Molecular Targets Underlying the Anti-inflammatory Effects of Thymoquinone in LPS activated BV-2 Cells

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Excessive production of pro-inflammatory cytokines in the brain have been implicated in several neurodegenerative diseases such as Alzheimer’s disease. Microglia is the primary immune cells of the brain, and when activated they release various pro-inflammatory cytokines. Natural compounds such as thymoquinone (TQ) that have an anti-inflammatory, anti-oxidant, and anticancer activities may offer a promising strategy for inflammation-mediated neurodegenerative disorders involving activated microglia cells. Our previous study showed that exposure to TQ in activated microglia reduces several cytokines/chemokines including IL-6, MCP-5, IP-10, MCP-1 and nitric oxide. The purpose of this study was to investigate the global molecular targets underlying the anti-inflammatory effects of TQ. In this study, microglia BV-2 cells were first stimulated for 1 hr. with 1μg/ml lipopolysaccharide (LPS); then incubated for 24 hr. in the presence or absence of 10 μM TQ. Genomic and proteomic approaches were used to identify target genes and proteins of TQ in activated microglia BV-2 cells. Genomic results showed that TQ significantly decreases gene expression of miR-155 by 3.9 folds, JAK2 by 2.2 folds, CCL5 by 13.2 folds, CCRL2 by 12 folds, and PTGS2 (COX2) by 3.3 folds in LPS-stimulated BV-2 cells. Proteomics results also showed that TQ significantly decreases protein expression of NOS by 10 folds and Tyrosine-protein kinase (SYK) by 8 folds. Our results showed that TQ significantly decreased genes and proteins involved in activated microglia-mediated inflammation. These results suggest that TQ could be an effective treatment for neuroinflammation that occurs in neurodegenerative diseases such as Alzheimer’s disease.

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