

'Cars' imaging reveals clues to myelin damage

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Researchers have discovered that calcium ions could play a crucial role in multiple sclerosis by activating enzymes that degrade the fatty sheath that insulates nerve fibers.

Learning exactly how the myelin sheath is degraded might enable scientists to determine how to halt disease progress and reverse damage by growing new myelin, said Ji-Xin Cheng, an assistant professor in Purdue University's Weldon School of Biomedical Engineering and Department of Chemistry.

"Although multiple sclerosis has been studied for many years, nobody knows exactly how the disease initially begins," he said. "The pathway is not clear."

Purdue researchers used an imaging technique called coherent anti-Stokes Raman scattering, or CARS, to study how the myelin sheath is degraded by a molecule called lysophosphatidylcholine, known as LPC. The LPC does not cause multiple sclerosis, but it is used extensively in laboratory research to study the deterioration of myelin, which insulates nerve fibers and enables them to properly conduct impulses in the spinal cord, brain and peripheral nervous system throughout the body.

The findings suggest that LPC causes sheath degradation by allowing an influx of calcium ions into the myelin. The increased concentration of calcium ions then activates two enzymes - calpain and cytosolic phospholipase A2 - which break down proteins and molecules in the

myelin called lipids.

"It is possible that the same pathway causes myelin degradation in people suffering from multiple sclerosis and spinal cord injuries," Cheng said.

The research demonstrates that CARS microscopy is a valuable research tool and could become a future clinical method to diagnose multiple sclerosis and detect damage to the spinal cord from accident trauma, which also causes the myelin to degrade, he said.

Research findings are detailed in a paper appearing online this month in the Journal of Neuroscience Research. The paper was authored by biomedical engineering doctoral student Yan Fu and postdoctoral research associate Haifeng Wang; Terry B. Huff, a graduate teaching assistant in the Department of Chemistry; Riyi Shi, an associate professor of basic medical sciences in Purdue's School of Veterinary Medicine and an associate professor of biomedical engineering; and Cheng.

"The findings of this study will help us to identify key steps in the progression of the demyelination, which is a hallmark of multiple sclerosis," said Shi, a researcher at Purdue's Institute for Applied Neurology and Center for Paralysis Research. "This information will also facilitate the design of pharmaceutical interventions that slow down or even reverse the development of the debilitating disease."

The researchers used CARS to study and take images of healthy and diseased myelin. The researchers showed that an enzyme called cytosolic phospholipase A2 contributes to myelin degradation by snipping off one of the two tails that make up lipid molecules contained in the myelin. Cutting off one of the tails turns the lipid molecules into LPC, amplifying the effect and further degrading the myelin.

The research was carried out in spinal cord tissues extracted from animals and in the sciatic nerves of living mice.

Findings were confirmed by comparing CARS results with electron microscope images and measurements of electrical impulses in spinal cord tissue that distinguish between normal and diseased myelin.

CARS imaging takes advantage of the fact that molecules vibrate at specific frequencies. In a CARS microscope, two laser beams are overlapped to produce a single beam having a new frequency representing the difference between the original two beams. This new frequency then drives specific molecules to vibrate together "in phase," amplifying the signals from those molecules.

Source: Purdue University

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