Gene name: ICAM1

External Ids for ICAM1 Gene: HGNC: 5344 NCBI Gene: 3383 Ensembl: ENSG00000090339 OMIM®: 147840 UniProtKB/Swiss-Prot: P05362

NCBI Gene Summary: This gene encodes a cell surface glycoprotein which is typically **expressed on endothelial cells and cells of the immune system**. It binds to integrins of type CD11a / CD18, or CD11b / CD18 and is also exploited by Rhinovirus as a receptor.

GeneCards Summary: ICAM1 (Intercellular Adhesion Molecule 1) is a Protein Coding gene. Diseases associated with ICAM1 include Malaria and Cerebral Malaria. Among its related pathways are Blood-Brain Barrier and Immune Cell Transmigration: VCAM-1/CD106 Signaling and **Cytokine Signaling in Immune system**. Gene Ontology (GO) annotations related to this gene include *signaling receptor activity* and *protein-containing complex binding*. An important paralog of this gene is ICAM3.

UniProtKB/Swiss-Prot Summary: ICAM proteins are ligands for the leukocyte adhesion protein LFA-1 (integrin alpha-L/beta-2). During leukocyte trans-endothelial migration, ICAM1 engagement promotes the assembly of endothelial apical cups through ARHGEF26/SGEF and RHOG activation. (ICAM1_HUMAN,P05362)

Cellular localization: mainly in extracellular and plasma membranes.

Full Name: *Intercellular Adhesion Molecule 1*

Protein Type: Cell adhesion molecule (part of the immunoglobulin superfamily)

🔬 Biological Function of ICAM1

- ICAM1 encodes a transmembrane glycoprotein expressed primarily on:
    1. Endothelial cells
    2. Immune cells (e.g., macrophages, T cells, dendritic cells)
    3. Epithelial cells during inflammation
- Key biological actions:
    1. Mediates cell-cell adhesion:
        - Forms a bridge between endothelial cells and circulating leukocytes (e.g., neutrophils, monocytes, lymphocytes).
    2. Facilitates leukocyte extravasation:
        - Enables firm adhesion and transmigration of immune cells across the vascular endothelium into tissues during infection or injury.
    3. Signal transduction:
        - Can transmit intracellular signals after ligand binding (e.g., leading to changes in endothelial cell permeability and cytokine production).

🛠️ Key Ligands for ICAM1:

- **LFA-1 (CD11a/CD18, ITGAL/ITGB2)** — on T cells and neutrophils.
- **Mac-1 (CD11b/CD18, ITGAM/ITGB2)** — mainly on neutrophils and monocytes.
- **Rhinovirus** — ICAM1 serves as a receptor for certain strains of the common cold virus.

🦠 Role of ICAM1 in Sepsis

In sepsis, ICAM1 plays a central role in the inflammatory cascade:

Early Sepsis:

- Upregulated rapidly on endothelial cells in response to:
    - Pro-inflammatory cytokines: TNF-α, IL-1β, IFN-γ.
- Function:
    - Promotes firm adhesion of leukocytes to the endothelium.
    - Facilitates diapedesis (the passage of immune cells into infected tissues).

Later or Severe Sepsis:

- Excessive ICAM1 expression can cause:
    - Vascular leakage and endothelial dysfunction.
    - Microvascular thrombosis (due to neutrophil and platelet aggregation).
    - Organ injury (lungs, kidneys, liver).
- Soluble ICAM1 (sICAM1) is shed into circulation during endothelial activation/injury and is a biomarker of endothelial damage.

📈 Clinical Relevance of ICAM1 in Sepsis

Diagnostic Role:

- Elevated plasma levels of soluble ICAM1 (sICAM1) are detected in septic patients.
- sICAM1 correlates with severity of endothelial injury.

Prognostic Role:

- Higher sICAM1 levels are associated with:
    - Increased risk of multiple organ failure (especially acute lung injury/ARDS).
    - Higher mortality rates in sepsis.

Therapeutic Interest:

- Blocking ICAM1 interactions has been explored experimentally to:
    - Reduce excessive leukocyte infiltration.
    - Prevent endothelial damage in sepsis and systemic inflammatory response syndrome (SIRS).
- Anti-ICAM1 therapies showed some promise in preclinical models but limited success in human trials so far.

🔬 Pathways Involving ICAM1

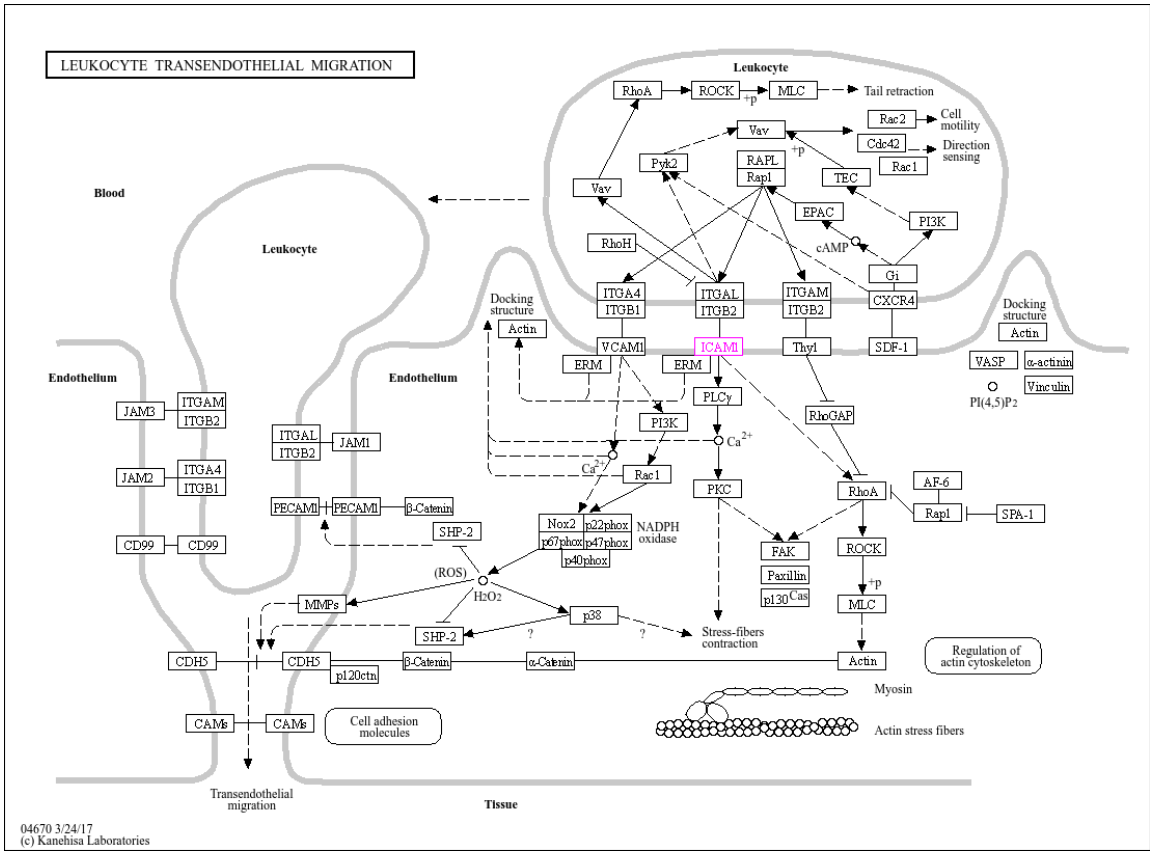
- **Leukocyte transendothelial migration (KEGG hsa04670)** → direct mediator of immune cell trafficking.
- **NF-κB signaling pathway (hsa04064)** → ICAM1 expression is induced downstream of NF-κB activation.

🧪 Supporting Literature

Doi: 10.1164/ajrccm.151.5.7735595 - Doi: 10.1097/01.shk.0000196497.49683.13

Doi: 10.1016/j.etp.2004.09.004 - Doi: 10.1016/j.jss.2007.07.021

KEGG:



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