ADRC Participant Access Request

Access Request Goal

Goal - Request for letter of support

Grant Deadline - 2024-03-07

Principal Investigator

Name	Jianhua Zhang
Title	professor
Institution	UAB
Email	zhanja@uab.edu (mailto:zhanja@uab.edu)
Phone	(205) 996-5153

No Co-PI listed in survey

Study and Theme Details

Hypothesis

dysregulation of metabolic networks is a key mechanism in AD which may be corrected by targeting the O-GlcNAc pathway

Specific Aims

Aim 1. Determine how dysregulation of metabolic and bioenergetic networks is related to O-GlcNAc in AD. Human AD has diverse etiology and pathological manifestations. To better understand sub-disease relevance of O-GlcNAc regulation of metabolic mechanisms, we will examine how the relationship between mitochondrial and metabolic characteristics and O-GlcNAcylation are divergent based on sex, ApoE4 status, and cognitive resilience. Additionally, differences in these regulation in different brain region and pathological features of AD will be examined to provide insights into biomarkers and treatment options. Furthermore, the levels of O-GlcNAcylation of a recently identified O-GlcNAc target from human AD and mouse studies, JMJD1C1,2, which regulates the expression of metabolic genes 3-5, will be determined in brain and plasma, based on sex, ApoE4 status, and cognitive resilience, as a potential mechanistic link and biomarker.
Aim 2. Demonstrate that metabolic, neuropathology and cognitive phenotypes can be reset by modulation of OGA and OGT activities in an AD model. To determine how O-GlcNAc enzymes regulate aspects of AD pathologies, we will modulate OGA and OGT activities in APPKI mice which exhibit significant Aβ burden, synaptic loss, neuroinflammation, and cognitive deficits30, and perform cognitive and neuropathological assessment, as well as metabolic characteristics, including spatial and cell type specific metabolomics, to provide insights into novel mechanisms.

This study is not related to Deep South disparities

Funding and IRB Details

Funding source - Not yet funded

IRB Contact - Not yet discussed project with IRB

Subject Sample Size and Profile

Sample size by cognitive ability

Normal Controls	40
MCI	40
Moderate to Severe	40
Total N	**120**

Additional inclusion/exclusion details

sex, age matched, equal ApoE4 carriers versus non carriers

Racial minorities and other stratifcation

This study does NOT test hypothesis on racial disparities

Additional stratification details

sex, ApoE genotype, LBD and TDP versus pure AD

Requested Resources

Banked biospecimen

Blood

Plasma (10ml)

Cells

PBMC
Fibroblasts

Statistical support

Would like to discuss statistics with the ADRC