CBRAIN Internships 2024

Following is the list of CBR's research projects in which internships are available. In the online application, please indicate up to 3 projects of your choice (i.e., 1st, 2nd, and 3rd preferences). The allotment of internships will depend on availability and the Mentors' recommendations.

Project 01: **Exploring Gait Variability using Prefrontal Cognitive Model in Aging and Neurodegeneration**

This study attempts to evaluate the impact of perturbation of prefrontal cognitive functions on gait variability in aging and neurodegeneration.

Keywords: Prefrontal functions, Gait variability, aging

Duration: **3 months**

Mentor: **Dr. Albert Stezin Sunny**

Project 02: **Differential effects of modulation of attentional control on constrained action in cognitive-motor functions in elderly**

This study attempts to evaluate the modulatory influence of non-invasive brain stimulation (transcranial direct current stimulation) on constrained action in different cognitive-motor functions in elderly.

Keywords: Non-invasive brain stimulation, Cognitive-motor functions, Aging, Gait

Duration: **3 months**

Mentor: **Dr. Albert Stezin Sunny**

Project 03: **Understanding the Population Level Genetic Basis of Aging**

This project will seek to find the genetic basis of aging in human populations and how they associate with complex disease susceptibilities, including manifestations of neurodegeneration. The student will peruse and get further trained in coding and computational and statistical analysis of large-scale genomics datasets.

Keywords: Aging, neurodegeneration, genomics, human genetics

Duration: **2 months**

Mentor: **Prof. Bratati Kahali**

Project 04: **Impact of brain stimulation on myelination**

The intern will be expected to study how brain stimulation impacts myelination using animal model, immunohistochemistry, and confocal imaging.

Keywords: Myelin, oligodendrocytes, brain immunostaining, microscopy, image processing

Duration: **3 months**

Mentor: **Dr. Chinnakkaruppan Adaikkan**

Project 05: **Impact of brain stimulation on neural dynamics**

The intern will be expected to perform signal processing to study neural dynamics in neurological conditions.

Keywords: MATLAB, signal processing, EEG, brain stimulation, brain connectivity

Duration: **3 months**

Mentor: **Dr. Chinnakkaruppan Adaikkan**

Project 06: **Extended High-frequency Audiometry in Indian Adults**

In research and clinical contexts, audiometric testing often excludes frequencies above 8 kHz. Young healthy ears have a sensitivity of 20 kHz. Testing in the extended high-frequency (EHF) range above 8 kHz may provide significant information regarding Basal (EHF) cochlear regions that are particularly vulnerable to the impacts of aging, diseases, ototoxic medications, and, possibly, noise exposure. EHF thresholds are highly susceptible to the early impacts of aging, and age-related EHF threshold increases are evident even in young populations. As a result, EHF loss may serve as an early warning sign of impairment, aiding in diagnosis and monitoring hearing health.

Keywords: Extended high frequency audiometry, Aging, Hearing, Cognition

Duration: **3 months**

Mentor: **Dr. Deepashri Agrawal**

Project 07: **Studying the association of cardiometabolic and vascular risk factors with dementia**

Emerging evidence suggests that cardiometabolic and vascular health significantly impacts cognitive function and brain health. This research seeks to robustly explore the role of cardiometabolic and vascular risk factors that may contribute to cognitive impairment and the pathogenesis of dementia in the aging Indian population. Towards this goal, the Centre for Brain Research, IISc is conducting two large-scale, community-based, prospective, aging cohort studies, in rural Karnataka and urban Bangalore. In these projects, aging adults from rural/urban India are studied longitudinally using multi-modal clinical, cognitive, and biochemical measurements and brain MRI. The rich data generated from these studies will serve as an invaluable platform to study how specific cardiometabolic and vascular risk profiles contribute to

dementia risk. This insight will, in turn, facilitate developing appropriate interventions that can help in preventing, delaying the onset, or mitigating the course of dementia.

Keywords: Aging, Dementia, Cardiometabolic Risk, Vascular Risk, Indians

Duration: **3 months**

Mentor: **Dr. Jonas S Sundarakumar**

Project 08: **Exploring the potential role of cardiac Autonomic Nervous System (ANS) dysfunction as an early biomarker for dementia.**

The impact of cardiac functioning on the brain, specifically on cognition, is complex and not well understood. In particular, the influence of the Cardiac Autonomic Nervous System regulation on cognitive process in brain aging is poorly understood. Preliminary studies have revealed that abnormalities in Cardiac Autonomic Nervous System (ANS) functions occur much before overt cognitive impairment can manifest. Further, dysfunction in this system can result in worse functional outcomes in persons with dementia. The goal of this project is to study the potential role of cardiac Autonomic Nervous System (ANS) in brain health and cognition and thereby, understand the role of cardiac ANS dysfunction in the risk for developing dementia and related neurodegenerative disorders. This, in turn, will pave way for developing appropriate strategies to prevent or delay the onset or slow down the progression of dementia and related disorders.

Keywords: Aging, Dementia, Cardiac Autonomic Nervous System (ANS), Indians

Duration: **3 months**

Mentor: **Dr. Jonas S Sundarakumar**

Project 09: **Diabetes as a vascular risk factor contributing to learning and memory deficit in a mouse model**

Diabetes is a prevalent risk factor for heart disease and stroke. Prolonged exposure to uncontrolled diabetes can damage many organs including the brain. Indian population is known to have the highest rate of diabetes incidence. Since our diet has a lot of sugar people tend to have a high risk of diabetes. Most people with diabetes with lack of exercise and being overweight can result in damage to blood vessels in the brain leading to cognitive decline. Brain depends on many chemicals supplied by blood through proper regulation of insulin, and high blood sugar can cause inflammation, therefore some of these changes can trigger cognitive decline. We are interested in studying such changes in the mouse model of diabetes to address the cause of cognitive decline. We want to look at changes in blood vessels for prolonged exposure to diabetes and how it contributes to learning and memory deficits by synaptic dysfunction. These findings provide evidence that could link diabetes with Alzheimer's disease, the most common cause of dementia.

Keywords: Diabetes, cognitive decline, Insulin resistance

Duration: **6 months**

Mentor: **Dr. Latha Diwakar**

Project 10: **Topological data analysis on MRI images**

Structural changes in brain due to neurodegeneration although subtle, need to be identified and quantified. Topological data analysis tools such as persistent homology are to be explored.

Keywords: MRI, image, structural analysis

Duration: **3 months**

Mentor: **Prof. Neelam Sinha**

Project 11: **Super resolution of MRI images**

Existing approaches for super resolution of natural images can not be applied straight forward to MRI images due to their fine anatomical details. Adaptation strategies need to be explored to maintain structural fidelity of super resolution.

Keywords: Deep learning, super resolution, MRI image

Duration: **3 months**

Mentor: **Prof. Neelam Sinha**

Project 12: **Evaluating the ACE2 gene polymorphisms association with Covid-19 infection and Cognitive impairment**

This study aims to investigate the relationship between ACE2 gene polymorphisms and their potential association with COVID-19 infection susceptibility and cognitive function. Utilizing participants from the TATA Longitudinal Study of Aging (TLSA) cohort, consisting of individuals from the Indian population, with 30% having a documented history of COVID-19 infection, we will explore genetic variations in the ACE2 gene among infected and uninfected individuals. Additionally, we will analyse the ACE2 polymorphism across the entire cohort to assess its correlation with cognitive decline which lead to uncover genetic factors that may influence susceptibility to COVID-19 and cognitive outcomes, contributing to our understanding of these complex relationships.

Keywords: Cognitive Impairment, Covid-19, TLSA cohort, ACE2 gene

Duration: **3 months**

Mentor: **Dr. Prathima Arvind**

Project 13: **Global Insights from Longitudinal Aging Cohorts: Unveiling Genetic Contributions to Cognitive Status**

This study investigates the genetic contributions to cognitive status within longitudinal aging cohorts worldwide. Utilizing data from diverse populations, we uncover significant insights into the role of genetics in both cognitive decline and preservation across aging trajectories. Furthermore, we examine the influence of environmental-genetic interactions, encompassing factors such as population demographics and lifestyle choices, on cognitive decline. By elucidating these interactions, our research sheds light on

the complex interplay between genetic predispositions and environmental influences, providing valuable insights for understanding cognitive aging and informing targeted interventions to promote cognitive health in aging populations.

Keywords: Aging Cohort, global population, genetics, lifestyle

Duration: **3 months**

Mentor: **Dr. Prathima Arvind**

Project 14: **The role of 2'O methylation in synaptic translation**

2'O methylation is a major modification on rRNA and plays a critical role in ribosome assembly and function. Altered 2'O methylation pattern leads to ribosome heterogeneity and specialised ribosomes. In this project, we want to explore the role of ribosome heterogeneity due to 2'O methylation in synaptic protein synthesis and its potential defects in AD.

Keywords: 2'O methylation, synaptic protein synthesis, specialised ribosomes, protein synthesis defects in AD

Duration: **3 months**

Mentor: **Prof. Ravi Muddashetty**

Project 15: **Mitochondrial translation defects in AD**

Mitochondria generate ATP and many critical metabolites and ROS as a by-product. Mitochondria has its own genome and its own protein synthesis machinery. Both proteins encoded by the nucleus and the ones encoded by mitochondria coordinate for the optimal function of mitochondria. In Alzheimer's Disease (AD) mitochondrial function is severely affected. In this project, we explore how mitochondrial protein synthesis is affected in AD neurons and how it contributes to synaptic pathology in AD.

Keywords: Mitochondria, mitochondrial protein synthesis, synaptic defects in AD

Duration: **3 months**

Mentor: **Prof. Ravi Muddashetty**

Project 16: **Understanding the early molecular mechanistic underpinnings of sex-specific differences in Alzheimer's disease pathology**

Women comprise two-thirds of people living with Alzheimer's disease (AD) regardless of age and ethnicity. Abnormal levels of estrogen are associated with cognitive and synaptic dysfunctions. We have shown that loss of synaptosomal Akt1-mTOR signaling in AD male mice occurs at an early age. However, the molecular mechanisms underpinning the regulation of and neuroprotection by estrogen in females compared with those in males during the pre-symptomatic age in AD remain unknown. The aim of the project will be to perform RNAseq from different brain regions of AD mice at pre-and post-symptomatic age and identify potential target(s) that affect the estrogen pathway at the synapse. The intern will learn

high-throughput RNA sequencing analysis utilizing different tools, which provides a great opportunity in their career in the computational or systems biology area.

Keywords: Alzheimer's disease, RNAseq, Bioinformatics, Computational biology, APP/PS1, AD mouse model

Duration: **3 months**

Mentor: **Dr. Reddy P Kommaddi**

Project 17: **The role of ubiquitination in beta-arrestins during AD pathogenesis**

Alzheimer's disease pathology has been associated with dysfunction of neurotransmitter-triggered G-protein-coupled receptors (GPCRs). Beta-arrestins control receptor desensitization and activate beta-arrestin-dependent signaling, which mediates GPCR function. Agonist-dependent beta-arrestin2 ubiquitination leads to rapid internalization and degradation of GPCRs. Although beta-arrestin2 ubiquitination plays an essential role in the endocytosis of GPCRs, there is little evidence connecting the role of beta-arrestins and synaptic plasticity. Thus, while beta-arrestin2 and GPCR dysfunction have been observed, it remains an open question whether these entities interact and what role does their ubiquitination plays in AD. The aim of the project will be to determine the role of synaptic beta-arrestin2 ubiquitination in the progression of AD pathology. The intern will learn and explore the wet lab environment and GPCRs biology with respect to neurodegeneration.

Keywords: Ubiquitination, GPCRs, Alzheimer's disease, SDS-PAGE, Immunoblot, Immunohistochemistry, AD mice

Duration: **3 months**

Mentor: **Dr. Reddy Kommaddi**

Project 18: **Identifying the genetic basis of mitochondrial function in human populations**

This is a computational bioinformatic project, in which we will use genomic data to identify genetic variants associated with mitochondrial function in Indian populations. This project will identify genetic risk and protective factors for mitochondrial dysfunction and aging.

Keywords: Bioinformatics, genomics, programming, sequencing

Duration: **3 months**

Mentor: **Dr. Shweta Ramdas**

Project 19: **Estimation of genetic risk scores for disease in Indian populations**

Genetic risk scores for Parksinson's disease have been established in European populations, and their utility in non-European and non East-Asian populations is relatively unknown. In this study, we will estimate the utility of European-derived genetic risk scores for traits including Parkinson's Disease in cohorts of Indian populations.

Keywords: Genomics, bioinformatics, genetics

Duration: **3 months**

Mentor: **Dr. Shweta Ramdas**

Project 20: **Locus coeruleus- ventral tegmental area (LC-VTA) crosstalk during early stages of Alzheimer's disease**

Mounting evidence suggests the pivotal involvement of monoamine dysfunction involving the LC and VTA years prior to the clinical onset of Alzheimer's disease (AD) resulting in the development of psychiatric symptoms. Nonetheless, numerous questions persist, such as the factors triggering this dysfunction, their reciprocal influence, and the underlying reasons driving these early neurodegenerative processes to develop AD. This study aims to investigate the cause underlying early LC-VTA dysfunction leading to psychiatric symptoms by studying the synaptic crosstalk between these two regions. Through intensive imaging and analysis, coupled with behavioral experiments, we seek to elucidate the dynamics of cross-talk between the LC and VTA at various stages of AD pathogenesis.

Keywords: Locus coeruleus, Ventral tegmental area, Alzheimer's disease

Duration: **3 months**

Mentor: **Dr. Smitha Karunakaran**

Project 21: **SENSEAGE - SENSE of Proprioception and AGE: Cognitive Correlations**

This study investigates the correlation between proprioception and cognitive function in the elderly. By examining proprioceptive sensitivity across various age groups, we aim to understand its impact on cognitive domains such as memory, attention, and spatial awareness. Preliminary findings suggest a significant link, indicating that enhanced proprioceptive training could potentially mitigate cognitive decline. This research underscores the importance of integrating sensory and cognitive assessments in geriatric care protocols to support healthy aging.

Keywords: Proprioception, sensation, aging

Duration: **2 months**

Mentor: **Prof. Thomas Gregor Issac**

Project 22: **NEUROIMAGINE - NEUROdegeneration IMAGery for INformation and Education**

The NEUROIMAGINE project aims to elevate public awareness on aging and dementia through compelling infographics and photographs. Over two months, this initiative will curate visual narratives that elucidate the complexities of neurodegenerative diseases, focusing on their impact, prevention, and management. By harnessing the power of visual storytelling, NEUROIMAGINE seeks to demystify dementia and promote cognitive health, encouraging community engagement and informed conversations. This project bridges the gap between scientific knowledge and public understanding, fostering a supportive environment for affected individuals and their families.

Keywords: Awareness, Aging, Dementia, photos and short videos

Duration: **2 months**

Mentor: **Prof. Thomas Gregor Issac**
