Neuron Regeneration From Neurotransmitter Biomimetic Polymers

A scientist at Georgia Tech has dreamed up a strategy that shows promise for regenerating damaged nervous system cells known as neurons. Currently there is no treatment for recovering human neurons after injury to the brain or spinal cord, since central nervous system neuron cells have very limited ability for self-repair and regeneration.

Here's how it would work. A biodegradable polymer that contains a chemical group mimicking the neurotransmitter acetylcholine would be surgically implanted in a patient. The chemicals would induce growth of axons and dendrites, projections that form the connections among neurons and between other cells. The biomimetic polymers would then guide the growth of the regenerating nerve.

"Regeneration in the central nervous system requires neural activity, not just neuronal growth factors thought a neurotransmitter might send the necessary signals," says Yadong Wang, assistant professor of biomedical engineering at Georgia Tech. She is the principal investigator of the study, which was published in the December 11, 2007 issue of the journal Advanced Materials.

Neurotransmitters and Polymers

Chemical neurotransmitters relay, modulate and amplify the signals between neurons and other cells. This study demonstrates that neurotransmitters into biodegradable polymers can result in a biomaterial that successfully promotes neurite growth, which is essential for victims of central nervous system injury, stroke or certain neurodegenerative diseases to recover sensory, motor, cognitive or autonomic functions.

"One of our ultimate goals is to create a conduit for nerve regeneration that guides the neurons to regenerate, but gradually degenerates so that it won't constrict the nerves permanently," explained Wang.

Polymers with different concentrations of the acetylcholine-mimicking groups were tested, but acetylcholine was chosen because it induces neurite outgrowth and promotes the formation and strengthening of synapses, or connections between neurons. Ganglia nerve samples were isolated, placed on the polymers and promoted the growth of new neurites from the ganglia.

Growth Inhibiting Materials Overcome

Since these neuron extensions must traverse growth inhibiting proteins in the nerves, Wang and Gumera tested the ability of the polymers to enhance the extension of sprouted neurites. More specifically, they assessed whether the ganglia sprouted at least 20 neurites in measured neurite length and neurite length distribution with an inverted phase contrast microscope.

"We found that adding 70 percent acetylcholine to the polymer induced regenerative responses similar to laminin, a benchmark nerve culture," said Wang. Seventy percent acetylcholine also led to a neurite growth rate of up to 0.7 millimeters per day, approximately half the thickness of a compact disc.

Laminin is a natural protein present in the nervous tissues, but it dissolves in water, making it difficult to incorporate into a conduit to support nerves for months. A synthetic polymer with acetylcholine functional groups, conversely, can be designed to be insoluble according to Wang.

Synapse Growth

Truly functional restoration after a nerve injury requires synapse formation, so the researchers also looked for the presence of synapses.
proteins on the newly formed neurites. With fluorescence imaging, they found that neurons cultured on these acetylcholine polymers expressed an established neuronal marker called synaptophysin.

To provide insights to new approaches in functional nerve regeneration, the researchers are currently investigating mechanisms by which neurons interact with these polymers. Since neurons that remain intact after severe injury have only a limited capacity to penetrate tissue, these new findings in nerve regeneration could help compensate for the lost connections.

"This polymer and approach aren’t limited to nerve regeneration though, they can probably be used for other neurodegenerative diseases as well," added Wang.

References:


Image: Phase-contrast micrograph of a ganglion on a 70 percent acetylcholine polymer that shows neurite growth. The figure is a series of 100x magnification images.

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