Alzheimer's biomarker sTREM2 plays a causal, potentially modifiable, role in disease

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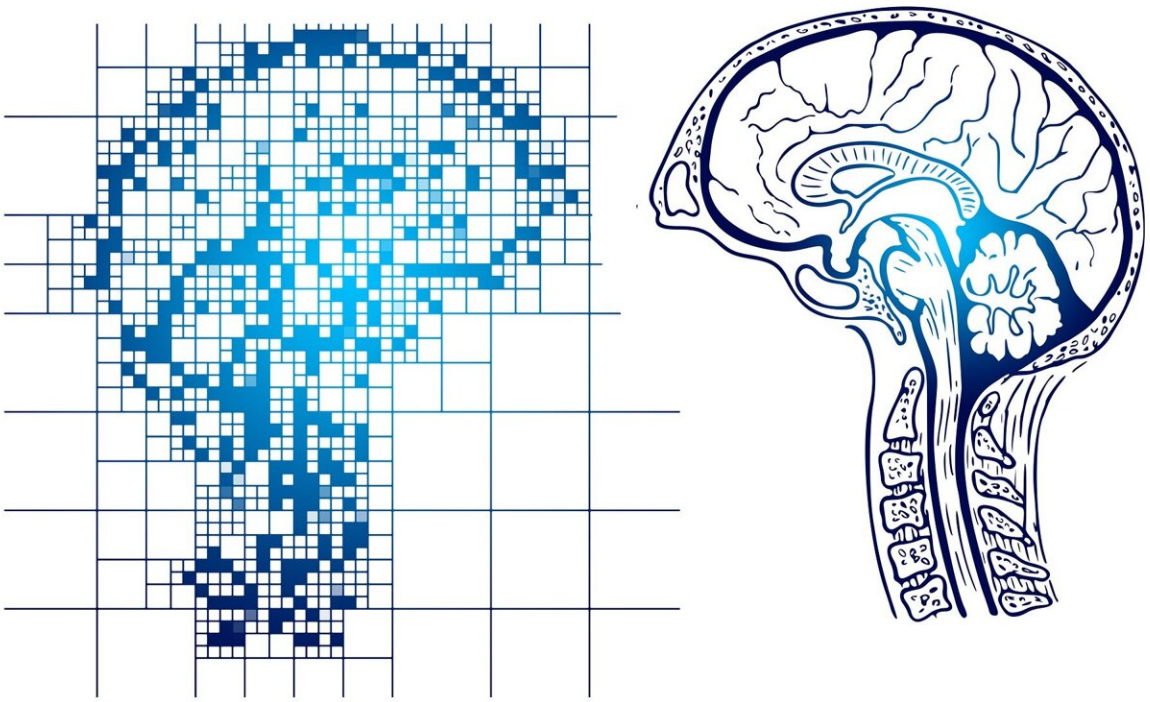

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The protein sTREM2 plays a crucial role in Alzheimer's disease, but the role is complex and poorly understood. In the early stages of the disease, sTREM2 levels in the cerebrospinal fluid fall relative to healthy people's,

but then the levels rise far above normal as the disease progresses. Why the levels fluctuate and whether the fluctuations reflect or cause disease progression is unknown.

In a study published in the journal *Molecular Neurodegeneration*, Carlos Cruchaga, the Barbara Burton & Reuben Morriss III Professor of Psychiatry at the School of Medicine, and colleagues identified four genomic regions linked to variations in sTREM2 levels, and then used functional analyses to pinpoint specific genes responsible for the association.

Then, using an approach known as Mendelian randomization, the researchers showed that sTREM2 is not just correlated with Alzheimer's but part of the causal pathway. The findings open up the possibility of targeting the newly identified genes to modulate sTREM2 levels and, potentially, change the course of the disease, Cruchaga said.

More information: Lihua Wang et al, Proteo-genomics of soluble TREM2 in cerebrospinal fluid provides novel insights and identifies novel modulators for Alzheimer's disease, *Molecular Neurodegeneration* (2024). DOI: 10.1186/s13024-023-00687-4

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