

## Regulating the orderly progression of oocyte meiotic maturation events in mammals

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Mammalian female germ cells enter meiosis during fetal development and, depending on species, they arrest at prophase of the first meiosis for months or years after birth. During follicle development, oocytes are still arrested at this stage although their size increases significantly. Only after puberty will the fully grown oocytes resume the first meiosis upon gonadotropin stimulation of the somatic cells surrounding mature follicles. The resumption of meiosis is indicated by germinal vesicle breakdown (GVBD), followed by chromatin condensation, spindle microtubule assembly, and the first meiotic spindle formation. It has long been known that maintenance of meiotic arrest requires a high level of intra-oocyte cyclic adenosine 3',5'-monophosphate (cAMP). Another second messenger, guanosine 3',5'-cyclic monophosphate (cGMP) also plays an important role in maintaining oocyte meiosis arrest. A high level of cGMP causes an increase in oocyte cAMP by acting on phosphodiesterase 3 (PDE3). The decrease in cGMP and cAMP provides the leading event for GVBD. In this research front, [Liu \*et al.\* \(2013\)](#) have summarised how the gonadotropin-stimulated GVBD occurs through regulating functions of natriuretic peptide precursor type C (NPPC) and natriuretic peptide receptor 2, a guanylyl cyclase in granulosa cells.

The oocyte loses its centrioles during oogenesis, and thus, different from mitotic cells, its meiotic spindle is organised by acentriolar centrosomes. Centrosome components including  $\gamma$ -tubulin, NuMA and several protein kinases have been shown to promote meiotic spindle microtubule nucleation and organisation at the spindle poles. The proper spindle organisation is important for correct chromosome alignment and separation. This research front also includes two research papers which show that UCHL5IP, one of the subunits of augmin that is important for  $\gamma$ -tubulin localisation in mitosis, also regulates meiotic spindle organisation and chromosome alignment. Knockdown of UCHL5IP disrupts spindle pole localisation of  $\gamma$ -tubulin and leads to spindle defects and chromosome misalignment ([Wang \*et al.\* 2013](#)). Histone modifications are also involved in proper distribution of chromosomes in the meiotic spindle. Knock-down of Suv4-20h, a histone methyltransferase (HMTase) that catalyses histone H4 lysine 20 dimethylation and trimethylation, causes an increased percentage of aberrant chromosome alignment in meiotic spindles ([Xiong \*et al.\* 2013](#)). The gradual understanding on regulation of meiotic spindle organisation and chromosome alignment will benefit oocyte quality improvement.

In mitotic cells, only when all chromosomes are well aligned at the middle plate of the spindle will the chromosomes separate into two daughter cells, and this is assured by spindle assembly checkpoint (SAC) proteins. If the SAC malfunctions, chromosome segregation error will occur, which causes aneuploidy followed by possible tumour formation or cell death. A high percentage of oocytes are aneuploid, which is a leading cause for female factor infertility. The percentage of oocyte aneuploidy is increased with advanced maternal age. Aneuploidy of oocytes will lead to embryo developmental failure, abortion or birth defects. It has recently been shown that SAC function also exists during oocyte meiotic maturation, although it is not as stringent as in mitotic cells. [Polanski \(2013\)](#) summarises our current knowledge on SAC function in chromosome separation with special reference to the SAC efficiency in mammalian oocytes as well as its clinical relevance.

Another unique characteristic of oocyte meiotic division is that the oocyte undergoes asymmetric division, producing a small first polar body (PB1) and a large secondary oocyte. Half of the homologous chromosomes are separated into the first polar body, while most maternal mRNA and proteins are left in the ooplasm, which provides nutrients for early embryo development. Upon SAC inactivation, the anaphase promoting complex (APC) is activated, allowing homologous chromosome segregation. Many events and molecules are involved in the cleavage of chromosome cohesion during oocyte meiosis. [Pomerantz and Dekel \(2013\)](#) review the sequence of events leading to chromosome segregation and PBI extrusion, and provide a comparison with the corresponding events in mitotic cell division.

In summary, in this research front on oocyte meiosis, we have included three review articles on the regulation of key meiotic events and two related research articles. These articles summarise the recent advancement of our understanding on oocyte meiotic maturation, and will be valuable for trainees and investigators in the field.

### References

- Liu, L., Kong, N., Xia, G., and Zhang, M. (2013). Molecular control of oocyte meiotic arrest and resumption. *Reprod. Fertil. Dev.* **25**, 463–471. doi:10.1071/RD12310
- Polanski, Z. (2013). Spindle assembly checkpoint regulation of chromosome segregation in mammalian oocytes. *Reprod. Fertil. Dev.* **25**, 472–483. doi:10.1071/RD12145

- Pomerantz, Y., and Dekel, N. (2013). Molecular participants in regulation of the meiotic cell cycle in mammalian oocytes. *Reprod. Fertil. Dev.* **25**, 484–494. doi:[10.1071/RD12242](https://doi.org/10.1071/RD12242)
- Wang, Y. P., Qi, S. T., Wei, Y., Ge, Z. J., Chen, L., Hou, Y., Ouyang, Y. C., Schatten, H., Zhao, J. G., and Sun, Q. Y. (2013). Knockdown of UCHL5IP causes abnormalities in  $\gamma$ -tubulin localisation, spindle organisation and chromosome alignment in mouse oocyte meiotic maturation. *Reprod. Fertil. Dev.* **25**, 495–502. doi:[10.1071/RD12300](https://doi.org/10.1071/RD12300)
- Xiong, K., Wu, W., Wang, X., Ma, X., Chen, J., and Liu, H. (2013). Mouse oocyte meiosis is disturbed by knockdown of Suv4-20h. *Reprod. Fertil. Dev.* **25**, 503–510. doi:[10.1071/RD12116](https://doi.org/10.1071/RD12116)