IN BRIEF

AUTOIMMUNITY

Functionally defective germline variants of sialic acid acetylesterase in autoimmunity

Surolia, I. *et al. Nature* 16 Jun 2010 (doi:10.1038/nature09115)

The enzyme sialic acid acetylesterase (SIAE) is a negative regulator of B cell receptor signalling, and mice with loss-of-function mutations in *Siae* develop an autoimmune syndrome. Previous genome-wide association studies did not detect an association between common variants of *SIAE* and autoimmune disease in humans. However, by identifying and analysing the function of a number of rare variants of *SIAE*, this study shows that rare functionally defective *SIAE* variants are enriched in patients with autoimmune diseases. When T cell lines were transfected with cDNAs encoding *SIAE* variants from either autoimmune or healthy subjects, the *SIAE* variants from the healthy controls encoded fully functional enzymes, but the variants identified in patients with autoimmune diseases encoded enzymes with a defect in catalytic activity or in secretion. These data show the importance of functional screening assays for identifying potential genetic risk factors for disease.

TUMOUR IMMUNOLOGY

Tumor-induced tolerance and immune suppression depend on the C/EBPβ transcription factor

Marigo, I. *et al. Immunity* 3 Jun 2010 (doi:10.1016/j.immuni.2010.05.010)

This study identifies C/EBPβ as a crucial transcriptional regulator of the myeloid-derived suppressor cells (MDSCs) that are induced by, and suppress the immune response to, tumour cells. Bronte and colleagues showed that they could generate mouse MDSCs *in vitro* — from bone marrow precursor cells cultured in the presence of granulocyte–macrophage colony-stimulating factor (GM-CSF) and interleukin-6 (IL-6) — that had similar phenotypical and functional properties to tumour-induced MDSCs. The exposure of mouse bone marrow cells to GM-CSF and IL-6 resulted in upregulation of C/EBPβ by these cells. The deletion of C/EBPβ in haematopoietic cells abrogated the T cell-suppressive activity of bone marrow-derived MDSCs *in vitro* and of splenic MDSCs in *in vivo* tumour models through decreased expression of arginase 1, nitric oxide synthase 2 and other components of the MDSC inhibitory machinery. C/EBPβ was also shown to control the immunoregulatory programme in human MDSCs.

T CELLS

Reprogramming of T cells to natural killer-like cells upon *Bcl11b* deletion.

Li, P. *et al. Science* 10 Jun 2010 (doi:10.1126/science.1188063)

Here the authors report that T cells can be reprogrammed as natural killer (NK)-like cells following deletion of B cell lymphoma 11b (*Bcl11b*). BCL-11b is highly expressed by thymocytes from the double negative 2 (DN2) stage of development and is crucial for T-lineage commitment. *Bcl11b*$^{-/-}$ DN1 and DN2 thymocytes that were cultured with OP9-DL1 stromal cells, which support T cell development, instead gave rise to cells expressing the NK cell marker NKp46 and not T cell genes *Cd3* or T cell receptor β-chain (*Tcrb*). In addition, these cells — termed induced T-to-NK (ITNK) cells — killed tumour cells *in vitro*, and their morphology and expression profiles were more akin to activated NK cells than T cells. Even mature CD4^{+}, CD8^{+} and γδ T cells with a conditional deletion of *Bcl11b* could be reprogrammed to be ITNK cells *in vitro*. Importantly, *Bcl11b*$^{-/-}$ thymocytes transferred into immunodeficient mice gave rise to ITNK cells that effectively prevented tumour metastasis *in vivo*.