IN BRIEF

THERAPEUTICS

Picking and choosing

Designing drugs against the fibroblast growth factor (FGF) pathway is complicated by the fact that there are several FGF family members with different biological activities. Blocking the hormonal FGFs causes toxicities; so, Harding *et al.* developed a soluble decoy receptor, FP-1039, that binds only the mitogenic FGFs. FP-1039 blocked FGF- and vascular endothelial growth factor (VEGF)-induced angiogenesis *in vivo*, and inhibited tumour growth in several xenograft mouse models with minimal toxicity. Xenografts of cancer cells with FGF pathway alterations were particularly sensitive to FP-1039.

ORIGINAL RESEARCH PAPER Harding, T. C. *et al.* Blockade of nonhormonal fibroblast growth factors by FP-1039 inhibits growth of multiple types of cancer. *Sci. Transl. Med.* **5**, 178ra39 (2013)

THERAPEUTICS

An alternative explanation

The heat shock protein 90 (HSP90) chaperone recruits protein kinase clients via cell division cycle 37 (CDC37). Polier *et al.* have found that CDC37 can directly prevent binding of ATP to kinases and so may affect kinase activity. Interestingly, the ATP-competitive kinase inhibitors vemurafenib (a BRAF inhibitor) and lapatinib (an ERBB2 and epidermal growth factor receptor inhibitor) block the binding of CDC37 to the oncogenic kinases BRAF and ERBB2, thus preventing them from accessing HSP90. As this leads to kinase degradation, it could account for some of the therapeutic effects of these inhibitors.

ORIGINAL RESEARCH PAPER Polier, S. *et al.* ATP-competitive inhibitors block protein kinase recruitment to the Hsp90-Cdc37 system. *Nature Chem. Biol.* 17 Mar 2013 (doi:10.1038/nchembio.1212)

BREAST CANCER

Improving mouse models

Knight *et al.* have developed a mouse model that resembles the claudin-low subtype of triple-negative breast cancer (TNBC) by expressing a weakly oncogenic MET receptor tyrosine kinase under the control of the mouse mammary tumour virus promoter concomitant with conditionally deleting *Trp53* in the mammary gland. Tumours in these mice have a similar molecular signature to human claudin-low TNBC, and require MET for proliferation and for maintaining the claudin-low morphological phenotype. Therefore, MET inhibitors may be effective against TNBC.

ORIGINAL RESEARCH PAPER Knight, J. F. *et al.* Met synergizes with p53 loss to induce mammary tumors that possess features of claudin-low breast cancer. *Proc. Natl Acad. Sci. USA* 18 Mar 2013 (doi:10.1073/pnas.1210353110)

IMMUNOTHERAPY

Modified CAR

Autologous chimeric antigen receptor (CAR)-modified T cells that target the B cell antigen CD19 and that express the CD137 (a costimulatory receptor) signalling domain have been used in adults with chronic lymphocytic leukaemia (CLL). Grupp *et al.* tested these cells in two children with relapsed and refractory pre-B cell acute lymphoblastic leukaemia (ALL). Although several adverse events occurred, both patients had a complete remission, and this is still ongoing in one patient after 11 months. The other patient relapsed after 2 months, with cells that no longer expressed CD19, indicating that other molecules may need to be targeted in some patients.

ORIGINAL RESEARCH PAPER Grupp, S. A. *et al.* Chimeric antigen receptor-modified T cells for acute lymphoid leukemia. *New Engl. J. Med.* 25 Mar 2013 (doi:10.1056/NEJMoa1215134)