IN BRIEF

NEUROSCIENCE

Optogenetic inhibition

Li, N. et al. *Elife* **8**, e48622 (2019).
Babl, S.S. et al. *Cell Rep*. https://doi.org/10.1016/j.celrep.2019.09.049 (2019).

Optogenetic inhibition is typically achieved by expressing an opsin of choice in the desired target region or across the whole brain, followed by illumination of the brain region of interest. However, inhibition can reach much farther than the illumination volume. Babl et al. and Li et al. have independently examined the spread of optogenetic silencing. Inhibition can be achieved directly by expressing an inhibitory opsin in the neurons of choice or indirectly by expressing channelrhodopsin2 in GABAergic interneurons. The findings suggest that the indirect strategy typically results in more widespread silencing than the direct strategy, and it requires less intense light. Conversely, optogenetic silencing can be confined to smaller areas by using a viral rather than a transgenic expression strategy. The results also showed that direct labeling of neurons with GtACR1, a potent inhibitory opsin, results in silencing as strong as that of the indirect strategy. However, at high light intensities, GtACR1 can have the opposite effect and result in activation, which should be avoided. These studies should provide guidance on which opsins to use in different scenarios. *NV*

https://doi.org/10.1038/s41592-019-0712-4

NANOBIOTECHNOLOGY

Aerolysin nanopores

Cao, C. et al. *Nat. Commun.* **10**, 4918 (2019).

Nanopores are useful tools for sensing, especially in regard to long-read DNA sequencing, as well as into proteomic applications and beyond. As such, a great deal of research has gone into identifying artificial and biological nanopores to optimize and expand their applicability. One well-characterized nanopore is aerolysin, a β-pore-forming toxin from *Aeromonas hydrophila*. To expand the versatility of aerolysin, Cao et al. first sought to understand the structure–function relationship of this pore. They used a range of computational and biophysical techniques to reveal that the ion selectivity and sensing are conferred by a combination of the narrow diameter of the protein's 'cap' and electrostatics. The researchers also identified mutants with improved molecular detection of nucleic acids and peptides. Their results highlight the utility of aerolysin and the benefits of mutational strategies for improving nanopore-based sensing. *RS*

https://doi.org/10.1038/s41592-019-0718-y

SENSORS AND PROBES

Small-molecule sensors

Glasgow, A. A. et al. *Science* **366**, 1024–1028 (2019).

The ability to sense small molecules with high sensitivity and specificity has yielded important insights into biology. Although fluorescent protein-based sensors for a wide range of small molecules have been developed, these often rely on specific cellular proteins that have evolved to bind the ligand of interest, and therefore broadly general strategies for making new sensors are lacking. Glasgow et al. have harnessed the power of computational protein design to address this challenge. In their approach, a binding site for a small molecule is designed and engineered into the binding interface of two proteins such that they only dimerize in the presence of the target molecule. These proteins are also fused to two halves of a split luminescent or fluorescent reporter, and only upon target binding and dimerization does the split reporter interact to yield signal. The researchers developed sensors against multiple targets and further showed that the crystal structures with bound ligand closely match the computational predictions. *RS*

https://doi.org/10.1038/s41592-019-0714-2

CELL BIOLOGY

Primate post-implantation development in a dish

Ma, H. et al. *Science* **366**, eaax7890 (2019).
Niu, Y. et al. *Science* **366**, eaaw5754 (2019).

The early post-implantation stage is critical in the development of a mammalian embryo. During this time, the association with maternal tissue is set up and strengthened, and the embryo itself undergoes formative rearrangements as the anterior–posterior axis emerges and the germ layers are formed. Mouse embryogenesis differs from human embryogenesis during this time, and more suitable models are therefore desirable. Ma et al. and Niu et al. have established culture conditions for macaque embryos that allow development up to 20 days post-fertilization. Embryos cultured under these conditions undergo the major developmental processes of primate post-implantation processes. They form epiblast and hypoblast lineages, they establish amniotic and yolk sac cavities, they generate primordial germ cells, they specify the anterior–posterior axis, and they gastrulate. This technology provides access to the transcriptomic and epitranscriptomic program at a crucial developmental stage and enables lineage studies in macaque embryos. *NV*

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