

The biochemical features, physiological aspects, and clinical applications of serum amyloid A : a review

Abstract:

Serum amyloid A (SAA) is one of the most abundant acute-phase proteins that exerts a key role in the inflammatory response, and is considered a clinically significant biomarker in many pathologies. Under inflammatory conditions, plasma SAA levels can rise over 1000-fold due to rapid hepatic production, which is largely regulated by interleukin-6 and other pro-inflammatory cytokines. In this review, we will summarize the biochemical properties, physiological functions, and clinical applications of SAA, emphasizing its biological significance in immune regulation, lipid metabolism, and tissue repair, respectively. Structurally, SAA is a small amphipathic protein which associates with high density lipoproteins (HDL) and performs its role in regulating cholesterol transport and modulating inflammatory signaling pathways. Physiologically, SAA plays a role in chemoattraction, and acts as a modulator of cytokine production and in host defense. Clinically, sustained increment of SAA has been associated with chronic inflammatory diseases and is the major precursor protein for AA amyloidosis, and an even more sensitive biomarker for disease activity and prognosis in several somatic illnesses such as infection, autoimmune disease, cardiovascular disorders and malignancies. Recent discoveries suggest that systemic amyloid A (SAA) can be more sensitive than C-reactive protein in clinical conditions. This review validates the potential diagnostic and prognostic power of SAA while addressing ongoing issues regarding assay standardization

and clinical implementation, justifying the eventual integration of SAA into routine laboratory practice.

Keywords: Acute Phase Proteins, SAA, FPR2, chromosome 11p15

Introduction

Serum amyloid A (SAA) is a family of acute-phase apolipoproteins whose circulating levels increase markedly in response to inflammation, infection, trauma, and other forms of physiological stress(1). Although SAA was originally described for its role in reactive amyloidosis, it is now recognized as a multifunctional protein with diverse roles in host defense, lipid metabolism, immune regulation, and pathogenesis of several diseases(2). The central importance of CRP in systemic biology and its clinical significance as a biomarker of inflammation and disease activity is evidenced by its dynamic synthesis pattern and dramatic serum level elevation—often as high as 1000-fold increase within 24–48 hours during acute-phase responses(3,4).

Biochemically, SAA constitutes a family of highly conserved proteins expressed from similar genes with the main isotypes—SAA1 and SAA2—synthesized mainly in the liver in response to pro-inflammatory cytokines such as interleukin-6 (IL-6), interleukin-1 β (IL-1 β), and tumor necrosis factor- α (TNF- α)(5). In an acute-phase response, circulating SAA binds to high-density lipoproteins (HDL), changing their structure and function(3). It comprises a lipophilic N-terminal domain which allows SAA to bind to HDL, and a versatile C-terminal region that can interact with a plethora of ligands and receptors, suggesting multifunctional immunomodulatory and lipid homeostatic roles(6).

In addition to its role as a simple biomarker of inflammation, SAA has important physiological roles. SAA may exert some cytokine-typical effects on leukocyte migration, cytokine production and immune cell activation as supported by several

preclinical and clinical studies. For instance, SAA interacts with pattern recognition receptors (PRRs) including Toll-like receptors (TLR2, TLR4) and formyl peptide receptors (FPRs), leading to downstream signaling pathways that alter innate immune responses(4). These interactions confirm a role of SAA in both the pro-inflammatory and anti-inflammatory pathways whereby SAA is implicated in the regulation of tissue repairing and the host defense process(7).

More importantly, SAA has a physiological relevance in lipid metabolism and cardiovascular disease. While HDL-bound SAA is low in non-inflammatory conditions, pathological SAA concentrations observed at both acute and chronic inflammation conditions displace apolipoprotein A-I (ApoA-I) from HDL, resulting in dysfunctional HDL that may reduce cholesterol efflux and drive atherogenesis(8). Accumulation of SAA modifies HDL-cholesterol and its protective functions in vivo and can predict mortality and cardiovascular risk in coronary disease, therefore related studies proved that the effects of high SAA levels are not benign(9).

Over the years evidence demonstrating the diagnostic and prognostic value of SAA measurement in many disease conditions has supported a broader application in the clinic(10). Compared with standard biomarkers such as C-reactive protein (CRP) and ESR, SAA concentrations in patients with rheumatic and autoimmune disorders correlate with clinical disease activity more sensitively, especially in cases of subclinical inflammation or biological therapy response(4). In a recent systematic review and meta-analysis, the authors confirmed that SAA levels are significantly higher in active compared to in remission and healthy controls, and that SAA has good diagnostic accuracy for the presence of rheumatic disease(9).

Aside from autoimmunity, SAA may have relevance in disorders from systemic lupus erythematosus, all the way down to aortic dissection. Indeed, elevated SAA levels have been reported in patients with active lupus in relation to systemic

inflammation and clinical markers of organ involvement, and SAA may complement as a disease severity measure(11). Elevation in SAA has also been associated with worse outcomes in acute aortic dissection and could therefore serve a role in risk stratification and prognostication(12).

The SAA has a historically nefarious role in AA amyloidosis, a life-threatening complication of chronic inflammation whereby aggregated insoluble fibrils of SAA fragments deposit in tissues like the kidney, liver, and heart, resulting in organ dysfunction(13). Though the structural basis of this misfolding and subsequent fibrillogenic formation has been historically investigated, recent advances in high-resolution structural biology have revealed the conformational mechanics of SAA and factors that pre-sent a propensity for pathological aggregation, with implications for disease mechanism and actionable therapeutic targets(14).

Although there have been advances in the biochemistry and clinical relevance of SAA, important gaps in understanding remain. However, the regulatory mechanisms that mediate its pleiotropic actions, isoform-specific functions, and context-dependent actions in acute versus chronic disease are poorly defined(15). In many other conditions, SAA is also a potential biomarker; however, the findings of the phylogenetic studies must be reproduced in the future using standardized assay techniques and clinical reference intervals, namely, data may not yet have been translated from research to clinical practice(4,9).

The SAA is a highly dynamic acute-phase protein with diverse involvement in inflammation, immunity, lipid metabolism and pathogenetic processes of human disease(16). Beyond its role as a biomarker of inflammation, the biochemical properties, physiological functions, and clinical applications of SAA highlight its potential as a therapeutic target. Continued advances in understanding the biological and regulatory mechanisms underlying SAA function, together with its

integration into clinical diagnostics, may further clarify its role in human health and disease(17).

Biochemical features of SAA

Serum amyloid A (SAA) are highly conserved acute-phase apolipoproteins with unique biochemical properties underlying their various biological and clinical functions. In human, SAA gene cluster is found in chromosome 11p15. SAA1 and SAA2 are the two major acute-phase isoforms, and SAA3 is a pseudogene(3), while SAA4 is constitutively expressed, and all of them are close to each other on the chromosome 1. SAA1 and SAA2 are hepatically synthesized proteins whose production is potently stimulated during inflammation by pro-inflammatory cytokines such as interleukin-6 (IL-6), interleukin-1 β (IL-1 β) and tumor necrosis factor- α (TNF- α), resulting in serum concentrations that can increase >1000-fold in as little as 24–48 hours(5).

The SAA is, biochemically, a small protein (~12 kDa) comprising 104–112 amino acids based on the isoform. The primary structure is characterized by an abundance of amphipathic α -helices which confer lipid-binding potential, allowing it to associate with high-density lipoprotein (HDL) particles in the plasma(18). Insertion into the phospholipid monolayer of HDL is mediated by the hydrophobic N-terminal region and the more flexible C-terminal region takes place in receptor binding and proteolytic processing. These structural principles illustrate how SAA operates as both an apolipoprotein and a signaling molecule(6).

One of the main biochemical hallmark of SAA is its active link with HDL. SAA, despite being a minor constituent of HDL at basal conditions, becomes the primary apolipoprotein during the acute-phase response, replacing apolipoprotein A-I (ApoA-I) and remarkably changing HDL structure and function(19). SAA-associated HDL has decreased cholesterol efflux capacity and defective antioxidant

function, thereby being a promising mediator of inflammation-associated dyslipidemia and atherosclerosis susceptibility. These effects are conferred by the high affinity of SAA for lipids and its ability to adopt alternative structure(6).

In a structurally unique manner, SAA exhibits incredible conformational flexibility, which is associated with its biological function as well as its potentially pathological activity in the context of amyloidosis(20). The SAA is mostly α -helical when bound to HDL, but when dissociated from HDL or cleaved proteolytically, it can refold to β -sheet rich structures that form aggregations and fibrils(21). Some N-terminal fragments are more amyloidogenic than others and, in fact, represent the most important building blocks of AA amyloid fibrils deposited in human tissue during chronic inflammatory disease(4).

In addition, SAA is highly heterogeneous biochemically due to genetic polymorphisms and post-translational modifications. Various allelic forms of SAA1 (e. 1, SAA1. 3, and SAA1. 5) differ in amino acid sequence, and exhibit varying levels of stability and amyloidogenicity, all of which contribute to individual susceptibility to AA amyloidosis(22). Oxidation and truncation are post-translational modifications which are also able to further diversify the species of SAA in plasma and modulate the receptor binding and aggregation phenotype of SAA(23).

The third major biochemical characteristic is the interaction of this protein with a multitude of cell surface receptors and other ligands. SAA is then taken up via pattern-recognition receptors including Toll-like receptors (TLR2 and TLR4), formyl peptide receptor 2 (FPR2), scavenger receptor class B type I (SR-BI), and the receptor for advanced glycation end products (RAGE), activating intracellular signaling pathways to regulate cytokine production, chemotaxis, and inflammatory gene expression(24). These interactions rely on different structural motifs of the

SAA molecule and demonstrate how the internal biochemical architecture of SAA facilitates its immunomodulatory activity(3).

Moreover, SAA has a high affinity for various extracellular matrix components and microbial ligands, such as heparan sulfate proteoglycans, lipopolysaccharide, and outer-membrane proteins of bacteria, supporting our understanding of SAA as an opsonizing-like molecule involved in innate immunity(25). SAA is known for its binding capabilities to both lipid and carbohydrate moieties, a feature which highlights the uniqueness of SAA in comparison to the more traditional inflammatory markers(18).

Physiological Aspects of SAA

Serum amyloid A (SAA) is an acute-phase protein with multiple functions that is a quintessential component of the physiological response to inflammation, infection, and tissue injury(26). Stably low (<10 mg/L) during homeostatic conditions due to low hepatic expression, the SAA pool expands dramatically upon induction of the acute-phase response, making it one of the most sensitive systemic inflammation responsive molecular biomarkers. This remarkable inducibility accentuates its role as a physiological mediator, not just a passive indicator of disease(4).

The SAA serves as an acute phase protein that is an important part of the innate immune system physiologically. Acute-phase SAA (SAA1 and SAA2) are produced primarily by hepatocytes, with production regulated primarily via IL-6, IL-1 β , and TNF- α via the JAK/STAT and NF- κ B signaling pathways(27). In addition to liver, extrahepatic expression takes place in adipocytes, macrophages, endothelial, and epithelial tissues, which allows local production of SAA at the site of inflammation. This synthesis at the tissue level enables SAA to take part directly in immune surveillance and inflammatory amplification(3).

Among physiological functions of SAA, recruitment and activation of leukocytes is one of its most relevant. SAA serves as a strong chemoattractant that attracts neutrophils (FPR2), monocytes and mast cells (TLR2/4) and T lymphocytes (RAGE)(28). The SAA thereby, through these interactions, promotes the chemotaxis and phagocytosis, and induces the secretion of pro-inflammatory cytokines and matrix-digesting exoenzymes. Such mechanisms promote the rapid trafficking of immune cells to the injured or infected tissue to aid in host defense and tissue repair(3,21).

Finally, as an acute-phase plasma protein, SAA also performs physiological roles related to lipid metabolism and cholesterol transport, thus connecting inflammation to metabolic control. The acute-phase response causes SAA to displace apolipoprotein A-I from HDL, resulting in SAA-rich HDL particles with different biological functions(29). This remodeling diminishes HDL cholesterol efflux and antioxidant capacity while augmenting its capacity for lipid and microbial component transport to the liver for clearance. While this switch is beneficial for the adaptive phase of inflammation, prolonged elevated levels of SAA disrupts lipid homeostasis and contributes to atherogenesis, highlighting the opposing physiological and pathological effects of SAA function(30).

Furthermore, a major physiological role played by SAA is its role in tissue remodeling and wound healing. The SAA activates the MAPK and PI3K/Akt signaling pathways, which then prompts fibroblast migration, angiogenesis, and secretion of extracellular matrix components. These actions help tissues to regenerate post-injury by coupling the resolution of inflammation with structural repair. The SAA also stimulates matrix metalloproteinases that enable the regulated degradation of the extracellular matrix to allow for infiltration of immune cells and tissue remodeling(4).

SAA also plays a regulatory role on the adaptive immune system. It plays a role in dendritic cell development and antigen presentation, T-cell polarization and B-cell antibody production, thus serving as a link between the innate and adaptive immune systems. By these mechanisms, SAA contributes to the state of immune memory and tolerance but ensures immune vigilance in physiological stress phases(3).The SAA is a hormone-like inflammatory mediator in metabolic tissues. SAA is expressed in adipose tissue, and especially in obesity, it plays an important role in low-grade chronic inflammation and insulin resistance. The SAA increases macrophage recruitment to white adipose tissue and induces an inflammatory response through the secretion of adipokines suggesting its physiological role in immunometabolism control(6).

Although SAA has protective functions, chronic elevation of SAA leads to pathological adaptation. Chronic inflammatory diseases like inflammatory bowel disease, rheumatoid arthritis and long-lasting infections have high levels of SAA for extended periods, predisposing to AA amyloidosis. In this case, the protein structure SAA deposits as amyloid fibrils in the organs and leads to renal, hepatic and cardiac dysfunction. Therefore, SAA acts as an inflammatory mediator with a physiological role; however, when failed regulation, it becomes pathogenic(23).

Clinical Importance of SAA

Literature has highlighted the role of serum amyloid A (SAA) and its diagnostic, prognostic and therapeutic monitoring application from simple infectious, inflammatory to metabolic diseases. Due to its quick and extreme rise in the acute-phase response, SAA frequently elevates more quickly and reaches a higher peak than C-reactive protein (CRP), distinguishing it as especially valuable for early detection of inflammation or inflammation in subclinical states. Such high

sensitivity makes SAA a promising clinical tool with a potential role in the evaluation of disease activity and clinical decision-making(4).

The SAA has one of the most well-established clinical uses, such as the monitoring of inflammatory and autoimmune diseases. SAA levels correlate well with disease severity and flare activity in rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis and inflammatory bowel disease(31). The SAA is correlated more closely with the current state of inflammation, performing better among other markers of inflammation, especially in patients receiving IL-6 inhibitors, where the synthesis of CRP is suppressed but SAA expresses a more sensitive trend as compared to its level of expression in normal individuals and among other markers of inflammation. As a result, SAA is increasingly identified as an adjunct biomarker to detect disease when traditional inflammatory markers are less reliable(3).

The SAA is also important for diagnostics and prognosis of infectious disease. Serum SAA concentrations increase dramatically, within hours of exposure to viruses, bacteria, or fungi, so this assay allows early detection of infection and distinction between infectious and non-infectious inflammatory states(10). The SAA has been found superior over CRP and procalcitonin in the diagnosis of neonatal sepsis and pediatric infections, diseases where early diagnosis is important for survival. Additionally, decreasing SAA concentrations during therapeutic antimicrobial trials can be used as a real-time monitor of treatment efficacy, enabling clinicians to personalize therapy and prevent potentially unnecessary exposure to antibiotics(6).

As a cardiovascular mediator and biomarker, SAA has attracted much attention in cardiovascular medicine. High SAA levels are independent predictors for atherosclerosis, myocardial infarction, and cardiovascular death. Clinically, the addition of SAA to traditional risk markers (eg, LDL-cholesterol and CRP)

improves risk stratification. In this regard, SAA causes endothelium dysfunction, promotes foam cell formation, and modifies HDL functionality, thereby connecting systemic inflammation to plaque vulnerability. This evidence endorses SAA as a clinical prognosticator in patients with coronary artery disease(32).

This is especially the case for SAA, which is clinically relevant, in particular, in the context of treatment with AA amyloidosis, a lethal complication of chronic inflammatory diseases. Continued high levels of SAA cause proteolytic degradation and depositing of amyloid A fibrils in organs, notably the kidneys, leading to proteinuria and progressive renal impairment(33). The SAA concentrations must be followed to predict the risk of amyloidosis and to assess the efficacy of treatment because long-term reduction of SAA to persistently less than 10 mg/L is powerfully linked both to improved survival and to reduction of amyloid deposits. SAA is therefore the pathogenic precursor of AA amyloidosis, and the most important clinical biomarker in its management(23).

The SAA is tremendous potential as a novel prognostic biomarker of tumor-associated inflammation in cancer. Increased SAA are associated with tumor stage, metastasis, and systemic inflammatory burden in lung colorectal breast and gastric cancers and poor survival. In our daily clinical practice SAA will be helpful in identification of high-risk patients, and even as a marker for response to therapy/chemotherapy or immunotherapy. The SAA can also be an adjunct marker in personalized cancer management due to its ability to reflect the inflammatory tumor microenvironment(3).

In addition to its status as a major research focus in metabolic and hormonal disorders, SAA has increasing clinical relevance. Background: Increased SAA is both a reflection of chronic low-grade inflammation in obesity and type two diabetes mellitus, but it may also predict the development of insulin resistance and cardiovascular risk as well as go more frequently with metabolic syndrome. The

SAA could play a role clinically by providing a means of identifying patients (who otherwise would be missed by glycemic and lipid parameters) who might benefit from early therapeutic lifestyle change or pharmacological intervention.(6).In obstetric and neonatal practice SAA is better than CRP for diagnosing maternal infection, chorioamnionitis, and neonatal sepsis. Rapid kinetics depicts an early diagnosis and can be treated early, which helps in reducing the morbidity. The SAA is therefore all the more important to its nature in that a multiplicity of inflammatory reactions needs to be detected early on to improve mother and fetus outcome(4).

Conclusion

The SAA is an acute-phase protein with complex biochemical, physiological, and clinical significance of inflammation. It has a distinct structure that allows it to respond to cytokine signaling in a faster manner than many other conventional disease indicators of inflammation and as such is considered sensitive to inflammatory activity. The SAA plays physiological roles in lipid transport, immune modulation and tissue repair bridging innate immunity with metabolic homeostasis. The biological laboratory parameter of SAA is more likely to predict clinical significance in inflammatory, infectious cardiovascular and malignant diseases and prolonged elevation of SAA levels clinically causes AA amyloidosis. Currently, given the necessity for assay standardization, controversies still exist: however, increasing evidence accumulate in favor of including SAA into routine practice. This is important to fully realize the diagnostic and therapeutic promise of this biomarker in future by harmonizing measurement technique with use of disease specific reference range in subsequent studies.

Reference

1. Ji A, Meredith LW, Shridas P. Serum Amyloid A: A Double-Edged Sword in Health and Disease. *Int J Mol Sci* [Internet]. 2025 May 9;26(10):4528. Available from: <https://www.mdpi.com/1422-0067/26/10/4528>
2. Jayaraman S, Urdaneta A, Bullitt E, Fändrich M, Gursky O. Lipid clearance and amyloid formation by serum amyloid A: exploring the links between beneficial and pathologic actions of an enigmatic protein. *J Lipid Res* [Internet]. 2023 Sep;64(9):100429. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S002227523001025>
3. Chang Y, Liu Y, Zou Y, Ye RD. Recent Advances in Studies of Serum Amyloid A: Implications in Inflammation, Immunity and Tumor Metastasis. *Int J Mol Sci* [Internet]. 2025 Jan 24;26(3):987. Available from: <https://www.mdpi.com/1422-0067/26/3/987>
4. Sorić Hosman I, Kos I, Lamot L. Serum Amyloid A in Inflammatory Rheumatic Diseases: A Compendious Review of a Renowned Biomarker. *Front Immunol* [Internet]. 2021 Feb 19;11. Available from: <https://www.frontiersin.org/articles/10.3389/fimmu.2020.631299/full>
5. Malle E, Madreiter-Sokolowski C, Windpassinger C. SAA4: An Underdog Within the Serum Amyloid a Superfamily? *Int J Mol Sci* [Internet]. 2026 Apr 28;27(9):3907. Available from: <https://www.mdpi.com/1422-0067/27/9/3907>
6. Moissl-Blanke AP, Delgado GE, Krämer BK, Siekmeier R, Duerschmied D, März W, et al. Serum Amyloid A (SAA) and Its Interaction with High-Density Lipoprotein Cholesterol (HDL-C): A Comprehensive Review. *Int J Mol Sci* [Internet]. 2025 Dec 25;27(1):241. Available from: <https://www.mdpi.com/1422-0067/27/1/241>
7. Ye RD, Sun L. Emerging functions of serum amyloid A in inflammation. *J Leukoc Biol* [Internet]. 2015 Dec 1;98(6):923–9. Available from: <https://academic.oup.com/jleukbio/article/98/6/923/6935992>
8. Webb NR. High-Density Lipoproteins and Serum Amyloid A (SAA). *Curr Atheroscler Rep* [Internet]. 2021 Feb 15;23(2):7. Available from: <https://link.springer.com/10.1007/s11883-020-00901-4>
9. Zinellu A, Mangoni AA. The potential role of serum amyloid A as biomarker of rheumatic diseases: a systematic review and meta-analysis. *Clin Exp Med* [Internet]. 2024 Jun 29;24(1):141. Available from: <https://link.springer.com/10.1007/s10238-024-01413-0>
10. Kang H, Park S. Diagnostic Performance and Prognostic Value of Serum Amyloid A in Patients with Bloodstream Infection. *Diagnostics* [Internet]. 2026 May 16;16(10):1510. Available from: <https://www.mdpi.com/2075-4418/16/10/1510>
11. Salman ZA. Evaluation of Serum Amyloid A and some Biochemical markers in Iraqi patients with systemic lupus erythematosus. *Al-Salam J Med Sci*

- [Internet]. 2024 Apr 27;3(2):22–9. Available from: <http://journal.alsalam.edu.iq/index.php/ajbms/article/view/245>
12. He Y, Ma C, Xing J, Wang S, Ji C, Han Y, et al. Serum amyloid a protein as a potential biomarker in predicting acute onset and association with in-hospital death in acute aortic dissection. *BMC Cardiovasc Disord* [Internet]. 2019 Dec 3;19(1):282. Available from: <https://bmccardiovascdisord.biomedcentral.com/articles/10.1186/s12872-019-1267-0>
13. Obici L, Merlini G. AA amyloidosis: basic knowledge, unmet needs and future treatments. *Swiss Med Wkly* [Internet]. 2012 May 20;142(2122):w13580. Available from: <https://smw.ch/index.php/smw/article/view/1486>
14. Simons JP, Al-Shawi R, Ellmerich S, Speck I, Aslam S, Hutchinson WL, et al. Pathogenetic mechanisms of amyloid A amyloidosis. *Proc Natl Acad Sci* [Internet]. 2013 Oct 19;110(40):16115–20. Available from: <https://pnas.org/doi/full/10.1073/pnas.1306621110>
15. García-Cortés CG, Parés-Matos EI. New Regulatory roles for Human Serum Amyloid A. *Int J Res Oncol* [Internet]. 2024;3(1). Available from: <http://www.ncbi.nlm.nih.gov/pubmed/39044740>
16. Mohanty T, Miličević K, Göthert H, Tillmann A, Padra M, Papareddy P, et al. Balancing inflammation: the specific roles of serum amyloid A proteins in sterile and infectious diseases. *Front Immunol* [Internet]. 2025 Feb 10;16. Available from: <https://www.frontiersin.org/articles/10.3389/fimmu.2025.1544085/full>
17. den Hartigh LJ, May KS, Zhang X-S, Chait A, Blaser MJ. Serum amyloid A and metabolic disease: evidence for a critical role in chronic inflammatory conditions. *Front Cardiovasc Med* [Internet]. 2023 Jun 15;10. Available from: <https://www.frontiersin.org/articles/10.3389/fcvm.2023.1197432/full>
18. Sack GH. Serum amyloid A – a review. *Mol Med* [Internet]. 2018 Dec 30;24(1):46. Available from: <https://molmed.biomedcentral.com/articles/10.1186/s10020-018-0047-0>
19. de Beer MC, Webb NR, Wroblewski JM, Noffsinger VP, Rateri DL, Ji A, et al. Impact of serum amyloid A on high density lipoprotein composition and levels. *J Lipid Res* [Internet]. 2010 Nov;51(11):3117–25. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0022227520409459>
20. Fan Y, Teng Vong C, D. Ye R. Serum Amyloid A and Immunomodulation. In: *Amyloid Diseases* [Internet]. IntechOpen; 2019. Available from: <https://www.intechopen.com/books/amyloid-diseases/serum-amyloid-a-and-immunomodulation>
21. Lu J, Yu Y, Zhu I, Cheng Y, Sun PD. Structural mechanism of serum

- amyloid A-mediated inflammatory amyloidosis. *Proc Natl Acad Sci* [Internet]. 2014 Apr 8;111(14):5189–94. Available from: <https://pnas.org/doi/full/10.1073/pnas.1322357111>
22. Sikora J, Kmochová T, Mušálková D, Pohludka M, Přikryl P, Hartmannová H, et al. A mutation in the SAA1 promoter causes hereditary amyloid A amyloidosis. *Kidney Int* [Internet]. 2022 Feb;101(2):349–59. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S008525382100867X>
23. Sun L, Ye RD. Serum amyloid A1: Structure, function and gene polymorphism. *Gene* [Internet]. 2016 May;583(1):48–57. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0378111916301408>
24. Eklund KK, Niemi K, Kovanen PT. Immune Functions of Serum Amyloid A. *Crit Rev Immunol* [Internet]. 2012;32(4):335–48. Available from: <http://www.dl.begellhouse.com/journals/2ff21abf44b19838,3348358a38f6810f,67a51fd719fc37f2.html>
25. Frame NM, Gursky O. Structure of serum amyloid A suggests a mechanism for selective lipoprotein binding and functions: <scp>SAA</scp> as a hub in macromolecular interaction networks. *FEBS Lett* [Internet]. 2016 Mar 6;590(6):866–79. Available from: <https://febs.onlinelibrary.wiley.com/doi/10.1002/1873-3468.12116>
26. Cheng J, Wang W, Cheng X, Li X, Lun L, Lian X, et al. The Acute-Phase Serum Amyloid A Promotes Cytokines Production in Oyster *Crassostrea gigas*. *Fishes* [Internet]. 2025 Feb 23;10(3):93. Available from: <https://www.mdpi.com/2410-3888/10/3/93>
27. Buck M, Gouwy M, Wang J, Snick J, Opdenakker G, Struyf S, et al. Structure and Expression of Different Serum Amyloid A (SAA) Variants and their Concentration-Dependent Functions During Host Insults. *Curr Med Chem* [Internet]. 2016 Jun 3;23(17):1725–55. Available from: <http://www.eurekaselect.com/openurl/content.php?genre=article&issn=0929-8673&volume=23&issue=17&spage=1725>
28. Abouelasrar Salama S, Gouwy M, Van Damme J, Struyf S. Acute-serum amyloid A and A-SAA-derived peptides as formyl peptide receptor (FPR) 2 ligands. *Front Endocrinol (Lausanne)* [Internet]. 2023 Feb 3;14. Available from: <https://www.frontiersin.org/articles/10.3389/fendo.2023.1119227/full>
29. Faty A, Ferré P, Commans S. The Acute Phase Protein Serum Amyloid A Induces Lipolysis and Inflammation in Human Adipocytes through Distinct Pathways. *Stadler K, editor. PLoS One* [Internet]. 2012 Apr 19;7(4):e34031. Available from: <https://dx.plos.org/10.1371/journal.pone.0034031>
30. Ronsein GE, Vaisar T. Inflammation, remodeling, and other factors affecting HDL cholesterol efflux. *Curr Opin Lipidol* [Internet]. 2017 Feb;28(1):52–9. Available from: <https://journals.lww.com/00041433-201702000-00009>

- 442 31. Zhou J, Dai Y, Lin Y, Chen K. Association between serum amyloid A and
443 rheumatoid arthritis: A systematic review and meta-analysis. *Semin Arthritis*
444 *Rheum* [Internet]. 2022 Feb;52:151943. Available from:
445 <https://linkinghub.elsevier.com/retrieve/pii/S0049017221002249>
- 446 32. Johnson BD, Kip KE, Marroquin OC, Ridker PM, Kelsey SF, Shaw LJ, et al.
447 Serum Amyloid A as a Predictor of Coronary Artery Disease and
448 Cardiovascular Outcome in Women. *Circulation* [Internet]. 2004 Feb
449 17;109(6):726–32. Available from:
450 <https://www.ahajournals.org/doi/10.1161/01.CIR.0000115516.54550.B1>
- 451 33. Mirioglu S, Uludag O, Hurdogan O, Kumru G, Berke I, Doumas SA, et al.
452 AA Amyloidosis: A Contemporary View. *Curr Rheumatol Rep* [Internet].
453 2024 Jul 3;26(7):248–59. Available from:
454 <https://link.springer.com/10.1007/s11926-024-01147-8>
- 455