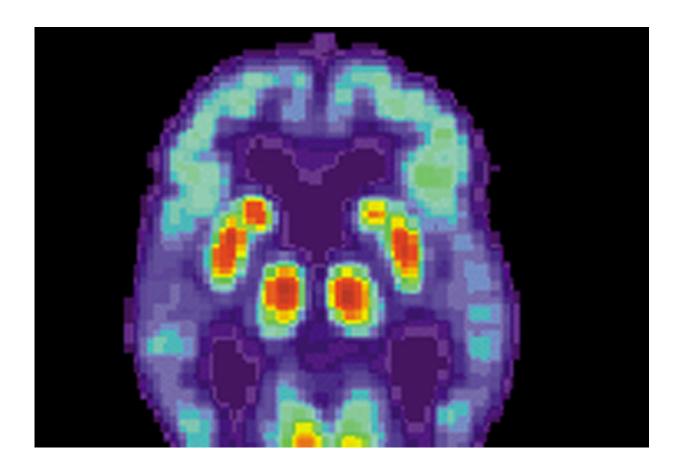


Researchers identify gene variant that protects against Alzheimer's disease

November 30 2017



PET scan of a human brain with Alzheimer's disease. Credit: public domain

Research published Wednesday in *Genome Medicine* details a novel and promising approach in the effort to treat Alzheimer's disease.



Brigham Young University professors Perry Ridge and John Kauwe led the discovery of a rare genetic <u>variant</u> that provides a protective effect for high-risk individuals—elderly people who carry known <u>genetic risk factors</u> for Alzheimer's— who never acquired the <u>disease</u>.

In other words, there's a specific reason why people who should get Alzheimer's remain healthy. Study authors believe this genetic function could be targeted with drugs to help reduce the risk of people getting the disease.

"Instead of identifying genetic variants that are causing disease, we wanted to identify genetic variants that are protecting people from developing disease," said Ridge, assistant professor of biology at BYU. "And we were able to identify a promising genetic variant."

That former approach to Alzheimer's disease has been generally effective in producing a list of genes that might impact risk for the disease, but it leaves researchers without sufficient data on what to do next. In this new approach, Ridge and Kauwe develop the biological mechanism by which a genetic variant actually impacts Alzheimer's disease.

Using data from the Utah Population Database—a 20-million-record database of the LDS Church's genealogical records combined with historical medical records from Utah—Ridge and Kauwe first identified families that had a large number of resilient individuals: those who carried the main genetic risk factor for Alzheimer's (E4 Allele) but remained healthy into advanced age.

Using whole genome sequencing and a linkage analysis methodology, they then looked for the DNA that those resilient individuals shared with each other that they didn't share with loved ones who died of Alzheimer's. They discovered the resilient subjects shared a variant in



the RAB10 gene while those who got the disease did not share the genetic variant.

Once the researchers identified the potentially protective gene variant, they over expressed it in cells and under expressed it in cells to see the impact on Alzheimer's disease related proteins. They learned that when this gene is reduced in your body, it has the potential to reduce your risk for Alzheimer's.

"There are currently no meaningful interventions for Alzheimer disease; No prevention, no modifying therapies, no cure," Kauwe said. "The discoveries we're reporting in this manuscript provide a new target with a new mechanism that we believe has great potential to impact Alzheimer's disease in the future."

More information: Linkage, whole genome sequence, and biological data implicate variants in RAB10 in Alzheimer's disease resilience, *Genome Medicine* (2017). DOI: 10.1186/s13073-017-0486-1

Provided by Brigham Young University

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