IN BRIEF

LYMPHOID ORGANOGENESIS

Tyrosine kinase receptor RET is a key regulator of Peyer's patch organogenesis.

Veiga-Fernandes, H. *et al. Nature* 25 February 2007 (doi:10.1038/nature05597)

The exact mechanisms involved in orchestrating intestinal organogenesis are not completely understood. In this study, Kioussis and colleagues examined the phenotype of the haematopoietic cells that give rise to lymphoid organ primordia. In addition to a previously described population, they identified a phenotypically distinct population of $CD4^{-}CD3^{-}CD127^{-}KIT^{+}CD11c^{+}$ haematopoietic cells, and showed that these cells have an important role in the formation of normal numbers of Peyer's patches during gut organogenesis. A proportion of these cells expressed the tyrosine kinase receptor RET, which is essential for the formation of the mammalian enteric nervous system. $Ret^{-/-}$ embryos had a defect in Peyer's patch primordia formation due to a failure in the aggregation of haematopoietic cells. The authors propose that activation of the RET signalling pathway has a crucial role in initiating the formation of the Peyer's patch primordium.

AUTOIMMUNITY

Dickkopf-1 is a master regulator of joint remodeling.

Diarra, D. *et al. Nature Med.* **13**, 156–163 (2007)

Rheumatic diseases show two main patterns of joint pathology: bone resorption (in which the bone and joint are progressively broken down), a hallmark of rheumatoid arthritis, and new bone formation, a hallmark of degenerative osteoarthritis. The molecular basis for these two patterns of joint disease is unknown. Diarra *et al.* proposed that regulators of bone formation, such as the *WNT* genes, are affected by joint pathology, and examined Dickkopf-1 (DKK1), a negative regulator of WNT signalling. Blocking the activity of DKK1 changed the pattern of bone destruction in a mouse model of rheumatoid arthritis to the bone-forming pattern of osteoarthritis. Although some bony nodules did form, there was no overall bone erosion. So, DKK1 seems to have a key role in joint remodelling, and might constitute an attractive therapeutic target for the modulation of joint architecture.

T CELLS

Alloreactive T cells respond specifically to multiple distinct peptide–MHC complexes.

Felix, N. J. *et al. Nature Immunol.* 25 February 2007 (doi:10.1038/ni1446)

Do endogenous peptides in complex with allogeneic MHC molecules (allopeptides) contribute to alloreactive T-cell responses? To address this issue, Allen and colleagues undertook a new approach that involved the screening of a large pool of T cells for reactivity against defined endogenous allopeptides. They identified nine alloreactive T-cell clones that responded to allopeptides, and three of these clones each responded to two or three distinct allopeptides that had no sequence homology. The recognition of each of these distinct peptide–MHC complexes by the alloreactive T cell was highly specific. In addition, the T-cell receptor (TCR) recognized different MHC contact residues for each interaction, resulting in slightly different TCR–MHC orientations depending on the peptide. The authors conclude that alloreactive T cells are not degenerate but are instead polyspecific, which provides an explanation for the high frequency of alloreactive T cells.

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