Nature Reviews Genetics | AOP, published online 12 August 2014

IN BRIEF

THERAPEUTICS

Targeting huntingtin through morpholino oligomers

Huntington's disease is caused by a mutant huntingtin (*HTT*) gene that contains an expanded tract of poly(CAG) repeats. Sun *et al.* designed phosphorodiamidate morpholino oligomers (PMOs, which are stable nucleic acid mimics) as antisense reagents to target the CAG tract in *HTT* mRNA. Applying the PMOs to *HTT*-mutant human neurons *in vitro* decreased HTT protein levels and reduced toxicity caused by mutant HTT. Furthermore, in two mouse models of Huntington's disease, intracranial injection of PMOs resulted in downregulation of mutant HTT levels and partially reduced disease symptoms.

ORIGINAL RESEARCH PAPER Sun, X. *et al.* Phosphorodiamidate morpholino oligomers suppress mutant huntingtin expression and attenuate neurotoxicity. *Hum. Mol. Genet.* http://dx.doi.org/10.1093/hmg/ddu349 (2014)

TECHNOLOGY

Using DNA repair to detect modified bases

There is great interest in characterizing the locations and functions of chemically modified bases in genomes. Bryan *et al.* report their Excision-seq method, in which DNA repair enzymes are used to cut genomic DNA at sites of the particular damaged bases they recognize, followed by high-throughput sequencing to characterize these cleavage sites. The researchers characterized the locations and sequence contexts of uracils (that is, demethylated thymines) in *Escherichia coli* and *Saccharomyces cerevisiae* genomes, and of ultraviolet-light-induced pyrimidine dimers in *S. cerevisiae*.

ORIGINAL RESEARCH PAPER Bryan, D. S. *et al.* High resolution mapping of modified DNA nucleobases using excision repair enzymes. *Genome Res.* http://dx.doi.org/10.1101/gr.174052.114 (2014)

NON-CODING RNA

MicroRNA stimulates mitochondrial translation

The muscle-specific microRNA miR-1 stimulates translation of various transcripts encoded by mitochondrial DNA, while repressing its nuclear DNA-encoded targets in the cytoplasm, report Zhang and colleagues. The observed effect is dependent on specific base-pairing between miR-1 and its target transcripts, as well as on the presence of Argonaute 2 (AGO2), which was shown by crosslinking and immunoprecipitation coupled with deep sequencing (CLIP–seq) to bind to the transcripts directly. The authors propose that AGO2 functions as a key mitochondrial translation initiation factor to facilitate ribosome–mRNA interactions.

ORIGINAL RESEARCH PAPER Zhang, X. *et al.* MicroRNA directly enhances mitochondrial translation during muscle differentiation. *Cell* http://dx.doi.org/10.1016/j.cell.2014.05.047 (2014)

DISEASE GENETICS

Loss of rescue factor unmasks epistatic mutation

Mutations in the mouse gene *n-Tr20*, which encodes a tRNA specifically expressed in the central nervous system, can slow translation at AGA codons by increasing ribosome pausing, thereby promoting neuronal death, a new study in *Science* shows. However, analyses of multiple strains of mice revealed that the neurodegeneration only manifests when the *n-Tr20* mutation co-occurs with a loss-of-function mutation in GTP-binding protein 2 (*Gtpbp2*). Co-immunoprecipitation and affinity capture experiments showed that GTPBP2 directly interacts with the ribosome recycling protein Pelota.

ORIGINAL RESEARCH PAPER Ishimura, R. *et al.* Ribosome stalling induced by mutation of a CNS-specific tRNA causes neurodegeneration. *Science* **345**, 455–459 (2014)