Importance of CENP-E in meiotic maturation of human oocytes

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Meiosis is a specialized cell division that generates oocytes with half the genome content of parental cells. Human oocyte meiosis is error prone which generates aneuploid eggs, leading to infertility and birth defects. Chromosome congression and alignment during meiosis is critical for correct chromosome segregation and the generation of euploid eggs. Centromere-associated protein-E (CENP-E) is a plus-end-directed kinesin and is required for the congression of pole-proximal chromosomes. In mitosis, it locates to outer kinetochores in prometaphase and mediates proper alignment of chromosomes at metaphase. Consequently, impaired CENP-E activity leads to prolonged activation of the spindle assembly checkpoint and a delay to the metaphase to anaphase transition.

However, the meiotic roles of CENP-E are not as fully investigated, especially in human oocytes. Furthermore, how the spindle checkpoint responds to different chromosome configurations in meiosis I is not well understood. In this study, we aim to understand the importance of CENP-E in generating euploid oocytes as well as determine how mammalian oocytes respond to polar chromosomes. To do this, we are taking a cross-species approach, employing mouse, bovine and human oocytes.

Using super-resolution microscopy, we found CENP-E localized to outer kinetochores and the microtubule plus ends in metaphase I and to the mid-body during anaphase I. Inhibition of CENP-E activity using the specific inhibitor GSK9293295 resulted in loss of its kinetochore localization and restricted it to the spindle poles. Initial experiments suggest that inhibition of CENP-E in mouse and bovine oocytes resulted in frequent polar chromosomes in metaphase I and metaphase II and abnormal spindle dynamics. Furthermore, inhibition of CENP-E activity significantly delayed completion of meiosis I. This preliminary data supports a role for CENP-E in chromosome alignment in meiosis I in mammalian oocytes and indicate that defective chromosome alignment causes cell cycle delay. Ongoing and future experiments are aimed at further elucidate the role of CENP-E in chromosome alignment in meiosis and towards understanding how chromosome alignment errors influence meiotic timing and oocyte maturation.