# Scientists program cells to carry out gene-guided construction projects

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The golden color illustrates the deposition of biocompatible polymers on two genetically targeted neurons at right, sparing neighboring cells. The selective deposition of these polymers, which can be electrically insulating or conductive, makes it possible to modulate target cell properties in living tissues and animals. Blue diamond particles represent the monomers to make the polymer diffusing globally through the tissue. The technology only enables polymers to form in targeted cells. Credit: Ella Maru Studio and Yoon Seok Kim/Jia Liu, Deisseroth/Bao laboratories, Stanford University

Stanford researchers have developed a technique that reprograms cells to use synthetic materials, provided by the scientists, to build artificial structures able to carry out functions inside the body.

"We turned cells into chemical engineers of a sort, that use materials we provide to construct functional polymers that change their behaviors in specific ways," said Karl Deisseroth, professor of bioengineering and of psychiatry and behavioral sciences, who co-led the work.

In the March 20 edition of *Science*, the researchers explain how they developed genetically targeted chemical assembly, or GTCA, and used the new method to build artificial structures on mammalian brain cells and on neurons in the tiny worm called *C. elegans*. The structures were made using two different biocompatible materials, each with a different electronic property. One material was an insulator, the other a conductor.

Study co-leader Zhenan Bao, professor and chair of chemical engineering, said that while the current experiments focused mainly on brain cells or neurons, GTCA should also work with other cell types. "We've developed a technology platform that can tap into the biochemical processes of cells throughout the body," Bao said.

The researchers began by genetically reprogramming the cells they wanted to affect. They did this by using standard bioengineering techniques to deliver instructions for adding an enzyme, called APEX2, into specific neurons.

Next, the scientists immersed the worms and other experimental tissues in a solution with two active ingredients—an extremely low, non-lethal dose of hydrogen peroxide, and billions of molecules of the raw material they wanted the cells to use for their building projects.

Contact between the hydrogen peroxide and the neurons with the APEX2 enzyme triggered a series of chemical reactions that fused the raw-material molecules together into a chain known as a polymer to form a mesh-like material. In this way, the researchers were able to weave artificial nets with either insulative or conductive properties around only the neurons they wanted.

The polymers changed the properties of the neurons. Depending on which polymer was formed, the neurons fired faster or slower, and when these polymers were created in cells of *C. elegans*, the worms' crawling movements were altered in opposite ways.

In the mammalian cell experiments, the researchers ran similar polymer-forming experiments on living slices from mouse brains and on cultured neurons from rat brains, and verified the conducting or insulating properties of the synthesized polymers. Finally, they injected a low-concentration hydrogen peroxide solution along with millions of the raw-material molecules into the brains of live mice to verify that these elements were not toxic together.

Rather than a medical application, Deisseroth says, "what we have are tools for exploration." But these tools could be used to study how multiple sclerosis, caused by the fraying of myelin insulation around nerves, might respond if diseased cells could be induced to form insulating polymers as replacements. Researchers might also explore whether forming conductive polymers atop misfiring neurons in autism or epilepsy might modify those conditions.

Going forward, the researchers would like to explore variants of their cell-targeted technology. GTCA could be used to produce a wide range of functional materials, implemented by diverse chemical signals. "We're imagining a whole world of possibilities at this new interface of chemistry and biology," Deisseroth said.

**More information:** J. Liu el al., "Genetically targeted chemical assembly of functional materials in living cells, tissues, and animals," *Science* (2020). science.sciencemag.org/cgi/doi … 1126/science.aay4866

K.J. Otto el al., "Neuron-targeted electrical modulation," *Science* (2020). science.sciencemag.org/cgi/doi … 1126/science.abb0216

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