THE ROLE OF PHOSPHOLIPASE A_2 IN AMYLOID β UPTAKE BY MICROGLIA

Li Dong

Dr. James Lee, Thesis Supervisor

ABSTRACT

The accumulation of amyloid-β (Aβ) is a key characteristic of Alzheimer's disease (AD). Microglia are the principle macrophages in the brain and are known to internalize Aβ, however the phagocytic function is impaired as AD progresses. Cytosolic phospholipase A_2 ($cPLA_2$) and calcium-independent PLA_2 ($iPLA_2$) are two major groups of PLA_2s that are involved in modulating membrane properties, intracellular trafficking and the cellular inflammatory responses. Here, we study the role of $cPLA_2$ and $iPLA_2$ in the uptake of $A\beta_{1-42}$ by microglia in vitro. We found that the uptake of $A\beta_{1-42}$ was rapid (<15 minutes) and remained unchanged up to 60 minutes. Also, inhibition of $cPLA_2$ greatly reduced $A\beta_{1-42}$ uptake while increasing $cPLA_2$ activation did not affect $A\beta_{1-42}$ uptake. $iPLA_2$ appears to reduce the rate of $A\beta_{1-42}$ uptake, but had no influence on the uptake level later on. Furthermore, $cPLA_2$ and $iPLA_2$ are not involved in intercellular processing of $A\beta_{1-42}$.