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IN BRIEF

IMMUNE REGULATION

Transcription factor T-bet regulates skin sclerosis through its function in innate immunity via IL-13.

Aliprantis, A. O. *et al. Proc. Natl Acad. Sci. USA* **104**, 2827–2830 (2007)

This study identifies a new role for the transcription factor T-bet in repressing dermal sclerosis, a fibrotic disease that is classically thought to be driven by T helper 2 (T_H2)-cell-derived cytokines. Surprisingly, mice that lacked an adaptive immune system (*Rag*$^{-/-}$ mice) remained susceptible to bleomycin-induced scleroderma, and mice that were also deficient in T-bet developed more severe scleroderma. The occurrence of severe disease in *Rag*$^{-/-}$*Tbet*$^{-/-}$ mice indicated that, instead of promoting T_H1-cell differentiation, T-bet attenuates disease by acting in innate immune cells. Further studies indicated that fibrotic disease in *Tbet*$^{-/-}$ mice was caused by increased levels of the profibrotic cytokine interleukin-13 (IL-13). So the authors propose that T-bet functions to attenuate scleroderma by repressing IL-13 production by innate immune cells.

LYMPHOCYTE MIGRATION

A central role for DOCK2 during interstitial lymphocyte motility and sphingosine-1-phosphate-mediated egress.

Nombela-Arrieta, C. *et al. J. Exp. Med.* 26 February 2007 (doi:10.1084/jem.20061780)

T cells are constantly on the move, even within secondary lymphoid organs; but what signalling pathways mediate such motility? Here, the authors investigated the roles of the signalling molecules DOCK2 (dedicator of cytokinesis 2) and PI3Kγ (phosphoinositide 3-kinase-γ), which are both downstream of G-protein-coupled receptors, such as chemokine receptors, in T-cell motility. Multiphoton intravital microscopy revealed that a lack of DOCK2 or both DOCK2 and PI3Kγ reduced T-cell motility in the T-cell area and B-cell follicle, respectively. PI3Kγ deficiency alone did not affect migration velocity, but increased the turning angles of T cells. Sphingosine 1-phosphate (S1P)-mediated egress of DOCK2-deficient T cells from lymph nodes was also impaired. And although egress was not affected in PI3Kγ-deficient T cells, F-actin polymerization triggered by S1P was reduced. So, DOCK2 and, to a lesser extent, PI3Kγ have central roles in signal transduction during interstitial lymphocyte migration and lymph-node egress.

B CELLS

Autoreactivity in human IgG$^+$ memory B cells.

Tiller, T. *et al. Immunity* **26**, 205–213 (2007)

The presence of low-affinity self-reactive antibodies in normal human serum (despite two checkpoints for removal of such antibodies during the maturation of naive B cells) has remained a mystery. In this paper, Tiller *et al.* investigated the source of these antibodies. They cloned, expressed and measured the reactivity of 141 antibodies from circulating human IgG$^+$ memory B cells from healthy donors. These B cells were found to frequently express low-affinity, non-pathogenic, self-reactive antibodies, including anti-nuclear antibodies and polyreactive antibodies, compared with naive B cells and IgM$^+$ memory B cells. The authors propose that abnormalities in checkpoint regulation or activation of peripheral self-reactive IgG$^+$ memory B cells could therefore contribute to the development of autoimmunity in susceptible individuals.