Gene name: **IFNA2**

External Ids for IFNA2 Gene: HGNC: 5423 NCBI Gene: 3440 Ensembl: ENSG00000188379
OMIM®: 147562 UniProtKB/Swiss-Prot: P01563

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. The encoded protein is effective in reducing the symptoms and duration of the common cold and in treating many types of cancer, including some hematological malignancies and solid tumors. A deficiency of type I interferon in the blood is thought to be a hallmark of severe COVID-19 and may provide a rationale for a combined therapeutic approach.

GeneCards Summary: IFNA2 (Interferon Alpha 2) is a Protein Coding gene. Diseases associated with IFNA2 include Lymphomatoid Granulomatosis and Hepatitis. 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 IFNA6.
UniProtKB/Swiss-Prot Summary: Produced by macrophages, IFN-alpha have antiviral activities. (IFNA2_HUMAN,P01563)
Cellular localization: mainly in extracellular.
Full Name: *Interferon Alpha 2*
Protein Type: Cytokine (member of the Type I interferon family)

🔬 Biological Function of IFNA2

- IFNA2 encodes interferon alpha-2, one of the most biologically active and clinically important subtypes of Type I interferons.
- It is produced primarily by:
  - Plasmacytoid dendritic cells (pDCs) during infection.
  - Monocytes/macrophages upon pathogen detection.
  - Some epithelial cells during viral and bacterial infections.
- Key actions of IFNA2:
  - Antiviral defense:
    - Induces transcription of interferon-stimulated genes (ISGs) to inhibit viral replication.
  - Immune regulation:
    - Activates natural killer (NK) cells.
    - Enhances antigen presentation by increasing MHC class I expression.
    - Promotes survival and activation of cytotoxic T cells (CD8+ T cells).
  - Inflammatory response:
    - Stimulates secretion of chemokines and pro-inflammatory cytokines.

🛠️ Mechanism of IFNA2 Action:

- Binds to Type I interferon receptor complex (IFNAR1/IFNAR2) on target cells.

- Activates the JAK-STAT signaling pathway:
    - Leads to formation of ISGF3 complex (STAT1-STAT2-IRF9).
    - Translocates to the nucleus to promote transcription of hundreds of ISGs.

These ISGs together create an antiviral, antiproliferative, and immunomodulatory environment.

🦠 Role of IFNA2 in Sepsis

- During early sepsis, IFNA2 is part of the rapid innate immune response triggered by both bacterial and viral infections.
- Dual role:
    - Early phase: Helps contain infections by boosting innate immune responses.
    - Late/prolonged phase: Overproduction of IFNA2 contributes to immunosuppression, T cell exhaustion, and persistent inflammation.

🧫 In bacterial sepsis:

- IFNA2 can be induced by bacterial components (e.g., via TLR4, TLR9 pathways).
- It is sometimes detrimental, promoting systemic inflammation and worsening septic shock.

🦠 In viral sepsis or mixed infections:

- IFNA2 is crucial for early viral control but may contribute to late immune dysfunction.

📈 Clinical Relevance of IFNA2 in Sepsis

Diagnostic Role:

- Elevated IFNA2 expression is detected in blood transcriptomes of septic patients.
- Contributes to a type I interferon signature, which is one of the hallmarks in certain sepsis subtypes.

Prognostic Role:

- High or sustained IFNA2 signaling correlates with:
    - Greater immune suppression.
    - Increased risk of secondary infections.
    - Higher mortality rates, especially in ICU patients.

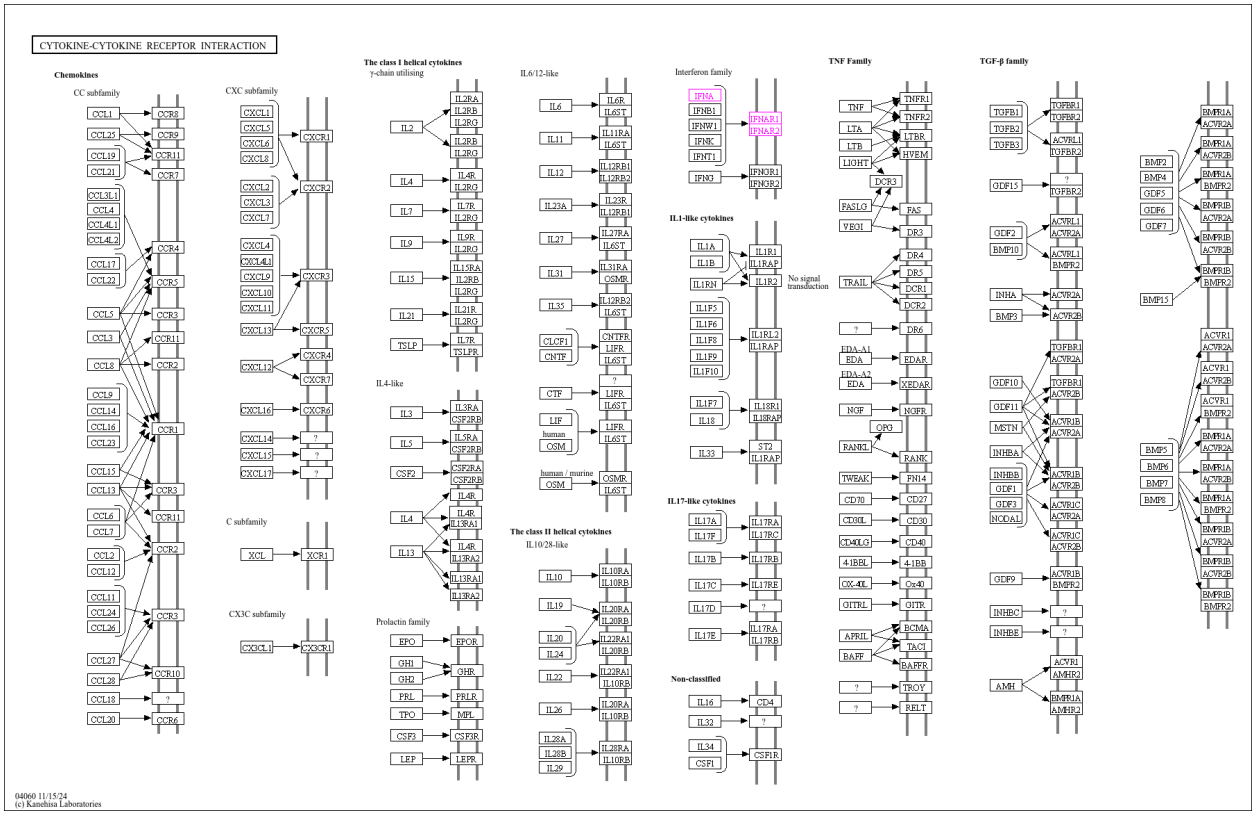
Therapeutic Interest:

- Targeting the IFNA2–IFNAR axis is considered for:
    - Reducing harmful hyperinflammation.
    - Reversing late-stage immunoparalysis.
- Some therapies aim to block IFNAR signaling in hyperinflammatory sepsis patients.

🧪 Supporting Literature

Doi: 10.3389/fimmu.2018.02061

KEGG:



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