IN BRIEF

INNATE IMMUNITY

Activation of innate immune antiviral responses by Nod2

Sabbah, A. *et al. Nature Immunol.* **10**, 1073–1081 (2009)

Nucleotide-binding oligomerization domain protein 2 (NOD2) is a cytoplasmic NOD-like receptor protein and has a well-described role in detecting bacterial peptidoglycan to trigger an innate immune response. This study shows that NOD2 also recognizes viruses and triggers an immune response during viral infection. Recognition of viral single-stranded RNA by NOD2 led to activation of interferon-regulatory factor 3, through mitochondrial antiviral signalling protein (MAVS), and induced the production of interferon-β (IFNβ). NOD2-deficient mice infected with respiratory syncytial virus (RSV) did not produce IFNβ efficiently, had higher viral titres and were more susceptible to respiratory disease pathogenesis caused by RSV than wild-type mice. This is the first report of NOD2 acting as a viral pattern recognition receptor and indicates the importance of NOD2 as a host antiviral defence mechanism.

TRANSPLANTATION

PKCθ is required for alloreactivity and GVHD but not for immune responses toward leukemia and infection in mice

Valenzuela, J. O. *et al. J. Clin. Invest.* 9 Nov 2009 (doi:10.1172/JCI39692)

Bone marrow transplants are used for the treatment of haematopoietic malignancies such as leukaemia. However, they can result in graft-versus-host disease (GVHD), in which the transplanted T cells attack the host's tissue. Protein kinase Cθ (PKCθ) is an important modulator of T cell receptor signalling and is involved in T cell survival and activation. This study shows that PKCθ-deficient $CD8^+$ T cells could still respond to and eradicate *Listeria monocytogenes* infection. Adoptive transfer of wild-type alloreactive $CD8^+$ T cells caused GVHD in all of the recipients, whereas most recipients of PKCθ-deficient alloreactive $CD8^+$ T cells remained free of GVHD. The authors show that a lack of PKCθ rendered T cells unable to make robust immune responses in response to low-affinity stimulation (such as an alloresponse) but did not affect high-affinity stimulation (such as an infection). This suggests that PKCθ might be a target to prevent GVHD but retain the beneficial effects of bone marrow transplantation.

TOLERANCE

PPARδ senses and orchestrates clearance of apoptotic cells to promote tolerance

Mukundan, L. *et al. Nature Med.* **15**, 1266–1272 (2009)

To limit potentially damaging autoimmune responses against self antigens, macrophages engulf and destroy apoptotic cells. This study identifies the lipid sensor peroxisome proliferator-activated receptor-δ (PPARδ) as a factor involved in sensing apoptotic cells. PPARδ expression is induced in macrophages following engulfment of apoptotic cells and promotes further apoptotic cell clearance by regulating the expression of opsonins that tag apoptotic cells for recognition and removal. Deletion of PPARδ in macrophages led to a decrease in apoptotic cell clearance and anti-inflammatory cytokine production. PPARδ-deficient mice were more likely to develop an autoimmune kidney disease (that mimics the human disease systemic lupus erythematosus) and had higher autoantibody levels than wild-type mice. These results show that PPARδ is a sensor of apoptotic cell engulfment and influences further apoptotic cell clearance, highlighting its importance in maintaining tolerance to self antigen to prevent autoimmune disease.