IN BRIEF

INNATE IMMUNITY

p38δ–PKD1–PTEN signalling promotes neutrophil chemotaxis

A new study shows that expression of the p38 δ-isoform (a member of the mitogen-activated protein kinase family) in neutrophils is essential for neutrophil chemotaxis. p38δ-deficient neutrophils had an impaired migratory capacity *in vitro* and failed to infiltrate the lungs in a mouse model of acute lung injury. The effect of p38δ on neutrophil extravasation and chemotaxis involved the inactivation of protein kinase D1 (PKD1). PKD1 was shown to phosphorylate the phosphoinositide 3-kinase (PI3K) regulatory subunit p85α, which in turn enhanced the activity of the lipid phosphatase PTEN. Thus, inactivation of PKD1 and PTEN downstream of p38δ appear to maintain the gradient of phosphatidylinositides (lipid targets of PI3K and PTEN) that is required for neutrophil chemotaxis.

ORIGINAL RESEARCH PAPER Ittner, A. *et al.* Regulation of PTEN activity by p38δ-PKD1 signaling in neutrophils confers inflammatory responses in the lung. *J. Exp. Med.* 5 Nov 2012 (doi:10.1084/jem.20120677)

T CELLS

The MALT1 switch in autoimmunity

MALT1 is a dual regulator of nuclear factor-κB (NF-κB) signalling: it functions as a scaffold to promote IκB kinase (IKK)-dependent activation of the canonical NF-κB pathway and proteolytically degrades several NF-κB-related factors, including the non-canonical NF-κB subunit RELB. Now, Brüstle *et al.* report a central role for MALT1 in the effector function of T helper 17 (T_H17) cells. MALT1-deficient mice were resistant to the induction of experimental autoimmune encephalomyelitis, despite infiltration of the brain by activated T cells after immunization. Moreover, MALT1-deficient T_H17 cells lacked pathogenicity and failed to produce the cytokines IL-17 and GM-CSF. Further analyses suggested that IKK activation and RELB degradation by MALT1 are two independent events that are required for the differentiation of T_H17 but not T_H1 cells. This function of MALT1 in T helper cell plasticity could be therapeutically targeted in autoimmune disorders.

ORIGINAL RESEARCH PAPER Brüstle, A. *et al.* The NF-κB regulator MALT1 determines the encephalitogenic potential of Th17 cells. *J. Clin. Invest.* 1 Nov 2012 (doi:10.1172/JCI63528)

INFLAMMATION

The GEF way to MYD88-dependent vascular permeabilization

The integrity of the vasculature is compromised under inflammatory conditions, partly as a result of low surface levels of the cell–cell adhesion molecule VE-cadherin. Now Zhu *et al.* delineate the signalling events that lead to vascular permeabilization following the stimulation of human endothelial cells with interleukin-1β (IL-1β). IL-1β induced NF-κB-independent activation of the GTPase ARF6, which promoted the endocytosis of VE-cadherin. The guanine nucleotide-exchange factor (GEF) ARNO was required for ARF6 activation and co-immunoprecipitated with the IL-1β signalling adaptor molecule MYD88. As the GEF inhibitor SecinH3 reduced vascular permeabilization and tissue inflammation in two models of inflammatory disease, specific targeting of this GEF-dependent arm of IL-1β signalling may be of therapeutic value.

ORIGINAL RESEARCH PAPER Zhu, W. *et al.* Interleukin receptor activates a MYD88–ARNO–ARF6 cascade to disrupt vascular stability. *Nature* 11 Nov 2012 (doi:10.1038/nature11603)