Gene name: **CD14**

External Ids for CD14 Gene: HGNC: 1628 NCBI Gene: 929 Ensembl: ENSG00000170458 OMIM®: 158120 UniProtKB/Swiss-Prot: P08571

NCBI Gene Summary: The protein encoded by this gene is a surface antigen that is preferentially expressed on monocytes/macrophages. It **cooperates with other proteins to mediate the innate immune response to bacterial lipopolysaccharide, and to viruses**. This gene has been identified as a target candidate in the treatment of SARS-CoV-2-infected patients to potentially lessen or inhibit a severe inflammatory response. Alternative splicing results in multiple transcript variants encoding the same protein.

GeneCards Summary: CD14 (CD14 Molecule) is a Protein Coding gene. Diseases associated with CD14 include Alagille Syndrome 1 and Croup. 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 *lipopolysaccharide binding* and *lipoteichoic acid binding*.

UniProtKB/Swiss-Prot Summary: Coreceptor for bacterial lipopolysaccharide (PubMed:1698311, 23264655). In concert with LBP, binds to monomeric lipopolysaccharide and delivers it to the LY96/TLR4 complex, thereby mediating the innate immune response to bacterial lipopolysaccharide (LPS) (PubMed:20133493, 22265692, 23264655). Acts via MyD88, TIRAP and TRAF6, leading to NF-kappa-B activation, cytokine secretion and the inflammatory response (PubMed:8612135). Acts as a coreceptor for TLR2:TLR6 heterodimer in response to diacylated lipopeptides and for TLR2:TLR1 heterodimer in response to triacylated lipopeptides, these clusters trigger signaling from the cell surface and subsequently are targeted to the Golgi in a lipid-raft dependent pathway (PubMed:16880211). Binds electronegative LDL (LDL(-)) and mediates the cytokine release induced by LDL(-) (PubMed:23880187). (CD14_HUMAN,P08571)

Cellular localization: mainly in golgi apparatus, extracellular and plasma membrane.

Full Name: *CD14 molecule* (Cluster of Differentiation 14)

Protein Type: Pattern recognition receptor (PRR), co-receptor

Forms: Exists in two forms:

Membrane-bound CD14 (mCD14) – anchored to the cell surface via a GPI-linkage.
Soluble CD14 (sCD14) – found circulating in blood.

Biological Function of CD14

- Key co-receptor for detecting bacterial components, especially lipopolysaccharide (LPS) from Gram-negative bacteria.
- Works together with TLR4 and MD-2 to recognize and respond to LPS.
- Can also detect other pathogen-associated molecular patterns (PAMPs), such as:
    - Lipoteichoic acid from Gram-positive bacteria
    - Peptidoglycan
    - Heat-shock proteins
- CD14 itself does not have a signaling domain but facilitates ligand recognition and transfer to TLR4, initiating intracellular immune signaling.

Main Actions of CD14:

- Binds LPS and presents it to the TLR4/MD-2 complex.
- Amplifies activation of NF-κB and MAPK pathways → drives cytokine production (TNF-α, IL-6, IL-1β).

- Enhances endocytosis of pathogens and apoptotic cells.
- Regulates both pro-inflammatory and anti-inflammatory responses depending on the context.

🦠 Role of CD14 in Sepsis

- Central player in the early innate immune response to bacterial infections.
- In Gram-negative sepsis:
    - CD14 is essential for LPS recognition.
    - Overactivation leads to excessive cytokine release (cytokine storm).
    - Contributes to systemic inflammation, vascular leakage, and organ dysfunction.
- In Gram-positive sepsis:
    - Also involved by recognizing bacterial lipoproteins and other cell wall components.
- Soluble CD14 (sCD14) increases during sepsis:
    - Helps detect pathogens even when cell-bound receptors are saturated.
    - Can also activate cells that don't express mCD14 (like endothelial and epithelial cells).

📈 Clinical Relevance of CD14 in Sepsis

Diagnostic Role:

- Elevated sCD14 levels in plasma/serum have been observed early in sepsis.
- Measurement of sCD14 and sCD14-ST (presepsin) is used clinically:
    - Presepsin is a cleavage product of sCD14 and is approved as a biomarker for sepsis diagnosis in some countries.
    - It rises earlier than procalcitonin (PCT) and CRP in some studies.

Prognostic Role:

- High levels of sCD14 or presepsin correlate with:
    - Increased severity of sepsis (higher SOFA scores).
    - Greater risk of progression to septic shock.
    - Higher ICU mortality.
- Persistent high sCD14 can indicate poor immune control and risk of organ failure.

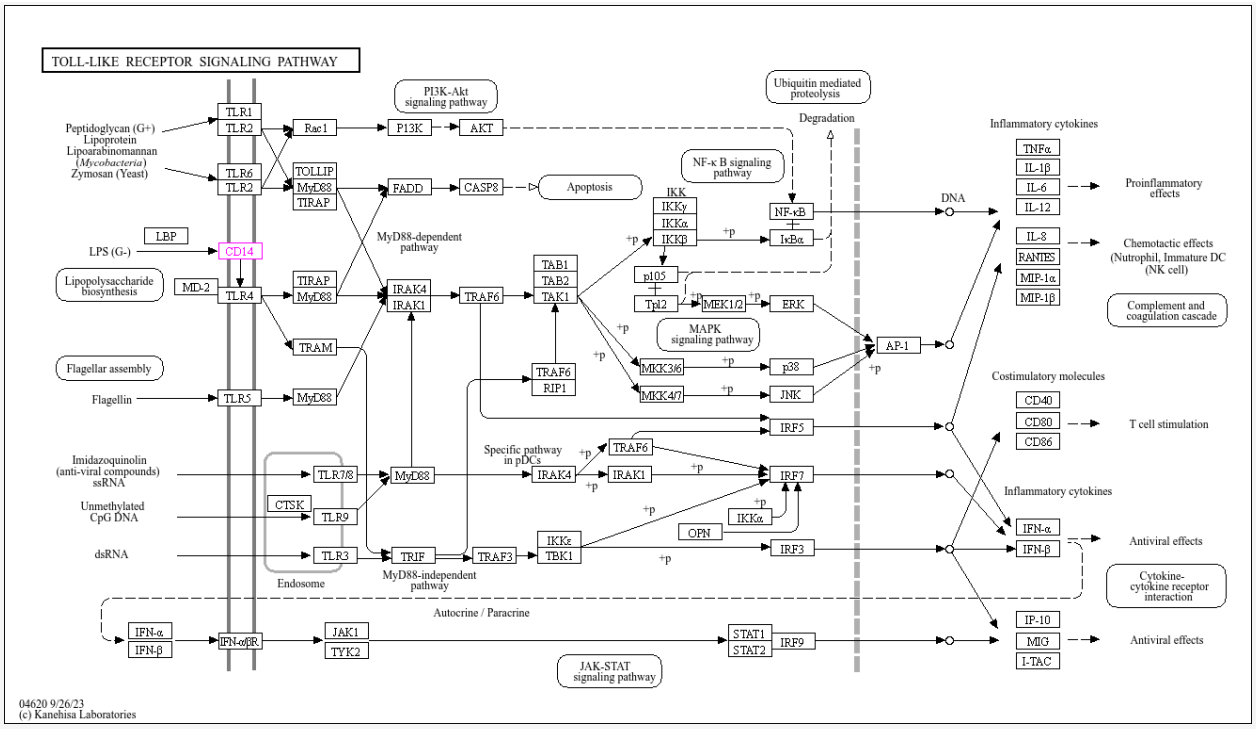
🧪 Experimental and Clinical Evidence

- In animal models, CD14-deficient mice have reduced inflammatory responses and better survival after LPS challenge.
- Human studies show elevated CD14 and presepsin levels correlate strongly with:
    - Need for mechanical ventilation
    - Acute kidney injury (AKI)
    - Overall severity of infection

🧪 Supporting Literature

doi: 10.5847/wjem.j.issn.1920-8642.2014.01.002
DOI: 10.1007/s10156-012-0435-2
DOI 10.1007/s10156-005-0400-4
DOI: 10.1097/01.shk.0000217815.57727.29

KEGG



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