IN BRIEF

SIGNALLING

Phosphorylation of the tumour suppressor Fat is regulated by its ligand Dachsous and the kinase discs overgrown

Sopko, R. *et al. Curr. Biol.* 18 Jun 2009 (doi:10.1016/j.cub.2009.05.049)

Helen McNeill and colleagues have shown that the *Drosophila melanogaster* tumour suppressor gene *fat* is regulated by Dachsous. They found that Fat (a cadherin) is cleaved into a 110 kDa and a 450 kDa protein. Fat^{110} is bound and phosphorylated by the casein kinase Discs overgrown, which seemed to be regulated by Dachsous, also a cadherin. These interactions seem to be important for the regulation of planar cell polarity and the Hippo cell growth pathway, disruption of which is implicated in tumorigenesis.

METASTASIS

Latent bone metastasis in breast cancer tied to Src-dependent survival signals

Zhang, X. H.-F. *et al. Cancer Cell* **16**, 67–78 (2009)

Late-onset metastasis, particularly to the bone, is a common occurrence in patients with breast cancer, but the mechanism(s) by which disseminated cancer cells survive for long periods of time in the metastatic microenvironment is largely unknown. Zhang and colleagues generated a gene expression signature using samples from more than 600 patients with breast cancer, which revealed that Src activation is associated with latent bone metastasis. Both CXCL12 and TNF-related apoptosis-inducing ligand (TRAIL) are particularly expressed in the bone microenvironment, and Src promoted survival by mediating CXCL12–CXCR4–Akt pathway activation and resistance to TRAIL.

METABOLISM

Mitochondrial STAT3 supports Ras-dependent oncogenic transformation

Gough, D. J. *et al. Science* **324**, 1713–1716 (2009)

Gough and colleagues found that signal transducer and activator of transcription 3 (STAT3) is required for HRAS-V12-mediated transformation. STAT3 is a transcription factor and when phosphorylated by tyrosine kinases it undergoes nuclear localization to activate target genes. Surprisingly, transactivation was not required for HRAS-V12-mediated transformation. Instead, mitochondrial STAT3 was sufficient and seemed to modulate metabolic pathways.

SIGNALLING

Genomic antagonism between retinoic acid and estrogen signalling in breast cancer

Hua, S. *et al. Cell* **137**, 1259–1271 (2009)

The retinoic acid receptors (RARs) are transcription factors that mediate the growth-inhibitory effects of retinoic acid and its derivatives, which are being developed as anticancer drugs. Hua and colleagues combined genome-wide chromatin immunoprecipitation and gene expression analyses in MCF7 breast cancer cells to identify RAR target genes. They found that RARs bound gene regulatory regions that overlap or are in close proximity to regions bound by oestrogen receptor-α, which has antagonistic effects. These data indicate that oestrogen and retinoic acid signalling exhibit extensive crosstalk.