Phosphoinositide Signaling Modulates Microglial Phagocytosis in Alzheimer's disease

Smita Eknath Desale

Subashchandrabose Chinnathambi

Video Byte

Keywords: phosphoinositides, PI3K signaling, actin remodeling, phagocytosis, dietary fatty acids, Alzheimer's disease, actin, cytoskeleton, Cell Communication and Signaling

Posted Date: October 16th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-978949/v1>

License: This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Alzheimer's disease affects 1 in 3 senior citizens worldwide. The hallmark of Alzheimer's is the accumulation of abnormal protein deposits, including Tau and amyloid β , in neurons and glial cells in the brain. These deposits disrupt signal transduction by affecting lipid-based secondary messengers in the brain called phosphatidylinositols (PIs). PIs drive the reorganization of the cytoskeleton in glial cells, affecting many cellular processes. These dynamic molecules are tightly regulated by their phosphorylation status, which influences their abundance and localization. Because microglia in the brain must respond to chemotactic and pro-inflammatory signals, disrupting PIs alters microglial function, resulting in hyperactivation and inflammation. PI signaling typically drives actin remodeling to modulate phagocytosis, allowing glial cells to clear amyloid β aggregates and debris. Unfortunately, extensive amyloid β accumulation disrupts PI signaling, altering cytoskeleton regulation. PI signaling can also be influenced by diet – in particular the balance of n-3 and n-6 polyunsaturated fatty acids. The critical role of PI signaling in modulating microglial phagocytosis makes this pathway an ideal target for new treatments for Alzheimer's disease, and while further study is needed to understand the mechanisms involved, altering fatty acid levels to modulate PI signaling may be a possible strategy.