Gene name: **CXCL8.** Previous HGNC Symbols: **IL8.**

External Ids for CXCL8 Gene: HGNC: 6025 NCBI Gene: 3576 Ensembl: ENSG00000169429 OMIM®: 146930 UniProtKB/Swiss-Prot: P10145

NCBI Gene Summary : The protein encoded by this gene is a member of the CXC chemokine family and is a major mediator of the inflammatory response. The encoded protein is commonly referred to as interleukin-8 (IL-8). IL-8 is secreted by mononuclear macrophages, neutrophils, eosinophils, T lymphocytes, epithelial cells, and fibroblasts. It functions as a chemotactic factor by guiding the neutrophils to the site of infection. Bacterial and viral products rapidly induce IL-8 expression. IL-8 also participates with other cytokines in the proinflammatory signaling cascade and plays a role in systemic inflammatory response syndrome (SIRS).

GeneCards Summary: CXCL8 (C-X-C Motif Chemokine Ligand 8) is a Protein Coding gene. Diseases associated with CXCL8 include Adult Respiratory Distress Syndrome and Melanoma. Among its related pathways are MIF Mediated Glucocorticoid Regulation and TGF-Beta Pathway. Gene Ontology (GO) annotations related to this gene include *chemokine activity* and *interleukin-8 receptor binding*. An important paralog of this gene is CXCL1.

UniProtKB/Swiss-Prot Summary: Chemotactic factor that mediates inflammatory response by attracting neutrophils, basophils, and T-cells to clear pathogens and protect the host from infection (PubMed:18692776, 7636208). Also plays an important role in neutrophil activation (PubMed:2145175, 9623510). Released in response to an inflammatory stimulus, exerts its effect by binding to the G-protein-coupled receptors CXCR1 and CXCR2, primarily found in neutrophils, monocytes and endothelial cells (PubMed:1840701, 1891716). G-protein heterotrimer (alpha, beta, gamma subunits) constitutively binds to CXCR1/CXCR2 receptor and activation by IL8 leads to beta and gamma subunits release from Galpha (GNAI2 in neutrophils) and activation of several downstream signaling pathways including PI3K and MAPK pathways (PubMed:11971003, 8662698).

Cellular location: extracellular region is the common part.

CXCL8, commonly known as interleukin-8 (IL-8), is a chemokine encoded by the CXCL8 gene. It is produced by various cell types, including macrophages, epithelial cells, airway smooth muscle cells, and endothelial cells. CXCL8 plays a pivotal role in the immune system by acting as a chemoattractant, primarily guiding neutrophils to sites of infection or inflammation. This chemotactic function is crucial for initiating and sustaining inflammatory responses.

In the context of sepsis—a severe systemic inflammatory response to infection—CXCL8 is significantly involved in the recruitment and activation of neutrophils. Elevated levels of CXCL8 have been observed in septic patients, correlating with disease severity and outcomes. The CXCL8-CXCR2 axis, in particular, mediates communication among hepatocytes, hepatic stellate cells, Kupffer cells, and liver sinusoidal endothelial cells, influencing liver inflammation during sepsis.

Additionally, studies have indicated that CXCL8 contributes to sepsis-induced acute kidney injury (AKI). In experimental models, antagonizing CXCL8 activity has shown protective effects against sepsis-induced AKI, suggesting its potential as a therapeutic target.

Diagnostic Role:

Elevated levels of CXCL8 have been observed in patients with sepsis, correlating with disease severity. Its measurement can aid in distinguishing sepsis from non-infectious inflammatory conditions, thereby assisting in early diagnosis. However, while CXCL8 is a sensitive marker, its specificity can be limited due to elevated levels in other inflammatory states.

Prognostic Role:

High concentrations of CXCL8 are associated with adverse outcomes in sepsis patients. Studies have demonstrated that increased CXCL8 levels correlate with higher mortality rates and the development of organ dysfunction, such as acute kidney injury (AKI). For instance, research indicates that CXCL8 contributes to sepsis-induced AKI, and antagonizing its activity has shown protective effects in experimental models.

Cytokine_cytokine receptor interactions: