DOI:
10.1038/nri1954

IN BRIEF

IMMUNOTHERAPY

Relating TCR–peptide–MHC affinity to immunogenicity for the design of tumor vaccines.

McMahan, R. H. *et al. J. Clin. Invest.* **116**, 2543–2551 (2006)

One strategy to increase the responsiveness of T cells to tumour-associated antigens (TAAs) is vaccination with mimotopes (mimics of tumour epitopes). Mimotopes can increase the proliferation of TAA-specific T cells, through increasing peptide–MHC–T-cell receptor (TCR) interactions, but this clonal expansion of T cells does not always correlate with reduced tumour growth. Using a combinatorial peptide library, the authors identified a panel of mimotopes of varying affinity for a TAA-specific TCR. Increased affinity of the peptide–MHC complex for the TCR correlated with increased activity of the T-cell clone *in vitro*. However, peptide–MHC complexes of high affinity were not functional *in vivo* and did not increase antitumour activity. The authors found that intermediate-affinity peptides elicited optimal protection against tumour growth, an important observation for the development of effective immunotherapy for cancer.

B CELLS

B-1 B lymphocytes require Blimp-1 for immunoglobulin secretion.

Savitsky, D. & Calame, K. *J. Exp. Med.* 5 Sep 2006 (doi:10.1084/jem.20060411)

The innate-like B-cell subset, B1 cells (which reside mainly in the pleural cavity, the peritoneal cavity and the gut), are defined by their ability to secrete 'natural' antibodies (such as IgM and IgA) in the absence of apparent infection or immunization. Unlike the mechanisms that regulate antibody secretion for conventional B cells (B2 cells), those for B1 cells are largely unexplored. This study shows that B1 and B2 cells use a common pathway for antibody secretion that involves the transcriptional repressor BLIMP1 (B-lymphocyte-induced maturation protein 1). Studies in BLIMP1-deficient mice showed that BLIMP1 is not required for the development or self-renewal of B1 cells but is crucial for the secretion of IgM. Accordingly, BLIMP1-deficient B1 cells do not repress PAX5 (paired box protein 5) expression or induce XBP1 (X-box-binding protein 1) expression, both of which are crucial steps in the pathway for antibody secretion.

REGULATORY T CELLS

Human $CD4^+$ $CD25^{hi}$ $Foxp3^+$ regulatory T cells are derived by rapid turnover of memory populations *in vivo*.

Vukmanovic-Stejic, M. *et al. J. Clin. Invest.* **116**, 2423–2433 (2006)

Naturally occurring regulatory T (T_{Reg}) cells, which are $CD4^+CD25^{hi}$ forkhead box P3 $(FOXP3)^+$, are thought to be derived mainly from the thymus. If this is the case, then why is the number of T_{Reg} cells maintained throughout life following involution of the thymus at puberty? By measuring *in vivo* incorporation of deuterium-labelled glucose into the DNA of dividing cells, Akbar and colleagues show that human T_{Reg} cells are highly proliferative. But they are also highly susceptible to apoptosis and have short telomeres and low telomerase activity. Therefore, they are unlikely to constitute a self-perpetuating, long-lived, thymus-derived population. Instead, the authors show that T_{Reg} cells are derived from antigen-stimulated memory T cells in the periphery. This provides the first evidence in humans of a population of adaptive T_{Reg} cells that is similar to that found in mice.