IN BRIEF

ALLERGY AND ASTHMA

House dust mite allergen induces asthma via Toll-like receptor 4 triggering of airway structural cells

Hammad, H. *et al. Nature Med.* **15**, 410–416 (2009)

Epithelial cells in the lung provide a barrier against inhaled allergens but they may also have a role in the induction of allergic airway inflammation owing to their expression of Toll-like receptors (TLRs). To assess this possibility, the authors generated radiation-chimeric mice in which the expression of TLR4 was restricted to radioresistant structural cells or to radiosensitive haematopoietic cells. Using these mice, the authors showed that the expression of TLR4 by lung structural cells (predominantly epithelial cells) but not by lung immune cells was necessary and sufficient for the activation of mucosal dendritic cells (DCs) and for the development of T helper 2-type allergic inflammation in response to house dust mite (HDM) extracts, which contain the TLR4 ligand lipopolysaccharide (LPS). Intrapulmonary administration of a TLR4 antagonist reduced HDM-driven inflammation and bronchial hyperreactivity. So, the recognition of LPS by airway structural cells drives airway inflammation through mucosal DCs.

T CELLS

A role for human skin-resident T cells in wound healing

Toulon, A. *et al. J. Exp. Med.* **206**, 743–750 (2009)

Human skin is populated by $\alpha\beta^+$ and $\gamma\delta^+$ T cells, but little is known about their functions. In mice, equivalent skin-resident T cells (which are exclusively $\gamma\delta^+$ T cells) have recently been shown to function in wound repair. This study shows that human skin T cells similarly promote wound healing by producing insulin-like growth factor 1 (IGF1). $\alpha\beta^+$ and $\gamma\delta^+$ T cells isolated from normal human skin were found to constitutively produce low levels of IGF1, and this could be upregulated following T cell stimulation *in vitro*. In skin organ cultures, wound closure was accelerated by the addition of stimulating CD3-specific antibody and inhibited by IGF1-specific antibody. Epidermal $\alpha\beta^+$ and $\gamma\delta^+$ T cells could be isolated from acute and chronic wounds, but those from chronic wounds failed to produce high levels of IGF1 and interleukin-2 following activation, indicating that the failure in wound healing could result from impaired responsiveness of skin T cells to activation.

IMMUNE RESPONSES

Syk kinase signalling couples to the Nlrp3 inflammasome for anti-fungal host defence

Gross, O. *et al. Nature* 1 Apr 2009 (doi:10.1038/nature07965)

This paper provides a molecular basis for the production of interleukin-1β (IL-1β) for antifungal defence. The pathway links sensing of fungus by pattern recognition receptors (PRRs) to activation of the NLRP3 (nucleotide-binding domain, leucine-rich-repeat-containing family protein 3) inflammasome, which results in caspase 1-mediated processing and secretion of IL-1β. Spleen tyrosine kinase (SYK), which is activated downstream of immunoreceptor tyrosine-based activation motif-containing PRRs such as dectin 1, was found to be crucial for inflammasome activation and IL-1β secretion in response to *Candida albicans* but not bacteria or a bacterial toxin. Additional signals required for inflammasome activation were shown to derive from potassium efflux and reactive oxygen species. The finding that NLRP3-deficient mice are highly susceptible to infection with *C. albicans* indicated that NLRP3 couples the fungus recognition signal to activation of the inflammasome component ASC (apoptosis-associated speck-like protein containing a CARD) and subsequent IL-1β production.