MEMBRANE DYNAMICS

A maturing model

Two diametrically opposed models have been proposed for transport of cargo through the Golgi. The vesicular transport model predicts that cargo travels from the *cis* to the *trans* region of the Golgi in vesicles that pinch off from one cisterna and fuse with the next. By contrast, the cisternal maturation model involves progression of whole cisternae from *cis* to *trans* and recycling of Golgi proteins from *trans* to *cis* to maintain Golgi architecture. Three papers in *The Journal of Cell Biology* provide new evidence in favour of cisternal maturation.

Luini and colleagues showed previously that procollagen-1 (PC-1), which forms aggregates that are too large to fit into vesicles, is transported through the Golgi by cisternal maturation. Using cells that express both PC-1 and the vesicular stomatitis virus G protein (VSVG), they now show that VSVG moves through the Golgi with identical kinetics to PC-1, hence it is probably transported by the same mechanism. So, cisternal maturation is not specific to large, aggregated proteins.

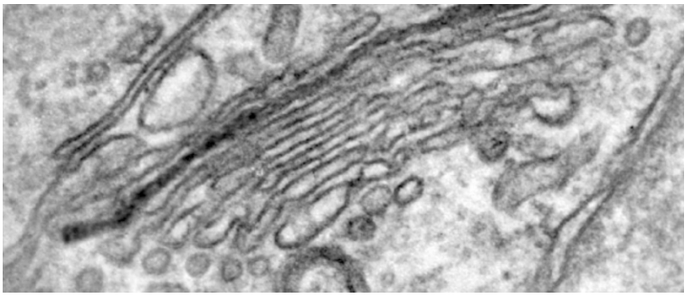
Moreover, the authors show that transport occurs without the cargo leaving the cisternal lumen. Indeed, serial cryosections followed by three-dimensional reconstruction confirmed that the large membrane distentions that contain PC-1 are continuous with the Golgi cisternae, and are not 'megavesicles' as proposed by others. And VSVG was not distributed throughout the Golgi in a gradient, as the vesicular transport model would predict, but was most often concentrated in one or two cisternae (see picture). Last, VSVG was depleted from peri-Golgi vesicles, indicating that these are unlikely to be cargo containers.

The content of peri-Golgi vesicles was analysed in more detail by Klumperman and colleagues using quantitative immunocryoelectron microscopy. They found that these vesicles — many of which were covered with COPI coats — lacked cargo, such as VSVG, but instead contained the Golgi enzyme mannosidase II and three proteins involved in membrane transport — giantin, the KDEL receptor and Bet1. So, peri-Golgi vesicles are probably not involved in anterograde transport, but in recycling of Golgi proteins, which would be compatible with a cisternal maturation model.

Nilsson and colleagues reached a similar conclusion using an *in vitro* budding assay. Here too, anterograde cargo, including the polymeric immunoglobulin receptor, apolipoprotein E and rat serum albumin, was absent from COPI vesicles, whereas Golgi-resident proteins including mannosidase II, GS28 and four members of the p24 family were present.

Although these findings will not end this debate, they might turn out to be key pieces in the complicated puzzle of biosynthetic transport.

Raluca Gagescu



References and links

ORIGINAL RESEARCH PAPERS Lanoix, J. *et al.* Sorting of Golgi resident proteins into different subpopulations of COPI vesicles: a role for ArfGAP1. *J. Cell Biol.* **155**, 1199–1212 (2001) | Martínez-Menárguez, J. A. *et al.* Peri-Golgi vesicles contain retrograde but not anterograde proteins consistent with the cisternal progression model of intra-Golgi transport. *J. Cell Biol.* **155**, 1213–1224 (2001) | Mironov, A. A. *et al.* Small cargo proteins and large aggregates can traverse the Golgi by a common mechanism without leaving the lumen of cisternae. *J. Cell Biol.* **155**, 1225–1238 (2001)

STRUCTURE WATCH

Water, water, everywhere...

Tonicity-responsive enhancer binding protein (TonEBP or nuclear factor of activated T cells 5 (NFAT5)) is the only mammalian transcription factor known to regulate gene expression in response to hypertonicity. Unlike other members of the NFAT transcription-factor family, TonEBP acts as a homodimer and binds asymmetric TonE sites with a low affinity. It has been unclear how TonEBP binds these sites, but Chen and colleagues have now determined the 2.86-Å crystal structure of TonEBP complexed with DNA.

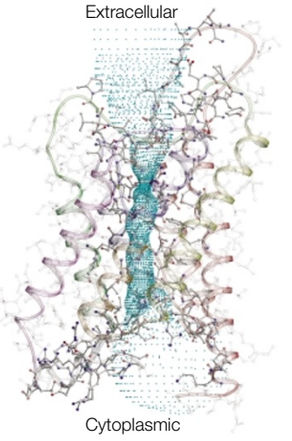
Each monomer of TonEBP has amino- and carboxy-terminal immunoglobulin-like domains that extend away from one another. In the homodimer, there are two interfaces. One — which is similar to that seen for nuclear factor (NF)-κB dimers — is between the carboxy-terminal domains, and the other — which is similar to the surface that NFAT uses to contact Fos–Jun — is between the amino-terminal domains. This homodimer forms a complete circle around the DNA, with DNA bound to one side.

The authors showed that this DNA encirclement probably increases the kinetic stability of TonEBP–DNA complexes, which helps to override TonEBP's low DNA-binding affinity. This work has added a sequence-specific transcription factor to the list of factors that bind DNA by encirclement, and has also revealed that the NFAT and NF-κB transcription factor families might be more closely related than was previously thought.

REFERENCE Stroud, J. C. *et al.* Structure of a TonEBP–DNA complex reveals DNA encircled by a transcription factor. *Nature Struct. Biol.* **9**, 90–94 (2002)

...for aquaporins to 'drink'

Aquaporins (AQPs) transport water across cell membranes in response to osmotic gradients. AQP1 allows water — but not ions (including protons) — to move freely and reversibly across cell membranes, but it is not clear how this water moves or how this specificity is achieved. Clearer insights have now been provided by Jap and co-workers, who have solved the crystal structure of bovine AQP1 to 2.2 Å resolution.



AQP1 functions as a tetramer, where each monomer has its own water channel. Each channel comprises an extracellular and cytoplasmic 'vestibule', connected by an extended narrow pore. In the crystal structure, only four bound water molecules interrupt this hydrophobic pore at three hydrophilic nodes, an arrangement that facilitates rapid water transport. The authors conclude that the transport of protons through this pore is probably energetically unfavourable, because of the lack of a hydrogen-bonded network of water molecules through which protons could 'shuttle'. They also found that residues of the constriction region — the narrowest point of the pore — are critical for conferring water specificity.

REFERENCE Sui, H. *et al.* Structural basis of water-specific transport through the AQP1 water channel. *Nature* **414**, 872–878 (2001)