# 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 ABREVIATIONS

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