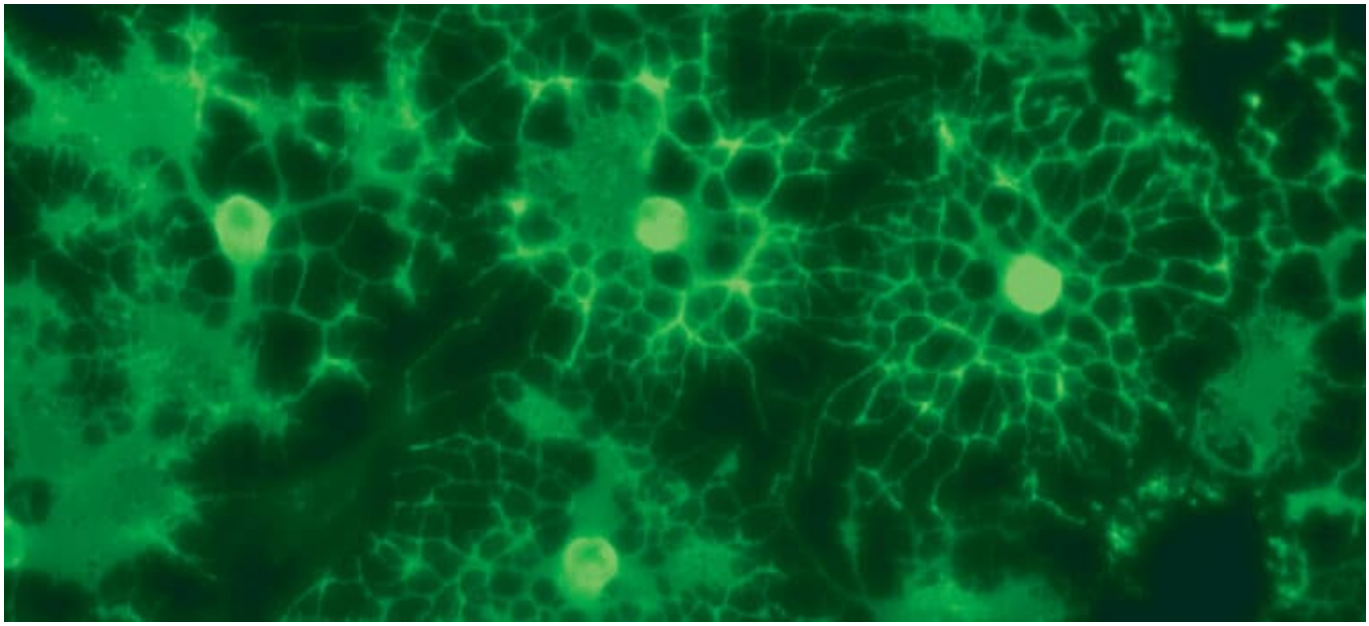
New hope for repairing myelin damage in MS



Stem cell therapies show early successes in lab models.

by Mary E. King, PhD

Dr. Jeffrey Cohen Photo courtesy of Dr. Jeffrey Cohen

Stem cell therapies are receiving considerable attention as possible methods to repair nerve damage that occurs in progressive forms of multiple sclerosis. Dr. Jeffrey Cohen, director of the Experimental Therapeutics Program at the Cleveland Clinic, and Paul Tesar, PhD, assistant professor of genetics and genome sciences at Case Western Reserve School of Medicine in Cleveland, are among many researchers advancing this field using several different approaches.

Why the intense interest? People with relapsing MS have a number of options for approved medications. These therapies target the immune system, slowing damage to the myelin, the insulating substance that surrounds the nerve fibers and which is a major target for the attack in MS. However, these therapies do not directly repair damage that has already occurred, and they are not helpful for many who have progressive MS.

Stem cell therapy holds the promise of actually repairing myelin, a restorative step that would be particularly helpful to people in the progressive phase of MS. Although some cell-based therapies have entered early clinical trials in humans, including one by Dr. Cohen and his collaborators, so far most of the research is being done in mice.

Promoting repair

"The specific type of stem cell that we study is called a mesenchymal stem cell (MSC)," Dr. Cohen says of his team's approach. "We isolate MSCs from the bone marrow of an adult and then multiply them in the lab," so they can be tested in a clinical trial.

Purified MSCs are then injected into the same adult's vein and travel through the bloodstream to the brain. What is most exciting, Dr. Cohen continues, is that "MSCs appear to seek out damaged areas and help promote myelin repair" in the brains of laboratory animals with experimental autoimmune encephalomyelitis (EAE), an MS-like disease. "We are hopeful that the same thing happens in people with MS."

MS Progression

Aiming for new heights: The Serial Unified Multicenter MS InvesTigation (SUMMIT) study is generating excitement in its quest to unravel the mystery of MS progression.

With funding from the U.S. Department of Defense, Dr. Cohen is now conducting an early stage clinical trial (called "phase 1") to test the safety and feasibility of using MSCs in people with MS. The study enrolled a total of 24 people. Final results are expected in early 2014 (Journal of the Neurological Sciences 2013; Jan 4). If the results are positive, Dr. Cohen hopes to initiate a larger, phase 2 trial to determine the effectiveness of MSC transplantation.

To facilitate the potential of this study, the National MS Society awarded a pilot grant to Dr. Cohen to help refine procedures for expanding patients' MSCs for injection and to see whether MSCs from people with MS differ from MSCs from people without MS.

As Dr. Cohen explains, "This is a very complicated undertaking; [stem cell therapy] is not like a drug, where you know exactly what you are giving to a patient. Stem cells are very dynamic, and they can change their function depending on where they find themselves. However, [if this approach works], it does offer a new strategy to repair damage in the progressive stage of MS."

Direct repair

What are stem cells?

Stem cells possess two key qualities: They divide and replicate when they are grown in the laboratory, and they have the potential to turn into a specialized cell, such as a brain or blood cell.

Mesenchymal stem cells (MSCs) can be isolated from many tissues. When injected into the bloodstream, they migrate directly into damaged or inflamed tissues, including the brain. MSCs do not directly repair the myelin that is damaged by the immune attack that occurs in MS. Instead, they seem to release chemicals that stimulate the natural repair processes of damaged tissue.

Oligodendrocyte progenitor cells (OPCs) develop into cells that do the actual job of repairing the myelin damage. However, because OPCs cannot move from the bloodstream into the brain across what is known as the "blood-brain barrier," these cells probably will need to be injected directly into the brain.

Dr. Tesar uses a different type of stem cell and a different approach in attempts to directly repair myelin. He explains, "The cell type we are most excited about as a cellular therapeutic is the oligodendrocyte progenitor cell (OPC)." When injected into the brain in animal models, these cells directly myelinate damaged nerve fibers.

Recent advances by Dr. Tesar and other investigators involve taking skin cells and converting them into OPCs in the laboratory. This procedure could potentially enable scientists to take a tiny piece of skin from an individual with MS, grow the skin cells in the lab, convert them to OPCs, and then inject the OPCs into the person's brain to repair the damage that has occurred in MS (Nature Biotechnology 2013; 31:426).

The National MS Society has current investments of more than $3 million to explore the potential of stem cell therapies.

One team, led by Dr. Steven Goldman at the University of Rochester, recently reported success transplanting stem cells derived from human skin into the brains of mice. The cells developed into myelin-making cells that formed new myelin quickly and efficiently. Dr. Goldman and his collaborators have leveraged $12.1 million in funding from New York State Stem Cell Science for clinical trials of stem cell strategies.

While Dr. Tesar's research is not yet ready for a clinical trial—additional questions about how OPCs behave long-term in animal models must be answered before they can be tested in humans—he is enthusiastic about its possibilities. "Cell transplantation is a completely new field for diseases of the brain. We are hoping that this type of research will change how we

treat MS.”

Mary E. King, PhD, is a freelance medical writer from Boulder, Colo.

Read more about Dr. Steven Goldman’s stem cell therapy study.

Read more about stem cell therapy in this downloadable PDF, “Stem Cell Therapies in MS.”