Cell type specific epigenetic analysis to understand complex mechanisms underlying Alzheimers disease phenotypes

https://neurodegenerationresearch.eu/survey/cell-type-specific-epigenetic-analysis-to-understand-complex-mechanisms-underlying-alzheimers-disease-phenotypes/

Principal Investigators

TSAI, LI-HUEI

Institution

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

Contact information of lead PI
Country

USA

Title of project or programme

Cell type specific epigenetic analysis to understand complex mechanisms underlying Alzheimers disease phenotypes

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NIH (NIA)

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€ 3,542,209.17

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01/08/2016

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1

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

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

Human Genome... Neurodegenerative... Neurosciences... Stem Cell Research... Stem Cell Research - Induced Pluripotent Stem Cell... Stem Cell Research - Induced Pluripotent Stem Cell - Human

Research Abstract
Alzheimer's disease (AD) is an age-related neurodegenerative disorder associated with severe memory impairments for which, currently, there is no cure. Studies in human patients and mouse models reveal disease profiles that involve the downregulation of genes involved in neural functions, such as synaptic transmission, and the upregulation of immune response and inflammatory genes. Although there are a number of neural cell types implicated in AD risk and etiology, including neurons and different types of glia, the majority of studies thus far have utilized total tissue. While these have offered great insight into AD, the establishment of techniques for analyzing cell type-specific mechanisms underlying AD etiology is critically important. In the current proposal, we will utilize a combination of molecular techniques to label and isolate populations of specific cell types, including glia and neurons, and to generate cell type-specific epigenetic and transcriptomic maps from mouse models of neurodegeneration, postmortem human brain, and human adult stem cell-derived cultures. Using integrative bioinformatic analysis, we will determine the pathways disrupted during early and late neurodegeneration. We believe these studies will provide invaluable information about the gene expression and cellular programs that mechanistically underlie AD in the human brain, and will identify novel targets for therapeutic strategies.

Lay Summary
To begin unraveling the complexity of AD, large-scale epigenetic and transcriptomic analyses, including studies from our labs, have used unbiased genome-wide approaches to address how neurodegeneration affects chromatin states and gene expression changes, respectively. However, although there are a number of neural cell types implicated in AD risk and etiology, including neurons and different types of glia, the majority of studies thus far have utilized total tissue and likely miss crucial cell type-specific information. In the current proposal, we will generate cell type-specific epigenetic and transcriptomic maps from mouse models of neurodegeneration, postmortem human brain, and human adult stem cell-derived cultures.

Further information available at:

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Investments > €500k

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United States of America

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