IN BRIEF

DEVELOPMENT

Drosophila SPARC is a self-protective signal expressed by loser cells during cell competition

Portela, M. *et al. Dev. Cell* **19**, 562–573 (2010)

Cell competition is important for eliminating suboptimal cells during development and might also have a role in cancer. A physiological mechanism that counteracts cell competition in *Drosophila melanogaster* development has now been identified. SPARC, a secreted glycoprotein involved in cell–cell and cell–matrix interactions, is upregulated in loser cells and transiently protects them from death by setting a higher threshold for caspase activation. This finding might have implications for cancer, consistent with earlier observations that SPARC is involved in tumour–stroma interactions.

THERAPY

DNA damage-mediated induction of a chemoresistant niche

Gilbert, L. A. & Hemann, M. T. *Cell* **143**, 355–366 (2010)

This study indicates that the tumour microenvironment has a role in chemotherapeutic responses. In a mouse model of Burkitt's lymphoma, administration of a DNA-damaging chemotherapeutic leads to the thymic release of two cytokines, interleukin-6 (IL-6) and tissue inhibitor of metalloproteinases 1 (TIMP1). IL-6 and TIMP1 signalling protects a thymic population of lymphoma cells from therapy-induced cell death, which can then serve as a reservoir for tumour relapse. Therefore, effective treatment regimens may need to also target chemotherapy-induced pro-survival mechanisms in the tumour microenvironment.

SMALL RNAS

A genetic defect in exportin-5 traps precursors microRNAs in the nucleus of cancer cells

Melo, S. *et al. Cancer Cell* **18**, 303–315 (2010)

A key step in the maturation of microRNAs (miRNAs) is the nucleocytoplasmic export through exportin 5 (XPO5) of the pre-miRNAs. Melo *et al.* have found mutations in *XPO5* in a set of cancer cell lines that prevent XPO5 binding to the pre-miRNAs. Overexpression of wild-type XPO5 rescued pre-miRNA export and processing in these cell lines. Moreover, cells overexpressing XPO5 showed lower tumorigenicity in nude mice, suggesting that *XPO5* could function as a tumour suppressor gene.

THERAPY

Alleviating cancer drug toxicity by inhibiting a baterial enzyme

Wallace, B. D. *et al. Science* **330**, 831–835 (2010)

CPT-11 is commonly used for the treatment of colorectal cancer (CRC), although its gastrointestinal side effects are a limiting factor in its efficacy. These are triggered by the production of CPT-11 metabolites by bacterial β-glucuronidase. Wallace *et al.* crystallized the bacterial β-glucuronidase and carried out a screening for inhibitors from which they validated four. These compounds specifically inhibited the bacterial enzyme, but not the mammalian enzyme, without affecting commensal bacteria or mammalian epithelial cell growth. Oral intake of one of the compounds successfully protected mice from CPT-11-mediated gastrointestinal toxicity.