

# THE ROLE OF CYTOSOLIC PHOSPHOLIPASE A2 IN MICROGLIAL SIGNALING PATHWAYS DURING NEUROINFLAMMATION

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## ABSTRACT

Oxidative and nitrosative stress plays an important role in neurodegenerative and neuroinflammatory diseases. Microglia are the primary innate immune cells in the central nervous system and the pathologic activation of microglia, secondary to neurodegenerative or neuroinflammatory processes, can lead to the release of pro-inflammatory/cytotoxic factors, which are critical in disease propagation. Cytosolic phospholipase A2 is the principle producers of arachidonic acid, the precursor for prostaglandins, prostacyclin and thromboxane during inflammation. Using cPLA knockout mice, we found that oxidative and nitrosative stress responses in microglia were significantly attenuated. Interestingly, unlike in macrophages, this process did not seem to involve the cyclooxygenases, but rather, the lipoxygenases, specifically LOX-12 and -15 instead. Botanical compounds, such as quercetin and honokiol, can suppress cPLA2, and thereby suppress inflammatory responses in microglia. Using an *in vivo* model of stroke, we observed that animals given certain botanical diets were partially protected from cerebral ischemia/reperfusion damage. Histologic results further support the important role of microglial cells in mediating the neuro-protective effects of the botanicals.