# In This Issue

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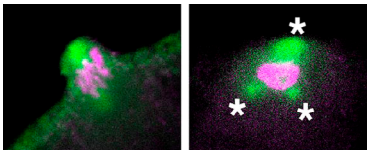
## Circumventing the Greatwall



Compared with a control oocyte (left), an oocyte injected with antibodies that inhibit Greatwall (right) resumes meiosis but forms a multipolar spindle (green) with misaligned chromosomes (magenta).

Okumura et al. reveal how cyclin B–Cdk1 can activate itself at the start of M phase without the help of Greatwall kinase.

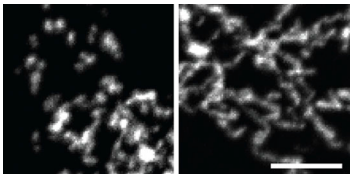
In order to push cells into M phase, cyclin B–Cdk1 must suppress the protein phosphatase PP2A-B55, which would otherwise oppose the cyclin-dependent kinase and prevent it from becoming fully active. Cyclin B–Cdk1 inhibits PP2A-B55 by activating a kinase called Greatwall. Greatwall, in turn, phosphorylates members of the Ensa/Arpp19 protein family, allowing them to bind and inhibit PP2A-B55. But some cell types, such as starfish oocytes, can fully activate cyclin B–Cdk1 and transition into M phase in the absence of Greatwall, suggesting that PP2A-B55 is inhibited by additional pathways.

Okumura et al. found that starfish oocytes lacking Greatwall still required Arpp19 for cyclin B–Cdk1 activation and meiotic M phase entry. Cyclin B–Cdk1 phosphorylated Arpp19 directly—on a different site to Greatwall—allowing it to partially inhibit PP2A-B55 even in Greatwall's absence. This partial inhibition was sufficient for cyclin B–Cdk1 to become fully activated and for oocytes to transition into M phase. Phosphorylation by Greatwall further increased Arpp19's ability to inhibit PP2A-B55, which could be important later in meiosis. Oocytes lacking Greatwall transitioned into M phase but failed to segregate their chromosomes, a defect rescued by injecting Arpp19 protein phosphorylated by Greatwall.

Senior author Takeo Kishimoto now wants to determine whether Greatwall kinase promotes M phase progression by phosphorylating additional substrates besides Arpp19.

Okumura, E., et al. 2014. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201307160.

## OPA1's shortcut to mitochondrial fission



The mitochondrial network is fragmented in a YME1L-deficient cell (left) but tubulated in a cell that also lacks the OMA1 protease (right).

Anand et al. reveal how a GTPase that promotes mitochondrial fusion is proteolytically cleaved to generate a shorter protein that stimulates the organelle's fission.

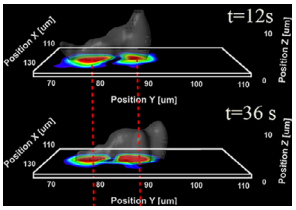
Mitochondria constantly fuse and split apart to maintain the organelle's function and regulate various cellular processes such as apoptosis. The dynamin-like GTPase OPA1 promotes fusion of the mitochondrial inner membrane. The full-length, membrane-bound form of OPA1 (L-OPA1) can be cleaved into a shorter, soluble fragment (S-OPA1) by the protease YME1L and, in response to stress, by OMA1. Mitochondrial fusion is thought to require both L- and S-OPA1, and, accordingly, when the balance of these isoforms is perturbed in cells lacking YME1L, the mitochondrial network becomes fragmented.

Anand et al. found, however, that completely inhibiting the generation of S-OPA1 by removing OMA1 from YME1L-null cells restored the formation of mitochondrial tubules. L-OPA1 was sufficient to promote mitochondrial fusion in these cells. In contrast, the researchers discovered that S-OPA1 is associated with mitochondrial fission. YME1L-null fibroblasts have fragmented mitochondria because OMA1 is hyperactive in these cells, generating excess S-OPA1.

OPA1 processing therefore regulates the balance of mitochondrial fission and fusion. Senior author Thomas Langer now wants to investigate how S-OPA1 promotes the organelle's fragmentation.

Anand, R., et al. 2014. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201308006.

## Tracking traction in amoeboid cells




A migrating cell (gray) forms two stable, stationary traction adhesions that exert force (magnitude indicated by heat map) on the underlying substrate.

Bastounis et al. examine how chemotaxing *Dictyostelium* cells generate traction.

*Dictyostelium* cells move rapidly toward a chemoattractant using an amoeboid mode of migration in which cycles of actin polymerization and contraction drive protrusion at the cell front and retraction of the cell's rear. The resulting forces must be transmitted to the underlying substrate in order to move the cell forward. In contrast to slower-moving fibroblasts, however, which contact the extracellular matrix via large, stable focal adhesions, *Dictyostelium* cells form small, transient attachments to their substrate. Bastounis et al. used Fourier traction force microscopy to measure where and when *Dictyostelium* cells transmit force to their surroundings.

Chemotaxing *Dictyostelium* cells tended to transmit force at 2–3 stable sites aligned along the cell's front-to-back axis. The researchers named these sites "traction adhesions." Cells formed new traction adhesions underneath their leading edge protrusions and lost them at the rear as their trailing edge retracted. The traction adhesions exerted strong contractile forces along the anterior–posterior axis of the cell, as well as perpendicularly aligned lateral forces that appeared to squeeze the cell and facilitate the formation of leading edge protrusions. Lateral forces were particularly important in cells migrating on sticky substrates and in cells lacking key actin-binding proteins. Myosin II–null cells couldn't contract along their anterior–posterior axis and therefore relied on lateral contractions for their limited motility, whereas cells lacking the actin cross-linker filamin used lateral forces to form leading edge protrusions in the absence of F-actin assembly.

Human neutrophils, which also use an amoeboid mode of migration, formed similar traction adhesions, the researchers found. The authors now want to examine how these sites are organized in cells migrating through 3D environments.

Bastounis, E., et al. 2014. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201307106.