to normal class I antigen expression and presentation merely by the replacement of the missing TAP subunits. The genes encoding LMP2/LMP7 did not appear to be required for antigen processing⁸; indeed the entire complex pattern of peptides loaded into class I MHC molecules in resting cells seemed unaffected either qualitatively or quantitatively by the lack of the two MHC-linked proteasome subunits⁹.

The new studies²⁻⁴ bring the LMP2/LMP7 chains back into consideration by showing that their presence or absence is associated with subtle changes of emphasis in the preferred cleavage specificity of the proteasome. All three groups used short fluorogenic oligopeptide substrates to test the cleavage specificity of proteasomes prepared from tissue culture cells. Driscoll *et al.*² and Gaczynska *et al.*³ worked with human hepatoma and macrophage cell lines, either resting or stimulated with γ -interferon, and lymphoblastoid cells carrying or lacking LMP2/LMP7 subunits genetically. They agree that the main change in specificity associated with expression of LMP2/LMP7 is an increase in the rate of cleavages leaving positively charged or hydrophobic carboxy-terminal (P1) amino acids. Gaczynska *et al.* also report a reduction in cleavages generating negatively charged carboxy termini not seen by Driscoll and colleagues.

Discrepancies

Boes *et al.*⁴, who worked on resting and γ -interferon-stimulated mouse fibroblasts, report a rather different result. They find a reduction in the efficiency of cleavages generating hydrophobic carboxy termini associated with the induction of the LMP2 chain (the LMP7 chain is constitutively expressed in the transformed fibroblasts used in this study), and no change in cleavages generating positively charged carboxy termini. It is too early to interpret the apparent discrepancies between the three sets of results, except to note the differences in species, cell type, protease preparation and substrates used.

The study of proteasome cleavage specificity has been overly influenced by previous experience with well-defined proteases such as trypsin and chymotrypsin, and the importance of sequence environment in determining cleavage by the proteasome has not yet been extensively investigated. Boes *et al.* approach this point in their *in vitro* analysis of cleavage of a synthetic 25-mer oligopeptide derived from a murine cytomegalovirus protein. Interestingly, the cleavage specificity of proteasomes from cells treated with γ -interferon differs from that of resting proteasomes not by the nature of the P1 amino acid, but by which of two instances of a favoured P1 amino acid (in

this case a tyrosine) is used.

There is an additional agenda in all these studies, namely, that the inclusion of the LMP2/LMP7 chain in the proteasome is good for antigen processing in some way. Driscoll *et al.* and Gaczynska *et al.* both emphasize that the carboxy-terminal amino acids of peptides actually loaded into class I MHC molecules are nearly always either positively charged or hydrophobic¹⁰. Thus the incorporation of LMP2/LMP7 into the proteasome would favour the generation of 'loadable' carboxy termini, and is at least consistent with the idea that proteasomes are responsible for creating the observed carboxy termini of naturally loaded peptides. The same argument appears not to hold for the amino termini where there is no consistency in the implied P1 amino acid (knowing the protein sequence from which they are derived), suggesting that the amino termini of loaded peptides are generated by a distinct proteolytic activity. In the same spirit, Boes *et al.* point out that the interferon-induced shift in preferred cleavage of their 25-mer would favour the release of a known 9-mer epitope.

The underlying issue is how typical class I peptides, which are normally 8–10 amino acids in length, are generated in their final form. Is it by proteolytic activity in the cytosol, followed by transport and loading? Or do they arise in two steps? That is, by a cytosolic step generating (on average) long peptides with hydrophobic or positively charged carboxy termini, followed by transport to the endoplasmic reticulum, assembly with the carboxy terminus correctly positioned in the peptide-binding groove, and amino-terminal trimming to optimal size, as proposed by Rammensee and colleagues¹¹. Some of the present data are at least consistent with this second notion. But there is still a grave shortage of relevant information, not least concerning the potentially selective properties of the peptide transporter^{12,13}. □

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DAEDALUS

Smoothed air

A SUBSONIC aircraft is designed to slip through the air with minimum drag. A warning pressure wave travels in front of it, diverging the air ahead slightly to let it through. But a supersonic aircraft cannot exploit this effect, for it travels faster than its own pressure wave. It just slams into static, unwarned air, kicking it aside as a conical shock wave which runs off with a vast amount of power, and hits the ground as a supersonic boom.

Daedalus has a way out. Suppose, he says, the aircraft projected ahead of it a contoured beam of some radiation absorbed by air. This could warm up the air ahead, and start it expanding out of the way of the approaching craft. By the time the craft arrived, the air ahead of it could be moving out of its way at just the right speed to accept the advancing shape quietly, radiating no energy as shock waves. Power would be needed to generate the radiation beam, but this would be saved by the vastly reduced load on the engines. In the ultimate limit, so much energy could be pumped into the air ahead that it would explode right out of the way of the advancing plane. The craft would then coast along in a continuously generated tunnel of vacuum, and would need no engine power at all. This, however, would probably consume more power in radiation than would be needed by the thirstiest conventional engines. Somewhere between these extremes lies the optimal minimum-power design.

Determining that design will pose the most complex and subtle mathematical problems. The aircraft and its advance radiation envelope have to match each other perfectly at cruising supersonic speed; in addition, the craft has to retain reasonable lift and stability in subsonic flight. Even Daedalus has no idea what the final result will look like. He is not even sure of the best radiation to use. Ion beams, some microwave and far infrared frequencies, and far ultraviolet are all absorbed by air. Far infrared, for which powerful laser sources are available, is probably the most immediately feasible choice.

The final technology should transform aviation. Aircraft designers will rush to redevelop the glittering supersonic, hypersonic, aerospace and ramjet vehicles stalled these past 20 years by high oil prices and supersonic-boom restrictions. Politicians and businessmen will flash round the world in a technomaniac dream, saving precious hours in which to savour at their destinations the leisurely, unchanging realities of baggage mishandling, customs and immigration formalities, traffic jams, and jet-lag. David Jones