

Gene name: **S100A12**

External Ids for S100A12 Gene: HGNC: [10489](#) NCBI Gene: [6283](#) Ensembl: [ENSG00000163221](#)
OMIM®: [603112](#) UniProtKB/Swiss-Prot: [P80511](#)

NCBI Gene Summary: The protein encoded by this gene is a member of the S100 family of proteins containing 2 EF-hand calcium-binding motifs. S100 proteins are localized in the cytoplasm and/or nucleus of a wide range of cells, and involved in the regulation of a number of cellular processes such as cell cycle progression and differentiation. S100 genes include at least 13 members which are located as a cluster on chromosome 1q21. This protein is proposed to be involved in specific calcium-dependent signal transduction pathways and its regulatory effect on cytoskeletal components may modulate various neutrophil activities. The protein includes an antimicrobial peptide which has antibacterial activity.

GeneCards Summary: S100A12 (S100 Calcium Binding Protein A12) is a Protein Coding gene. Diseases associated with S100A12 include [Kawasaki Disease](#) and [Mooren's Ulcer](#). Among its related pathways are [Toll Like Receptor 7/8 \(TLR7/8\) Cascade](#) and [Innate Immune System](#). Gene Ontology (GO) annotations related to this gene include *calcium ion binding* and *RAGE receptor binding*. An important paralog of this gene is [S100A9](#).

UniProtKB/Swiss-Prot Summary: S100A12 is a calcium-, zinc- and copper-binding protein which plays a prominent role in the regulation of inflammatory processes and immune response. Its proinflammatory activity involves recruitment of leukocytes, promotion of cytokine and chemokine production, and regulation of leukocyte adhesion and migration. Acts as an alarmin or a danger associated molecular pattern (DAMP) molecule and stimulates innate immune cells via binding to receptors for advanced glycation endproducts (AGER). Binding to AGER activates the MAP-kinase and NF-kappa-B signaling pathways leading to production of pro-inflammatory cytokines and up-regulation of cell adhesion molecules ICAM1 and VCAM1. Acts as a monocyte and mast cell chemoattractant. Can stimulate mast cell degranulation and activation which generates chemokines, histamine and cytokines inducing further leukocyte recruitment to the sites of inflammation. Can inhibit the activity of matrix metalloproteinases; MMP2, MMP3 and MMP9 by chelating Zn(2+) from their active sites. Possesses filaricide and filaria static activity. Calcitermin possesses antifungal activity against *C.albicans* and is also active against *E.coli* and *P.aeruginosa* but not *L.monocytogenes* and *S.aureus*.

Cellular localization: cytosol, nucleus, cytoskeleton, extracellular, plasma membrane.

Full Name: *S100 calcium-binding protein A12*

Aliases: Calgranulin C, EN-RAGE (extracellular newly identified RAGE-binding protein), ...

Gene Family: S100 family of EF-hand calcium-binding proteins

Biological Function

S100A12 is a pro-inflammatory, calcium-binding protein mainly secreted by:

- Activated neutrophils
- Monocytes/macrophages

While related to S100A8/A9, S100A12 functions independently and binds strongly to the RAGE receptor (Receptor for Advanced Glycation End-products) – initiating and amplifying immune signaling.


Key Functions:

- Acts as a DAMP (damage-associated molecular pattern) → triggers immune responses
- Promotes secretion of pro-inflammatory cytokines (such as, IL-6, TNF- α)
- Increases endothelial permeability and leukocyte adhesion
- Contributes to vascular inflammation and tissue damage

S100A12 in Sepsis

In sepsis, S100A12 plays a central role in triggering and sustaining inflammation, particularly by:

- Binding to RAGE, leading to NF- κ B activation and cytokine storm
- Enhancing endothelial activation and permeability, contributing to hypotension and edema
- Driving immune cell recruitment to infection sites

 It is an early responder in sepsis pathogenesis and a marker of neutrophil-driven inflammation.

 S100A12 is especially relevant in:

- Pediatric sepsis (strong neutrophilic response)
- Acute lung injury
- Cardiovascular complications in systemic inflammation

Diagnostic and Prognostic Value

Diagnostic:

- S100A12 is elevated in serum of sepsis patients vs. controls.
- May outperform CRP or procalcitonin in early infection stages in some contexts.

Prognostic: Severity (such as, SOFA score)

- Poor outcomes and ICU admission
- Increased mortality risk in sepsis and septic shock

Measurable in serum or plasma → potential clinical biomarker

Supporting Literature

Doi: 10.1164/rccm.201209-1602OC

Doi: 10.1097/SHK.0b013e31829fbc38

Doi: 10.3389/fcvm.2024.1401314

Enrichr-KG:

