IN BRIEF

INNATE IMMUNITY

Selective modulation of TLR4-activated inflammatory responses by altered iron homeostasis in mice

Wang, L. *et al. J. Clin. Invest.* 5 Oct 2009 (doi:10.1172/JCI39939)

This study helps to explain the increased susceptibility to certain bacterial infections of patients with type I haemochromatosis, who have a mutation in the haemochromatosis gene, *HFE*, resulting in dysregulated iron homeostasis; this could affect both the host immune response and microbial growth, but the precise mechanisms of disease have been unclear. HFE-deficient mice have decreased production of tumour necrosis factor and interleukin-6 by macrophages in response to *Salmonella typhimurium* or lipopolysaccharide. This was shown to be a result of low concentrations of intracellular iron in peritoneal macrophages, which specifically inhibited Toll-like receptor 4 signalling through the adaptor proteins TRAM and TRIF but not through MYD88 and MAL (also known as TIRAP). Deliberately lowering iron levels in macrophages using small-molecule inhibitors of the HFE pathway decreased the severity of intestinal inflammation induced by various means, which potentially offers a new anti-inflammatory strategy.

LYMPHOID ORGANOGENESIS

Id2-, RORγt-, and LTβR-independent initiation of lymphoid organogenesis in ocular immunity

Nagatake, T. *et al. J. Exp. Med.* 12 Oct 2009 (doi:10.1084/jem.20091436)

Tear-duct-associated lymphoid tissue (TALT) in humans has been proposed to provide mucosal immune surveillance in the eye in a similar manner to mucosa-associated lymphoid tissue (MALT) in the nasopharynx and gut, but the extent of any similarity between these tissues has been unclear. In contrast to the embryonic genesis of MALT in the gut, TALT develops postnatally in mice, similar to nasopharynx-associated MALT. Mouse TALT could take up ocularly administered antigens through M cells and form germinal centres. However, the initiation of TALT development did not require the transcriptional regulators Id2 or RORγt, which regulate the differentiation of lymphoid tissue inducer (LTi) cells, and did not require signalling through the interleukin-7 receptor (expressed by LTi cells) or lymphotoxin-β receptor (triggered by LTi cells). Therefore, TALT genesis is distinct from that of other secondary lymphoid tissues, despite similar function.

T CELL RESPONSES

Evidence of premature immune aging in patients thymectomized during early childhood

Sauce, D. *et al. J. Clin. Invest.* **119**, 3070–3078 (2009)

Given that the thymus atrophies from early adolescence and is routinely resected during heart surgery, how important is the thymus in maintaining a normal T cell compartment? Appay and colleagues report that young adults who were thymectomized during early childhood, owing to congenital heart defects, show signs of a prematurely aged immune system. Childhood thymectomy was associated with a substantial loss of naive T cells, an accumulation of memory T cells and increased markers of inflammation, features normally associated with the T cell compartment in the elderly. The most extensive alterations to the T cell compartment were found in individuals that had strong T cell responses to cytomegalovirus, suggesting that infection may exhaust the naive T cell pool in the absence of adequate T cell renewal from the thymus.