**Research Now** is a quarterly feature of **Momentum**, produced by the Society's Research and Clinical Programs Department.

**Sara Bernstein**, Editor, **Research Now**

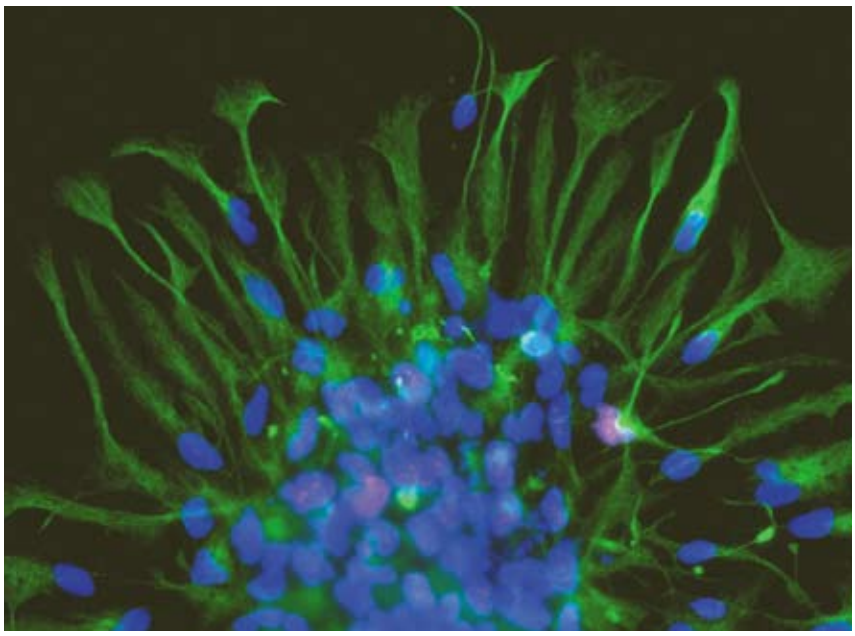
**Cathy Carlson**, Senior Director, Research Information

**INSIDE:**

**64** **Following MS research down every path**

**66** **Targeting MS pain**

The National MS Society is proud to be a source of information about MS. Our comments are based on professional advice, published experience and expert opinion, but do not represent individual therapeutic recommendation or prescription. For specific information and advice, consult your personal physician.



STEFANO PLUCHINO

# Cell therapy for MS

by Sara Bernstein

The Holy Grail of multiple sclerosis research is repairing damage to restore function. Although there are therapies that modify the course of the most common forms of MS, none has been proven to repair damage once it occurs. One strategy is the exciting frontier of cell transplantation or cell therapy. This approach may stimulate the brain's natural capacity for repair and may provide an outside source of replacement cells.

MS is not an easy target for cell-based therapies though, because as a chronic disease it involves repeated assaults on brain and spinal cord tissues, and the damage occurs at many sites. For a cell therapy to work, the supply of cells would have to be vast, and the cells would probably have to be able to migrate to several areas concurrently. Ideally, new cells would be safeguarded from immune assaults that damaged the original tissue.

In May 2009 the MS societies of the United Kingdom and the United States held an international meeting in London to build

**Keep up on MS research**

Subscribe to the monthly National MS eNEWS to get the latest research news in your inbox. Go to **nationalMSsociety.org/signup** to create your user profile and start receiving the eNEWS and other Society communications.

And visit **nationalMSsociety.org/research** regularly for full coverage on everything from research breakthroughs to clinical trials near you.

consensus on clinical trials of all types of stem cell therapies in MS. The resulting guidelines for researchers and clinicians, slated to be published soon, should encourage consistency between studies and speed up the development of potential cell therapies.

### Which cells?

Finding the best source of replacement cells and how to deliver them are just a few of the challenges being addressed by research teams around the world, including the four international teams collaborating as part of the National MS Society's Nervous System Repair and Protection initiative, launched through the Promise: 2010 campaign.

First let's distinguish these strategies from a similar-sounding procedure being investigated in MS. It is variously called "hematopoietic stem cell therapy," "bone marrow transplantation," and "autologous stem cell transplantation." This procedure aims to **reboot the immune system** by repopulating the body with new immune cells that will no longer attack the brain and spinal cord. There is no proof yet that it can "cure" a person with MS, but research is ongoing worldwide to determine whether it can halt progression or bring on remission of disease.

Here are just a few candidates under study for cell transplantation **to induce protection or repair** in MS.

### Mastering mesenchymal stem cells

Adult mesenchymal (pronounced messENkimmul) stem cells are present in many tissues of the body, including the bone marrow and fat (adipose tissue). Dimitrios Karussis, MD, PhD, and colleagues (Hadassah-Hebrew University Hospital, Jerusalem) showed how they could protect the nervous system in mice with chronic EAE, an MS-like disease. In treated mice, 86% to 95% of nerve fibers were left intact, versus 45% in untreated controls. **Archives of Neurology** 2008;65:753–61

These and other preclinical results led Mark Freedman, MD (University of Ottawa), and Antonio Ucelli, MD (University of Genoa), to launch a unique effort to translate these findings to clinical trials. Realizing that initial studies each would involve very few people, in 2009 they invited investigators interested in mesenchymal research to share evidence and form a consensus on conducting clinical trials so that results of small studies could be compared.

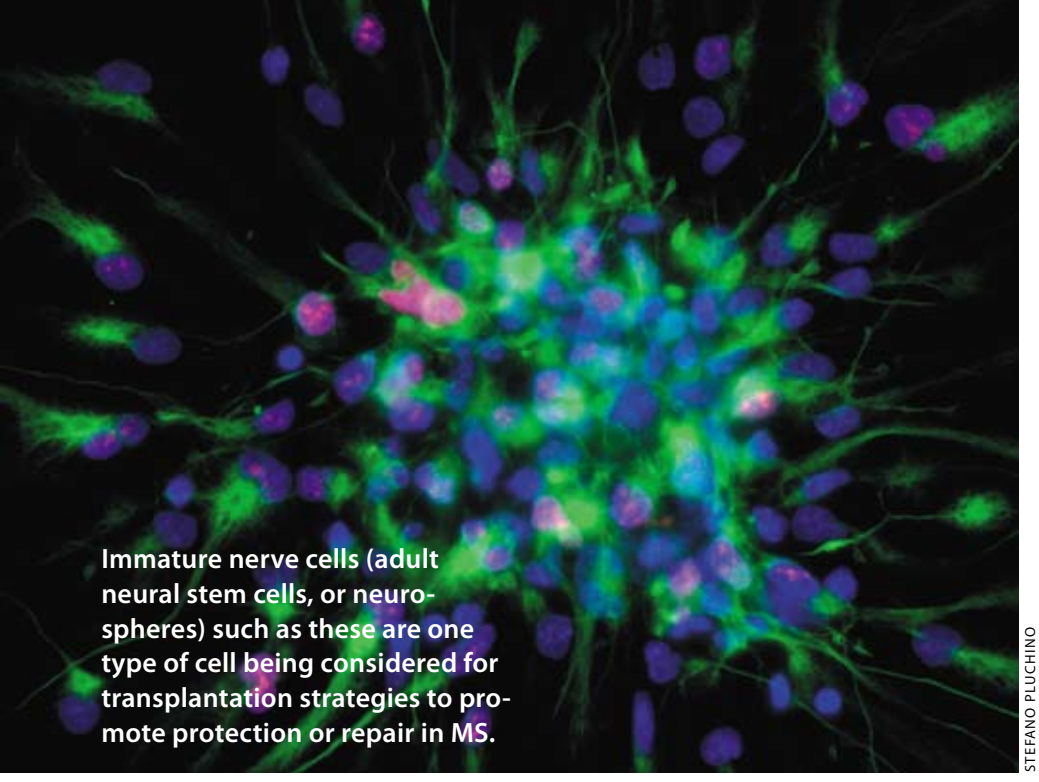
The International Mesenchymal Stem Cell Transplantation Study Group's consensus report lays out their recommendations for study details such as inclusion/exclusion criteria, stem cell product, and measuring outcomes. "We hope that other researchers who are interested in pursuing MSCT as a potential treatment for MS will join in," they wrote. **Multiple Sclerosis** 2010 Jan 19 [Epub ahead of print]

As of this writing, at least five small clinical trials of mesenchymal stem cell transplantation are underway in people with MS; four are being conducted by members of the MSCT study group. More information is available on **clinicaltrials.gov**, and on our Web site at **nationalMSsociety.org/mescell**.

### The promise of neurospheres

In 2003, Stefano Pluchino, MD, and Gianvito Martino, MD (San Raffaele Hospital, Milan) reported that immature nerve cells (adult mouse neural stem cells, or neurospheres) injected into the blood or brain cavities of mice with EAE could move throughout the brain and spinal cord to sites of tissue damage, promote repair of nerve-insulating myelin, decrease damage to nerve fibers, and reverse clinical disease. **Nature** 2003;422:688–694 Dr. Martino has since joined forces with the Nervous System Repair and Protection Initiative team based at the Universities of Cambridge and Edinburgh. He is investigating these immune mechanisms further, and is planning early clinical trials of neurosphere transplants in people with MS.

Jeffery Kocsis, PhD (Yale University) is a pioneer in the study of cell-based therapeutic strategies for MS. With funding from a Collaborative MS Research Center Award from the Society, his team investigated a novel source of neural stem cells in the adult



Immature nerve cells (adult neural stem cells, or neurospheres) such as these are one type of cell being considered for transplantation strategies to promote protection or repair in MS.

STEFANO PLUCHINO

brain—the olfactory bulb, which controls perception of odors. They isolated neural stem cells from the olfactory bulb of rats, and then introduced these cells into areas of myelin damage in the spinal cord of other rats. The cells survived, integrated into the areas of damage, and extensive myelin repair was observed. 2009; **PLos one** 4(9):e7260 Research on this strategy continues.

## Making the myelin makers

Although myelin-making cells—oligodendrocytes—are lost in MS, research indicates that the capacity for repair exists in people with the disease, but fails for some unknown reason. The Society is funding some of the best minds in cell transplantation to tackle this problem, and several are studying how to take advantage of immature oligodendrocytes—known as oligodendrocyte precursor cells (OPCs).

Steven A. Goldman, MD, PhD (University of Rochester Medical Center), is among the leaders focusing on the potential of cell therapy to treat MS. His team showed that transplanting OPCs into mice that normally make no myelin results in almost complete restoration of their previously lost neurological function. **Cell Stem Cell** 2008;2:553–65 This Society-funded project was supported in full by gifts from the Charles and Margery Barancik Foundation and the Alan Buegeleisen Research Fund. Now they are exploring these findings in other mouse models, including a model that resembles progressive MS. Dr. Goldman also is working with Ian D. Duncan, BVMS, PhD, FRCPath (University of Wisconsin, Madison), whose Repair initiative team is investigating novel methods of encouraging and tracking OPCs in novel animal models and exploring other sources of replacement cells.

Thomas Lane, PhD (University of California, Irvine) is leading a new Collaborative MS Research Center focusing on cell therapy. He has been funded to study messenger chemicals, called chemokines, for clues to stopping the influx of damaging immune cells in MS, but now is looking at them as possible vehicles for allowing the migration of OPCs into sites needing repair. These studies require major sources of cells, which is the focus of team member Hans Keirstead, PhD, who has extensive expertise in generating stem cell lines.

Another potential source of myelin-making cells is in the body's periphery. "Schwann cells" are very good at repairing myelin lost from nerves in the arms or legs, but do not normally cross into the central nervous system. Anne Baron-Van Evercooren, PhD, and colleagues at INSERM in Paris, as well as other teams, have found that altering gene activity in Schwann cells could enhance their migration to lesion sites and promote their repair activities in the central nervous system of mice. **Brain** 2010;133:406–420

## Fast-paced field

These studies are just a small sample of research going on around the world on cell therapy for MS. Cell therapy is truly an exciting strategy that brings much promise for restoring function in people with MS.