IN BRIEF

DENDRITIC CELLS

IFN-dependent DC maturation

The full maturation of dendritic cells (DCs) induced by the Toll-like receptor 3 (TLR3) and melanoma differentiation-associated gene 5 (MDA5) agonist polyinosinic–polycytidylic acid (polyI:C) requires type I interferon (IFN) signalling. This study looked at the molecular mechanism by which type I IFNs contribute to DC maturation *in vivo*. Surprisingly, most changes in DC gene expression in response to polyI:C depended on type I IFN signalling rather than on TLR3 or MDA5 signalling. In the presence of an inflammatory milieu containing type I IFNs, direct signalling through TLR3 or MDA5 was not required for DC maturation. Furthermore, type I IFNs regulated the metabolic reprogramming of DCs from oxidative phosphorylation to glycolysis through the increased expression of hypoxia-inducible factor 1α (HIF1α), which is proposed to meet the increased energy demands of activated mature DCs and to promote DC survival. In support of this, the T cell response after immunization with polyI:C and a DC-targeted antigen was decreased in mice with HIF1α-deficient DCs compared with wild-type mice.

ORIGINAL RESEARCH PAPER Pantel, A. *et al.* Direct type I IFN but not MDA5/TLR3 activation of dendritic cells is required for maturation and metabolic shift to glycolysis after polyI:C stimulation. *PLoS Biol.* **12**, e1001759 (2014)

TUMOUR IMMUNOLOGY

Next-generation antibody overcomes resistance

This study proposes a strategy to overcome the intrinsic resistance of tumours that can develop in response to therapeutic antibodies targeting oncogenic proteins. The results indicate that type I interferons (IFNs) are required for the antitumour response induced by oncogene-specific antibodies in mice and that exogenous administration of type I IFN can improve the response even for antibody-resistant tumours. To avoid the problems associated with systemic IFN injection, the authors used an EGFR-specific antibody–IFNβ fusion protein to target IFNβ to $EGFR^+$ tumours. The fusion protein was more effective than EGFR-specific antibody alone in controlling the growth and metastasis of antibody-sensitive tumours and it was also effective against antibody-resistant tumours. This effect was T cell-dependent and involved increased cross-presentation of tumour antigens by dendritic cells stimulated with IFNβ.

ORIGINAL RESEARCH PAPER Yang, X. *et al.* Targeting the tumor microenvironment with interferon-β bridges innate and adaptive immune responses. *Cancer Cell* http://dx.doi.org/10.1016/j.ccr.2013.12.004 (2014)

AUTOIMMUNITY

A link between autoimmunity and cancer?

Certain patients with the autoimmune disease scleroderma who have autoantibodies specific for RNA polymerase III subunit (RPC1; encoded by *POLR3A*) develop cancer around the same time as the autoimmune disease. This study found that tumours from six of eight scleroderma patients with RPC1-specific autoantibodies had genetic alterations affecting the *POLR3A* locus, whereas no *POLR3A* alterations were detected in tumours from eight scleroderma patients with other autoantibodies. $CD4^+$ T cells specific for the mutant RPC1 peptides were identified in two of the three patients analysed. These T cells did not cross-react with the native RPC1 protein but the autoantibodies in these patients recognized both native and mutant RPC1. So, the data suggest that the mutant RPC1 generated in tumour cells acts as an immunogen for $CD4^+$ T cells; these cells may help to control the cancer through immunoediting, but may also promote a cross-reactive humoral immune response that triggers scleroderma.

ORIGINAL RESEARCH PAPER Joseph, C. G. *et al.* Association of the autoimmune disease scleroderma with an immunologic response to cancer. *Science* **343**, 152–157 (2014)