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Role for Moesin in Lipopolysaccharide-Stimulated Signal Transduction

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Moesin is a 78-kDa protein with diverse functions in linking the cytoskeleton to the membrane while controlling cell shape, adhesion, locomotion, and signaling. The aim of this study was to characterize the expression and localization of moesin in mononuclear phagocytes by using confocal microscopy, flow cytometry, immunoprecipitation, and Western blotting and to analyze the function of moesin as a lipopolysaccharide receptor, utilizing an antisense oligonucleotide approach to knock down the moesin gene. Results revealed that moesin is expressed on the surface of monocytes/macrophages and surface expression is increased after lipopolysaccharide stimulation. The total protein mass of moesin is increased in monocytes after lipopolysaccharide stimulation. Immunoprecipitation showed that moesin coprecipitates with TLR4, a well-known lipopolysaccharide receptor, suggesting an early role of moesin in the formation of the initiation complex for lipopolysaccharide signaling. Two antisense and two control sense oligonucleotides were synthesized and introduced every 4 h for 48 h in adherent macrophage-like cells. Cells were then stimulated with lipopolysaccharide for 4 h, and the supernatants were assayed for tumor necrosis factor alpha (TNF-α) production. Cell lysates were assayed for moesin expression by Western blotting immediately after the 48-h treatment period and also after 116 h of recovery to assess the return of moesin expression and function. Moesin gene expression was completely suppressed after 48 h of incubation with antisense oligonucleotides. The antisense elimination of moesin gene expression led to a significant reduction of lipopolysaccharide-induced TNF-α secretion. Restoration of moesin gene expression led to restoration of TNF-α production. These data suggest an important role for moesin in lipopolysaccharide-induced TNF-α production, highlighting its importance in lipopolysaccharide-mediated signal transduction.