Nature Reviews Molecular Cell Biology | Published online 19 Dec 2016

IN BRIEF

ORGANELLE DYNAMICS

Controlling phase separation of P granules

Caenorhabditis elegans germ cell granules (P granules) are RNA and protein condensates that are associated with RNA metabolism. In *C. elegans* zygotes, P granules are spatially restricted to the posterior pole and, similarly to other non-membranous organelles, their formation is driven by liquid–liquid phase separation. Seydoux and colleagues revealed that MEG-3 — a protein with an intrinsically disordered region (IDR) — is the main driver of P granule assembly and that its IDR drives phase separation, which is further enhanced by its interaction with RNA. The authors propose that the RNA-binding protein MEX-5, which is enriched at the anterior pole, limits RNA availability and thereby constrains efficient MEG-3-driven phase separation at the anterior and promotes P granule formation at the posterior. This mechanism sheds new light on the spatial regulation of non-membranous organelle assembly and distribution.

ORIGINAL ARTICLE Smith, J. *et al.* Spatial patterning of P granules by RNA-induced phase separation of the intrinsically-disordered protein MEG-3. *eLife* http://dx.doi.org/10.7554/eLife.21337 (2016)

GENOME ENGINEERING

NHEJ and CRISPR–Cas9 improve gene therapy

The repair of DNA double-strand breaks by non-homologous end-joining (NHEJ) is efficient in non-dividing cells, but its use for site-specific transgene integration has not been shown. Suzuki *et al.* developed homology-independent targeted integration (HITI) for CRISPR–Cas9- and NHEJ-based gene knock-in. HITI successfully mediated site-directed GFP knock-in in postmitotic cultured mouse and human neurons. To improve applicability *in vivo*, HITI constructs were sub-cloned into adeno-associated virus (AAV). Following systemic delivery in mice, HITI was 90–95% on-target in muscle and heart tissues, with minimal NHEJ-associated mutagenesis. HITI–AAV was tested in the RCS rat, which is a model for retinitis pigmentosa (inherited retinal degeneration) caused by mutations in exon 2 of the *Mertk* gene. Injection of HITI–AAV–*Mertk* exon 2 into the eyes of RCS rats led to MERTK expression and this significantly improved retinal physiology and function.

ORIGINAL ARTICLE Suzuki, K. *et al. In vivo* genome editing via CRISPR/Cas9 mediated homology-independent targeted integration. *Nature* **540**, 144–149 (2016)

RNA DECAY

NoBody binds to mRNA decapping proteins

Recent studies have revealed that genomes contain thousands of small open reading frames that encode microproteins, but the functional significance of microproteins is unclear. D'Lima *et al.* now report the identification of a human microprotein, NoBody (non-annotated P-body dissociating polypeptide), that interacts with the mRNA decapping complex. Functional proteomics studies showed that NoBody interacts with the decapping complex, which removes the 5′cap from mRNAs to promote decay, by directly binding to enhancer of decapping protein 4. At low expression levels, NoBody localized to cytoplasmic P-bodies (RNA–protein granules that are involved in mRNA decay). NoBody overexpression induced the dispersal of P-bodies, whereas silencing its expression increased the number of P-bodies. Moreover, NoBody overexpression increased the levels of a nonsense-mediated decay substrate, which suggests that NoBody inhibits mRNA decay, although the exact mechanisms remain to be elucidated.

ORIGINAL ARTICLE D'Lima, N. G. *et al.* A human microprotein that interacts with the mRNA decapping complex. *Nat. Chem. Biol.* http://dx.doi.org/10.1038/nchembio.2249 (2016)