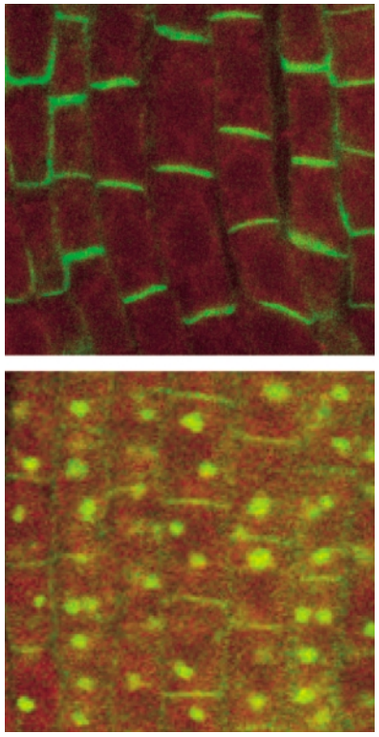


PLANT HORMONES

Pinning down auxin transport

Of the main plant hormones, our understanding of auxin signalling is better than most. Auxin is synthesized in newly formed organs and is then transported to the rest of the plant. In *Arabidopsis*, the directionality of this transport is thought to result from the static, polar distribution of putative auxin-efflux carriers called PINs. Reporting in *Nature*, Geldner *et al.* show that one of these, PIN1, does not stay at the plasma membrane, but that it rapidly cycles between the plasma membrane and an unknown cellular compartment. Their results further indicate that auxin-specific transport inhibitors can actually disturb general transport of membrane proteins.

Previous studies have shown that PIN1 is found at the basal end of cells (figure, top), and that this polar localization is required for normal transport of auxin. *gnom* mutants are defective in normal PIN1 localization, and they fail to establish tissue polarity (and presumably normal auxin transport). Geldner *et al.* investigated why PIN1 is mislocalized in *gnom* mutants.

GNOM encodes a brefeldin A (BFA)-sensitive regulator of vesicular transport. Treating wild-type roots with BFA abolished membrane localization of PIN1, which led to its accumulation in an intracellular compartment (figure, bottom). This process was rapidly reversible, insensitive to protein-synthesis inhibitors, and dependent on actin. These remarkable results indicate that the highly stable pool of PIN1 protein rapidly cycles between the plasma membrane and an undefined intracellular compartment along the cytoskeleton.

How, then, do the 'auxin-transport' inhibitors work? Geldner *et al.* examined the effects of an inhibitor called TIBA in concert with BFA. Pre- or co-treatment with TIBA prevented PIN1 from leaving the plasma membrane, and treating roots with TIBA after BFA prevented PIN1 from returning to the plasma membrane after BFA was removed. The effect of TIBA is not specific to PIN1, so these results indicate that TIBA could interfere with the general movement of proteins in the cell, at the level of the transport route itself.

Sarah Cooney, Nature

References and links

ORIGINAL RESEARCH PAPER Geldner, N., Friml, J., Stierhof, Y.-D., Jürgens, G. & Palme, K. Auxin transport inhibitors block PIN1 cycling and vesicle transport. *Nature* **413**, 425–428 (2001)

MEMBRANE DYNAMICS

Life without caveolae

The function of caveolae — flask-shaped invaginations at the plasma membrane — has remained elusive for almost 50 years. Reporting in *Science*, Kurzchalia and colleagues now describe a new tool that might shed light on the functions of this mysterious organelle — a caveolin-1 knockout (*cav-1*$^{-/-}$) mouse.

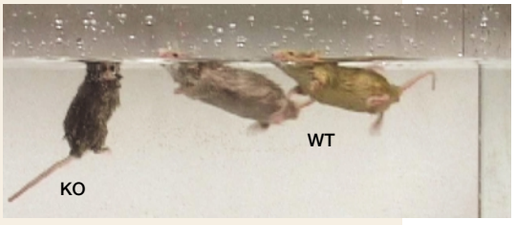
Caveolin-1 is the main protein constituent of caveolae; and it was shown years ago to be sufficient to generate caveolae in lymphocytes, which normally do not contain caveolae. Kurzchalia and colleagues now confirm that caveolin-1 is essential for the formation of these organelles, as *cav-1*$^{-/-}$ mice completely lack caveolae. So, by knocking out a single protein, the authors have in fact knocked out an organelle — a remarkable feat in itself.

Caveolae are often considered a specialized type of lipid raft — lateral aggregates of cholesterol and glycosphingolipids that concentrate certain proteins. But lipid-raft preparations from *cav-1*$^{-/-}$ mice did not show any gross defects in composition, which indicates that caveolin-1 and/or caveolae are not required for the organization of these membrane domains.

The authors then tested a few of the postulated functions of caveolae. They found that transcytosis — which is thought to be the mechanism by which albumin crosses the endothelium — is probably not dependent on caveolae, as the albumin concentration in the cerebrospinal fluid remained unchanged in *cav-1*$^{-/-}$ mice. Also, caveolae are probably not required for cholesterol transport, as the blood lipoprotein composition and the cholesterol content of high-density lipoprotein were unchanged in the knockout mice.

However, caveolin-1 and/or caveolae do function in signalling during several physiological processes. Isolated aortic rings of *cav-1*$^{-/-}$ mice did not establish a steady contractile tone, and their relaxation after acetylcholine stimulation was highly increased. Both processes are known to be mediated by NO, and, indeed, the basal release of NO was 31% higher and cGMP levels were three times higher in *cav-1*$^{-/-}$ mice. So, caveolin-1 and/or caveolae are probably negative regulators of NO-mediated vascular relaxation. Loss of caveolin-1 and/or caveolae also resulted in a markedly decreased response to vasoconstrictors, such as angiotensin II, endothelin-1 or phorbol ester in vascular smooth muscle cells. Last, the myogenic tone of these cells was reduced.

In addition to the marked defects in vascular



physiology, *cav-1*$^{-/-}$ mice also displayed uncontrolled hyperproliferation of angioblastic cells and fibrosis in lung alveolar septa, which implicates caveolin-1 and/or caveolae in the local control of cell proliferation.

Remarkably, despite the profound dysfunction of the vascular system and the pathomorphological defects in lung alveolar septa, *cav-1*$^{-/-}$ mice were viable, and had only relatively minor physical disabilities — for example, they could not swim as long as their wild-type littermates. To explain the non-lethal phenotype, the authors propose that lipid rafts, which seem to be normal in these mice, could carry out many of the functions that are proposed for caveolae.

Raluca Gagescu

References and links

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FURTHER READING Simons, K. & Toomre, D. Lipid rafts and signal transduction. *Nature Rev. Mol. Cell Biol.* **1**, 31–39 (2001)