

IN BRIEF

➔ BREAST CANCER

Channelling oncogenicity

The chromosomal region 11q13 is amplified in ~15% of breast cancers, and Britschgi *et al.* investigated whether one of the genes in this region, the *ANO1* calcium-activated chloride channel, could be a driver oncogene. Overexpression of *ANO1* in breast cancer cells without an 11q13 amplification increased proliferation *in vitro*, whereas *ANO1* knockdown in 11q13-amplified cells reduced their proliferation *in vitro* and decreased their growth as xenografts in mice. Thus, *ANO1* might be an oncogenic driver and a putative therapeutic target.

ORIGINAL RESEARCH PAPER Britschgi, A. *et al.* Calcium-activated chloride channel *ANO1* promotes breast cancer progression by activating EGFR and CAMK signaling. *Proc. Natl Acad. Sci. USA* 19 Feb 2013 (doi:10.1073/pnas.1217072110)

➔ SIGNALLING

A smooth alternative?

The membrane protein Smoothed (SMO) is an oncogenic effector of Hedgehog (HH) signalling and is a drug target for cancers such as basal-cell carcinomas (BCCs), but resistance mutations in SMO have emerged. From a proteomics screen to search for additional HH pathway components as alternative drug targets, Atwood *et al.* found the polarity protein atypical protein kinase $C\iota/\lambda$ (aPKC ι/λ), and they showed that it acts downstream of SMO in the activation of the GLI1 transcription factor. An inhibitor of aPKC ι/λ suppressed both the growth of therapy-naive allografted BCCs in mice and also the proliferation of SMO-inhibitor-resistant BCC cells *in vitro*.

ORIGINAL RESEARCH PAPER Atwood, S. X. *et al.* GLI activation by atypical protein kinase $C\iota/\lambda$ regulates the growth of basal cell carcinomas. *Nature* **494**, 484–488 (2013)

➔ IMMUNOTHERAPY

A vehicle for inflammation

Aldara is a topical cream formulation of imiquimod (IMQ) that stimulates an antitumour inflammatory immune response for the treatment of non-melanoma skin cancers. Walter *et al.* examined the effects of Aldara on the skin of healthy mice and found that much of the inflammatory response is independent of the action of IMQ on its target Toll-like receptor 7 (TLR7): various aspects of the immune response occurred using cream without IMQ or when applying Aldara to *Tlr7*-null mice. Other components of the cream, such as isostearic acid, were found to be important for inducing an immune response.

ORIGINAL RESEARCH PAPER Walter, A. *et al.* Aldara activates TLR7-independent immune defence. *Nature Commun.* **4**, 1560 (2013)

➔ SIGNALLING

Chemokine underpinnings of a tumour

Malignant peripheral nerve sheath tumours (MPNSTs) commonly occur in patients with neurofibromatosis type 1 (NF1). To identify potential molecular drivers, Mo *et al.* analysed the gene expression signatures in MPNSTs that arose in *Nf1*-deficient mice. They found upregulation of CXCR4, which is a receptor for the CXCL12 chemokine. Similar signalling alterations were also found in human *NF1*-deficient MPNSTs. Crucially, knockdown or small-molecule inhibition of CXCR4 slowed the growth of MPNSTs in mice, highlighting the potential value of CXCR4 as a therapeutic target.

ORIGINAL RESEARCH PAPER Mo, W. *et al.* CXCR4/CXCL12 mediate autocrine cell-cycle progression in NF1-associated malignant peripheral nerve sheath tumors. *Cell* **152**, 1077–1090 (2013)