IN BRIEF

ANTIVIRAL IMMUNITY

A wake up call for antiviral T cells

This report shows that interleukin-33 (IL-33) released from necrotic cells drives potent cytotoxic T lymphocyte (CTL) responses during virus infection. In mice infected with lymphocytic choriomeningitis virus (LCMV), IL-33 signalled via the IL-33 receptor subunit ST2 on virus-specific CTLs to promote their proliferation and acquisition of effector functions. Radio-resistant, non-haematopoietic cells in the spleen were identified as the main source of IL-33 during virus infection. Mice deficient in ST2 or IL-33 had an impaired ability to induce CTLs during infection with various wild-type RNA or DNA viruses, but had similar levels of CTL induction to wild-type mice in response to replication-deficient virus strains. The authors proposed that IL-33 could be used to mimic the presence of viral replication. In support of this idea, co-delivery of IL-33 markedly increased CTL induction in mice vaccinated with attenuated-virus vectors or virus-like particles.

ORIGINAL RESEARCH PAPER Bonilla, W. V. *et al.* The alarmin interleukin-33 drives protective antiviral $CD8^+$ T cell responses. *Science* 9 Feb 2012 (doi:10.1126/science.1215418)

APOPTOSIS

Stress triggers the healing process

To maintain tissue homeostasis, apoptotic cells release factors that trigger the proliferation of surrounding cells. This process is known as 'compensatory proliferation' but is incompletely understood. As production of reactive oxygen species (ROS) is associated with apoptosis, the authors of this study proposed that ROS might trigger compensatory proliferation. They found that cells produce interleukin-11 (IL-11) in response to oxidative stress, but not in response to tumour necrosis factor or lipopolysaccharide. Oxidative stress induced the phosphorylation of the kinase ERK2 and the activation of the transcription factor FOS-related antigen 1, which promoted *Il11* gene transcription. In a mouse model of acute liver injury, IL-11 was released by dying hepatocytes in a ROS-dependent manner and triggered the proliferation of neighbouring hepatocytes by activating STAT3. In the same model, treatment of mice with an IL-11 receptor agonist enhanced hepatocyte proliferation and reduced liver injury, whereas liver injury was exacerbated in mice deficient in the IL-11 receptor.

ORIGINAL RESEARCH PAPER Nishina, T. *et al.* Interleukin-11 links oxidative stress and compensatory proliferation. *Sci. Signal.* **5**, ra5 (2012)

T CELL DEVELOPMENT

Inflammasome blockade keeps the thymus young

This study suggests that activation of the NOD-, LRR- and pyrin domain-containing 3 (NLRP3) inflammasome contributes to thymic involution and decreases thymic export of naive T cells in aged individuals. The authors found that myeloid cells in the mouse thymus showed an age-dependent progressive increase in the activation of caspase 1. Aged mice had higher levels of free cholesterol and ceramides, and these age-related 'danger' signals could promote caspase 1 activation in macrophages. Notably, age-related caspase 1 activation and thymic involution was reduced in mice deficient in the inflammasome components NLRP3 and ASC. Furthermore, aged NLRP3- or ASC-deficient mice had increased numbers of cortical epithelial cells and T cell progenitors and a more diverse peripheral T cell repertoire compared with wild-type controls. Aged NLRP3-deficient mice also showed increased T cell reconstitution in a model of haematopoietic stem cell transplantation. The authors suggest that pharmacological inhibition of the inflammasome could boost immune function in elderly patients.

ORIGINAL RESEARCH PAPER Youm, Y.-H. *et al.* The NLRP3 inflammasome promotes age-related thymic demise and immunosenescence. *Cell Rep.* **1**, 56–68 (2012)