Gene name: **PLAUR**

External Ids for PLAUR Gene: HGNC: 9053 NCBI Gene: 5329 Ensembl: ENSG00000011422 OMIM®: 173391 UniProtKB/Swiss-Prot: Q03405

NCBI Gene Summary: This gene encodes the receptor for urokinase plasminogen activator and, given its role in localizing and promoting plasmin formation, likely influences many normal and pathological processes related to cell-surface plasminogen activation and localized degradation of the extracellular matrix. It binds both the proprotein and mature forms of urokinase plasminogen activator and permits the activation of the receptor-bound pro-enzyme by plasmin. The protein lacks transmembrane or cytoplasmic domains and may be anchored to the plasma membrane by a glycosyl-phosphatidylinositol (GPI) moiety following cleavage of the nascent polypeptide near its carboxy-terminus. However, a soluble protein is also produced in some cell types. Alternative splicing results in multiple transcript variants encoding different isoforms. The proprotein experiences several post-translational cleavage reactions that have not yet been fully defined.

GeneCards Summary: PLAUR (Plasminogen Activator, Urokinase Receptor) is a Protein Coding gene. Diseases associated with PLAUR include Ureter, Cancer Of and Diphtheria. Among its related pathways are Innate Immune System and Metabolism of proteins. Gene Ontology (GO) annotations related to this gene include *signaling receptor binding* and *signaling receptor activity*. An important paralog of this gene is LYPD3.

UniProtKB/Swiss-Prot Summary: Acts as a receptor for urokinase plasminogen activator (PubMed:15677461). Plays a role in localizing and promoting plasmin formation. Mediates the proteolysis-independent signal transduction activation effects of U-PA. It is subject to negative-feedback regulation by U-PA which cleaves it into an inactive form. (UPAR_HUMAN,Q03405)

Cellular localization: mostly extracellular and plasma membrane.

Full Name: *Plasminogen Activator, Urokinase Receptor*

Protein Name: **uPAR** (Urokinase-type Plasminogen Activator Receptor)

Protein Type: GPI-anchored cell surface receptor (not transmembrane)

🔬 Biological Function of PLAUR (uPAR)

PLAUR encodes the uPAR protein, which acts as the receptor for urokinase-type plasminogen activator (uPA or PLAU).

🛠️ Main Functions:

1. Regulates extracellular matrix degradation:
    - uPAR binds uPA, which converts plasminogen → plasmin.
    - Plasmin degrades fibrin and activates matrix metalloproteinases (MMPs) → enabling cell migration, tissue remodeling, and invasion.
2. Promotes immune cell migration:
    - uPAR is involved in leukocyte adhesion, chemotaxis, and transendothelial migration.
3. Modulates immune responses and inflammation:
    - Influences macrophage and neutrophil activation.
    - Can regulate cytokine release and toll-like receptor (TLR) signaling.
4. Signal transduction (indirectly):
    - Despite lacking a cytoplasmic domain, uPAR interacts with:
        - Integrins

        - Vitronectin
          EGFR and other co-receptors
          → leading to intracellular signaling (MAPK, PI3K/AKT pathways).

🦠 Role of PLAUR/uPAR in Sepsis

PLAUR plays a key role in sepsis, especially in linking coagulation, fibrinolysis, and inflammation:

Early Sepsis:

- uPAR is upregulated on monocytes, neutrophils, and endothelial cells.
- Promotes:
    - Immune cell migration
    - Tissue infiltration
    - Microbial clearance

Severe/Late Sepsis:

- Excessive uPAR activity leads to:
    - Excess fibrinolysis and matrix degradation → contributing to vascular leakage and organ damage.
    - Enhanced cytokine production → worsening the cytokine storm.
    - Release of soluble uPAR (suPAR) into plasma, a marker of systemic inflammation and immune activation.

📈 Clinical Relevance of PLAUR in Sepsis

Diagnostic Role:

- Soluble uPAR (suPAR) levels are elevated in sepsis and correlate with:
    - Inflammation severity and Immune cell activation

Prognostic Role:

- High suPAR levels predict:
    - Poor clinical outcomes
    - Higher mortality risk
    - Organ dysfunction (such as, ARDS, AKI)
- suPAR is used as a prognostic biomarker in ICU settings.

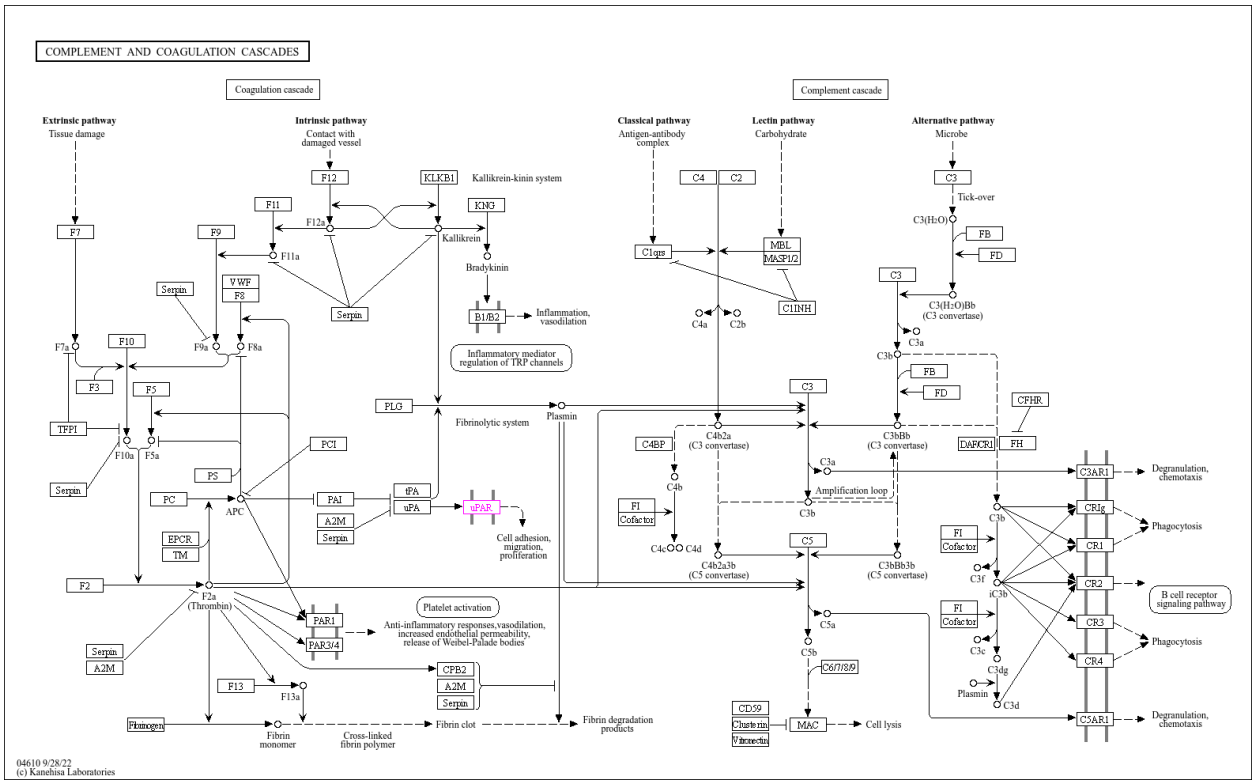
Therapeutic Potential:

- Targeting the uPA-uPAR system is being explored to:
    - Reduce excessive inflammation
    - Preserve vascular integrity
    - Modulate immune responses

🧪 Supporting Literature

Doi:10.1186/1741-7015-10-2 - Doi:10.1097/SHK.0000000000001434 - Doi:10.1007/s11739-015-1268-7

KEGG:



Enrichr-KG