Biological Scaffold Allows Nerve Cells to Grow and Form Connections

ROSSLYN, VA., June 30, 2000 -- Biomedical engineers have taken a very early step toward reversing paralysis by developing a biological scaffold that stimulates nerve cells to grow and network.
Paralysis from spinal injuries and other nerve damage tends to be irreversible because the human body virtually ceases nerve-cell production after the prenatal years. The brain actually secretes molecules that prevent the regeneration of neurons.

But Whitaker Investigator Shuguang Zhang, Ph.D., associate director of the Center for Biomedical Engineering at the Massachusetts Institute of Technology, Todd C. Holmes, Ph.D., of New York University, and their colleagues have found a material that seems to rob these inhibitor molecules of their effect.

The material is a new type of self-assembling biological scaffold on which neurons will grow, reach out to neighboring neurons, and form channels of communication among themselves. These are the essential ingredients for repairing nerve damage.

In the June 6 issue of *Proceedings of the National Academy of Sciences*, Zhang and his group report a series of successful experiments with the scaffolds, which are made of fragments of proteins, the building blocks of the human body. These protein fragments are known as peptides.

The researchers placed the peptides in a salt solution. The salt causes the peptides to assemble themselves into thin sheets composed of 99 percent water and 1 percent peptides. Within the sheet, the peptides appear as individual interwoven fibers that form a matrix or scaffold.

The researchers placed several different types of neuronal cells on the peptide scaffolds and found that the nerve cells grew along the peptide fibers. The neurons also sent out projections called axons that formed functional synaptic connections with other neurons. It is between these synaptic connections that nerve cells communicate with one another.

"This is an important property for further development on the self-assembling peptide scaffolds for neurorepair, neuroengineering, and other general applications for tissue engineering," Zhang said.

These peptides exhibit other features that make them especially attractive for a wide-range of medical and biological uses. In Zhang's and Holmes's experiments with rodent neurons, the peptides caused no inflammation and no immune response—two potentially major obstacles for clinical applications.

The self-assembling peptides can arrange themselves into fibers, tubules, and a variety of geometrical layers and can be designed to degrade and disappear from the body over time. They can adapt to changes in acidity, mechanical force, temperature, pressure, electrical current, magnetic fields and light. They are also stable at up to 350 degrees Centigrade and can be produced economically in vast quantities.

"These new biological materials will become increasingly important in developing approaches for a wide range of innovative medical technologies," Zhang said. "These technologies include controlled drug release, new scaffolds for cell-based therapies, tissue engineering and biomineralization for hard tissue repair."

But it will be a long time before they could be available for patient use.

Further research will be needed to determine the molecular mechanisms by which the peptide scaffolds encourage nerve cells attachment and axon growth. Zhang's group speculates that two independent processes may be involved in the attachment of neurons to the peptide scaffold and the subsequent growth of axons.

In their experiments, the group compared the behavior of neurons grown on the peptide scaffolds with neurons grown on a commercially available surface called Matrigel and found no difference between the two. Matrigel, however, contains natural collagen, growth factors and other proteins that encourage cell growth, while Zhang's peptides do not. But because of their simplicity, the peptide scaffolds can be placed in many different biological environments without hampering their performance.

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"The self-assembling peptide scaffold described here belongs to a class of biologically inspired materials," Zhang said. "The self-assembly event creating the peptide scaffold takes place under physiological conditions and they are readily transportable to different environments."

"In combination with stem cell technology, we can anticipate the encapsulation of stem cells in the self-assembled peptide scaffold, allowing them to differentiate into desired cell types with specific growth factors and cytokines, and then the application of cell-scaffold systems into needed tissues," Zhang said.

"These biocompatible and biodegradable peptide scaffolds developed through molecular self-assembly will likely have a broad range of applications for tissue repair and tissue engineering," he said.

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