Gene name: **LBP**

External Ids for LBP Gene: HGNC: 6517 NCBI Gene: 3929 Ensembl: ENSG00000129988 OMIM®: 151990 UniProtKB/Swiss-Prot: P18428

NCBI Gene Summary: The protein encoded by this gene is involved in the acute-phase immunologic response to gram-negative bacterial infections. Gram-negative bacteria contain a glycolipid, lipopolysaccharide (LPS), on their outer cell wall. Together with bactericidal permeability-increasing protein (BPI), the encoded protein binds LPS and interacts with the CD14 receptor, probably playing a role in regulating LPS-dependent monocyte responses. Studies in mice suggest that the encoded protein is necessary for the rapid acute-phase response to LPS but not for the clearance of LPS from circulation.

GeneCards Summary: LBP (Lipopolysaccharide Binding Protein) is a Protein Coding gene. Diseases associated with LBP include Alcoholic Hepatitis and Peritonitis. Among its related pathways are Bacterial infections in CF airways and Toll Like Receptor 7/8 (TLR7/8) Cascade. Gene Ontology (GO) annotations related to this gene include *signaling receptor binding* and *lipopolysaccharide binding*. An important paralog of this gene is BPI.

UniProtKB/Swiss-Prot Summary: Plays a role in the innate immune response. Binds to the lipid A moiety of bacterial lipopolysaccharides (LPS), a glycolipid present in the outer membrane of all Gram-negative bacteria (PubMed:24120359, 7517398). Acts as an affinity enhancer for CD14, facilitating its association with LPS. Promotes the release of cytokines in response to bacterial lipopolysaccharide (PubMed:24120359, 7517398)

Cellular localization: mainly in the extracellular region.

The **LBP** gene encodes **lipopolysaccharide-binding protein**, a crucial component of the innate immune system. LBP is primarily produced by hepatocytes and circulates in the bloodstream, where it plays a pivotal role in recognizing and responding to Gram-negative bacterial infections.

Function in Sepsis: In sepsis—a severe systemic inflammatory response to infection—LBP facilitates the immune system's recognition of lipopolysaccharides (LPS), components of the outer membrane of Gram-negative bacteria:

- **LPS Recognition and Transfer:** LBP binds to LPS and transfers it to the CD14 receptor on immune cells, such as macrophages and monocytes. This interaction triggers signaling pathways leading to the production of pro-inflammatory cytokines, initiating an immune response to combat the infection.
- **Amplification of Inflammatory Response:** While LBP-mediated recognition of LPS is essential for pathogen defense, excessive LBP activity can lead to an overwhelming inflammatory response, contributing to the pathogenesis of sepsis and its associated complications.

Genetic Variations and Sepsis Susceptibility: Genetic polymorphisms in the LBP gene have been associated with variations in individual susceptibility to sepsis:

- **rs2232618 Polymorphism:** This single nucleotide polymorphism (SNP) results in an amino acid substitution (Phe436Leu) in the LBP protein. Studies have shown that individuals carrying the variant allele have an increased risk of developing sepsis following trauma. For instance, research

involving Chinese trauma patients demonstrated a significant association between the rs2232618 polymorphism and heightened sepsis susceptibility.

- **Gender-Specific Associations:** Certain LBP gene polymorphisms have been linked to sepsis predisposition in a gender-specific manner. For example, the Gly98 allele has been associated with an increased risk of sepsis in male patients but not in females.

Diagnostic and Prognostic Role: Elevated serum LBP levels have been observed in sepsis patients, correlating with disease severity and outcomes. Serial measurements of LBP can aid in identifying patients at higher risk for adverse outcomes, including the development of acute respiratory distress syndrome (ARDS). A study reported that increased LBP levels at 48 hours were associated with higher mortality in severe sepsis patients.

Therapeutic Implications: Given its role in modulating the inflammatory response to Gram-negative bacterial infections, LBP represents a potential therapeutic target. Modulating LBP activity could help balance the necessary immune response to clear infections while preventing excessive inflammation that leads to tissue damage and organ dysfunction.