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Authors
Ünal, Elçin
Torres, Jorge Z

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Ensuring fidelity of chromosome segregation

Elçin Ünal[a,*] and Jorge Z. Torres[b,*]
[a]Department of Molecular and Cell Biology, University of California, Berkeley, Berkeley, CA 94720; [b]Department of Chemistry and Biochemistry, University of California, Los Angeles, Los Angeles, CA 90095

At the 2017 first joint ASCB EMBO Meeting, the fields of cell division, cell cycle, and cell death took the center stage in three separate Minisymposia. In this review, we highlight some of the topics presented in the Minisymposium entitled "Ensuring Fidelity of Chromosome Segregation."

From centromeres to kinetochores: keeping chromosomes under control

How cells establish and maintain centromere identity was the focus of two separate talks: First, **Barbara Mellone** (University of Connecticut) presented an elegant genetic system for creating ectopic centromeres in *Drosophila*. This is accomplished by targeting CAL1, a centromere-specific histone assembly factor, through a LacI-CAL1 chimeric protein that binds to the lacO arrays inserted at distinct genomic locations. Her group found that ectopic centromeres are mostly functional and cause severe genomic instability but, interestingly, in some cases can be inactivated. Further investigation will reveal whether and how the activity state of these ectopic centromeres is propagated throughout animal development. **Shannon McNulty** (Sullivan lab, Duke University) reported on the identification and function of noncoding alpha satellite RNAs. Using cytological and molecular techniques, her group found that each human centromere produces a unique set of noncoding alpha satellite RNAs, which function in *cis* to recruit at least two key centromere proteins: CENP-A and CENP-C. This exciting discovery reveals that RNAs present at active centromeres play a crucial role in kinetochore assembly and cell cycle progression.

Moving outward from centromeres, **Kelly Salmon** (Compton lab, Geisel School of Medicine at Dartmouth) presented a role for the condensin complexes in mitotic chromosome movement. Her group found that depletion of the CAP-D3 condensin subunit results in abnormal chromosome oscillations, which arise due to a failure in the recruitment of two chromokinesins, Kid and Kif4A, to chromosomes.

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MBoC is pleased to publish this summary of the Minisymposium on "Ensuring Fidelity of Chromosome Segregation," held at the 2017 ASCB EMBO Meeting, Philadelphia, PA, December 4, 2017.
*Address correspondence to: Elçin Ünal (elcin@berkeley.edu) and Jorge Z. Torres (torres@chem.ucla.edu).
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Carissa Heath (Wignall lab, Northwestern University) presented a follow-up talk on chromokinesins. Her group found that Kif4 plays an essential role in mouse oocyte meiosis through its dynamic localization to mediate chromosome segregation and midzone formation.

Elçin Ünal (University of California, Berkeley) described a novel mechanism that ensures timely function of kinetochores in budding yeast, through modulating the Ndc80 subunit abundance. Meiosis-specific transcription from the distal *NDC80* promoter inhibits Ndc80 protein synthesis through two parallel pathways: the distal promoter transcript cannot be translated, and its transcription interferes with the proximal promoter in *cis*, therefore repressing the expression of the protein-coding mRNA. Interestingly, this dual mechanism is used genome-wide, in conditions demanding rapid and dynamic changes in gene expression.

Forming and monitoring microtubule action on chromosomes

The second half of the Minisymposium mainly focused on nonchromosomal factors that ensure high-fidelity chromosome segregation. **Vitali Sikirzhytski** (Khodjakov lab, Wadsworth Center) presented work that elucidates how kinetochore fibers (K-fibers) are formed. Using correlative light/electron microscopy (CLEM) and live-cell recordings, his group found that microtubule nucleation around kinetochores governs mitotic spindle assembly in human cells. Furthermore, the formation of nascent K-fibers is facilitated by the motor activity of CENP-E, which brings the plus ends of the initially disoriented microtubules into the kinetochore, thereby converting lateral interactions into end-on attachments. **Patrik Risteski** (Tolić lab, Ruđer Bošković Institute) described the role of a different set of microtubule fibers, called the bridging fibers, in chromosome segregation. Using laser-cutting experiments, his group found that kinetochores could segregate without any connection to one spindle pole. This separation requires the bridging fiber, which connects sister kinetochore fibers. K-fibers and bridging fibers appear to be cross-linked. Thus, microtubule sliding within the bridging fiber works together with the shortening of kinetochore fibers to segregate chromosomes.

Finally, the spindle assembly checkpoint (SAC) was the highlight of two exciting talks. **Jorge Torres** (University of California, Los Angeles) presented results from a genetic high-throughput screen to identify novel SAC components. Utilizing siRNA libraries and drugs targeting the kinome along with cell cycle sensor cell lines and synchronization experiments, the Torres lab identified novel kinases and phosphatases crucial for SAC function. These enzymes all localize to the kinetochores from prometaphase to metaphase, a time when the SAC is active, and their mechanisms of action are being currently investigated. **Pablo Lara-Gonzalez** (Desai lab, University of California, San Diego) presented his finding that components of the SAC are repurposed in development to control germ cell proliferation. Using *Caenorhabditis elegans*, his group showed that mutants of the SAC component Mad2 have a severe defect in fertility that arises from defects in mitotic entry in germ cell precursors. Interestingly, this function is unrelated to the well-understood role of Mad2 in the SAC. Using separation-of-function mutants, Pablo identified the molecular pathway used by Mad2 to promote mitotic entry. These data revealed a new mechanism of cell cycle control in germ cells and, possibly, other tissues.