

Discovery of a treatment to block the progression of multiple sclerosis

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Demyelination by MS. The CD68 colored tissue shows several macrophages in the area of the lesion. Original scale 1:100. Credit: <u>CC BY-SA 3.0</u> Marvin 101/Wikipedia

A drug that could halt the progression of multiple sclerosis may soon be developed thanks to a discovery by a team at the CHUM Research Centre and the University of Montreal. The researchers have identified a



molecule called MCAM, and they have shown that blocking this molecule could delay the onset of the disease and significantly slow its progression. These encouraging results from in vitro tests in humans and in vivo tests in mice were published today in the *Annals of Neurology*. "We believe we have identified the first therapy that will impact the quality of life of people with multiple sclerosis by significantly reducing the disability and the disease's progression," said Dr. Alexandre Prat, lead author of the study, researcher at the CRCHUM, and professor in the Department of Neurosciences at the University of Montreal.

Multiple sclerosis (MS) is a neurological disease that is characterized by paralysis, numbness, loss of vision, and gait and balance deficits that lead to chronic disability. There is no effective cure. The disease particularly affects young adults in northern countries. In Canada, nearly 75,000 people have MS.

The brain is normally protected from attacks by the <u>blood-brain barrier</u>. The blood-brain barrier prevents immune cells - lymphocytes - from entering the central nervous system. In people with MS, there is often leakage. Two types of lymphocytes, CD4 and CD8, find a way to cross this protective barrier. They attack the brain by destroying the <u>myelin</u> <u>sheath</u> that protects neurons, resulting in decreased transmission of nerve impulses, and plaque formation.

In 2008, Dr. Prat's team identified a <u>cell adhesion molecule</u>, called MCAM (Melanoma Cell Adhesion Molecule), which plays a crucial role in dysregulation of the immune system observed in <u>multiple sclerosis</u>. "Our studies have shown that MCAM is necessary for the migration of CD4 and CD8 across the blood-brain barrier. If we block the interaction of MCAM with the protein to which it normally binds, we decrease the disease's activity," he said. Independently, the biotechnology company Prothena Corporation plc also discovered complementary data regarding MCAM, which led to an ongoing collaboration between the CRCHUM



and Prothena.

The results are extremely positive. "We observed a decrease of approximately 50% of the disease in mice with experimental autoimmune encephalomyelitis (EAE), the most widely used animal model of MS. What is especially significant is that we can stop the disease from the first symptoms in addition to having an impact on its progression, which is a first," noted Prat.

MS develops in most patients in two phases. For 10 to 15 years, there are outbreaks of symptoms interspersed with remissions. Later, the diseases progresses and the disability worsens, leading to the use of a cane or wheelchair. Currently, none of the drugs available on the market affect the disease's progression.

Prothena has developed a potentially disease-modifying antibody, called PRX003, which is designed, to inhibit MCAM function and thus prevent migration of destructive lymphocytes into tissue. Prothena expects to initiate clinical trials of PRX003 in healthy volunteers by the end of June, and anticipates a study in patients with psoriasis in 2016. Beyond psoriasis, anti-MCAM antibodies may be useful for treating a variety of diseases, including progressive forms of multiple sclerosis.

More information: *Annals of Neurology*: <u>onlinelibrary.wiley.com/doi/10 ... 2/ana.24415/abstract</u>

Provided by University of Montreal

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