Nature Reviews Cancer | AOP, published online 23 November 2016

IN BRIEF

METASTASIS

Caught in a trap

Neutrophils can capture and kill pathogens by releasing DNA and associated proteolytic enzymes into the extracellular space, forming structures known as neutrophil extracellular traps (NETs). Park *et al.* have shown that in the absence of infection, metastatic breast cancer cells can stimulate neutrophils to form metastasis-promoting NETs. Treatment with NET-digesting DNase I inhibited migration and invasion of breast cancer cells *in vitro* and reduced lung metastases *in vivo* when mice were treated with DNase I-coated nanoparticles. NETs were also observed in tumour samples from patients with triple-negative breast cancer, raising the possibility of targeting NETs to prevent metastasis.

ORIGINAL ARTICLE Park, J. *et al.* Cancer cells induce metastasis-supporting neutrophil extracellular DNA traps. *Sci. Transl Med.* **8**, 361ra138 (2016)

TUMOUR METABOLISM

When metabolic and epigenetic states converge

Metabolic and epigenetic states in cells can be linked when intermediary metabolism generates substrates for chromatin regulation. Kottakis *et al.* have found that synergistic liver kinase B1 (LKB1) loss and KRAS activation can promote mTOR-mediated serine biosynthesis pathway dependency during pancreatic tumorigenesis. The subsequent generation of *S*-adenosylmethionine (SAM) drives increased DNA methylation, with specific enrichment of methylation of retrotransposons that are transcriptionally silenced as a consequence. These data indicate that DNA methyltransferase inhibitors may be effective in cancers with LKB1 mutations.

ORIGINAL ARTICLE Kottakis, F. *et al.* LKB1 loss links serine metabolism to DNA methylation and tumorigenesis. *Nature* http://dx.doi.org/10.1038/nature20132 (2016)

TUMOUR IMMUNOLOGY

The consequences of concomitant challenges

Kohlhapp *et al.* found that acute influenza infection accelerates cancer-specific death of immunocompetent mice injected with B16 melanoma cells. Infection caused $CD8^+$ T cells to move from the tumour to the site of infection, thus allowing increased tumour growth; this could be reversed by treatment with programmed cell death protein 1 (PD1) antibodies. These results might explain the data that non-oncogenic infections increase cancer-specific death in patients.

ORIGINAL ARTICLE Kohlhapp, F. J. *et al.* Non-oncogenic acute viral infections disrupt anti-cancer responses and lead to accelerated cancer-specific host death. *Cell Rep.* **17**, 957–965 (2016)

IMMUNOTHERAPY

Powerful combinations

Immunotherapies are not effective in all cancer patients, likely due in part to immunosuppressive networks in advanced tumours. Moynihan *et al.* found that combination immunotherapy consisting of four components (a tumour antigen-targeting antibody, extended half-life recombinant interleukin-2, a programmed cell death protein 1 (PD1) antibody and a T cell vaccine) could eliminate large tumours in syngeneic mouse tumour models and a genetically engineered mouse model of melanoma. This response required many different immune cell subsets. Importantly, the regimen also seemed to have minimal toxicity.

ORIGINAL ARTICLE Moynihan, K. D. *et al.* Eradication of large established tumors in mice by combination immunotherapy that engages innate and adaptive immune responses. *Nat. Med.* http://dx.doi.org/10.1038/nm.4200 (2016)