IN BRIEF

INNATE IMMUNITY

Phagocytes come back even stronger

Lauvau and colleagues have shown that inflammatory monocytes and neutrophils become better pathogen killers during memory responses. The authors found that the enhanced clearance of the intracellular pathogen *Listeria monocytogenes* following re-infection was associated with increased reactive oxygen species (ROS)-mediated bacterial killing. Indeed, higher numbers of ROS-producing inflammatory monocytes and neutrophils were detected during the memory response, and these inflammatory phagocytes produced higher levels of ROS on a per cell basis, had an increased phagosomal pH and had elevated levels of autophagy compared with cells during the primary response. These enhanced phagocyte functions were decreased in the presence of neutralizing antibodies specific for CC-chemokine ligand 3 (CCL3) or CD8, suggesting that, during a memory response, CCL3 produced by memory $CD8^+$ T cells helps to 'license' monocytes and neutrophils to more effectively kill intracellular pathogens.

ORIGINAL RESEARCH PAPER Narni-Mancinelli, E. *et al.* Inflammatory monocytes and neutrophils are licensed to kill during memory responses *in vivo*. *PLoS Pathog.* **7**, e1002457 (2011)

B CELLS

Protective role of innate-like B cells in sepsis

This study describes a protective immune role for a previously uncharacterized population of innate-like B cells. When mice were systemically treated with lipopolysaccharide (LPS) or infected with *Escherichia coli*, cells that produced granulocyte–macrophage colony-stimulating factor (GM-CSF) accumulated in the spleen. Surprisingly, most of these cells were IgM^+ B cells, and transfer studies showed that they develop from innate-like B-1 cells. In response to LPS, peritoneal B-1 cells proliferated, migrated to the spleen and gave rise to the $GM\text{-}CSF^+$ B cell population. Development of the $GM\text{-}CSF^+$ B cells depended on BAFFR, TLR4 and MYD88, and these cells were retained in the spleen by the integrins VLA4 and LFA1. In a model of sepsis, mice with a B cell-restricted deficiency in GM-CSF showed increased neutrophil infiltration to the peritoneum. However, these neutrophils had impaired phagocytic activity, and the mice experienced a severe cytokine storm and died. This suggests that GM-CSF-producing B cells contribute to bacterial clearance by promoting neutrophil phagocytic functions.

ORIGINAL RESEARCH PAPER Rauch, P. J. *et al.* Innate response activator B cells protect against microbial sepsis. *Science* 12 Jan 2012 (doi:10.1126/science.1215173)

MACROPHAGES

Linking lysosome function to macrophage homeostasis

A recent study in *Science* reveals that equilibrative nucleoside transporter 3 (ENT3) is essential for both lysosomal function and macrophage homeostasis. Similarly to patients with lysosomal storage disease owing to *ENT3* mutations, ENT3-deficient mice were found to develop splenomegaly as a result of increased macrophage proliferation (histiocytosis). In the absence of functional ENT3, nucleosides accumulated in the lysosomes, leading to lysosomal alkalization. This, in turn, compromised lysosomal function, as indicated by a delay in the degradation of apoptotic cells and live bacteria by ENT3-deficient macrophages. Furthermore, the lysosomal degradation of the macrophage colony-stimulating factor 1 (CSF1)–CSF1 receptor complex was impaired in ENT3-deficient macrophages, resulting in persistent CSF1-mediated signalling, which was suggested to underlie the increase in macrophage proliferation. These findings suggest a link between lysosomal storage disease and macrophage histiocytosis.

ORIGINAL RESEARCH PAPER Hsu, C.-L. *et al.* Equilibrative nucleoside transporter 3 deficiency perturbs lysosome function and macrophage homeostasis. *Science* **335**, 89–92 (2012)