IN BRIEF

GENOMIC INSTABILITY

Tetraploidy tolerance promotes cancer evolution

Aneuploidy has long been associated with genetic instability and tumorigenesis. Dewhurst *et al.* examined the evolution and consequences of chromosomal aberrations using long-term culture of a diploid colon cancer progenitor cell line. Tetraploids — rare cells that survive genome doubling — have a greater tolerance for further chromosomal abnormalities. Furthermore, tetraploidy was associated with a low probability of disease-free survival.

ORIGINAL RESEARCH PAPER Dewhurst, S. M. *et al.* Tolerance of whole-genome doubling propagates chromosomal instability and accelerates cancer genome evolution. *Cancer Discov.* **4**, 175–185 (2014)

GENETICS

BRAF mutation drives rare brain tumour

Craniopharyngiomas are a rare and exceedingly difficult-to-treat type of brain tumour that can be further divided into papillary and adamantinomatous subtypes. A whole-exome sequencing study of patient tumour samples identified a single driver mutation in each subtype: a $BRAF^{V600E}$ mutation for papillary craniopharyngiomas and a β-catenin mutation for adamantinomatous craniopharyngiomas. These mutations are mutually exclusive and clonal, and they can be used to classify these tumour types in patients. Furthermore, there are currently targeted therapies for the $BRAF^{V600E}$ mutation that could be used to treat papillary craniopharyngiomas.

ORIGINAL RESEARCH PAPER Brastianos, P. K. *et al.* Exome sequencing identifies *BRAF* mutations in papillary craniopharyngiomas. *Nature Genet.* **46**, 161–165 (2014)

SIGNALLING

ERβ activation drives gender bias in lymphoma

Lymphomas show a higher incidence and poorer prognosis in males than in females, which suggests a role for endocrine regulation in this cancer. Yakimchuk *et al.* used xenograft mouse models of human lymphomas to show that ligand-mediated oestrogen receptor-β (ERβ) activation inhibits angiogenesis and lymphangiogenesis. These effects are not thought to be mediated by the microenvironment, as there was no difference between wild-type and ERβ-deficient mice engrafted with lymphoma cells. Furthermore, they showed that human lymphoma biopsies express ERβ, which suggests that ERβ agonists could be a viable therapy for lymphoma.

ORIGINAL RESEARCH PAPER Yakimchuk, K. *et al.* Inhibition of lymphoma vascularization and dissemination by estrogen receptor β agonists. *Blood* http://dx.doi.org/10.1182/blood-2013-07-517292 (2014)

THERAPEUTICS

SMAC mimetics deal a blow to tumours

SMAC mimetic compounds (SMCs) activate apoptosis by binding to the inhibitor of apoptosis (IAP) proteins and have had disappointing effects as single agents. SMCs might only be effective in tumours in which death-inducing proteins are generated in substantial amounts. A new study combined SMCs with agents such as oncolytic viruses that generate cytokines such as tumour necrosis factor. The combination induced 'bystander death' of cancer cells and led to significant tumour regression and extended survival in mice. Thus, this combination might be a viable treatment for human cancers.

ORIGINAL RESEARCH PAPER Beug, S. T. *et al.* Smac mimetics and innate immune stimuli synergize to promote tumor death. *Nature Biotech.* **32**, 182–190 (2014)