IN BRIEF

DNA DAMAGE

Cooperative functions of Chk1 and Chk2 reduce tumour susceptibility *in vivo*

Niida, H. *et al. EMBO J.* 10 Sep 2010 (doi:10.1038/emboj.2010.218)

The checkpoint kinases CHK1 and CHK2 function in DNA damage response signalling to mediate cell cycle checkpoint arrest and DNA repair, and are thought to contribute to the suppression of tumorigenesis. However, neither *Chek1*$^{+/-}$ nor *Chek2*$^{+/-}$ mice are predisposed to develop tumours, suggesting that they might have redundant roles in tumour suppression. So, Nakanishi and colleagues investigated the effects of the combined loss of CHK1 and CHK2 and found that *Chek1*$^{+/-}$;*Chek2*$^{-/-}$ and *Chek1*$^{+/-}$;*Chek2*$^{+/-}$ mice (*Chek1* ablation is lethal) had an increased susceptibility for developing lymphomas, sarcomas and carcinomas, suggesting that CHK1 and CHK2 are haploinsufficient tumour suppressors. The loss of CHK1 and CHK2 increased spontaneous DNA damage, and the authors identified independent and cooperative roles for CHK1 and CHK2 in the activation of cell cycle checkpoints and apoptosis.

TUMORIGENESIS

Spontaneous tumorigenesis in mice overexpressing the p53-negative regulator Mdm4

Xiong, S. *et al. Cancer Res.* **70**, OF1–7 (2010)

MDM4 is a protein involved in the negative regulation of the tumour suppressor p53 and is sometimes overexpressed in tumours that retain expression of wild-type p53. However, whether the increased expression of MDM4 is functionally important is unclear. To address this, Guillermina Lozano and colleagues generated transgenic mice expressing high levels of MDM4. They found that these mice often developed sarcomas. Mice that are nullizygous or heterozygous for *Trp53* develop mainly lymphomas, so to examine whether MDM4 overexpression can alter the tumour spectrum, the authors generated *Mdm4*-transgenic mice on a *Trp53*-heterozygous background. Tumours rapidly arose in these mice and were predominately carcinomas rather than lymphomas. Interestingly, the wild-type *Trp53* allele was maintained in these tumours, suggesting that overexpression of MDM4 is oncogenic, and cooperates with heterozygous p53.

RNA-BINDING PROTEINS

A Pumilio-induced RNA structure switch in p27-3′ UTR controls miR-221 and miR-222 accessibility

Kedde, M. *et al. Nature Cell Biol.* 5 Sep 2010 (doi:101038/ncb2105)

MicroRNAs (miRNAs) and RNA-binding proteins (RBPs) interact with 3′ untranslated regions (3′ UTRs) to regulate gene expression. Reuven Agami and collaborators have described how the RBP Pumilio and the miRNAs miR-221 and miR-222 share an affinity for the 3′ UTR of the tumour suppressor *CDKN1B*, which encodes the cyclin-dependent kinase inhibitor p27. In quiescent BJ primary fibroblasts that are stimulated with a growth factor, Pumilio interacts with the *CDKN1B* 3′ UTR and induces a conformational change in this region, which was revealed by secondary structure prediction software. This change allows more efficient binding by miR-221 and miR-222 and represses *CDKN1B* expression. Downregulation of p27 permitted BJ cells to enter the S phase of the cell cycle.