In This Issue

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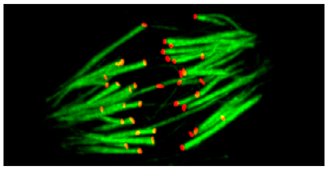
CDK1 makes the meiotic spindle wait



In an oocyte with enhanced CDK1 activity, every kinetochore (red) forms a stable, end-on attachment to a spindle microtubule (green).

A delay in cyclin-dependent kinase activity prevents meiotic chromosomes from prematurely attaching to spindle microtubules, Davydenko et al. report.

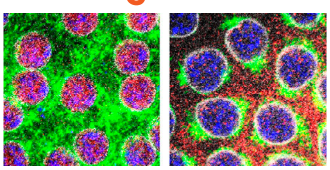
In somatic cells, the mitotic spindle assembles and forms stable attachments to the kinetochores of sister chromatids in a matter of minutes. In mammalian oocytes undergoing meiosis I, however, multiple microtubule-organizing centers take several hours to assemble a bipolar spindle, and kinetochore–microtubule interactions aren't stabilized for a few hours after that, probably to prevent chromosomes from forming incorrect attachments while the spindle is still multipolar. How oocytes delay the formation of stable kinetochore–microtubule attachments is unclear, however.

Davydenko et al. wondered whether the cyclin-dependent kinase CDK1 might be involved in timing attachment stabilization. CDK1 activity rises sharply at the beginning of mitosis, but in oocytes the kinase's activity increases slowly during meiosis I, reaching a peak at the end of metaphase when kinetochore–microtubule attachments are stabilized. Reducing CDK1 activity delayed the formation of stable attachments still further, whereas prematurely boosting CDK1's function caused oocytes to stabilize their kinetochore–microtubule interactions earlier than normal. This led to frequent errors in chromosome segregation, supporting the idea that oocytes delay attachment stabilization to avoid forming incorrect kinetochore–microtubule connections.

CDK1 phosphorylates numerous substrates, including many kinetochore-associated proteins. Which of these help to stabilize kinetochore–microtubule attachments is an important question for the future, says senior author Michael Lampson.

Davydenko, O., et al. 2013. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201303019.

Moving the Greatwall



Gwl (red) localizes to the nuclei (blue) of early *Drosophila* embryos during interphase (left) but exits during prophase (right) while the nuclear envelope (white) is still intact.

Wang et al. reveal how a mitotic kinase moves in and out of the nucleus to promote cell cycle progression.

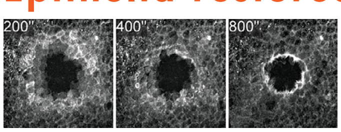
Cyclin B and the cyclin-dependent kinase Cdk1 push cells into mitosis by phosphorylating numerous substrates in the nucleus and cytoplasm. The Greatwall (Gwl) kinase aids mitotic entry by inhibiting the phosphatase PP2A-B55, which would otherwise dephosphorylate cyclin B–Cdk1's targets. Cdk1 activates Gwl at the start of mitosis, but Wang et al. discovered that Gwl's localization is also regulated to ensure cells enter mitosis on time.

Gwl localizes to the nucleus of interphase cells, but Wang et al. noticed that the kinase exits the nucleus a few minutes before the nuclear envelope breaks down in prophase. The researchers identified two nuclear localization signals in Gwl's central domain. Cdk1 and the mitotic kinase Polo phosphorylated this region of Gwl to promote the protein's exclusion from the nucleus. Polo phosphorylation prompted the scaffold protein 14-3-3ε to bind and retain Gwl in the cytoplasm, possibly by masking the protein's nuclear localization signals.

Gwl mutants lacking the nuclear localization signals permanently resided in the cytoplasm. These mutants failed to rescue the mitotic defects of flies lacking Gwl, suggesting that Gwl needs to localize to the nucleus during interphase, perhaps so that it can be activated by cyclin B–Cdk1. However, Gwl mutants that remained in the nucleus throughout prophase also delayed mitosis, indicating that Gwl's early exit from the nucleus is required for mitotic progression. Senior author Vincent Archambault now wants to investigate how Gwl's activity and localization are reversed at the end of mitosis and to determine which Cdk1 substrates Gwl is required to protect.

Wang, P., et al. 2013. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201211141.

Epithelia restored by healing waves



A wave of actomyosin assembly converges to form a cable around the edge of a wound.

Waves of actomyosin assembly and constriction help repair epithelial wounds, Antunes et al. reveal.

When epithelial tissues are punctured, the cells around the wound edge assemble an actomyosin cable that constricts like a purse string to draw the wound closed. The events that lead up to cable formation are poorly understood, however, prompting Antunes et al. to study the earliest stages of the wound response in the epithelial notum of *Drosophila* pupae.

Live imaging revealed that, within minutes of wounding, cells set back from the wound initiated a wave of actin filament assembly that flowed through neighboring cells toward the wound edge. These actin filaments recruited myosin II and drove a wave of apical cell constriction that propagated into the epithelial cells surrounding the wound. Depleting cells of the actin-nucleating formin protein Dia or the contractility-promoting kinase ROCK blocked the waves of actin polymerization and cell constriction, inhibiting actomyosin cable assembly and wound closure.

Calcium signaling forms a key part of the early wound response in many tissues. Knocking down the calcium channel TRPM diminished the influx of calcium into cells surrounding epithelial wounds, impairing actomyosin flow and cable assembly. Down-regulating the calcium-activated, actin-severing protein Gelsolin had a similar effect, suggesting that calcium may initiate actomyosin flow by inducing the remodeling of existing actin filaments. Senior author Antonio Jacinto now wants to investigate in more detail how calcium signals and mechanical forces guide actomyosin flow toward the wound edge to promote cable assembly and wound healing.

Antunes, M., et al. 2013. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201211039.