT	inner membrane protein, mitochondrial (mitofilin)

---

---

IMP3	imp3, u3 small nucleolar ribonucleoprotein, homolog (yeast)
IMP4	imp4, u3 small nucleolar ribonucleoprotein, homolog (yeast)
IMP41	inositol(myo)-1(or 4)-monophosphatase 1
IMPDH1	imp (inosine monophosphate) dehydrogenase 1
IMPDH2	imp (inosine monophosphate) dehydrogenase 2
INA	internekin neuronal intermediate filament protein, alpha
ING5	inhibitor of growth family, member 5
INPP4B	inositol polyphosphate-4-phosphatase, type ii, 105kda
INPP5F	inositol polyphosphate-5-phosphatase f
INSIG1	insulin induced gene 1
INT4	integrator complex subunit 4
IPO11	importin 11
IPO4	importin 4
IPO7	importin 7
IPO8	importin 8
IRAK1BP1	interleukin-1 receptor-associated kinase 1 binding protein 1
IRF2BP2	interferon regulatory factor 2 binding protein 2
ISC2L1	interferon stimulated exonuclease gene 20kda-like 1
ISLR2	immunoglobulin superfamily containing leucine-rich repeat 2
ISOC1	isochorismatase domain containing 1
ISOC2	isochorismatase domain containing 2
ITGA9	integrin, alpha 9
ITGAE	integrin, alpha e (antigen cd103, human mucosal lymphocyte antigen 1; alpha polypeptide)
ITGAV	integrin, alpha v (vitronectin receptor, alpha polypeptide, antigen cd51)
ITGB1BP1	integrin beta 1 binding protein 1
ITGB3BP	integrin beta 3 binding protein (beta3-endonexin)
ITGB4BP	integrin beta 4 binding protein
ITPA	inosine triphosphatase (nucleoside triphosphate pyrophosphatase)
ITPR1	inositol 1,4,5-triphosphate receptor, type 1
ITSN1	intersectin 1 (sh3 domain protein)
IVD	isovaleryl coenzyme a dehydrogenase
JAM2	junctional adhesion molecule 2
JAZF1	juxtaposed with another zinc finger gene 1
JMJD2B	jumonji domain containing 2b
JPH1	junctionophilin 1
JRK	jerky homolog (mouse)
JTV1	jtv1 gene
KARS	lysyl-trna synthetase
KATNA1	katanin p60 (atpase-containing) subunit a 1
KATNB1	katanin p80 (wd repeat containing) subunit b 1
KBTBD6	kelch repeat and btb (poz) domain containing 6
KBTBD7	kelch repeat and btb (poz) domain containing 7
KBTBD8	kelch repeat and btb (poz) domain containing 8
KCNH2	potassium voltage-gated channel, subfamily h (eag-related), member 2
KCNJ8	potassium inwardly-rectifying channel, subfamily j, member 8
KCNK1	potassium channel, subfamily k, member 1
KCNK3	potassium channel, subfamily k, member 3
KCNMA1	potassium large conductance calcium-activated channel, subfamily m, alpha member 1
KCNQ2	potassium voltage-gated channel, kqt-like subfamily, member 2
KCNT1	potassium channel, subfamily t, member 1
KCTD12	potassium channel tetramerisation domain containing 12
KCTD3	potassium channel tetramerisation domain containing 3
KDEL1	kdel (lys-asp-glu-leu) containing 1
KDEL1R1	kdel (lys-asp-glu-leu) endoplasmic reticulum protein retention receptor 1
KHDRBS1	kh domain containing, rna binding, signal transduction associated 1
KHDRBS3	kh domain containing, rna binding, signal transduction associated 3
KHSRP	kh-type splicing regulatory protein (fuse binding protein 2)
KIAA0020	kiaa0020
KIAA0101	kiaa0101
KIAA0133	kiaa0133
KIAA0141	kiaa0141
KIAA0179	kiaa0179
KIAA0182	kiaa0182
KIAA0196	kiaa0196
KIAA0241	kiaa0241
KIAA0247	kiaa0247
KIAA0391	kiaa0391
KIAA0409	kiaa0409
KIAA0427	kiaa0427
KIAA0586	kiaa0586
KIAA0664	kiaa0664
KIAA0690	kiaa0690
KIAA0859	kiaa0859 protein
KIAA0971	kiaa0971
KIAA1143	kiaa1143
KIAA1160	kiaa1160 protein
KIAA1166	kiaa1166
KIAA1429	kiaa1429
KIAA1576	kiaa1576 protein
KIAA1604	kiaa1604 protein
KIAA1698	kiaa1698
KIAA1712	kiaa1712
KIAA1754	kiaa1754
KIAA1794	kiaa1794
KIAA1797	kiaa1797
KIAA1853	kiaa1853
KIAA1967	kiaa1967
KIF14	kinesin family member 14
KIF1C	kinesin family member 1c
KIF2	kinesin heavy chain member 2
KIF20A	kinesin family member 20a

---



---

KIF21A	kinesin family member 21a
KIF22	kinesin family member 22
KIF23	kinesin family member 23
KIF2C	kinesin family member 2c
KIF4A	kinesin family member 4a
KIF5B	kinesin family member 5b
KLF15	kruppel-like factor 15
KLF6	kruppel-like factor 6
KLHDC4	kelch domain containing 4
KLHL18	kelch-like 18 (drosophila)
KLHL25	kelch-like 25 (drosophila)
KLHL5	kelch-like 5 (drosophila)
KLHL8	kelch-like 8 (drosophila)
KNTC2	kinetochore associated 2
KPNA1	karyopherin alpha 1 (importin alpha 5)
KPNA2	karyopherin alpha 2 (rag cohort 1, importin alpha 1)
KPNA5	karyopherin alpha 5 (importin alpha 6)
Kua-UEV	ubiquitin-conjugating enzyme e2 variant 1
LACE1	lactation elevated-1
LAMA1	laminin, alpha 1
LAMA4	laminin, alpha 4
LAMB1	laminin, beta 1
LAP3	leucine aminopeptidase 3
LAPTM4A	lysosomal-associated protein transmembrane 4 alpha
LAPTM4B	lysosomal associated protein transmembrane 4 beta
LARP2	la ribonucleoprotein domain family, member 2
LARP4	la ribonucleoprotein domain family, member 4
LARP6	la ribonucleoprotein domain family, member 6
LARS2	leucyl-trna synthetase 2, mitochondrial
LAS1L	las1-like (s. cerevisiae)
LBR	lamin b receptor
LBX2	ladybird homeobox homolog 2 (drosophila)
LDB2	lim domain binding 2
LDHA	lactate dehydrogenase a
LDHB	lactate dehydrogenase b
LDLRAD3	low density lipoprotein receptor class a domain containing 3
LDOC1	leucine zipper, down-regulated in cancer 1
LEO1	leo1, paf1/rna polymerase ii complex component, homolog (s. cerevisiae)
LETM1	leucine zipper-ef-hand containing transmembrane protein 1
LFNG	lunatic fringe homolog (drosophila)
LGTN	ligatin
LHFP	lipoma hmgic fusion partner
LHFP2	lipoma hmgic fusion partner-like 2
LIG3	ligase iii, dna, atp-dependent
LIMA1	lim domain and actin binding 1
LIMS1	lim and senescent cell antigen-like domains 1
LIN28B	lin-28 homolog b (c. elegans)
LIPA	lipase a, lysosomal acid, cholesterol esterase (wolman disease)
LIPT1	lipoyltransferase 1
LITAF	lipopolysaccharide-induced tnfr factor
LMNA	lamin a/c
LMNB1	lamin b1
LMNB2	lamin b2
LMO1	lim domain only 1 (rhombotin 1)
LMO3	lim domain only 3 (rhombotin-like 2)
LMO4	lim domain only 4
LOC113179	hypothetical protein bc011824
LOC113444	hypothetical protein bc011880
LOC115098	hypothetical protein bc013949
LOC126208	hypothetical protein loc126208
LOC133619	hypothetical protein mgc12103
LOC134147	similar to mouse 2310016a09rik gene
LOC144097	hypothetical protein bc007540
LOC150223	hypothetical protein loc150223
LOC151194	similar to hepatocellular carcinoma-associated antigen hca557b
LOC153364	similar to metallo-beta-lactamase superfamily protein
LOC168850	hypothetical protein loc168850
LOC198437	ba299n6.3
LOC201725	hypothetical protein loc201725
LOC221143	hypothetical protein loc221143
LOC283174	hypothetical protein loc283174
LOC283932	hypothetical protein loc283932
LOC283951	hypothetical protein loc283951
LOC387882	hypothetical protein
LOC388610	hypothetical loc388610
LOC400451	hypothetical gene supported by ak075564; bc060873
LOC440157	hypothetical gene supported by ak096951; bc066547
LOC441046	hypothetical loc 441046
LOC51255	hypothetical protein loc51255
LOC51334	mesenchymal stem cell protein dsc54
LOC554235	hypothetical protein loc554235
LOC56902	putative 28 kda protein
LOC89944	hypothetical protein bc008326
LOC90355	hypothetical gene supported by af038182; bc009203
LOC90580	hypothetical protein bc011833
LOC90624	hypothetical protein loc90624
LOC91137	hypothetical protein bc017169
LOC91461	hypothetical protein bc007901
LOC92345	hypothetical protein bc008207
LOC93343	hypothetical protein bc011840
LOC93622	hypothetical protein bc006130

---

---

LOC96610	hypothetical protein similar to k1aa0187 gene product
LONPL, WDR51B	peroxisomal lon protease like
LOX	lysyl oxidase
LPHN3	latrophilin 3
LRFN2	leucine rich repeat and fibronectin type iii domain containing 2
LRFN4	leucine rich repeat and fibronectin type iii domain containing 4
LRP5	low density lipoprotein receptor-related protein 5
LRP5L	low density lipoprotein receptor-related protein 5-like
LRP8	low density lipoprotein receptor-related protein 8, apolipoprotein e receptor
LRRC34	leucine rich repeat containing 34
LRRC41	leucine rich repeat containing 41
LRRC47	leucine rich repeat containing 47
LRRC59	leucine rich repeat containing 59
LRRC8B	leucine rich repeat containing 8 family, member b
LRRC8C	leucine rich repeat containing 8 family, member c
LRRK1	leucine-rich repeat kinase 1
LRRN1	leucine rich repeat neuronal 1
LRRN3	leucine rich repeat neuronal 3
LRRN6C	leucine rich repeat neuronal 6c
LSG1	large subunit gtpase 1 homolog (s. cerevisiae)
LSM12	lsm12 homolog (s. cerevisiae)
LSM14A	lsm14 homolog a (scd6, s. cerevisiae)
LSM3	lsm3 homolog, u6 small nuclear rna associated (s. cerevisiae)
LSM4	lsm4 homolog, u6 small nuclear rna associated (s. cerevisiae)
LSM5	lsm5 homolog, u6 small nuclear rna associated (s. cerevisiae)
LSM6	lsm6 homolog, u6 small nuclear rna associated (s. cerevisiae)
LSM7	lsm7 homolog, u6 small nuclear rna associated (s. cerevisiae)
LTA4H	leukotriene a4 hydrolase
LTV1	ltv1 homolog (s. cerevisiae)
LUC7L2	cgi-59 protein
LY6E	lymphocyte antigen 6 complex, locus e
LYAR	hypothetical protein flj20425
LYL1	lymphoblastic leukemia derived sequence 1
LYN	v-yes-1 yamaguchi sarcoma viral related oncogene homolog
LYPLA1	lysophospholipase i
LYPLA2	lysophospholipase ii
LYPLAL1	lysophospholipase-like 1
LZIC	leucine zipper and ctnnbp1 domain containing
M6PRBP1	mannose-6-phosphate receptor binding protein 1
MAD2L1	mad2 mitotic arrest deficient-like 1 (yeast)
MAD2L1BP	mad2l1 binding protein
MAFB	v-maf musculoaponeurotic fibrosarcoma oncogene homolog b (avian)
MAGEA3	melanoma antigen family a, 3
MAGEF1	melanoma antigen family f, 1
Magmas	mitochondria-associated protein involved in granulocyte-macrophage colony-stimulating factor signal transduction
MAGOH	mago-nashi homolog, proliferation-associated (drosophila)
MAML1	mastermind-like 1 (drosophila)
MAOB	monoamine oxidase b
MAP1A	microtubule-associated protein 1a
MAP2K2	mitogen-activated protein kinase kinase 2
MAP2K6	mitogen-activated protein kinase kinase 6
MAP3K11	mitogen-activated protein kinase kinase kinase 11
MAP3K7	mitogen-activated protein kinase kinase kinase 7
MAPK10	mitogen-activated protein kinase 10
MAPK4	mitogen-activated protein kinase 4
MAPKAP1	mitogen-activated protein kinase associated protein 1
MAPKAPK3	mitogen-activated protein kinase-activated protein kinase 3
MAPKAPK5	mitogen-activated protein kinase-activated protein kinase 5
MARCKS	myristoylated alanine-rich protein kinase c substrate
MARS2	methionine-trna synthetase 2 (mitochondrial)
MAT2B	dtbp-4-keto-6-deoxy-d-glucose 4-reductase
MATN3	matrilin 3
MATR3	matrin 3
MBNL1	muscleblind-like (drosophila)
MCCC2	methylcrotonoyl-coenzyme a carboxylase 2 (beta)
MCEE	methylmalonyl coa epimerase
MCM10	mcm10 minichromosome maintenance deficient 10 (s. cerevisiae)
MCM4	mcm4 minichromosome maintenance deficient 4 (s. cerevisiae)
MCM6	mcm6 minichromosome maintenance deficient 6 (mis5 homolog, s. pombe) (s. cerevisiae)
MCM7	mcm7 minichromosome maintenance deficient 7 (s. cerevisiae)
MCPI1	microcephaly, primary autosomal recessive 1
MCRS1	microspherule protein 1
MCTS1	malignant t cell amplified sequence 1
MDH2	malate dehydrogenase 2, nad (mitochondrial)
ME1	malic enzyme 1, nadp(+)-dependent, cytosolic
ME2	malic enzyme 2, nad(+)-dependent, mitochondrial
ME3	malic enzyme 3, nadp(+)-dependent, mitochondrial
MED25	mediator of rna polymerase ii transcription, subunit 25 homolog (yeast)
MED28	mediator of rna polymerase ii transcription, subunit 28 homolog (yeast)
MED6	mediator of rna polymerase ii transcription, subunit 6 homolog (yeast)
MED8	mediator of rna polymerase ii transcription, subunit 8 homolog (yeast)
MESDC1	mesoderm development candidate 1
METAP1	methionyl aminopeptidase 1
METTL5	methyltransferase like 5
METTL7A	methyltransferase like 7a
MFAP4	microfibrillar-associated protein 4
MFSO2	major facilitator superfamily domain containing 2
MGC10992	hypothetical protein loc92922
MGC10993	hypothetical protein mgc10993
MGC11257	hypothetical protein mgc11257
MGC13057	hypothetical protein mgc13057

---

---

MGC13096	hypothetical protein mgc13096
MGC13170	multidrug resistance-related protein
MGC14141	hypothetical protein mgc14141
MGC15476	thymus expressed gene 3-like
MGC15523	hypothetical protein mgc15523
MGC23909	hypothetical protein mgc23909
MGC2408	hypothetical protein mgc2408
MGC24975	hypothetical protein mgc24975
MGC2747	hypothetical protein mgc2747
MGC2749	hypothetical protein mgc2749
MGC3101	hypothetical protein mgc3101
MGC33648	hypothetical protein mgc33648
MGC3731	hypothetical protein mgc3731
MGC4093	hypothetical protein mgc4093
MGC42367	similar to 2010300c02rik protein
MGC45800	hypothetical protein loc90768
MGC5242	hypothetical protein mgc5242
MGC5297	hypothetical protein mgc5297
MGC5509	hypothetical protein mgc5509
MGC61571	hypothetical protein mgc61571
MGC7036	hypothetical protein mgc7036
MGC70924	hypothetical loc284338
MGC72075	hypothetical protein mgc72075
MGC88387	similar to hspc296
MGST2	microsomal glutathione s-transferase 2
mimitin	myc-induced mitochondria protein
MINA	myc induced nuclear antigen
MKI67IP	mk167 (fha domain) interacting nucleolar phosphoprotein
MKKS	mckusick-kaufman syndrome
MLFIIP	mlf1 interacting protein
MLSTD1	male sterility domain containing 1
MMAB	hypothetical protein mgc20496
MMACHC	methylmalonic aciduria (cobalamin deficiency) cblc type, with homocystinuria
MMP2	matrix metalloproteinase 2 (gelatinase a, 72kda gelatinase, 72kda type iv collagenase)
MNAT1	menage a trois homolog 1, cyclin h assembly factor (xenopus laevis)
MOCS1	molybdenum cofactor synthesis 1
MON1A	mon1 homolog a (yeast)
MORC4	morc family cw-type zinc finger 4
MORF4L2	mortality factor 4 like 2
MOSC2	moco sulphurase c-terminal domain containing 2
MPDU1	mannose-p-dolichol utilization defect 1
MPHOSPH9	m-phase phosphoprotein 9
MPP6	membrane protein, palmitoylated 6 (maguk p55 subfamily member 6)
MPST	mercaptopyruvate sulfurtransferase
MPV17	mpv17 transgene, murine homolog, glomerulosclerosis
MPZL1	myelin protein zero-like 1
MRE11A	mre11 meiotic recombination 11 homolog a (s. cerevisiae)
M-RIP	myosin phosphatase-rho interacting protein
MRPL1	bm022 protein
MRPL11	cgi-113 protein
MRPL12	mitochondrial ribosomal protein l12
MRPL13	mitochondrial ribosomal protein l13
MRPL15	mitochondrial ribosomal protein l15
MRPL16	mitochondrial ribosomal protein l16
MRPL17	mitochondrial ribosomal protein l17
MRPL18	mitochondrial ribosomal protein l18
MRPL19	mitochondrial ribosomal protein l19
MRPL2	mitochondrial ribosomal protein l2
MRPL20	mitochondrial ribosomal protein l20
MRPL21	mitochondrial ribosomal protein l21
MRPL22	mitochondrial ribosomal protein l22
MRPL23	mitochondrial ribosomal protein l23
MRPL24	mitochondrial ribosomal protein l24
MRPL27	mitochondrial ribosomal protein l27
MRPL3	mitochondrial ribosomal protein l3
MRPL30	mitochondrial ribosomal protein l30
MRPL36	mitochondrial ribosomal protein l36
MRPL37	mitochondrial ribosomal protein l37
MRPL39	mitochondrial ribosomal protein l39
MRPL4	mitochondrial ribosomal protein l4
MRPL42	mitochondrial ribosomal protein l42
MRPL44	mitochondrial ribosomal protein l44
MRPL45	mitochondrial ribosomal protein l45
MRPL47	mitochondrial ribosomal protein l47
MRPL48	mitochondrial ribosomal protein l48
MRPL50	mitochondrial ribosomal protein l50
MRPL51	mitochondrial ribosomal protein l51
MRPL52	mitochondrial ribosomal protein l52
MRPL54	mitochondrial ribosomal protein l54
MRPL9	mitochondrial ribosomal protein l9
MRPS10	mitochondrial ribosomal protein s10
MRPS11	hypothetical protein flj22512
MRPS12	mitochondrial ribosomal protein s12
MRPS15	mitochondrial ribosomal protein s15
MRPS17	mitochondrial ribosomal protein s17
MRPS18A	mitochondrial ribosomal protein s18a
MRPS18B	mitochondrial ribosomal protein s18b
MRPS18C	mitochondrial ribosomal protein s18c
MRPS2	mitochondrial ribosomal protein s2
MRPS21	mitochondrial ribosomal protein s21
MRPS25	mitochondrial ribosomal protein s25

---

---

MRPS26	mitochondrial ribosomal protein s26
MRPS27	mitochondrial ribosomal protein s27
MRPS28	mitochondrial ribosomal protein s28
MRPS30	mitochondrial ribosomal protein s30
MRPS34	mitochondrial ribosomal protein s34
MRPS35	mitochondrial ribosomal protein s35
MRPS5	mitochondrial ribosomal protein s5
MRPS6	mitochondrial ribosomal protein s6
MRPS7	mitochondrial ribosomal protein s7
MRPS9	mitochondrial ribosomal protein s9
MRRF	mitochondrial ribosome recycling factor
MRS2L	mrs2-like, magnesium homeostasis factor (s. cerevisiae)
MSH2	mutS homolog 2, colon cancer, nonpolyposis type 1 (e. coli)
MSI1	musashi homolog 1 (drosophila)
MSI2	musashi homolog 2 (drosophila)
MSL3L1	male-specific lethal 3-like 1 (drosophila)
MSN	moesin
MSRA	methionine sulfoxide reductase a
MSRB2	methionine sulfoxide reductase b2
MSX2	msh homeobox homolog 2 (drosophila)
MT	malonyl-coa:acyl carrier protein transacylase, mitochondrial
MT1A	metallothionein 1a (functional)
MT1X	metallothionein 1x
MT2A	metallothionein 2a
MTA1	metastasis associated 1
MTA2	metastasis associated 1 family, member 2
MTA3	metastasis associated 1 family, member 3
MTAP	methylthioadenosine phosphorylase
MTDH	metadherin
MTERFD1	mtorf domain containing 1
MTFMT	mitochondrial methionyl-trna formyltransferase
MTFR1	mitochondrial fission regulator 1
MTG1	mitochondrial gtpase 1 homolog (s. cerevisiae)
MTHFD1	methylenetetrahydrofolate dehydrogenase (nadp+ dependent) 1, methenyltetrahydrofolate cyclohydrolase, formyltetrahydrofolate synthetase
MTHFD1L	methylenetetrahydrofolate dehydrogenase (nadp+ dependent) 1-like
MTHFD2	methylenetetrahydrofolate dehydrogenase (nadp+ dependent) 2, methenyltetrahydrofolate cyclohydrolase
MTIF2	mitochondrial translational initiation factor 2
MTIF3	mitochondrial translational initiation factor 3
MTMR12	myotubularin related protein 12
MTMR2	myotubularin related protein 2
MTP18	mitochondrial protein 18 kda
MTR	5-methyltetrahydrofolate-homocysteine methyltransferase
MTRF1L	mitochondrial translational release factor 1-like
MTRR	5-methyltetrahydrofolate-homocysteine methyltransferase reductase
MULK	multiple substrate lipid kinase
MUTED	muted homolog (mouse)
MVK	mevalonate kinase (mevalonic aciduria)
MXRA7	flj46603 protein
MYB	v-myb myeloblastosis viral oncogene homolog (avian)
MYBBP1A	myb binding protein (p160) 1a
MYC	v-myc myelocytomatosis viral oncogene homolog (avian)
MYD88	myeloid differentiation primary response gene (88)
MYLIP	myosin regulatory light chain interacting protein
MYO10	myosin x
MYO1B	myosin ib
MYO5A	myosin va (heavy polypeptide 12, myoxin)
MYOHD1	myosin head domain containing 1
MYOZ3	myozenin 3
NACA	nascent-polypeptide-associated complex alpha polypeptide
NAGPA	n-acetylglucosamine-1-phosphodiester alpha-n-acetylglucosaminidase
NANS	n-acetylneuraminic acid synthase (sialic acid synthase)
NAP1L1	nucleosome assembly protein 1-like 1
NAP1L4	nucleosome assembly protein 1-like 4
NAPG	n-ethylmaleimide-sensitive factor attachment protein, gamma
NARF	nuclear prelamin a recognition factor
NARG1	nmda receptor regulated 1
NARS	asparaginyl-trna synthetase
NARS2	asparaginyl-trna synthetase 2 (mitochondrial)(putative)
NAT10	n-acetyltransferase 10
NBN	nibrin
NCBP1	nuclear cap binding protein subunit 1, 80kda
NCDN	neurochondrin
NCK2	nck adaptor protein 2
NCL	nucleolin
NCOA4	nuclear receptor coactivator 4
NDIFP2	nedd4 family interacting protein 2
NDN	necdin homolog (mouse)
NDUFA10	nadh dehydrogenase (ubiquinone) 1 alpha subcomplex, 10, 42kda
NDUFA11	nadh dehydrogenase (ubiquinone) 1 alpha subcomplex, 11, 14.7kda
NDUFA12	nadh dehydrogenase (ubiquinone) 1 alpha subcomplex, 12
NDUFA5	nadh dehydrogenase (ubiquinone) 1 alpha subcomplex, 5, 13kda
NDUFA8	nadh dehydrogenase (ubiquinone) 1 alpha subcomplex, 8, 19kda
NDUFA9	nadh dehydrogenase (ubiquinone) 1 alpha subcomplex, 9, 39kda
NDUFAB1	nadh dehydrogenase (ubiquinone) 1, alpha/beta subcomplex, 1, 8kda
NDUFB3	nadh dehydrogenase (ubiquinone) 1 beta subcomplex, 3, 12kda
NDUFB7	nadh dehydrogenase (ubiquinone) 1 beta subcomplex, 7, 18kda
NDUFB9	nadh dehydrogenase (ubiquinone) 1 beta subcomplex, 9, 22kda
NDUFC1	nadh dehydrogenase (ubiquinone) 1, subcomplex unknown, 1, 6kda
NDUFS3	nadh dehydrogenase (ubiquinone) fe-s protein 3, 30kda (nadh-coenzyme q reductase)
NDUFS4	nadh dehydrogenase (ubiquinone) fe-s protein 4, 18kda (nadh-coenzyme q reductase)
NDUFS6	nadh dehydrogenase (ubiquinone) fe-s protein 6, 13kda (nadh-coenzyme q reductase)

---

---

NDUFS7	nadh dehydrogenase (ubiquinone) fe-s protein 7, 20kda (nadh-coenzyme q reductase)
NDUF58	nadh dehydrogenase (ubiquinone) fe-s protein 8, 23kda (nadh-coenzyme q reductase)
NDUFV1	nadh dehydrogenase (ubiquinone) flavoprotein 1, 51kda
NDUFV2	nadh dehydrogenase (ubiquinone) flavoprotein 2, 24kda
NDUFV3	nadh dehydrogenase (ubiquinone) flavoprotein 3, 10kda
NECAP2	necap endocytosis associated 2
NEF3	neurofilament 3 (150kda medium)
NEFH	neurofilament, heavy polypeptide 200kda
NEFL	neurofilament, light polypeptide 68kda
NEIL2	hypothetical protein mgc2832
NEIL3	nei endonuclease viii-like 3 (e. coli)
NEK1	nima (never in mitosis gene a)-related kinase 1
NEK2	nima (never in mitosis gene a)-related kinase 2
NELL1	nel-like 1 (chicken)
NET1	neuroepithelial cell transforming gene 1
NETO2	hypothetical protein flj10430
NEUROG3	neurogenin 3
NFATC3	nuclear factor of activated t-cells, cytoplasmic, calcineurin-dependent 3
NFE2L3	nuclear factor (erythroid-derived 2)-like 3
NFIC	nuclear factor i/c (ccat-binding transcription factor)
NFIX	nuclear factor i/x (ccat-binding transcription factor)
NFKB1	nuclear factor of kappa light polypeptide gene enhancer in b-cells 1 (p105)
NFKBIB	nuclear factor of kappa light polypeptide gene enhancer in b-cells inhibitor, beta
NFX1	nuclear transcription factor, x-box binding 1
NFXL1	nuclear transcription factor, x-box binding-like 1
NFYC	nuclear transcription factor y, gamma
NHLRC2	hypothetical protein flj20147
NHN1	conserved nuclear protein nhn1
NHP2L1	nhp2 non-histone chromosome protein 2-like 1 (s. cerevisiae)
NID1	nidogen 1
NIF3LBP1	ngg1 interacting factor 3 like 1 binding protein 1
NIFUN	nifu-like n-terminal domain containing
NIN	ninein (gsk3b interacting protein)
NIP7	nuclear import 7 homolog (s. cerevisiae)
NIPA2	non imprinted in prader-willi/angelman syndrome 2
NTT2	nitrilase family, member 2
NKAP	nf-kappab activating protein
NKD1	naked cuticle homolog 1 (drosophila)
NLE1	notchless homolog 1 (drosophila)
NLN	neurolysin (metallopeptidase m3 family)
NMD3	nmd3 homolog (s. cerevisiae)
NME1	non-metastatic cells 1, protein (nm23a) expressed in
NME1-NME2	nme1-nme2 protein
NME4	non-metastatic cells 4, protein expressed in
NME7	non-metastatic cells 7, protein expressed in (nucleoside-diphosphate kinase)
NMNAT2	nicotinamide nucleotide adenyltransferase 2
NMT1	n-myristoyltransferase 1
NMU	neuromedin u
NNAT	neuronatin
NNT	nicotinamide nucleotide transhydrogenase
NOC2L	nucleolar complex associated 2 homolog (s. cerevisiae)
NOC3L	nucleolar complex associated 3 homolog (s. cerevisiae)
NOC4L	nucleolar complex associated 4 homolog (s. cerevisiae)
NOL1	nucleolar protein 1, 120kda
NOL11	nucleolar protein 11
NOL4	nucleolar protein 4
NOL5A	nucleolar protein 5a (56kda with kke/d repeat)
NOL6	nucleolar protein family 6 (rna-associated)
NOL7	nucleolar protein 7, 27kda
NOLA1	nucleolar protein family a, member 1 (h/aca small nucleolar mps)
NOLA2	nucleolar protein family a, member 2 (h/aca small nucleolar mps)
NOLA3	nucleolar protein family a, member 3 (h/aca small nucleolar mps)
NOLC1	nucleolar and coiled-body phosphoprotein 1
NOP5/NOP58	hypothetical protein hspc120
NOSIP	nitric oxide synthase interacting protein
NP	ortholog of mouse neuropoietin (pseudogene in humans)
N-PAC	uncharacterized bone marrow protein bm045
NPFFR2	neuropeptide g protein-coupled receptor; neuropeptide ff 2
NPL	n-acetylneuraminate pyruvate lyase (dihydrodipicolinate synthase)
NPM1	nucleophosmin (nucleolar phosphoprotein b23, numatrin)
NPY	neuropeptide y
NQO1	nad(p)h dehydrogenase, quinone 1
NQO2	nad(p)h dehydrogenase, quinone 2
NR2C2	nuclear receptor subfamily 2, group c, member 2
NRBF2	nuclear receptor binding factor 2
NRCAM	neuronal cell adhesion molecule
NRD1	nardilysin (n-arginine dibasic convertase)
NS4ATP2	ns4atp2
NSDHL	nad(p) dependent steroid dehydrogenase-like
NSF	n-ethylmaleimide-sensitive factor
NSMAF	neutral sphingomyelinase (n-smase) activation associated factor
NSMCE1	non-smc element 1 homolog (s. cerevisiae)
NSUN2	nol1/nop2/sun domain family, member 2
NSUN6	nol1/nop2/sun domain family, member 6
NT5C3	5'-nucleotidase, cytosolic iii
NT5C3L	5'-nucleotidase, cytosolic iii-like
NT5DC2	5'-nucleotidase domain containing 2
NT5DC3	5'-nucleotidase domain containing 3
NTHL1	nth endonuclease iii-like 1 (e. coli)
NUBP1	nucleotide binding protein 1 (mind homolog, e. coli)
NUBPL	nucleotide binding protein-like

---

NUCKS1	nuclear casein kinase and cyclin-dependent kinase substrate 1
NUDC	nuclear distribution gene c homolog (a. nidulans)
NUDCD2	nudc domain containing 2
NUDT1	nudix (nucleoside diphosphate linked moiety x)-type motif 1
NUDT11	nudix (nucleoside diphosphate linked moiety x)-type motif 11
NUDT15	nudix (nucleoside diphosphate linked moiety x)-type motif 15
NUDT16	nudix (nucleoside diphosphate linked moiety x)-type motif 16
NUDT18	nudix (nucleoside diphosphate linked moiety x)-type motif 18
NUDT21	nudix (nucleoside diphosphate linked moiety x)-type motif 21
NUDT3	diphosphoinositol polyphosphate phosphohydrolase
NUDT5	nudix (nucleoside diphosphate linked moiety x)-type motif 5
NUDT6	nudix (nucleoside diphosphate linked moiety x)-type motif 6
NUDT8	nudix (nucleoside diphosphate linked moiety x)-type motif 8
NUP107	nucleoporin 107kda
NUP155	nucleoporin 155kda
NUP160	nucleoporin 160kda
NUP188	nucleoporin 188kda
NUP210	nucleoporin 210kda
NUP37	nucleoporin 37kda
NUP43	nucleoporin 43kda
NUP50	nucleoporin 50kda
NUP54	nucleoporin 54kda
NUP85	nucleoporin 85kda
NUP88	nucleoporin 88kda
NUP93	nucleoporin 93kda
NUP98	nucleoporin 98kda
NUTF2	nuclear transport factor 2
NXT2	nuclear transport factor 2-like export factor 2
OAF	oaf homolog (drosophila)
OAS3	2'-5'-oligoadenylate synthetase 3, 100kda
OAT	ornithine aminotransferase (gyrate atrophy)
OBFC1	oligonucleotide/oligosaccharide-binding fold containing 1
OBFC2A	oligonucleotide/oligosaccharide-binding fold containing 2a
OBFC2B	oligonucleotide/oligosaccharide-binding fold containing 2b
OCA2	oculocutaneous albinism ii (pink-eye dilution homolog, mouse)
ODC1	ornithine decarboxylase 1
ODF2	outer dense fiber of sperm tails 2
OCFOD1	2-oxoglutarate and iron-dependent oxygenase domain containing 1
OGFR	opioid growth factor receptor
OIP5	opa interacting protein 5
OLFM1	olfactomedin 1
OLFML3	olfactomedin-like 3
OMA1	oma1 homolog, zinc metallopeptidase (s. cerevisiae)
OPA1	optic atrophy 1 (autosomal dominant)
OPRS1	opioid receptor, sigma 1
ORAOV1	oral cancer overexpressed 1
ORC1L	origin recognition complex, subunit 1-like (yeast)
ORC3L	origin recognition complex, subunit 3-like (yeast)
ORC6L	origin recognition complex, subunit 6 homolog-like (yeast)
OSGEP	o-sialoglycoprotein endopeptidase
OSRF	osmosis responsive factor
OTUB2	otu domain, ubiquitin aldehyde binding 2
OXA1L	oxidase (cytochrome c) assembly 1-like
OXCT2	3-oxoacid coa transferase 2
OXSRI	oxidative-stress responsive 1
P15RS	hypothetical protein flj10656
P4HA1	procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide i
P4HB	procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), beta polypeptide
PA2G4	proliferation-associated 2g4, 38kda
PABPC1	poly(a) binding protein, cytoplasmic 2
PABPC4	poly(a) binding protein, cytoplasmic 4 (inducible form)
PAFAH1B2	platelet-activating factor acetylhydrolase, isoform ib, beta subunit 30kda
PAICS	phosphoribosylaminoimidazole carboxylase, phosphoribosylaminoimidazole succinocarboxamide synthetase
PAK1IP1	pak1 interacting protein 1
PAK4	p21(cdkn1a)-activated kinase 4
PAK7	p21(cdkn1a)-activated kinase 7
PANK1	pantothenate kinase 1
PAPD1	pap associated domain containing 1
PAPOLA	poly(a) polymerase alpha
PAPSS1	3'-phosphoadenosine 5'-phosphosulfate synthase 1
PAPSS2	3'-phosphoadenosine 5'-phosphosulfate synthase 2
PAQR3	progesterin and adiponectin receptor family member iii
PAQR8	progesterin and adiponectin receptor family member viii
PARK7	parkinson disease (autosomal recessive, early onset) 7
PARP4	poly (adp-ribose) polymerase family, member 4
PARVB	parvin, beta
PAXIP1	pax interacting (with transcription-activation domain) protein 1
PBEF1	pre-b-cell colony enhancing factor 1
PBK	pdz binding kinase
PCAF	p300/cbp-associated factor
PCBF1	poly(rc) binding protein 1
PCBF3	poly(rc) binding protein 3
PCCA	propionyl coenzyme a carboxylase, alpha polypeptide
PCCB	propionyl coenzyme a carboxylase, beta polypeptide
PCDH17	protocadherin 17
PCDH18	protocadherin 18
PCGF1	polycomb group ring finger 1
PCGF6	polycomb group ring finger 6
PCK2	phosphoenolpyruvate carboxykinase 2 (mitochondrial)
PCNA	proliferating cell nuclear antigen
PCNXL2	pecanex-like 2 (drosophila)

---

PCSK7	proprotein convertase subtilisin/kexin type 7
PCTP	phosphatidylcholine transfer protein
PCYT1B	phosphate cytidylyltransferase 1, choline, beta
PDCD11	programmed cell death 11
PDCD2	programmed cell death 2
PDCD4	programmed cell death 4 (neoplastic transformation inhibitor)
PDCD7	programmed cell death 7
PDCD8	programmed cell death 8 (apoptosis-inducing factor)
PDCL3	phosducin-like 3
PDE2A	phosphodiesterase 2a, cgmp-stimulated
PDE3B	phosphodiesterase 3b, cgmp-inhibited
PDE4D	phosphodiesterase 4d, camp-specific (phosphodiesterase e3 dunce homolog, drosophila)
PDE7B	phosphodiesterase 7b
PDF	peptide deformylase-like protein
PDGFRB	platelet-derived growth factor receptor, beta polypeptide
PDHA1	pyruvate dehydrogenase (lipoamide) alpha 1
PDHX	pyruvate dehydrogenase complex, component x
PDIA5	protein disulfide isomerase family a, member 5
PDIA6	protein disulfide isomerase family a, member 6
PK3	pyruvate dehydrogenase kinase, isozyme 3
PDLM1	pdz and lim domain 1 (elfin)
PDLM4	pdz and lim domain 4
PDSS1	prenyl (decaprenyl) diphosphate synthase, subunit 1
PDXP	pyridoxal (pyridoxine, vitamin b6) phosphatase
PDZD8	pdz domain containing 8
PEBP1	phosphatidylethanolamine binding protein 1
PECI	peroxisomal d3,d2-enoyl-coa isomerase
PECR	peroxisomal trans-2-enoyl-coa reductase
PEF1	pef protein with a long n-terminal hydrophobic domain
PEMT	phosphatidylethanolamine n-methyltransferase
PEO1	progressive external ophthalmoplegia 1
PEPD	peptidase d
PER2	period homolog 2 (drosophila)
PES1	pescadillo homolog 1, containing brct domain (zebrafish)
PET112L	pet112-like (yeast)
PEX13	peroxisome biogenesis factor 13
PEX26	peroxisome biogenesis factor 26
PFA5	phosphoribosylformylglycinamide synthase (figar amidotransferase)
PFDN1	prefoldin subunit 1
PFDN2	prefoldin subunit 2
PFKFB3	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3
PFKM	phosphofructokinase, muscle
PFKP	phosphofructokinase, platelet
PFN1	profilin 1
PFN2	profilin 2
Pfs2	dna replication complex gins protein psf2
PGAM1	phosphoglycerate mutase 1 (brain)
PGAM4	phosphoglycerate mutase family member 4
PGBD3	excision repair cross-complementing rodent repair deficiency, complementation group 6
PGK1	phosphoglycerate kinase 1
PGM1	phosphoglucomutase 1
PGM2	phosphoglucomutase 2
PHACTR1	kiaa1733 protein
PHACTR3	phosphatase and actin regulator 3
PHB	prohibitin
PHF16	phd finger protein 16
PHF17	phd finger protein 17
PHF19	phd finger protein 19
PHF20L1	phd finger protein 20-like 1
PHF22	phd finger protein 22
PHGDHL1	phosphoglycerate dehydrogenase like 1
PHKA1	phosphorylase kinase, alpha 1 (muscle)
PHKB	phosphorylase kinase, beta
PHTF2	putative homeodomain transcription factor 2
PHYH2	phytanoyl-coa 2-hydroxylase 2
PHYHIPL	phytanoyl-coa 2-hydroxylase interacting protein-like
PI4K2B	phosphatidylinositol 4-kinase type 2 beta
PIAS2	protein inhibitor of activated stat, 2
PIGA	phosphatidylinositol glycan, class a (paroxysmal nocturnal hemoglobinuria)
PIGH	phosphatidylinositol glycan, class h
PICK	phosphatidylinositol glycan, class k
PIGW	phosphatidylinositol glycan, class w
PIK3C3	phosphoinositide-3-kinase, class 3
PIM3	pim-3 oncogene
PINX1	pin2-interacting protein 1
PIR	pirin (iron-binding nuclear protein)
PITPNC1	phosphatidylinositol transfer protein, cytoplasmic 1
PIWIL1	piwi-like 1 (drosophila)
PKM2	pyruvate kinase, muscle
PKMYT1	protein kinase, membrane associated tyrosine/threonine 1
PKN1	protein kinase n1
PKP2	plakophilin 2
PKP4	plakophilin 4
PLAA	phospholipase a2-activating protein
PLAGL2	pleiomorphic adenoma gene-like 2
PLCL2	phospholipase c-like 2
PLEKHC1	pleckstrin homology domain containing, family c (with ferm domain) member 1
PLEKHJ1	pleckstrin homology domain containing, family j member 1
PLEKHK1	pleckstrin homology domain containing, family k member 1
PLEKHO1	pleckstrin homology domain containing, family o member 1
PLK4	polo-like kinase 4 (drosophila)

---

---

PLOD3	procollagen-lysine, 2-oxoglutarate 5-dioxygenase 3
PLP2	proteolipid protein 2 (colonic epithelium-enriched)
PLRG1	pleiotropic regulator 1 (prl1 homolog, arabidopsis)
PLS1	plastin 1 (i isoform)
PLS3	plastin 3 (t isoform)
PMF1	polyamine-modulated factor 1
PMM2	phosphomannomutase 2
PMP22	peripheral myelin protein 22
PMPCA	peptidase (mitochondrial processing) alpha
PMPCB	peptidase (mitochondrial processing) beta
PMVK	phosphomevalonate kinase
PNKD	paroxysmal nonkinesigenic dyskinesia
PNMT	phenylethanolamine n-methyltransferase
PNPO	pyridoxine 5'-phosphate oxidase
PNPT1	polyribonucleotide nucleotidyltransferase 1
PNRC2	proline-rich nuclear receptor coactivator 2
PODXL	podocalyxin-like
PODXL2	podocalyxin-like 2
POLA2	polymerase (dna directed), alpha 2 (70kd subunit)
POLD2	polymerase (dna directed), delta 2, regulatory subunit 50kda
POLDIP2	polymerase (dna-directed), delta interacting protein 2
POLE2	polymerase (dna directed), epsilon 2 (p59 subunit)
POLE3	polymerase (dna directed), epsilon 3 (p17 subunit)
POLE4	polymerase (dna-directed), epsilon 4 (p12 subunit)
POLM	polymerase (dna directed), mu
POLR1B	similar to dna-directed rna polymerase i (135 kda)
POLR1C	polymerase (rna) i polypeptide c, 30kda
POLR1D	polymerase (rna) i polypeptide d, 16kda
POLR2C	polymerase (rna) ii (dna directed) polypeptide c, 33kda
POLR2D	polymerase (rna) ii (dna directed) polypeptide d, 44kda
POLR2E	polymerase (rna) ii (dna directed) polypeptide e, 25kda
POLR2F	polymerase (rna) ii (dna directed) polypeptide f
POLR2H	polymerase (rna) ii (dna directed) polypeptide h
POLR2I	polymerase (rna) ii (dna directed) polypeptide i, 14.5kda
POLR3A	polymerase (rna) iii (dna directed) polypeptide a, 155kda
POLR3B	polymerase (rna) iii (dna directed) polypeptide b
POLR3D	polymerase (rna) iii (dna directed) polypeptide d, 44kda
POLR3E	polymerase (rna) iii (dna directed) polypeptide e (80kd)
POLR3F	polymerase (rna) iii (dna directed) polypeptide f, 39 kda
POLR3K	polymerase (rna) iii (dna directed) polypeptide k, 12.3 kda
POLRMT	polymerase (rna) mitochondrial (dna directed)
PON2	paraoxonase 2
POP1	processing of precursor 1, ribonuclease p/mrp subunit (s. cerevisiae)
POP7	processing of precursor 7, ribonuclease p subunit (s. cerevisiae)
POPDC2	popeye domain containing 2
POPDC3	popeye domain containing 3
POU3F2	pou domain, class 3, transcription factor 2
PPA1	pyrophosphatase (inorganic) 1
PPA2	pyrophosphatase (inorganic) 2
PPAN	peter pan homolog (drosophila)
PPAP2B	phosphatidic acid phosphatase type 2b
PPAPDC2	phosphatidic acid phosphatase type 2 domain containing 2
PPARB	ppar binding protein
PPAT	phosphoribosyl pyrophosphate amidotransferase
PPEF1	protein phosphatase, ef-hand calcium binding domain 1
PPFIBP1	ptprf interacting protein, binding protein 1 (liprin beta 1)
PPFIBP2	ptprf interacting protein, binding protein 2 (liprin beta 2)
PPHLN1	hypothetical protein hspc206
PPIAL4	peptidylprolyl isomerase a (cyclophilin a)-like 4
PPID	peptidylprolyl isomerase d (cyclophilin d)
PPIE	peptidylprolyl isomerase e (cyclophilin e)
PPIH	peptidylprolyl isomerase h (cyclophilin h)
PPIL1	peptidylprolyl isomerase (cyclophilin)-like 1
PPIL5	peptidylprolyl isomerase (cyclophilin)-like 5
PPM1D	protein phosphatase 1d magnesium-dependent, delta isoform
PPM1F	protein phosphatase 1f (pp2c domain containing)
PPM1G	protein phosphatase 1g (formerly 2c), magnesium-dependent, gamma isoform
PPP1CA	protein phosphatase 1, catalytic subunit, alpha isoform
PPP1CB	protein phosphatase 1, catalytic subunit, beta isoform
PPP1CC	protein phosphatase 1, catalytic subunit, gamma isoform
PPP1R14A	protein phosphatase 1, regulatory (inhibitor) subunit 14a
PPP1R7	protein phosphatase 1, regulatory subunit 7
PPP1R8	protein phosphatase 1, regulatory (inhibitor) subunit 8
PPP1R9B	protein phosphatase 1, regulatory subunit 9b, spinophilin
PPP2CA	protein phosphatase 2 (formerly 2a), catalytic subunit, alpha isoform
PPP2R2B	protein phosphatase 2 (formerly 2a), regulatory subunit b (pr 52), beta isoform
PPP2R2D	protein phosphatase 2, regulatory subunit b, delta isoform
PPP2R3B	protein phosphatase 2 (formerly 2a), regulatory subunit b'', beta
PPP2R4	protein phosphatase 2a, regulatory subunit b' (pr 53)
PPP2R5C	protein phosphatase 2, regulatory subunit b (b56), gamma isoform
PPP2R5D	protein phosphatase 2, regulatory subunit b (b56), delta isoform
PPP4R2	protein phosphatase 4, regulatory subunit 2
PPP6C	protein phosphatase 6, catalytic subunit
PPRC1	peroxisome proliferative activated receptor, gamma, coactivator-related 1
PPT1	palmitoyl-protein thioesterase 1 (ceroid-lipofuscinosis, neuronal 1, infantile)
PQBPI	polyglutamine binding protein 1
PRAME	melanoma antigen preferentially expressed in tumors
PRC1	protein regulator of cytokinesis 1
PRDM8	pr domain containing 8
PRDX1	peroxiredoxin 1
PRDX3	peroxiredoxin 3

---



---

PRDX4	peroxiredoxin 4
PRDX6	peroxiredoxin 6
PREI3	preimplantation protein 3
PREP	prolyl endopeptidase
PRKAR1B	protein kinase, camp-dependent, regulatory, type i, beta
PRKAR2A	protein kinase, camp-dependent, regulatory, type ii, alpha
PRKCA	protein kinase c, alpha
PRKCD	protein kinase c, delta
PRKCI	protein kinase c, iota
PRKCQ	protein kinase c, theta
PRKCZ	protein kinase c, zeta
PRKDC	protein kinase, dna-activated, catalytic polypeptide
PRKX	protein kinase, x-linked
PRMT1	protein arginine methyltransferase 1
PRMT3	protein arginine methyltransferase 3
PRMT5	protein arginine methyltransferase 5
PRMT6	protein arginine methyltransferase 6
PRMT7	protein arginine methyltransferase 7
PRNPIP	prion protein interacting protein
PRO1853	hypothetical protein pro1853
PROM1	prominin 1
PRPF18	prp18 pre-mrna processing factor 18 homolog (yeast)
PRPF19	prp19/psa4 pre-mrna processing factor 19 homolog (s. cerevisiae)
PRPF38A	prp38 pre-mrna processing factor 38 (yeast) domain containing a
PRPF8	prp8 pre-mrna processing factor 8 homolog (yeast)
PRPS1, PRPS2	phosphoribosyl pyrophosphate synthetase 1
PRR11	proline rich 11
PRR5	rho gtpase activating protein 8
PRR6	proline rich 6
PRRX2	paired related homeobox 2
PRSS23	protease, serine, 23
PRSS35	protease, serine, 35
PSAT1	phosphoserine aminotransferase 1
PSCD1	pleckstrin homology, sec7 and coiled-coil domains 1(cytohesin 1)
PSD3	pleckstrin and sec7 domain containing 3
PSIP1	pc4 and sfrs1 interacting protein 1
PSMA1	proteasome (prosome, macropain) subunit, alpha type, 1
PSMA2	proteasome (prosome, macropain) subunit, alpha type, 2
PSMA3	proteasome (prosome, macropain) subunit, alpha type, 3
PSMA4	proteasome (prosome, macropain) subunit, alpha type, 4
PSMA5	proteasome (prosome, macropain) subunit, alpha type, 5
PSMA6	proteasome (prosome, macropain) subunit, alpha type, 6
PSMA7	proteasome (prosome, macropain) subunit, alpha type, 7
PSMB3	proteasome (prosome, macropain) subunit, beta type, 3
PSMB5	proteasome (prosome, macropain) subunit, beta type, 5
PSMB6	proteasome (prosome, macropain) subunit, beta type, 6
PSMB7	proteasome (prosome, macropain) subunit, beta type, 7
PSMC2	proteasome (prosome, macropain) 26s subunit, atpase, 2
PSMC3	proteasome (prosome, macropain) 26s subunit, atpase, 3
PSMC4	proteasome (prosome, macropain) 26s subunit, atpase, 4
PSMC5	proteasome (prosome, macropain) 26s subunit, atpase, 5
PSMD11	proteasome (prosome, macropain) 26s subunit, non-atpase, 11
PSMD13	proteasome (prosome, macropain) 26s subunit, non-atpase, 13
PSMD14	proteasome (prosome, macropain) 26s subunit, non-atpase, 14
PSMD3	proteasome (prosome, macropain) 26s subunit, non-atpase, 3
PSMD5	proteasome (prosome, macropain) 26s subunit, non-atpase, 5
PSMD6	proteasome (prosome, macropain) 26s subunit, non-atpase, 6
PSMD8	proteasome (prosome, macropain) 26s subunit, non-atpase, 8
PSME3	proteasome (prosome, macropain) activator subunit 3 (pa28 gamma; ki)
PSME4	proteasome (prosome, macropain) activator subunit 4
PSPC1	paraspeckle component 1
PSRC1	proline/serine-rich coiled-coil 1
PTD015	ptd015 protein
PTDSS1	phosphatidylserine synthase 1
PTEN	phosphatase and tensin homolog (mutated in multiple advanced cancers 1)
PTGES	prostaglandin e synthase
PTGES2	prostaglandin e synthase 2
PTGES3	prostaglandin e synthase 3 (cytosolic)
PTGFRN	prostaglandin f2 receptor negative regulator
PTK9L	ptk9l protein tyrosine kinase 9-like (a6-related protein)
PTMA	prothymosin, alpha (gene sequence 28)
PTMS	parathymosin
PTN	pleiotrophin (heparin binding growth factor 8, neurite growth-promoting factor 1)
PTP4A3	protein tyrosine phosphatase type iva, member 3
PTPLA	protein tyrosine phosphatase-like (proline instead of catalytic arginine), member a
PTPN2	protein tyrosine phosphatase, non-receptor type 2
PTPRO	protein tyrosine phosphatase, receptor type, o
PTPRU	protein tyrosine phosphatase, receptor type, u
PTRH1	peptidyl-trna hydrolase 1 homolog (s. cerevisiae)
PTRH2	peptidyl-trna hydrolase 2
PTS	6-pyruvoyltetrahydropterin synthase
PTTG1	pituitary tumor-transforming 1
PUS1	pseudouridylate synthase 1
PUS3	pseudouridylate synthase 3
PUSL1	pseudouridylate synthase-like 1
PVR	poliovirus receptor
PWP1	pwp1 homolog (s. cerevisiae)
PWWP2	pwwp domain containing 2
PX19	px19-like protein
PYCR1	pyrroline-5-carboxylate reductase 1
QIL1	qil1 protein

---

---

QTRTD1	queuine trna-ribosyltransferase domain containing 1
R3HDM1	r3h domain containing 1
RAB1B	rab1b, member ras oncogene family
RAB32	rab32, member ras oncogene family
RAB33A	rab33a, member ras oncogene family
RAB3C	rab3c, member ras oncogene family
RAB4A	rab4a, member ras oncogene family
RAB6A	rab6a, member ras oncogene family
RABEPK	rab9 effector protein with kelch motifs
RABGGTA	rab geranylgeranyltransferase, alpha subunit
RABGGTB	rab geranylgeranyltransferase, beta subunit
RABL2A	rab, member of ras oncogene family-like 2a
RABL3	rab, member of ras oncogene family-like 3
RAC2	ras-related c3 botulinum toxin substrate 2 (rho family, small gtp binding protein rac2)
RAC3	ras-related c3 botulinum toxin substrate 3 (rho family, small gtp binding protein rac3)
RAD23B	rad23 homolog b (s. cerevisiae)
RAD51	rad51 homolog (reca homolog, e. coli) (s. cerevisiae)
RAD51AP1	rad51 associated protein 1
RAD54B	fibrinogen silencer binding protein
RAF1	v-raf-1 murine leukemia viral oncogene homolog 1
RAI14	retinoic acid induced 14
RALBP1	rala binding protein 1
RALY	rna binding protein, autoantigenic (hnmp-associated with lethal yellow homolog (mouse))
RAMP3	receptor (calcitonin) activity modifying protein 3
RAN	ran, member ras oncogene family
RANBP1	ran binding protein 1
RANBP5	ran binding protein 5
RANGAP1	ran gtpase activating protein 1
RAP1GDS1	rap1, gtp-gdp dissociation stimulator 1
RAPGEF4	rap guanine nucleotide exchange factor (gef) 4
RARS	arginyl-trna synthetase
RASL11B	ras-like, family 11, member b
RASSF2	ras association (ralgds/af-6) domain family 2
RAVER2	hypothetical protein flj10770
RB1	retinoblastoma 1 (including osteosarcoma)
RBBP5	retinoblastoma binding protein 5
RBM13	rna binding motif protein 13
RBM14	rna binding motif protein 14
RBM15	rna binding motif protein 15
RBM18	rna binding motif protein 18
RBM28	rna binding motif protein 28
RBM3	rna binding motif (rnp1, rrm) protein 3
RBM34	rna binding motif protein 34
RBM4	rna binding motif protein 4
RBMX	rna binding motif protein, x-linked
RBMXL1	kynurenine aminotransferase iii
RBPMS2	rna binding protein with multiple splicing 2
RBPSUH	recombining binding protein suppressor of hairless (drosophila)
RBX1	ring-box 1
RC74	integrator complex subunit 9
RCC1	regulator of chromosome condensation 1
RCL1	rna terminal phosphate cyclase-like 1
RCN1	reticulocalbin 1, ef-hand calcium binding domain
RDBP	rd rna binding protein
RDX	radixin
KEEP4	receptor accessory protein 4
RELN	reelin
REP15	rab15 effector protein
RER1	rer1 retention in endoplasmic reticulum 1 homolog (s. cerevisiae)
REXO2	rex2, rna exonuclease 2 homolog (s. cerevisiae)
RFC2	replication factor c (activator 1) 2, 40kda
RFC3	replication factor c (activator 1) 3, 38kda
RFC5	replication factor c (activator 1) 5, 36.5kda
RFP	ret finger protein
RFWD3	ring finger and wd repeat domain 3
RFXAP	regulatory factor x-associated protein
RG9MTD1	rna (guanine-9-) methyltransferase domain containing 1
RGS10	regulator of g-protein signalling 10
RGS12	regulator of g-protein signalling 12
RGS19	regulator of g-protein signalling 19
RHBD3	rhomboid domain containing 3
RHBD2	rhomboid 5 homolog 2 (drosophila)
RHOA	ras homolog gene family, member a
RHOB	ras homolog gene family, member b
RHOBTB3	rho-related btb domain containing 3
RHOG	ras homolog gene family, member g (rho g)
RHOT1	ras homolog gene family, member t1
RIMS4	regulating synaptic membrane exocytosis 4
RIOK1	rio kinase 1 (yeast)
RIOK2	rio kinase 2 (yeast)
RIS1	ras-induced senescence 1
RKHD2	ring finger and kh domain containing 2
RLF	rearranged l-myc fusion
RNASEH2A	ribonuclease h2, large subunit
RND3	rho family gtpase 3
RNF10	ring finger protein 10
RNF113A	ring finger protein 113a
RNF126	ring finger protein 126
RNF13	ring finger protein 13
RNF130	ring finger protein 130
RNF165	chromosome 18 open reading frame 23

---

---

RNF26	ring finger protein 26
RNF8	ring finger protein 8
RNMTL1	rna methyltransferase like 1
RNU3IP2	rna, u3 small nucleolar interacting protein 2
RNUT1	rna, u transporter 1
RNUXA	rna u, small nuclear rna export adaptor (phosphorylation regulated)
ROBO1	roundabout, axon guidance receptor, homolog 1 (drosophila)
ROR2	receptor tyrosine kinase-like orphan receptor 2
RORB	rar-related orphan receptor b
RP11-19J3.3	hypothetical protein mgc88047
RP9	retinitis pigmentosa 9 (autosomal dominant)
RPA1	replication protein a1, 70kda
RPA3	replication protein a3, 14kda
RPE	ribulose-5-phosphate-3-epimerase
RPH3A	rabphilin 3a homolog (mouse)
RPIA	ribose 5-phosphate isomerase a (ribose 5-phosphate epimerase)
RPL10A	ribosomal protein l10a
RPL13	ribosomal protein l13
RPL13A	ribosomal protein l13a
RPL14	ribosomal protein l14
RPL19	ribosomal protein l19
RPL23A	ribosomal protein l23a
RPL26	ribosomal protein l26
RPL26L1	ribosomal protein l26-like 1
RPL27A	ribosomal protein l27a
RPL28	ribosomal protein l28
RPL29	ribosomal protein l29
RPL32	ribosomal protein l32
RPL34	ribosomal protein l34
RPL36	ribosomal protein l36
RPL37A	ribosomal protein l37a
RPL39L	ribosomal protein l39-like
RPL41	ribosomal protein l41
RPL6	ribosomal protein l6
RPL7	ribosomal protein l7
RPL7A	ribosomal protein l7a
RPL7L1	ribosomal protein l7-like 1
RPLP0	ribosomal protein, large, p0
RPLP1	ribosomal protein, large, p1
RPN2	ribophorin ii
RPP40	ribonuclease p 40kda subunit
RPS15	ribosomal protein s15
RPS17	ribosomal protein s17
RPS19BP1	ribosomal protein s19 binding protein 1
RPS21	ribosomal protein s21
RPS26	ribosomal protein s26
RPS29	ribosomal protein s29
RPS6KA2	ribosomal protein s6 kinase, 90kda, polypeptide 2
RPS6KB2	ribosomal protein s6 kinase, 70kda, polypeptide 2
RPS7	ribosomal protein s7
RPSA	ribosomal protein sa
RPUSD1	rna pseudouridylylate synthase domain containing 1
RPUSD2	rna pseudouridylylate synthase domain containing 2
RPUSD3	rna pseudouridylylate synthase domain containing 3
RPUSD4	rna pseudouridylylate synthase domain containing 4
RQCDC1	rcd1 required for cell differentiation1 homolog (s. pombe)
RRAS2	related ras viral (r-ras) oncogene homolog 2
RRM1	ribonucleotide reductase m1 polypeptide
RRM2	ribonucleotide reductase m2 polypeptide
RRS1	rrs1 ribosome biogenesis regulator homolog (s. cerevisiae)
RSAD1	radical s-adenosyl methionine domain containing 1
RSBN1L	round spermatid basic protein 1-like
RSL1D1	ribosomal l1 domain containing 1
RSU1	ras suppressor protein 1
RTCD1	rna terminal phosphate cyclase domain 1
RTN4IP1	reticulon 4 interacting protein 1
RUVBL1	ruvb-like 1 (e. coli)
RUVBL2	ruvb-like 2 (e. coli)
RWDD4A	rwd domain containing 4a
RXRA	retinoid x receptor, alpha
RYK	ryk receptor-like tyrosine kinase
S100A4	s100 calcium binding protein a4 (calcium protein, calvasculin, metastasin, murine placental homolog)
S100A6	s100 calcium binding protein a6 (calcyclin)
SAAL1	serum amyloid a-like 1
SAFB2	scaffold attachment factor b2
SALL4	sal-like 4 (drosophila)
SAMD11	sterile alpha motif domain containing 11
SAMD13	sterile alpha motif domain containing 13
SAMM50	sorting and assembly machinery component 50 homolog (s. cerevisiae)
SAP30	sin3a-associated protein, 30kda
SARIA	sar1 gene homolog a (s. cerevisiae)
SARS	seryl-trna synthetase
SARS2	seryl-trna synthetase 2
SAS10	disrupter of silencing 10
SATB1	special at-rich sequence binding protein 1 (binds to nuclear matrix/scaffold-associating dna's)
SAV1	salvador homolog 1 (drosophila)
SBD5	shwachman-bodian-diamond syndrome
SC65	synaptonemal complex protein sc65
SCAMP1	secretory carrier membrane protein 1
SCARB1	scavenger receptor class b, member 1
SCC-112	scc-112 protein

---

---

SCGN	secretagogin, ef-hand calcium binding protein
SCML2	sex comb on midleg-like 2 (drosophila)
SCNM1	sodium channel modifier 1
SCRIB	scribbled homolog (drosophila)
SCRT2	scratch homolog 2, zinc finger protein (drosophila)
SDC1	syndecan 1
SDC2	syndecan 2 (heparan sulfate proteoglycan 1, cell surface-associated, fibroglycan)
SDCCAG10	serologically defined colon cancer antigen 10
SDCCAG3	serologically defined colon cancer antigen 3
SDF2L1	stromal cell-derived factor 2-like 1
SDHA	succinate dehydrogenase complex, subunit a, flavoprotein (fp)
SDHB	succinate dehydrogenase complex, subunit b, iron sulfur (ip)
SDHD	succinate dehydrogenase complex, subunit d, integral membrane protein
SEC11L3	sec11-like 3 (s. cerevisiae)
SEC13L1	sec13-like 1 (s. cerevisiae)
SEC22L1	sec22 vesicle trafficking protein-like 1 (s. cerevisiae)
SEC22L2	sec22 vesicle trafficking protein-like 2 (s. cerevisiae)
SEC22L3	sec22 vesicle trafficking protein-like 3 (s. cerevisiae)
SEC24D	sec24 related gene family, member d (s. cerevisiae)
SEC61A1	sec61 alpha 1 subunit (s. cerevisiae)
SEC61B	sec61 beta subunit
SEC61G	sec61 gamma subunit
SEC63	sec63-like (s. cerevisiae)
SEH1L	seh1-like (s. cerevisiae)
SELI	selenoprotein i
SEMA3C	sema domain, immunoglobulin domain (ig), short basic domain, secreted, (semaphorin) 3c
SENP2	sumo1/sentrin/smt3 specific peptidase 2
SEPHS1	selenophosphate synthetase 1
SEPN1	selenoprotein n, 1
SEPW1	selenoprotein w, 1
SEPX1	selenoprotein x, 1
SERBP1	serpine1 mrna binding protein 1
SERF1B	small edrk-rich factor 1a (telomeric)
SERP1	stress-associated endoplasmic reticulum protein 1
SERPINA5	serpin peptidase inhibitor, clade a (alpha-1 antiproteinase, antitrypsin), member 5
SERPINB6	serpin peptidase inhibitor, clade b (ovalbumin), member 6
SERPINF1	serpin peptidase inhibitor, clade f (alpha-2 antiplasmin, pigment epithelium derived factor), member 1
SERTAD4	serta domain containing 4
SESN1	sestrin 1
SETD8	set domain containing (lysine methyltransferase) 8
SETMAR	set domain and mariner transposase fusion gene
SF1	splicing factor 1
SF3A3	splicing factor 3a, subunit 3, 60kda
SF3B14	splicing factor 3b, 14 kda subunit
SFPQ	splicing factor proline/glutamine-rich (polypyrimidine tract binding protein associated)
SFRP1	secreted frizzled-related protein 1
SFRS1	splicing factor, arginine/serine-rich 1 (splicing factor 2, alternate splicing factor)
SFRS10	splicing factor, arginine/serine-rich 10 (transformer 2 homolog, drosophila)
SFRS11	splicing factor, arginine/serine-rich 11
SFRS2	splicing factor, arginine/serine-rich 2
SFRS3	splicing factor, arginine/serine-rich 3
SFRS9	splicing factor, arginine/serine-rich 9
SFXN1	likely ortholog of mouse sideroflexin 1
SFXN2	sideroflexin 2
SFXN4	sideroflexin 4
SGK	serum/glucocorticoid regulated kinase
SGOL1	shugoshin-like 1 (s. pombe)
SGTA	small glutamine-rich tetratricopeptide repeat (tpr)-containing, alpha
SH2BP1	sh2 domain binding protein 1 (tetratricopeptide repeat containing)
SH3D19	sh3 domain protein d19
SH3PX3	sh3 and px domain containing 3
SH3PXD2B	hypothetical protein flj20831
SHB	src homology 2 domain containing adaptor protein b
SHFM1	split hand/foot malformation (ectrodactyly) type 1
SHMT2	serine hydroxymethyltransferase 2 (mitochondrial)
SIAH2	seven in absentia homolog 2 (drosophila)
SIL1	sil1 homolog, endoplasmic reticulum chaperone (s. cerevisiae)
SIP1	survival of motor neuron protein interacting protein 1
SITPEC	signaling intermediate in toll pathway, evolutionarily conserved
SIVA	cd27-binding (siva) protein
SIX3	sine oculis homeobox homolog 3 (drosophila)
SIX6	sine oculis homeobox homolog 6 (drosophila)
SKIV2L	superkiller viralicidic activity 2-like (s. cerevisiae)
SKIV2L2	superkiller viralicidic activity 2-like 2 (s. cerevisiae)
SKP2	s-phase kinase-associated protein 2 (p45)
SLC16A10	hypothetical protein pro0813
SLC16A9	solute carrier family 16 (monocarboxylic acid transporters), member 9
SLC1A5	solute carrier family 1 (neutral amino acid transporter), member 5
SLC20A2	solute carrier family 20 (phosphate transporter), member 2
SLC25A10	solute carrier family 25 (mitochondrial carrier; dicarboxylate transporter), member 10
SLC25A11	solute carrier family 25 (mitochondrial carrier; oxoglutarate carrier), member 11
SLC25A12	solute carrier family 25 (mitochondrial carrier, aralar), member 12
SLC25A13	solute carrier family 25, member 13 (citrin)
SLC25A15	solute carrier family 25 (mitochondrial carrier; ornithine transporter) member 15
SLC25A17	solute carrier family 25 (mitochondrial carrier; peroxisomal membrane protein, 34kda), member 17
SLC25A19	solute carrier family 25 (mitochondrial deoxynucleotide carrier), member 19
SLC25A23	solute carrier family 25 (mitochondrial carrier; phosphate carrier), member 23
SLC25A3	solute carrier family 25 (mitochondrial carrier; phosphate carrier), member 3
SLC25A37	solute carrier family 25, member 37
SLC25A5	solute carrier family 25 (mitochondrial carrier; adenine nucleotide translocator), member 5
SLC25A6	solute carrier family 25 (mitochondrial carrier; adenine nucleotide translocator), member 6

---

---

SLC27A2	fatty-acid-coenzyme a ligase, very long-chain 1
SLC29A1	solute carrier family 29 (nucleoside transporters), member 1
SLC29A3	solute carrier family 29 (nucleoside transporters), member 3
SLC2A1	solute carrier family 2 (facilitated glucose transporter), member 1
SLC2A6	solute carrier family 2 (facilitated glucose transporter), member 6
SLC30A1	solute carrier family 30 (zinc transporter), member 1
SLC35A4	solute carrier family 35, member a4
SLC35F2	solute carrier family 35, member f2
SLC35F3	solute carrier family 35, member f3
SLC36A4	solute carrier family 36 (proton/amino acid symporter), member 4
SLC39A10	solute carrier family 39 (zinc transporter), member 10
SLC39A11	solute carrier family 39 (metal ion transporter), member 11
SLC39A3	solute carrier family 39 (zinc transporter), member 3
SLC39A8	solute carrier family 39 (zinc transporter), member 8
SLC43A1	solute carrier family 43, member 1
SLC45A3	solute carrier family 45, member 3
SLC5A6	solute carrier family 5 (sodium-dependent vitamin transporter), member 6
SLC6A15	solute carrier family 6, member f5
SLC6A2	solute carrier family 6 (neurotransmitter transporter, noradrenalin), member 2
SLC7A14	solute carrier family 7 (cationic amino acid transporter, y+ system), member 14
SLC7A2	solute carrier family 7 (cationic amino acid transporter, y+ system), member 2
SLC7A5	solute carrier family 7 (cationic amino acid transporter, y+ system), member 5
SLC7A6	solute carrier family 7 (cationic amino acid transporter, y+ system), member 6
SLC8A3	solute carrier family 8 (sodium-calcium exchanger), member 3
SLC9A1	solute carrier family 9 (sodium/hydrogen exchanger), member 1 (antiporter, na+/h+, amiloride sensitive)
SLC9A3R1	solute carrier family 9 (sodium/hydrogen exchanger), member 3 regulator 1
SLC04A1	solute carrier organic anion transporter family, member 4a1
SMAD6	smad, mothers against dpp homolog 6 (drosophila)
SMAD7	smad, mothers against dpp homolog 7 (drosophila)
SMAD9	smad, mothers against dpp homolog 9 (drosophila)
SMAP1	stromal membrane-associated protein 1
SMARCA4	swi/snf related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4
SMARCA5	swi/snf related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 5
SMARCB1	swi/snf related, matrix associated, actin dependent regulator of chromatin, subfamily b, member 1
SMARCD1	swi/snf related, matrix associated, actin dependent regulator of chromatin, subfamily d, member 1
SMARCD2	swi/snf related, matrix associated, actin dependent regulator of chromatin, subfamily d, member 2
SMN1	survival of motor neuron 1, telomeric
SMNDC1	survival motor neuron domain containing 1
SMO	smoothened homolog (drosophila)
SMU1	smu-1 suppressor of mec-8 and unc-52 homolog (c. elegans)
SMUG1	single-strand-selective monofunctional uracil-dna glycosylase 1
SMYD2	set and mynd domain containing 2
SMYD3	set and mynd domain containing 3
SNAIL	snail homolog 1 (drosophila)
SNAIL2	snail homolog 2 (drosophila)
SNAP23	synaptosomal-associated protein, 23kda
SNAP91	synaptosomal-associated protein, 91kda homolog (mouse)
SNAPC3	small nuclear rna activating complex, polypeptide 3, 50kda
NDI1	staphylococcal nuclease domain containing 1
SNF8	snf8, escrt-ii complex subunit, homolog (s. cerevisiae)
SNRPA	small nuclear ribonucleoprotein polypeptide a
SNRPA1	small nuclear ribonucleoprotein polypeptide a'
SNRPB	small nuclear ribonucleoprotein polypeptides b and b1
SNRPB2	small nuclear ribonucleoprotein polypeptide b''
SNRPC	small nuclear ribonucleoprotein polypeptide c
SNRPD1	small nuclear ribonucleoprotein d1 polypeptide 16kda
SNRPD2	small nuclear ribonucleoprotein d2 polypeptide 16.5kda
SNRPF	small nuclear ribonucleoprotein polypeptide f
SNRPG	small nuclear ribonucleoprotein polypeptide g
SNX2	sorting nexin 2
SNX5	sorting nexin 5
SNX8	sorting nexin 8
SOD2	superoxide dismutase 2, mitochondrial
SOX11	sry (sex determining region y)-box 11
SOX13	sry (sex determining region y)-box 13
SOX7	sry (sex determining region y)-box 7
SP1	sp1 transcription factor
SPA17	sperm autoantigenic protein 17
SPAG5	sperm associated antigen 5
SPAG7	sperm associated antigen 7
SPATA5L1	spermatogenesis associated 5-like 1
SPATS2	spermatogenesis associated, serine-rich 2
SPBC25	spindle pole body component 25 homolog (s. cerevisiae)
SPCS2	signal peptidase complex subunit 2 homolog (s. cerevisiae)
SPCS3	signal peptidase complex subunit 3 homolog (s. cerevisiae)
SPFH2	spfh domain family, member 2
SPHAR	s-phase response (cyclin-related)
SPPL2A	signal peptide peptidase-like 2a
SPR	sepiapterin reductase (7,8-dihydrobiopterin:nadp+ oxidoreductase)
SPRY2	sprouty homolog 2 (drosophila)
SPTBN2	spectrin, beta, non-erythrocytic 2
SPTY2D1	spt2, suppressor of ty, domain containing 1 (s. cerevisiae)
SRC	v-src sarcoma (schmidt-ruppin a-2) viral oncogene homolog (avian)
SRCRB4D	scavenger receptor cysteine rich domain containing, group b (4 domains)
SRD5A1	steroid-5-alpha-reductase, alpha polypeptide 1 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 1)
SREBF2	sterol regulatory element binding transcription factor 2
SRFBP1	serum response factor binding protein 1
SRGAP1	slit-robo rho gtpase activating protein 1
SRI	sorcin
SRM	spermidine synthase
SRP19	signal recognition particle 19kda

---

SRP72	signal recognition particle 72kda
SRP9	signal recognition particle 9kda
SRPK1	sfrs protein kinase 1
SRPRB	signal recognition particle receptor, b subunit
SRRM1	serine/arginine repetitive matrix 1
SRrp35	serine-arginine repressor protein (35 kda)
SSI8	synovial sarcoma translocation, chromosome 18
SSI8L2	synovial sarcoma translocation gene on chromosome 18-like 2
SSB	sjogren syndrome antigen b (autoantigen la)
SSBP1	single-stranded dna binding protein 1
SSBP3	single stranded dna binding protein 3
SSBP4	hypothetical protein mgc3181
SSH2	slingshot homolog 2 (drosophila)
SSNA1	sjogren's syndrome nuclear autoantigen 1
SSR1	signal sequence receptor, alpha (translocon-associated protein alpha)
SSR2	signal sequence receptor, beta (translocon-associated protein beta)
SSRP1	structure specific recognition protein 1
SSSCA1	sjogren's syndrome/scleroderma autoantigen 1
SSTR2	somatostatin receptor 2
SSU72	ssu72 rna polymerase ii ctd phosphatase homolog (yeast)
ST3GAL5	st3 beta-galactoside alpha-2,3-sialyltransferase 5
ST3GAL6	st3 beta-galactoside alpha-2,3-sialyltransferase 6
ST6GAL1	st6 beta-galactosamide alpha-2,6-sialyltransferase 1
ST6GALNAC3	st6 (alpha-n-acetyl-neuraminy-2,3-beta-galactosyl-1,3)-n-acetylgalactosaminide alpha-2,6-sialyltransferase 3
ST6GALNAC5	st6 (alpha-n-acetyl-neuraminy-2,3-beta-galactosyl-1,3)-n-acetylgalactosaminide alpha-2,6-sialyltransferase 5
ST8SIA2	st8 alpha-n-acetyl-neuraminide alpha-2,8-sialyltransferase 2
ST8SIA3	st8 alpha-n-acetyl-neuraminide alpha-2,8-sialyltransferase 3
STAMPB	stam binding protein
STAMPB1	stam binding protein-like 1
STARD3NL	stard3 n-terminal like
STARD7	start domain containing 7
STAT1P1	signal transducer and activator of transcription 3 interacting protein 1
STAU2	staufen, rna binding protein, homolog 2 (drosophila)
STC2	stanniocalcin 2
STEAP1	six transmembrane epithelial antigen of the prostate 1
STEAP3	steap family member 3
STIP1	stress-induced-phosphoprotein 1 (hsp70/hsp90-organizing protein)
STK17B	serine/threonine kinase 17b (apoptosis-inducing)
STK32C	serine/threonine kinase 32c
STK39	serine threonine kinase 39 (ste20/sps1 homolog, yeast)
STMN1	stathmin 1/oncoprotein 18
STOM	stomatin
STOML2	stomatin (epb72)-like 2
STON1	stonin 1
STRA6	stimulated by retinoic acid gene 6 homolog (mouse)
STRAP	serine/threonine kinase receptor associated protein
STRBP	spermatid perinuclear rna binding protein
STRN3	striatin, calmodulin binding protein 3
STT3B	stt3, subunit of the oligosaccharyltransferase complex, homolog b (s. cerevisiae)
STX10	syntaxin 10
STX6	syntaxin 6
STX8	syntaxin 8
STXBP4	syntaxin binding protein 4
STXBP5	syntaxin binding protein 5 (tomosyn)
SUCLA2	succinate-coa ligase, adp-forming, beta subunit
SUCLG1	succinate-coa ligase, gdp-forming, alpha subunit
SUCLG2	succinate-coa ligase, gdp-forming, beta subunit
SUGT1	sgt1, suppressor of g2 allele of skp1 (s. cerevisiae)
SUHW3	suppressor of hairy wing homolog 3 (drosophila)
SUHW4	suppressor of hairy wing homolog 4 (drosophila)
SULT1A4	sulfotransferase family, cytosolic, 1a, phenol-preferring, member 3
SUMF2	sulfatase modifying factor 2
SUMO2	smt3 suppressor of mif two 3 homolog 2 (yeast)
SUMO3	smt3 suppressor of mif two 3 homolog 3 (yeast)
SUPT3H	suppressor of ty 3 homolog (s. cerevisiae)
SUPV3L1	suppressor of var1, 3-like 1 (s. cerevisiae)
SURB7	srb7 suppressor of rna polymerase b homolog (yeast)
SURF2	surfeit 2
SURF6	surfeit 6
SUV39H1	suppressor of variegation 3-9 homolog 1 (drosophila)
SUV420H1	suppressor of variegation 4-20 homolog 1 (drosophila)
SUV420H2	suppressor of variegation 4-20 homolog 2 (drosophila)
SVH	svh protein
SYAP1	hypothetical protein flj14495
SYNCRIP	synaptotagmin binding, cytoplasmic rna interacting protein
SYNJ2	synaptojanin 2
SYPL1	synaptophysin-like 1
TACC3	transforming, acidic coiled-coil containing protein 3
TAF1B	tata box binding protein (tbp)-associated factor, rna polymerase i, b, 63kda
TAFA	taf4 rna polymerase ii, tata box binding protein (tbp)-associated factor, 135kda
TAFA5	taf5 rna polymerase ii, tata box binding protein (tbp)-associated factor, 100kda
TAFA5L	taf5-like rna polymerase ii, p300/cbp-associated factor (pcaf)-associated factor, 65kda
TAFA9	taf9 rna polymerase ii, tata box binding protein (tbp)-associated factor, 32kda
TAGLN2	transgelin 2
TAGLN3	transgelin 3
TALDO1	transaldolase 1
TARBP2	tar (hiv-1) rna binding protein 2
TARS	threonyl-trna synthetase
TARSL1	threonyl-trna synthetase-like 1
TATDN1	tatd dnase domain containing 1
TAX1BP3	tax1 (human t-cell leukemia virus type i) binding protein 3

---

TBC1D22A	tbcl domain family, member 22a
TBC1D4	tbcl domain family, member 4
TBC1D7	tbcl domain family, member 7
TBCC	tubulin-specific chaperone c
TBPL1	tbp-like 1
TBRG4	transforming growth factor beta regulator 4
TBX2	t-box 2
TBX3	t-box 3 (ulnar mammary syndrome)
TCEA1	transcription elongation factor a (sii), 1
TCEB1	transcription elongation factor b (siii), polypeptide 1 (15kda, elongin c)
TCEB2	transcription elongation factor b (siii), polypeptide 2 (18kda, elongin b)
TCERG1	transcription elongation regulator 1
TCF12	transcription factor 12 (htf4, helix-loop-helix transcription factors 4)
TCF15	transcription factor 15 (basic helix-loop-helix)
TCF7	transcription factor 7 (t-cell specific, hmg-box)
TCF7L2	transcription factor 7-like 2 (t-cell specific, hmg-box)
TCHP	trichoplein, keratin filament binding
TCP1	t-complex 1
TCP11L1	t-complex 11 (mouse) like 1
TDRD3	tudor domain containing 3
TEAD2	tea domain family member 2
TEAD4	tea domain family member 4
TEX10	testis expressed sequence 10
TEX261	testis expressed sequence 261
TFAF4	transcription factor ap-4 (activating enhancer binding protein 4)
TFB1M	transcription factor b1, mitochondrial
TFB2M	transcription factor b2, mitochondrial
TFCP2	transcription factor cp2
TFDP1	transcription factor dp-1
TFPI2	tissue factor pathway inhibitor 2
TGDS	tdp-glucose 4,6-dehydratase
TGIF2	hypothetical protein loc57163
THADA	thyroid adenoma associated
THEM2	thioesterase superfamily member 2
THNSL1	threonine synthase-like 1 (bacterial)
THOC1	tho complex 1
THOC3	tho complex 3
THOC4	tho complex 4
THOP1	thimet oligopeptidase 1
THRAP4	thyroid hormone receptor associated protein 4
THRAP5	thyroid hormone receptor associated protein 5
THUMPD2	thump domain containing 2
THY1	thy-1 cell surface antigen
THYN1	thymocyte nuclear protein 1
TIAL1	tial1 cytotoxic granule-associated rna binding protein-like 1
TIMM10	translocase of inner mitochondrial membrane 10 homolog (yeast)
TIMM17B	translocase of inner mitochondrial membrane 17 homolog b (yeast)
TIMM23	translocase of inner mitochondrial membrane 23 homolog (yeast)
TIMM44	translocase of inner mitochondrial membrane 44 homolog (yeast)
TIMM8A	translocase of inner mitochondrial membrane 8 homolog a (yeast)
TIMM8B	translocase of inner mitochondrial membrane 8 homolog b (yeast)
TIMM9	translocase of inner mitochondrial membrane 9 homolog (yeast)
TIPRL	tip41, tor signalling pathway regulator-like (s. cerevisiae)
TJP2	tight junction protein 2 (zona occludens 2)
TK1	thymidine kinase 1, soluble
TKT	transketolase (wernicke-korsakoff syndrome)
TLE1	transducin-like enhancer of split 1 (e(sp1) homolog, drosophila)
TLE3	transducin-like enhancer of split 3 (e(sp1) homolog, drosophila)
TLK1	tousled-like kinase 1
TLK2	tousled-like kinase 2
TLN2	talin 2
TLX2	t-cell leukemia homeobox 2
TMC6	transmembrane channel-like 6
TMED3	transmembrane emp24 protein transport domain containing 3
TMED5	transmembrane emp24 protein transport domain containing 5
TMEM100	transmembrane protein 100
TMEM103	transmembrane protein 103
TMEM109	transmembrane protein 109
TMEM11	transmembrane protein 11
TMEM118	transmembrane protein 118
TMEM119	transmembrane protein 119
TMEM123	transmembrane protein 123
TMEM126A	transmembrane protein 126a
TMEM126B	transmembrane protein 126b
TMEM14A	transmembrane protein 14a
TMEM20	transmembrane protein 20
TMEM35	transmembrane protein 35
TMEM38B	transmembrane protein 38b
TMEM48	transmembrane protein 48
TMEM5	transmembrane protein 5
TMEM70	transmembrane protein 70
TMEM93	transmembrane protein 93
TMEM97	transmembrane protein 97
TMEM99	transmembrane protein 99
TMPO	thymopoietin
TNC	tenascin c (hexabrachion)
TNFAIP6	tumor necrosis factor, alpha-induced protein 6
TNFRSF21	tumor necrosis factor receptor superfamily, member 21
TNFSF5IP1	tumor necrosis factor superfamily, member 5-induced protein 1
TNIP2	tnfaip3 interacting protein 2
TNN	tenascin n

---

---

TNRC5	trinucleotide repeat containing 5
TNS1	tensin 1
TOE1	hypothetical protein flj13949
TOM1L1	target of myb1-like 1 (chicken)
TOMM20	translocase of outer mitochondrial membrane 20 homolog (yeast)
TOMM22	translocase of outer mitochondrial membrane 22 homolog (yeast)
TOMM34	translocase of outer mitochondrial membrane 34
TOMM40	translocase of outer mitochondrial membrane 40 homolog (yeast)
TOMM70A	translocase of outer mitochondrial membrane 70 homolog a (yeast)
TOP2A	topoisomerase (dna) ii alpha 170kda
TOR2A	torsin family 2, member a
TP53	tumor protein p53 (li-fraumeni syndrome)
TP53BP2	tumor protein p53 binding protein, 2
TP53I3	tumor protein p53 inducible protein 3
TP53RK	tp53 regulating kinase
TPCN2	two pore segment channel 2
TPPI	triosephosphate isomerase 1
TPM1	tropomyosin 1 (alpha)
TPM4	tropomyosin 4
TPP2	tripeptidyl peptidase ii
TPRKB	tp53rk binding protein
TPST2	tyrosylprotein sulfotransferase 2
TPX2	tpx2, microtubule-associated, homolog (xenopus laevis)
TRA2A	transformer-2 alpha
TRAK1	trafficking protein, kinesin binding 1
TRAM1L1	translocation associated membrane protein 1-like 1
TRAP1	tnf receptor-associated protein 1
TRFP	trf (tata binding protein-related factor)-proximal homolog (drosophila)
TRG20	hypothetical protein mge5309
TRIAP1	tp53 regulated inhibitor of apoptosis 1
TRIB1	tribbles homolog 1 (drosophila)
TRIM25	tripartite motif-containing 25
TRIM28	tripartite motif-containing 28
TRIM9	tripartite motif-containing 9
TRIP12	thyroid hormone receptor interactor 12
TRIP13	thyroid hormone receptor interactor 13
TRIT1	trna isopentenyltransferase 1
TRMT1	trm1 trna methyltransferase 1 homolog (s. cerevisiae)
TRMT12	trna methyltransferase 12 homolog (s. cerevisiae)
TRMU	trna 5-methylaminomethyl-2-thiouridylate methyltransferase
TRNT1	trna nucleotidyl transferase, cca-adding, 1
TRUB2	trub pseudouridine (psi) synthase homolog 2 (e. coli)
TSEN2	trna splicing endonuclease 2 homolog (s. cerevisiae)
TSFM	ts translation elongation factor, mitochondrial
TSNAX	translin-associated factor x
TSPAN13	tetraspanin 13
TSPAN33	tetraspanin 33
TSPAN6	tetraspanin 6
TSPAN8	tetraspanin 8
TSPYL5	tspy-like 5
TSR1	tsr1, 20s rna accumulation, homolog (yeast)
TSSC1	tumor suppressing subtransferable candidate 1
TSSC4	tumor suppressing subtransferable candidate 4
TST	thiosulfate sulfurtransferase (rhodanese)
TTC4	tetratricopeptide repeat domain 4
TTF1	transcription termination factor, ma polymerase i
TTF2	transcription termination factor, ma polymerase ii
TTK	ttk protein kinase
TTL12	tubulin tyrosine ligase-like family, member 12
TTL4	tubulin tyrosine ligase-like family, member 4
TUB	tubby homolog (mouse)
TUBB2C	tubulin, beta 2c
TUBB4	tubulin, beta 4
TUBB8	tubulin, beta 8
TUBG1	tubulin, gamma 1
TUBGCP3	tubulin, gamma complex associated protein 3
TUFM	tu translation elongation factor, mitochondrial
TWIST1	twist homolog 1 (acrocephalosyndactyly 3; saethre-hotzen syndrome) (drosophila)
TWISTNB	twist neighbor
TXN	thioredoxin
TXNDC	thioredoxin domain containing
TXNDC5	thioredoxin domain containing 5
TXNDC9	thioredoxin domain containing 9
TXNL1	thioredoxin-like 1
TXNL4A	thioredoxin-like 4a
TXNL5	thioredoxin-like 5
TXNRD1	thioredoxin reductase 1
TXNRD2	thioredoxin reductase 2
TYMS	thymidylate synthetase
TYRP1	tyrosinase-related protein 1
TYSD1	trypsin domain containing 1
U2AF1	u2(rnu2) small nuclear rna auxiliary factor 1
U2AF2	u2 (rnu2) small nuclear rna auxiliary factor 2
UAP1	udp-n-acteylglucosamine pyrophosphorylase 1
UBA2	sumo-1 activating enzyme subunit 2
UBADC1	ubiquitin associated domain containing 1
UBE2C	ubiquitin-conjugating enzyme e2c
UBE2D4	ubiquitin-conjugating enzyme e2d 4 (putative)
UBE2E2	ubiquitin-conjugating enzyme e2e 2 (ubc4/5 homolog, yeast)
UBE2E3	ubiquitin-conjugating enzyme e2e 3 (ubc4/5 homolog, yeast)
UBE2G1	ubiquitin-conjugating enzyme e2g 1 (ubc7 homolog, yeast)

---



---

UBE2H	ubiquitin-conjugating enzyme e2h (ubc8 homolog, yeast)
UBE2I	ubiquitin-conjugating enzyme e2i (ubc9 homolog, yeast)
UBE2M	ubiquitin-conjugating enzyme e2m (ubc12 homolog, yeast)
UBE2O	ubiquitin-conjugating enzyme e2o
UBE2R2	ubiquitin-conjugating enzyme e2r 2
UBE2S	ubiquitin-conjugating enzyme e2s
UBE2T	ubiquitin-conjugating enzyme e2t (putative)
UBE2V2	ubiquitin-conjugating enzyme e2 variant 2
UBE3C	ubiquitin protein ligase e3c
UBE4A	ubiquitination factor e4a (ufd2 homolog, yeast)
UBIAD1	ubia prenyltransferase domain containing 1
UBL7	ubiquitin-like 7 (bone marrow stromal cell-derived)
UBPH	ubiquitin-binding protein homolog
UBQLN1	ubiquilin 1
UBQLN2	ubiquilin 2
UBR1	ubiquitin protein ligase e3 component n-recognin 1
UBR2	ubiquitin protein ligase e3 component n-recognin 2
UBXD1	ubx domain containing 1
UCHL1	ubiquitin carboxyl-terminal esterase I1 (ubiquitin thiolesterase)
UCHL3	ubiquitin carboxyl-terminal esterase I3 (ubiquitin thiolesterase)
UCHL5	ubiquitin carboxyl-terminal hydrolase I5
UCK2	uridine-cytidine kinase 2
UCP2	uncoupling protein 2 (mitochondrial, proton carrier)
UCRC	ubiquinol-cytochrome c reductase complex (7.2 kd)
UFC1	ubiquitin-fold modifier conjugating enzyme 1
UGDH	udp-glucose dehydrogenase
UHRF1	ubiquitin-like, containing phd and ring finger domains, 1
UIP1	three prime repair exonuclease 2
UMPS	uridine monophosphate synthetase (orotate phosphoribosyl transferase and orotidine-5'-decarboxylase)
UNC13B	unc-13 homolog b (c. elegans)
UNC13D	unc-13 homolog d (c. elegans)
UNC5A	unc-5 homolog a (c. elegans)
UNC5B	unc-5 homolog b (c. elegans)
UQCRB	ubiquinol-cytochrome c reductase binding protein
UQCRC1	ubiquinol-cytochrome c reductase core protein i
UQCRC2	ubiquinol-cytochrome c reductase core protein ii
UQCRH	ubiquinol-cytochrome c reductase hinge protein
UROS	uroporphyrinogen iii synthase (congenital erythropoietic porphyria)
USF1	upstream transcription factor 1
USF2	upstream transcription factor 2, c-fos interacting
USMG5	upregulated during skeletal muscle growth 5 homolog (mouse)
USP10	ubiquitin specific peptidase 10
USP13	ubiquitin specific peptidase 13 (isopeptidase t-3)
USP14	ubiquitin specific peptidase 14 (trna-guanine transglycosylase)
USP15	ubiquitin specific peptidase 15
USP3	ubiquitin specific peptidase 3
USP38	ubiquitin specific peptidase 38
USP39	ubiquitin specific peptidase 39
USP46	ubiquitin specific peptidase 46
USP48	hypothetical protein flj11328
USP7	ubiquitin specific peptidase 7 (herpes virus-associated)
UTP11L	utp11-like, u3 small nucleolar ribonucleoprotein, (yeast)
UTP14A	utp14, u3 small nucleolar ribonucleoprotein, homolog a (yeast)
UXT	ubiquitously-expressed transcript
VAR5	valyl-tma synthetase
VDAC1	voltage-dependent anion channel 1
VDAC2	voltage-dependent anion channel 2
VDAC3	voltage-dependent anion channel 3
VIM	vimentin
VKORC1	vitamin k epoxide reductase complex, subunit 1
VKORC1L1	vitamin k epoxide reductase complex, subunit 1-like 1
VPS26B	vacuolar protein sorting 26 homolog b (yeast)
VPS29	vacuolar protein sorting 29 (yeast)
VPS33A	vacuolar protein sorting 33a (yeast)
VPS37B	vacuolar protein sorting 37b (yeast)
VPS72	vacuolar protein sorting 72 (yeast)
VRK1	vaccinia related kinase 1
VTI1B	vesicle transport through interaction with t-snares homolog 1b (yeast)
WASF1	was protein family, member 1
WASF3	was protein family, member 3
WBSCR1	williams-beuren syndrome chromosome region 1
WBSCR16	williams-beuren syndrome chromosome region 16
WBSCR22	putative methyltransferase
WDR12	wd repeat domain 12
WDR18	wd repeat domain 18
WDR20	wd repeat domain 20
WDR21A	wd repeat domain 21a
WDR34	wd repeat domain 34
WDR35	wd repeat domain 35
WDR41	wd repeat domain 41
WDR46	wd repeat domain 46
WDR5	wd repeat domain 5
WDR50	wd repeat domain 50
WDR51A	wd repeat domain 51a
WDR57	wd repeat domain 57 (u5 snrnp specific)
WDR61	wd repeat domain 61
WDR68	wd repeat domain 68
WDR70	wd repeat domain 70
WDR74	wd repeat domain 74
WDR75	wd repeat domain 75
WDR77	wd repeat domain 77

---

---

WDR79	wd repeat domain 79
WDR81	wd repeat domain 81
WDSOF1	wd repeats and sof1 domain containing
WEE1	wee1 homolog (s. pombe)
WHSC2	wolf-hirschhorn syndrome candidate 2
WIBG	within bgcn homolog (drosophila)
WNK2	serologically defined colon cancer antigen 43
WRNIP1	werner helicase interacting protein 1
WWC1	ww, c2 and coiled-coil domain containing 1
WWOX	putative oxidoreductase
WWP1	ww domain containing e3 ubiquitin protein ligase 1
XBP1	x-box binding protein 1
KKRX	xk, kell blood group complex subunit-related, x-linked
XPNPEP2	x-prolyl aminopeptidase (aminopeptidase p) 2, membrane-bound
XPO4	exportin 4
XPO5	exportin 5
XPO6	exportin 6
XPOT	exportin, trna (nuclear export receptor for trnas)
XPR1	xenotropic and polytropic retrovirus receptor
XRCC6	x-ray repair complementing defective repair in chinese hamster cells 6 (ku autoantigen, 70kda)
XRCC6BP1	xrcc6 binding protein 1
XTP3TPA	xtp3-transactivated protein a
YARS	tyrosyl-trna synthetase
YARS2	tyrosyl-trna synthetase 2 (mitochondrial)
YBX1	y box binding protein 1
YES1	v-yes-1 yamaguchi sarcoma viral oncogene homolog 1
YIF1B	yip1 interacting factor homolog b (s. cerevisiae)
YME1L1	yme1-like 1 (s. cerevisiae)
YOD1	yod1 otu deubiquinating enzyme 1 homolog (yeast)
YWHAB	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, beta polypeptide
YWHAE	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon polypeptide
YWHAG	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, gamma polypeptide
ZAK	sterile alpha motif and leucine zipper containing kinase azk
ZBTB2	zinc finger and btb domain containing 2
ZBTB24	zinc finger and btb domain containing 24
ZC3H3	zinc finger ccch-type containing 3
ZC3HAV1	zinc finger ccch-type, antiviral 1
ZC3HC1	zinc finger, c3hc-type containing 1
ZCCHC17	zinc finger, ccch domain containing 17
ZCCHC3	zinc finger, ccch domain containing 3
ZCCHC9	zinc finger, ccch domain containing 9
ZCSL2	zinc finger, cs1-type containing 2
ZDHHHC23	zinc finger, dhhc-type containing 23
ZDHHHC24	zinc finger, dhhc-type containing 24
ZDHHHC9	zinc finger, dhhc-type containing 9
ZFAND1	zinc finger, an1-type domain 1
ZFHXB1B	zinc finger homeobox 1b
ZFP106	zinc finger protein 106 homolog (mouse)
ZFP64	zinc finger protein 64 homolog (mouse)
ZFPM1	zinc finger protein, multitype 1
ZGPAT	zinc finger, ccch-type with g patch domain
ZHX3	zinc fingers and homeoboxes 3
ZIC2	zic family member 2 (odd-paired homolog, drosophila)
ZMPSTE24	zinc metalloproteinase (ste24 homolog, yeast)
ZMYM1	zinc finger, mym-type 1
ZMYND19	zinc finger, mynd-type containing 19
ZNF114	zinc finger protein 114
ZNF121	zinc finger protein 121 (clone zhc32)
ZNF179	zinc finger protein 179
ZNF207	zinc finger protein 207
ZNF24	zinc finger protein 24 (kox 17)
ZNF256	zinc finger protein 256
ZNF259	zinc finger protein 259
ZNF286	zinc finger protein 286
ZNF313	zinc finger protein 313
ZNF330	zinc finger protein 330
ZNF365	zinc finger protein 365
ZNF385	zinc finger protein 385
ZNF408	zinc finger protein 408
ZNF414	zinc finger protein 414
ZNF423	zinc finger protein 423
ZNF444	zinc finger protein 444
ZNF462	zinc finger protein 462
ZNF503	zinc finger protein 503
ZNF511	zinc finger protein 511
ZNF536	zinc finger protein 536
ZNF551	zinc finger protein 551
ZNF585A	zinc finger protein 585a
ZNF586	zinc finger protein 586
ZNF593	zinc finger protein 593
ZNF609	zinc finger protein 609
ZNF621	zinc finger protein 621
ZNF622	zinc finger protein 622
ZNF659	zinc finger protein 659
ZNF691	zinc finger protein 691
ZNF695	zinc finger protein 695
ZNF696	zinc finger protein 696
ZNF7	zinc finger protein 7 (kox 4, clone hf.16)
ZNF704	zinc finger protein 704
ZNF714	zinc finger protein 714
ZNF74	zinc finger protein 74 (cos52)

---

---

ZNF9	zinc finger protein 9 (a cellular retroviral nucleic acid binding protein)
ZNFN1A5	zinc finger protein, subfamily 1a, 5
ZNHIT2	zinc finger, hit type 2
ZNRD1	zinc ribbon domain containing, 1
ZSCAN2	zinc finger and scan domain containing 2
ZSCAN5	zinc finger and scan domain containing 5
ZWINT	zw10 interactor

## Supplementary Table 5: Gene Lists of up-regulated miR-17 targets and down-regulated brain-enriched miRNA targets

### miR-17 family targets which were up-regulated during differentiation

Gene Symbol	Gene Name
ABCA1	atp-binding cassette, sub-family a (abc1), member 1
ABCC5	atp-binding cassette, sub-family c (cfr/mrp), member 5
ABCG4	atp-binding cassette, sub-family g (white), member 4
ABHD3	abhydrolase domain containing 3
ABI3BP	abi gene family, member 3 (nesh) binding protein
ABR	active bcr-related gene
ACCN2	amiloride-sensitive cation channel 2, neuronal
ACTN1	actinin, alpha 1
ACTR1A	arp1 actin-related protein 1 homolog a, centractin alpha (yeast)
ACVR1B	activin a receptor, type ib
ADAM19	adam metallopeptidase domain 19 (meltrin beta)
ADCY6	adenylate cyclase 6
ADD3	adducin 3 (gamma)
AFTIPHILIN	aftiphilin protein
AK3	adenylate kinase 3
AKAP13	lymphoid blast crisis oncogene
ALS2	amyotrophic lateral sclerosis 2 (juvenile)
AMFR	autocrine motility factor receptor
ANK2	ankyrin 2, neuronal
ANKFY1	ankyrin repeat and fyve domain containing 1
ANKRD12	ankyrin repeat domain 12
AP2M1	adaptor-related protein complex 2, mu 1 subunit
APEG1	aortic preferentially expressed gene 1
APPL	adaptor protein containing ph domain, ptb domain and leucine zipper motif 1
APRN	androgen-induced proliferation inhibitor
ARHGAP1	rho gtpase activating protein 1
ARHGAP12	hypothetical protein fj10971
ARHGAP20	rho gtpase activating protein 20
ARHGAP21	rho gtpase activating protein 21
ARHGEF11	rho guanine nucleotide exchange factor (gef) 11
ARHGEF18	rho/rac guanine nucleotide exchange factor (gef) 18
ARHGEF3	rho guanine nucleotide exchange factor (gef) 3
ARIH2	ariadne homolog 2 (drosophila)
ARL4C	adp-ribosylation factor-like 4c
ARL8B	adp-ribosylation factor-like 8b
ARPP-21	cyclic amp-regulated phosphoprotein, 21 kd
ARRDC4	arrestin domain containing 4
ASXL2	additional sex combs like 2 (drosophila)
ATP1B1	atpase, na+/k+ transporting, beta 1 polypeptide
ATP2A2	atpase, ca++ transporting, cardiac muscle, slow twitch 2
ATP6V1B2	atpase, h+ transporting, lysosomal 56/58kda, v1 subunit b2
ATXN1	ataxin 1
ATXN2	ataxin 2
AUTS2	autism susceptibility candidate 2
AXIN2	axin 2 (conductin, axil)
B4GALT5	udp-gal:betaglcnac beta 1,4- galactosyltransferase, polypeptide 5
BAC1H2	btb and cnc homology 1, basic leucine zipper transcription factor 2
BAI3	brain-specific angiogenesis inhibitor 3
BAZZB	dkfzp434h071 protein
BCAP29	b-cell receptor-associated protein 29
BCL2L1	bcl2-like 1
BCL2L2	bcl2-like 2
BCL9L	b-cell cl/lymphoma 9-like
BDNF	brain-derived neurotrophic factor
BIRC6	baculoviral iap repeat-containing 6 (apollon)
Bles03	basophilic leukemia expressed protein bles03
BM88	bm88 antigen
BNC2	basonuclin 2
BRPF3	bromodomain and phd finger containing, 3
BRUNOL6	bruno-like 6, rna binding protein (drosophila)
BSC12	bernardinelli-seip congenital lipodystrophy 2 (seipin)
BSDC1	bsd domain containing 1
BSN	bassoon (presynaptic cytomatrix protein)
BTBD10	btb (poz) domain containing 10
BTG1	b-cell translocation gene 1, anti-proliferative
BTG2	btg family, member 2
BTG3	btg family, member 3
BZRAP1	benzodiazapine receptor (peripheral) associated protein 1
C10orf6	chromosome 10 open reading frame 6
C14orf147	chromosome 14 open reading frame 147
C15orf17	chromosome 15 open reading frame 17
C16orf28	chromosome 16 open reading frame 28
C16orf7	chromosome 16 open reading frame 7
C16orf9	chromosome 16 open reading frame 9
C1orf21	chromosome 1 open reading frame 21
C1QDC1	c1q domain containing 1
C20orf35	chromosome 20 open reading frame 35
C20orf46	chromosome 20 open reading frame 46
C5orf13	chromosome 5 open reading frame 13
C5orf5	chromosome 5 open reading frame 5

---

C6orf134	chromosome 6 open reading frame 134
C9orf5	chromosome 9 open reading frame 5
CA10	carbonic anhydrase x
CACNA1C	calcium channel, voltage-dependent, 1 type, alpha 1c subunit
CALM1	calmodulin 1 (phosphorylase kinase, delta)
CAMK2G	calcium/calmodulin-dependent protein kinase (cam kinase) ii gamma
CAMK2N1	calcium/calmodulin-dependent protein kinase ii inhibitor 1
CAMSAP1L1	calmodulin regulated spectrin-associated protein 1-like 1
CAMTA1	calmodulin binding transcription activator 1
CBX4	chromobox homolog 4 (pc class homolog, drosophila)
CBX7	chromobox homolog 7
CCDC24	coiled-coil domain containing 24
CCM2	cerebral cavernous malformation 2
CCND1	cyclin d1
CCPG1	cell cycle progression 1
CDC2L5	cell division cycle 2-like 5 (cholinesterase-related cell division controller)
CDC2L6	cell division cycle 2-like 6 (cdk8-like)
CDC42EP2	cdc42 effector protein (rho gtpase binding) 2
CDH2	cadherin 2, type 1, n-cadherin (neuronal)
CDK6	cyclin-dependent kinase 6
CDKN1C	cyclin-dependent kinase inhibitor 1c (p57, kip2)
CEP350	centrosomal protein 350kda
CEP70	centrosomal protein 70kda
CETN2	centrin, ef-hand protein, 2
CGGBP1	cgg triplet repeat binding protein 1
CGI-38	cgi-38 protein
CHD5	chromodomain helicase dna binding protein 5
CHD5	coronary heart disease, susceptibility to, 5
CHD9	hypothetical protein bc022889
CHRNB1	cholinergic receptor, nicotinic, beta 1 (muscle)
CHST1	carbohydrate (keratan sulfate gal-6) sulfotransferase 1
CHST7	carbohydrate (n-acetylglucosamine 6-o) sulfotransferase 7
CIC	capicua homolog (drosophila)
CLASP2	cytoplasmic linker associated protein 2
CLCF1	cardiotrophin-like cytokine factor 1
CLDN12	claudin 12
CLIPR-59	clip-170-related protein
CNIH2	cornichon homolog 2 (drosophila)
CNOT4	ccr4-not transcription complex, subunit 4
CNR1	cannabinoid receptor 1 (brain)
CNTFR	ciliary neurotrophic factor receptor
CNTNAP1	contactin associated protein 1
COL17A1	collagen, type xvii, alpha 1
COL23A1	collagen, type xxiii, alpha 1
Contact	
COP57A	cop9 constitutive photomorphogenic homolog subunit 7a (arabidopsis)
COX7A2L	cytochrome c oxidase subunit viia polypeptide 2 like
CPEB1	cytoplasmic polyadenylation element binding protein 1
CPEB3	cytoplasmic polyadenylation element binding protein 3
CREB5	camp responsive element binding protein 5
CREBBP	creb binding protein (rubinstein-taybi syndrome)
CRMP1	collapsin response mediator protein 1
CRTC2	creb regulated transcription coactivator 2
CSMD2	cub and sushi multiple domains 2
CSNK2A2	casein kinase 2, alpha prime polypeptide
CSPG3	chondroitin sulfate proteoglycan 3 (neurocan)
CTNNBIP1	catenin, beta interacting protein 1
CUL5	cullin 5
CXorf45	chromosome x open reading frame 45
CXXC5	ccc finger 5
CYLD	cylindromatosis (turban tumor syndrome)
CYP26B1	cytochrome p450, family 26, subfamily b, polypeptide 1
DAAM1	dishevelled associated activator of morphogenesis 1
DACH1	dachshund homolog 1 (drosophila)
DAG1	dystroglycan 1 (dystrophin-associated glycoprotein 1)
DAZAP2	daz associated protein 2
DCAMKL2	doublecortin and cam kinase-like 2
DCBLD2	discoidin, cub and lcl domain containing 2
DCX	doublecortin; lissencephaly, x-linked (doublecortin)
DDEF2	development and differentiation enhancing factor 2
DDR1	discoidin domain receptor family, member 1
DDX26	dkfzp434b105 protein
DDX42	dead (asp-glu-ala-asp) box polypeptide 42
DHDDS	dehydrodolichyl diphosphate synthase
DIRAS2	diras family, gtp-binding ras-like 2
DKFZp761i2123	hypothetical protein dkfzp761i2123
DKK1	dickkopf homolog 1 (xenopus laevis)
DKK2	dickkopf homolog 2 (xenopus laevis)
DKK3	dickkopf homolog 3 (xenopus laevis)
DLL1	delta-like 1 (drosophila)
DLST	dihydrolipoamide s-succinyltransferase (e2 component of 2-oxo-glutarate complex)
DMTF1	cyclin d binding myb-like transcription factor 1
DNAJB1	dnaj (hsp40) homolog, subfamily b, member 1
DNAJB5	dnaj (hsp40) homolog, subfamily b, member 5
DNAJB6	dnaj (hsp40) homolog, subfamily b, member 6
DNAJB9	dnaj (hsp40) homolog, subfamily b, member 9
DNAJC14	cytokine induced protein 29 kda
DNAL4	dynein, axonemal, light polypeptide 4
DOCK9	dedicator of cytokinesis 9
DPYSL2	dihydropyrimidinase-like 2
DUSP10	dual specificity phosphatase 10

---

---

DUSP16	dual specificity phosphatase 16
DUSP6	dual specificity phosphatase 6
DUSP8	dual specificity phosphatase 8
DYNC1I2	dynein, cytoplasmic 1, intermediate chain 2
DYNC1L2	dynein, cytoplasmic 1, light intermediate chain 2
DYNLT3	dynein, light chain, tctex-type 3
DYRK1A	dual-specificity tyrosine-(γ)-phosphorylation regulated kinase 1a
EDEM1	er degradation enhancer, mannosidase alpha-like 1
EGR1	early growth response 1
EIF1B	eukaryotic translation initiation factor 1b
EIF4A2	eukaryotic translation initiation factor 4a, isoform 2
EIF5A2	eukaryotic translation initiation factor 5a2
ELOVL4	elongation of very long chain fatty acids (fen1/elo2, sur4/elo3, yeast)-like 4
EP300	e1a binding protein p300
EPAS1	endothelial pas domain protein 1
EPB41L1	erythrocyte membrane protein band 4.1-like 1
EPC1	enhancer of polycomb homolog 1 (drosophila)
ETV5	ets variant gene 5 (ets-related molecule)
EV15L	ecotropic viral integration site 5-like
EXTL3	exostoses (multiple)-like 3
EYA1	eyes absent homolog 1 (drosophila)
FALZ	fetal alzheimer antigen
FAM38A	family with sequence similarity 38, member a
FAM43A	family with sequence similarity 43, member a
FAM45A	family with sequence similarity 45, member a
FAM57A	family with sequence similarity 57, member a
FAM8A1	family with sequence similarity 8, member a1
FBXL2	f-box and leucine-rich repeat protein 2
FBXL20	f-box and leucine-rich repeat protein 20
FBXL5	f-box and leucine-rich repeat protein 5
FBXO11	f-box only protein 11
FBXO21	f-box protein 21
FBXO34	f-box protein 34
FGF11	fibroblast growth factor 11
FHL2	four and a half lim domains 2
FLJ10154	hypothetical protein flj10154
FLJ14503	
FLJ20558	hypothetical protein flj20558
FLJ31818	hypothetical protein flj31818
FLJ31951	hypothetical protein flj31951
FLJ37266	hypothetical protein loc283225
FLJ38101	hypothetical protein flj38101
FLJ40142	flj40142 protein
FLJ45187	flj45187 protein
FLNC	filamin c, gamma (actin binding protein 280)
FLOT2	flotillin 2
FMN2	formin 2
FNBP1	formin binding protein 1
FNBP4	formin binding protein 4
FOXC1	forkhead box c1
FOXJ2	forkhead box j2
FOXJ3	forkhead box j3
FRMD4A	ferm domain containing 4a
FSTL1	folliculin-like 1
FTS	fused toes homolog (mouse)
FVT1	follicular lymphoma variant translocation 1
FZD7	frizzled homolog 7 (drosophila)
GAB2	grb2-associated binding protein 2
GAS1	growth arrest-specific 1
GATAD2B	gata zinc finger domain containing 2b
GFPT2	glutamine-fructose-6-phosphate transaminase 2
GLRB	glycine receptor, beta
GNAI2	guanine nucleotide binding protein (g protein), alpha inhibiting activity polypeptide 2
GNAO1	guanine nucleotide binding protein (g protein), alpha activating activity polypeptide o
GNAQ	guanine nucleotide binding protein (g protein), q polypeptide
GOLGA1	golgi autoantigen, golgin subfamily a, 1
GOLGA3	golgi autoantigen, golgin subfamily a, 3
GRIK2	glutamate receptor, ionotropic, kainate 2
GRIK4	glutamate receptor, ionotropic, kainate 4
GTPBP2	gtp binding protein 2
GULP1	gulp, engulfment adaptor ptb domain containing 1
H3F3B	h3 histone, family 3a
HAND1	heart and neural crest derivatives expressed 1
HARSL	histidyl-trna synthetase-like
HBP1	hmg-box transcription factor 1
HCN3	hyperpolarization activated cyclic nucleotide-gated potassium channel 3
HDAC4	histone deacetylase 4
HDDC3	hd domain containing 3
HELZ	helicase with zinc finger
HIC1	hypermethylated in cancer 1
HIF1AN	hypoxia-inducible factor 1, alpha subunit inhibitor
HIVEP1	human immunodeficiency virus type i enhancer binding protein 1
HIVEP2	human immunodeficiency virus type i enhancer binding protein 2
HNRPU	heterogeneous nuclear ribonucleoprotein u (scaffold attachment factor a)
HOXC8	homeobox c8
HRIHFB2122	
IGF2R	insulin-like growth factor 2 receptor
IGSF4	immunoglobulin superfamily, member 4
IGSF4B	immunoglobulin superfamily, member 4b
IGSF4C	immunoglobulin superfamily, member 4c
IGSF4D	immunoglobulin superfamily, member 4d

---

---

IL17RD	interleukin 17 receptor d
ILF3	interleukin enhancer binding factor 3, 90kda
IQWD1	iq motif and wd repeats 1
IRF1	interferon regulatory factor 1
IRS2	insulin receptor substrate 2
ITGB1	integrin, beta 1 (fibronectin receptor, beta polypeptide, antigen cd29 includes mdf2, msk12)
ITM2C	integral membrane protein 2c
IDL	intersex-like (drosophila)
JAG1	jagged 1 (alagille syndrome)
JARID1B	jumonji, at rich interactive domain 1b (rbp2-like)
JOSD1	josephin domain containing 1
JUN	v-jun sarcoma virus 17 oncogene homolog (avian)
KBTBD2	kelch repeat and btb (poz) domain containing 2
KCND1	potassium voltage-gated channel, shal-related subfamily, member 1
KCNJ2	potassium inwardly-rectifying channel, subfamily j, member 2
KCNQ2	potassium voltage-gated channel, kqt-like subfamily, member 2
KIAA0240	kiaa0240
KIAA0323	kiaa0323
KIAA0350	kiaa0350 protein
KIAA0376	kiaa0376 protein
KIAA0494	kiaa0494
KIAA0513	kiaa0513
KIAA0828	kiaa0828 protein
KIAA0831	kiaa0831
KIAA1128	kiaa1128
KIAA1267	dkfzp727c091 protein
KIAA1370	kiaa1370
KIAA1522	kiaa1522
KIAA1598	kiaa1598
KIAA1600	kiaa1600
KIAA1961	kiaa1961 gene
KIF1B	kinesin family member 1b
KIF3B	kinesin family member 3b
KIF3C	kinesin family member 3c
KIT	v-kit hardy-zuckerman 4 feline sarcoma viral oncogene homolog
KLC2	kinesin light chain 2
KLF10	kruppel-like factor 10
KLF11	kruppel-like factor 11
KLF12	kruppel-like factor 12
KLF13	kruppel-like factor 13
KLHL13	kelch-like 13 (drosophila)
KLHL3	kelch-like 3 (drosophila)
LASS6	lag1 longevity assurance homolog 6 (s. cerevisiae)
LEFTY1	left-right determination factor 1
LEMD3	lem domain containing 3
LIFR	leukemia inhibitory factor receptor
LIMK1	lim domain kinase 1
LKAP	limkain b1
LMAN2L	lectin, mannose-binding 2-like
LOC129285	smooth muscle myosin heavy chain 11 isoform sm1-like
LOC153222	adult retina protein
LONRF1	lon peptidase n-terminal domain and ring finger 1
LONRF2	lon peptidase n-terminal domain and ring finger 2
LPHN2	latrophilin 2
LPP	lim domain containing preferred translocation partner in lipoma
LRIQ1	leucine-rich repeats and immunoglobulin-like domains 1
LRRFIP2	leucine rich repeat (in flil) interacting protein 2
LZTFL1	leucine zipper transcription factor-like 1
MAFG	v-maf musculoaponeurotic fibrosarcoma oncogene homolog g (avian)
MAGI2	membrane associated guanylate kinase, ww and pdz domain containing 2
MAP2K4	mitogen-activated protein kinase kinase 4
MAP3K12	mitogen-activated protein kinase kinase kinase 12
MAP3K4	mitogen-activated protein kinase kinase kinase 4
MAP3K5	mitogen-activated protein kinase kinase kinase 5
MAP3K8	mitogen-activated protein kinase kinase kinase 8
MAP3K9	mitogen-activated protein kinase kinase kinase 9
MAP4	microtubule-associated protein 4
MAP4K1	mitogen-activated protein kinase kinase kinase kinase 1
MAP4K5	mitogen-activated protein kinase kinase kinase kinase 5
MAPK3	mitogen-activated protein kinase 3
MAPK6	mitogen-activated protein kinase 6
MAPK8IP3	mitogen-activated protein kinase 8 interacting protein 3
MAPK9	mitogen-activated protein kinase 9
MAPRE3	microtubule-associated protein, rp/eb family, member 3
MBTPS1	membrane-bound transcription factor peptidase, site 1
MECP2	methyl cpq binding protein 2 (rett syndrome)
MEF2C	mads box transcription enhancer factor 2, polypeptide c (myocyte enhancer factor 2c)
MEF2D	mads box transcription enhancer factor 2, polypeptide d (myocyte enhancer factor 2d)
MEIS1	meis1, myeloid ecotropic viral integration site 1 homolog (mouse)
MGC3123	hypothetical protein mgc3123
MGC33486	hypothetical protein mgc33486
MGC40405	hypothetical protein mgc40405
MGEA5	meningioma expressed antigen 5 (hyaluronidase)
MID1IP1	mid1 interacting protein 1 (gastrulation specific g12-like (zebrafish))
MKRN1	makorin, ring finger protein, 1
MLL	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, drosophila)
MLL5	hypothetical protein flj10078
MLR2	ligand-dependent corepressor
MMD	monocyte to macrophage differentiation-associated
MNT	max binding protein
MOAP1	modulator of apoptosis 1

---

---

MON2	mon2 homolog (yeast)
MPPED2	metallophosphoesterase domain containing 2
MTF1	metal-regulatory transcription factor 1
MTMR3	myotubularin related protein 3
MXI1	max interactor 1
MYST4	myst histone acetyltransferase (monocytic leukemia) 4
NAGK	n-acetylglucosamine kinase
NANOS1	nanos homolog 1 (drosophila)
NAPB	neuritis with brachial predilection
NAPB	n-ethylmaleimide-sensitive factor attachment protein, beta
NAV1	hypothetical protein mgc14961
NBEA	neurobeachin
NCOA1	nuclear receptor coactivator 1
NCOA3	nuclear receptor coactivator 3
NCOA7	nuclear receptor coactivator 7
NCSTN	nicastrin
NDEL1	nude nuclear distribution gene e homolog like 1 (a. nidulans)
NDRG4	ndrg family member 4
NEBL	nebulette
NEDD4L	neural precursor cell expressed, developmentally down-regulated 4-like
NEDD9	neural precursor cell expressed, developmentally down-regulated 9
NEUROG2	neurogenin 2
NFAT5	nuclear factor of activated t-cells 5, tonicity-responsive
NFIA	nuclear factor i/a
NFIB	nuclear factor i/b
NIP30	nefa-interacting nuclear protein nip30
NKIRAS1	nfkB inhibitor interacting ras-like 1
NLGN1	neuroligin 1
NLGN2	neuroligin 2
NPC1	niemann-pick disease, type c1
NPC1	nasopharyngeal carcinoma 1
NPEPL1	aminopeptidase-like 1
NR2F2	nuclear receptor subfamily 2, group f, member 2
NRBP1	nuclear receptor binding protein 1
NTE	neuropathy target esterase
NXPH1	neurexophilin 1
OACT2	o-acyltransferase (membrane bound) domain containing 2
OACT5	o-acyltransferase (membrane bound) domain containing 5
OCRL	oculocerebrorenal syndrome of lowe
of	
OLFM3	olfactomedin 3
OSBPL5	kiaa1534 protein
OSTM1	osteopetrosis associated transmembrane protein 1
OTUD4	kiaa1046 protein
P2RX4	purinergic receptor p2x, ligand-gated ion channel, 4
PAFAH1B1	platelet-activating factor acetylhydrolase, isoform ib, alpha subunit 45kda
PALLD	palladin, cytoskeletal associated protein
PAM	peptidylglycine alpha-amidating monooxygenase
PANX2	pannexin 2
PAPPA	pregnancy-associated plasma protein a, pappalysin 1
PBX3	pre-b-cell leukemia transcription factor 3
PCDHA4	protocadherin alpha 4
PCGF2	polycomb group ring finger 2
PCGF4	polycomb group ring finger 4
PCNP	pest-containing nuclear protein
PDAP1	pdgfa associated protein 1
PDGFRA	platelet-derived growth factor receptor, alpha polypeptide
PDPR	pyruvate dehydrogenase phosphatase regulatory subunit
PGM2L1	phosphoglucomutase 2-like 1
PHC1	polyhomeotic-like 1 (drosophila)
PHF1	phd finger protein 1
PHF12	phd finger protein 12
PHF13	phd finger protein 13
PHF15	phd finger protein 15
PHF2	phd finger protein 2
PIAS3	protein inhibitor of activated stat, 3
PIB5PA	inositol polyphosphate 5-phosphatase
PIK3R1	phosphoinositide-3-kinase, regulatory subunit 1 (p85 alpha)
PIP5K1C	phosphatidylinositol-4-phosphate 5-kinase, type i, gamma
PIP5K2C	phosphatidylinositol-4-phosphate 5-kinase, type ii, gamma
PISD	phosphatidylserine decarboxylase
PKD1	polycystic kidney disease 1 (autosomal dominant)
PLCB1	phospholipase c, beta 1 (phosphoinositide-specific)
PLCG1	phospholipase c, gamma 1
PLEKHA1	pleckstrin homology domain containing, family a (phosphoinositide binding specific) member 1
PLEKHA6	pleckstrin homology domain containing, family a member 6
PLEKHH1	pleckstrin homology domain containing, family h (with myth4 domain) member 1
PLEKHM1	pleckstrin homology domain containing, family m (with run domain) member 1
POGZ	pogo transposable element with znf domain
POLQ	polymerase (dna directed), theta
PPCS	phosphopantothienoylcysteine synthetase
PPF1A3	protein tyrosine phosphatase, receptor type, f polypeptide (ptprf), interacting protein (liprin), alpha 3
PPP2R2C	protein phosphatase 2 (formerly 2a), regulatory subunit b (pr 52), gamma isoform
PPP3CB	protein phosphatase 3 (formerly 2b), catalytic subunit, beta isoform (calcineurin a beta)
PPP3R1	protein phosphatase 3 (formerly 2b), regulatory subunit b, 19kda, alpha isoform (calcineurin b, type i)
PRDM4	pr domain containing 4
PRKCE	protein kinase c, epsilon
PRO0149	pro0149 protein
PSAP	prosaposin (variant gaucher disease and variant metachromatic leukodystrophy)
PSD2	pleckstrin and sec7 domain containing 2
PTCH	patched homolog (drosophila)

---



---

PTPRA	protein tyrosine phosphatase, receptor type, a
PTPRM	protein tyrosine phosphatase, receptor type, m
PUM2	pumilio homolog 2 (drosophila)
PURA	purine-rich element binding protein a
PURB	purine-rich element binding protein b
PVRL2	poliovirus receptor-related 2 (herpesvirus entry mediator b)
RAB10	rab10, member ras oncogene family
RAB11FIP2	rab11 family interacting protein 2 (class i)
RAB22A	rab22a, member ras oncogene family
RAB23	rab23, member ras oncogene family
RAB2B	rab2b, member ras oncogene family
RAB4B	rab4b, member ras oncogene family
RAB5B	rab5b, member ras oncogene family
RAB6B	rab6b, member ras oncogene family
RAB7	rab7, member ras oncogene family
RABGAP1	rab gtpase activating protein 1
RAD23A	rad23 homolog a (s. cerevisiae)
RAD9A	rad9 homolog a (s. pombe)
RAI17	retinoic acid induced 17
RAI2	retinoic acid induced 2
RALGDS	ral guanine nucleotide dissociation stimulator
RALGPS1	ral gef with ph domain and sh3 binding motif 1
RAP2C	rap2c, member of ras oncogene family
RAPGEFL1	rap guanine nucleotide exchange factor (gef)-like 1
RARB	retinoic acid receptor, beta
RB1CC1	rb1-inducible coiled-coil 1
RBJ	ras-associated protein rap1
RBL2	retinoblastoma-like 2 (p130)
RBM9	rna binding motif protein 9
RBMS1	rna binding motif, single stranded interacting protein 1
RCE1	rce1 homolog, prenyl protein peptidase (s. cerevisiae)
RCOR3	rest corepressor 3
RECK	reversion-inducing-cysteine-rich protein with kazal motifs
RET	ret proto-oncogene (multiple endocrine neoplasia and medullary thyroid carcinoma 1, hirschsprung disease)
REV1L	rev1-like (yeast)
REV3L	rev3-like, catalytic subunit of dna polymerase zeta (yeast)
RFX1	regulatory factor x, 1 (influences hla class ii expression)
RGL1	ral guanine nucleotide dissociation stimulator-like 1
RGS17	regulator of g-protein signalling 17
RHOC	ras homolog gene family, member c
RHPN2	rhophilin, rho gtpase binding protein 2
RIMS3	regulating synaptic membrane exocytosis 3
RIN2	ras and rab interactor 2
RNF103	ring finger protein 103
RNF144	ring finger protein 144
RNF167	ring finger protein 167
RNF38	hypothetical protein flj21343
RNF41	ring finger protein 41
RNF44	ring finger protein 44
RNH1	ribonuclease/angiogenesis inhibitor 1
RPS6KA2	ribosomal protein s6 kinase, 90kda, polypeptide 2
RPS6KA4	ribosomal protein s6 kinase, 90kda, polypeptide 4
RPS6KA5	ribosomal protein s6 kinase, 90kda, polypeptide 5
RRAGB	ras-related gtp binding b
RSBN1	round spermatid basic protein 1
RSPRY1	ring finger and spry domain containing 1
RTN1	reticulin 1
RTN2	reticulin 2
RTN3	reticulin 3
RUNX1	runt-related transcription factor 1 (acute myeloid leukemia 1; aml1 oncogene)
RUNX1T1	runt-related transcription factor 1; translocated to, 1 (cyclin d-related)
RYBP	ring1 and yy1 binding protein
SARI1B	sar1 gene homolog b (s. cerevisiae)
SCAMP5	secretory carrier membrane protein 5
SCARB2	scavenger receptor class b, member 2
SCHIP1	schwannomin interacting protein 1
SCOC	short coiled-coil protein
SCRN1	secernin 1
SEMA4B	sema domain, immunoglobulin domain (ig), transmembrane domain (tm) and short cytoplasmic domain, (semaphorin) 4b
SEMA6A	ht018 protein
SERTAD3	serta domain containing 3
Service	
SFRS5	splicing factor, arginine/serine-rich 5
SGIP1	sh3-domain grb2-like (endophilin) interacting protein 1
SH3BGRL2	sh3 domain binding glutamic acid-rich protein like 2
SH3BP4	sh3-domain binding protein 4
SHANK2	sh3 and multiple ankyrin repeat domains 2
SHC4	shc (src homology 2 domain containing) family, member 4
SIGIRR	single immunoglobulin and toll-interleukin 1 receptor (tir) domain
SIPAIL2	signal-induced proliferation-associated 1 like 2
SIRT7	pyrroline-5-carboxylate reductase 1
Site	
SLC1A2	solute carrier family 1 (glial high affinity glutamate transporter), member 2
SLC25A1	solute carrier family 25 (mitochondrial carrier; citrate transporter), member 1
SLC25A27	solute carrier family 25, member 27
SLC2A4RG	slc2a4 regulator
SLC30A3	solute carrier family 30 (zinc transporter), member 3
SLC30A7	solute carrier family 30 (zinc transporter), member 7
SLC31A2	solute carrier family 31 (copper transporters), member 2
SLC36A1	lysosomal amino acid transporter 1
SLC39A1	solute carrier family 39 (zinc transporter), member 1

---

---

SLC6A17	hypothetical protein loc284462
SLC9A6	solute carrier family 9 (sodium/hydrogen exchanger), member 6
SLIT2	slit homolog 2 (drosophila)
SMAD5	smad, mothers against dpp homolog 5 (drosophila)
SMOC1	sparc related modular calcium binding 1
SNIP1	smad nuclear interacting protein 1
SNN	stannin
SNRK	snf related kinase
SNX16	sorting nexin 16
SNX27	sorting nexin family member 27
SOC5	suppressor of cytokine signaling 5
SORCS1	sortilin-related vps10 domain containing receptor 1
SORL1	sortilin-related receptor, l(dlr class) a repeats-containing
SOX4	sry (sex determining region y)-box 4
SOX9	sry (sex determining region y)-box 9 (campomelic dysplasia, autosomal sex-reversal)
SPEN	spen homolog, transcriptional regulator (drosophila)
SPHK2	sphingosine kinase 2
SPIRE1	spire homolog 1 (drosophila)
SPRYD3	spry domain containing 3
SPTBN4	spectrin, beta, non-erythrocytic 4
SQSTM1	sequestosome 1
SREBF1	sterol regulatory element binding transcription factor 1
SRGAP3	slit-robo rho gtpase activating protein 3
SRR	serine racemase
SRRM2	serine/arginine repetitive matrix 2
SSI1L1	synovial sarcoma translocation gene on chromosome 18-like 1
STAT3	signal transducer and activator of transcription 3 (acute-phase response factor)
STK11IP	serine/threonine kinase 11 interacting protein
STK19	serine/threonine kinase 19
STMN4	stathmin-like 4
STX1A	syntaxin 1a (brain)
STX3A	syntaxin 3a
STXBP1	syntaxin binding protein 1
SURF4	surfeit 4
SUZ12	suppressor of zeste 12 homolog (drosophila)
SYDE1	synapse defective 1, rho gtpase, homolog 1 (c. elegans)
SYN1	synapsin i
SYN2	synapsin ii
SYNGR1	synaptogyrin 1
SYT1	synaptotagmin i
SYT11	synaptotagmin xi
SYT13	synaptotagmin xiii
TACC2	transforming, acidic coiled-coil containing protein 2
TANC1	tetratricopeptide repeat, ankyrin repeat and coiled-coil containing 1
TAOK1	tao kinase 1
TARDBP	tar dna binding protein
TAX1BP1	tax1 (human t-cell leukemia virus type i) binding protein 1
TBC1D20	tbc1 domain family, member 20
TCERGIL	transcription elongation regulator 1-like
TCF4	transcription factor 4
Term of Service   Contact Us   Site Map	
TGOLN2	trans-golgi network protein 2
TIA1	tia1 cytotoxic granule-associated rna binding protein
TJP1	tight junction protein 1 (zona occludens 1)
TLX3	t-cell leukemia homeobox 3
TMEM15	transmembrane protein 15
TMEM16C	transmembrane protein 16c
TMEM16F	transmembrane protein 16f
TMEM32	transmembrane protein 32
TMEM55B	transmembrane protein 55b
TMEM87A	transmembrane protein 87a
TMEPA1	transmembrane, prostate androgen induced rna
TNFAIP1	tumor necrosis factor, alpha-induced protein 1 (endothelial)
TNFRSF12A	tumor necrosis factor receptor superfamily, member 12a
TNRC6A	trinucleotide repeat containing 6a
TP53INP1	tumor protein p53 inducible nuclear protein 1
TP53INP2	tumor protein p53 inducible nuclear protein 2
TPP1	tripeptidyl peptidase i
TRAK2	trafficking protein, kinesin binding 2
TRIB2	tribbles homolog 2 (drosophila)
TRIM2	tripartite motif-containing 2
TSC1	tuberous sclerosis 1
TSC22D2	tsc22 domain family, member 2
TSC22D3	tsc22 domain family, member 3
TSGA14	testis specific, 14
TSPYL2	tspy-like 2
TUBB2B	tubulin, beta 2b
TULP4	tubby like protein 4
TUSC2	tumor suppressor candidate 2
TXNDC12	thioredoxin domain containing 12 (endoplasmic reticulum)
TXNIP	thioredoxin interacting protein
UBE2D2	ubiquitin-conjugating enzyme e2d 2 (ubc4/5 homolog, yeast)
UBE2H	ubiquitin-conjugating enzyme e2h (ubc8 homolog, yeast)
UBE2J1	ubiquitin-conjugating enzyme e2, j1 (ubc6 homolog, yeast)
UBE2Q2	ubiquitin-conjugating enzyme e2q (putative) 2
UBE2W	ubiquitin-conjugating enzyme e2w (putative)
UBE2Z	ubiquitin-conjugating enzyme e2z (putative)
UBL3	ubiquitin-like 3
UBLCP1	ubiquitin-like domain containing ctd phosphatase 1
UBTD1	ubiquitin domain containing 1
UCP3	uncoupling protein 3 (mitochondrial, proton carrier)

---

---

UNC84A	unc-84 homolog a (c. elegans)
USF2	upstream transcription factor 2, c-fos interacting
USP32	ubiquitin specific peptidase 32
USP34	ubiquitin specific peptidase 34
UTX	ubiquitously transcribed tetratricopeptide repeat, x chromosome
VAMP1	vesicle-associated membrane protein 1 (synaptobrevin 1)
VAMP2	vesicle-associated membrane protein 2 (synaptobrevin 2)
VAMP3	vesicle-associated membrane protein 3 (cellubrevin)
VAT1	vesicle amine transport protein 1 homolog (t. californica)
VCL	vinculin
VGLL4	vestigial like 4 (drosophila)
VP54B	vacuolar protein sorting 4b (yeast)
WAC	ww domain containing adaptor with coiled-coil
WASL	wiskott-aldrich syndrome-like
WBP2	ww domain binding protein 2
WBSCR18	williams beuren syndrome chromosome region 18
WDR22	wd repeat domain 22
WDR26	wd repeat domain 26
WDR42A	wd repeat domain 42a
WDR44	wd repeat domain 44
WNT3	wingless-type mmtv integration site family, member 3
WSB1	wd repeat and socs box-containing 1
YPEL4	yippee-like 4 (drosophila)
YPEL5	yippee-like 5 (drosophila)
ZAK	sterile alpha motif and leucine zipper containing kinase azk
ZBTB4	zinc finger and btb domain containing 4
ZBTB7A	zinc finger and btb domain containing 7a
ZDHHC1	zinc finger, dhhc-type containing 1
ZDHHC17	zinc finger, dhhc-type containing 17
ZDHHC7	zinc finger, dhhc-type containing 7
ZFAND3	zinc finger, an1-type domain 3
ZFHX4	zinc finger homeodomain 4
ZFP91	zinc finger protein 91 homolog (mouse)
ZFYVE21	zinc finger, fyve domain containing 21
ZFYVE26	zinc finger, fyve domain containing 26
ZHX2	zinc fingers and homeoboxes 2
ZKSCAN1	zinc finger with krab and scan domains 1
ZMYND11	zinc finger, mynd domain containing 11
ZNFI61	zinc finger protein 161
ZNFI238	zinc finger protein 238
ZNFI289	zinc finger protein 289, id1 regulated
ZNFI3	zinc finger protein 3 (a8-51)
ZNFI319	zinc finger protein 319
ZNFI436	zinc finger protein 436
ZNFI518	zinc finger protein 518
ZNFI608	dkfzp434m098 protein
ZYG11BL	zyg-11 homolog b (c. elegans)-like
ZYX	zyxin

## "Brain-enriched" group of targets which were down-regulated during differentiation

Gene Symbol	Gene Name
ABCC4	atp-binding cassette, sub-family c (cftr/mrp), member 4
ABCG1	atp-binding cassette, sub-family g (white), member 1
ABHD5	abhydrolase domain containing 5
ACSL1	fatty-acid-coenzyme a ligase, long-chain 1
ACTB, ACTG1	actin, beta
ACTR3	arp3 actin-related protein 3 homolog (yeast)
ADCY1	adenylate cyclase 1 (brain)
ADCY9	adenylate cyclase 9
ADORA2B	adenosine a2b receptor
AK2	adenylate kinase 2
AKT1S1	akt1 substrate 1 (proline-rich)
ALDH9A1	aldehyde dehydrogenase 9 family, member a1
ANP32B	acidic (leucine-rich) nuclear phosphoprotein 32 family, member b
ANXA11	annexin a11
ANXA5	annexin a5
ARG2	arginase, type ii
ASAM	adipocyte-specific adhesion molecule
ASCC2	hypothetical protein dkfzp586o0223
ASF1A	asf1 anti-silencing function 1 homolog a (s. cerevisiae)
ATG4C	atg4 autophagy related 4 homolog c (s. cerevisiae)
ATP1A1	atpase, na+/k+ transporting, alpha 1 polypeptide
ATP6V0A2	atpase, h+ transporting, lysosomal v0 subunit a2
BCAT2	branched chain aminotransferase 2, mitochondrial
BCKDHA	branched chain keto acid dehydrogenase e1, alpha polypeptide
BCL11A	b-cell cl/lymphoma 11a (zinc finger protein)
BRP44L	brain protein 44-like
C10orf42	hypothetical protein flj21463
C14orf130	chromosome 14 open reading frame 130
C1GALT1	core 1 synthase, glycoprotein-n-acetylgalactosamine 3-beta-galactosyltransferase, 1
C9orf72	hypothetical protein flj11109
C9orf88	chromosome 9 open reading frame 88
CAMKK2	calcium/calmodulin-dependent protein kinase kinase 2, beta
CAPN2	calpain 2, (m/ii) large subunit
CAPZA1	capping protein (actin filament) muscle z-line, alpha 1
CASC3	cancer susceptibility candidate 3
CAST	calpastatin
CBLN2	cerebellin 2 precursor
CBX1	chromobox homolog 1 (hp1 beta homolog drosophila )
CCDC43	coiled-coil domain containing 43
CCDC6	coiled-coil domain containing 6
CCDC71	coiled-coil domain containing 71
CCNG1	cyclin g1
CCNJ	cyclin j
CDC44	cell division cycle associated 4
CDH11	cadherin 11, type 2, ob-cadherin (osteoblast)
CECR6	cat eye syndrome chromosome region, candidate 6
CHSY1	carbohydrate (chondroitin) synthase 1
CNOT7	ccr4-not transcription complex, subunit 7
CNTN1	contactin 1
COL4A1	collagen, type iv, alpha 1
CSTF3	cleavage stimulation factor, 3' pre-ma, subunit 3, 77kda
CTDSP1	ctd (carboxy-terminal domain, ma polymerase ii, polypeptide a) small phosphatase 1
CTDSP2	ctd (carboxy-terminal domain, ma polymerase ii, polypeptide a) small phosphatase 2
CUL4A	cullin 4a
CXCR4	chemokine (c-x-c motif) receptor 4
DAZAP1	daz associated protein 1
DCP2	dcp2 decapping enzyme homolog (s. cerevisiae)
DHCR24	24-dehydrocholesterol reductase
DKFZP564J0863	dkfzp564j0863 protein
DLG5	discs, large homolog 5 (drosophila)
DLX5	distal-less homeobox 5
DOLPP1	dolichyl pyrophosphate phosphatase 1
DRD2	dopamine receptor d2
DSCR1	down syndrome critical region gene 1
DTNA	dystrobrevin, alpha
DYNC1I1	dynein, cytoplasmic 1, intermediate chain 1
E2F5	e2f transcription factor 5, p130-binding
E2F7	e2f transcription factor 7
EEFSEC	eukaryotic elongation factor, selenocysteine-tma-specific
EGLN3	hypothetical protein flj21620
EHD4	eh-domain containing 4
EIF1AX	eukaryotic translation initiation factor 1a, x-linked
EIF3S1	eukaryotic translation initiation factor 3, subunit 1 alpha, 35kda
EIF4EBP2	eukaryotic translation initiation factor 4e binding protein 2
ELMO1	engulfment and cell motility 1
ELOVL1	cgi-88 protein
ELOVL5	elovl family member 5, elongation of long chain fatty acids (fen1/elo2, sur4/elo3-like, yeast)
ELOVL6	elovl family member 6, elongation of long chain fatty acids (fen1/elo2, sur4/elo3-like, yeast)
EPHA2	eph receptor a2
ERF	ets2 repressor factor
ESRRG	estrogen-related receptor gamma
ETF1	eukaryotic translation termination factor 1
ETS1	v-ets erythroblastosis virus e26 oncogene homolog 1 (avian)
EXOSC9	exosome component 9
EZH2	enhancer of zeste homolog 2 (drosophila)
FAM35A	family with sequence similarity 35, member a
FAM53B	family with sequence similarity 53, member b

---

FBXL11	f-box and leucine-rich repeat protein 11
FCHSD2	fch and double sh3 domains 2
FGFR1OP	fgfr1 oncogene partner
FKBP1A	fk506 binding protein 1a, 12kda
FLJ14768	hypothetical protein flj14768
FLJ20152	hypothetical protein flj20152
FLJ22222	hypothetical protein flj22222
FLRT3	fibronectin leucine rich transmembrane protein 3
FMNL2	formin-like 2
FN5	fn5 protein
FOXP1	forkhead box p1
FXR1	fragile x mental retardation, autosomal homolog 1
G3BP	ras-gtpase-activating protein sh3-domain-binding protein
GABPB2	ga binding protein transcription factor, beta subunit 1, 53kda
GALNT1	udp-n-acetyl-alpha-d-galactosamine:polypeptide n-acetylgalactosaminyltransferase 1 (galnac-t1)
GLTP	glycolipid transfer protein
GNAI3	guanine nucleotide binding protein (g protein), alpha inhibiting activity polypeptide 3
GNG12	guanine nucleotide binding protein (g protein), gamma 12
GNNPAT1	glucosamine-phosphate n-acetyltransferase 1
GPAM	glycerol-3-phosphate acyltransferase, mitochondrial
GPM6B	glycoprotein m6b
GRIA3	glutamate receptor, ionotropic, ampa 3
GRIN1	glutamate receptor, ionotropic, n-methyl d-aspartate 1
GRSF1	g-rich rna sequence binding factor 1
GTF2I	general transcription factor ii, i
GYS1	glycogen synthase 1 (muscle)
HADHA	hydroxyacyl-coenzyme a dehydrogenase/3-ketoacyl-coenzyme a thiolase/enoyl-coenzyme a hydratase (trifunctional protein), alpha subunit
HADHSC	l-3-hydroxyacyl-coenzyme a dehydrogenase, short chain
HDAC9	histone deacetylase 9
HIC2	hypermethylated in cancer 2
HIP1	huntingtin interacting protein 1
HIST1H4K	h4 histone, family 2
HNRPF	heterogeneous nuclear ribonucleoprotein f
HNRPK	heterogeneous nuclear ribonucleoprotein k
HNRPLL	heterogeneous nuclear ribonucleoprotein l-like
IARS2	isoleucine-trna synthetase 2, mitochondrial
IGF2BP3	insulin-like growth factor 2 mrna binding protein 3
IPO11	importin 11
IPO7	importin 7
IQGAP1	iq motif containing gtpase activating protein 1
ITSN1	intersectin 1 (sh3 domain protein)
JAZF1	juxtaposed with another zinc finger gene 1
KATNA1	katanin p60 (atpase-containing) subunit a 1
KCNQ2	potassium voltage-gated channel, kqt-like subfamily, member 2
KCTD12	potassium channel tetramerisation domain containing 12
KIAA0963	kiaa0963
KIAA1576	kiaa1576 protein
KIAA1967	kiaa1967
KIF1C	kinesin family member 1c
KIF2	kinesin heavy chain member 2
KLHL18	kelch-like 18 (drosophila)
LDB2	lim domain binding 2
LGTN	ligatin
LHFP	lipoma hmgic fusion partner
LIN28B	lin-28 homolog b (c. elegans)
LITAF	lipopolysaccharide-induced tnfr factor
LMNA	lamin a/c
LMNB1	lamin b1
LMO3	lim domain only 3 (rhombotin-like 2)
LMO4	lim domain only 4
LOC133619	hypothetical protein mgc12103
LOC144097	hypothetical protein bc007540
LOC153364	similar to metallo-beta-lactamase superfamily protein
LOC400451	hypothetical gene supported by ak075564; bc060873
LSM12	lsm12 homolog (s. cerevisiae)
LUC7L2	cgi-59 protein
M6PRBP1	mannose-6-phosphate receptor binding protein 1
MAML1	mastermind-like 1 (drosophila)
MAP1A	microtubule-associated protein 1a
MAP3K7	mitogen-activated protein kinase kinase kinase 7
MAPK4	mitogen-activated protein kinase 4
MARCKS	myristoylated alanine-rich protein kinase c substrate
MED8	mediator of rna polymerase ii transcription, subunit 8 homolog (yeast)
MESDC1	mesoderm development candidate 1
MORC4	morc family cw-type zinc finger 4
MPZL1	myelin protein zero-like 1
MRPS7	mitochondrial ribosomal protein s7
MTDH	metadherin
MTHFD2	methylenetetrahydrofolate dehydrogenase (nadp+ dependent) 2, methenyltetrahydrofolate cyclohydrolase
MTMR12	myotubularin related protein 12
MYLIP	myosin regulatory light chain interacting protein
MYO10	myosin x
MYOHD1	myosin head domain containing 1
NAGPA	n-acetylglucosamine-1-phosphodiester alpha-n-acetylglucosaminidase
NARG1	nmda receptor regulated 1
NCK2	nck adaptor protein 2
NCOA4	nuclear receptor coactivator 4
NDUFS4	nadh dehydrogenase (ubiquinone) fe-s protein 4, 18kda (nadh-coenzyme q reductase)
NEF3	neurofilament 3 (150kda medium)
NEK2	nima (never in mitosis gene a)-related kinase 2
NFIX	nuclear factor i/x (ccat-binding transcription factor)

---

---

NFKB1	nuclear factor of kappa light polypeptide gene enhancer in b-cells 1 (p105)
NKAP	nf-kappab activating protein
NME4	non-metastatic cells 4, protein expressed in
NMT1	n-myristoyltransferase 1
NRCAM	neuronal cell adhesion molecule
NSMAF	neutral sphingomyelinase (n-smase) activation associated factor
NSUN2	nol1/nop2/sun domain family, member 2
NUDCD2	nude domain containing 2
NUMA1	nuclear mitotic apparatus protein 1
NUTF2	nuclear transport factor 2
NXN	nucleoredoxin
NXT2	nuclear transport factor 2-like export factor 2
OPRS1	opioid receptor, sigma 1
ORCSL	origin recognition complex, subunit 5-like (yeast)
OXSR1	oxidative-stress responsive 1
P15RS	hypothetical protein flj10656
P4HA1	procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide i
PAK7	p21(cdkn1a)-activated kinase 7
PANK1	pantothenate kinase 1
PAQR8	progesterin and adipog receptor family member viii
PARP1	poly (adp-ribose) polymerase family, member 1
PBEF1	pre-b-cell colony enhancing factor 1
PCAF	p300/cbp-associated factor
PDE2A	phosphodiesterase 2a, cgmp-stimulated
PDE7B	phosphodiesterase 7b
PDIA5	protein disulfide isomerase family a, member 5
PFN2	profilin 2
PGM1	phosphoglucomutase 1
PHF16	phd finger protein 16
PHF19	phd finger protein 19
PHF20L1	phd finger protein 20-like 1
PHTF2	putative homeodomain transcription factor 2
PI4K2B	phosphatidylinositol 4-kinase type 2 beta
PLAGL2	pleiomorphic adenoma gene-like 2
PLEKHC1	pleckstrin homology domain containing, family c (with ferm domain) member 1
PLOD3	procollagen-lysine, 2-oxoglutarate 5-dioxygenase 3
PLP2	proteolipid protein 2 (colonic epithelium-enriched)
PMP22	peripheral myelin protein 22
PODXL	podocalyxin-like
POU3F2	pou domain, class 3, transcription factor 2
PPM1F	protein phosphatase 1f (pp2c domain containing)
PPP1CC	protein phosphatase 1, catalytic subunit, gamma isoform
PPP2R5D	protein phosphatase 2, regulatory subunit b (b56), delta isoform
PRNP1P	prion protein interacting protein
PRPS1	phosphoribosyl pyrophosphate synthetase 1
PSME3	proteasome (prosome, macropain) activator subunit 3 (pa28 gamma; ki)
PTEN	phosphatase and tensin homolog (mutated in multiple advanced cancers 1)
PTGFRN	prostaglandin f2 receptor negative regulator
RAB1B	rab1b, member ras oncogene family
RAB6A	rab6a, member ras oncogene family
RAF1	v-raf-1 murine leukemia viral oncogene homolog 1
RAI14	retinoic acid induced 14
RALBP1	rala binding protein 1
RANBP5	ran binding protein 5
KEEP4	receptor accessory protein 4
RHBDF2	rhomboid 5 homolog 2 (drosophila)
RHOG	ras homolog gene family, member g (rho g)
RHOT1	ras homolog gene family, member t1
RIMS4	regulating synaptic membrane exocytosis 4
RNF130	ring finger protein 130
ROR2	receptor tyrosine kinase-like orphan receptor 2
RORB	rar-related orphan receptor b
RPIA	ribose 5-phosphate isomerase a (ribose 5-phosphate epimerase)
RF56KA2	ribosomal protein s6 kinase, 90kda, polypeptide 2
RQCD1	rcd1 required for cell differentiation1 homolog (s. pombe)
RWDD4A	rwd domain containing 4a
RXRA	retinoid x receptor, alpha
SDC1	syndecan 1
SDC2	syndecan 2 (heparan sulfate proteoglycan 1, cell surface-associated, fibroglycan)
SDF2L1	stromal cell-derived factor 2-like 1
SEC13L1	sec13-like 1 (s. cerevisiae)
SEC61A1	sec61 alpha 1 subunit (s. cerevisiae)
SELI	selenoprotein i
SERP1	stress-associated endoplasmic reticulum protein 1
SERTAD4	serta domain containing 4
SFRS1	splicing factor, arginine/serine-rich 1 (splicing factor 2, alternate splicing factor)
SFRS10	splicing factor, arginine/serine-rich 10 (transformer 2 homolog, drosophila)
SFXN2	sideroflexin 2
SGK	serum/glucocorticoid regulated kinase
SKP2	s-phase kinase-associated protein 2 (p45)
SLC29A1	solute carrier family 29 (nucleoside transporters), member 1
SLC35A4	solute carrier family 35, member a4
SMAD7	smad, mothers against dpp homolog 7 (drosophila)
SOX13	sry (sex determining region y)-box 13
SP1	sp1 transcription factor
SPPL2A	signal peptide peptidase-like 2a
SPRY2	sprouty homolog 2 (drosophila)
SPTY2D1	spt2, suppressor of ty, domain containing 1 (s. cerevisiae)
ST6GALNAC3	st6 (alpha-n-acetyl-neuraminyl-2,3-beta-galactosyl-1,3)-n-acetylglactosaminide alpha-2,6-sialyltransferase 3
STARD7	start domain containing 7
STK39	serine threonine kinase 39 (ste20/sps1 homolog, yeast)

---

---

STMN1	stathmin 1/oncoprotein 18
STRN3	striatin, calmodulin binding protein 3
SUCLG2	succinate-coa ligase, gdp-forming, beta subunit
SUGT1	sgt1, suppressor of g2 allele of skp1 (s. cerevisiae)
SUV39H1	suppressor of variegation 3-9 homolog 1 (drosophila)
SYAP1	hypothetical protein flj14495
SYPL1	synaptophysin-like 1
TBC1D22A	tbc1 domain family, member 22a
TCF12	transcription factor 12 (htf4, helix-loop-helix transcription factors 4)
TCF3	transcription factor 3 (e2a immunoglobulin enhancer binding factors e12/e47)
TEX261	testis expressed sequence 261
TFAP4	transcription factor ap-4 (activating enhancer binding protein 4)
TFDP2	transcription factor dp-2 (e2f dimerization partner 2)
TIPRL	tip41, tor signalling pathway regulator-like (s. cerevisiae)
TJP2	tight junction protein 2 (zona occludens 2)
TLK1	tousled-like kinase 1
TLK2	tousled-like kinase 2
TMEM109	transmembrane protein 109
TOE1	hypothetical protein flj13949
TOM1L1	target of myb1-like 1 (chicken)
TOMM34	translocase of outer mitochondrial membrane 34
TPCN2	two pore segment channel 2
TPP2	tripeptidyl peptidase ii
TPST2	tyrosylprotein sulfotransferase 2
TRIM9	tripartite motif-containing 9
TUBG1	tubulin, gamma 1
TXNDC	thioredoxin domain containing
TXNDC5	thioredoxin domain containing 5
TYSD1	trypsin domain containing 1
UBE2H	ubiquitin-conjugating enzyme e2h (ubc8 homolog, yeast)
UBE2V2	ubiquitin-conjugating enzyme e2 variant 2
UBE4A	ubiquitination factor e4a (ufd2 homolog, yeast)
UHRF1	ubiquitin-like, containing phd and ring finger domains, 1
USF2	upstream transcription factor 2, c-fos interacting
USP14	ubiquitin specific peptidase 14 (trna-guanine transglycosylase)
USP38	ubiquitin specific peptidase 38
USP46	ubiquitin specific peptidase 46
USP48	hypothetical protein flj11328
VDAC3	voltage-dependent anion channel 3
VIM	vimentin
VPS37B	vacuolar protein sorting 37b (yeast)
WASF1	was protein family, member 1
WDR20	wd repeat domain 20
WEE1	wee1 homolog (s. pombe)
XPO4	exportin 4
XPO5	exportin 5
YME1L1	yme1-like 1 (s. cerevisiae)
YOD1	yod1 otu deubiquinating enzyme 1 homolog ( yeast)
ZCCHC3	zinc finger, cchc domain containing 3
ZDHHC23	zinc finger, dhhc-type containing 23
ZFX1B	zinc finger homeobox 1b
ZMPSTE24	zinc metallopeptidase (ste24 homolog, yeast)
ZNF313	zinc finger protein 313
ZNF503	zinc finger protein 503

---

## **APPENDIX II: SUPPLEMENTARY DATA FOR CHAPTER 3**

**Supplementary Table 1: Detailed demographic information for 97 postmortem DLPFC samples**

Sample	Age Group	Age	Gender	RIN	pH	PMI	Race	Cohort	qPCR
1	Neonate	0.15	M	2.80	6.36	24.0	W	U Maryland	*
2	Neonate	0.15	M	7.50	6.86	11.0	C	U Maryland	*
3	Neonate	0.15	M	7.75	6.63	17.0	AA	U Maryland	*
4	Neonate	0.18	F	7.05	6.48	19.0	C	U Maryland	*
5	Neonate	0.19	F	5.20	6.36	21.0	H	U Maryland	*
6	Neonate	0.20	M	4.10	6.12	24.0	C	U Maryland	*
7	Neonate	0.21	M	7.75	6.60	28.0	AA	U Maryland	*
8	Infant	0.25	F	8.45	6.54	14.0	AA	U Maryland	*
9	Infant	0.32	M	6.73	6.36	19.0	C	U Maryland	*
10	Infant	0.35	M	7.95	6.66	27.0	C	U Maryland	*
11	Infant	0.38	M	6.90	6.54	9.0	AA	U Maryland	*
12	Infant	0.39	M	7.70	6.81	5.0	AA	U Maryland	*
13	Infant	0.48	F	6.50	6.47	18.0	AA	U Maryland	*
14	Infant	0.52	F	7.65	6.82	22.0	AA	U Maryland	*
15	Infant	0.54	M	3.55	6.17	10.0	AA	U Maryland	*
16	Infant	0.54	M	7.40	6.71	24.0	AA	U Maryland	*
17	Infant	0.67	F	5.85	6.58	21.0	AA	U Maryland	*
18	Infant	0.82	M	7.30	6.65	18.0	AA	U Maryland	*
19	Infant	0.91	F	6.57	6.38	10.0	AA	U Maryland	*
20	Infant	0.91	M	7.40	6.87	18.0	AA	U Maryland	*
21	Toddler	1.58	F	7.35	6.90	24.0	C	U Maryland	*
22	Toddler	2.00	M	6.90	6.89	13.0	AA	U Maryland	*
23	Toddler	2.19	M	7.00	6.64	27.0	AA	U Maryland	*
24	Toddler	2.45	F	6.75	6.74	22.0	AA	U Maryland	*
25	Toddler	2.47	F	5.70	6.45	20.0	C	U Maryland	*
26	Toddler	2.75	M	3.80	6.16	14.0	W	U Maryland	*
27	Toddler	4.64	M	6.00	6.92	18.0	C	U Maryland	*
28	Toddler	4.86	M	7.70	6.74	19.0	AA	U Maryland	*
29	School Age	5.39	M	7.70	6.74	17.0	C	U Maryland	*
30	School Age	6.88	M	4.10	6.05	18.0	C	U Maryland	*
31	School Age	7.84	M	7.00	6.78	18.0	AA	U Maryland	*
32	School Age	8.01	M	7.05	6.76	5.0	C	U Maryland	*
33	School Age	8.14	F	6.85	6.78	20.0	AA	U Maryland	*
34	School Age	8.92	F	6.67	6.41	12.0	C	U Maryland	*
35	School Age	11.54	F	6.00	6.44	12.0	C	U Maryland	*
36	School Age	12.42	M	8.05	6.82	16.0	C	U Maryland	*
37	School Age	12.97	F	6.55	6.85	18.0	C	U Maryland	*
38	Teenage	15.00	M	5.63	6.76	13.0	AA	U Maryland	*
39	Teenage	16.34	F	6.67	6.60	20.0	C	U Maryland	*
40	Teenage	16.68	F	7.30	6.81	16.0	C	U Maryland	*
41	Teenage	17.05	M	6.33	6.69	25.0	C	U Maryland	*
42	Teenage	17.38	M	6.00	6.84	17.0	C	U Maryland	*
43	Teenage	17.49	M	6.45	6.67	16.0	C	U Maryland	*
44	Teenage	17.69	M	7.80	6.83	16.0	AA	U Maryland	*
45	Teenage	17.82	M	4.50	6.80	12.0	C	U Maryland	*
46	Teenage	18.00	M	7.00	6.79	33.0	C	NSW TRC	
47	Young Adult	20.14	M	5.80	6.50	18.0	AA	U Maryland	*
48	Young Adult	21.00	F	8.10	6.83	39.5	C	NSW TRC	
49	Young Adult	21.93	M	6.85	6.96	13.0	C	U Maryland	*
50	Young Adult	21.97	M	6.85	6.25	7.0	AA	U Maryland	*
51	Young Adult	22.51	M	5.45	6.75	12.0	C	U Maryland	*
52	Young Adult	22.92	M	6.93	6.84	4.0	AA	U Maryland	*
53	Young Adult	24.00	M	7.10	6.95	43.0	C	NSW TRC	
54	Young Adult	24.93	M	7.50	6.92	7.0	C	U Maryland	*



55	Young Adult	25.10	F	6.80	6.54	32.0	C	U Maryland	*
56	Young Adult	25.38	F	7.35	6.73	16.0	C	U Maryland	*
57	Adult	33.00	F	8.00	6.91	24.0	C	NSW TRC	*
58	Adult	34.00	M	7.10	6.51	20.5	C	NSW TRC	*
59	Adult	35.99	M	7.25	6.73	13.0	C	U Maryland	*
60	Adult	37.00	M	6.90	6.23	11.0	C	NSW TRC	
61	Adult	37.00	M	7.60	6.80	21.0	C	NSW TRC	
62	Adult	37.00	M	7.50	6.94	24.0	C	NSW TRC	
63	Adult	38.00	M	7.70	6.73	13.5	C	NSW TRC	
64	Adult	38.42	F	7.00	6.98	19.0	AA	U Maryland	*
65	Adult	38.63	M	6.90	6.37	8.0	AA	U Maryland	*
66	Adult	42.94	M	6.25	6.49	18.0	C	U Maryland	*
67	Adult	43.00	M	7.40	6.71	13.0	C	NSW TRC	
68	Adult	44.00	M	7.20	6.72	50.0	C	NSW TRC	
69	Adult	46.00	M	6.70	5.84	29.0	C	NSW TRC	
70	Adult	46.00	M	7.30	6.65	25.0	C	NSW TRC	
71	Adult	46.18	M	7.43	6.75	18.0	AA	U Maryland	*
72	Adult	47.44	M	6.35	6.56	12.0	C	U Maryland	*
73	Adult	49.00	F	8.30	6.64	15.0	C	NSW TRC	
74	Adult	49.22	F	5.85	6.78	7.0	AA	U Maryland	*
75	Elderly	50.00	M	6.90	6.61	19.0	C	NSW TRC	
76	Elderly	50.00	M	8.10	6.68	29.0	C	NSW TRC	
77	Elderly	51.00	F	7.70	7.15	37.5	C	NSW TRC	
78	Elderly	53.00	M	7.10	6.70	27.0	C	NSW TRC	
79	Elderly	54.00	M	6.00	6.80	29.0	C	NSW TRC	
80	Elderly	55.00	M	7.30	7.19	20.0	C	NSW TRC	
81	Elderly	56.00	F	7.10	6.47	23.0	C	NSW TRC	
82	Elderly	56.00	M	7.10	6.64	24.0	C	NSW TRC	
83	Elderly	56.00	M	6.20	6.98	37.0	C	NSW TRC	
84	Elderly	57.00	M	8.40	6.86	18.0	C	NSW TRC	
85	Elderly	58.00	M	7.60	6.56	12.0	C	NSW TRC	
86	Elderly	59.00	M	7.40	6.96	20.0	C	NSW TRC	
87	Elderly	60.00	M	7.10	6.02	25.0	C	NSW TRC	
88	Elderly	60.00	M	7.80	6.55	13.0	C	NSW TRC	
89	Elderly	60.00	F	7.40	6.52	21.0	C	NSW TRC	
90	Elderly	60.00	M	6.90	6.95	21.5	C	NSW TRC	
91	Elderly	61.00	M	6.60	6.31	27.5	C	NSW TRC	
92	Elderly	62.00	M	7.50	6.57	37.5	C	NSW TRC	
93	Elderly	64.00	M	7.00	7.01	39.5	C	NSW TRC	
94	Elderly	73.00	M	8.10	6.57	48.0	C	NSW TRC	
95	Elderly	74.00	M	7.40	6.31	10.0	C	NSW TRC	
96	Elderly	78.00	M	7.50	6.29	6.5	C	NSW TRC	
97	Elderly	78.00	F	6.10	6.37	11.0	C	NSW TRC	

C: Caucasian; AA: African-American; H: Hispanic; PMI: postmortem interval (hours); RIN: RNA integrity number; \* Samples were included in qPCR validation. NSW TRC; NSW Tissue Resource Centre, University of Sydney, Australia

**Supplementary Table 2: Oligonucleotide Sequences**

Name	Sequence	Target
U49-F	ATCACTAATAGGAAGTGCCGTC	U49 snoRNA
U49-R	ACAGGAGTAGTCTTCGTCAGT	U49 snoRNA
U44-F	TGATAGCAAATGCTGACTGA	U44 snoRNA
U44-R	CAGTTAGAGCTAATTAAGACCT	U44 snoRNA
U6-probe	GCCATGCTAATCTTCTCTGTATC	U6 snRNA
U6-F339	CGGCAGCACATATACTAAAATTGG	U6 snRNA
107-F	AGCAGCATTGTACAG	miR-107
107-R	<u>GTAAAACGACGGCCAGT</u> TGATAGCC	miR-107
16-F	TAGCAGCACATCAT	miR-16
16-R	<u>GTAAAACGACGGCCAGT</u> TGTAAACC	miR-16
181b-F	TTTCTAACATTTCATTGCT	miR-181b
181b-R	CAACCTTCTCCACCGAC	miR-181b
219-F	T+GAT+TGTCCAAAC	miR-219
219-R	<u>GTAAAACGACGGCCAGT</u> AGAATTGC	miR-219
195-F	T+AGCAGCACAGA	miR-195
195-R	<u>GTAAAACGACGGCCAGT</u> GCCAATATT	miR-195
17-F	CAAAGTGCTTACAGT	miR-17
17-R	<u>GTAAAACGACGGCCAGT</u> CTACCTG	miR-17
GUSB-F	GCCAATGAAACCAGGTATCCC	GUSB
GUSB-R	GCTCAAGTAAACAGGCTGTTTTCC	GUSB
HMBS-F	GAGAGTGATTCGCGTGGGTA	HMBS
HMBS-R	CAGGGTACGAGGCTTTCAAT	HMBS
DICER1-F	CACATCAATAGATACTGTGCT	DICER
DICER-R	TTGGTGGACCAACAATGGAGG	DICER
DGCR8-F	GCTGAGGAAAGGGAGGAG	DGCR8
DGCR8-R	ACGTCCACGGTGACACAG	DGCR8
DROSHA-F	AAGCGTTAATAGGAGCTGTTTACT	DROSHA
DROSHA-R	CGTCCAAATAACTGCTTGGCT	DROSHA
XPO5-F	ATATATGAGGCACTGCGCC	EXPORTIN-5
XPO5-R	AAACTGGTCCAGTGAGTCCTT	EXPORTIN-5

The direction of primers with respect to the target sequence was denoted in the name as either F or R for forward and reverse respectively. Underlined sequence is not gene specific and was used to provide a primer recognition sequence. The positions of LNA modified bases are preceded by a “+” symbol.

**Supplementary Table 3: Spearman correlations of miRNA expression and demographic variables**

miRNA		Age	RIN	pH	PMI
let7a	Correlation Coefficient	-.250 <sup>*</sup>	-.156	-.205 <sup>*</sup>	-.261 <sup>***</sup>
	Sig. (2-tailed)	.014	.127	.044	.010
	N	97	97	97	97
let7b	Correlation Coefficient	-.511 <sup>***</sup>	-.213 <sup>*</sup>	-.144	-.349 <sup>**</sup>
	Sig. (2-tailed)	.000	.036	.160	.000
	N	97	97	97	97
let7c	Correlation Coefficient	-.487 <sup>***</sup>	-.241 <sup>*</sup>	-.201 <sup>*</sup>	-.295 <sup>**</sup>
	Sig. (2-tailed)	.000	.018	.049	.003
	N	97	97	97	97
let7d	Correlation Coefficient	-.355 <sup>**</sup>	-.206 <sup>*</sup>	-.208 <sup>*</sup>	-.266 <sup>**</sup>
	Sig. (2-tailed)	.000	.043	.041	.009
	N	97	97	97	97
let7e	Correlation Coefficient	-.409 <sup>**</sup>	-.152	-.174	-.337 <sup>***</sup>
	Sig. (2-tailed)	.000	.138	.088	.001
	N	97	97	97	97
let7f	Correlation Coefficient	-.455 <sup>**</sup>	-.194	-.154	-.302 <sup>**</sup>
	Sig. (2-tailed)	.000	.057	.132	.003
	N	97	97	97	97
let7g	Correlation Coefficient	-.416 <sup>**</sup>	-.200 <sup>*</sup>	-.145	-.296 <sup>**</sup>
	Sig. (2-tailed)	.000	.050	.155	.003
	N	97	97	97	97
let7i	Correlation Coefficient	-.445 <sup>**</sup>	-.195	-.116	-.276 <sup>**</sup>
	Sig. (2-tailed)	.000	.056	.256	.006
	N	97	97	97	97
miR1	Correlation Coefficient	-.465 <sup>**</sup>	-.152	.022	-.290 <sup>**</sup>
	Sig. (2-tailed)	.000	.138	.834	.004
	N	97	97	97	97
miR7	Correlation Coefficient	-.437 <sup>***</sup>	-.179	-.150	-.306 <sup>**</sup>
	Sig. (2-tailed)	.000	.079	.142	.002
	N	97	97	97	97
miR9	Correlation Coefficient	-.410 <sup>**</sup>	-.138	-.188	-.278 <sup>**</sup>
	Sig. (2-tailed)	.000	.178	.065	.006
	N	97	97	97	97
miR16	Correlation Coefficient	-.463 <sup>**</sup>	-.210 <sup>*</sup>	-.163	-.310 <sup>**</sup>
	Sig. (2-tailed)	.000	.039	.111	.002
	N	97	97	97	97
miR21	Correlation Coefficient	-.270 <sup>**</sup>	-.172	-.186	-.250 <sup>*</sup>
	Sig. (2-tailed)	.008	.093	.068	.013
	N	97	97	97	97
miR22	Correlation Coefficient	-.549 <sup>***</sup>	-.209 <sup>*</sup>	-.140	-.354 <sup>***</sup>
	Sig. (2-tailed)	.000	.040	.171	.000
	N	97	97	97	97
miR24	Correlation Coefficient	-.298 <sup>**</sup>	-.183	-.163	-.276 <sup>**</sup>
	Sig. (2-tailed)	.003	.072	.110	.006
	N	97	97	97	97
miR25	Correlation Coefficient	.345 <sup>***</sup>	.072	-.106	.013
	Sig. (2-tailed)	.001	.481	.300	.897
	N	97	97	97	97
miR28	Correlation Coefficient	.157	.060	-.106	.076
	Sig. (2-tailed)	.125	.562	.302	.458
	N	97	97	97	97
miR31	Correlation Coefficient	.483 <sup>***</sup>	.216 <sup>*</sup>	.138	.243 <sup>*</sup>
	Sig. (2-tailed)	.000	.034	.177	.017
	N	97	97	97	97
miR32	Correlation Coefficient	-.527 <sup>***</sup>	-.257 <sup>*</sup>	-.072	-.353 <sup>**</sup>
	Sig. (2-tailed)	.000	.011	.483	.000
	N	97	97	97	97
miR33	Correlation Coefficient	-.421 <sup>**</sup>	-.176	-.061	-.302 <sup>**</sup>
	Sig. (2-tailed)	.000	.085	.555	.003
	N	97	97	97	97
miR92	Correlation Coefficient	.323 <sup>**</sup>	.130	-.084	-.003
	Sig. (2-tailed)	.001	.205	.414	.976
	N	97	97	97	97
miR93	Correlation Coefficient	-.363 <sup>**</sup>	-.172	-.199	-.313 <sup>**</sup>
	Sig. (2-tailed)	.000	.093	.051	.002
	N	97	97	97	97
miR95	Correlation Coefficient	-.517 <sup>***</sup>	-.185	-.176	-.315 <sup>**</sup>
	Sig. (2-tailed)	.000	.069	.085	.002
	N	97	97	97	97
miR98	Correlation Coefficient	-.258 <sup>*</sup>	-.149	-.260 <sup>*</sup>	-.156
	Sig. (2-tailed)	.011	.146	.010	.128
	N	97	97	97	97
miR100	Correlation Coefficient	-.085	-.149	-.105	-.205 <sup>*</sup>
	Sig. (2-tailed)	.406	.147	.306	.044
	N	97	97	97	97
miR101	Correlation Coefficient	-.456 <sup>**</sup>	-.210 <sup>*</sup>	-.165	-.307 <sup>**</sup>
	Sig. (2-tailed)	.000	.039	.106	.002
	N	97	97	97	97
miR103	Correlation Coefficient	-.516 <sup>***</sup>	-.203 <sup>*</sup>	-.142	-.330 <sup>**</sup>
	Sig. (2-tailed)	.000	.046	.166	.001
	N	97	97	97	97
miR105	Correlation Coefficient	-.446 <sup>**</sup>	-.108	-.145	-.193
	Sig. (2-tailed)	.000	.291	.156	.059

	N	97	97	97	97
miR107	Correlation Coefficient	-.489"	-.124	-.151	-.245'
	Sig. (2-tailed)	.000	.228	.139	.015
	N	97	97	97	97
miR126	Correlation Coefficient	-.450"	-.216'	-.158	-.290"
	Sig. (2-tailed)	.000	.033	.123	.004
	N	97	97	97	97
miR127	Correlation Coefficient	-.345"	-.084	-.137	-.195
	Sig. (2-tailed)	.001	.416	.181	.055
	N	97	97	97	97
miR129	Correlation Coefficient	-.086	-.052	-.156	-.138
	Sig. (2-tailed)	.401	.611	.126	.176
	N	97	97	97	97
miR132	Correlation Coefficient	-.486"	-.169	-.147	-.323"
	Sig. (2-tailed)	.000	.098	.150	.001
	N	97	97	97	97
miR134	Correlation Coefficient	-.141	-.005	-.111	.000
	Sig. (2-tailed)	.169	.962	.278	1.000
	N	97	97	97	97
miR136	Correlation Coefficient	-.438"	-.168	-.042	-.263"
	Sig. (2-tailed)	.000	.101	.680	.009
	N	97	97	97	97
miR137	Correlation Coefficient	-.442"	-.201'	-.159	-.283"
	Sig. (2-tailed)	.000	.048	.120	.005
	N	97	97	97	97
miR138	Correlation Coefficient	-.432"	-.179	-.201'	-.222'
	Sig. (2-tailed)	.000	.079	.048	.029
	N	97	97	97	97
miR139	Correlation Coefficient	-.488"	-.217'	-.171	-.304"
	Sig. (2-tailed)	.000	.033	.094	.002
	N	97	97	97	97
miR140	Correlation Coefficient	-.292"	-.186	-.168	-.279"
	Sig. (2-tailed)	.004	.068	.099	.006
	N	97	97	97	97
miR141	Correlation Coefficient	-.258'	-.250'	-.170	-.185
	Sig. (2-tailed)	.011	.013	.097	.069
	N	97	97	97	97
miR143	Correlation Coefficient	-.384"	-.178	-.179	-.297"
	Sig. (2-tailed)	.000	.081	.080	.003
	N	97	97	97	97
miR144	Correlation Coefficient	-.477"	-.203'	-.063	-.363"
	Sig. (2-tailed)	.000	.046	.542	.000
	N	97	97	97	97
miR145	Correlation Coefficient	-.227'	-.121	-.201'	-.234'
	Sig. (2-tailed)	.025	.240	.048	.021
	N	97	97	97	97
miR149	Correlation Coefficient	-.342"	-.029	-.138	-.151
	Sig. (2-tailed)	.001	.776	.177	.139
	N	97	97	97	97
miR150	Correlation Coefficient	-.080	-.069	-.123	-.222'
	Sig. (2-tailed)	.435	.499	.228	.029
	N	97	97	97	97
miR151	Correlation Coefficient	.007	-.133	-.122	-.147
	Sig. (2-tailed)	.946	.195	.236	.151
	N	97	97	97	97
miR152	Correlation Coefficient	-.344"	-.247'	-.149	-.278"
	Sig. (2-tailed)	.001	.015	.145	.006
	N	97	97	97	97
miR153	Correlation Coefficient	-.498"	-.166	-.149	-.311"
	Sig. (2-tailed)	.000	.103	.145	.002
	N	97	97	97	97
miR154	Correlation Coefficient	-.068	.008	-.046	-.049
	Sig. (2-tailed)	.509	.938	.653	.632
	N	97	97	97	97
miR155	Correlation Coefficient	-.392"	-.153	-.120	-.222'
	Sig. (2-tailed)	.000	.133	.241	.028
	N	97	97	97	97
miR182	Correlation Coefficient	-.404"	-.223'	.049	-.211'
	Sig. (2-tailed)	.000	.028	.633	.038
	N	97	97	97	97
miR183	Correlation Coefficient	-.255'	-.095	-.048	-.082
	Sig. (2-tailed)	.012	.357	.639	.425
	N	97	97	97	97
miR185	Correlation Coefficient	-.294"	-.232'	-.096	-.355"
	Sig. (2-tailed)	.003	.022	.350	.000
	N	97	97	97	97
miR186	Correlation Coefficient	-.375"	-.186	-.163	-.227'
	Sig. (2-tailed)	.000	.069	.111	.025
	N	97	97	97	97
miR187	Correlation Coefficient	-.508"	-.121	-.085	-.228'
	Sig. (2-tailed)	.000	.238	.405	.025
	N	97	97	97	97
miR188	Correlation Coefficient	-.358"	-.137	-.105	-.184
	Sig. (2-tailed)	.000	.182	.308	.071
	N	97	97	97	97
miR189	Correlation Coefficient	.442"	.130	.018	.060
	Sig. (2-tailed)	.000	.204	.864	.560
	N	97	97	97	97
miR190	Correlation Coefficient	-.431"	-.153	-.087	-.314"
	Sig. (2-tailed)	.000	.133	.396	.002
	N	97	97	97	97

miR191	Correlation Coefficient	-.357"	-.200"	-.139	-.230'
	Sig. (2-tailed)	.000	.050	.175	.023
	N	97	97	97	97
miR192	Correlation Coefficient	.109	.040	-.151	.039
	Sig. (2-tailed)	.286	.696	.139	.705
	N	97	97	97	97
miR194	Correlation Coefficient	.103	.052	-.236'	.039
	Sig. (2-tailed)	.315	.615	.020	.707
	N	97	97	97	97
miR195	Correlation Coefficient	-.220'	-.157	-.212'	-.208'
	Sig. (2-tailed)	.031	.126	.037	.041
	N	97	97	97	97
miR197	Correlation Coefficient	-.138	-.061	-.199	-.095
	Sig. (2-tailed)	.178	.555	.051	.354
	N	97	97	97	97
miR202	Correlation Coefficient	-.132	.033	-.152	-.139
	Sig. (2-tailed)	.196	.747	.138	.174
	N	97	97	97	97
miR203	Correlation Coefficient	.112	.079	.015	.028
	Sig. (2-tailed)	.275	.441	.883	.782
	N	97	97	97	97
miR204	Correlation Coefficient	-.254'	-.151	-.116	-.270"
	Sig. (2-tailed)	.012	.141	.257	.007
	N	97	97	97	97
miR205	Correlation Coefficient	-.663"	-.302"	-.133	-.359"
	Sig. (2-tailed)	.000	.003	.195	.000
	N	97	97	97	97
miR206	Correlation Coefficient	-.175	-.091	-.178	-.232'
	Sig. (2-tailed)	.086	.373	.082	.022
	N	97	97	97	97
miR210	Correlation Coefficient	-.331"	-.173	.002	-.284"
	Sig. (2-tailed)	.001	.090	.983	.005
	N	97	97	97	97
miR211	Correlation Coefficient	.108	.087	.042	-.193
	Sig. (2-tailed)	.291	.395	.681	.058
	N	97	97	97	97
miR212	Correlation Coefficient	-.447"	-.134	-.103	-.196
	Sig. (2-tailed)	.000	.191	.316	.055
	N	97	97	97	97
miR213	Correlation Coefficient	-.034	-.079	-.211'	-.096
	Sig. (2-tailed)	.739	.441	.038	.350
	N	97	97	97	97
miR214	Correlation Coefficient	-.024	.095	.027	-.111
	Sig. (2-tailed)	.815	.353	.792	.279
	N	97	97	97	97
miR215	Correlation Coefficient	-.007	.012	-.059	-.011
	Sig. (2-tailed)	.948	.904	.565	.914
	N	97	97	97	97
miR218	Correlation Coefficient	-.503"	-.164	-.149	-.287"
	Sig. (2-tailed)	.000	.109	.145	.004
	N	97	97	97	97
miR219	Correlation Coefficient	-.052	-.109	-.108	-.279"
	Sig. (2-tailed)	.615	.287	.292	.006
	N	97	97	97	97
miR221	Correlation Coefficient	-.350"	-.178	-.197	-.261"
	Sig. (2-tailed)	.000	.080	.053	.010
	N	97	97	97	97
miR222	Correlation Coefficient	-.006	.139	.056	-.017
	Sig. (2-tailed)	.952	.175	.588	.865
	N	97	97	97	97
miR223	Correlation Coefficient	-.126	-.170	-.173	-.199
	Sig. (2-tailed)	.219	.096	.090	.050
	N	97	97	97	97
miR296	Correlation Coefficient	-.233'	.114	.071	-.133
	Sig. (2-tailed)	.022	.267	.488	.193
	N	97	97	97	97
miR301	Correlation Coefficient	-.202'	-.131	-.310"	-.198
	Sig. (2-tailed)	.048	.200	.002	.052
	N	97	97	97	97
miR320	Correlation Coefficient	-.258'	-.092	-.119	-.241'
	Sig. (2-tailed)	.011	.370	.248	.017
	N	97	97	97	97
miR323	Correlation Coefficient	-.332"	-.077	-.086	-.092
	Sig. (2-tailed)	.001	.455	.401	.368
	N	97	97	97	97
miR326	Correlation Coefficient	-.186	-.050	-.124	-.144
	Sig. (2-tailed)	.068	.629	.228	.159
	N	97	97	97	97
miR328	Correlation Coefficient	.272"	.188	.015	-.023
	Sig. (2-tailed)	.007	.065	.887	.825
	N	97	97	97	97
miR329	Correlation Coefficient	-.282"	-.165	-.110	-.135
	Sig. (2-tailed)	.005	.107	.282	.188
	N	97	97	97	97
miR330	Correlation Coefficient	.294"	.042	-.030	-.112
	Sig. (2-tailed)	.004	.684	.773	.275
	N	97	97	97	97
miR331	Correlation Coefficient	-.375"	-.145	-.165	-.288"
	Sig. (2-tailed)	.000	.157	.106	.004
	N	97	97	97	97
miR335	Correlation Coefficient	-.427"	-.161	-.156	-.221'

miR338	Sig. (2-tailed)	.000	.116	.127	.030
	N	97	97	97	97
	Correlation Coefficient	-.156	-.177	-.205 <sup>*</sup>	-.221 <sup>*</sup>
miR339	Sig. (2-tailed)	.127	.083	.044	.029
	N	97	97	97	97
	Correlation Coefficient	-.112	-.148	.055	-.123
miR340	Sig. (2-tailed)	.274	.149	.594	.230
	N	97	97	97	97
	Correlation Coefficient	-.022	-.013	-.185	-.001
miR342	Sig. (2-tailed)	.831	.900	.070	.990
	N	97	97	97	97
	Correlation Coefficient	-.355 <sup>**</sup>	-.167	-.143	-.257 <sup>*</sup>
miR345	Sig. (2-tailed)	.000	.102	.162	.011
	N	97	97	97	97
	Correlation Coefficient	-.447 <sup>**</sup>	-.181	-.121	-.387 <sup>**</sup>
miR346	Sig. (2-tailed)	.000	.076	.239	.000
	N	97	97	97	97
	Correlation Coefficient	.514 <sup>**</sup>	.135	.042	.192
miR361	Sig. (2-tailed)	.000	.188	.679	.059
	N	97	97	97	97
	Correlation Coefficient	-.393 <sup>**</sup>	-.178	-.204 <sup>*</sup>	-.242 <sup>*</sup>
miR362	Sig. (2-tailed)	.000	.081	.045	.017
	N	97	97	97	97
	Correlation Coefficient	-.402 <sup>**</sup>	-.248 <sup>*</sup>	-.113	-.352 <sup>**</sup>
miR363	Sig. (2-tailed)	.000	.014	.270	.000
	N	97	97	97	97
	Correlation Coefficient	-.298 <sup>**</sup>	-.199	-.158	-.262 <sup>**</sup>
miR365	Sig. (2-tailed)	.003	.050	.123	.010
	N	97	97	97	97
	Correlation Coefficient	-.382 <sup>**</sup>	-.279 <sup>**</sup>	-.112	-.328 <sup>**</sup>
miR368	Sig. (2-tailed)	.000	.006	.274	.001
	N	97	97	97	97
	Correlation Coefficient	-.549 <sup>**</sup>	-.159	-.187	-.291 <sup>**</sup>
miR370	Sig. (2-tailed)	.000	.120	.067	.004
	N	97	97	97	97
	Correlation Coefficient	-.181	.006	.031	-.018
miR372	Sig. (2-tailed)	.076	.951	.760	.862
	N	97	97	97	97
	Correlation Coefficient	-.146	-.192	-.123	-.159
miR374	Sig. (2-tailed)	.153	.059	.229	.119
	N	97	97	97	97
	Correlation Coefficient	-.432 <sup>**</sup>	-.199	-.188	-.289 <sup>**</sup>
miR377	Sig. (2-tailed)	.000	.051	.065	.004
	N	97	97	97	97
	Correlation Coefficient	-.360 <sup>**</sup>	-.189	-.227 <sup>*</sup>	-.282 <sup>**</sup>
miR378	Sig. (2-tailed)	.000	.063	.025	.005
	N	97	97	97	97
	Correlation Coefficient	-.252 <sup>*</sup>	.027	-.117	.100
miR379	Sig. (2-tailed)	.013	.789	.253	.328
	N	97	97	97	97
	Correlation Coefficient	-.438 <sup>**</sup>	-.179	-.194	-.251 <sup>*</sup>
miR381	Sig. (2-tailed)	.000	.080	.057	.013
	N	97	97	97	97
	Correlation Coefficient	-.522 <sup>**</sup>	-.187	-.149	-.303 <sup>**</sup>
miR382	Sig. (2-tailed)	.000	.067	.145	.003
	N	97	97	97	97
	Correlation Coefficient	-.538 <sup>**</sup>	-.147	-.088	-.223 <sup>*</sup>
miR383	Sig. (2-tailed)	.000	.151	.393	.028
	N	97	97	97	97
	Correlation Coefficient	-.511 <sup>**</sup>	-.136	-.101	-.222 <sup>*</sup>
miR384	Sig. (2-tailed)	.000	.184	.323	.029
	N	97	97	97	97
	Correlation Coefficient	-.440 <sup>**</sup>	-.207 <sup>*</sup>	-.093	-.302 <sup>**</sup>
miR410	Sig. (2-tailed)	.000	.042	.364	.003
	N	97	97	97	97
	Correlation Coefficient	-.453 <sup>**</sup>	-.192	-.185	-.245 <sup>*</sup>
miR411	Sig. (2-tailed)	.000	.059	.070	.016
	N	97	97	97	97
	Correlation Coefficient	-.447 <sup>**</sup>	-.142	-.137	-.289 <sup>**</sup>
miR412	Sig. (2-tailed)	.000	.165	.181	.004
	N	97	97	97	97
	Correlation Coefficient	.356 <sup>**</sup>	.216 <sup>*</sup>	.065	.230 <sup>*</sup>
miR421	Sig. (2-tailed)	.000	.034	.526	.024
	N	97	97	97	97
	Correlation Coefficient	-.392 <sup>**</sup>	-.230 <sup>*</sup>	-.186	-.288 <sup>**</sup>
miR423	Sig. (2-tailed)	.000	.023	.068	.004
	N	97	97	97	97
	Correlation Coefficient	-.288 <sup>**</sup>	-.147	-.112	-.293 <sup>**</sup>
miR424	Sig. (2-tailed)	.004	.152	.273	.004
	N	97	97	97	97
	Correlation Coefficient	-.574 <sup>**</sup>	-.255 <sup>*</sup>	-.180	-.289 <sup>**</sup>
miR425	Sig. (2-tailed)	.000	.012	.078	.004
	N	97	97	97	97
	Correlation Coefficient	.489 <sup>**</sup>	.142	.041	.175
miR429	Sig. (2-tailed)	.000	.164	.689	.086
	N	97	97	97	97
	Correlation Coefficient	.199	.044	-.082	.042
miR431	Sig. (2-tailed)	.051	.670	.424	.685
	N	97	97	97	97
	Correlation Coefficient	-.086	.032	-.055	.033
	Sig. (2-tailed)	.403	.757	.589	.747
	N				
	Correlation Coefficient				

	N	97	97	97	97
miR432	Correlation Coefficient	-.384**	-.114	-.075	-.162
	Sig. (2-tailed)	.000	.265	.464	.113
	N	97	97	97	97
miR433	Correlation Coefficient	-.068	.060	.050	-.069
	Sig. (2-tailed)	.510	.557	.625	.503
	N	97	97	97	97
miR448	Correlation Coefficient	-.529**	-.150	-.115	-.156
	Sig. (2-tailed)	.000	.141	.260	.126
	N	97	97	97	97
miR449	Correlation Coefficient	.203*	.256*	-.015	.303**
	Sig. (2-tailed)	.046	.012	.880	.003
	N	97	97	97	97
miR450	Correlation Coefficient	-.610**	-.205*	-.164	-.298**
	Sig. (2-tailed)	.000	.044	.108	.003
	N	97	97	97	97
miR451	Correlation Coefficient	-.289**	-.179	-.189	-.223*
	Sig. (2-tailed)	.004	.079	.063	.028
	N	97	97	97	97
miR453	Correlation Coefficient	.352**	.073	-.112	.054
	Sig. (2-tailed)	.000	.479	.274	.603
	N	97	97	97	97
miR455	Correlation Coefficient	-.521**	-.124	-.140	-.309**
	Sig. (2-tailed)	.000	.226	.170	.002
	N	97	97	97	97
miR483	Correlation Coefficient	-.287**	.030	-.163	-.166
	Sig. (2-tailed)	.004	.772	.112	.104
	N	97	97	97	97
miR484	Correlation Coefficient	-.220*	-.057	-.182	-.233*
	Sig. (2-tailed)	.030	.582	.074	.022
	N	97	97	97	97
miR486	Correlation Coefficient	-.119	.045	.068	-.050
	Sig. (2-tailed)	.244	.659	.509	.624
	N	97	97	97	97
miR488	Correlation Coefficient	-.476**	-.093	-.197	-.238*
	Sig. (2-tailed)	.000	.366	.053	.019
	N	97	97	97	97
miR490	Correlation Coefficient	-.397**	-.065	-.036	-.135
	Sig. (2-tailed)	.000	.526	.728	.189
	N	97	97	97	97
miR491	Correlation Coefficient	.052	-.002	-.014	-.073
	Sig. (2-tailed)	.616	.988	.893	.477
	N	97	97	97	97
miR494	Correlation Coefficient	-.477**	-.169	-.162	-.193
	Sig. (2-tailed)	.000	.097	.113	.058
	N	97	97	97	97
miR495	Correlation Coefficient	-.319**	-.153	-.120	-.214*
	Sig. (2-tailed)	.001	.136	.240	.035
	N	97	97	97	97
miR496	Correlation Coefficient	-.557**	-.184	-.139	-.237*
	Sig. (2-tailed)	.000	.072	.173	.019
	N	97	97	97	97
miR497	Correlation Coefficient	-.202*	-.091	-.192	-.173
	Sig. (2-tailed)	.047	.376	.059	.091
	N	97	97	97	97
miR498	Correlation Coefficient	-.422**	-.145	-.088	-.292**
	Sig. (2-tailed)	.000	.156	.394	.004
	N	97	97	97	97
miR499	Correlation Coefficient	.262**	.008	-.134	-.077
	Sig. (2-tailed)	.009	.941	.190	.452
	N	97	97	97	97
miR500	Correlation Coefficient	.117	-.033	.024	-.088
	Sig. (2-tailed)	.254	.745	.814	.393
	N	97	97	97	97
miR502	Correlation Coefficient	-.374**	-.080	-.265**	-.234*
	Sig. (2-tailed)	.000	.438	.009	.021
	N	97	97	97	97
miR503	Correlation Coefficient	-.636**	-.212*	-.123	-.176
	Sig. (2-tailed)	.000	.037	.231	.084
	N	97	97	97	97
miR504	Correlation Coefficient	.253*	.215*	-.084	.152
	Sig. (2-tailed)	.012	.035	.414	.138
	N	97	97	97	97
miR505	Correlation Coefficient	-.564**	-.228*	-.193	-.295**
	Sig. (2-tailed)	.000	.024	.058	.003
	N	97	97	97	97
miR506	Correlation Coefficient	-.597**	-.124	-.181	-.309**
	Sig. (2-tailed)	.000	.228	.076	.002
	N	97	97	97	97
miR507	Correlation Coefficient	.544**	.249*	-.084	.244*
	Sig. (2-tailed)	.000	.014	.412	.016
	N	97	97	97	97
miR522	Correlation Coefficient	-.301**	-.045	-.086	-.226*
	Sig. (2-tailed)	.003	.662	.403	.026
	N	97	97	97	97
miR523	Correlation Coefficient	.291**	.114	-.085	.014
	Sig. (2-tailed)	.004	.267	.408	.889
	N	97	97	97	97
miR525	Correlation Coefficient	.339**	.059	-.099	.044
	Sig. (2-tailed)	.001	.568	.335	.669
	N	97	97	97	97

miR532	Correlation Coefficient	.174	-.013	-.248*	-.131
	Sig. (2-tailed)	.088	.902	.015	.201
	N	97	97	97	97
miR539	Correlation Coefficient	-.401**	-.203*	-.087	-.238*
	Sig. (2-tailed)	.000	.046	.395	.019
	N	97	97	97	97
miR544	Correlation Coefficient	-.397**	-.167	-.122	-.282**
	Sig. (2-tailed)	.000	.102	.233	.005
	N	97	97	97	97
miR545	Correlation Coefficient	-.518**	-.205*	-.128	-.376**
	Sig. (2-tailed)	.000	.044	.212	.000
	N	97	97	97	97
miR550	Correlation Coefficient	-.347**	-.141	-.212*	-.240*
	Sig. (2-tailed)	.001	.167	.038	.018
	N	97	97	97	97
miR553	Correlation Coefficient	-.273**	-.198	-.058	-.119
	Sig. (2-tailed)	.007	.052	.575	.248
	N	97	97	97	97
miR554	Correlation Coefficient	.473**	.106	-.028	.299**
	Sig. (2-tailed)	.000	.300	.786	.003
	N	97	97	97	97
miR555	Correlation Coefficient	-.173	-.023	-.097	-.175
	Sig. (2-tailed)	.090	.824	.343	.087
	N	97	97	97	97
miR559	Correlation Coefficient	-.452**	-.302**	-.164	-.244*
	Sig. (2-tailed)	.000	.003	.108	.016
	N	97	97	97	97
miR560	Correlation Coefficient	-.083	-.111	-.123	-.080
	Sig. (2-tailed)	.416	.280	.231	.435
	N	97	97	97	97
miR563	Correlation Coefficient	.021	-.071	-.006	.032
	Sig. (2-tailed)	.835	.487	.957	.757
	N	97	97	97	97
miR564	Correlation Coefficient	.185	.052	-.131	.010
	Sig. (2-tailed)	.070	.612	.201	.920
	N	97	97	97	97
miR565	Correlation Coefficient	.134	.134	-.127	.016
	Sig. (2-tailed)	.190	.192	.216	.875
	N	97	97	97	97
miR566	Correlation Coefficient	.024	.055	-.036	.022
	Sig. (2-tailed)	.815	.592	.726	.830
	N	97	97	97	97
miR567	Correlation Coefficient	.354**	.142	-.228*	.090
	Sig. (2-tailed)	.000	.164	.025	.383
	N	97	97	97	97
miR568	Correlation Coefficient	.043	-.048	-.046	-.092
	Sig. (2-tailed)	.677	.638	.658	.372
	N	97	97	97	97
miR569	Correlation Coefficient	-.166	-.053	-.123	-.139
	Sig. (2-tailed)	.105	.606	.228	.175
	N	97	97	97	97
miR570	Correlation Coefficient	-.014	-.017	-.148	-.198
	Sig. (2-tailed)	.894	.869	.149	.052
	N	97	97	97	97
miR571	Correlation Coefficient	.467**	.131	-.072	.145
	Sig. (2-tailed)	.000	.202	.483	.156
	N	97	97	97	97
miR572	Correlation Coefficient	.205*	.064	-.015	.157
	Sig. (2-tailed)	.044	.536	.883	.125
	N	97	97	97	97
miR573	Correlation Coefficient	.129	-.093	-.167	-.025
	Sig. (2-tailed)	.208	.366	.102	.806
	N	97	97	97	97
miR574	Correlation Coefficient	.325**	.042	.022	-.107
	Sig. (2-tailed)	.001	.684	.831	.298
	N	97	97	97	97
miR576	Correlation Coefficient	-.331**	-.299**	-.208*	-.314**
	Sig. (2-tailed)	.001	.003	.041	.002
	N	97	97	97	97
miR577	Correlation Coefficient	-.377**	-.197	.002	-.326**
	Sig. (2-tailed)	.000	.053	.986	.001
	N	97	97	97	97
miR578	Correlation Coefficient	-.429**	-.139	-.003	-.344**
	Sig. (2-tailed)	.000	.173	.980	.001
	N	97	97	97	97
miR580	Correlation Coefficient	-.194	-.032	-.097	-.182
	Sig. (2-tailed)	.057	.757	.344	.074
	N	97	97	97	97
miR581	Correlation Coefficient	.179	.146	-.088	.134
	Sig. (2-tailed)	.079	.154	.389	.190
	N	97	97	97	97
miR582	Correlation Coefficient	-.371**	-.149	-.131	-.253*
	Sig. (2-tailed)	.000	.144	.201	.013
	N	97	97	97	97
miR583	Correlation Coefficient	.382**	.138	-.051	.148
	Sig. (2-tailed)	.000	.178	.621	.148
	N	97	97	97	97
miR584	Correlation Coefficient	.237*	.025	-.003	-.034
	Sig. (2-tailed)	.019	.811	.977	.741
	N	97	97	97	97
miR585	Correlation Coefficient	.003	-.056	-.111	-.086



	Sig. (2-tailed)	.979	.588	.279	.404
	N	97	97	97	97
miR586	Correlation Coefficient	-.268"	.047	-.083	-.143
	Sig. (2-tailed)	.008	.646	.418	.162
	N	97	97	97	97
miR590	Correlation Coefficient	-.525"	-.181	-.155	-.317"
	Sig. (2-tailed)	.000	.075	.129	.002
	N	97	97	97	97
miR591	Correlation Coefficient	-.093	-.120	-.186	-.169
	Sig. (2-tailed)	.363	.242	.068	.098
	N	97	97	97	97
miR592	Correlation Coefficient	-.263"	-.108	-.135	-.187
	Sig. (2-tailed)	.009	.294	.186	.067
	N	97	97	97	97
miR594	Correlation Coefficient	.344"	.123	-.143	.204'
	Sig. (2-tailed)	.001	.230	.162	.045
	N	97	97	97	97
miR596	Correlation Coefficient	.076	-.060	-.217'	-.268"
	Sig. (2-tailed)	.458	.557	.033	.008
	N	97	97	97	97
miR597	Correlation Coefficient	-.310"	-.170	-.050	-.350"
	Sig. (2-tailed)	.002	.095	.628	.000
	N	97	97	97	97
miR598	Correlation Coefficient	.048	-.030	-.075	.040
	Sig. (2-tailed)	.640	.774	.468	.696
	N	97	97	97	97
miR600	Correlation Coefficient	-.609"	-.231'	-.150	-.341"
	Sig. (2-tailed)	.000	.023	.142	.001
	N	97	97	97	97
miR602	Correlation Coefficient	.614"	.109	.070	.356"
	Sig. (2-tailed)	.000	.288	.497	.000
	N	97	97	97	97
miR603	Correlation Coefficient	.337"	.138	.070	.232'
	Sig. (2-tailed)	.001	.178	.493	.022
	N	97	97	97	97
miR609	Correlation Coefficient	.318"	-.045	-.135	.058
	Sig. (2-tailed)	.002	.665	.186	.570
	N	97	97	97	97
miR610	Correlation Coefficient	.454"	.064	-.170	.348"
	Sig. (2-tailed)	.000	.531	.097	.000
	N	97	97	97	97
miR614	Correlation Coefficient	.313"	.025	-.178	.089
	Sig. (2-tailed)	.002	.806	.081	.384
	N	97	97	97	97
miR615	Correlation Coefficient	.336"	.120	-.139	.066
	Sig. (2-tailed)	.001	.244	.175	.521
	N	97	97	97	97
miR617	Correlation Coefficient	.016	-.077	-.189	-.069
	Sig. (2-tailed)	.880	.454	.064	.500
	N	97	97	97	97
miR618	Correlation Coefficient	-.055	.118	-.090	-.016
	Sig. (2-tailed)	.590	.250	.379	.873
	N	97	97	97	97
miR619	Correlation Coefficient	.475"	.145	-.040	.202'
	Sig. (2-tailed)	.000	.158	.699	.048
	N	97	97	97	97
miR622	Correlation Coefficient	.515"	.160	-.013	.415"
	Sig. (2-tailed)	.000	.116	.898	.000
	N	97	97	97	97
miR624	Correlation Coefficient	-.167	-.192	-.099	-.183
	Sig. (2-tailed)	.102	.059	.337	.073
	N	97	97	97	97
miR625	Correlation Coefficient	-.348"	-.235'	-.077	-.332"
	Sig. (2-tailed)	.000	.021	.451	.001
	N	97	97	97	97
miR627	Correlation Coefficient	-.062	-.128	-.089	-.177
	Sig. (2-tailed)	.546	.211	.384	.082
	N	97	97	97	97
miR628	Correlation Coefficient	-.074	.104	-.032	-.064
	Sig. (2-tailed)	.474	.311	.757	.533
	N	97	97	97	97
miR631	Correlation Coefficient	-.704"	-.245'	-.154	-.321"
	Sig. (2-tailed)	.000	.016	.133	.001
	N	97	97	97	97
miR632	Correlation Coefficient	.511"	.158	.032	.377"
	Sig. (2-tailed)	.000	.121	.754	.000
	N	97	97	97	97
miR641	Correlation Coefficient	.433"	.100	-.133	.072
	Sig. (2-tailed)	.000	.328	.194	.482
	N	97	97	97	97
miR642	Correlation Coefficient	.360"	.046	.097	-.041
	Sig. (2-tailed)	.000	.658	.342	.691
	N	97	97	97	97
miR643	Correlation Coefficient	.226'	.054	-.196	.009
	Sig. (2-tailed)	.026	.601	.054	.933
	N	97	97	97	97
miR645	Correlation Coefficient	-.571"	-.225'	-.151	-.395"
	Sig. (2-tailed)	.000	.027	.140	.000
	N	97	97	97	97
miR646	Correlation Coefficient	.206'	-.028	-.258'	-.055
	Sig. (2-tailed)	.043	.787	.011	.595

	N	97	97	97	97
miR647	Correlation Coefficient	-.506"	-.139	-.126	-.258'
	Sig. (2-tailed)	.000	.175	.220	.011
	N	97	97	97	97
miR651	Correlation Coefficient	-.274"	-.078	-.146	-.221'
	Sig. (2-tailed)	.007	.448	.154	.029
	N	97	97	97	97
miR652	Correlation Coefficient	-.224'	-.015	.059	-.179
	Sig. (2-tailed)	.028	.884	.565	.079
	N	97	97	97	97
miR653	Correlation Coefficient	.176	-.091	-.008	-.119
	Sig. (2-tailed)	.084	.374	.937	.247
	N	97	97	97	97
miR654	Correlation Coefficient	-.159	.050	-.057	.056
	Sig. (2-tailed)	.120	.625	.579	.585
	N	97	97	97	97
miR655	Correlation Coefficient	-.513"	-.158	-.124	-.197
	Sig. (2-tailed)	.000	.122	.226	.054
	N	97	97	97	97
miR656	Correlation Coefficient	-.422"	-.124	-.069	-.166
	Sig. (2-tailed)	.000	.226	.499	.105
	N	97	97	97	97
miR657	Correlation Coefficient	-.463"	-.229'	-.044	-.389"
	Sig. (2-tailed)	.000	.024	.668	.000
	N	97	97	97	97
miR659	Correlation Coefficient	.030	-.007	-.121	-.104
	Sig. (2-tailed)	.770	.944	.237	.310
	N	97	97	97	97
miR660	Correlation Coefficient	-.467"	-.296"	-.159	-.372"
	Sig. (2-tailed)	.000	.003	.119	.000
	N	97	97	97	97
miR663	Correlation Coefficient	.176	.134	.209'	.236'
	Sig. (2-tailed)	.085	.191	.040	.020
	N	97	97	97	97
miR668	Correlation Coefficient	.386"	.264"	.035	.213'
	Sig. (2-tailed)	.000	.009	.732	.037
	N	97	97	97	97
miR671	Correlation Coefficient	-.280"	-.040	.055	.030
	Sig. (2-tailed)	.006	.698	.590	.769
	N	97	97	97	97
miR766	Correlation Coefficient	.179	.215'	-.041	.162
	Sig. (2-tailed)	.080	.034	.692	.112
	N	97	97	97	97
miR801	Correlation Coefficient	.345"	.211'	.120	.391"
	Sig. (2-tailed)	.001	.038	.240	.000
	N	97	97	97	97
miR802	Correlation Coefficient	-.359"	-.126	-.302"	-.243'
	Sig. (2-tailed)	.000	.220	.003	.016
	N	97	97	97	97
miR106a	Correlation Coefficient	-.285"	-.065	-.258'	-.191
	Sig. (2-tailed)	.005	.527	.011	.062
	N	97	97	97	97
miR106b	Correlation Coefficient	-.533"	-.213'	-.164	-.314"
	Sig. (2-tailed)	.000	.036	.108	.002
	N	97	97	97	97
miR122a	Correlation Coefficient	-.396"	-.155	-.124	-.152
	Sig. (2-tailed)	.000	.129	.224	.138
	N	97	97	97	97
miR124a	Correlation Coefficient	-.430"	-.175	-.146	-.314"
	Sig. (2-tailed)	.000	.087	.153	.002
	N	97	97	97	97
miR125a	Correlation Coefficient	-.298"	-.162	-.234'	-.272"
	Sig. (2-tailed)	.003	.113	.021	.007
	N	97	97	97	97
miR125b	Correlation Coefficient	-.196	-.163	-.237'	-.229'
	Sig. (2-tailed)	.055	.110	.019	.024
	N	97	97	97	97
miR126star	Correlation Coefficient	-.518"	-.215'	-.122	-.335"
	Sig. (2-tailed)	.000	.034	.235	.001
	N	97	97	97	97
miR128a	Correlation Coefficient	-.325"	-.112	-.206'	-.186
	Sig. (2-tailed)	.001	.276	.043	.069
	N	97	97	97	97
miR128b	Correlation Coefficient	-.333"	-.065	-.149	-.138
	Sig. (2-tailed)	.001	.525	.144	.177
	N	97	97	97	97
miR130a	Correlation Coefficient	-.460"	-.196	-.207'	-.279"
	Sig. (2-tailed)	.000	.054	.042	.006
	N	97	97	97	97
miR130b	Correlation Coefficient	-.607"	-.237'	-.210'	-.316"
	Sig. (2-tailed)	.000	.020	.039	.002
	N	97	97	97	97
miR133a	Correlation Coefficient	.497"	.281"	.111	.095
	Sig. (2-tailed)	.000	.005	.277	.353
	N	97	97	97	97
miR133b	Correlation Coefficient	.244'	.071	-.100	.034
	Sig. (2-tailed)	.016	.489	.327	.741
	N	97	97	97	97
miR135a	Correlation Coefficient	-.338"	-.181	-.116	-.228'
	Sig. (2-tailed)	.001	.076	.258	.024
	N	97	97	97	97

miR135b	Correlation Coefficient	-.056	.168	-.189	.229 <sup>*</sup>
	Sig. (2-tailed)	.584	.099	.064	.024
	N	97	97	97	97
miR1423p	Correlation Coefficient	-.324 <sup>***</sup>	-.164	-.151	-.271 <sup>***</sup>
	Sig. (2-tailed)	.001	.109	.140	.007
	N	97	97	97	97
miR1425p	Correlation Coefficient	-.328 <sup>***</sup>	-.193	-.157	-.253 <sup>*</sup>
	Sig. (2-tailed)	.001	.058	.124	.012
	N	97	97	97	97
miR146a	Correlation Coefficient	-.374 <sup>***</sup>	-.147	-.202 <sup>*</sup>	-.147
	Sig. (2-tailed)	.000	.151	.047	.150
	N	97	97	97	97
miR146b	Correlation Coefficient	-.190	-.148	-.070	-.217 <sup>*</sup>
	Sig. (2-tailed)	.062	.147	.498	.033
	N	97	97	97	97
miR148a	Correlation Coefficient	-.556 <sup>***</sup>	-.169	-.189	-.234 <sup>*</sup>
	Sig. (2-tailed)	.000	.098	.064	.021
	N	97	97	97	97
miR148b	Correlation Coefficient	-.328 <sup>***</sup>	-.253 <sup>*</sup>	-.137	-.292 <sup>***</sup>
	Sig. (2-tailed)	.001	.012	.182	.004
	N	97	97	97	97
miR154star	Correlation Coefficient	.036	.009	-.090	.021
	Sig. (2-tailed)	.726	.933	.383	.842
	N	97	97	97	97
miR15a	Correlation Coefficient	-.398 <sup>***</sup>	-.210 <sup>*</sup>	-.171	-.318 <sup>***</sup>
	Sig. (2-tailed)	.000	.039	.095	.001
	N	97	97	97	97
miR15b	Correlation Coefficient	-.629 <sup>***</sup>	-.247 <sup>*</sup>	-.134	-.363 <sup>***</sup>
	Sig. (2-tailed)	.000	.015	.189	.000
	N	97	97	97	97
miR173p	Correlation Coefficient	-.318 <sup>***</sup>	-.147	-.148	-.142
	Sig. (2-tailed)	.002	.150	.148	.165
	N	97	97	97	97
miR175p	Correlation Coefficient	-.553 <sup>***</sup>	-.218 <sup>*</sup>	-.293 <sup>***</sup>	-.234 <sup>*</sup>
	Sig. (2-tailed)	.000	.032	.004	.021
	N	97	97	97	97
miR181a	Correlation Coefficient	-.295 <sup>***</sup>	-.192	-.199	-.281 <sup>***</sup>
	Sig. (2-tailed)	.003	.060	.051	.005
	N	97	97	97	97
miR181b	Correlation Coefficient	-.444 <sup>***</sup>	-.217 <sup>*</sup>	-.121	-.318 <sup>***</sup>
	Sig. (2-tailed)	.000	.033	.239	.002
	N	97	97	97	97
miR181c	Correlation Coefficient	-.354 <sup>***</sup>	-.124	-.172	-.241 <sup>*</sup>
	Sig. (2-tailed)	.000	.225	.092	.017
	N	97	97	97	97
miR181d	Correlation Coefficient	-.437 <sup>***</sup>	-.111	-.194	-.188
	Sig. (2-tailed)	.000	.278	.056	.065
	N	97	97	97	97
miR182star	Correlation Coefficient	-.418 <sup>***</sup>	-.213 <sup>*</sup>	-.202 <sup>*</sup>	-.251 <sup>*</sup>
	Sig. (2-tailed)	.000	.037	.047	.013
	N	97	97	97	97
miR18a	Correlation Coefficient	.123	.065	-.205 <sup>*</sup>	.060
	Sig. (2-tailed)	.229	.530	.044	.561
	N	97	97	97	97
miR18astar	Correlation Coefficient	-.327 <sup>***</sup>	-.209 <sup>*</sup>	-.140	-.183
	Sig. (2-tailed)	.001	.040	.170	.073
	N	97	97	97	97
miR18b	Correlation Coefficient	.199	.106	-.154	.072
	Sig. (2-tailed)	.051	.301	.132	.485
	N	97	97	97	97
miR193a	Correlation Coefficient	-.441 <sup>***</sup>	-.211 <sup>*</sup>	.051	-.376 <sup>***</sup>
	Sig. (2-tailed)	.000	.038	.619	.000
	N	97	97	97	97
miR193b	Correlation Coefficient	.165	.160	.095	.069
	Sig. (2-tailed)	.107	.118	.353	.502
	N	97	97	97	97
miR196a	Correlation Coefficient	-.558 <sup>***</sup>	-.210 <sup>*</sup>	-.024	-.206 <sup>*</sup>
	Sig. (2-tailed)	.000	.039	.813	.043
	N	97	97	97	97
miR196b	Correlation Coefficient	.048	-.194	-.280 <sup>***</sup>	.010
	Sig. (2-tailed)	.639	.057	.006	.926
	N	97	97	97	97
miR199a	Correlation Coefficient	-.110	.070	-.026	-.160
	Sig. (2-tailed)	.283	.495	.797	.118
	N	97	97	97	97
miR199astar	Correlation Coefficient	-.106	.003	-.160	-.198
	Sig. (2-tailed)	.302	.973	.117	.052
	N	97	97	97	97
miR199b	Correlation Coefficient	-.427 <sup>***</sup>	-.041	-.205 <sup>*</sup>	-.234 <sup>*</sup>
	Sig. (2-tailed)	.000	.691	.044	.021
	N	97	97	97	97
miR19a	Correlation Coefficient	-.562 <sup>***</sup>	-.213 <sup>*</sup>	-.178	-.337 <sup>***</sup>
	Sig. (2-tailed)	.000	.036	.081	.001
	N	97	97	97	97
miR19b	Correlation Coefficient	-.449 <sup>***</sup>	-.236 <sup>*</sup>	-.244 <sup>*</sup>	-.266 <sup>***</sup>
	Sig. (2-tailed)	.000	.020	.016	.008
	N	97	97	97	97
miR200a	Correlation Coefficient	.287 <sup>***</sup>	.041	.029	.007
	Sig. (2-tailed)	.004	.688	.781	.946
	N	97	97	97	97
miR200astar	Correlation Coefficient	-.237 <sup>*</sup>	-.101	-.137	-.096

	Sig. (2-tailed)	.019	.324	.180	.349
	N	97	97	97	97
miR200b	Correlation Coefficient	-.352**	-.334**	-.137	-.288**
	Sig. (2-tailed)	.000	.001	.179	.004
	N	97	97	97	97
miR200c	Correlation Coefficient	-.294**	-.196	-.014	-.161
	Sig. (2-tailed)	.003	.054	.890	.115
	N	97	97	97	97
miR202star	Correlation Coefficient	.383**	.111	-.090	.133
	Sig. (2-tailed)	.000	.280	.379	.193
	N	97	97	97	97
miR20a	Correlation Coefficient	-.387**	-.194	-.192	-.295**
	Sig. (2-tailed)	.000	.056	.060	.003
	N	97	97	97	97
miR20b	Correlation Coefficient	-.120	-.136	-.166	-.152
	Sig. (2-tailed)	.243	.183	.103	.137
	N	97	97	97	97
miR23a	Correlation Coefficient	-.476**	-.222'	-.139	-.294**
	Sig. (2-tailed)	.000	.029	.173	.003
	N	97	97	97	97
miR23b	Correlation Coefficient	-.434**	-.226'	-.151	-.330**
	Sig. (2-tailed)	.000	.026	.139	.001
	N	97	97	97	97
miR26a	Correlation Coefficient	-.251'	-.158	-.191	-.253'
	Sig. (2-tailed)	.013	.123	.061	.013
	N	97	97	97	97
miR26b	Correlation Coefficient	-.504**	-.219'	-.143	-.341**
	Sig. (2-tailed)	.000	.031	.161	.001
	N	97	97	97	97
miR27a	Correlation Coefficient	-.292**	-.107	-.162	-.248'
	Sig. (2-tailed)	.004	.295	.112	.014
	N	97	97	97	97
miR27b	Correlation Coefficient	-.368**	-.248'	-.126	-.330**
	Sig. (2-tailed)	.000	.014	.220	.001
	N	97	97	97	97
miR2993p	Correlation Coefficient	-.281**	-.035	-.067	-.194
	Sig. (2-tailed)	.005	.734	.514	.057
	N	97	97	97	97
miR2995p	Correlation Coefficient	-.211'	-.066	-.147	-.144
	Sig. (2-tailed)	.038	.521	.150	.159
	N	97	97	97	97
miR29a	Correlation Coefficient	-.448**	-.211'	-.132	-.329**
	Sig. (2-tailed)	.000	.038	.198	.001
	N	97	97	97	97
miR29b	Correlation Coefficient	-.078	-.140	-.175	-.203'
	Sig. (2-tailed)	.447	.171	.087	.046
	N	97	97	97	97
miR29c	Correlation Coefficient	-.435**	-.207'	-.100	-.356**
	Sig. (2-tailed)	.000	.042	.330	.000
	N	97	97	97	97
miR302b	Correlation Coefficient	.517**	.140	.067	.268**
	Sig. (2-tailed)	.000	.172	.513	.008
	N	97	97	97	97
miR302bstar	Correlation Coefficient	.374**	.097	-.112	.168
	Sig. (2-tailed)	.000	.346	.274	.101
	N	97	97	97	97
miR302cstar	Correlation Coefficient	-.098	-.218'	-.071	-.101
	Sig. (2-tailed)	.340	.032	.489	.323
	N	97	97	97	97
miR302d	Correlation Coefficient	.105	-.081	-.079	-.043
	Sig. (2-tailed)	.307	.430	.441	.679
	N	97	97	97	97
miR30a3p	Correlation Coefficient	-.344**	-.174	-.113	-.301**
	Sig. (2-tailed)	.001	.088	.272	.003
	N	97	97	97	97
miR30a5p	Correlation Coefficient	-.410**	-.203'	-.171	-.300**
	Sig. (2-tailed)	.000	.046	.093	.003
	N	97	97	97	97
miR30b	Correlation Coefficient	-.440**	-.190	-.164	-.332**
	Sig. (2-tailed)	.000	.062	.108	.001
	N	97	97	97	97
miR30c	Correlation Coefficient	-.360**	-.179	-.199	-.302**
	Sig. (2-tailed)	.000	.079	.051	.003
	N	97	97	97	97
miR30d	Correlation Coefficient	-.310**	-.151	-.217'	-.236'
	Sig. (2-tailed)	.002	.140	.033	.020
	N	97	97	97	97
miR30e3p	Correlation Coefficient	-.134	-.103	-.190	-.186
	Sig. (2-tailed)	.190	.317	.063	.068
	N	97	97	97	97
miR30e5p	Correlation Coefficient	-.320**	-.211'	-.143	-.281**
	Sig. (2-tailed)	.001	.038	.162	.005
	N	97	97	97	97
miR3243p	Correlation Coefficient	-.217'	-.128	-.131	-.171
	Sig. (2-tailed)	.033	.212	.200	.093
	N	97	97	97	97
miR3245p	Correlation Coefficient	-.333**	-.125	-.128	-.193
	Sig. (2-tailed)	.001	.222	.213	.058
	N	97	97	97	97
miR33b	Correlation Coefficient	.085	-.104	.025	-.236'
	Sig. (2-tailed)	.408	.313	.810	.020

	N	97	97	97	97
miR34a	Correlation Coefficient	.341"	.130	.102	-.026
	Sig. (2-tailed)	.001	.205	.319	.799
	N	97	97	97	97
miR34b	Correlation Coefficient	.030	-.064	-.005	-.204'
	Sig. (2-tailed)	.769	.533	.960	.045
	N	97	97	97	97
miR34c	Correlation Coefficient	.119	-.024	.045	-.191
	Sig. (2-tailed)	.246	.814	.659	.061
	N	97	97	97	97
miR363star	Correlation Coefficient	.443"	.185	.010	.238'
	Sig. (2-tailed)	.000	.069	.924	.019
	N	97	97	97	97
miR3693p	Correlation Coefficient	-.488"	-.149	-.114	-.221'
	Sig. (2-tailed)	.000	.145	.267	.030
	N	97	97	97	97
miR3695p	Correlation Coefficient	-.203'	-.081	-.141	-.246'
	Sig. (2-tailed)	.047	.430	.167	.015
	N	97	97	97	97
miR376a	Correlation Coefficient	-.490"	-.162	-.182	-.227'
	Sig. (2-tailed)	.000	.114	.075	.026
	N	97	97	97	97
miR376astar	Correlation Coefficient	-.400"	-.155	-.208'	-.172
	Sig. (2-tailed)	.000	.130	.041	.092
	N	97	97	97	97
miR376b	Correlation Coefficient	-.490"	-.115	-.188	-.270"
	Sig. (2-tailed)	.000	.262	.065	.007
	N	97	97	97	97
miR3803p	Correlation Coefficient	-.199	-.057	-.193	-.209'
	Sig. (2-tailed)	.051	.578	.059	.040
	N	97	97	97	97
miR3805p	Correlation Coefficient	-.307"	-.192	-.203'	-.232'
	Sig. (2-tailed)	.002	.059	.046	.022
	N	97	97	97	97
miR4093p	Correlation Coefficient	-.379"	-.016	-.066	-.096
	Sig. (2-tailed)	.000	.876	.520	.348
	N	97	97	97	97
miR4095p	Correlation Coefficient	-.474"	-.171	-.079	-.289"
	Sig. (2-tailed)	.000	.094	.444	.004
	N	97	97	97	97
miR422b	Correlation Coefficient	-.489"	-.044	-.121	-.124
	Sig. (2-tailed)	.000	.668	.238	.226
	N	97	97	97	97
miR4255p	Correlation Coefficient	-.092	-.114	-.163	-.140
	Sig. (2-tailed)	.369	.264	.112	.171
	N	97	97	97	97
miR432star	Correlation Coefficient	-.540"	-.121	-.032	-.201'
	Sig. (2-tailed)	.000	.239	.757	.048
	N	97	97	97	97
miR449b	Correlation Coefficient	.194	-.013	-.107	-.092
	Sig. (2-tailed)	.057	.902	.296	.369
	N	97	97	97	97
miR452star	Correlation Coefficient	-.401"	-.309"	-.249'	-.221'
	Sig. (2-tailed)	.000	.002	.014	.029
	N	97	97	97	97
miR4543p	Correlation Coefficient	-.461"	-.203'	-.211'	-.303"
	Sig. (2-tailed)	.000	.046	.038	.003
	N	97	97	97	97
miR4853p	Correlation Coefficient	-.019	-.011	-.107	.078
	Sig. (2-tailed)	.850	.913	.296	.449
	N	97	97	97	97
miR4855p	Correlation Coefficient	.089	.038	-.001	-.055
	Sig. (2-tailed)	.385	.715	.991	.593
	N	97	97	97	97
miR487a	Correlation Coefficient	-.304"	-.152	-.135	-.130
	Sig. (2-tailed)	.002	.138	.189	.206
	N	97	97	97	97
miR487b	Correlation Coefficient	-.414"	-.146	-.120	-.276"
	Sig. (2-tailed)	.000	.154	.242	.006
	N	97	97	97	97
miR4935p	Correlation Coefficient	-.289"	-.170	-.133	-.244'
	Sig. (2-tailed)	.004	.096	.193	.016
	N	97	97	97	97
miR5123p	Correlation Coefficient	.371"	.121	.026	.118
	Sig. (2-tailed)	.000	.237	.798	.250
	N	97	97	97	97
miR5125p	Correlation Coefficient	.324"	.105	-.042	.202'
	Sig. (2-tailed)	.001	.306	.685	.048
	N	97	97	97	97
miR5163p	Correlation Coefficient	-.247"	-.108	-.140	-.221'
	Sig. (2-tailed)	.015	.292	.171	.029
	N	97	97	97	97
miR517a	Correlation Coefficient	.278"	.037	-.122	.047
	Sig. (2-tailed)	.006	.716	.236	.650
	N	97	97	97	97
miR517b	Correlation Coefficient	-.375"	-.207"	-.193	-.356"
	Sig. (2-tailed)	.000	.042	.058	.000
	N	97	97	97	97
miR517c	Correlation Coefficient	.174	-.063	-.076	-.072
	Sig. (2-tailed)	.089	.538	.461	.486
	N	97	97	97	97

miR518a	Correlation Coefficient	.452"	.134	-.105	.182
	Sig. (2-tailed)	.000	.190	.306	.075
	N	97	97	97	97
miR518b	Correlation Coefficient	.499"	.291"	.035	.328"
	Sig. (2-tailed)	.000	.004	.734	.001
	N	97	97	97	97
miR518cstar	Correlation Coefficient	-.110	-.072	-.219'	-.074
	Sig. (2-tailed)	.281	.486	.031	.471
	N	97	97	97	97
miR518d	Correlation Coefficient	.338"	.037	-.100	.038
	Sig. (2-tailed)	.001	.717	.328	.712
	N	97	97	97	97
miR518e	Correlation Coefficient	-.209'	-.182	-.152	-.258'
	Sig. (2-tailed)	.040	.075	.137	.011
	N	97	97	97	97
miR519a	Correlation Coefficient	.071	.125	-.099	.004
	Sig. (2-tailed)	.489	.224	.336	.967
	N	97	97	97	97
miR519b	Correlation Coefficient	.370"	.153	-.015	.181
	Sig. (2-tailed)	.000	.134	.883	.077
	N	97	97	97	97
miR519c	Correlation Coefficient	-.183	.031	-.221'	-.133
	Sig. (2-tailed)	.072	.764	.030	.193
	N	97	97	97	97
miR519e	Correlation Coefficient	.129	.157	-.210'	.109
	Sig. (2-tailed)	.208	.123	.039	.290
	N	97	97	97	97
miR520c	Correlation Coefficient	.142	.096	.004	-.025
	Sig. (2-tailed)	.166	.351	.967	.810
	N	97	97	97	97
miR520dstar	Correlation Coefficient	-.497"	-.173	-.087	-.300"
	Sig. (2-tailed)	.000	.091	.398	.003
	N	97	97	97	97
miR525star	Correlation Coefficient	-.518"	-.190	-.144	-.293"
	Sig. (2-tailed)	.000	.062	.160	.004
	N	97	97	97	97
miR526c	Correlation Coefficient	-.272"	-.034	-.085	-.181
	Sig. (2-tailed)	.007	.742	.407	.075
	N	97	97	97	97
miR5423p	Correlation Coefficient	-.446"	-.097	-.171	-.139
	Sig. (2-tailed)	.000	.347	.095	.175
	N	97	97	97	97
miR5425p	Correlation Coefficient	-.603"	-.234'	-.125	-.245'
	Sig. (2-tailed)	.000	.021	.221	.016
	N	97	97	97	97
miR548a	Correlation Coefficient	.371"	.072	-.161	.117
	Sig. (2-tailed)	.000	.485	.116	.253
	N	97	97	97	97
miR548b	Correlation Coefficient	-.419"	-.154	-.088	-.296"
	Sig. (2-tailed)	.000	.131	.390	.003
	N	97	97	97	97
miR548c	Correlation Coefficient	-.274"	-.061	-.123	-.261"
	Sig. (2-tailed)	.007	.556	.228	.010
	N	97	97	97	97
miR551a	Correlation Coefficient	.377"	.141	-.136	.131
	Sig. (2-tailed)	.000	.169	.183	.199
	N	97	97	97	97
miR551b	Correlation Coefficient	-.457"	-.175	-.169	-.238'
	Sig. (2-tailed)	.000	.086	.097	.019
	N	97	97	97	97
miR7675p	Correlation Coefficient	-.307"	-.043	-.246'	-.120
	Sig. (2-tailed)	.002	.675	.015	.243
	N	97	97	97	97
miR7683p	Correlation Coefficient	-.104	-.076	-.183	-.120
	Sig. (2-tailed)	.310	.460	.073	.241
	N	97	97	97	97
miR7685p	Correlation Coefficient	.119	.038	.085	.138
	Sig. (2-tailed)	.246	.710	.406	.177
	N	97	97	97	97
miR7693p	Correlation Coefficient	.195	.148	.019	.211'
	Sig. (2-tailed)	.056	.148	.851	.038
	N	97	97	97	97
miR7695p	Correlation Coefficient	-.365"	-.118	-.119	-.198
	Sig. (2-tailed)	.000	.250	.247	.052
	N	97	97	97	97
miR7705p	Correlation Coefficient	-.118	-.063	-.106	-.063
	Sig. (2-tailed)	.250	.540	.302	.542
	N	97	97	97	97
miR92b	Correlation Coefficient	.088	.133	-.213'	.042
	Sig. (2-tailed)	.393	.192	.036	.681
	N	97	97	97	97
miR99a	Correlation Coefficient	-.481"	-.187	-.166	-.316"
	Sig. (2-tailed)	.000	.066	.104	.002
	N	97	97	97	97
miR99b	Correlation Coefficient	-.308"	-.169	-.102	-.259'
	Sig. (2-tailed)	.002	.097	.321	.010
	N	97	97	97	97
miR9star	Correlation Coefficient	-.399"	-.179	-.179	-.293"
	Sig. (2-tailed)	.000	.079	.079	.004
	N	97	97	97	97

---

**Supplementary Table 4: miRNA displaying expression changes across the lifespan.**

Name	df	F	Sig.
<b>miRNA decreasing with age</b>			
let7b	7	4.311	0.0004
let7c	7	3.733	0.0014
let7d	7	2.226	0.0393
let7f	7	3.166	0.0049
miR-101	7	2.748	0.0125
miR-103	7	4.243	0.0004
miR-105	7	3.738	0.0014
miR-106a	7	2.535	0.0200
miR-106b	7	4.913	0.0001
miR-107	7	2.959	0.0078
miR-126	7	3.064	0.0062
miR-126*	7	5.939	1.103E-05
miR-130a	7	3.323	0.0034
miR-130b	7	7.775	2.55E-07
miR-132	7	2.614	0.0168
miR-135a	7	2.779	0.0116
miR-136	7	3.947	0.0009
miR-137	7	2.729	0.0130
miR-138	7	2.624	0.0164
miR-139	7	2.757	0.0122
miR-146a	7	2.721	0.0132
miR-148a	7	6.138	7.244E-06
miR-153	7	4.582	0.0002
miR-15b	7	8.26	9.83E-08
miR-16	7	2.612	0.0169
miR-17-3p	7	2.443	0.0245
miR-17-5p	7	8.765	3.7E-08
miR-181b	7	2.139	0.0474
miR-187	7	3.899	0.0009
miR-190	7	3.419	0.0028
miR-199b	7	2.992	0.0072
miR-19a	7	5.593	2.304E-05
miR-19b	7	3.075	0.0060
miR-200a*	7	2.204	0.0412
miR-212	7	2.605	0.0171
miR-218	7	3.862	0.0010
miR-22	7	5.115	6.47E-05
miR-23a	7	3.827	0.0011
miR-23b	7	2.578	0.0182
miR-26b	7	4.088	0.0006
miR-29c	7	2.377	0.0283
miR-33	7	3.41	0.0028
miR-335	7	3.35	0.0032
miR-345	7	2.962	0.0077
miR-365	7	3.636	0.0017
miR-368	7	5.667	1.969E-05
miR-369-3p	7	4.772	0.0001
miR-374	7	3.364	0.0031
miR-376a	7	4.386	0.0003
miR-376a*	7	2.9	0.0089
miR-376b	7	5.526	2.661E-05
miR-379	7	3.828	0.0011

---

miR-381	7	4.143	0.0005
miR-382	7	4.551	0.0002
miR-383	7	4.839	0.0001
miR-410	7	2.907	0.0088
miR-422b	7	4.12	0.0006
miR-424	7	6.56	3.002E-06
miR-450	7	8.183	1.142E-07
miR-454-3p	7	3.586	0.0019
miR-488	7	3.713	0.0014
miR-490	7	3.239	0.0042
miR-494	7	4.56	0.0002
miR-503	7	8.417	7.24E-08
miR-526c	7	2.593	0.0176
miR-542-3p	7	3.98	0.0008
miR-545	7	5.292	4.405E-05
miR-550	7	2.477	0.0227
miR-551b	7	4.298	0.0004
miR-578	7	2.948	0.0080
miR-7	7	2.49	0.0221
miR-7675p	7	3.038	0.0065
miR-95	7	4.605	0.0002
<b>miRNA increasing with age</b>			
miR-133a	7	3.634	0.0017
miR-133b	7	2.855	0.0098
miR-135b	7	6.233	5.933E-06
miR-189	7	2.611	0.0169
miR-200a*	7	2.204	0.0412
miR-302b*	7	4.428	0.0003
miR-302d	7	3.564	0.0020
miR-31	7	4.622	0.0002
miR-363*	7	5.913	1.166E-05
miR-425	7	3.4	0.0029
miR-504	7	2.847	0.0100
miR-507	7	6.659	2.444E-06
miR-512-3p	7	4.579	0.0002
miR-517a	7	3.282	0.0038
miR-518a	7	4.575	0.0002
miR-518d	7	3.338	0.0033
miR-519b	7	4.721	0.0002
miR-525	7	3.022	0.0068
miR-548a	7	3.656	0.0016
miR-551a	7	2.734	0.0128
miR-564	7	2.287	0.0344
miR-571	7	4.367	0.0003
miR-583	7	3.45	0.0026
miR-614	7	3.559	0.0020
miR-615	7	3.212	0.0044
miR-641	7	3.522	0.0022
miR-668	7	3.226	0.0043
miR-766	7	2.923	0.0084

A total of 74 miRNA displayed a decrease in expression and 28 miRNA displayed an increase in expression throughout aging. PMI was the second most influential factor and was therefore used as a covariate in ANCOVA analysis.

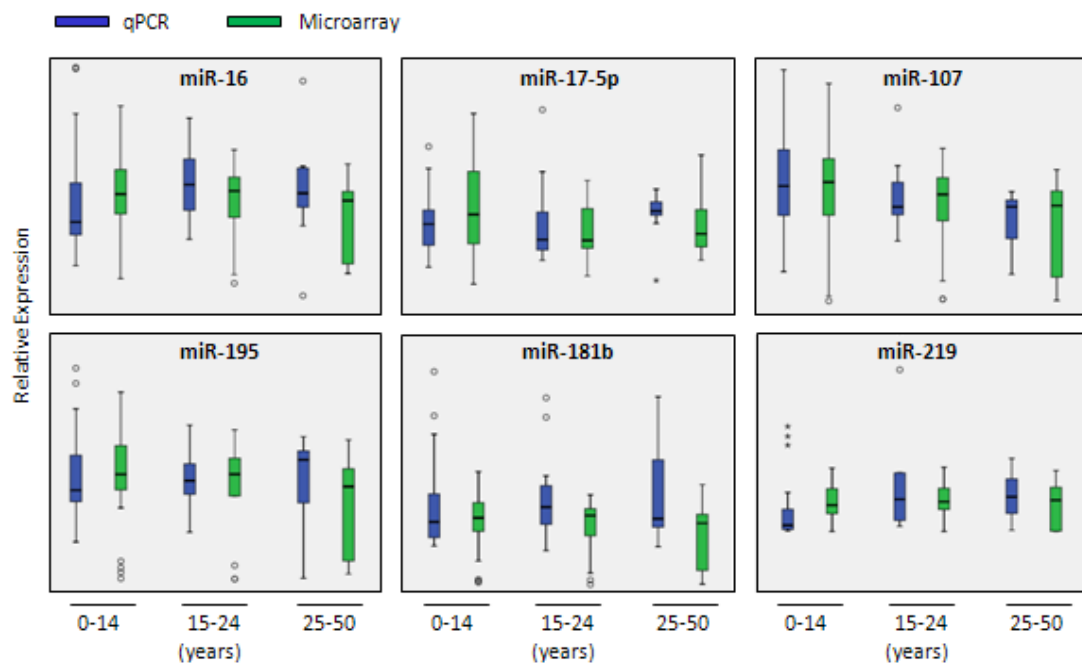
---



**Supplementary Table 5: Target gene pathway analysis**

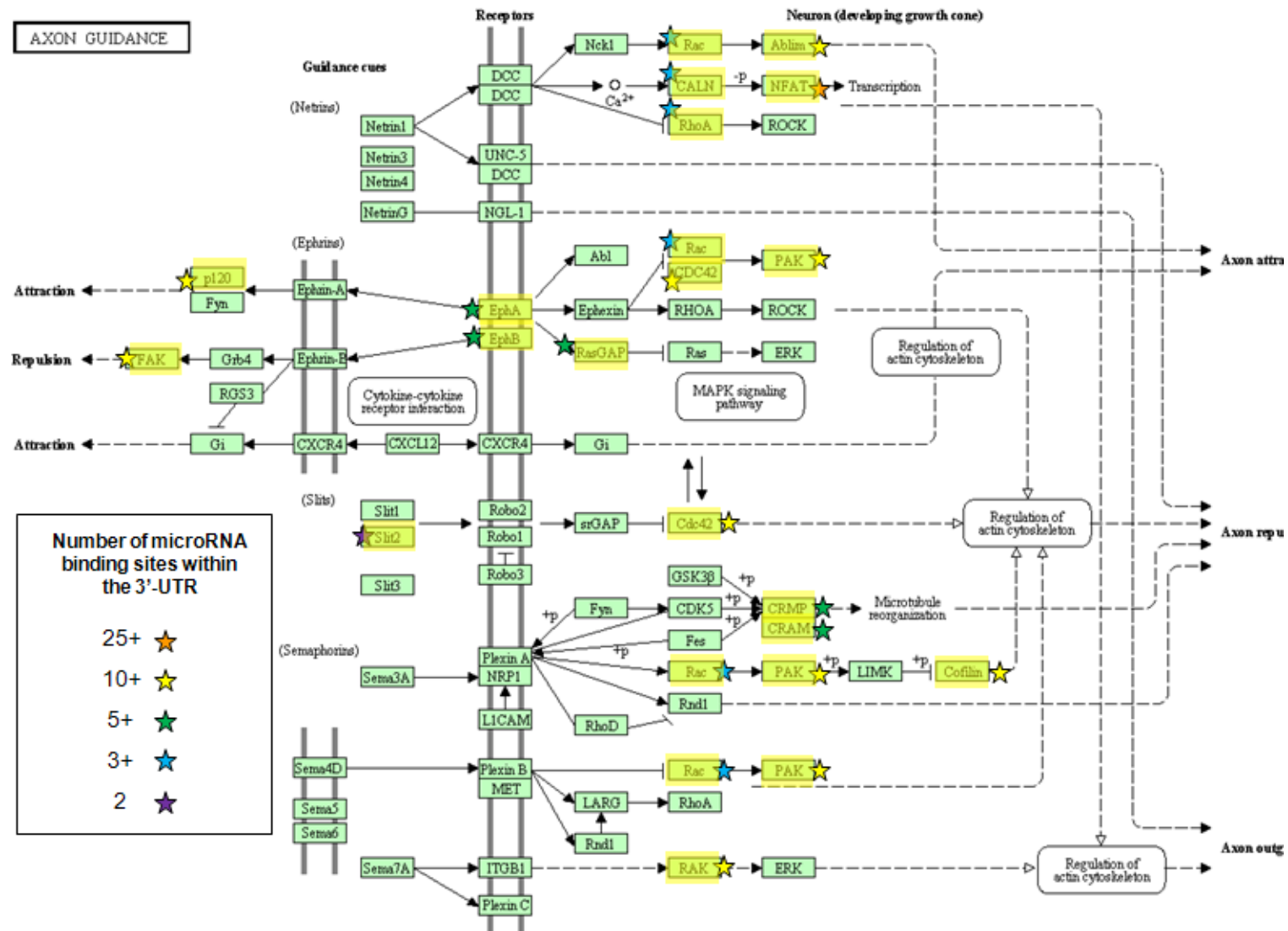
Category	Term	Count	%	PValue	Fold Enrichment	Bonferroni	Benjamini	FDR
<b>Targets of miRNAs increasing with age/genes decreasing with age</b>								
GENETIC_ASSOCIATION_DB_DISEASE_CL ASS	PSYCH	19	0.785	2.52E-04	2.36	0.0040318	0.004032	0.179148
GOTERM_BP_ALL	GO:0007399-nervous system development	41	1.695	1.79E-08	2.65	2.82E-05	2.82E-05	2.99E-05
GOTERM_BP_ALL	GO:0032502-developmental process	76	3.142	6.93E-07	1.70	0.0011	5.46E-04	0.0012
GOTERM_BP_ALL	GO:0048856-anatomical structure development	65	2.687	8.68E-07	1.81	0.0014	4.55E-04	0.0015
GOTERM_BP_ALL	GO:0022008-neurogenesis	26	1.075	1.34E-06	3.04	0.0021	5.28E-04	0.0022
GOTERM_BP_ALL	GO:0048731-system development	58	2.398	1.32E-05	1.75	0.0206	0.0042	0.0221
GOTERM_BP_ALL	GO:0007275-multicellular organismal development	66	2.728	3.05E-05	1.62	0.0468	0.0080	0.0509
GOTERM_BP_ALL	GO:0048699-generation of neurons	22	0.909	4.53E-05	2.76	0.0688	0.0101	0.0757
GOTERM_BP_ALL	GO:0031346-positive regulation of cell projection organization	7	0.289	4.97E-05	10.46	0.0752	0.0097	0.0830
GOTERM_BP_ALL	GO:0048869-cellular developmental process	45	1.860	5.09E-05	1.85	0.0770	0.0089	0.0850
GOTERM_BP_ALL	GO:0030154-cell differentiation	43	1.778	8.87E-05	1.84	0.1303	0.0139	0.15
GOTERM_BP_ALL	GO:0006928-cell motion	19	0.785	1.45E-04	2.81	0.2045	0.0206	0.24
GOTERM_BP_ALL	GO:0007155-cell adhesion	24	0.992	1.49E-04	2.41	0.2091	0.0194	0.25
GOTERM_BP_ALL	GO:0022610-biological adhesion	24	0.992	1.52E-04	2.40	0.2130	0.0183	0.25
GOTERM_BP_ALL	GO:0031344-regulation of cell projection organization	8	0.331	2.66E-04	6.31	0.3426	0.0295	0.44
GOTERM_BP_ALL	GO:0045893-positive regulation of transcription, DNA-dependent	18	0.744	4.53E-04	2.65	0.5103	0.0465	0.76
GOTERM_BP_ALL	GO:0051254-positive regulation of RNA metabolic process	18	0.744	4.99E-04	2.63	0.5438	0.0479	0.83
GOTERM_BP_ALL	GO:0010557-positive regulation of macromolecule biosynthetic process	21	0.868	0.0010	2.26	0.7941	0.0888	1.66
GOTERM_BP_ALL	GO:0007417-central nervous system development	16	0.661	0.0011	2.64	0.8176	0.0902	1.79
GOTERM_BP_ALL	GO:0051130-positive regulation of cellular component organization	10	0.413	0.0011	3.88	0.8260	0.0879	1.84
GOTERM_BP_ALL	GO:0050794-regulation of cellular process	119	4.919	0.0014	1.23	0.8967	0.1073	2.38
GOTERM_BP_ALL	GO:0030182-neuron differentiation	16	0.661	0.0015	2.57	0.8992	0.1035	2.41
GOTERM_BP_ALL	GO:0006357-regulation of transcription from RNA polymerase II promoter	22	0.909	0.0015	2.13	0.9104	0.1038	2.53
GOTERM_BP_ALL	GO:0065007-biological regulation	128	5.291	0.0016	1.20	0.9246	0.1063	2.71
GOTERM_BP_ALL	GO:0051960-regulation of nervous system development	10	0.413	0.0017	3.66	0.9283	0.1040	2.76
GOTERM_BP_ALL	GO:0031328-positive regulation of cellular biosynthetic process	21	0.868	0.0017	2.15	0.9363	0.1043	2.88
GOTERM_BP_ALL	GO:0048523-negative regulation of cellular process	39	1.612	0.0018	1.65	0.9443	0.1051	3.02
GOTERM_BP_ALL	GO:0060491-regulation of cell projection assembly	4	0.165	0.0020	15.61	0.9540	0.1078	3.22
GOTERM_BP_ALL	GO:0016337-cell-cell adhesion	12	0.496	0.0020	3.05	0.9541	0.1042	3.22
GOTERM_BP_ALL	GO:0009891-positive regulation of biosynthetic process	21	0.868	0.0021	2.12	0.9617	0.1064	3.40
GOTERM_BP_ALL	GO:0010604-positive regulation of macromolecule metabolic process	24	0.992	0.0024	1.97	0.9765	0.1175	3.90
GOTERM_BP_ALL	GO:0050767-regulation of neurogenesis	9	0.372	0.0025	3.81	0.9816	0.1209	4.15
GOTERM_BP_ALL	GO:0048519-negative regulation of biological process	41	1.695	0.0027	1.59	0.9851	0.1231	4.37
GOTERM_BP_ALL	GO:0045941-positive regulation of transcription	18	0.744	0.0028	2.24	0.9876	0.1245	4.55
GOTERM_BP_ALL	GO:0007420-brain development	12	0.496	0.0028	2.92	0.9877	0.1214	4.56
GOTERM_BP_ALL	GO:0009893-positive regulation of metabolic process	25	1.033	0.0028	1.91	0.9880	0.1188	4.59
GOTERM_BP_ALL	GO:0045664-regulation of neuron differentiation	8	0.331	0.0029	4.22	0.9889	0.1176	4.67
KEGG_PATHWAY	hsa04360:Axon guidance	7	0.289	0.0039	4.52	0.2834	0.2834	4.09
KEGG_PATHWAY	hsa04514:Cell adhesion molecules (CAMs)	7	0.289	0.0043	4.42	0.3116	0.1703	4.57
<b>Targets of miRNAs decreasing with age/genes increasing with age</b>								
GENETIC_ASSOCIATION_DB_DISEASE_CL ASS	PSYCH	14	0.528	0.0063	2.13	0.0964	0.0964	4.40
GENETIC_ASSOCIATION_DB_DISEASE	seizures	3	0.113	0.0019	42.06	0.3061	0.3061	2.33
GENETIC_ASSOCIATION_DB_DISEASE	schizophrenia	10	0.377	0.0043	2.92	0.5637	0.3394	5.21
GOTERM_BP_ALL	GO:0006810-transport	66	2.487	7.16E-09	2.00	9.19E-06	9.19E-06	1.17E-05
GOTERM_BP_ALL	GO:0051234-establishment of localization	66	2.487	1.09E-08	1.98	1.40E-05	6.98E-06	1.77E-05

GOTERM_BP_ALL	GO:0051179-localization	67	2.524	4.88E-07	1.79	6.26E-04	2.09E-04	7.96E-04
GOTERM_BP_ALL	GO:0051641-cellular localization	26	0.980	2.15E-04	2.23	0.2410	0.0666	0.35
GOTERM_BP_ALL	GO:0051649-establishment of localization in cell	24	0.904	3.81E-04	2.25	0.3870	0.0932	0.62
GOTERM_BP_ALL	GO:0006996-organelle organization	32	1.206	4.81E-04	1.92	0.4606	0.0978	0.78
GOTERM_BP_ALL	GO:0015031-protein transport	21	0.791	0.0013	2.20	0.8153	0.2144	2.12
GOTERM_BP_ALL	GO:0046907-intracellular transport	19	0.716	0.0014	2.31	0.8420	0.2060	2.32
GOTERM_BP_ALL	GO:0008104-protein localization	23	0.867	0.0014	2.08	0.8446	0.1869	2.34
GOTERM_BP_ALL	GO:0045184-establishment of protein localization	21	0.791	0.0015	2.18	0.8481	0.1717	2.36
GOTERM_BP_ALL	GO:0006812-cation transport	17	0.641	0.0015	2.45	0.8585	0.1629	2.45
GOTERM_BP_ALL	GO:0030036-actin cytoskeleton organization	10	0.377	0.0021	3.53	0.9349	0.2036	3.41
GOTERM_BP_ALL	GO:0016192-vesicle-mediated transport	17	0.641	0.0023	2.35	0.9479	0.2033	3.68
KEGG_PATHWAY	hsa04666:Fc gamma R-mediated phagocytosis	8	0.301	3.79E-04	5.79	0.0354	0.0354	0.42
KEGG_PATHWAY	hsa04370:VEGF signaling pathway	6	0.226	0.0042	5.50	0.3296	0.1812	4.52
Schizophrenia-associated miRNA (decreasing with age) targets + genes increase with age								
GENETIC_ASSOCIATION_DB_DISEASE_CL ASS	PSYCH	16	0.509	0.006783	1.99	0.1032	0.1032	4.71825
GENETIC_ASSOCIATION_DB_DISEASE	seizures	3	0.095	0.00285	34.41	0.5307	0.5307	3.672995
GOTERM_BP_ALL	GO:0051234-establishment of localization	73	2.322	4.97E-09	1.94	0.0000	0.0000	8.17E-06
GOTERM_BP_ALL	GO:0006810-transport	72	2.290	8.01E-09	1.93	0.0000	0.0000	1.32E-05
GOTERM_BP_ALL	GO:0051179-localization	76	2.417	6.54E-08	1.79	0.0001	0.0000	1.07E-04
GOTERM_BP_ALL	GO:0051641-cellular localization	32	1.018	6.10E-06	2.43	0.0083	0.0021	0.0100
GOTERM_BP_ALL	GO:0006996-organelle organization	40	1.272	7.88E-06	2.12	0.0107	0.0022	0.0129
GOTERM_BP_ALL	GO:0051649-establishment of localization in cell	28	0.891	6.45E-05	2.32	0.0845	0.0146	0.11
GOTERM_BP_ALL	GO:0046907-intracellular transport	22	0.700	3.95E-04	2.36	0.4175	0.0743	0.65
GOTERM_BP_ALL	GO:0007010-cytoskeleton organization	17	0.541	4.62E-04	2.75	0.4683	0.0759	0.76
GOTERM_BP_ALL	GO:0006812-cation transport	19	0.604	8.42E-04	2.42	0.6842	0.1202	1.37
GOTERM_BP_ALL	GO:0033365-protein localization in organelle	9	0.286	0.0011	4.35	0.7742	0.1383	1.77
GOTERM_BP_ALL	GO:0019226-transmission of nerve impulse	14	0.445	0.0014	2.82	0.8540	0.1605	2.28
GOTERM_BP_ALL	GO:0008104-protein localization	25	0.795	0.0015	2.00	0.8695	0.1561	2.42
GOTERM_BP_ALL	GO:0033036-macromolecule localization	28	0.891	0.0024	1.84	0.9639	0.2255	3.91
GOTERM_BP_ALL	GO:0030001-metal ion transport	16	0.509	0.0025	2.43	0.9664	0.2152	3.99
GOTERM_BP_ALL	GO:0065008-regulation of biological quality	35	1.113	0.0025	1.68	0.9686	0.2061	4.07
GOTERM_BP_ALL	GO:0015031-protein transport	22	0.700	0.0025	2.04	0.9691	0.1953	4.09
GOTERM_BP_ALL	GO:0045184-establishment of protein localization	22	0.700	0.0028	2.02	0.9792	0.2038	4.55
KEGG_PATHWAY	hsa04666:Fc gamma R-mediated phagocytosis	7	0.223	0.0021	5.13	0.1776	0.1776	2.28
KEGG_PATHWAY	hsa04360:Axon guidance	8	0.254	0.0021	4.32	0.1814	0.0952	2.33
KEGG_PATHWAY	hsa04370:VEGF signaling pathway	6	0.191	0.0040	5.57	0.3085	0.1157	4.25
KEGG_PATHWAY	hsa04114:Oocyte meiosis	7	0.223	0.0044	4.43	0.3354	0.0971	4.70



**Supplementary Figure 1: miRNA microarray quantitative real-time PCR validation.** Box plots demonstrate the relative expression of each miRNA in each of the three age groups; 0-14 years, 15-24 years and 25-50 years. Data obtained using qPCR are displayed in blue; microarray data in green.

**Supplementary Figure 2: The axon guidance pathway is heavily regulated by age-related miRNA.** The colored stars indicate the number of miRNA binding sites each gene is predicted to have. Yellow shading indicates that particular gene was altered in the predicted direction.



## **APPENDIX III: SUPPLEMENTARY DATA FOR CHAPTER 4**

**Supplementary Table 1: miRNA expressed in STG using DNA microarrays**

<b>miRNA</b>	<b>Expression in human tissue</b>	<b>Reference</b>
hsa-let-7a	Abundant expression across organs	[1, 2]
hsa-let-7b	Abundant expression across organs	[1, 2]
hsa-let-7c	Abundant expression across organs	[2]
hsa-let-7d	Abundant expression across organs	[2]
hsa-let-7e	Abundant expression across organs	[2]
hsa-let-7f	Abundant expression across organs	[2]
hsa-let-7g	Medium expression across organs	[2]
hsa-let-7i	Medium expression across organs	[2]
hsa-miR-100	Low-Med expression across organs	[1]
hsa-miR-103	Low expression across organs	[1, 2]
hsa-miR-105	Low expression in adult frontal cortex	[3]
hsa-miR-107	Low expression across organs	[1, 2]
hsa-miR-124a	Neuron specific	[4]
hsa-miR-125a	Neuron, astrocyte enriched	[4]
hsa-miR-125b	Neuron, astrocyte enriched	[4]
hsa-miR-126	Abundant expression across organs	[2]
hsa-miR-127	Low-Med expression across organs / Medium expression in Brain	[1, 2]
hsa-miR-128a	Neuron, astrocyte enriched	[4]
hsa-miR-128b	Neuron, astrocyte enriched	[4]
hsa-miR-130a	Low-Med expression across organs	[3]
hsa-miR-132	Brain enriched	[1]
hsa-miR-138	Brain enriched	[1]
hsa-miR-139	Medium expression across organs / Med-High expression in Brain	[1, 2]
hsa-miR-143	Abundant expression across organs	[2]
hsa-miR-145	Abundant expression across organs	[2]
hsa-miR-149	Low expression across organs / Low-Med expression in Brain	[2]
hsa-miR-15a	Medium expression across organs	[1, 2]
hsa-miR-15b	Medium expression across organs	[1, 2]
hsa-miR-16	Low-Med expression across organs	[2]
hsa-miR-17-5p	Medium expression across organs	[1, 2]
hsa-miR-181a	Low expression across organs / Medium expression in Brain	[2]
hsa-miR-181b	Low-Med expression across organs / Medium expression in Brain	[1, 2]
hsa-miR-181c	Low expression across organs	[2]
hsa-miR-185	Low-Med expression across organs	[2]
hsa-miR-191	Low-Med expression across organs	[2]
hsa-miR-195	Immune enriched / Medium expression in Brain	[2]
hsa-miR-198	Low expression across organs	[2]
hsa-miR-20	Low-Med expression across organs	[1, 2]
hsa-miR-200c	Low expression across organs	[2]
hsa-miR-204	Low-Med expression across organs	[2]
hsa-miR-21	Med-High expression across organs	[2]
hsa-miR-218	Low expression across organs	[1, 2]
hsa-miR-219	Brain enriched	[1, 2]
hsa-miR-22	Low-Med expression across organs	[1, 2]
hsa-miR-221	Low-Med expression across organs	[2]

---

hsa-miR-222	Low-Med expression across organs/ Medium expression in Brain	[1, 2]
hsa-miR-23a	Astrocyte enriched	[4]
hsa-miR-23b	Astrocyte enriched	[4]
hsa-miR-24	Low expression across organs	[1, 2]
hsa-miR-26a	Neuron, astrocyte enriched	[4]
hsa-miR-26b	Neuron, astrocyte enriched	[4]
hsa-miR-27a	Abundant expression across organs	[2]
hsa-miR-27b	Medium expression across organs	[1]
hsa-miR-28	Low-Med expression across organs	[1, 2]
hsa-miR-29a	Astrocyte enriched	[4]
hsa-miR-29b	Astrocyte enriched	[4]
hsa-miR-29c	Astrocyte enriched	[4]
hsa-miR-30a-5p	Low-Med expression across organs	[1]
hsa-miR-30b	Abundant expression across organs	[1]
hsa-miR-30c	Abundant expression across organs	[1]
hsa-miR-30d	Low-Med expression across organs	[1]
hsa-miR-324-5p	Low-Med expression across organs	[3]
hsa-miR-335	Medium expression across organs	[2]
hsa-miR-338	Brain enriched	[1]
hsa-miR-342	Medium expression across organs	[2]
hsa-miR-34a	Low expression across organs	[2]
hsa-miR-361	Low expression across organs	[3]
hsa-miR-368	Low-Med expression across organs	[3]
hsa-miR-373*	Expressed in human embryonic stem cells	[5]
hsa-miR-7	Brain enriched	[1]
hsa-miR-9	Brain specific	[1, 4]
hsa-miR-9*	Brain enriched	[1, 4]
hsa-miR-95	Low expression across organs	[1, 2]
hsa-miR-98	Low-Med expression across organs	[2]
hsa-miR-99a	Low-Med expression across organs	[2]
hsa-miR-99b	Low-Med expression across organs	[2]

[1] Sempere *et al.* (2004); [2] Baskerville & Bartel (2005); [3] Landgraf *et al.* (2007);  
4] Smirnova *et al.* (2005); [5] Suh *et al.* (2004)

**Supplementary Table 2a: miR-181b targets - miRanda algorithm (web version)**

Gene	Ensembl Id	Gene Description	Number of Hits	Location
ACSL1	ENST00000281455	ENSG00000151726 (ACSL1): ENSEMBL: Long-chain-fatty-acid--CoA ligase 2 (EC 6.2.1.3) (Long-chain acyl-CoA synthetase 2) (LACS 2). [SWISSPROT:P33121]	1	1408
ACSL1	ENST00000359903	ENSG00000151726 (ACSL1): ENSEMBL: Long-chain-fatty-acid--CoA ligase 2 (EC 6.2.1.3) (Long-chain acyl-CoA synthetase 2) (LACS 2). [SWISSPROT:P33121]	1	1408
ACVR2	ENST00000241416	ENSG00000121989 (ACVR2): ENSEMBL: Activin receptor type II precursor (EC 2.7.1.37) (ACTR-II) (ACTRIIA). [SWISSPROT:P27037]	1	469
ADAMTS18	ENST00000282849	ENSG00000140873 (ADAMTS18): ENSEMBL: ADAMTS-18 precursor (EC 3.4.24.-) (A disintegrin and metalloproteinase with thrombospondin motifs 18) (ADAM-TS 18) (ADAM-TS18). [SWISSPROT:Q8TE60]	1	1329
ADCY9	ENST00000348726	ENSG00000162104 (ADCY9): ENSEMBL: Adenylate cyclase, type IX (EC 4.6.1.1) (ATP pyrophosphate-lyase) (Adenyllyl cyclase). [SWISSPROT:O60503]	1	2537
ADCY9	ENST00000294016	ENSG00000162104 (ADCY9): ENSEMBL: Adenylate cyclase, type IX (EC 4.6.1.1) (ATP pyrophosphate-lyase) (Adenyllyl cyclase). [SWISSPROT:O60503]	1	2537
AGPAT1	ENST00000306095	ENSG00000168448 (AGPAT1): ENSEMBL: 1-acyl-sn-glycerol-3-phosphate acyltransferase alpha (EC 2.3.1.51) (1- AGP acyltransferase 1) (1-AGPAT 1) (Lysophosphatidic acid acyltransferase-alpha) (LPAAT-alpha) (1-acylglycerol-3-phosphate O- acyltransferase 1) (G15 protein). [SWISSPROT:Q99943]	1	129
AGPAT1	ENST00000336984	ENSG00000168448 (AGPAT1): ENSEMBL: 1-acyl-sn-glycerol-3-phosphate acyltransferase alpha (EC 2.3.1.51) (1- AGP acyltransferase 1) (1-AGPAT 1) (Lysophosphatidic acid acyltransferase-alpha) (LPAAT-alpha) (1-acylglycerol-3-phosphate O- acyltransferase 1) (G15 protein). [SWISSPROT:Q99943]	1	129
AKAP6	ENST00000280979	ENSG00000151320 (AKAP6): ENSEMBL: A-kinase anchor protein 6 (Protein kinase A anchoring protein 6) (PRKA6) (A-kinase anchor protein 100 kDa) (AKAP 100) (mAKAP). [SWISSPROT:Q13023]	1	3077
ARHGEF2	ENST00000313695	ENSG00000116584 (ARHGEF2): ENSEMBL: Rho guanine nucleotide exchange factor 2 (GEF-H1 protein) (Proliferating cell nuclear antigen p40). [SWISSPROT:Q92974]	1	650
ARHGEF2	ENST00000361247	ENSG00000116584 (ARHGEF2): ENSEMBL: Rho guanine nucleotide exchange factor 2 (GEF-H1 protein) (Proliferating cell nuclear antigen p40). [SWISSPROT:Q92974]	1	650
ARHGEF2	ENST00000356361	ENSG00000116584 (ARHGEF2): ENSEMBL: Rho guanine nucleotide exchange factor 2 (GEF-H1 protein) (Proliferating cell nuclear antigen p40). [SWISSPROT:Q92974]	1	650
ARL3	ENST00000260746	ENSG00000138175 (ARL3): ENSEMBL: ADP-ribosylation factor-like protein 3. [SWISSPROT:P36405]	1	2357
ARL5	ENST00000355116	ENSG00000162980 (ARL5): ENSEMBL: ADP-ribosylation factor-like protein 5. [SWISSPROT:Q9Y689]	1	326
ARL5	ENST00000295087	ENSG00000162980 (ARL5): ENSEMBL: ADP-ribosylation factor-like protein 5. [SWISSPROT:Q9Y689]	1	326
ASAH2	ENST00000341534_P	ENSG00000188611 (ASAH2): ENSEMBL: N-acylsphingosine amidohydrolase 2; mitochondrial ceramidase; acid ceramidase; non-lysosomal ceramidase; neutral/alkaline ceramidase. [RefSeq:NM_019893]	1	526
ATP11C	ENST00000361648	ENSG00000101974 (ATP11C): ENSEMBL: Potential phospholipid-transporting ATPase 1G (EC 3.6.3.1) (ATPase class I type 11C) (ATPase 1G) (Fragment). [SWISSPROT:Q8NB49]	1	1068
ATP11C	ENST00000327569	ENSG00000101974 (ATP11C): ENSEMBL: Potential phospholipid-transporting ATPase 1G (EC 3.6.3.1) (ATPase class I type 11C) (ATPase 1G) (Fragment). [SWISSPROT:Q8NB49]	1	1068
ATP2B2	ENST00000352432	ENSG00000157087 (ATP2B2): ENSEMBL: Plasma membrane calcium-transporting ATPase 2 (EC 3.6.3.8) (PMCA2) (Plasma membrane calcium pump isoform 2) (Plasma membrane calcium ATPase isoform 2). [SWISSPROT:Q01814]	1	310
ATP2B2	ENST00000343816	ENSG00000157087 (ATP2B2): ENSEMBL: Plasma membrane calcium-transporting ATPase 2 (EC 3.6.3.8) (PMCA2) (Plasma membrane calcium pump isoform 2) (Plasma membrane calcium ATPase isoform 2). [SWISSPROT:Q01814]	1	310
ATP2B2	ENST00000360273	ENSG00000157087 (ATP2B2): ENSEMBL: Plasma membrane calcium-transporting ATPase 2 (EC 3.6.3.8) (PMCA2) (Plasma membrane calcium pump isoform 2) (Plasma membrane calcium ATPase isoform 2). [SWISSPROT:Q01814]	1	310
BACH2	ENST00000257749	ENSG00000112182 (BACH2): ENSEMBL: Transcription regulator protein BACH2 (BTB and CNC homolog 2). [SWISSPROT:Q9BYV9]	1	335
BACH2	ENST00000343122	ENSG00000112182 (BACH2): ENSEMBL: Transcription regulator protein BACH2 (BTB and CNC homolog 2). [SWISSPROT:Q9BYV9]	1	335
BAZ2A	ENST00000179765	ENSG00000076108 (BAZ2A): ENSEMBL: Bromodomain adjacent to zinc finger domain 2A (Transcription termination factor-1 interacting protein 5) (TTF-I interacting protein 5) (Tip5) (hWalp3). [SWISSPROT:Q9UIF9]	1	375
BHLHB2	ENST00000256495	ENSG00000134107 (BHLHB2): ENSEMBL: Class B basic helix-loop-helix protein 2 (bHLHB2) (Differentially expressed in chondrocytes protein 1) (DEC1) (Enhancer-of-split and hairy-related protein 2) (SHARP-2) (Stimulated with retinoic acid 13). [SWISSPROT:O14503]	1	1296
BIRC6	ENST00000261359_P	ENSG00000115760 (BIRC6): ENSEMBL: Baculoviral IAP repeat-containing protein 6 (Ubiquitin-conjugating BIR-domain enzyme apollon). [SWISSPROT:Q9NR09]	1	280
BTBD3	ENST00000337608	ENSG00000132640 (BTBD3): ENSEMBL: BTB/POZ domain containing protein 3. [SWISSPROT:Q9Y2F9]	1	2870
BTBD3	ENST00000254977	ENSG00000132640 (BTBD3): ENSEMBL: BTB/POZ domain containing protein 3. [SWISSPROT:Q9Y2F9]	1	2870
C14orf4	ENST00000238647	ENSG00000119669 (C14orf4): ENSEMBL: Protein C14orf4 (My039 protein). [SWISSPROT:Q9H1B7]	1	659
C17orf31	ENST00000263073	ENSG00000070366 (C17orf31): ENSEMBL: Est1p-like protein A; ever shorter telomeres 1A. [RefSeq:NM_017575]	1	439
C5orf6	ENST00000239906	ENSG00000120709 (C5orf6): ENSEMBL: putative nuclear protein. [RefSeq:NM_016605]	1	224
C9orf54	ENST00000349214	ENSG00000148343 (C9orf54): ENSEMBL	1	1441
C9orf54	ENST00000358369	ENSG00000148343 (C9orf54): ENSEMBL	1	1441
C9orf54	ENST00000277475	ENSG00000148343 (C9orf54): ENSEMBL	1	1441
CACNA2D2	ENST00000360963	ENSG000000007402 (CACNA2D2): ENSEMBL: calcium channel, voltage-dependent, alpha 2/delta subunit 2; alpha 2 delta calcium channel subunit. [RefSeq:NM_006030]	1	802
CACNA2D2	ENST00000266039	ENSG000000007402 (CACNA2D2): ENSEMBL: calcium channel, voltage-dependent, alpha 2/delta subunit 2; alpha 2 delta calcium channel subunit. [RefSeq:NM_006030]	1	802
CACNB2	ENST00000362084	ENSG00000165995 (CACNB2): ENSEMBL: Dihydropyridine-sensitive L-type, calcium channel beta-2 subunit (CAB2) (Voltage-dependent calcium channel beta-2 subunit) (Lambert- Eaton myasthenic syndrome antigen B) (MYSB). [SWISSPROT:Q08289]	1	1150
CACNB2	ENST00000340194	ENSG00000165995 (CACNB2): ENSEMBL: Dihydropyridine-sensitive L-type, calcium channel beta-2 subunit (CAB2) (Voltage-dependent calcium channel beta-2 subunit) (Lambert- Eaton myasthenic syndrome antigen B) (MYSB). [SWISSPROT:Q08289]	1	1150
CACNB2	ENST00000340232	ENSG00000165995 (CACNB2): ENSEMBL: Dihydropyridine-sensitive L-type, calcium channel	1	1150

		beta-2 subunit (CAB2) (Voltage-dependent calcium channel beta-2 subunit) (Lambert- Eaton myasthenic syndrome antigen B) (MYSB). [SWISSPROT:Q08289]		
CACNB2	ENST00000324631	ENSG00000165995 (CACNB2): ENSEMBL: Dihydropyridine-sensitive L-type, calcium channel beta-2 subunit (CAB2) (Voltage-dependent calcium channel beta-2 subunit) (Lambert- Eaton myasthenic syndrome antigen B) (MYSB). [SWISSPROT:Q08289]	1	1150
CACNB2	ENST00000282343	ENSG00000165995 (CACNB2): ENSEMBL: Dihydropyridine-sensitive L-type, calcium channel beta-2 subunit (CAB2) (Voltage-dependent calcium channel beta-2 subunit) (Lambert- Eaton myasthenic syndrome antigen B) (MYSB). [SWISSPROT:Q08289]	1	1150
CACNB2	ENST00000352115	ENSG00000165995 (CACNB2): ENSEMBL: Dihydropyridine-sensitive L-type, calcium channel beta-2 subunit (CAB2) (Voltage-dependent calcium channel beta-2 subunit) (Lambert- Eaton myasthenic syndrome antigen B) (MYSB). [SWISSPROT:Q08289]	1	1150
CACNB2	ENST00000359991	ENSG00000165995 (CACNB2): ENSEMBL: Dihydropyridine-sensitive L-type, calcium channel beta-2 subunit (CAB2) (Voltage-dependent calcium channel beta-2 subunit) (Lambert- Eaton myasthenic syndrome antigen B) (MYSB). [SWISSPROT:Q08289]	1	1150
CBX7	ENST00000216133	ENSG00000100307 (CBX7): ENSEMBL: Chromobox protein homolog 7. [SWISSPROT:Q95931]	1	2601
CD4	ENST00000011653	ENSG00000010610 (CD4): ENSEMBL: T-cell surface glycoprotein CD4 precursor (T-cell surface antigen T4/Leu-3). [SWISSPROT:P01730]	1	55
CDH13	ENST00000268613	ENSG00000140945 (CDH13): ENSEMBL: Cadherin-13 precursor (Truncated-cadherin) (T-cadherin) (T-cad) (Heart-cadherin) (H-cadherin) (P105). [SWISSPROT:P55290]	1	205
CFL2	ENST00000298159	ENSG00000165410 (CFL2): ENSEMBL: Cofilin, muscle isoform (Cofilin 2). [SWISSPROT:Q9Y281]	1	111
CFL2	ENST00000341223	ENSG00000165410 (CFL2): ENSEMBL: Cofilin, muscle isoform (Cofilin 2). [SWISSPROT:Q9Y281]	1	111
CLCNKA	ENST00000331433	ENSG00000186510 (CLCNKA): ENSEMBL: Chloride channel protein CIC-KA (CIC-K1). [SWISSPROT:P51800]	1	203
CNNM2	ENST00000278072	ENSG00000148842 (CNNM2): ENSEMBL: cyclin M2 isoform 3; ancient conserved domain protein 2. [RefSeq:NM_199077]	1	714
CNNM2	ENST00000345419	ENSG00000148842 (CNNM2): ENSEMBL: cyclin M2 isoform 3; ancient conserved domain protein 2. [RefSeq:NM_199077]	1	714
CNOT2	ENST00000229195_P	ENSG00000111596 (CNOT2): ENSEMBL: CCR4-NOT transcription complex, subunit 2; NOT2 (negative regulator of transcription 2, yeast) homolog. [RefSeq:NM_014515]	1	906
CPEB1	ENST00000261723	ENSG00000103723 (CPEB1): ENSEMBL: cytoplasmic polyadenylation element binding protein 1. [RefSeq:NM_030594]	1	483
CPNE2	ENST00000290776	ENSG00000140848 (CPNE2): ENSEMBL: Copine II. [SWISSPROT:Q96FN4]	1	221
CSNK1G1	ENST00000303032	ENSG00000169118 (CSNK1G1): ENSEMBL: Casein kinase I, gamma 1 isoform (EC 2.7.1.-) (CKI-gamma 1). [SWISSPROT:Q9HCP0]	1	188
CTDSPL	ENST00000273179	ENSG00000144677 (CTDSPL): ENSEMBL: Nuclear LIM interactor-interacting factor 1 (NLI-interacting factor 1) (NIF-like protein) (YA22 protein) (HYA22). [SWISSPROT:O15194]	1	104
CUGBP1	ENST00000338267	ENSG00000149187 (CUGBP1): ENSEMBL: CUG triplet repeat RNA-binding protein 1 (CUG-BP1) (RNA-binding protein BRUNOL-2) (Deadenylation factor CUG-BP) (50 kDa Nuclear polyadenylated RNA-binding protein) (EDEN-BP). [SWISSPROT:Q92879]	1	904
CUGBP1	ENST00000358597	ENSG00000149187 (CUGBP1): ENSEMBL: CUG triplet repeat RNA-binding protein 1 (CUG-BP1) (RNA-binding protein BRUNOL-2) (Deadenylation factor CUG-BP) (50 kDa Nuclear polyadenylated RNA-binding protein) (EDEN-BP). [SWISSPROT:Q92879]	1	816
CUGBP1	ENST00000361904	ENSG00000149187 (CUGBP1): ENSEMBL: CUG triplet repeat RNA-binding protein 1 (CUG-BP1) (RNA-binding protein BRUNOL-2) (Deadenylation factor CUG-BP) (50 kDa Nuclear polyadenylated RNA-binding protein) (EDEN-BP). [SWISSPROT:Q92879]	1	816
DAZAP2	ENST00000332845	ENSG00000183283 (DAZAP2): ENSEMBL: DAZ associated protein 2; deleted in azoospermia associated protein 2. [RefSeq:NM_014764]	1	216
DCAMKL1	ENST00000360631	ENSG00000133083 (DCAMKL1): ENSEMBL: Serine/threonine-protein kinase DCAMKL1 (EC 2.7.1.-) (Doublecortin-like and CAM kinase-like 1). [SWISSPROT:O15075]	1	361
DCAMKL1	ENST00000255448	ENSG00000133083 (DCAMKL1): ENSEMBL: Serine/threonine-protein kinase DCAMKL1 (EC 2.7.1.-) (Doublecortin-like and CAM kinase-like 1). [SWISSPROT:O15075]	1	361
DDIT4	ENST00000307365	ENSG00000168209 (DDIT4): ENSEMBL: RTP801; HIF-1 responsive RTP801. [RefSeq:NM_019058]	1	531
DDX3X	ENST00000308665	ENSG00000124487 (DDX3X): ENSEMBL: DEAD-box protein 3 (Helicase-like protein 2) (HLP2) (DEAD-box, X isoform). [SWISSPROT:O00571]	1	1883
DNAJA4	ENST00000343789	ENSG00000140403 (DNAJA4): ENSEMBL: DnaJ homolog subfamily A member 4. [SWISSPROT:Q8WW22]	1	20
EED	ENST00000263360	ENSG00000074266 (EED): ENSEMBL: embryonic ectoderm development isoform a; WD protein associating with integrin cytoplasmic tails 1. [RefSeq:NM_003797]	1	637
EED	ENST00000327320	ENSG00000074266 (EED): ENSEMBL: embryonic ectoderm development isoform a; WD protein associating with integrin cytoplasmic tails 1. [RefSeq:NM_003797]	1	637
EED	ENST00000351625	ENSG00000074266 (EED): ENSEMBL: embryonic ectoderm development isoform a; WD protein associating with integrin cytoplasmic tails 1. [RefSeq:NM_003797]	1	107
EGR3	ENST00000317216	ENSG00000179388 (EGR3): ENSEMBL: Early growth response protein 3 (EGR-3) (Zinc finger protein pilot). [SWISSPROT:Q06889]	1	1696
ENAH	ENST00000358675	ENSG00000154380 (ENAH): ENSEMBL: enabled homolog. [RefSeq:NM_018212]	2	2667, 2789
ENAH	ENST00000284563	ENSG00000154380 (ENAH): ENSEMBL: enabled homolog. [RefSeq:NM_018212]	2	2667, 2789
EPB41LAB	ENST00000262536	ENSG00000095203 (EPB41LAB): ENSEMBL: Band 4.1-like protein 4B (EHM2 protein) (FERM-containing protein CG1). [SWISSPROT:Q9H329]	1	1023
ESM1	ENST00000296723	ENSG00000164283 (ESM1): ENSEMBL: Endothelial cell-specific molecule 1 precursor (ESM-1 secretory protein) (ESM-1). [SWISSPROT:Q9NQ30]	1	1273
ETV6	ENST00000266427	ENSG00000139083 (ETV6): ENSEMBL: Transcription factor ETV6 (ETS-related protein Tel1) (Tel) (ETS translocation variant 6). [SWISSPROT:P41212]	1	4211
FALZ	ENST00000342579	ENSG00000171634 (FALZ): ENSEMBL: Fetal Alzheimer antigen (Fetal Alz-50-reactive clone 1). [SWISSPROT:Q12830]	1	858
FALZ	ENST00000306378	ENSG00000171634 (FALZ): ENSEMBL: Fetal Alzheimer antigen (Fetal Alz-50-reactive clone 1). [SWISSPROT:Q12830]	1	858
FALZ	ENST00000321892	ENSG00000171634 (FALZ): ENSEMBL: Fetal Alzheimer antigen (Fetal Alz-50-reactive clone 1). [SWISSPROT:Q12830]	1	858
FALZ	ENST00000335221	ENSG00000171634 (FALZ): ENSEMBL: Fetal Alzheimer antigen (Fetal Alz-50-reactive clone 1). [SWISSPROT:Q12830]	1	858
FBXO33	ENST00000298097	ENSG00000165355 (FBXO33): ENSEMBL: F-box only protein 33. [RefSeq:NM_203301]	1	1661
FIGN	ENST00000333129	ENSG00000182263 (FIGN): ENSEMBL: fidgetin. [RefSeq:NM_018086]	1	12
FKBP1A	ENST00000262925	ENSG00000088832 (FKBP1A): ENSEMBL: FK506-binding protein 1A (EC 5.2.1.8) (Peptidyl-prolyl cis-trans isomerase) (PPIase) (Rotamase) (12 kDa FKBP) (FKBP-12) (Immunophilin FKBP12). [SWISSPROT:P20071]	1	126
FUT11	ENST00000339365	ENSG00000176986 (FUT11): ENSEMBL: Protein transport protein Sec24C (SEC24-related protein C). [SWISSPROT:P53992]	1	230
FUT11	ENST00000345254	ENSG00000176986 (FUT11): ENSEMBL: Protein transport protein Sec24C (SEC24-related protein C). [SWISSPROT:P53992]	1	230



GARP	ENST00000260061	ENSG00000137507 (GARP): ENSEMBL: GARP protein precursor (Garpin) (Glycoprotein A repetitions predominant). [SWISSPROT:Q14392]	1	2038
GAS7	ENST00000361018	ENSG00000007237 (GAS7): ENSEMBL: Growth-arrest-specific protein 7 (GAS-7). [SWISSPROT:O60861]	1	6333
GAS7	ENST00000323816	ENSG00000007237 (GAS7): ENSEMBL: Growth-arrest-specific protein 7 (GAS-7). [SWISSPROT:O60861]	1	6333
GCC2	ENST00000258451	ENSG00000135968 (GCC2): ENSEMBL: GRIP and coiled-coil domain-containing protein 2 (Golgi coiled coil protein GCC185) (CTCL tumor antigen se1-1) (CLL-associated antigen KW-11). [SWISSPROT:Q81WJ2]	1	1423
GCC2	ENST00000309863	ENSG00000135968 (GCC2): ENSEMBL: GRIP and coiled-coil domain-containing protein 2 (Golgi coiled coil protein GCC185) (CTCL tumor antigen se1-1) (CLL-associated antigen KW-11). [SWISSPROT:Q81WJ2]	1	1423
GDA	ENST00000228018	ENSG00000119125 (GDA): ENSEMBL: Guanine deaminase (EC 3.5.4.3) (Guanase) (Guanine aminase) (Guanine aminohydrolase) (GAH) (p51-nedasin). [SWISSPROT:Q9Y2T3]	1	616
GDA	ENST00000358399	ENSG00000119125 (GDA): ENSEMBL: Guanine deaminase (EC 3.5.4.3) (Guanase) (Guanine aminase) (Guanine aminohydrolase) (GAH) (p51-nedasin). [SWISSPROT:Q9Y2T3]	1	616
GLS	ENST00000320717	ENSG00000115419 (GLS): ENSEMBL: Glutaminase, kidney isoform, mitochondrial precursor (EC 3.5.1.2) (GLS) (L-glutamine amidohydrolase) (K-glutaminase). [SWISSPROT:O94925]	1	2401
GOLGA1	ENST00000259462	ENSG00000136935 (GOLGA1): ENSEMBL: Golgi autoantigen, golgin subfamily A member 1 (Golgin-97). [SWISSPROT:Q92805]	1	671
GRIA2	ENST00000264426	ENSG00000120251 (GRIA2): ENSEMBL: Glutamate receptor 2 precursor (GluR-2) (GluR-B) (GluR-K2) (Glutamate receptor ionotropic, AMPA 2). [SWISSPROT:P42262]	1	122
GRIA2	ENST00000296526	ENSG00000120251 (GRIA2): ENSEMBL: Glutamate receptor 2 precursor (GluR-2) (GluR-B) (GluR-K2) (Glutamate receptor ionotropic, AMPA 2). [SWISSPROT:P42262]	1	122
GRIK2	ENST00000333309	ENSG00000164418 (GRIK2): ENSEMBL: Glutamate receptor, ionotropic kainate 2 precursor (Glutamate receptor 6) (GluR-6) (GluR6) (Excitatory amino acid receptor 4) (EAA4). [SWISSPROT:Q13002]	1	231
GRIK2	ENST00000296893	ENSG00000164418 (GRIK2): ENSEMBL: Glutamate receptor, ionotropic kainate 2 precursor (Glutamate receptor 6) (GluR-6) (GluR6) (Excitatory amino acid receptor 4) (EAA4). [SWISSPROT:Q13002]	1	231
GRM1	ENST00000282753	ENSG00000152822 (GRM1): ENSEMBL: Metabotropic glutamate receptor 1 precursor (mGluR1). [SWISSPROT:Q13255]	1	1187
GRM1	ENST00000355289	ENSG00000152822 (GRM1): ENSEMBL: Metabotropic glutamate receptor 1 precursor (mGluR1). [SWISSPROT:Q13255]	1	1187
GRM5	ENST00000357667_P	ENSG00000168959 (GRM5): ENSEMBL: Metabotropic glutamate receptor 5 precursor (mGluR5). [SWISSPROT:P41594]	1	416
HAVCR2	ENST00000307851	ENSG00000135077 (HAVCR2): ENSEMBL: T cell immunoglobulin mucin 3; T cell immunoglobulin mucin-3; kidney injury molecule-3. [RefSeq:NM_032782]	1	214
HECA	ENST00000230165	ENSG00000112406 (HECA): ENSEMBL: headcase homolog; hHDC for homolog of Drosophila headcase. [RefSeq:NM_016217]	1	407
HEY2	ENST00000258012	ENSG00000135547 (HEY2): ENSEMBL: hairy/enhancer-of-split related with YRPW motif 2; gridlock; HES-related repressor protein 1. [RefSeq:NM_012259]	1	1087
HIPK1	ENST00000361587	ENSG00000163349 (HIPK1): ENSEMBL: Homeodomain-interacting protein kinase 1 (EC 2.7.1.-). [SWISSPROT:Q86Z02]	1	3141
HIPK1	ENST00000340480	ENSG00000163349 (HIPK1): ENSEMBL: Homeodomain-interacting protein kinase 1 (EC 2.7.1.-). [SWISSPROT:Q86Z02]	1	3141
HIPK1	ENST00000349025	ENSG00000163349 (HIPK1): ENSEMBL: Homeodomain-interacting protein kinase 1 (EC 2.7.1.-). [SWISSPROT:Q86Z02]	1	3141
HMBS	ENST00000278715	ENSG00000149397 (HMBS): ENSEMBL: Porphobilinogen deaminase (EC 2.5.1.61) (Hydroxymethylbilane synthase) (HMBS) (Pre-uroporphyrinogen synthase) (PBG-D). [SWISSPROT:P08397]	1	208
HOXA1	ENST00000343060	ENSG00000105991 (HOXA1): ENSEMBL: Homeobox protein Hox-A1 (Hox-1F). [SWISSPROT:P49639]	1	1384
HOXA11	ENST00000006015	ENSG00000005073 (HOXA11): ENSEMBL: Homeobox protein Hox-A11 (Hox-1I). [SWISSPROT:P31270]	1	1195
HOXB5	ENST00000239151	ENSG00000120075 (HOXB5): ENSEMBL: Homeobox protein Hox-B5 (Hox-2A) (HHO.C10) (HU-1). [SWISSPROT:P09067]	1	252
HOXC8	ENST00000040584	ENSG00000037965 (HOXC8): ENSEMBL: Homeobox protein Hox-C8 (Hox-3A). [SWISSPROT:P31273]	2	1160, 1275
ING5	ENST00000313552	ENSG00000168395 (ING5): ENSEMBL: inhibitor of growth family, member 5. [RefSeq:NM_032329]	1	4248
ING5	ENST00000340585	ENSG00000187524 (ING5): ENSEMBL: inhibitor of growth family, member 5. [RefSeq:NM_032329]	1	4248
ING5	ENST00000339171	ENSG00000187524 (ING5): ENSEMBL: inhibitor of growth family, member 5. [RefSeq:NM_032329]	1	4248
KCNH8	ENST00000328405	ENSG00000183960 (KCNH8): ENSEMBL: Potassium voltage-gated channel subfamily H member 8 (Ether-a-go-go-like potassium channel 3) (ELK channel 3) (ELK3) (ELK1) (hElk1). [SWISSPROT:Q96L42]	1	628
KIF3B	ENST00000262652	ENSG00000101350 (KIF3B): ENSEMBL: Kinesin-like protein KIF3B (Microtubule plus end-directed kinesin motor 3B) (HH0048). [SWISSPROT:O15066]	1	3124
KPNA1	ENST00000344337	ENSG00000114030 (KPNA1): ENSEMBL: Importin alpha-1 subunit (Karyopherin alpha-1 subunit) (SRP1-beta) (RAG cohort protein 2) (Nucleoprotein interactor 1) (NPI-1). [SWISSPROT:P52294]	1	611
KPNA4	ENST00000334256	ENSG00000186432 (KPNA4): ENSEMBL: Importin alpha-4 subunit (Karyopherin alpha-4 subunit) (Qip1 protein). [SWISSPROT:O00629]	1	459
KPNB1	ENST00000290158	ENSG00000108424 (KPNB1): ENSEMBL: Importin beta-1 subunit (Karyopherin beta-1 subunit) (Nuclear factor P97) (Importin 90). [SWISSPROT:Q14974]	1	78
KPNB3	ENST00000357602	ENSG00000065150 (KPNB3): ENSEMBL: Importin beta-3 subunit (Karyopherin beta-3 subunit) (Ran-binding protein 5). [SWISSPROT:O00410]	1	571
KPNB3	ENST00000261574	ENSG00000065150 (KPNB3): ENSEMBL: Importin beta-3 subunit (Karyopherin beta-3 subunit) (Ran-binding protein 5). [SWISSPROT:O00410]	1	571
LRRN1	ENST00000319331	ENSG00000175928 (LRRN1): ENSEMBL: leucine rich repeat neuronal 1. [RefSeq:NM_020873]	1	535
MADH7	ENST00000262158	ENSG00000101665 (MADH7): ENSEMBL: Mothers against decapentaplegic homolog 7 (SMAD 7) (Mothers against DPP homolog 7) (Smad7) (hSMAD7). [SWISSPROT:O15105]	1	1449
MAMDC2	ENST00000324072	ENSG00000165072 (MAMDC2): ENSEMBL: MAM domain containing 2; MAM domain containing 1. [RefSeq:NM_153267]	1	327
MAP1A	ENST00000300231	ENSG00000166963 (MAP1A): ENSEMBL: Microtubule-associated protein 1A (MAP 1A) (Proliferation-related protein p80) [Contains: MAP1 light chain LC2]. [SWISSPROT:P78559]	1	937
MAP3K10	ENST00000253055	ENSG00000130758 (MAP3K10): ENSEMBL: Mitogen-activated protein kinase kinase kinase 10 (EC 2.7.1.37) (Mixed lineage kinase 2) (Protein kinase MST). [SWISSPROT:Q02779]	1	15
MAP3K12	ENST00000267079	ENSG00000139625 (MAP3K12): ENSEMBL: Mitogen-activated protein kinase kinase kinase 12 (EC 2.7.1.37) (Leucine-zipper protein kinase) (ZPK). [SWISSPROT:Q12852]	1	168
MAP3K12	ENST00000333964_P	ENSG00000139625 (MAP3K12): ENSEMBL: Mitogen-activated protein kinase kinase kinase 12 (EC 2.7.1.37) (Leucine-zipper protein kinase) (ZPK). [SWISSPROT:Q12852]	1	24
MBNL1	ENST00000357472	ENSG00000152601 (MBNL1): ENSEMBL: Muscledblind-like protein (Triplet-expansion RNA-binding protein). [SWISSPROT:Q9NR56]	1	563

MBNL1	ENST00000324196	ENSG00000152601 (MBNL1): ENSEMBL: Muscleblind-like protein (Triplet-expansion RNA-binding protein). [SWISSPROT:Q9NR56]	1	563
MBNL1	ENST00000355460	ENSG00000152601 (MBNL1): ENSEMBL: Muscleblind-like protein (Triplet-expansion RNA-binding protein). [SWISSPROT:Q9NR56]	1	563
MBNL1	ENST00000282488	ENSG00000152601 (MBNL1): ENSEMBL: Muscleblind-like protein (Triplet-expansion RNA-binding protein). [SWISSPROT:Q9NR56]	1	563
MBNL1	ENST00000282486	ENSG00000152601 (MBNL1): ENSEMBL: Muscleblind-like protein (Triplet-expansion RNA-binding protein). [SWISSPROT:Q9NR56]	1	563
MBNL1	ENST00000324210	ENSG00000152601 (MBNL1): ENSEMBL: Muscleblind-like protein (Triplet-expansion RNA-binding protein). [SWISSPROT:Q9NR56]	1	563
MLF1	ENST00000312827	ENSG00000178053 (MLF1): ENSEMBL: Myeloid leukemia factor 1 (Myelodysplasia-myeloid leukemia factor 1). [SWISSPROT:P58340]	1	111
MLF1	ENST00000312799	ENSG00000178053 (MLF1): ENSEMBL: Myeloid leukemia factor 1 (Myelodysplasia-myeloid leukemia factor 1). [SWISSPROT:P58340]	1	111
MLF1	ENST00000355893	ENSG00000178053 (MLF1): ENSEMBL: Myeloid leukemia factor 1 (Myelodysplasia-myeloid leukemia factor 1). [SWISSPROT:P58340]	1	111
MLF1	ENST00000359117	ENSG00000178053 (MLF1): ENSEMBL: Myeloid leukemia factor 1 (Myelodysplasia-myeloid leukemia factor 1). [SWISSPROT:P58340]	1	111
MTPN	ENST00000356707	ENSG00000105887 (MTPN): ENSEMBL: Myotrophin (V-1 protein). [SWISSPROT:P58546]	1	1385
MTPN	ENST00000222605	ENSG00000105887 (MTPN): ENSEMBL: Myotrophin (V-1 protein). [SWISSPROT:P58546]	1	1385
MYH10	ENST00000269243	ENSG00000133026 (MYH10): ENSEMBL: Myosin heavy chain, nonmuscle type B (Cellular myosin heavy chain, type B) (Nonmuscle myosin heavy chain-B) (NMMHC-B). [SWISSPROT:P35580]	1	973
MYO9B	ENST00000319396	ENSG00000099331 (MYO9B): ENSEMBL: Myosin IXb (Unconventional myosin-9b). [SWISSPROT:Q13459]	1	668
NAT5	ENST00000310450	ENSG00000173418 (NAT5): ENSEMBL: N-acetyltransferase 5 (EC 2.3.1.-). [SWISSPROT:Q9Y6D2]	1	423
NAT5	ENST00000334982	ENSG00000173418 (NAT5): ENSEMBL: N-acetyltransferase 5 (EC 2.3.1.-). [SWISSPROT:Q9Y6D2]	1	423
NCALD	ENST00000311028	ENSG00000104490 (NCALD): ENSEMBL: Neurocalcin delta. [SWISSPROT:P29554]	1	856
NCALD	ENST00000220931	ENSG00000104490 (NCALD): ENSEMBL: Neurocalcin delta. [SWISSPROT:P29554]	1	856
NCOA2	ENST00000267974	ENSG00000140396 (NCOA2): ENSEMBL: Nuclear receptor coactivator 2 (NCoA-2) (Transcriptional intermediary factor 2). [SWISSPROT:Q15596]	1	299
NEFH	ENST00000310624	ENSG00000100285 (NEFH): ENSEMBL: Neurofilament triplet H protein (200 kDa neurofilament protein) (Neurofilament heavy polypeptide) (NF-H). [SWISSPROT:P12036]	1	338
NEFH	ENST00000328842	ENSG00000100285 (NEFH): ENSEMBL: Neurofilament triplet H protein (200 kDa neurofilament protein) (Neurofilament heavy polypeptide) (NF-H). [SWISSPROT:P12036]	1	338
NFX1	ENST00000263220	ENSG00000086102 (NFX1): ENSEMBL: Transcriptional repressor NF-X1 (EC 6.3.2.-) (Nuclear transcription factor, X box-binding, 1). [SWISSPROT:Q12986]	1	125
NFX1	ENST00000360404	ENSG00000086102 (NFX1): ENSEMBL: Transcriptional repressor NF-X1 (EC 6.3.2.-) (Nuclear transcription factor, X box-binding, 1). [SWISSPROT:Q12986]	1	125
NPEPPS	ENST00000322157	ENSG00000141279 (NPEPPS): ENSEMBL: Puromycin-sensitive aminopeptidase (EC 3.4.11.-) (PSA). [SWISSPROT:P55786]	1	103
NPHP4	ENST00000253998	ENSG00000131697 (NPHP4): ENSEMBL: Nephrocystin 4 (Nephroretinin). [SWISSPROT:O75161]	1	1142
NR6A1	ENST00000344523	ENSG00000148200 (NR6A1): ENSEMBL: Orphan nuclear receptor NR6A1 (Germ cell nuclear factor) (GCNF) (Retinoid receptor-related testis specific receptor) (RTR). [SWISSPROT:Q15406]	1	181
NSMAF	ENST00000038176	ENSG00000035681 (NSMAF): ENSEMBL: Protein FAN (Factor associated with N-SMase activation) (Factor associated with neutral-sphingomyelinase activation). [SWISSPROT:Q92636]	1	62
OSBPL3	ENST00000352860	ENSG00000070882 (OSBPL3): ENSEMBL: Oxysterol binding protein-related protein 3 (OSBP-related protein 3) (ORP-3). [SWISSPROT:Q9H4L5]	1	242
OSBPL3	ENST00000353930	ENSG00000070882 (OSBPL3): ENSEMBL: Oxysterol binding protein-related protein 3 (OSBP-related protein 3) (ORP-3). [SWISSPROT:Q9H4L5]	1	242
OSBPL3	ENST00000313367	ENSG00000070882 (OSBPL3): ENSEMBL: Oxysterol binding protein-related protein 3 (OSBP-related protein 3) (ORP-3). [SWISSPROT:Q9H4L5]	1	242
OSBPL8	ENST00000261183	ENSG000000091039 (OSBPL8): ENSEMBL: Oxysterol binding protein-related protein 8 (OSBP-related protein 8) (ORP-8). [SWISSPROT:Q9BZF1]	1	3586
OSBPL8	ENST00000313439	ENSG000000091039 (OSBPL8): ENSEMBL: Oxysterol binding protein-related protein 8 (OSBP-related protein 8) (ORP-8). [SWISSPROT:Q9BZF1]	1	3586
PAPOLG	ENST00000238714	ENSG00000115421 (PAPOLG): ENSEMBL	1	491
PDE3A	ENST00000325802	ENSG00000172572 (PDE3A): ENSEMBL	1	928
PDE3A	ENST00000359062	ENSG00000172572 (PDE3A): ENSEMBL	1	928
PDGFRA	ENST00000257290	ENSG00000134853 (PDGFRA): ENSEMBL: Alpha platelet-derived growth factor receptor precursor (EC 2.7.1.112) (PDGF-R-alpha) (CD140a antigen). [SWISSPROT:P16234]	1	2734
PERQ1	ENST00000275732	ENSG00000146830 (PERQ1): ENSEMBL: PERQ amino acid rich with GYF domain protein 1. [SWISSPROT:O75420]	1	856
PKNOX2	ENST00000298282	ENSG00000165495 (PKNOX2): ENSEMBL: Homeobox protein PKNOX2 (PBX/knotted homeobox 2) (Homeobox protein PREP-2). [SWISSPROT:Q96KN3]	1	2010
PLA2G4A	ENST00000264143	ENSG00000116711 (PLA2G4A): ENSEMBL: Cytosolic phospholipase A2 (CPLA2) [Includes: Phospholipase A2 (EC 3.1.1.4) (Phosphatidylcholine 2-acylhydrolase); Lysophospholipase (EC 3.1.1.5)]. [SWISSPROT:P47712]	1	350
PLAG1	ENST00000316981	ENSG00000181690 (PLAG1): ENSEMBL: pleiomorphic adenoma gene 1; Pleomorphic adenoma gene 1. [RefSeq:NM_002655]	2	3476, 4370
PLEKHA3	ENST00000234453	ENSG00000116095 (PLEKHA3): ENSEMBL: pleckstrin homology domain containing, family A (phosphoinositide binding specific) member 3; pleckstrin homology domain-containing, family A (phosphoinositide binding specific) member 3. [RefSeq:NM_019091]	1	203
PLXNA4	ENST00000251675	ENSG00000189437 (PLXNA4): ENSEMBL	2	967, 1732
POU3F2	ENST00000328345	ENSG00000184486 (POU3F2): ENSEMBL: POU domain, class 3, transcription factor 2 (Nervous-system specific octamer-binding transcription factor N-Oct-3) (Brain-specific homeobox/POU domain protein 2) (Brain-2) (Brn-2 protein). [SWISSPROT:P20265]	1	1955
PPAP2B	ENST00000294390	ENSG00000162407 (PPAP2B): ENSEMBL: phosphatidic acid phosphatase type 2B; phosphatidic acid phosphohydrolase; vascular endothelial growth factor and type I collagen inducible; type-2 phosphatidic acid phosphatase-beta. [RefSeq:NM_003713]	1	67
PPP1R12B	ENST00000336894	ENSG00000077157 (PPP1R12B): ENSEMBL: Protein phosphatase 1 regulatory subunit 12B (Myosin phosphatase targeting subunit 2) (Myosin phosphatase target subunit 2). [SWISSPROT:O60237]	1	207
PPP1R12B	ENST00000361863	ENSG00000077157 (PPP1R12B): ENSEMBL: Protein phosphatase 1 regulatory subunit 12B (Myosin phosphatase targeting subunit 2) (Myosin phosphatase target subunit 2). [SWISSPROT:O60237]	1	207
PPP1R12B	ENST00000356764	ENSG00000077157 (PPP1R12B): ENSEMBL: Protein phosphatase 1 regulatory subunit 12B (Myosin phosphatase targeting subunit 2) (Myosin phosphatase target subunit 2). [SWISSPROT:O60237]	1	207

PPP1R12B	ENST00000290419	ENSG00000077157 (PPP1R12B): ENSEMBL: Protein phosphatase 1 regulatory subunit 12B (Myosin phosphatase targeting subunit 2) (Myosin phosphatase target subunit 2). [SWISSPROT:O60237]	1	207
PRDM1	ENST00000071246	ENSG00000057657 (PRDM1): ENSEMBL: PR-domain zinc finger protein 1 (Beta-interferon gene positive- regulatory domain 1 binding factor) (BLIMP-1) (Positive regulatory domain 1-binding factor 1) (PRDI-binding factor-1) (PRDI-BF1). [SWISSPROT:O75626]	1	2248
RAD21	ENST00000297338	ENSG00000164754 (RAD21): ENSEMBL: Double-strand-break repair protein rad21 homolog (hHR21) (Nuclear matrix protein 1) (NXP-1) (SCC1 homolog). [SWISSPROT:O60216]	1	1401
RIN2	ENST00000255006	ENSG00000132669 (RIN2): ENSEMBL: Ras and Rab interactor 2 (Ras interaction/interference protein 2) (Ras inhibitor JC265) (Ras association domain family 4). [SWISSPROT:Q8WYP3]	1	811
RNF110	ENST00000337952	ENSG00000056661 (RNF110): ENSEMBL: DNA-binding protein Mel-18 (RING finger protein 110) (Zinc finger protein 144). [SWISSPROT:P35227]	1	519
RNF110	ENST00000360797	ENSG00000056661 (RNF110): ENSEMBL: DNA-binding protein Mel-18 (RING finger protein 110) (Zinc finger protein 144). [SWISSPROT:P35227]	1	519
RPS6KA3	ENST00000321410	ENSG00000177189 (RPS6KA3): ENSEMBL: Ribosomal protein S6 kinase alpha 3 (EC 2.7.1.37) (S6K-alpha 3) (90 kDa ribosomal protein S6 kinase 3) (p90-RSK 3) (Ribosomal S6 kinase 2) (RSK-2) (pp90RSK2) (Insulin-stimulated protein kinase 1) (ISPK-1). [SWISSPROT:P51812]	1	619
SEMA4C	ENST00000305476	ENSG00000168758 (SEMA4C): ENSEMBL: sema domain, immunoglobulin domain (Ig), transmembrane domain TM; semaf; semac1. [RefSeq:NM_017789]	1	562
SEMA4G	ENST00000210633	ENSG00000095539 (SEMA4G): ENSEMBL: Semaphorin 4G precursor. [SWISSPROT:Q9NTN9]	1	1318
SEMA4G	ENST00000355853	ENSG00000095539 (SEMA4G): ENSEMBL: Semaphorin 4G precursor. [SWISSPROT:Q9NTN9]	1	1318
SEN1	ENST00000004980	ENSG00000079387 (SEN1): ENSEMBL: Sentrin-specific protease 1 (EC 3.4.22.-) (Sentrin/SUMO-specific protease SENP1). [SWISSPROT:Q9P0U3]	1	1553
SEN1	ENST00000339976	ENSG00000079387 (SEN1): ENSEMBL: Sentrin-specific protease 1 (EC 3.4.22.-) (Sentrin/SUMO-specific protease SENP1). [SWISSPROT:Q9P0U3]	1	1553
SEPT3	ENST00000328414	ENSG00000100167 (SEPT3): ENSEMBL: Neuronal-specific septin 3. [SWISSPROT:Q9UH03]	1	3106
SEPT3	ENST00000334525	ENSG00000100167 (SEPT3): ENSEMBL: Neuronal-specific septin 3. [SWISSPROT:Q9UH03]	1	1425
SEPT3	ENST00000291236	ENSG00000100167 (SEPT3): ENSEMBL: Neuronal-specific septin 3. [SWISSPROT:Q9UH03]	1	3106
SHOC2	ENST00000265277	ENSG00000108061 (SHOC2): ENSEMBL: Leucine-rich repeat protein SHOC-2 (Ras-binding protein Sur-8). [SWISSPROT:Q9UQ13]	1	959
SHOC2	ENST00000359438	ENSG00000108061 (SHOC2): ENSEMBL: Leucine-rich repeat protein SHOC-2 (Ras-binding protein Sur-8). [SWISSPROT:Q9UQ13]	1	959
SIAT7E	ENST00000318803	ENSG00000117069 (SIAT7E): ENSEMBL: Alpha-N-acetylgalactosaminide alpha-2,6-sialyltransferase V (GD1 alpha synthase) (GalNAc alpha-2,6-sialyltransferase V) (ST6GalNAc V) (Sialyltransferase 7E). [SWISSPROT:Q9BVH7]	1	189
SIRT1	ENST00000212015	ENSG00000096717 (SIRT1): ENSEMBL: NAD-dependent deacetylase sirtuin 1 (EC 3.5.1.-) (hSIRT1) (hSIR2) (SIR2-like protein 1). [SWISSPROT:Q96EB6]	1	45
SIX2	ENST00000303077	ENSG00000170577 (SIX2): ENSEMBL: Homeobox protein SIX2 (Sine oculis homeobox homolog 2). [SWISSPROT:Q9NPC8]	1	887
SLC19A2	ENST00000236137	ENSG00000117479 (SLC19A2): ENSEMBL: Thiamine transporter 1 (THTR-1) (ThTr1) (Thiamine carrier 1) (TC1). [SWISSPROT:O60779]	1	33
SLC19A2	ENST00000302778	ENSG00000117479 (SLC19A2): ENSEMBL: Thiamine transporter 1 (THTR-1) (ThTr1) (Thiamine carrier 1) (TC1). [SWISSPROT:O60779]	1	33
SLC24A3	ENST00000328041	ENSG00000185052 (SLC24A3): ENSEMBL: Sodium/potassium/calcium exchanger 3 precursor (Na <sup>+</sup> /K <sup>+</sup> /Ca <sup>2+</sup> - exchange protein 3). [SWISSPROT:Q9HC58]	1	1546
SLC35C2	ENST00000317734	ENSG000000080189 (SLC35C2): ENSEMBL: Solute carrier family 35 member C2 (Ovarian cancer overexpressed gene 1 protein) (CGI-15). [SWISSPROT:Q9NQQ7]	1	623
SLC35C2	ENST00000243896	ENSG000000080189 (SLC35C2): ENSEMBL: Solute carrier family 35 member C2 (Ovarian cancer overexpressed gene 1 protein) (CGI-15). [SWISSPROT:Q9NQQ7]	1	623
SLITRK1	ENST00000314878	ENSG00000178235 (SLITRK1): ENSEMBL: slit and trk like 1 protein; slit and trk like gene 1. [RefSeq:NM_052910]	1	449
SLK	ENST00000278065	ENSG00000065613 (SLK): ENSEMBL: serine/threonine kinase 2; Ste20-like kinase; Ste20-related serine/threonine kinase; CTCL tumor antigen se20-9. [RefSeq:NM_014720]	1	1685
SLK	ENST00000192055	ENSG00000065613 (SLK): ENSEMBL: serine/threonine kinase 2; Ste20-like kinase; Ste20-related serine/threonine kinase; CTCL tumor antigen se20-9. [RefSeq:NM_014720]	1	1685
SOX5	ENST00000309359	ENSG00000134532 (SOX5): ENSEMBL: Transcription factor SOX-5. [SWISSPROT:P35711]	1	363
SOX6	ENST00000316399	ENSG00000110693 (SOX6): ENSEMBL: Transcription factor SOX-6. [SWISSPROT:P35712]	1	389
SOX6	ENST00000340278	ENSG00000110693 (SOX6): ENSEMBL: Transcription factor SOX-6. [SWISSPROT:P35712]	1	389
SOX6	ENST00000336941	ENSG00000110693 (SOX6): ENSEMBL: Transcription factor SOX-6. [SWISSPROT:P35712]	1	389
SOX6	ENST00000352083	ENSG00000110693 (SOX6): ENSEMBL: Transcription factor SOX-6. [SWISSPROT:P35712]	1	389
SOX6	ENST00000357817	ENSG00000110693 (SOX6): ENSEMBL: Transcription factor SOX-6. [SWISSPROT:P35712]	1	389
SPRY4	ENST00000344120	ENSG00000187678 (SPRY4): ENSEMBL: Sprouty homolog 4 (Spry-4). [SWISSPROT:Q9C004]	1	2000
SPRY4	ENST00000359661	ENSG00000187678 (SPRY4): ENSEMBL: Sprouty homolog 4 (Spry-4). [SWISSPROT:Q9C004]	1	1994
SS18L1	ENST00000331758	ENSG00000184402 (SS18L1): ENSEMBL: SS18-like protein 1 (SYT homolog-1). [SWISSPROT:O75177]	1	2551
SS18L1	ENST00000216863	ENSG00000184402 (SS18L1): ENSEMBL: SS18-like protein 1 (SYT homolog-1). [SWISSPROT:O75177]	1	2551
STC1	ENST00000290271	ENSG00000159167 (STC1): ENSEMBL: Stanniocalcin 1 precursor (STC-1). [SWISSPROT:P52823]	1	462
SYNCRIP	ENST00000257768	ENSG00000135316 (SYNCRIP): ENSEMBL: synaptotagmin binding, cytoplasmic RNA interacting protein; NS1-associated protein 1. [RefSeq:NM_006372]	1	1203
TARDBP	ENST00000240185	ENSG00000120948 (TARDBP): ENSEMBL: TAR DNA-binding protein-43 (TDP-43). [SWISSPROT:Q13148]	1	1034
TBL1X	ENST00000217964	ENSG00000101849 (TBL1X): ENSEMBL: Transducin beta-like 1X protein (Transducin-beta-like 1, X-linked). [SWISSPROT:O60907]	1	30
TENS1	ENST00000311160	ENSG00000136205 (TENS1): ENSEMBL: tensin-like SH2 domain containing 1; tumor endothelial marker 6; thyroid specific PTB domain protein; tensin 3; tensin-like SH2 domain-containing 1; H_NH0549I23.2. [RefSeq:NM_022748]	1	2817
TENS1	ENST00000275514	ENSG00000136205 (TENS1): ENSEMBL: tensin-like SH2 domain containing 1; tumor endothelial marker 6; thyroid specific PTB domain protein; tensin 3; tensin-like SH2 domain-containing 1; H_NH0549I23.2. [RefSeq:NM_022748]	1	2817
TENS1	ENST00000355730	ENSG00000136205 (TENS1): ENSEMBL: tensin-like SH2 domain containing 1; tumor endothelial marker 6; thyroid specific PTB domain protein; tensin 3; tensin-like SH2 domain-containing 1; H_NH0549I23.2. [RefSeq:NM_022748]	1	2817
TGIF2	ENST00000237533	ENSG00000118707 (TGIF2): ENSEMBL	1	453
TMF1	ENST00000356248_P	ENSG00000144747 (TMF1): ENSEMBL: TATA element modulatory factor (TMF). [SWISSPROT:P82094]	1	884

TNFRSF11B	ENST00000297350	ENSG00000164761 (TNFRSF11B): ENSEMBL: Tumor necrosis factor receptor superfamily member 11B precursor (Osteoprotegerin) (Osteoclastogenesis inhibitory factor). [SWISSPROT:O00300]	1	724
TRIM3	ENST00000359518	ENSG00000110171 (TRIM3): ENSEMBL: Tripartite motif protein 3 (RING finger protein 22) (Brain-expressed RING finger protein). [SWISSPROT:O75382]	1	76
TRIM3	ENST00000345851	ENSG00000110171 (TRIM3): ENSEMBL: Tripartite motif protein 3 (RING finger protein 22) (Brain-expressed RING finger protein). [SWISSPROT:O75382]	1	76
TRIM3	ENST00000336043	ENSG00000110171 (TRIM3): ENSEMBL: Tripartite motif protein 3 (RING finger protein 22) (Brain-expressed RING finger protein). [SWISSPROT:O75382]	1	76
TSGA14	ENST00000343969	ENSG00000106477 (TSGA14): ENSEMBL: testis specific, 14; testis specific protein A14. [RefSeq:NM_018718]	1	2300
TSGA14	ENST00000223208	ENSG00000106477 (TSGA14): ENSEMBL: testis specific, 14; testis specific protein A14. [RefSeq:NM_018718]	1	2300
TTBK1	ENST00000259750	ENSG00000146216 (TTBK1): ENSEMBL	1	1986
TTN	ENST00000359218	ENSG00000155657 (TTN): ENSEMBL: titin isoform novex-3; connectin; CMH9, included; cardiomyopathy, dilated 1G (autosomal dominant). [RefSeq:NM_133379]	1	58568
TTN	ENST00000342175	ENSG00000155657 (TTN): ENSEMBL: titin isoform novex-3; connectin; CMH9, included; cardiomyopathy, dilated 1G (autosomal dominant). [RefSeq:NM_133379]	1	58568
TXNDC7	ENST00000272227	ENSG00000143870 (TXNDC7): ENSEMBL: Protein disulfide isomerase A6 precursor (EC 5.3.4.1) (Protein disulfide isomerase P5). [SWISSPROT:Q15084]	1	270
WASL	ENST00000223023	ENSG00000106299 (WASL): ENSEMBL: Neural Wiskott-Aldrich syndrome protein (N-WASP). [SWISSPROT:O00401]	1	457
WDR20	ENST00000299135	ENSG00000140153 (WDR20): ENSEMBL: WD-repeat protein 20 (DMR protein). [SWISSPROT:Q8TBZ3]	1	56
WDR20	ENST00000342702	ENSG00000140153 (WDR20): ENSEMBL: WD-repeat protein 20 (DMR protein). [SWISSPROT:Q8TBZ3]	1	56
WDR20	ENST00000355079	ENSG00000140153 (WDR20): ENSEMBL: WD-repeat protein 20 (DMR protein). [SWISSPROT:Q8TBZ3]	1	56
YWHAB	ENST00000217069	ENSG00000166913 (YWHAB): ENSEMBL: 14-3-3 protein beta/alpha (Protein kinase C inhibitor protein-1) (KCIP-1) (Protein 1054). [SWISSPROT:P31946]	1	1793
YWHAB	ENST00000353703	ENSG00000166913 (YWHAB): ENSEMBL: 14-3-3 protein beta/alpha (Protein kinase C inhibitor protein-1) (KCIP-1) (Protein 1054). [SWISSPROT:P31946]	1	1793
YWHAG	ENST00000307630	ENSG00000170027 (YWHAG): ENSEMBL: 14-3-3 protein gamma (Protein kinase C inhibitor protein-1) (KCIP-1). [SWISSPROT:P35214]	1	2702
ZDHHC3	ENST00000296127	ENSG00000163812 (ZDHHC3): ENSEMBL: Zinc finger DHHC domain containing protein 3 (Zinc finger protein 373) (DHHCI protein). [SWISSPROT:Q9NYG2]	1	54
ZDHHC3	ENST00000342790	ENSG00000163812 (ZDHHC3): ENSEMBL: Zinc finger DHHC domain containing protein 3 (Zinc finger protein 373) (DHHCI protein). [SWISSPROT:Q9NYG2]	1	54
ZFP36L1	ENST00000336440	ENSG00000185650 (ZFP36L1): ENSEMBL: Butyrate response factor 1 (TIS11B protein) (EGF-response factor 1) (ERF-1). [SWISSPROT:Q07352]	1	1709
ZIC1	ENST00000282928	ENSG00000152977 (ZIC1): ENSEMBL: Zinc finger protein ZIC 1 (Zinc finger protein of the cerebellum 1). [SWISSPROT:Q15915]	1	526
ZIC2	ENST00000245295	ENSG00000043355 (ZIC2): ENSEMBL: Zinc finger protein ZIC 2 (Zinc finger protein of the cerebellum 2). [SWISSPROT:O95409]	1	695
ZNF12	ENST00000356901	ENSG00000174652 (ZNF12): ENSEMBL: Zinc finger protein 266 (Zinc finger protein HZF1) (Fragment). [SWISSPROT:Q14584]	1	50
ZNF12	ENST00000361451	ENSG00000174652 (ZNF12): ENSEMBL: Zinc finger protein 266 (Zinc finger protein HZF1) (Fragment). [SWISSPROT:Q14584]	1	50
ZNF12	ENST00000355921	ENSG00000174652 (ZNF12): ENSEMBL: Zinc finger protein 266 (Zinc finger protein HZF1) (Fragment). [SWISSPROT:Q14584]	1	50
ZNF12	ENST00000361151	ENSG00000174652 (ZNF12): ENSEMBL: Zinc finger protein 266 (Zinc finger protein HZF1) (Fragment). [SWISSPROT:Q14584]	1	50
ZNF364	ENST00000262881	ENSG00000121848 (ZNF364): ENSEMBL: Zinc finger protein 364 (Fragment). [SWISSPROT:Q9Y4L5]	1	104
ZSWIM1	ENST00000305256	ENSG00000168612 (ZSWIM1): ENSEMBL: Zinc finger SWIM domain containing protein 1. [SWISSPROT:Q9BR11]	1	589

**Supplementary Table 2b: miR-181b targets - TargetCombo (Union) - Diana-microT, PicTar, TargetScanS, miRanda**

Program	Gene Symbol	Description
PicTar	SEP3	Neuronal-specific septin-3. [Source:Uniprot/SWISSPROT;Acc:Q9UHH03]
TargetScanS	SEP3	Neuronal-specific septin-3. [Source:Uniprot/SWISSPROT;Acc:Q9UHH03]
miRanda	SEP3	Neuronal-specific septin-3. [Source:Uniprot/SWISSPROT;Acc:Q9UHH03]
PicTar	ABI3BP	Target of Nesh-SH3 precursor (Tarsh) (Nesh-binding protein) (NeshBP) (ABI gene family member 3-binding protein). [Source:Uniprot/SWISSPROT;Acc:Q7Z7G0]
TargetScanS	ABI3BP	Target of Nesh-SH3 precursor (Tarsh) (Nesh-binding protein) (NeshBP) (ABI gene family member 3-binding protein). [Source:Uniprot/SWISSPROT;Acc:Q7Z7G0]
TargetScanS	ABTB2	Ankyrin repeat and BTB/POZ domain-containing protein 2. [Source:Uniprot/SWISSPROT;Acc:Q8N961]
TargetScanS	ACCN2	
PicTar	ACSL1	Long-chain-fatty-acid-CoA ligase 1 (EC 6.2.1.3) (Long-chain acyl-CoA synthetase 1) (LACS 1) (Palmitoyl-CoA ligase 1) (Long-chain fatty acid CoA ligase 2) (Long-chain acyl-CoA synthetase 2) (LACS 2) (Acyl-CoA synthetase 1) (ACS1) (Palmitoyl-CoA ligase 2). [Source:Uniprot/SWISSPROT;Acc:P33121]
TargetScanS	ACSL1	Long-chain-fatty-acid-CoA ligase 1 (EC 6.2.1.3) (Long-chain acyl-CoA synthetase 1) (LACS 1) (Palmitoyl-CoA ligase 1) (Long-chain fatty acid CoA ligase 2) (Long-chain acyl-CoA synthetase 2) (LACS 2) (Acyl-CoA synthetase 1) (ACS1) (Palmitoyl-CoA ligase 2). [Source:Uniprot/SWISSPROT;Acc:P33121]
PicTar	ACTL6A	Actin-like protein 6A (53 kDa BRG1-associated factor A) (Actin-related protein Baf53a) (ArpNbeta). [Source:Uniprot/SWISSPROT;Acc:Q96019]
PicTar	ACTL6A	Actin-like protein 6A (53 kDa BRG1-associated factor A) (Actin-related protein Baf53a) (ArpNbeta). [Source:Uniprot/SWISSPROT;Acc:Q96019]
PicTar	ACTL6A	Actin-like protein 6A (53 kDa BRG1-associated factor A) (Actin-related protein Baf53a) (ArpNbeta). [Source:Uniprot/SWISSPROT;Acc:Q96019]
TargetScanS	ACVR2	
PicTar	ACVR2A	Activin receptor type 2A precursor (EC 2.7.1.37) (Activin receptor type IIA) (ACTR-IIA) (ACTRIIA). [Source:Uniprot/SWISSPROT;Acc:P27037]
miRanda	ACVR2A	Activin receptor type 2A precursor (EC 2.7.1.37) (Activin receptor type IIA) (ACTR-IIA) (ACTRIIA). [Source:Uniprot/SWISSPROT;Acc:P27037]
TargetScanS	AD-020	
PicTar	ADAM11	ADAM 11 precursor (A disintegrin and metalloproteinase domain 11) (Metalloproteinase-like, disintegrin-like, and cysteine-rich protein) (MDC). [Source:Uniprot/SWISSPROT;Acc:O75078]
TargetScanS	ADAM11	ADAM 11 precursor (A disintegrin and metalloproteinase domain 11) (Metalloproteinase-like, disintegrin-like, and cysteine-rich protein) (MDC). [Source:Uniprot/SWISSPROT;Acc:O75078]
PicTar	ADAMTS1	ADAMTS-1 precursor (EC 3.4.24.-) (A disintegrin and metalloproteinase with thrombospondin motifs 1) (ADAM-TS 1) (ADAM-TS1) (METH-1). [Source:Uniprot/SWISSPROT;Acc:Q9UHH8]
TargetScanS	ADAMTS1	ADAMTS-1 precursor (EC 3.4.24.-) (A disintegrin and metalloproteinase with thrombospondin motifs 1) (ADAM-TS 1) (ADAM-TS1) (METH-1). [Source:Uniprot/SWISSPROT;Acc:Q9UHH8]
PicTar	ADAMTS18	ADAMTS-18 precursor (EC 3.4.24.-) (A disintegrin and metalloproteinase with thrombospondin motifs 18) (ADAM-TS 18) (ADAM-TS18). [Source:Uniprot/SWISSPROT;Acc:Q8TE60]
TargetScanS	ADAMTS18	ADAMTS-18 precursor (EC 3.4.24.-) (A disintegrin and metalloproteinase with thrombospondin motifs 18) (ADAM-TS 18) (ADAM-TS18). [Source:Uniprot/SWISSPROT;Acc:Q8TE60]
TargetScanS	ADAMTS5	ADAMTS-5 precursor (EC 3.4.24.-) (A disintegrin and metalloproteinase with thrombospondin motifs 5) (ADAM-TS 5) (ADAM-TS5) (Aggrecanase-2) (ADMP-2) (ADAM-TS 11). [Source:Uniprot/SWISSPROT;Acc:Q9UNAO]
PicTar	ADARB1	Double-stranded RNA-specific editase 1 (EC 3.5.-.-) (dsRNA adenosine deaminase) (RNA-editing deaminase 1) (RNA-editing enzyme 1). [Source:Uniprot/SWISSPROT;Acc:P78563]
PicTar	ADARB1	Double-stranded RNA-specific editase 1 (EC 3.5.-.-) (dsRNA adenosine deaminase) (RNA-editing deaminase 1) (RNA-editing enzyme 1). [Source:Uniprot/SWISSPROT;Acc:P78563]
TargetScanS	ADARB1	Double-stranded RNA-specific editase 1 (EC 3.5.-.-) (dsRNA adenosine deaminase) (RNA-editing deaminase 1) (RNA-editing enzyme 1). [Source:Uniprot/SWISSPROT;Acc:P78563]
PicTar	ADCY1	Adenylate cyclase type I (EC 4.6.1.1) (ATP pyrophosphate-lyase 1) (Ca(2+)/calmodulin-activated adenyllyl cyclase). [Source:Uniprot/SWISSPROT;Acc:Q08828]
TargetScanS	ADCY1	Adenylate cyclase type I (EC 4.6.1.1) (ATP pyrophosphate-lyase 1) (Ca(2+)/calmodulin-activated adenyllyl cyclase). [Source:Uniprot/SWISSPROT;Acc:Q08828]
PicTar	ADCY9	Adenylate cyclase type IX (EC 4.6.1.1) (ATP pyrophosphate-lyase 9) (Adenyllyl cyclase 9). [Source:Uniprot/SWISSPROT;Acc:O60503]
TargetScanS	ADCY9	Adenylate cyclase type IX (EC 4.6.1.1) (ATP pyrophosphate-lyase 9) (Adenyllyl cyclase 9). [Source:Uniprot/SWISSPROT;Acc:O60503]
PicTar	ADM	ADM precursor [Contains: Adrenomedullin (AM); Proadrenomedullin N-20 terminal peptide (ProAM-N20) (ProAM N-terminal 20 peptide) (PAMP)]. [Source:Uniprot/SWISSPROT;Acc:P35318]
TargetScanS	ADM	ADM precursor [Contains: Adrenomedullin (AM); Proadrenomedullin N-20 terminal peptide (ProAM-N20) (ProAM N-terminal 20 peptide) (PAMP)]. [Source:Uniprot/SWISSPROT;Acc:P35318]
miRanda	ADM	ADM precursor [Contains: Adrenomedullin (AM); Proadrenomedullin N-20 terminal peptide (ProAM-N20) (ProAM N-terminal 20 peptide) (PAMP)]. [Source:Uniprot/SWISSPROT;Acc:P35318]
TargetScanS	ADRBK1	Beta-adrenergic receptor kinase 1 (EC 2.7.1.126) (Beta-ARK-1) (G- protein coupled receptor kinase 2). [Source:Uniprot/SWISSPROT;Acc:P25098]
miRanda	AFF4	ALL1 fused gene from 5q31 [Source:RefSeq_peptide;Acc:NP_055238]
TargetScanS	AFIIPHILIN	
PicTar	AGPAT1	1-acyl-sn-glycerol-3-phosphate acyltransferase alpha (EC 2.3.1.51) (1- AGP acyltransferase 1) (1-AGPAT 1) (Lysophosphatidic acid acyltransferase-alpha) (LPAAT-alpha) (1-acylglycerol-3-phosphate O- acyltransferase 1) (G15 protein). [Source:Uniprot/SWISSPROT;Acc:Q99943]
PicTar	AGPAT1	1-acyl-sn-glycerol-3-phosphate acyltransferase alpha (EC 2.3.1.51) (1- AGP acyltransferase 1) (1-AGPAT 1) (Lysophosphatidic acid acyltransferase-alpha) (LPAAT-alpha) (1-acylglycerol-3-phosphate O- acyltransferase 1) (G15 protein). [Source:Uniprot/SWISSPROT;Acc:Q99943]
TargetScanS	AGPAT1	1-acyl-sn-glycerol-3-phosphate acyltransferase alpha (EC 2.3.1.51) (1- AGP acyltransferase 1) (1-AGPAT 1) (Lysophosphatidic acid acyltransferase-alpha) (LPAAT-alpha) (1-acylglycerol-3-phosphate O- acyltransferase 1) (G15 protein). [Source:Uniprot/SWISSPROT;Acc:Q99943]
TargetScanS	AKAP6	A-kinase anchor protein 6 (Protein kinase A-anchoring protein 6) (PRKA6) (A-kinase anchor protein 100 kDa) (AKAP 100) (mAKAP). [Source:Uniprot/SWISSPROT;Acc:Q13023]
PicTar	AKAP7	A-kinase anchor protein 7 isoform gamma (Protein kinase A-anchoring protein 7 isoform gamma) (A-kinase-anchoring protein 18). [Source:Uniprot/SWISSPROT;Acc:Q9P0M2]
TargetScanS	AKT3	RAC-gamma serine/threonine-protein kinase (EC 2.7.1.37) (RAC-PK-gamma) (Protein kinase Akt-3) (Protein kinase B, gamma) (PKB gamma) (STK-2). [Source:Uniprot/SWISSPROT;Acc:Q9Y243]
PicTar	ALS2	Alsln (Amyotrophic lateral sclerosis protein 2). [Source:Uniprot/SWISSPROT;Acc:Q96Q42]
TargetScanS	ALS2CR3	
PicTar	ANGPT2	Angiopoietin-2 precursor (ANG-2). [Source:Uniprot/SWISSPROT;Acc:O15123]
TargetScanS	ANKFY1	Ankyrin repeat and FYVE domain protein 1 (Ankyrin repeats hooked to a zinc finger motif). [Source:Uniprot/SWISSPROT;Acc:Q9P2R3]
PicTar	ANKRD13C	ankyrin repeat domain 13C [Source:RefSeq_peptide;Acc:NP_110443]
miRanda	ANKRD13C	ankyrin repeat domain 13C [Source:RefSeq_peptide;Acc:NP_110443]
PicTar	ANKRD15	Ankyrin repeat domain-containing protein 15 (Kidney ankyrin repeat- containing protein). [Source:Uniprot/SWISSPROT;Acc:Q14678]
TargetScanS	ANKRD15	Ankyrin repeat domain-containing protein 15 (Kidney ankyrin repeat- containing protein). [Source:Uniprot/SWISSPROT;Acc:Q14678]
PicTar	ANKRD43	ankyrin repeat domain 43 [Source:RefSeq_peptide;Acc:NP_787069]
TargetScanS	APIG1	AP-1 complex subunit gamma-1 (Adapter-related protein complex 1 gamma- 1 subunit) (Gamma-adaptin) (Adaptor protein complex AP-1 gamma-1 subunit) (Golgi adaptor HA1/AP1 adaptin subunit gamma-1) (Clathrin assembly protein complex 1 gamma-1 large chain). [Source:Uniprot/SWISSPROT;Acc:O43747]
miRanda	APBB1	Amyloid beta A4 precursor protein-binding family B member 1 (Fe65 protein). [Source:Uniprot/SWISSPROT;Acc:O00213]
miRanda	APC	Adenomatous polyposis coli protein (Protein APC). [Source:Uniprot/SWISSPROT;Acc:P25054]
TargetScanS	APG5L	
PicTar	API5	Apoptosis inhibitor 5 (API-5) (Fibroblast growth factor 2-interacting factor) (FIF) (XAGL protein) (AAC-11).

		[Source:Uniprot/SWISSPROT;Acc:Q9BZZ5]
TargetScanS	APLP2	Amyloid-like protein 2 precursor (Amyloid protein homolog) (APPH) (CDEI box-binding protein) (CDEBP). [Source:Uniprot/SWISSPROT;Acc:Q06481]
TargetScanS	ARF3	ADP-ribosylation factor 3. [Source:Uniprot/SWISSPROT;Acc:P61204]
miRanda	ARF4	ADP-ribosylation factor 4. [Source:Uniprot/SWISSPROT;Acc:P18085]
PicTar	ARFGEF2	Brefeldin A-inhibited guanine nucleotide-exchange protein 2 (Brefeldin A-inhibited GEP 2). [Source:Uniprot/SWISSPROT;Acc:Q9Y6D5]
TargetScanS	ARFGEF2	Brefeldin A-inhibited guanine nucleotide-exchange protein 2 (Brefeldin A-inhibited GEP 2). [Source:Uniprot/SWISSPROT;Acc:Q9Y6D5]
TargetScanS	ARHGEF7	Rho guanine nucleotide exchange factor 7 (PAK-interacting exchange factor beta) (Beta-Pix) (COOL-1) (p85). [Source:Uniprot/SWISSPROT;Acc:Q14155]
PicTar	ARID3B	AT rich interactive domain 3B (BRIGHT- like) protein [Source:RefSeq_peptide;Acc:NP_006456]
miRanda	ARID5B	AT-rich interactive domain-containing protein 5B (ARID domain- containing protein 5B) (Mrf1-like) (Modulator recognition factor 2) (MRF-2). [Source:Uniprot/SWISSPROT;Acc:Q14865]
TargetScanS	ARIH2	Protein ariadne-2 homolog (ARI-2) (Triad1 protein). [Source:Uniprot/SWISSPROT;Acc:Q95376]
TargetScanS	ARL3	ADP-ribosylation factor-like protein 3. [Source:Uniprot/SWISSPROT;Acc:P36405]
TargetScanS	ARL5	
PicTar	ARL5A	ADP-ribosylation factor-like protein 5A. [Source:Uniprot/SWISSPROT;Acc:Q9Y689]
PicTar	ARL5A	ADP-ribosylation factor-like protein 5A. [Source:Uniprot/SWISSPROT;Acc:Q9Y689]
PicTar	ARNT2	Aryl hydrocarbon receptor nuclear translocator 2 (ARNT protein 2). [Source:Uniprot/SWISSPROT;Acc:Q9HBZ2]
TargetScanS	ARNT2	Aryl hydrocarbon receptor nuclear translocator 2 (ARNT protein 2). [Source:Uniprot/SWISSPROT;Acc:Q9HBZ2]
TargetScanS	ARRDC3	arrestin domain containing 3 [Source:RefSeq_peptide;Acc:NP_065852]
TargetScanS	ARSJ	
TargetScanS	ATF7	Cyclic AMP-dependent transcription factor ATF-7 (Activating transcription factor 7) (Transcription factor ATF-A). [Source:Uniprot/SWISSPROT;Acc:P17544]
PicTar	ATG5	Autophagy protein 5 (APG5-like) (Apoptosis-specific protein). [Source:Uniprot/SWISSPROT;Acc:Q9H1Y0]
PicTar	ATP11C	Probable phospholipid-transporting ATPase 1G (EC 3.6.3.1) (ATPase class I type 11C) (ATPase 1G) (ATPase 1Q) (ATPase class VI type 11C). [Source:Uniprot/SWISSPROT;Acc:Q8NB49]
TargetScanS	ATP11C	Probable phospholipid-transporting ATPase 1G (EC 3.6.3.1) (ATPase class I type 11C) (ATPase 1G) (ATPase 1Q) (ATPase class VI type 11C). [Source:Uniprot/SWISSPROT;Acc:Q8NB49]
PicTar	ATP1B1	Sodium/potassium-transporting ATPase beta-1 chain (Sodium/potassium- dependent ATPase beta-1 subunit). [Source:Uniprot/SWISSPROT;Acc:P05026]
PicTar	ATP1B1	Sodium/potassium-transporting ATPase beta-1 chain (Sodium/potassium- dependent ATPase beta-1 subunit). [Source:Uniprot/SWISSPROT;Acc:P05026]
TargetScanS	ATP1B1	Sodium/potassium-transporting ATPase beta-1 chain (Sodium/potassium- dependent ATPase beta-1 subunit). [Source:Uniprot/SWISSPROT;Acc:P05026]
miRanda	ATP1B1	Sodium/potassium-transporting ATPase beta-1 chain (Sodium/potassium- dependent ATPase beta-1 subunit). [Source:Uniprot/SWISSPROT;Acc:P05026]
PicTar	ATP2A2	Sarcoplasmic/endoplasmic reticulum calcium ATPase 2 (EC 3.6.3.8) (Calcium pump 2) (SERCA2) (SR Ca(2+)-ATPase 2) (Calcium-transporting ATPase sarcoplasmic reticulum type, slow twitch skeletal muscle isoform) (Endoplasmic reticulum class 1/2 Ca(2+) ATPase). [Source:Uniprot/SWISSPROT;Acc:P16615]
TargetScanS	ATP2A2	Sarcoplasmic/endoplasmic reticulum calcium ATPase 2 (EC 3.6.3.8) (Calcium pump 2) (SERCA2) (SR Ca(2+)-ATPase 2) (Calcium-transporting ATPase sarcoplasmic reticulum type, slow twitch skeletal muscle isoform) (Endoplasmic reticulum class 1/2 Ca(2+) ATPase). [Source:Uniprot/SWISSPROT;Acc:P16615]
TargetScanS	ATP2B1	Plasma membrane calcium-transporting ATPase 1 (EC 3.6.3.8) (PMCA1) (Plasma membrane calcium pump isoform 1) (Plasma membrane calcium ATPase isoform 1). [Source:Uniprot/SWISSPROT;Acc:P20020]
PicTar	ATP2B2	Plasma membrane calcium-transporting ATPase 2 (EC 3.6.3.8) (PMCA2) (Plasma membrane calcium pump isoform 2) (Plasma membrane calcium ATPase isoform 2). [Source:Uniprot/SWISSPROT;Acc:Q01814]
TargetScanS	ATP2B2	Plasma membrane calcium-transporting ATPase 2 (EC 3.6.3.8) (PMCA2) (Plasma membrane calcium pump isoform 2) (Plasma membrane calcium ATPase isoform 2). [Source:Uniprot/SWISSPROT;Acc:Q01814]
miRanda	ATP6V0D1	Vacuolar ATP synthase subunit d (EC 3.6.3.14) (V-ATPase d subunit) (Vacuolar proton pump d subunit) (V-ATPase AC39 subunit) (V-ATPase 40 kDa accessory protein) (P39) (32 kDa accessory protein). [Source:Uniprot/SWISSPROT;Acc:P61421]
TargetScanS	ATP8B2	Probable phospholipid-transporting ATPase 1D (EC 3.6.3.1) (ATPase class I type 8B member 2). [Source:Uniprot/SWISSPROT;Acc:P98198]
PicTar	ATRN	Attractin precursor (Mahogany homolog) (DPPT-L). [Source:Uniprot/SWISSPROT;Acc:Q75882]
PicTar	ATXN1	Ataxin-1 (Spinocerebellar ataxia type 1 protein). [Source:Uniprot/SWISSPROT;Acc:P54253]
TargetScanS	ATXN1	Ataxin-1 (Spinocerebellar ataxia type 1 protein). [Source:Uniprot/SWISSPROT;Acc:P54253]
PicTar	B4GALT1	Beta-1,4-galactosyltransferase 1 (EC 2.4.1.-) (Beta-1,4-GalTase 1) (Beta4Gal-T1) (b4Gal-T1) (UDP-galactose:beta-N-acetylglucosamine beta-1,4-galactosyltransferase 1) (UDP-Gal:beta-GlcNAc beta-1,4- galactosyltransferase 1) [Includes: Lactose synthase A pr [Source:Uniprot/SWISSPROT;Acc:P15291]
TargetScanS	B4GALT1	Beta-1,4-galactosyltransferase 1 (EC 2.4.1.-) (Beta-1,4-GalTase 1) (Beta4Gal-T1) (b4Gal-T1) (UDP-galactose:beta-N-acetylglucosamine beta-1,4-galactosyltransferase 1) (UDP-Gal:beta-GlcNAc beta-1,4- galactosyltransferase 1) [Includes: Lactose synthase A pr [Source:Uniprot/SWISSPROT;Acc:P15291]
PicTar	BACH2	Transcription regulator protein BACH2 (BTB and CNC homolog 2). [Source:Uniprot/SWISSPROT;Acc:Q9BYV9]
TargetScanS	BACH2	Transcription regulator protein BACH2 (BTB and CNC homolog 2). [Source:Uniprot/SWISSPROT;Acc:Q9BYV9]
miRanda	BACH2	Transcription regulator protein BACH2 (BTB and CNC homolog 2). [Source:Uniprot/SWISSPROT;Acc:Q9BYV9]
PicTar	BAI3	Brain-specific angiogenesis inhibitor 3 precursor. [Source:Uniprot/SWISSPROT;Acc:Q60242]
TargetScanS	BAI3	Brain-specific angiogenesis inhibitor 3 precursor. [Source:Uniprot/SWISSPROT;Acc:Q60242]
TargetScanS	BAIAP2	Brain-specific angiogenesis inhibitor 1-associated protein 2 (BAI1- associated protein 2) (BAI2 protein) (Insulin receptor substrate p53) (IRSp53) (Insulin receptor substrate protein of 53 kDa) (Insulin receptor substrate p53/p5 [Source:Uniprot/SWISSPROT;Acc:Q9UQB8]
PicTar	BAZZA	Bromodomain adjacent to zinc finger domain 2A (Transcription termination factor I-interacting protein 5) (TTF-I-interacting protein 5) (Tip5) (hWALp3). [Source:Uniprot/SWISSPROT;Acc:Q9UIF9]
TargetScanS	BAZZA	Bromodomain adjacent to zinc finger domain 2A (Transcription termination factor I-interacting protein 5) (TTF-I-interacting protein 5) (Tip5) (hWALp3). [Source:Uniprot/SWISSPROT;Acc:Q9UIF9]
PicTar	BAZZB	Bromodomain adjacent to zinc finger domain 2B (hWALp4). [Source:Uniprot/SWISSPROT;Acc:Q9UIF8]
TargetScanS	BAZZB	Bromodomain adjacent to zinc finger domain 2B (hWALp4). [Source:Uniprot/SWISSPROT;Acc:Q9UIF8]
DIANA-microT	BCL11B	B-cell lymphoma/leukemia 11B (B-cell CLL/lymphoma 11B) (Radiation- induced tumor suppressor gene 1 protein) (hRit1) (COUP-TF- interacting protein 2). [Source:Uniprot/SWISSPROT;Acc:Q9C0K0]
TargetScanS	BCL2	Apoptosis regulator Bcl-2. [Source:Uniprot/SWISSPROT;Acc:P10415]
PicTar	BCL2L11	Bcl-2-like protein 11 (Bcl2-interacting mediator of cell death). [Source:Uniprot/SWISSPROT;Acc:Q43521]
PicTar	BCL2L11	Bcl-2-like protein 11 (Bcl2-interacting mediator of cell death). [Source:Uniprot/SWISSPROT;Acc:Q43521]
PicTar	BCL2L11	Bcl-2-like protein 11 (Bcl2-interacting mediator of cell death). [Source:Uniprot/SWISSPROT;Acc:Q43521]
TargetScanS	BCL2L11	Bcl-2-like protein 11 (Bcl2-interacting mediator of cell death). [Source:Uniprot/SWISSPROT;Acc:Q43521]
TargetScanS	BCL6	B-cell lymphoma 6 protein (BCL-6) (Zinc finger protein 51) (LAZ-3 protein) (BCL-5) (Zinc finger and BTB domain-containing protein 27). [Source:Uniprot/SWISSPROT;Acc:P41182]
PicTar	BCL7A	B-cell CLL/lymphoma 7A isoform a [Source:RefSeq_peptide;Acc:NP_066273]
TargetScanS	BCL9	B-cell lymphoma 9 protein (Bcl-9) (Legless homolog). [Source:Uniprot/SWISSPROT;Acc:Q00512]
PicTar	BCLAF1	Bcl-2-associated transcription factor 1 (Btf). [Source:Uniprot/SWISSPROT;Acc:Q9N9F8]
TargetScanS	BCLAF1	Bcl-2-associated transcription factor 1 (Btf). [Source:Uniprot/SWISSPROT;Acc:Q9N9F8]
PicTar	BHLHB2	Class B basic helix-loop-helix protein 2 (bHLHB2) (Differentially expressed in chondrocytes protein 1) (DEC1) (Enhancer-of-split and hairy-related protein 2) (SHARP-2) (Stimulated with retinoic acid 13). [Source:Uniprot/SWISSPROT;Acc:Q14503]
TargetScanS	BHLHB2	Class B basic helix-loop-helix protein 2 (bHLHB2) (Differentially expressed in chondrocytes protein 1) (DEC1) (Enhancer-of-split and hairy-related protein 2) (SHARP-2) (Stimulated with retinoic acid 13). [Source:Uniprot/SWISSPROT;Acc:Q14503]
miRanda	BHLHB2	Class B basic helix-loop-helix protein 2 (bHLHB2) (Differentially expressed in chondrocytes protein 1) (DEC1) (Enhancer-of-split and hairy-related protein 2) (SHARP-2) (Stimulated with retinoic acid 13). [Source:Uniprot/SWISSPROT;Acc:Q14503]
miRanda	BHLHB3	Class B basic helix-loop-helix protein 3 (bHLHB3) (Differentially expressed in chondrocytes protein 2) (hDEC2) (Enhancer-of-split and hairy-related protein 1) (SHARP-1). [Source:Uniprot/SWISSPROT;Acc:Q9C0J9]
miRanda	BHLHB5	basic helix-loop-helix domain containing, class B, 5 [Source:RefSeq_peptide;Acc:NP_689627]
PicTar	BICD2	Cytoskeleton-like bicaudal D protein homolog 2. [Source:Uniprot/SWISSPROT;Acc:Q8TD16]

miRanda	BIRC6	Baculoviral IAP repeat-containing protein 6 (Ubiquitin-conjugating BIR-domain enzyme apollon). [Source:Uniprot/SWISSPROT;Acc:Q9NR09]
TargetScanS	BMPER	BMP-binding endothelial regulator protein precursor (Bone morphogenetic protein-binding endothelial cell precursor-derived regulator) (Crossveinless-2 protein) (hCV2). [Source:Uniprot/SWISSPROT;Acc:Q8N8U9]
TargetScanS	BMPR2	Bone morphogenetic protein receptor type II precursor (EC 2.7.1.37) (BMP type II receptor) (BMPR-II). [Source:Uniprot/SWISSPROT;Acc:Q13873]
TargetScanS	BNC2	Zinc finger protein basonuclin-2. [Source:Uniprot/SWISSPROT;Acc:Q6ZN30]
PicTar	BRD1	Bromodomain-containing protein 1 (BR140-like protein). [Source:Uniprot/SWISSPROT;Acc:Q95696]
TargetScanS	BRD1	Bromodomain-containing protein 1 (BR140-like protein). [Source:Uniprot/SWISSPROT;Acc:Q95696]
PicTar	BTBD3	BTB/POZ domain-containing protein 3. [Source:Uniprot/SWISSPROT;Acc:Q9Y2F9]
TargetScanS	BTBD3	BTB/POZ domain-containing protein 3. [Source:Uniprot/SWISSPROT;Acc:Q9Y2F9]
miRanda	BTBD3	BTB/POZ domain-containing protein 3. [Source:Uniprot/SWISSPROT;Acc:Q9Y2F9]
TargetScanS	C10orf22	
TargetScanS	C10orf6	
TargetScanS	C10orf78	
TargetScanS	C11orf30	
TargetScanS	C13orf10	
TargetScanS	C13orf25	
TargetScanS	C14orf4	
TargetScanS	C17orf39	
TargetScanS	C1orf16	
TargetScanS	C4orf16	
TargetScanS	C5orf5	
TargetScanS	C6orf62	
TargetScanS	C9orf54	
DIANA-microT	CAB39	Calcium-binding protein 39 (Protein Mo25). [Source:Uniprot/SWISSPROT;Acc:Q9Y376]
PicTar	CAB39	Calcium-binding protein 39 (Protein Mo25). [Source:Uniprot/SWISSPROT;Acc:Q9Y376]
TargetScanS	CACNA2D2	calcium channel, voltage-dependent, alpha 2/delta subunit 2 isoform b [Source:RefSeq_peptide;Acc:NP_006021]
PicTar	CACNB2	Voltage-dependent L-type calcium channel beta-2 subunit (CAB2) (Calcium channel, voltage-dependent, beta 2 subunit) (Lambert-Eaton myasthenic syndrome antigen B) (MYSB). [Source:Uniprot/SWISSPROT;Acc:Q08289]
PicTar	CACNB2	Voltage-dependent L-type calcium channel beta-2 subunit (CAB2) (Calcium channel, voltage-dependent, beta 2 subunit) (Lambert-Eaton myasthenic syndrome antigen B) (MYSB). [Source:Uniprot/SWISSPROT;Acc:Q08289]
TargetScanS	CACNB2	Voltage-dependent L-type calcium channel beta-2 subunit (CAB2) (Calcium channel, voltage-dependent, beta 2 subunit) (Lambert-Eaton myasthenic syndrome antigen B) (MYSB). [Source:Uniprot/SWISSPROT;Acc:Q08289]
PicTar	CAMK2G	Calcium/calmodulin-dependent protein kinase type II gamma chain (EC 2.7.1.123) (CaM-kinase II gamma chain) (CaM kinase II gamma subunit) (CaMK-II gamma subunit). [Source:Uniprot/SWISSPROT;Acc:Q13555]
PicTar	CAMK2G	Calcium/calmodulin-dependent protein kinase type II gamma chain (EC 2.7.1.123) (CaM-kinase II gamma chain) (CaM kinase II gamma subunit) (CaMK-II gamma subunit). [Source:Uniprot/SWISSPROT;Acc:Q13555]
TargetScanS	CAMK2G	Calcium/calmodulin-dependent protein kinase type II gamma chain (EC 2.7.1.123) (CaM-kinase II gamma chain) (CaM kinase II gamma subunit) (CaMK-II gamma subunit). [Source:Uniprot/SWISSPROT;Acc:Q13555]
miRanda	CAMK2G	Calcium/calmodulin-dependent protein kinase type II gamma chain (EC 2.7.1.123) (CaM-kinase II gamma chain) (CaM kinase II gamma subunit) (CaMK-II gamma subunit). [Source:Uniprot/SWISSPROT;Acc:Q13555]
PicTar	CAMSAP1	calmodulin regulated spectrin-associated protein 1 [Source:RefSeq_peptide;Acc:NP_056262]
TargetScanS	CAMSAP1	calmodulin regulated spectrin-associated protein 1 [Source:RefSeq_peptide;Acc:NP_056262]
miRanda	CAMSAP1L1	calmodulin regulated spectrin-associated protein 1-like 1 [Source:RefSeq_peptide;Acc:NP_982284]
TargetScanS	CAMTA2	calmodulin binding transcription activator 2 [Source:RefSeq_peptide;Acc:NP_055914]
DIANA-microT	CARD11	Caspase recruitment domain-containing protein 11 (CARD-containing MAGUK protein 3) (Carma 1). [Source:Uniprot/SWISSPROT;Acc:Q9BXL7]
PicTar	CARD11	Caspase recruitment domain-containing protein 11 (CARD-containing MAGUK protein 3) (Carma 1). [Source:Uniprot/SWISSPROT;Acc:Q9BXL7]
TargetScanS	CARD11	Caspase recruitment domain-containing protein 11 (CARD-containing MAGUK protein 3) (Carma 1). [Source:Uniprot/SWISSPROT;Acc:Q9BXL7]
TargetScanS	CARF	
TargetScanS	CARM1	Histone-arginine methyltransferase CARM1 (EC 2.1.1.125) (EC 2.1.1.-) (Protein arginine N-methyltransferase 4) (Coactivator-associated arginine methyltransferase 1). [Source:Uniprot/SWISSPROT;Acc:Q86X55]
PicTar	CBFA2T2	Protein CBFA2T2 (MTG8-like protein) (MTG8-related protein 1) (Myeloid translocation-related protein 1) (ETO homologous on chromosome 20) (p85). [Source:Uniprot/SWISSPROT;Acc:O43439]
TargetScanS	CBFA2T2	Protein CBFA2T2 (MTG8-like protein) (MTG8-related protein 1) (Myeloid translocation-related protein 1) (ETO homologous on chromosome 20) (p85). [Source:Uniprot/SWISSPROT;Acc:O43439]
PicTar	CBFA2T3	myeloid translocation gene-related protein 2 isoform MTG16b [Source:RefSeq_peptide;Acc:NP_787127]
TargetScanS	CBFA2T3	myeloid translocation gene-related protein 2 isoform MTG16b [Source:RefSeq_peptide;Acc:NP_787127]
PicTar	CBLB	CBL-B E3 ubiquitin protein ligase (EC 6.3.2.-) (Signal transduction protein CBL-B) (SH3-binding protein CBL-B) (Casitas B-lineage lymphoma proto-oncogene b) (RING finger protein 56). [Source:Uniprot/SWISSPROT;Acc:Q13191]
TargetScanS	CBLB	CBL-B E3 ubiquitin protein ligase (EC 6.3.2.-) (Signal transduction protein CBL-B) (SH3-binding protein CBL-B) (Casitas B-lineage lymphoma proto-oncogene b) (RING finger protein 56). [Source:Uniprot/SWISSPROT;Acc:Q13191]
TargetScanS	CBX4	Chromobox protein homolog 4 (Polycomb 2 homolog) (Pc2) (hPc2). [Source:Uniprot/SWISSPROT;Acc:O00257]
PicTar	CBX7	Chromobox protein homolog 7. [Source:Uniprot/SWISSPROT;Acc:O95931]
TargetScanS	CBX7	Chromobox protein homolog 7. [Source:Uniprot/SWISSPROT;Acc:O95931]
TargetScanS	CCAR1	cell-cycle and apoptosis regulatory protein 1 [Source:RefSeq_peptide;Acc:NP_060707]
TargetScanS	CDC6	Coiled-coil domain-containing protein 6 (H4 protein) (Papillary thyroid carcinoma-encoded protein). [Source:Uniprot/SWISSPROT;Acc:Q16204]
PicTar	CCNJ	cyclin J [Source:RefSeq_peptide;Acc:NP_061957]
TargetScanS	CCNJ	cyclin J [Source:RefSeq_peptide;Acc:NP_061957]
miRanda	CCNJ	cyclin J [Source:RefSeq_peptide;Acc:NP_061957]
TargetScanS	CCNK	Cyclin-K. [Source:Uniprot/SWISSPROT;Acc:O75909]
PicTar	CD163	CD163 antigen isoform a [Source:RefSeq_peptide;Acc:NP_004235]
PicTar	CD163	CD163 antigen isoform a [Source:RefSeq_peptide;Acc:NP_004235]
TargetScanS	CD163	CD163 antigen isoform a [Source:RefSeq_peptide;Acc:NP_004235]
miRanda	CD24	Signal transducer CD24 precursor. [Source:Uniprot/SWISSPROT;Acc:P25063]
TargetScanS	CD2AP	CD2-associated protein (Cas ligand with multiple SH3 domains) (Adapter protein CMS). [Source:Uniprot/SWISSPROT;Acc:Q9Y5K6]
PicTar	CD4	T-cell surface glycoprotein CD4 precursor (T-cell surface antigen T4/Leu-3). [Source:Uniprot/SWISSPROT;Acc:P01730]
TargetScanS	CD4	T-cell surface glycoprotein CD4 precursor (T-cell surface antigen T4/Leu-3). [Source:Uniprot/SWISSPROT;Acc:P01730]
TargetScanS	CD69	Early activation antigen CD69 (Early T-cell activation antigen p60) (GP32/28) (Leu-23) (MLR-3) (EA1) (BL-AC/P26) (Activation inducer molecule) (AIM). [Source:Uniprot/SWISSPROT;Acc:Q07108]
TargetScanS	CDC42BPA	Serine/threonine-protein kinase MRCK alpha (EC 2.7.1.37) (CDC42- binding protein kinase alpha) (Myotonic dystrophy kinase-related CDC42-binding kinase alpha) (Myotonic dystrophy protein kinase-like alpha) (MRCK alpha) (DMPK-like alpha). [Source:Uniprot/SWISSPROT;Acc:Q5V725]
PicTar	CDC73	Parafibromin (Cell division cycle protein 73 homolog) (Hyperparathyroidism 2 protein). [Source:Uniprot/SWISSPROT;Acc:Q6P1J9]
miRanda	CDH11	Cadherin-11 precursor (Osteoblast-cadherin) (OB-cadherin) (OSF-4). [Source:Uniprot/SWISSPROT;Acc:P55287]
PicTar	CDH13	Cadherin-13 precursor (Truncated-cadherin) (T-cadherin) (T-cad) (Heart-cadherin) (H-cadherin) (P105). [Source:Uniprot/SWISSPROT;Acc:P55290]
TargetScanS	CDH13	Cadherin-13 precursor (Truncated-cadherin) (T-cadherin) (T-cad) (Heart-cadherin) (H-cadherin) (P105). [Source:Uniprot/SWISSPROT;Acc:P55290]
miRanda	CDH2	Neural-cadherin precursor (N-cadherin) (Cadherin-2) (CDw325 antigen). [Source:Uniprot/SWISSPROT;Acc:P19022]
miRanda	CDH8	Cadherin-8 precursor. [Source:Uniprot/SWISSPROT;Acc:P55286]
TargetScanS	CDON	surface glycoprotein, Ig superfamily member [Source:RefSeq_peptide;Acc:NP_058648]
TargetScanS	CDX2	Homeobox protein CDX-2 (Caudal-type homeobox protein 2) (CDX-3). [Source:Uniprot/SWISSPROT;Acc:Q99626]
PicTar	CDYL	Chromodomain Y-like protein (CDY-like). [Source:Uniprot/SWISSPROT;Acc:Q9Y232]

PicTar	CDYL	Chromodomain Y-like protein (CDY-like). [Source:Uniprot/SWISSPROT;Acc:Q9Y232]
PicTar	CDYL	Chromodomain Y-like protein (CDY-like). [Source:Uniprot/SWISSPROT;Acc:Q9Y232]
TargetScanS	CDYL	Chromodomain Y-like protein (CDY-like). [Source:Uniprot/SWISSPROT;Acc:Q9Y232]
TargetScanS	CELSR3	SH3 adapter protein SPIN90 (NCK-interacting protein with SH3 domain) (SH3 protein interacting with Nck, 90 kDa) (VacA-interacting protein, 54 kDa) (VIP54) (AF3p21) (Diaphanous protein-interacting protein) (Dia-interacting protein 1) (DIP-1). [Source:Uniprot/SWISSPROT;Acc:Q9NZQ3]
TargetScanS	CENTB2	Centaurin-beta 2 (Cnt-b2). [Source:Uniprot/SWISSPROT;Acc:Q15057]
TargetScanS	CGBBP1	
PicTar	CHD7	Chromodomain-helicase-DNA-binding protein 7 (EC 3.6.1.-) (ATP- dependent helicase CHD7) (CHD-7) (Fragment). [Source:Uniprot/SWISSPROT;Acc:Q9P2D1]
TargetScanS	CHD7	Chromodomain-helicase-DNA-binding protein 7 (EC 3.6.1.-) (ATP- dependent helicase CHD7) (CHD-7) (Fragment). [Source:Uniprot/SWISSPROT;Acc:Q9P2D1]
miRanda	CHD7	Chromodomain-helicase-DNA-binding protein 7 (EC 3.6.1.-) (ATP- dependent helicase CHD7) (CHD-7) (Fragment). [Source:Uniprot/SWISSPROT;Acc:Q9P2D1]
PicTar	CHD9	chromodomain helicase DNA binding protein 9 [Source:RefSeq_peptide;Acc:NP_079410]
TargetScanS	CHD9	chromodomain helicase DNA binding protein 9 [Source:RefSeq_peptide;Acc:NP_079410]
PicTar	CHN2	Beta-chimaerin (Beta-chimerin) (Rho-GTPase-activating protein 3). [Source:Uniprot/SWISSPROT;Acc:P52757]
TargetScanS	CHPPR	
TargetScanS	CIT	Citron Rho-interacting kinase (EC 2.7.1.37) (CRIK) (Rho-interacting, serine/threonine-protein kinase 21). [Source:Uniprot/SWISSPROT;Acc:O14578]
miRanda	CKS1B	Cyclin-dependent kinases regulatory subunit 1 (CKS-1). [Source:Uniprot/SWISSPROT;Acc:P61024]
PicTar	CLASP1	CLIP-associating protein 1 (Cytoplasmic linker-associated protein 1) (Multiple asters homolog 1). [Source:Uniprot/SWISSPROT;Acc:Q7Z460]
TargetScanS	CLASP1	CLIP-associating protein 1 (Cytoplasmic linker-associated protein 1) (Multiple asters homolog 1). [Source:Uniprot/SWISSPROT;Acc:Q7Z460]
PicTar	CLOCK	Circadian locomotor output cycles kaput protein (hCLOCK). [Source:Uniprot/SWISSPROT;Acc:O15516]
miRanda	CLTC	Clathrin heavy chain 1 (CLH-17). [Source:Uniprot/SWISSPROT;Acc:Q00610]
PicTar	CNR1	Cannabinoid receptor 1 (CB1) (CB-R) (CANN6). [Source:Uniprot/SWISSPROT;Acc:P21554]
TargetScanS	CNR1	Cannabinoid receptor 1 (CB1) (CB-R) (CANN6). [Source:Uniprot/SWISSPROT;Acc:P21554]
PicTar	CNTN4	Contactin-4 precursor (Brain-derived immunoglobulin superfamily protein 2) (BIG-2). [Source:Uniprot/SWISSPROT;Acc:Q81WV2]
TargetScanS	CNTN4	Contactin-4 precursor (Brain-derived immunoglobulin superfamily protein 2) (BIG-2). [Source:Uniprot/SWISSPROT;Acc:Q81WV2]
TargetScanS	CNTNAP2	Contactin-associated protein-like 2 precursor (Cell recognition molecule Caspr2). [Source:Uniprot/SWISSPROT;Acc:Q9UHC6]
TargetScanS	CNTNAP3	Contactin-associated protein-like 3 precursor (Cell recognition molecule Caspr3). [Source:Uniprot/SWISSPROT;Acc:Q9BZ76]
miRanda	COL2A1	Collagen alpha-1(I) chain precursor [Contains: Chondrocalcin]. [Source:Uniprot/SWISSPROT;Acc:P02458]
PicTar	CPD	Carboxypeptidase D precursor (EC 3.4.17.22) (Metallo-carboxypeptidase D) (gp180). [Source:Uniprot/SWISSPROT;Acc:O75976]
TargetScanS	CPD	Carboxypeptidase D precursor (EC 3.4.17.22) (Metallo-carboxypeptidase D) (gp180). [Source:Uniprot/SWISSPROT;Acc:O75976]
miRanda	CPD	Carboxypeptidase D precursor (EC 3.4.17.22) (Metallo-carboxypeptidase D) (gp180). [Source:Uniprot/SWISSPROT;Acc:O75976]
PicTar	CPEB4	cytoplasmic polyadenylation element binding protein 4 [Source:RefSeq_peptide;Acc:NP_085130]
TargetScanS	CPEB4	cytoplasmic polyadenylation element binding protein 4 [Source:RefSeq_peptide;Acc:NP_085130]
TargetScanS	CPNE2	Copine-2 (Copine II). [Source:Uniprot/SWISSPROT;Acc:Q96FN4]
PicTar	CREB1	cAMP response element-binding protein (CREB). [Source:Uniprot/SWISSPROT;Acc:P16220]
TargetScanS	CREB1	cAMP response element-binding protein (CREB). [Source:Uniprot/SWISSPROT;Acc:P16220]
PicTar	CREBBP	CREB-binding protein (EC 2.3.1.48). [Source:Uniprot/SWISSPROT;Acc:Q92793]
PicTar	CRIM1	Cysteine-rich motor neuron 1 protein precursor (CRIM-1) (Cysteine-rich repeat-containing protein 552). [Source:Uniprot/SWISSPROT;Acc:Q9NZV1]
TargetScanS	CRIM1	Cysteine-rich motor neuron 1 protein precursor (CRIM-1) (Cysteine-rich repeat-containing protein 552). [Source:Uniprot/SWISSPROT;Acc:Q9NZV1]
miRanda	CRSP7	CRSP complex subunit 7 (Cofactor required for Sp1 transcriptional activation subunit 7) (Transcriptional coactivator CRSP70) (Activator-recruited cofactor 70 kDa component) (ARC70). [Source:Uniprot/SWISSPROT;Acc:O95402]
PicTar	CSDA	DNA-binding protein A (Cold shock domain-containing protein A) (Single-strand DNA-binding protein NF-GMB). [Source:Uniprot/SWISSPROT;Acc:P16989]
miRanda	CSNK1G1	Casein kinase I isoform gamma-1 (EC 2.7.1.-) (CKI-gamma 1). [Source:Uniprot/SWISSPROT;Acc:Q9HCF0]
TargetScanS	CSNK2A2	Casein kinase II subunit alpha' (CK II) (EC 2.7.1.37). [Source:Uniprot/SWISSPROT;Acc:P19784]
TargetScanS	CSTF3	Cleavage stimulation factor, 77 kDa subunit (CSTF 77 kDa subunit) (CF- 1 77 kDa subunit) (Cstf-77). [Source:Uniprot/SWISSPROT;Acc:Q12996]
DIANA-microT	CTCF	Transcriptional repressor CTCF (CCCTC-binding factor) (CTCFL paralog) (11-zinc finger protein). [Source:Uniprot/SWISSPROT;Acc:P49711]
PicTar	CTCF	Transcriptional repressor CTCF (CCCTC-binding factor) (CTCFL paralog) (11-zinc finger protein). [Source:Uniprot/SWISSPROT;Acc:P49711]
TargetScanS	CTDSPL	CTD small phosphatase-like protein (CTDSP-like) (Small C-terminal domain phosphatase 3) (Small CTD phosphatase 3) (SCFP3) (Nuclear LIM interactor-interacting factor 1) (NLI-interacting factor 1) (NIF-like protein) (RBSFP3) (YA22 protein) (HYA22). [Source:Uniprot/SWISSPROT;Acc:O15194]
miRanda	CTDSPL	CTD small phosphatase-like protein (CTDSP-like) (Small C-terminal domain phosphatase 3) (Small CTD phosphatase 3) (SCFP3) (Nuclear LIM interactor-interacting factor 1) (NLI-interacting factor 1) (NIF-like protein) (RBSFP3) (YA22 protein) (HYA22). [Source:Uniprot/SWISSPROT;Acc:O15194]
TargetScanS	CTNND1	Catenin delta-1 (p120 catenin) (p120(ctn)) (Cadherin-associated Src substrate) (CAS) (p120(cas)). [Source:Uniprot/SWISSPROT;Acc:O60716]
TargetScanS	CTTNBP2	cortactin binding protein 2 [Source:RefSeq_peptide;Acc:NP_219499]
PicTar	CTTNBP2NL	CTTNBP2 N-terminal-like protein. [Source:Uniprot/SWISSPROT;Acc:Q9P2B4]
PicTar	CUL3	Cullin-3 (CUL-3). [Source:Uniprot/SWISSPROT;Acc:Q13618]
TargetScanS	CUL3	Cullin-3 (CUL-3). [Source:Uniprot/SWISSPROT;Acc:Q13618]
TargetScanS	CXXC5	CXXC finger 5 [Source:RefSeq_peptide;Acc:NP_057547]
miRanda	CYCS	Cytochrome c. [Source:Uniprot/SWISSPROT;Acc:P99999]
PicTar	CYR61	Protein CYR61 precursor (Cysteine-rich, angiogenic inducer, 61) (Insulin-like growth factor-binding protein 10) (IGF1 protein). [Source:Uniprot/SWISSPROT;Acc:O00622]
PicTar	DAZAP2	DAZ-associated protein 2 (Deleted in azoospermia-associated protein 2). [Source:Uniprot/SWISSPROT;Acc:Q15038]
TargetScanS	DAZAP2	DAZ-associated protein 2 (Deleted in azoospermia-associated protein 2). [Source:Uniprot/SWISSPROT;Acc:Q15038]
TargetScanS	DCBLD2	Discoidin, CUB and LCCL domain-containing protein 2 precursor (Endothelial and smooth muscle cell-derived neuropilin-like protein) (CUB, LCCL and coagulation factor V/VIII-homology domains protein 1). [Source:Uniprot/SWISSPROT;Acc:Q96PD2]
PicTar	DCUN1D1	DCN1-like protein 1 (Defective in cullin neddylation protein 1-like protein 1) (DCUN1 domain-containing protein 1) (Squamous cell carcinoma-related oncogene). [Source:Uniprot/SWISSPROT;Acc:Q96GG9]
miRanda	DDIT4	RTP801 [Source:RefSeq_peptide;Acc:NP_061931]
TargetScanS	DDX3X	ATP-dependent RNA helicase DDX3X (EC 3.6.1.-) (DEAD box protein 3, X- chromosomal) (Helicase-like protein 2) (HLP2) (DEAD box, X isoform). [Source:Uniprot/SWISSPROT;Acc:O00571]
TargetScanS	DDX3Y	ATP-dependent RNA helicase DDX3Y (EC 3.6.1.-) (DEAD box protein 3, Y- chromosomal). [Source:Uniprot/SWISSPROT;Acc:O15523]
TargetScanS	DEK	Protein DEK. [Source:Uniprot/SWISSPROT;Acc:P35659]
PicTar	DERL1	Derlin-1 (Degradation in endoplasmic reticulum protein 1) (Der1-like protein 1) (DERtrin-1). [Source:Uniprot/SWISSPROT;Acc:Q9BUN8]
TargetScanS	DERL1	Derlin-1 (Degradation in endoplasmic reticulum protein 1) (Der1-like protein 1) (DERtrin-1). [Source:Uniprot/SWISSPROT;Acc:Q9BUN8]
miRanda	DHX15	Putative pre-mRNA-splicing factor ATP-dependent RNA helicase DHX15 (EC 3.6.1.-) (DEAH box protein 15) (ATP-dependent RNA helicase #46). [Source:Uniprot/SWISSPROT;Acc:O43143]
PicTar	DHX57	DEAH (Asp-Glu-Ala-Asp/His) box polypeptide 57 [Source:RefSeq_peptide;Acc:NP_945314]
TargetScanS	DHX57	DEAH (Asp-Glu-Ala-Asp/His) box polypeptide 57 [Source:RefSeq_peptide;Acc:NP_945314]
TargetScanS	DKFZP434C212	
TargetScanS	DKFZp434H2226	
TargetScanS	DKFZp547A023	
TargetScanS	DKFZp547G0215	
TargetScanS	DKFZP566D1346	
TargetScanS	DKFZP566M1046	
TargetScanS	DKFZp761C169	
TargetScanS	DLG2	Discs large homolog 2 (Postsynaptic density protein PSD-93) (Channel- associated protein of synapse-110) (Chapsyn-110). [Source:Uniprot/SWISSPROT;Acc:Q15700]



TargetScanS	DLGAP2	Disks large-associated protein 2 (DAP-2) (SAP90/PSD-95-associated protein 2) (SAPAP2) (PSD-95/SAP90-binding protein 2) (Fragment). [Source:Uniprot/SWISSPROT;Acc:Q9P1A6]
PicTar	DLX1	Homeobox protein DLX-1. [Source:Uniprot/SWISSPROT;Acc:P56177]
TargetScanS	DNAJA3	DnaJ homolog subfamily A member 3, mitochondrial precursor (Tumorous imaginal discs protein Tid56 homolog) (DnaJ protein Tid-1) (hTid-1). [Source:Uniprot/SWISSPROT;Acc:Q96EY1]
PicTar	DNAJB5	DnaJ homolog subfamily B member 5 (Heat shock protein Hsp40-3) (Heat shock protein cognate 40) (Hsc40) (Hsp40-2). [Source:Uniprot/SWISSPROT;Acc:O75953]
TargetScanS	DNAJC13	DnaJ homolog subfamily C member 13 (Required for receptor-mediated endocytosis 8). [Source:Uniprot/SWISSPROT;Acc:O75165]
TargetScanS	DNCL12	
TargetScanS	DOCK10	Dedicator of cytokinesis protein 10 (Protein zizimin 3). [Source:Uniprot/SWISSPROT;Acc:Q96BY6]
TargetScanS	DOCK7	Dedicator of cytokinesis protein 7. [Source:Uniprot/SWISSPROT;Acc:Q96N67]
PicTar	DPP10	Inactive dipeptidyl peptidase 10 (Dipeptidyl peptidase X) (Dipeptidyl peptidase-like protein 2) (DPL2) (Dipeptidyl peptidase IV-related protein 3) (DPRP-3). [Source:Uniprot/SWISSPROT;Acc:Q8N608]
PicTar	DPP10	Inactive dipeptidyl peptidase 10 (Dipeptidyl peptidase X) (Dipeptidyl peptidase-like protein 2) (DPL2) (Dipeptidyl peptidase IV-related protein 3) (DPRP-3). [Source:Uniprot/SWISSPROT;Acc:Q8N608]
TargetScanS	DPP10	Inactive dipeptidyl peptidase 10 (Dipeptidyl peptidase X) (Dipeptidyl peptidase-like protein 2) (DPL2) (Dipeptidyl peptidase IV-related protein 3) (DPRP-3). [Source:Uniprot/SWISSPROT;Acc:Q8N608]
miRanda	DPP10	Inactive dipeptidyl peptidase 10 (Dipeptidyl peptidase X) (Dipeptidyl peptidase-like protein 2) (DPL2) (Dipeptidyl peptidase IV-related protein 3) (DPRP-3). [Source:Uniprot/SWISSPROT;Acc:Q8N608]
PicTar	DPYSL2	Dihydropyrimidinase-related protein 2 (DRP-2) (Collapsin response mediator protein 2) (CRMP-2) (N2A3). [Source:Uniprot/SWISSPROT;Acc:Q16555]
TargetScanS	DPYSL2	Dihydropyrimidinase-related protein 2 (DRP-2) (Collapsin response mediator protein 2) (CRMP-2) (N2A3). [Source:Uniprot/SWISSPROT;Acc:Q16555]
PicTar	DUSP5	Dual specificity protein phosphatase 5 (EC 3.1.3.48) (EC 3.1.3.16) (Dual specificity protein phosphatase hVH3). [Source:Uniprot/SWISSPROT;Acc:Q16690]
TargetScanS	DUSP5	Dual specificity protein phosphatase 5 (EC 3.1.3.48) (EC 3.1.3.16) (Dual specificity protein phosphatase hVH3). [Source:Uniprot/SWISSPROT;Acc:Q16690]
TargetScanS	DUSP6	Dual specificity protein phosphatase 6 (EC 3.1.3.48) (EC 3.1.3.16) (Mitogen-activated protein kinase phosphatase 3) (MAP kinase phosphatase 3) (MKP-3) (Dual specificity protein phosphatase PYST1). [Source:Uniprot/SWISSPROT;Acc:Q16828]
miRanda	DYNCIII	Cytoplasmic dynein 1 intermediate chain 1 (Dynein intermediate chain 1, cytosolic) (DH1C-1) (Cytoplasmic dynein intermediate chain 1). [Source:Uniprot/SWISSPROT;Acc:O14576]
PicTar	DYNC1L12	Cytoplasmic dynein 1 light intermediate chain 2 (Dynein light intermediate chain 2, cytosolic) (LIC53/55) (LIC-2). [Source:Uniprot/SWISSPROT;Acc:O43237]
PicTar	E2F5	Transcription factor E2F5 (E2F-5). [Source:Uniprot/SWISSPROT;Acc:Q15329]
TargetScanS	E2F5	Transcription factor E2F5 (E2F-5). [Source:Uniprot/SWISSPROT;Acc:Q15329]
miRanda	E2F5	Transcription factor E2F5 (E2F-5). [Source:Uniprot/SWISSPROT;Acc:Q15329]
TargetScanS	E2F7	E2F transcription factor 7 [Source:RefSeq_peptide;Acc:NP_976328]
TargetScanS	EDG1	Sphingosine 1-phosphate receptor Edg-1 (Sphingosine 1-phosphate receptor 1) (S1P1). [Source:Uniprot/SWISSPROT;Acc:P21453]
miRanda	EDG1	Sphingosine 1-phosphate receptor Edg-1 (Sphingosine 1-phosphate receptor 1) (S1P1). [Source:Uniprot/SWISSPROT;Acc:P21453]
PicTar	EED	embryonic ectoderm development isoform a [Source:RefSeq_peptide;Acc:NP_003788]
TargetScanS	EED	embryonic ectoderm development isoform a [Source:RefSeq_peptide;Acc:NP_003788]
PicTar	EEF1A1	Elongation factor 1-alpha 1 (EF-1-alpha-1) (Elongation factor 1 A-1) (eEF1A-1) (Elongation factor Tu) (EF-Tu). [Source:Uniprot/SWISSPROT;Acc:P68104]
TargetScanS	EGR1	Early growth response protein 1 (EGR-1) (Krox-24 protein) (Transcription factor Zif268) (Nerve growth factor-induced protein A) (NGFI-A) (Transcription factor ETR103) (Zinc finger protein 225) (AT225). [Source:Uniprot/SWISSPROT;Acc:P18146]
miRanda	EGR1	Early growth response protein 1 (EGR-1) (Krox-24 protein) (Transcription factor Zif268) (Nerve growth factor-induced protein A) (NGFI-A) (Transcription factor ETR103) (Zinc finger protein 225) (AT225). [Source:Uniprot/SWISSPROT;Acc:P18146]
PicTar	EGR3	Early growth response protein 3 (EGR-3) (Zinc finger protein pilot). [Source:Uniprot/SWISSPROT;Acc:Q06889]
TargetScanS	EGR3	Early growth response protein 3 (EGR-3) (Zinc finger protein pilot). [Source:Uniprot/SWISSPROT;Acc:Q06889]
PicTar	EIF4A2	Eukaryotic initiation factor 4A-II (EC 3.6.1.-) (ATP-dependent RNA helicase eIF4A-2) (eIF4A-II) (eIF-4A-II). [Source:Uniprot/SWISSPROT;Acc:Q14240]
TargetScanS	EIF4A2	Eukaryotic initiation factor 4A-II (EC 3.6.1.-) (ATP-dependent RNA helicase eIF4A-2) (eIF4A-II) (eIF-4A-II). [Source:Uniprot/SWISSPROT;Acc:Q14240]
TargetScanS	Ells1	
TargetScanS	ELOVL2	Elongation of very long chain fatty acids protein 2. [Source:Uniprot/SWISSPROT;Acc:Q9NXB9]
PicTar	EN1	Homeobox protein engrailed-1 (Hu-En-1). [Source:Uniprot/SWISSPROT;Acc:Q05925]
TargetScanS	EN1	Homeobox protein engrailed-1 (Hu-En-1). [Source:Uniprot/SWISSPROT;Acc:Q05925]
PicTar	EN2	Homeobox protein engrailed-2 (Hu-En-2). [Source:Uniprot/SWISSPROT;Acc:P19622]
TargetScanS	EN2	Homeobox protein engrailed-2 (Hu-En-2). [Source:Uniprot/SWISSPROT;Acc:P19622]
TargetScanS	ENAH	Enabled protein homolog. [Source:Uniprot/SWISSPROT;Acc:Q8N857]
miRanda	EP300	E1A-associated protein p300 (EC 2.3.1.48). [Source:Uniprot/SWISSPROT;Acc:Q09472]
TargetScanS	EPB49	Dematin (Erythrocyte membrane protein band 4.9). [Source:Uniprot/SWISSPROT;Acc:Q08495]
miRanda	EPC1	Enhancer of polycomb homolog 1. [Source:Uniprot/SWISSPROT;Acc:Q9H2F5]
PicTar	EPC2	enhancer of polycomb homolog 2 [Source:RefSeq_peptide;Acc:NP_056445]
TargetScanS	EPC2	enhancer of polycomb homolog 2 [Source:RefSeq_peptide;Acc:NP_056445]
miRanda	EPC2	enhancer of polycomb homolog 2 [Source:RefSeq_peptide;Acc:NP_056445]
PicTar	EPHA4	Ephrin type-A receptor 4 precursor (EC 2.7.1.112) (Tyrosine-protein kinase receptor SEK) (Receptor protein-tyrosine kinase HEK8). [Source:Uniprot/SWISSPROT;Acc:P54764]
TargetScanS	EPHA4	Ephrin type-A receptor 4 precursor (EC 2.7.1.112) (Tyrosine-protein kinase receptor SEK) (Receptor protein-tyrosine kinase HEK8). [Source:Uniprot/SWISSPROT;Acc:P54764]
TargetScanS	EPHA7	Ephrin type-A receptor 7 precursor (EC 2.7.1.112) (Tyrosine-protein kinase receptor EHK-3) (EPH homology kinase 3) (Receptor protein-tyrosine kinase HEK11). [Source:Uniprot/SWISSPROT;Acc:Q15375]
TargetScanS	EPS15	Epidermal growth factor receptor substrate 15 (Protein Eps15) (AF-1p protein). [Source:Uniprot/SWISSPROT;Acc:P42566]
PicTar	EPS8	Epidermal growth factor receptor kinase substrate 8. [Source:Uniprot/SWISSPROT;Acc:Q12929]
TargetScanS	ERF	ETS domain-containing transcription factor ERF (Ets2 repressor factor). [Source:Uniprot/SWISSPROT;Acc:P50548]
TargetScanS	ERG	Transcriptional regulator ERG (Transforming protein ERG). [Source:Uniprot/SWISSPROT;Acc:P11308]
PicTar	ESM1	Endothelial cell-specific molecule 1 precursor (ESM-1 secretory protein) (ESM-1). [Source:Uniprot/SWISSPROT;Acc:Q9NQ30]
TargetScanS	ESM1	Endothelial cell-specific molecule 1 precursor (ESM-1 secretory protein) (ESM-1). [Source:Uniprot/SWISSPROT;Acc:Q9NQ30]
PicTar	ESR1	Estrogen receptor (ER) (Estradiol receptor) (ER-alpha). [Source:Uniprot/SWISSPROT;Acc:P03372]
TargetScanS	ESR1	Estrogen receptor (ER) (Estradiol receptor) (ER-alpha). [Source:Uniprot/SWISSPROT;Acc:P03372]
PicTar	ETF1	Eukaryotic peptide chain release factor subunit 1 (eRF1) (Eukaryotic release factor 1) (TB3-1) (C11 protein). [Source:Uniprot/SWISSPROT;Acc:P62495]
TargetScanS	ETF1	Eukaryotic peptide chain release factor subunit 1 (eRF1) (Eukaryotic release factor 1) (TB3-1) (C11 protein). [Source:Uniprot/SWISSPROT;Acc:P62495]
PicTar	ETS1	C-ets-1 protein (p54). [Source:Uniprot/SWISSPROT;Acc:P14921]
TargetScanS	ETS1	C-ets-1 protein (p54). [Source:Uniprot/SWISSPROT;Acc:P14921]
PicTar	ETV6	Transcription factor ETV6 (ETS-related protein Tel1) (Tel) (ETS translocation variant 6). [Source:Uniprot/SWISSPROT;Acc:P41212]
TargetScanS	ETV6	Transcription factor ETV6 (ETS-related protein Tel1) (Tel) (ETS translocation variant 6). [Source:Uniprot/SWISSPROT;Acc:P41212]
PicTar	EYA1	Eyes absent homolog 1 (EC 3.1.3.48). [Source:Uniprot/SWISSPROT;Acc:Q99502]
PicTar	EYA1	Eyes absent homolog 1 (EC 3.1.3.48). [Source:Uniprot/SWISSPROT;Acc:Q99502]
TargetScanS	EYA3	Eyes absent homolog 3 (EC 3.1.3.48). [Source:Uniprot/SWISSPROT;Acc:Q99504]
PicTar	EYA4	Eyes absent homolog 4 (EC 3.1.3.48). [Source:Uniprot/SWISSPROT;Acc:Q95677]
TargetScanS	FALZ	Fetal Alzheimer antigen (Fetal Alz-50-reactive clone 1). [Source:Uniprot/SWISSPROT;Acc:Q12830]
TargetScanS	FAM19A2	Protein FAM19A2 precursor (Chemokine-like protein TFA-2). [Source:Uniprot/SWISSPROT;Acc:Q8N3H0]
TargetScanS	FAM3C	Protein FAM3C precursor (Protein GS3786). [Source:Uniprot/SWISSPROT;Acc:Q92520]
miRanda	FAM46B	

PicTar	FAM73B	
PicTar	FBN2	Fibrillin-2 precursor. [Source:Uniprot/SWISSPROT;Acc:P35556]
PicTar	FBXO11	F-box only protein 11 (Vitiligo-associated protein VIT-1). [Source:Uniprot/SWISSPROT;Acc:Q86XK2]
TargetScanS	FBXO11	F-box only protein 11 (Vitiligo-associated protein VIT-1). [Source:Uniprot/SWISSPROT;Acc:Q86XK2]
PicTar	FBXO33	F-box only protein 33. [Source:Uniprot/SWISSPROT;Acc:Q7Z6M2]
TargetScanS	FBXO33	F-box only protein 33. [Source:Uniprot/SWISSPROT;Acc:Q7Z6M2]
miRanda	FBXO33	F-box only protein 33. [Source:Uniprot/SWISSPROT;Acc:Q7Z6M2]
miRanda	FIGN	fidgetin [Source:RefSeq_peptide;Acc:NP_060556]
PicTar	FKBP1A	FK506-binding protein 1A (EC 5.2.1.8) (Peptidyl-prolyl cis-trans isomerase) (PPIase) (Rotamase) (12 kDa FKBP) (FKBP-12) (Immunophilin FKBP12). [Source:Uniprot/SWISSPROT;Acc:P62942]
TargetScanS	FKBP1C	
PicTar	FKBP4	FK506-binding protein 4 (EC 5.2.1.8) (Peptidyl-prolyl cis-trans isomerase) (PPIase) (Rotamase) (p59 protein) (HSP-binding immunophilin (HBI) (FKBP52 protein) (52 kDa FK506-binding protein) (FKBP59). [Source:Uniprot/SWISSPROT;Acc:Q02790]
TargetScanS	FLJ11730	
TargetScanS	FLJ12443	
TargetScanS	FLJ13576	
TargetScanS	FLJ14503	
TargetScanS	FLJ16517	
TargetScanS	FLJ20160	
TargetScanS	FLJ20273	
TargetScanS	FLJ22688	
TargetScanS	FLJ23749	
TargetScanS	FLJ31951	
TargetScanS	FLJ32679	
TargetScanS	FLJ38973	
TargetScanS	FLT1	Vascular endothelial growth factor receptor 1 precursor (EC 2.7.1.112) (VEGFR-1) (Vascular permeability factor receptor) (Tyrosine-protein kinase receptor FLT) (Flt-1) (Tyrosine-protein kinase FRT) (Fms-like tyrosine kinase 1). [Source:Uniprot/SWISSPROT;Acc:P17948]
miRanda	FMNL2	formin-like 2 isoform A [Source:RefSeq_peptide;Acc:NP_001004421]
TargetScanS	FMR1	Fragile X mental retardation 1 protein (Protein FMR-1) (FMRP). [Source:Uniprot/SWISSPROT;Acc:Q06787]
PicTar	FNDC3A	Fibronectin type-III domain-containing protein 3a. [Source:Uniprot/SWISSPROT;Acc:Q9Y2H6]
TargetScanS	FNDC3A	Fibronectin type-III domain-containing protein 3a. [Source:Uniprot/SWISSPROT;Acc:Q9Y2H6]
miRanda	FNDC3A	Fibronectin type-III domain-containing protein 3a. [Source:Uniprot/SWISSPROT;Acc:Q9Y2H6]
PicTar	FNDC3B	fibronectin type III domain containing 3B [Source:RefSeq_peptide;Acc:NP_073600]
TargetScanS	FNDC3B	fibronectin type III domain containing 3B [Source:RefSeq_peptide;Acc:NP_073600]
miRanda	FNDC3B	fibronectin type III domain containing 3B [Source:RefSeq_peptide;Acc:NP_073600]
PicTar	FOS	Proto-oncogene protein c-fos (Cellular oncogene fos) (G0/G1 switch regulatory protein 7). [Source:Uniprot/SWISSPROT;Acc:P01100]
TargetScanS	FOS	Proto-oncogene protein c-fos (Cellular oncogene fos) (G0/G1 switch regulatory protein 7). [Source:Uniprot/SWISSPROT;Acc:P01100]
miRanda	FOXC1C,	
	FOXG1B	Forkhead box protein G1C (Forkhead-related protein FKHL3) (HFK3) (Fragment). [Source:Uniprot/SWISSPROT;Acc:Q14488]
PicTar	FOXPI	
TargetScanS	FOXPI	Forkhead box protein P1. [Source:Uniprot/SWISSPROT;Acc:Q9H334]
miRanda	FXR2	Forkhead box protein P1. [Source:Uniprot/SWISSPROT;Acc:Q9H334]
TargetScanS	G3BP2	Fragile X mental retardation syndrome-related protein 2. [Source:Uniprot/SWISSPROT;Acc:P51116]
PicTar	GABRA1	
TargetScanS	GABRA1	Gamma-aminobutyric-acid receptor alpha-1 subunit precursor (GABA(A) receptor). [Source:Uniprot/SWISSPROT;Acc:P14867]
		Gamma-aminobutyric-acid receptor alpha-1 subunit precursor (GABA(A) receptor). [Source:Uniprot/SWISSPROT;Acc:P14867]
PicTar	GALNT1	Polypeptide N-acetylgalactosaminyltransferase 1 (EC 2.4.1.41) (Protein-UDP acetylgalactosaminyltransferase 1) (UDP- GalNAc:polypeptide N-acetylgalactosaminyltransferase 1) (Polypeptide GalNAc transferase 1) (GalNAc-T1) (pp-GaNTase 1) [Contains: Polypeptid [Source:Uniprot/SWISSPROT;Acc:Q10472]
PicTar	GATA6	Transcription factor GATA-6 (GATA-binding factor 6). [Source:Uniprot/SWISSPROT;Acc:Q92908]
TargetScanS	GATA6	Transcription factor GATA-6 (GATA-binding factor 6). [Source:Uniprot/SWISSPROT;Acc:Q92908]
miRanda	GATA6	Transcription factor GATA-6 (GATA-binding factor 6). [Source:Uniprot/SWISSPROT;Acc:Q92908]
TargetScanS	GDPD1	glycerophosphodiester phosphodiesterase domain containing 1 [Source:RefSeq_peptide;Acc:NP_872375]
miRanda	GFAP	Glial fibrillary acidic protein, astrocyte (GFAP). [Source:Uniprot/SWISSPROT;Acc:P14136]
TargetScanS	GHITM	Growth hormone-inducible transmembrane protein (Dermal papilla derived protein 2) (Transmembrane BAX inhibitor motif-containing protein 5). [Source:Uniprot/SWISSPROT;Acc:Q9H3K2]
miRanda	GJA1	Gap junction alpha-1 protein (Connexin-43) (Cx43) (Gap junction 43 kDa heart protein). [Source:Uniprot/SWISSPROT;Acc:P17302]
TargetScanS	GLCC1I	glucocorticoid induced transcript 1 [Source:RefSeq_peptide;Acc:NP_612435]
miRanda	GLMN	Giolulin (FKBP-associated protein) (FK506-binding protein-associated protein) (FAP). [Source:Uniprot/SWISSPROT;Acc:Q92990]
PicTar	GLS	Glutaminase kidney isoform, mitochondrial precursor (EC 3.5.1.2) (GLS) (L-glutamine amidohydrolase) (K-glutaminase). [Source:Uniprot/SWISSPROT;Acc:O94925]
TargetScanS	GLS	Glutaminase kidney isoform, mitochondrial precursor (EC 3.5.1.2) (GLS) (L-glutamine amidohydrolase) (K-glutaminase). [Source:Uniprot/SWISSPROT;Acc:O94925]
TargetScanS	GMFB	Glia maturation factor beta (GMF-beta). [Source:Uniprot/SWISSPROT;Acc:P60983]
TargetScanS	GNAI1	Guanine nucleotide-binding protein G(i), alpha-1 subunit (Adenylate cyclase-inhibiting G alpha protein). [Source:Uniprot/SWISSPROT;Acc:P63096]
TargetScanS	GNAO1	Guanine nucleotide-binding protein G(o), alpha subunit 1. [Source:Uniprot/SWISSPROT;Acc:P09471]
PicTar	GOLGA1	Golgin subfamily A member 1 (Golgin-97). [Source:Uniprot/SWISSPROT;Acc:Q92805]
TargetScanS	GOLGA1	Golgin subfamily A member 1 (Golgin-97). [Source:Uniprot/SWISSPROT;Acc:Q92805]
miRanda	GPC4	Glypican-4 precursor (K-glypican). [Source:Uniprot/SWISSPROT;Acc:O75487]
PicTar	GPDL1	glycerol-3-phosphate dehydrogenase 1-like [Source:RefSeq_peptide;Acc:NP_055956]
TargetScanS	GPDL1	glycerol-3-phosphate dehydrogenase 1-like [Source:RefSeq_peptide;Acc:NP_055956]
TargetScanS	GPM6A	Neuronal membrane glycoprotein M6-a (M6a). [Source:Uniprot/SWISSPROT;Acc:P51674]
PicTar	GPR124	Probable G-protein coupled receptor 124 precursor (Tumor endothelial marker 5). [Source:Uniprot/SWISSPROT;Acc:Q96PE1]
TargetScanS	GRB10	Growth factor receptor-bound protein 10 (GRB10 adaptor protein) (Insulin receptor-binding protein GRB-IR). [Source:Uniprot/SWISSPROT;Acc:Q13322]
miRanda	GRB10	Growth factor receptor-bound protein 10 (GRB10 adaptor protein) (Insulin receptor-binding protein GRB-IR). [Source:Uniprot/SWISSPROT;Acc:Q13322]
TargetScanS	GREM1	Gremlin-1 precursor (Cysteine knot superfamily 1, BMP antagonist 1) (Proliferation-inducing gene 2 protein) (Increased in high glucose protein 2) (IHG-2) (Down-regulated in Mos-transformed cells protein). [Source:Uniprot/SWISSPROT;Acc:O60565]
miRanda	GREM2	Gremlin-2 precursor (Cysteine knot superfamily 1, BMP antagonist 2) (Protein related to DAN and cerberus). [Source:Uniprot/SWISSPROT;Acc:Q9H772]
TargetScanS	GRIA2	Glutamate receptor 2 precursor (GluR-2) (GluR-B) (GluR-K2) (Glutamate receptor ionotropic, AMPA 2) (AMPA-selective glutamate receptor 2). [Source:Uniprot/SWISSPROT;Acc:P42262]
miRanda	GRIA2	Glutamate receptor 2 precursor (GluR-2) (GluR-B) (GluR-K2) (Glutamate receptor ionotropic, AMPA 2) (AMPA-selective glutamate receptor 2). [Source:Uniprot/SWISSPROT;Acc:P42262]
TargetScanS	GRID1	Glutamate receptor delta-1 subunit precursor (GluR delta-1). [Source:Uniprot/SWISSPROT;Acc:Q9ULK0]
PicTar	GRIK2	Glutamate receptor, ionotropic kainate 2 precursor (Glutamate receptor 6) (GluR-6) (GluR6) (Excitatory amino acid receptor 4) (EAA4). [Source:Uniprot/SWISSPROT;Acc:Q13002]
TargetScanS	GRIK2	Glutamate receptor, ionotropic kainate 2 precursor (Glutamate receptor 6) (GluR-6) (GluR6) (Excitatory amino acid receptor 4) (EAA4). [Source:Uniprot/SWISSPROT;Acc:Q13002]
TargetScanS	GRK6	G protein-coupled receptor kinase 6 (EC 2.7.1.-) (G protein-coupled receptor kinase GRK6). [Source:Uniprot/SWISSPROT;Acc:P43250]
TargetScanS	GRM5	Metabotropic glutamate receptor 5 precursor (mGluR5). [Source:Uniprot/SWISSPROT;Acc:P41594]
TargetScanS	GRM7	Metabotropic glutamate receptor 7 precursor (mGluR7). [Source:Uniprot/SWISSPROT;Acc:Q14831]
miRanda	GSP7I	G1 to S phase transition protein 1 homolog (GTP-binding protein GSTI- HS). [Source:Uniprot/SWISSPROT;Acc:P15170]
TargetScanS	HCN2	Potassium/sodium hyperpolarization-activated cyclic nucleotide-gated channel 2 (Brain cyclic nucleotide gated channel 2) (BCNG-2). [Source:Uniprot/SWISSPROT;Acc:Q9UL51]
PicTar	HECA	Headcase protein homolog (hHDC). [Source:Uniprot/SWISSPROT;Acc:Q9UB19]

TargetScanS	HECA	Headcase protein homolog (hHDC). [Source:Uniprot/SWISSPROT;Acc:Q9UBI9]
PicTar	HERPUD1	Homocysteine-responsive endoplasmic reticulum-resident ubiquitin-like domain member 1 protein (Methyl methanesulfonate (MMF)-inducible fragment protein 1). [Source:Uniprot/SWISSPROT;Acc:Q15011]
TargetScanS	HEY2	hairly/enhancer-of-split related with YRPW motif 2 [Source:RefSeq_peptide;Acc:NP_036391]
PicTar	HIC2	Hypermethylated in cancer 2 protein (Hic-2) (Hic-3) (HIC1-related gene on chromosome 22) (Zinc finger and BTB domain-containing protein 30). [Source:Uniprot/SWISSPROT;Acc:Q96JB3]
TargetScanS	HIC2	Hypermethylated in cancer 2 protein (Hic-2) (Hic-3) (HIC1-related gene on chromosome 22) (Zinc finger and BTB domain-containing protein 30). [Source:Uniprot/SWISSPROT;Acc:Q96JB3]
TargetScanS	HIS1	
PicTar	HLF	Hepatic leukemia factor. [Source:Uniprot/SWISSPROT;Acc:Q16534]
TargetScanS	HLF	Hepatic leukemia factor. [Source:Uniprot/SWISSPROT;Acc:Q16534]
miRanda	HLF	Hepatic leukemia factor. [Source:Uniprot/SWISSPROT;Acc:Q16534]
TargetScanS	HMGB1	High mobility group protein 1 (HMG-1) (High mobility group protein B1). [Source:Uniprot/SWISSPROT;Acc:P09429]
TargetScanS	HMGB2	High mobility group protein 2 (HMG-2). [Source:Uniprot/SWISSPROT;Acc:P26583]
miRanda	HNRPA3	Heterogeneous nuclear ribonucleoprotein A3 (hnRNP A3). [Source:Uniprot/SWISSPROT;Acc:P51991]
TargetScanS	HNRPH1	Heterogeneous nuclear ribonucleoprotein H (hnRNP H). [Source:Uniprot/SWISSPROT;Acc:P31943]
miRanda	HNRPH2	Heterogeneous nuclear ribonucleoprotein H' (hnRNP H') (FTP-3). [Source:Uniprot/SWISSPROT;Acc:P55795]
TargetScanS	HNRPK	Heterogeneous nuclear ribonucleoprotein K (hnRNP K) (Transformation up-regulated nuclear protein) (TUNP). [Source:Uniprot/SWISSPROT;Acc:P61978]
TargetScanS	HOXA1	Homeobox protein Hox-A1 (Hox-1F). [Source:Uniprot/SWISSPROT;Acc:P49639]
PicTar	HOXA11	Homeobox protein Hox-A11 (Hox-1I). [Source:Uniprot/SWISSPROT;Acc:P31270]
TargetScanS	HOXA11	Homeobox protein Hox-A11 (Hox-1I). [Source:Uniprot/SWISSPROT;Acc:P31270]
miRanda	HOXA11	Homeobox protein Hox-A11 (Hox-1I). [Source:Uniprot/SWISSPROT;Acc:P31270]
miRanda	HOXB4	Homeobox protein Hox-B4 (Hox-2F) (Hox-2.6). [Source:Uniprot/SWISSPROT;Acc:P17483]
PicTar	HOXB5	Homeobox protein Hox-B5 (Hox-2A) (HHO.C10) (HU-1). [Source:Uniprot/SWISSPROT;Acc:P09067]
TargetScanS	HOXB5	Homeobox protein Hox-B5 (Hox-2A) (HHO.C10) (HU-1). [Source:Uniprot/SWISSPROT;Acc:P09067]
TargetScanS	HOXB8	Homeobox protein Hox-B8 (Hox-2D) (Hox-2.4). [Source:Uniprot/SWISSPROT;Acc:P17481]
miRanda	HOXC13	Homeobox protein Hox-C13 (Hox-3G). [Source:Uniprot/SWISSPROT;Acc:P31276]
PicTar	HOXC8	Homeobox protein Hox-C8 (Hox-3A). [Source:Uniprot/SWISSPROT;Acc:P31273]
TargetScanS	HOXC8	Homeobox protein Hox-C8 (Hox-3A). [Source:Uniprot/SWISSPROT;Acc:P31273]
TargetScanS	HP53	Hermansky-Pudlak syndrome 3 protein. [Source:Uniprot/SWISSPROT;Acc:Q969F9]
PicTar	HRB	Nucleoporin-like protein RIP (HIV-1 Rev-binding protein) (Rev- interacting protein) (Rev/Rex activation domain-binding protein). [Source:Uniprot/SWISSPROT;Acc:P52594]
TargetScanS	HRB	Nucleoporin-like protein RIP (HIV-1 Rev-binding protein) (Rev- interacting protein) (Rev/Rex activation domain-binding protein). [Source:Uniprot/SWISSPROT;Acc:P52594]
TargetScanS	HRPT2	
TargetScanS	HSHIN1	
miRanda	HSP90B1	Endoplasmic precursor (94 kDa glucose-regulated protein) (GRP94) (gp96 homolog) (Tumor rejection antigen 1). [Source:Uniprot/SWISSPROT;Acc:P14625]
TargetScanS	HSPA5	78 kDa glucose-regulated protein precursor (GRP 78) (Immunoglobulin heavy chain-binding protein) (BiP) (Endoplasmic reticulum luminal Ca(2+)-binding protein grp78). [Source:Uniprot/SWISSPROT;Acc:P11021]
miRanda	HSPA5	78 kDa glucose-regulated protein precursor (GRP 78) (Immunoglobulin heavy chain-binding protein) (BiP) (Endoplasmic reticulum luminal Ca(2+)-binding protein grp78). [Source:Uniprot/SWISSPROT;Acc:P11021]
miRanda	HTR1B	5-hydroxytryptamine 1B receptor (5-HT-1B) (Serotonin receptor 1B) (5-HT1B) (5-HT-1D-beta) (Serotonin 1D beta receptor) (512). [Source:Uniprot/SWISSPROT;Acc:P28222]
miRanda	HTR2C	5-hydroxytryptamine 2C receptor (5-HT-2C) (Serotonin receptor 2C) (5-HT2C) (5-HTR2C) (5HT-1C). [Source:Uniprot/SWISSPROT;Acc:P28335]
TargetScanS	HYOU1	150 kDa oxygen-regulated protein precursor (Orp150) (Hypoxia up-regulated 1). [Source:Uniprot/SWISSPROT;Acc:Q9Y4L1]
PicTar	ID4	DNA-binding protein inhibitor ID-4 (Inhibitor of DNA binding 4). [Source:Uniprot/SWISSPROT;Acc:P47928]
PicTar	IGSF4D	immunoglobulin superfamily, member 4D [Source:RefSeq_peptide;Acc:NP_694854]
PicTar	IL1A	Interleukin-1 alpha precursor (IL-1 alpha) (Hematopoietin-1). [Source:Uniprot/SWISSPROT;Acc:P01583]
TargetScanS	IL1A	Interleukin-1 alpha precursor (IL-1 alpha) (Hematopoietin-1). [Source:Uniprot/SWISSPROT;Acc:P01583]
TargetScanS	ILF3	Interleukin enhancer-binding factor 3 (Nuclear factor of activated T- cells 90 kDa) (NF-AT-90) (Double-stranded RNA-binding protein 76) (DRBP76) (Translational control protein 80) (TCP80) (Nuclear factor associated with dsRNA) (NFAR) (M-phase phosphoprote [Source:Uniprot/SWISSPROT;Acc:Q12906]
TargetScanS	IMP-2	
TargetScanS	IMP-3	
TargetScanS	INO80	
PicTar	INOC1	INO80 complex homolog 1 [Source:RefSeq_peptide;Acc:NP_060023]
TargetScanS	INPP5A	Type 1 inositol-1,4,5-trisphosphate 5-phosphatase (EC 3.1.3.56) (5PTase). [Source:Uniprot/SWISSPROT;Acc:Q14642]
TargetScanS	INPP5E	72 kDa inositol polyphosphate 5-phosphatase (EC 3.1.3.36) (Phosphatidylinositol-4,5-bisphosphate 5-phosphatase) (Phosphatidylinositol polyphosphate 5-phosphatase type IV). [Source:Uniprot/SWISSPROT;Acc:Q9NRR6]
TargetScanS	IQGAP2	Ras GTPase-activating-like protein IQGAP2. [Source:Uniprot/SWISSPROT;Acc:Q13576]
TargetScanS	IQSEC2	IQ motif and Sec7 domain 2 [Source:RefSeq_peptide;Acc:NP_055890]
PicTar	IRS2	Insulin receptor substrate 2 (IRS-2). [Source:Uniprot/SWISSPROT;Acc:Q9Y4H2]
TargetScanS	IRS2	Insulin receptor substrate 2 (IRS-2). [Source:Uniprot/SWISSPROT;Acc:Q9Y4H2]
PicTar	ITGA3	Integrin alpha-3 precursor (Galactoprotein B3) (GAPB3) (VLA-3 alpha chain) (FRP-2) (CD49c antigen) [Contains: Integrin alpha-3 heavy chain; Integrin alpha-3 light chain]. [Source:Uniprot/SWISSPROT;Acc:P26006]
TargetScanS	ITGA3	Integrin alpha-3 precursor (Galactoprotein B3) (GAPB3) (VLA-3 alpha chain) (FRP-2) (CD49c antigen) [Contains: Integrin alpha-3 heavy chain; Integrin alpha-3 light chain]. [Source:Uniprot/SWISSPROT;Acc:P26006]
miRanda	ITGB3BP	Nuclear receptor-interacting factor 3 (Integrin beta-3-binding protein) (Beta3-endonexin). [Source:Uniprot/SWISSPROT;Acc:Q13352]
PicTar	ITGB8	Integrin beta-8 precursor. [Source:Uniprot/SWISSPROT;Acc:P26012]
TargetScanS	ITGB8	Integrin beta-8 precursor. [Source:Uniprot/SWISSPROT;Acc:P26012]
miRanda	ITM2A	Integral membrane protein 2A (E25 protein). [Source:Uniprot/SWISSPROT;Acc:O43736]
TargetScanS	ITSN1	Intersectin-1 (SH3 domain-containing protein 1A) (SH3P17). [Source:Uniprot/SWISSPROT;Acc:Q15811]
PicTar	IVNS1ABP	influenza virus NS1A binding protein isoform a [Source:RefSeq_peptide;Acc:NP_006460]
PicTar	JARID1A	Jumonji/ARID domain-containing protein 1A (Retinoblastoma-binding protein 2) (RBBP-2). [Source:Uniprot/SWISSPROT;Acc:P29375]
TargetScanS	JAZF1	
miRanda	JOSD1	Josephin-1 (Josephin domain containing 1). [Source:Uniprot/SWISSPROT;Acc:Q15040]
miRanda	KBTBD9	Kelch repeat and BTB domain-containing protein 9. [Source:Uniprot/SWISSPROT;Acc:Q96CT2]
miRanda	KCNH8	Potassium voltage-gated channel subfamily H member 8 (Voltage-gated potassium channel subunit Kv12.1) (Ether-a-go-go-like potassium channel 3) (ELK channel 3) (ELK3) (ELK1) (hElk1). [Source:Uniprot/SWISSPROT;Acc:Q96L42]
miRanda	KCNJ3	G protein-activated inward rectifier potassium channel 1 (GIRK1) (Potassium channel, inwardly rectifying subfamily J member 3) (Inward rectifier K(+) channel Kir3.1). [Source:Uniprot/SWISSPROT;Acc:P48549]
PicTar	KCNK10	Potassium channel subfamily K member 10 (Outward rectifying potassium channel protein TREK-2) (TREK-2 K(+) channel subunit). [Source:Uniprot/SWISSPROT;Acc:P57789]
TargetScanS	KCNK10	Potassium channel subfamily K member 10 (Outward rectifying potassium channel protein TREK-2) (TREK-2 K(+) channel subunit). [Source:Uniprot/SWISSPROT;Acc:P57789]
miRanda	KCN53	Potassium voltage-gated channel subfamily S member 3 (Voltage-gated potassium channel subunit Kv9.3) (Delayed-rectifier K(+) channel alpha subunit 3). [Source:Uniprot/SWISSPROT;Acc:Q9BQ31]
TargetScanS	KIAA0182	
PicTar	KIAA0195	
TargetScanS	KIAA0195	
TargetScanS	KIAA0252	
miRanda	KIAA0355	
TargetScanS	KIAA0376	
PicTar	KIAA0423	

TargetScanS	KIAA0423	
TargetScanS	KIAA0433	
PicTar	KIAA0528	
TargetScanS	KIAA0528	
TargetScanS	KIAA0663	
TargetScanS	KIAA0664	Putative eukaryotic translation initiation factor 3 subunit (eIF-3). [Source:Uniprot/SWISSPROT;Acc:O75153]
TargetScanS	KIAA0789	
PicTar	KIAA0802	
TargetScanS	KIAA0802	
TargetScanS	KIAA0992	
TargetScanS	KIAA1102	
TargetScanS	KIAA1117	
PicTar	KIAA1128	granule cell antiserum positive 14 [Source:RefSeq_peptide;Acc:NP_061872]
TargetScanS	KIAA1212	Hook-related protein 1 [Source:RefSeq_peptide;Acc:NP_060554]
TargetScanS	KIAA1217	
TargetScanS	KIAA1463	
TargetScanS	KIAA2022	
TargetScanS	KIF3B	Kinesin-like protein KIF3B (Microtubule plus end-directed kinesin motor 3B) (HH0048). [Source:Uniprot/SWISSPROT;Acc:O15066]
PicTar	KIT	Mast/stem cell growth factor receptor precursor (EC 2.7.1.112) (SCFR) (Proto-oncogene tyrosine-protein kinase Kit) (c-kit) (CD117 antigen). [Source:Uniprot/SWISSPROT;Acc:P10721]
PicTar	KLF15	Kruppel-like factor 15 (Kidney-enriched kruppel-like factor). [Source:Uniprot/SWISSPROT;Acc:Q9UIH9]
TargetScanS	KLF15	Kruppel-like factor 15 (Kidney-enriched kruppel-like factor). [Source:Uniprot/SWISSPROT;Acc:Q9UIH9]
PicTar	KLF6	Core promoter element-binding protein (Kruppel-like factor 6) (B-cell derived protein 1) (Proto-oncogene BCD1) (Transcription factor Zf9) (GC-rich sites-binding factor GBF). [Source:Uniprot/SWISSPROT;Acc:Q99612]
TargetScanS	KLF6	Core promoter element-binding protein (Kruppel-like factor 6) (B-cell derived protein 1) (Proto-oncogene BCD1) (Transcription factor Zf9) (GC-rich sites-binding factor GBF). [Source:Uniprot/SWISSPROT;Acc:Q99612]
PicTar	KLHL2	Kelch-like protein 2 (Actin-binding protein Mayven). [Source:Uniprot/SWISSPROT;Acc:O95198]
TargetScanS	KLHL2	Kelch-like protein 2 (Actin-binding protein Mayven). [Source:Uniprot/SWISSPROT;Acc:O95198]
TargetScanS	KLHL5	Kelch-like protein 5. [Source:Uniprot/SWISSPROT;Acc:Q96PQ7]
PicTar	KPNA1	Importin alpha-1 subunit (Karyopherin alpha-1 subunit) (SRP1-beta) (RAG cohort protein 2) (Nucleoprotein interactor 1) (NPI-1). [Source:Uniprot/SWISSPROT;Acc:P52294]
TargetScanS	KPNA1	Importin alpha-1 subunit (Karyopherin alpha-1 subunit) (SRP1-beta) (RAG cohort protein 2) (Nucleoprotein interactor 1) (NPI-1). [Source:Uniprot/SWISSPROT;Acc:P52294]
PicTar	KPNB1	Importin beta-1 subunit (Karyopherin beta-1 subunit) (Nuclear factor P97) (Importin 90). [Source:Uniprot/SWISSPROT;Acc:Q14974]
TargetScanS	KPNB1	Importin beta-1 subunit (Karyopherin beta-1 subunit) (Nuclear factor P97) (Importin 90). [Source:Uniprot/SWISSPROT;Acc:Q14974]
miRanda	KPNB1	Importin beta-1 subunit (Karyopherin beta-1 subunit) (Nuclear factor P97) (Importin 90). [Source:Uniprot/SWISSPROT;Acc:Q14974]
PicTar	LBR	Lamin-B receptor (Integral nuclear envelope inner membrane protein) (LMN2R). [Source:Uniprot/SWISSPROT;Acc:Q14739]
PicTar	LBR	Lamin-B receptor (Integral nuclear envelope inner membrane protein) (LMN2R). [Source:Uniprot/SWISSPROT;Acc:Q14739]
TargetScanS	LBR	Lamin-B receptor (Integral nuclear envelope inner membrane protein) (LMN2R). [Source:Uniprot/SWISSPROT;Acc:Q14739]
DIANA-microT	LEF1	Lymphoid enhancer-binding factor 1 (LEF-1) (T cell-specific transcription factor 1-alpha) (TCF1-alpha). [Source:Uniprot/SWISSPROT;Acc:Q9UJU2]
PicTar	LEMD3	Inner nuclear membrane protein Man1 (LEM domain containing protein 3). [Source:Uniprot/SWISSPROT;Acc:Q9Y2U8]
TargetScanS	LEMD3	Inner nuclear membrane protein Man1 (LEM domain containing protein 3). [Source:Uniprot/SWISSPROT;Acc:Q9Y2U8]
TargetScanS	LIF	Leukemia inhibitory factor precursor (LIF) (Differentiation- stimulating factor) (D factor) (Melanoma-derived LPL inhibitor) (MLPLI) (Emfilermin). [Source:Uniprot/SWISSPROT;Acc:P15018]
TargetScanS	Lin10	
PicTar	LIN28	lin-28 homolog [Source:RefSeq_peptide;Acc:NP_078950]
TargetScanS	LIN28	lin-28 homolog [Source:RefSeq_peptide;Acc:NP_078950]
PicTar	LIN28B	lin-28 homolog B [Source:RefSeq_peptide;Acc:NP_001004317]
PicTar	LIN7C	LIN-7 homolog C (LIN-7C) (Mammalian LIN-seven protein 3) (MALS-3) (Vertebrate LIN 7 homolog 3) (Veli-3 protein). [Source:Uniprot/SWISSPROT;Acc:Q9NUP9]
TargetScanS	LIN7C	LIN-7 homolog C (LIN-7C) (Mammalian LIN-seven protein 3) (MALS-3) (Vertebrate LIN 7 homolog 3) (Veli-3 protein). [Source:Uniprot/SWISSPROT;Acc:Q9NUP9]
PicTar	LMO1	Rhombotin-1 (Cysteine-rich protein TTG-1) (T-cell translocation protein 1) (LIM-only protein 1). [Source:Uniprot/SWISSPROT;Acc:P25800]
TargetScanS	LMO1	Rhombotin-1 (Cysteine-rich protein TTG-1) (T-cell translocation protein 1) (LIM-only protein 1). [Source:Uniprot/SWISSPROT;Acc:P25800]
PicTar	LMO3	LIM-only protein 3 (Neuronal-specific transcription factor DAT1) (Rhombotin-3). [Source:Uniprot/SWISSPROT;Acc:Q8TAP4]
PicTar	LMO3	LIM-only protein 3 (Neuronal-specific transcription factor DAT1) (Rhombotin-3). [Source:Uniprot/SWISSPROT;Acc:Q8TAP4]
TargetScanS	LMO3	LIM-only protein 3 (Neuronal-specific transcription factor DAT1) (Rhombotin-3). [Source:Uniprot/SWISSPROT;Acc:Q8TAP4]
miRanda	LMO3	LIM-only protein 3 (Neuronal-specific transcription factor DAT1) (Rhombotin-3). [Source:Uniprot/SWISSPROT;Acc:Q8TAP4]
TargetScanS	LOC113251	
TargetScanS	LOC134218	
TargetScanS	LOC134548	
TargetScanS	LOC151963	
TargetScanS	LOC153222	
TargetScanS	LOC159090	
TargetScanS	LOC168850	
TargetScanS	LOC283174	
TargetScanS	LOC283768	
TargetScanS	LOC345667	
TargetScanS	LOC388272	
TargetScanS	LOC390535	
PicTar	LONRF1	
miRanda	LONRF1	
PicTar	LPP	Lipoma-preferred partner (LIM domain-containing preferred translocation partner in lipoma). [Source:Uniprot/SWISSPROT;Acc:Q93052]
TargetScanS	LPP	Lipoma-preferred partner (LIM domain-containing preferred translocation partner in lipoma). [Source:Uniprot/SWISSPROT;Acc:Q93052]
TargetScanS	LPPR4	
PicTar	LRBA	Lipopolysaccharide-responsive and beige-like anchor protein (CDC4-like protein) (Beige-like protein). [Source:Uniprot/SWISSPROT;Acc:P50851]
TargetScanS	LRBA	Lipopolysaccharide-responsive and beige-like anchor protein (CDC4-like protein) (Beige-like protein). [Source:Uniprot/SWISSPROT;Acc:P50851]
DIANA-microT	LRFN2	Leucine-rich repeat and fibronectin type-III domain-containing protein 2 precursor. [Source:Uniprot/SWISSPROT;Acc:Q9ULH4]
TargetScanS	LRP12	Low-density lipoprotein receptor-related protein 12 precursor (Suppressor of tumorigenicity protein 7). [Source:Uniprot/SWISSPROT;Acc:Q9Y561]
TargetScanS	LRP4	Low-density lipoprotein receptor-related protein 4 precursor (Multiple epidermal growth factor-like domains 7). [Source:Uniprot/SWISSPROT;Acc:O75096]
PicTar	LRRC32	Leucine-rich repeat-containing protein 32 precursor (GARP protein) (Garpin) (Glycoprotein A repetitions predominant). [Source:Uniprot/SWISSPROT;Acc:Q14392]
TargetScanS	LRRC32	Leucine-rich repeat-containing protein 32 precursor (GARP protein) (Garpin) (Glycoprotein A repetitions predominant). [Source:Uniprot/SWISSPROT;Acc:Q14392]
PicTar	LRRC8D	Leucine-rich repeat-containing protein 8D. [Source:Uniprot/SWISSPROT;Acc:Q7L1W4]
PicTar	LRRN1	Leucine-rich repeats neuronal protein 1 precursor (Neuronal leucine- rich repeat protein 1) (NLRR-1). [Source:Uniprot/SWISSPROT;Acc:Q6UXK5]
TargetScanS	LRRN1	Leucine-rich repeats neuronal protein 1 precursor (Neuronal leucine- rich repeat protein 1) (NLRR-1). [Source:Uniprot/SWISSPROT;Acc:Q6UXK5]
miRanda	LRRN1	Leucine-rich repeats neuronal protein 1 precursor (Neuronal leucine- rich repeat protein 1) (NLRR-1). [Source:Uniprot/SWISSPROT;Acc:Q6UXK5]
TargetScanS	LUZP1	leucine zipper protein 1 [Source:RefSeq_peptide;Acc:NP_361013]

TargetScanS	LYCAT	lysocardiolipin acyltransferase isoform 1 [Source:RefSeq_peptide;Acc:NP_872357]
TargetScanS	MAEA	macrophage erythroblast attacher isoform 2 [Source:RefSeq_peptide;Acc:NP_005873]
PicTar	MAGI1	Membrane-associated guanylate kinase, WW and PDZ domain-containing protein 1 (BAP-1) (Membrane-associated guanylate kinase inverted 1) (MAGI-1) (Atrophin-1-interacting protein 3) (AIP3) (WW domain-containing protein 3) (WWP3) ([Source:Uniprot/SWISSPROT;Acc:Q96QZ7])
PicTar	MAK3	Mak3 homolog [Source:RefSeq_peptide;Acc:NP_079422]
PicTar	MAK3	Mak3 homolog [Source:RefSeq_peptide;Acc:NP_079422]
PicTar	MAMDC2	MAM domain-containing protein 2 precursor. [Source:Uniprot/SWISSPROT;Acc:Q7Z304]
TargetScanS	MAMDC2	MAM domain-containing protein 2 precursor. [Source:Uniprot/SWISSPROT;Acc:Q7Z304]
PicTar	MAP1A	Microtubule-associated protein 1A (MAP 1A) (Proliferation-related protein p80) [Contains: MAP1 light chain LC2]. [Source:Uniprot/SWISSPROT;Acc:P78559]
TargetScanS	MAP1A	Microtubule-associated protein 1A (MAP 1A) (Proliferation-related protein p80) [Contains: MAP1 light chain LC2]. [Source:Uniprot/SWISSPROT;Acc:P78559]
PicTar	MAP1B	Microtubule-associated protein 1B (MAP 1B) [Contains: MAP1 light chain LC1]. [Source:Uniprot/SWISSPROT;Acc:P46821]
PicTar	MAP1B	Microtubule-associated protein 1B (MAP 1B) [Contains: MAP1 light chain LC1]. [Source:Uniprot/SWISSPROT;Acc:P46821]
TargetScanS	MAP1B	Microtubule-associated protein 1B (MAP 1B) [Contains: MAP1 light chain LC1]. [Source:Uniprot/SWISSPROT;Acc:P46821]
PicTar	MAP3K10	Mitogen-activated protein kinase kinase kinase 10 (EC 2.7.1.37) (Mixed lineage kinase 2) (Protein kinase MST). [Source:Uniprot/SWISSPROT;Acc:Q02779]
TargetScanS	MAP3K10	Mitogen-activated protein kinase kinase kinase 10 (EC 2.7.1.37) (Mixed lineage kinase 2) (Protein kinase MST). [Source:Uniprot/SWISSPROT;Acc:Q02779]
miRanda	MAP3K10	Mitogen-activated protein kinase kinase kinase 10 (EC 2.7.1.37) (Mixed lineage kinase 2) (Protein kinase MST). [Source:Uniprot/SWISSPROT;Acc:Q02779]
PicTar	MAP3K3	Mitogen-activated protein kinase kinase kinase 3 (EC 2.7.1.37) (MAPK/ERK kinase kinase 3) (MEK kinase 3) (MEKK 3). [Source:Uniprot/SWISSPROT;Acc:Q99759]
TargetScanS	MAP3K3	Mitogen-activated protein kinase kinase kinase 3 (EC 2.7.1.37) (MAPK/ERK kinase kinase 3) (MEK kinase 3) (MEKK 3). [Source:Uniprot/SWISSPROT;Acc:Q99759]
TargetScanS	MAP3K7IP2	Mitogen-activated protein kinase kinase kinase 7-interacting protein 2 (TAK1-binding protein 2). [Source:Uniprot/SWISSPROT;Acc:Q9NYI8]
TargetScanS	MAP4K4	Mitogen-activated protein kinase kinase kinase 4 (EC 2.7.1.37) (MAPK/ERK kinase kinase kinase 4) (MEK kinase kinase 4) (MEKKK 4) (HPK/GCK-like kinase HGK) (Nck-interacting kinase). [Source:Uniprot/SWISSPROT;Acc:Q95819]
TargetScanS	MARCKS	Myristoylated alanine-rich C-kinase substrate (MARCKS) (Protein kinase C substrate, 80 kDa protein, light chain) (PKCSL) (80K-L protein). [Source:Uniprot/SWISSPROT;Acc:P29966]
TargetScanS	MAT2A	S-adenosylmethionine synthetase isoform type-2 (EC 2.5.1.6) (Methionine adenosyltransferase 2) (AdoMet synthetase 2) (Methionine adenosyltransferase II) (MAT-II). [Source:Uniprot/SWISSPROT;Acc:P31153]
miRanda	MAT2A	S-adenosylmethionine synthetase isoform type-2 (EC 2.5.1.6) (Methionine adenosyltransferase 2) (AdoMet synthetase 2) (Methionine adenosyltransferase II) (MAT-II). [Source:Uniprot/SWISSPROT;Acc:P31153]
TargetScanS	MBNL2	muscleblind-like 2 isoform 1 [Source:RefSeq_peptide;Acc:NP_659002]
PicTar	MECP2	Methyl-CpG-binding protein 2 (MeCP-2 protein) (MeCP2). [Source:Uniprot/SWISSPROT;Acc:P51608]
TargetScanS	MECP2	Methyl-CpG-binding protein 2 (MeCP-2 protein) (MeCP2). [Source:Uniprot/SWISSPROT;Acc:P51608]
miRanda	MECP2	Methyl-CpG-binding protein 2 (MeCP-2 protein) (MeCP2). [Source:Uniprot/SWISSPROT;Acc:P51608]
PicTar	MEIS2	Homeobox protein Meis2 (Meis1-related protein 1). [Source:Uniprot/SWISSPROT;Acc:O14770]
PicTar	MEIS2	Homeobox protein Meis2 (Meis1-related protein 1). [Source:Uniprot/SWISSPROT;Acc:O14770]
PicTar	MEIS2	Homeobox protein Meis2 (Meis1-related protein 1). [Source:Uniprot/SWISSPROT;Acc:O14770]
TargetScanS	METAP1	Methionine aminopeptidase 1 (EC 3.4.11.18) (MetAp 1) (MAP 1) (Peptidase M 1). [Source:Uniprot/SWISSPROT;Acc:P53582]
TargetScanS	MG29	
TargetScanS	MGAT2	Alpha-1,6-mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltransferase (EC 2.4.1.143) (Mannoside acetylglucosaminyltransferase 2) (N-glycosyl-oligosaccharide-glycoprotein N-acetylglucosaminyltransferase II) (Beta-1,2-N-acetylglucosaminyltransferase II) ([Source:Uniprot/SWISSPROT;Acc:Q10469])
TargetScanS	MGC14276	
TargetScanS	MGC33555	
TargetScanS	MGC39518	
TargetScanS	MGC42090	
PicTar	MINK1	Missshapen-like kinase 1 (EC 2.7.1.37) (Mitogen-activated protein kinase kinase kinase kinase 6) (MAPK/ERK kinase kinase kinase 6) (MEK kinase kinase 6) (MEKKK 6) (Missshapen/NIK-related kinase) (GCK family kinase MiNK). [Source:Uniprot/SWISSPROT;Acc:Q8N4C8]
TargetScanS	MINK1	Missshapen-like kinase 1 (EC 2.7.1.37) (Mitogen-activated protein kinase kinase kinase kinase 6) (MAPK/ERK kinase kinase kinase 6) (MEK kinase kinase 6) (MEKKK 6) (Missshapen/NIK-related kinase) (GCK family kinase MiNK). [Source:Uniprot/SWISSPROT;Acc:Q8N4C8]
TargetScanS	MKNK2	MAP kinase-interacting serine/threonine-protein kinase 2 (EC 2.7.1.37) (MAP kinase signal-integrating kinase 2) (Mnk2). [Source:Uniprot/SWISSPROT;Acc:Q9HBH9]
TargetScanS	MLLT2	
PicTar	MMP14	Matrix metalloproteinase-14 precursor (EC 3.4.24.80) (MMP-14) (Membrane-type matrix metalloproteinase 1) (MT-MMP 1) (MTMMP1) (Membrane-type-1 matrix metalloproteinase) (MT1-MMP) (MT1MMP) (MMP- X1). [Source:Uniprot/SWISSPROT;Acc:P50281]
TargetScanS	MMP14	Matrix metalloproteinase-14 precursor (EC 3.4.24.80) (MMP-14) (Membrane-type matrix metalloproteinase 1) (MT-MMP 1) (MTMMP1) (Membrane-type-1 matrix metalloproteinase) (MT1-MMP) (MT1MMP) (MMP- X1). [Source:Uniprot/SWISSPROT;Acc:P50281]
miRanda	MMP16	Matrix metalloproteinase-16 precursor (EC 3.4.24.-) (MMP-16) (Membrane-type matrix metalloproteinase 3) (MT-MMP 3) (MTMMP3) (Membrane-type-3 matrix metalloproteinase) (MT3-MMP) (MT3MMP) (MMP- X2). [Source:Uniprot/SWISSPROT;Acc:P51512]
miRanda	MMP24	Matrix metalloproteinase-24 precursor (EC 3.4.24.-) (MMP-24) (Membrane-type matrix metalloproteinase 5) (MT-MMP 5) (Membrane-type-5 matrix metalloproteinase) (MT5-MMP). [Source:Uniprot/SWISSPROT;Acc:Q9Y5R2]
TargetScanS	MPP5	MAGUK p55 subfamily member 5. [Source:Uniprot/SWISSPROT;Acc:Q8N3R9]
TargetScanS	MSCP	
TargetScanS	MSI1	RNA-binding protein Musashi homolog 1 (Musashi-1). [Source:Uniprot/SWISSPROT;Acc:O43347]
TargetScanS	MSI2	RNA-binding protein Musashi homolog 2 (Musashi-2). [Source:Uniprot/SWISSPROT;Acc:Q96DH6]
PicTar	MSL2L1	ring finger protein 184 [Source:RefSeq_peptide;Acc:NP_060603]
miRanda	MSL2L1	ring finger protein 184 [Source:RefSeq_peptide;Acc:NP_060603]
PicTar	MTCH2	Mitochondrial carrier homolog 2 (Met-induced mitochondrial protein). [Source:Uniprot/SWISSPROT;Acc:Q9Y6C9]
PicTar	MTMR12	myotubularin related protein 12 [Source:RefSeq_peptide;Acc:NP_061934]
TargetScanS	MTMR9	Myotubularin-related protein 9. [Source:Uniprot/SWISSPROT;Acc:Q96QG7]
PicTar	MTFN	Myotrophin (V-1 protein). [Source:Uniprot/SWISSPROT;Acc:P58546]
TargetScanS	MTFN	Myotrophin (V-1 protein). [Source:Uniprot/SWISSPROT;Acc:P58546]
miRanda	MTSS1	Metastasis suppressor protein 1 (Missing in metastasis protein) (Metastasis suppressor YGL-1). [Source:Uniprot/SWISSPROT;Acc:O43312]
TargetScanS	MYCBP2	Probable ubiquitin ligase protein MYCBP2 (EC 6.3.2.-) (Myc binding protein 2) (Protein associated with Myc) (Pam/highwire/rpm-1 protein). [Source:Uniprot/SWISSPROT;Acc:O75592]
PicTar	MYCN	N-myc proto-oncogene protein. [Source:Uniprot/SWISSPROT;Acc:P04198]
PicTar	MYH10	Myosin-10 (Myosin heavy chain, nonmuscle IIb) (Nonmuscle myosin heavy chain IIb) (NMMHC II-b) (NMMHC-IIb) (Cellular myosin heavy chain, type B) (Nonmuscle myosin heavy chain-B) (NMMHC-B). [Source:Uniprot/SWISSPROT;Acc:P35580]
TargetScanS	MYH10	Myosin-10 (Myosin heavy chain, nonmuscle IIb) (Nonmuscle myosin heavy chain IIb) (NMMHC II-b) (NMMHC-IIb) (Cellular myosin heavy chain, type B) (Nonmuscle myosin heavy chain-B) (NMMHC-B). [Source:Uniprot/SWISSPROT;Acc:P35580]
miRanda	MYH10	Myosin-10 (Myosin heavy chain, nonmuscle IIb) (Nonmuscle myosin heavy chain IIb) (NMMHC II-b) (NMMHC-IIb) (Cellular myosin heavy chain, type B) (Nonmuscle myosin heavy chain-B) (NMMHC-B). [Source:Uniprot/SWISSPROT;Acc:P35580]
TargetScanS	MYO1C	Myosin Ic (Myosin I beta) (MMI-beta) (MMIb). [Source:Uniprot/SWISSPROT;Acc:O00159]
miRanda	MYST2	Histone acetyltransferase MYST2 (EC 2.3.1.48) (MYST protein 2) (MOZ, YBF2/SAS3, SAS2 and TIP60 protein 2) (Histone acetyltransferase binding to hORC1). [Source:Uniprot/SWISSPROT;Acc:O95251]
miRanda	MYST4	Histone acetyltransferase MYST4 (EC 2.3.1.48) (EC 2.3.1.-) (MYST protein 4) (MOZ, YBF2/SAS3, SAS2 and TIP60 protein 4) (Histone acetyltransferase MOZ2) (Monocytic leukemia zinc finger protein-related factor) (Histone acetyltransferase MORF). [Source:Uniprot/SWISSPROT;Acc:Q8WYB5]
PicTar	NAALADL2	N-acetylated alpha-linked acidic dipeptidase 2 [Source:RefSeq_peptide;Acc:NP_996898]
TargetScanS	NAB1	NGFI-A-binding protein 1 (EGR-1-binding protein 1) (Transcriptional regulatory protein p54). [Source:Uniprot/SWISSPROT;Acc:Q13506]
TargetScanS	NAP1L5	nucleosome assembly protein 1-like 5 [Source:RefSeq_peptide;Acc:NP_715638]
PicTar	NARG1	NMDA receptor-regulated protein 1 (N-terminal acetyltransferase) (Tubedown-1 protein) (Tbdn100) (Gastric cancer antigen Ga19).

		[Source:Uniprot/SWISSPROT;Acc:Q9BXJ9]
PicTar	NAT5	N-acetyltransferase 5 (EC 2.3.1.-). [Source:Uniprot/SWISSPROT;Acc:P61599]
PicTar	NAT5	N-acetyltransferase 5 (EC 2.3.1.-). [Source:Uniprot/SWISSPROT;Acc:P61599]
TargetScanS	NAT5	N-acetyltransferase 5 (EC 2.3.1.-). [Source:Uniprot/SWISSPROT;Acc:P61599]
TargetScanS	NBEA	Protein neurobeachin (Lysosomal trafficking regulator 2) (Protein BCL8B). [Source:Uniprot/SWISSPROT;Acc:Q8NFP9]
PicTar	NCALD	Neurocalcin delta. [Source:Uniprot/SWISSPROT;Acc:P61601]
TargetScanS	NCALD	Neurocalcin delta. [Source:Uniprot/SWISSPROT;Acc:P61601]
miRanda	NCN	neurochondrin isoform 1 [Source:RefSeq_peptide;Acc:NP_055099]
PicTar	NCOA2	Nuclear receptor coactivator 2 (NCoA-2) (Transcriptional intermediary factor 2). [Source:Uniprot/SWISSPROT;Acc:Q15596]
TargetScanS	NCOA2	Nuclear receptor coactivator 2 (NCoA-2) (Transcriptional intermediary factor 2). [Source:Uniprot/SWISSPROT;Acc:Q15596]
miRanda	NCOA2	Nuclear receptor coactivator 2 (NCoA-2) (Transcriptional intermediary factor 2). [Source:Uniprot/SWISSPROT;Acc:Q15596]
		Bifunctional heparan sulfate N-deacetylase/N-sulfotransferase 2 (EC 2.8.2.8) (Glucosaminyl N-deacetylase/N-sulfotransferase 2) (NDST- 2) (N-heparan sulfate sulfotransferase 2) (N-HSST 2) [Includes: Heparan sulfate N-deacetylase 2 (3,-,-,-); Heparan sulfat
miRanda	NDST2	[Source:Uniprot/SWISSPROT;Acc:P52849]
		Neurofilament triplet H protein (200 kDa neurofilament protein) (Neurofilament heavy polypeptide) (NF-H).
miRanda	NEFH	[Source:Uniprot/SWISSPROT;Acc:P12036]
miRanda	NEUROD1	Neurogenic differentiation factor 1 (NeuroD1) (NeuroD). [Source:Uniprot/SWISSPROT;Acc:Q13562]
miRanda	NEUROG2	Neurogenin 2. [Source:Uniprot/SWISSPROT;Acc:Q9HZA3]
PicTar	NFAT5	Nuclear factor of activated T cells 5 (T cell transcription factor NFAT5) (NF-AT5) (Tonicity-responsive enhancer-binding protein) (TonE-binding protein) (TonEBP). [Source:Uniprot/SWISSPROT;Acc:Q94916]
PicTar	NFAT5	Nuclear factor of activated T cells 5 (T cell transcription factor NFAT5) (NF-AT5) (Tonicity-responsive enhancer-binding protein) (TonE-binding protein) (TonEBP). [Source:Uniprot/SWISSPROT;Acc:Q94916]
TargetScanS	NFAT5	Nuclear factor of activated T cells 5 (T cell transcription factor NFAT5) (NF-AT5) (Tonicity-responsive enhancer-binding protein) (TonE-binding protein) (TonEBP). [Source:Uniprot/SWISSPROT;Acc:Q94916]
PicTar	NIPBL	Nipped-B-like protein (Delangin) (SCC2 homolog). [Source:Uniprot/SWISSPROT;Acc:Q6KC79]
TargetScanS	NIPBL	Nipped-B-like protein (Delangin) (SCC2 homolog). [Source:Uniprot/SWISSPROT;Acc:Q6KC79]
PicTar	NKX2-2	Homeobox protein Nkx-2.2 (Homeobox protein NK-2 homolog B). [Source:Uniprot/SWISSPROT;Acc:Q95096]
PicTar	NLK	Serine/threonine kinase NLK (EC 2.7.1.37) (Nemo-like kinase) (LAK1 protein). [Source:Uniprot/SWISSPROT;Acc:Q9UBE8]
TargetScanS	NLK	Serine/threonine kinase NLK (EC 2.7.1.37) (Nemo-like kinase) (LAK1 protein). [Source:Uniprot/SWISSPROT;Acc:Q9UBE8]
PicTar	NMT2	Glycylpeptide N-tetradecanoyltransferase 2 (EC 2.3.1.97) (Peptide N- myristoyltransferase 2) (Myristoyl-CoA:protein N-myristoyltransferase 2) (NMT 2) (Type II N-myristoyltransferase). [Source:Uniprot/SWISSPROT;Acc:Q60551]
TargetScanS	NMT2	Glycylpeptide N-tetradecanoyltransferase 2 (EC 2.3.1.97) (Peptide N- myristoyltransferase 2) (Myristoyl-CoA:protein N-myristoyltransferase 2) (NMT 2) (Type II N-myristoyltransferase). [Source:Uniprot/SWISSPROT;Acc:Q60551]
TargetScanS	NOG	Noggin precursor. [Source:Uniprot/SWISSPROT;Acc:Q13253]
PicTar	NOVA1	RNA-binding protein Nova-1 (Neuro-oncological ventral antigen 1) (Onconeural ventral antigen 1) (Paraneoplastic Ri antigen) (Ventral neuron-specific protein 1). [Source:Uniprot/SWISSPROT;Acc:P51513]
TargetScanS	NOVA1	RNA-binding protein Nova-1 (Neuro-oncological ventral antigen 1) (Onconeural ventral antigen 1) (Paraneoplastic Ri antigen) (Ventral neuron-specific protein 1). [Source:Uniprot/SWISSPROT;Acc:P51513]
PicTar	NPC1	Niemann-Pick C1 protein precursor. [Source:Uniprot/SWISSPROT;Acc:O15118]
TargetScanS	NPD014	
PicTar	NPEPPS	Puromycin-sensitive aminopeptidase (EC 3.4.11.-) (PSA). [Source:Uniprot/SWISSPROT;Acc:P55786]
TargetScanS	NPEPPS	Puromycin-sensitive aminopeptidase (EC 3.4.11.-) (PSA). [Source:Uniprot/SWISSPROT;Acc:P55786]
miRanda	NPEPPS	Puromycin-sensitive aminopeptidase (EC 3.4.11.-) (PSA). [Source:Uniprot/SWISSPROT;Acc:P55786]
PicTar	NPM1	Nucleophosmin (NPM) (Nucleolar phosphoprotein B23) (Numatrin) (Nucleolar protein NO38). [Source:Uniprot/SWISSPROT;Acc:P06748]
PicTar	NPTN	Stromal cell-derived receptor 1 precursor (SDR-1). [Source:Uniprot/SWISSPROT;Acc:Q9Y639]
PicTar	NPTXR	Neuronal pentraxin receptor. [Source:Uniprot/SWISSPROT;Acc:Q95502]
PicTar	NPTXR	Neuronal pentraxin receptor. [Source:Uniprot/SWISSPROT;Acc:Q95502]
TargetScanS	NPTXR	Neuronal pentraxin receptor. [Source:Uniprot/SWISSPROT;Acc:Q95502]
miRanda	NR1D2	Orphan nuclear receptor NR1D2 (Rev-erb-beta) (EAR-1R) (Orphan nuclear hormone receptor BD73). [Source:Uniprot/SWISSPROT;Acc:Q14995]
PicTar	NR4A3	Orphan nuclear receptor NR4A3 (Nuclear hormone receptor NOR-1) (Neuron-derived orphan receptor 1) (Mitogen-induced nuclear orphan receptor). [Source:Uniprot/SWISSPROT;Acc:Q92570]
PicTar	NR4A3	Orphan nuclear receptor NR4A3 (Nuclear hormone receptor NOR-1) (Neuron-derived orphan receptor 1) (Mitogen-induced nuclear orphan receptor). [Source:Uniprot/SWISSPROT;Acc:Q92570]
PicTar	NR4A3	Orphan nuclear receptor NR4A3 (Nuclear hormone receptor NOR-1) (Neuron-derived orphan receptor 1) (Mitogen-induced nuclear orphan receptor). [Source:Uniprot/SWISSPROT;Acc:Q92570]
TargetScanS	NR4A3	Orphan nuclear receptor NR4A3 (Nuclear hormone receptor NOR-1) (Neuron-derived orphan receptor 1) (Mitogen-induced nuclear orphan receptor). [Source:Uniprot/SWISSPROT;Acc:Q92570]
miRanda	NR4A3	Orphan nuclear receptor NR4A3 (Nuclear hormone receptor NOR-1) (Neuron-derived orphan receptor 1) (Mitogen-induced nuclear orphan receptor). [Source:Uniprot/SWISSPROT;Acc:Q92570]
DIANA-microT	NR6A1	Orphan nuclear receptor NR6A1 (Germ cell nuclear factor) (GCNF) (Retinoid receptor-related testis-specific receptor) (RTR). [Source:Uniprot/SWISSPROT;Acc:Q15406]
PicTar	NR6A1	Orphan nuclear receptor NR6A1 (Germ cell nuclear factor) (GCNF) (Retinoid receptor-related testis-specific receptor) (RTR). [Source:Uniprot/SWISSPROT;Acc:Q15406]
TargetScanS	NR6A1	Orphan nuclear receptor NR6A1 (Germ cell nuclear factor) (GCNF) (Retinoid receptor-related testis-specific receptor) (RTR). [Source:Uniprot/SWISSPROT;Acc:Q15406]
miRanda	NRP1	Neuropilin-1 precursor (Vascular endothelial cell growth factor 165 receptor) (CD304 antigen). [Source:Uniprot/SWISSPROT;Acc:O14786]
TargetScanS	NRXN1	
PicTar	NSMAF	Protein FAN (Factor associated with N-SMase activation) (Factor associated with neutral sphingomyelinase activation). [Source:Uniprot/SWISSPROT;Acc:Q92636]
TargetScanS	NSMAF	Protein FAN (Factor associated with N-SMase activation) (Factor associated with neutral sphingomyelinase activation). [Source:Uniprot/SWISSPROT;Acc:Q92636]
miRanda	NUP153	Nuclear pore complex protein Nup153 (Nucleoporin Nup153) (153 kDa nucleoporin). [Source:Uniprot/SWISSPROT;Acc:P49790]
PicTar	OACT2	O-acyltransferase (membrane bound) domain containing 2 [Source:RefSeq_peptide;Acc:NP_620154]
TargetScanS	OACT2	O-acyltransferase (membrane bound) domain containing 2 [Source:RefSeq_peptide;Acc:NP_620154]
miRanda	OACT2	O-acyltransferase (membrane bound) domain containing 2 [Source:RefSeq_peptide;Acc:NP_620154]
miRanda	OFD1	Oral-facial-digital syndrome 1 protein (Protein 71-7A). [Source:Uniprot/SWISSPROT;Acc:Q75665]
PicTar	OGT	UDP-N-acetylglucosamine-peptide N-acetylglucosaminyltransferase 110 kDa subunit (EC 2.4.1.-) (O-GlcNAc transferase p110 subunit). [Source:Uniprot/SWISSPROT;Acc:O15294]
PicTar	OGT	UDP-N-acetylglucosamine-peptide N-acetylglucosaminyltransferase 110 kDa subunit (EC 2.4.1.-) (O-GlcNAc transferase p110 subunit). [Source:Uniprot/SWISSPROT;Acc:O15294]
TargetScanS	OGT	UDP-N-acetylglucosamine-peptide N-acetylglucosaminyltransferase 110 kDa subunit (EC 2.4.1.-) (O-GlcNAc transferase p110 subunit). [Source:Uniprot/SWISSPROT;Acc:O15294]
DIANA-microT	OPN1SW	Blue-sensitive opsin (BOP) (Blue cone photoreceptor pigment). [Source:Uniprot/SWISSPROT;Acc:P03999]
PicTar	OSBP.L3	Oxysterol-binding protein-related protein 3 (OSBP-related protein 3) (ORP-3). [Source:Uniprot/SWISSPROT;Acc:Q9H4L5]
TargetScanS	OSBP.L3	Oxysterol-binding protein-related protein 3 (OSBP-related protein 3) (ORP-3). [Source:Uniprot/SWISSPROT;Acc:Q9H4L5]
PicTar	OSBP.L8	Oxysterol-binding protein-related protein 8 (OSBP-related protein 8) (ORP-8). [Source:Uniprot/SWISSPROT;Acc:Q9BZF1]
PicTar	OSBP.L8	Oxysterol-binding protein-related protein 8 (OSBP-related protein 8) (ORP-8). [Source:Uniprot/SWISSPROT;Acc:Q9BZF1]
TargetScanS	OSBP.L8	Oxysterol-binding protein-related protein 8 (OSBP-related protein 8) (ORP-8). [Source:Uniprot/SWISSPROT;Acc:Q9BZF1]
miRanda	OSBP.L8	Oxysterol-binding protein-related protein 8 (OSBP-related protein 8) (ORP-8). [Source:Uniprot/SWISSPROT;Acc:Q9BZF1]
miRanda	OTUD1	OTU domain containing 1. [Source:Uniprot/SPTREMBL;Acc:Q5VV17]
PicTar	OTUD4	OTU domain-containing protein 4 (HIV-1-induced protein HIN-1). [Source:Uniprot/SWISSPROT;Acc:Q01804]
miRanda	PACS2	phosphofurin acidic cluster sorting protein 2 [Source:RefSeq_peptide;Acc:NP_056012]
TargetScanS	PAFAH1B1	Platelet-activating factor acetylhydrolase IB alpha subunit (PAF acetylhydrolase 45 kDa subunit) (PAF-AH 45 kDa subunit) (PAF-AH alpha) (PAFAH alpha) (Lissencephaly-1 protein) (LIS-1). [Source:Uniprot/SWISSPROT;Acc:P43034]
miRanda	PAIP1	Polyadenylate-binding protein-interacting protein 1 (Poly(A)-binding protein-interacting protein 1) (PABP-interacting protein 1) (PAIP-1). [Source:Uniprot/SWISSPROT;Acc:Q9H074]

PicTar	PAK4	Serine/threonine-protein kinase PAK 4 (EC 2.7.1.37) (p21-activated kinase 4) (PAK-4). [Source:Uniprot/SWISSPROT;Acc:O96013]
TargetScanS	PAK4	Serine/threonine-protein kinase PAK 4 (EC 2.7.1.37) (p21-activated kinase 4) (PAK-4). [Source:Uniprot/SWISSPROT;Acc:O96013]
TargetScanS	PAK7	Serine/threonine-protein kinase PAK 7 (EC 2.7.1.37) (p21-activated kinase 7) (PAK-7) (PAK-5). [Source:Uniprot/SWISSPROT;Acc:Q9P286]
PicTar	PAM	Peptidyl-glycine alpha-amidating monooxygenase precursor (EC 1.14.17.3) (PAM). [Source:Uniprot/SWISSPROT;Acc:P19021]
TargetScanS	PAM	Peptidyl-glycine alpha-amidating monooxygenase precursor (EC 1.14.17.3) (PAM). [Source:Uniprot/SWISSPROT;Acc:P19021]
PicTar	PAPOLG	Poly(A) polymerase gamma (EC 2.7.7.19) (PAP gamma) (Polynucleotide adenyllyltransferase gamma) (SRP RNA 3' adenylating enzyme). [Source:Uniprot/SWISSPROT;Acc:Q9BWT3]
TargetScanS	PAPOLG	Poly(A) polymerase gamma (EC 2.7.7.19) (PAP gamma) (Polynucleotide adenyllyltransferase gamma) (SRP RNA 3' adenylating enzyme). [Source:Uniprot/SWISSPROT;Acc:Q9BWT3]
miRanda	PAPOLG	Poly(A) polymerase gamma (EC 2.7.7.19) (PAP gamma) (Polynucleotide adenyllyltransferase gamma) (SRP RNA 3' adenylating enzyme). [Source:Uniprot/SWISSPROT;Acc:Q9BWT3]
miRanda	PARP8	poly (ADP-ribose) polymerase family, member 8 [Source:RefSeq_peptide;Acc:NP_078891]
PicTar	PAWR	PRKC apoptosis WT1 regulator protein (Prostate apoptosis response-4 protein) (Par-4). [Source:Uniprot/SWISSPROT;Acc:Q96IZ0]
PicTar	PBX3	Pre-B-cell leukemia transcription factor 3 (Homeobox protein PBX3). [Source:Uniprot/SWISSPROT;Acc:P40426]
TargetScanS	PBX3	Pre-B-cell leukemia transcription factor 3 (Homeobox protein PBX3). [Source:Uniprot/SWISSPROT;Acc:P40426]
PicTar	PCAF	Histone acetyltransferase PCAF (EC 2.3.1.48) (P300/CBP-associated factor) (P/CAF) (Histone acetylase PCAF). [Source:Uniprot/SWISSPROT;Acc:Q92831]
TargetScanS	PCAF	Histone acetyltransferase PCAF (EC 2.3.1.48) (P300/CBP-associated factor) (P/CAF) (Histone acetylase PCAF). [Source:Uniprot/SWISSPROT;Acc:Q92831]
PicTar	PCBP1	Poly(rC)-binding protein 1 (Alpha-CP1) (hnrNP-E1) (Nucleic acid-binding protein SUB2.3). [Source:Uniprot/SWISSPROT;Acc:Q15365]
miRanda	PCDH8	Protocadherin 8 precursor (Arcadlin). [Source:Uniprot/SWISSPROT;Acc:O95206]
PicTar	PCDHA1	Protocadherin alpha 1 precursor (PCDH-alpha1). [Source:Uniprot/SWISSPROT;Acc:Q9Y5I3]
TargetScanS	PCDHA1	Protocadherin alpha 1 precursor (PCDH-alpha1). [Source:Uniprot/SWISSPROT;Acc:Q9Y5I3]
TargetScanS	PCDHA10	
TargetScanS	PCDHA11	
TargetScanS	PCDHA12	
PicTar	PCDHA13	Protocadherin alpha C2 precursor (PCDH-alpha-C2). [Source:Uniprot/SWISSPROT;Acc:Q9Y5I4]
PicTar	PCDHA13	Protocadherin alpha C2 precursor (PCDH-alpha-C2). [Source:Uniprot/SWISSPROT;Acc:Q9Y5I4]
TargetScanS	PCDHA13	Protocadherin alpha C2 precursor (PCDH-alpha-C2). [Source:Uniprot/SWISSPROT;Acc:Q9Y5I4]
TargetScanS	PCDHA2	Protocadherin alpha 2 precursor (PCDH-alpha2). [Source:Uniprot/SWISSPROT;Acc:Q9Y5H9]
PicTar	PCDHA3	Protocadherin alpha 3 precursor (PCDH-alpha3). [Source:Uniprot/SWISSPROT;Acc:Q9Y5H8]
TargetScanS	PCDHA3	Protocadherin alpha 3 precursor (PCDH-alpha3). [Source:Uniprot/SWISSPROT;Acc:Q9Y5H8]
PicTar	PCDHA4	Protocadherin alpha 4 precursor (PCDH-alpha4). [Source:Uniprot/SWISSPROT;Acc:Q9UN74]
TargetScanS	PCDHA4	Protocadherin alpha 4 precursor (PCDH-alpha4). [Source:Uniprot/SWISSPROT;Acc:Q9UN74]
PicTar	PCDHA5	Protocadherin alpha 5 precursor (PCDH-alpha5). [Source:Uniprot/SWISSPROT;Acc:Q9Y5H7]
TargetScanS	PCDHA5	Protocadherin alpha 5 precursor (PCDH-alpha5). [Source:Uniprot/SWISSPROT;Acc:Q9Y5H7]
PicTar	PCDHA6	Protocadherin alpha 6 precursor (PCDH-alpha6). [Source:Uniprot/SWISSPROT;Acc:Q9UN73]
TargetScanS	PCDHA6	Protocadherin alpha 6 precursor (PCDH-alpha6). [Source:Uniprot/SWISSPROT;Acc:Q9UN73]
PicTar	PCDHA7	Protocadherin alpha 7 precursor (PCDH-alpha7). [Source:Uniprot/SWISSPROT;Acc:Q9UN72]
TargetScanS	PCDHA7	Protocadherin alpha 7 precursor (PCDH-alpha7). [Source:Uniprot/SWISSPROT;Acc:Q9UN72]
PicTar	PCDHA8	Protocadherin alpha 8 precursor (PCDH-alpha8). [Source:Uniprot/SWISSPROT;Acc:Q9Y5H6]
TargetScanS	PCDHA8	Protocadherin alpha 8 precursor (PCDH-alpha8). [Source:Uniprot/SWISSPROT;Acc:Q9Y5H6]
PicTar	PCDHA9	Protocadherin alpha 9 precursor (PCDH-alpha9). [Source:Uniprot/SWISSPROT;Acc:Q9Y5H5]
TargetScanS	PCDHA9	Protocadherin alpha 9 precursor (PCDH-alpha9). [Source:Uniprot/SWISSPROT;Acc:Q9Y5H5]
PicTar	PCDHAC1	Protocadherin alpha C2 precursor (PCDH-alpha-C2). [Source:Uniprot/SWISSPROT;Acc:Q9Y5I4]
TargetScanS	PCDHAC1	Protocadherin alpha C2 precursor (PCDH-alpha-C2). [Source:Uniprot/SWISSPROT;Acc:Q9Y5I4]
PicTar	PCDHAC2	Protocadherin alpha C2 precursor (PCDH-alpha-C2). [Source:Uniprot/SWISSPROT;Acc:Q9Y5I4]
TargetScanS	PCDHAC2	Protocadherin alpha C2 precursor (PCDH-alpha-C2). [Source:Uniprot/SWISSPROT;Acc:Q9Y5I4]
PicTar	PCF11	Pre-mRNA cleavage complex II protein Pcf11 (Fragment). [Source:Uniprot/SWISSPROT;Acc:O94913]
PicTar	PCGF2	Polycomb group RING finger protein 2 (DNA-binding protein Mel-18) (RING finger protein 110) (Zinc finger protein 144). [Source:Uniprot/SWISSPROT;Acc:P35227]
TargetScanS	PCGF2	Polycomb group RING finger protein 2 (DNA-binding protein Mel-18) (RING finger protein 110) (Zinc finger protein 144). [Source:Uniprot/SWISSPROT;Acc:P35227]
TargetScanS	PCNP	
TargetScanS	PCTK2	Serine/threonine-protein kinase PCTAIRE-2 (EC 2.7.1.37) (PCTAIRE-motif protein kinase 2). [Source:Uniprot/SWISSPROT;Acc:Q00537]
miRanda	PCTK2	Serine/threonine-protein kinase PCTAIRE-2 (EC 2.7.1.37) (PCTAIRE-motif protein kinase 2). [Source:Uniprot/SWISSPROT;Acc:Q00537]
TargetScanS	PDCD4	programmed cell death 4 isoform 1 [Source:RefSeq_peptide;Acc:NP_055271]
PicTar	PDE3A	cGMP-inhibited 3',5'-cyclic phosphodiesterase A (EC 3.1.4.17) (Cyclic GMP-inhibited phosphodiesterase A) (CGI-PDE A). [Source:Uniprot/SWISSPROT;Acc:Q14432]
TargetScanS	PDE3A	cGMP-inhibited 3',5'-cyclic phosphodiesterase A (EC 3.1.4.17) (Cyclic GMP-inhibited phosphodiesterase A) (CGI-PDE A). [Source:Uniprot/SWISSPROT;Acc:Q14432]
PicTar	PDGFRA	Alpha platelet-derived growth factor receptor precursor (EC 2.7.1.112) (PDGF-R-alpha) (CD140a antigen). [Source:Uniprot/SWISSPROT;Acc:P16234]
TargetScanS	PDGFRA	Alpha platelet-derived growth factor receptor precursor (EC 2.7.1.112) (PDGF-R-alpha) (CD140a antigen). [Source:Uniprot/SWISSPROT;Acc:P16234]
TargetScanS	PDHX	Pyruvate dehydrogenase protein X component, mitochondrial precursor (Dihydrolipoamide dehydrogenase-binding protein of pyruvate dehydrogenase complex) (Lipoyl-containing pyruvate dehydrogenase complex component X) (E3-binding protein) (E3BP) (proX). [Source:Uniprot/SWISSPROT;Acc:O00330]
miRanda	PDIA5	Protein disulfide-isomerase A5 precursor (EC 5.3.4.1) (Protein disulfide isomerase-related protein). [Source:Uniprot/SWISSPROT;Acc:Q14554]
PicTar	PDIA6	Protein disulfide-isomerase A6 precursor (EC 5.3.4.1) (Protein disulfide isomerase P5) (Thioredoxin domain-containing protein 7). [Source:Uniprot/SWISSPROT;Acc:Q15084]
TargetScanS	PDIA6	Protein disulfide-isomerase A6 precursor (EC 5.3.4.1) (Protein disulfide isomerase P5) (Thioredoxin domain-containing protein 7). [Source:Uniprot/SWISSPROT;Acc:Q15084]
PicTar	PKD4	[Pyruvate dehydrogenase [lipoamide]] kinase isozyme 4, mitochondrial precursor (EC 2.7.1.99) (Pyruvate dehydrogenase kinase isoform 4). [Source:Uniprot/SWISSPROT;Acc:Q16654]
TargetScanS	PKD4	[Pyruvate dehydrogenase [lipoamide]] kinase isozyme 4, mitochondrial precursor (EC 2.7.1.99) (Pyruvate dehydrogenase kinase isoform 4). [Source:Uniprot/SWISSPROT;Acc:Q16654]
miRanda	PEL12	Protein pellino homolog 2 (Pellino-2). [Source:Uniprot/SWISSPROT;Acc:Q9HAT8]
PicTar	PER2	Period circadian protein 2. [Source:Uniprot/SWISSPROT;Acc:O15055]
TargetScanS	PER2	Period circadian protein 2. [Source:Uniprot/SWISSPROT;Acc:O15055]
miRanda	PHF12	PHD finger protein 12 (PHD factor 1) (Pfi). [Source:Uniprot/SWISSPROT;Acc:Q96QT6]
PicTar	PHF15	PHD finger protein 15. [Source:Uniprot/SWISSPROT;Acc:Q9NQCI]
TargetScanS	PHF15	PHD finger protein 15. [Source:Uniprot/SWISSPROT;Acc:Q9NQCI]
TargetScanS	PHF2	PHD finger protein 2 (GRCS). [Source:Uniprot/SWISSPROT;Acc:O75151]
TargetScanS	PHF20L1	PHD finger protein 20-like 1 isoform 2 [Source:RefSeq_peptide;Acc:NP_940915]
PicTar	PHF3	PHD finger protein 3. [Source:Uniprot/SWISSPROT;Acc:Q92576]
TargetScanS	PHF3	PHD finger protein 3. [Source:Uniprot/SWISSPROT;Acc:Q92576]
PicTar	PHIP	pleckstrin homology domain interacting protein [Source:RefSeq_peptide;Acc:NP_060404]
PicTar	PHLDA1	Pleckstrin homology-like domain family A member 1 (T-cell death-associated gene 51 protein) (Apoptosis-associated nuclear protein) (Proline- and histidine-rich protein) (Proline- and glutamine-rich protein) (PQ-rich protein). [Source:Uniprot/SWISSPROT;Acc:Q8WV24]
TargetScanS	PHLDA1	Pleckstrin homology-like domain family A member 1 (T-cell death-associated gene 51 protein) (Apoptosis-associated nuclear protein) (Proline- and histidine-rich protein) (Proline- and glutamine-rich protein) (PQ-rich protein). [Source:Uniprot/SWISSPROT;Acc:Q8WV24]
PicTar	PHOX2B	Paired mesoderm homeobox protein 2B (Paired-like homeobox 2B) (PHOX2B homeodomain protein) (Neuroblastoma Phox) (NBPhox). [Source:Uniprot/SWISSPROT;Acc:Q99453]
TargetScanS	PHOX2B	Paired mesoderm homeobox protein 2B (Paired-like homeobox 2B) (PHOX2B homeodomain protein) (Neuroblastoma Phox) (NBPhox). [Source:Uniprot/SWISSPROT;Acc:Q99453]
TargetScanS	PHTF2	putative homeodomain transcription factor 2 [Source:RefSeq_peptide;Acc:NP_065165]

TargetScanS	PI4K2B	phosphatidylinositol 4-kinase type-II beta [Source:RefSeq_peptide;Acc:NP_060793]
TargetScanS	PI4KII	
PicTar	PIAS3	Protein inhibitor of activated STAT protein 3. [Source:Uniprot/SWISSPROT;Acc:Q9Y6X2]
TargetScanS	PICALM	Phosphatidylinositol-binding clathrin assembly protein (Clathrin assembly lymphoid myeloid leukemia protein). [Source:Uniprot/SWISSPROT;Acc:Q13492]
PicTar	PIK3R3	Phosphatidylinositol 3-kinase regulatory gamma subunit (PI3-kinase p85-gamma subunit) (PtdIns-3-kinase p85-gamma) (p55PIK). [Source:Uniprot/SWISSPROT;Acc:Q92569]
TargetScanS	PIK3R3	Phosphatidylinositol 3-kinase regulatory gamma subunit (PI3-kinase p85-gamma subunit) (PtdIns-3-kinase p85-gamma) (p55PIK). [Source:Uniprot/SWISSPROT;Acc:Q92569]
TargetScanS	PIP3AP	
PicTar	PKNOX1	Homeobox protein PKNOX1 (PBX/knotted homeobox 1) (Homeobox protein PREP-1). [Source:Uniprot/SWISSPROT;Acc:P55347]
PicTar	PKNOX2	Homeobox protein PKNOX2 (PBX/knotted homeobox 2) (Homeobox protein PREP-2). [Source:Uniprot/SWISSPROT;Acc:Q96KN3]
TargetScanS	PKNOX2	Homeobox protein PKNOX2 (PBX/knotted homeobox 2) (Homeobox protein PREP-2). [Source:Uniprot/SWISSPROT;Acc:Q96KN3]
miRanda	PKNOX2	Homeobox protein PKNOX2 (PBX/knotted homeobox 2) (Homeobox protein PREP-2). [Source:Uniprot/SWISSPROT;Acc:Q96KN3]
PicTar	PLAG1	pleiomorphic adenoma gene 1 [Source:RefSeq_peptide;Acc:NP_002646]
TargetScanS	PLAG1	pleiomorphic adenoma gene 1 [Source:RefSeq_peptide;Acc:NP_002646]
PicTar	PLCL2	phospholipase C-like 2 [Source:RefSeq_peptide;Acc:NP_055999]
TargetScanS	PLCL2	phospholipase C-like 2 [Source:RefSeq_peptide;Acc:NP_055999]
TargetScanS	PLEKHA3	Pleckstrin homology domain-containing family A member 3 (Phosphoinositol 4-phosphate adaptor protein 1) (FAPP-1). [Source:Uniprot/SWISSPROT;Acc:Q9HB20]
miRanda	PLEKHA3	Pleckstrin homology domain-containing family A member 3 (Phosphoinositol 4-phosphate adaptor protein 1) (FAPP-1). [Source:Uniprot/SWISSPROT;Acc:Q9HB20]
PicTar	PLEKHJ1	pleckstrin homology domain containing, family J member 1 [Source:RefSeq_peptide;Acc:NP_060519]
TargetScanS	PLEKHJ1	pleckstrin homology domain containing, family J member 1 [Source:RefSeq_peptide;Acc:NP_060519]
TargetScanS	PLS1	Plastin-1 (I-plastin) (Intestine-specific plastin). [Source:Uniprot/SWISSPROT;Acc:Q14651]
TargetScanS	PLS3	Plastin-3 (T-plastin). [Source:Uniprot/SWISSPROT;Acc:P13797]
PicTar	PNRC2	Proline-rich nuclear receptor coactivator 2. [Source:Uniprot/SWISSPROT;Acc:Q9NPJ4]
TargetScanS	PNRC2	Proline-rich nuclear receptor coactivator 2. [Source:Uniprot/SWISSPROT;Acc:Q9NPJ4]
TargetScanS	PODXL	Podocalyxin-like protein 1 precursor. [Source:Uniprot/SWISSPROT;Acc:O00592]
TargetScanS	POM121	Nuclear envelope pore membrane protein POM 121 (Pore membrane protein of 121 kDa) (P145). [Source:Uniprot/SWISSPROT;Acc:Q9Y2N3]
miRanda	POM121	Nuclear envelope pore membrane protein POM 121 (Pore membrane protein of 121 kDa) (P145). [Source:Uniprot/SWISSPROT;Acc:Q9Y2N3]
miRanda	POU3F1	POU domain, class 3, transcription factor 1 (Octamer-binding transcription factor 6) (Oct-6) (POU-domain transcription factor SCIP). [Source:Uniprot/SWISSPROT;Acc:Q03052]
miRanda	POU3F2	POU domain, class 3, transcription factor 2 (Nervous system-specific octamer-binding transcription factor N-Oct-3) (Brain-specific homeobox/POU domain protein 2) (Brain-2) (Protein Brn-2). [Source:Uniprot/SWISSPROT;Acc:P20265]
TargetScanS	PPAP2B	Lipid phosphate phosphohydrolase 3 (EC 3.1.3.4) (Phosphatidic acid phosphatase 2b) (Phosphatidate phosphohydrolase type 2b) (PAP2b) (PAP- 2b) (PAP2-beta) (Vascular endothelial growth factor and type I collagen-inducible protein) (VCIP). [Source:Uniprot/SWISSPROT;Acc:O14495]
miRanda	PPAP2B	Lipid phosphate phosphohydrolase 3 (EC 3.1.3.4) (Phosphatidic acid phosphatase 2b) (Phosphatidate phosphohydrolase type 2b) (PAP2b) (PAP- 2b) (PAP2-beta) (Vascular endothelial growth factor and type I collagen-inducible protein) (VCIP). [Source:Uniprot/SWISSPROT;Acc:O14495]
PicTar	PPARGC1A	Peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PPAR gamma coactivator 1-alpha) (PPARGC-1-alpha) (PGC-1-alpha) (Ligand effect modulator 6). [Source:Uniprot/SWISSPROT;Acc:Q9UBK2]
TargetScanS	PPFIA1	Liprin-alpha-1 (Protein tyrosine phosphatase receptor type f polypeptide-interacting protein alpha-1) (PTPRF-interacting protein alpha-1) (LAR-interacting protein 1) (LIP.1). [Source:Uniprot/SWISSPROT;Acc:Q13136]
miRanda	PPIL1	Peptidyl-prolyl cis-trans isomerase-like 1 (EC 5.2.1.8) (PPIase) (Rotamase). [Source:Uniprot/SWISSPROT;Acc:Q9Y3C6]
TargetScanS	PPM1B	Protein phosphatase 2C isoform beta (EC 3.1.3.16) (PP2C-beta). [Source:Uniprot/SWISSPROT;Acc:O75688]
miRanda	PPM1E	protein phosphatase 1E [Source:RefSeq_peptide;Acc:NP_055721]
PicTar	PPP1CB	Serine/threonine-protein phosphatase PPI-1-beta catalytic subunit (EC 3.1.3.16) (PP-1B). [Source:Uniprot/SWISSPROT;Acc:P62140]
PicTar	PPP1CB	Serine/threonine-protein phosphatase PPI-1-beta catalytic subunit (EC 3.1.3.16) (PP-1B). [Source:Uniprot/SWISSPROT;Acc:P62140]
TargetScanS	PPP1CB	Serine/threonine-protein phosphatase PPI-1-beta catalytic subunit (EC 3.1.3.16) (PP-1B). [Source:Uniprot/SWISSPROT;Acc:P62140]
PicTar	PPP1R12B	Protein phosphatase 1 regulatory subunit 12B (Myosin phosphatase targeting subunit 2) (Myosin phosphatase target subunit 2). [Source:Uniprot/SWISSPROT;Acc:O60237]
TargetScanS	PPP1R12B	Protein phosphatase 1 regulatory subunit 12B (Myosin phosphatase targeting subunit 2) (Myosin phosphatase target subunit 2). [Source:Uniprot/SWISSPROT;Acc:O60237]
miRanda	PPP3CA	Serine/threonine-protein phosphatase 2B catalytic subunit alpha isoform (EC 3.1.3.16) (Calmodulin-dependent calcineurin A subunit alpha isoform) (CAM-FRP catalytic subunit). [Source:Uniprot/SWISSPROT;Acc:Q08209]
PicTar	PPP3R1	Calcineurin subunit B isoform 1 (Protein phosphatase 2B regulatory subunit 1) (Protein phosphatase 3 regulatory subunit B alpha isoform 1). [Source:Uniprot/SWISSPROT;Acc:P63098]
TargetScanS	PPP3R1	Calcineurin subunit B isoform 1 (Protein phosphatase 2B regulatory subunit 1) (Protein phosphatase 3 regulatory subunit B alpha isoform 1). [Source:Uniprot/SWISSPROT;Acc:P63098]
PicTar	PRDM10	PR-domain zinc finger protein 10. [Source:Uniprot/SWISSPROT;Acc:Q9NQV6]
PicTar	PRDM10	PR-domain zinc finger protein 10. [Source:Uniprot/SWISSPROT;Acc:Q9NQV6]
TargetScanS	PRICKLE2	Prickle-like protein 2. [Source:Uniprot/SWISSPROT;Acc:Q7Z3G6]
TargetScanS	PRKAG2	5'-AMP-activated protein kinase, gamma-2 subunit (AMPK gamma-2 chain) (AMPK gamma2) (H91620p). [Source:Uniprot/SWISSPROT;Acc:Q9UGJ0]
miRanda	PRKAG2	5'-AMP-activated protein kinase, gamma-2 subunit (AMPK gamma-2 chain) (AMPK gamma2) (H91620p). [Source:Uniprot/SWISSPROT;Acc:Q9UGJ0]
PicTar	PRKCD	Protein kinase C delta type (EC 2.7.1.-) (nPKC-delta). [Source:Uniprot/SWISSPROT;Acc:Q05655]
PicTar	PRKCD	Protein kinase C delta type (EC 2.7.1.-) (nPKC-delta). [Source:Uniprot/SWISSPROT;Acc:Q05655]
TargetScanS	PRKCD	Protein kinase C delta type (EC 2.7.1.-) (nPKC-delta). [Source:Uniprot/SWISSPROT;Acc:Q05655]
miRanda	PRKCD	Protein kinase C delta type (EC 2.7.1.-) (nPKC-delta). [Source:Uniprot/SWISSPROT;Acc:Q05655]
PicTar	PRKCE	Protein kinase C epsilon type (EC 2.7.1.-) (nPKC-epsilon). [Source:Uniprot/SWISSPROT;Acc:Q02156]
TargetScanS	PRKCE	Protein kinase C epsilon type (EC 2.7.1.-) (nPKC-epsilon). [Source:Uniprot/SWISSPROT;Acc:Q02156]
TargetScanS	PROX1	Homeobox prospero-like protein PROX1 (PROX 1). [Source:Uniprot/SWISSPROT;Acc:Q92786]
PicTar	PSAP	Proactivator polypeptide precursor [Contains: Saposin A (Protein A); Saposin B-Val; Saposin B (Sphingolipid activator protein 1) (SAP-1) (Cerebroside sulfate activator) (CSAct) (Dispersin) (Sulfatide/GM1 activator); Saposin C (Co-beta-glucosidase) (A1 act [Source:Uniprot/SWISSPROT;Acc:P07602]
TargetScanS	PSAP	Proactivator polypeptide precursor [Contains: Saposin A (Protein A); Saposin B-Val; Saposin B (Sphingolipid activator protein 1) (SAP-1) (Cerebroside sulfate activator) (CSAct) (Dispersin) (Sulfatide/GM1 activator); Saposin C (Co-beta-glucosidase) (A1 act [Source:Uniprot/SWISSPROT;Acc:P07602]
miRanda	PSMF1	Proteasome inhibitor P131 subunit (hP131). [Source:Uniprot/SWISSPROT;Acc:Q92530]
miRanda	PSMF1	Proteasome inhibitor P131 subunit (hP131). [Source:Uniprot/SWISSPROT;Acc:Q92530]
miRanda	PSPC1	paraspeckle protein 1 [Source:RefSeq_peptide;Acc:NP_060752]
miRanda	PTCH	Protein patched homolog 1 (PTC1) (PTC). [Source:Uniprot/SWISSPROT;Acc:Q13635]
miRanda	PTCHD1	patched domain containing 1 [Source:RefSeq_peptide;Acc:NP_775766]
PicTar	PTPN9	Tyrosine-protein phosphatase non-receptor type 9 (EC 3.1.3.48) (Protein-tyrosine phosphatase MEG2) (PTPase-MEG2). [Source:Uniprot/SWISSPROT;Acc:P43378]
TargetScanS	PTPN9	Tyrosine-protein phosphatase non-receptor type 9 (EC 3.1.3.48) (Protein-tyrosine phosphatase MEG2) (PTPase-MEG2). [Source:Uniprot/SWISSPROT;Acc:P43378]
miRanda	PTPRR	Receptor-type tyrosine-protein phosphatase R precursor (EC 3.1.3.48) (Protein-tyrosine phosphatase PCPTP1) (NC-PTPCOM1) (Ch-1PTPase). [Source:Uniprot/SWISSPROT;Acc:Q15256]
PicTar	PUM1	Pumilio homolog 1 (Pumilio-1) (HsPUM). [Source:Uniprot/SWISSPROT;Acc:Q14671]
TargetScanS	PUM1	Pumilio homolog 1 (Pumilio-1) (HsPUM). [Source:Uniprot/SWISSPROT;Acc:Q14671]
miRanda	PUM1	Pumilio homolog 1 (Pumilio-1) (HsPUM). [Source:Uniprot/SWISSPROT;Acc:Q14671]
miRanda	PURA	Transcriptional activator protein Pur-alpha (Purine-rich single- stranded DNA-binding protein alpha). [Source:Uniprot/SWISSPROT;Acc:Q00577]



PicTar	PURB	Transcriptional activator protein Pur-beta (Purine-rich element- binding protein B). [Source:Uniprot/SWISSPROT;Acc:Q96QR8]
TargetScanS	PURB	Transcriptional activator protein Pur-beta (Purine-rich element- binding protein B). [Source:Uniprot/SWISSPROT;Acc:Q96QR8]
miRanda	PURB	Transcriptional activator protein Pur-beta (Purine-rich element- binding protein B). [Source:Uniprot/SWISSPROT;Acc:Q96QR8]
TargetScanS	QKI	quaking homolog, KH domain RNA binding isoform HQK-7 [Source:RefSeq_peptide;Acc:NP_996736]
PicTar	RAB11A	Ras-related protein Rab-11A (Rab-11) (YL8). [Source:Uniprot/SWISSPROT;Acc:P62491]
TargetScanS	RAB11A	Ras-related protein Rab-11A (Rab-11) (YL8). [Source:Uniprot/SWISSPROT;Acc:P62491]
PicTar	RAB11FIP2	Rab11 family-interacting protein 2 (Rab11-FIP2) (NRip11). [Source:Uniprot/SWISSPROT;Acc:Q7L804]
TargetScanS	RAB11FIP2	Rab11 family-interacting protein 2 (Rab11-FIP2) (NRip11). [Source:Uniprot/SWISSPROT;Acc:Q7L804]
TargetScanS	RAB3IL1	RAB3A interacting protein (rabin3)-like 1 [Source:RefSeq_peptide;Acc:NP_037533]
TargetScanS	RABGEF1	Rab5 GDP/GTP exchange factor (Rabaptin 5-associated exchange factor for Rab5) (Rabex-5). [Source:Uniprot/SWISSPROT;Acc:Q9UJ41]
PicTar	RAD21	Double-strand-break repair protein rad21 homolog (hHR21) (Nuclear matrix protein 1) (NXP-1) (SCC1 homolog). [Source:Uniprot/SWISSPROT;Acc:O60216]
TargetScanS	RAD21	Double-strand-break repair protein rad21 homolog (hHR21) (Nuclear matrix protein 1) (NXP-1) (SCC1 homolog). [Source:Uniprot/SWISSPROT;Acc:O60216]
TargetScanS	RAI1	Retinoic acid-induced protein 1. [Source:Uniprot/SWISSPROT;Acc:Q7Z5J4]
TargetScanS	RALA	Ras-related protein Ral-A. [Source:Uniprot/SWISSPROT;Acc:P11233]
PicTar	RAN	GTP-binding nuclear protein Ran (GTPase Ran) (Ras-like protein TC4) (Androgen receptor-associated protein 24). [Source:Uniprot/SWISSPROT;Acc:P62826]
TargetScanS	RAN	GTP-binding nuclear protein Ran (GTPase Ran) (Ras-like protein TC4) (Androgen receptor-associated protein 24). [Source:Uniprot/SWISSPROT;Acc:P62826]
TargetScanS	RANBP5	Importin beta-3 (Karyopherin beta-3) (Ran-binding protein 5) (RanBP5). [Source:Uniprot/SWISSPROT;Acc:O00410]
miRanda	RANBP9	Ran-binding protein 9 (RanBP9) (RanBP7) (Ran-binding protein M) (RanBPM) (BPM90) (BPM-L). [Source:Uniprot/SWISSPROT;Acc:Q96559]
PicTar	RAP1B	Ras-related protein Rap-1b precursor (GTP-binding protein smg p21B). [Source:Uniprot/SWISSPROT;Acc:P61224]
TargetScanS	RAP1B	Ras-related protein Rap-1b precursor (GTP-binding protein smg p21B). [Source:Uniprot/SWISSPROT;Acc:P61224]
TargetScanS	RASL10B	RAS-like, family 10, member B [Source:RefSeq_peptide;Acc:NP_201572]
TargetScanS	RASSF1	Ras association domain family 1 (Ras association, RafGDS/AF-6, domain family 1). [Source:Uniprot/SWISSPROT;Acc:Q9NS23]
PicTar	RBBP7	Histone-binding protein RBBP7 (Retinoblastoma-binding protein 7) (RBBP-7) (Retinoblastoma-binding protein p46) (Histone acetyltransferase type B subunit 2). [Source:Uniprot/SWISSPROT;Acc:Q16576]
TargetScanS	RBBP7	Histone-binding protein RBBP7 (Retinoblastoma-binding protein 7) (RBBP-7) (Retinoblastoma-binding protein p46) (Histone acetyltransferase type B subunit 2). [Source:Uniprot/SWISSPROT;Acc:Q16576]
PicTar	RBM22	RNA binding motif protein 22 [Source:RefSeq_peptide;Acc:NP_060517]
TargetScanS	RBM22	RNA binding motif protein 22 [Source:RefSeq_peptide;Acc:NP_060517]
miRanda	RBM22	RNA binding motif protein 22 [Source:RefSeq_peptide;Acc:NP_060517]
TargetScanS	RBM25	Probable RNA-binding protein 25 (RNA-binding motif protein 25) (RNA- binding region-containing protein 7) (Protein S164). [Source:Uniprot/SWISSPROT;Acc:P49756]
PicTar	RECK	Reversion-inducing cysteine-rich protein with Kazal motifs precursor (hRECK) (Suppressor of tumorigenicity 15) (ST15). [Source:Uniprot/SWISSPROT;Acc:O95980]
miRanda	RECK	Reversion-inducing cysteine-rich protein with Kazal motifs precursor (hRECK) (Suppressor of tumorigenicity 15) (ST15). [Source:Uniprot/SWISSPROT;Acc:O95980]
PicTar	RFP2	Ret finger protein 2 (Leukemia-associated protein 5) (B-cell chronic lymphocytic leukemia tumor suppressor Leu5) (Putative tumor suppressor RFP2) (Tripartite motif protein 13) (RING finger protein 77). [Source:Uniprot/SWISSPROT;Acc:O60858]
PicTar	RFP2	Ret finger protein 2 (Leukemia-associated protein 5) (B-cell chronic lymphocytic leukemia tumor suppressor Leu5) (Putative tumor suppressor RFP2) (Tripartite motif protein 13) (RING finger protein 77). [Source:Uniprot/SWISSPROT;Acc:O60858]
PicTar	RFP2	Ret finger protein 2 (Leukemia-associated protein 5) (B-cell chronic lymphocytic leukemia tumor suppressor Leu5) (Putative tumor suppressor RFP2) (Tripartite motif protein 13) (RING finger protein 77). [Source:Uniprot/SWISSPROT;Acc:O60858]
PicTar	RGMA	Repulsive guidance molecule A precursor (RGM domain family member A). [Source:Uniprot/SWISSPROT;Acc:Q96B86]
TargetScanS	RGMA	Repulsive guidance molecule A precursor (RGM domain family member A). [Source:Uniprot/SWISSPROT;Acc:Q96B86]
TargetScanS	RIN2	Ras and Rab interactor 2 (Ras interaction/interference protein 2) (Ras inhibitor JC265) (Ras association domain family 4). [Source:Uniprot/SWISSPROT;Acc:Q8WYP3]
PicTar	RKHD2	ring finger and KH domain containing 2 [Source:RefSeq_peptide;Acc:NP_057710]
TargetScanS	RKHD2	ring finger and KH domain containing 2 [Source:RefSeq_peptide;Acc:NP_057710]
PicTar	RKHD3	ring finger and KH domain containing 3 [Source:RefSeq_peptide;Acc:NP_115622]
TargetScanS	RKHD3	ring finger and KH domain containing 3 [Source:RefSeq_peptide;Acc:NP_115622]
PicTar	RLF	Zinc finger protein Rlf (Rearranged L-myc fusion gene protein) (Zn-15- related protein). [Source:Uniprot/SWISSPROT;Acc:Q13129]
TargetScanS	RLF	Zinc finger protein Rlf (Rearranged L-myc fusion gene protein) (Zn-15- related protein). [Source:Uniprot/SWISSPROT;Acc:Q13129]
miRanda	RLF	Zinc finger protein Rlf (Rearranged L-myc fusion gene protein) (Zn-15- related protein). [Source:Uniprot/SWISSPROT;Acc:Q13129]
PicTar	RNF182	ring finger protein 182 [Source:RefSeq_peptide;Acc:NP_689950]
TargetScanS	RNF182	ring finger protein 182 [Source:RefSeq_peptide;Acc:NP_689950]
PicTar	RNF2	RING finger protein 2 (RING finger protein 1B) (RING finger protein BAP-1) (DinG protein) (Huntingtin-interacting protein 2-interacting protein 3) (HIP2-interacting protein 3). [Source:Uniprot/SWISSPROT;Acc:Q99496]
PicTar	RNF34	RING finger protein 34 (RING finger protein RIFF) (FYVE-RING finger protein Momo) (Human RING finger homologous to inhibitor of apoptosis protein) (hRfI) (Caspases-8 and -10-associated RING finger protein 1) (CARP-1) (Caspase regulator CARP1). [Source:Uniprot/SWISSPROT;Acc:Q969K3]
TargetScanS	RNF34	RING finger protein 34 (RING finger protein RIFF) (FYVE-RING finger protein Momo) (Human RING finger homologous to inhibitor of apoptosis protein) (hRfI) (Caspases-8 and -10-associated RING finger protein 1) (CARP-1) (Caspase regulator CARP1). [Source:Uniprot/SWISSPROT;Acc:Q969K3]
miRanda	RNF44	ring finger protein 44 [Source:RefSeq_peptide;Acc:NP_055716]
TargetScanS	RNF6	RING finger protein 6 (RING-H2 protein). [Source:Uniprot/SWISSPROT;Acc:Q9Y252]
TargetScanS	RORB	Nuclear receptor ROR-beta (Nuclear receptor RZR-beta). [Source:Uniprot/SWISSPROT;Acc:Q92753]
TargetScanS	RP42	
DIANA-microT	RP56KA3	Ribosomal protein S6 kinase alpha 3 (EC 2.7.1.37) (S6K-alpha 3) (90 kDa ribosomal protein S6 kinase 3) (p90-RSK 3) (Ribosomal S6 kinase 2) (RSK-2) (pp90RSK2) (Insulin-stimulated protein kinase 1) (ISPK-1). [Source:Uniprot/SWISSPROT;Acc:P51812]
TargetScanS	RP56KA3	Ribosomal protein S6 kinase alpha 3 (EC 2.7.1.37) (S6K-alpha 3) (90 kDa ribosomal protein S6 kinase 3) (p90-RSK 3) (Ribosomal S6 kinase 2) (RSK-2) (pp90RSK2) (Insulin-stimulated protein kinase 1) (ISPK-1). [Source:Uniprot/SWISSPROT;Acc:P51812]
TargetScanS	RP56KB1	Ribosomal protein S6 kinase 1 (EC 2.7.1.37) (S6K) (S6K1) (70 kDa ribosomal protein S6 kinase 1) (p70 S6 kinase alpha) (p70(S6K)-alpha) (p70-S6K) (p70-alpha). [Source:Uniprot/SWISSPROT;Acc:P23443]
PicTar	RRAGA	Ras-related GTP binding A [Source:RefSeq_peptide;Acc:NP_006561]
miRanda	RRM2	Ribonucleoside-diphosphate reductase M2 subunit (EC 1.17.4.1) (Ribonucleotide reductase small subunit) (Ribonucleotide reductase small chain). [Source:Uniprot/SWISSPROT;Acc:P31350]
PicTar	RSBN1	round spermatid basic protein 1 [Source:RefSeq_peptide;Acc:NP_060834]
TargetScanS	RSBN1	round spermatid basic protein 1 [Source:RefSeq_peptide;Acc:NP_060834]
PicTar	RSN	Restin (Cytoplasmic linker protein 170 alpha-2) (CLIP-170) (Reed- Sternberg intermediate filament-associated protein) (Cytoplasmic linker protein 1). [Source:Uniprot/SWISSPROT;Acc:P30622]
TargetScanS	RSN	Restin (Cytoplasmic linker protein 170 alpha-2) (CLIP-170) (Reed- Sternberg intermediate filament-associated protein) (Cytoplasmic linker protein 1). [Source:Uniprot/SWISSPROT;Acc:P30622]
PicTar	RSPO2	
PicTar	RTF1	Paf1/RNA polymerase II complex component [Source:RefSeq_peptide;Acc:NP_055953]
PicTar	RUNX1	Runt-related transcription factor 1 (Core-binding factor, alpha 2 subunit) (CBF-alpha 2) (Acute myeloid leukemia 1 protein) (Oncogene AML-1) (Polyomavirus enhancer-binding protein 2 alpha B subunit) (PEBP2-alpha B) (PEA2-alpha B) (SL3-3 enhancer factor 1) [Source:Uniprot/SWISSPROT;Acc:Q01196]
PicTar	RUNX1	Runt-related transcription factor 1 (Core-binding factor, alpha 2 subunit) (CBF-alpha 2) (Acute myeloid leukemia 1 protein) (Oncogene AML-1) (Polyomavirus enhancer-binding protein 2 alpha B subunit) (PEBP2-alpha B) (PEA2-alpha B) (SL3-3 enhancer factor 1) [Source:Uniprot/SWISSPROT;Acc:Q01196]
TargetScanS	RUNX1	Runt-related transcription factor 1 (Core-binding factor, alpha 2 subunit) (CBF-alpha 2) (Acute myeloid leukemia 1 protein) (Oncogene AML-1) (Polyomavirus enhancer-binding protein 2 alpha B subunit) (PEBP2-alpha B) (PEA2-alpha B) (SL3-3 enhancer factor 1) [Source:Uniprot/SWISSPROT;Acc:Q01196]
miRanda	RUNX1T1	Protein CBF42T1 (Protein MTC8) (Protein ETO) (Eighth twenty one protein) (Cyclin D-related protein) (Zinc finger MYND domain- containing

		protein 2). [Source:Uniprot/SWISSPROT;Acc:Q06455]
miRanda	RYBP	RING1 and YY1-binding protein (Death effector domain-associated factor) (DED-associated factor) (YY1 and E4TF1-associated factor 1) (Apoptin-associating protein 1) (APAP-1). [Source:Uniprot/SWISSPROT;Acc:Q8N488]
PicTar	S100PBP	S100P binding protein Riken isoform a [Source:RefSeq_peptide;Acc:NP_073590]
TargetScanS	S100PBP	
TargetScanS	SACM1L	
TargetScanS	SAMHD1	SAM domain and HD domain-containing protein 1 (Dendritic cell-derived IFNG-induced protein) (DCIP) (Monocyte protein 5) (MOP-5). [Source:Uniprot/SWISSPROT;Acc:Q9Y3Z3]
PicTar	SCHIP1	schwannomin interacting protein 1 [Source:RefSeq_peptide;Acc:NP_055390]
TargetScanS	SCHIP1	schwannomin interacting protein 1 [Source:RefSeq_peptide;Acc:NP_055390]
TargetScanS	SCML2	Sex comb on midleg-like protein 2. [Source:Uniprot/SWISSPROT;Acc:Q9UQR0]
TargetScanS	SCOC	short coiled-coil protein [Source:RefSeq_peptide;Acc:NP_115936]
PicTar	SDF2L1	Stromal cell-derived factor 2-like protein 1 precursor (SDF2-like protein 1) (PWP1-interacting protein 8). [Source:Uniprot/SWISSPROT;Acc:Q9HCN8]
TargetScanS	SDFR1	
miRanda	SDK1	Protein sidekick-1 precursor. [Source:Uniprot/SWISSPROT;Acc:Q7Z5N4]
PicTar	SEC24C	Protein transport protein Sec24C (SEC24-related protein C). [Source:Uniprot/SWISSPROT;Acc:P53992]
PicTar	SEC24C	Protein transport protein Sec24C (SEC24-related protein C). [Source:Uniprot/SWISSPROT;Acc:P53992]
TargetScanS	SEC24C	Protein transport protein Sec24C (SEC24-related protein C). [Source:Uniprot/SWISSPROT;Acc:P53992]
PicTar	SEL1L	Sel-1 homolog precursor (Suppressor of lin-12-like protein) (Sel-1L). [Source:Uniprot/SWISSPROT;Acc:Q9UBV2]
TargetScanS	SEL1L	Sel-1 homolog precursor (Suppressor of lin-12-like protein) (Sel-1L). [Source:Uniprot/SWISSPROT;Acc:Q9UBV2]
PicTar	SEMA4C	Semaphorin-4C precursor. [Source:Uniprot/SWISSPROT;Acc:Q9C0C4]
miRanda	SEMA4C	Semaphorin-4C precursor. [Source:Uniprot/SWISSPROT;Acc:Q9C0C4]
TargetScanS	SEMA4G	Semaphorin-4G precursor. [Source:Uniprot/SWISSPROT;Acc:Q9NTN9]
miRanda	SEMA7A	Semaphorin-7A precursor (Semaphorin L) (Sema L) (Semaphorin K1) (Sema K1) (John-Milton-Hargen human blood group Ag) (JMH blood group antigen) (CD108 antigen) (CDw108). [Source:Uniprot/SWISSPROT;Acc:O75326]
PicTar	SEN1P	Sentrin-specific protease 1 (EC 3.4.22.-) (Sentrin/SUMO-specific protease SENP1). [Source:Uniprot/SWISSPROT;Acc:Q9P0U3]
TargetScanS	SEN1P	Sentrin-specific protease 1 (EC 3.4.22.-) (Sentrin/SUMO-specific protease SENP1). [Source:Uniprot/SWISSPROT;Acc:Q9P0U3]
TargetScanS	SEN2P	Sentrin-specific protease 2 (EC 3.4.22.-) (Sentrin/SUMO-specific protease SENP2) (SMT3-specific isopeptidase 2) (Smt3ip2) (Axam2). [Source:Uniprot/SWISSPROT;Acc:Q9HC62]
PicTar	SEN7P	Sentrin-specific protease 7 (EC 3.4.22.-) (Sentrin/SUMO-specific protease SENP7) (SUMO-1-specific protease 2). [Source:Uniprot/SWISSPROT;Acc:Q9BQF6]
PicTar	SERPINB5	Maspin precursor (Protease inhibitor 5). [Source:Uniprot/SWISSPROT;Acc:P36952]
miRanda	SERPINF2	Alpha-2-antiplasmin precursor (Alpha-2-plasmin inhibitor) (Alpha-2-Pi) (Alpha-2-AP). [Source:Uniprot/SWISSPROT;Acc:P08697]
TargetScanS	SERTAD2	SERTA domain-containing protein 2 (Transcriptional regulator interacting with the PHD-bromodomain 2) (TRIP-Br2). [Source:Uniprot/SWISSPROT;Acc:Q14140]
miRanda	SETD7	Histone-lysine N-methyltransferase, H3 lysine-4 specific SET7 (EC 2.1.1.43) (Histone H3-K4 methyltransferase) (H3-K4-HMTase) (SET domain-containing protein 7) (Set9) (SET17/9). [Source:Uniprot/SWISSPROT;Acc:Q8WTS6]
PicTar	SF3B1	Splicing factor 3B subunit 1 (Spliceosome-associated protein 155) (SAP 155) (SF3b155) (Pre-mRNA-splicing factor SF3b 155 kDa subunit). [Source:Uniprot/SWISSPROT;Acc:O75533]
miRanda	SFPQ	Splicing factor, proline- and glutamine-rich (Polypyrimidine tract- binding protein-associated splicing factor) (PTB-associated splicing factor) (PSF) (DNA-binding p52/p100 complex, 100 kDa subunit) (100-kDa DNA-pairing protein) (hPOMp100). [Source:Uniprot/SWISSPROT;Acc:P23246]
TargetScanS	SFRS7	Splicing factor, arginine/serine-rich 7 (Splicing factor 9G8). [Source:Uniprot/SWISSPROT;Acc:Q16629]
PicTar	SGPP1	Sphingosine-1-phosphate phosphatase 1 (EC 3.1.3.-) (Sphingosine-1- phosphatase 1) (SPPase1) (Spp1) (hSPPase1). [Source:Uniprot/SWISSPROT;Acc:Q9BX95]
PicTar	SH2D3C	SH2 domain containing 3C isoform 2 [Source:RefSeq_peptide;Acc:NP_733745]
miRanda	SHOX2	Short stature homeobox protein 2 (Paired-related homeobox protein SHOT) (Homeobox protein Ogl2X). [Source:Uniprot/SWISSPROT;Acc:O60902]
TargetScanS	ShrmL	
miRanda	SIDT2	SID1 transmembrane family member 2 precursor. [Source:Uniprot/SWISSPROT;Acc:Q8NB9J]
TargetScanS	SIPAIL2	Signal-induced proliferation-associated 1-like protein 2. [Source:Uniprot/SWISSPROT;Acc:Q9P2F8]
PicTar	SIRT1	NAD-dependent deacetylase sirtuin-1 (EC 3.5.1.-) (hSIRT1) (hSIR2) (SIR2-like protein 1). [Source:Uniprot/SWISSPROT;Acc:Q96EB6]
TargetScanS	SIRT1	NAD-dependent deacetylase sirtuin-1 (EC 3.5.1.-) (hSIRT1) (hSIR2) (SIR2-like protein 1). [Source:Uniprot/SWISSPROT;Acc:Q96EB6]
miRanda	SIRT1	NAD-dependent deacetylase sirtuin-1 (EC 3.5.1.-) (hSIRT1) (hSIR2) (SIR2-like protein 1). [Source:Uniprot/SWISSPROT;Acc:Q96EB6]
PicTar	SIX2	Homeobox protein SIX2 (Sine oculis homeobox homolog 2). [Source:Uniprot/SWISSPROT;Acc:Q9NPC8]
TargetScanS	SIX2	Homeobox protein SIX2 (Sine oculis homeobox homolog 2). [Source:Uniprot/SWISSPROT;Acc:Q9NPC8]
TargetScanS	SLC25A25	solute carrier family 25, member 25 isoform a [Source:RefSeq_peptide;Acc:NP_443133]
miRanda	SLC25A25	solute carrier family 25, member 25 isoform a [Source:RefSeq_peptide;Acc:NP_443133]
TargetScanS	SLC2A3	Solute carrier family 2, facilitated glucose transporter member 3 (Glucose transporter type 3, brain). [Source:Uniprot/SWISSPROT;Acc:P11169]
PicTar	SLC31A1	High-affinity copper uptake protein 1 (hCTR1) (Copper transporter 1) (Solute carrier family 31 member 1). [Source:Uniprot/SWISSPROT;Acc:O15431]
TargetScanS	SLC38A2	solute carrier family 38, member 2 [Source:RefSeq_peptide;Acc:NP_061849]
miRanda	SLC44A1	Choline transporter-like protein 1 (Solute carrier family 44 member 1) (CD92 antigen) (CDw92). [Source:Uniprot/SWISSPROT;Acc:Q8WW15]
PicTar	SLC9A6	Sodium/hydrogen exchanger 6 (Na <sup>+</sup> /H <sup>+</sup> exchanger 6) (NHE-6) (Solute carrier family 9 member 6). [Source:Uniprot/SWISSPROT;Acc:Q92581]
TargetScanS	SLC9A6	Sodium/hydrogen exchanger 6 (Na <sup>+</sup> /H <sup>+</sup> exchanger 6) (NHE-6) (Solute carrier family 9 member 6). [Source:Uniprot/SWISSPROT;Acc:Q92581]
PicTar	SLITRK1	SLIT and NTRK-like protein 1 precursor (Leucine-rich repeat-containing protein 12). [Source:Uniprot/SWISSPROT;Acc:Q96PX8]
TargetScanS	SLITRK1	SLIT and NTRK-like protein 1 precursor (Leucine-rich repeat-containing protein 12). [Source:Uniprot/SWISSPROT;Acc:Q96PX8]
miRanda	SLITRK1	SLIT and NTRK-like protein 1 precursor (Leucine-rich repeat-containing protein 12). [Source:Uniprot/SWISSPROT;Acc:Q96PX8]
PicTar	SLITRK2	SLIT and NTRK-like protein 2 precursor. [Source:Uniprot/SWISSPROT;Acc:Q9H156]
TargetScanS	SLITRK2	SLIT and NTRK-like protein 2 precursor. [Source:Uniprot/SWISSPROT;Acc:Q9H156]
PicTar	SLITRK3	SLIT and NTRK-like protein 3 precursor. [Source:Uniprot/SWISSPROT;Acc:Q94933]
miRanda	SLK	serine/threonine kinase 2 [Source:RefSeq_peptide;Acc:NP_055535]
TargetScanS	SLMAP	sarcolemma associated protein [Source:RefSeq_peptide;Acc:NP_009090]
PicTar	SMAD7	Mothers against decapentaplegic homolog 7 (SMAD 7) (Mothers against DPP homolog 7) (Smad7) (hSMAD7). [Source:Uniprot/SWISSPROT;Acc:O15105]
TargetScanS	SMAD7	Mothers against decapentaplegic homolog 7 (SMAD 7) (Mothers against DPP homolog 7) (Smad7) (hSMAD7). [Source:Uniprot/SWISSPROT;Acc:O15105]
miRanda	SMAD7	Mothers against decapentaplegic homolog 7 (SMAD 7) (Mothers against DPP homolog 7) (Smad7) (hSMAD7). [Source:Uniprot/SWISSPROT;Acc:O15105]
TargetScanS	SMAP1	stromal membrane-associated protein [Source:RefSeq_peptide;Acc:NP_068759]
TargetScanS	SMBP	
PicTar	SNN	Stannin (AG8_1). [Source:Uniprot/SWISSPROT;Acc:O75324]
miRanda	SOC6	Suppressor of cytokine signaling 6 (SOC6) (Suppressor of cytokine signaling 4) (SOC6-4) (Cytokine-inducible SH2 protein 4) (CIS-4). [Source:Uniprot/SWISSPROT;Acc:O14544]
PicTar	SON	SON protein (SON3) (Negative regulatory element-binding protein) (NRE- binding protein) (DBP-5) (Bax antagonist selected in saccharomyces 1) (BASS1). [Source:Uniprot/SWISSPROT;Acc:P18583]
PicTar	SON	SON protein (SON3) (Negative regulatory element-binding protein) (NRE- binding protein) (DBP-5) (Bax antagonist selected in saccharomyces 1) (BASS1). [Source:Uniprot/SWISSPROT;Acc:P18583]
miRanda	SORCS1	VPS10 domain-containing receptor SorCS1 precursor (hSorCS). [Source:Uniprot/SWISSPROT;Acc:Q8WY21]
PicTar	SOX5	Transcription factor SOX-5. [Source:Uniprot/SWISSPROT;Acc:P35711]
PicTar	SOX5	Transcription factor SOX-5. [Source:Uniprot/SWISSPROT;Acc:P35711]
PicTar	SOX5	Transcription factor SOX-5. [Source:Uniprot/SWISSPROT;Acc:P35711]
TargetScanS	SOX5	Transcription factor SOX-5. [Source:Uniprot/SWISSPROT;Acc:P35711]
TargetScanS	SOX6	Transcription factor SOX-6. [Source:Uniprot/SWISSPROT;Acc:P35712]

TargetScanS	SP7	Transcription factor Sp7 (Zinc finger protein osterix). [Source:Uniprot/SWISSPROT;Acc:Q8TDD2]
miRanda	SPFH1	SPFH domain-containing protein 1 precursor (Protein KE04). [Source:Uniprot/SWISSPROT;Acc:O75477]
TargetScanS	SPIRE1	spire homolog 1 [Source:RefSeq_peptide;Acc:NP_064533]
PicTar	SPRY4	Sprouty homolog 4 (Spry-4). [Source:Uniprot/SWISSPROT;Acc:Q9C004]
TargetScanS	SPRY4	Sprouty homolog 4 (Spry-4). [Source:Uniprot/SWISSPROT;Acc:Q9C004]
miRanda	SREBF1	Sterol regulatory element-binding protein 1 (SREBP-1) (Sterol regulatory element-binding transcription factor 1). [Source:Uniprot/SWISSPROT;Acc:P36956]
TargetScanS	SRGAP1	SLIT-ROBO Rho GTPase-activating protein 1 (srGAP1) (Rho-GTPase- activating protein 13). [Source:Uniprot/SWISSPROT;Acc:Q7Z6B7]
DIANA-microT	SRPK2	Serine/threonine-protein kinase SRPK2 (EC 2.7.1.37) (Serine/arginine- rich protein-specific kinase 2) (SR-protein-specific kinase 2) (SFRS protein kinase 2). [Source:Uniprot/SWISSPROT;Acc:P78362]
TargetScanS	SRPK2	Serine/threonine-protein kinase SRPK2 (EC 2.7.1.37) (Serine/arginine- rich protein-specific kinase 2) (SR-protein-specific kinase 2) (SFRS protein kinase 2). [Source:Uniprot/SWISSPROT;Acc:P78362]
PicTar	SS18L1	SS18-like protein 1 (SYT homolog 1). [Source:Uniprot/SWISSPROT;Acc:O75177]
PicTar	SS18L1	SS18-like protein 1 (SYT homolog 1). [Source:Uniprot/SWISSPROT;Acc:O75177]
TargetScanS	SS18L1	SS18-like protein 1 (SYT homolog 1). [Source:Uniprot/SWISSPROT;Acc:O75177]
miRanda	SS18L1	SS18-like protein 1 (SYT homolog 1). [Source:Uniprot/SWISSPROT;Acc:O75177]
miRanda	SS18L1	SS18-like protein 1 (SYT homolog 1). [Source:Uniprot/SWISSPROT;Acc:O75177]
miRanda	SSR1	Translocon-associated protein alpha subunit precursor (TRAP-alpha) (Signal sequence receptor alpha subunit) (SSR-alpha). [Source:Uniprot/SWISSPROT;Acc:P43307]
PicTar	SSX2IP	Afadin- and alpha-actinin-binding protein (ADIP) (Afadin DIL domain- interacting protein) (SSX2-interacting protein). [Source:Uniprot/SWISSPROT;Acc:Q9Y2D8]
TargetScanS	SSX2IP	Afadin- and alpha-actinin-binding protein (ADIP) (Afadin DIL domain- interacting protein) (SSX2-interacting protein). [Source:Uniprot/SWISSPROT;Acc:Q9Y2D8]
PicTar	ST8SIA4	CMP-N-acetylneuraminate-poly-alpha-2,8-sialyltransferase (EC 2.4.99.-) (Alpha-2,8-sialyltransferase 8D) (ST8Sia IV) (Polysialyltransferase- 1). [Source:Uniprot/SWISSPROT;Acc:Q92187]
TargetScanS	ST8SIA4	CMP-N-acetylneuraminate-poly-alpha-2,8-sialyltransferase (EC 2.4.99.-) (Alpha-2,8-sialyltransferase 8D) (ST8Sia IV) (Polysialyltransferase- 1). [Source:Uniprot/SWISSPROT;Acc:Q92187]
miRanda	STAT3	Signal transducer and activator of transcription 3 (Acute-phase response factor). [Source:Uniprot/SWISSPROT;Acc:P40763]
PicTar	STC1	Stanniocalcin-1 precursor (STC-1). [Source:Uniprot/SWISSPROT;Acc:P52823]
TargetScanS	STC1	Stanniocalcin-1 precursor (STC-1). [Source:Uniprot/SWISSPROT;Acc:P52823]
TargetScanS	STIM2	Stromal interaction molecule 2 precursor. [Source:Uniprot/SWISSPROT;Acc:Q9P246]
miRanda	STK24	Serine/threonine-protein kinase 24 (EC 2.7.1.37) (STE20-like kinase MST3) (MST-3) (Mammalian STE20-like protein kinase 3). [Source:Uniprot/SWISSPROT;Acc:Q9Y6E0]
DIANA-microT	STRBP	spermatid perinuclear RNA-binding protein [Source:RefSeq_peptide;Acc:NP_060857]
PicTar	STRBP	spermatid perinuclear RNA-binding protein [Source:RefSeq_peptide;Acc:NP_060857]
miRanda	STXBP6	Syntaxin-binding protein 6 (Amisyn). [Source:Uniprot/SWISSPROT;Acc:Q8NFX7]
TargetScanS	SUHW4	suppressor of hairy wing homolog 4 isoform 1 [Source:RefSeq_peptide;Acc:NP_060131]
PicTar	SYNE1	Nesprin-1 (Nuclear envelope spectrin repeat protein 1) (Synaptic nuclear envelope protein 1) (Syne-1) (Myocyte nuclear envelope protein 1) (Myne-1) (Enaptin). [Source:Uniprot/SWISSPROT;Acc:Q8NF91]
TargetScanS	SYNE1	Nesprin-1 (Nuclear envelope spectrin repeat protein 1) (Synaptic nuclear envelope protein 1) (Syne-1) (Myocyte nuclear envelope protein 1) (Myne-1) (Enaptin). [Source:Uniprot/SWISSPROT;Acc:Q8NF91]
PicTar	SYNPR	Synaptoporin. [Source:Uniprot/SWISSPROT;Acc:Q8TBG9]
TargetScanS	SYNPR	Synaptoporin. [Source:Uniprot/SWISSPROT;Acc:Q8TBG9]
miRanda	SYNPR	Synaptoporin. [Source:Uniprot/SWISSPROT;Acc:Q8TBG9]
TargetScanS	SYPL	
TargetScanS	SYT3	Synaptotagmin-3 (Synaptotagmin III) (SytlIII). [Source:Uniprot/SWISSPROT;Acc:Q9BQG1]
TargetScanS	TAB3	
PicTar	TAF5	Transcription initiation factor TFIID subunit 5 (Transcription initiation factor TFIID 100 kDa subunit) (TAF(II)100) (TAFII-100) (TAFII100). [Source:Uniprot/SWISSPROT;Acc:Q15542]
PicTar	TAF9B	Transcription initiation factor TFIID subunit 9B (Transcription initiation factor TFIID subunit 9-like protein) (Transcription- associated factor TAFII31L) (Neuronal cell death-related protein 7) (DN-7). [Source:Uniprot/SWISSPROT;Acc:Q9HBM6]
TargetScanS	TA-KRP	
PicTar	TARDBP	TAR DNA-binding protein 43 (TDP-43). [Source:Uniprot/SWISSPROT;Acc:Q13148]
TargetScanS	TARDBP	TAR DNA-binding protein 43 (TDP-43). [Source:Uniprot/SWISSPROT;Acc:Q13148]
PicTar	TBC1D1	TBC1 domain family member 1. [Source:Uniprot/SWISSPROT;Acc:Q86T10]
TargetScanS	TBC1D4	TBC1 domain family member 4 (Akt substrate of 160 kDa) (AS160). [Source:Uniprot/SWISSPROT;Acc:O60343]
TargetScanS	TBL1X	F-box-like/WD-repeat protein TBL1X (Transducin beta-like 1X protein) (Transducin-beta-like 1, X-linked) (SMAF55). [Source:Uniprot/SWISSPROT;Acc:O60907]
TargetScanS	TBL1XR1	F-box-like/WD-repeat protein TBL1XR1 (Transducin beta-like 1X-related protein 1) (Nuclear receptor corepressor/HDAC3 complex subunit TBLR1) (TBL1-related protein 1). [Source:Uniprot/SWISSPROT;Acc:Q9BZK7]
PicTar	TBPL1	TATA box-binding protein-like protein 1 (TBP-like protein 1) (TATA box-binding protein-related factor 2) (TBP-related factor 2) (STUD protein) (21-kDa TBP-like protein). [Source:Uniprot/SWISSPROT;Acc:P62380]
TargetScanS	TBPL1	TATA box-binding protein-like protein 1 (TBP-like protein 1) (TATA box-binding protein-related factor 2) (TBP-related factor 2) (STUD protein) (21-kDa TBP-like protein). [Source:Uniprot/SWISSPROT;Acc:P62380]
miRanda	TBPL1	TATA box-binding protein-like protein 1 (TBP-like protein 1) (TATA box-binding protein-related factor 2) (TBP-related factor 2) (STUD protein) (21-kDa TBP-like protein). [Source:Uniprot/SWISSPROT;Acc:P62380]
TargetScanS	TCBA1	T-cell lymphoma breakpoint-associated target 1 [Source:RefSeq_peptide;Acc:NP_699186]
PicTar	TCERG1	Transcription elongation regulator 1 (TATA box-binding protein- associated factor 2S) (Transcription factor CA150). [Source:Uniprot/SWISSPROT;Acc:O14776]
TargetScanS	TCERG1	Transcription elongation regulator 1 (TATA box-binding protein- associated factor 2S) (Transcription factor CA150). [Source:Uniprot/SWISSPROT;Acc:O14776]
miRanda	TCHH	Trichohyalin. [Source:Uniprot/SWISSPROT;Acc:Q07283]
TargetScanS	TEAD1	Transcriptional enhancer factor TEF-1 (TEA domain family member 1) (TEAD-1) (Protein GT-IIC) (Transcription factor 13) (NTEF-1). [Source:Uniprot/SWISSPROT;Acc:P28347]
TargetScanS	TGFBRI	TGF-beta receptor type I precursor (EC 2.7.1.37) (TGFR-1) (TGF-beta type I receptor) (Serine/threonine-protein kinase receptor R4) (SKR4) (Activin receptor-like kinase 5) (ALK-5). [Source:Uniprot/SWISSPROT;Acc:P36897]
miRanda	TGIF2	Homeobox protein TGIF2 (TGFB-induced factor 2) (5'-TG-3'-interacting factor 2) (TGF(beta)-induced transcription factor 2). [Source:Uniprot/SWISSPROT;Acc:Q9GZN2]
PicTar	TIMP3	Metalloproteinase inhibitor 3 precursor (TIMP-3) (Tissue inhibitor of metalloproteinases-3) (MIG-5 protein). [Source:Uniprot/SWISSPROT;Acc:P35625]
TargetScanS	TIMP3	Metalloproteinase inhibitor 3 precursor (TIMP-3) (Tissue inhibitor of metalloproteinases-3) (MIG-5 protein). [Source:Uniprot/SWISSPROT;Acc:P35625]
miRanda	TIMP3	Metalloproteinase inhibitor 3 precursor (TIMP-3) (Tissue inhibitor of metalloproteinases-3) (MIG-5 protein). [Source:Uniprot/SWISSPROT;Acc:P35625]
TargetScanS	TLP19	
TargetScanS	TM9SF4	Transmembrane 9 superfamily protein member 4. [Source:Uniprot/SWISSPROT;Acc:Q92544]
TargetScanS	TMCC1	Transmembrane and coiled-coil domains protein 1. [Source:Uniprot/SWISSPROT;Acc:O94876]
PicTar	TMED5	Transmembrane emp24 domain-containing protein 5 precursor. [Source:Uniprot/SWISSPROT;Acc:Q9Y3A6]
TargetScanS	TMED5	Transmembrane emp24 domain-containing protein 5 precursor. [Source:Uniprot/SWISSPROT;Acc:Q9Y3A6]
TargetScanS	TMEFF1	transmembrane protein with EGF-like and two follistatin-like domains 1 [Source:RefSeq_peptide;Acc:NP_003683]
DIANA-microT	TMEM117	
TargetScanS	TMEM16A	transmembrane protein 16A [Source:RefSeq_peptide;Acc:NP_060513]
miRanda	TMEM16D	transmembrane protein 16D [Source:RefSeq_peptide;Acc:NP_849148]
PicTar	TMEM28	Transmembrane protein 28 (TED protein). [Source:Uniprot/SWISSPROT;Acc:O75949]
miRanda	TMEM48	transmembrane protein 48 [Source:RefSeq_peptide;Acc:NP_060557]
TargetScanS	TNFRSF11B	Tumor necrosis factor receptor superfamily member 11B precursor (Osteoprotegerin) (Osteoclastogenesis inhibitory factor). [Source:Uniprot/SWISSPROT;Acc:O00300]

miRanda	TNFRSF19L	Tumor necrosis factor receptor superfamily member 19L precursor (Receptor expressed in lymphoid tissues). [Source:Uniprot/SWISSPROT;Acc:Q969Z4]
PicTar	TNFSF11	Tumor necrosis factor ligand superfamily member 11 (Receptor activator of nuclear factor kappa B ligand) (RANKL) (TNF-related activation-induced cytokine) (TRANCE) (Osteoprotegerin ligand) (OPGL) (Osteoclast differentiation factor) (ODF) (CD254 antigen) [Source:Uniprot/SWISSPROT;Acc:O14788]
PicTar	TNFSF11	Tumor necrosis factor ligand superfamily member 11 (Receptor activator of nuclear factor kappa B ligand) (RANKL) (TNF-related activation-induced cytokine) (TRANCE) (Osteoprotegerin ligand) (OPGL) (Osteoclast differentiation factor) (ODF) (CD254 antigen) [Source:Uniprot/SWISSPROT;Acc:O14788]
TargetScanS	TNFSF11	Tumor necrosis factor ligand superfamily member 11 (Receptor activator of nuclear factor kappa B ligand) (RANKL) (TNF-related activation-induced cytokine) (TRANCE) (Osteoprotegerin ligand) (OPGL) (Osteoclast differentiation factor) (ODF) (CD254 antigen) [Source:Uniprot/SWISSPROT;Acc:O14788]
TargetScanS	TNP1	Spermatid nuclear transition protein 1 (STP-1) (TP-1). [Source:Uniprot/SWISSPROT;Acc:P09430]
miRanda	TNS3	tensin-like SH2 domain containing 1 [Source:RefSeq_peptide;Acc:NP_073585]
PicTar	TOM1L1	TOM1-like 1 protein (Target of myb-like 1 protein) (Src-activating and signaling molecule protein). [Source:Uniprot/SWISSPROT;Acc:O75674]
TargetScanS	TOM1L1	TOM1-like 1 protein (Target of myb-like 1 protein) (Src-activating and signaling molecule protein). [Source:Uniprot/SWISSPROT;Acc:O75674]
miRanda	TOP2B	DNA topoisomerase 2-beta (EC 5.99.1.3) (DNA topoisomerase II, beta isozyme). [Source:Uniprot/SWISSPROT;Acc:Q02880]
TargetScanS	TOX	
miRanda	TP53NP2	Tumor protein p53-inducible nuclear protein 2 (p53-inducible protein U) (PIG-U). [Source:Uniprot/SWISSPROT;Acc:Q8XDH6]
TargetScanS	TRA1	
PicTar	TRAK2	Amyotrophic lateral sclerosis 2 chromosomal region candidate gene 3 protein (Trafficking protein, kinesin-binding 2). [Source:Uniprot/SWISSPROT;Acc:O60296]
PicTar	TRIM2	Tripartite motif protein 2 (RING finger protein 86). [Source:Uniprot/SWISSPROT;Acc:Q9C040]
TargetScanS	TRIM2	Tripartite motif protein 2 (RING finger protein 86). [Source:Uniprot/SWISSPROT;Acc:Q9C040]
DIANA-microT	TRIM3	Tripartite motif protein 3 (RING finger protein 22) (Brain-expressed RING finger protein) (RING finger protein 97). [Source:Uniprot/SWISSPROT;Acc:O75382]
TargetScanS	TRIM3	Tripartite motif protein 3 (RING finger protein 22) (Brain-expressed RING finger protein) (RING finger protein 97). [Source:Uniprot/SWISSPROT;Acc:O75382]
TargetScanS	TRIM39	Tripartite motif protein 39 (RING finger protein 23) (Testis-abundant finger protein). [Source:Uniprot/SWISSPROT;Acc:Q9HCM9]
PicTar	TRIM9	Tripartite motif protein 9 (RING finger protein 91). [Source:Uniprot/SWISSPROT;Acc:Q9C026]
TargetScanS	TRIM9	Tripartite motif protein 9 (RING finger protein 91). [Source:Uniprot/SWISSPROT;Acc:Q9C026]
miRanda	TSCL1	Hamartin (Tuberous sclerosis 1 protein). [Source:Uniprot/SWISSPROT;Acc:Q92574]
PicTar	TSC22D2	TSC22 domain family protein 2 (TSC22-related-inducible leucine zipper protein 4). [Source:Uniprot/SWISSPROT;Acc:O75157]
TargetScanS	TSC22D2	TSC22 domain family protein 2 (TSC22-related-inducible leucine zipper protein 4). [Source:Uniprot/SWISSPROT;Acc:O75157]
TargetScanS	TTBK1	tau tubulin kinase 1 [Source:RefSeq_peptide;Acc:NP_115927]
miRanda	TTBK1	tau tubulin kinase 1 [Source:RefSeq_peptide;Acc:NP_115927]
TargetScanS	TULP4	Tubby-like protein 4 (Tubby superfamily protein). [Source:Uniprot/SWISSPROT;Acc:Q9NRJ4]
PicTar	UBE2B	Ubiquitin-conjugating enzyme E2 B (EC 6.3.2.19) (Ubiquitin-protein ligase B) (Ubiquitin carrier protein B) (HR6B) (hHR6B) (E2-17 kDa). [Source:Uniprot/SWISSPROT;Acc:P63146]
TargetScanS	UBE2B	Ubiquitin-conjugating enzyme E2 B (EC 6.3.2.19) (Ubiquitin-protein ligase B) (Ubiquitin carrier protein B) (HR6B) (hHR6B) (E2-17 kDa). [Source:Uniprot/SWISSPROT;Acc:P63146]
TargetScanS	UBE3C	Ubiquitin-protein ligase E3C (EC 6.3.2.-). [Source:Uniprot/SWISSPROT;Acc:Q15386]
TargetScanS	UBL3	Ubiquitin-like protein 3 (HCG-1 protein). [Source:Uniprot/SWISSPROT;Acc:O95164]
PicTar	UBP1	upstream binding protein 1 (LBP-1a) [Source:RefSeq_peptide;Acc:NP_055332]
TargetScanS	UBP1	upstream binding protein 1 (LBP-1a) [Source:RefSeq_peptide;Acc:NP_055332]
miRanda	UCHL5	Ubiquitin carboxyl-terminal hydrolase isozyme L5 (EC 3.4.19.12) (UCH- L5) (Ubiquitin thiolesterase L5) (Ubiquitin C-terminal hydrolase UCH37). [Source:Uniprot/SWISSPROT;Acc:Q9Y5K5]
miRanda	UGT8	2-hydroxyacylsphingosine 1-beta-galactosyltransferase precursor (EC 2.4.1.45) (UDP-galactose-ceramide galactosyltransferase) (Ceramide UDP-galactosyltransferase) (Cerebroside synthase). [Source:Uniprot/SWISSPROT;Acc:Q16880]
miRanda	UHRF2	Ubiquitin-like PHD and RING finger domain-containing protein 2 (EC 6.3.2.-) (Ubiquitin-like-containing PHD and RING finger domains protein 2) (Np95/ICBP90-like RING finger protein) (Np95-like RING finger protein) (Nuclear zinc finger protein Np97) (RING f [Source:Uniprot/SWISSPROT;Acc:Q96PU4]
TargetScanS	USP15	Ubiquitin carboxyl-terminal hydrolase 15 (EC 3.1.2.15) (Ubiquitin thiolesterase 15) (Ubiquitin-specific-processing protease 15) (Deubiquitinating enzyme 15) (Unph-2) (Unph4). [Source:Uniprot/SWISSPROT;Acc:Q9Y4E8]
TargetScanS	USP33	Ubiquitin carboxyl-terminal hydrolase 33 (EC 3.1.2.15) (Ubiquitin thiolesterase 33) (Ubiquitin-specific-processing protease 33) (Deubiquitinating enzyme 33) (VHL-interacting deubiquitinating enzyme 1). [Source:Uniprot/SWISSPROT;Acc:Q8TEY7]
TargetScanS	USP8	Ubiquitin carboxyl-terminal hydrolase 8 (EC 3.1.2.15) (Ubiquitin thiolesterase 8) (Ubiquitin-specific processing protease 8) (Deubiquitinating enzyme 8) (hUBPy). [Source:Uniprot/SWISSPROT;Acc:P40818]
miRanda	VAV3	Protein vav-3. [Source:Uniprot/SWISSPROT;Acc:Q9UKW4]
miRanda	VCIP1P1	Deubiquitinating protein VCIP135 (EC 3.4.22.-) (Valosin-containing protein p97/p47 complex-interacting protein p135) (Valosin-containing protein p97/p47 complex-interacting protein 1). [Source:Uniprot/SWISSPROT;Acc:Q96JH7]
TargetScanS	VGLL4	Transcription cofactor vestigial-like protein 4 (Vgl-4). [Source:Uniprot/SWISSPROT;Acc:Q14135]
miRanda	VLDLR	Very low-density lipoprotein receptor precursor (VLDL receptor) (VLDL- R). [Source:Uniprot/SWISSPROT;Acc:P98155]
miRanda	VSNL1	Visinin-like protein 1 (VILIP) (Hippocalcin-like protein 3) (HLP3). [Source:Uniprot/SWISSPROT;Acc:P62760]
PicTar	WDR20	WD-repeat protein 20 (DMR protein). [Source:Uniprot/SWISSPROT;Acc:Q8TBZ3]
TargetScanS	WDR20	WD-repeat protein 20 (DMR protein). [Source:Uniprot/SWISSPROT;Acc:Q8TBZ3]
PicTar	WDR37	WD-repeat protein 37. [Source:Uniprot/SWISSPROT;Acc:Q9Y2I8]
TargetScanS	WDR37	WD-repeat protein 37. [Source:Uniprot/SWISSPROT;Acc:Q9Y2I8]
TargetScanS	WDR40B	WD repeat domain 40B [Source:RefSeq_peptide;Acc:NP_848565]
miRanda	WDR42A	H326 [Source:RefSeq_peptide;Acc:NP_056541]
miRanda	WDR42A	H326 [Source:RefSeq_peptide;Acc:NP_056541]
TargetScanS	WDR9	
PicTar	WNT11	Protein Wnt-11 precursor. [Source:Uniprot/SWISSPROT;Acc:O96014]
PicTar	WSB1	WD repeat and SOCS box-containing protein 1 (WSB-1) (SOCS box- containing WD protein SWiP-1). [Source:Uniprot/SWISSPROT;Acc:Q9Y6I7]
PicTar	WSB1	WD repeat and SOCS box-containing protein 1 (WSB-1) (SOCS box- containing WD protein SWiP-1). [Source:Uniprot/SWISSPROT;Acc:Q9Y6I7]
TargetScanS	WSB1	WD repeat and SOCS box-containing protein 1 (WSB-1) (SOCS box- containing WD protein SWiP-1). [Source:Uniprot/SWISSPROT;Acc:Q9Y6I7]
PicTar	XPO4	Exportin-4 (Exp4). [Source:Uniprot/SWISSPROT;Acc:Q9C0E2]
TargetScanS	YT521	
PicTar	YTHDF2	YTH domain protein 2 (High-glucose-regulated protein 8) (NY-REN-2 antigen) (CLL-associated antigen KW-14). [Source:Uniprot/SWISSPROT;Acc:Q9Y5A9]
TargetScanS	YTHDF2	YTH domain protein 2 (High-glucose-regulated protein 8) (NY-REN-2 antigen) (CLL-associated antigen KW-14). [Source:Uniprot/SWISSPROT;Acc:Q9Y5A9]
PicTar	YTHDF3	YTH domain family, member 3 [Source:RefSeq_peptide;Acc:NP_689971]
TargetScanS	YTHDF3	YTH domain family, member 3 [Source:RefSeq_peptide;Acc:NP_689971]
PicTar	YWHAG	14-3-3 protein gamma (Protein kinase C inhibitor protein 1) (KCIP-1). [Source:Uniprot/SWISSPROT;Acc:P61981]
TargetScanS	YWHAG	14-3-3 protein gamma (Protein kinase C inhibitor protein 1) (KCIP-1). [Source:Uniprot/SWISSPROT;Acc:P61981]
miRanda	YWHAG	14-3-3 protein gamma (Protein kinase C inhibitor protein 1) (KCIP-1). [Source:Uniprot/SWISSPROT;Acc:P61981]
TargetScanS	YY1	Transcriptional repressor protein YY1 (Yin and yang 1) (YY-1) (Delta transcription factor) (NF-E1). [Source:Uniprot/SWISSPROT;Acc:P25490]
TargetScanS	ZA20D2	Zinc finger A20 domain-containing protein 2 (Zinc finger protein 216). [Source:Uniprot/SWISSPROT;Acc:O76080]
PicTar	ZA20D3	zinc finger, A20 domain containing 3 [Source:RefSeq_peptide;Acc:NP_061879]
TargetScanS	ZA20D3	zinc finger, A20 domain containing 3 [Source:RefSeq_peptide;Acc:NP_061879]
PicTar	ZBTB4	Zinc finger and BTB domain-containing protein 4 (KAISO-like zinc finger protein 1) (KAISO-L1). [Source:Uniprot/SWISSPROT;Acc:Q9P1Z0]
TargetScanS	ZBTB4	Zinc finger and BTB domain-containing protein 4 (KAISO-like zinc finger protein 1) (KAISO-L1). [Source:Uniprot/SWISSPROT;Acc:Q9P1Z0]
PicTar	ZC3H6	Zinc finger CCH4-type domain-containing protein 6. [Source:Uniprot/SWISSPROT;Acc:P61129]
TargetScanS	ZC3HDC6	

TargetScanS	ZCCHC3	Zinc finger CCHC domain-containing protein 3. [Source:Uniprot/SWISSPROT;Acc:Q9NUD5]
PicTar	ZDHHHC3	Palmitoyltransferase ZDHHHC3 (EC 2.3.1.-) (Zinc finger DHHC domain- containing protein 3) (DHHC-3) (Zinc finger protein 373) (DHHHC1 protein). [Source:Uniprot/SWISSPROT;Acc:Q9NYG2]
PicTar	ZDHHHC7	Palmitoyltransferase ZDHHHC7 (EC 2.3.1.-) (Zinc finger DHHC domain- containing protein 7) (DHHC-7) (Zinc finger protein 370). [Source:Uniprot/SWISSPROT;Acc:Q9NXF8]
TargetScanS	ZDHHHC7	Palmitoyltransferase ZDHHHC7 (EC 2.3.1.-) (Zinc finger DHHC domain- containing protein 7) (DHHC-7) (Zinc finger protein 370). [Source:Uniprot/SWISSPROT;Acc:Q9NXF8]
TargetScanS	ZF	
TargetScanS	ZFOC1	
PicTar	ZFP36L1	Butyrate response factor 1 (TIS11B protein) (EGF-response factor 1) (ERF-1). [Source:Uniprot/SWISSPROT;Acc:Q07352]
PicTar	ZIC1	Zinc finger protein ZIC 1 (Zinc finger protein of the cerebellum 1). [Source:Uniprot/SWISSPROT;Acc:Q15915]
miRanda	ZIC1	Zinc finger protein ZIC 1 (Zinc finger protein of the cerebellum 1). [Source:Uniprot/SWISSPROT;Acc:Q15915]
PicTar	ZIC2	Zinc finger protein ZIC 2 (Zinc finger protein of the cerebellum 2). [Source:Uniprot/SWISSPROT;Acc:Q95409]
PicTar	ZIC3	Zinc finger protein ZIC 3 (Zinc finger protein of the cerebellum 3). [Source:Uniprot/SWISSPROT;Acc:Q60481]
TargetScanS	ZIC3	Zinc finger protein ZIC 3 (Zinc finger protein of the cerebellum 3). [Source:Uniprot/SWISSPROT;Acc:Q60481]
miRanda	ZIC3	Zinc finger protein ZIC 3 (Zinc finger protein of the cerebellum 3). [Source:Uniprot/SWISSPROT;Acc:Q60481]
PicTar	ZNF207	Zinc finger protein 207. [Source:Uniprot/SWISSPROT;Acc:O43670]
TargetScanS	ZNF207	Zinc finger protein 207. [Source:Uniprot/SWISSPROT;Acc:O43670]
miRanda	ZNF238	Zinc finger protein 238 (Transcriptional repressor RP58) (58 kDa repressor protein) (Zinc finger protein C2H2-171) (Translin-associated zinc finger protein 1) (TAZ-1) (Zinc finger and BTB domain-containing protein 18). [Source:Uniprot/SWISSPROT;Acc:Q99592]
PicTar	ZNF281	Zinc finger protein 281 (Zinc finger DNA-binding protein 99) (Transcription factor ZBP-99) (GC-box-binding zinc finger protein 1). [Source:Uniprot/SWISSPROT;Acc:Q9Y2X9]
miRanda	ZNF281	Zinc finger protein 281 (Zinc finger DNA-binding protein 99) (Transcription factor ZBP-99) (GC-box-binding zinc finger protein 1). [Source:Uniprot/SWISSPROT;Acc:Q9Y2X9]
miRanda	ZNF282	Zinc finger protein 282 (HTLV-I U5RE-binding protein 1) (HUB-1). [Source:Uniprot/SWISSPROT;Acc:Q9UDV7]
miRanda	ZNF443	Zinc finger protein 443 (Kruppel-type zinc finger protein ZK1). [Source:Uniprot/SWISSPROT;Acc:Q9Y2A4]
miRanda	ZNF516	Zinc finger protein 516. [Source:Uniprot/SWISSPROT;Acc:Q92618]
PicTar	ZNF533	Zinc finger protein 533. [Source:Uniprot/SWISSPROT;Acc:Q569K4]
TargetScanS	ZNF536	zinc finger protein 536 [Source:RefSeq_peptide;Acc:NP_055532]
miRanda	ZNF592	Zinc finger protein 592. [Source:Uniprot/SWISSPROT;Acc:Q92610]
PicTar	ZNF615	Zinc finger protein 615. [Source:Uniprot/SWISSPROT;Acc:Q8N8J6]
TargetScanS	ZNF615	Zinc finger protein 615. [Source:Uniprot/SWISSPROT;Acc:Q8N8J6]
PicTar	ZNF655	Zinc finger protein 655 (Vav-interacting Kruppel-like protein). [Source:Uniprot/SWISSPROT;Acc:Q8N720]
TargetScanS	ZNF655	Zinc finger protein 655 (Vav-interacting Kruppel-like protein). [Source:Uniprot/SWISSPROT;Acc:Q8N720]
miRanda	ZNF677	zinc finger protein 677 [Source:RefSeq_peptide;Acc:NP_872415]

**Supplementary Table 2c: Functional Annotation Clustering of miR-181b gene targets – Enrichment Score: 5.35**

Cluster 1	Category	No. genes	p value	Genes
GOTERM_BP_ALL	development	36	2.11E-07	ARHGEF2, CACNB2, CD4, CUGBP1, DCAMKL1, EGR3, ENAH, ESM1, FALZ, GAS7, GDA, HECA, HEY2, HOXA1, HOXA11, HOXB5, HOXC8, KIF3B, MBNL1, MLF1, MTPN, MYH10, NEFH, RPS6KA3, SEMA4C, SEMA4G, SIRT1, SIX2, SOX6, SPRY4, TNFRSF11B, TRIM3, TTN, YWHAG, ZIC1, ZIC2
SP_PIR_KEYWORDS	developmental protein	16	5.09E-07	HECA, DCAMKL1, ENAH, GAS7, HOXA1, HOXA11, HOXB5, HOXC8, MLF1, SEMA4C, SEMA4G, SIRT1, SIX2, SPRY4, ZIC1, ZIC2
GOTERM_BP_ALL	nervous system development	16	3.47E-06	DCAMKL1, ENAH, FALZ, GAS7, GDA, HEY2, MBNL1, MTPN, NEFH, RPS6KA3, SEMA4C, SEMA4G, TRIM3, YWHAG, ZIC1, ZIC2
GOTERM_BP_ALL	system development	16	3.84E-06	DCAMKL1, ENAH, FALZ, GAS7, GDA, HEY2, MBNL1, MTPN, NEFH, RPS6KA3, SEMA4C, SEMA4G, TRIM3, YWHAG, ZIC1, ZIC2
SP_PIR_KEYWORDS	neurogenesis	7	5.35E-06	DCAMKL1, ENAH, GAS7, SEMA4C, SEMA4G, ZIC1, ZIC2
GOTERM_BP_ALL	cell differentiation	15	3.43E-05	CD4, CUGBP1, DCAMKL1, ENAH, GAS7, MBNL1, MLF1, MTPN, SEMA4C, SEMA4G, SIRT1, TTN, YWHAG, ZIC1, ZIC2
SP_PIR_KEYWORDS	differentiation	9	1.31E-04	DCAMKL1, ENAH, GAS7, MLF1, SEMA4C, SEMA4G, SIRT1, ZIC1, ZIC2
Cluster 2	Category	No. genes	p value	
SP_PIR_KEYWORDS	nuclear protein	45	2.94E-07	
GOTERM_MF_ALL	transcription regulator activity	28	1.73E-06	
SP_PIR_KEYWORDS	transcription	27	3.25E-06	
GOTERM_MF_ALL	transcription factor activity	22	9.24E-06	
SP_PIR_KEYWORDS	transcription regulation	26	1.43E-05	
SP_PIR_KEYWORDS	dna-binding	25	4.96E-05	
GOTERM_BP_ALL	regulation of biological process	48	1.55E-04	
GOTERM_BP_ALL	regulation of metabolism	36	2.86E-04	
GOTERM_BP_ALL	regulation of cellular process	45	2.93E-04	
GOTERM_BP_ALL	regulation of cellular metabolism	35	3.70E-04	
GOTERM_BP_ALL	regulation of physiological process	44	4.07E-04	
GOTERM_CC_ALL	nucleus	51	4.65E-04	
GOTERM_MF_ALL	DNA binding	31	5.01E-04	
GOTERM_BP_ALL	regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	33	6.46E-04	
GOTERM_BP_ALL	regulation of transcription, DNA-dependent	31	7.66E-04	
GOTERM_BP_ALL	regulation of cellular physiological process	42	8.84E-04	
GOTERM_BP_ALL	regulation of transcription	32	0.0011	
GOTERM_BP_ALL	transcription	33	0.0011	
GOTERM_BP_ALL	transcription, DNA-dependent	31	0.0013	
GOTERM_BP_ALL	nucleobase, nucleoside, nucleotide and nucleic acid metabolism	42	0.0030	
GOTERM_MF_ALL	nucleic acid binding	38	0.0088	
GOTERM_CC_ALL	intracellular membrane-bound organelle	59	0.0296	
GOTERM_CC_ALL	membrane-bound organelle	59	0.0298	
GOTERM_CC_ALL	intracellular organelle	67	0.0480	
GOTERM_CC_ALL	organelle	67	0.0483	
GOTERM_CC_ALL	intracellular	76	0.1020	

**Supplementary Table 2d: KEGG Pathway Analysis of miR-181b gene targets**

Category	Term	Count	P Value	Genes
KEGG_PATHWAY	HSA04720:LONG-TERM POTENTIATION	11	1.65E-04	CAMK2G, RPS6KA3, EP300, RAP1B, CREBBP, PPP3CA, PPP3R1, PPP1CB, GRM5, GRIA2, ADCY1, MAP3K3, PTPRR, RPS6KA3, DUSP5, MINK1, CACNA2D2, IL1A, MKNK2, PPP3CA, HSPA5, PPP3R1, PDGFRA, MAP4K4, FOS, MAP3K10, DUSP6, RAP1B, CACNB2, AKT3, MAP3K7IP2, NLK, PPM1B, TGFBR1,
KEGG_PATHWAY	HSA04010:MAPK SIGNALING PATHWAY	23	0.0011	PAK7, PIK3R3, CD4, PAK4, VAV3, CARD11, CBLB, PPP3CA, PPP3R1, AKT3, NFAT5, FOS,
KEGG_PATHWAY	HSA04660:T CELL RECEPTOR SIGNALING PATHWAY	12	0.0013	NEFH, EP300, BCL2, CREBBP, HSPA5, ALS2, GFAP,
KEGG_PATHWAY	HSA01510:NEURODEGENERATIVE DISORDERS	7	0.0021	TBL1XR1, PPP3CA, CREBBP, PRICKLE2, PPP3R1, WNT11, NFAT5, CSNK2A2, APC, CAMK2G, TBL1X, LEF1, EP300, SENP2, NLK,
KEGG_PATHWAY	HSA04310:WNT SIGNALING PATHWAY	15	0.0022	GNAI1, EPHA4, SEMA4G, DPYSL2, PPP3CA, PPP3R1, SRGAP1, EPHA7, NFAT5, SEMA4C, PAK7, PAK4, SEMA7A, NRP1,
KEGG_PATHWAY	HSA04360:AXON GUIDANCE	14	0.0034	ACVR2A, RPS6KB1, NOG, ID4, EP300, CREBBP, BMPR2, E2F5, SMAD7, TGFBR1,
KEGG_PATHWAY	HSA04350:TGF-BETA SIGNALING PATHWAY	10	0.0063	PIK3R3, RPS6KB1, SOCS6, TSC1, CBLB, PDE3A, MKNK2, PPP1CB, SREBF1, IRS2, PPARGC1A, PRKAG2, AKT3,
KEGG_PATHWAY	HSA04910:INSULIN SIGNALING PATHWAY	13	0.0090	CTNND1, LEF1, EP300, CREBBP, BAIAP2, SSX2IP, CSNK2A2, NLK, TGFBR1,
KEGG_PATHWAY	HSA04520:ADHERENS JUNCTION	9	0.0127	PIK3R3, VAV3, CARD11, PPP3CA, PPP3R1, AKT3, NFAT5, FOS,
KEGG_PATHWAY	HSA04662:B CELL RECEPTOR SIGNALING PATHWAY	8	0.0180	PER2, BHLHB2, BHLHB3, CLOCK,
KEGG_PATHWAY	HSA04710:CIRCADIAN RHYTHM	4	0.0193	NEFH, BCL2, PPP3CA, ALS2,
KEGG_PATHWAY	HSA05030:AMYOTROPHIC LATERAL SCLEROSIS (ALS)	4	0.0272	

**Supplementary Table 2e: miR-181b targets - Down regulated in the STG (Bowden et al., 2007)**

Program	Gene Symbol	Description
TargetScanS	ANKFY1	Ankyrin repeat and FYVE domain protein 1 (Ankyrin repeats hooked to a zinc finger motif). [Source:Uniprot/SWISSPROT;Acc:Q9P2R3]
PicTar	C5orf5	Protein C5orf5 (GAP-like protein N61). [Source:Uniprot/SWISSPROT;Acc:Q9NYF5]
PicTar	CDYL	Chromodomain Y-like protein (CDY-like). [Source:Uniprot/SWISSPROT;Acc:Q9Y232]
TargetScanS	CNTNAP2	Contactin-associated protein-like 2 precursor (Cell recognition molecule Caspr2). [Source:Uniprot/SWISSPROT;Acc:Q9UHC6]
PicTar	EEF1A1	Elongation factor 1-alpha 1 (EF-1-alpha-1) (Elongation factor 1 A-1) (eEF1A-1) (Elongation factor Tu) (EF-Tu). [Source:Uniprot/SWISSPROT;Acc:P68104]
PicTar	EPHA4	Ephrin type-A receptor 4 precursor (EC 2.7.1.112) (Tyrosine-protein kinase receptor SEK) (Receptor protein-tyrosine kinase HEK8). [Source:Uniprot/SWISSPROT;Acc:P54764]
TargetScanS	EPHA4	
miRanda	FXR2	Fragile X mental retardation syndrome-related protein 2. [Source:Uniprot/SWISSPROT;Acc:P51116]
PicTar	GOLGA1	Golgin subfamily A member 1 (Golgin-97). [Source:Uniprot/SWISSPROT;Acc:Q92805]
TargetScanS	GOLGA1	
miRanda	GREM2	Gremlin-2 precursor (Cysteine knot superfamily 1, BMP antagonist 2) (Protein related to DAN and cerberus). [Source:Uniprot/SWISSPROT;Acc:Q9H772]
TargetScanS	GRIA2	Glutamate receptor 2 precursor (GluR-2) (GluR-B) (GluR-K2) (Glutamate receptor ionotropic, AMPA 2) (AMPA-selective glutamate receptor 2). [Source:Uniprot/SWISSPROT;Acc:P42262]
TargetScanS	HYOU1	150 kDa oxygen-regulated protein precursor (Orp150) (Hypoxia up-regulated 1). [Source:Uniprot/SWISSPROT;Acc:Q9Y4L1]
TargetScanS	INPP5A	Type I inositol-1,4,5-trisphosphate 5-phosphatase (EC 3.1.3.56) (5PTase). [Source:Uniprot/SWISSPROT;Acc:Q14642]
TargetScanS	MAEA	macrophage erythroblast attacher isoform 2 [Source:RefSeq_peptide;Acc:NP_005873]
TargetScanS	MPP5	MAGUK p55 subfamily member 5. [Source:Uniprot/SWISSPROT;Acc:Q8N3R9]
TargetScanS	MTMR9	Myotubularin-related protein 9. [Source:Uniprot/SWISSPROT;Acc:Q96QG7]
PicTar	PHF3	PHD finger protein 3. [Source:Uniprot/SWISSPROT;Acc:Q92576]
TargetScanS	PPAP2B	Lipid phosphate phosphohydrolase 3 (EC 3.1.3.4) (Phosphatidic acid phosphatase 2b) (Phosphatidate phosphohydrolase type 2b) (PAP2b) (PAP- 2b) (PAP2-beta) (Vascular endothelial growth factor and type I collagen-inducible protein) (VCIP). [Source:Uniprot/SWISSPROT;Acc:O14495]
miRanda	PPAP2B	
TargetScanS	RBM25	Probable RNA-binding protein 25 (RNA-binding motif protein 25) (RNA-binding region-containing protein 7) (Protein S164). [Source:Uniprot/SWISSPROT;Acc:P49756]
PicTar	RRAGA	Ras-related GTP binding A [Source:RefSeq_peptide;Acc:NP_006561]
TargetScanS	VGLL4	Transcription cofactor vestigial-like protein 4 (Vgl-4). [Source:Uniprot/SWISSPROT;Acc:Q14135]
miRanda	VSNL1	Visinin-like protein 1 (VILIP) (Hippocalcin-like protein 3) (HLP3). [Source:Uniprot/SWISSPROT;Acc:P62760]
TargetScanS	YY1	Transcriptional repressor protein YY1 (Yin and yang 1) (YY-1) (Delta transcription factor) (NF-E1). [Source:Uniprot/SWISSPROT;Acc:P25490]
miRanda web	GDA	Guanine deaminase (EC 3.5.4.3) (Guanase) (Guanine aminase) (Guanine aminohydrolase) (GAH) (p51-nedasin). [Source:Uniprot/SWISSPROT;Acc:Q9Y2T3]



## APPENDIX IV: SUPPLEMENTARY DATA FOR CHAPTER 5

**Supplementary Table 1: Demographic information for STG and DLPFC postmortem tissue.**

STG Cohort										
Pair	Diagnosis	Sex	Age	Hemi	PMI	pH	COD	Toxicology	DOI	CPE
1	CRS	M	51	L	21	6.02	IHD <sup>c, g</sup>	Thioridazine 2.2mg/L (fatal), Mesoridazine 2.4mg/L (toxic/fatal)	24	100 - 700
2	CPS	M	57	L	33	6.40	Coronary artery thrombosis <sup>a, e</sup>	Thioridazine 0.6mg/L, Seraline <0.1mg/L	26	100 - 400
3	CPS	M	52	R	8	6.10	IHD <sup>a, f</sup>	Temazepam <0.1mg/L	31	260 - 600
4	CUS	M	44	L	35	6.55	Hanging suicide <sup>a</sup>	Urine THC detected	17	500 - 1000
5	CPS	M	30	L	24	6.60	CO poisoning <sup>d, b</sup>	Carbon Monoxide 74% saturation, Clozapine 0.7mg/L	3.5	130 - 975
6	CDS	M	32	L	25	6.24	Hanging suicide <sup>a</sup>	N/A	13	780
7	CPS	M	51	R	18	6.62	IHD <sup>a, f</sup>	N/A	30	300 - 1300
8	CRS	F	51	L	12	5.40	Emphema <sup>a</sup>	Lithium 20mg/L (fatal), Midazolam 0.02mg/L	16	112 - 1000
9	CDS	F	67	R	27	6.20	IHD <sup>a, f</sup>	Benztropine, Mesoridazine, Thioridazine & Paracetamol detected	46	150 - 1100
10	CPS	M	75	L	36	6.40	IHD <sup>a, f</sup>	Olanzapine - 0.2 mg/L, Fluvoxamine - 0.7 mg/L	44	200 - 1200
11	CPS	M	54	R	27	6.20	Coronary artery thrombosis <sup>a, f</sup>	Chlorpromazine: 0.7mg/L, Diazepam: <0.1mg/L, Nordiazepam: 0.1mg/L, Insulin: 2 uU/mL	35	50 - 600
12	CPS	F	61	R	49	6.70	Ischaemic heart disease <sup>c, f</sup>	Clozapine 1.1 mg/L; Diazepam 0.2 mg/L; Laudanosine 0.4 mg/L; Nordiazepam 0.4 mg/L; Olanzapine 0.2 mg/L	42	800 - 1500
13	CUS	M	67	R	5	6.40	Cardiovascular disease <sup>c, g</sup>	Negative	41	200 - 2400
14	CPS	M	57	R	48	6.70	ASCVD <sup>a, e</sup>	Carbamazepine 10 mg/L, Citalopram 0.2 mg/L, Quetiapine <0.1 mg/L	17	225 - 975
15	CPS	M	40	R	21.5	6.20	Dihydrocodeine toxicity and obstructive sleep apnoea <sup>a</sup>	Valproic acid 20mg/L, Dihydrocodeine 0.7mg/L, Quetiapine 0.3mg/L, Sertraline 0.3mg/L	23	225 - 1800
16	CPS	F	66	R	12.5	6.30	Faecoloid peritonitis <sup>a, f</sup>	Negative	30	1200 - 2500
17	CPS	F	61	R	39	6.60	Undetermined <sup>b, e</sup>	Thioridazine & Mesoridazine detected	32	100 - 600
18	CPS	F	61	L	19	6.10	Sepsis and chronic renal failure <sup>a</sup>	Morphine: 0.06 mg/L, Codeine: 0.05 mg/L, Carbamazepine: 7 mg/L, Pethidine: 0.1 mg/L, Paracetamol: 6mg/L, Metoclopramide 0.1mg/L, Diazepam: <0.1 mg/L	39	300 - 400
19	CPS	M	33	L	48	6.70	Hanging suicide <sup>a</sup>	Doxylamine: 0.9mg/L, Olanzapine: 0.2mg/L, Paracetamol: 3mg/L	10	222
20	CUS	M	52	R	46	6.40	Cardiomegaly <sup>b, f</sup>	N/A	32	17 - 1165
21	CPS	F	54	R	29	6.50	Asthma <sup>a, f</sup>	Citalopram 0.6 mg/L	35	15 - 600
Mean (SD)			52.7 (11.7)		28.9 (13.4)	6.4 (0.3)				
1	CON	M	50	L	19	6.26	IHD <sup>e</sup>	Negative		
2	CON	M	58	L	38	6.50	IHD <sup>e</sup>	N/A		
3	CON	M	59	R	20	6.56	Coronary thrombosis <sup>f</sup>	Negative		
4	CON	M	43	L	13	6.43	Thrombotic coronary artery occlusion <sup>f</sup>	Negative		
5	CON	M	34	L	20.5	6.73	Asthma <sup>e</sup>	N/A		
6	CON	M	38	L	13.5	6.00	ASCVD <sup>e</sup>	Negative		
7	CON	M	46	R	25	6.70	Cardiac arrest	Negative		
8	CON	F	52	L	9.5	5.80	IHD	N/A		
9	CON	F	70	R	30	6.80	IHD <sup>g</sup>	Blood EtOH: 0.251g per 100mL, Paracetamol <3mg/L		
10	CON	M	73	L	10	6.20	Cardiac arrest	N/A		
11	CON	M	56	R	37	6.80	Pulmonary thromboembolus	N/A		
12	CON	F	56	R	23	6.70	Pulmonary thromboembolus <sup>e</sup>	N/A		
13	CON	M	69	R	16	6.60	Cardiac atheroma <sup>h, g</sup>	Paracetamol 23 mg/L, 1% blood saturation of CO (low)		
14	CON	M	56	R	24	6.50	Coronary artery atheroma <sup>f</sup>	N/A		
15	CON	M	37	L	21	6.60	IHD	Negative		
16	CON	F	71	L	16	6.20	Adenocarcinoma of the pancreas <sup>e</sup>	N/A		
17	CON	F	52	L	11	6.20	Ischaemic heart disease <sup>f</sup>	N/A		
18	CON	M	46	L	29	6.70	Pulmonary thromboembolus <sup>e</sup>	N/A		
19	CON	M	46	L	29	6.10	MI <sup>g</sup>	N/A		
20	CON	M	53	R	27	6.60	MI	N/A		

21	CON	F	49	R	15	6.90	Arrhythmogenic right ventricular dysplasia	Chloride ions 118 mmol/L		
Mean (SD)			53.2 (11.4)		21.4 (8.5)	6.5 (0.3)				
DLPFC Cohort										
Pair	Diagnosis	Sex	Age	Hemi	PMI	pH	COD	Toxicology	DOI	CPE
1	CPS	M	57	R	48	6.70	ASCVD <sup>a,c</sup>	Carbamazepine 10 mg/L, Citalopram 0.2 mg/L, Quetiapine <0.1 mg/L	17	225 - 975
2	CPS	M	40	R	21.5	6.20	Dihydrocodeine toxicity and obstructive sleep apnoea <sup>a</sup>	Valproic acid 20mg/L, Dihydrocodeine 0.7mg/L, Quetiapine 0.3mg/L, Sertraline 0.3mg/L	23	225 - 1800
3	CPS	F	61	L	19	6.10	Sepsis and chronic renal failure <sup>a</sup>	Morphine: 0.06 mg/L, Codeine: 0.05 mg/L, Carbamazepine: 7 mg/L, Pethidine: 0.1 mg/L, Paracetamol: 6mg/L, Metoclopramide 0.1mg/L, Diazepam: <0.1 mg/L	39	300 - 400
4	CDS	M	32	L	25	6.24	Hanging suicide <sup>a</sup>	N/A	13	780
5	CPS	M	30	L	24	6.60	CO poisoning <sup>d,b</sup>	Carbon Monoxide 74% saturation, Clozapine 0.7mg/L	3.5	130 - 975
6	CPS	M	51	R	18	6.62	IHD <sup>a,f</sup>	N/A	30	300 - 1300
7	CPS	M	54	R	27	6.20	Coronary artery thrombosis <sup>a,i</sup>	Chlorpromazine: 0.7mg/L, Diazepam: <0.1mg/L, Nordiazepam: 0.1mg/L, Insulin: 2 uU/mL	35	50 - 600
8	CUS	M	44	L	35	6.55	Hanging suicide <sup>a</sup>	Urine THC detected	17	500 - 1000
9	CPS	F	66	R	12.5	6.30	Faecoid peritonitis <sup>a,f</sup>	Negative	30	1200 - 2500
10	CPS	M	75	L	36	6.40	IHD <sup>a,f</sup>	Olanzapine - 0.2 mg/L, Fluvoxamine - 0.7 mg/L	44	200 - 1200
11	CPS	M	54	R	27	6.20	Coronary artery thrombosis <sup>a,i</sup>	Chlorpromazine: 0.7mg/L, Diazepam: <0.1mg/L, Nordiazepam: 0.1mg/L, Insulin: 2 uU/mL	35	50 - 600
12	CPS	M	33	L	48	6.70	Hanging suicide <sup>a</sup>	Doxylamine: 0.9mg/L, Olanzapine: 0.2mg/L, Paracetamol: 3mg/L	10	222
13	CUS	M	52	R	46	6.40	Cardiomegaly <sup>b,f</sup>	N/A	32	17 - 1165
14	CPS	F	54	R	29	6.50	Asthma <sup>a,f</sup>	Citalopram 0.6 mg/L	35	15 - 600
15	CUS	F	55	L	33.5	6.70	Amisulpride toxicity and ASCVD	Amisulpride 18/mg/L, Clozapine 1.4 mg/L	38	75 - 4650
Mean (SD)			50.5 (12.7)		29.9 (11.0)	6.4 (0.2)				
1	CON	M	56	R	24	6.50	Coronary artery atheroma <sup>i</sup>	N/A		
2	CON	M	37	L	21	6.60	IHD	Negative		
3	CON	F	56	R	23	6.70	Pulmonary thromboembolus <sup>a</sup>	N/A		
4	CON	M	37	R	24	6.37	Electrocution	N/A		
5	CON	M	34	L	20.5	6.73	Asthma <sup>a</sup>	N/A		
6	CON	M	53	L	16	6.84	Dilated cardiomyopathy	N/A		
7	CON	M	60	R	25	6.70	Bacterial Peritonitis, ascites, carcinomatosis, gastrointestinal stomach tumor	N/A		
8	CON	M	44	L	50	6.60	IHD	N/A		
9	CON	F	71	L	16	6.20	Adenocarcinoma of the pancreas <sup>a</sup>	N/A		
10	CON	M	78	L	6.5	6.20	Dehydration, adenocarcinoma (lung), adenocarcinoma (rectum), Multiple Metastases	N/A		
11	CON	F	60	L	21	6.80	IHD	N/A		
12	CON	M	46	L	29	6.10	MI <sup>g</sup>	N/A		
13	CON	M	53	R	27	6.60	MI	N/A		
14	CON	F	49	R	15	6.90	Arrhythmogenic right ventricular dysplasia	Chloride ions 118 mmol/L		
15	CON	F	52	L	11	6.20	Ischaemic heart disease <sup>i</sup>	N/A		
Mean (SD)			52.4 (12.2)		21.9 (9.9)	6.5 (0.3)				

**Abbreviations:** CRS: chronic residual schizophrenia; CPS: chronic paranoid schizophrenia; CUS: chronic undifferentiated schizophrenia; CDS: chronic disorganised schizophrenia; CON: control subject; Hemi: brain hemisphere; PMI: postmortem interval (hours); COD: cause of death; DOI: duration of illness (years); CPE: chlorpromazine equivalent (mg/day); IHD: Ischaemic heart disease; MI: myocardial infarction; ASCVD: Atherosclerotic cardiovascular disease.

a: Schizophrenia subjects medicated with predominately typical antipsychotics over their lifetime; b: Medicated with predominately atypical antipsychotics over their lifetime; c: Medicated with only typical antipsychotics over their lifetime; d: Medicated equally with typical and atypical antipsychotics over their lifetime; e: Moderate nicotine consumption; f: Heavy nicotine consumption; g: Moderate alcohol consumption; h: Heavy alcohol consumption; i: Calculated using the mean CPE dosage for each subject. All toxicology results are from blood unless otherwise stated (e.g. urine). All subjects are of Caucasian descent. Mean PMI is higher in the schizophrenia cohort; 7.5h (p = 0.065) and 8.0h (p = 0.045) in the STG and DLPFC respectively.

**Supplementary Table 2: Differentially Expressed miRNA by microarray as determined by SAM analysis**

STG	miRNA	Relative Expression Value	Microarray fold-change	FDR (%)	p-value	RT-PCR validation
1	hsa-let-7e	35988	1.42	0	<0.001	*
2	hsa-miR-107	7563	1.42	0	0.018	*
3	hsa-miR-125b	13635	1.29	3.84	0.168	
4	hsa-miR-128a	12396	1.32	0	0.140	
5	hsa-miR-128b	12670	1.44	0	0.110	
6	hsa-miR-129	5657	1.48	0	0.088	
7	hsa-miR-130a	2555	1.44	0	0.037	
8	hsa-miR-133b	2145	1.43	0	0.064	
9	hsa-miR-138	9339	1.56	0	0.003	
10	hsa-miR-146b	1683	1.51	0	0.062	
11	hsa-miR-148a	824	1.56	0	0.002	
12	hsa-miR-150	2912	1.31	0	0.025	
13	hsa-miR-152	858	1.60	0	0.011	
14	hsa-miR-155	3606	1.52	0	0.096	
15	hsa-miR-15a	4619	1.39	0	0.044	*
16	hsa-miR-15b	3917	1.53	0	0.007	*
17	hsa-miR-16	8209	1.54	0	0.136	*
18	hsa-miR-17-3p	1388	1.64	0	0.053	
19	hsa-miR-17-5p	4812	1.33	0	0.136	
20	hsa-miR-195	4750	1.42	0	0.008	*
21	hsa-miR-197	10552	1.24	0	0.109	
22	hsa-miR-199a*	1100	1.59	0	0.061	
23	hsa-miR-19a	963	1.65	0	0.018	*
24	hsa-miR-20a	9012	1.71	0	0.030	*
25	hsa-miR-222	5853	1.35	0	0.109	
26	hsa-miR-23a	12987	1.51	0	0.102	
27	hsa-miR-24	887	1.54	0	0.050	
28	hsa-miR-26b	19121	1.62	0	0.006	*
29	hsa-miR-27b	8698	1.28	0	0.196	
30	hsa-miR-28	3596	1.47	0	0.107	
31	hsa-miR-296	3499	1.58	0	0.048	
32	hsa-miR-328	5943	1.30	3.84	0.239	
33	hsa-miR-330	1968	1.55	0	0.098	
34	hsa-miR-335	11056	1.54	0	0.033	
35	hsa-miR-338	25545	1.55	0	0.238	*
36	hsa-miR-339	1254	1.63	0	0.054	
37	hsa-miR-340	1159	1.48	0	0.043	
38	hsa-miR-373*	14328	1.31	0	0.144	
39	hsa-miR-381	1420	1.61	0	0.003	
40	hsa-miR-409-5p	2579	1.57	0	0.054	
41	hsa-miR-432*	3530	1.34	0	0.090	
42	hsa-miR-452*	1477	1.60	0	0.074	
43	hsa-miR-455	556	1.78	0	0.014	
44	hsa-miR-484	2277	1.45	0	0.021	
45	hsa-miR-485-5p	906	1.60	0	0.012	

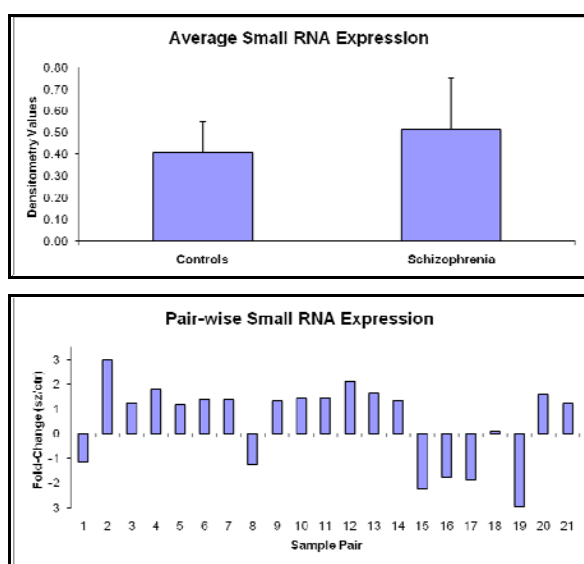
46	hsa-miR-486	5375	1.40	0	0.122
47	hsa-miR-487a	7270	1.52	0	0.020
48	hsa-miR-489	1506	1.62	0	0.006
49	hsa-miR-494	26241	1.57	0	0.125
50	hsa-miR-499	2086	1.49	0	0.023
51	hsa-miR-502	10657	1.38	0	0.212
52	hsa-miR-517a	3261	1.56	0	0.054
53	hsa-miR-517c	912	1.71	0	0.008
54	hsa-miR-518b	2954	1.43	0	0.042
55	hsa-miR-519d	47530	1.41	0	0.064
56	hsa-miR-520a*	1164	1.56	0	0.053
57	hsa-miR-520g	1748	1.67	0	0.361
58	hsa-miR-9*	7050	1.28	3.84	0.170
59	hsa-miR-99a	3439	1.39	0	0.053

DLPFC	miRNA	Relative Expression Value	Microarray fold-change	FDR (%)	p-value	RT-PCR validation
1	hsa-let-7d	25656	1.30	0	0.019	*
2	hsa-miR-101	6327	1.23	0	0.071	
3	hsa-miR-105	2930	1.26	0	0.045	
4	hsa-miR-126*	1303	1.61	0	0.035	
5	hsa-miR-128a	11797	1.19	0	0.033	*
6	hsa-miR-153	6314	1.37	0	0.091	
7	hsa-miR-16	3073	1.20	0	0.111	*
8	hsa-miR-181a	3362	1.27	0	0.048	*
9	hsa-miR-181b	3263	1.20	0	0.052	*
10	hsa-miR-181d	3263	1.23	0	0.087	
11	hsa-miR-184	19899	1.18	0	0.100	
12	hsa-miR-199a	1191	1.41	0	0.086	
13	hsa-miR-20a	2041	1.29	0	0.058	*
14	hsa-miR-219	6716	1.42	0	0.084	*
15	hsa-miR-223	3203	1.42	0	0.090	
16	hsa-miR-27a	4104	1.27	0	0.014	*
17	hsa-miR-29c	18919	1.23	0	0.091	*
18	hsa-miR-302a*	950	1.28	0	0.009	
19	hsa-miR-302b*	1591	1.21	0	0.039	
20	hsa-miR-31	578	1.35	0	0.024	
21	hsa-miR-33	623	1.64	0	0.009	
22	hsa-miR-338	12394	1.33	0	0.033	*
23	hsa-miR-409-3p	803	1.26	0	0.035	
24	hsa-miR-512-3p	915	1.23	0	0.035	
25	hsa-miR-519b	3226	1.42	0	0.109	
26	hsa-miR-7	3112	1.47	0	0.011	

**Supplementary Table 3: Total RNA analysis**

Sample Pair	Controls	Schizophrenia	Ratio (sz/ctr)	Fold change
1	0.5591	0.4910	0.8782	-1.1386
2	0.3876	1.1565	2.9838	2.9838
3	0.4292	0.5366	1.2502	1.2502
4	0.2925	0.5211	1.7815	1.7815
5	0.5847	0.6840	1.1699	1.1699
6	0.4699	0.6501	1.3834	1.3834
7	0.2931	0.3963	1.3524	1.3524
8	0.8053	0.6484	0.8052	-1.2419
9	0.5083	0.6709	1.3198	1.3198
10	0.4128	0.5915	1.4330	1.4330
11	0.4465	0.6497	1.4553	1.4553
12	0.3373	0.7120	2.1110	2.1110
13	0.4243	0.6851	1.6148	1.6148
14	0.4362	0.5872	1.3460	1.3460
15	0.3089	0.1395	0.4515	-2.2147
16	0.3748	0.2134	0.5694	-1.7561
17	0.3668	0.1981	0.5399	-1.8521
18	0.1521	0.3763	2.4746	0.0614
19	0.5035	0.1715	0.3407	-2.9354
20	0.2721	0.4285	1.5749	1.5749
21	0.2197	0.2659	1.2104	1.2104

	Controls	Schizophrenia
Average	0.4088	0.5130
SD	0.14	0.24
Ratio (sz/ctr)	1.26	
p value	0.0471	(un-paired)
	0.0281	(paired)



**Supplementary Table 4: Over-represented KEGG pathways predicted to be regulated by miR-107 and the miR-15 family**

KEGG Pathway Term	Count	Genes
Wnt signaling pathway	17	TBL1XR1, BTRC, NFATC3, LRP6, WNT7A, CREBBP, APC, PPP2R1A, SMAD3, NFATC4, PPP3CB, CAMK2G, WNT3A, FZD10, FZD7, SIAH1, AXIN2
MAPK signaling pathway	17	PPM1A, MAP3K4, AKT3, PDGFRB, MAP3K3, RPS6KA3, MAP2K3, MAP2K1, FGF2, NFATC4, BDNF, PPP3CB, CDC42, RAF1, CACNB1, CRKL, MRAS
Focal adhesion	16	ZYX, ITGA9, BCL2, AKT3, PIK3R1, PDGFRB, LAMC1, RELN, MAP2K1, CDC42, RAF1, COL1A1, BIRC4, ITGA2, CRKL, VCL
Regulation of actin cytoskeleton	13	ITGA9, PIK3R1, PDGFRB, APC, MAP2K1, FGF2, CDC42, PPP1R12B, RAF1, CRKL, ITGA2, MRAS, VCL
Axon guidance	12	SEMA3D, PLXNA2, EPHA1, EPHA7, NFATC4, PPP3CB, CDC42, NFATC3, SEMA6D, EFN1, EFN2, GNAI3
Colorectal cancer	11	APC, MAP2K1, BCL2, SMAD3, AKT3, RAF1, PIK3R1, PDGFRB, FZD10, FZD7, AXIN2
Ubiquitin mediated proteolysis	11	UBE2A, CUL5, UBE2R2, FBXW7, BTRC, CUL2, SIAH1, BIRC4, UBE2Q1, PIAS1, UBE2J1
Cell cycle	11	CDC25A, YWHAG, YWHAQ, CHEK1, SMAD3, CDK6, WEE1, CCNE1, E2F3, CREBBP, YWHAH
Small cell lung cancer	10	BCL2, CDK6, AKT3, CCNE1, PIK3R1, E2F3, BIRC4, ITGA2, PIAS1, LAMC1
Chronic myeloid leukemia	10	MAP2K1, SMAD3, CDK6, AKT3, RUNX1, RAF1, PIK3R1, E2F3, CRKL, BCR
Prostate cancer	10	MAP2K1, BCL2, AKT3, CCNE1, RAF1, PIK3R1, E2F3, PDGFRB, CREB5, CREBBP
Melanogenesis	10	MAP2K1, RAF1, CAMK2G, WNT3A, GNAO1, FZD10, FZD7, WNT7A, GNAI3, CREBBP
Insulin signaling pathway	10	RPS6KB1, TRIP10, PPARGC1A, MAP2K1, AKT3, RAF1, FASN, PIK3R1, CRKL, FLOT2
VEGF signaling pathway	9	MAP2K1, NFATC4, PPP3CB, CDC42, AKT3, RAF1, PIK3R1, NFATC3, SH2D2A
TGF-beta signaling pathway	9	ACVR2A, RPS6KB1, PPP2R1A, BMPR1B, CHRD, SMAD3, CREBBP, SMAD5, SMAD7
Acute myeloid leukemia	8	RUNX1T1, RPS6KB1, PIM1, MAP2K1, AKT3, RUNX1, RAF1, PIK3R1,
ErbB signaling pathway	8	RPS6KB1, MAP2K1, AKT3, RAF1, PIK3R1, CAMK2G, CRKL, NRG1
Melanoma	8	MAP2K1, FGF2, CDK6, AKT3, RAF1, PIK3R1, E2F3, PDGFRB
Glioma	8	MAP2K1, CDK6, AKT3, RAF1, PIK3R1, CAMK2G, E2F3, PDGFRB
Pancreatic cancer	8	MAP2K1, SMAD3, CDK6, CDC42, AKT3, RAF1, PIK3R1, E2F3
Renal cell carcinoma	8	MAP2K1, CUL2, CDC42, AKT3, RAF1, PIK3R1, CRKL, CREBBP
Non-small cell lung cancer	7	MAP2K1, CDK6, AKT3, RAF1, PIK3R1, E2F3, RASSF5,
Long-term potentiation	7	GRIN1, MAP2K1, PPP3CB, RAF1, CAMK2G, RPS6KA3, CREBBP
Basal cell carcinoma	6	APC, WNT3A, FZD10, FZD7, WNT7A, AXIN2
Endometrial cancer	6	APC, MAP2K1, AKT3, RAF1, PIK3R1, AXIN2
mTOR signaling pathway	6	RPS6KB1, CAB39, AKT3, PIK3R1, RPS6KA3, EIF4B
p53 signaling pathway	6	CHEK1, PPM1D, CDK6, CCNE1, BAI1, SIAH1
Neurodegenerative Diseases	5	APP, FBXW7, BCL2, APBA1, CREBBP
Circadian rhythm	3	CLOCK, BHLHB3, PER1

\*Shaded terms indicate relevance to schizophrenia

**Supplementary Table 5: Investigating miRNA/target gene relationships by luciferase reporter gene assay.**

	RGS4	GRM7	GRIN3A	HTR2A	RELN	VSNL1	DLG4	DRD1	PLEXN A2
<b>miR-107</b>	+	+	+	*	+			#	
<b>miR-15a</b>	#	#	#		+	#		*	
<b>miR-15b</b>	#	#	+	#	#		*		
<b>miR-16</b>	#	+	#		#	#	#	*	*
<b>miR-195</b>	#		#	*	#	*			
<p>+ denotes miRNA/target gene interactions in which synthetic miRNA transfection caused suppression of luciferase activity and anti-miR transfections caused a relief of existing endogenous suppression (increase in luciferase activity). * denotes miRNA/target gene interactions in which anti-miR transfections caused an increase in luciferase activity only. # denotes miRNA/target gene interactions in which synthetic miRNA transfections caused a suppression of luciferase activity only.</p>									

## APPENDIX V: SUPPLEMENTARY DATA FOR CHAPTER 6

**Supplementary Table 1: BA46 schizophrenia and non-psychiatric control cohort demographics and tissue characterisation.**

Pair	Diag	Sex	Age	pH	PMI	Hemi	Cause of death	Toxicology	APD	CPE	AO	DOI
1	CRS	F	51	5.7	12	R	Li toxicity & congestive cardiac failure	Li 20mg/L (fatal), Midazolam 0.02mg/L	T	570	35	16
2	CDS	M	56	6.2	15	L	Chronic airways disease	NAD	TO	450	21	35
3	CUS	M	52	6.4	46	R	Cardiomegaly (cardiomyopathy)	N/A	A	500	19	33
4	CRS	M	51	6.5	21	L	Ischaemic heart disease	Thioridazine 2.2mg/L (fatal), Mesoridazine 2.4mg/L (fatal)	TO	-	27	24
5	CPS	M	54	6.2	27.5	R	Coronary artery thrombosis	Chlorpromazine: 0.7mg/L-Diazepam: <0.1mg/L, Nordiazepam: 0.1mg/L, Insulin: 2 uU/mL	T	1560	19	35
6	CPS	F	58	6.3	19	R	Sepsis & chronic renal failure	Morphine: 0.06 mg/L, Codeine: 0.05 mg/L, Carbamazepine: 7 mg/L, Pethidine: 0.1 mg/L, Paracetamol: 6mg/L, Metoclopramide 0.1mg/L, Diazepam: <0.1 mg/L	T	450	19	39
7	CPS	F	66	6.3	12.5	R	Faecaloid peritonitis	N/A	T	-	19	47
8	CUS	F	55	6.3	33.5	L	AMS toxicity & coronary artery disease	Amisulpride 18mg/L, Clozapine 1.4mg/L	T	1300	17	38
9	CPS	M	55	6.4	72	R	Ischaemic heart disease	Metoprolol: 0.2mg/L	TO	-	30	26
10	CPS	F	54	6.4	29	R	Asthma	Citalopram 0.6 mg/L	T	700	19	35
11	CDS	F	67	6.4	27	L	Empyema	Benzotropine 0.2mg/L, Mesoridazine 0.9mg/L, Thioridazine 0.6mg/L, Paracetamol < 3.0mg/L	TO	350	21	46
12	CPS	M	75	6.6	36	L	Ischaemic heart disease	Olanzapine - 0.2 mg/L, Fluvoxamine - 0.7 mg/L	T	500	<33	44
13	CPS	M	40	6.5	21.5	L	Dihydrocodeine toxicity & sleep apnoea	Valproic acid 20mg/L, Dihydrocodeine 0.7mg/L, Quetiapine 0.3mg/l, Sertraline 0.3mg/L	T	986	17	23
14	CUS	M	44	6.5	27-43.5	L	Hanging	Urine THC detected	T	500	27	17
15	CUS	M	27	6.6	10	L	Clozapine toxicity	Clozapine 8.6mg/L (fatal)	T	300	18	11
16	CPS	M	51	6.7	18	L	Ischaemic heart disease	N/A	T	150	21	30
17	CPS	M	52	6.7	8.35	R	Ischaemic heart disease	Temazepam <0.1mg/L	T	680	21	31
18	CPS	M	33	6.8	48	L	Hanging	Doxylamine: 0.9mg/L, Olanzapine: 0.2mg/L, Paracetamol: 3mg/L	A	250	22	12
19	CPS	M	30	6.8	24	L	CO poisoning - suicide	CO 74% saturation, Clozapine 0.7mg/L, HIV -	A/T	300	26	3.5
20	CDS	F	56	6.8	34	L	Pulmonary thrombo-embolism	Paracetamol 4.5mg/L	TO	760	17	40
21	CUS	M	27	6.8	38.5	L	Myocarditis	Clozapine 0.9mg/L	A	200	23	4
22	CPS	M	57	7	33-38	L	Cardiac arrythmia	Thioridazine 0.6mg/L, Seraline <0.1mg/L	T	700	30	26
23	CPS	M	57	6.7	48	R	Atherosclerotic cardiovascular disease	Carbamazepine 10 mg/L, Citalopram 0.2 mg/L, Quetiapine <0.1 mg/L	T	618	40	17
24	CPS	M	27	6.8	33	R	Hanging	Negative	T	-	19	9
25	CDS	M	59	6.9	26.5	R	Unknown	N/A	T	750	21	39
26	CUS	M	67	6.8	5	L	Ischaemic heart disease	N/A	TO	1340	26	41
27	CPS	F	61	6.9	42	R	Ischaemic heart disease	Clozapine 1.1 mg/L, Diazepam 0.2 mg/L, Audanosine 0.4 mg/L, Nordiazepam 0.4 mg/L, Olanzapine 0.2 mg/L	TO	1200	19	42
28	CDS	M	32	7	26	L	Hanging	Negative	T	190	19	13
29	CPS	F	56	7.1	39	R	Undetermined (obesity / hepatic fatty changes)	Thioridazine (1mg/L) & Mesoridazine (0.6mg/L)	T	580	24	32
30	CUS	F	68	6.2	32	L	Acute pancreatitis	EtOH 0.055 µ/100ml, Paracetamol 3 mg/L	T	190	23	46
31	BPT	M	34	7	26	R	Hanging	Carbamazepine (1mg/L)	A	250	27	8
32	CDPS	F	33	6.9	50	R	Hanging	Negative	AO	95	14	19
33	BPT	M	57	6.4	28	R	Chronic obstructive airway disease	Paracetamol 3 mg/L, Li 4.6 mg/L	T	415	30	27
34	BPT	F	61	6.4	17	R	Myocarditis	Clozapine 0.4mg/L, Li: 0.1mg/L, nil EtOH	T	100	31	30
35	CDPS	M	30	7	26	L	Hanging	Venlafaxine 0.9mg/l	A	285	27	4
36	CDPS	F	73	6.9	17-19	L	Right ventricular dysplasia	Doxepin 0.1 mg/L, Chlorpheniramine 01, Trifluoperazine 01, Codeine 0.05, Pseudoephedrine 0.1, Paracetamol 10 mg/L	TO	300	36	37
37	CDPS	M	73	6.8	14	L	Asphyxia	Fluoxetine - 0.2 mg/l, 7-Amino nitrazepam - 0.1 mg/l, Diazepam - <0.1 mg/l, Paracetamol - <3 mg/l	T	380	21	50
Mean (SD)			51.3 (14.1)	6.6 (0.3)	28.2 (13.8)					542 (374)	23.5 (6.0)	27.8 (13.6)
1	CTR	M	46	5.8	29	L	Acute myocardial infarction	N/A				
2	CTR	M	60	6	25	R	Bacterial peritonitis, ascites, carcinomatosis	Negative				



3	CTR	M	37	6.2	11	R	Pulmonary embolism	Negative
4	CTR	M	56	6.6	24	R	Coronary artery atheroma	N/A
5	CTR	M	61	6.3	27.5	R	Unknown	N/A
6	CTR	M	74	6.3	10	L	Respiratory arrest	N/A
7	CTR	F	78	6.4	11	R	Pulmonary fibrosis	N/A
8	CTR	F	56	6.5	23	R	Massive pulmonary thrombo-embolus	N/A
9	CTR	F	60	6.5	21	L	Ischaemic heart disease	EtOH: 0.251g per 100mL, Paracetamol <3mg/L
10	CTR	M	60	6.6	13	L	Acute myocardial infarction	Negative
11	CTR	M	58	6.6	12	L	Ischaemic heart disease	N/A
12	CTR	M	73	6.6	48	R	Ischaemic heart disease	N/A
13	CTR	M	46	6.7	25	R	Mitral valve prolapse	Negative
14	CTR	F	49	6.6	15	R	Arrhythmogenic right ventricular dysplasia	Chloride ion 118 mmol/L
15	CTR	M	34	6.5	20.5	R	Acute exacerbation of asthma	N/A
16	CTR	M	44	6.7	50	L	Ischaemic heart disease	Negative
17	CTR	M	50	6.6	19	L	Ischaemic heart disease	NAD
18	CTR	M	43	6.7	13	R	Thrombotic coronary artery occlusion	Negative
19	CTR	M	38	6.7	13.5	L	Atherosclerotic cardiovascular disease	N/A
20	CTR	M	54	6.8	29	R	Coronary artery atheroma	Negative
21	CTR	M	18	6.8	33	L	Probable hypertrophic cardiomyopathy	Paracetamol (24mg/L) & Lignocaine (1mg/L)
22	CTR	F	51	7.2	37.5	R	Acute myocardial infarction	N/A
23	CTR	M	53	6.7	27	R	Acute myocardial infarct	N/A
24	CTR	F	33	6.9	24	L	Cardiac arrhythmia; myocardial fibrosis	EtOH not detected
25	CTR	M	59	7	20	R	Coronary thrombosis	N/A
26	CTR	M	56	7	37	R	Hypertension & cardiomegaly	N/A
27	CTR	M	57	6.9	18	L	Ischaemic heart disease	HIV negative
28	CTR	M	37	6.9	24	R	Electrocution	Codeine <0.5 mg/L, paracetamol 3 mg/L, lignocaine <0.5 mg/L
29	CTR	M	55	7.2	20	L	Cardiac arrest	N/A
30	CTR	M	78	6.3	6.5	L	Dehydration, adenocarcinoma	N/A
31	CTR	M	37	6.8	21	L	Ischaemic heart disease	N/A
32	CTR	F	21	6.8	39.5	R	Primary cardiac arrhythmia	N/A
33	CTR	M	62	6.6	37.5	R	Acute myocardial infarction	Negative
34	CTR	M	50	6.7	29	R	Ischaemic heart disease	Negative
35	CTR	M	24	7	43	R	Idiopathic cardiac arrhythmia	Negative
36	CTR	M	64	7	39.5	R	Coronary artery thrombosis	Negative
37	CTR	M	60	7	21.5	R	Ischaemic heart disease	N/A
Mean (SD)			51.1 (14.6)	6.7 (0.3)	24.8 (11.0)			

Diag, diagnosis; CRS, chronic residual schizophrenia; CDS, chronic disorganized schizophrenia; CUS, chronic undifferentiated schizophrenia; CPS, chronic paranoid schizophrenia; BPT, bipolar type; CDPS, chronic depressive schizophrenia; CTR, control; PMI, post mortem interval (hours); Hemi, brain hemisphere; APD, antipsychotic drug class (A, predominantly atypical; T, predominantly typical; TO, typical only; A/T, equal); CPE, chlorpromazine equivalent (mg/day); AO, age of onset; DOI, duration of illness (years); Demographic variables age (p=0.95), pH (p=0.49), PMI (p=0.23) and RIN (p=0.81) do not differ between schizophrenia and control cohorts (two-tailed Student's t-test).

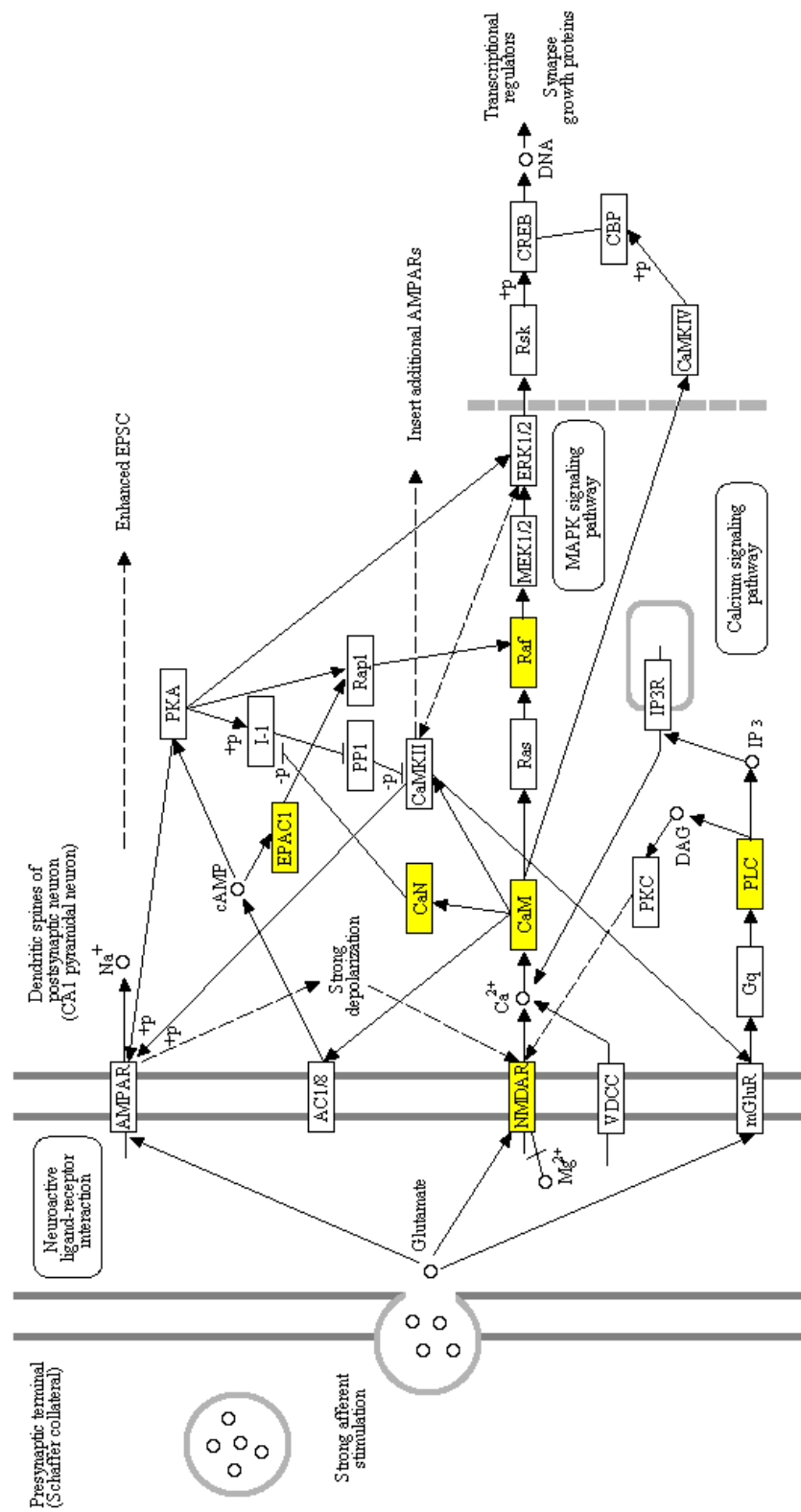
**Supplementary Table 2: miRNA and biogenesis gene expression correlation matrix. Blue shaded cells represent significant correlations.**

Correlations										
		miR-17	miR-328	miR--134	miR-107	miR-652	miR-382	DGCR8	DROSHA	DICER
miR-17	Correlation	1	.470**	.405**	.434**	.141	.089	-.046	-.094	.359**
	p value		.000	.000	.000	.240	.466	.700	.442	.002
miR-328	Correlation	.470**	1	.588**	.855**	.089	.315**	.099	-.023	.226
	p value	.000		.000	.000	.463	.008	.407	.852	.058
miR-134	Correlation	.405**	.588**	1	.676**	.321**	.267*	.066	.185	.117
	p value	.000	.000		.000	.006	.025	.584	.127	.331
miR-107	Correlation	.434**	.855**	.676**	1	.112	.300*	.114	.036	.206
	p value	.000	.000	.000		.354	.012	.342	.768	.085
miR-652	Correlation	.141	.089	.321**	.112	1	.550**	.049	.091	.139
	p value	.240	.463	.006	.354		.000	.685	.467	.255
miR-382	Correlation	.089	.315**	.267*	.300*	.550**	1	.311**	.035	.297*
	p value	.466	.008	.025	.012	.000		.009	.779	.014
DGCR8	Correlation	-.046	.099	.066	.114	.049	.311**	1	.083	.084
	p value	.700	.407	.584	.342	.685	.009		.504	.492
DROSHA	Correlation	-.094	-.023	.185	.036	.091	.035	.083	1	.251*
	p value	.442	.852	.127	.768	.467	.779	.504		.040
DICER	Correlation	.359**	.226	.117	.206	.139	.297*	.084	.251*	1
	p value	.002	.058	.331	.085	.255	.014	.492	.040	
* Two-tailed Pearson Correlation is significant at the 0.05 level;** 0.01 level										



**B**

**LONG-TERM POTENTIATION**



**Supplement 4: Over-represented KEGG Pathways predicted to be regulated by up-regulated microRNA in BA46:** Multi-hit analysis. Pathways relevant to schizophrenia are highlighted in white.

Term	Count	%	P Value	Genes	Fold Enrichment	Bonferroni	Benjamini	FDR
hsa04810: Regulation of actin cytoskeleton	40	2.24	2.71E-05	FGFR2, FGF5, ENAH, PDGFB, DIAPH2, MRAS, WASF1, DIAPH3, SSH2, WASF2, FGF11, PIP5K1B, ABI2, ARPC4, ITGB1, VCL, PTK2, PFN2, TIAM2, ITGB8, ARPC2, TIAM1, RAC1, PPP1R12A, PDGFD, FGF1, PIK3R1, FN1, ROCK1, ROCK2, ARHGEF7, MYLK2, ACTN2, PPP1CA, ITGA5, CFL2, PDGFRA, CRK, MYLK, MYH10	1.99	0.004631	0.004631	0.033
hsa05200: Pathways in cancer	54	3.02	3.05E-05	FGF5, PDGFB, PPARG, MITF, FGF11, PTEN, CCNE1, MAX, PAX8, FAS, FGF1, CHUK, AKT3, CSF2RA, PLD1, CTBP2, RUNX1T1, CDK6, CTNNA2, RAD51, CCDC6, HIF1A, VEGFA, PDGFRA, MAPK9, LAMC1, FGFR2, EGLN3, PML, BCL2L1, ITGB1, TPM3, IGF1R, PTK2, BCL2, RAC1, NKX3-1, RUNX1, PIK3R1, FN1, COL4A1, EPAS1, VHL, CREBBP, TGFBR2, COL4A6, STAT3, DVL1, RASSF5, CDKN1A, LAMA3, ETS1, RASSF1, CRK	1.76	0.00521	0.002608	0.037
hsa04360: Axon guidance	26	1.45	2.71E-04	ABLIM1, ABLIM3, ITGB1, PTK2, ROBO1, RAC1, NFAT5, PPP3CB, UNC5D, ROBO2, PPP3CA, NFATC1, ROCK1, ROCK2, DPYSL5, EPHA5, EPHA4, EPHA7, SEMA6C, SEMA4G, SEMA6D, RGS3, CFL2, SEMA4C, SEMA4B, SRGAP2	2.16	0.045232	0.01531	0.330
hsa04350: TGF-beta signaling pathway	20	1.12	3.05E-04	LTBP1, ROCK1, E2F5, ROCK2, SMAD6, SMAD5, CREBBP, TGFBR2, BMPR2, RPS6KB2, RPS6KB1, SMAD1, ACVR2A, ACVR2B, ZFYVE16, SMURF2, CHRD, CUL1, TFDP1, BMPR1A	2.46	0.050817	0.012954	0.371
hsa04510: Focal adhesion	35	1.96	3.63E-04	PDGFB, COL2A1, ITGB1, PTEN, VCL, IGF1R, PTK2, PDPK1, ARHGAP5, ITGB8, BCL2, RAC1, PPP1R12A, SHC1, PDGFD, COL11A1, AKT3, PIK3R1, SHC4, FN1, COL4A1, ROCK1, ROCK2, MYLK2, ACTN2, COL4A6, PPP1CA, LAMA3, ITGA5, VEGFA, PDGFRA, MAPK9, LAMC1, CRK, MYLK	1.86	0.060186	0.012338	0.442
hsa04720: Long-term potentiation	17	0.95	3.73E-04	CREBBP, GRM1, ITPR1, PPP1CA, RPS6KA3, PLCB4, GRIA2, CAMK4, GRIN2C, CAMK2D, PPP1R12A, PPP3CB, PRKACB, PPP3CA, CACNA1C, PLCB1, CALM1	2.681962	0.061757	0.010568	0.454
hsa04722: Neurotrophin signaling pathway	24	1.34	8.98E-04	YWHAZ, MAPKAPK2, RPS6KA3, BDNF, YWHAH, CAMK4, MAP3K3, MAPK14, BCL2, GAB1, RAC1, NTRK2, CAMK2D, SH2B3, MAPK9, SORT1, SHC1, SH2B1, CRK, FRS2, PIK3R1, AKT3, CALM1, SHC4	2.076358	0.142467	0.021717	1.091

