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ORGANELLE BIOGENESIS

The building blocks of the secretory pathway

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> …the architecture and function of the secretory pathway is maintained by 1,430 proteins…

Understanding how an organelle functions is helped enormously if you know all the proteins from which it is composed. Reporting in *Cell*, Gilchrist *et al.* provide a proteomic analysis of the endoplasmic reticulum (ER) and Golgi apparatus from liver cells, providing new insights into the roles of these organelles in the secretory pathway.

Gilchrist *et al.* studied the proteome of both the rough and smooth ER, and in doing so expanded the number of different proteins associated with the ER from 500 to over 1,200. Of the ER proteins with a known function, most are associated with protein synthesis, folding and modification, as would be expected of an organelle that forms an early compartment in the secretory pathway. Other significant groups include proteins that interact with the actin cytoskeleton, such as myosins, and proteins that function in metabolism and detoxification, such as the cytochrome P450 enzymes.

The proteomics approach the researchers used provides a quantitative readout of protein expression that helps to identify possible contaminants in the sample from true organelle-resident proteins. This approach has been validated with other cellular targets, such as the nuclear pore complex, and, therefore, the authors are confident that this represents the almost complete set of ER proteins.

As a comprehensive proteomics analysis of the Golgi apparatus has previously been reported, the authors focused their efforts on understanding the importance of small transport vesicles — coatomer complex protein-I (COPI) vesicles — that form in the Golgi. The function of these vesicles is controversial and two roles have been proposed; COPI vesicles could mediate the forward transport of cargo proteins through the Golgi, or the retrograde retrieval of Golgi-resident proteins back through the apparatus.

Cargo proteins were found to be largely excluded from COPI vesicles, whereas the vesicles were enriched with Golgi-resident proteins, supporting a function for COPI vesicles in retrograde transport. Interestingly, several Golgi-resident proteins were separated between the COPI vesicles and Golgi fractions to different extents, indicating that perhaps a regulated sorting mechanism, rather than a random process, controls the delivery of proteins into nascent COPI vesicles.

Analysis of the data set shows that a large proportion of ER proteins are also found in the Golgi, as might be expected considering that the two organelles lie next to each other in the secretory pathway. It also reveals that the architecture and function of the secretory pathway is maintained by 1,430 proteins, including 345 proteins that have no known function. Understanding how these proteins cooperate will keep cell biologists busy for a long time.

James Pickett

ORIGINAL RESEARCH PAPER Gilchrist, A. *et al.* Quantitative proteomics analysis of the secretory pathway. *Cell* **127**, 1265–1281 (2006)
FURTHER READING Yates, J. R. 3rd *et al.* Proteomics of organelles and large cellular structures. *Nature Rev. Mol. Cell Biol.* **6**, 702–714 (2005)
WEB SITES
John Bergeron's laboratory:
http://people.mcgill.ca/john.bergeron
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