

IN BRIEF

 TUMOUR IMMUNOLOGY**How does IL-12 enhance antitumour responses?**

Transfer of tumour-specific CD8⁺ T cells that produce interleukin-12 (IL-12) was recently used to effectively treat mice with established tumours, but the underlying mechanism was unknown. Now, Kerkar *et al.* report that expression of the IL-12 receptor and interferon- γ by host haematopoietic cells (but not by the transferred CD8⁺ T cells) is required for IL-12-mediated tumour eradication. Interestingly, IL-12 upregulated the expression of MHC class I molecules and pro-inflammatory genes in tumour-resident myeloid cells and increased the cross-presentation of natural tumour antigens. Moreover, tumour-derived macrophages, dendritic cells and myeloid-derived suppressor cells from treated mice had an enhanced capacity to stimulate naive CD8⁺ T cells *in vitro*. Thus, IL-12 can be used in tumour immunotherapy to reverse the immunosuppressive function of tumour-resident myeloid cells.

ORIGINAL RESEARCH PAPER Kerkar, S. P. *et al.* IL-12 triggers a programmatic change in dysfunctional myeloid-derived cells within mouse tumors. *J. Clin. Invest.* 7 Nov 2011 (doi:10.1172/JCI58814)

 VACCINES**An effective PRR-targeting adjuvant in humans**

Studies in mice have supported the notion that agonists of pattern recognition receptors (PRRs) are promising vaccine adjuvant candidates. One such candidate is a type of synthetic double-stranded RNA (dsRNA) — polyinosinic-polycytidylic acid stabilized with poly-L-lysine (polyI:CLC) — which is an agonist of Toll-like receptor 3 (TLR3) and the cytosolic RNA helicase MDA5. But is polyI:CLC effective in humans? This study shows that subcutaneous injection of healthy volunteers with a single dose of polyI:CLC was tolerated, although local and systemic reactogenicity was noted. A systems-wide analysis of innate immune responses in these volunteers showed that polyI:CLC reliably induces an interferon response, and also induces other components of the main effector pathways of innate immunity, such as the inflammasome, complement and nuclear factor- κ B pathways. The pathways induced by polyI:CLC were similarly induced by the highly efficacious yellow fever vaccine, so synthetic dsRNA can be considered a true viral mimic for use as a vaccine adjuvant.

ORIGINAL RESEARCH PAPER Caskey, M. *et al.* Synthetic double-stranded RNA induces innate immune responses similar to a live viral vaccine in humans. *J. Exp. Med.* 7 Nov 2011 (doi:10.1084/jem.20111171)

 INNATE IMMUNITY**STAT6 activation in response to viral nucleic acids**

Signal transducer and activator of transcription 6 (STAT6) is activated by a Janus kinase (JAK) downstream of cytokine receptor signalling. This study describes the activation of STAT6 by viral nucleic acids. STAT6 was found to interact with STING (an adaptor protein involved in sensing nucleic acids) and the kinase TBK1 after infection with DNA viruses, and with STING, TBK1 and the adaptor protein MAVS after infection with RNA viruses. These interactions resulted in TBK1-dependent (but JAK-independent) STAT6 activation. Of note, the phosphorylation pattern of virus-activated STAT6 is different from that observed following cytokine stimulation. Moreover, STAT6 activation in response to viral nucleic acids upregulated the expression of CC-chemokine ligand 2 (CCL2), CCL20 and CCL26. Interestingly, STAT6-deficient mice had impaired survival following viral infection, suggesting that non-classical activation of STAT6 is crucial for antiviral immune responses.

ORIGINAL RESEARCH PAPER Chen, H. *et al.* Activation of STAT6 by STING is critical for antiviral innate immunity. *Cell* **147**, 436–446 (2011)