# IN BRIEF

## TUMORIGENESIS

### Preneoplastic lesion growth driven by the death of adjacent normal stem cells

Chao, D. L., Eck, J. T., Brash, D. E., Maley, C. C. & Luebeck, E. G. *Proc. Natl Acad. Sci. USA* **105**, 15034–15039 (2008)

How do premalignant lesions expand once the initial mutation(s) has occurred? A mathematical model that limited mutant cell growth to spaces left by the death of normal adjacent stem cells was a better predictor of the expansion of ultraviolet B-induced mutant p53 clones in mouse skin than models of exponential cell proliferation. These findings might help explain why mutagens such as ultraviolet B that usually induce cell death can also induce cell proliferation.

## GENOMIC INSTABILITY

### Loss of the epigenetic tumour suppressor SNF5 leads to cancer without genomic instability

McKenna, E. S. *et al. Mol. Cell. Biol.* **28**, 6223–6233 (2008)

Whether or not cells require unstable genomes to become tumorigenic or metastatic is still a matter for debate. This paper shows that the need for genomic instability can be circumvented through the disruption of the SWI–SNF chromatin-remodelling complex. The tumour suppressor SNF5 is a component of this complex. SNF5-null cells are diploid and genomically stable, but show epigenetically based changes in gene transcription that are sufficient to induce aggressive tumour growth.

## CELL CYCLE

### AP4 encodes a c-MYC-inducible repressor of *p21*

Jung, P. *et al. Proc. Natl Acad. Sci. USA* **105**, 15046–15051 (2008)

This study reports a novel mechanism of p21 downregulation by the oncoprotein MYC. p21 is a central regulator of cell cycle inhibition and its loss allows cells to continue replication of their DNA in the presence of DNA damage. The authors found that expression of p21 could be altered by MYC binding to *AP4* regulatory motifs, thus altering AP4 expression. AP4 is a transcriptional activator and repressor, and regulates expression of *CDKN1A*, the gene that encodes p21, by binding sites in the *CDKN1A* promoter. AP4 sensitizes cells to DNA-damaging agents, which are commonly used in cancer therapy. Therefore, modulation of processes that are regulated by AP4 may have therapeutic value.

## SIGNALLING

### Defective Notch activation in microenvironment leads to myeloproliferative disease

Kim, Y.-W. *et al. Blood* 25 Sep 2008 (doi:10.1182/blood-2008-03-148999)

Inactivation of mind bomb 1 (*Mib1*), an essential component of Notch ligand endocytosis, in non-haematopoietic cells led to the development of myeloproliferative disease in conditional knockout mice. The introduction of a constitutively active form of Notch into the *Mib1*-null background significantly suppressed disease progression, which suggested that myeloproliferative disease development is caused by defective activation of Notch in non-haematopoietic cells. Therefore, Notch ligand–receptor interactions between the non-haematopoietic cells that constitute the cellular microenvironment are absolutely required for normal haematopoiesis.