

THE CONTROL OF CHROMOSOME SEGREGATION IN MOUSE OOCYTES

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PhD Thesis

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I hereby certify that the work embodied in this thesis contains published papers of which I am a joint author. I have included as part of the thesis a written statement, endorsed by my supervisor, attesting to my contribution to the joint publications (Appendix I).

Simon Lane, 2nd April 2012

This page is dedicated to Dr. C. K. Mercer

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ABSTRACT

This thesis explores the first meiotic division in mouse oocytes, using imaging of fluorescent chimeras by confocal and epifluorescence microscopy in real time and of fixed specimens following immunocytochemistry. The activities of the spindle assembly checkpoint (SAC) and the anaphase promoting complex (APC) are examined with respect to the timing of germinal vesicle breakdown, spindle formation, chromosome alignment, and polar body extrusion. The activation of the APC, an event that in mitosis is prevented until proper attachment of all chromosomes is achieved, is shown not to be strictly coupled to bivalent alignment in prometaphase I. Instead the metaphase to anaphase transition is begun following the attachment of the majority of kinetochores and is characterised by sub-optimal activity of the APC. It is shown that this uncoupling of the SAC and chromosome alignment has the potential to generate aneuploidy. These findings have implications for the high aneuploidy rates deriving from the first meiotic division, which are often responsible for miscarriage in humans.

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LIST OF COMMONLY USED ABBREVIATIONS

APC – Anaphase Promoting Complex
CDK – Cyclin Dependent Kinase
CPC – Chromosomal Passenger Complex
GVBD – Germinal Vesicle Breakdown
ICC – Immunocytochemistry
MCC – Mitotic Checkpoint Complex
MI – Meiosis I
MII – Meiosis II
PBE – Polar Body Extrusion
PGC – Primordial Germ Cell
SAC – Spindle Assembly Checkpoint
SC – Synaptonemal Complex

