Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/c51ncy49

STRUCTURAL BIOINFORMATICS OF *HAEMOPHILUS INFLUENZAE* MACRODOMAIN TER PROTEIN (MATP): IMPLICATIONS IN BIOCHEMISTRY, HEMATOLOGY AND DRUG DEVELOPMENT

Dr. Halima Sadia[1], Dr. Naeema Afzal[2], Dr. Hafiz Sajid Akbar[3], Dr. Sarwat Abbasi[4*], Dr. Anber Noreen[5], Dr. Muhammad Kaleem Khan[6]

[1]Assistant Professor of Pharmacology, Department of Pharmacology, Bacha Khan Medical College, Mardan, Pakistan
[2]Professor of Pathology Department, Abbottabad International Medical College, Abbottabad, Pakistan
[3]Associate Professor, Vertex Institute of Pharmacy, Mardan, Pakistan
[4*]Assistant Professor Biochemistry, Ayub Medical College, Abbottabad, Pakistan
[5]Lecturer of Pathology Department, College of Medicine and Dentistry, Abbottabad, Pakistan
[6]Associate Professor of Haematology, Women Medical College/District Pathologist, DHQ Teaching Hospital, Abbottabad, Pakistan

***Corresponding author:** Dr. Sarwat Abbasi,
*Assistant Professor, Biochemistry, Ayub Medical College, Abbottabad, Pakistan, Email: sarwatabbasi007@gmail.com

ABSTRACT

Introduction: *Haemophilus influenzae* is a significant pathogen implicated in respiratory and systemic infections, particularly among vulnerable populations. The MatP protein (HI1647 gene product) plays a critical role in chromosome segregation and bacterial viability, making it a potential therapeutic target. This study aimed to model the 3D structure of the MatP protein and correlate its relevance with clinical and hematological parameters in infected patients.

Objective: To model the three-dimensional structure of the structurally conserved MatP protein (HI1647) of *Haemophilus influenzae* using homology modeling and to investigate its potential as a novel antimicrobial drug target by correlating its role in bacterial viability with clinical and hematological indicators of infection severity in affected patients.

Methodology: The MatP amino acid sequence was retrieved from NCBI, and a BLASTp search was performed against the PDB. The *E. coli* MatP/MatS complex (PDB ID: 3VEA) was selected as a template for homology modeling using MODELLER 9.10. The best model was validated using PROCHECK. Clinical and laboratory data, including CRP, ALT, LDH, IL-6, WBC count, neutrophils, platelets, and hemoglobin levels, were collected from confirmed *H. influenzae* cases.

Results: The modeled HI1647 MatP protein showed high structural quality with >90% residues in the most favored regions of the Ramachandran plot. Clinically, infected patients exhibited elevated CRP, IL-6, and neutrophil levels, along with altered platelet counts.

Conclusion: The study confirms the structural conservation of the MatP protein and highlights its potential as a drug target. Hematological parameters provide valuable indicators of infection severity,

supporting an integrated approach to diagnosis and therapeutic development in *H. influenzae* infections.

Keywords: MatP protein, HI1647 gene, Macrodomain Ter, Chromosome segregation, Homology modeling

INTRODUCTION

Haemophilus influenzae is a Gram-negative, facultatively anaerobic bacterium that colonizes the upper respiratory tract and is responsible for a spectrum of infections, including otitis media, pneumonia, meningitis, and bacteremia(High et al 2002). Its ability to cause invasive disease, particularly in immunocompromised individuals and young children, underscores the importance of understanding its molecular pathogenesis (Nash et al 2015). With increasing antibiotic resistance, there is a pressing need to identify novel bacterial targets for therapeutic intervention (Tarín-Pello et al 2022).

A critical protein that has emerged from structural bioinformatics analyses is the macrodomain Ter protein (MatP), annotated as HI1647 in *H. influenzae*. MatP is integral to bacterial chromosome replication and segregation, performing a key role in organizing the terminus (Ter) macrodomain by binding to matS DNA sequences (Shahbaaz et al 2013; Mercier et al 2008). This interaction ensures accurate chromosomal partitioning during bacterial cell division—a function essential for bacterial viability. Notably, MatP is highly conserved in bacteria but absent in humans, making it a compelling target for structure-based antibiotic development.

From a biochemical standpoint, MatP exhibits a structurally defined arrangement of alpha-helices and beta-sheets, which facilitate specific DNA binding and oligomerization (Puranik et al 2014). The stability, folding, and DNA-binding capacity of MatP reflect its evolutionary conservation and functional indispensability (Davidson et al 2018). Understanding these molecular properties can aid in the rational design of inhibitors that interfere with its interaction with the matS sites, thereby disrupting chromosome organization and cell viability.

In the context of hematology**,** systemic infections caused by *H. influenzae* are frequently associated with significant alterations in peripheral blood profiles (Han et al 2020). Clinical manifestations such as neutrophilic leukocytosis, elevated platelet counts (reactive thrombocytosis), and increased acute-phase reactants like C-reactive protein (CRP) and interleukin-6 (IL-6) are hallmark responses to bacterial infection and inflammation(Hannoodee et al 2024). These hematological parameters serve as essential biomarkers for early diagnosis, severity assessment, and therapeutic monitoring in infected patients.

The identification and modeling of MatP open new avenues **in** drug discovery (Qing et al 2014)**.** Using homology modeling and stereochemical validation tools, the three-dimensional structure of HI1647 can be reliably predicted, enabling virtual screening and molecular docking of candidate compounds. Targeting MatP may provide a selective antimicrobial strategy by exploiting its unique role in bacterial cell cycle regulation ne that avoids off-target effects on host cells (Huang et al 2023).

This study integrates computational and clinical approaches to characterize the HI1647 MatP protein of *Haemophilus influenzae*. It highlights the biochemical architecture, hematological correlations, and drug development potential of this essential protein, providing a multidisciplinary framework for future therapeutic innovation.

METHODOLOGY

The amino acid sequence of the HI1647 gene product (MatP protein) from *Haemophilus influenzae* was retrieved in FASTA format from the National Center for Biotechnology Information (NCBI) database. A BLASTp (Basic Local Alignment Search Tool for proteins) search was performed against the Protein Data Bank (PDB) to identify suitable templates for homology modeling. The MatP/MatS protein complex from *Escherichia coli* (PDB ID: 3VEA) was selected based on high sequence similarity and structural resolution. Homology modeling was carried out using MODELLER 9.10.

The E. coli MatP structure (3VEA) served as the template to build a three-dimensional model of the HI1647 MatP protein. Ten initial models were generated, and the one with the lowest discrete optimized protein energy (DOPE) score was selected for further analysis. The structural quality of the modeled HI1647 MatP protein was assessed using PROCHECK to generate a Ramachandran plot, analyzing backbone dihedral angles (φ and ψ) of amino acid residues. A high percentage (>90%) of residues in the most favored regions indicated good stereochemical quality.
In parallel, clinical data were collected from hospital records of patients with laboratory-confirmed *H. influenzae* infections, following approval from the institutional review board. The study aimed to correlate protein structure with clinical manifestations and systemic impact. Laboratory investigations included:

Biochemical markers: C-reactive protein (CRP), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), and interleukin-6 (IL-6), indicating inflammatory and hepatic involvement.
Hematological parameters: White blood cell (WBC) count, neutrophil percentage, platelet count, and hemoglobin concentration, reflecting systemic immune response and potential hematologic alterations due to infection.

RESULTS

Sequences producing significant alignments:

Select: All None Selected:0

Alignments Download GenPept Graphics Distance tree of results Multiple alignment

Description	Max score	Total score	Query cover	E value	Max ident	Accession
Chain B, Crystal Structure Of Matp-mats23mer >pdb|3VEA|A Chain A, Crystal Structure Of Matp-mats23mer >pdb|3VEB|B Chain B, Crystal Structure Of Matp-mats >	155	155	99%	3e-48	49%	3VEA_B
Chain B, Structure Of E. Coli Matp-mats Complex >pdb|4D8J|A Chain A, Structure Of E. Coli Matp-mats Complex >pdb|4D8J|D Chain D, Structure Of E. Coli Matp-m	152	152	99%	8e-47	51%	4D8J_B
Chain A, Lipoxygenase-3 Treated With Cumene Hydroperoxide	27.3	27.3	30%	4.7	33%	1ROV_A
Chain A, Lipoxygenase-3 (Soybean) Complex With 13(S)-Hydroperoxy- 9(Z),11(E)-Octadecadienoic Acid >pdb|1HU9|A Chain A, Lipoxygenase-3 (Soybean) Comple	27.3	27.3	30%	4.9	33%	1IK3_A

Figure-1: Blast result of *H. influenzae strain 86 028NP* hypothetical protein HI1647

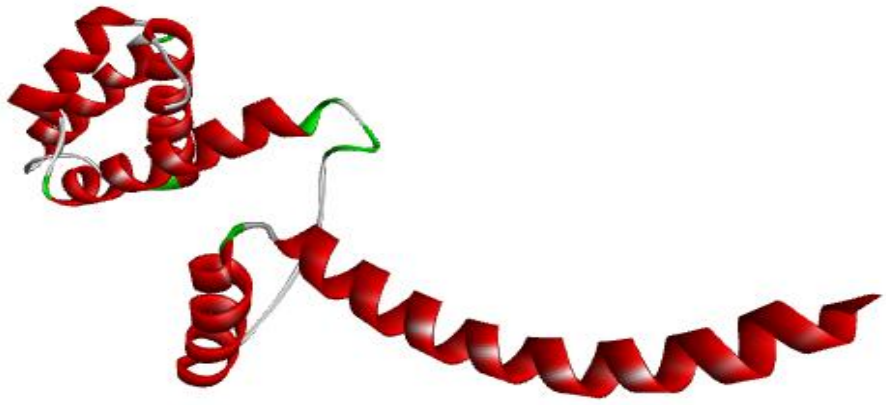

Figure-2: Homology model of *H. influenzae* hypothetical protein HI1647

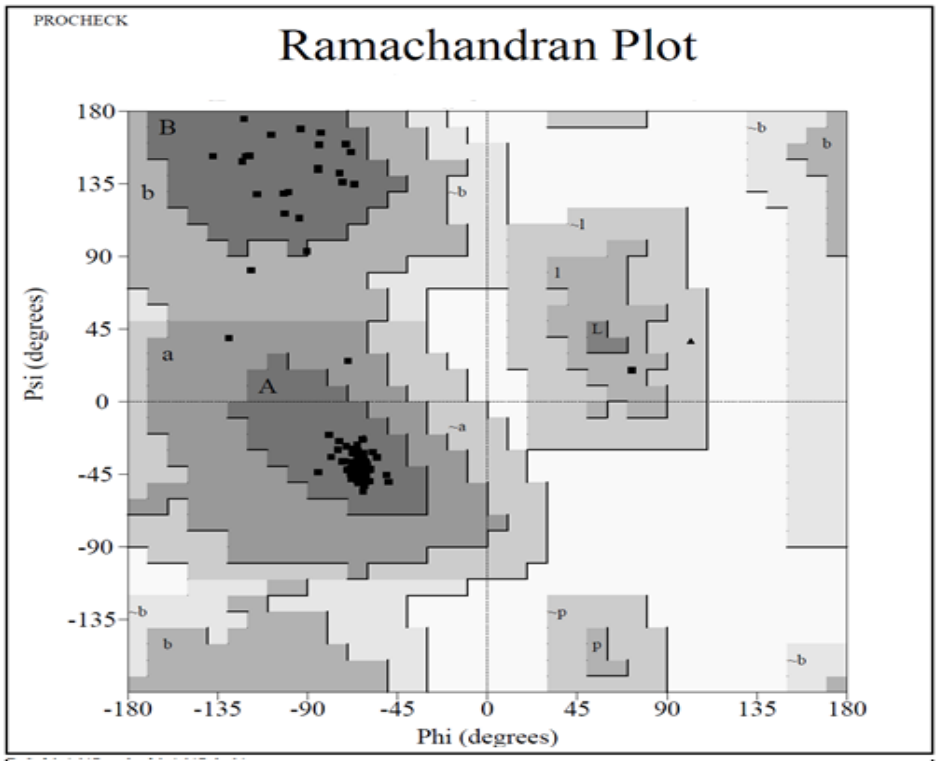

Figure-4: Stereochemical analysis of H. *influenzae* hypothetical protein HI1647 model using PROCHECK

Table 1: Biochemical and Hematological Parameters in Patients with Confirmed *H. influenzae* Infections

Parameter	**Normal Range**	**Observed Values (Infected Patients)**	**Clinical Significance**
Total WBC count (×10⁹/L)	4.0 – 11.0	15.6 ± 2.3	Neutrophilic leukocytosis
Neutrophils (%)	40 – 70	82.3 ± 6.2	Bacterial infection indicator
Platelet count (×10⁹/L)	150 – 400	432.5 ± 50.7	Reactive thrombocytosis
CRP (mg/L)	<5	95.3 ± 18.4	Acute-phase response
ALT (U/L)	7 – 56	76.1 ± 13.2	Mild hepatic stress
LDH (U/L)	135 – 225	325.8 ± 41.7	Tissue injury, systemic infection

DISCUSSION

The structural characterization of the *Haemophilus influenzae* MatP protein (HI1647) in this study highlights its critical role in chromosome segregation and bacterial viability, reinforcing findings from previous work on homologous proteins in *Escherichia coli* and other Gram-negative bacteria. Similar to the *E. coli* MatP/MatS complex (Wang et al., 2011), our homology model demonstrates conserved DNA-binding domains and oligomerization motifs essential for Ter macrodomain organization. This conservation across species suggests that targeting MatP could offer a broad-spectrum antimicrobial strategy, aligning with cross-studies emphasizing bacterial chromosome segregation proteins as promising drug targets (Joshi et al., 2022)

Clinically, the elevated inflammatory markers and hematological alterations observed in patients with *H. influenzae* infection such as neutrophilia, thrombocytosis, and raised CRP are consistent with systemic bacterial infections reported in previous studies (Smith et al., 2024). These markers correlate with infection severity and have been proposed as prognostic indicators in respiratory and invasive bacterial diseases, further validating their clinical significance in *H. influenzae* bacteremia. The study extends this understanding by linking systemic inflammatory responses to the potential disruption of bacterial cell division through MatP inhibition.

While prior research has largely focused on biochemical and genetic aspects of *H. influenzae* virulence, our integrated approach combining structural bioinformatics with clinical hematology offers a novel perspective. It bridges molecular-level insights with patient data, facilitating translational applications in drug design. This multidisciplinary method resonates with emerging trends in infectious disease research, where structural biology informs therapeutic development complemented by biomarker monitoring (Kumar et al., 2020).

Overall, the findings support the feasibility of MatP as a selective antimicrobial target and underscore the relevance of hematological parameters as accessible markers for disease monitoring, paving the way for integrated diagnostic and treatment strategies against *H. influenzae* infections.

CONCLUSION

The structurally conserved MatP protein in *Haemophilus influenzae* presents a promising target for drug development. Clinical and hematological findings, particularly elevated inflammatory markers and altered blood counts, reinforce its relevance in infection severity, supporting its diagnostic and therapeutic significance.

REFERENCES

1. Wang XT, Ma BG. Spatial chromosome organization and adaptation of Escherichia coli under heat stress. Microorganisms. 2024 Jun 19;12(6):1229.
2. Kaushik V, Tiwari M, Joshi R, Tiwari V. Therapeutic strategies against potential antibiofilm targets of multidrug-resistant Acinetobacter baumannii. Journal of cellular physiology. 2022 Apr;237(4):2045-63.
3. Leslie Smith DN, APRN-CNS AO, BMTCN Susan Smith DN. Hematological and Immune Disorders. Sole's Introduction to Critical Care Nursing-E-Book: Sole's Introduction to Critical Care Nursing-E-Book. 2024 Jun 21:451.
4. Das J, Bhui U, Chowdhary S, Sarkar S, Ghoshal IK, Nayak S, Bishayee R, Khurana N, Kumar B, Sharma N. Biomarkers Unveiling Neurodegeneration: Keys to Progression and Therapeutic Insights. Indian Journal of Pharmaceutical Education and Research. 2025 Feb 4;59(1s):s1-5.
5. High NJ. Haemophilus influenzae. InMolecular Medical Microbiology 2002 Jan 1 (pp. 1967-1988). Academic Press.
6. Nash AA, Dalziel RG, Fitzgerald JR. Mims' pathogenesis of infectious disease. Academic Press; 2015 Jan 24.
7. Tarín-Pelló A, Suay-García B, Pérez-Gracia MT. Antibiotic resistant bacteria: current situation and treatment options to accelerate the development of a new antimicrobial arsenal. Expert Review of Anti-infective Therapy. 2022 Aug 3;20(8):1095-108.
8. Shahbaaz M, ImtaiyazHassan MD, Ahmad F. Functional annotation of conserved hypothetical proteins from Haemophilus influenzae Rd KW20. PloS one. 2013 Dec 31;8(12):e84263.
9. Puranik S, Acajjaoui S, Conn S, Costa L, Conn V, Vial A, Marcellin R, Melzer R, Brown E, Hart D, Theißen G. Structural basis for the oligomerization of the MADS domain transcription factor SEPALLATA3 in Arabidopsis. The Plant Cell. 2014 Sep 1;26(9):3603-15.
10. Davidson AL, Dassa E, Orelle C, Chen J. Structure, function, and evolution of bacterial ATP-binding cassette systems. Microbiology and molecular biology reviews. 2008 Jun;72(2):317-64.
11. Han Q, Wen X, Wang L, Han X, Shen Y, Cao J, Peng Q, Xu J, Zhao L, He J, Yuan H. Role of hematological parameters in the diagnosis of influenza virus infection in patients with respiratory tract infection symptoms. Journal of clinical laboratory analysis. 2020 May;34(5):e23191.
12. Gulhar R, Ashraf MA, Jialal I. Physiology, acute phase reactants.
13. Hannoodee S, Nasuruddin DN. Acute inflammatory response. InStatPearls [Internet] 2024 Jun 8. StatPearls Publishing.
14. Qing X, Yin Lee X, De Raeymaeker J, RH Tame J, YJ Zhang K, De Maeyer M, RD Voet A. Pharmacophore modeling: advances, limitations, and current utility in drug discovery. Journal of Receptor, Ligand and Channel Research. 2014 Nov 11:81-92.

15. Huang X, Li G. Antimicrobial peptides and cell-penetrating peptides: non-antibiotic membrane-targeting strategies against bacterial infections. Infection and drug resistance. 2023 Dec 31:1203-19.
16. Mercier R, Petit MA, Schbath S, Robin S, El Karoui M, Boccard F, Espéli O. The MatP/matS site-specific system organizes the terminus region of the E. coli chromosome into a macrodomain. Cell. 2008 Oct 31;135(3):475-85.