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Targeting Pro-Inflammatory Function of Microglia Using Small Molecules to Combat Neurodegeneration

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ABSTRACT

Microglia are the brain's resident immune cells that are responsible for maintaining homeostasis in healthy conditions. During injury or infection, resting microglia get activated and produce pro-inflammatory cytokines such as IL-1b, IL-1a, IL-6, etc. along with reactive oxygen species like nitric oxide (NO) to combat neuroinflammatory diseases such as Alzheimer's disease (AD). Inflammation is characterized by the activation of resident-immune cells in the brain called microglia that respond to the eat-me signals released by the toxic amyloid beta peptides as well as the dying neurons in the microenvironment. Recent studies have shown that activated microglia induce neuronal death by secreting IL-1a, TNF-a, and C1q. However, the cellular and molecular mechanisms in this process are not well understood. Furthermore, it has been previously shown that IL-1a and TNF-a promote neuronal death via the activation of astrocytes during inflammation. We used BV2 mouse microglia to investigate the IL-1a and TNF-a cytokine production in response to LPS activation using enzyme-linked immunosorbent assay (ELISA). In addition, the viability of the cells along with their NO production was evaluated using cell titer blue assay (CTB) and Griess assay. In this study, we show that small molecules can be used in single treatment and in combination to combat the inflammatory functions of microglia. These small molecules that modulate microglial functions may play an important role in developing new therapeutics for neuroinflammation.

KEYWORDS

Microglia, cytokine, neuroinflammation, Alzheimer's