authors deciphered which of the molecular components of the apoptotic pathway affected the break-up of mitochondria, and they incorporate mitochondrial disruption into a new working model of apoptosis in *C. elegans*. They propose that, in cells that are destined to die, the pro-apoptotic protein EGL-1 binds to, and activates, CED-9. CED-9 then activates DRP-1, which mediates mitochondrial disruption. How exactly mitochondrial fragmentation contributes to cell death in *C. elegans* remains unclear, but the authors suggest that, as these organelles fragment, a pro-apoptotic molecule might be liberated that potentiates the activity of the adaptor protein CED-4. CED-4 activates the caspase CED-3, and the enhanced activity of this enzyme results in efficient programmed cell death.

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References and links

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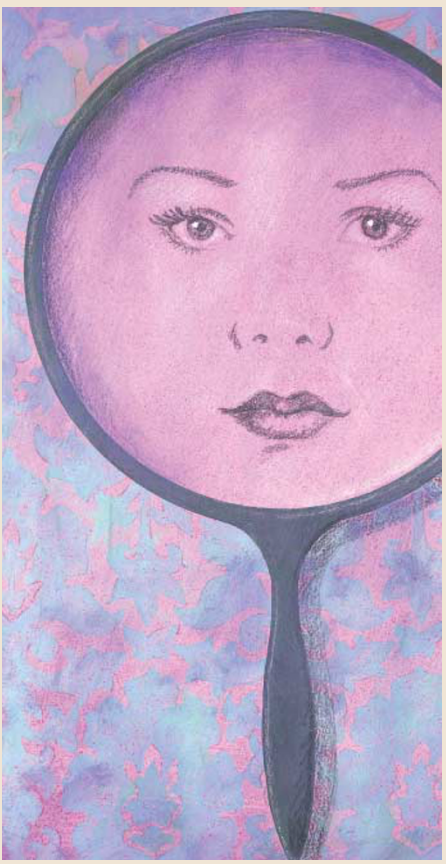

MEMBRANE TRAFFICKING

Controlling the flow

There are various hypotheses regarding the flow of material within the Golgi stack. For example, some researchers believe that anterograde movement occurs through the maturation of the Golgi cisternae and that retrograde transport is mediated by coatomer protein complex-I (COPI) vesicles, whereas others believe that vesicles mediate both anterograde and retrograde transport. However, the various hypotheses are not mutually exclusive, but they do require the strict control of the flow pattern of COPI vesicles. So, how might COPI vesicles be targeted to particular cisternae?

Golgin-family proteins have been proposed to be involved in intra-Golgi transport by functioning as tethers for COPI vesicles, and the well-characterized golgins giantin and GM130 link COPI vesicles to p115 on the *cis*-Golgi network (CGN). In *Science*, Warren and colleagues now describe the characterization of the golgin-84–CASP tether, and their results indicate that subpopulations of COPI vesicles are defined by their golgin tethers.

First, they showed that the golgin-84–CASP tether is asymmetric — that is, golgin-84 was found on COPI vesicles, whereas CASP was located in Golgi membranes. Next, they determined the protein composition of the COPI vesicles that bind CASP. Surprisingly, they lacked any p24-family members, proteins that are thought to be involved in COPI-vesicle biogenesis. Other proteins must therefore nucleate the budding of COPI vesicles that use the golgin-84–CASP tether. Interestingly, the vesicles were enriched for mannosidase-I and -II, which reside in *cis* and *medial* cisternae, but not for a representative cargo protein destined for the plasma membrane. These data therefore indicate that the vesicles are involved in retrograde transport.

Warren and co-workers then looked at the protein composition of COPI vesicles that bind p115. They found that they contained all of the p24-family members and a representative cargo protein, but were depleted of mannosidase-I and -II. This indicates that these vesicles bud from the CGN, where p24 proteins are localized, and move in an anterograde direction. However, this movement must be limited to the early part of the Golgi stack (for example, from the CGN to the *cis*-cisternae), because p115 is limited to these membranes.

Finally, the authors confirmed the role of the golgin-84–CASP tether in retrograde transport by studying the cycling of a Golgi enzyme through the endoplasmic reticulum (ER). They inhibited the export of a labelled Golgi enzyme from the ER, and observed that it was gradually relocated to the ER. The injection of soluble golgin-84 or CASP during this time substantially inhibited this retrograde movement (agents that disrupted the p115 tether had only a modest effect). However, they also showed that soluble golgin-84 or CASP did not affect the retrograde movement of COPI vesicles (carrying a recycling protein, ERGIC53) from the CGN to the ER.

It therefore seems that the retrograde movement of CASP-binding COPI vesicles occurs within the Golgi, and not from the Golgi to the ER. A two-step retrograde pathway — "…the first step mediated by intra-Golgi COPI transport to the CGN, the second by a COPI-independent pathway to the ER" — might explain why earlier work did not identify a role for COPI vesicles in the retrograde transport of Golgi enzymes to the ER despite the presence of such enzymes in these vesicles. Furthermore, this study has shown that golgin tethers define subpopulations of COPI vesicles, and this information will help us to further our understanding of the intra-Golgi flow of material in the future.

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References and links

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