

# SECRETORY PHOSPHOLIPASE A2-IIA IN ALZHEIMER'S DISEASE AND INFLAMMATORY RESPONSES IN ASTROCYTES

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## ABSTRACT

Alzheimer's disease (AD) is a progressive, fatal neurodegenerative disease marked with dementia. Secretory phospholipase A2-IIA (sPLA2-IIA) is an inflammatory protein known to have a role in the pathogenesis of multiple inflammatory diseases and is implicated in several neurodegenerative diseases. In AD, astrocytes become reactive and have increased expression of inflammatory cytokines such as IL-1 $\beta$  and TNF- $\alpha$ , and undergo increased oxidative stress. In these studies, we show that sPLA2-IIA mRNA is up-regulated in AD brains (compared to non-demented elderly brains). To further elucidate involvement of oxidative pathways in induction of sPLA2-IIA mRNA and protein by pro-inflammatory cytokines, we performed in vitro studies with immortalized astrocytes (DITNC) and various inhibitors and antioxidants. The results of these studies suggest the involvement of oxidative pathways, possibly the NADPH oxidase pathway. These results, taken together, identify sPLA2-IIA as an inflammatory factor for Alzheimer's disease, and support the involvement of NADPH oxidase in the cytokine induction of sPLA2-IIA in astrocytes and the possibility of using botanical antioxidants to ameliorate the inflammatory response in these cells.