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Quercetin Ameliorates Cognitive Impairment in Depression by Targeting HSP90 to Inhibit NLRP3 Inflammasome Activation

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Abstract

Cognitive dysfunction was a common symptom of major depressive disorder (MDD). In previous studies, psychological stress leads to activation and proliferation of microglial cells in different brain regions. Quercetin, a bioflavonoid derived from vegetables and fruits, exerts anti-inflammatory effects in various diseases. To demonstrate the role of quercetin in the hippocampal inflammatory response in depress mice. The chronic unpredictable stress (CUS) depressive mice model built is used to explore the protective effects of quercetin on depression. Neurobehavioral test, protein expression of NOD-like receptor thermal protein domain associated protein 3 (NLRP3) and heat shock protein 90 (HSP90), and cytokines (IL-6, IL-1β, MCP-1, and TNF-α) were assessed. Quercetin ameliorated depressive-like behavior and cognitive impairment, and quercetin attenuates neuroinflammation and by targeting HSP90 to inhibit NLRP3 inflammasome activation. Quercetin inhibited the increase of HSP90 levels in the hippocampus and reverses inflammation-induced cognitive impairment. Besides, quercetin inhibited the increased level of cytokines (IL-6, IL-1β,

MCP-1, and TNF-α) in the hippocampus of the depressive model mouse and the increased level of cytokines (IL-6, IL-1β, and MCP-1) in microglia. The current study indicated that quercetin mitigated depressive-like behavior and by targeting HSP90 to inhibit NLRP3 inflammasome activation in microglia and depressive mice model, meanwhile ameliorated cognitive impairment in depression. Quercetin has huge potential for the novel pharmacological efficacy of antidepressant therapy.