Characterizing the Role of Microglial Quaking (Qki) in the Progression of Alzheimer’s Disease (AD)

Adithya Nair 1,3 Takese McKenzie 2,3 Jian Hu 2,3

1 Baylor University, University Outreach Summer Program, Waco, TX
2 The University of Texas MD Anderson UTHealth Graduate School of Biomedical Sciences, Neuroscience Graduate Program, Houston, TX
3 The University of Texas MD Anderson Cancer Center, Department of Cancer Biology, Houston, TX

Introduction

- Alzheimer’s disease (AD) is a prominent neurodegenerative disorder characterized by the presence of amyloid plaques and microglial dysfunction.
- Microglia are resident immune cells that phagocytose plaque and debris.
- Quaking (Qki) is an RNA binding protein present in multiple brain glial cell types.
- Qki regulates microglial phagocytosis.
- Qki expression is upregulated in AD patients.

Hypothesis: Qki promotes microglial phagocytosis to attenuate AD progression

Methods

Experimental Outline:

- Human AD Brain Samples
- 5xFAD mice crossed with Qki mice
- Immunofluorescent Staining
- Imaging

Results

Diverse Amyloid Plaque Burden is Present in Human AD Brain

Microglial Qki Expression Negatively Correlates with Amyloid Burden in AD Patients

Conclusion

- Qki can act as a stress responder protein and promotes the phagocytosis of amyloid plaques.
- With excessive amyloid burden, microglial phagocytosis may decrease as Qki expression in the microglia decreases.
- Qki expression is important for microglial function in the context of AD.

Future Directions

- Characterize the changes in microglia states with Qki loss in AD via single-cell RNA seq and IF
- Identify the microglial pathways that are regulated by Qki in AD
- Propose Potential Qki Rescue Experiment: PPARβ agonist KD3010
- Characterize onset of cognitive and motor deficit in Qki KO 5xFAD mice

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References