IN BRIEF

HIV

Long-term control of HIV by *CCR5* delta32/delta32 stem-cell transplantation

Hütter, G. *et al. N. Engl. J. Med.* **360**, 692–698 (2009)

Antiretroviral therapies have proven useful in delaying the progression to AIDS in people infected with HIV, but long-term treatment can result in serious side effects, and the virus can become resistant to such therapies. It is well established that people who are homozygous for the Δ32 allele of *CCR5* (CC-chemokine receptor 5) have cells that do not express this receptor and are resistant to infection with the R5 strains of HIV, even when they have been exposed to the virus many times. Hütter and colleagues built on this knowledge to test a new approach for treating HIV infection. They treated an HIV-positive patient with acute myeloid leukaemia using transplanted stem cells from a donor who was homozygous for the *CCR5* Δ32 allele. Antiretroviral therapy was discontinued, but the patient remained free of detectable virus in the bloodstream and had no recurrence of leukaemia up to 20 months after the transplant. Furthermore, the $CD4^+$ T-cell count returned to the normal range.

INNATE IMMUNITY

Cytosolic viral sensor RIG-I is a 5′-triphosphate-dependent translocase on double-stranded RNA

Myong S. *et al. Science* **323**, 1070–1074 (2009)

Retinoic acid-inducible gene I (RIG-I) is a cytosolic viral sensor that detects RNA, leading to the induction of type I interferon expression. Known pathogen-associated molecular patterns for RIG-I include viral RNA 5′-triphosphates and double-stranded RNA (dsRNA) itself, but it is unclear whether RIG-I integrates such signals or whether they trigger RIG-I independently. The results from this study suggest that RIG-I does indeed integrate the two signals — recognition of 5′-triphosphates by RIG-I leads to RIG-I dimerization and activation of a translocase domain, such that RIG-I then preferentially translocates on dsRNA in *cis*. The authors propose that this induces a signalling conformation in RIG-I. So, integration of these two viral molecular patterns might be a means by which RIG-I verifies the specificity for viral RNA.

TOLERANCE

MerTK regulates thymic selection of autoreactive T cells

Wallet, M. A. *et al. Proc. Natl Acad. Sci. USA* 27 Feb 2009 (doi:10.1073/pnas.0900683106)

The gene encoding the receptor tyrosine kinase MER (*Mertk*) is found in the type 1 diabetes genetic susceptibility locus in mice. To investigate the role of MER in diabetes, Wallet *et al.* generated non-obese diabetic (NOD) mice that lack functional MER. In contrast to MER-sufficient NOD mice, the mutant mice did not develop diabetes. Few T cells infiltrated the pancreatic islets of $Mertk^{-/-}$ NOD mice, and of these, the percentage of cells specific for diabetogenic β-cell antigens was reduced, suggesting that autoreactive T cells might have been deleted from the repertoire of these mice. Using fetal thymic organ cultures established from $Merkt^{-/-}$ or $Merkt^{+/-}$ NOD mouse embryos, the authors confirmed that autoreactive $Merkt^{-/-}$ thymocytes were more efficiently deleted than autoreactive $Merkt^{+/-}$ thymocytes. This was due to the enhanced capacity of $Merkt^{-/-}$ thymic dendritic cells to promote negative selection, thereby supporting a new role for MER in the regulation of negative selection and susceptibility to type 1 diabetes.