NEUROSCIENCE

Trapping fluorescence in the soma

Tethering fluorescent proteins to ribosomes clears up background signals when imaging neural circuits.

In vivo studies of neural circuitry often involve imaging fluorescent reporters. However, fluorescently labeled cell bodies are embedded in between neurites from other fluorescent neurons, leading to high background. To overcome this problem, fluorescent reporters have been targeted to the soma by fusing them to soma-targeting peptides. The team of Jennifer Garrison from the Buck Institute for Research On Aging in Novato, California, and their collaborators from the University of California, San Francisco have developed an alternative strategy for soma-targeting fluorescent reporters.

When the researchers imaged GFP in cells containing an Nano-L10 transgene, they observed exceptionally bright signals. The Nano-L10 transgene leads to the expression of a GFP nanobody on the surface of ribosomes, which then recruits GFP and in turn concentrates GFP in the cell body.

The researchers extended this approach to the calcium sensor GCaMP6. Here, the researchers directly fused the sensor to the ribosomal protein L10 to generate ribo-GCaMP6. When ribo-GCaMP6 was expressed in the mouse brain, the sensor was tightly restricted to neuronal cell bodies and faithfully reported neuronal activity.

Ribo-GCaMP6 proved to be useful in a variety of different scenarios. The researchers imaged neuronal activity in the mouse visual cortex in response to visual stimuli, using two-photon microscopy, and in the medial prefrontal cortex of behaving mice through a GRIN lens, using single-photon microscopy. Furthermore, they applied ribo-GCaMP6 in *Caenorhabditis elegans*, where soma-targeting showed advantages over the commonly used nuclear targeting of calcium sensors.

Notably, ribo-GCaMP6 does not lead to any toxicity, which Garrison ascribes to quality control mechanisms around ribosome biology. "Over at least six months, we didn't see anything that was toxic or we didn't see a decrease in signal fidelity, which was really fantastic," says Garrison. She hopes that the tools will be useful to the community. "I'm really excited to see how people use the tools to make discoveries."

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