



Neurons Can Be Reprogrammed to Take on New Identities ALS Association Funded Study Finds

In work supported by The ALS Association and funded through The Milton Safenowitz Post-Doctoral Fellowship Program, researchers have for the first time reprogrammed a neuron from one type into another and have done so in a living organism. The finding will help scientists better understand how to control neuronal development and may one day aid in treating diseases in which neurons die, such as amyotrophic lateral sclerosis (ALS). The study was published in the journal Nature Cell Biology.

ALS is a progressive neurodegenerative disease that affects nerve cells in the brain and the spinal cord. Eventually, people with ALS lose the ability to initiate and control muscle movement, which often leads to total paralysis and death within two to five years of diagnosis. There is no cure and no life-prolonging treatments for the disease.

“This discovery tells us again that the brain is a somehow flexible system and gives us more evidence that reprogramming neurons to take on new identities and, perhaps, that new functions are possible,” said Lucie Bruijn, PhD, Chief Scientist for The Association. “For those working to treat neurodegenerative diseases, that is reassuring.”

The outermost layer of the brain, called the cerebral cortex, contains multiple different types of neurons. During embryonic development, each type takes on its unique identity, which remains unchanged throughout the life of the organism. Working in newborn mice, the researchers in this study used two different techniques to convert one type of cortex neuron into a second type. The second type, called corticofugal projection neurons, are significant for ALS, as they include corticospinal motor neurons that die in the disease.

The newly converted projection neurons were able to make connections with other neurons characteristic of their new identity, rather than their original identity. Those connections are vital to proper neuronal function. The conversion was performed shortly after the mice were born. Further experiments will be needed to determine if and how it is possible to perform such a conversion later in life.

“Understanding the constraints and possibilities of nervous system development allows us to consider new experiments and new strategies for therapy development,” Dr. Bruijn said. “The most immediate importance of this finding is likely to be in laboratory, where it will help us understand more about how the nervous system may respond when neurons are injured, as they are in ALS.”

The research was performed by Caroline Rouaux, PhD and Paola Arlotta, PhD, of the Department of Stem Cell and Regenerative Biology at Harvard University in Cambridge, Mass. Dr. Arlotta is an Associate Professor at Harvard University and a New York Stem Cell Foundation-Robertson Investigator. Dr. Rouaux received The Milton-Safenowitz Post-Doctoral fellowship from The ALS Association when in Arlotta’s laboratory in 2007 and 2008 and has recently become an Assistant Professor at National Institute of Health and Medical Research (INSERM) in Strasbourg, France, where she continues her work in ALS research together with other leaders in the field.

The Milton Safenowitz Post-Doctoral Fellowship for ALS Research Award encourages and facilitates promising young scientists to enter the ALS field.

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