



October 10, 2007

## **Antibody Leads to Repair of Myelin Sheath in Lab Study of Multiple Sclerosis and Related Disorders, Mayo Clinic Study Shows**

AMY REYES

ROCHESTER, Minn. — Mayo Clinic researchers have found that a human antibody administered in a single low dose in laboratory mouse models can repair myelin, the insulating covering of nerves that when damaged can lead to multiple sclerosis and other disorders of the central nervous system.

The study will be presented on Oct. 9 at the American Neurological Association meeting in Washington, D.C.

"The repair of chronic spinal cord injury is seldom modeled in laboratory studies, but it is an important reality for the treatment of humans. The concept of using natural human antibodies to treat disease of this kind has not yet been tested in humans, but these research findings are very promising," says Moses Rodriguez, M.D., a Mayo Clinic neurologist and the study's corresponding author. "The findings could eventually lead to new treatments that could limit permanent disability," states Arthur Warrington, Ph.D., a Mayo Clinic scientist and study author.

Myelin repair normally occurs spontaneously, but in multiple sclerosis and other disorders of the central nervous system, the myelin repair process occurs very slowly or fails altogether. Researchers are trying to determine how to speed up the myelin healing process, which they hope will eventually lead to new treatments for patients.

The antibody, which was genetically engineered from a single cell, binds to myelin and the surface of cells in the brain and spinal cord, then it triggers the cells to begin the repair process called remyelination. This antibody is the first known reagent designed to induce repair by acting within the central nervous system at the damage sites on cells responsible for myelin synthesis.

The study uses laboratory mouse models of chronic progressive multiple sclerosis in humans. The severity of the disease and also success of the treatment were largely defined by how naturally active the mice were, particularly during the night because mice are nocturnal and are especially active at this time. They received a single dose of the antibody. A minimum of 25 mcg/kg was needed to trigger remyelination, which is equivalent to about 2 mg in the average adult, considered a very low dose. The myelin repair plateaued after five weeks in the mice models.

In addition, when combined with daily methylprednisolone, (an immune modulating steroid) the antibody still promotes remyelination in mouse models. This is an important fact because the first multiple sclerosis patients treated with the antibody will have been treated first with methylprednisolone.

As a naturally occurring protein of the immune system, antibodies do not appear to carry any side effects, nor are they toxic — even when administered at 4,000 times the minimal effective dose — though the concept has not yet been tested in humans, the researchers say.

In summary, this antibody:

- \* Promotes remyelination with a single dose as low as 25 mcg/kg in mice models
- \* The remyelination plateaus at five weeks after a single dose
- \* Converts a model of chronic immune mediated demyelination to one that repairs with the speed of a toxin induced model of demyelination

In terms of replicating the findings in humans, the researchers have already produced the antibody through genetic engineering and conducted preliminary toxicology experiments in mice showing that 1,000 times the therapeutic dose is not toxic. The study continues to be explored in animal models and eventually, in clinical trials.

In short, the critical finding is that when combined with methylprednisolone, the antibody still effectively promotes remyelination and does not make the mice worse, Dr. Warrington states.

#### About Multiple Sclerosis:

Multiple sclerosis (MS) is a chronic, potentially debilitating disease that affects the central nervous system, which is made up of the brain and spinal cord. Multiple sclerosis is widely believed to be an autoimmune disease, a condition in which the immune system attacks components of the body as if they're foreign.

Multiple sclerosis affects an estimated 300,000 people in the United States and probably more than 1 million people around the world, including twice as many women as men. Most people experience their first signs or symptoms between ages 20 and 40.

#### Collaboration and Support

The study was funded by the National Institutes of Health, the National Multiple Sclerosis Society, Multiple Sclerosis Society of Canada, the Hilton Foundation and Mr. and Mrs. Eugene Applebaum.

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