Gene name: ITGAM **Previous HGNC Symbols for ITGAM Gene:** CR3A, CD11B
External Ids for ITGAM Gene: HGNC: 6149 NCBI Gene: 3684 Ensembl: ENSG00000169896
OMIM®: 120980 UniProtKB/Swiss-Prot: P11215

NCBI Gene Summary: This gene encodes the integrin alpha M chain. Integrins are heterodimeric integral membrane proteins composed of an alpha chain and a beta chain. This I-domain containing alpha integrin combines with the beta 2 chain (ITGB2) to form a leukocyte-specific integrin referred to as macrophage receptor 1 ('Mac-1'), or inactivated-C3b (iC3b) receptor 3 ('CR3'). The alpha M beta 2 integrin is **important in the adherence of neutrophils and monocytes to stimulated endothelium, and also in the phagocytosis of complement coated particles**. Multiple transcript variants encoding different isoforms have been found for this gene.
GeneCards Summary: ITGAM (Integrin Subunit Alpha M) is a Protein Coding gene. Diseases associated with ITGAM include Systemic Lupus Erythematosus 6 and Neutropenia, Severe Congenital, X-Linked. Among its related pathways are Apoptotic Pathways in Synovial Fibroblasts and Integrin Pathway. Gene Ontology (GO) annotations related to this gene include *protein heterodimerization activity* and *protein binding*. An important paralog of this gene is ITGAX.
UniProtKB/Swiss-Prot Summary: Integrin ITGAM/ITGB2 is implicated in various adhesive interactions of monocytes, macrophages and granulocytes as well as in mediating the uptake of complement-coated particles and pathogens (PubMed:20008295, 9558116). It is identical with CR-3, the receptor for the iC3b fragment of the third complement component. It probably recognizes the R-G-D peptide in C3b. Integrin ITGAM/ITGB2 is also a receptor for fibrinogen, factor X and ICAM1. It recognizes P1 and P2 peptides of fibrinogen gamma chain. Regulates neutrophil migration (PubMed:28807980). In association with beta subunit ITGB2/CD18, required for CD177-PRTN3-mediated activation of TNF primed neutrophils (PubMed:21193407). May regulate phagocytosis-induced apoptosis in extravasated neutrophils (By similarity). May play a role in mast cell development (By similarity). Required with TYROBP/DAP12 in microglia to control production of microglial superoxide ions which promote the neuronal apoptosis that occurs during brain development (By similarity). (ITAM_HUMAN,P11215)

Cellular localization: mostly extracellular and plasma membrane.
Full Name: *Integrin Subunit Alpha M*

- Also Known As:
  - CD11b
  - Complement receptor 3 alpha chain (CR3 alpha)
  - Mac-1 alpha chain

- Protein Type:
  - Cell surface receptor (integrin family)
  - Forms part of the Mac-1 complex or CR3 complex (with ITGB2/CD18)

🔬 Biological Function of ITGAM

- ITGAM encodes CD11b, which partners with CD18 (encoded by ITGB2) to form Mac-1 or Complement Receptor 3 (CR3).

- Key biological actions:
    - Leukocyte adhesion:
        - Binds to ICAM-1 on endothelial cells to allow immune cells to migrate from blood into tissues (extravasation).
    - Phagocytosis:
        - Binds complement fragments like iC3b, promoting uptake and destruction of opsonized microbes.
    - Inflammatory response regulation:
        - Helps clear pathogens, dead cells, and debris.
        - Modulates TLR signaling to control inflammation.
    - Cell migration and chemotaxis:
        - Directs neutrophils, monocytes, and macrophages to sites of infection or injury.

🛠️ Specific Ligands for ITGAM:

- **iC3b** (inactivated complement C3 fragment)
- **ICAM-1** (Intercellular Adhesion Molecule 1)
- **Fibrinogen**
- **Lipopolysaccharide (LPS)** (weak binding)

🦠 Role of ITGAM in Sepsis

- Very important during infection and sepsis because:
    - It enables immune cells to adhere to blood vessels and migrate into infected tissues.
    - It enhances phagocytosis of bacteria and apoptotic cells, helping clear infections.
    - It modulates inflammatory responses to prevent excessive tissue damage.

- In sepsis:
    - ITGAM expression is upregulated on neutrophils and monocytes.
    - Facilitates neutrophil recruitment, a hallmark of early immune activation.
    - However, excessive activation of ITGAM can contribute to vascular injury and organ dysfunction due to over-infiltration of leukocytes.

📈 Clinical Relevance of ITGAM in Sepsis

Diagnostic Role:

- Increased ITGAM/CD11b expression on neutrophils and monocytes is an early marker of systemic inflammation and sepsis.
- Surface CD11b is used experimentally to detect early leukocyte activation in sepsis.

Prognostic Role:

- High CD11b expression correlates with:
    - Higher severity of systemic inflammatory response
    - Development of multiple organ dysfunction
    - Potentially higher mortality
- Persistent neutrophil ITGAM overexpression may predict prolonged immune activation and poor outcomes.

Therapeutic Interest:

- Blocking CD11b-mediated adhesion has been explored experimentally to reduce tissue injury during systemic inflammation and sepsis.
- However, therapeutic inhibition must be careful, because you don't want to impair pathogen clearance.

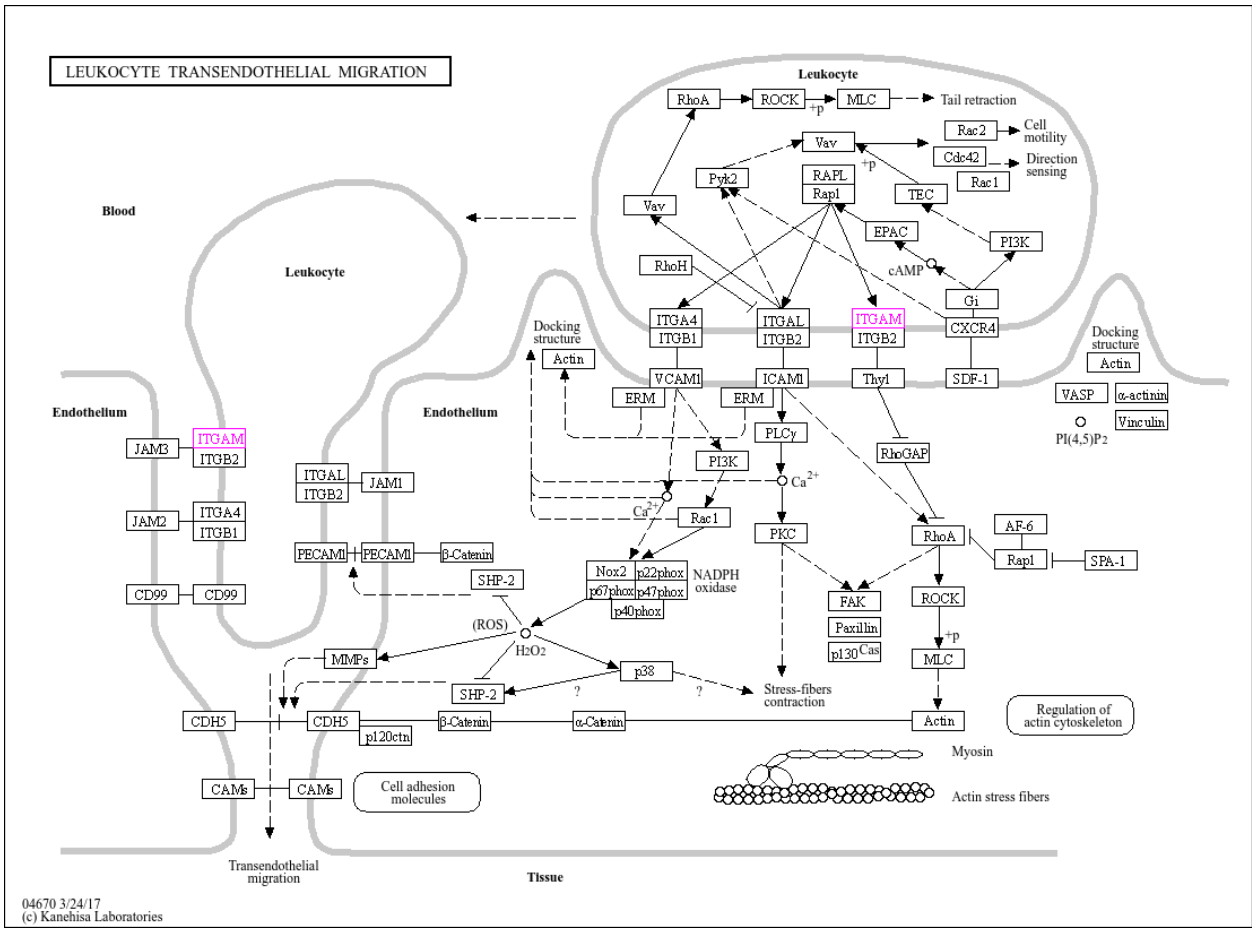
🔬 Pathways Involving ITGAM

- **Leukocyte transendothelial migration (KEGG hsa04670)**
- **Complement and coagulation cascades (KEGG hsa04610)** (through complement receptor functions)
- **Phagosome pathway (KEGG hsa04145)**
- **Toll-like receptor modulation** (indirectly through control of neutrophil responses)

🧪 Supporting Literature

DOI: 10.1097/01.shk.0000217815.57727.29
DOI: 10.1111/aas.12515
DOI:10.1016/j.humimm.2009.01.009
DOI: 10.1097/SHK.0000000000000250
DOI: 10.1186/s12964-025-02098-y

KEGG:



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