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Team of researchers finds possible new genetic risk for Alzheimer's disease

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Researchers have identified a gene that appears to increase a person's risk of developing late-onset Alzheimer's disease, the most common form of the disease. The gene, abbreviated as MTHFD1L, is on chromosome six, and was identified in a genome-wide association study. Details are published September 23 in the journal *PLoS Genetics*.

The collaborative team of researchers was led by Margaret A. Pericak-Vance, PhD, Director of the John P. Hussman Institute for Human Genomics at the University of Miami Miller School of Medicine; Joseph D. Buxbaum, PhD, Department of Psychiatry, Mount Sinai School of Medicine; and Jonathan L. Haines, PhD, Vanderbilt Center for Human Genetics Research, Vanderbilt University. The researchers were able to identify small differences in the genetic sequences of the MTHFD1L gene in people with and without Alzheimer's disease. The team found that individuals with the variation may be nearly twice as likely to develop Alzheimer's disease as people without the variation. The researchers observed the gene variation throughout the human genomes of 2,269 people with late-onset Alzheimer's disease and 3,107 without the disease.

"Identifying this gene is important because the gene is known to be involved in influencing the body's levels of homocysteine, and high levels of homocysteine are a strong risk factor for late-onset Alzheimer disease," said Dr. Pericak-Vance. "In addition, variations of the MTHFD1L gene have been reported to possibly increase the risk of coronary artery disease. Since the function of blood vessels in the brain

may affect Alzheimer's disease, this finding may help us understand how homocysteine levels and blood vessel function in the brain affect Alzheimer's disease."

"This finding gives us unique insight into possible interactions between genetic and environmental risk factors that contribute to AD," said Dr. Buxbaum. "We know of environmental and lifestyle factors that can impact homocysteine levels, and it will be important to understand whether variations of the MTHFD1L gene can modulate these effects."

"By applying the new tools of genomics we are now making rapid progress in finding out what genetic changes are involved in Alzheimer's disease. These findings will lead to a better understanding of what's happening in Alzheimer's disease, and how we can improve treatments," said Dr. Haines.

More information: Naj AC, Beecham GW, Martin ER, Gallins PJ, Powell EH, et al. (2010) Dementia Revealed: Novel Chromosome 6 Locus for Late-Onset Alzheimer Disease Provides Genetic Evidence for Folate-Pathway Abnormalities. PLoS Genet 6(9): e1001130. doi:10.1371/journal.pgen.1001130

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