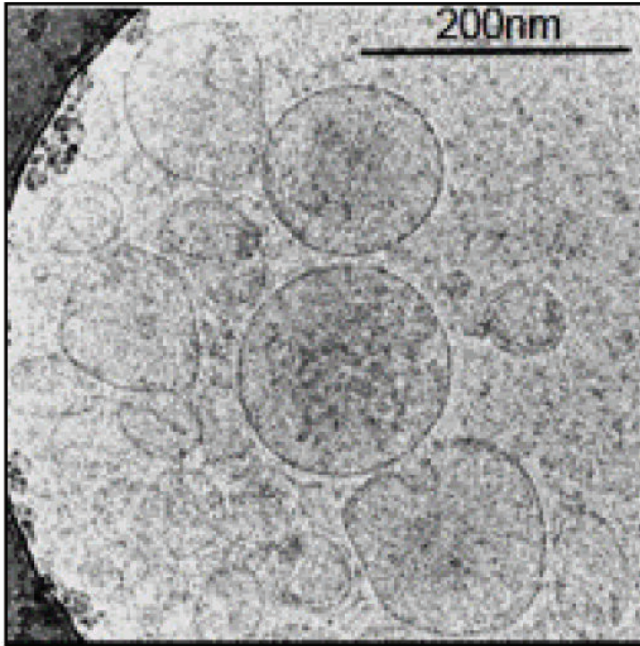


A novel immunotherapy proves effective in animal models of multiple sclerosis

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The purified oligodendrocyte extracellular vesicles under an electron microscope. Credit: G. Casella et al., *Science Translational Medicine* (2020)

Multiple sclerosis (MS) is an autoimmune disorder that develops as the body's immune system attacks the central nervous system. Specifically, it attacks the protective layer surrounding nerve cells, called the myelin sheath. Current MS therapies aim to counter this inflammatory response by suppressing the immune system, which can lead to serious side effects like a higher risk of infection, and even cancer. Jefferson researchers have found a way to prevent immune cells from attacking myelin and halt disease progression, while leaving the rest of the immune system intact, in mouse models of MS. The study was published in *Science Translational Medicine* on November 4th.

"There are many possible immune-activating

antigens in the myelin sheath, but the biggest hurdle is that we don't know which component of myelin is triggering the immune response in MS patients," says senior author Abdolmohamad Rostami, MD, Ph.D., Professor and Chairman of the Department of Neurology at Sidney Kimmel Medical College—Thomas Jefferson University and Vickie and Jack Farber Institute for Neuroscience—Jefferson Health. "Previous studies have used single myelin antigens or combinations of antigens to prevent auto-immunity in animal models, but in humans they have had limited success."

For answers, the researchers turned to [cells](#) called oligodendrocytes. These cells wrap their cell membrane around nerve cells to produce the myelin sheath. Tiny sacs called extracellular vesicles (EVs) can be harvested from cultured oligodendrocytes. The researchers found that these EVs contain almost all the relevant myelin antigens. With all of the antigens present, there'd be a higher chance that these vesicles could halt the autoimmune attack on myelin.

"The neat thing about these EVs is that they give us an opportunity to treat the disease in an antigen-specific way, without having to know the exact identity of the target antigen," explains Dr. Rostami. "It covers all the bases."

The researchers were able to safely inject the EVs intravenously in three different mouse models of MS representing early and late stages of the disease. When administered before disease developed, the EVs had a prophylactic effect, preventing the onset of symptoms like decrease in mobility and paralysis. When given after disease onset, EVs significantly reduced severity of disease in all three models, to the point that the animals could walk again.

"The antigens involved in the auto-immune response can differ between MS patients, and even

change over time in an individual patient," explains Dr. Rostami. "The fact that our approach was effective in different experimental models shows this could act as a universal therapy."

Importantly, the researchers found that the experimental therapy only affected immune cells that were attacking the myelin layer. The rest of the immune system was intact and not weakened at all.

"This is a huge advantage of our antigen-specific method over current therapies, which are like a sledgehammer to the immune system," says Dr. Rostami, "and what makes it so novel."

Translating the approach to the clinical setting, the team found that they were able to isolate the vesicles from human-derived oligodendrocytes. These human vesicles, like those from mice, also contained multiple [myelin](#) antigens, and therefore could have the same therapeutic effect in patients.

Dr. Rostami and his team are now working on getting the intravenous EVs approach patented, which could be a revolutionary step for MS treatment.

"This study was made possible by a talented group of scientists, especially Giacomo Casella, a postdoctoral fellow in our laboratory, and Bogoljub Ciric, and Guang-Xin Zhang, faculty members here at Jefferson," says Dr. Rostami.

More information: G. Casella et al., "Oligodendrocyte-derived extracellular vesicles as antigen-specific therapy for autoimmune neuroinflammation in mice," *Science Translational Medicine* (2020). [stm.sciencemag.org/lookup/doi/...scitranslmed.aba0599](https://stm.sciencemag.org/lookup/doi/10.1126/scitranslmed.aba0599)

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