Gene name: TLR2

External Ids for TLR2 Gene: HGNC: 11848 NCBI Gene: 7097 Ensembl: ENSG00000137462 OMIM®: 603028 UniProtKB/Swiss-Prot: O60603

NCBI Gene Summary: The protein encoded by this gene is a member of the Toll-like receptor (TLR) family which plays a fundamental **role in pathogen recognition and activation of innate immunity.** TLRs are highly conserved from Drosophila to humans and share structural and functional similarities. This protein is a cell-surface protein that can form heterodimers with other TLR family members to recognize conserved molecules derived from microorganisms known as pathogen-associated molecular patterns (PAMPs). Activation of TLRs by PAMPs leads to an up-regulation of signaling pathways to modulate the host's inflammatory response. This gene is also thought to promote apoptosis in response to bacterial lipoproteins. This gene has been implicated in the pathogenesis of several autoimmune diseases. Alternative splicing results in multiple transcript variants.

GeneCards Summary: TLR2 (Toll Like Receptor 2) is a Protein Coding gene. Diseases associated with TLR2 include Leprosy 3 and Colorectal Cancer. Among its related pathways are Toll Like Receptor 7/8 (TLR7/8) Cascade and Diseases of Immune System. Gene Ontology (GO) annotations related to this gene include *protein heterodimerization activity* and *transmembrane signaling receptor activity*. An important paralog of this gene is TLR6.

UniProtKB/Swiss-Prot Summary: Cooperates with LY96 to mediate the innate immune response to bacterial lipoproteins and other microbial cell wall components. Cooperates with TLR1 or TLR6 to mediate the innate immune response to bacterial lipoproteins or lipopeptides (PubMed:17889651, 21078852). Acts via MYD88 and TRAF6, leading to NF-kappa-B activation, cytokine secretion and the inflammatory response. May also activate immune cells and promote apoptosis in response to the lipid moiety of lipoproteins (PubMed:10426995, 10426996). Recognizes mycoplasmal macrophage-activating lipopeptide-2kD (MALP-2), soluble tuberculosis factor (STF), phenol-soluble modulin (PSM) and B.burgdorferi outer surface protein A lipoprotein (OspA-L) cooperatively with TLR6 (PubMed:11441107). Stimulation of monocytes in vitro with M.tuberculosis PstS1 induces p38 MAPK and ERK1/2 activation primarily via this receptor, but also partially via TLR4 (PubMed:16622205). MAPK activation in response to bacterial peptidoglycan also occurs via this receptor (PubMed:16622205). Acts as a receptor for M.tuberculosis lipoproteins LprA, LprG, LpqH and PstS1, some lipoproteins are dependent on other coreceptors (TLR1, CD14 and/or CD36); the lipoproteins act as agonists to modulate antigen presenting cell functions in response to the pathogen (PubMed:19362712). M.tuberculosis HSP70 (dnaK) but not HSP65 (groEL-2) acts via this protein to stimulate NF-kappa-B expression (PubMed:15809303). Recognizes M.tuberculosis major T-antigen EsxA (ESAT-6) which inhibits downstream MYD88-dependent signaling (shown in mouse) (By similarity). Forms activation clusters composed of several receptors depending on the ligand, these clusters trigger signaling from the cell surface and subsequently are targeted to the Golgi in a lipid-raft dependent pathway. Forms the cluster TLR2:TLR6:CD14:CD36 in response to diacylated lipopeptides and TLR2:TLR1:CD14 in response to triacylated lipopeptides (PubMed:16880211). Required for normal uptake of M.tuberculosis, a process that is inhibited by M.tuberculosis LppM (By similarity). (TLR2_HUMAN,O60603)

Cellular localization: mostly in golgi apparatus and plasma membrane.
TLR2 stands for *Toll-like Receptor 2*, a member of the TLR family that plays a crucial role in the innate immune system.

TLR2 is a transmembrane pattern recognition receptor (PRR) that detects microbial components from pathogens.

🔬 Biological Function

- TLR2 recognizes pathogen-associated molecular patterns (PAMPs), particularly from Gram-positive bacteria, fungi, and certain viruses.
- It forms heterodimers with other TLRs:
    - With TLR1 → detects triacylated lipopeptides.
    - With TLR6 → detects diacylated lipoproteins.
- Upon activation, it triggers intracellular signaling cascades, leading to:
    - Activation of NF-κB and MAPK pathways.
      Production of pro-inflammatory cytokines (TNF-α, IL-6, IL-1β).
    - Upregulation of costimulatory molecules on antigen-presenting cells.

🦠 Role of TLR2 in Sepsis

- TLR2 is highly active during bacterial infections, especially Gram-positive sepsis (e.g., Staphylococcus, Streptococcus).
- It contributes to the early detection of invading microbes and initiates inflammatory signaling.
- TLR2 signaling can be both protective and detrimental:
    - Early response: enhances pathogen clearance.
    - Overactivation: leads to cytokine storm, tissue damage, and organ dysfunction.
- In polymicrobial sepsis models, TLR2-deficient mice sometimes have better survival due to reduced inflammation.

🧪 Expression and Regulation

- TLR2 is expressed on:
    - **Monocytes/macrophages**
    - **Neutrophils**
    - **Dendritic cells**
    - **Endothelial and epithelial cells**
- Expression is **upregulated by LPS, IFN-γ, IL-1β**, and other TLR agonists.
- It is tightly regulated by **negative feedback loops**, such as SOCS proteins and microRNAs, to prevent excessive inflammation.

📈 Clinical Relevance in Sepsis

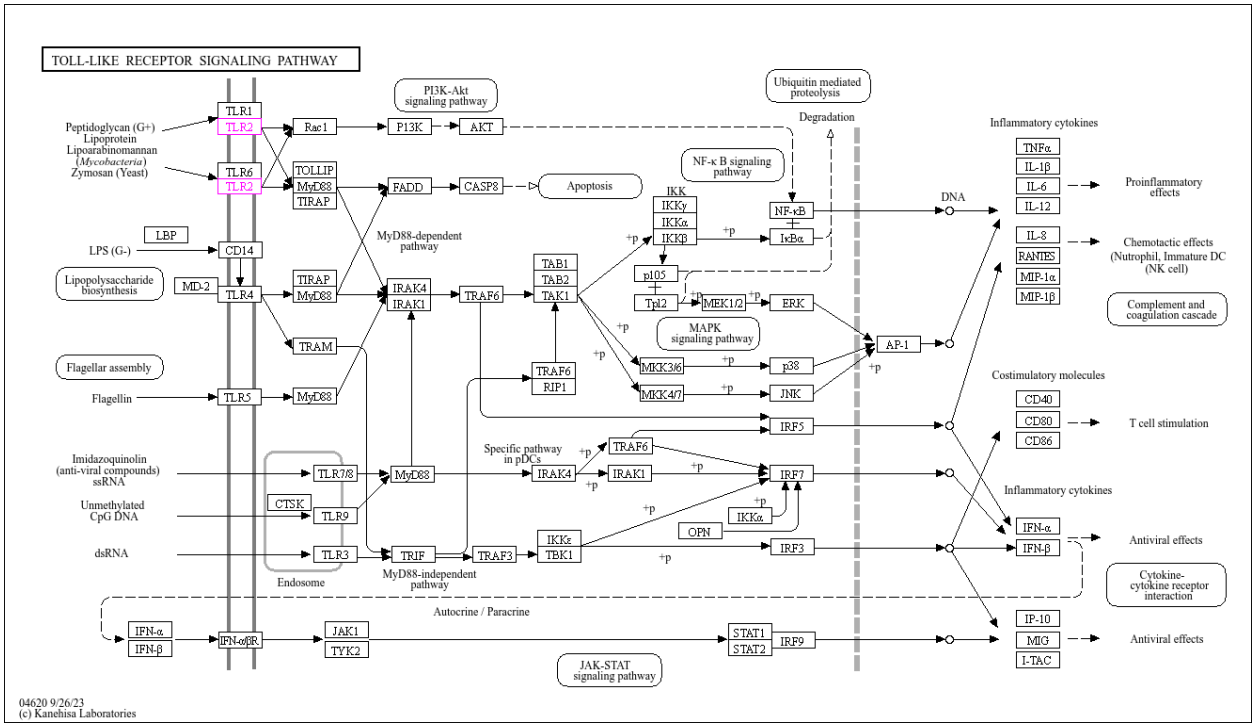
- TLR2 expression is elevated in the blood and tissues of patients with bacterial sepsis.
- Its levels are correlated with systemic inflammation markers, including IL-6 and CRP.
  Genetic polymorphisms in TLR2 (like, **Arg753Gln**) are linked to:
    - Increased risk of sepsis.
    - Altered immune responses to bacterial infection.

- Targeting TLR2 or its downstream pathways (such as, MyD88) is being explored to modulate sepsis-induced inflammation.

🧪 Supporting Literature

Doi: 10.1097/01.shk.0000142256.23382.5d — Doi:10.1111/j.1365-2249.2004.02433.x

KEGG:



Enrichr-KG: