IN BRIEF

SEQUENCING TECHNOLOGIES

Microdroplet-based PCR enrichment for large-scale targeted sequencing

Tewhey, R. *et al. Nature Biotech.* 1 Nov 2009 (doi:10.1038/nbt.1583)

Human genome sequencing using unchained base reads on self-assembling DNA nanoarrays

Drmanac, R. *et al. Science* 5 Nov 2009 (doi:10.1126/science.1181498)

Genome sequencing for large-scale population-based studies requires technologies that are reliable, high-throughput and affordable — aims that are addressed by two recent papers. Tewhey and colleagues describe a new approach for targeted sequencing — a strategy that will remain important until the cost of whole-genome sequencing falls. They developed an enrichment approach that involves singleplex PCR carried out in microdroplets. This method enables 1.5 million parallel amplifications, achieves high levels of specificity and sensitivity, and has advantages over other enrichment methods in terms of the uniformity of coverage and the ability to capture sequences that have highly similar counterparts elsewhere in the genome. Drmanac and colleagues report a new genome sequencing platform that should reduce the cost of whole-genome sequencing. They used combinatorial probe anchor ligation chemistry (cPAL) in combination with DNA nanoballs on patterned nanoarrays to sequence three human genomes, at a coverage of between 45- and 87-fold. The method is highly accurate and benefits from an average cost of just US$4,400 per genome for consumables.

DEVELOPMENT

Analysis of cell fate from single-cell gene expression profiles in *C. elegans*

Liu, X. *et al. Cell* **139**, 623–633 (2009)

The authors created a single-cell resolution gene expression database for *Caenorhabditis elegans* using an automated, high-throughput method to analyse images of worms expressing fluorescent reporter constructs for 93 genes. As the cell lineage pattern in *C. elegans* is invariant, they could track the expression patterns in distinct cell lineages during development. They found that cells with identical fates can be formed by different transcriptional programmes. The digital gene expression atlas generated in this study is expected to be a useful resource for examining the molecular characteristics of cell fate.

POPULATION GENETICS

The relationship between imputation error and statistical power in genetic association studies in diverse populations

Huang, L., Wang, C. & Rosenberg, N. A. *Am. J. Hum. Genet.* 22 Oct 2009 (doi:10.1016/j.ajhg.2009.09.017)

In case–control association studies, imputation strategies are a powerful means of testing markers that have not actually been genotyped. The authors relate the imputation error rate to loss of statistical power across 29 populations: each 1% rise in the error rate requires a substantial increase in sample size (5–13%) to maintain power. Size increases could be up to 150% in populations in which genotypes are difficult to impute. These data should help to inform study designs and develop resources to minimize imputation error.