PROJECT DESCRIPTION

TITLE: Characterization of innate lymphoid cells in a mouse model of Alzheimer's disease
PI: Erin Reed, Assistant Professor, Department of Pharmaceutical Sciences
SITE: NEOMED, Rootstown campus

ABSTRACT: Alzheimer's disease (AD) is the primary cause of dementia, characterized by robust inflammation within the brain that accompanies the pathological hallmarks of amyloid plaques and neurofibrillary tau tangles. Microglia, the resident innate immune cells of the brain, mediate this process, driving AD pathogenesis; however, they also signal to circulating peripheral immune cells to instruct their function and phenotype. These peripheral cells similarly contribute to the inflammatory environment of the AD brain, but how they contribute to disease processes remains unclear. We hypothesize innate lymphoid cells (ILCs) from the circulation localize at brain-border interfaces (meninges and choroid plexus) to modulate parenchymal AD pathology through their actions on B cells. We propose to determine the localization and composition of ILCs during disease onset and progression, their reliance on specific signaling pathways for their action, and their influence on B cells.

SIGNIFICANCE: Successful completion of this research project will provide critical insights to the mechanisms giving rise to immune dysregulation and neuroinflammation in AD. Understanding these processes have the potential to become the basis for new therapeutic strategies.

GOALS & OBJECTIVES: The student working on this project will participate in characterizing ILCs in the brain and at the interfaces through genetic and immunohistochemical approaches to define their location, temporal dynamics, and phenotypes.

RESEARCH METHODS: To identify ILCs, the student working on this project will use a combination of genetic and immunolabeling approaches. A mouse model of AD has been generated where specific cell populations express fluorescent proteins. Brain tissue and meninges from these transgenic mice will be collected. The student will perform immunohistochemistry and microscopy on tissue slices and meningeal wholemounts to assess cell number and location. Brains and meninges will also be analyzed by flow cytometry for labeling efficiency and cell phenotype.

DATA ANALYSIS: The student will be taught how to use the microscope for data acquisition and ImageJ for analysis. They will also be taught how to use the FACSDiva program for flow cytometry data acquisition and FlowJo for analysis. Microsoft Excel will be used to perform statistical analyses of all data generated.

STUDENT CONTRIBUTION TO OVERALL INVESTIGATION: The overall investigation of peripheral immune cell participation in AD pathogenesis will be aided immensely by successful contributions of the student in characterizing the fate and functions of immune cells in the brain and its interfaces. To date, there has been little investigation of some cell populations and studies of others has produced conflicting reports. As these peripheral immune cells function in various disease processes, the student contribution stands to be significant in advancing the project.

STUDENT TRAINING/MENTORING PLAN

Training/mentoring: The student joining this project will be mentored and trained by the PI and the postdoc who developed and is currently working on the project. The PI will meet weekly, or more often if needed/desired, with the student and postdoc to discuss the goals and progress of

the project, review data, etc. The postdoc will provide daily technical oversight and mentorship. The group (PI, postdoc, and student) will also read and discuss papers related to the project on a regular basis.

Available resources: The laboratory is fully equipped and/or has access to all the equipment necessary to carry out these experiments. The requisite IACUC and IBC approvals have been attained. Many of the mice have been generated, and some tissue for analysis has been collected. Additional animals will be available for collection and analysis in Summer 2026.

Site: This research project will be carried out within the Department of Pharmaceutical Sciences at NEOMED. The laboratory is located on the 4th floor of the RGE building.