



OCT scans such as this one may provide a “window” for tracking nerve repair in clinical trials.

ELIZA GORDON-LIPKIN

## Nervous system repair: The next frontier in MS research

by John R. Richert, MD

People often ask me what’s coming down the pipeline for MS—what’s the next breakthrough. I tend to point out that within a few years we’ll likely have more effective and more convenient weapons to fight the immune activity that underlies multiple sclerosis. The next frontier is to find ways to repair the damage that MS does to brain and spinal cord tissues, ultimately to restore function.

Myelin—the insulating material that is wrapped around the nerve fibers (axons)—protects the axons and also helps nurture

them. When myelin is stripped away by the immune system, the axons and their cell bodies become vulnerable. Damage to both the myelin and the nerve

fibers leads to the progressive disability experienced by many people with MS. That’s why it’s so important that we find ways to protect and repair

these vital tissues.

One of two 2008 North American Education Programs focuses on nervous system repair. The program, being released this month, is a collaboration between our own Society and the MS Society of Canada. Some

The next frontier: find ways to repair MS damage and restore function.

of the repair strategies covered by the program are outlined briefly below.

### Stimulating the brain's repair capacity

The body attempts to repair myelin damage and often succeeds, especially early in the MS disease process. Work is underway to understand why some lesions are repaired and others are not, and on deciphering the molecular signals that are sent out at sites of injury to recruit the body's own repair cells.

The hope is to find ways to mimic these signals to stimulate repair. Also under investigation are a host of proteins known as "growth factors" for their roles in turning on different stages of myelin formation and nerve growth. Investigators have developed high-speed screening systems to identify molecules that may stimulate tissue repair.

Another approach is to identify and block natural processes that may actually **inhibit** the body's ability to repair nervous system damage.

### Prospects for cell therapy

What about supplying new cells to do the repair work? Right now this work is going on largely in rodents and other animals to work out safety issues and to figure out the optimal source of cells to transplant, how to obtain enough cells for transplant, the best mode of delivery, and other issues. There are also concerns

that certain types of transplanted cells could multiply uncontrollably and give rise to tumors.

Many readers will have heard of bone marrow stem cell transplantation to treat some forms of cancer. Over the years, there have also been efforts to determine whether this procedure (called autologous hematopoietic stem cell transplantation) can stop MS by "rebooting" a person's immune system. There have been mixed results, and further trials are ongoing to determine whether this invasive procedure can stop disease activity or even restore some functions.

But now researchers at the University of Bristol in the UK have announced the beginning of a study involving a handful of people with MS who would receive infusions of a different type of their own bone marrow-derived stem cells, called "mes-

enchymal stem cells," with the aim of repairing nervous system damage.

There has been some debate as to whether there is enough information on mesenchymal stem cells to warrant proceeding with a clinical trial at this time. The scientific world will be watching to see what can be learned about the safety of this type of cell therapy. Some fear that if this trial is not successful from the safety standpoint, it would set nervous system repair research back a number of years. It will be important to interpret the results in the context of what we know and don't know about the basic biology of mesenchymal stem cells.

### Tracking repair

One thing that's missing is a "window" into the brain to see whether any repair or protection interventions will work, and to track how well they enhance repair. New imaging methods to assess the health of nerve tissue and to quantify damage and responses to therapy are under development.

One new tool is a high-resolution imaging technique called optical coherence tomography, or OCT (see picture, page 71). A recent report suggested that OCT-detected thinning of the nerve layer at the back of the eye echoes evidence of brain shrinkage in MS, suggesting it may be a useful tool for tracking repair in clinical trials.



Dr. Richert

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—Caroline Whitacre, PhD

This study involved a team of investigators from Baltimore, Philadelphia, Dallas and Birmingham who were formerly working individually on this problem. This kind of collaboration, on an even larger scale, is what it will take to properly tackle questions surrounding nervous system repair for people with MS.

### Big science + wide collaboration = progress

Achieving nervous system repair requires lots of money and many collaborations between researchers across disciplines. The National MS Society alone is investing \$38 million for multi-year projects focusing on virtually every aspect of myelin formation, nerve function in MS, and repair of the brain and spinal cord. This includes our flagship Nervous System Repair and Protection initiative being funded through the Promise: 2010 campaign. The four international repair teams are becoming a catalyst pushing this field forward.

Few scientific fields are changing as quickly as the landscape of nervous system tissue repair. There are hundreds of scientists around the world who stay awake at night thinking their way through these issues. This exciting area may ultimately lead to ways to reverse the damage and restore nerve function in people with MS.

Dr. John Richert is executive vice president for our Research and Clinical Programs.

SHERYL TAYLOR



## We've come a long way: Research featured at National Conference

At the 2007 National Conference of the National MS Society in Dallas, Caroline C. Whitacre, PhD (The Ohio State University, Columbus) delivered the keynote address on multiple sclerosis research.

“When I began my research career in the 1970s, there were no approved therapies for MS and knowledge of the immune system was limited,” said Dr. Whitacre, whose career was launched with a postdoctoral fellowship award from the Society. “Today, we are making progress in virtually every field that impacts MS.”

Dr. Whitacre cited the following strides:

- Finding genes that make people susceptible to whatever triggers MS—a recent genome-wide study identified two new genetic variations.
- Discovering possible trig-

gers, such as smoking or viral infection, and possible protective factors, such as sun exposure.

- Understanding the potential of cell transplants for stimulating repair—studies show that immature nerve cells can repair damage in mice with MS-like disease.

- Translating knowledge of gender differences to clinical trials—the nationwide study of oral estriol in 130 women with MS.

Dr. Whitacre has been at the forefront of research into gender differences, and presented new findings on the widespread immune suppression which occurs during pregnancy.

“Pregnancy is the best treatment for multiple sclerosis,” Dr. Whitacre said. “We need to take advantage of this naturally-occurring suppression. The best is yet to come!”