Ganoderma Lucidum Polysaccharides Enhance CD14 Endocytosis of LPS and Promote TLR4 Signal Transduction of Cytokine Expression

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We have previously reported that a well-characterized glycoprotein fraction containing fucose residues in an extract of Ganoderma lucidum polysaccharides (EORP) exerts certain immuno-modulation activity by stimulating the expression of inflammatory cytokines via TLR4. Continuing our studies, we have demonstrated that EORP increases the surface expression of CD14 and TLR4 within murine macrophages J774A.1 cells in vitro, and further promotes LPS binding and uptake by J774A.1 cells in a CD14-dependent fashion. Moreover, we observed the co-localization of internalized LPS with lysosome- and Golgi-apparatus markers within 5 min after J774A.1 cells stimulated with LPS. In addition, EORP pretreatment of J774A.1 cells and human blood-derived primary macrophages, followed by LPS stimulation, results in the super-induction of interleukin-1beta (IL-1) expression. Endocytosis inhibitors: such as cytochalasin D and colchicine effectively block EORP-enhanced LPS internalization by J774A.1 cells; yet they fail to decrease the LPS-induced phosphorylation of certain mitogen-activated protein kinases, and IL-1 mRNA and proIL-1 protein expression, indicating that LPS internalization by J774A.1 cells is not associated with LPS-dependent activation. Our current results could provide a potential EORP-associated protection mechanism for bacteria infection by enhancing IL-1 expression and the clearance of contaminated LPS by macrophages.