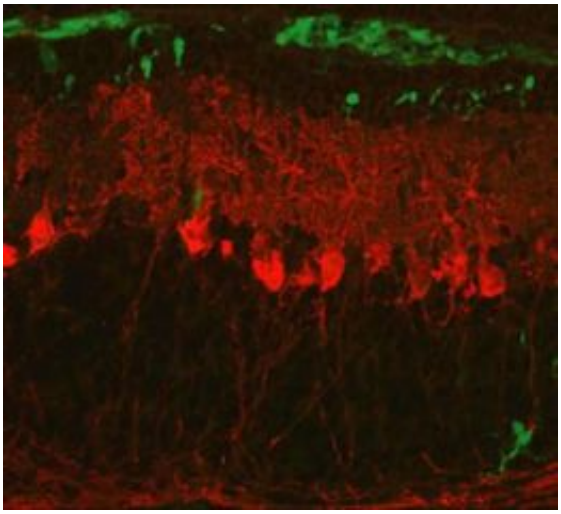
Chemical cues turn embryonic stem cells into cerebellar neurons

March 14 2007



When differentiated embryonic stem cells were implanted into the cerebellums of newborn mice (green), they migrated to the internal granule layer -- the area where fully differentiated granule neurons extend dendrites (bottom right). Credit: The Rockefeller University

In order to differentiate and specialize, stem cells require very specific environmental cues in a very specific order, and scientists have so far been unable to prod them to go through each of the necessary steps. But now, for the first time, a study in mice by Rockefeller University scientists shows that embryonic stem cells implanted in the brain appear to develop into fully differentiated granule neurons, the most plentiful neuron in the cerebellum. The findings were reported Feb. 20 in the

online edition of *Proceedings of the National Academy of Sciences*.

Embryonic stem cells have shown a great deal of promise for alleviating heart disease and regenerating organs. But for some of the conditions for which people hold out the most hope -- Alzheimer's and Parkinson's, for example -- there's been little evidence to date that stem cells can work. Part of the problem is that neural stem cells, especially those involved in brain development, specialize as they mature and lose their ability to diversify. They require very specific environmental cues in a very specific order, and scientists have so far been unable to prod them to go through each of the necessary steps. But now, for the first time, a new study in mice shows that embryonic stem cells implanted in the brain appear to develop into fully differentiated granule neurons, the most plentiful neurons in the cerebellum.

The cerebellum, which is tucked into the lower, rear portion of the mammalian brain, contains neural circuits that are responsible for motor learning, motor memory and sensory perception. It's also the location of 40 percent of pediatric brain tumors. Mary E. Hatten, Rockefeller's Frederick P. Rose Professor and head of the Laboratory of Developmental Neurobiology, has been studying granule cells for 30 years; she sees her results as a step toward understanding how embryonic stem cells could be regulated in vivo and ultimately used for cell replacement therapy, especially after childhood tumors, in the central nervous system.

Hatten and postdoc Enrique Salero found that in order to get the embryonic stem cells to differentiate, progressing through each of the known steps of granule neuron maturation as they did so, the cells had to be treated with signals that induce specific transcription factors - proteins that can turn genes on and off - in a specific order. The researchers then implanted the newly differentiated cells into a specific spot in the brains of newborn mice, the gray layer on the surface of the

cerebellum called the cerebellar cortex. Once in the brain, the cells extended parallel fibers, migrated to and incorporated themselves into the internal granule cell layer, and extended short projections called dendrites, something that neurons use to communicate with each other. Each of these steps, Hatten says, is characteristic of a typical granule cell.

Salero and Hatten then looked for evidence that their embryonic stem cells had not just gone through the developmental steps of young granule neurons, but that they also had the known markers of young granule neurons, including those indicating that the neurons had formed in the cerebellum. "We're excited about this paper because it's the first time that anybody has shown that a cell not only migrates to where it's supposed to go, but extends dendrites," Hatten says. "So they're actually in the synaptic network that's sitting on the cortex."

Hatten isn't yet convinced that the cells differentiated into true granule neurons. "There is such wild-eyed enthusiasm over stem cells," she says, "but it's very hard to know when you've provided sufficient evidence that a cell is actually what you say it is." So her next step will be to work with Nathaniel Heintz, an HHMI investigator and Rockefeller's James and Marilyn Simons Professor, to determine how close a genetic match the native granule cells are to the embryonic stem cell-derived versions.

"This whole field of stem cell biology is exciting, but also frightening because of the potential harm that could be done," Hatten says. "We have made a lot of progress with stem cells outside the brain, especially with the heart and skin. But neurons in the brain seem to undergo more complicated genetic changes as they progress through a long series of maturation steps. So we want to be absolutely sure that we're generating neurons that will aid, rather than hamper, brain function."

Source: Rockefeller University

Citation: Chemical cues turn embryonic stem cells into cerebellar neurons (2007, March 14) retrieved 6 May 2024 from https://medicalxpress.com/news/2007-03-chemical-cues-embryonic-stem-cells.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.