IN BRIEF

INNATE IMMUNITY

Statins enhance formation of phagocyte extracellular traps

Chow, O. A. *et al. Cell Host Microbe* **8**, 445–454 (2010)

Statins inhibit cholesterol synthesis and are prescribed to those at high risk of developing cardiovascular disease. The widespread use of these drugs has promoted interest in their other effects: this study shows that statins affect phagocyte functions. Pre-treatment with statins increased the capacity of human neutrophils and macrophages to kill various bacteria *in vitro*, but paradoxically, statins decreased the ability of neutrophils to phagocytose *Staphylococcus aureus* or induce the oxidative burst. Instead, statins promoted microbial killing by inducing phagocyte production of extracellular traps (mesh-like structures composed of nuclear DNA, histones and antimicrobial peptides). In a model of *S. aureus*-induced pneumonia, pre-treating mice with statins decreased bacterial loads and pathology in the lungs, and this was associated with increased formation of extracellular traps. Patients with pneumonia or sepsis have better survival rates if they are receiving statin therapy; this study may explain these findings.

INFLAMMATION

A role for mitochondria in NLRP3 inflammasome activation

Zhou, R. *et al. Nature* 1 Dec 2010 (doi:10.1038/nature09663)

The NLRP3 (NOD-, LRR- and pyrin domain-containing 3) inflammasome is activated in response to pathogens or damaged cells and promotes the maturation of inflammatory cytokines, such as interleukin-1β (IL-1β). It is currently unclear how diverse danger signals activate the NLRP3 inflammasome, but one model proposes that the generation of reactive oxygen species (ROS) is involved. This study shows that stressed mitochondria are a rich source of ROS that trigger inflammasome activation. Inhibition of mitochondrial function led to ROS release and subsequent IL-1β induction in wild-type, but not NLRP3-deficient, macrophages. Healthy cells remove ROS-generating mitochondria through mitophagy, a specialized form of autophagy, and inhibiting mitophagy in macrophages led to inflammasome activation. These findings could explain the link between mitochondrial malfunction and chronic inflammatory diseases.

MHC MOLECULES

Structure of a classical MHC class I molecule that binds “non-classical” ligands

Hee, C. S. *et al. PLoS Biol.* **8**, e1000557 (2010)

This paper reports the crystal structure of one variant of the polymorphic YF1 MHC class I molecule in chickens, showing that this unusual molecule represents a structural link between the peptide-presenting classical MHC class I molecules and the lipid-presenting non-classical MHC class I molecules (CD1 molecules) that are present in mammals. The YF1*7.1 heavy chain associates with β2-microglobulin to form the typical structure of a classical MHC class I molecule, with anti-parallel β-helices forming the binding groove. However, the binding groove of YF1*7.1 is narrower than that of classical MHC class I molecules and is lined by hydrophobic residues. Binding assays showed that YF1*7.1 can bind lipid antigens, and modelling studies suggested that the type of lipid that is bound might be affected by allelic differences in the binding groove. So, the presentation of a large repertoire of lipids, which is accomplished using multiple non-polymorphic *CD1* genes in mammals, might be achieved by multiple alleles of a single *YF1* gene in chickens (which have only two *CD1* genes).