Ras makes a pit stop

Ras proteins are restless, continually flitting from the cell membrane to the Golgi apparatus and back again. Misaki et al. reveal that the proteins enter recycling endosomes during the journey to the plasma membrane. One mystery is why Ras proteins—which spur cell growth, differentiation, and survival—move so often. The clutered cell interior has also made it difficult to discern how the proteins travel. Proteins heading for the Golgi might zip through the cytosol or hitchhike in endosomes. Some evidence suggests that they pass through recycling endosomes, whereas other studies indicate they shun the endocytic pathway altogether.

Misaki et al. used COS-1 cells in which recycling endosomes are easier to observe because they gather in the so-called Golgi ring near the organelle, separate from early and late endosomes. The researchers found that Ras proteins do spend time in recycling endosomes, but only on the outbound leg from the Golgi to the cell membrane. Addition of two palmitoyl groups directs Ras to recycling endosomes, the team discovered.

The researchers think that an unidentified vesicle ferries the proteins from the Golgi to the recycling endosomes. Whether recycling endosomes deliver Ras proteins to the cell membrane or send them to the vesicles to other carriers is unclear. Receptors such as the epidermal growth factor receptor also slip into recycling endosomes and might activate Ras proteins there.

CLIP catches enzymes in the act

Prooprotein convertases (PCs) are big shots in the body because they snip and turn on numerous hormones, receptors, adhesion molecules, and other crucial proteins implicated in Alzheimer's disease. Cancer cells and pathogens such as HIV often co-opt the enzymes for nefarious ends. For example, PCs turn on matrix metalloproteinases that clear away extracellular matrix and allow cancer cells to spread. But the enzymes' widespread distribution and overlapping functions have made it difficult to tease out what jobs individual enzymes perform.

To simplify the task, Mesnard and Constam devised a method to determine when and where PCs are working. They fused yellow and blue fluorescent proteins to create a biosensor they call CLIP. When PCs are absent, the two colors remain fused yellow and blue fluorescence. But active PCs cut CLIP and separate the colors. Researchers can thus track PC activity inside a cell and at its surface, or even in whole tissues. Mesnard and Constam used the approach to find out when two PCs, PACE4 and Furin, switch on in early mouse embryos. The enzymes were on the job before the blastocyst implanted, earlier than expected. The researchers say that CLIP could improve drug design, allowing scientists to pin down where certain PCs are functioning in diseases and monitor the effectiveness of inhibitors dispatched to those sites.

How a virus enters without breaking

Viruses enter cells by remodeling their membranes, allowing them to fuse. VSV carries a surface glycoprotein called G. Previous work indicated that G has at least three configurations—a pre-fusion state, an intermediate form that interacts with the target cell membrane, and a post-fusion conformation. Using electron microscopy and tomography, Libersou et al. tracked enzymes’ activity in the act.