Gene name: **P2RX7**

External Ids for P2RX7 Gene: HGNC: 8537 NCBI Gene: 5027 Ensembl: ENSG00000089041
OMIM®: 602566 UniProtKB/Swiss-Prot: Q99572

NCBI Gene Summary: The product of this gene belongs to the family of purinoceptors for ATP. This receptor functions as a ligand-gated ion channel and is responsible for ATP-dependent lysis of macrophages through the formation of membrane pores permeable to large molecules. Activation of this nuclear receptor by ATP in the cytoplasm may be a mechanism by which cellular activity can be coupled to changes in gene expression. Multiple alternatively spliced variants have been identified, most of which fit nonsense-mediated decay (NMD) criteria.

GeneCards Summary: P2RX7 (Purinergic Receptor P2X 7) is a Protein Coding gene. Diseases associated with P2RX7 include Leukemia, Chronic Lymphocytic and Tularemia. Among its related pathways are Inflammasomes and Platelet homeostasis. Gene Ontology (GO) annotations related to this gene include *protein homodimerization activity* and *signaling receptor activity*. An important paralog of this gene is P2RX4.

UniProtKB/Swiss-Prot Summary: Receptor for ATP that acts as a ligand-gated ion channel. Responsible for ATP-dependent lysis of macrophages through the formation of membrane pores permeable to large molecules. Could function in both fast synaptic transmission and the ATP-mediated lysis of antigen-presenting cells. In the absence of its natural ligand, ATP, functions as a scavenger receptor in the recognition and engulfment of apoptotic cells (PubMed:21821797, 23303206). (P2RX7_HUMAN,Q99572)

Cellular localization: mostly in plasma membranes.

Full Name: *Purinergic Receptor P2X, Ligand Gated Ion Channel 7*

Protein Type: ATP-gated ion channel (P2X receptor family)

Key Role: Senses extracellular ATP as a danger signal and mediates inflammation and cell death.

Biological Function of P2RX7

- P2RX7 is a membrane ion channel activated by high concentrations of extracellular ATP, typically released from:
  - Dying or stressed cells
  - Damaged tissues
  - Infections and trauma
- Upon activation:
  - Opens a cation channel allowing Na^+ and Ca^{2+} influx and K^+ efflux.
  - Sustained activation can lead to formation of a large pore permeable to molecules up to ~900 Da.
- Major downstream effects include:
  - Activation of the NLRP3 inflammasome.
  - Processing and secretion of pro-inflammatory cytokines, especially IL-1β and IL-18.
  - Induction of pyroptosis, a highly inflammatory form of programmed cell death.

P2RX7's Role in Sepsis

- ATP release into extracellular spaces is a hallmark of tissue injury and infection, which happens massively during sepsis.

- P2RX7 senses this ATP and triggers strong inflammatory responses:
    - Promotes NLRP3 inflammasome activation → leading to IL-1β release.
    - Induces vascular permeability, worsening hypotension and edema.
    - Facilitates immune cell recruitment and activation.
- In severe sepsis, overactivation of P2RX7 contributes to:
    - Cytokine storm
    - Endothelial dysfunction
    - Multi-organ damage
- Some evidence suggests that P2RX7 activation also contributes to immune exhaustion if sustained too long.

📈 Clinical Relevance in Sepsis

Diagnostic Implication:

- P2RX7 activity correlates with elevated levels of inflammatory cytokines like **IL-1β** and **IL-18** in septic patients.
- Markers of inflammasome activation (partially downstream of P2RX7) are elevated in early and severe sepsis.

Prognostic Implication:

- Higher P2RX7 expression or activation correlates with:
    - Worse clinical outcomes
    - Higher organ dysfunction scores
    - Increased risk of septic shock and mortality
- Inhibition of P2RX7 in experimental models reduces sepsis severity and improves survival rates.

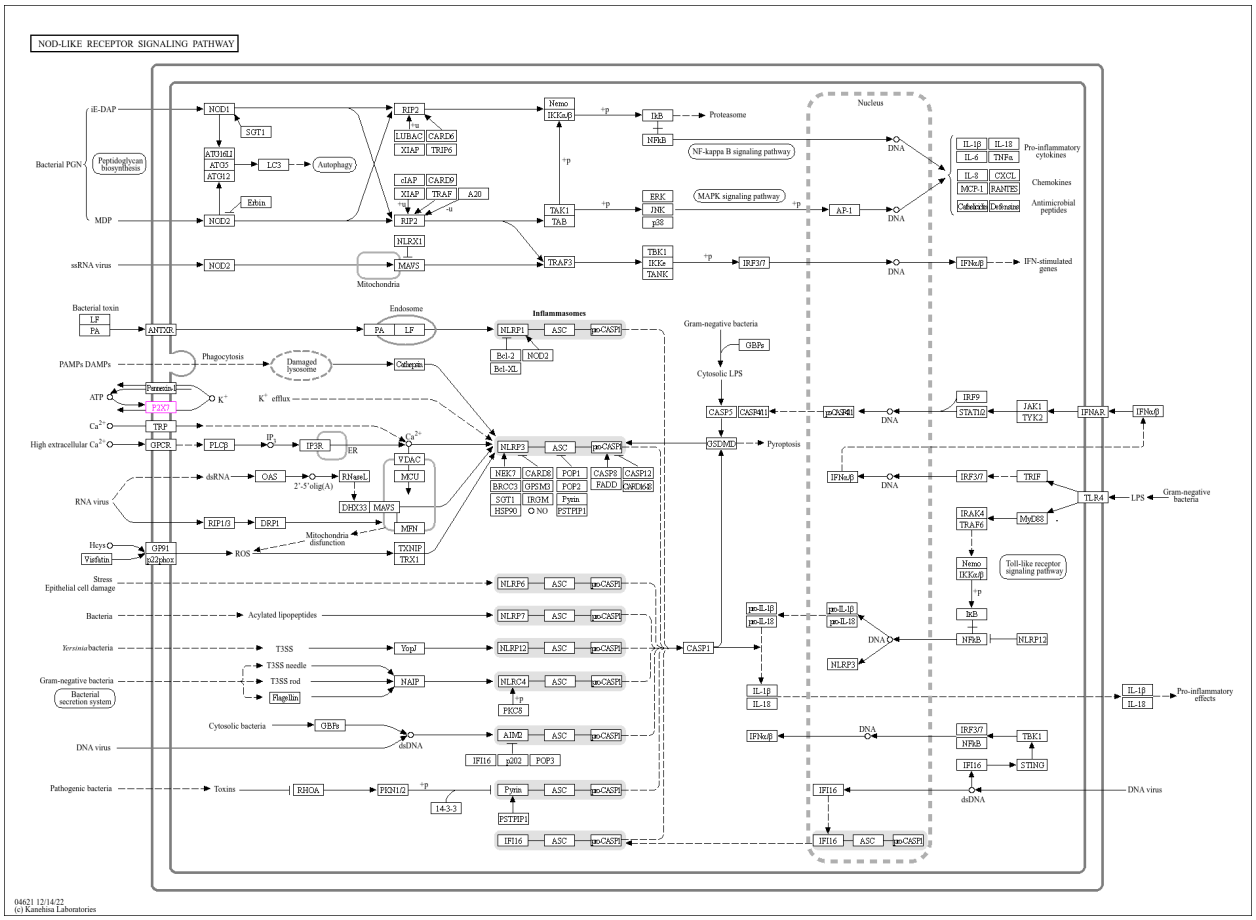
Therapeutic Target:

- P2RX7 antagonists are under investigation for:
    - Sepsis
    - Autoimmune diseases
    - Inflammatory disorders
- The goal is to prevent excessive IL-1β release and inflammasome activation.

🧪 Supporting Literature

Doi: 10.1038/s41467-019-10626-x
Doi: 10.1007/s12035-016-0168-9
Doi: 10.7554/eLife.60849
Doi: 10.1007/s11302-020-09746-7

KEGG:



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