
Credit: Dušan Zidar/Alamy

used for inferences about transcriptional or post-transcriptional gene regulatory mechanisms, such as enhancers or heterochromatic domains (demarcated by histone marks) or microRNAs (based on sequence and expression data), and to dissect their relative contributions to gene expression.

This study highlights that mRNA expression levels are predictable to a substantial degree from features derived solely from genomic sequence; the authors estimate that "promoter sequences alone explain ~50% of gene expression variability in humans". Future algorithms that incorporate non-promoter regulatory elements could improve this prediction model.

Linda Koch

ORIGINAL ARTICLE Agarwal, V. & Shendure, J. Predicting mRNA abundance directly from genomic sequence using deep convolutional neural networks. *Cell Rep.* **31**, 107663 (2020)
RELATED ARTICLES Eraslan, G. et al. Deep learning: new computational modelling techniques for genomics. *Nat. Rev. Genet.* **20**, 389–403 (2019)

> "competitive fitness of a mutant clone is dependent on the genotype of its neighbours"

observed clonal dynamics for a number of simple scenarios.

Next, the authors experimentally validated two key predictions of the NCF model. First, they showed that expansion of highly competitive clones carrying a dominant-negative inhibitor of Notch signalling (*DN-Maml1*) was constrained in DEN-treated mice compared with untreated controls. This finding indicates that clone growth is restricted by the presence of other mutant clones with similar competitive fitness. Second, they used lineage analysis of cells at different positions within *DN-Maml1* clones to confirm that winner clones expand more where they border loser cells than where they are surrounded by other winners.

The authors propose that clonal competition in human ageing oesophageal epithelium, and possibly other tissues, may occur by similar mechanisms to those uncovered in the mouse.

Dorothy Clyde

ORIGINAL ARTICLE Colom, B. et al. Spatial competition shapes the dynamic mutational landscape of normal esophageal epithelium. *Nat. Genet.* https://doi.org/10.1038/s41588-020-0624-3 (2020)

CHROMOSOME BIOLOGY

Sequencing sperm to untangle meiotic variation

Human meiosis is highly variable. While existing methods have provided useful insight into this variation, they are limited by the number of meiotic phenotypes, gametes or individuals that can be analysed in parallel. Now, a study in *Nature* describes Sperm-seq, a single-cell sequencing approach that enables genome-wide analysis of multiple meiotic phenotypes in thousands of sperm simultaneously.


Credit: Ed Buziak/Alamy

Bell et al. used Sperm-seq and accompanying computational methods to sequence and analyse 31,228 sperm cell genomes from 20 young donors (18–38 years old). The team focused on a range of meiotic phenotypes, including recombination rate, crossover location and spacing, and aneuploidy.

First, phased parental haplotypes were inferred for each donor genome. Then, crossover events in each sperm genome were identified and located based on switches from one parental haplotype to the other. A total of 813,122 crossovers were detected across all cells. Among donors, recombination rates ranged from 22.2 to 28.1 crossovers per cell (s.d. 1.53). Variation between gametes, which ranged from 17 to 37 events per cell (s.d. 4.23), was higher than between individuals. Notably, the global recombination rate in individuals was indicative of the crossover rate at each chromosome; and, in gametes, the number of crossover events in one-half of the genome reflected the number in the other half. Thus, factors affecting crossover frequency act throughout the nucleus, rather than locally.

Analyses of crossover location and spacing revealed that both parameters varied greatly among donors, with use of proximal (centromeric) crossover zones more variable than distal (telomeric) zones. However, use of distal zones and crossover spacing were found to be inversely correlated with recombination rate. These relationships held true when the analysis was restricted to chromosomes with exactly two crossovers and applied both to donors and to single cells. Taken together, these observations suggest that variation in crossover location and spacing reflects underlying biological variation between people and between cells rather than an indirect effect of the number of crossovers on a chromosome.

Aneuploidy was detected for all chromosomes and donors, ranging from 0.010 to 0.046 aneuploidy events per cell in donors, a 4.5-fold difference that seemed to reflect true inter-individual variation. Crossovers are thought to protect against aneuploidy during maternal meiosis. Analysis of chromosome gains originating in meiosis I (when recombination occurs) suggested that crossovers are similarly protective in sperm, as 36% fewer crossovers were detected than matched, properly segregated chromosomes.

Taken together, the study shows that certain meiotic phenotypes, such as high recombination rate, closely spaced crossovers and proximally located crossovers, co-vary across chromosomes, gametes and donors. The authors propose that inter-cell and inter-individual variation in meiotic chromosome compaction — and therefore the number of crossover events — could explain this covariance.

Dorothy Clyde

ORIGINAL ARTICLE Bell, A. D. et al. Insights into variation in meiosis from 31,228 human sperm genomes. *Nature* https://doi.org/10.1038/s41586-020-2347-0 (2020)