Twin pairs discordant for Alzheimer's disease have peripheral blood DNA methylation differences in genes associated with neuronal functions and pathologies

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Alzheimer's disease is the most common cause of dementia worldwide. The neurodegenerative changes in Alzheimer's disease start to progress years before the first clinical symptoms. There is an urgent need for new diagnostic markers and treatment methods that enable early disease intervention. Despite a partial role for genetic risk factors, environmental factors and other disorders also affect the disease pathogenesis potentially through epigenetic mechanisms. Epigenetic changes in Alzheimer's disease are not well-known.

To identify epigenetic markers for Alzheimer's disease we have analysed DNA methylation differences in blood of twin pairs discordant for the disease. Twin pairs from the Finnish Twin Cohort were included in the genome-wide analysis with Reduced Representation Bisulfite Sequencing (RRBS). Validation of the most significant methylation marks in Swedish twin cohorts with targeted bisulphite pyrosequencing is ongoing. In addition, we have characterized cell-free methylated DNA and miRNA markers in plasma of twin pairs discordant for cognitive functions.

The differentially methylated sites in peripheral blood of Finnish twin pairs discordant for Alzheimer's disease are mostly located close to genes that are involved in neurological functions and pathologies. Single cell RNA-sequencing revealed no disease associated changes in blood cell subtypes. However, based on our results, a subset of the genes show Alzheimer's disease associated DNA methylation and/or gene expression changes in brain. Further studies are required for evaluating the diagnostic value of the peripheral blood DNA methylation markers in Alzheimer's disease.