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IN BRIEF

TECHNOLOGY

Less could be more for genome editing

Zinc finger nucleases (ZFNs) enable genome editing by generating site-specific double-stranded DNA breaks, but these lesions are prone to mutagenic repair by non-homologous end joining (NHEJ). Kim *et al.* engineered an inactivating mutation into one of the two FokI nuclease domains of a ZFN, resulting in a 'nickase' that made only single-stranded DNA breaks. These nickases successfully achieved genome editing in human cells, albeit with a lower efficiency than ZFNs. Importantly, nickases did not cause the NHEJ-mediated mutagenic insertions and deletions that are characteristic of ZFNs.

ORIGINAL RESEARCH PAPER Kim, E. *et al.* Precision genome engineering with programmable DNA-nicking enzymes. *Genome Res.* 20 Apr 2012 (doi:10.1101/gr.138792.112)

GENE–ENVIRONMENT INTERACTIONS

Environmental effects on disease gene penetrance

Homozygous mutations in *HES7* and *MESP2* — which encode Notch signalling pathway transcription factors — cause the spinal curvature defect congenital scoliosis. In a human mutation screen, Sparrow *et al.* found that heterozygous mutations in these genes also cause the condition, albeit at lower penetrance. Using mice heterozygous for these genes, the authors revealed that penetrance is increased by hypoxia during gestation. Transient hypoxia during mouse gestation disrupted embryonic WNT, fibroblast growth factor (FGF) and Notch signalling, providing a potential mechanistic explanation for how these genetic and environmental factors converge.

ORIGINAL RESEARCH PAPER Sparrow, D. B. *et al.* A mechanism for gene-environment interaction in the etiology of congenital scoliosis. *Cell* **149**, 295–306 (2012)

DISEASE GENETICS

Population differentiation in type 2 diabetes risk

Here the authors used a novel method to identify the distribution of disease risk allele frequencies across geographically distinct populations. They found that type 2 diabetes (T2D) risk alleles showed greater geographical differences in frequencies compared with risk alleles for other diseases and that their frequency decreased in the direction of human migration from Africa into East Asia. This was shown to contribute to the differing genetic susceptibility of these populations to T2D. One possible cause of this frequency variation is the differing energy storage and usage appropriate to the populations' environments.

ORIGINAL RESEARCH PAPER Chen, R. *et al.* Type 2 diabetes risk alleles demonstrate extreme directional differentiation among human populations, compared to other diseases. *PLoS Genet.* **8**, e1002621 (2012)

STEM CELLS

Mouse genetically tractable fertilization agent

Haploid embryonic stem cells have been previously derived and shown to be amenable to genetic analysis. This paper describes the derivation of mouse androgenetic haploid embryonic stem cells (AG-haESCs) that can be used to derive live mice; the use of haploid cells might provide a simple way to generate genetically manipulated animals. AG-haESCs maintain paternal imprints and contribute to multiple tissues when injected into diploid blastocysts. Injection of AG-haESCs into MII oocytes also leads to fertile offspring, and AG-haESCs can be genetically manipulated.

ORIGINAL RESEARCH PAPER Yang, H. *et al.* Generation of genetically modified mice by oocyte injection of androgenetic haploid embryonic stem cells. *Cell* **149**, 605–617 (2012)