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NEW PERSPECTIVES ON UNDERSTANDING, PREVENTING AND TREATING VASCULAR DEMENTIA

A study conducted by the Geneva University Hospitals (HUG) and the University of Geneva (UNIGE) sheds significant light on the understanding of age-related dementias, particularly those of vascular origin, which are the most common after Alzheimer's disease. The study highlights the key role of a brain molecule, the chemokine receptor 5 (CCR5), in the neuronal death observed during the development of vascular dementia. This discovery offers promising avenues for prevention, enabling the early identification of people at risk and appropriate action. The study is published in the journal [Alzheimer's and Dementia](#).

Dementia is a group of brain diseases that share similar symptoms, such as memory, language, orientation, and behavioural issues. Vascular dementia generally develops in the elderly, affecting between 1% and 4% of people over the age of 65, according to *Alzheimer's Switzerland*. It is caused by vascular lesions that disrupt the blood supply to the brain, leading to the death of neurons. There is currently no cure for vascular dementia, and the only way to combat it is prevention by controlling risk factors such as high blood pressure, high cholesterol, diabetes and smoking. Preventive measures would become more effective with the discovery of new disease biomarkers that would enable a better identification of people at risk. And this is what the HUG and UNIGE team succeeded in by discovering the role of the CCR5 receptor in the development of vascular dementia.

A new biomarker for dementia

The study focused on CCR5, a receptor protein linked to chemokines, chemical messengers of the immune system. The team led by Dina Zekry, Head of the division of Internal Medicine for the Aged at the HUG and Associate Professor in the Department of Rehabilitation and Geriatrics at the UNIGE Faculty of Medicine, in collaboration with the team led by Karl-Heinz Krause, a senior physician in the Department of Diagnostics and Medicine at the HUG and Full Professor in the Department of Pathology and Immunology at the UNIGE Faculty of Medicine, who were both responsible for the study. They discovered that CCR5 plays a crucial role in brain cells response to oxidative stress, a mechanism involved in the death of neurons. They also found a link between a specific genetic variant of CCR5 and that of another protein, apolipoprotein E (ApoE), known for its role in age-related dementia.

This complex genetic association considerably increases the risk of vascular dementia. "People over the age of 80 who carry this specific genotype are eleven times more likely to develop vascular dementia," explains Benjamin Tournier, PhD, a biologist in the Department of Psychiatry at the HUG, and a researcher in the Department of Psychiatry at the UNIGE Faculty of Medicine and first author of the study.

This research of translational nature, a concept that aims to translate fundamental discoveries into concrete clinical applications, has made it possible to clarify the probable mechanisms of dementia through a series of experiments. The research team first highlighted the potential role of CCR5 in ischaemic mechanisms by examining mouse neurons "in vitro". They then studied variations in the CCR5 and ApoE genes in a group of 362 people (205 without dementia and 189 with dementia) who agreed to give blood samples annually for a duration of five years. These findings were then verified on another cohort in Italy (157 individuals without dementia and 620 individuals with dementia), consolidating the robustness of the discovery.

A major step towards prevention and treatment

Prof Zekry emphasises the importance of this discovery as a new target for understanding and treating age-related dementia. "This is a major advance that opens doors for the early identification of individuals at risk and for the development of targeted therapies. It offers considerable hope for our society with regard to neurocognitive diseases as a whole". New treatment strategies could also emerge from these results aiming at improving the quality of life and functionality of those affected.

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