

Scientists make strides toward defining genetic signature of Alzheimer's disease

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Scientists have new information about the complex genetic signature associated with Alzheimer's disease, the leading cause of cognitive decline and dementia in the elderly. The research, published by Cell Press in the January issue of the *American Journal of Human Genetics*, uses a powerful, high-resolution analysis to look for genes associated with this devastating neurodegenerative disorder.

Previous research linked late-onset Alzheimer's disease, the most common form, with the apolipoprotein E gene. However, the genetics of the disease are complex and are not well understood. "Though apolipoprotein E has been universally confirmed as a risk gene for late-onset Alzheimer's disease, the gene is neither necessary nor sufficient to cause AD and as much as 50% of the genetic risk effect remains unexplained," says senior study author Dr. Margaret A. Pericak-Vance from the Miami Institute for Human Genomics at the University of Miami in Florida.

To gain further insight into the genetics of late-onset Alzheimer's disease, Dr. Pericak-Vance and colleagues completed a sophisticated and comprehensive genetic analysis of 492 late-onset Alzheimer's disease patients and 498 control individuals. The analysis was powerful enough to detect single nucleotide polymorphisms (SNPs) that are significantly more prevalent in individuals with Alzheimer's disease than they are in controls. A SNP is a variation of a single nucleotide of DNA.

The researchers confirmed the known apolipoprotein E association and identified a new association with a SNP on chromosome 12q13. The SNP is close to the gene for the vitamin D receptor, which has previously been linked with memory performance. "There is no known connection between this SNP and the vitamin D receptor, but the region between the two is largely uncharacterized, and it is possible that our SNP is in a region that may play some sort of regulatory role," offers Dr. Jonathan Haines, co-director of the

project at Vanderbilt University's Center for Human Genetics Research.

The team also identified four other regions of interest and validated several candidate genes that exhibited a promising genome-wide association with Alzheimer's disease. "Detailed functional examination of these signals and genes may lead to a better understanding of the complex pathophysiology of Alzheimer's disease," concludes Dr. Pericak-Vance.

Source: Cell Press

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