IN BRIEF

ANTIVIRALS

Engineered T cells as broad-spectrum antivirals

Immunocompromised individuals often have a number of active viral infections. Here, the development of an adoptive transfer strategy is presented, using multivirus-specific T cells (mVSTs) generated by direct stimulation of peripheral blood mononuclear cells with overlapping peptide libraries that incorporate antigens from five common viruses. The mVSTs were tested in a small clinical trial in recipients of allogenic transplants with up to four active infections, where they showed sustained and broad antiviral activity. Importantly, mVSTs can be rapidly produced and tailored to desired specifications.

ORIGINAL RESEARCH PAPER Papadopoulou, A. *et al.* Activity of broad-spectrum T cells as treatment for AdV, EBV, CMV, BKV, and HHV6 infections after HSCT. *Sci. Transl. Med.* **6**, 242ra83 (2014)

CANCER

Epigenetic target in Hedgehog-driven tumours

The Hedgehog (Hh) pathway can drive oncogenesis, and current strategies to target it mainly focus on inhibitors of the G protein-coupled receptor Smoothened (SMO). SMO activates the downstream transcription factors GLI1 and GLI2, which transactivate Hh target genes. SMO inhibitors have demonstrated clinical efficacy, but resistance usually develops. Tang *et al.* now report that the epigenetic regulator BRD4, a BET bromodomain protein, controls GLI transcription by binding to the GLI1 and GLI2 promoters. The BRD4 inhibitor JQ1 was shown to downregulate Hh signalling, and had antitumour activity even in tumours that were resistant to SMO inhibitors.

ORIGINAL RESEARCH PAPER Tang, Y. *et al.* Epigenetic targeting of Hedgehog pathway transcriptional output through BET bromodomain inhibition. *Nature Med.* **20**, 732–740 (2014)

MALARIA

Complete protection with AMA1–RON2 complex?

The apical membrane antigen 1 (AMA1), a crucial protein for the invasion of *Plasmodium* merozoites into red blood cells, is a leading malaria vaccine candidate, but has shown little efficacy in clinical trials so far. Here, the authors show that vaccination with a complex of AMA1 and rhoptry neck protein 2 (RON2) can induce antibody-mediated complete protection against a lethal *Plasmodium yoelii* challenge in mice. It is likely that the protein complex mimics the functional form of the proteins more closely, thereby inducing more potent protective antibodies.

ORIGINAL RESEARCH PAPER Srinivasan, P. *et al.* Immunization with a functional protein complex required for erythrocyte invasion protects against lethal malaria. *Proc. Natl Acad. Sci. USA* **111**, 10311–10316 (2014)

CANCER

PLK4 inhibitor shows potent antitumour activity

Polo-like kinase 4 (PLK4) was identified as an anticancer target in an RNA interference (RNAi) screen in human breast cancers and cell lines, and the small molecule CFI-400945 was found to be a potent, selective and orally available PLK4 inhibitor. *In vitro* studies showed that CFI-400945 treatment recapitulates the hallmarks of genetic PLK4 inhibition, and *in vivo* studies showed it was well tolerated and had potent antitumour activity in breast cancer xenograft models, particularly those deficient in the tumour suppressor PTEN — a synthetic lethal interaction partner of PLK4. CFI-400945 has entered Phase I clinical trials.

ORIGINAL RESEARCH PAPER Mason, J. M. *et al.* Functional characterization of CFI-400945, a Polo-like kinase 4 inhibitor, as a potential anticancer agent. *Cancer Cell* **26**, 163–176 (2014)