IN BRIEF

EVOLUTION

Reconstructing essentiality

Recently originated 'young' genes can rapidly evolve essential functions, although the underlying mechanisms are largely unclear. Ross *et al*. carried out phylogenetic and functional analyses to show that the *Drosophila melanogaster* gene *Umbrea*, which arose <15 million years ago through duplication of the non-essential gene heterochromatin protein 1b (*HP1b*), evolved novel functions that conferred essentiality. These included alterations to protein–protein interaction domains that conferred Umbrea with centromere localization and an indispensable role in chromosome segregation.

ORIGINAL RESEARCH PAPER Ross, B. D. *et al.* Stepwise evolution of essential centromere function in a *Drosophila* neogene. *Science* **340**, 1211–1214 (2013)

EPIGENETICS

Mechanistic insight into epigenetic inheritance

Paramutation is a non-Mendelian inheritance phenomenon in which one allele alters the epigenetic state of a second allele, probably through an RNA signal; this 'paramutated' state of the second allele can be inherited by progeny independently of the first allele. Kiani *et al*. found that establishment and trangenerational transmission of paramutated *Kit* and *Sox9* alleles in mice requires *Dnmt2*, which is thought to be primarily an RNA methyltransferase. Further analyses revealed hypomethylation of *Kit* transcripts in *Dnmt2*-null mice without detectable methylation changes at the *Kit* genomic locus. Thus, DNMT2-mediated methylation may be required for the activity or stability of transgenerational RNAs in mice.

ORIGINAL RESEARCH PAPER Kiani, J. *et al.* RNA-mediated epigenetic heredity requires the cytosine methyltransferase Dnmt2. *PLoS Genet.* **9**, e1003498 (2013)

COMPLEX DISEASE

Limited role of rare variants in autoimmunity

One proposed explanation for the 'missing heritability' of common diseases is an important contribution of rare variants. To identify associations between rare variants and autoimmune diseases, these authors sequenced the exons of 25 genes that had previously been implicated in these disorders in 24,892 cases and 17,019 controls. Despite the large sample size, little evidence was found for an important role of rare variants in autoimmune disease susceptibility, indicating that further large-scale exome-resequencing studies are unlikely to be informative for these conditions.

ORIGINAL RESEARCH PAPER Hunt, K. A. *et al.* Negligible impact of rare autoimmune-locus coding-region variants on missing heritability. *Nature* 22 May 2013 (doi:10.1038/nature12170)

GENE REGULATION

Better screening for alternative splicing regulators

Although high-throughput screening methods have boosted efforts to identify regulators of alternative splicing, issues such as false positives can be problematic. This study describes a strategy that uses two complementary minigene reporters to identify positive and negative splicing regulators of particular exons. False positives are eliminated by combining results from the two reporters. The authors used this strategy to identify several previously unknown alternative splicing regulators for an exon of the *Dlg4* gene in a high-throughput screen in mammalian cells.

ORIGINAL RESEARCH PAPER Zheng, S. *et al.* A broadly applicable high-throughput screening strategy identifies new regulators of *Dlg4* (*Psd-95*) alternative splicing. *Genome Res.* 1 May 2013 (doi:10.1101/gr.147546.112).