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IN BRIEF

IMMUNOTHERAPY

Interferon's helping hand with chemotherapy efficacy

It has been known for some time that some of the anticancer effects of chemotherapy originate from an immune-based response. Now, researchers have uncovered this mechanism in more detail in a mouse study published in *Nature Medicine*. The investigators showed that anthracyclines can cause a rapid production of type I interferon by tumour cells that is caused by activation of the Toll-like receptor 3 (Tlr3). The type I interferon molecules are able to trigger autocrine and paracrine signalling loops that release CXC chemokine ligand 10 (CXCL10). Tumours in mice that lacked Tlr3 failed respond to chemotherapy unless type I interferon or CXCL10 was present. Moreover, in several independent patient cohorts who had breast cancer associated with a poor prognosis, a type I interferon-like molecular signature was able to predict clinical response to treatment with chemotherapy.

Original article Sistigu, A. *et al*. Cancer cell–autonomous contribution of type I interferon signalling to the efficacy of chemotherapy. *Nat. Med*. doi:10.1038/nm.3708

BREAST CANCER

Paradoxical role of angiogenesis in breast cancer metastasis

The tumour microenvironment has a key role in cancer growth. A high number of macrophages is associated with poor patient prognosis and survival, and with high expression levels of the chemoattractant CCL2. Inhibition of CCL2 reduces metastasis in mice; however, a study has now shown that interruption of CCL2 inhibition paradoxically led to accelerated metastases and death in four syngeneic mouse models of breast cancer. This surprising result is explained by the release of monocytes from the bone marrow that caused enhanced cancer-cell mobilization from the primary tumour, resulting in increased blood vessel formation in an IL-6 and VEGFA-dependent manner. Inhibition of IL-6 and CCL2 showed a marked reduction in metastasis and increased survival, implicating CCL2 as a potential therapeutic target. This study highlights the importance of the tumour microenvironment as a critical determinant of anticancer therapy.

Original article Bonapace, L. *et al*. Cessation of CCL2 inhibition accelerates breast cancer metastasis by promoting angiogenesis. *Nature* doi:10.1038/nature13862

GENETICS

Somatic genomic engineering approach in cancer

Cancer is a complex and multistep process that develops as a result of mutations and other alterations in oncogenes and tumour suppressor genes. Nevertheless, pinpointing which mutations are causally involved in carcinogenesis is a key challenge. Researchers have now developed a novel CRISPR/Cas9-based approach for the functional investigation of genes involved in lung cancer. Using a $KRAS^{G12D}$ mouse model, they functionally characterized a panel of tumour suppressor genes with known loss-of-function alterations. By combining Cre-dependent somatic activation of $KRAS^{G12D}$ with CRISPR/Cas9-mediated genomic editing of tumour suppressor genes, distinct molecular and histopathological lung cancer phenotypes were determined. These data illustrate how this rapid approach could help to characterize and dissect the complex mutations in other cancers.

Original article Sánchez-Rivera, F. J. *et al*. Rapid modelling of cooperating genetic events in cancer through somatic genome editing. *Nat. Med*. doi:10.1038/nature13906