TOOLBOX

Easy-to-make solution turns brains transparent

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Gummy mice: After soaking for two weeks in a simple chemical cocktail, mouse embryos become transparent.

Three common laboratory chemicals are all scientists need to create see-through brains ideal for visualizing complex neural circuits, according to a study published 30 August in *Nature Neuroscience*[1].

The basic architecture of individual neurons is well known, but **mapping the millions of connections** that make up the brain's neural circuits remains a challenge. Because light can only penetrate a short depth into opaque substances, microscopy techniques rely on **slicing brain regions into thin sections** that are subsequently reconstructed into three-dimensional images.

Another option is to use commercially available solutions that can render tissues transparent. These are typically expensive, however, and because their composition is unknown to researchers, they cannot be optimized for different experiments. These reagents also partially quench the fluorescent signals that researchers rely upon to visualize neurons.

The ideal solution, it turns out, is already sitting above most researchers' benches: A compound made up of urea, glycerol and Triton X-100, dubbed Sca*l*e, renders a mouse brain transparent after soaking for two weeks.

Clear vision: *Researchers can delve into the mouse hippocampus and visualize the interactions between neural stem cells (green) and blood vessels (red).*

Light can penetrate more than twice as far into brain slices treated with Sca*l*e compared with FocusClear or MountClear, two commercially available reagents, according to the study. Sugar solution, which is also sometimes used for this purpose, is not as efficient as either Sca*l*e or the other commercial reagents.

Fluorescent molecules retained their fluorescence when photographed over time in Sca*l*e, but not in BABB, another commercially available reagent.

The researchers used Sca*l*e-treated brains and embryos containing fluorescent neurons to visualize neural circuits. They also looked at the association between fluorescently labeled neural stem cells and blood vessels in the hippocampus of adult mice. Because blood vessels are fragile, traditional sectioning techniques cannot trace these interactions.

Commercially available solutions shrink tissues, whereas Sca*l*e expands tissues by about 1.25 percent, which can affect light transmission. The researchers created an optimized version of Sca*l*e that preserves the size of brain tissue, but takes up to a month to render the samples fully transparent.

REFERENCES:

1. Hama H. *et al. Nat. Neurosci.* Epub ahead of print (2011) **PubMed**