Gene name: MMP9 **Previous HGNC Symbols for MMP9 Gene:** CLG4B
External Ids for MMP9 Gene: HGNC: 7176 NCBI Gene: 4318 Ensembl: ENSG00000100985
OMIM®: 120361 UniProtKB/Swiss-Prot: P14780
NCBI Gene Summary: Proteins of the matrix metalloproteinase (MMP) family are involved in the breakdown of extracellular matrix in normal physiological processes, such as embryonic development, reproduction, and tissue remodeling, as well as in disease processes, such as arthritis and metastasis. Most MMP's are secreted as inactive proproteins which are activated when cleaved by extracellular proteinases. The enzyme encoded by this gene degrades type IV and V collagens. Studies in rhesus monkeys suggest that the enzyme is involved in IL-8-induced mobilization of hematopoietic progenitor cells from bone marrow, and murine studies suggest a role in tumor-associated tissue remodeling.

GeneCards Summary: MMP9 (Matrix Metallopeptidase 9) is a Protein Coding gene. Diseases associated with MMP9 include Metaphyseal Anadysplasia 2 and Metaphyseal Anadysplasia. Among its related pathways are Collagen chain trimerization and Matrix metalloproteinases. Gene Ontology (GO) annotations related to this gene include *identical protein binding* and *metalloendopeptidase activity*. An important paralog of this gene is MMP2.
UniProtKB/Swiss-Prot Summary: Matrix metalloproteinase that plays an essential role in local proteolysis of the extracellular matrix and in leukocyte migration (PubMed:12879005, 1480034, 2551898). Could play a role in bone osteoclastic resorption (By similarity). Cleaves KiSS1 at a Gly-|-Leu bond (PubMed:12879005). Cleaves NINJ1 to generate the Secreted ninjurin-1 form (PubMed:32883094). Cleaves type IV and type V collagen into large C-terminal three quarter fragments and shorter N-terminal one quarter fragments (PubMed:1480034). Degrades fibronectin but not laminin or Pz-peptide. (MMP9_HUMAN,P14780)

Cellular localization: mostly in extracellular.
Full Name: *Matrix Metallopeptidase 9*
Protein Type: Zinc-dependent matrix metalloproteinase (MMP)
Family: MMPs (enzymes that degrade extracellular matrix)

🔬 Biological Function of MMP9

MMP9 is a secreted enzyme that breaks down components of the extracellular matrix (ECM), playing critical roles in:

🛠️ Main Functions:

1. **ECM remodeling**:
    - Degrades type IV collagen, gelatin, elastin, and fibronectin
    - Enables cell migration, angiogenesis, and wound repair
2. **Leukocyte migration**:

    - Facilitates immune cell entry into tissues by breaking down basement membranes

3. **Modulation of inflammation**:
    - Can activate or inactivate cytokines and chemokines
    - Releases matrix-bound growth factors

4. **Stored in immune cells**:
    - Primarily in neutrophils, also in monocytes/macrophages
    - Released from granules upon activation

🦠 Role of MMP9 in Sepsis

MMP9 is strongly induced during inflammation, especially in sepsis.

Early Sepsis:

- Released by neutrophils and monocytes at infection sites
- Promotes:
    - Leukocyte recruitment
    - Tissue infiltration
    - Bacterial clearance

Excessive or Prolonged Sepsis:

- High MMP9 levels contribute to:
    - Endothelial barrier breakdown
    - Capillary leakage
    - Tissue and organ injury
    - Exacerbated inflammation via cytokine release
- MMP9 dysregulation is linked to acute lung injury (ALI)/ARDS, AKI, and multi-organ dysfunction

📈 Clinical Relevance of MMP9 in Sepsis

Diagnostic Role:

- Elevated plasma MMP9 is observed in:
    - Bacterial sepsis
    - COVID-19-related cytokine storms
    - Acute lung injury (ARDS)
- Can serve as a biomarker of neutrophil activation and vascular damage

Prognostic Role:

- High MMP9 levels are associated with:
    - Increased disease severity
    - Poor oxygenation (in ARDS)
    - Higher mortality

Therapeutic Interest:

- MMP9 inhibitors may reduce:
    - Vascular permeability
    - Neutrophil-mediated tissue injury
- Experimental therapies include:
    - Doxycycline (broad-spectrum MMP inhibitor)
    - Small-molecule MMP blockers (in preclinical stages)

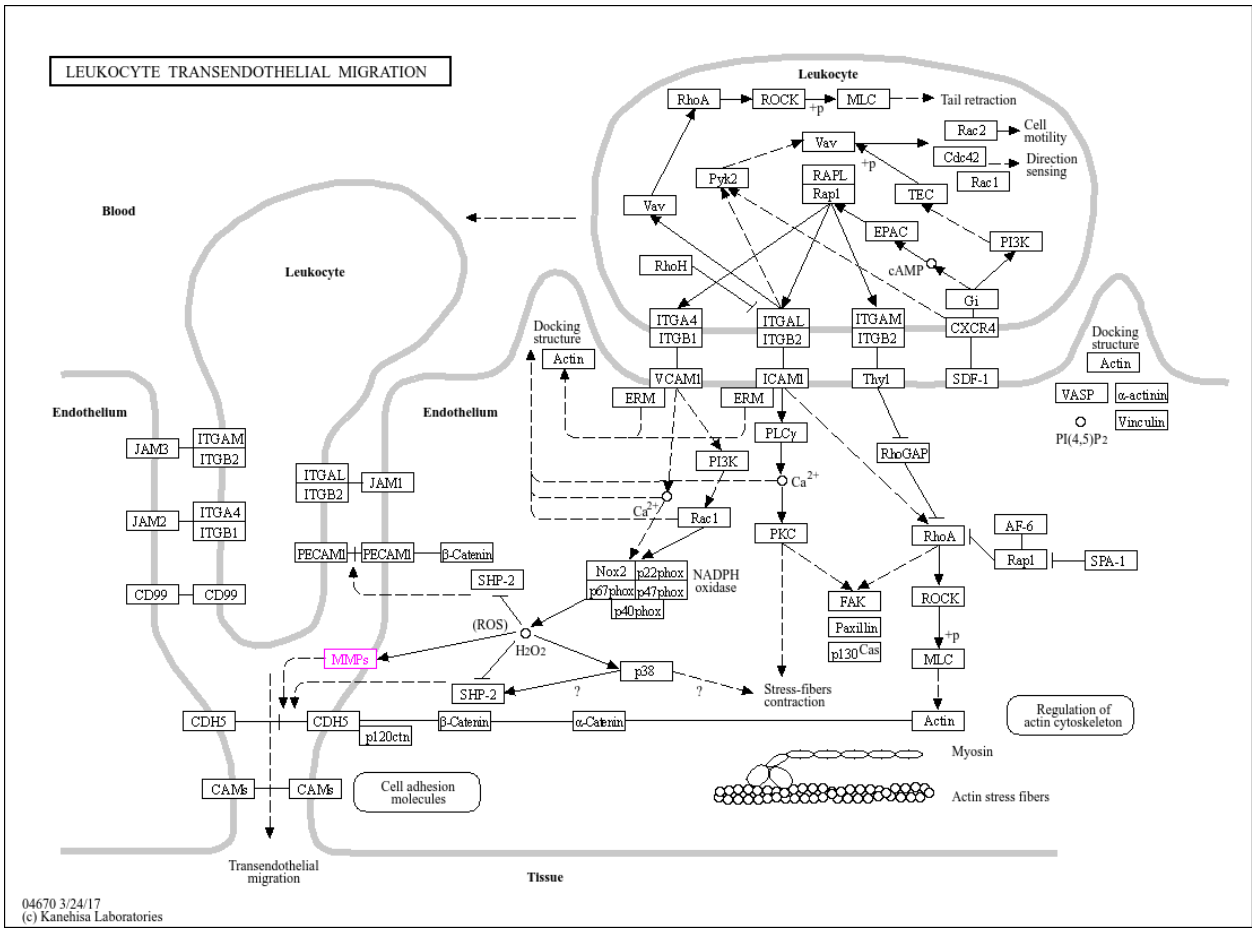
🔬 Pathways Involving MMP9

- **Leukocyte transendothelial migration (hsa04670)** — helps break basement membranes
- **Toll-like receptor signaling (indirect)**
- **Neutrophil degranulation** (Reactome)
- **Cytokine regulation and resolution of inflammation**

🧪 Supporting Literature

Doi: 10.4049/jimmunol.176.6.3735
Doi: 10.1155/2021/8889313
Doi: 10.1007/s12035-013-8433-7
Doi: 10.1038/ncomms4880
Doi: 10.1016/j.ijbiomac.2025.143024

KEGG:



ENrichr-KG: