Gene name: **OLFM4**
External Ids for OLFM4 Gene: HGNC: 17190 NCBI Gene: 10562 Ensembl: ENSG00000102837
OMIM®: 614061 UniProtKB/Swiss-Prot: Q6UX06

NCBI Gene Summary: This gene was originally cloned from human myeloblasts and found to be selectively expressed in inflammed colonic epithelium. This gene encodes a member of the olfactomedin family. The encoded protein is an antiapoptotic factor that promotes tumor growth and is an extracellular matrix glycoprotein that facilitates cell adhesion.

GeneCards Summary: OLFM4 (Olfactomedin 4) is a Protein Coding gene. Diseases associated with OLFM4 include Atrophy Of Prostate and Gallbladder Benign Neoplasm. Among its related pathways are **Innate Immune System** and Adhesion. Gene Ontology (GO) annotations related to this gene include *protein homodimerization activity* and *cadherin binding*. An important paralog of this gene is OLFM1.

UniProtKB/Swiss-Prot Summary: May promote proliferation of pancreatic cancer cells by favoring the transition from the S to G2/M phase. In myeloid leukemic cell lines, inhibits cell growth and induces cell differentiation and apoptosis. May play a role in the inhibition of EIF4EBP1 phosphorylation/deactivation. Facilitates cell adhesion, most probably through interaction with cell surface lectins and cadherin. (OLFM4_HUMAN,Q6UX06)
Cellular localization: mainly in mitochondria, extracellular matrix and plasma membrane.
Full Name: *Olfactomedin 4*
Protein Type: Glycoprotein; secreted and cell surface protein.
Belongs to: The olfactomedin family (characterized by a conserved olfactomedin domain).

🔬 Biological Function of OLFM4

- Primarily expressed in neutrophils (especially a subset called OLFM4+ neutrophils) and some epithelial tissues (like intestinal crypts).
- Functions inside cells:
  - Binds to proteins involved in innate immunity and inflammation regulation.
  - May modulate cell adhesion, apoptosis, and immune cell survival.
- Major extracellular role:
  - When released during neutrophil activation or degranulation, OLFM4 can influence inflammation, pathogen clearance, and tissue injury.

🛠️ Main Actions of OLFM4:

- Modulates neutrophil responses:
  - Not all neutrophils express OLFM4; ~20–25% of neutrophils are OLFM4+ under normal conditions, but this proportion increases during sepsis.
- Suppresses bacterial killing in some contexts:
  - OLFM4+ neutrophils are less efficient at killing bacteria compared to OLFM4- neutrophils.
- Regulates apoptosis and survival:
  - OLFM4 can inhibit caspase-3 activity, delaying neutrophil apoptosis.
- Participates in NET formation:
  - Found within neutrophil extracellular traps (NETs) released during severe infections.

🦠 Role of OLFM4 in Sepsis

- In sepsis, OLFM4 expression dramatically increases, both in neutrophils and as a soluble protein in plasma.
- High OLFM4 levels are associated with:
    - Severe systemic inflammation
    - Multi-organ dysfunction
    - Poor bacterial clearance
    - Worse clinical outcomes
- OLFM4+ neutrophils accumulate during sepsis and may contribute to:
    - Uncontrolled inflammation
    - Impaired pathogen elimination
    - Tissue damage due to excessive NET formation
- OLFM4 is also found elevated in:
    - Septic shock
    - Pediatric sepsis
    - Sepsis-associated acute lung injury

📈 Clinical Relevance of OLFM4 in Sepsis

Diagnostic Role:

- Plasma OLFM4 levels are significantly higher in septic patients compared to healthy individuals.
- Could serve as a biomarker of neutrophil activation and severity of inflammation.

Prognostic Role:

- High OLFM4 expression correlates with:
    - Higher organ failure scores (SOFA)
    - Higher risk of septic shock
    - Increased ICU mortality
- Persistent OLFM4 elevation suggests ongoing dysregulated innate immune response.

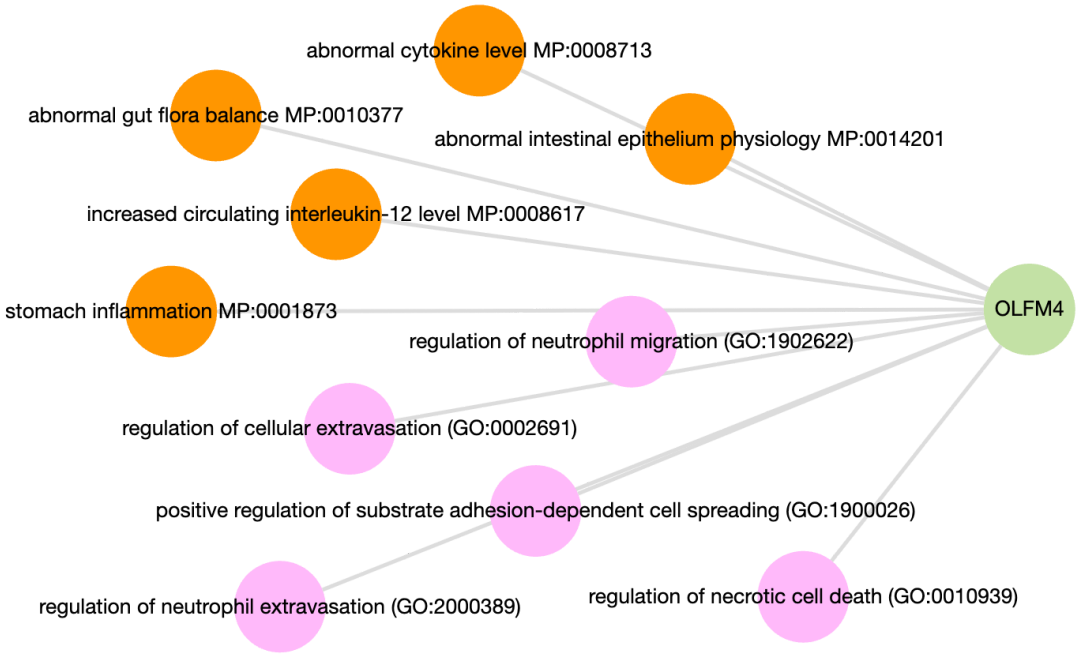
Therapeutic Interest:

- Targeting OLFM4-expressing neutrophils might be a future strategy to modulate neutrophil function in sepsis without broadly suppressing immunity.

🧪 Supporting Literature

Doi: 10.1097/CCM.0000000000002102
Doi: 10.1152/ajplung.00090.2020
Doi: 10.1093/ofid/ofac061
Doi: 10.1159/000527649

Enrichr-KG


abnormal cytokine level MP:0008713
abnormal gut flora balance MP:0010377
abnormal intestinal epithelium physiology MP:0014201
increased circulating interleukin-12 level MP:0008617
stomach inflammation MP:0001873
OLFM4
regulation of neutrophil migration (GO:1902622)
regulation of cellular extravasation (GO:0002691)
positive regulation of substrate adhesion-dependent cell spreading (GO:1900026)
regulation of neutrophil extravasation (GO:2000389)
regulation of necrotic cell death (GO:0010939)