Possible new target for treatment of multiple sclerosis found

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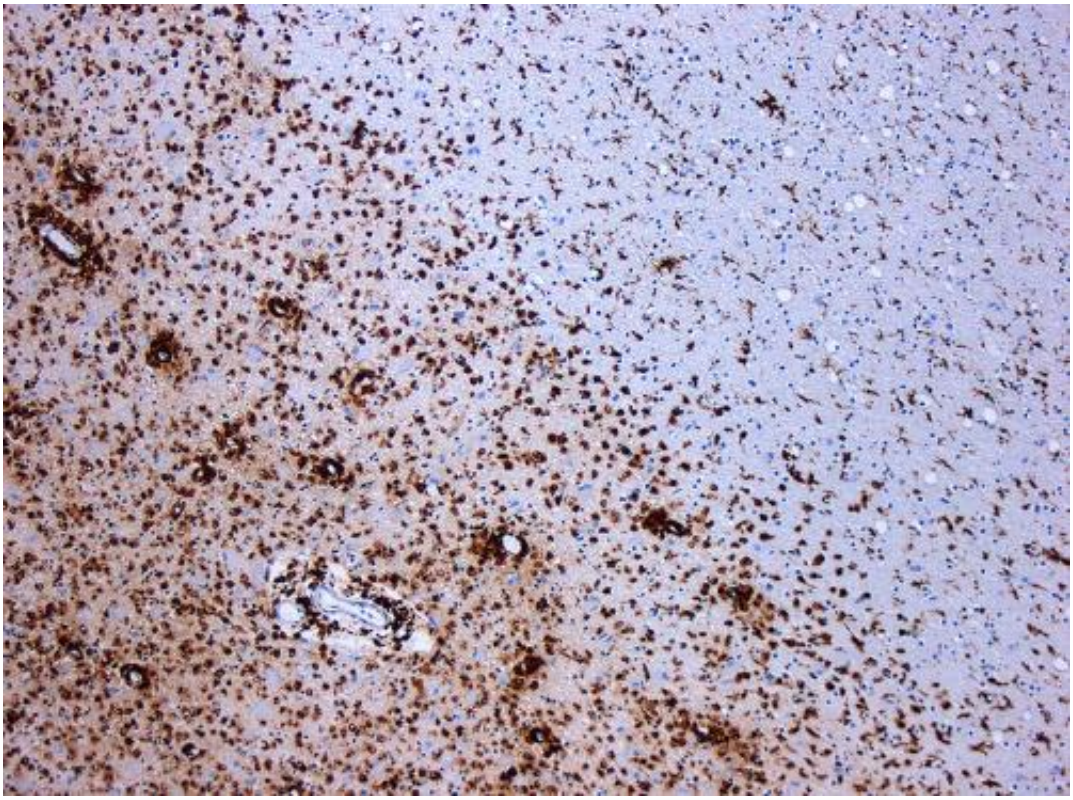

Demyelination by MS. The CD68 colored tissue shows several macrophages in the area of the lesion. Original scale 1:100. Credit: CC BY-SA 3.0 Marvin 101/Wikipedia

In the relentless battle against multiple sclerosis (MS), U of A researchers recently discovered an entirely new cellular mechanism—an underlying defect in brain cells—that may to be blame for the disease,

and a potential hallmark that may be a target for future treatment.

The finding opens the door to a brand new avenue of study in the battle against the cryptic autoimmune disorder that strikes more Canadians than any other nationality worldwide, said Fabrizio Giuliani, study co-author, U of A neurologist and medical director of the Northern Alberta MS Clinic.

"Scientists have been pointing to the mitochondria, the powerhouse of the cell, as a possible link to MS, but have not been able to decipher how they malfunction. Ours is the first study that combines clinical and lab experiments to explain how mitochondria become defective in MS patients," said Thomas Simmen, study co-author and cell biology professor.

Specifically, using human brain tissue samples, the researchers discovered how two sub-components within a cell are miscommunicating in patients with MS, and identified how at least one protein (Rab32) is swooping in to trigger the dangerous dysfunction.

"A part of the cell that stores calcium (ER or endoplasmic reticulum) gets too close to the part of the cell that creates energy (mitochondria) when massive amounts of Rab32 are present in the brain of MS patients. The resulting miscommunication with the calcium supply triggers the mitochondria to misbehave, ultimately causing toxicity for brain cells in MS patients," explained Simmen.

In healthy brain tissue samples, there's virtually no Rab32 present, he added.

Researchers don't know why or what causes an unwelcome influx of Rab32 but they theorize the defect could originate at the base of the ER.

With this finding in hand, not only can scientists search for effective treatments that target Rab32, added Simmen, they can embark on determining whether there are other proteins that may be at play.

"Rab32 is just one of the proteins that is having the effect of drawing the ER and mitochondria too close. There are dozens of other possibilities," he said.

This discovery may give hope to the 100,000 Canadians living with MS who have had to rely on partially effective treatments that aim to reduce inflammation, and, sometimes, controversial experiential treatments such as the vein-widening treatment.

The study, conducted with researchers at the University of Exeter, was recently published in the *Journal of Neuroinflammation*.

More information: Yohannes Haile et al, Rab32 connects ER stress to mitochondrial defects in multiple sclerosis, *Journal of Neuroinflammation* (2017). DOI: 10.1186/s12974-016-0788-z

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