

IN BRIEF

DNA ELEMENTS**Determinants of site-specific hypermutation**

Rearranged antibody genes in B lymphocytes are subjected to somatic hypermutation mediated by activation-induced cytidine deaminase (AID) in order to increase antibody diversity. Buerstedde *et al.* used a fluorescent reporter system for somatic hypermutation in a B cell line to test the ability of mouse and human regulatory elements to enhance somatic hypermutation. They found that different immunoglobulin enhancer and enhancer-like elements cooperated to promote somatic hypermutation, which may be important for restricting AID-mediated mutagenesis to appropriate loci.

ORIGINAL RESEARCH PAPER Buerstedde, J. M. *et al.* Targeting of somatic hypermutation by immunoglobulin enhancer and enhancer-like sequences. *PLoS Biol.* **12**, e1001831 (2014)

TECHNOLOGY***In vivo* correction of genetic disease in adult mice**

The CRISPR–Cas9 gene editing system can introduce or correct specific mutations in various species. Yin *et al.* used a mouse model of hereditary tyrosinemia type 1, which is a liver disease caused by a homozygous mutation in the fumarylacetoacetate hydrolase (*Fah*) gene. By hydrodynamically injecting *Fah*-targeted CRISPR–Cas9 reagents into diseased adult *Fah*^{mut/mut} mice, they were able to correct the genetic defect and achieve wild-type FAH expression in ~1 in 250 hepatocytes. The selective advantage of *Fah*-corrected hepatocytes led to their expansion in the liver during the following 30 days to constitute ~33% of liver cells and alleviate pathological symptoms.

ORIGINAL RESEARCH PAPER Yin, H. *et al.* Genome editing with Cas9 in adult mice corrects a disease mutation and phenotype. *Nature Biotech.* <http://dx.doi.org/10.1038/nbt.2884> (2014)

DISEASE GENETICS**Non-invasive monitoring of resistance mutations**

Cancers frequently develop resistance to anticancer therapies, but opportunities to obtain tissue samples for molecular analyses of resistance mutations are typically limited. Mohan *et al.* used high-throughput sequencing to analyse the tumour-derived DNA in the blood of ten patients with colorectal cancer who were undergoing treatment with epidermal growth factor receptor (EGFR)-targeted antibodies. They found that acquired focal amplifications (rather than point mutations) in genes that are known to be involved in the response to EGFR-targeted agents were predictive of therapeutic resistance. Such monitoring may aid optimization of treatment regimens.

ORIGINAL RESEARCH PAPER Mohan, S. *et al.* Changes in colorectal carcinoma genomes under anti-EGFR therapy identified by whole-genome plasma DNA sequencing. *PLoS Genet.* **10**, e1004271 (2014)

TRANSPOSABLE ELEMENTS**A pluripotency role for a retroviral element**

Human endogenous retroviruses (HERVs) are kept silent to a large extent to minimize retrotransposition and genomic instability. Lu *et al.* studied the HERV-H subfamily, which are selectively re-expressed in embryonic stem cells. They found that HERV-H knockdown induced differentiation, indicating that HERV-H expression has an active and useful role in maintaining pluripotency. Mechanistic investigations revealed that HERV-H transcripts bind to OCT4 and co-activators to contribute to a pluripotency-associated transcriptional network.

ORIGINAL RESEARCH PAPER Lu, X. *et al.* The retrovirus HERVH is a long noncoding RNA required for human embryonic stem cell identity. *Nature Struct. Mol. Biol.* <http://dx.doi.org/10.1038/nsm.2799> (2014)