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IN BRIEF

EVOLUTION

Flu fitness model may inform vaccine selection

A new fitness model has been developed that predicts evolution of the seasonal human influenza A/H3N2 virus from genomic data. The model is based on the fitness effects of mutations in antibody-binding epitope and in non-epitope regions of haemagglutinin, which is a surface protein of the virus. Beneficial mutations in epitopes and harmful (that is, deleterious) mutations in non-epitope regions are used to infer fitness of individual strains. Predictions of growth and decline of viral groups (that is, clades) in one year on the basis of frequency and fitness of individual strains in a previous year were accurate 93% and 76% of the time, respectively.

ORIGINAL RESEARCH PAPER Łuksza, M. & Lässig, M. A predictive fitness model for influenza. *Nature* http://dx.doi.org/10.1038/nature13087 (2014)

ANIMAL MODELS

High-precision gene editing in monkeys is feasible

Successful application of the CRISPR–Cas method for genome editing has been reported in cynomolgus monkeys (*Macaca fascicularis*). The researchers injected the components of the system, *Cas9* mRNA and mixtures of 5 single-chain guide RNAs into 186 zygotes, 83 of which were transferred into 29 surrogate females. A total of ten pregnancies were established. So far, a female twin pair harbouring Cas9–RNA-mediated site-specific modifications in the simultaneously targeted genes *Pparg* and *Rag1* has been born. Of note, no off-target mutations were detected in either animal.

ORIGINAL RESEARCH PAPER Niu, Y. *et al.* Generation of gene-modified cynomolgus monkey via Cas9/RNA-mediated gene targeting in one-cell embryos. *Cell* **156**, 836–843 (2014)

DISEASE GENETICS

Insights into missing heritability

The significant association with prostate cancer risk of a newly identified cluster of common, low-penetrance germline single-nucleotide polymorphisms (SNPs) across the *HOXB* locus can be attributed to a previously identified rare, higher-penetrance causal variant. The study suggests the existence of a 'synthetic association' in cancer; that is, the genome-wide association (GWA) signal detected through the common SNPs is actually driven by the rare variant. This phenomenon could underlie other associations identified by GWA studies, which might account for a proportion of the missing heritability of complex diseases, propose Saunders and colleagues.

ORIGINAL RESEARCH PAPER Saunders, E. J. *et al.* Fine-mapping the *HOXB* region detects common variants tagging a rare coding allele: evidence for synthetic association in prostate cancer. *PLoS Genet.* **10**, e1004129 (2014)

EPIGENETICS

Mechanisms underlying fragile X syndrome

Fragile X syndrome is caused by silencing of the fragile X mental retardation 1 gene (*FMR1*) and consequent loss of its associated protein product. Silencing of *FMR1* was known to correlate with the presence of trinucleotide repeats adjacent to the *FMR1* promoter. Colak *et al.* now demonstrate that *FMR1* silencing is due to direct binding of the trinucleotide repeat region of *FMR1* mRNA to the *FMR1* promoter DNA. Formation of such DNA–mRNA duplexes may represent a general mechanism of epigenetic silencing in nucleotide repeat disorders.

ORIGINAL RESEARCH PAPER Colak, D. *et al.* Promoter-bound trinucleotide repeat mRNA drives epigenetic silencing in fragile X syndrome. *Science* **343**, 1002–1005 (2014)