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*$^{-/-}$ or *Socs3*$^{-/-}$ macrophages were analysed in the absence or presence of polarizing stimuli, and their function was tested in a mouse model of sepsis. *Socs2*$^{-/-}$ macrophages were biased towards the M1 subset, whereas *Socs3*$^{-/-}$ macrophages had a stable M2 profile. Moreover, compared with controls, *Socs2*$^{-/-}$ macrophages had higher levels of phosphorylated STAT1 (signal transducer and activator of transcription 1) following stimulation with interferon-γ, and *Socs3*$^{-/-}$ 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*$^{-/-}$ and *Socs3*$^{-/-}$ 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*$^{-/-}$ 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*$^{-/-}$ 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-κB 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_H1) and T_H2 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_H1 and T_H2 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)