IN BRIEF

HAEMATOPOIESIS

Aryl hydrocarbon receptor antagonists promote the expansion of human hematopoietic stem cells

Boitano, A. E. *et al. Science* 5 Aug 2010 (doi:10.1126/science.1191536)

The clinical use of haematopoietic stem cells (HSCs) has been restricted by a lack of defined culture conditions for proliferating HSCs without loss of pluripotency. Stored cord blood is a potential source of HLA-matched HSCs for allogeneic transplantation, but cord blood generally contains only a small proportion of HSCs. This study shows that the addition of the purine derivative StemReginin 1 (SR1) increases the number of $CD34^+$ cells when primary human $CD34^+$ HSCs from peripheral or cord blood are cultured with a cytokine cocktail that otherwise induces differentiation and the loss of CD34 expression. Human cord-blood-derived $CD34^+$ cells were more efficient at engrafting immunodeficient mice after culture with SR1 and they retained multilineage potential for long-term engraftment. SR1 mediates these effects by directly antagonizing signalling through the human aryl hydrocarbon receptor, although the downstream mechanisms are unknown.

ANTIBODIES

PTIP promotes chromatin changes critical for immunoglobulin class switch recombination

Daniel, J. A. *et al. Science* 29 Jul 2010 (doi:10.1126/science.1187942)

During class-switch recombination (CSR) in B cells, rearrangement of the immunoglobulin loci requires both transcription, to make the DNA accessible to activation-induced cytidine deaminase (AID), and repair of AID-mediated double-strand breaks. PAX-interacting protein 1 (PTIP) associates with methyltransferases that catalyse histone methylation of actively transcribed genes and interacts with components of the DNA damage response and repair pathway, so the authors looked at the role of PTIP in CSR. B cell-specific PTIP-deficient mice had a selective decrease in histone methylation of the immunoglobulin heavy-chain switch regions *Igh*-γ2b and *Igh*-γ3 in B cells, which correlated with decreased transcription initiation at these regions and decreased IgG2b and IgG3 class switching. In PTIP-deficient B cells transfected with a mutant form of PTIP that does not form DNA damage foci, CSR was restored less effectively than in cells transfected with wild-type PTIP, independent of any effect on switch-region transcription. So, PTIP both targets AID to and repairs DNA damage at switch regions during CSR.

NATURAL KILLER CELLS

Central nervous system (CNS)-resident natural killer cells suppress Th17 responses and CNS autoimmune pathology

Hao, J. *et al. J. Exp. Med.* 9 Aug 2010 (doi:10.1084/jem.20092749)

Most studies addressing the roles of natural killer (NK) cells in autoimmunity have focused on peripheral NK cells; this study shows that tissue-resident NK cells suppress pro-inflammatory T cell development in the central nervous system (CNS) and prevent autoimmune responses at this site. In a model of experimental autoimmune encephalomyelitis (EAE), disease was exacerbated in CX_3C-chemokine receptor 1 (CX_3CR1)-deficient mice (which are deficient in CNS-resident NK cells but have normal NK cell numbers elsewhere), and this was associated with increased numbers of interferon-γ- and interleukin-17 (IL-17)-producing T cells. Expansion of CNS-resident NK cell populations by administration of IL-2 complexes decreased the severity of EAE in wild-type mice but had no effect in CX_3CR1-deficient mice. The anti-inflammatory effects of NK cells seem to be due to their interaction with microglial cells in the CNS.