Nature Reviews Genetics | Published online 9 May 2016

IN BRIEF

GENETIC ENGINEERING

A CORRECT step forward in disease modelling

A CRISPR–Cas9-based strategy enables the targeted introduction of homozygous or heterozygous sequence changes by homology-directed repair. The CORRECT (consecutive re-guide or re-Cas steps to erase CRISPR–Cas-blocked targets) method allows for the introduction of targeted modifications together with silent CRISPR–Cas-blocking mutations aimed at preventing 're-editing' due to high nuclease activity. Subsequent removal of the blocking mutations leaves only the intended modification. Using CORRECT, Paquet *et al.* generate human induced pluripotent stem cells with heterozygous and homozygous mutations in *APP* (which encodes amyloid-β precursor protein) and *PSEN1* (which encodes presenilin 1), genes linked to the development of dominant early-onset Alzheimer disease. Cortical neurons derived from these cells exhibited disease-associated phenotypes dependent on genotype.

ORIGINAL ARTICLE Paquet, D. *et al.* Efficient introduction of specific homozygous and heterozygous mutations using CRISPR/Cas9. *Nature* http://dx.doi.org/10.1038/nature17664 (2016)

GENETIC VARIATION

Genomic monomorphism off the scale

The generality of the small-population paradigm in conservation genetics is called into question by a recent report in *Current Biology*. It has long been thought that loss of genetic variation drives the extinction of isolated populations. However, an analysis of complete genome sequence data from Channel Island foxes (*Urocyon littoralis*) reveals a striking absence of genome-wide variation in these animals. Island fox populations have persisted over thousands of years despite extremely small population sizes and exhibit a two- to threefold increase in the homozygous state of deleterious variants, such as loss-of-function or missense variants. These findings suggest that selection has not purged harmful variants. Moreover, the San Nicolas Island fox exhibits what the authors call 'genomic flatlining', that is, a near absence of genetic variation, except in a few genes known to have high levels of ancestral variation, for example, olfactory receptor genes.

ORIGINAL ARTICLE Robinson, J. A. *et al.* Genomic flatlining in the endangered island fox. *Curr. Biol.* http://dx.doi.org/10.1016/j.cub.2016.02.062 (2016)

BIOINFORMATICS

Benchmarking transcript expression quantification

A new study presents a set of assessment metrics and visualization techniques for the statistical evaluation of algorithms for quantifying RNA sequencing data. The benchmarks are available as a R/Bioconductor package (http://bioconductor.org/packages/rnaseqcomp). The new set of interpretable assessment metrics relate to the quantification of differential, rather than absolute, expression levels. The authors apply these benchmarks, using two data sets, to seven competing algorithms, including mapping methods such as STAR, TopHat2 and Bowtie2, as well as quantification methods such as Cufflinks, eXpress, Flux Capacitor, kallisto, RSEM, Sailfish and Salmon. Taken together, the benchmarks reveal differences between the algorithms, and the overall performance for the quantification of differential gene expression was poor. An additional webtool (available at http://rafalab.rc.fas.harvard.edu/rnaseqbenchmark) enables users to evaluate the specificity and sensitivity of additional methods.

ORIGINAL ARTICLE Teng, M. *et al.* A benchmark for RNA-seq quantification pipelines. *Genome Biol.* **17**, 74 (2016)