IN BRIEF

EPIGENETICS

TRIM24 links a non-canonical histone signature to breast cancer

Tsai, W.-W. *et al. Nature* **468**, 927–932 (2010)

Tsai, Wang and colleagues showed that the tandem plant homeodomain (PHD) and bromodomain motifs within tripartite motif-containing 24 (TRIM24; also known as TIF1α) behave as a functional unit in order to recognize histone H3 that is both unmodified at K4 and acetylated at K23. This domain structure seems to selectively transactivate oestrogen receptor-α (ERα; which binds to TRIM24) target genes that regulate proliferation and tumour development. Indeed, TRIM24 is often overexpressed in breast tumours, and this correlated with reduced survival in patients.

MELANOMA

The histone variant macroH2A suppresses melanoma progression through regulation of CDK8

Kapoor, A. *et al. Nature* **468**, 1105–1109 (2010)

The macroH2A histone variants are associated with condensed chromatin and are thought to fine-tune the expression of developmental transcriptional programmes. Kapoor and colleagues showed that knock down of macroH2A isoforms increased the growth of melanoma cells *in vitro* and *in vivo*, and increased metastasis *in vivo*. They found that upregulation of cyclin-dependent kinase 8 (CDK8) mediated — at least partially — the effects of macroH2A knockdown. Indeed, an inverse correlation between CDK8 and macroH2A expression was found in human melanoma samples.

METABOLISM

ATM activates the pentose phosphate pathway promoting anti-oxidant defence and DNA repair

Cosentino, C. *et al. EMBO J.* 14 Dec 2010 (doi:10.1038/emboj.2010.330)

The kinase ataxia telangiectasia-mutated (ATM) is involved in the response to double-strand breaks (DSBs) and possibly oxidative stress. Cosentino and colleagues showed that ATM activates the pentose phosphate pathway (PPP) by phosphorylating heat shock protein 27 (HSP27), which consequently binds to and activates the rate-limiting enzyme of the PPP: glucose-6-phosphate dehydrogenase (G6PD). This activation of the PPP increased nucleotide production, and G6PD-deficient cells exhibit impaired DSB repair, which suggests that ATM promotes the synthesis of nucleotides for DSB repair. The PPP also generates the antioxidant cofactor NADPH; these roles of ATM may function in the barrier to tumorigenesis.

BREAST CANCER

HIV tropism and decreased risk of breast cancer

Hessol, N. A. *et al. PLoS One* **5**,e14349 (2010)

HIV infection is associated with a decreased prevalence of breast cancer. To examine the role of HIV subtypes on breast cancer risk, Hessol ***et al.*** studied the HIV co-receptor tropisms in HIV-infected patients with and without breast cancer. CXCR4-tropic HIV infections were under-represented in patients with breast cancer, suggesting that this HIV subtype specifically confers breast cancer protection. This is consistent with an emerging model suggesting that CXCR4, which is expressed on ductal breast cells during tumorigenesis, is a novel therapeutic target for breast cancer.