Another way to break down

When yeast secretory proteins are improperly folded, the ER quality control system directs them into the HRD/DER pathway, which targets the proteins for degradation. Blocking the HRD/DER pathway, however, does not completely stop degradation, implying that there must be an alternative way to destroy misfolded secretory proteins. Haynes et al., reporting on page 91, have now characterized that pathway, and suggest that it may serve to handle the overflow when the HRD/DER system gets swamped.

In the HRD/DER pathway, the ubiquitin ligase Hrd1p tags defective proteins, such as a misfolded mutant form of carpoxypeptidase Y (CPY*), for degradation. The authors found that overexpressing CPY* appears to saturate the HRD/DER system, allowing direct observation of the new pathway, named Hrd1p-independent proteolysis (HIP). HIP requires ER-to-Golgi vesicular transport, and uses the ubiquitin ligase Rsp5p instead of Hrd1p.

Blocking both the HRD/DER and HIP pathways completely blocks CPY* degradation, so there do not appear to be any additional pathways for this substrate. Haynes et al. suggest that HRD/DER may be a low-capacity system that handles routine protein-folding problems, whereas HIP could act as a high-capacity system, possibly boosted by the unfolded protein response, to respond when large numbers of proteins are misfolded.

Coordinating myosin with mitosis

Early in Drosophila development, the embryo is a syncytium, and the cloud of dividing nuclei expands along the long axis of the embryo. This nuclear axial expansion requires tight coordination between mitosis and the actin–myosin cytoskeleton; but how do these two systems communicate? On page 127, Royou et al. show that a spatially and temporally regulated cycle of myosin recruitment to and dispersion from the embryo cortex in this system is indirectly controlled by the cell cycle regulator Cdc2. A similar mechanism may be at work in other types of mitotic cells.

Using time-lapse confocal microscopy of embryos expressing fluorescently tagged myosin, the authors found that cytoplasmic myosin is repeatedly recruited and dispersed with the same rhythm as the mitotic cycle. Myosin is recruited only to the cortical regions above the cloud of nuclei, and each cycle of recruitment is accompanied by a cortical contraction, coinciding with interphase. The myosin then disperses, and the cortex relaxes during metaphase. The cycles of contraction and relaxation may cause a cytoplasmic flux that drives the nuclei poleward.

Cdc2 activity regulates this process indirectly, acting through Rho kinase. Since ordinary mitotic cells must coordinate actin–myosin cytoskeletal movements with the cell cycle to form the contractile ring, this pathway may be a general feature of eukaryotic mitosis.