ADRC Participant Access Request

Access Request Goal

Goal - Formal requst for ADRC data

Principal Investigator

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

Co-PI

Name	Rati Chkheidze
Title	Assistant professor of pathology
Institution	UAB

Email	rchkheidze@uabmc.edu (mailto:rchkheidze@uabmc.edu)
Phone	(205) 975-6126

Study and Theme Details

Hypothesis

mitochondrial dysfunction in Alzheimer’s disease is dependent on brain regions and correlates with neuropathological parameters and the extent of neuroinflammation

Specific Aims

Aim1: Determine if different regions of the same Alzheimer’s disease brain exhibit different mitochondrial dysfunction.

We will perform studies of 3 de-identified Alzheimer’s disease post-mortem brains with correlated pathological index including age, sex, , date of death, , PMI, clinical diagnosis, associated tau, amyloid, TDP and synuclein pathologies. Prefrontal cortex, hippocampus and visual cortex (3 regions) will be dissected. From each regions we will dissect 3 different 1-2 cm2 tissues. Mitochondrial complexes I, II, III, IV, citrate synthase and lactate dehydrogenase activities will be measured using Seahorse XF analyser. mtDNA copy number and mtDNA damage will be quantified by PCR based method.

Aim2: Determine if mitochondrial function in different regions of Alzheimer’s disease brains correlates with protein aggregation pathologies.

Tau, p-tau, amyloid, TDP and a-synuclein antibodies will be used for immunohistochemistry to quantify pathology. Immunohistochemistry of autophagy regulators will be used to correlate protein aggregates with

mechanisms that target protein clearance. Bi-variant analyses will be used to determine if mitochondrial dysfunction in different brain regions correlates with the extent of protein aggregation pathologies.

Aim3: Determine if mitochondrial function in different regions of Alzheimer's disease brains correlates with neuroinflammatory pathologies.

NeuN, MAP2, GFAP, S100b, CD163, TMEM119, CD11b, CD45, and IBA1 immunohistochemistry, western blots and quantitative RT-PCR of mRNA will be performed to measure extent of neuroinflammation and distribution of different cell populations in tissue samples. Bi-variant analyses will be used to determine if mitochondrial dysfunction in different brain regions correlates with the extent of neuroinflammation.

This study is not related to Deep South disparities

Funding and IRB Details

Funding source - Not yet funded

IRB Contact - IRB contacted for discussion / pending approval

IRB Protocol # - IRB-300008063

Subject Sample Size and Profile

Sample size by cognitive ability

Moderate to Severe	3
Total N	**3**

Additional inclusion/exclusion details

1 sample of pure AD tauopathy, 1 sample of mixed AD pathology with synuclein pathology, 1 sample of AD pathology with TDP43 pathology, 3 regions each brain: hippocampus, prefrontal cortex and visual cortex, both frozen and fixed

Racial minorities and other stratifcation

This study does NOT test hypothesis on racial disparities

Requested Resources

Existing data

Demographics	Required
Medical History	Required
Social Determinants	Required
Clinical Exam	Required
Cognitive Testing	Required
MRI	Required
Amyloid PET	Required
Tau PET	Required
CSF	Required
Blood Test	Required
AD Blood Biomarkers	Required
Genetics	Required

Banked biospecimen

Brain tissue

Fixed
Frozen
Parafin
Region (hippocampus, prefrontal cortex, visual cortex)

Statistical support

Would like to discuss statistics with the ADRC