In A Nutshell
March 2018
Myelin Repair Research

Here are a couple of re-myelinization research projects:
1. A three-year research project titled "Targeting Extracellular Sulfatases to Accelerate Oligodendrocyte Progenitor-Based Myelin Repair and Regeneration" has been funded by the NMSS in the amount of $580,000.
Its primary goal is to determine the role of heparin sulfate proteoglycan (HSPG) sulfation and delineate sulfatase enzymes as novel and efficacious drug targets for regenerative therapy in MS, according to Fraser J. Sim, PHD , associate professor of pharmacology and toxicology and principal investigator on the grant.
The brain contains a population of neural stem/progenitor cells that remain dormant during adulthood.
These cells are commonly referred to as oligodendrocyte progenitor cells (OPCs) and give rise to specialized cells known as oligodendrocytes.
Oligodendrocytes and the myelin that they produce are vital for normal neurological function.
When oligodendrocytes are lost or damaged in demyelinating diseases such as multiple sclerosis this contributes to severe and progressive disability, Sim notes.
"Importantly, OPCs can generate new oligodendrocytes, restoring lost myelin and promoting functional regeneration," he says. "As such, OPCs represent a promising untapped source of stem/progenitors that when properly stimulated could lead to significant regeneration in MS and other diseases."
Unfortunately, in MS the inhibitory tissue environment prevents OPC-mediated regeneration, Sim says.
"Sulfation is a biochemical modification that alters how the tissue environment signals to OPCs," he says. "As such, it is in a unique position to alter the chemical communication of OPCs with the inhibitory MS environment."
"We hypothesize that by blocking sulfatases we will improve both spontaneous myelin repair, but also further potentiate the ability of transplanted human cells to repair the MS brain," Sim adds. "This is important as future transplantation therapies will need to overcome the same inhibitory environment that prevents spontaneous repair."
Sim says the project is significant, as it will define a new role for HSPG sulfation and sulfatases in myelin repair.
"We will characterize the potential of a new drug and identify novel approaches to enhance myelin repair by stem/progenitor cells," he says. "Furthermore, we anticipate that modification of human OPC sulfation will make cells resistant to the otherwise inhibitory environment and thereby significantly increase the likelihood of success for future stem cell-based transplantation therapy in demyelinating disease."

2. Inhibiting an oxidative stress enzyme reduced nerve cell damage and promoted the formation of new nerve cells, a multiple sclerosis study in mice showed.

It also helped regenerate cells that produce the nerve cell-protecting myelin sheath, researchers said. The team used a mouse model of the progressive form of MS in their work.

Oxidative stress is caused by an imbalance between the body's production of potentially harmful reactive oxygen species and its ability to contain them. Oxidative stress leads to immune cells releasing reactive oxygen species. This release promotes nerve cell damage and degeneration of the myelin sheath.

Myeloid cells are one type of immune cell that releases reactive oxygen species. Although the cells' name is similar to the name myelin, they have nothing to do with myelin production.

Myeloperoxidase is one of the most potent oxidative-promoting enzymes that myeloid cells release when they generate inflammation in response to an injury or threat.

Because the release leads to cell damage, researchers hypothesized that inhibiting the enzyme could have positive effects.

The team decided to treat a mouse model of the progressive form of MS with a myeloperoxidase inhibitor called N-acetyl lysyltyrosylcysteine amide.

They divided the mice into two groups, with one receiving the inhibitor and the other a placebo. They administered the inhibitor into the abdomens of the first group, with some getting injections once a day and some two injections. The controls received a saline solution called PBS in matching amounts.

The key finding was that the inhibitor significantly reduced the disease scores of the mice, compared with the controls, even at the lower of the two doses. Researchers said the results supported the notion that myeloperoxidase plays a key role in the damage seen in progressive MS.

The team also analyzed levels of myeloperoxidase in the mice's spinal cords. The levels increased significantly after the mice were engineered to have MS. But treatment with the inhibitor stopped the increase.

Inhibiting myeloperoxidase "not only reduced the level of oxidative stress, but also the number of myeloid [immune] cells" in the central nervous system of the mice with MS, the researchers wrote.

Since nerve cell damage and loss of the protective myelin sheath are hallmarks of MS, the team also looked at whether the inhibitor could alleviate these problems. It found that it did.

In addition, the team discovered that the inhibitor promoted the formation of nerve cells in mice with MS and helped regenerate oligodendrocytes — cells responsible for myelin production in the central nervous system.

"Taken together, our data suggests that targeting MPO [myeloperoxidase] should be a good therapeutic approach for reducing oxidative injury and preserving neuronal [nerve cell] function in progressive MS patients," the team concluded

Just For Fun

Has anyone succumb to the flu this season? There is nothing about the flu that is "Fun" but I read an inspiring article written by a person with MS who was recovering from the flu. This ties in with the rejuvenating of myelin. Of course we have no control over how or when that will be discovered. We do have some control over how we cope recovering from the flu. She writes that "our bodies are trying to preserve themselves from the constant attacks they're under, our spirits are revitalizing, and our minds are calling to memory all the times we made it through the most difficult occurrences of life. Our minds are preparing us for physical, psychological, and spiritual warfare against the spirit of illness and adversity."

"Even the darkest night will end … and the sun will rise." –Victor Hugo, "Les Miserables."

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