Gene name: IFNG

External Ids for IFNG Gene: HGNC: 5438 NCBI Gene: 3458 Ensembl: ENSG00000111537 OMIM®: 147570 UniProtKB/Swiss-Prot: P01579.

NCBI Gene Summary for IFNG Gene: This gene encodes a soluble cytokine that is a member of the type II interferon class. The encoded protein is **secreted by cells of both the innate and adaptive immune systems.** The active protein is a homodimer that binds to the interferon gamma receptor which triggers a cellular response to viral and microbial infections. Mutations in this gene are associated with an increased susceptibility to viral, bacterial and parasitic infections and to several autoimmune diseases.

GeneCards Summary for IFNG Gene: IFNG (Interferon Gamma) is a Protein Coding gene. Diseases associated with IFNG include Immunodeficiency 69 and Hepatitis C Virus. Among its related pathways are Antiviral mechanism by IFN-stimulated genes and Gene expression (Transcription). Gene Ontology (GO) annotations related to this gene include *cytokine activity* and *type II interferon receptor binding*.

UniProtKB/Swiss-Prot Summary for IFNG Gene: Type II interferon produced by immune cells such as T-cells and NK cells that plays crucial roles in antimicrobial, antiviral, and antitumor responses by activating effector immune cells and enhancing antigen presentation (PubMed:16914093, 8666937). Primarily signals through the JAK-STAT pathway after interaction with its receptor IFNGR1 to affect gene regulation (PubMed:8349687). Upon IFNG binding, IFNGR1 intracellular domain opens out to allow association of downstream signaling components JAK2, JAK1 and STAT1, leading to STAT1 activation, nuclear translocation and transcription of IFNG-regulated genes. Many of the induced genes are transcription factors such as IRF1 that are able to further drive regulation of a next wave of transcription (PubMed:16914093).

Cellular location: mainly extracellular region.
Full Name: *Interferon gamma*
Protein Product: **IFN-γ** (the cytokine)

🧪 Key Points About IFNG / IFN-γ

- Type: Type II interferon (not Type I like IFNB1 or IFNA1/2).
- Produced by:
  - Activated T helper 1 (Th1) cells
  - Cytotoxic CD8+ T cells
  - Natural Killer (NK) cells
- Major functions:
  - Activates macrophages → increases their ability to kill ingested microbes.
  - Boosts antigen presentation by upregulating MHC class I and II molecules.
  - Drives Th1-type immune responses, promoting cell-mediated immunity (very important for clearing intracellular pathogens like viruses and some bacteria).

    - Stimulates production of chemokines to recruit more immune cells.

- Receptor:
    - Binds to IFN-γ receptor (IFNGR1 and IFNGR2) on target cells.
    - Activates the JAK-STAT1 pathway, particularly forming STAT1 homodimers.

🦠 Biological role In Sepsis:

- Early stage:
    - IFN-γ production is beneficial → helps eliminate pathogens by activating macrophages.
- Late stage or uncontrolled production:
    - May cause excessive inflammation and tissue damage.
    - Or paradoxically, low IFN-γ levels in late sepsis contribute to immune exhaustion and secondary infections.

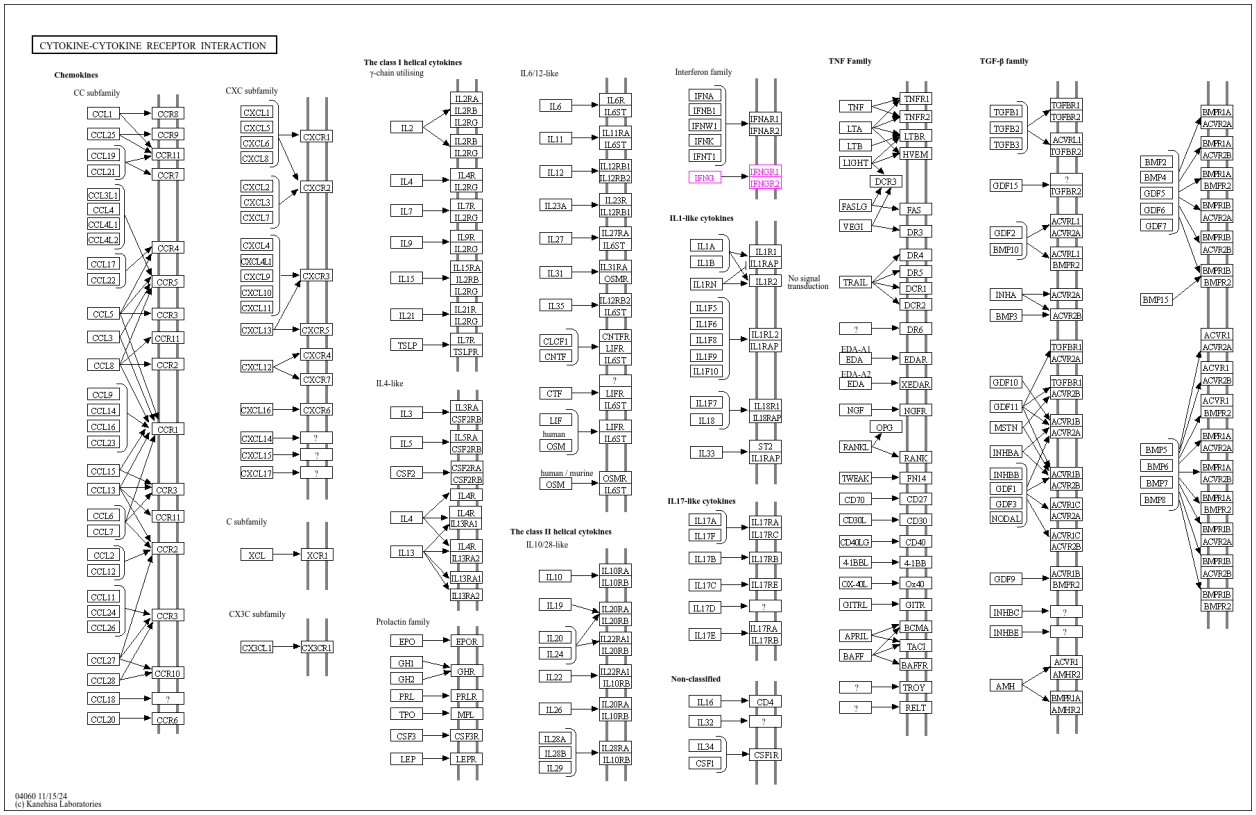
📈 Evidence in Sepsis Studies

- **Diagnostic Role:** Elevated levels of IFN-γ have been observed in septic patients, reflecting its involvement in the inflammatory cascade. However, its diagnostic utility is limited due to the intricate balance between pro-inflammatory and anti-inflammatory phases in sepsis, which can influence IFN-γ levels variably.
- **Prognostic Role:** The prognostic significance of IFN-γ in sepsis is nuanced. Some studies suggest that sustained high levels may correlate with adverse outcomes, while others indicate that IFN-γ can help reverse sepsis-induced immunosuppression by promoting metabolic pathways in immune cells. For instance, IFN-γ has been shown to regulate immunosuppression in septic mice by promoting glycolysis through the PI3K/AKT/mTOR pathway.

🧪 Supporting Literature

Doi: 10.1016/j.lfs.2017.07.010
Doi: 10.1186/s12879-019-4526-x
Doi: 10.1371/journal.pone.0068218

KEGG pathway:



Enrichr-KG: