IN BRIEF

IMMUNOTHERAPY

Promising results from autologous T cell transfer

Davila and colleagues report a Phase I trial using CD19-specific chimeric antigen receptor (CAR)-engineered T cells for autologous transplant. The 16 patients with relapsed or refractory B cell acute lymphoblastic leukaemia (B-ALL) exhibited an 88% overall complete response rate. The authors also characterized diagnostic criteria and identified an already available test for the development of severe cytokine release syndrome, which is a complication of T cell transplant that requires therapeutic intervention.

ORIGINAL RESEARCH PAPER Davila, M. L. *et al.* Efficacy and toxicity management of 19-28z CAR T cell therapy in B cell acute lymphoblastic leukemia. *Sci. Trans. Med.* **6**, 224ra25 (2014)

THERAPY

Combination and dosing schedule are key

The inhibition of mutant BRAF has been shown to induce ERK activation in RAS-mutant cells, which can lead to tumorigenesis. A patient with BRAF-V600E-mutant melanoma undergoing treatment with the BRAF inhibitor vemurafenib developed NRAS-mutant leukaemia, and Abdel-Wahab and colleagues tested whether combined BRAF and MEK inhibition would control both malignancies. They found that intermittent treatment (to keep toxicities under control) with vemurafenib plus concurrent intermittent treatment with the MEK inhibitor cobimetinib caused remission of the melanoma and suppressed progression, proliferation and ERK activation of the leukaemia. These responses have, so far, lasted for 20 months.

ORIGINAL RESEARCH PAPER Abdel-Wahab, O. *et al.* Efficacy of intermittent combined RAF and MEK inhibition in a patient with concurrent BRAF and NRAS mutant malignancies. *Cancer Discov.* http://dx.doi.org/10.1158/2159-8290.CD-13-1038 (2014)

SIGNALLING

Connecting metabolism and proliferation

The metabolic enzyme pyruvate kinase M2 (PKM2) was recently shown to have protein kinase activity, and Keller *et al.* now report that the metabolite SAICAR, which is found in proliferating cells, binds to PKM2 and induces its kinase activity. Moreover, they found that more than 100 proteins are phosphorylated by PKM2–SAICAR, including ERK1 and ERK2, indicating that PKM2 connects metabolism with proliferation.

ORIGINAL RESEARCH PAPER Keller, K. E. *et al.* SAICAR induces protein kinase activity of PKM2 that is necessary for sustained proliferative signaling of cancer cells. *Mol. Cell* **53**, 700–709 (2014)

INFLAMMATION

Determinants of neoplastic sites

Why do some neoplasms form in certain sites and not in others? For example, serrated polyps develop only in the caecum of transgenic mice that express heparin-binding EGF-like growth factor (HB-EGF) throughout the intestine, indicating that non-genetic factors may be involved. Bongers *et al.* showed that alteration of the intestinal microbiome, such as through treatment with antibiotics, inhibited serrated polyp formation in the caecum. Although the offending microbial factors were not identified, the authors found that the development of serrated polyps was associated with reduced epithelial barrier function, bacterial invasion and inflammation. In particular, neutrophil depletion significantly reduced serrated polyp formation.

ORIGINAL RESEARCH PAPER Bongers, G. *et al.* Interplay of host microbiota, genetic perturbations, and inflammation promotes local development of intestinal neoplasms in mice. *J. Exp. Med.* **211**, 457–472 (2014)