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# IN BRIEF

## CANCER IMMUNOTHERAPY

### Targeting regulatory T cells

The immunosuppressive actions of regulatory T ($T_{reg}$) cells have limited the success of cancer immunotherapies. Grinberg-Bleyer *et al.* show that ablation of the canonical nuclear factor κB (NF-κB) subunit c-rel specifically impairs the generation and maintenance of activated $T_{reg}$ cells and reduces growth of transplanted melanoma cells in mice. Daily injections of the FDA-approved drug pentoxyfylline (PTXF; which inhibits c-rel) similarly reduced the rate of tumour growth in a mouse melanoma transplantation model by altering $T_{reg}$ cell identity and function. Furthermore, combining PTXF with anti-PD1 immunotherapy had an additive effect in treating established melanoma in mice.

**ORIGINAL ARTICLE** Grinberg-Bleyer, Y. *et al.* NF-κB c-rel is crucial for the regulatory T cell immune checkpoint in cancer. *Cell* **170**, 1096–1108 (2017).

## TRANSPLANTATION

### Combining OX40L and mTOR blockade

Controlling alloimmunity after transplantation remains a significant challenge, as existing immunosuppressive agents typically inhibit both effector T ($T_{eff}$) and regulatory T ($T_{reg}$) cells. Using the non-human primate graft-versus-host disease (GVHD) model, Tkachev *et al.* now demonstrate that the combination of the mTOR inhibitor sirolimus with an antibody against the tumour necrosis factor superfamily member OX40L (KY1005) synergistically controls T cell activation after haematopoietic stem cell transplantation while permitting robust regulatory T cell reconstitution. This results in prolonged GVHD-free survival of more than 100 days.

**ORIGINAL ARTICLE** Tkachev, V. *et al.* Combined OX40L and mTOR blockade controls effector T cell activation while preserving Treg reconstitution after transplant. *Sci. Transl Med.* **9**, eaan3085 (2017)

## HIV

### Trispecific antibodies block infection

The use of broadly neutralizing antibodies (bnAbs) isolated from HIV-infected individuals in the development of an effective AIDS vaccine has been limited by potency and breadth of protection. Now, Xu *et al.* report the generation of multi-specific antibodies derived from bnAbs with specificities for three independent HIV-1 envelope determinants: the CD4 binding site, the membrane-proximal external region and the V1V2 glycan site. In contrast to single bnAbs, these trispecific antibodies conferred complete immunity against a mixture of two different simian–human immunodeficiency viruses (SHIVs) in non-human primates.

**ORIGINAL ARTICLE** Xu, L. *et al.* Trispecific broadly neutralizing HIV antibodies mediate potent SHIV protection in macaques. *Science* http://dx.doi.org/10.1126/science.aan8630 (2017).

## CANCER

### Reducing melanoma in redheads

The G protein-coupled melanocortin-1 receptor (MC1R) mediates melanin production, which protects the skin from UV radiation. However, almost all red-haired individuals have a variant of MC1R with reduced or absent signalling capacity and are therefore at higher risk of developing melanomas. Chen *et al.* report that palmitate enhances downstream MC1R signalling in cells that express variants of the protein that are associated with red hair. Palmitate increased MC1R palmitoylation, which promoted interaction of the receptor with the cell membrane. Treatment of MC1R-variant mice with palmostatin B (a small molecule that enhances palmitoylation) before UV treatment delayed and reduced melanoma incidence.

**ORIGINAL ARTICLE** Chen, S. *et al.* Palmitoylation-dependent activation of MC1R prevents melanomagenesis. *Nature* **549**, 399–403 (2017)