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IN BRIEF

EPIGENOMICS

Sperm as obesity propagator?

Donkin *et al.* propose that dynamic changes in the epigenome of human spermatozoa in response to the environment may underlie the heritability of obesity. Micrococcal nuclease sequencing (MNase-seq), small non-coding RNA (sncRNA) sequencing and reduced-representation bisulfite sequencing (RRBS) were used to characterize nucleosome positioning, sncRNA expression, and DNA methylation, respectively, in spermatozoa from 13 lean, glucose-tolerant and 10 obese, glucose-intolerant men. These approaches yielded a comprehensive epigenomic profile specific to obesity; sncRNA expression and DNA methylation patterns differed substantially between lean and obese men. In a separate cohort of men with morbid obesity, weight loss (resulting from bariatric surgery) led to marked remodelling of the obesity-associated DNA methylation pattern of spermatozoa. DNA methylation was affected mainly in genetic loci that have previously been implicated in the central control of appetite.

ORIGINAL ARTICLE Donkin, I. *et al.* Obesity and bariatric surgery drive epigenetic variation of spermatozoa in humans. *Cell Metab.* http://dx.doi.org/10.1016/j.cmet.2015.11.004 (2015)

TECHNIQUE

Mapping open chromatin in single cells

A new high-resolution approach for the genome-wide detection of DNase I hypersensitive sites (DHSs) can be applied to single cells. Approximately 317,000 unique reads and 38,000 DHSs, on average, were detected per single cell by single-cell DNase sequencing (scDNase-seq). The authors show that pooled DHSs of five single NIH3T3 cells correlate significantly with those of 1,000 cells, and single-cell DHS patterns are highly reproducible between individual cells. Single-cell DHSs predicted enhancers that regulate cell-specific gene expression programmes, and cell-to-cell variations of individual DHSs were predictive of gene expression. scDNase-seq of cells dissected from formalin-fixed paraffin-embedded tissue slides obtained from patients with thyroid cancer identified thousands of tumour-specific DHSs.

ORIGINAL ARTICLE Jin, W. *et al.* Genome-wide detection of DNase I hypersensitive sites in single cells and FFPE tissue samples. *Nature* http://dx.doi.org/10.1038/nature15740 (2015)

GENETIC SCREENS

CRISPR knockout screens for human fitness genes

A new high-complexity, genome-scale CRISPR–Cas9 guide RNA (gRNA) library is presented in *Cell*. The Toronto KnockOut (TKO) library includes a total of 176,500 sequences that target 17,661 protein-coding genes. The authors used the library to screen five human cell lines to identify those genes for which knockouts would result in substantial fitness defects. The TKO library enabled the identification of a greater number of fitness genes than previous RNA interference or CRISPR screens. Further investigations distinguished core from context-dependent fitness genes, giving insights into cell-type-specific biological processes. A data-driven approach was used to identify context-specific oncogenic drivers.

ORIGINAL ARTICLE Hart, T. *et al.* High-resolution CRISPR screens reveal fitness genes and genotype-specific cancer liabilities. *Cell* http://dx.doi.org/10.1016/j.cell.2015.11.015 (2015)