Stem-Cell Repair Kit for Stroke

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A novel matrix of neural stem cells and a biodegradable polymer can quickly repair brain damage from stroke in rats. Within just seven days of injecting the concoction directly into the damaged part of the brain, new nerve tissue grew to fill stroke-induced cavities.

Scientists say that the key to the advance, published today in the journal Biomaterials, is the use of a biodegradable polymer called PLGA, which ensures that the stem cells remain in the area of stroke damage and establish connections with surrounding brain tissue. By reducing the number of stray stem cells, the system is likely to be safer as well as more effective than other methods, the researchers add.

Strokes, which occur due to bleeds or blocked blood vessels in the brain, cause some brain tissue to die. This dead tissue is then removed by the immune system, leaving a hole. "We would expect to see a much better improvement in the outcome after a stroke if we can fully replace the lost brain tissue, and that is what we have been able to do with our technique," says Mike Modo, a neurobiologist at the Institute of Psychiatry at King's College London, who oversaw the research.

Earlier studies had indicated that using support structures, including carbon nanotubes, might help stem cells that were introduced to replace the brain tissue damaged by a stroke. But the latest research, sponsored by the Biotechnology and Biological Sciences Research Council, appears to take the process a significant step farther. The team was able to show that the hole in the brains of rats caused by a stroke was completely filled with "primitive" new nerve tissue within seven days. This raises the possibility of radically better treatments for a condition that is the leading cause of adult disability in industrialized countries.

The researchers injected particles of the PLGA polymer loaded with neural stem cells directly into the stroke cavities. Once inside the brain, the particles link up to form complex scaffolds. Modo's team used MRI scans to pinpoint where the stem-cell injections were needed and to monitor the development of new brain tissue. "Over a few days we can see cells migrating along the scaffold particles and forming a primitive brain tissue that interacts with the host brain," says Modo. "Gradually, the particles biodegrade, leaving more gaps and conduits for tissue, fibers, and blood vessels to move into." The next step, he says, will be to add the growth factor VEGF, which should encourage blood vessels to enter the new tissue and speed its development into mature tissue.

"This project is an excellent example where, by understanding the importance of biomaterial scaffolds, the cells are better able to populate the void left by the injury," says Jonathan Cooper, a bioengineer at the University of Glasgow. "Not only does the biomaterial act as a support for the cells when they are seeded into the void, but as the scaffold is degraded, it provides the physical space for new blood vessels to form."

The key to the advance was the ability of the new polymer to encourage the growth and differentiation of the neural stem cells at three different scales, says Modo's colleague Kevin Shakesheff, a tissue engineer at Nottingham University. "At the large scale, it enables the void formed by the injury to get new blood vessels very quickly, which is vital if the new tissue is to survive. At the cellular level, the scaffold surface allows stem-cell receptors to attach to it. And at the molecular level, it will allow cells to mix with the right growth factors."

Shakesheff says that extensive testing is needed before human trials of the matrix can begin. He hopes, however, that the PLGA polymer will be marketed within 12 months for use in bone surgery.