IN BRIEF

METASTASIS

CXCR2-targeted therapy for pancreatic cancer

Steele *et al.* found that C-X-C chemokine receptor type 2 (CXCR2) expression in neutrophils and myeloid-derived suppressor cells (MDSCs) at tumour borders correlates with poor prognosis in pancreatic ductal adenocarcinoma (PDAC). Genetic ablation and inhibition of CXCR2 in PDAC mouse models reduced metastasis but only inhibition slowed tumorigenesis, suggesting different roles for CXCR2 at different tumour stages. CXCR2 was also implicated in immune cell migration and metastatic niche establishment. CXCR2 blockade increased sensitivity to gemcitabine and programmed cell death protein 1 (PD1) antibodies, underscoring CXCR2 as a therapeutic target for late-stage PDAC.

ORIGINAL ARTICLE Steele, C. W. *et al.* CXCR2 inhibition profoundly suppresses metastases and augments immunotherapy in pancreatic ductal adenocarcinoma. *Cancer Cell* https://dx.doi.org/10.1016/j.ccell.2016.04.014 (2016)

GENETICS

Transfer RNAs in the driver's seat

Transfer RNAs (tRNAs) may not be silent partners in mRNA translation. Goodarzi *et al.* developed a high-throughput tRNA profiling method, which showed that specific tRNAs are upregulated in breast cancer cells with increased metastatic potential. Changing the tRNA expression landscape drives the stability and translation of transcripts enriched for their cognate codons. $tRNA^{Glu}_{UUC}$ was found to directly induce exosome component 2 (*EXOSC2*) and *GRIPAP1* expression to support metastatic colonization, highlighting the dynamic contribution of tRNAs to cancer progression.

ORIGINAL ARTICLE Goodarzi, H. *et al.* Modulated expression of specific tRNAs drives gene expression and cancer progression. *Cell* **165**, 1416–1427 (2016)

PANCREATIC CANCER

Connecting obesity and cancer mechanistically

How obesity worsens outcomes in pancreatic ductal adenoocarcinoma (PDAC) is not clear. Incio *et al.* showed that obesity promoted desmoplasia, increased tumour growth and impaired delivery of chemotherapy in mouse models of PDAC; these phenotypes were reversed by inhibition of angiotensin II receptor type 1 (AT1). Desmoplasia was promoted by crosstalk between pancreatic stellate cells, neutrophils and adipocytes, and loss of this network prevented tumour growth. Obese patients with PDAC also had increased desmoplasia and reduced chemotherapy response, indicating the therapeutic relevance of this pathway.

ORIGINAL ARTICLE Incio, J. *et al.* Obesity-induced inflammation and desmoplasia promote pancreatic cancer progression and resistance to chemotherapy. *Cancer Discov.* https://dx.doi.org/10.1158/2159-8290.CD-15-1177 (2016)

EPIGENETICS

Histone mutations reprogramme chondroblastoma

Lysine-to-methionine mutations in histone H3.3 at position 36 (H3.3K36M) occur in >90% of chondroblastomas. Fang *et al.* found that the global reduction in H3K36 methylation observed in chondrocytes and chondroblastoma cells with H3.3K36M results from inhibition of the methyltransferases MMSET and NSD2 and SET domain containing 2 (SETD2), and that these epigenomic changes affect the expression of genes involved in many cancer-associated pathways.

ORIGINAL ARTICLE Fang, D. *et al.* The histone H3.3K36M mutation reprograms the epigenome of chondroblastomas. *Science* **352**, 1344–1348 (2016)