IN BRIEF

THERAPEUTICS

Providing protection

Tissue injury during chemoradiotherapy presents a substantial clinical challenge. Zhou *et al.* found that the induction of intestinal stem cell (ISC) proliferation during lethal doses of chemoradiotherapy reduced gut damage in mice bearing intestinal tumours without compromising therapeutic efficacy, and therefore improved the survival of the mice. The SLIT2–roundabout 1 (ROBO1) signalling pathway was shown to have a role in promoting ISC proliferation, and treatment of mice with a short pulse of the WNT agonist R-spondin 1, along with recombinant SLIT2, protected animals from death.

ORIGINAL RESEARCH PAPER Zhou, W. J. *et al.* Induction of intestinal stem cells by R-spondin 1 and Slit2 augments chemoradioprotection. *Nature* http://dx.doi.org/10.1038/nature12416 (2013)

TUMOUR SUPPRESSORS

Nuclear PTEN

The tumour suppressor PTEN antagonizes PI3K signalling in the cytoplasm. PTEN can also be found in the nucleus, where its function is unclear. Bassi *et al.* have shown that sumoylation of PTEN promotes nuclear localization, and genotoxic stress (ionizing radiation (IR)) leads to decreased levels of nuclear PTEN. Nuclear PTEN was required for the repair of DNA double-strand breaks, and lack of sumoylated PTEN increased the sensitivity of cells to IR. Furthermore $PTEN^{-/-}$ xenograft tumours were sensitive to the combination of a genotoxic agent (cisplatin or IR) and a PI3K inhibitor, thus this combination may have therapeutic potential against PTEN-null tumours.

ORIGINAL RESEARCH PAPER Bassi, C. *et al.* Nuclear PTEN controls DNA repair and sensitivity to genotoxic stress. *Science* **341**, 395–399 (2013)

GENETICS

Synonymous is not always the same

Synonymous mutations (in which the protein sequence remains the same) can affect protein function; however, these are not often considered in analyses of mutations in cancers. Using whole-genome and exome sequencing of 29 melanomas, Gartner *et al.* identified a recurrent synonymous mutation in BCL2-like 12 (*BCL2L12*) that increased the levels of *BCL2L12* mRNA and protein, owing to the disruption of a microRNA binding site. This in turn led to increased cell survival. These data suggest that so-called silent mutations may have a functional role in cancers.

ORIGINAL RESEARCH PAPER Gartner, J. J. *et al.* Whole-genome sequencing identifies a recurrent functional synonymous mutation in melanoma. *Proc. Natl Acad. Sci. USA* http://dx.doi.org/10.1073/pnas.1304227110 **(2013)**

ONCOGENES

Exchange needed

GDP–GTP exchange factors (GEFs) promote the activity of RHO GTPases. Menacho-Márquez *et al.* have examined the role of VAV family GEFs in squamous cell carcinomas. They found that loss of both *Vav2* and *Vav3* in mice reduced the formation of carcinogen-induced skin tumours, and identified roles for VAV2 and VAV3 in both tumour initiation and promotion. Mechanistically, VAV2 and VAV3 promoted the proliferation of keratinocytes and the recruitment of inflammatory cells. Loss of either VAV2 or VAV3 alone did not prevent tumours, suggesting that both proteins are required.

ORIGINAL RESEARCH PAPER Menacho-Márquez, M. *et al.* The Rho exchange factors Vav2 and Vav3 favor skin tumor initiation and promotion by engaging extracellular signaling loops. *PLoS Biol.* **11**, e1001615 (2013)