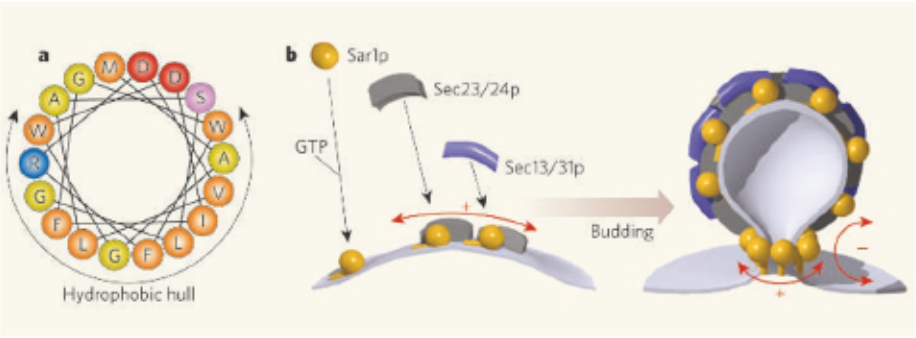

Figure 1 | Sar1p in budding and fission. **a**, The N-terminal 18 amino acids of Sar1p form an amphipathic helix, seen here as though looking along the central axis with each amino acid identified by a one-letter code. The highly hydrophobic amino acids (orange) constitute a wide side, whereas polar amino acids (red, negatively charged; blue, positively charged; purple, hydroxylated) make up a smaller one. Other amino acids are in yellow. **b**, On activation by GTP, Sar1p inserts its N-terminal helix into the membrane. Lee *et al.*[2] show that, once there, it bends the membrane outwards (+) and recruits the Sec23/24p complex, which polymerizes into a coat with Sec13/31p. Eventually, the coated bud is attached to the membrane by a small neck, with a negative curvature (−) in one direction and a positive curvature (+) in the other. Several Sar1p N-terminal helices may orientate parallel to the main neck axis, where they might further constrict the membrane and help fission and release of the bud.

swapped Sar1p mutant, yet free vesicles are scarce. In line with this, follow-up experiments conducted on membranes derived from endoplasmic reticulum show that an intact N terminus in Sar1p is key to the efficient release of COPII vesicles. So, if there is no doubt that the spherical shell formed by Sec23/24p and Sec13/31p is central to the sculpting of the membrane, Lee and colleagues' study[2] implies that the N terminus of Sar1p is not merely a simple piece of tape that sticks the COPII coat to the membrane, but that it has an active role in membrane deformation and fission.

The N-terminal helix of Sar1p is amphipathic — that is, it has a hydrophobic face and a hydrophilic face. The wide hydrophobic 'hull' should insert between the lipid acyl chains of the membrane, while the polar hydrophilic side interacts with the lipid heads and the watery environment of the cytoplasm (Fig. 1a). From model studies, we know that this kind of helix is designed to float on biological membranes, with the axis lying at the interface between the polar and nonpolar lipid regions[4]. The membrane is a tightly packed bilayer of lipids, so when the N-terminal helices from numerous Sar1p proteins adsorb on its surface, they will expand the outer layer and, because the bilayer has a finite area, compress the inner layer. As a result, the membrane will bend and dome. Indeed, when Lee *et al.* replaced bulky amino acids in the hydrophobic side of the helix with smaller ones, Sar1p was less able to make tubules from the liposomes and to generate transport vesicles from isolated membranes *in vitro*.

Because Sar1p recruits Sec23/24p, which has a three-dimensional structure that is adapted to a convex surface, it is easy to imagine how the two proteins work in concert to bend the membrane at early stages of coat assembly[5] (Fig. 1b). However, the role of Sar1p at the fission step is less intuitive. The curvature of the bud neck resembles that of a horse saddle, being negative in one direction and positive in the other. If the N-terminal helix of Sar1p invades the neck, its most plausible orientation is to align along the neck axis (Fig. 1b). A ring of parallel helices emerging from the coat edge may further constrict the neck and help membrane fission. Notably, COPII-coated buds on liposomes show a wider neck with N-terminal Sar1p mutants than with the unmutated form (Figs 3 and 8 in ref. 2).

The formation of clathrin-coated vesicles, which transport cargoes from the cell surface, follows an analogous process to that of COPII vesicles in that a short N-terminal helix of the protein epsin allows the plasma membrane to deform[6]. However, the epsin helix is shorter and has a smaller hydrophobic hull. Moreover, its polar side contains several electrically charged residues that bind specifically to PIP_2, a negatively charged lipid that is a hallmark of the plasma membrane. So if the insertion of hydrophobic residues from amphipathic helices seems to be a common mechanism for inducing membrane curvature, subtle changes in the sequence may govern the ability to deform specific cellular membranes.

Hydrophobic and polar residues form the two broad classes of the amino-acid alphabet, and their segregation is the basis of the amphipathic helix. Yet hydrophobic amino acids vary in size, and this should influence the helix 'footprint' on the membrane. Likewise, the polar amino acids (such as hydroxylated, basic or acidic residues) in the other side do not interact to the same extent with the lipid polar heads[7,8]. No doubt, the language of membrane-deforming helices at the complex membrane–water interface is very rich and remains to be translated. ■

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MYCOLOGY

The whiff of danger

You don't take the death cap (*Amanita phalloides*) home for tea. This species, pictured here, is infamously poisonous, with many other mushrooms being toxic to a greater or lesser degree.

Thomas N. Sherratt, David M. Wilkinson and Roderick S. Bain have addressed two issues raised by the existence of poisonous mushrooms (*Am. Nat.* doi:10.1086/497399). The first question was what purposes possession of poisons might serve in mushrooms. One possibility is that toxins are simply a metabolic by-product. Another that has been suggested by several authors is that they act as a deterrent to predators, which might otherwise destroy the mushroom before its spores have matured and dispersed. Fungus-loving vertebrates could in particular be highly destructive.

An evolutionary principle is that if you as an organism go to the bother of being unpalatable, you might as well signal that fact. Does this apply in mushrooms? To investigate this second issue, Sherratt *et al.* turned to data compilation and neural-network analysis. They made use of modern evolutionary trees to judge the incidence of poisonousness in mushrooms, then analysed data sets, culled from field guides, to see whether poisonous species tend to have particular ecological correlates — whether, for instance, they are more colourful, more aggregated or have a more noticeable odour.

Overall odour (and not cap colour) came out as the best predictor of toxicity, a result that was supported by pairwise comparisons of related poisonous and edible forms. Given that many animals forage by night, and that nocturnal mammals tend to have relatively poor colour vision, the authors suspect that odour provides the more effective signal.

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Sherratt *et al.* make plain that their study is correlative only, and that — for them and others — this is a work in progress. There is rich scope for further investigation of the hypothesis that poisonous mushrooms use odours as warning signals, and of the likely exceptions.
Tim Lincoln