Nervous System Repair – Reversing Damage to Regain Function

Repairing the nervous system, in particular myelin, the coating that surrounds and protects axons (nerve wires) and which is damaged by MS, was just a dream just a few years ago. Today it holds significant promise as a strategy to restore the function that MS has taken from people; and reducing or stopping MS progression. This remarkable progress is due to the National MS Society’s comprehensive efforts and multi-million dollar research investments.

We are at a pivotal moment in time where breakthrough solutions can change the world for everyone with MS. Among the approaches being taken are:

- Clinical trials to stimulate the natural capacity of the brain to repair itself.
- Tests of the ability of stem cells to treat MS damage.
- Finding ways to protect the nervous system to allow natural myelin repair to occur.
- Developing better ways to track successful repair.

This exciting research area has been gaining momentum since the Society’s 2005 global initiative funded four collaborative teams who were focused on nervous system protection and repair. Over five years, the teams engaged more than 100 investigators, produced over 180 research papers, identified new therapeutic targets and launched clinical trials to test neuroprotective strategies. Today the Society is supporting 87 research projects in nervous system repair, with multi-year commitments totaling over $35 million.

Promoting natural capacity for repair

Research shows that the brain does repair myelin to some extent, but myelin repair may stall. While we don’t fully understand why repair fails in MS, early clinical trials are now underway to test their ability to stimulate myelin repair. The Society is supporting research looking at key molecules that are important to the cells that make myelin (oligodendrocytes) and that may serve as targets for promoting myelin repair. Promising solutions to restore function are now at our fingertips:

- Jonah Chan, PhD (University of California, San Francisco) won the Society’s first Barancik Prize for Innovation in MS research for creating novel technology that enables screening of thousands of molecules for their myelin repair potential. The strategy identified one drug that is now in clinical trials, possibly bringing potential treatments to market more quickly.
- Acorda Therapeutics is launching a Phase I clinical trial to test an antibody called “rHlgM22,” which promotes myelin repair in mice. Early Society support to Dr. Moses Rodriguez at the Mayo Clinic helped his team to uncover this antibody’s myelin repair properties.
- Several Society-supported commercial research initiatives are exploring ways to enhance the ability of oligodendrocytes to proliferate in areas of myelin damage to facilitate repair. For example, we’re supporting ENDECE Neural to further develop NDC-1308, a form of hormone that has shown early potential to promote nerve repair.

“Regenerating lost brain tissue is the next frontier in MS – to add repair to what we can already do to fight inflammation – to dramatically delay or prevent disease progression.”

Bruce Trapp, PhD
Cleveland Clinic Foundation
Stem cell therapy
The Society has been supporting research for over a decade into the potential of different types of stem cells, including adult cells derived from bone marrow, fat and skin. Additional research is needed to determine whether this approach will help people with MS, but exciting progress has been made already:

- A team led by Steven A. Goldman, MD, PhD (University of Rochester) successfully transplanted 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.
- Researchers in Italy led by Gianvito Martino, MD (Ospedale di San Raffaele in Milan) have forced mouse skin stem cells to become myelin-making cells and put them into the spinal cord. The cells promoted recovery in mice with MS-like disease, but didn’t actually make myelin. The cells appear to release growth chemicals that stimulate natural repair processes and reduce inflammation.
- The Society helped fund the development of Athersys’ MultiStem adult stem cell platform for the treatment of MS, including progressive forms of the disease. MultiStem appears to stimulate production of molecules that regulate the immune system, protect damaged cells, and promote repair.
- A Phase I clinical trial at Cleveland Clinic is testing individual’s own adult stem cells isolated from the bone marrow to both inhibit immune activity and improve natural repair processes in people with relapsing MS. This study is funded by the Congressionally Directed Medical Research Program, and the Society funded the team’s pilot study comparing stem cells from people with and without MS.

Protecting the nervous system
To stop further damage and allow natural myelin repair to occur, the Society is funding clinical trials of potential therapies that will protect the nervous system. For example:

- Ibudilast – a repurposed drug with protective potential for progressive forms of MS (funded with the Cleveland Clinic Foundation and National Institutes of Health’s NeuroNEXT Network)
- Lipoic acid – antioxidant may help block nerve fiber damage in MS
- Phenytoin – reduces entry of sodium, linked to increased disease activity, into nerve fibers (collaboration with United Kingdom MS Society)
- The MS-SMART trial which is testing three therapies that may have nerve-protecting properties in secondary-progressive MS (funded in collaboration with the United Kingdom MS Society)
- A trial of the sex hormone estriol, linked to protection seen in pregnancy, added to Copaxone (funded with NIH)

Tracking repair
The Society fuels research to find ways to detect whether the nervous system is being repaired or protected by therapies in future clinical trials. Approaches include:

- Non-conventional brain imaging and scanning nerves at the back of the eye
- Biomarkers in the blood or spinal fluid – which could be “footprints” that indirectly indicate the success of a repair therapy
- Better clinical readouts – called outcome measurements -- that can determine whether a repair or protection therapy is working, without waiting years to watch the disease course

Finding Repair Solutions
Achieving success in the Society’s priority area of nervous system repair would provide life-changing advances for people with MS. It could allow us to restore neurological function for people with all types of MS, including progressive forms of the disease.