Footprinting the yeast genome

Eukaryotic genomes are highly organized systems of DNA interacting with regulatory proteins. Over the years, several technologies have been developed to identify the DNA motifs that certain proteins bind to, but they require a priori knowledge of the bound proteins and protein-specific reagents, and they do not provide nucleotide-level resolution. Stamatoyanopoulos and colleagues wanted an unbiased look at the genome-wide protein occupancy on DNA in vivo. They mapped genome-wide DNase I cleavage sites in yeast by deep sequencing and analyzed the resulting protected protein footprints for known and de novo protein binding motifs. Their data also allowed them to position the nucleosomes flanking the binding sites and thus combine protein binding data with chromatin structure information.

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Facilitating stem cell transplants

With their potential for differentiation, stem cells are ideal candidates for transplants to replace diseased tissue; however, as with all transplants, the risk of rejection by the host is high. Two research teams have tackled the question of how graft rejection can be circumvented in a rat and mouse model, respectively. Kelly and colleagues exposed neonatal rats to human stem cells and showed that these desensitized rats, while fully immunocompetent, tolerated engraftment of the human stem cells in their brains. Waskow, Rodewald and co-workers created a universal recipient mouse that tolerates engraftment of allogeneic hematopoietic stem cells into its bone marrow without prior irradiation.

Brief Communications p267, p271

Cell surface scans with a hopping probe

Several approaches exist to map the surface of cells, but achieving high resolution under physiological conditions in living cells remains a challenge. Korchev, Klenerman, Frolenkov and colleagues now present hopping probe ion conductance microscopy (HPICM). The method is based on scanning ion conductance microscopy, which is limited to relatively flat surfaces. By using the nanopipette probe in ‘hopping mode’, where it repeatedly approaches the sample from a position above the topological features being scanned, HPICM can be applied to live cells with substantial surface topologies. The researchers imaged live mammalian auditory hair cells and networks of hippocampal neurons at a resolution of tens of nanometers.

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Finding rare alleles

Many diseases are the result of a large number of genetic variants that, individually, are often rare and consequently difficult to find. High-throughput sequencing has advanced their identification, and several diseases have been associated with certain sequence variants, most commonly single-nucleotide polymorphisms (SNPs). Despite its power, the inherent limitation of deep sequencing is the error rate of the technology, below which it is impossible to discern whether a variant is due to a mutation or a sequencing error. Mitra and colleagues developed a new SNP calling algorithm, based on large deviation theory, which takes the position in the sequencing read and the identity of the two upstream bases into account. They sequenced over a thousand patients at select loci and detected variants with a minor allele frequency as low as 0.5%.

Brief Communication p263

Watching fruit flies interact

The quantitative study of animal behavior requires laborious observation. But computers can help. Anderson, Perona and colleagues report a method based on machine vision to analyze social interactions in pairs of Drosophila. Applied to videos of fly pairs, the new software can accurately identify the individual stereotypical actions of fly courtship and aggression. It also detects expected differences in fly behavior resulting from either genetic or circuit-level perturbation. Notably, the method allows a dramatic reduction in the time and effort involved in such experiments, thus opening up the study of Drosophila social interaction to genetic and other screens.

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