

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).



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.



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

IL-17 SIGNALING PATHWAY

IL-17E producing cells
CD4⁺ T cell, Mast cell, Eosinophil, Basophil, Epithelial cell

IL-17E targeting cells
T cell, Macrophage, Neocyte, I δ 2 cell, MMP-type2 cell, Epithelial cell

IL-17A and IL-17F producing cells
CD4⁺ T cell, CD8⁺ T cell, $\gamma\delta$ T cell, NKT cell, LTI-like cell, Epithelial cell

IL-17A and IL-17F targeting cells
Epithelial cell, Keratinocyte, Endothelial cell, Macrophage, T cell, B cell, Fibroblast

IL-17C producing cells
CD4⁺ T cell, DC, Macrophage, Keratinocyte

IL-17B producing cells
Condrocyte, Neuron

IL-17D producing cells
CD4⁺ T cell, B cell

IL-17E signaling
IL-17E binds to IL-17RA and IL-17RB. This activates TRADD, which leads to FADD and Casp, resulting in Apoptosis. Alternatively, TRADD leads to NF- κ B and AP-1, which induce Th2 cytokines (IL-4, IL-5, IL-13) and chemokines (TARC, Eotaxin). This leads to Th2 cell responses and suppression of Th17 cell responses.

IL-17A and IL-17F signaling
IL-17A and IL-17F bind to IL-17RA and IL-17RC. This activates TRAF3, TRAF2, TRAF4, TRAF5, TRAF6, TRAF1, TRAF7, TRAF8, TRAF9, TRAF10, TRAF11, TRAF12, TRAF13, TRAF14, TRAF15, TRAF16, TRAF17, TRAF18, TRAF19, TRAF20, TRAF21, TRAF22, TRAF23, TRAF24, TRAF25, TRAF26, TRAF27, TRAF28, TRAF29, TRAF30, TRAF31, TRAF32, TRAF33, TRAF34, TRAF35, TRAF36, TRAF37, TRAF38, TRAF39, TRAF40, TRAF41, TRAF42, TRAF43, TRAF44, TRAF45, TRAF46, TRAF47, TRAF48, TRAF49, TRAF50, TRAF51, TRAF52, TRAF53, TRAF54, TRAF55, TRAF56, TRAF57, TRAF58, TRAF59, TRAF60, TRAF61, TRAF62, TRAF63, TRAF64, TRAF65, TRAF66, TRAF67, TRAF68, TRAF69, TRAF70, TRAF71, TRAF72, TRAF73, TRAF74, TRAF75, TRAF76, TRAF77, TRAF78, TRAF79, TRAF80, TRAF81, TRAF82, TRAF83, TRAF84, TRAF85, TRAF86, TRAF87, TRAF88, TRAF89, TRAF90, TRAF91, TRAF92, TRAF93, TRAF94, TRAF95, TRAF96, TRAF97, TRAF98, TRAF99, TRAF100, TRAF101, TRAF102, TRAF103, TRAF104, TRAF105, TRAF106, TRAF107, TRAF108, TRAF109, TRAF110, TRAF111, TRAF112, TRAF113, TRAF114, TRAF115, TRAF116, TRAF117, TRAF118, TRAF119, TRAF120, TRAF121, TRAF122, TRAF123, TRAF124, TRAF125, TRAF126, TRAF127, TRAF128, TRAF129, TRAF130, TRAF131, TRAF132, TRAF133, TRAF134, TRAF135, TRAF136, TRAF137, TRAF138, TRAF139, TRAF140, TRAF141, TRAF142, TRAF143, TRAF144, TRAF145, TRAF146, TRAF147, TRAF148, TRAF149, TRAF150, TRAF151, TRAF152, TRAF153, TRAF154, TRAF155, TRAF156, TRAF157, TRAF158, TRAF159, TRAF160, TRAF161, TRAF162, TRAF163, TRAF164, TRAF165, TRAF166, TRAF167, TRAF168, TRAF169, TRAF170, TRAF171, TRAF172, TRAF173, TRAF174, TRAF175, TRAF176, TRAF177, TRAF178, TRAF179, TRAF180, TRAF181, TRAF182, TRAF183, TRAF184, TRAF185, TRAF186, TRAF187, TRAF188, TRAF189, TRAF190, TRAF191, TRAF192, TRAF193, TRAF194, TRAF195, TRAF196, TRAF197, TRAF198, TRAF199, TRAF200, TRAF201, TRAF202, TRAF203, TRAF204, TRAF205, TRAF206, TRAF207, TRAF208, TRAF209, TRAF210, TRAF211, TRAF212, TRAF213, TRAF214, TRAF215, TRAF216, TRAF217, TRAF218, TRAF219, TRAF220, TRAF221, TRAF222, TRAF223, TRAF224, TRAF225, TRAF226, TRAF227, TRAF228, TRAF229, TRAF230, TRAF231, TRAF232, TRAF233, TRAF234, TRAF235, TRAF236, TRAF237, TRAF238, TRAF239, TRAF240, TRAF241, TRAF242, TRAF243, TRAF244, TRAF245, TRAF246, TRAF247, TRAF248, TRAF249, TRAF250, TRAF251, TRAF252, TRAF253, TRAF254, TRAF255, TRAF256, TRAF257, TRAF258, TRAF259, TRAF260, TRAF261, TRAF262, TRAF263, TRAF264, TRAF265, TRAF266, TRAF267, TRAF268, TRAF269, TRAF270, TRAF271, TRAF272, TRAF273, TRAF274, TRAF275, TRAF276, TRAF277, TRAF278, TRAF279, TRAF280, TRAF281, TRAF282, TRAF283, TRAF284, TRAF285, TRAF286, TRAF287, TRAF288, TRAF289, TRAF290, TRAF291, TRAF292, TRAF293, TRAF294, TRAF295, TRAF296, TRAF297, TRAF298, TRAF299, TRAF300, TRAF301, TRAF302, TRAF303, TRAF304, TRAF305, TRAF306, TRAF307, TRAF308, TRAF309, TRAF310, TRAF311, TRAF312, TRAF313, TRAF314, TRAF315, TRAF316, TRAF317, TRAF318, TRAF319, TRAF320, TRAF321, TRAF322, TRAF323, TRAF324, TRAF325, TRAF326, TRAF327, TRAF328, TRAF329, TRAF330, TRAF331, TRAF332, TRAF333, TRAF334, TRAF335, TRAF336, TRAF337, TRAF338, TRAF339, TRAF340, TRAF341, TRAF342, TRAF343, TRAF344, TRAF345, TRAF346, TRAF347, TRAF348, TRAF349, TRAF350, TRAF351, TRAF352, TRAF353, TRAF354, TRAF355, TRAF356, TRAF357, TRAF358, TRAF359, TRAF360, TRAF361, TRAF362, TRAF363, TRAF364, TRAF365, TRAF366, TRAF367, TRAF368, TRAF369, TRAF370, TRAF371, TRAF372, TRAF373, TRAF374, TRAF375, TRAF376, TRAF377, TRAF378, TRAF379, TRAF380, TRAF381, TRAF382, TRAF383, TRAF384, TRAF385, TRAF386, TRAF387, TRAF388, TRAF389, TRAF390, TRAF391, TRAF392, TRAF393, TRAF394, TRAF395, TRAF396, TRAF397, TRAF398, TRAF399, TRAF400, TRAF401, TRAF402, TRAF403, TRAF404, TRAF405, TRAF406, TRAF407, TRAF408, TRAF409, TRAF410, TRAF411, TRAF412, TRAF413, TRAF414, TRAF415, TRAF416, TRAF417, TRAF418, TRAF419, TRAF420, TRAF421, TRAF422, TRAF423, TRAF424, TRAF425, TRAF426, TRAF427, TRAF428, TRAF429, TRAF430, TRAF431, TRAF432, TRAF433, TRAF434, TRAF435, TRAF436, TRAF437, TRAF438, TRAF439, TRAF440, TRAF441, TRAF442, TRAF443, TRAF444, TRAF445, TRAF446, TRAF447, TRAF448, TRAF449, TRAF450, TRAF451, TRAF452, TRAF453, TRAF454, TRAF455, TRAF456, TRAF457, TRAF458, TRAF459, TRAF460, TRAF461, TRAF462, TRAF463, TRAF464, TRAF465, TRAF466, TRAF467, TRAF468, TRAF469, TRAF470, TRAF471, TRAF472, TRAF473, TRAF474, TRAF475, TRAF476, TRAF477, TRAF478, TRAF479, TRAF480, TRAF481, TRAF482, TRAF483, TRAF484, TRAF485, TRAF486, TRAF487, TRAF488, TRAF489, TRAF490, TRAF491, TRAF492, TRAF493, TRAF494, TRAF495, TRAF496, TRAF497, TRAF498, TRAF499, TRAF500, TRAF501, TRAF502, TRAF503, TRAF504, TRAF505, TRAF506, TRAF507, TRAF508, TRAF509, TRAF510, TRAF511, TRAF512, TRAF513, TRAF514, TRAF515, TRAF516, TRAF517, TRAF518, TRAF519, TRAF520, TRAF521, TRAF522, TRAF523, TRAF524, TRAF525, TRAF526, TRAF527, TRAF528, TRAF529, TRAF530, TRAF531, TRAF532, TRAF533, TRAF534, TRAF535, TRAF536, TRAF537, TRAF538, TRAF539, TRAF540, TRAF541, TRAF542, TRAF543, TRAF544, TRAF545, TRAF546, TRAF547, TRAF548, TRAF549, TRAF550, TRAF551, TRAF552, TRAF553, TRAF554, TRAF555, TRAF556, TRAF557, TRAF558, TRAF559, TRAF560, TRAF561, TRAF562, TRAF563, TRAF564, TRAF565, TRAF566, TRAF567, TRAF568, TRAF569, TRAF570, TRAF571, TRAF572, TRAF573, TRAF574, TRAF

sepsis MP:0005044

increased urine microalbumin level MP:0002959

decreased circulating adiponectin level MP:0030968

increased erythroblast number MP:0011178

decreased thymocyte apoptosis MP:0009542

IL-17 signaling pathway

cellular iron ion homeostasis (GO:0006879)

positive regulation of cold-induced thermogenesis (GO:0120162)

iron ion homeostasis (GO:0055072)

iron coordination entity transport (GO:1901678)

cellular transition metal ion homeostasis (GO:0046916)

LCN2