Role of microRNA dysregulation in Alzheimer's Disease

From 2011-05-01 to 2016-04-30, closed project

Objective

Alzheimer's Disease (AD) is a major health problem in aging societies. Remarkable progress in the study of the rare genetic forms of the disease has led to the identification of several key players like APP and the secretases, but the molecular basis of sporadic AD remains largely unresolved. The convergence of several factors (multicausality) has to be considered. miRNAs are crucially involved in normal brain functioning and integrity. Evidence obtained from analyzing a limited number of brains indicates that miRNA expression is affected in sporadic AD. We propose the hypothesis that such changes can affect normal functioning of neurons increasing their susceptibility to AD. We will document in 3 brain regions in >100 sporadic AD patients and in >100 controls alterations in miRNA expression and explore whether similar alterations can be detected in cerebrospinal fluid. This part of the study will firmly establish which miRNAs are altered in AD. We will then investigate the functional relevance of those miRNAs by gain and loss of function experiments in brains of zebra fish and mice. We will determine the target genes of the miRNA with genetic and proteomic approaches, and establish the functional networks controlled by those miRNA. We anticipate that this will lead to complete novel insights in the role of miRNAs in AD and in maintenance of brain integrity. Our work is likely to have diagnostic relevance for AD and will identify novel drug targets for the disease.

Related information

Report Summaries

Final Report Summary - MIRNA_AD (Role of microRNA dysregulation in Alzheimer's Disease)

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Subjects

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