Changes associated with Alzheimer's disease detectable in blood samples

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Researchers have discovered changes in blood samples associated with Alzheimer's disease. A new international study examined disease-discordant twin pairs: one sibling who suffered from Alzheimer's disease and one who was cognitively healthy. The researchers used the latest genome-wide methods to find out whether the twins' blood samples had any disease-related differences in epigenetic marks, which are sensitive to changes in environmental and lifestyle factors. Differences in epigenetic marks between the sibling who suffered from Alzheimer's disease and the healthy sibling were discovered in multiple genomic regions.

Development of the late-onset form of Alzheimer's disease is affected by genetic and environmental factors, including lifestyle. Environmental factors can alter function of the genes associated with the disease by modifying their epigenetic regulation, e.g. by influencing the bond formation of methyl groups in the DNA's regulatory regions which control function of the genes.

By measuring methylation levels in the DNA isolated from the Finnish twins' blood samples, the researchers discovered epigenetic marks associated with Alzheimer's disease in multiple genomic regions. One of the marks appeared stronger in the brain samples of the patients suffering from Alzheimer's disease. The link between this mark and Alzheimer's disease was confirmed in the Swedish twin cohorts.

The researchers observed that the strength of the mark was influenced not only by the disease, but also age, gender and APOE genotype, which is known to associate with the risk of developing Alzheimer's disease. Furthermore, the mark was stronger in those twins with Alzheimer's disease who had been smoking.

The function of the gene where the mark is located is still not well understood. The gene product is suspected to inhibit activity of certain brain enzymes that edit the code translated from DNA to direct the formation of proteins. In a previous study conducted on mice, it was noticed that removing this genomic region caused learning and memory problems which are central symptoms of Alzheimer's disease.

One of the leaders of the research group, Docent at the University of Turku, Riikka Lund explains that even though the results offer new information about the molecular mechanisms of Alzheimer's disease, more research is needed on whether the discovered epigenetic marks could be utilised in diagnostics.

"The challenges of utilising these marks include for example the variation of the DNA methylation level between individuals. More research is also needed to clarify the potential impact of the marks on disease mechanisms and to identify the brain regions and cell types affected," Lund says.

More information: Mikko Konki et al. Peripheral

blood DNA methylation differences in twin pairs discordant for Alzheimer's disease, *Clinical Epigenetics* (2019). DOI: 10.1186/s13148-019-0729-7

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