IN BRIEF

EPIGENETICS

Epimutation of *SDH*

Epimutations are heritable changes in gene expression that are not caused by genetic alterations. Whereas some gastrointestinal stromal tumours (GISTs) are known to have mutations in succinate dehydrogenase (SDH) subunits, such as *SDHC*, some GISTs have defects in SDH activity without having a detectable mutation. Killian ***et al.*** assessed 59 SDH-defective human GIST samples and found 16 with no detectable mutation. DNA methylation and expression profiling revealed *SDHC* promoter epimutation in 15 of these cases, which also had mosaic epimutation of *SDHC* in blood and saliva samples.

ORIGINAL RESEARCH PAPER Killian, J. K. ***et al.*** Recurrent epimutation of *SDHC* in gastrointestinal stromal tumors. *Sci. Transl Med.* **6**, 268ra177 (2014)

INFLAMMATION

Red meat protein in human tissues

The consumption of red meat is associated with an increased risk of carcinoma. Samraj ***et al.*** found that red meat is specifically enriched with the non-human sialic acid *N*-glycolylneuraminic acid (Neu5Gc). When glycosidically bound, Neu5Gc is bioactive and incorporated into tissues, where it acts as an antigen and could then activate an immune response if antibodies against Neu5Gc were present. Indeed, humanized mice that were fed bioavailable Neu5Gc and treated with Neu5Gc antibodies developed systemic inflammation and had a higher incidence of liver tumours.

ORIGINAL RESEARCH PAPER Samraj, A. N. ***et al.*** A red meat-derived glycan promotes inflammation and cancer progression. *Proc. Natl Acad. Sci. USA* http://dx.doi.org/10.1073/pnas.1417508112 (2014)

VIRAL TUMORIGENESIS

Similar but different

Hu ***et al.*** analysed 130 samples of cervical intraepithelial neoplasia and cervical carcinoma, and identified human papillomavirus (HPV) integration sites. They confirmed previously reported integration sites and also identified new ones. In addition, they uncovered changes in gene expression resulting from viral integration, including increased levels of MYC. Importantly, they found that there were sequence microhomologies between the HPV genome and the integration sites, strongly indicating that viral integration occurs via microhomology-mediated DNA repair.

ORIGINAL RESEARCH PAPER Hu, Z. ***et al.*** Genome-wide profiling of HPV integration in cervical cancer identifies clustered genomic hot spots and a potential microhomology-mediated integration mechanism. *Nature Genet.* http://dx.doi.org/10.1038/ng.3178 (2015)

INFLAMMATION

Immune responses to commensal bacteria

A polymorphism in Toll-like receptor 5 (*TLR5*^{R392X}), which prevents the ability to respond to flagellin, occurs in ~7% of humans. Mice without this polymorphism respond to flagellin from commensal bacteria; this leads to increased systemic interleukin-6 (IL-6) levels and immunosuppression, resulting in the progression of existing tumours. In tumour-bearing mice expressing TLR5-R392X, IL-17 was upregulated and tumour growth was more restrained; this difference was abrogated when commensal bacteria were ablated. Patients with ovarian or breast cancer also had the different cytokine profiles according to the presence of the *TLR5*^{R392X} polymorphism.

ORIGINAL RESEARCH PAPER Rutkowski, M. R. ***et al.*** Microbially driven TLR5-dependent signaling governs distal malignant progression through tumor-promoting inflammation. *Cancer Cell* **27**, 27–40 (2015)