GEORGE STREET Journal
A PUBLICATION FOR THE BROWN UNIVERSITY COMMUNITY
March 26, 2004

Laser-wielding students explore ways to jump-start nerve growth

Group Research Project is under direction of Hoffman-Kim

by **Adam Voiland '05**

Six undergraduate students participating in a Group Research Project (GRP) under the direction of Assistant Professor of Medical Science and Engineering Diane Hoffman-Kim are using sophisticated laser techniques to determine what makes nerves grow. The research eventually may help scientists develop treatments for people with spinal cord injuries, as well as developmental neurological disorders.

It could also explain why damaged neurons from the brain and spinal cord - the central nervous system - shrivel into scarred stumps after traumatic injury while those from the body's peripheral nervous system possess the ability to spontaneously regenerate.

Assistant Professor of Medical Science and Engineering Diane Hoffman-Kim, seated, and Beth Toste '04

Growth-encouraging as well as growth-discouraging cues are found near central and peripheral nerve cells, but in different combinations and abundances. Whether a nerve cell grows depends on how it incorporates these contrasting signals. In a developing baby, for example, growth-promoting cues outweigh growth-inhibiting cues, resulting in the active growth of neurons in the spine and brain.

Nerves from the peripheral nervous system are surrounded by sheet-like Schwann cells, which wrap tightly around neurons and provide an environment that encourages growth. In contrast, nerves from the central nervous system find themselves hemmed in after injury by cells called oligodendrocytes, which produce cues that discourage growth.

One strategy, then, to jump-start damaged central nervous system cells is to surround them with growth-promoting Schwann cells. Hoffman-Kim's group takes Schwann cells from the thigh of a rat and places them around spinal and brain cells in an effort to overcome the inhibitory environment of the central nervous system.

"The basic question we address is how to recreate the environment of a peripheral nervous system cell in the central nervous environment," Hoffman-Kim said. Six undergraduates and two graduate students have participated in the group research project called "Nerve Guidance in (Simplified) Complex Environments."

"We call it 'simplified' because we're working with cells in a dish," Hoffman-Kim said. "We're trying to decipher, one by one, the multiple varied biological processes that exist in the live animal. It's complex because even though it's in a dish, we're using sophisticated biomedical engineering technology to manipulate cells with an incredible amount of precision."

Most scientists think that even mature, damaged central nervous system nerves can grow under the right environmental conditions. After injury, central nervous system nerves do, in fact, make modest efforts at repair. These efforts, however, are soon squelched by growth-inhibiting cues from the environment.

Why would nerves want to inhibit their own growth? Growth inhibitors provide a cellular scaffold in developing nerve systems so that neurons only sprout where they are intended. Like red traffic lights at a busy intersection, inhibitors ensure that only certain neurons grow, so that the

proper connections are made. Without inhibitors, a frenzy of growth would occur, causing chaos at the molecular scale and ultimately nervous system failure.

Hoffman-Kim thinks that nerve cells ultimately make growth decisions by balancing multiple factors, including the abundance of each type of growth cue and the spatial arrangement of the cells that produce the cues. To test this hypothesis she and her students use lasers and rubber molds to precisely position nerve cells in relation to one another. The group is also using a technique called Chromophore Assisted Laser Inactivation to zap, and thus inactivate, certain proteins in living cells which influence nerve growth.

By having such precise control over cell position and the concentration of growth cues, the group hopes to develop a more quantitative understanding of how the environment directs nerve growth. Scientists "have been putting peripheral cells into the central nervous system for quite a while, but we haven't understood what was happening in enough detail," she said. "Hopefully, this work will change that."

Hoffman-Kim credits the undergraduates participating in the GRP for helping to prepare data that was critical for securing grant funding. GRPs are small teams of undergraduate students who work with a faculty member on a project that contributes to the faculty member's research. Students participating in a GRP receive course credit for their work and take an active part in every facet of the research.

"Brown definitely has a great research atmosphere that is very friendly to undergrads. They really give a lot of opportunities that wouldn't be available at other universities," said Alex Toy '04, one of the students working with Hoffman-Kim. "It's great that professors here are so welcoming."

The other undergraduates working with Hoffman are Ronald Beimel '06, Joshua Goldner '05, Shaily Kapur '04, Beth Toste '04, and Pearl Yu '04. The graduate students working on the project are Daniele Gazzola and Jan Bruder. Hoffman-Kim plans to present the results of her research in two or three scientific conferences this coming fall.