IN BRIEF

INNATE IMMUNITY

NLRC5 negatively regulates the NF-κB and type I interferon signaling pathways

Cui, J. *et al. Cell* **141**, 483–496 (2010)

NLRC5 (NLR family, CARD containing 5) is a member of the NOD-like receptor family of intracellular pathogen recognition receptors, but its physiological function is not known. Cui ***et al.*** show that NLRC5 is a cytoplasmic protein induced by nuclear factor-κB (NF-κB). NLRC5 inhibits NF-κB activation by various cytokine- and Toll-like receptor-mediated signals through its direct interaction with the NF-κB-activating kinases IKKα and IKKβ in both mouse and human cells. NLRC5 blocks the phosphorylation and kinase activity of the IKKs through its LRR domain. Furthermore, NLRC5 interacts with the viral sensors RIG-I and MDA5 and blocks binding to the adaptor signalling molecule MAVS, thereby inhibiting type I interferon responses. Knockdown of NLRC5 expression enhances NF-κB activation and inflammatory responses, as well as antiviral immunity. So, NLRC5 is a key negative regulator of two important innate immune signalling pathways.

CYTOKINES

Functional crosstalk between type I and II interferon through the regulated expression of STAT1

Gough, D. J. *et al. PLoS Biol.* 27 Apr 2010 (doi:10.1371/journal.pbio.1000361)

Low levels of constitutively produced type I interferon (IFN) can prime cells for increased responsiveness to other cytokines, but the molecular basis for this has been unclear. Gough ***et al.*** now show that priming by type I IFNs induces expression of signal transducer and activator of transcription 1 (STAT1), thereby enhancing subsequent signalling induced by IFNγ. Unstimulated fibroblasts were shown to constitutively produce low levels of IFNβ in a JUN-dependent manner. *Jun*$^{-/-}$ fibroblasts had lower levels of STAT1 but increased STAT1 expression following culture with conditioned medium from wild-type cells, indicating that IFNβ (identified as the STAT1-inducing factor in the conditioned medium) induces STAT1 in both an autocrine and paracrine manner. Antiviral effects of IFNγ are less potent in IFNα/β receptor 1 (*Ifnar1*)$^{-/-}$ mice; however, overexpression of *Stat1* in *Ifnar1*$^{-/-}$ cells could override the requirement for type I IFN priming and enable IFNγ-mediated protection of these cells from cytopathic virus infection.

ANTIBODY RESPONSES

Batf coordinates multiple aspects of B and T cell function required for normal antibody responses

Betz, B. C. *et al. J. Exp. Med.* **207**, 933–942 (2010)

BATF (basic leucine zipper transcription factor, ATF-like) is a member of the activator protein 1 family of transcription factors, and a recent study has shown that it has a central role in T helper 17 (T_H17) cell differentiation. Using mice that can not produce BATF (*Batf*$^{\Delta Z/\Delta Z}$ mice), this study confirms the role of BATF in T_H17 cells and describes additional roles for BATF in lymphocyte development and humoral immunity. *Batf*$^{\Delta Z/\Delta Z}$ mice had decreased numbers of peripheral CD4$^+$ T cells, specifically T_H2, T_H17 and follicular T helper cells, but normal B cell numbers. However, no germinal centres developed in antigen-challenged *Batf*$^{\Delta Z/\Delta Z}$ mice, and antibody production was severely impaired. Adoptive transfer of wild-type but not *Batf*$^{\Delta Z/\Delta Z}$ CD4$^+$ T cells restored antibody production. In addition, *Batf*$^{\Delta Z/\Delta Z}$ B cells do not express activation-induced cytidine deaminase or undergo class-switch recombination in response to T cell-independent antigen.