# TOOLS IN BRIEF

NEUROSCIENCE

## Optogenetic access to opioid signaling

Despite the clinical interest in opioid drugs, the function of opioid receptors is difficult to study with high spatial, temporal and cell type–specific precision. Siuda *et al*. generated a light-controlled opioid-like receptor called opto-MOR. This designed receptor is a hybrid between the intensely studied mu-opioid receptor (MOPR) and a rat rhodopsin and is made possible by the structural similarities of the parent molecules. Opto-MOR exhibits expression levels similar to those of MOPR and activates the same signaling pathways when stimulated with blue light. The researchers applied the tool to study the effects of opioid signaling in different regions of the mouse brain. For instance, activation of opto-MOR in the ventral pallidum led to aversive behaviors, whereas the same manipulation in the rostromedial tegmental nucleus had the opposite effect.

Siuda, E.R. *et al. Neuron* **86**, 923–935 (2015).

STEM CELLS

## Sub-primed pluripotent stem cells

Embryonic stem cells derived from the mouse inner cell mass and epiblast stem cells (EpiSCs) from the post-implantation embryo (corresponding to 'primed' human embryonic stem cells) represent two time points in development. Wu *et al*. reasoned that spatial positioning in the early embryo may also define other distinct stem cell populations. By optimizing epiblast cell culture conditions, they identified stable, region-selective pluripotent stem cells (rsEpiPSCs) that resemble EpiSCs but selectively engraft to the posterior of epiblast-stage embryos. rsEpiPSCs are derived with perfect success, and they proliferate more rapidly and show high cloning efficiencies compared with traditional EpiSCs. The new cell type has distinct transcriptional, methylation and metabolic profiles. Similar culture conditions can derive human rsEpiPSCs. The ease of isolating and manipulating these cells makes them valuable for future stem cell work.

Wu, J. *et al. Nature* **521**, 316–321 (2015).

CELL BIOLOGY

## Efficient transduction of proteins into eukaryotic cells

The direct delivery of a protein into eukaryotic cells allows scientists to study its function without resorting to genetic manipulation. However, existing methods are inefficient or require the protein to be tagged with a cell-penetrating peptide. D'Astolfo *et al*. describe a method called induced transduction by osmocytosis and propanebetaine (iTOP) for the delivery of native proteins and other compounds into cells. In iTOP, cells are mixed with the protein of interest and a special buffer containing sodium chloride and nondetergent sulfobetaine 201. Upon incubation, the protein is efficiently delivered to cells in a concentration-dependent manner. The authors demonstrated the method in multiple cell types, including stem cells, and used it to deliver Cas9 and a guide RNA to demonstrate gene targeting without exogenous gene expression.

D'Astolfo, D.S. *et al. Cell* **161**, 674–690 (2015).

NEUROSCIENCE

## Neurons on the blink

Optogenetic approaches to activate neurons are widely used in neuroscience, but inhibitory tools are less well established. Cosentino *et al*. engineered a blue light–induced $K^+$ channel by fusing the viral $K^+$ channel Kcv with the LOV2-J$\alpha$ light switch and optimizing the dynamic range and expression level of the engineered protein. The resulting channel, named BLINK1, is selective for potassium ions and is highly conductive. Its slow activation and deactivation kinetics make the channel an ideal tool for applications that require neural inactivation over long periods of time. The researchers demonstrated the *in vivo* suitability of BLINK1 in zebrafish. Under blue light illumination, fewer larvae showed an escape response after touch if injected with mRNA encoding BLINK1, behavior consistent with the inhibitory role of BLINK1.

Cosentino, C. *et al. Science* **348**, 707–710 (2015).