TOOLBOX

Tiny square rafts help neurons thrive in lab

BY **MARISSA FESSENDEN**

8 APRIL 2015

Screening solution: A chemotherapy drug activates the gene UBE3A (green) in neurons from mice modeling Angelman syndrome.

A convoy of miniature plastic rafts boosts survival in cultured neurons, using a method that may aid autism research. The technique provides an easier, more versatile way to grow many thousands of neurons spun from the stem cells of people with complex disorders.

To mature into neurons, stem cells need to be close to their neighbors. Scientists typically culture large numbers of the cells in tiny wells to crowd them. But the small volumes of fluid in these wells can quickly evaporate, starving the cells.

To bypass this problem, researchers developed a way to use a much larger culture dish by populating it with 1,600 polystyrene rafts. These rafts, each 500 square micrometers, tightly cluster the neurons by providing miniature platforms on which to grow. The rafts start out embedded in a flexible layer of silicone at the bottom of the dish, which is about the size of a quarter. Bending this layer releases the rafts, allowing them to float freely. The researchers described the method 10 February in *Scientific Reports*[1].

They tested the system, distributed by **Cell Microsystems**, by adding roughly 1 million neurons isolated from a human embryonic stem cell line to a raft-lined dish. The neurons stuck to the bottom of the dish. Two days later, the researchers used a metal probe to bend the silicone layer

and pop out the neuron-coated rafts.

After five days, they verified that the genes typically expressed in neurons were active in the cultured cells, showing that the method does not alter gene expression. The rafts also had significantly fewer dead and dying cells compared with cells cultured in a 384-well plate.

In another experiment, the researchers showed that neurons derived from the stem cells of a person with **fragile X syndrome** also maintain molecular signatures of that disorder.

Healthy-looking cells thrive on the rafts for up to 14 days, at which point they can be plated into tissue culture dishes and coaxed into becoming different types of neurons. Alternatively, the free-floating rafts can be divvied up and plopped into tiny wells for high-throughput drug screening.

The researchers used neurons from mice showing characteristics of **Angelman syndrome**, a disorder that bears some similarities to autism, to screen compounds that might revive **UBE3A**, a gene normally silenced in the disorder. One compound that showed promise in a previous screen activated the gene in neurons cultured on the rafts.

References:

1. Neidringhaus M. *et al. Sci. Rep.* **5**, 8353 (2015) **PubMed**