IN BRIEF

GENOMICS

Exploring class 1 CRISPR systems

Nat. Biotechnol. http://doi.org/dcg9 (2019).

The CRISPR–Cas systems comprise two classes: multi-subunit effector class 1 and single-effector class 2. Class 2 systems, such as Cas9 and Cas12a, have been widely used as genome-editing tools. The more complicated class 1 systems, although accounting for the majority (about 90%) of CRISPR–Cas systems, have rarely been repurposed for genome editing. The reason behind the unpopularity is that class 1 systems rely on multiple Cas subunits to form a complex known as Cascade (CRISPR-associated complex for antiviral defense). Pickar-Oliver et al. explored type I variants of class 1 systems from *Escherichia coli* and *Listeria monocytogenes*. The expression and the formation of Cascade complexes are validated in bacterial cells and human cells. To demonstrate utility in human cells, they reprogrammed Cascade for targeted transcriptional modulation by tethering an activation domain or a repression domain to the Cascade complex. The multiple Cas subunits offer more options for fusing functional domains with improved flexibility. *LT*

https://doi.org/10.1038/s41592-019-0642-1

NEUROSCIENCE

Massively parallel intracellular recordings

Nat. Biomed. Eng. http://doi.org/dchb (2019).

Multi-electrode arrays can record from thousands of neurons, but these recordings are extracellular and do not pick up subthreshold events that allow assessment of synaptic connectivity. Such measurements have been the domain of patch-clamp electrodes, with the caveat of low throughput. Abbott et al. describe complementary metal-oxide-semiconductor (CMOS) neuroelectronic interphases (CNEI) that can intracellularly record from thousands of neurons simultaneously. The CNEIs can be operated in either pseudocurrent clamp or in pseudovoltage clamp, in analogy to the recording modes of patch-clamp electrodes. The researchers demonstrated the capabilities of their CNEIs by acquiring intracellular recordings from cultured neurons while pharmacologically manipulating the cultures. In addition, the researchers assessed synaptic connectivity at a network-wide scale. Recordings can last for several minutes and, with the ability of monitoring thousands of neurons, datasets can be acquired at unprecedented scale with the CNEI technology. *NV*

https://doi.org/10.1038/s41592-019-0644-z

GENE EXPRESSION

The *C. elegans* embryonic transcriptome

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Caenorhabditis elegans has an invariant lineage during development, and is an ideal model organism for studying gene-expression dynamics in different lineages and cell types. Single-cell RNA-seq has been used to profile transcriptomic heterogeneity and changes in *C. elegans* development, however, challenges such as confounding factors and limited data still exist. To portray a near-complete atlas of *C. elegans* embryonic transcriptome, Packer et al. generated single-cell RNA-seq data for 86,024 embryonic cells covering 87% of lineage branches. Integration with other data, such as bulk RNA-seq time series and fluorescent reporter imaging data from the EPiC and WormBase, allowed them to manually annotate 93% of cells in the dataset with a cell type or a cell lineage. Detailed analysis of this comprehensive resource revealed transcription factors underlying cell fate determination, global patterns of gene expression, and correlations between cell lineage and the transcriptome. *LT*

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MICROSCOPY

MIET with graphene

Nat. Photon. http://doi.org/c93w (2019).

Single-molecule localization microscopy approaches achieve high lateral localization accuracy and precision. However, methods for achieving similarly high axial localization precision have tended to be more specialized or technically complex. Metal-induced energy transfer (MIET) is an established approach for accurate determination of an emitter's axial position, based on the fluorescence modulation caused by the electromagnetic coupling of an emitter to surface plasmons in an underlying metal layer. Ghosh et al. now further improve this approach by demonstrating that replacing the metal layer with a graphene layer also allows for electromagnetic coupling, but with a smaller coupling range, which leads to a tenfold improvement in axial localization determination compared to conventional MIET. The researchers demonstrated that their approach can achieve sub-nanometer localization accuracy with low photon budgets, an impressive achievement for localization microscopy. *RS*

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