Gene name: **CCL25** **Previous HGNC Symbols for CCL25 Gene:** SCYA25

External Ids for CCL25 Gene: HGNC: 10624 NCBI Gene: 6370 Ensembl: ENSG00000131142 OMIM®: 602565 UniProtKB/Swiss-Prot: O15444

NCBI Gene Summary: This antimicrobial gene belongs to the subfamily of small cytokine CC genes. Cytokines are a family of secreted proteins involved in immunoregulatory and inflammatory processes. The CC cytokines are proteins characterized by two adjacent cysteines. The cytokine encoded by this gene displays chemotactic activity for dendritic cells, thymocytes, and activated macrophages but is inactive on peripheral blood lymphocytes and neutrophils. The product of this gene binds to chemokine receptor CCR9.

GeneCards Summary: CCL25 (C-C Motif Chemokine Ligand 25) is a Protein Coding gene. Diseases associated with CCL25 include Ileitis and Cholangitis, Primary Sclerosing. Among its related pathways are MIF Mediated Glucocorticoid Regulation and TGF-Beta Pathway. Gene Ontology (GO) annotations related to this gene include *hormone activity* and *chemokine receptor binding*. An important paralog of this gene is CCL16.

UniProtKB/Swiss-Prot Summary: Potentially involved in T-cell development. Recombinant protein shows chemotactic activity on thymocytes, macrophages, THP-1 cells, and dendritics cells but is inactive on peripheral blood lymphocytes and neutrophils. Binds to CCR9.

CCL25, also known as **C-C motif chemokine ligand 25** or **thymus-expressed chemokine (TECK)**, is a member of the CC chemokine family. It is primarily expressed in the thymus and small intestine, where it plays a crucial role in the development and migration of T lymphocytes by binding to its receptor, **CCR9**.

Function in Sepsis: In sepsis—a severe systemic inflammatory response to infection—CCL25 has been implicated in modulating immune responses and contributing to organ-specific inflammation:

- **Acute Lung Injury (ALI):** Elevated serum levels of CCL25 have been observed in sepsis patients, particularly those with acute lung injury. Experimental studies indicate that inhibition of CCL25 can alleviate sepsis-induced acute lung injury by reducing inflammation and decreasing endothelial permeability. This suggests that CCL25 contributes to the pathogenesis of lung injury during sepsis.
- **Thymic Atrophy:** Sepsis-induced thymic atrophy, characterized by a reduction in thymic size and cellularity, has been associated with defects in early lymphopoiesis. Studies have shown that sepsis leads to a dramatic decline in early T-lineage progenitors (ETPs) in the thymus, which correlates with thymic atrophy. The chemotaxis of bone marrow lymphoid progenitors towards chemokines, including CCL25, is impaired during sepsis, contributing to reduced thymic output and subsequent immunosuppression.

Pathways Involved in Sepsis:

CCL25 is involved in several key pathways during sepsis:

- **Chemotaxis and Immune Cell Trafficking:** By binding to CCR9, CCL25 directs the migration of immune cells, particularly T lymphocytes, to specific tissues. In sepsis, dysregulation of this

pathway can lead to inappropriate immune cell localization, contributing to tissue damage and impaired immune responses.

- **Inflammatory Signaling:** CCL25 can influence inflammatory responses by modulating the recruitment and activation of immune cells. Elevated levels of CCL25 during sepsis may exacerbate inflammation, leading to organ dysfunction.

Diagnostic and Prognostic Role: **Biomarker Potential:** Increased serum levels of CCL25 in sepsis patients suggest its potential as a biomarker for disease severity, particularly in cases complicated by acute lung injury. However, further clinical studies are needed to validate its diagnostic and prognostic utility.

Therapeutic Implications: **Targeting CCL25:** Given its role in sepsis-induced acute lung injury, targeting CCL25 or its receptor CCR9 may offer therapeutic benefits. Inhibition of CCL25 has been shown to reduce inflammation and improve outcomes in experimental models, indicating a potential avenue for therapeutic intervention.