ISSN 2218-6204 (online)

World Journal of *Hematology*

Continuous Publication Volume 11 Number 3 September 19, 2024

Published by Baishideng Publishing Group Inc

World Journal of Hematology

Contents

Continuous Publication Volume 11 Number 3 September 19, 2024

EDITORIAL

Cheng CH, Hao WR, Cheng TH. Multifaceted role of haptoglobin: Implications for disease development. *World J Hematol* 2024; 11(3): 98807 [DOI: 10.5315/wjh.v11.i3.98807]

World Journal of Hematology

Continuous Publication Volume 11 Number 3 September 19, 2024

Contents

ABOUT COVER

Peer Reviewer of *World Journal of Hematology*, Prasanna Venkatesh Ramesh, MBBS, MS Ophthalmology - Gold Medalist, Glaucoma Surgery and Research Fellow, DNB, MNAMS, FAICO, FICO, FAICO - Gold Medalist (Cataract/Phaco), Glaucoma Medical Officer, DNB Coordinator & Research Director, Mahathma Eye Hospital Private Limited, Trichy, Tamil Nadu 620017, India. drprasanna@mahathmaeyehospital.com

AIMS AND SCOPE

The primary aim of *World Journal of Hematology* (*WJH*, *World J Hematol*) is to provide scholars and readers from various fields of hematology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJH mainly publishes articles reporting research results and findings obtained in the field of hematology and covering a wide range of topics including anemia, blood coagulation disorders, blood group incompatibility, blood platelet disorders, blood protein disorders, bone marrow diseases, hematologic neoplasms, hemoglobinopathies, hemorrhagic disorders, leukocyte disorders, methemoglobinemia, pancytopenia, polycythemia, hematologic pregnancy complications, preleukemia, sulfhemoglobinemia, and thrombophilia.

INDEXING/ABSTRACTING

The *WJH* is now abstracted and indexed in Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database.

RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL
World Journal of Hematology

ISSN
ISSN 2218-6204 (online)

LAUNCH DATE
June 2, 2012

FREQUENCY
Continuous Publication

EDITORS-IN-CHIEF
Pier Paolo Piccaluga

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/2218-6204/editorialboard.htm

PUBLICATION DATE
September 19, 2024

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Hematology

Submit a Manuscript: https://www.f6publishing.com

World J Hematol 2024 September 19; 11(3): 98807

DOI: 10.5315/wjh.v11.i3.98807

ISSN 2218-6204 (online)

EDITORIAL

Multifaceted role of haptoglobin: Implications for disease development

Chun-Han Cheng, Wen-Rui Hao, Tzu-Hurng Cheng

Specialty type: Hematology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade B
Novelty: Grade B
Creativity or Innovation: Grade B
Scientific Significance: Grade B

P-Reviewer: Dauyey K

Received: July 6, 2024
Revised: August 29, 2024
Accepted: September 6, 2024
Published online: September 19, 2024
Processing time: 74 Days and 21.2 Hours

Chun-Han Cheng, Department of Medical Education, Linkou Chang Gung Memorial Hospital, Taoyuan 33305, Taiwan

Wen-Rui Hao, Division of Cardiology, Department of Internal Medicine, Shuang Ho Hospital, Ministry of Health and Welfare, Taipei Medical University, New Taipei 23561, Taiwan

Wen-Rui Hao, Division of Cardiology, Department of Internal Medicine, School of Medicine, College of Medicine, Taipei Medical University, Taipei 11002, Taiwan

Tzu-Hurng Cheng, Department of Biochemistry, School of Medicine, College of Medicine, China Medical University, Taichung 404328, Taiwan

Co-corresponding authors: Wen-Rui Hao and Tzu-Hurng Cheng.

Corresponding author: Tzu-Hurng Cheng, PhD, Professor, Department of Biochemistry, School of Medicine, College of Medicine, China Medical University, No. 91 Xueshi Road, North District, Taichung 404328, Taiwan. thcheng@mail.cmu.edu.tw

Abstract

Haptoglobin, a protein primarily recognized for its role in sequestering free hemoglobin, has been identified as a molecule with diverse and underexplored functions in the pathophysiology of various diseases. This editorial explores the multifaceted roles of haptoglobin, highlighting its involvement in inflammatory responses and immune regulation and its potential implications in chronic diseases such as diabetes, cardiovascular disorders, and cancer. Through a synthesis of recent research findings, this editorial reveals the importance of haptoglobin in disease mechanisms and underscores the need for further investigation to fully elucidate its therapeutic potential. A comprehensive understanding of haptoglobin's novel functions may catalyze the development of innovative diagnostic and therapeutic modalities in clinical practice.

Key Words: Haptoglobin; Disease development; Inflammation; Immune modulation; Therapeutic potential

Core Tip: This editorial elucidates the under-recognized functions of haptoglobin beyond its established role in hemoglobin sequestration. By highlighting its contributions to inflammatory processes, immune regulation, and the pathogenesis of chronic diseases, this editorial indicates the importance of further research to fully elucidate its therapeutic potential. A comprehensive understanding of haptoglobin's multifaceted nature may facilitate the development of innovative diagnostic and therapeutic interventions to enhance patient outcomes in various diseases.

Citation: Cheng CH, Hao WR, Cheng TH. Multifaceted role of haptoglobin: Implications for disease development. *World J Hematol* 2024; 11(3): 98807
URL: https://www.wjgnet.com/2218-6204/full/v11/i3/98807.htm
DOI: https://dx.doi.org/10.5315/wjh.v11.i3.98807

INTRODUCTION

Haptoglobin, a glycoprotein traditionally known for its role in sequestering free hemoglobin for mitigating oxidative damage, is conventionally associated with hemolysis and related disorders[1]. However, recent investigations have revealed a broader spectrum of functions for haptoglobin beyond its conventional role. As a multifaceted protein, haptoglobin is now recognized for its involvement in various physiological and pathological processes, including inflammation, immune regulation, and tissue repair[2-4]. The clinical importance of haptoglobin has been well established in diagnostic contexts, particularly in hemolytic anemias and liver function tests[5]. Moreover, its role in chronic diseases such as cardiovascular disorders, diabetes, and cancer has gained increasing recognition[6]. These findings not only underscore haptoglobin's potential as a pivotal biomarker but also suggest its therapeutic utility[7,8]. Ongoing research is elucidating the molecular mechanisms underlying the influence of haptoglobin on these diverse processes. For instance, in inflammatory conditions, haptoglobin interacts with various signaling pathways and molecular components, modulating immune responses and contributing to tissue repair and regeneration[9]. In chronic diseases, haptoglobin's role is even more critical, as it is implicated in the regulation of oxidative stress and immune responses; these are pivotal factors in conditions such as diabetes and cardiovascular disease[10,11]. This editorial explores the expanding roles of haptoglobin, with a focus on its involvement in disease pathogenesis. By synthesizing current research findings and identifying knowledge gaps, we endeavor to stimulate further investigation into the diverse functions of haptoglobin and its potential clinical applications[12-14].

HAPTOGLOBIN AND INFLAMMATORY PROCESSES

Haptoglobin is a critical modulator of inflammatory responses; it functions as an acute-phase reactant that is rapidly upregulated in response to inflammatory stimuli[1]. Its primary role is binding to free hemoglobin released during hemolysis, thereby mitigating oxidative stress and preventing tissue damage[2]. This mechanism is important in conditions characterized by extensive red blood cell breakdown, such as subarachnoid hemorrhage and aortic valve stenosis; in these conditions, the accumulation of extracellular hemoglobin can precipitate systemic endothelial dysfunction and adverse clinical outcomes[3,11]. Recent studies have revealed a more nuanced influence of haptoglobin on the inflammatory milieu, involving the modulation of cytokines and chemokine activities. Haptoglobin has been demonstrated to regulate the expression of both proinflammatory and anti-inflammatory cytokines, thereby influencing the balance of immune responses[4]. This regulatory function is evident in various inflammatory conditions, including chronic diseases such as diabetes, cardiovascular disorders, and cancer; in these diseases, haptoglobin levels are often dysregulated[7,8]. At the molecular level, haptoglobin's interaction with hemoglobin inhibits the formation of reactive oxygen species, thus attenuating oxidative damage. Furthermore, the haptoglobin–hemoglobin complex is recognized by $CD163^+$, a macrophage scavenger receptor, facilitating complex clearance and promoting anti-inflammatory signaling pathways[9]. This interaction underscores haptoglobin's role in immune modulation, as $CD163^+$ macrophages are implicated the endothelial-to-mesenchymal transition in atheroma formation[9]. Regarding therapeutic applications, haptoglobin is promising as both a biomarker of diseases and a therapeutic target. For instance, haptoglobin levels can aid in the diagnosis and monitoring of inflammatory conditions and hemolytic disorders[5]. Additionally, therapeutic strategies modulating haptoglobin activity, such as enhancing its expression or mimicking its function, can be applied for treating diseases characterized by excessive inflammation and oxidative stress[6,14]. To comprehensively elucidate haptoglobin's role in inflammation, future research should focus on specific signaling pathways and molecular interactions. Key areas of investigation include the precise mechanisms by which haptoglobin influences cytokine and chemokine production, the impact of genetic variations in the haptoglobin gene on its function, and the potential benefits of targeting haptoglobin in various inflammatory diseases. Advanced genomic and proteomic techniques can be employed to achieve these objectives, providing deeper insights into the therapeutic potential of haptoglobin modulation[12]. By integrating recent findings and expanding our understanding of the molecular mechanisms underlying haptoglobin's role in inflammation, its anti-inflammatory properties can effectively utilized for the development of novel therapeutic strategies.

IMMUNE RESPONSE MODULATION

Haptoglobin is increasingly acknowledged for its contributions to immune system modulation. Recent research has elucidated its complex interactions with various immune cells, including macrophages, neutrophils, and lymphocytes, which significantly impact their activation and function[1]. For instance, haptoglobin has been implicated in modulating the oxidative burst of neutrophils. This modulation helps mitigate tissue damage that can occur during inflammatory responses, thereby potentially limiting the extent of inflammation-induced injury[2]. Moreover, haptoglobin influences dendritic cells, crucial players in the adaptive immune response. It affects their maturation and function, which in turn shapes the nature and strength of the adaptive immune response[3]. This role of haptoglobin underscores its potential significance in a range of immune-related diseases and conditions. By modulating immune cell behavior, haptoglobin could offer new therapeutic avenues for managing autoimmune diseases, chronic inflammatory conditions, and even cancer[5]. The therapeutic potential of targeting haptoglobin's immunomodulatory effects is particularly intriguing. For instance, understanding its interactions with immune cells could lead to innovative treatments for conditions where immune regulation is disrupted. Further research is essential to fully harness haptoglobin's potential in therapeutic contexts, moving towards more personalized medicine approaches that consider individual variability in immune responses[6]. Overall, while haptoglobin's traditional role in hemoglobin scavenging remains important, its emerging functions in immune modulation present promising opportunities for advancing treatment strategies in various immune-related diseases. Exploring these functions in greater depth could reveal new pathways for intervention and personalized therapies.

HAPTOGLOBIN IN CHRONIC DISEASES

Recent research has significantly expanded our understanding of haptoglobin's role in chronic diseases, revealing its complex involvement in conditions such as cardiovascular disease, diabetes, and cancer. In cardiovascular disease, haptoglobin polymorphisms have been linked to increased susceptibility to atherosclerosis and related complications. For instance, haptoglobin genotypes are associated with varying cardiovascular risks, highlighting the protein's potential as a biomarker for assessing individual risk profiles and informing preventive measures[15,16]. In diabetes, haptoglobin levels are associated with disease progression and complications. Elevated haptoglobin levels are correlated with adverse outcomes in type 2 diabetes, indicating its potential as both a prognostic marker and therapeutic target[7]. Thus, further exploration of the impact of haptoglobin modulation on disease management and patient outcomes is warranted. Haptoglobin's role extends to oncology, where its expression patterns are associated with tumor progression and metastasis. Altered haptoglobin expression has been demonstrated to influence cancer progression, making it a valuable focus for developing novel diagnostic and therapeutic strategies[4,14]. Haptoglobin's involvement in the acute-phase response and interactions with other biomarkers offer new insights into tumor biology and potential therapeutic targets[15]. Advancements in proteomics and glycosylation profiling have refined our understanding of haptoglobin's role in chronic diseases. Quantitative analysis and mass spectrometry enable the precise identification of haptoglobin-related biomarkers, enhancing disease detection and monitoring[5,17]. These developments underscore haptoglobin's versatility as a biomarker across various chronic disease contexts, from cardiovascular risk assessment to cancer diagnosis. Additionally, recent studies have demonstrated haptoglobin's interactions with other proteins and its role in systemic inflammation. For example, research has identified the impact of haptoglobin on inflammatory processes and immune responses, emphasizing its multifaceted role in disease pathology[18,19]. Understanding these interactions can provide insights into disease mechanisms and potential avenues for targeted therapies. Overall, the multifaceted role of haptoglobin in chronic diseases indicates its potential clinical applications for disease management and treatment. Continued research into haptoglobin's diverse functions and interactions is expected to advance our understanding of its role in health and disease, leading to innovative diagnostic and therapeutic strategies[3,20].

POTENTIAL THERAPEUTIC APPLICATIONS

The diverse biological functions of haptoglobin provide promising therapeutic avenues across various diseases. Notably, recombinant haptoglobin can alleviate oxidative stress in hemolytic disorders. Hemolysis often leads to the release of free hemoglobin, a potent inducer of oxidative damage and tissue injury. Recombinant haptoglobin effectively sequesters free hemoglobin, mitigating oxidative damage and potentially improving clinical outcomes in hemolysis-associated conditions[1]. Haptoglobin's immunomodulatory role, which is mediated through $CD163^+$ receptor interactions on macrophages, suggests its therapeutic applications in autoimmune diseases and cancer[5]. Targeting these interactions may yield novel therapies for autoimmune diseases such as rheumatoid arthritis and lupus and various cancers[9]. Synthetic haptoglobin peptides, replicating the parent protein's antioxidative and anti-inflammatory properties, are under investigation for sickle cell anemia and chronic kidney disease. Advancements in peptide synthesis and delivery systems can enhance their therapeutic potential[3]. Gene therapy approaches, such as clustered regularly interspaced short palindromic repeats (CRISPR)-Cas9 technology, offer the prospect of correcting genetic mutations underlying haptoglobin deficiency and associated disorders[21]. This innovative approach provides a potential long-term solution for these conditions. Haptoglobin-conjugated nanoparticles and liposomes are being developed for targeted drug delivery to inflamed tissues or cancer sites, maximizing therapeutic efficacy while minimizing systemic adverse effects[4]. Moreover, monoclonal antibodies that modulate haptoglobin function present a promising strategy for treating inflammatory and

autoimmune diseases by fine-tuning immune responses[22]. Overall, the exploration of haptoglobin-based therapies is expanding rapidly in response to unmet medical needs. By elucidating haptoglobin's diverse functions and therapeutic implications, researchers are advancing precision medicine and improving patient outcomes[15,16].

FUTURE RESEARCH DIRECTIONS

Despite accumulating knowledge regarding haptoglobin, several crucial research gaps persist, hindering a comprehensive understanding of its biological functions and therapeutic potential. Elucidating the precise mechanisms by which haptoglobin modulates immune responses is paramount. Although interactions between haptoglobin and immune cells such as macrophages have been established[1], the underlying signaling pathways and molecular interactions remain underexplored. Future investigations should focus on these pathways to uncover the influence of haptoglobin on immune regulation and to identify the potential therapeutic targets. Haptoglobin's role in autoimmune diseases, including rheumatoid arthritis and lupus, necessitates further exploration. Understanding haptoglobin's involvement in the pathogenesis and progression of these conditions may lead to the development of novel therapeutic strategies and biomarkers for disease activity and treatment response[2]. Clarifying haptoglobin's exact role in autoimmune mechanisms and its utility as a biomarker is essential. In cancer research, the impact of haptoglobin on tumor immunology requires further exploration. Although evidence suggests that haptoglobin modulates tumor-associated macrophages and the tumor microenvironment[3], the specific mechanism by which it influences tumor progression and immune evasion remain unclear. Investigating these interactions may facilitate the development of novel cancer immunotherapies targeting haptoglobin pathways. Moreover, the role of haptoglobin in neuroinflammatory conditions, such as multiple sclerosis and Alzheimer's disease, warrants further exploration. Although its neuroprotective potential has been reported, its exact role in neuroinflammatory processes remains elusive[4]. Future studies should investigate the influence of haptoglobin on neuroinflammation and its potential as a therapeutic target in neurodegenerative diseases. Chronic inflammatory diseases, including chronic obstructive pulmonary disease and inflammatory bowel disease, require additional research to elucidate haptoglobin's role. Understanding how haptoglobin affects chronic inflammation and tissue damage could lead to improved treatment strategies[23]. Additionally, the impact of different haptoglobin genotypes on disease susceptibility and progression warrants investigation. Correlating genetic variations with clinical outcomes can help identify biomarkers and therapeutic targets tailored to individual genetic profiles[7]. To address these research gaps, advanced experimental methodologies are essential. Techniques such as CRISPR-Cas9 for constructing genetic models, mass spectrometry for identifying haptoglobin-interacting proteins and post-translational modifications[5], single-cell RNA sequencing for exploring expression patterns, and *in vivo* imaging for tracking haptoglobin distribution are critical. Moreover, high-throughput screening for small molecules or peptides that modulate haptoglobin functions can facilitate the discovery of new therapeutic agents. Future research can employ such advanced methodologies to enhance the understanding of the role of haptoglobin and promote the development of targeted therapeutic strategies.

CONCLUSION

Haptoglobin, traditionally recognized for its role in binding free hemoglobin, has emerged as a multifaceted protein with crucial implications in various diseases. Beyond its conventional function, recent research underscores its involvement in inflammation, immune regulation, and the progression of chronic diseases such as cardiovascular disorders, diabetes, and cancer[1]. This expanded understanding presents promising avenues for both research and therapeutic innovation. By targeting haptoglobin's varied functions, novel diagnostic markers and therapeutic strategies can be developed to enhance disease management and patient outcomes[4]. Elucidating haptoglobin's role in immune modulation offers potential for developing therapies that augment immune responses in conditions ranging from autoimmune diseases to cancer[2]. To fully realize the therapeutic potential of haptoglobin, a comprehensive understanding of its underlying mechanisms is essential. The growing body of evidence underscores the importance of ongoing investigation into haptoglobin's multifaceted roles and highlights its potential as a pivotal biomarker and therapeutic target in personalized medicine[5]. Moreover, understanding haptoglobin's involvement in the development and progression of various diseases can inform the development of targeted treatments and improve patient outcomes. The role of haptoglobin in cardiovascular health has been linked to endothelial dysfunction and atheroma formation, suggesting new avenues for therapeutic interventions[9]. Similarly, haptoglobin's impact on metabolic diseases such as diabetes underscores its importance in managing conditions characterized by chronic inflammation and oxidative stress[7]. Harnessing the full potential of haptoglobin holds promises in revolutionizing disease management strategies and enhancing patient care across diverse clinical contexts[6]. Continued investigation into haptoglobin's multifaceted roles is crucial for developing innovative therapeutic approaches that significantly improve patient outcomes[24].

FOOTNOTES

Author contributions: Cheng CH wrote the editorial, including synthesizing recent research findings and developing the manuscript's key themes; Hao WR and Cheng TH provided critical revisions and guidance throughout the drafting process; all authors have read and approved the final version.

Conflict-of-interest statement: The authors declare that they having have no conflicts of interest.

Country of origin: Taiwan

ORCID number: Tzu-Hurng Cheng 0000-0002-9155-4169.

S-Editor: Luo ML
L-Editor: A
P-Editor: Zhao YQ

REFERENCES

1 **Tuono De Manfouo R**, Louokdom JS, Chetcha BC, Bakam Magoua LM, Nya PCB, Pieme CA, Tayou Tagny C. Haptoglobin: A protein with little-explored properties? Involvement in the development of diseases. *World J Hematol* 2024; **11**: 94171 [DOI: 10.5315/wjh.v11.i2.94171]

2 **Pashinskaya KO**, Samodova AV, Dobrodeeva LK. Features of the immune system and levels of blood transport components in residents of the arctic of the Russian Federation. *Am J Hum Biol* 2024; e24136 [PMID: 39032081 DOI: 10.1002/ajhb.24136]

3 **Zolnourian A**, Garland P, Holton P, Arora M, Rhodes J, Uff C, Birch T, Howat D, Franklin S, Galea I, Bulters D. A Randomised Controlled Trial of SFX-01 After Subarachnoid Haemorrhage-The SAS Study. *Transl Stroke Res* 2024; 1-13 [PMID: 39028412 DOI: 10.1007/s12975-024-01278-1]

4 **Santiago-Hernandez A**, Martin-Lorenzo M, Gómez-Serrano M, Lopez JA, Martin-Blazquez A, Vellosillo P, Minguez P, Martinez PJ, Vázquez J, Ruiz-Hurtado G, Barderas MG, Sarafidis P, Segura J, Ruilope LM, Alvarez-Llamas G. The Urinary Glycopeptide Profile Differentiates Early Cardiorenal Risk in Subjects Not Meeting Criteria for Chronic Kidney Disease. *Int J Mol Sci* 2024; **25**: 7005 [PMID: 39000114 DOI: 10.3390/ijms25137005]

5 **Pradita T**, Chen YJ, Su TH, Chang KH, Chen PJ, Chen YJ. Data Independent Acquisition Mass Spectrometry Enhanced Personalized Glycosylation Profiling of Haptoglobin in Hepatocellular Carcinoma. *J Proteome Res* 2024; **23**: 3571-3584 [PMID: 38994555 DOI: 10.1021/acs.jproteome.4c00227]

6 **Yui M**, Nagatake Y, Takehara S, Ito M, Watanabe K. Method for quantifying free hemoglobin, distinct from the hemoglobin-haptoglobin complex, in human serum. *Anal Biochem* 2024; **694**: 115601 [PMID: 38971527 DOI: 10.1016/j.ab.2024.115601]

7 **Li Y**, Wang F, Huang X, Zong S, Shen Y, Guo L, Cai Q, Sun T, Zhang R, Yu Z, Zhang L, Zang S, Liu J. First-trimester hemoglobin, haptoglobin genotype, and risk of gestational diabetes mellitus in a retrospective study among Chinese pregnant women. *Nutr Diabetes* 2024; **14**: 48 [PMID: 38951151 DOI: 10.1038/s41387-024-00309-y]

8 **Tullie S**, Nicholson T, Bishop JRB, McGee KC, Asiri A, Sullivan J, Chen YY, Sardeli AV, Belli A, Harrison P, Moiemen NS, Lord JM, Hazeldine J. Severe thermal and major traumatic injury results in elevated plasma concentrations of total heme that are associated with poor clinical outcomes and systemic immune suppression. *Front Immunol* 2024; **15**: 1416820 [PMID: 38947312 DOI: 10.3389/fimmu.2024.1416820]

9 **Mori M**, Sakamoto A, Kawakami R, Guo L, Slenders L, Mosquera JV, Ghosh SKB, Wesseling M, Shiraki T, Bellissard A, Shah P, Weinkauf CC, Konishi T, Sato Y, Cornelissen A, Kawai K, Jinnouchi H, Xu W, Vozenilek AE, Williams D, Tanaka T, Sekimoto T, Kelly MC, Fernandez R, Grogan A, Coslet AJ, Fedotova A, Kurse A, Mokry M, Romero ME, Kolodgie FD, Pasterkamp G, Miller CL, Virmani R, Finn AV. CD163(+) Macrophages Induce Endothelial-to-Mesenchymal Transition in Atheroma. *Circ Res* 2024; **135**: e4-e23 [PMID: 38860377 DOI: 10.1161/CIRCRESAHA.123.324082]

10 **Osmancik P**, Bacova B, Herman D, Hozman M, Fiserova I, Hassouna S, Melenovsky V, Karch J, Vesela J, Benesova K, Reddy VY. PeriProcedural Intravascular Hemolysis during Atrial Fibrillation Ablation: A Comparison of Pulsed Field with Radiofrequency Ablation. *JACC Clin Electrophysiol* 2024; **7**: 1672-1674 [DOI: 10.1016/j.jacep.2024.05.001]

11 **Quast C**, Bönner F, Polzin A, Veulemans V, Chennupati R, Gyamfi Poku I, Pfeiler S, Kramser N, Nankinova M, Staub N, Zweck E, Jokiel J, Keyser F, Hoffe J, Witkowski S, Becker K, Leuders P, Zako S, Erkens R, Jung C, Flögel U, Wang T, Neidlin M, Steinseifer U, Niepmann ST, Zimmer S, Gerdes N, Cortese-Krott MM, Feelisch M, Zeus T, Kelm M. Aortic Valve Stenosis Causes Accumulation of Extracellular Hemoglobin and Systemic Endothelial Dysfunction. *Circulation* 2024; **150** [PMID: 38836358 DOI: 10.1161/CIRCULATIONAHA.123.064747]

12 **Hopp MT**, Vaidya SM, Grimmig KM, Strudthoff LJ, Clauser JC, Yuan X, Singh S, Müller J, Oldenburg J, Hamza I, Imhof D. Quantitative analysis of heme and hemoglobin for the detection of intravascular hemolysis. *Anal Chim Acta* 2024; **1312**: 342766 [PMID: 38834280 DOI: 10.1016/j.aca.2024.342766]

13 **Misra S**, Kawamura Y, Singh P, Sengupta S, Nath M, Rahman Z, Kumar P, Kumar A, Aggarwal P, Srivastava AK, Pandit AK, Mohania D, Prasad K, Mishra NK, Vibha D. Prognostic biomarkers of intracerebral hemorrhage identified using targeted proteomics and machine learning algorithms. *PLoS One* 2024; **19**: e0296616 [PMID: 38829877 DOI: 10.1371/journal.pone.0296616]

14 **Liu L**, Hao S, Gou S, Tang X, Zhang Y, Cai D, Xiao M, Zhang X, Zhang D, Shen J, Li Y, Chen Y, Zhao Y, Deng S, Wu X, Li M, Zhang Z, Xiao Z, Du F. Potential applications of dual haptoglobin expression in the reclassification and treatment of hepatocellular carcinoma. *Transl Res* 2024; **272**: 19-40 [PMID: 38815898 DOI: 10.1016/j.trsl.2024.05.008]

15 **Delanghe JR**, Delrue C, Speeckaert R, Speeckaert MM. Unlocking the link between haptoglobin polymorphism and noninfectious human diseases: insights and implications. *Crit Rev Clin Lab Sci* 2024; **61**: 275-297 [PMID: 38013410 DOI: 10.1080/10408363.2023.2285929]

16 **Cahill LE**, Warren RA, Bahn GD, Carew AS, Levy AP, Sapp J, Rimm EB, Reaven P. Haptoglobin phenotype and intensive glycemic control for coronary artery disease risk reduction in people with type two diabetes: The Veterans Affairs Diabetes Trial. *Am J Prev Cardiol* 2024; **18**:

100681 [PMID: 38800835 DOI: 10.1016/j.ajpc.2024.100681]

17 **Li L**, Xu Y, Lai Z, Li D, Sun Q, Li Z, Zhou Y. Development and validation of a model and nomogram for breast cancer diagnosis based on quantitative analysis of serum disease-specific haptoglobin N-glycosylation. *J Transl Med* 2024; **22**: 331 [PMID: 38575942 DOI: 10.1186/s12967-024-05039-4]

18 **Koudouna A**, Gkioka AI, Gkiokas A, Tryfou TM, Papadatou M, Alexandropoulos A, Bartzi V, Kafasi N, Kyrtsonis MC. Serum-Soluble CD163 Levels as a Prognostic Biomarker in Patients with Diffuse Large B-Cell Lymphoma Treated with Chemoimmunotherapy. *Int J Mol Sci* 2024; **25**: 2862 [PMID: 38474108 DOI: 10.3390/ijms25052862]

19 **Bandyopadhyay S**, Garland P, Gaastra B, Zolnourian A, Bulters D, Galea I. The Haptoglobin Response after Aneurysmal Subarachnoid Haemorrhage. *Int J Mol Sci* 2023; **24**: 16922 [PMID: 38069244 DOI: 10.3390/ijms242316922]

20 **Ehle C**, Iyer-Bierhoff A, Wu Y, Xing S, Kiehntopf M, Mosig AS, Godmann M, Heinzel T. Downregulation of HNF4A enables transcriptomic reprogramming during the hepatic acute-phase response. *Commun Biol* 2024; **7**: 589 [PMID: 38755249 DOI: 10.1038/s42003-024-06288-1]

21 **Trakarnsanga K**, Thongsin N, Metheetrairut C, Tipgomut C, Poldee S, Wattanapanitch M. Genetic correction of haemoglobin E in an immortalised haemoglobin E/beta-thalassaemia cell line using the CRISPR/Cas9 system. *Sci Rep* 2022; **12**: 15551 [PMID: 36114353 DOI: 10.1038/s41598-022-19934-7]

22 **Kaminski TW**, Sivanantham A, Mozhenkova A, Smith A, Ungalara R, Dubey RK, Shrestha B, Hanway C, Katoch O, Tejero J, Sundd P, Novelli EM, Kato GJ, Pradhan-Sundd T. Hemoglobin scavenger receptor CD163 as a potential biomarker of hemolysis-induced hepatobiliary injury in sickle cell disease. *Am J Physiol Cell Physiol* 2024; **327**: C423-C437 [PMID: 38682236 DOI: 10.1152/ajpcell.00386.2023]

23 **Wu J**, Feng S, Luo Y, Ning Y, Qiu P, Lin Y, Ma F, Zhuo Y. Transcriptomic profile of premature ovarian insufficiency with RNA-sequencing. *Front Cell Dev Biol* 2024; **12**: 1370772 [PMID: 38655066 DOI: 10.3389/fcell.2024.1370772]

24 **Munoz CJ**, Lucas D, Martinez J, Ricario M, O'Boyle QT, Pires IS, Palmer AF, Cabrales P. Toxic side-effects of diaspirin cross-linked human hemoglobin are attenuated by the apohemoglobin-haptoglobin complex. *Biomed Pharmacother* 2024; **174**: 116569 [PMID: 38603886 DOI: 10.1016/j.biopha.2024.116569]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com