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IN BRIEF

TECHNOLOGY

Characterizing CRISPR off-target effects

Off-target mutagenesis is an emerging problem when inducing site-specific DNA breaks for genome editing. Cho *et al.* used high-throughput DNA sequencing to characterize off-target mutagenesis in human cells during editing by the RNA-guided CRISPR–Cas system. They found that off-target mutagenesis occurs frequently at sites that differ by one nucleotide from the intended target site but substantially less frequently at sites with more than one mismatch. Off-target mutagenesis could be reduced through careful design of the guide RNA sequence and by using alternative nucleases to induce paired single-strand rather than double-strand DNA breaks.

ORIGINAL RESEARCH PAPER Cho, S. W. *et al.* Analysis of off-target effects of CRISPR/Cas-derived RNA-guided endonucleases and nickases. *Genome Res.* http://www.dx.doi.org/10.1101/gr.162339.113 (2013)

GENOMICS

Scaffolding DNA assemblies by 3D proximity

The short length of reads from current high-throughput sequencing technologies leads to ambiguities when mapping the genomic location of these reads. Kaplan and Dekker show that Hi-C chromosome conformation capture data, which report the three-dimensional (3D) proximity of DNA regions in cells, contain valuable information on the *cis*-connectivity of DNA. Supplementing human sequence contigs with Hi-C data from human cells facilitated the mapping of previously unmapped contigs and the *de novo* assembly of a genome scaffold. The method may be applicable to genomes of various species.

ORIGINAL RESEARCH PAPER Kaplan, N. & Dekker, J. High-throughput genome scaffolding from *in vivo* DNA interaction frequency. *Nature Biotech.* http://dx.doi.org/10.1038/nbt.2768 (2013)

NETWORKS

Integrating GWASs and protein interactions

Han *et al.* integrated data from genome-wide association studies (GWASs) with data from a human protein interaction network and identified a network of 39 genes that are associated with alcohol dependence. These genes are involved in processes that are relevant to underlying risk for alcohol dependence and are specific for this disorder, as they were not found to be significantly associated with three other complex human disorders. The unbiased nature of this approach and the focus on biological function at the protein level provide advantages over traditional pathway analysis methods.

ORIGINAL RESEARCH PAPER Han, S. *et al.* Integrating GWASs and human protein interaction networks identifies a gene subnetwork underlying alcohol dependence. *Am. J. Hum. Genet.* http://dx.doi.org/10.1016/j.ajhg.2013.10.021 (2013)

COMPLEX TRAITS

Non-coding polymorphism in *IRF4* reveals function

Interferon regulatory factor 4 (*IRF4*) had been associated with human pigmentation but, until now, had no known role in melanocyte pigmentation. The authors examined a single-nucleotide polymorphism in an intron of *IRF4* from a previous genome-wide association study and found that the associated allele impairs binding by transcription factor AP-2α (TFAP2A) and microphthalmia-associated transcription factor (MITF). In addition, cooperation of MITF, TFAP2A and IRF4 was found to be required for activation of the pigmentation enzyme tyrosinase.

ORIGINAL RESEARCH PAPER Praetorius, C. *et al.* A polymorphism in IRF4 affects human pigmentation through a tyrosinase-dependent MITF/TFAP2A pathway. *Cell* **155**, 1022–1033 (2013)