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IN BRIEF

REGULATORY T CELLS

Foxp3 controls regulatory T-cell function by interacting with AML1/Runx1.

Ono, M. *et al. Nature* **446**, 685–689 (2007)

Forkhead box P3 (FOXP3) is a crucial regulator of the development and function of naturally occurring $CD4^+CD25^+$ regulatory T (T_{Reg}) cells. However, the molecular events associated with its function were not known. Sakaguchi and colleagues now show that the transcription factor acute myeloid leukaemia 1 (AML1; also known as RUNX1) specifically binds to the genes encoding interleukin-2 (IL-2) and interferon-γ (IFNγ), and enhances their expression in $CD4^+$ T cells. Because FOXP3 repressed the expression of these cytokines in T_{Reg} cells, the authors examined whether FOXP3 interacted with AML1 in these cells. They showed that FOXP3 physically interacted with AML1 and repressed AML1-induced IL-2 and IFNγ expression. In addition, the formation of the FOXP3–AML1 complex upregulated the expression of T_{Reg}-cell-associated molecules, such as CD25, CTLA4 and GITR, and controlled the suppressive function of these cells. So, this study provides a model for the transcriptional control of T_{Reg}-cell function by FOXP3, through its interaction with AML1.

LYMPHOCYTE MIGRATION

Lymph node topology dictates T cell migration behavior.

Beltman, J. B. *et al. J. Exp. Med.* 26 March 2007 (doi:10.1084/jem.20061278)

T-cell activation by dendritic cells (DCs) occurs in secondary lymphoid organs, and the anatomical structure of these organs is thought to have an important role in the development of an immune response. Here, Beltman *et al.* used a three-dimensional model of the lymph node to examine T-cell motility. They show that the fluctuations in T-cell velocity are determined by the dense lymph-node environment and not by an intrinsic motility mechanism. The model also predicted that T cells form small, dynamic, local streams that are constantly changing direction, which was confirmed *in vivo*. In addition, this model allowed the authors to estimate that T cells can scan about 100 different DCs, and that DCs scan about 2,000 different T cells per hour. So, using this spatially explicit model, the authors concluded that the lymph-node environment dictates T-cell motility and migration.

MAST CELLS

The sphingosine kinase–sphingosine-1-phosphate axis is a determinant of mast cell function and anaphylaxis.

Olivera, A. *et al. Immunity* **26**, 287–297 (2007)

The stimulation of mast cells by allergens induces two mammalian sphingosine kinases (SPHK1 and SPHK2) to produce sphingosine 1-phosphate (S1P), but little is known about their specific role in regulating immune-cell function. Here, Olivera *et al.* used mice in which either one or both of the *Sphk1* and *Sphk2* genes were deleted to investigate their role in mast-cell function. They showed that, unexpectedly, SPHK2, but not SPHK1, is the main regulator of S1P production, mediating several mast-cell signals and functions. An *in vivo* anaphylaxis challenge showed that the responsiveness of mast cells is determined by circulating amounts of S1P and by a partnership between SPHK1 (as an extrinsic regulator) and SPHK2 (as an intrinsic regulator). So, SPHKs and S1P have a key role in mast-cell responsiveness.