

Gene name: **ARG1**

External Ids for ARG1 Gene: HGNC: [663](#) NCBI Gene: [383](#) Ensembl: [ENSG00000118520](#) OMIM®: [608313](#)
UniProtKB/Swiss-Prot: [P05089](#)

NCBI Gene Summary: Arginase catalyzes the hydrolysis of arginine to ornithine and urea. At least two isoforms of mammalian arginase exist (types I and II) which differ in their tissue distribution, subcellular localization, immunological cross reactivity and physiologic function. The type I isoform encoded by this gene, is a cytosolic enzyme and expressed predominantly in the liver as a component of the urea cycle.

GeneCards Summary: ARG1 (Arginase 1) is a Protein Coding gene. Diseases associated with ARG1 include [Argininemia](#) and [Urea Cycle Disorder](#). Among its related pathways are [superpathway of L-citrulline metabolism](#) and [Innate Immune System](#). Gene Ontology (GO) annotations related to this gene include *manganese ion binding* and *arginase activity*. An important paralog of this gene is [ARG2](#).

UniProtKB/Swiss-Prot Summary: Key element of the urea cycle converting L-arginine to urea and L-ornithine, which is further metabolized into metabolites proline and polyamides that drive collagen synthesis and bioenergetic pathways critical for cell proliferation, respectively; the urea cycle takes place primarily in the liver and, to a lesser extent, in the kidneys. ([ARG1_HUMAN,P05089](#))

Cellular localization: lysosome, cytosol, nucleus, extracellular.

Full Name: *Arginase 1*

Protein Type: Enzyme (cytosolic arginase)



Biological Function of ARG1

- ARG1 encodes the enzyme arginase 1, which catalyzes the conversion of L-arginine → urea + ornithine.
- It's a key component of the urea cycle, helping eliminate excess nitrogen.
- Tissue expression:
 - Highly expressed in the liver (for urea metabolism).
 - Also expressed in myeloid immune cells, particularly neutrophils, monocytes, and myeloid-derived suppressor cells (MDSCs).



Major Immune-Related Functions of ARG1:

- **Regulates immune responses via L-arginine metabolism:**
 - Depletes extracellular L-arginine, which is essential for T cell proliferation.
 - Therefore, ARG1 acts as an immunosuppressive enzyme in inflamed tissues.

- **Suppresses T cell activity** by:
 - Inhibiting TCR signaling.
 - Reducing CD3 ζ chain expression in T cells.
- **Promotes resolution of inflammation:**
 - Through modulation of macrophage and neutrophil function.

Role of ARG1 in Sepsis

ARG1 plays a dual and time-dependent role in sepsis:

Early Sepsis:

- Arginase-1 may help limit tissue damage by regulating excessive nitric oxide (NO) production (via competition with iNOS for arginine).
- Produced by activated neutrophils and monocytes as a regulatory mechanism.

Late/Severe Sepsis:

- Overexpression of ARG1 contributes to immune suppression:
 - Depletes arginine → suppresses T cell responses.
 - Leads to T cell exhaustion, impaired pathogen clearance, and secondary infections.
- Found in sepsis-associated myeloid-derived suppressor cells (MDSCs), which dampen adaptive immunity.

Clinical Relevance of ARG1 in Sepsis

Diagnostic Role:

- ARG1 is strongly upregulated in sepsis — detectable in:
 - Whole blood
 - Neutrophil transcriptomes
 - Plasma protein levels
- Considered a marker of emergency myelopoiesis and innate immune activation.

Prognostic Role:

- High ARG1 levels are associated with:

- Worse immune suppression
- Poor lymphocyte recovery
- Higher mortality rates
- Organ dysfunction, especially related to endothelial damage and shock

Therapeutic Interest:

- Blocking ARG1 activity (such as, with small molecule inhibitors) is being explored to:
 - Preserve T cell function
 - Improve outcomes in sepsis-induced immune suppression, cancer, and chronic infections



Pathways Involving ARG1

- **Urea cycle and nitrogen metabolism**
- **Amino acid metabolism** (especially L-arginine)
- **Regulation of T cell-mediated immunity**
- **Sepsis immunosuppression pathways** (via MDSC and neutrophil activity)



Supporting Literature

Doi: 10.3390/genes10121005

Doi: 10.1186/s40560-015-0124-1

Doi: 10.1186/s41065-022-00240-1

Doi: 10.1080/2162402X.2021.1956143

ARG1

- pale liver MP:0000603
- abnormal hepatobiliary system morphology MP:0002138
- abnormal homeostasis MP:0001764
- increased circulating ammonia level MP:0005309
- abnormal circulating amino acid level MP:0005311
- Arginine biosynthesis
- Arginine and proline metabolism
- Amoebiasis
- urea cycle (GO:0000050)
- negative regulation of response to interferon-gamma (GO:0060331)
- negative regulation of interferon-gamma-mediated signaling pathway (GO:0060336)
- arginine catabolic process (GO:0006527)
- ornithine metabolic process (GO:0006591)