TOOLBOX

Viral sidekick allows CRISPR to reliably edit neuron DNA

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A new trick involving a virus gives the CRISPR enzyme system the ability to edit the genome of a neuron more predictably than was previously possible[1].

The technique enables researchers to target any brain area in mice of any age. The researchers described the approach 15 November in *Neuron*.

Genome editing with CRISPR breaks DNA strands at specific locations. The cell repairs the damage using one of two methods. In one of them, proteins find the broken ends and quickly fuse them together, causing the cell to unpredictably insert or delete DNA letters.

The other method, homology-directed repair, is more precise: The cell connects the broken strands using a DNA template that overlaps either side of the break. By providing the template, scientists can add, modify or delete a desired sequence where CRISPR cuts. However, this method does not work reliably in non-dividing cells, including most neurons, because the cellular machinery involved only shows up during cell division.

So the researchers packaged the genes for the machinery into a virus that can infect neurons. The virus carries the DNA template along with RNA snippets that guide the CRISPR enzyme, called CAS9, to a specific location in the genome. Its payload also includes a tag that attaches to the target gene and glows when the desired type of gene editing occurs.

The researchers targeted the gene for CaMKIIa, an enzyme that shows up exclusively in neurons. They injected the virus into the brains of newborn mice genetically engineered to make CAS9. A week later, they found glowing spots in brain slices from the mice, indicating that the gene was successfully edited in mature neurons.

The researchers also injected ordinary mice with a virus that carried the genes for CAS9, as well as

another virus that delivered the rest of the gene-editing cargo. Again, the mature neurons glowed. Up to 30 percent of the neurons in the slices showed signs of editing.

The researchers used the technique to edit two other genes in the mouse genome. The method also works in rat neurons and is likely to translate to other animals as well, the researchers say.

REFERENCES:

1. Nishiyama J. *et al. Neuron* **96**, 755-768 (2017) **PubMed**