
RESTORING FUNCTION

Myelin's Growth, Injury and Repair

Myelin insulates the wire-like extensions of nerve cells, speeding nerve conduction and protecting the nerve from harm. Because myelin is thought to be the main target of the immune attack that underlies MS, it's vital that we understand its development, function and repair.

The National MS Society has current, multi-year commitments of \$18.5 million to support research projects focusing on myelin biology in MS.

Regina C. Armstrong, PhD

Uniformed Services Univ. of the Hlth. Sci.
Bethesda, MD

Area: National Capital Chapter/Region B

Award: Research Grant

Term/Amount: 11/1/09-10/31/12: \$419,685

"Regulation of oligodendrocyte maturation: a key to endogenous cell remyelination" Molecular mechanisms that control myelin development and repair.

Myelin, the substance that wraps and protects nerve fibers, is damaged in the central nervous system (CNS: brain, spinal cord and optic nerves) in MS. Cells known as oligodendrocytes make and maintain myelin in the CNS. During development, oligodendrocyte precursor (OP) cells give rise to oligodendrocytes. Although OP cells persist in the adult CNS and appear to respond to some MS damage by maturing and repairing some of the damaged myelin, for reasons that are not yet clear, they are not able to keep up with the damage.

In this research project, Regina Armstrong, PhD, will study signaling molecules that regulate how OP cells develop into

oligodendrocytes. These signaling molecules act in the control center, or nucleus, of OP cells and oligodendrocytes to control whether genes that have the instructions for proteins critical for myelin development are "turned on," enabling the cells to make myelin. Dr. Armstrong intends to look at how the molecules influence myelin production in cells grown in the laboratory, as well as in the CNS of animals when myelin is developing.

This work could provide new understanding of how the cells that make myelin develop and lead to new ways to stimulate the repair of myelin damaged by MS.

Li-Jin Chew, PhD

The Children's National Medical Center
Washington, DC

Area: National Capital Chapter/Region B

Award: Research Grant

Term/Amount: 11/1/09-10/31/12: \$384,918

"Mechanisms of inhibition of oligodendrocyte differentiation by interferon gamma" Exploring signals that may inhibit tissue repair in MS and ways to overcome them.

Myelin in the brain and spinal cord is formed by oligodendrocytes – cells whose cell membranes ensheath the wire-like axons that send and receive nerve signals. Research indicates that oligodendrocyte precursors (OPCs) – immature cells that might induce myelin repair – are not depleted in areas of damage, but instead are increasingly prevented from developing to maturity. After myelin is damaged by the immune attacks in MS, these cells move into place but some stay in an immature state inside damaged areas, reducing the amount of tissue repair.

Dr. Li-Jin Chew hopes to study how the MS lesion environment could inhibit cell repair. The inflammatory immune protein known as interferon gamma (IFN gamma) is produced in lesions. Her team has preliminary data that treating OPCs with IFN gamma may prevent OPC development by activating an enzyme known as MAP kinase. They are planning to activate and inhibit this protein in OPCs in the laboratory and in mouse models to determine its effects on cell development.

Understanding how the lesion environment prevents remyelination will provide clues to overcoming these effects to stimulate tissue repair in MS.

Teresa L. Wood, PhD

Univ. of Medicine and Dentistry of NJ
Newark, NJ

Area: New Jersey Metro Chapter/Region A
Term/Amount: 11/1/09-10/31/13; \$872,519

“The mTOR Pathway: A master regulator of oligodendrocyte differentiation” Investigating how to make immature cells form mature cells that manufacture new myelin to repair MS damage.

Myelin, the protective coating of nerve fibers, and oligodendrocytes, the cells that make and maintain myelin, are both damaged in MS. Without their protective coating, nerve fibers fail to carry nerve signals properly, leading to the symptoms of MS, and the nerve fibers can also be damaged in MS. Immature oligodendrocytes, known as oligodendrocyte progenitor cells (OPCs) exist in the adult nervous system. However, they fail to differentiate (develop) to the extent needed to continually replace all of the oligodendrocytes damaged by MS.

OPC differentiation is a complex process involving "turning on" a number of genes

that control the manufacture of myelin. A number of chemicals inside the cells are involved in the signals that turn on the genes for myelin manufacture. In this research project, Teresa Wood, PhD, in collaboration with seven other researchers in her own and outside institutions, is investigating one of the chemical signaling pathways known as the mTOR pathway. It acts to turn on a number of the genes involved in making proteins essential to myelin development and Dr. Wood intends to discover details of how it works.

The results of this project could lead to new ways to coax OPCs to develop into oligodendrocytes to repair myelin damaged by MS. A treatment that repairs damaged myelin could restore nerve function and help reverse symptoms of MS.

RESTORING FUNCTION

Nervous System Repair

Decades of research into nerve physiology and the biology of myelin and glial cells that support nerve cells have been laying the groundwork for finding ways to restore normal function in individuals with MS.

The National MS Society has current, multi-year commitments of \$33 million to support research projects focusing on finding ways to repair the nervous system and restore lost function in people with MS.