IN BRIEF

IMMUNOTHERAPY

Treat your mouse like a 'man

In cancer immunotherapy, lymphocytes can be modified to express T cell receptors (TCRs) specific for particular tumour antigens. However, these antigens are mostly self-antigens, and T cells that bind strongly to self-antigens are eliminated to avoid autoimmune responses. Obenaus *et al.* have developed a new strategy for generating T cells that can recognize tumours as exogenous antigens. They generated transgenic mice with T cells expressing a repertoire of human TCRs instead of mouse TCRs. They then inoculated human cancer antigens into these mice, inducing a reactive T cell response. The authors isolated the TCRs specific for certain tumour antigens and observed an antitumour effect *in vivo* in a different animal model. The DNA encoding the resulting high-affinity TCRs could then be transferred into human T cells for adoptive therapy.

ORIGINAL RESEARCH PAPER Obenaus, M. *et al.* Identification of human T-cell receptors with optimal affinity to cancer antigens using antigen-negative humanized mice. *Nature Biotech.* **33**, 402–407 (2015)

WILDLIFE CANCER

Outbreak of leukaemia in clams

Metzger *et al.* have found that a leukaemia-like type of cancer in soft-shell clams that is causing substantial population loss worldwide is transmissible. The authors found that the genotypes of the clam leukaemic cells were different from their hosts and nearly identical to the genotypes of other neoplastic cells in clams from dispersed locations. This suggests that the cancer is spreading as a clonal transmissible cell derived from a single original clam.

ORIGINAL RESEARCH PAPER Metzger, M. J. *et al.* Horizontal transmission of clonal cancer cells causes leukemia in soft-shell clams. *Cell* **161**, 255–263 (2015)

GENETICS

Slowing premature ageing

Mice with alterations in ataxia telangiectasia and Rad3-related (ATR) kinase age prematurely. López-Contreras *et al.* have shown that mice carrying extra alleles of the regulatory subunit of the ribonucleotide reductase complex (RRM2TG) have increased levels of nucleotides and reduced chromosomal breakage at fragile sites. Moreover, increased levels of RRM2 extended the lifespan of mice with reduced ATR levels and alleviated the severity of the pathologies associated with premature ageing, including cancer.

ORIGINAL RESEARCH PAPER López-Contreras, A. J. *et al.* Increased *Rrm2* gene dosage reduces fragile site breakage and prolongs survival of ATR mutant mice. *Genes Dev.* **29**, 690–695 (2015)

CELL SIGNALLING

Scaffolding proteins under hypoxia

Scaffold proteins are key in the regulation of signalling molecules. Finger *et al.* have revealed that hypoxia regulates expression of a variant of the scaffold protein A-kinase anchor protein 12 (AKAP12v2). This scaffolding protein regulates protein kinase A (PKA)-mediated phosphorylation events, and inhibition of AKAP12v2 decreased cell invasion and migration *in vitro*, as well as tumour growth and metastasis in an *in vivo* orthotopic mouse model of melanoma.

ORIGINAL RESEARCH PAPER Finger E. C. *et al.* Hypoxic induction of AKAP12 variant 2 shifts PKA-mediated protein phosphorylation to enhance migration and metastasis of melanoma cells. *Proc. Natl Acad. Sci. USA* **112**, 4441–4446 (2015)