Gene name: **IFNA1**

External Ids for IFNA1 Gene: HGNC: 5417 NCBI Gene: 3439 Ensembl: ENSG00000197919
OMIM®: 147660 UniProtKB/Swiss-Prot: P01562

NCBI Gene Summary: This gene is a member of the alpha interferon gene cluster on chromosome 9. The encoded cytokine is a member of the type I interferon family that is produced in response to viral infection as a key part of the innate immune response with potent antiviral, antiproliferative and immunomodulatory properties. This cytokine, like other type I interferons, binds a plasma membrane receptor made of IFNAR1 and IFNAR2 that is ubiquitously expressed, and thus is able to act on virtually all body cells. This cytokine is upregulated in preeclamptic placentas and is thought to be a mediator of preeclampsia.

GeneCards Summary: IFNA1 (Interferon Alpha 1) is a Protein Coding gene. Diseases associated with IFNA1 include Hepatitis and Newcastle Disease. Among its related pathways are Overview of interferons-mediated signaling pathway and SARS-CoV-2 Infection. Gene Ontology (GO) annotations related to this gene include *cytokine activity* and *type I interferon receptor binding*. An important paralog of this gene is IFNA13.
UniProtKB/Swiss-Prot Summary: Produced by macrophages, IFN-alpha have antiviral activities. Interferon stimulates the production of two enzymes: a protein kinase and an oligoadenylate synthetase. (IFNA1_HUMAN,P01562)

Cellular localization: mainly in extracellular.
Full Name: *Interferon Alpha 1*
Protein Type: Cytokine (type I interferon family)

Biological Function of IFNA1

- IFNA1 encodes interferon alpha-1, part of the Type I interferon family (includes multiple IFN-α subtypes and IFN-β).
- Produced mainly by:
  - Plasmacytoid dendritic cells (pDCs) — the professional producers of type I IFNs.
  - Monocytes/macrophages and infected epithelial cells during strong stimulation.
- Key actions of IFNA1:
  - Antiviral defense: Induces antiviral proteins that block virus replication.
  - Immune modulation:
    - Activates natural killer (NK) cells.
    - Enhances antigen presentation by dendritic cells and macrophages.
    - Increases MHC class I expression on cells.
  - Regulates inflammation:
    - Stimulates the production of additional cytokines and chemokines.
    - Bridges innate and adaptive immunity (especially early CD8+ T cell activation).

🛠️ Mechanism of IFNA1 Action:

- Binds to the type I interferon receptor complex (IFNAR1/IFNAR2) on target cells.
- Activates the JAK-STAT signaling pathway:
    - Leads to transcription of hundreds of interferon-stimulated genes (ISGs).
    - Induces an "antiviral state" in infected and neighboring cells.

🦠 Role of IFNA1 in Sepsis

- During early sepsis, IFNA1 is produced as part of the host's defense against infection (both bacterial and viral).
- Dual role:
    - Protective early on: Enhances pathogen clearance.
    - Harmful if excessive: Sustained or dysregulated IFNA1 response leads to immune exhaustion, systemic inflammation, and worsened organ damage.

🧫 In bacterial sepsis:

- IFNA1 is induced by bacterial products (via TLR4, TLR9, cGAS-STING pathways).
- Overproduction may contribute to sepsis-induced immunosuppression and T cell dysfunction.

🦠 In viral sepsis or secondary infections:

- IFNA1 is even more critical in controlling viral replication and spread.

📈 Clinical Relevance in Sepsis

Diagnostic Role:

- Elevated IFNA1 and type I interferon signatures can be detected early in severe infections.
- Transcriptomic profiling shows upregulated IFNA1 in sepsis caused by both bacteria and viruses.

Prognostic Role:

- High IFNA1 responses are associated with:
    - Immune exhaustion (especially of T cells).
    - Worse outcomes (higher mortality).
    - Greater risk of secondary infections (due to impaired adaptive immunity).
- A "Type I IFN signature" is sometimes used to stratify patients based on their immune status during sepsis.

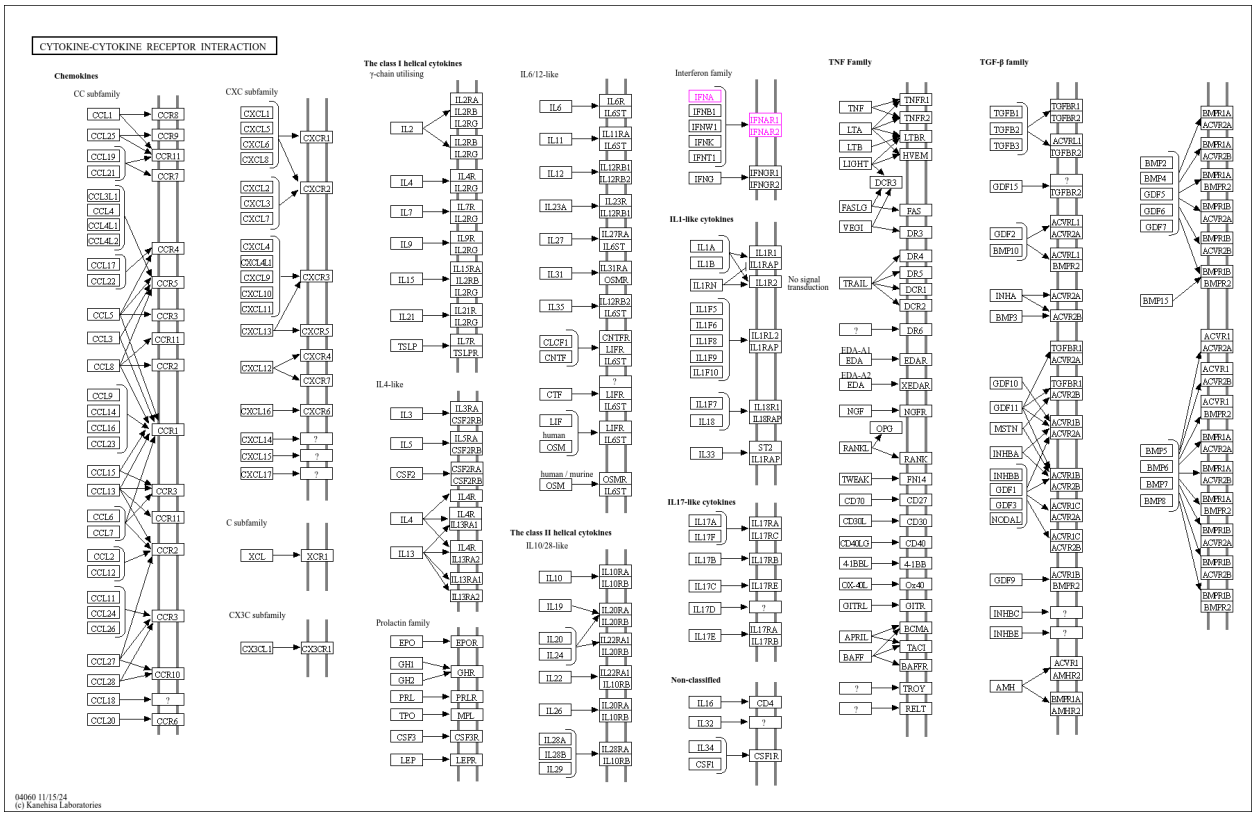
Therapeutic Interest:

- Blocking type I IFN signaling (such as anti-IFNAR antibodies) is under investigation for treating hyperinflammatory syndromes and late-phase sepsis.

🧪 Supporting Literature

Doi: 10.4049/jimmunol.177.8.5623
Doi: 10.1016/j.tim.2021.01.007
Doi: 10.1016/j.chom.2016.05.016
Doi: 10.1128/IAI.00829-06

KEGG:



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