IN BRIEF

GENE REGULATION

Novel mRNA quality control mechanism

Recent findings point to a novel translational quality control pathway for secretory proteins that pre-empts mutant protein production and aggregation by inducing mRNA degradation. Karamyshev *et al.* found that the pathway is triggered if signal sequences within the nascent chain fail to interact correctly with the signal recognition particle (SRP) when exiting the ribosome, which shifts the proximity of the nascent chain from the SRP to the protein argonaute2 (AGO2). Knockdown or overexpression of AGO2 prevented or induced degradation of mRNA containing mutated signal sequences, respectively. Finally, knockdown of SRP54 was shown to also promote the degradation of secretory protein mRNA.

ORIGINAL RESEARCH PAPER Karamyshev, A. L. *et al.* Inefficient SRP interaction with a nascent chain triggers a mRNA quality control pathway. *Cell* **156**, 146–157 (2014)

GENE THERAPY

Clinical trial suggests triple gene therapy is safe

A Phase I/II trial suggests that a new triple gene therapy called ProSavin, which is based on lentiviral vectors, is tolerable and safe. In the trial, 15 refractory individuals aged 48–65 years with advanced Parkinson's disease were given low, medium or high doses of ProSavin, which was injected directly into the dopamine-depleted striatum — the region of the brain that controls movement — to provide a continuous and stable source of the neurotransmitter. Motor symptoms significantly improved after 6 and 12 months, whereas adverse effects of the treatment were mild to moderate. The authors warn about over-interpreting results regarding the efficacy of this approach; however, its safety could provide a proof of principle for future studies.

ORIGINAL RESEARCH PAPER Palfi, S. *et al.* Long-term safety and tolerability of ProSavin, a lentiviral vector-based gene therapy for Parkinson's disease: a dose escalation, open-label, phase 1/2 trial. *Lancet* http://dx.doi.org/10.1016/S0140-6736(13)61939-X (2014)

TECHNOLOGY

Tagging mRNAs in living cells

Analysis of RNAs in their endogenous environment could provide unique insights into cell-type-specific gene expression and RNA dynamics. However, visualizing individual RNA molecules within or isolating RNAs from a live single cell has remained challenging. Two recent reports look to drive the field forward in that respect. Park *et al.* engineered a transgenic mouse model that expresses fluorescently labelled endogenous β-actin mRNA to visualize its localization and movement. Experiments in cultured neurons and acute brain slices showed that β-actin mRNA molecules undergo continuous assembly and disassembly in large mRNA–protein complexes. The authors believe that their live-cell imaging technique is applicable to other genes to investigate the dynamic regulation of individual components of the transcriptome. In the second study, Lovatt *et al.* describe an mRNA capture methodology that enables the isolation of mRNA from live single cells in intact complex tissues. They engineered a chemical compound called the TIVA (transcriptome *in vivo* analysis) tag that enters live cells and, upon photoactivation, anneals to mRNA. TIVA–mRNA hybrids can be isolated through an affinity tag incorporated into the TIVA tag, and subsequent RNA sequencing thus yields the transcriptome profile of a single cell.

ORIGINAL RESEARCH PAPERS Park, H. Y. *et al.* Visualization of dynamics of single endogenous mRNA labeled in live mouse. *Science* **343**, 422–424 (2014) | Lovatt, D. *et al.* Transcriptome *in vivo* analysis (TIVA) of spatially defined single cells in live tissue. *Nature Methods* **11**, 190–196 (2014)