Uncovering the multiple sclerosis protein

BY NICOLE YADA

A white-matter component called myelin basic protein (MBP) has long been known to be implicated in the formation of multiple sclerosis. But exactly how it functions remains largely a mystery.

To help address the matter, physics Prof. Vladimir Ladizhansky and molecular and cellular biology Prof. George Harauz are working together to identify the structure of MBP, one of the proteins that make up a large portion of the myelin sheath.

The myelin sheath is responsible for causing rapid nerve conduction in higher vertebrates. In fact, myelinated axons transmit nerve impulses 100 times faster than non-myelinated axons.

In MS sufferers, the sheath loses myelin. This degeneration causes nerve transmission to slow, negatively affecting the brain's ability to communicate with the spinal cord. As a result, neurologically based co-ordination problems become apparent.

"If you want to look at intelligent design for MS drugs, you'll want to know the molecular basis of this protein," says Ladizhansky.

About one-third of the body's proteins cannot be crystallized, including MBP. So Harauz and Ladizhansky are using solid-state nuclear magnetic resonance spectroscopy to gain a better understanding of MBP at its atomic level.

MBP is "floppy" by nature, with the appearance of a folded string. When the MBP sample is placed in the magnetic field, the nuclei (which behave like small magnets) align, and the strength of interaction between the nuclei is measured. A strong signal means there's a short distance between those segments of the protein. The many distance measurements can then be converted into a structure.

What causes the degeneration of MBP (and consequent development of MS) remains unknown. After age 20, the amount of myelin in a healthy person's body is normally consistent throughout the rest of their lives. However, until age 20, myelin development remains vulnerable to irregular activity in the enzymes responsible for protein processing and modification.

While this much is known, it is necessary to identify the MBP structure to establish how and why the protein degenerates. Knowing the MBP structure will enable researchers to understand key facts, such as how myelin damage spreads and what the genetic component is for MS.

Determining the structure of the myelin-based protein is important for understanding how and why it degenerates in multiple sclerosis, say Profs. Vladimir Ladizhansky (left) and George Harauz.

"By the time MS is diagnosed, a significant portion of the MBP has already been lost," says Harauz. An in-depth understanding of this protein means a method for replacing lost myelin will come closer to being a reality.

This research is funded by Canadian Institutes of Health Research and the Natural Sciences and Engineering Research Council.

| Photo by Kyle Rodriguez