IN BRIEF

NEUTROPHILS

Disrupting the 'neutrostat' in LAD-I

Patients with leukocyte adhesion deficiency type I (LAD-I) — which results from mutation of the CD18 subunit of β2 integrins — have recurrent microbial infections and periodontal bone loss. A new study shows that bone loss in patients and in mouse models is not due to defective neutrophil extravasation and impaired surveillance of periodontal infection, but is caused by the excessive production of interleukin-17 (IL-17). These data support the 'neutrostat' model of neutrophil homeostasis, whereby the phagocytosis of apoptotic neutrophils in tissue sites suppresses the production of IL-23 and hence IL-17, which leads to the downregulation of granulopoiesis; this feedback regulation is disrupted in patients with LAD-I. This is the first study to link neutrostat disruption to IL-17-driven pathology, and has implications for therapeutic targeting of the IL-23–IL-17 axis in patients with LAD-I.

ORIGINAL RESEARCH PAPER Moutsopoulos, N. M. *et al.* Defective neutrophil recruitment in leukocyte adhesion deficiency type I disease causes local IL-17-driven inflammatory bone loss. *Sci. Transl Med.* **6**, 229ra40 (2014)

PARASITE IMMUNITY

Innate immune response to the liver stage of malaria

After a mosquito bite, the sporozoite forms of *Plasmodium* spp. — the causative agents of malaria — enter the bloodstream and are transported to the liver where they replicate inside hepatocytes. Blood-stage *Plasmodium* infection has been shown to induce innate immune responses, but whether the liver stage of malaria infection activates the innate immune system is less clear. Using RNA sequencing techniques, Kappe and colleagues analysed gene expression data from mouse livers after infection with attenuated *Plasmodium yoelii*, which only develop into liver-stage forms. They found that the parasites induced an innate immune response in the liver that was mediated by type I interferons (IFNs) and IFNγ, and mice that lacked IFNγ, the type I IFN receptor or IFN-regulatory factor 3 could not suppress liver-stage infection. Thus, in mice, innate immune responses are induced during malaria liver-stage infection, and this response can limit parasite development prior to the infection of red blood cells.

ORIGINAL RESEARCH PAPER Miller, J. L. *et al.* Interferon-mediated innate immune responses against malaria parasite liver stages. *Cell Rep.* http://dx.doi.org/10.1016/j.celrep.2014.03.018 (2014)

NEUTROPHILS

Sensing calcium to kill

Calcium influx is important for several neutrophil effector functions, but the effects of altered calcium signalling have not been investigated in neutrophils *in vivo*. Now, Zhang *et al.* show that the calcium-sensing molecule stromal interaction molecule 1 (STIM1) is important for neutrophil-mediated killing of bacteria. Mouse neutrophils that lacked *Stim1* showed a loss of store-operated Ca^{2+} entry (SOCE), which mediates a sustained increase in cytosolic Ca^{2+} concentration. Mice that lacked *Stim1* were more susceptible to infection with *Listeria monocytogenes* and *Staphylococcus aureus* than wild-type mice owing to diminished neutrophil superoxide production. These mice also showed increased protection from tissue damage in a model of hepatic ischaemia and reperfusion injury. The authors speculate that blockade of SOCE in neutrophils could provide a novel approach to treat inflammation-induced tissue damage.

ORIGINAL RESEARCH PAPER Zhang, H. *et al.* STIM1 calcium sensor is required for activation of the phagocyte oxidase during inflammation and host defense. *Blood* **123**, 2238–2249 (2014)