MedicalXpress

Study sheds light on the biology of progressive form of multiple sclerosis, suggests a new potential path for treatment

February 8 2017

A research team led by scientists from Brigham and Women's Hospital has revealed how an FDA-approved drug works in the central nervous system in mice to suppress chronic inflammation. The drug, known as FTY720 (or Fingolimod) interferes with signals sent through sphingosine-1-phosphate receptors, and appears to reduce the pathogenic activities of astrocytes. The findings suggest the treatment may hold promise for a progressive and difficult-to-treat form of multiple sclerosis (MS) known as secondary progressive MS (SPMS).

"One of the most important unmet clinical needs in MS is to design therapeutic approaches for the progressive phase of the disease," said senior author Francisco Quintana, PhD, a researcher in the Ann Romney Center for Neurologic Diseases at BWH. "And a key unanswered question related to that is, what are the biological processes that drive disease pathogenesis at this stage?"

MS is a chronic autoimmune disease that affects the central nervous system. It frequently begins with a relapsing-remitting course that often gives way to second phase, SPMS, which is characterized by severe and irreversible neurological decline. Unfortunately, there are few therapies that target this form of MS. Notably, treatments for the relapsing-remitting phase of the disease are ineffective against SPMS.

The current study, published in *PNAS* and led by Quintana and his

colleagues, sheds new light on the role of sphingosine-1-phosphate, a type of lipid, and its receptors in SPMS. The researchers found that blockage of these signals with FTY720 had important effects on astrocytes in both mice and humans, decreasing their pro-inflammatory and neurotoxic properties while also increasing the cells' anti-inflammatory capabilities.

Although the findings are noteworthy, the neuroprotective effects Quintana and his colleagues observe are not as strong as those they have recorded in previous studies of other drugs. Nevertheless, the results suggest FTY720 may help mitigate some aspects of SPMS in humans. A clinical trial of a highly related drug, led by Novartis, is now underway and encouraging preliminary results have been recently released, Quintana said.

More information: Veit Rothhammer et al, Sphingosine 1-phosphate receptor modulation suppresses pathogenic astrocyte activation and chronic progressive CNS inflammation, *Proceedings of the National Academy of Sciences* (2017). DOI: 10.1073/pnas.1615413114

Provided by Brigham and Women's Hospital