

While risk for dementia expression is determined by multiple associated pathologies, Alzheimer's disease (AD) is the most common pathology associated with cognitive decline and transition to dementia. Epidemiologic studies link traffic-related air pollution (TRAP) to increased AD risk and AD biomarker expression. While preclinical studies support a causal relationship between TRAP and increased AD risk, many of these studies used concentrated ambient particles or diesel exhaust that do not recapitulate the complexity of real-life TRAP exposure for humans. Additionally, the mechanisms by which TRAP promotes AD pathology are still unclear. Utilizing an innovative TRAP exposure paradigm that mimics human exposure to TRAP, I seek to investigate the role of the lung-brain axis in mediating TRAP effects on AD-relevant phenotypes in a transgenic rat model of AD. Specifically, I hypothesize that TRAP-induced lung inflammation promotes blood-brain barrier (BBB) dysfunction leading to aberrant microglial activation, which increases severity of and/or decreases time to onset of AD phenotypes in genetically susceptible rats. I will investigate TGF $\beta$ -induced endothelial-mesenchymal transition in brain endothelial cells and consequent increased BBB permeability and its relationship to increased neuroinflammation in a rat model of AD.