

## IN BRIEF

 **MACROPHAGES****SOCS2 and SOCS3 in macrophage polarization**

M1 macrophages are pro-inflammatory, whereas M2 macrophages are involved in tissue repair. Here, Spence *et al.* study the role of suppressor of cytokine signalling 2 (SOCS2) and SOCS3 in macrophage polarization. The phenotypes of *Socs2*<sup>-/-</sup> or *Socs3*<sup>-/-</sup> macrophages were analysed in the absence or presence of polarizing stimuli, and their function was tested in a mouse model of sepsis. *Socs2*<sup>-/-</sup> macrophages were biased towards the M1 subset, whereas *Socs3*<sup>-/-</sup> macrophages had a stable M2 profile. Moreover, compared with controls, *Socs2*<sup>-/-</sup> macrophages had higher levels of phosphorylated STAT1 (signal transducer and activator of transcription 1) following stimulation with interferon- $\gamma$ , and *Socs3*<sup>-/-</sup> macrophages had higher levels of active STAT6 in response to interleukin-4. As the blockade of these cytokines partially reversed the polarization bias of *Socs2*<sup>-/-</sup> and *Socs3*<sup>-/-</sup> macrophages, SOCS2 and SOCS3 may control macrophage polarization by regulating cytokine-STAT signalling.

**ORIGINAL RESEARCH PAPER** Spence, S. *et al.* Suppressors of cytokine signaling 2 and 3 diametrically control macrophage polarization. *Immunity* 21 Nov 2012 (doi:10.1016/j.immuni.2012.09.013)

 **MUCOSAL IMMUNOLOGY****IRF3 maintains gut homeostasis**

Here, Negishi *et al.* investigate the role of interferon-regulatory factor 3 (IRF3) in intestinal homeostasis. *Irf3*<sup>-/-</sup> mice showed more severe symptoms of dextran sulphate sodium-induced colitis and impaired disease recovery compared with control mice. Thymic stromal lymphopoietin (TSLP) and interleukin-33 (IL-33) have homeostatic functions in the gut, and their expression levels were lower in *Irf3*<sup>-/-</sup> mice than in wild-type controls, both in the steady state and during colitis. IRF3-dependent expression of TSLP and IL-33 was induced in response to faecal (possibly microbiota-derived) nucleic acids and involved signalling through one of the adaptor proteins MAVS and STING. Finally, IRF3 cooperated with nuclear factor- $\kappa$ B to promote *Tslp* transcription. Further molecular links between the intestinal microbiota and IRF3-dependent homeostasis remain to be identified.

**ORIGINAL RESEARCH PAPER** Negishi, H. *et al.* Essential contribution of IRF3 to intestinal homeostasis and microbiota-mediated *Tslp* gene induction. *Proc. Natl Acad. Sci. USA* 3 Dec 2012 (doi:10.1073/pnas.1219482110)

 **GENE REGULATION****STATs control subset-specific enhancer activation**

Enhancers are upstream genetic elements that promote transcription, and their activation is marked by several epigenetic changes, including monomethylation of histone H3 lysine 4 and binding of the acetyltransferase p300. Genome-wide analyses of enhancer activation in T helper 1 (T<sub>H</sub>1) and T<sub>H</sub>2 cells revealed very distinct profiles. Interestingly, analyses in T helper cells deficient for key signal transducer and activation of transcription (STAT) proteins showed that STATs bind to subset-specific enhancers and control the recruitment of p300 and, thereby, enhancer activation. Overexpression of the master transcriptional regulators T-bet and GATA3 in STAT-deficient T<sub>H</sub>1 and T<sub>H</sub>2 cells, respectively, was not sufficient to restore the profile of enhancer activation. Thus, STATs seem to link cytokine signals to transcriptional regulation.

**ORIGINAL RESEARCH PAPER** Vahedi, G. *et al.* STATs shape the active enhancer landscape of T cell populations. *Cell* 151, 981–993 (2012)