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Researchers at UPMC, Stanford test stem cells to enhance stroke recovery

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By Mark Roth / Pittsburgh Post-Gazette

Doctors have known for years that when people suffer a stroke, their brains furiously try to repair themselves, but the improvement often plateaus after several weeks or months.

Now, researchers at UPMC and Stanford University hope they can enhance recovery by infusing millions of stem cells directly into patients' brains. Using cells developed by a San Francisco-area company called SanBio, the two institutions have carried out the procedure on six patients so far and plan to enroll another 12 in a two-year safety trial of the new therapy.

The cells were culled from adult bone marrow and given a booster containing a gene known as Notch, which is involved in the development of infant brains.

No adverse reactions have occurred in the first half-dozen patients, each of whom got 2.5 million stem cells. During the procedure, doctors sedate the patient, numb the person's skull, bore a hole through the skull and insert a metal tube into the brain near the area of the stroke damage, said Douglas Kondziolka, a neurosurgeon who heads the UPMC branch of the trial. The stem cells are then infused into the brain through the tube.

Doctors won't know the outcome for several months, but tests in laboratory rats by Cesario Borlongan at the University of South Florida have shown that the stem cells improved motor function in animals that had suffered a stroke, and the cells secreted several growth and anti-inflammatory factors in the lab.

Ernest Yankee, SanBio's vice president of development, said if there are no safety issues, the company hopes to begin testing the stem cells' clinical effectiveness within the next two years.

Mr. Borlongan, a neuroscientist at South Florida, said that when people suffer a stroke from a clot blocking blood flow to the brain, there is a central area of damage and then a surrounding, partially damaged area known as the penumbra.

In the animals, the stem cells seem to work primarily by repairing the penumbra area. Not only do they secrete factors that help new neurons and blood vessels grow, but they also promote the growth of cellular scaffolding to support the brain repair, he said.

Interestingly, he said, the stem cells themselves disappear a few weeks after they are put in, but their beneficial effects seem to persist.

"We think what our cells are doing is providing an environment for improvement," SanBio's Mr. Yankee said.

This is not the first time UPMC has been involved in stem cell therapy for stroke.

About a decade ago, Dr. Kondziolka led a trial of a different stem cell line in older stroke patients, and it showed promise, but money to support the experiments ran out when the New York Stock Exchange's tech investment bubble burst in 2000.

Because the current stem cells are a different type, researchers had to start all over again with animal and safety tests. "Every time a new cell line gets developed, you have to go back to the drawing board," he said.

The current trial is still enrolling patients. They must be adults and must have experienced their strokes between six months and three years ago. They also must have persistent motor difficulties that have plateaued, he said.

Anyone who wants more information can contact study coordinator Julia Billigen at 412-605-3959 or BilligenJB@upmc.edu.

The UPMC-Stanford trial is the only one in the U.S. putting these stem cells directly into patients' brains. In the United Kingdom, a British company called ReNeuron Ltd. is using a similar procedure on stroke patients with stem cells developed from fetal brain tissue.

Mr. Borlongan said the potential of this therapy comes from the fact that whole cells are secreting a "cocktail" of growth and anti-inflammatory factors into people's brains. Still, he noted that 178 drugs and biologic agents already have helped repair brain damage in animals but have never successfully worked in humans.

"As a result," he said, "we in the field of stem cells are very cautious that we don't fall into giving this too much hype."

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