

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)