IN BRIEF

GENETICS

Mutation identified for an inherited cancer

Hereditary mixed polyposis syndrome (HMPS) frequently leads to colorectal carcinoma. Copy number analyses in the chromosomal region thought to harbour the causal genetic lesion identified a 40 kb duplication — encompassing the 3′ end of the *SCG5* gene and the region upstream of the gremlin 1 (*GREM1*) gene — in affected individuals. Tissue expression analyses indicated that the duplication causes GREM1 to be misexpressed in epithelial cells of colonic crypts. As GREM1 is an antagonist of bone morphogenetic protein (BMP) signalling this might explain the tumorigenic effects of the duplication.

ORIGINAL RESEARCH PAPER Jaeger, E. *et al.* Hereditary mixed polyposis syndrome is caused by a 40-kb upstream duplication that leads to increased and ectopic expression of the BMP antagonist GREM1. *Nature Genet.* 6 May 2012 (doi:10.1038/ng.2263)

MIGRATION

Transporting ions and moving cells

Expression of the Na^+–K^+–Cl^- cotransporter 1 (NKCC1; also known as SLC12A2) has been associated with glioblastoma cell invasion and aggressiveness. The authors found that knockdown or inhibition of NKCC1 in glioma cells resulted in reduced invasion and that this was accompanied by larger cell–matrix focal adhesions and lower cell traction forces. Therefore, NKCC1 might promote cell motility and invasion by regulating cell adhesion dynamics in addition to known roles in controlling cell size through ion transport.

ORIGINAL RESEARCH PAPER Garzon-Muvdi, T. *et al.* Regulation of brain tumor dispersal by NKCC1 through a novel role in focal adhesion regulation. *PLoS Biol.* **10**, e1001320 (2012)

GENOMIC INSTABILITY

Potential predictive value of somatic mosaicism

Two studies analysed chromosomal abnormalities in buccal and blood cells from more than 100,000 individuals of different ages. Detectable abnormalities increased with age and were higher in patients with either solid or haematological cancers compared with cancer-free individuals (0.97% versus 0.74%). This indicates that genomic instability underlies both somatic cell mosaicism and cancer risk. Crucially, abnormalities in samples from undiagnosed individuals were predictive of future cancer diagnoses, so this approach may be a useful future screening tool.

ORIGINAL RESEARCH PAPERS Laurie, C. C. *et al.* Detectable clonal mosaicism from birth to old age and its relationship to cancer. *Nature Genet.* 6 May 2012 (doi:10.1038/ng.2271) | Jacobs, K. B. *et al.* Detectable clonal mosaicism and its relationship to aging and cancer. *Nature Genet.* 6 May 2012 (doi:10.1038/ng.2270)

THERAPY

Enhancing efficacy by reducing side effects

To overcome the myelosuppression that is a common side effect of chemotherapy, Adair *et al.* modified *ex vivo* the haematopoietic stem cells (HSCs) from three patients with glioblastoma to express a mutant form of 6-*O*-methylguanine-DNA methyltransferase (MGMT). This enzyme enhances the repair of DNA lesions caused by alkylating chemotherapies. Re-injection of the MGMT-modified HSCs, which successfully engrafted, enabled the patients to tolerate higher doses of chemotherapy, with some evidence of disease stabilization and improved survival.

ORIGINAL RESEARCH PAPER Adair, J. E. *et al.* Extended survival of glioblastoma patients after chemoprotective HSC gene therapy. *Sci. Transl Med.* **4**, 133ra57 (2012)