Nanomedicine opens the way for nerve cell regeneration

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The ability to regenerate nerve cells in the body could reduce the effects of trauma and disease in a dramatic way. In two presentations at the NSTI Nanotech 2007 Conference, researchers describe the use of nanotechnology to enhance the regeneration of nerve cells.

In the first method, developed at the University of Miami, researchers show how magnetic nanoparticles (MNPs) may be used to create mechanical tension that stimulates the growth and elongation of axons of the central nervous system neurons. The second method from the University of California, Berkeley uses aligned nanofibers containing one or more growth factors to provide a bioactive matrix where nerve cells can regrow.

It is known that injured neurons in the central nervous system (CNS) do not regenerate, but it is not clear why. Adult CNS neurons may lack an intrinsic capacity for rapid regeneration, and CNS glia create an inhibitory environment for growth after injury. Can these challenges be overcome even before we fully understand them at a molecular level "why axons in central nervous system do not regenerate?" Dr. Mauris N. De Silva describes the novel nanotechnology based approach designed that includes the use of magnetic nanoparticles and magnetic fields for addressing the challenges associated with regeneration of central nervous system after injury. "By providing mechanical tension to the regrowing axon, we may be able to enhance the regenerative axon growth in vivo". This mechanically induced neurite outgrowth may provide a possible method for bypassing the inhibitory interface and the tissue beyond a

CNS related injury. Using optic nerve and spinal cord tissues as in vivo models and dissociated retinal ganglion neurons as an in vitro model, De Silva and his colleagues are currently investigating how these magnetic nanoparticles can be incorporated into neurons and axons at the site of injury. Although, this study is at a very preliminary stage to explore the possibility of using magnetic nanoparticles for enhancing in vivo axon regeneration, this work may have significant implications for the treatment of spinal cord injuries, and is a vital "next step" in bringing this new technology to clinical use.

The second presentation focuses on peripheral nerve injury, which affects 2.8% of all trauma patients and quite often results in lifelong disability. Since peripheral nerves relay signals between the brain and the rest of the body, injury to these nerves results in loss of sensory and motor function. Upper extremity paralysis alone affects more than 300,000 individuals annually in the US. The most serious form of peripheral nerve injury is complete severance of the nerve. The severed nerve can regenerate; the nerve fibers from the nerve end closest to the spinal cord have to grow across the injury gap, enter the other nerve segment and then work their way through to their end targets (skin, muscle, etc). Usually, when the gap between the severed nerve endings is larger than a few millimeters, the nerve does not regenerate on its own. If left untreated, the end result is permanent sensory and motor paralysis. A few hundred thousand people suffer from this debilitating condition annually in the US.

Currently, the most successful form of treatment is to take a section of healthy nerve (autograft) from another part of the patient's body to bridge the damaged one. This autograft then serves as a guide for nerve fibers to cross the injury gap. Although successful, this autograft procedure has major drawbacks including loss of function at the donor site, multiple surgeries and, quite often, it's just not possible to find a suitable nerve to use as a graft. Various synthetic nerve grafts are currently available but none work better than the autograft and can't bridge gaps larger than 4 centimeters.

Researchers at the University of California, Berkeley have developed a technology that has the potential to serve as a better alternative than currently available synthetic nerve grafts. The graft material is composed entirely of aligned nanoscale polymer fibers. These polymer fibers act as physical guides for regenerating nerve fibers. They have also developed a way to make these aligned nanofibers bioactive by attaching various biochemicals directly onto the surfaces of the nanofibers. Thus, the bioactive aligned nanofiber technology mimics the nerve autograft by providing both physical and biochemical cues to enhance and direct nerve growth.

This technology has been tested by culturing rat nerve tissue ex vivo on our bioactive aligned nanofiber scaffolds. When the nerve tissue was cultured on unaligned nanofibers there was no nerve fiber growth onto the scaffolds. However, on aligned nanofiber scaffolds, they not only observed nerve fibers growing from the tissue but the nerve fibers were aligned in the same orientation as the nanofibers. Furthermore, when there were biochemicals present on the nanofibers, the nerve fiber growth was enhanced 5 fold. In a matter of just 5 days, nerve fibers had extended 4 millimeters from the nerve tissue in a bipolar fashion on the bioactive aligned nanofiber scaffolds. Thus, this technology can induce, enhance and direct nerve fiber regeneration in a straight and organized manner.

In order to make the technology clinically viable, they have also developed a novel graft fabrication technology in their laboratory. The most common method for fabricating polymer nanofibers is to use an electrical field to "spin" very thin fibers. This technique is called electrospinning and can be used to make nanofiber scaffolds in various shapes such as sheets and tubes. They have made a key innovation to this technology that enables us to fabricate tubular nerve grafts composed entirely of polymer nanofibers aligned along the length of tubes. This technology also allows customization of the length, diameter and thickness of the aligned tubular nanofiber grafts. The group will evaluate the performance of these aligned nanofiber nerve grafts in small animal pre-clinical studies starting in mid-May.

The technology presented herein is being patented by the University of California, Berkeley and has been licensed to NanoNerve, Inc.

According to Principal Investigator, Shyam Patel, "Speed is the key to successful nerve regeneration. Our aligned nanofiber technology takes full advantage of the fact that the shortest distance between damaged nerve endings is a straight line. It directs straightforward nerve growth and never lets them stray from the fast lane."

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