Gene name: IL10

External Ids for IL10 Gene: HGNC: 5962 NCBI Gene: 3586 Ensembl: ENSG00000136634 OMIM®: 124092 UniProtKB/Swiss-Prot: P22301

NCBI Gene Summary: The protein encoded by this gene is a cytokine produced primarily by monocytes and to a lesser extent by lymphocytes. This cytokine has pleiotropic effects in immunoregulation and inflammation. It down-regulates the expression of Th1 cytokines, MHC class II Ags, and costimulatory molecules on macrophages. It also enhances B cell survival, proliferation, and antibody production. This cytokine can block NF-kappa B activity, and is involved in the regulation of the JAK-STAT signaling pathway. Knockout studies in mice suggested the function of this cytokine as an essential immunoregulator in the intestinal tract.

GeneCards Summary: IL10 (Interleukin 10) is a Protein Coding gene. Diseases associated with IL10 include Graft-Versus-Host Disease and Human Immunodeficiency Virus Type 1. Among its related pathways are MIF Mediated Glucocorticoid Regulation and ADORA2B mediated anti-inflammatory cytokines production. Gene Ontology (GO) annotations related to this gene include *cytokine activity* and *interleukin-10 receptor binding*. An important paralog of this gene is IL20.

UniProtKB/Swiss-Prot Summary: Major immune regulatory cytokine that acts on many cells of the immune system where it has profound anti-inflammatory functions, limiting excessive tissue disruption caused by inflammation. Mechanistically, IL10 binds to its heterotetrameric receptor comprising IL10RA and IL10RB leading to JAK1 and STAT2-mediated phosphorylation of STAT3 (PubMed:16982608). In turn, STAT3 translocates to the nucleus where it drives expression of anti-inflammatory mediators (PubMed:18025162). Targets antigen-presenting cells (APCs) such as macrophages and monocytes and inhibits their release of pro-inflammatory cytokines including granulocyte-macrophage colony-stimulating factor /GM-CSF, granulocyte colony-stimulating factor/G-CSF, IL-1 alpha, IL-1 beta, IL-6, IL-8 and TNF-alpha (PubMed:11564774, 1940799, 7512027).

Cellular localization: extracellular region.

Interleukin-10 (**IL-10**) is a pivotal anti-inflammatory cytokine encoded by the **IL10** gene. It plays a crucial role in regulating immune responses by inhibiting the production of pro-inflammatory cytokines, thereby maintaining immune homeostasis and preventing excessive tissue damage during inflammatory processes.

Function in Sepsis: In sepsis—a severe, systemic inflammatory response to infection—IL-10 serves as a counter-regulatory mechanism to the overwhelming pro-inflammatory milieu. Its primary functions during sepsis include:

- Modulation of Immune Response: IL-10 suppresses the production of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, thereby mitigating the hyperinflammatory state characteristic of sepsis.
- **Prevention of Tissue Damage:** By limiting excessive inflammation, IL-10 helps prevent collateral tissue damage, which is crucial for maintaining organ function during sepsis.
- Induction of Immunosuppression: While beneficial in controlling inflammation, elevated IL-10 levels can lead to immunosuppression, increasing susceptibility to secondary infections and potentially worsening outcomes in septic patients.

Diagnostic and Prognostic Role:

- Diagnostic Marker: Elevated serum IL-10 levels have been observed in septic patients, distinguishing them from those with non-infectious inflammatory conditions. However, due to its anti-inflammatory nature, IL-10 is often considered alongside pro-inflammatory markers to improve diagnostic accuracy.
- Prognostic Indicator: High IL-10 levels have been associated with increased mortality in sepsis, reflecting the balance between pro- and anti-inflammatory responses. Studies have shown that initial serum IL-10 levels can serve as outcome predictors in pediatric sepsis patients, with higher levels correlating with poorer outcomes.

Genetic Associations: Polymorphisms in the IL10 gene have been studied for their potential influence on sepsis susceptibility and outcomes. Meta-analyses suggest that certain IL10 polymorphisms may be associated with an increased risk of sepsis, particularly in specific populations.

Therapeutic Implications: Given its dual role in modulating inflammation and inducing immunosuppression, IL-10 presents a complex target for therapeutic intervention in sepsis. Strategies aimed at modulating IL-10 levels must carefully balance the suppression of harmful inflammation with the maintenance of adequate immune function to combat infections.

Cytokine_cytokine receptor interaction:

