論 文 要 旨

Atractylenolide-III suppresses lipopolysaccharide-induced inflammation Via downregulation of toll-like receptor 4 in mouse microglia

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Atractylenolide-III (AIII), a sesquiterpene compound isolated from the rhizome of Atractylodes macrocephala, has been reported to have anti-inflammatory effects in the peripheral organs. However, its effects on brain inflammation remain elusive. The present study investigated the effects of AIII on the response to lipopolysaccharide (LPS) in mouse microglia and clarified the underlying mechanism. In this study, treatment of MG6 cells with AIII (100 μM) significantly decreased the mRNA expression and protein levels of toll-like receptor 4 (TLR4). In addition, pretreatment of MG6 cells and primary cultured microglia cells with AIII (100 μM) significantly decreased the mRNA expression and protein levels of tumor necrosis factor-α, interleukin-1β, interleukin-6, inducible nitric oxide synthase, and cyclooxygenase-2 induced by LPS (5 ng/mL) without cytotoxicity. Subsequently, pretreatment with AIII significantly suppressed the phosphorylation of p38 mitogen-activated protein kinase (p38 MAPK) and c-Jun NH2-terminal kinase (JNK) after LPS stimulation in MG6 cells. These results showed that AIII downregulated TLR4 expression, leading to suppression of the p38 MAPK and JNK pathways, which in turn inhibited the production of pro-inflammatory cytokines and enzymes in LPS-stimulated microglia. Our findings, therefore, suggest the potential for AIII as a therapeutic agent for the treatment of brain inflammation, particularly in microglia-associated inflammation.