Most cell-surface receptors are recycled from 'early' or 'sorting' endosomes (that is, those first encountered by endocytic tracers) where the pH is mildly acidic, favouring dissociation of the cargo from receptors. The released luminal contents are collected in large vacuolar portions of sorting endosomes, and the receptors are laterally segregated into long tubular extensions. The vacuoles then dissociate and move along microtubules towards the centre of the cell, where they start to mature. Maturation involves the removal of residual, recycling surface receptors, delivery of lysosomal hydrolases, and involution of the surrounding membrane to form multivesicular bodies[3].

At the end of this process, the so-called 'late' endosomes contain large amounts of intraluminal membrane, and they are enriched in lysosomal hydrolases and lysosomal membrane proteins. Having delivered their cargo of lysosomal hydrolases, MPRs are removed and recycled to the trans-Golgi network before the late endosomes fuse with the lysosomes. The mechanisms underlying maturation of the late endosomes and the sorting and retrieval of recycling receptors are poorly understood. Perplexingly, the recycling MPRs are concentrated on the intraluminal membrane, whereas lysosomal membrane proteins are found on the limiting membrane of the late endosome[4].

Cell biologists are only beginning to understand why cellular membranes contain so many types of phospholipid, and what particular species of lipid do in signal transduction, vesicle formation and fusion, and membrane protein-sorting[5–7]. The finding that LBPA is a 'marker' lipid of late endosomes (and lysosomes[8]) raises the question, what late-endosome-specific function might this unique lipid fulfil? Its structure may provide some clues. The small, negatively charged headgroup and polyunsaturated acyl-chain composition[9] would be expected to result in physical properties similar to those of cardiolipin, which is a marker lipid in the highly convoluted inner mitochondrial membrane. Cardiolipin tends to adopt the non-bilayer lipid structures that might facilitate the mixing of lipid bilayers required for membrane fusion.

There are several possibilities for the function of LBPA. It may play a structural role in the maturation of late endosomes — its tendency not to form a bilayer could help in developing the complex intraluminal membrane system. Alternatively, its unique structure means that LBPA is resistant to phospholipases, so it may stabilize the late-endosome/lysosomal membranes against degradation. In this case, however, we might expect to find LBPA on external, rather than internal, membranes.

LBPA may also be involved in protein sorting by the late endosomes. Indeed, other species of lipid with long-chain fatty acids, such as sphingomyelins, can form microdomains in the plane of the membrane that is implicated in protein sorting in polarized cells[6]. The exclusive localization of LBPA, within the internal membranes of late endosomes, suggests that these membranes represent a specialized functional domain. Furthermore, Kobayashi *et al.*[1] have shown that uptake of anti-LBPA antibodies into late endosomes perturbs the normal recycling of the MPR back to the trans-Golgi network. And the closely related lipid semi-LBPA has been shown[10] to be enriched in tubular vesicular elements of the trans-Golgi network, where protein sorting is known to occur.

Late endosomes/lysosomes are degradative organelles, so LBPA may be involved in lipid catabolism. For example, fatty acyltransferases[11] for LBPA exist in lysosomal fractions from rat liver, so LBPA could be involved in the sequestration and eventual transport of fatty-acid catabolites generated by lysosomal phospholipases. The effect of anti-LBPA antibodies on late endosomes — accumulation of membranes — is suggestive of other lysosomal storage diseases resulting from the aberrant accumulation of digestive products. Whether perturbation of any of these functions of LBPA accounts for the symptoms associated with antiphospholipid syndrome remains to be seen.

The work of Kobayashi *et al.* adds to the growing appreciation of the part played by lipids in membrane transport and sorting. Because the structure of lipids can be rapidly altered by the modification or removal of headgroups, or by acyl-exchange reactions, their associated functional properties can be tightly regulated. And given that cells contain over 200 unique species of lipid, it is not unlikely that others will turn out to be 'marker' lipids, involved in the structure and function of specific organelles. □

Sandra L. Schmid is in the Department of Cell Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, California 92037, USA.
e-mail: slschmid@scripps.edu
Pieter R. Cullis is in the Department of Biochemistry, University of British Columbia, 2146 Health Sciences Mall, Vancouver, British Columbia, Canada V6T 1Z3.
e-mail pieterc@unixg.ubc.ca

1. Kobayashi, T. *et al. Nature* **392,** 193–197 (1998).
2. Mellman, I. *Annu. Rev. Cell Dev. Biol.* **12,** 575–625 (1996).
3. Futter, C. E., Pearse, A., Hewlett, L. J. & Hopkins, C. R. *J. Cell Biol.* **132,** 1011–1023 (1996).
4. Griffiths, G., Hoflack, B., Simons, K., Mellman, I. & Kornfeld, S. *Cell* **52,** 329–341 (1988).
5. DeCamilli, P., Emr, S. D., McPherson, P. S. & Novick, P. *Science* **271,** 1533–1539 (1996).
6. Simons, K. & Ikonen, E. *Nature* **387,** 569–572 (1997).
7. Chernomordik, L., Kozlov, M. M. & Zimmerberg, J. *J. Membr. Biol.* **146,** 1–14 (1995).
8. Wherrett, J. R. & Huterer, S. *J. Biol. Chem.* **247,** 4144–4120 (1992).
9. Stremmel, W. & Debuch, H. *Hoppe-Seyler's Z. Physiol. Chem.* **357,** 803–810 (1976).
10. Cluett, E. B., Kuismanen, E. & Machamer, C. E. *Mol. Biol. Cell* **8,** 2233–2240 (1997).
11. Huterer, S. J. & Wherret, J. R. *Biochem. Cell Biol.* **68,** 366–372 (1990).

Daedalus

Breathable water

When animals came out of the sea, they had to learn to breathe air. In fact, says Daedalus, they never did. They took their own water with them. Even today, we still breathe water: we absorb the oxygen which dissolves in the moist lining of our lungs.

So why can't we still breathe water? Sadly, bulk water contains too little oxygen for our modern needs — only about 0.7% by volume, compared to 21% in air. But Daedalus has a way out. Imagine, he says, a dense foam of tiny air-bubbles in water. If all the bubbles had the same diameter, and were packed closely together, they could not easily rise to the surface. The result would be a curiously viscous stable foam, analogous to those 'rigid' close-packed emulsions of oil in water, whose droplets can hardly move past one another.

To make this foam breathable, Daedalus will dissolve suitable salts in it, bringing it into osmotic balance with lung tissue, and will add the natural polysaccharides that give saliva and sputum their viscosity, and a detergent like the one that helps the lungs to expand. He will aerate the solution through a battery of uniform nozzles, compress it briefly to collapse bubbles smaller than the standard size, and drain it to pack the remainder tight. It will then contain 74% of air by volume, giving it a density of 0.26 g ml^{-1}.

Daedalus's 'Liquid Air' will be a novel environment. You will sink into it, but will still feel somewhat buoyed up. It will be easier to move through than water, more opaque and sound-deadening than the densest fog, and rather an effort to breathe. Extra oxygen may be needed to make it feel comfortable and safe. But then the novelty of the experience, the sense of entering a silent, private fluid world, should make the Liquid Air immersion bath a popular relaxation.

Other more serious uses should also develop. With its high water content, Liquid Air will be utterly fireproof. Pumped in volume from fire-tenders, it will blanket rescuers as they enter burning buildings; injected into threatened aircraft, it will extinguish fires and blind and disorientate hijackers. Even better, bullets and explosion-fragments would be rapidly halted by Liquid Air. Pumped into and around suspicious vehicles and packages, it would damp an explosion wonderfully. The blast would expend its energy in 'inverting' the air–water emulsion to a dense spray of liquid droplets.

David Jones