

The role of aging-associated microRNAs in Alzheimers disease

<https://neurodegenerationresearch.eu/survey/the-role-of-aging-associated-micrnas-in-alzheimers-disease/>

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Country

USA

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The role of aging-associated microRNAs in Alzheimers disease

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NIH (NIA)

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01/09/2016

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1

The project/programme is most relevant to:

Alzheimer's disease & other dementias

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Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Biotechnology... Brain Disorders... Dementia... Genetics... Neurodegenerative... Neurosciences

Research Abstract

PROJECT SUMMARY/ABSTRACT Mounting evidence suggests that epigenetic changes,

including microRNA (miRNA) dysregulation, contribute to aging, psychiatric disorders and neurodegenerative disorders. Although modulations of miRNA function have generated promising clinical data for several diseases, miRNA's roles in brain aging and Alzheimer's disease (AD) have not been investigated thoroughly. During AD pathogenesis, dysregulation of insulin signaling is evident. Abnormal accumulation of Tau and amyloid beta is hypothesized to initiate a pathogenic cascade leading to AD. Given the critical role of these protein aggregations in AD, strategies to modulate tau and amyloid beta are actively being pursued as therapies. Toward that end, we seek to define the role of microRNAs (miRNAs), specifically miR-17-92, in AD pathogenesis. Instead of setting up a hypothesis based on the previously well-known proteins and concepts, we performed unbiased transcriptomics profiling experiments and identified miR-17-92 as the most strongly dysregulated miRNAs during brain aging.

Remarkably, our finding is consistent with a recent landmark study by the NIH Common Fund's Genotype-Tissue Expression (GTEx) consortium's data using 11 human brain subregions. We hypothesize that such dysregulation of miR-17-92 expression may directly contribute to aging process. Therefore, it will be critical to understand the functional effect of miR-17-92 decline on brain aging and try to restore its levels to ameliorate aging effect and AD pathogenesis.

Mounting studies recently suggests that miRNA dysregulation may contribute to several neurodegenerative disorders, including AD. Interestingly, we found that miR-17-92 regulates tau phosphorylation and APP expression level possibly by modulating insulin signaling pathway. In this application, we propose to investigate the role of miR-17-92 in cognition and Alzheimer's disease. We will determine how miR-17-92 affects learning and memory and AD-related neuropathology using novel AAV Tau mouse model and APP knock-in mouse model.

Furthermore using several innovative in vivo methods, we will investigate the mechanism underlying the role of miR-17-92 in Tau and Abeta metabolism.

Lay Summary

PROJECT NARRATIVE Alzheimer's disease is clinically characterized by progressive memory loss and pathologically characterized by the accumulation of toxic protein, such as amyloid beta and Tau. In this project, we propose to study roles of a newly discovered biomolecule, microRNA, in cognition and toxic protein aggregation. Our study will offer novel mechanistic insights into Alzheimer's disease pathogenesis and brain aging.

Further information available at:

Types:

Investments > €500k

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United States of America

Diseases:

Alzheimer's disease & other dementias

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