IN BRIEF

T-CELL DEVELOPMENT

Natural agonists for aryl hydrocarbon receptor in culture medium are essential for optimal differentiation of Th17 cells

Veldhoen, M. *et al. J. Exp. Med.* 29 Dec 2009 (doi:10.1084/jem.20081438)

Owing to the relevance of T helper 17 (T_H17) cells in several autoimmune and inflammatory diseases, efforts are being made to characterize the factors that influence their differentiation. Recently, ligation of the aryl hydrocarbon receptor (AHR) — which binds several environmental pollutants and endogenous ligands derived from aromatic amino acids — on T cells has been linked with T_H17-cell differentiation. Now, Stockinger and colleagues show that the amount of AHR agonists in the culture medium contributes to T_H17-cell differentiation *in vitro*. Iscove's modified Dulbecco's medium (IMDM), which contains high levels of aromatic amino acids, supported T_H17-cell differentiation better than RPMI, a more commonly used culture medium. These results help to clarify discrepancies between the reported efficacy of T_H17-cell generation *in vitro* and increase our understanding of the differentiation requirements of this T-cell subset.

AUTOIMMUNITY

Distinct roles of helper T cell subsets in systemic autoimmune disease

Hoyer, K.K. *et al. Blood* **113**, 389–395 (2008)

With the discovery of T helper 17 (T_H17) cells, the examination of the role of different T_H-cell subsets in autoimmunity has been a topic of great interest. In this study, Hoyer ***et al.*** examined the contribution of the T_H1-type cytokine interferon-γ (IFNγ) and the T_H17-type cytokine interleukin-17 (IL-17) in the development of autoimmunity. *Il2*$^{-/-}$ mice (which develop spontaneous systemic autoimmune disease and die of haemolytic anaemia) had increased levels of IFNγ and IL-17 compared with wild-type mice. Mice that lacked both IL-2 and IFNγ had higher rates of survival than *Il2*$^{-/-}$ mice, and this was due to decreased production of autoantibodies and macrophage-mediated phagocytosis owing to a lack of IFNγ. However, these mice eventually died as a result of colonic inflammation, which was accompanied by increased levels of *Il17* mRNA. The authors concluded that T_H1 cells drive early autoimmune responses, whereas T_H17 cells are probably responsible for chronic tissue inflammation.

T-CELL DEVELOPMENT

Cutting Edge: Ikaros is a regulator of Th2 cell differentiation

Quirion, M. R. *et al. J. Immunol.* **182**, 741–745 (2009)

The transcription factor Ikaros is a key regulator of haematopoiesis and early lymphocyte development. Now, Quirion ***et al.*** have identified a regulatory role for Ikaros in T helper 2 (T_H2)-cell differentiation. Naive Ikaros-deficient T cells stimulated under T_H2-cell polarizing conditions did not express the T_H2-type cytokines interleukin-4 (IL-4) and IL-5, but did express the T_H1-type cytokine interferon-γ (IFNγ), suggesting a positive regulatory role for Ikaros in T_H2-cell development. Histone 3 acetylation levels at the T_H2-cytokine locus in both undifferentiated and T_H2-polarized Ikaros-deficient T cells were reduced compared with wild-type control cells. In addition, the expression levels of T_H2-cell-associated transcription factors were reduced in T_H2-polarized Ikaros-deficient T cells, whereas those of T_H1-cell-associated transcription factors were increased. So, Ikaros regulates T_H2-cell differentiation directly, by regulating chromatin accessibility, and indirectly, through the regulation of lineage-specific transcription factors.