Implanted neurons, grown in the lab, take charge of brain circuitry

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Among the many hurdles to be cleared before human embryonic stem cells can achieve their therapeutic potential is determining whether or not transplanted cells can functionally integrate into target organs or tissues.

Writing today in the Proceedings of the National Academy of Sciences, a team of Wisconsin scientists reports that neurons, forged in the lab from blank slate human embryonic stem cells and implanted into the brains of mice, can successfully fuse with the brain's wiring and both send and receive signals.

Neurons are specialized, impulse conducting cells that are the most elementary functional unit of the central nervous system. The 100 billion or so neurons in the human brain are constantly sending and receiving the signals that govern everything from walking and talking to thinking. The work represents a crucial step toward deploying customized cells to repair damaged or diseased brains, the most complex human organ.

"The big question was can these cells integrate in a functional way," says Jason P. Weick, the lead author of the new study and a staff scientist at the University of Wisconsin-Madison's Waisman Center. "We show for the first time that these transplanted cells can both listen and talk to surrounding neurons of the adult brain."

The Wisconsin team tested the ability of their lab grown neurons to integrate into the brain's circuitry by transplanting the cells into the adult

mouse hippocampus, a well-studied region of the brain that plays a key role in processing memory and spatial navigation. The capacity of the cells to integrate was observed in live tissue taken from the animals that received the cell transplants.

Weick and colleagues also reported that the human neurons adopted the rhythmic firing behavior of many brain cells talking to one another in unison. And, perhaps more importantly, that the human cells could modify the way the neural network behaved.

A critical tool that allowed the UW group to answer this question was a new technology known as optogenetics, where light, instead of electric current, is used to stimulate the activity of the neurons.

"Previously, we've been limited in how efficiently we could stimulate transplanted cells. Now we have a tool that allows us to specifically stimulate only the transplanted human cells, and lots of them at once in a non-invasive way," says Weick.

Weick explains that the capacity to modulate the implanted cells was a necessary step in determining the function of implanted cells because previous technologies were too imprecise and unreliable to accurately determine what transplanted neurons were doing.

Embryonic stem cells, and the closely related induced pluripotent stem cells can give rise to all of the 220 types of tissues in the human body, and have been directed in the lab to become many types of cells, including brain cells.

The appeal of human embryonic stem cells and induced pluripotent cells is the potential to manufacture limitless supplies of healthy, specialized cells to replace diseased or damaged cells. Brain disorders such as Parkinson's disease and amyotrophic lateral sclerosis, more widely

known as Lou Gehrig's disease, are conditions that scientists think may be alleviated by using healthy lab grown cells to replace faulty ones. Multiple studies over the past decade have shown that both embryonic stem cells and induced cells can alleviate deficits of these disorders in animal models.

The new study opens the door to the potential for clinicians to deploy light-based stimulation technology to manipulate transplanted tissue and cells. "The marriage between stem cells and optogenetics has the potential to assist in the treatment of a number of debilitating neurodegenerative disorders," notes Su-Chun Zhang, a UW-Madison professor of neuroscience and an author of the new PNAS report. "You can imagine that if the transplanted cells don't behave as they should, you could use this system to modulate them using light."

Provided by University of Wisconsin-Madison