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PRESS RELEASE

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A promising target for multiple sclerosis

A team from UNIGE and HUG has discovered a subgroup of immune cells particularly involved in the disease, paving the way for more precise treatments and avoiding certain side effects.

Multiple sclerosis, which affects around one in 500 people in Switzerland, is an autoimmune disease in which immune cells attack the central nervous system, causing irreversible damage. Current treatments involve blocking the immune system to prevent it from attacking the body. Although effective, these drugs can trigger potentially serious infections. A team from the University of Geneva (UNIGE) and Geneva University Hospitals (HUG), in collaboration with the University of Pennsylvania, has identified a subtype of immune cells in newly diagnosed patients that may play a decisive role in disease progression. A treatment targeting these cells specifically could effectively control the disease while avoiding certain side effects. These findings have been published in the *journal Annals of Neurology*.

Multiple sclerosis is characterised by lesions in the myelin, a membrane that protects neurons and is essential for the transmission of nerve impulses. This results in motor, sensory, visual and cognitive disorders that can lead to disability.

"Over the past twenty years, major progress has been made in both early diagnosis and the development of immunosuppressive drugs. These treatments inhibit the process of nervous system degradation by limiting inflammatory flare-ups, which has led to a real improvement in the quality of life of those affected," says Patrice Lalive, professor in the Department of Clinical Neurosciences and the Department of Pathology and Immunology at UNIGE Faculty of Medicine, and head of the Neuroimmunology Unit at the HUG, who led the study. "However, these treatments indiscriminately destroy immune cells, paving the way for all kinds of infections and significant side effects."

A minority cell receptor

For more than 10 years, Patrice Lalive's team has been conducting research on a cell signalling pathway (a mechanism that allows cells to perceive their environment and communicate with each other), the c-Met/HGF pathway, which is involved in neuroinflammation. "Initial laboratory studies highlighted the role of this c-Met receptor in this process," explains Patrice Lalive. "Here, we wanted to examine what actually happens in our patients."

The research team compared the white blood cells present in the blood and cerebrospinal fluid of around thirty people with recently diagnosed multiple sclerosis who had not yet received any treatment with those of individuals without multiple sclerosis.

High resolution pictures

"We detected the presence of lymphocytes expressing the c-Met receptor in people with multiple sclerosis, which were absent in the control group," explains Gautier Breville, a research physician in Prof. Lalive's team and first author of the study. "Furthermore, these c-Met expressing lymphocytes, which make up only 5-6% of white blood cells in the cerebrospinal fluid, appeared to be particularly inflammatory and toxic, and were able to cross the blood-brain barrier more easily to attack the brain."

First steps towards targeted therapy

Thus, the abnormal pro-inflammatory mechanism of multiple sclerosis appears to promote the expression of c-Met in a small proportion of lymphocytes. "This process could be a real opportunity to develop treatments that target only c-Met-carrying lymphocytes, sparing the rest of the immune system necessary for the defence against infections. Would this be enough to limit the progression of the disease? That is what we now want to verify by identifying molecules that target c-Met," concludes Patrice Lalive.

contact

Patrice Lalive
Associate Professor
Department of Clinical Neuroscience
Department of Pathology and Immunology
Faculty of Medicine
UNIGE

Head
Neuroimmunology Unit
HUG

+41 22 372 83 57
patrice.lalive@hug.ch

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UNIVERSITÉ DE GENÈVE
Communication Department
24 rue du Général-Dufour
CH-1211 Geneva 4

Tel. +41 22 379 77 17

media@unige.ch
www.unige.ch