IN BRIEF

T CELL RESPONSES

NFIL3 clocks out T_H17 cells

Hooper and colleagues show that the transcription factor NFIL3 integrates signals from the circadian clock to regulate T helper 17 (T_H17) cell development in mice. NFIL3 suppressed T_H17 cell development by repressing *Rorc* (which encodes RORγt) transcription, and NFIL3 itself was suppressed by the clock regulator REV-ERBα. *Nfil3* and *Rorc* were expressed in opposite phases of the circadian cycle, with *Nfil3* expression lower during the day (a 12-hour light cycle) and higher at night (a 12-hour dark cycle). Accordingly, $CD4^+$ T cells isolated from mice during the day showed a higher propensity for differentiating into T_H17 cells following *in vitro* polarization. Notably, mice exposed to chronic light-cycle perturbations had increased frequencies of T_H17 cells in the spleen and small intestine, and were more susceptible to chemically induced colitis than mice maintained under a normal light cycle. Interestingly, *Nfil3* polymorphisms, night-shift work and jet lag are all linked to human inflammatory diseases — the authors suggest that this could be due to the disruption of circadian pathways that regulate pro-inflammatory immune responses.

ORIGINAL RESEARCH PAPER Yu, X. *et al.* T_H17 cell differentiation is regulated by the circadian clock. *Science* http://dx.doi.org/10.1126/science.1243884 (2013)

AUTOIMMUNITY

Altered microbiota linked to rheumatoid arthritis

In mouse models of arthritis, the introduction of a single species of intestinal bacteria is sufficient to induce joint inflammation in otherwise healthy animals. Littman and colleagues now report that patients with new-onset rheumatoid arthritis (NORA) have an increased abundance of the bacterial species *Prevotella copri* in their faeces compared with patients with chronic, treated rheumatoid arthritis (CRA), patients with psoriasis or healthy controls. *P. copri* was present in the microbiota of 75% of patients with NORA, but only in 21.4% of healthy controls. Sequencing experiments showed that *P. copri* strains vary among individuals, and the authors could associate particular open-reading frames (ORFs) within the *P. copri* genome with strains isolated from either healthy individuals or patients with NORA. These ORFs could be useful biomarkers for distinguishing healthy microbiota from disease-associated microbiota, although it remains to be determined whether expansion of *P. copri* is a causative factor in the development of rheumatoid arthritis.

ORIGINAL RESEARCH PAPER Scher, J. U. *et al.* Expansion of intestinal *Prevotella copri* correlates with enhanced susceptibility to arthritis. *eLIFE* http://dx.doi.org/10.7554/eLife.01202 (2013)

PARASITE IMMUNITY

IL-6 helps the regulators rein in T_H2 cells

This study shows an unexpected role for interleukin-6 (IL-6) during infection with *Heligmosomoides polygyrus*. Mice deficient in IL-6 developed more potent T helper 2 (T_H2) cell responses to *H. polygyrus* and had increased resistance to chronic infection. IL-6 deficiency led to increased eosinophilia and higher levels of IgE, but did not affect type 2 innate lymphoid cells. T_H17 cell numbers were increased in *H. polygyrus*-infected IL-6-deficient mice, but their depletion had no effect on worm burdens. However, IL-6-deficient mice had an altered regulatory T (T_{Reg}) cell phenotype (characterized by lower expression of FOXP3, Helios and GATA3, and increased production of IL-2 and IL-17), and restoration of normal T_{Reg} cell function decreased the T_H2 cell response to *H. polygyrus*. This suggests that IL-6 stabilizes T_{Reg} cells during helminth infection.

ORIGINAL RESEARCH PAPER Smith, K. A. & Maizels, R. M. IL-6 controls susceptibility to helminth infection by impeding Th2 responsiveness and altering the Treg phenotype in vivo. *Eur. J. Immunol.* http://dx.doi.org/10.1002/eji.201343746 (2013)