ANIMAL DISEASE MODELS

A Saethre-Chotzen fish

Teng, C.S. et al. *eLife doi:* https://doi.org/10.7554/eLife.37024 (2018)

Children born with Saethre-Chotzen syndrome experience premature fusion of the bones of their skull, which impedes the growth of the brain and the symmetrical development of the head and face. It's a rare genetic disease caused by mutations in one of two genes involved in the development of cranial sutures, the sites where cranial bones come together. Mouse models can recapitulate the syndrome, but only offer researchers a post-natal view.

To study potential pre-natal factors that could influence Saethre-Chotzen syndrome, researchers at the University of Southern California developed a zebrafish model. Even though different cell lineages are involved in the fish and in mammals, the underlying processes that direct cranial suture development and fusion appear to be conserved: mutant zebrafish developed cranial defects, related to abnormalities in their stem cells, early in their embryonic development. *EPN*

https://doi.org/10.1038/s41684-018-0212-7

NEUROSCIENCE

Waking up with the thalamus

Ren, S. et al. *Science* **362**, 429–434 (2018)

How does your brain actually wake you up? It's been a mystery, but new research in mice suggests the thalamus has something to do with it.

In humans, injuries to the thalamus can result in comas. So the research team started by looking at neuronal activity in the thalamus of mice as they slept and woke normally. They observed that neurons in the paraventricular region of the thalamus were more active than others while the animals were awake. Activity in those neurons declined as the mice transitioned into sleep, and increased as they started to wake up. When the researchers inhibited those neurons, the mice became and stayed sleepy; when they activated them, the mice woke up. *EPN*

https://doi.org/10.1038/s41684-018-0213-6

TARGETED GENE REPAIR

Base editors versus PKU

Villiger, L. et al. *Nat. Med.* **24**, 1519–1525 (2018)

Phenylketonuria (PKU) is a heritable disease caused by loss-of-function mutations to enzymes involved in liver cell metabolism. Special diets can help prevent symptoms in humans and adding the missing enzyme can treat the condition in PKU mouse models, but there is no cure. The genetic basis of the disease makes it a candidate for gene editing, but previous attempts to edit the mouse liver haven't proved particularly efficient.

Base editing might be a more fruitful strategy, suggests new research from a team of Swiss researchers. Such approaches are able to change a base in a DNA sequence without having to break and the repair both strands, reducing potential off-target effects. The researchers delivered the base editor in two portions to the liver of adult mice modeling PKU via dual adeno-associated viral vectors and observed correction rates up to 63%. *EPN*

https://doi.org/10.1038/s41684-018-0214-5

FLUORESCENCE IMAGING

The brain sees red

Kannan, M. et al. *Nat. Methods* https://doi.org/10.1038/s41592-018-0188-7 (2018)

VARNAM is the Sanskrit word for 'hue' and also the acronym for a new genetically encoded voltage indicator recently developed by researchers at Yale and Stanford universities. Short for "voltage-activated red neuronal activity monitor," the indicator fluoresces at the red end of the visual spectrum whenever it detects a voltage change, such as the firing of a neuron. VARNAM is faster, brighter, and more sensitive than previously engineered red fluorescent indicators.

The researchers describe the screening process to identify VARNAM and demonstrate its functionality in murine brain slices, *Drosophila*, and behaving adult mice in *Nature Methods*. The indicator can be used alone or alongside other colored optical tools to provide multispectral functional imaging in vivo. *EPN*

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