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RESEARCH NEWS

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Neural Stem Cells Can Develop into Functional Neurons

Researchers have found that neural stem cells isolated from the brains of adult rats can mature into functional neurons. Stem cells, which are found in tissues throughout the body, are immature progenitor cells that give rise to more specialized cells that form tissues and organs.

The scientists emphasized that although their studies show that adult stem cells have the capacity to develop into functioning brain cells, their findings do not mean that clinical application of adult neural stem cells is imminent. The studies were published April 15, 2002, in an advance online article in *Nature Neuroscience* by Howard Hughes Medical Institute (HHMI) investigator Charles F. Stevens and colleagues Hong-jun Song, an HHMI research associate, and Fred H. Gage at The Salk Institute.

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> **— Charles F. Stevens**

According to Stevens, previous experiments showed that adult neural stem cells bear certain molecular markers that suggested that they could become neurons. "It's absolutely clear that embryonic stem cells can make perfectly good neurons, otherwise there would be no development of the brain," said Stevens. "But nobody had demonstrated before that adult stem cells can generate fully functional neurons, beyond just having particular protein markers."

To see whether adult neural stem cells possessed the ability to develop into functional neurons, Gage and his colleagues first isolated stem cells from the hippocampal region of the rat brain and then tagged the cells with fluorescent molecules that made it possible for the researchers to track the stem cells as they developed. The scientists "co-cultured" these tagged cells along with normal adult neurons on a carpet of supporting cells called astrocytes, which are known to produce chemical signals that trigger neuronal growth.

“The normal neurons were necessary to show that our stem-cell-generated neurons were genuine, in the sense that they could incorporate into the neural circuitry that attempts to become established in cell culture,” explained Stevens.

In their initial studies, the scientists found that the fluorescently tagged stem cells developed normal neuronal structures, including the long, cable-like axons and branching dendrites that form connections with other neurons. The researchers observed that the axons and dendrites produced protein markers that were characteristic of normal neurons.

By recording electrical signals from the cultured cells when they were stimulated, the scientists observed that functioning connections, called synapses, were established between the stem-cell-derived neurons and normal adult neurons. Synapses are the junctions between neurons where nerve impulses are transmitted. Electron microscope studies of the synapses revealed that they appeared normal.

The researchers also showed that the stem-cell-derived neurons produced neurotransmitters, chemical signals by which neurons communicate to each other across synapses.

“However, we did find that the stem-cell-derived neurons did not make as many synapses as normal neurons,” said Stevens. “It might be that adult stem cells by themselves don’t give rise to cells with sufficient synapses; that we didn’t give them the right environment for synaptic production, or that these particular cultured cells might have contained mutations that reduced synapse production.”

To test whether astrocytes played a role in triggering the maturation of adult neural stem cells, the scientists cultured the cells with both neonatal and adult astrocytes. The studies showed that both types of astrocytes produced factors that supported stem cell maturation.

According to Stevens, the observation that adult neural stem cells can mature into functional neurons could have clinical implications. “There has been considerable debate about whether adult neural stem cells, as well as embryonic stem cells, could be used to regenerate damaged brain tissue,” he said. “These findings give some indication that if we ever reach the point where stem cell therapy is feasible to treat such disease, there’s some hope that adult stem cells might work.”

But Stevens emphasized that extensive comparative studies of both embryonic and adult neural stem cells will be needed before their relative advantages and disadvantages can be determined.

“It is absolutely vital to continue research using embryonic neural stem cells,” he said. “It may be that, for reasons we don’t yet understand, adult stem cells will never be useful in therapy and that we will always need embryonic cells. Or, it may be the other way around. We just don’t know.”