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Stem Cell Work Shows Promise and Risks

Parkinson's Treatment Tried in Rats Reduced Symptoms but Caused Tumors

By Rick Weiss
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Nerve cells grown from human embryonic stem cells and injected into the brains of rats with a syndrome mimicking Parkinson's disease significantly reduced the animals' symptoms, but the treatment also caused tumors in the rodents' brains, scientists reported yesterday.

Researchers said the work showed both the potential benefits and risks of human embryonic stem cells, which have been highly touted for their capacity to replace diseased tissue but are controversial because they are derived through the destruction of human embryos.

"The behavioral data validate the utility of the approach. But it also raises a cautionary flag and says we are not ready for prime time yet," said lead researcher Steven A. Goldman, a professor of neurology and neurosurgery at the University of Rochester Medical Center.

Goldman said he suspected that with modest changes in technique, researchers will be able to keep the benefits of the treatment while eliminating or reducing the chances of getting the cancerlike growths. But he conceded that much more basic research would have to be done before scientists -- or regulators -- were likely to be convinced of the approach's safety.

In the experiments, Goldman and colleagues from the Weill Medical College of Cornell University in New York treated laboratory-cultured human embryonic stem cells in a new way that coaxed many to become a kind of neuron that produces dopamine, a neurotransmitter. Those cells are gradually lost in Parkinson's disease, depriving the body of that essential chemical messenger.

The disease causes motor problems such as trembling and muscle rigidity and a gradual decline in mental functioning.

The team injected the cells into the brains of rats, which had been given a chemical that causes damage similar to that seen in Parkinson's. The new cells integrated into the animals' brains and produced copious amounts of dopamine. As a result, the animals' motor coordination improved almost to the point of being normal, according to the report in yesterday's online edition of the journal *Nature Medicine*.

But when the animals were autopsied after three months and their brains were examined microscopically, the team found multiple tumors, indicating that some of the injected cells did not settle into the job of being neurons but rather had begun to grow uncontrollably.

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The results were similar to those of other experiments published Oct. 12 in the online journal *Stem Cells* by a team led by Ole Isacson, a Harvard Medical School professor of neuroscience and neurology. In that case, the stem cells were cultivated differently, produced less dopamine and had fewer beneficial effects. But some grew out of control.

"I think it is a terrific demonstration that we are midway between earliest discovery and clinical application," Isacson said Friday.

Goldman and Isacson said they are developing technologies for culling from a developing stem cell population those cells that are not fully committing themselves to becoming neurons -- or selecting such fully committed cells from a larger, mixed population.

"We still have so little experience with these cells, but if we keep doing the work and we do it carefully, then I believe that in the long run it will help patients," Isacson said.

Thomas Okarma, president of Geron, a California company that hopes to gain Food and Drug Administration permission to treat spinal-cord-injury patients with modified embryonic stem cells next year, said his company's cells have shown no sign of causing tumor growth in any of its animal studies.

But he said the FDA has asked for additional extensive data on exactly that question before it will give its final okay.

"What they worry about, and rightly so, is there are rogue undifferentiated cells lurking in the cell population that we haven't detected," Okarma said.

Geron cultivates its embryonic stem cells differently than others, he said, adding that no tumors have been seen in animals up to nine months after injections into the rodents' injured spinal cords. Moreover, he said, the cells survive and help the animals recover, in part by secreting special factors that spur new nerve growth around the injury.

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