Medical Xpress

A new gene thought to be the cause in early-onset forms of Alzheimer's disease

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A new gene that causes early-onset of Alzheimer's disease has been discovered by the research team of Dominique Campion at the Insert unit 1079 "Genetics of cancer and neuropsychiatric diseases" in Rouen. The research scientists showed that in the families of 5 of 14 patients suffering from the disease, mutations were detected on the gene SORL1. This gene regulates the production of a peptide involved in Alzheimer's disease. The results of this study have been published in the review *Molecular Psychiatry* issued April 3rd.

Precise genetic mutations have been seen to play a part in early-onset forms of Alzheimer's disease. However, there is a sub-population of patients in whom there is no mutation of these genes. So how can these patients, in whom there are no pre-established mutations, be suffering from early-onset Alzheimer's?

To reply to this question, the research team working under the leadership of Dominique Campion and Didier Hannequin (Inserm unit 1079 and Centre national de référence malades Alzheimer jeunes, University hospital Rouen), studied the genes from 130 families suffering from early-onset forms of Alzheimer's disease. These families were identified by 23 French hospital teams within the framework of the "Alzheimer Plan". Of these families, 116 presented mutations on the already known genes. But in the 14 remaining families, there was no mutation at all observed on these genes.

A study of the genome of the 14 families using new whole DNA

sequencing techniques showed evidence of mutations on a new SORL1 gene. The SORL1 gene is a coding gene for a protein involved in the production of the beta-amyloid peptide. This protein is known to affect the functioning of the brain cells (see insert).

Two of the identified mutations are responsible for an under-expression of SORL1, resulting in an increase in the production of the beta-amyloid peptide. "The mutations observed on SORL1 seem to contribute to the development of early-onset Alzheimer's disease. However, we still need to identify more clearly the way in which these mutations are transmitted on the SORL1 gene within families" states Dominique Campion.

Alzheimer's disease is one of the main causes of dependency among the elderly. It results from neuron degradation in different areas of the brain. Its symptoms include increased alterations to memory, cognitive functions and behaviour disorders that lead to a progressive loss of independence.

Alzheimer's disease is characterized by the development of two types of lesion in the brain: amyloid plaques and neurofibrillary degenerescence. Amyloid plaques are caused by extracellular accumulation of a peptide, beta-amyloid peptide (Aβ) in specific areas of the brain. Neurofibrillary degenerescences are intraneuronal lesions caused by abnormal filamentary aggregation of a protein known as a Tau protein.

More information: High frequency of potentially pathogenic SORL1 mutations in autosomal dominant early-onset Alzheimer disease,

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