IN BRIEF

INFLAMMATION

A genome-wide association study identifies *IL23R* as an inflammatory bowel disease gene.

Duerr, R. H. *et al. Science* 26 Oct 2006 (doi:10.1126/science.1135245)

Genetic factors are known to have an important role in susceptibility to the inflammatory bowel diseases (IBDs) Crohn's disease and ulcerative colitis. This study identifies the *IL23R* gene, which encodes a subunit of the interleukin-23 receptor, as a new locus associated with IBD. A non-synonymous single-nucleotide polymorphism, resulting in an arginine-to-glutamine substitution at position 381 of IL-23R, was shown to protect against the development of Crohn's disease. This focus on *IL23R* ties in with the known pro-inflammatory role of IL-23, in part through activation of IL-17-producing T cells, and indicates that modification of the IL-23R signalling pathway could be a therapeutic strategy for IBD.

THYMOCYTE DEVELOPMENT

Control of thymocyte development and recombination-activating gene expression by the zinc finger protein Zfp608.

Zhang, F., Thomas, L. R., Oltz, E. M. & Aune, T. M. *Nature Immunol.* 22 Oct 2006 (doi:10.1038/ni1397)

This study mapped the mutation in a previously described congenic strain of mice, which have defects in natural killer T (NKT)- and T-cell development, to the gene encoding the zinc-finger protein ZFP608 on chromosome 18. Wild-type mice have high expression of ZFP608 in neonatal thymus only, whereas the congenic mice had sustained thymocyte expression of ZFP608 throughout life. Expression of ZFP608 negatively regulated expression of *Rag1* (recombination-activating gene 1) and *Rag2*, causing a block in thymocyte development at the double-negative to double-positive transition. The authors speculate that the high-level expression of ZFP608 *in utero* normally inhibits development of the adaptive immune system until after birth to prevent fetal recognition of the mother as foreign.

TECHNIQUE

Humanized mice mount specific adaptive and innate immune responses to EBV and TSST-1.

Melkus, M. W. *et al. Nature Med.* 22 Oct 2006 (doi:10.1038/nm1431)

The authors describe a new model of human haematopoiesis, by combining two previous systems that have used non-obese diabetic and severe combined immunodeficient (NOD/SCID) mice transplanted with haematopoietic $CD34^+$ cells or SCID mice implanted with human fetal thymic and liver tissue (SCID-hu thy-liv mice). In the new model, NOD/SCID-hu thy-liv mice transplanted with $CD34^+$ cells had increased systemic reconstitution with human T cells, B cells, monocytes/macrophages and dendritic cells compared with previous models. Importantly, in these mice, thymocytes develop in human thymic tissue in the context of autologous MHC restriction and the mice mounted MHC-restricted human T-cell responses to Epstein–Barr virus. They also mounted innate immune responses to the superantigen toxic shock syndrome toxin 1, which shows that human T cells and human dendritic cells can interact and respond appropriately in these mice.