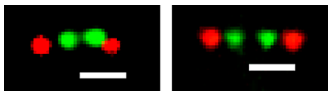
In This Issue

Text by Ben Short
bshort@rockefeller.edu

Spindle microtubules sustain the tension



Compared with a wild-type cell (left), sister pericentromeres (green) are stretched farther apart in a yeast cell lacking topoisomerase II (right). Spindle poles are labeled red.

Chacón et al. reveal how the mitotic spindle maintains a constant level of tension on correctly attached chromosomes.

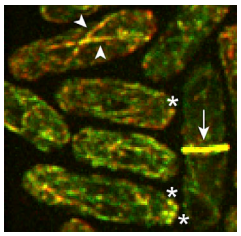
When sister chromatids attach to microtubules emanating from opposite spindle poles, the chromatin that surrounds and connects the chromatids' centromeres is thought to come under tension, generating a mechanical signal that permits the cell to separate the chromosomes and exit mitosis. But it is unclear how much tension pericentromeric chromatin experiences and how cells cope with fluctuations in this force.

By measuring the inherent stiffness of pericentromeric chromatin and how much it became stretched during metaphase, Chacón et al. calculated that each budding yeast pericentromere experiences around 5 pN of tension when correctly attached to the mitotic spindle, more than enough to activate downstream signaling events. The researchers then investigated how pericentromeric tension was affected by changes in pericentromere structure. Pericentromeres were much more flexible in yeast lacking the DNA-packaging enzyme topoisomerase II, but they still experienced 5 pN of tension during metaphase because the mitotic spindle contrived to pull sister centromeres further apart than normal. The spindle achieved this feat by growing longer than it did in wild-type cells, while simultaneously shortening the kinetochore microtubules that directly attach to chromosomes.

Modeling experiments suggested that changes in pericentromeric tension can induce compensatory changes in kinetochore microtubule dynamics, which could help prevent natural variations in pericentromere structure from falsely activating checkpoint pathways that delay mitotic exit. Senior author Melissa Gardner now wants to investigate how tension regulates kinetochore microtubules and to determine how much pericentromeric tension can decrease without activating the spindle checkpoint.

Chacón, J.M., et al. 2014. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201312024.

The fellowship of the Rng



Myo51 (green) and Rng8 (red) colocalize in cytoplasmic puncta (asterisks), actin cables (arrowheads), and the contractile cytokinetic ring (arrow).

Wang et al. reveal how two proteins cluster the myosin motor Myo51 to promote assembly of the fission yeast cytokinetic ring.

Fission yeast assemble a contractile ring from myosin II–containing precursor nodes scattered around the cell equator. The motor protein captures actin filaments nucleated from neighboring nodes and pulls the structures together until they coalesce into a compact actomyosin ring. The type V myosin Myo51 also contributes to ring formation by promoting the delivery of additional actin filaments to the cell equator. But Myo51's precise function and how it is regulated during cytokinesis remain unclear.

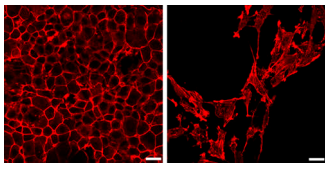
Wang et al. identified two coiled-coil proteins, which they named Rng8 and Rng9, that colocalized with Myo51 on actin cables and the cytokinetic ring. Deleting Rng8 or Rng9 largely abolished Myo51's recruitment to these structures, thereby delaying node coalescence and ring assembly.

All three proteins interacted with each other in vivo, forming higher-order clusters containing multiple Myo51 dimers. These clusters were able to move without interruption along actin filaments, transporting artificial cargoes long distances across the cell. In the absence of Rng8 or Rng9, however, Myo51 only formed individual dimers that failed to move processively on actin cables.

Rng8 and Rng9 therefore support Myo51's function in cytokinesis by regulating the motor's localization and oligomerization. Senior author Jian-Qiu Wu now wants to investigate the motor complex's behavior in vitro and to identify any cargoes (besides actin filaments) that it might transport to promote contractile ring assembly and stability.

Wang, N., et al. 2014. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201308146.

Tenascin-X and the pick of destiny



Breast epithelial cells (left) stained for F-actin (red) show a characteristic epithelial morphology on control coverslips but adopt a mesenchymal phenotype when plated on the FBG domain of TNX (right).

Alcaraz et al. describe how the extracellular matrix protein tenascin-X (TNX) controls cell plasticity by activating the TGF-β signaling pathway.

In addition to their structural and mechanical roles, extracellular matrix proteins often have signaling functions that influence cell fate choices. Type I collagen, for example, induces epithelial-to-mesenchymal transitions (EMTs) by regulating several cell-signaling pathways. The matrix protein TNX binds to multiple collagens and helps assemble them into functional three-dimensional networks, but whether TNX also has signaling functions is unknown.

Alcaraz et al. found that breast epithelial cells quickly switched to a mesenchymal fate when plated onto coverslips coated with the fibrinogen-like (FBG) domain of TNX. This transition depended on the TGF-β signaling pathway. TGF-β is secreted in an inactive complex, in which the mature cytokine is masked by an inhibitory peptide. The FBG domain of TNX bound and activated the latent TGF-β complex, probably by inducing a conformational change that exposes the cytokine to its cell surface receptor.

Alcaraz et al. identified the integrin α11β1 as the adhesion receptor that binds to the FBG domain of TNX, and they showed that knocking down the α11 subunit blocked TGF-β signaling and EMT. Senior author Ulrich Valcourt now wants to investigate whether the integrin plays an active role in the process or whether it simply docks cells close to the sites where TNX activates latent TGF-β. He also plans to examine the pathway's role in events that involve TGF-β–induced EMT, such as wound healing and cancer metastasis.

Alcaraz, L.B., et al. 2014. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201308031.

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