In This Issue

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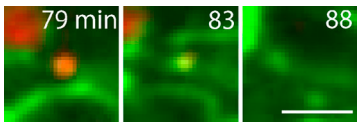
Apoptotic regulators dispose of the midbody



In this time-lapse series, a Q cell midbody (red) is degraded in the lysosome (green) of a hyp7 cell.

A pathway that clears up the remains of dead cells also removes the debris generated during cell division, Chai et al. report.

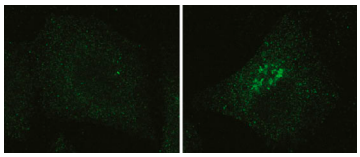
The midbody is a microtubule-rich structure that connects the two daughter cells at the end of mitosis. When cytokinesis is completed, the midbody is either shed into the extracellular space or retained by one of the daughter cells, potentially influencing its developmental fate. Chai et al. found that, in *C. elegans*, asymmetrically dividing Q neuroblasts discard their midbodies into their surroundings.

The Q cell midbodies were subsequently engulfed and degraded by a neighboring epithelial cell called hyp7, which also internalizes the corpses of apoptotic Q cells during development. Mutations in the genes that promote apoptotic cell engulfment blocked midbody clearance, indicating that hyp7 cells use the same pathway to internalize Q cell corpses and cytokinetic midbodies. Indeed, Chai et al. found that, just like apoptotic cells, Q cell midbodies expose phosphatidylserine on their outer surface and that blocking this lipid signal prevented the hyp7 cell from recognizing and engulfing the remnants of Q cell divisions.

Apoptotic engulfment genes also regulated midbody clearance in other *C. elegans* cell lineages. But senior author Guangshuo Ou now wants to study the function of the midbodies produced by worm epithelial stem cells, which are specifically retained by the daughter cell that remains undifferentiated.

Chai, Y., et al. 2012. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201209050.

Secretory proteins hail a cab at the TGN



A secretory protein (green) is exocytosed from control cells (left) but retained in the Golgi of cells lacking Cab45 (right).

Von Blume et al. reveal how a calcium-binding protein helps sort secretory cargo at the trans-Golgi network (TGN).

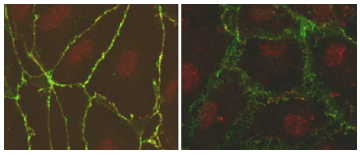
After moving through the secretory pathway from the ER to the Golgi apparatus, proteins are sorted at the TGN for delivery to their final destinations. How soluble proteins are selected for secretion outside of the cell is unclear, though the sorting process appears to rely on an ATPase called SPCA1, which pumps calcium ions into the TGN lumen when activated by the actin-severing protein cofilin. Cells lacking either SPCA1 or cofilin exocytose reduced amounts of many secretory proteins while incorrectly secreting other proteins that are normally retained in the Golgi complex or delivered to lysosomes.

Von Blume et al. found that a calcium-binding Golgi protein called Cab45 helps regulate calcium levels and protein sorting at the TGN. Calcium import through SPCA1 was required to retain Cab45 in the Golgi lumen, and Cab45, in turn, was required to maintain normal calcium levels inside the TGN. Cab45 bound to several secretory proteins in a calcium-dependent manner, and exocytosis of these proteins was inhibited in Cab45's absence. Lysosomal proteins, on the other hand, were secreted from cells lacking Cab45, suggesting that Cab45 operates in the same sorting pathway as SPCA1 and cofilin.

The researchers now want to identify additional components of the pathway to determine how Cab45 packs secretory proteins into transport vesicles destined for the plasma membrane.

Von Blume, J., et al. 2012. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201207180.

How endothelial junctions get deep-Syx'd



Endothelial junctions marked by VE-cadherin (green) and ZO-1 (red) are intact in control cells (left) but disrupted in the absence of Syx (right).

Ngok et al. describe how two growth factors control the localization of a guanine nucleotide exchange factor (GEF) to exert opposing effects on vascular permeability.

Vascular endothelial growth factor (VEGF) increases blood vessel leakiness by disrupting the junctions between endothelial cells, whereas Angiopoietin-1 (Ang1) stabilizes intercellular adhesions to decrease vascular permeability. Intercellular junctions are regulated by Rho family GTPases and by polarity proteins like the Crumbs complex. Ngok et al. discovered that a GEF called Syx localizes to endothelial cell junctions by binding to the Crumbs complex member Mupp1. Syx stabilized intercellular adhesions by locally activating RhoA and its downstream effector, the formin Dia.

VEGF disrupted endothelial cell contacts by displacing Syx from intercellular junctions. The growth factor inhibited Syx's association with Mupp1 by stimulating its phosphorylation by protein kinase D1 (PKD1). A non-phosphorylatable Syx mutant remained bound to Mupp1 at cell junctions and prevented VEGF from destabilizing cell–cell contacts. Ang1 also prevented VEGF from displacing Syx and disrupting intercellular adhesions, but Ang1 was unable to stabilize junctions in the absence of Syx.

Mice lacking Syx had leaky blood vessels, resulting in edemas and reduced heart function. Increased vascular permeability is associated with many human diseases, including strokes and tumor metastasis. The authors now want to investigate whether promoting Syx's localization to endothelial cell junctions, by inhibiting PKD1 for example, could be used to prevent vascular leakiness.

Ngok, S.P., et al. 2012. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201207009.