IN BRIEF

CANCER STEM CELLS

Upping the stemness during tumour progression

Using four mouse models of squamous skin cancer and limiting dilution serial transplantation, Lapouge and colleagues found that cells from benign papillomas formed tumours in recipient mice at a low frequency and only when cancer-associated fibroblasts or endothelial cells were present in the transplanted mixture. This indicates that there are few cancer stem cells (CSCs) in papillomas, which grow rapidly. Conversely, the number of CSCs increased with tumour invasiveness, indicating that the proportion of CSCs in squamous skin tumours changes as they progress.

ORIGINAL RESEARCH PAPER Lapouge, G. *et al.* Skin squamous cell carcinoma propagating cells increase with tumour progression and invasiveness. *EMBO J.* 27 Nov 2012 (doi:10.1038/emboj.2012.312)

METABOLISM

Transporting drugs

Glycolysis is often upregulated in tumour cells but it can be inhibited by 3-bromopyruvate. Birsoy and colleagues found that monocarboxylate transporter 1 (MCT1) is required for 3-bromopyruvate uptake. The expression of *SLC16A1* (which encodes MCT1) mRNA is a determinant of tumour cell sensitivity to 3-bromopyruvate, and its forced expression in tumour cells rendered xenografts sensitive to 3-bromopyruvate, indicating that MCT1 could be a biomarker of sensitivity to this drug.

ORIGINAL RESEARCH PAPER Birsoy, K. *et al.* MCT1-mediated transport of a toxic molecule is an effective strategy for targeting glycolytic tumors. *Nature Genet.* 2 Dec 2012 (doi:10.1038/ng.2471)

SIGNALLING

Modifying responses

Monoubiquitylation activates RAS isoforms through an unknown mechanism. Using NMR spectroscopy, computational modelling and biochemistry, Baker and colleagues found that KRAS monoubiquitylation does not affect GTP binding, GTP hydrolysis or the regulation of RAS–GDP exchange. Rather, monoubiquitylation of K147 substantially reduced the response of KRAS to GTPase-activating proteins, which results in prolonged activation of KRAS (as it remains GTP bound).

ORIGINAL RESEARCH PAPER Baker, R. *et al.* Site-specific monoubiquitination activates Ras by impeding GTPase-activating protein function. *Nature Struct. Mol. Biol.* 25 Nov 2012 (doi:10.1038/nsmb.2430)

CHROMOSOME INSTABILITY

A different kind of chromosome instability

BUB1 is an activator of the spindle assembly checkpoint, and its altered expression promotes tumorigenesis, which is associated with aneuploidy and chromosome missegregation. Ricke and colleagues generated knock-in mice expressing a kinase-dead BUB1 mutant, which was expressed at normal levels. Surprisingly, these mice did not develop tumours and were not more susceptible to carcinogenesis (unlike mice with altered expression of BUB1), despite aneuploidy and errors in chromosome segregation. This indicates that the type of chromosome instability induced in these knock-in mice does not promote tumorigenesis and so further investigation is required.

ORIGINAL RESEARCH PAPER Ricke, R. M. *et al.* Bub1 kinase activity drives error correction and mitotic checkpoint control but not tumor suppression. *J. Cell Biol.* 3 Dec 2012 (doi:10.1083/jcb.201205115)