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PP2A in meiotic oocytes

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Meiosis is a specialized type of cell division in which one round of DNA replication is followed by 2 consecutive rounds of chromosome segregation. It occurs in eukaryotes during the generation of haploid gametes or spores. In meiosis I, homologous chromosomes (4n) are paired into bivalents and then separated to produce 2 haploid 2n cells. In meiosis II, sister chromatids are further separated to form a total of 4 haploid 1n cells.[1] Missegregation of meiotic chromosomes in mammals can lead to infertility, miscarriage, or birth defects. Notably, meiosis, especially female meiosis, which usually occurs after a prolonged arrest of oocytes in meiosis I, is error prone and the error rate markedly increases with age.

Precise chromosome segregation requires bipolar microtubule (MT)-kinetochore (KT) attachment of all chromosomes and timely disjunction of bivalents (meiosis I) or sister chromatids (meiosis II and mitosis). In mitotic cells, the bipolar MT-KT attachment is achieved when a pair of MT bundles from opposite spindle poles is attached separately to the 2 sister KTs of a chromosome ("end-on" attachment). Sister chromatids are stuck together by the protein complex cohesin till the inactivation of a machinery termed spindle assembly checkpoint after all the properly attached chromosomes are aligned at the metaphase plate.[2] Distinct from mitosis, however, during meiosis I sister KTs are attached to MTs from the same poles and, since the paired homologous chromosomes are held together by chiasma, cohesin needs to be protected from degradation. Furthermore, as female meiosis in most animals occurs in the absence of the centrosome, both the spindle formation and the chromosome alignment are mechanistically distinct from those in mitosis.[1]

Protein phosphatase 2A (PP2A) is a major serine/threonine phosphatase in eukaryotic cells. The PP2A holoenzyme is composed of a structural A subunit (PP2Aa), a regulatory B subunit, and a catalytic C subunit (PP2Ac). Each of the A and C subunits has 2 paralogs or isoforms in mammals, whereas isoforms of the B subunit are currently classified into 4 families, each containing 2-5 members. PP2A promotes stable MT-KT interaction in mitosis.[2] It is required for persistent sister chromatid cohesion in meiosis I in yeast or mitosis in human.[3] Studies also suggest that PP2A is involved in multiple steps of murine oocyte meiosis, including spindle formation, MT-KT attachment, and sister chromatid cohesion.[4-6] Complete genetic inactivation of PP2A in oocytes, however, had not been performed to directly verify these reported meiotic roles.

In this volume, Tang and colleagues generated conditional knockout mice whose oocytes were deficient in genes encoding all the PP2Ac paralogs (PP2Acα and PP2Acβ) from primary follicular stages.[7] They found that the paralogs are functionally redundant, because only the loss of both PP2Acα and PP2Acβ resulted in female infertility. The double knockout did not affect ovary morphology, ovarian folliculogenesis, or germinal vesicle breakdown (GVBD), the hallmark of meiotic resumption. Meiosis I of the DKO oocytes, however, was severely blocked. Following GVBD, spindles became elongated or multipolar. Bivalents were poorly stretched and rarely bioriented. KTs tended to be either unattached to spindle MTs or exhibited only transient (lateral) or incorrect (merotelic) attachment. Live imaging revealed that chromosomes failed to either congress to or stably aligned at the metaphase plate. Sister chromatid cohesion, however, was not perturbed. PP2A is believed to stabilize the MT-KT attachment by counteracting with Aurora B/C kinases.[2,6] Consistently, the authors observed increased phosphorylation levels of Aurora B/C substrates, KNL1 and histone H3, in the DKO oocytes. Furthermore, treating the oocytes with an Aurora B/C inhibitor, hesperadin, improved their chromosome alignment, bivalent stretching, and KT-MT attachments.

Thus, Tang and colleagues confirm the roles of PP2A in spindle organization and proper MT-KT attachment in meiosis I. Their study, however, does not support its role in protecting cohesin from premature degradation. Such a discrepancy apparently needs clarification in the future.

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Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

References

[1] Clift D and M. Schuh. Nat Rev Mol Cell Biol 2013; 14:549-62; PMID:23942453; http://dx.doi.org/10.1038/nrm3643
[2] Godek KM, et al. Nat Rev Mol Cell Biol 2015; 16:57-64; PMID:25466864; http://dx.doi.org/10.1038/nrm3916
[3] Rivera T, et al. Bioessays 2006; 28:775-9; PMID:16927389; http://dx.doi.org/10.1002/bies.20448
[4] Rattani A, et al. Elife 2013; 2:e01133; PMID:24192037; http://dx.doi.org/10.7554/eLife.01133
[5] Hu MW, et al. Biol Reprod 2014; 91:19; PMID:24899574; http://dx.doi.org/10.1095/biolreprod.114.120220
[6] Yoshida S, et al. Dev Cell 2015; 33:589-602; PMID:26028219; http://dx.doi.org/10.1016/j.devcel.2015.04.020
[7] Tang A, et al. Cell Cycle 2016; 15(11):1450-61; PMID: 27096707; http://dx.doi/org/10.1080/15384101.2016.1175256