

IN BRIEF

 GENOMIC INSTABILITY**Histone mismanagement**

The alternative lengthening of telomeres (ALT) pathway is a mechanism of maintaining telomere length and is activated in 10–15% of cancers. However, the mechanism of ALT activation is poorly understood. O'Sullivan and colleagues show that knockdown of both ASF1A and ASF1B (histone chaperones that are involved in histone management) in several human cell lines induced phenotypic markers of ALT pathway activity. After further analyses, the authors propose that the ALT pathway may be activated by defects in histone management.

ORIGINAL RESEARCH PAPER O'Sullivan, R. J. *et al.* Rapid induction of alternative lengthening of telomeres by depletion of the histone chaperone ASF1. *Nature Struct. Mol. Biol.* **21**, 167–174 (2014)

 BREAST CANCER**Breast cancer classification**

Phenotypic similarities between haematological tumour cells and normal haematopoiesis are key to classifying haematological malignancies, and this requires characterization of cells during normal haematopoiesis. Santagata *et al.* set about characterizing the cell types in normal breast epithelium to see whether they could use this information to classify breast tumours. Using 15,000 normal breast cells and breast epithelial markers, they identified 11 differentiation states, which were used to classify breast tumours into four subtypes based on the expression of certain receptors. These subtypes were distinct from standard molecular subtyping and they could be used to refine the classification system.

ORIGINAL RESEARCH PAPER Santagata, S. *et al.* Taxonomy of breast cancer based on normal cell phenotype predicts outcome. *J. Clin. Invest.* **124**, 859–870 (2014)

 NEUROBLASTOMA**A new gene that promotes NMYC activity**

Suenaga *et al.* found that a *cis*-antisense gene of MYCN, called NCYM, encodes a protein that, like NMYC, is involved in the pathogenesis of neuroblastoma. They found that NCYM is co-amplified with MYCN in primary human neuroblastoma samples. Also, unlike *Mycn* transgenic mice, *Mycn;Ncym* transgenic mice developed metastatic neuroblastoma, which is reminiscent of human neuroblastoma with NMYC amplification. The authors showed that NCYM inhibits the activity of glycogen synthase kinase 3 β (GSK3 β), which targets NMYC for degradation, suggesting that NCYM promotes tumorigenesis by stabilizing NMYC.

ORIGINAL RESEARCH PAPER Suenaga, Y. *et al.* NCYM, a *cis*-antisense gene of MYCN, encodes a *de novo* evolved protein that inhibits GSK3 β resulting in the stabilization of MYCN in human neuroblastomas. *PLoS Genet.* **10**, e1003996 (2014)

 ALTERNATIVE SPLICING**Driving too much wound healing in the skin**

Jensen *et al.* generated a conditional transgenic mouse that expressed the alternative splicing factor serine/arginine-rich splicing factor 6 (SRSF6) in the skin. They found that SRSF6 induction caused substantial hyperplasia and skin thickening, which was enhanced by epidermal injury. SRSF6 induction also caused the activation of genes that are involved in wound healing. The authors found that SRSF6 is overexpressed in several types of skin cancer. Together, these data indicate that SRSF6 is a proto-oncogene that drives wound healing and hyperplasia.

ORIGINAL RESEARCH PAPER Jensen, M. A. *et al.* Splicing factor SRSF6 promotes hyperplasia of sensitized skin. *Nature Struct. Mol. Biol.* **21**, 189–197 (2014)