# IN BRIEF

## IMMUNOTHERAPY

### Effective tumor treatment targeting a melanoma/melanocyte-associated antigen triggers severe ocular autoimmunity.

Palmer, D. C. *et al. Proc. Natl Acad. Sci USA* **105**, 8061–8066 (2008)

The development of autoimmune responses can be a serious consequence of immunotherapeutic regimens that target non-mutated self antigens. Experiments in mice and clinical trials in humans with malignant melanoma indicate that the more aggressive the immune-based therapy (such as lymphodepletion followed by the adoptive transfer of $CD8^+$ T cells that target melanocytes and administration of interleukin-2) the more likely it is that tumours will regress, but that side effects, such as vitiligo and melanocyte-targeted ocular autoimmunity, will occur. The authors suggest that immunotherapy regimens that target unique tumour-associated antigens may prove to be more prudent strategies in the future.

## REGULATORY T CELLS

### Two functional subsets of FOXP3$^+$ regulatory T cells in human thymus and periphery.

Ito, T. *et al. Immunity* **28**, 870–880 (2008)

It is generally thought that the thymus produces a homogeneous population of regulatory T ($T_{Reg}$) cells that is characterized by the expression of CD4, CD25 and the transcription factor forkhead box P3 (FOXP3). However, Ito *et al.* found two subsets of $CD4^+CD25^+FOXP3^+$ $T_{Reg}$ cells in the thymus and periphery that were defined by the expression of inducible T-cell co-stimulator (ICOS). The two subsets showed different mechanisms of action: $ICOS^+$ $T_{Reg}$ cells produced interleukin-10 (IL-10) to suppress dendritic-cell (DC) function and transforming growth factor-β (TGFβ) to suppress T-cell function, whereas $ICOS^-$ $T_{Reg}$ cells mainly used TGFβ for their suppressive activity. The survival and proliferation of the $ICOS^+$ and $ICOS^-$ $T_{Reg}$-cell subsets were differentially regulated by signals from ICOS ligand (on plasmacytoid DCs) and CD80 and/or CD86 (on myeloid DCs), respectively. This suggests that the two subsets might be selected and 'educated' by different populations of DCs in the thymus.

## ANTIBODY RESPONSES

### Rapid cloning of high-affinity human monoclonal antibodies against influenza virus.

Wrammert, J. *et al. Nature* **453**, 667–671 (2008)

Although it is known that antibodies are crucial for the protection from influenza virus, the nature of the B-cell responses that underlie antibody generation in response to viral infection are not well understood. Here, Wilson and colleagues demonstrate that vaccination of humans against the influenza virus elicits the massive generation of antibody-secreting cells (ASCs) that peak in numbers around 7 days post-vaccination. This early burst of ASCs was found to consist of a high proportion of influenza-virus-specific cells that bound the virus with high affinity and therefore probably contributed to immune protection *in vivo*. Furthermore, the authors demonstrate that high-affinity, virus-specific antibodies could be purified from ASCs induced following vaccination. This provides hope that such techniques for the rapid isolation of human antibodies will be useful for the treatment or diagnosis of influenza virus infection.