INEFFICIENT METHYL GROUP ASSIMILATION PATHWAY IS RELATED WITH THE DEVELOPMENT AND SEVERITY OF ALZHEIMER'S DISEASE

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In the beginning of 90s, four genes related to Alzheimer's disease (AD) were identified (APP, PSEN1, PSEN2 and APOE). Thereafter, few genes have been found with the potential to increase the list, awaiting to be consistently validated.

More than ask for independent polymorphisms we try to follow a different strategy looking for the accumulation of some of them congregated on the same pathway. The pathway analyzed in this study is central to the assimilation of methyl groups, and has been selected for different reasons. First, the polymorphisms C677T-\text{MTFHR}, A66G-\text{MTRR} and A2756G-\text{MTR} have been associated with AD independently. Second, the methyl groups are crucial in the epigenetic control of the genes, which deregulation has been related with AD. And finally, the methyl groups come exclusively from the diet, which has also been reported to be associated with AD.

Our working hypothesis is based on the concept that the accumulation of polymorphisms that affect the activity of the enzymes in the studied pathway has an additive effect and is related with the onset and severity of AD.

Aiming to proof this, we sequenced the different polymorphisms and found a correlation of \(r=0.68\) between AD onset and the number of polymorphisms. Furthermore the correlation between the number of polymorphisms and the severity of AD was \(r=0.83\).

The accumulation of polymporphisms generates a less efficient pathway that can result in altered epigenetic patterns. To test this possibility, we performed an Infinium Methylation DNA array which results are upcoming and will be further discussed.