

Salk scientists advance ultrasound technology for neurological therapy

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The emerging technology of sonogenetics—a technique where cells are controlled by sound—offers the potential to one day replace pharmaceutical drugs or invasive surgical treatments for neurological conditions like epilepsy, Parkinson's disease or posttraumatic stress disorder.

The Salk Institute scientist who pioneered the idea of using ultrasonic waves to stimulate [neurons](#) and coined the term "sonogenetics" will participate in the Defense Advanced Research Projects Agency's ElectRx program, aiming to take his lab's work to the next level with \$750,000 in new funding.

"We initiated this project about six years ago, when we first brought ultrasound into the laboratory to study a biological system," says Salk Associate Professor Sreekanth Chalasani, the principal investigator of the grant. "We wanted to know whether ultrasound could stimulate behavior in the nematode—a simple organism whose basic neurological circuitry has similarities to our own—and, strikingly, we found that it could."

In 2012, Chalasani received a Salk Innovation Grant to explore his idea of genetically engineering neurons in the worm to respond to sound waves. He [first demonstrated the technique on nematodes in 2015](#), showing that low-intensity ultrasound waves propagating into the worms caused a chemically sensitive molecular channel called TRP-4 to open and activate brain cells. His team then used molecular biology techniques to add the TRP-4 channel to neurons that don't usually react to ultrasound, successfully activating them and influencing the worms' behavior. The lab leveraged the early success of their approach into a grant from the National Institutes of Health's (NIH) Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative to explore additional molecular channels that could be targeted with ultrasound. The team also showed

the technique works in a mouse model.

Before the development of sonogenetics, scientists used a tool called optogenetics to stimulate neurons with light. While optogenetics continues to be a highly valuable tool for neuroscience research, the approach has some therapeutic limitations.

"With optogenetics, you need to surgically implant some sort of probe or light-emitting device in or very near the tissue that you are targeting," says Yusuf Tufail, a research scientist in the Chalasani lab. "But with sonogenetics, you don't need surgery, because the genetic components that make neurons sensitive to ultrasound can be delivered via therapeutic viruses, and then the ultrasound stimulation is applied from outside the body, just like a pregnancy ultrasound."

Now, the team aims to search for additional proteins that will respond to [ultrasound](#)—but rather than activate neurons, these proteins would inhibit cells. Methods to both noninvasively inhibit as well as activate neurons have immense potential for therapies.

"Sonogenetics is a very exciting way in which we could potentially treat different [neurological conditions](#) without having to invasively implant electrodes into patients," says Corinne Lee-Kubli, a research associate in the Chalasani lab. "Parkinson's disease, neuropathic pain, PTSD and movement disorders, such as paralysis, could theoretically all benefit from a sonogenetics approach."

With this new support, the team will build novel, custom-made instruments to develop and assess the technology.

Adds Chalasani, "We are excited with the results that we have obtained. We're excited with the prospects of this technology, which we think could revolutionize the fields of both neuroscience and

medicine."

Provided by Salk Institute

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