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Destroying the messenger

An E2 ubiquitination enzyme is meant to shuffle ubiquitins through its active site and on to substrates so that the substrates are marked for destruction. But a polyubiquitin chain on the active site of Ubc7 can result in the downfall of this E2, according to Tommer Ravid and Mark Hochstrasser (Yale University, New Haven, CT). The result gives clues about how polyubiquitin chains are built.

If Ubc7 strays away from its binding partner Cue1 on the yeast ER, it is destroyed. The Yale team found that this destruction required both polyubiquitination on the active site cysteine of Ubc7 and release from Cue1's grip. Similar in vitro evidence that polyubiquitin chains can form on an E2 active site was recently presented by Li et al. (*Nature*. 2007. doi:10.1038/nature05542).

The reaction may work via a seesaw mechanism between dimeric E2s. In this model, one E2 receives first a single ubiquitin and then on top of that the entire growing polyubiquitin chain from the other E2. This frees up the active site of the second E2 to receive another single ubiquitin. Eventually the fully grown chain can be transferred to another substrate.

The seesaw model contrasts with the original model of sequential addition. In the sequential model, it was not clear how the enzyme would reach out to the distant end of a substrate's growing ubiquitin chain to add additional ubiquitins. JCB

Reference: Ravid, T., and M. Hochstrasser. 2007. *Nat. Cell Biol.* doi:10.1038/ncb1558.

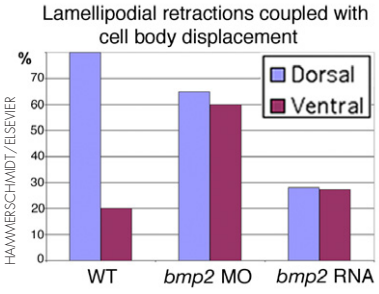
Migrating toward adhesion

A morphogen can determine the direction of cell movement by creating an adhesion gradient, according to Sophia von der Hardt, Matthias Hammerschmidt (Max-Planck, Freiburg, Germany), and colleagues.

The bone morphogenetic proteins (Bmps) are better known as factors that determine cell fate decisions. Bmps appear to affect migration, but this might have been a side-effect of changes in cell fate.

The German group therefore implanted a Bmp-containing bead on the opposite side of a fish embryo from Bmp's normal source. Cells responded by moving away from the bead. Bmp receptors were needed not in the migrating cells but in the surrounding cells on which they migrated. This suggested that the surrounding cells might be creating a gradient of adhesion that was guiding the migrating cells.

Sure enough, the migrating cells showed equal numbers of protrusions at the front and back, but only the protrusions facing away from a Bmp source were able to grab on securely enough to pull the cell body forward.



Based on an adhesion gradient, dorsal but not ventral retractions are productive.

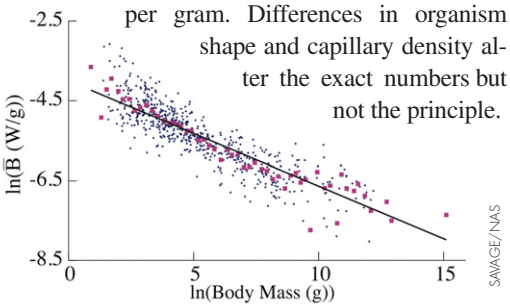
Other developmental pathways also regulate adhesion. This has been presumed to affect cell survival or cohesion of migrating masses of cells, but the creation of an adhesion gradient is another possibility. JCB

Reference: von der Hardt, S., et al. 2007. *Curr. Biol.* doi:10.1016/j.cub.2007.02.013.

Big mammals have big (or slow) cells

Cells use two basic strategies to adapt to the size of the organism in which they reside, say Van Savage (Harvard Medical School, Boston, MA), Geoffrey West (Santa Fe Institute, Santa Fe, NM), and colleagues. Depending on how often they divide, comparable cells in a mouse and an elephant differ in either metabolic rate or cell volume, but usually not both.

The need for such adaptation stems from simple geometry. As body volume increases, surface area increases more slowly. So an elephant radiates and loses less energy per gram than a mouse and thus requires less replacement energy per gram. Differences in organism shape and capillary density alter the exact numbers but not the principle.



Bigger animals have lower metabolic rates (B).

Thus, what Savage and others call the "cell is a cell is a cell" theory cannot hold. With energy consumed per unit volume decreasing with increasing animal size, average cell volume and average cellular metabolic rate cannot both remain constant.

There are at least two possible solutions. Under theory one, average cell volume stays constant but each cell in the larger organism consumes less energy. Theory two keeps energy consumption per cell constant but the cells in the larger organism are larger so that there are fewer of them per unit volume.

Digging through the literature, the researchers found that rapidly dividing cell types were a close fit to theory one. Slower metabolism in these cells in larger organisms may explain why these animals accumulate damage and age more slowly.

Cells such as neurons and adipocytes, however, divide infrequently and must maintain their structural integrity using a constant energy supply. Their variation fit theory two.

The findings reflect the extent to which organisms also affect cells, says Savage. "For a cell type to exist in an organism it has to adapt to an organism," he says. He plans to study the phenomenon in yeast that can be manipulated to grow at different sizes and metabolic rates. JCB

Reference: Savage, V.M., et al. 2007. *Proc. Natl. Acad. Sci. USA*. doi:10.1073/pnas.0611235104.