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saw similar discrimination against youthful proteins when they treated the cells to spur production of reactive oxygen species. Older proteins escaped destruction even though they incurred damage.

The results indicate that young proteins pass through a vulnerable stage that lasts around an hour. Folding into shape would probably take a few minutes at most, say the authors. But the proteins might also have to join with other proteins to form complexes, undergo structural modifications, or move to their home in the cell, during which time they are prone to damage and thus to destruction.

Medicherla, B., and A.L. Goldberg. 2008. *J. Cell Biol.* doi:10.1083/jcb.200803022.

How a cell puts itself on the menu

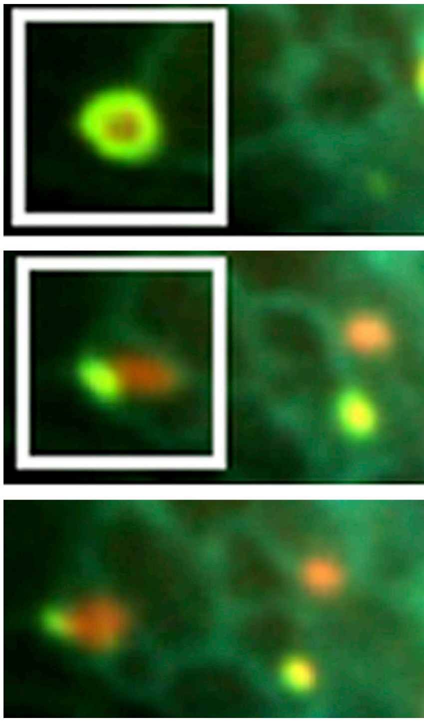
It could be starving or just cleaning up, but a cell sometimes devours a portion of its own cytoplasm, a process called autophagy. Two groups help clarify the workings of this form of self-eating. Axe et al. identify a cellular nursery for the membrane pouches that perform autophagy. Cao et al. reveal a method for pinning down the activity of autophagy control proteins.

During autophagy, a membrane container called an autophagosome scoops up some of the cell's contents, which the lysosome then digests. This cannibalism not only recycles nutrients for famished cells, it helps purge marred proteins. Too little or too much autophagy might cause illnesses such as Alzheimer's disease and certain types of cancer.

A stubborn mystery is where the autophagosome membrane comes from. Does it derive from the endoplasmic reticulum, as many scientists think? Or does it form when lipids in the cytoplasm rendezvous? Axe et al. attacked the question by tracking a phospholipid named PI(3)P that's essential for making an autophagosome. In starving cells a bud rich in PI(3)P bulged from the ER. This outgrowth, which the researchers dubbed an omegasome, spawned autophagosomes. The team observed new autophagosomes appearing inside the omegasome and then breaking free. Whether the omegasome separates from the ER or remains attached is unclear, the researchers say. But they conclude that the results support an ER origin for the autophagosome.

More than 20 proteins collaborate to orchestrate autophagy, but researchers are still trying to work out each protein's job. Instead of following the typical strategy of eliminating two or three of these proteins, Cao et al. went whole hog, deleting all 24 of the known yeast autophagy proteins. The team then added back different combinations of proteins to test hypotheses about their functions. For example, previous work suggested that the protein Atg17 is a pioneer that draws other proteins to the developing autophagosome. However, the researchers found that two other proteins are also necessary to instigate autophagosome formation.

Axe, E.L., et al. 2008. *J. Cell Biol.* doi:10.1083/jcb.200803137.
Cao, Y., et al. 2008. *J. Cell Biol.* doi:10.1083/jcb.200801035.



A newborn autophagosome (red) emerges from an omegasome (green circle).

Arp2/3 phosphorylation kickstarts cells

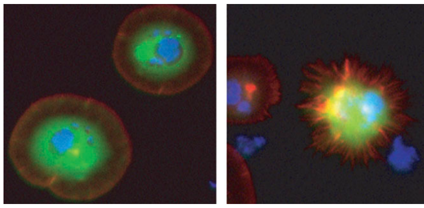
Crawl or stay put—it seems like a simple choice. But LeClaire et al. show that the decision is more complex than previously thought.

A cell slithers by extending a membrane protrusion, or lamellipodium, driven by newly assembled actin filaments. A seven-part protein complex called Arp2/3 controls the lengthening and branching of these filaments. Researchers thought that binding of a pair of so-called nucleation promoting factors, WASP and Scar, was sufficient to switch on Arp2/3. However, LeClaire et al. determined that phosphorylation of Arp2/3's subunits also was essential for the complex's activation—and thus for actin elongation and lamellipodia extension.

Arp2/3 works by attaching to the side of an existing actin filament and then spurring a branch to grow. To nail down which action phosphorylation controls, the team used several methods to dislodge phosphates. After treatment Arp2/3 could still grab hold of an actin fiber, but it couldn't perform capping, an essential step that prevents the newly formed actin filament from breaking apart. The cells also could not extend lamellipodia.

The work suggests that Arp2/3 serves as a command center, receiving input not just from WASP and Scar, but also from phosphate-adding enzymes. The researchers think that this complexity provides the cell with more precise control over its movement.

LeClaire, L.L., et al. 2008. *J. Cell Biol.* doi:10.1083/jcb.200802145.



In controls, lamellipodia spread out evenly around the cells (left). But cells lacking part of the Arp2/3 complex sprout abnormal, spiky extensions (right).