IN BRIEF

CELL SIGNALLING

Migration fizzles out

Uncovering the signalling pathways by which growth factors regulate epithelial–mesenchymal transition (EMT) could guide the development of new therapies for cancer metastasis. Gujral *et al.* found that the WNT receptor Frizzled 2 (FZD2) and its ligands WNT5a and WNT5b are elevated in human samples of metastatic tumours. A pharmacological and genetic screen in cancer cell lines revealed that FZD2 drives EMT and cell migration through a new, non-canonical pathway that includes FYN and STAT3. Reducing FZD2 expression by RNA interference or blocking the activity with anti-FZD2 antibodies reduced WNT5-mediated cell migration *in vitro* and inhibited tumour growth and metastasis in a mouse xenograft model.

ORIGINAL RESEARCH PAPER Gujral, T. S. *et al.* A noncanonical Frizzled2 pathway regulates epithelial-mesenchymal transition and metastasis. *Cell* **159**, 844–856 (2014)

IMMUNOTHERAPY

CAR T cell distribution centres

Using chimeric antigen receptor (CAR) T cell therapy in solid tumours requires effective T cell tumour infiltration and functional persistence. Adusumilli *et al.* have found that, in an orthotopic model of lung cancer, administering mesothelin-targeted CAR T cells directly to the lung required fewer cells and achieved longer-term remission than doing so intravenously. This therapeutic efficacy was dependent on early activation of $CD4^+$ T cells and CD28-dependent $CD4^+$ T cell-mediated cytotoxicity, and was also effective at eliminating tumours in extrathoracic, disseminated sites.

ORIGINAL RESEARCH PAPER Adusumilli, P. S. *et al.* Regional delivery of mesothelin-targeted CAR T cell therapy generates potent and long-lasting CD4-dependent tumor immunity. *Sci. Trans. Med.* **6**, 261ra151 (2014)

THERAPY

Caution for targeting the microenvironment

Targeting chemokine (C-C motif) ligand 2 (CCL2) paracrine signalling from tumour cells to monocytes has been shown to inhibit metastasis. Using four syngeneic mouse models of metastatic breast cancer, Bonapace *et al.* showed that cessation of CCL2 inhibition increased cancer cell dissemination and monocyte release from the bone marrow, leading to increased metastasis and decreased survival. Importantly, combined inhibition of CCL2 and interleukin-6 (IL-6) reduced metastasis and improved survival. As CCL2 inhibition is being developed for anticancer therapy, this paper identifies the need for caution and a clearer understanding of targeting the tumour microenvironment.

ORIGINAL RESEARCH PAPER Bonapace, L. *et al.* Cessation of CCL2 inhibition accelerates breast cancer metastasis by promoting angiogenesis. *Nature* **515**, 130–133 (2014)

SIGNALLING

Intrinsic intrigue

Scheeren *et al.* have found a cell-intrinsic role for Toll-like receptor 2 (TLR2) in tumorigenesis. They found that ablation of *Tlr2* or myeloid differentiation primary response gene 88 (*Myd88*; which functions downstream of TLR2) reduced inflammation-induced tumorigenesis of intestinal epithelium. Furthermore, deletion of *Tlr2* and *Myd88* in mammary epithelium reduced the mammary repopulating unit frequency, and TLR2 inhibition reduced the growth of human breast cancers.

ORIGINAL RESEARCH PAPER Scheeren, F. A. *et al.* A cell-intrinsic role for TLR2–MYD88 in intestinal and breast epithelial and oncogenesis. *Nature Cell Biol.* http://dx.doi.org/10.1038/ncb3058 (2014)