IN BRIEF

ANTICANCER DRUGS

Targeting receptor–regulator interactions

Dysregulated androgen receptor (AR) signalling is a hallmark of advanced prostate cancer. This study showed that disrupting an interaction between the AR and a co-regulator protein could be beneficial. The authors structurally designed a peptidomimetic that disrupted the interaction between the scaffold protein PELP1 (proline-, glutamic acid- and leucine-rich protein 1) and the AR by targeting the LXXLLL motif. In cells, the compound prevented nuclear translocation of the AR and inhibited androgen-induced proliferation, and it inhibited tumour growth in a mouse xenograft model of prostate cancer.

ORIGINAL RESEARCH PAPER Ravindranathan, P. *et al.* Peptidomimetic targeting of critical androgen receptor–coregulator interactions in prostate cancer. *Nature Comm.* **4,** 1923 (2013)

CANCER

A new way to restore tumour suppressor function

The tumour suppressor PTEN is an antagonist of the phosphoinositide 3-kinase (PI3K) pathway that is mutated in several cancers. Hopkins *et al.* identified a translational variant of PTEN, dubbed PTEN-long, that was a secreted, membrane-permeable lipid phosphatase that interacted with cell surface proteins and could enter other cells. *In vitro*, administration of PTEN-long antagonized PI3K signalling and it reduced tumour growth in a mouse model. The authors suggest that recombinant PTEN-long could provide therapeutic benefit by delivering functional tumour suppressor protein to cells.

ORIGINAL RESEARCH PAPER Hopkins, B. D. *et al.* A secreted PTEN phosphatase that enters cells to alter signaling and survival. *Science* http:dx.doi.org/10.1126/science.1234907 (2013)

TARGET PROFILING

Chaperones as thermodynamic sensors

The interaction between a particular kinase and its chaperone proteins results in a change in the thermodynamic stability of the kinase. Using the HSP90 (heat shock protein 90) chaperone, Taipale *et al.* exploited this fact to create a thermodynamic sensor assay to profile the target specificity of 30 kinase inhibitors against >300 kinases in living cells. For example, they identified the *ETV6–NTRK3* fusion oncogene as a new target of crizotinib. The assay could be extended to other chaperone–target interactions (HSP70–steroid hormone receptor and CDC37–kinase interactions), which suggests that the method could also be applicable to other small-molecule–target interactions.

ORIGINAL RESEARCH PAPER Taipale, M. *et al.* Chaperones as thermodynamic sensors of drug–target interactions reveal kinase inhibitor specificities in living cells. *Nature Biotech.* **31,** 630–637 (2013)

DERMAL DISORDERS

Boosting hair follicle regeneration

In rodents, but not in humans, hair follicles can regenerate during wound healing. This study showed that fibroblast growth factor 9 (FGF9) is responsible for the regeneration of hair follicles after skin wounding in mice. FGF9 produced by γδ T cells activates WNT in wound fibroblasts, which then express FGF9; this further amplifies WNT activity in the wound dermis during skin regeneration. The paucity of dermal γδ T cells in humans could explain their inability to regenerate hair. Overexpression of FGF9 increased the number of neogenic hair follicles in mice, which suggests that targeting FGF9 might induce hair follicle regeneration in humans.

ORIGINAL RESEARCH PAPER Gay, D. *et al.* Fgf9 from dermal γδ T cells induces hair follicle neogenesis after wounding. *Nature Med.* **19,** 916–923 (2013)