IN BRIEF

SYNTHETIC BIOLOGY

Post-transcriptional synthetic circuits

Therapeutic applications of gene delivery have so far relied on the introduction of foreign DNA, an approach that carries a risk of harmful genomic integration. Wroblewska *et al.* have now created RNA-only synthetic regulatory circuits using RNA-encoded RNA-binding proteins and demonstrated their functionality in mammalian cells. They engineered a multi-input cell-type classifier, encoded as modified RNA, that can distinguish HeLa cells from other cell types in a fluorescence assay on the basis of their microRNA expression profiles. By incorporating a pro-apoptotic gene as the circuit output, they were able to selectively kill HeLa cells in a mixed-cell population without affecting the viability of other cell types. The researchers also constructed a repression cascade and a switch circuit, which were functional when encoded on modified RNA or self-replicating RNA, facilitating transient or long-term expression, respectively. The researchers suggest that RNA circuits offer potential benefits for applications *in vivo*, particularly those in which safety is a concern.

ORIGINAL RESEARCH PAPER Wroblewska, L. *et al.* Mammalian synthetic circuits with RNA binding proteins for RNA-only delivery. *Nat. Biotechnol.* **33**, 839–841 (2015)

CANCER GENETICS

Improved prediction of relapse in breast cancer

Assessing the presence of circulating tumour DNA in plasma samples enables the early prediction of relapse among patients who received therapy for breast cancer and are apparently disease-free. These findings stem from a study involving 55 women who had been treated with neoadjuvant chemotherapy and surgery for early breast cancer. From an analysis of the mutations present in the primary tumours of each patient, the researchers developed personalized digital PCR assays that they later used to monitor the existence of minimal residual disease in plasma samples collected either at a single time point after surgery or serially during follow-up. This approach led to detection of metastatic relapse with high accuracy and sensitivity, particularly when performed in serial samples (for which detection occurred at a median of 7.9 months before clinical relapse). This procedure could be used to identify patients at high risk of relapse and to tailor therapy to their specific mutation profiles.

ORIGINAL RESEARCH PAPER Garcia-Murillas, I. *et al.* Mutation tracking in circulating tumor DNA predicts relapse in early breast cancer. *Sci. Transl. Med.* **7**, 302ra133 (2015)

EVOLUTIONARY GENETICS

Alternative splicing shapes vertebrate evolution

A single alternative splicing event might have had far-reaching consequences in the evolution of the nervous system in vertebrates, Gueroussov *et al.* report. The new findings show that one exon of the transcript encoding polypyrimidine tract-binding protein 1 (PTBP1) is skipped in mammals, whereas in other vertebrates this exon is present. PTBP1 binds to many RNAs to regulate alternative splicing on a large scale. Experiments in mammalian cells showed that the absence of exon 9 (exon 8 in some species) represses the activity of PTBP1 so that a mammalian-specific alternative splicing programme is activated during neuronal differentiation. Deletion of exon 9 leads to the appearance of mammalian-like features in chicken cells. These findings underscore the importance of differences in alternative splicing programming in vertebrate evolution.

ORIGINAL RESEARCH PAPER Gueroussov, S. *et al.* An alternative splicing event amplifies evolutionary differences between vertebrates. *Science* **349**, 868–873 (2015)