IN BRIEF

INNATE IMMUNITY

Innate lymphoid cells drive interleukin-23-dependent innate intestinal pathology

Buonocore, S. *et al. Nature* **464,** 1371–1375 (2010)

The production of interleukin-17 (IL-17) and interferon-γ (IFNγ) during colitis is often attributed to $CD4^+$ T cells. However, these pro-inflammatory cytokines are also detected in T cell-independent models of intestinal inflammation. This study identifies an IL-23-responsive population of innate immune cells that can promote inflammation by producing IL-17 and IFNγ. These cells are $CD45^+THY1^+$ but do not express a range of other leukocyte lineage markers (LIN^-), suggesting that they are distinct from traditional innate immune cells. The $CD45^+THY1^+LIN^-$ population expanded during innate colitis and spontaneously produced IL-17 and IFNγ *ex vivo*. IL-23 enhanced both the frequency and cytokine-producing ability of $CD45^+THY1^+LIN^-$ cells, and antibody-mediated depletion of these cells abrogated disease in innate models of colitis. Notably, a similar population of $CD45^+THY1^+LIN^-$ cells was detected in both immunocompetent mice and in patients with inflammatory bowel disease (IBD). These data show crucial pro-inflammatory roles for $CD45^+THY1^+LIN^-$ cells and suggest that they could be a new therapeutic target for IBD.

IMMUNE REGULATION

Statin-induced Kruppel-like factor 2 expression in human and mouse T cells reduces inflammatory and pathogenic responses

Bu, D. *et al. J. Clin. Invest.* 3 May 2010 (doi:10.1172/JCI41384)

Statins are known to have various immunomodulatory effects that are independent of their cholesterol-lowering capabilities and, in this study, they are shown to act directly on T cells, diminishing their proliferation and interferon-γ (IFNγ) production. Treatment of mouse or human T cells with statins led to increased expression of the transcription factor Kruppel-like factor 2 (KLF2). KLF2 expression has been linked to T cell quiescence and is normally downregulated following T cell activation. Statin treatment blocked this reduction and inhibited T cell function. In a mouse model of myocarditis induced by heart-antigen-specific $CD8^+$ T cells, statin treatment and retrovirus-mediated overexpression of KLF2 in T cells similarly lowered T cell pathogenicity *in vivo* and ameliorated the disease.

T CELL DEVELOPMENT

Neural crest-derived pericytes promote egress of mature thymocytes at the corticomedullary junction

Zachariah, M. A. & Cyster, J. G. *Science* 22 Apr 2010 (doi:10.1126/science.1188222)

Following their positive selection in the medulla, thymocytes upregulate sphingosine 1-phosphate receptor 1 (S1P1) to exit the thymus and enter the blood. Until now, the route of thymocyte egress and the source of S1P were unknown. This study shows that mature thymocytes exit through blood vessels at the corticomedullary junction facilitated by S1P production by pericytes (specialized cells that surround thymic blood vessels). Forced expression of S1P1 by immature thymocytes led to premature egress of these cells into the periphery, as well as accumulation at sites close to thymic blood vessels in association with basement membrane epithelial cells and pericytes. CD69 (which regulates S1P1 function) was found to delay thymocyte egress to allow full maturation before cells exit through blood vessels in the corticomedullary junction in an S1P-dependent manner. The authors estimate that ~1 million thymocytes in young mice exit through this route each day.