Analysis of Alzheimer's Disease Associated DNA Methylation Changes in Peripheral Blood with Reduced Representation Bisulphite Sequencing

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Alzheimer's disease is a chronic neurodegenerative disorder that greatly decreases patients' quality of life and causes massive challenges for public health and economy. Accounting for more than 50 % of dementia cases, it is the leading cause for dementia in the Western world. Alzheimer's disease is mainly a disease of the elderly and its prevalence is increasing as the populations age. Alzheimer's disease diagnostics and treatment still face many challenges. Neurological and psychiatric testing, sometimes in addition to bioimaging, are the standard methods in Alzheimer's disease diagnostics. These methods can usually detect AD in only such a late point, when the disease is too far progressed and the neuropathological changes cannot be restored.

The recent discoveries on Alzheimer's disease have revealed that it is a more systemic disease than was previously assumed. Especially immune and blood-circulatory systems have significant roles in the pathogenesis. Many external factors, including living environment, lifestyle and other diseases can alter Alzheimer's disease risk, which indicates some epigenetic changes affect the disease pathogenesis. Promising findings on epigenetic changes in Alzheimer's disease have already been made in several laboratories.

Our goals in this research project were to implement a novel genome-wide DNA methylation assay multiplexed Reduced Representation Bisulphite Sequencing (mRRBS), validate the method for DNA methylation analysis of peripheral blood samples and to assess the quality and reliability of the sequencing data. Our sample material (n=69) consisted of peripheral blood samples from 9 monozygotic and 12 dizygotic twin pairs discordant for Alzheimer's disease, and 18 non-twin case and 9 control subjects.

We succeeded in establishing the mRRBS and the sequencing library preparation worked well with peripheral blood DNA in practise. Our results suggest that the sequencing coverage threshold that has been established in literature is inadequate for detecting DNA methylation accurately. The data produced will be reanalysed with the new threshold values and supported by resequencing part of the samples.

Key Terms: Alzheimer's disease, DNA methylation, Epigenomics, Reduced Representation Bisulphite Sequencing, Peripheral blood