Gene name: **PDCD1** **Previous HGNC Symbols for PDCD1 Gene:** SLEB2

External Ids for PDCD1 Gene: HGNC: 8760 NCBI Gene: 5133 Ensembl: ENSG00000188389
OMIM®: 600244 UniProtKB/Swiss-Prot: Q15116

NCBI Gene Summary: Programmed cell death protein 1 (PDCD1) is an **immune-inhibitory receptor expressed in activated T cells**; it is involved in the regulation of T-cell functions, including those of effector CD8+ T cells. In addition, this protein can also promote the differentiation of CD4+ T cells into T regulatory cells. PDCD1 is expressed in many types of tumors including melanomas, and has demonstrated to play a role in anti-tumor immunity. Moreover, this protein has been shown to be involved in safeguarding against autoimmunity, however, it can also contribute to the inhibition of effective antitumor and antimicrobial immunity.
GeneCards Summary: PDCD1 (Programmed Cell Death 1) is a Protein Coding gene. Diseases associated with PDCD1 include Autoimmune Disease With Mycobacterium Tuberculosis and Systemic Lupus Erythematosus 2. Among its related pathways are Infectious disease and SARS-CoV-2 Infection. Gene Ontology (GO) annotations related to this gene include *obsolete signal transducer activity*.
UniProtKB/Swiss-Prot Summary: Inhibitory receptor on antigen activated T-cells that plays a critical role in induction and maintenance of immune tolerance to self (PubMed:21276005). Delivers inhibitory signals upon binding to ligands CD274/PDCD1L1 and CD273/PDCD1LG2 (PubMed:21276005). Following T-cell receptor (TCR) engagement, PDCD1 associates with CD3-TCR in the immunological synapse and directly inhibits T-cell activation (By similarity). Suppresses T-cell activation through the recruitment of PTPN11/SHP-2: following ligand-binding, PDCD1 is phosphorylated within the ITSM motif, leading to the recruitment of the protein tyrosine phosphatase PTPN11/SHP-2 that mediates dephosphorylation of key TCR proximal signaling molecules, such as ZAP70, PRKCQ/PKCtheta and CD247/CD3zeta (By similarity). (PDCD1_HUMAN,Q15116) The PDCD1-mediated inhibitory pathway is exploited by tumors to attenuate anti-tumor immunity and escape destruction by the immune system, thereby facilitating tumor survival (PubMed:28951311). The interaction with CD274/PDCD1L1 inhibits cytotoxic T lymphocytes (CTLs) effector function (PubMed:28951311). The blockage of the PDCD1-mediated pathway results in the reversal of the exhausted T-cell phenotype and the normalization of the anti-tumor response, providing a rationale for cancer immunotherapy (PubMed:22658127, 25034862, 25399552). (PDCD1_HUMAN,Q15116)

Cellular localization: mostly in plasma membranes.
Full Name: *Programmed Cell Death 1*
Protein Name: **PD-1** (Programmed Death-1 receptor)
Protein Type:

- Immune checkpoint receptor
- Transmembrane protein in the CD28/CTLA4 family

Biological Function of PDCD1 (PD-1)

- PDCD1 encodes PD-1, an inhibitory receptor expressed primarily on:
    - T cells (especially activated T cells)
    - B cells

    - Natural killer (NK) cells
    - Some monocytes and dendritic cells under certain conditions

- Key biological actions:
    - Inhibits immune cell activation to prevent overactive immune responses.
    - Maintains peripheral tolerance (prevents autoimmune reactions).
    - Regulates the balance between immune activation and exhaustion.

🛠️ How PDCD1/PD-1 Works:

- When PD-1 binds to its ligands:
    - PD-L1 (CD274) or PD-L2 (PDCD1LG2),
- It delivers an inhibitory signal into the immune cell.
- This leads to:
    - Decreased TCR (T-cell receptor) signaling.
    - Reduced proliferation of T cells.
    - Lower cytokine production (like IFN-γ, IL-2).
    - Promotion of T cell exhaustion and apoptosis under chronic stimulation.

🦠 Role of PDCD1 in Sepsis

- In early sepsis, the immune system is highly activated ("cytokine storm").
- But in prolonged or severe sepsis, the body often switches to an immune suppression phase ("immunoparalysis").
- During late sepsis:
    - PD-1 expression is massively upregulated on:
        - CD4+ and CD8+ T cells
        - NK cells
        - Monocytes
    - This drives immune exhaustion, leading to:
        - Impaired pathogen clearance.
        - Increased susceptibility to secondary infections.
        - Poor wound healing.
        - Higher risk of death.

🔴 High PD-1 expression is a hallmark of immune dysfunction in sepsis.

📈 Clinical Relevance of PDCD1 in Sepsis

Diagnostic Role:

- Elevated PD-1 expression can be detected on circulating T cells and monocytes in septic patients.
- Serves as a marker of immunosuppression and T cell exhaustion.

Prognostic Role:

- **Higher PD-1 levels** correlate with:
    - Increased likelihood of secondary infections (nosocomial infections).
    - Higher rates of ICU-acquired infections.
    - Increased mortality rates.
- Persistent PD-1 elevation is associated with failure to clear pathogens and poor sepsis recovery.

Therapeutic Interest:

- PD-1/PD-L1 blockade therapies (immune checkpoint inhibitors) are being investigated to:
    - Restore immune function in septic patients.
    - Improve pathogen clearance and patient survival.
- Preclinical trials (such as, PD-1 blockade in septic mice) showed improved survival and bacterial clearance.

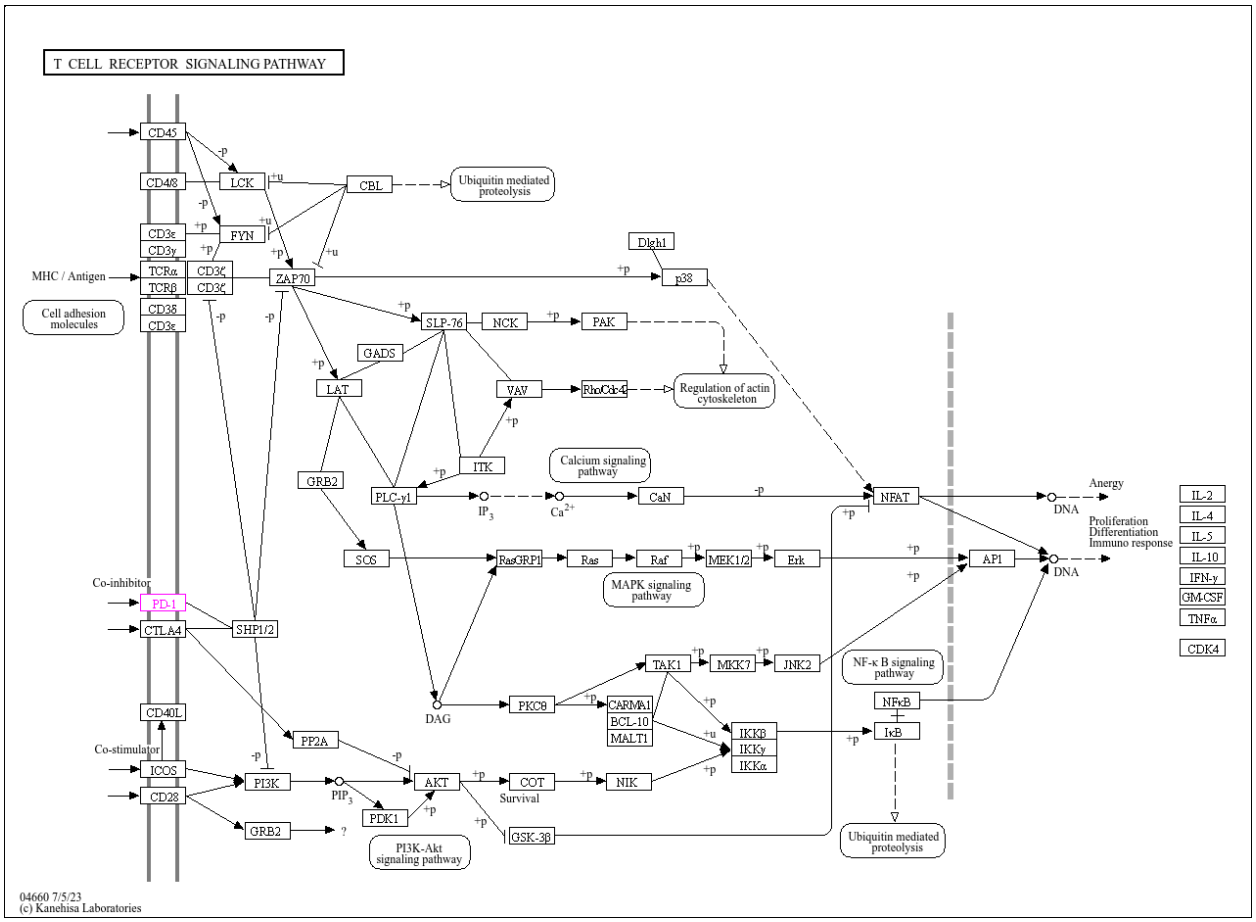
🔬 Pathways Involving PDCD1

- **T cell receptor signaling pathway (KEGG hsa04660)** → modulates T cell activation.
- **Apoptosis and exhaustion pathways** → controls T cell lifespan.
- **PD-1 checkpoint pathway in cancer (KEGG hsa05235)** → well-characterized in tumors, but same inhibitory pathways operate in sepsis.
- **Cytokine-cytokine receptor interaction pathway (hsa04060)** → via its interaction with PD-L1 and PD-L2.

🧪 Supporting Literature

Doi: 10.1111/sji.13049
Doi: 10.3389/fimmu.2020.624279
Doi: 10.3389/fimmu.2018.02008

KEGG:



Enrichr-KG