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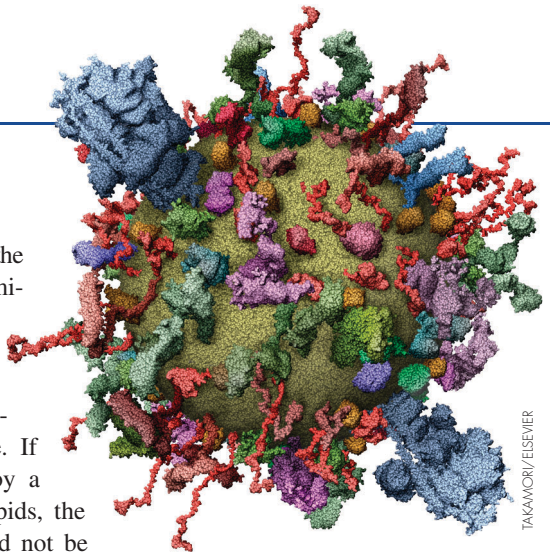
Synaptic vesicle structure

The first molecular level model of an organelle is described by Shigeo Takamori, Reinhard Jahn (Max-Planck Institute, Göttingen, Germany), and colleagues. Proteomics, quantitative measurements, and molecular modeling give them a view of an average synaptic vesicle.

The first surprise is that the vesicle is almost smothered in proteins. The group started by identifying 410 proteins associated with purified brain synaptic vesicles, but "if you want to put 400 proteins in the model it exceeds the amount of surface area available," says Takamori. They suspect that many of the proteins are passengers on only a few vesicles, so instead they measured the copy number of the more abundant proteins. By putting just these 27 proteins in the model, they accounted for almost 70% by mass of the vesicles' protein complement.

Even with these few proteins, "the vesicles are really protein dominated," says Takamori. Transmembrane domains take up approximately 20% of the surface, with their attached globular domains shading far more. If each protein was surrounded by a monomeric collar of phospholipids, the majority of phospholipids would not be free. The amount of protein and lipid clustering is not yet known, however.

The model "provides a point of departure for understanding the molecular mechanism of trafficking, docking, and fusion of a trafficking organelle," says Takamori. The synaptic vesicle and its proteins have been studied in detail, but quantitative information has been lacking. The new model suggests that quantities of certain fusion proteins are large enough not to be rate limiting. The presence of more than the expected diversity of other proteins, such as Rabs, is still to be explained as either contamination or signs of unexpected side-trips by the vesicles. JCB


TAKAMORI/ELSEVIER

A synaptic vesicle, up close and personal.

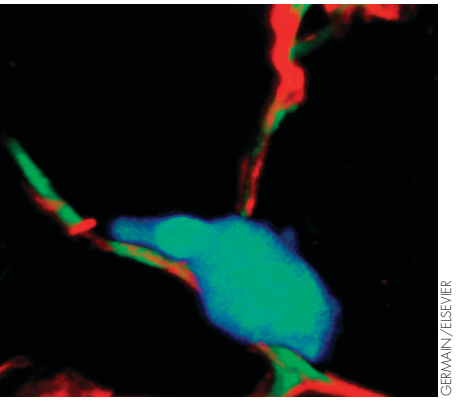
Reference: Takamori, S., et al. 2006. *Cell.* 127:831–846.

Lymphocyte tracks

Lymphocytes wander around lymph nodes to find their rare target: the dendritic cells that carry an antigen that they recognize. But this apparently random wandering is orchestrated, say Marc Bajénoff, Ronald Germain (NIAID, Bethesda, MD), and colleagues. The cells use a fibroblast network as train tracks to guide them on their travels.

Past experiments using similar intravital microscopy methods have not systematically visualized these train tracks, although lymphocytes were seen to make suspiciously sharp turns. "Lymphocytes have been swimming in an inky void, but that's an artifact of the method," says Germain. For the first time his colleagues labeled not just the added lymphocytes but also the stromal host cells constituting the backbone of the lymph node.

In both static and live images, T and B cells were seen associated with and crawling along fibroblastic reticular cells (FRCs) in the T cell area. B cells also crossed over and moved along a follicular dendritic cell (FDC) network in the B cell area. Approximately 90% of lymphocyte turns were associated with FRC or FDC fibers running at the corresponding angles.


GERMAIN/ELSEVIER

A T cell (blue) hugs an FRC fiber to guide its travels.

The networks probably help out in a couple of ways. First, lymphocytes crawling along the networks should more easily meet their target dendritic cells, which are also attached to the networks. Second, the networks are covered with motility-stimulating factors that may help keep the lymphocytes moving. The group hopes to determine the signals that maintain both the movement along and attachment to the networks, and to see whether other cells or signals can divert lymphocytes from their network-determined pathways. JCB

Reference: Bajénoff, M., et al. 2006. *Immunity.* doi:10.1016/j.immuni.2006.10.011.

Moving cells link membrane and actin

Exocytosis and actin polymerization during cell movement are tied together by Xiaofeng Zuo, Wei Guo (University of Pennsylvania, Philadelphia, PA), and colleagues. They find that Exo70, a component of the exocytosis machine called the exocyst, binds to the Arp2/3 complex, a regulator of actin polymerization that helps push out the front of migrating cells.

It has long been thought that exocytosis is directed to the front of moving cells. The added membrane helps the front of the cell to push outwards, and recycles adhesion proteins from the cell rear.

The link to the actin polymerization machinery started with interaction assays using yeast proteins, and was extended to mammalian proteins. The proteins colocalized at the front of moving cells, and depletion of Exo70 decreased lamellipodial size, cell migration speed, and directional persistence.

Overexpressed Exo70 could induce protrusions, but not if its Arp2/3 interaction domain was deleted. EGF induced greater interaction between Exo70 and Arp2/3, and recruited both to the leading edge.

Future work will clarify whether Exo70 is primarily bringing Arp2/3 to the membrane or kinetically regulating its activity. The study underlines, says Guo, that "cell migration is a really coordinated process." JCB

Reference: Zuo, X., et al. 2006. *Nat. Cell Biol.* doi:10.1038/ncb1505.