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In addition to the recognition of peptide–MHC complexes by the classical antigen-recognition receptors of T cells and B cells, several other ligand–receptor interactions are used by cells of the immune system to allow the recognition of foreign antigens and to maintain tolerance to self.

For example, lipid-antigen recognition by T cells involves the surveillance of lipid–CD1 complexes at the surface of antigen-presenting cells. On page 387, Branch Moody, Dirk Zajonc and Ian Wilson describe how analysing the crystal structures of lipid-bound CD1 proteins — in particular, looking at the differences between the antigen-binding grooves of CD1a, CD1b and CD1d — can lead to insights into the ligand specificity of these proteins.

By contrast, natural killer (NK) cells are known to use a form of 'missing-self' recognition to monitor the expression of MHC class I molecules by self and non-self cells. Vinay Kumar and Megan McNerney (page 363) now describe an additional system, based on the recognition of non-MHC ligands by inhibitory receptors at the surface of NK cells, that can maintain appropriate NK-cell function even in conditions in which the levels of self MHC class I molecules are reduced, such as in individuals who are deficient in MHC class I molecules.

However, despite such varied and elaborate systems to ensure both self-tolerance and appropriate responses to pathogens, defects can and do arise. The Opinion article by David Dunne and Anne Cooke, on page 420, proposes that the increasing incidence of some autoimmune diseases, such as type 1 diabetes, in the developed world can be explained in terms of our co-evolution with parasites. They suggest that, as hygiene levels improve, the very relationship that led to the evolution of these immune-recognition systems might now be causing disease in the absence of the immune stimuli provided by parasites.


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