

IN BRIEF

DENDRITIC CELLS**Lipid accumulation and dendritic cell dysfunction in cancer**

Herber, D. L. *et al. Nature Med.* **16**, 880–886 (2010)

The unexpected finding that dendritic cells (DCs) generated in tumour cell-conditioned medium had an accumulation of lipids led Herber *et al.* to investigate how this might affect DC function. Lipids were found to accumulate in DCs from tumour-bearing mice and humans, and this was shown to result from the upregulation of macrophage scavenger receptor 1 (MSR1) expression by DCs. Although lipid accumulation did not affect DC maturation or expression of MHC and co-stimulatory molecules, lipid-laden DCs from tumour-bearing mice had a reduced capacity to stimulate T cells, owing to defects in the processing of soluble antigens. Treatment of tumour-bearing mice with an inhibitor of fatty acid synthesis decreased the number of lipid-laden DCs and restored their ability to stimulate T cells. Moreover, administration of the inhibitor together with a DC-based vaccine led to more potent antitumour effects than administration of the vaccine alone, suggesting that manipulating lipid levels in DCs may improve immune responses to cancer.

ANTIBODIES**IgT, a primitive immunoglobulin class specialized in mucosal immunity**

Zhang, Y.-A. *et al. Nature Immunol.* 1 Aug 2010 (doi:10.1038/ni.1913)

By describing the existence of a mucosal antibody known as IgT in teleost fish, this study challenges the paradigm that specialized immunoglobulin isotypes for mucosal and systemic responses arose during tetrapod evolution. Zhang *et al.* show that IgT exists as a monomer in the serum of trout, but is found at the highest levels in the gut mucus in a polymeric form. A distinct B cell subset that expresses IgT and not IgM was identified and mainly found in the trout gut. The phagocytic activity, proliferative capacity and ability to secrete immunoglobulin of these IgT⁺ B cells was similar to that of IgM⁺ B cells. However, in response to a gut-tropic parasitic infection, survival of the fish was associated with an accumulation of IgT⁺ B cells and high levels of parasite-specific IgT in the gut; IgM⁺ B cell numbers and IgM levels did not change, suggesting that fish IgT is the functional equivalent to mammalian IgA.

INFECTIOUS DISEASE**Serine protease activity contributes to control of *Mycobacterium tuberculosis* in hypoxic lung granulomas in mice**

Reece, S. T. *et al. J. Clin. Invest.* 2 Aug 2010 (doi:10.1172/JCI42796)

Caseous necrotic granulomas containing hypoxic regions form in the lungs of patients with tuberculosis and are particularly problematic as bacteria in these structures are resistant to most antibiotics. However, research into these granulomas has been difficult as they do not form in mice that are infected with *Mycobacterium tuberculosis*. This study shows that blockade of interferon- γ and tumour necrosis factor in inducible nitric oxide synthase 2-deficient mice during *M. tuberculosis* infection leads to the formation of hypoxic, caseous granulomas, which resemble those seen in infected humans. Serine proteases were found to be upregulated in hypoxic granulomas in both mice and humans, and these proteases helped to control intracellular bacterial growth. The authors suggest that the targeting of serine proteases could be an effective therapy for tuberculosis; their mouse model is also likely to be an invaluable tool for further research into hypoxic granulomas.