IN BRIEF

TUMORIGENESIS

LIN28 addiction

Nguyen *et al.* found that inducible overexpression of the RNA binding protein LIN28B is sufficient to drive liver cancers in mice. Knocking down *Lin28b* increased overall survival and reduced tumour burden, indicating that LIN28B is also necessary for tumour maintenance. *Igf2* mRNA binding proteins (IGF2BPs) are overexpressed in human liver tumours, and knockdown of *Igf2bp3* markedly reduced cell proliferation. This reduction was even higher when LIN28B was overexpressed, suggesting that IGF2BP3 might act as a downstream effector of LIN28B and that these two RNA-binding protein families may work synergistically to promote liver cancer development.

ORIGINAL RESEARCH PAPER Nguyen, L. H. *et al.* *Lin28b* is sufficient to drive liver cancer and necessary for its maintenance in murine models. *Cancer Cell* **26,** 248–261 (2014)

IMAGING

Delivered to your door

Biological barriers that limit delivery of imaging and therapeutic agents to the tumour pose a technological challenge. One of those barriers, the vascular endothelium, uses vesicles called caveolae to transport proteins across the cell. Annexin A1 (AnnA1) was enriched in the caveolae at the blood–tumour interface of both human and mouse tumours, so the authors generated a fluorescent-conjugated AnnA1 antibody. When injected intravenously in a mouse model of breast cancer, the antibody rapidly crossed the blood vessels and was taken up by tumours, where it remained for over one hour.

ORIGINAL RESEARCH PAPER Oh, P. *et al.* *In vivo* proteomic imaging analysis of caveolae reveals pumping system to penetrate solid tumors. *Nature Med.* **20**, 1062–1068 (2014)

TARGETED THERAPIES

Insights from exceptional responders

Lovly *et al.* have identified a therapeutic synergism between inhibitors of ALK and insulin-like growth factor 1 receptor (IGF1R) by analysing the response of a patient with *ALK*-positive lung cancer to a treatment combination that included an IGF1R inhibitor. The authors found that the IGF1R pathway was activated in ALK inhibition-resistant cells, and that an IGF1R-specific monoclonal antibody sensitized cells to ALK inhibition.

ORIGINAL RESEARCH PAPER Lovly, C. M. *et al.* Rationale for co-targeting IGF-1R and ALK in *ALK* fusion–positive lung cancer. *Nature Med.* **20**, 1027–1034 (2014)

GENETICS

Working in pairs

An analysis of 51 malignant peripheral nerve sheath tumours (MPNSTs) from patients with neurofibromatosis type I with and without mutations in *NF1*, has identified mutations in one of the components of the Polycomb repressive complex 2 (PRC2), *SUZ12*. Mutations in *Suz12* and *Nf1* cooperated to promote development of MPNSTs and gliomas in mice, and *SUZ12* loss promoted an epigenetic switch from histone H3 lysine 37 trimethylation (H3K37me3) to H3K27 acetylation (H3K27ac), a transcriptional activating signal that recruits bromodomain proteins. *SUZ12*-mutant MPNSTs were sensitive to the bromodomain inhibitor JQ1. Treatment with JQ1 in combination with MEK inhibitors promoted tumour regression and suppressed RAS transcriptional output, suggesting that SUZ12 loss might be amplifying RAS-driven transcription.

ORIGINAL RESEARCH PAPER De Raedt, T. *et al.* PRC2 loss amplifies Ras-driven transcription and confers sensitivity to BRD4-based therapies. *Nature* http://dx.doi.org/10.1038/nature13561 (2014)