Gene name: **LCN2**

External Ids for LCN2 Gene: HGNC: 6526 NCBI Gene: 3934 Ensembl: ENSG00000148346 OMIM®: 600181 UniProtKB/Swiss-Prot: P80188

NCBI Gene Summary: This gene encodes a protein that belongs to the lipocalin family. Members of this family transport small hydrophobic molecules such as lipids, steroid hormones and retinoids. The protein encoded by this gene is a neutrophil gelatinase-associated lipocalin and **plays a role in innate immunity** by limiting bacterial growth as a result of sequestering iron-containing siderophores. The presence of this protein in blood and urine is an early biomarker of acute kidney injury. This protein is thought to be involved in multiple cellular processes, including maintenance of skin homeostasis, and suppression of invasiveness and metastasis. Mice lacking this gene are more susceptible to bacterial infection than wild type mice.

GeneCards Summary: LCN2 (Lipocalin 2) is a Protein Coding gene. Diseases associated with LCN2 include Pyuria and Proctitis. Among its related pathways are Innate Immune System and Cytokine Signaling in Immune system. Gene Ontology (GO) annotations related to this gene include *protein homodimerization activity* and *iron ion binding*. An important paralog of this gene is LCN12.

UniProtKB/Swiss-Prot Summary: Iron-trafficking protein involved in multiple processes such as apoptosis, innate immunity and renal development (PubMed:12453413, 20581821, 27780864). Binds iron through association with 2,3-dihydroxybenzoic acid (2,3-DHBA), a siderophore that shares structural similarities with bacterial enterobactin, and delivers or removes iron from the cell, depending on the context. Iron-bound form (holo-24p3) is internalized following binding to the SLC22A17 (24p3R) receptor, leading to release of iron and subsequent increase of intracellular iron concentration. In contrast, association of the iron-free form (apo-24p3) with the SLC22A17 (24p3R) receptor is followed by association with an intracellular siderophore, iron chelation and iron transfer to the extracellular medium, thereby reducing intracellular iron concentration. Involved in apoptosis due to interleukin-3 (IL3) deprivation: iron-loaded form increases intracellular iron concentration without promoting apoptosis, while iron-free form decreases intracellular iron levels, inducing expression of the proapoptotic protein BCL2L11/BIM, resulting in apoptosis (By similarity). Involved in innate immunity; limits bacterial proliferation by sequestering iron bound to microbial siderophores, such as enterobactin (PubMed:27780864). Can also bind siderophores from M.tuberculosis (PubMed:15642259, 21978368). (NGAL_HUMAN,P80188)

Cellular localization: mainly in extracellular.
Full Name: *Lipocalin 2*
Aliases: Neutrophil gelatinase-associated lipocalin (NGAL), 24p3, siderocalin, …
Protein Type: Secreted glycoprotein; member of the lipocalin family (small secreted proteins that transport small hydrophobic molecules).

Biological Function of LCN2

- Produced mainly by:
  - Neutrophils (stored in granules, released upon activation).
  - Epithelial cells (especially during stress or infection).
  - Liver cells during systemic inflammation.
- Main biological roles:

    - Sequesters iron by binding bacterial siderophores (iron-chelating molecules).
    - Inhibits bacterial growth by depriving bacteria of iron (essential for their survival).
    - Acts as an acute-phase protein, rapidly upregulated during infection and injury.
    - Modulates immune responses, cell differentiation, apoptosis, and tissue remodeling.

🦠 Role of LCN2 in Sepsis

- In sepsis, **LCN2 is massively upregulated**, mainly from:
    - Activated neutrophils.
    - Inflamed tissues (like kidneys, liver, lungs).
- **Functions during sepsis**:
    - Early host defense: limits bacterial proliferation by iron deprivation.
    - Prolonged inflammation: high LCN2 levels contribute to immune activation and potential tissue injury.
    - Kidney stress and injury marker: since LCN2 is released during acute kidney injury (AKI), which is common in sepsis.

🛠️ Key Actions of LCN2:

- **Antimicrobial defense**:
    - Captures iron-loaded siderophores to starve bacteria.
    - Especially important against Gram-negative pathogens.
- **Inflammatory regulation**:
    - Can enhance pro-inflammatory cytokine production.
    - Regulates neutrophil recruitment and activation.
- **Tissue protection**:
    - Plays a dual role — both protective (limiting infection) and damaging (promoting inflammation and fibrosis under chronic activation).

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📈 Clinical Relevance of LCN2 in Sepsis

Diagnostic Role:

- Plasma and urine LCN2/NGAL levels rise early in sepsis and bacterial infections.
- Considered one of the earliest markers of infection and organ damage, especially acute kidney injury (AKI) during sepsis.

Prognostic Role:

- High LCN2 levels correlate with:
    - Sepsis severity
    - Development of multi-organ failure (especially renal failure)
    - Poor prognosis and higher mortality

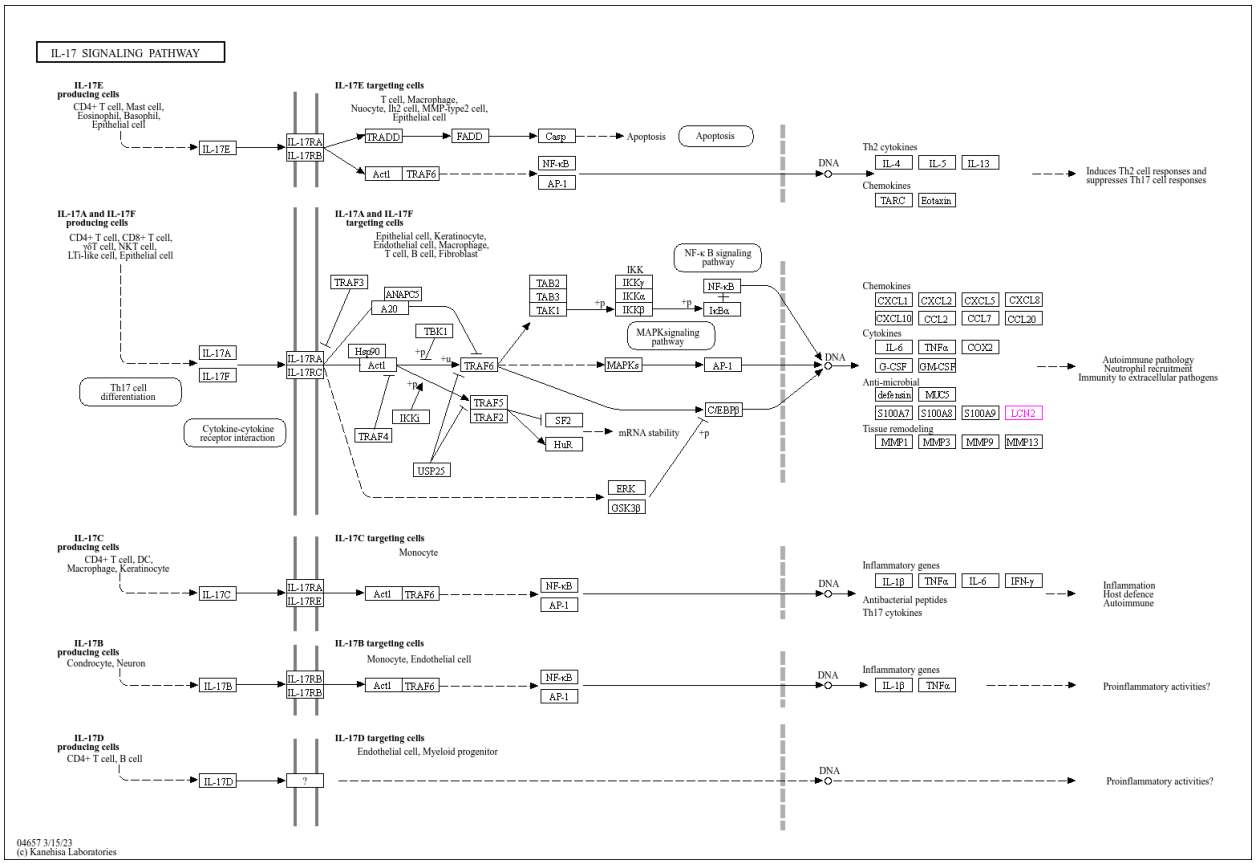
Therapeutic Interest:

- Monitoring LCN2 levels could help predict septic complications early, especially renal dysfunction.
- Potential target for limiting excessive inflammation while preserving antimicrobial defense.

🧪 Supporting Literature

doi: 10.3389/fcvm.2022.1009726
doi:10.1152/ajplung.00380.2014
doi: 10.1177/1753425914548491
doi: 10.1038/nature03104
doi: 10.1016/j.clinbiochem.2013.05.069
doi: 10.4049/jimmunol.1200892

KEGG:



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