IN BRIEF

GENOMICS

Sequence-based prediction of variants' effects

Zhou, J. et al. *Nat. Genet.* https://doi.org/10.1038/s41588-018-0160-6 (2018).

Inspired by Harry Potter's rallying cry "Expecto Patronum," which summons a protective spirit out of thin air, Zhou et al. developed their own version of ExPecto to predict tissue-specific gene expression from DNA sequence alone. ExPecto is a deep learning framework trained on sequences from over 200 tissues and cell types; it does not require information on variants for training and can therefore assess the transcriptional effect of any mutation, observed or yet unobserved, within a radius of up to 40 kb around promoters. The researchers confirmed ExPecto's predictions with known expression quantitative trait loci and massively parallel reporter assays and used its output to prioritize variants in genome-wide association studies. They show that some putative functional single-nucleotide polymorphisms exert allele-specific regulation. ExPecto allows the definition of a variation potential for each gene, and the systematic probing of tissue-specific effects of any mutation on gene expression. *NR*

https://doi.org/10.1038/s41592-018-0087-y

CHEMISTRY

Self-assembled 'silicages'

Ma, K. et al. *Nature* **558**, 577–580 (2018).

Self-assembled nanostructures with highly symmetrical, cage-like polyhedral shapes are usually made of programmable organic biomaterials such as DNA. Wiesner and colleagues have now developed a system for the self-assembly of inorganic silica nanostructures that are directed by surfactant micelles. The researchers took advantage of cryo-EM and single-particle 3D reconstruction to accurately identify <10-nm individual silica nanoparticles with dodecahedral cage-like features, called 'silicages'. It is likely that these nano-sized silicages are formed via Coulomb interaction between positively charged surfactant micelles and negatively charged silica clusters in aqueous solutions. This micelle-directed assembly method enables researchers to distinguish the inside and outside of the cage, which holds great potential for applications ranging from catalysis to drug delivery. Additionally, these self-assembled nanoscale inorganic cages are not limited to silica materials, but also can be produced from gold, silver, and vanadium oxide. *LT*

https://doi.org/10.1038/s41592-018-0088-x

GENOMICS

Tumor genetic analysis from single-cell RNA-seq data

Fan, J. et al. *Genome Res.* https://doi.org/10.1101/gr.228080.117 (2018).

Single-cell RNA-seq offers a powerful way to dissect expression in heterogeneous tumors, but it cannot relate expression differences to genetic clones. Sequencing of both DNA and RNA from individual cells is possible, but it remains relatively costly. As an alternative, Fan et al. have developed a hidden Markov model integrated Bayesian approach for detecting copy-number variants (CNVs) and loss of heterozygosity from single-cell RNA-seq data (HoneyBADGER). The software identifies candidate focal CNVs by jointly analyzing single-nucleotide polymorphisms in a given region for allelic imbalance, taking the expected rate of monoallelic detection into account. The researchers show that the tool can genotype large deletions and CNVs in simulated data, multiple myeloma, acute myeloid leukemia, and breast cancer samples, even from 3′-tag RNA-seq data. Their analysis identifies some transcriptional signatures that correspond to genetic clones, and others that do not. *TN*

https://doi.org/10.1038/s41592-018-0089-9

NEUROSCIENCE

Improving retrograde labeling of neurons

Li, S.-J. et al. *Neuron* **98**, 905–917 (2018).

Retrograde labeling of neurons via viral infection at their terminals allows the neurons to be manipulated on the basis of their projections. However, current viral tools have disadvantages such as neurotoxicity and limited tropism. CAV-2 (canine adenovirus type 2) is a good example: this benign virus has been used for retrograde labeling but can infect only a narrow range of neurons. Li et al. have now overcome CAV-2's limited tropism by establishing a complementation strategy. They transduce cells of interest with an adeno-associated virus (AAV) vector that delivers a receptor called CAR, which is recognized by CAV-2 and facilitates its uptake. CAV-2 can then deliver Cre to the cells, leading to the expression of Cre-dependent effector genes. Furthermore, Li et al. generated a suite of AAV vectors that encode Cre-dependent effectors such as fluorescent proteins, calcium sensors or channelrhodopsin. This strategy allowed the researchers to label projection neurons that have not been amenable to retrograde targeting. The approach also works in rats. *NV*

https://doi.org/10.1038/s41592-018-0090-3

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