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Enhanced white blood cells heal mice with MS-like disease

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Genetically engineered immune cells seem to promote healing in mice infected with a neurological disease similar to multiple sclerosis (MS), cleaning up lesions and allowing the mice to regain use of their legs and tails.

The new finding, by a team of University of Wisconsin School of Medicine and Public Health researchers, suggests that immune cells could be engineered to create a new type of treatment for people with MS.

Currently, there are few good medications for MS, an autoimmune inflammatory disease that affects some 400,000 people in the United States, and none that reverse progress of the disease.

Dr. Michael Carrithers, assistant professor of neurology, led a team that created a specially designed macrophage – an immune cell whose name means "big eater." Macrophages rush to the site of an injury or infection, to destroy bacteria and viruses and clear away damaged tissue. The research team added a human gene to the mouse immune cell, creating a macrophage that expressed a sodium channel called NaVI.5, which seems to enhance the cell's immune response.

But because macrophages can also be part of the autoimmune response that damages the protective covering (myelin) of the nerves in people with MS, scientists weren't sure whether the NaV1.5 macrophages would help or make the disease worse.

When the mice developed experimental autoimmune encephalomyelitis – the mouse version of MS—they found that the NaV1.5 macrophages sought out the lesions caused by the disease and promoted recovery.

"This finding was unexpected because we weren't sure how much damage they would do, versus how much cleaning up they would do," Carrithers says. "Some people thought the mice would get more ill, but we found that it protected them and they either had no disease or a very mild case."

In follow-up experiments, regular mice that do not express the human gene were treated with the NaV1.5 macrophages after the onset of symptoms, which include weakness of the back and front limbs. The majority of these mice developed complete paralysis of their hindlimbs. Almost all of the mice that were treated with the Na1.5 macrophages regained the ability to walk. Mice treated with placebo solution or regular mouse macrophages that did not have NaV1.5 did not show any recovery or became more ill. In treated mice, the research team also found the NaV1.5 macrophages at the site of the lesions, and found smaller lesions and less damaged tissue in the treated mice.

Because the NaV1.5 variation is present in human immune cells, Carrithers says, "The questions are, 'Why are these repair mechanisms deficient in patients with MS and what can we do to enhance them?' " He says the long-range goal is to develop the NaV1.5 enhanced macrophages as a treatment for people with MS.

Carrithers is a neurologist who treats patients with multiple sclerosis at University of Wisconsin Hospital and Clinics and the William S. Middleton Veterans' Hospital in Madison. His research team includes Kusha Rahgozar, Erik Wright and Lisette Carrithers. The research was supported by a prior National MS Society research grant and a current VA Merit Award from the Biomedical Laboratory Research and

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The study is being published in the June issue of the *Journal of Neuropathology and Experimental Neurology*.

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