Microglia Cell Signaling in Models of Parkinson’s Disease

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Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder that affects the dopaminergic neurons in the substantia nigra in elderly population (1). Microglia, the resident macrophage-like cells located in the central nervous system, mediates synaptic pruning, perform phagocytosis of cellular deposits and waste, and release pro and anti-inflammatory responses contributing to neurodegeneration or neuroprotection (2). Microglia polarizes into different M1 and M2 phenotypes. These phenotypes modulate and release pro and anti-inflammatory responses contributing to pruning, perform phagocytosis of cellular depositions and waste, alpha-synuclein fibrils (3).

Figure 1. Dopaminergic neurons carrying mutated alpha-synuclein releases stress signals that activates astrocytes and microglia. The accumulation of α-syn leads to oxidative stress and proinflammatory responses in which microglia is polarized to M1 phenotype. M1 microglia secrete inflammatory responses such as TNF-α which is a pro-inflammatory cytokine. M2 microglia secrete anti-inflammatory responses such as IL-4 which is an anti-inflammatory cytokine.

Our overall hypothesis is that DHA derivative, Maresin 1, induce the second step in the polarization from M1 to M2, leading to a decrease in the inflammatory signals and increasing the LAP activity of microglial cells.

Methods

This hypothesis was tested “in vivo” in a 6-hydroxydopamine (6-HODA) toxicity rat model and “in vitro”, in adult rat brain cultures of microglial cells treated with TNF-alpha, C1q and IL-alpha or alpha-synuclein fibrils to induce M1 polarization.

Immunocytochemistry was used to detect p65 nuclear translocation and LC3 decorated vesicles, and immunohistochemistry using IBA1 was used to detect microglial cells in different areas of the rat brain. Images were taken using a Fluoview 1200 confocal microscope. The confocal capture z-stacks were processed using Imaris 9.7 and the data was statistically analyzed.

References


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