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IN BRIEF

GENE-BASED THERAPY

RNA therapy for myotonic dystrophy

Working in a mouse model of myotonic dystrophy type 1 (DM1), the authors designed antisense oligonucleotides (ASOs) that target nuclear retained transcripts of a human *ACTAC1* transgene containing an expanded CUG tract (CUG^{exp}). The ASOs were optimized for processing by the RNAaseH pathway. Injecting these mice with ASOs caused a rapid knockdown of CUG^{exp} as well as changes in the transcriptome that were consistent with the splice factor muscleblind being released from CUG^{exp} sequestration, which is a mechanism by which the aberrant transcripts are thought to cause disease. Histological features of the disease were also corrected, and this is a promising advance for therapy.

ORIGINAL RESEARCH PAPER Wheeler, T. M. *et al.* Targeting nuclear RNA for *in vivo* correction of myotonic dystrophy. *Nature* **488**, 111–115 (2012)

GENOMICS

Mitochondrial mutations may explain why women live longer than men

Mutations in mitochondrial DNA respond only to selection acting on females, theoretically allowing harmful male-specific mutations to accumulate in the mitochondrial genome: a phenomenon previously termed the 'mother's curse'. This paper presents experimental evidence from *Drosophila melanogaster* indicating that mitochrondrial genomes carry numerous variants dispersed across the genome that affect male-specific patterns of ageing. The authors suggest that the mitochondrial genome is a 'hotspot' for mutations that influence these sex-specific differences in ageing and that mitochondrial genetic variation may influence the patterns of sexual dimorphism observed in ageing across animals.

ORIGINAL RESEARCH PAPER Camus, M. F. *et al.* Mitochondria, maternal inheritance, and male aging. *Curr. Biol.* **22**, 1–5 (2012)

CANCER GENETICS

Evaluating oncogene cooperativities

The authors developed a mouse cancer model to evaluate oncogene cooperativity in the development of tumours. Stochastic gene expression was induced using a 'Multi-Hit' transgene containing three oncogenes that can be independently activated by the Cre recombinase to mimic the stepwise development of specific cancers. The authors suggest that future experiments using this model may show whether pathway interactions are affected by tumour suppressor functions, and they suggest that the model could be useful in predicting the effectiveness of drug treatments.

ORIGINAL RESEARCH PAPER Musteanu, M. *et al.* A mouse model to identify cooperating signaling pathways in cancer. *Nature Methods* 10 Jul 2012 (doi:10.1038/nmeth.2130)

DNA METHYLATION

Variation in methylomes of neonatal twins

Inter-individual differences in DNA methylation are thought to contribute to disease risk, but what influences these differences in methylation? This paper provides valuable insight by presenting the genome-wide methylation profiles of neonatal mono- and dizygotic twins. The differences they detect within twin pairs highlight the importance of intra-uterine environment and/or stochastic effects in early development.

ORIGINAL RESEARCH PAPER Gordon, L. *et al.* Neonatal DNA methylation profile in human twins is specified by a complex interplay between intrauterine environmental and genetic factors, subject to tissue-specific influence. *Genome Res.* **22**, 1395–1406 (2012)