combined with lack of evidence of extensive spontaneous internalization of cell-surface class II molecules, suggested that these are newly synthesized MHC proteins on their way to the surface. The findings implied that class II MHC molecules are present from the earliest contact between antigen and the cellular processing machinery, and may potentially bind antigenic peptides as soon as they become available, shielding them for further degradation[12,13].

Such early rendezvous of class II MHC and antigen was not observed by Peters *et al.*[1]. Although agreeing that it is newly synthesized class II molecules rather than those recycled from the cell surface that are detected in the endocytotic system, they find that class II MHC proteins in the endocytotic pathway are confined primarily to structures resembling lysosomes; that is, much further along the pathway than early endosomes. According to this picture, endocytosed antigens must run nearly the full gamut of acid pH and endosomal proteolysis before having the opportunity to bind class II molecules, suggesting that antigenic peptides would have to be hardy survivors of the endosomal degradative system. In this regard, Peters *et al.* observed that it took 20–50 minutes for a proteolytically resistant endocytosed molecule to reach the lysomsome-like compartments containing class II molecules; meanwhile, the more readily degraded bovine serum albumin molecule was detected there only poorly, implying that proteolysis takes its toll of material moving in to deeper structures.

Clearly, there are labile T-cell determinants that are not presented well from endocytosed antigens[14] or whose presentation is markedly enhanced by inhibition of cellular proteolytic activity[15,16]. Whether this functional degradation of T-cell determinants observed in biological assays results from a prolonged trip towards class II MHC in an increasingly harsh endosomal environment requires direct information; failure to detect molecules by electron microscopy does not necessarily mean that T-cell epitopes could not be pulled from the digest by MHC molecules. Further, although the lag period of 30–60 minutes needed for endocytosed antigen to become available for T-cell recognition[17] fits neatly with the time taken by antigen to travel to the lysosome-like MHC-containing structures, it is not established that this is the rate-limiting step in antigen presentation. On the other hand, the observation by Peters *et al.* that intracellular class II MHC molecules have half-lives of hours may explain why antigen presentation can persist for hours after cellular protein synthesis has been inhibited[18].

How can the findings of Guagliardi *et al.*[11] and Peters *et al.*[1] be reconciled? Information is needed on how results could be affected by use of different cell lines, or cells cultured under different conditions. The degree of resolution of molecules is also a consideration, but here one would expect that the thawed cryosections used by Peters *et al.* would be more sensitive than the plastic-embedded material of Guagliardi *et al.* In any event, no technique has yet revealed where the association between antigen and class II molecules actually occurs. Experiments addressing functional association — that is, experiments using T-cell recognition — will probably be required in order to resolve this issue.

There are also pressing questions on the related immunology. For instance, is there a way by which endogenously synthesized antigens (for a review see ref. 19) could enter a compartment to associate with class II MHC, other than by uptake at the cell surface? Are there mechanisms in the class II/antigen presentation system similar to those uncovered for class I, such as molecules which actively translocate peptides to compartments for MHC association, or the need to form a complex with antigen as a prerequisite for transport of MHC to the cell surface? Finally, can the observation that protein antigens are presented by intact antigen-presenting cells faster and at much lower concentrations than expected from studies with isolated molecules[20] be explain by how peptide and MHC meet in specialized intracellular compartments? □

Charles J. Hackett is at The Wistar Institute, 36th and Spruce Streets, Philadelphia, Pennsylvania 19104, USA.

Come in LDEF, your time is up

THE first satellite to be recovered by a space shuttle, the Long Duration Exposure Facility (LDEF) was retrieved by Columbia on 12 January 1990. It is seen here in its last moments in free-fall. LDEF was launched in 1984 to study the effects of cosmic dust and rays. The experiment reported by Fishman *et al.* on page 678 of this issue may indicate the kind of surprises in store for participants in the project. Amongst the gases and ions swept up by LDEF during its mission were prodigious quantities of beryllium-7. Produced by cosmic-ray interactions with air at an altitude of 40 km, 270 km below LDEF's orbit, ^{7}Be has a half-life of only 53 days, so that the authors are at a loss to explain how it came to be trapped by the satellite. □

1. Peters, P.J., Neefjes, J.J., Oorschot, V., Ploegh, H.L. & Geuze, H.J. *Nature* **349**, 669–676 (1991).
2. Yewdell, J.W. & Bennink, J.R. *Cell* **62**, 203–206 (1990).
3. Parham, P. *Nature* **348**, 674–675 (1990).
4. Townsend, A. *et al. Nature* **340**, 443–448 (1989).
5. Teyton, L. *et al. Nature* **348**, 39–44 (1990).
6. Bakke, O. & Dobberstein, B. *Cell* **63**, 707–716 (1990).
7. Neefjes, J.J., Stollorz, V., Peters, P.J., Geuze, H.J. & Pleogh, H.L. *Cell* **61**, 171–183 (1990).
8. Gruenberg, J. & Howell, K.E. *A. Rev. cell. Biol.* **5**, 453–481 (1989).
9. Griffiths, G., Back, R. & Marsh, M. *J. Cell Biol.* **109**, 2703–2720 (1989).
10. Blum, J.S. & Cresswell, P. *Proc. natn. Acad. Sci. U.S.A.* **85**, 3975–3973 (1988).
11. Guagliardi, L.E. *et al. Nature* **343**, 133–139 (1990).
12. Leyva-Cobian, F. & Unanue, E.R. *J. Immun.* **141**, 1445–1450 (1988).
13. Werdelin, O. *Scand. J. Immun.* **24**, 625–636 (1986).
14. Eisenlohr, L.G. & Hackett, C.J. *J. exp. Med.* **169**, 921–931 (1989).
15. Buus, S. & Werdelin, O. *J. Immun.* **136**, 452–453 (1986).
16. Gradehandt, G., Hampl, J., Milbradt, S. & Rude, E. *Eur. J. Immun.* **20**, 2637–2641 (1990).
17. Roosnek, E. *et al. J. Immun.* **140**, 4079–4082 (1988).
18. St-Pierre, Y. & Watts, T.H. *J. Immun.* **145**, 812–818 (1990).
19. Long, E.O. *Immun. Today* **10**, 232–234 (1989).
20. Sadegh-Nasseri, S. & McConnell, H. *Nature* **337**, 272–276 (1989).