IN BRIEF

MYELOID DEVELOPMENT

Mice with a human innate compartment

Immunodeficient mice reconstituted with human haematopoietic cells (termed humanized mice) are a powerful tool for studying human immune function *in vivo*. However, human innate immune cell development is not supported by current humanized mouse strains. Two new strains of humanized mice, termed MITRG and MISTRG, have been developed that support human monocyte, macrophage and natural killer (NK) cell development. A knock-in gene replacement strategy was used to replace genes encoding cytokines that are important for myeloid cell development — M-CSF, IL-3–GM-CSF and thrombopoietin — with their human counterparts in immunodeficient *Rag2*$^{-/-}$*Il2rg*$^{-/-}$ mice (MITRG mice). MISTRG mice also carry a transgene encoding human SIRPα, which is thought to have a role in NK cell survival. The human monocytes and macrophages were fully functional in MITRG and MISTRG mice, and *trans*-presentation of IL-15 by these cells supported the development of functional human NK cells in MISTRG mice. Furthermore, immunosuppressive macrophages infiltrated and supported the growth of engrafted tumours in both mouse strains, similar to what has been observed in human tumours.

ORIGINAL RESEARCH PAPER Rongvaux, A. *et al.* Development and function of human innate immune cells in a humanized mouse model. *Nature Biotech.* http://dx.doi.org/10.1038/nbt.2858 (2014)

HIV

Gene therapy for HIV?

For the first time, researchers show that it is safe and effective to genetically modify cells to increase resistance to HIV infection in humans. They used a zinc-finger nuclease to target and inactivate the HIV coreceptor CC-chemokine receptor 5 (CCR5) in CD4$^+$ T cells, which were then infused into 12 patients with chronic aviraemic HIV infection who were receiving antiretroviral treatment. The modified T cells readily engrafted and persisted (with a mean half-life of 48 weeks) in all 12 individuals. One individual suffered an adverse reaction to the transplant. Analysis of viraemia following the interruption of antiretroviral treatment in six participants revealed that the modified T cells had a survival advantage over unmodified T cells. Strikingly, the virus remained undetectable in one patient for the period of treatment interruption. This patient was later found to be heterozygous for the *CCR5* deletion, which suggests that this therapy could be most effective in individuals with only one functional copy of *CCR5*.

ORIGINAL RESEARCH PAPER Tebas, P. *et al.* Gene editing of *CCR5* in autologous CD4 T cells of persons infected with HIV. *N. Engl. J. Med.* **370**, 901–910 (2014)

INFLAMMATION

IL-21 stokes brain inflammation

Much of the secondary tissue damage associated with ischaemic stroke is caused by inflammation, but the factors involved in this neuroinflammation remain unclear. This study showed that interleukin-21 (IL-21) expression is greatly increased in the brain of mice following cerebral ischaemic reperfusion injury, that *Il21*$^{-/-}$ mice have reduced brain injury, and that IL-21 blockade in wild-type mice greatly reduced infarct size. Infiltrating CD4$^+$ T cells were found to be the main source of IL-21 in the post-ischaemic brain in mice. Furthermore, CD4$^+$IL-21$^+$ T cells were shown to surround acute stroke lesions in human post-mortem tissue, which suggests that IL-21 may have a role in tissue injury following stroke in humans.

ORIGINAL RESEARCH PAPER Clarkson, B. D. S. *et al.* T cell-derived interleukin (IL)-21 promotes brain injury following stroke in mice. *J. Exp. Med.* http://dx.doi.org/10.1084/jem.20131377 (2014)