Changed plasma membrane properties and its interaction to the cytoskeleton due to LPS binding

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Keywords: *Lypopolysaccharides, membrane mechanics, vesicles, optical tweezers*

Abstract

Lypopolysaccharides (LPS) are large amphiphilic molecules consisting of hydrophobic component (lipid A) and a polysaccharide composed of O-antigen. LPS are found in the outer membrane of Gram-negative bacteria and elicit strong immune response. In normal healthy individuals plasma concentrations of LPS range from undetectable levels to 0.2 ng/ml, prolonged physiological stress can elevate plasma LPS to 2 ng/ml and severe diseases to 10 or even 20 ng/ml.

LPS binds to LPS binding protein present in cholesterol reach domains of the plasma membrane. Its binding elicits a signal transduction cascade in which CD14 and Toll-like receptor 4 play a very important role. The biochemical path caused by LPS binding is extensively studied and well-understood. But binding of a molecule that is big like LPS to plasma membrane could influence also the membrane mechanical properties and this aspect is often neglected by strictly biochemical approach. Cell membrane is inseparably connected to the cytoskeleton and a redistribution of the cytoskeleton is also expected.

Motivated by this we studied how binding of LPS changes the mechanical properties of vesicles and cells from concentrations that among others corresponds the levels at prolonged stress (0.2 ng/ml). In synthetic vesicles consisting from two phases (ordered and disordered) and in vesicles made from plasma membrane the shape changes due to LPS binding were studied. In human umbilical vein endothelial cells the reorganization of actin filaments, microtubules and vimentin was observed with confocal microscopy. Optical tweezers were utilized to quantify membrane tether extraction, which provides information about the interconnections between the plasma membrane and the cytoskeleton.

Mechanical properties are increasingly recognized as an important factor for many vital cellular processes and cellular pathologies so the aim of our study was to shed some light also on physical aspect caused by LPS binding which could supplement the biochemical findings.