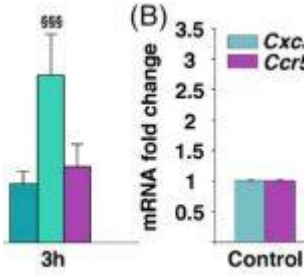
New biomarker for vascular dementia



Vascular dementia, a debilitating condition, arises from vascular lesions that disrupt the blood supply to the brain, resulting in neuron loss. Currently, there's no cure for this condition, and prevention through risk factor management remains the primary defense, encompassing control of high blood pressure, cholesterol, diabetes, and smoking.

The battle against vascular dementia would gain significant ground with the discovery of novel disease biomarkers enabling better risk identification. In a new study, researchers described the pivotal role of the CCR5 receptor in the development of vascular dementia (Figure 1). This receptor, intricately connected to chemokines, the immune system's messengers, emerged as a key player.

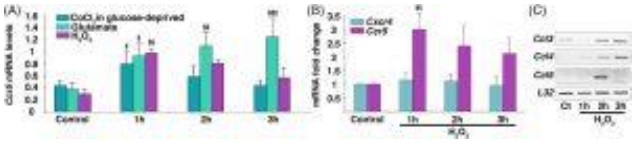


Figure 1: Oxidative stress increases Ccr5 expression and induces CCR5 ligands. *(A) Induction of Ccr5 mRNA expression by oxidative stress in wild-type primary neurons. Wild-type primary neurons at day 10 in vitro were treated*

*for the indicated time with CoCl2 (500 μM) in a glucose-deprived (GD) medium, glutamate (100 μM), H2O2 (30 μM), or vehicle (control, Ct). The levels of mRNA were determined by Real-Time PCR (n = 4). (B) The levels of Ccr5 and Cxcr4 mRNA were determined by Real-Time PCR.**p < 0.01 H2O2 1h versus control. (C) Induction of CCR5 ligands (Ccl3, Ccl4, and Ccl5) by H2O2 (30 μM). RT-PCR was performed by using the ribosomal L32 house-keeping gene as control. Similar results were obtained from four independent experiments. §p < 0.05, §§p < 0.01, and §§§p < 0.001 as compared to the respective group control, using one-way ANOVA followed by Tukey post-hoc test.*

The study illuminated how CCR5 is central to brain cells' response to oxidative stress, a process implicated in neuronal degradation. A specific genetic variant of CCR5 exhibited a profound connection with apolipoprotein E (ApoE), a known actor in age-related dementia. This intricate genetic interplay substantially heightens the risk of vascular dementia.

To decipher the mechanisms at play, the research team meticulously examined mouse neurons in vitro, focusing on CCR5's involvement in ischemic processes. Subsequently, they explored variations in the CCR5 and ApoE genes in a cohort of

individuals, who generously provided annual blood samples over five years.

This discovery marks a significant leap forward, offering the prospect of early risk identification and the development of precisely targeted therapies. It’s a beacon of hope for individuals vulnerable to vascular dementia and a promising stride toward a future with more effective prevention and treatment strategies.

Journal article: B. B., Tournier, et al. 2023. CCR5 deficiency: Decreased neuronal resilience to oxidative stress and increased risk of vascular dementia. *Alzheimer’s & Dementia*.

Summary by Stefan Botha