Understanding, Preventing, Diagnosing, and Treating Alzheimer's Disease: Two Additional Late-Onset Alzheimer's Disease Risk Factor Genes Identified

Two new risk factor genes, SORL1 and GAB2, for late onset Alzheimer's disease have been discovered. Their discovery was made possible through the use of new technology, large databases, and collaboration involving scientists around the world.

Lead Agency: National Institute on Aging (NIA)/National Institutes of Health (NIH)

Agency Mission:

- Support and conduct genetic, biological, clinical, behavioral, social, and economic research related to the aging process, diseases and conditions associated with aging, and other special problems and needs of older Americans.
- Foster the development of research and clinician scientists in aging.
- Communicate information about aging and advances in research on aging to the scientific community, health care providers, and the public.

Principle Investigator:

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Partner Agencies:

National Human Genome Research Institute

GAB2:
Kronos Life Sciences Laboratories.

SORL1:
Alzheimer Association
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General Description:

Two Additional Late-Onset Alzheimer's Disease Risk Factor Genes Identified
The etiology of Alzheimer's disease (AD) is complex, likely involving both genetic and environmental components. Until recently, only one gene, APOE-ε4, had been linked with late-onset AD, the more common form of the disease. In the past year, multinational research teams using state-of-the-art genome-wide association study (GWAS) technology, which involves rapidly scanning for markers across the complete set of DNA of many people to find genetic variations related to a particular disease, have identified two new genes that may influence risk of late-onset AD, the more common form of the disease.

SORL1: Researchers found evidence suggesting that faulty versions of the SORL1 gene contribute to formation of amyloid plaques, a hallmark sign of Alzheimer's in the brains of people with the disease. They identified 29 variants that mark relatively short segments of DNA where disease-causing changes could lie. The study did not, however, identify specific genetic changes that result in Alzheimer's.

GAB2: Investigators found that the GAB2 gene modifies late onset AD risk in APOE-ε4 carriers and influences AD neuropathology.

Excellence: What makes this project exceptional?

A particularly compelling aspect of these findings is the use of publicly available data from a genome-wide association study to confirm the identification of a risk factor gene. These findings demonstrate the tremendous benefit of highly collaborative interaction, sample sharing, and rapid analysis which greatly increase the likelihood of finding new risk factor genes more quickly and inexpensively.

Significance: How is this research relevant to older persons, populations and/or an aging society?

As many as 4.5 million Americans currently have Alzheimer's disease. A better understanding of its underlying causes may ultimately lead to preventive interventions.

Effectiveness: What is the impact and/or application of this research to older persons?

Further research is needed to determine the specific mutations and pathways through which genes for late-onset AD influence risk.

Innovativeness: Why is this research exciting or newsworthy?

Previously, only one gene for late-onset AD had been identified. These discoveries provide new clues as to AD's pathogenesis.