MEMBRANE TRAFFICKING

Organelle blueprints unveiled

In a recent issue of *Cell*, Jahn and colleagues report a comprehensive stock-take of the lipid and protein composition of a synaptic vesicle. As well as being a testament to patience and a precise scientific technique, this study provides an insight into the life cycle of these neurotransmitter-loaded organelles, which are concentrated at presynaptic nerve endings.

The authors first catalogued the proteins that are expressed in highly purified synaptic vesicles by mass spectrometry. This proteomics approach identified many of the core proteins already known to be essential for synaptic vesicle function as well as a diverse set of other trafficking proteins associated with both endocytic and other exocytic pathways. Although some of the proteins identified might be contaminants, this finding indicates that synaptic vesicles are less isolated from other organelles of the secretory pathway than previously thought.

The quantitative measurement of protein expression revealed that many of the most important proteins on the vesicle are found in multiple copies; the most abundant is the SNARE protein synaptobrevin-2, which interacts with proteins on the plasma membrane to mediate fusion. Several synaptic vesicle proteins have previously been suggested to bind synaptobrevin-2 stoichiometrically, and constitutively inactivate it: however, the relatively low abundance of these proteins makes this unlikely.

Putting these data together with measurements of the physical parameters of a synaptic vesicle, Jahn and colleagues were able to construct a three-dimensional model of a synaptic vesicle. The structure is dominated by proteins and contains over 600 membrane-spanning domains, which occupy ~20% of the total membrane volume. This extraordinarily high density of proteins means that the membrane bilayer is probably highly ordered, with most phospholipids organized around the transmembrane helices. Synaptic vesicle membranes contain large amounts of cholesterol that might help to keep membranes fluid in this densely populated environment. The large vacuolar H^+-ATPase is present only in a single copy on most vesicles, and this asymmetry might have implications for how a vesicle can approach and dock on the plasma membrane.

This study provides the most detailed description of a synaptic vesicle so far, albeit an average one generated from a large vesicle population, and it raises some important questions. Are populations of synaptic vesicles — both those found in the same nerve terminal and between nerves — really homogeneous? Could differences in protein expression control the different release probabilities observed for vesicles, and could they determine whether the vesicle collapses into the plasma membrane or is retrieved intact after fusion? Further quantitative studies should help expand our understanding of both organelle trafficking and membrane fusion.

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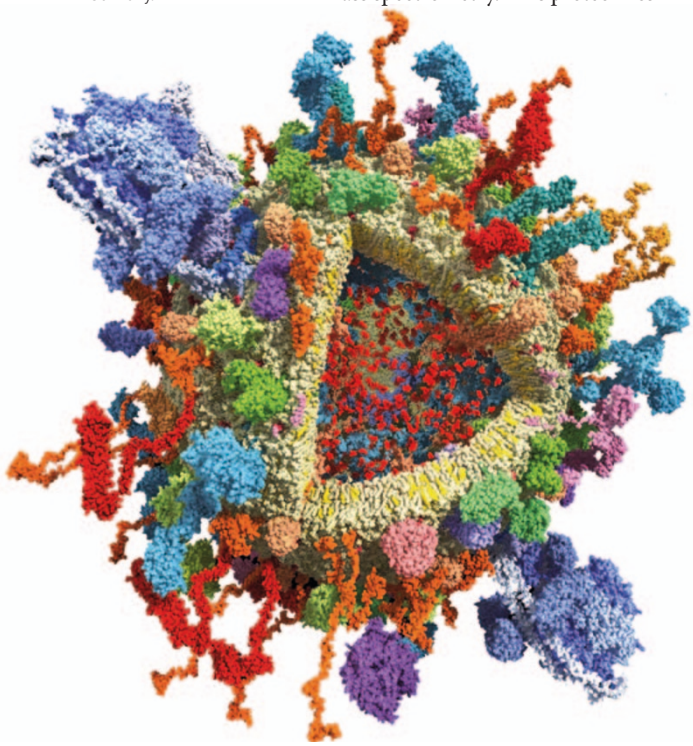

▼ Space-filling model of the main synaptic proteins on an average synaptic vesicle. Part of the vesicle is cut away to show the glutamate-filled lumen. Image generated by H. Grubmüller, Max Planck Institute for Biophysical Chemistry, Göttingen, Germany.

ORIGINAL RESEARCH PAPER Takamori, S. *et al.* Molecular anatomy of a trafficking organelle. *Cell* **127**, 831–846 (2006)
FURTHER READING Jahn, R. & Scheller, R. H. SNAREs — engines for membrane fusion. *Nature Rev. Mol. Cell Biol.* **7**, 631–643 (2006)
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