

# EXPLORING HISTONE DERIVED NOVEL ANTI-MICROBIAL PEPTIDES IN ARCHAEBACTERIA



Ishika Rai  
B.Tech (IT & MI), University of Delhi, Delhi-110007, India



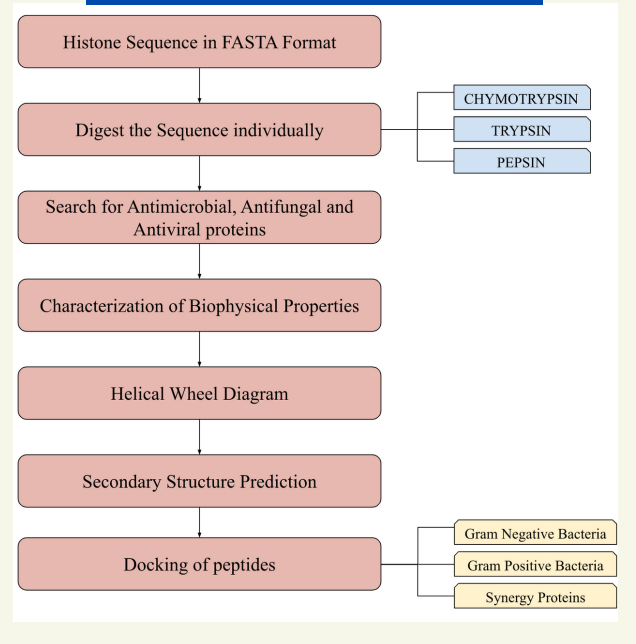
Mentor  
Dr. Jogeshwar S. Purohit

## ABSTRACT

In this study, we investigated the potential of using archaeal histones (HMfB and H1b) to exert their antimicrobial activity in humans. We used computational methods to explore the molecular properties of some ligands and various anti-inflammatory peptides (AMPs).

We found that peptides that exhibit antibacterial properties with higher affinity for some ligands than others are a promising starting point for the development of new antibiotics. AMP's ability to bind suggests that it may have antibacterial and anti-fungal properties, making it a potential drug for the treatment of infections with antibiotics.

## METHODOLOGY



## OBJECTIVES

The aim of the study was to provide insights into the factors that contribute to the antimicrobial activity of the histone proteins and to provide a basis for further experimental studies to validate these findings.

- Digestion of Histone sequences with Chymotrypsin, Trypsin and Pepsin using WebExPasy
- Finding the peptides showing anti-microbial activity using CAMP database
- Scoring anti-microbial peptides on the basis of their anti-fungal, anti-viral and biophysical properties.
- Creating a helical wheel diagram to analyze helical region of the peptides
- Evaluating these peptides for their MOTIFs and in vivo aggregation properties
- Docking of relevant peptides with specific proteins to predict the efficacy of the peptides as an anti-microbial agent

## WHAT IS KNOWN

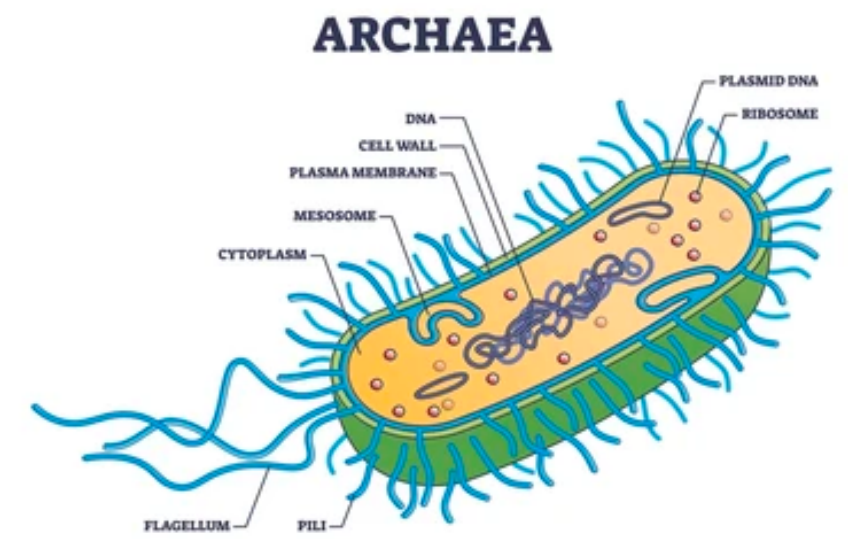
Prior to this project, it was already known that histone proteins are important in regulating gene expression and chromatin organization in eukaryotic organisms. However, the study of histone proteins in archaea is a relatively new field, and their functions and properties are not well understood.

## WHAT IS NEW

In this project, we have applied computational methods to investigate the potential antimicrobial properties of archaeobacterial histone proteins. Our findings suggest that these proteins possess conserved motifs and biochemical properties that are associated with antimicrobial activity. Additionally, our molecular docking studies suggest that these proteins have the potential to interact with the cell membranes of pathogens.

## INTRODUCTION

Archaea are a group of prokaryotes with unique features compared to other organisms. They are often found in hot springs, salt pans, and deep-sea hydrothermal vents. One of the key factors involved in these processes is the histone proteins found in archaeal cells. The archaeal histones are characterized by small, efficient, and unique folding patterns that allow them to interact with DNA in a specific way and have been shown to be involved in DNA packaging, gene editing, and DNA repair. A particularly interesting feature of archaeal histones is their antimicrobial properties. Histones have been shown to play a role in the regulation of the human immune system. The immunological properties of histones have important implications for human health. They can be used as a new class of antibiotics in the treatment of diseases caused by bacteria that have become resistant to antibiotics.



## RESULTS

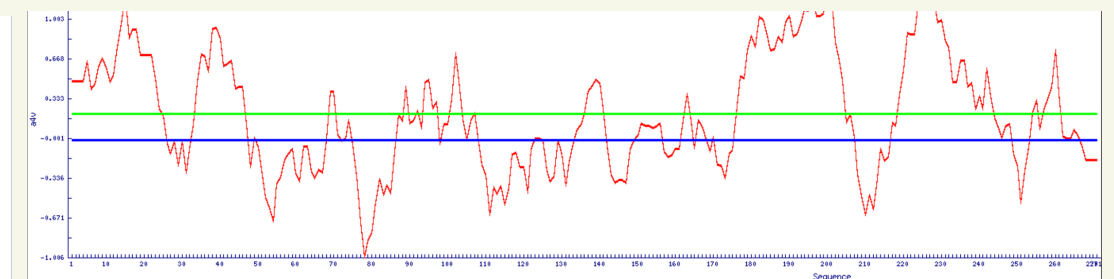
### PROTEIN SEQUENCE H1b

S. NO	PEPTIDE	AMP	SVN	RF	ANN	DA	ANTI-FUNGAL	ANTI-VIRAL
1	HM-1 AANVEKANTDOR	Y	0.544	0.595	1	0.857	N	N
2	VNMTAESPAASDF	N	0.044	0.027	0	0.008	-	-
3	HM-2 QVNFRL	Y	0.794	0.227	1	0.971	N	N
4	LQRLAPECV	N	0.022	0.342	0	0.001	-	-
5	HM-3 SDTARRKARKVVDLKLKSDVVP ADCLVDRLSRCEVNAALTSGL PATKDTLRLMDSYKREGGAVVY EVGERTVF	Y	0.959	0.808	1	1	N	N
6	SDTARRKARKVVDGL	N	0.235	0.477	0	0.091	-	-
7	HM-4 QLRLKSDVVPADCLVDRLSR L	Y	0.923	0.649	1	0.725	N	N
8	KSDVVPADCI	N	0.742	0.549	0	0.022	-	-
9	PATKDTLRL	N	0.048	0.234	0	0.002	-	-
10	QKADMSYKRESDVF	N	0.2	0.396	0	0.004	-	-
11	LSVVV	N	0.029	0.444	0	0	-	-

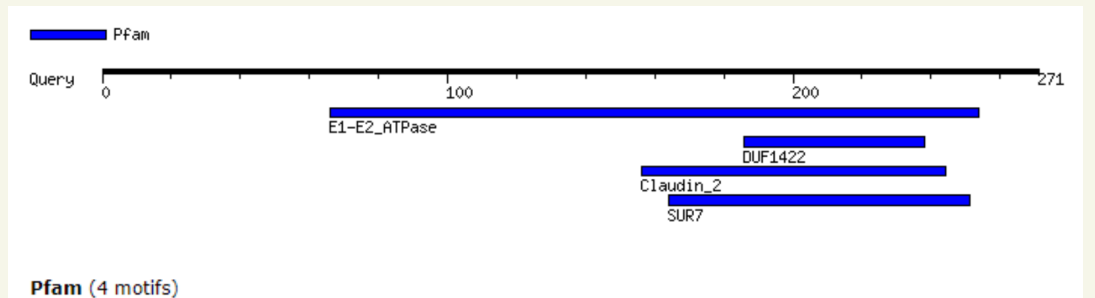
Scoring of sequences for anti-microbial and various properties

Cleavage map with Chymotrypsin

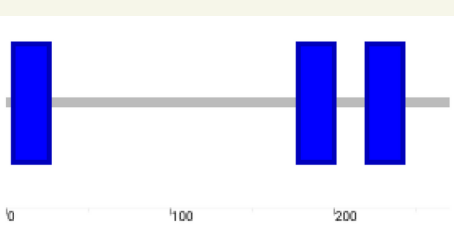
Cleavage map with Trypsin



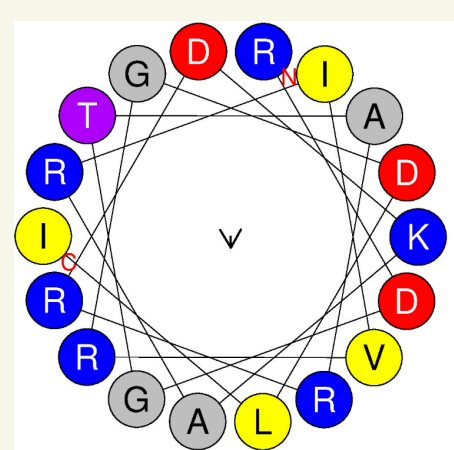
In-Vivo Aggregation of the peptide



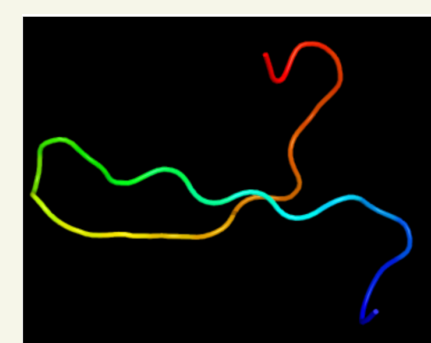
MOTIF of the peptide



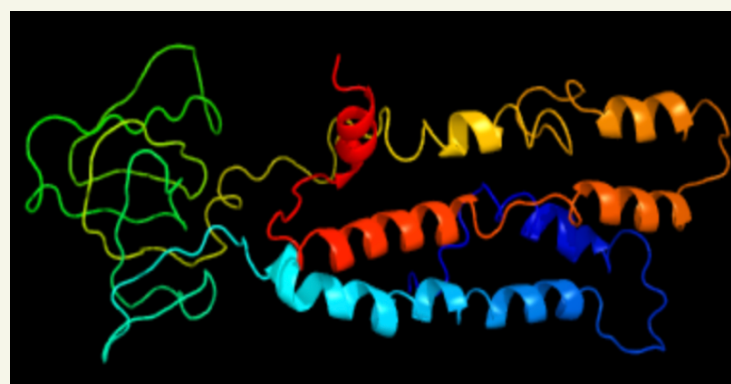
Domains in the Histone Protein



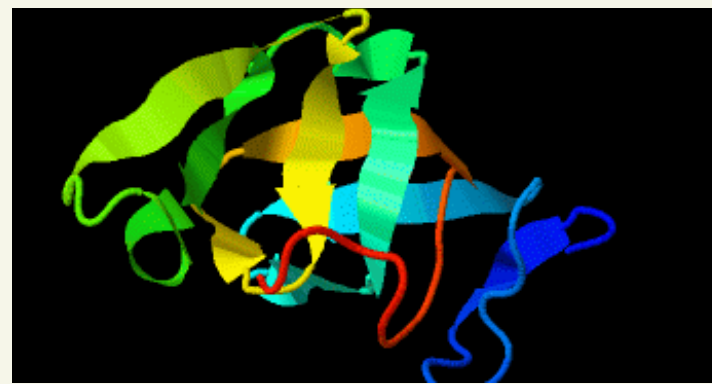
Helical Wheel of the peptide



Protein Folding Structure of HMfB-3



Protein Folding Structure of the Peptide



Molecular Docking of the Peptide with DNA Gyrase



Molecular Docking of HMfB-3 with DNA Gyrase

## CONCLUSION

In conclusion, our study has shown that archaeobacterial histone proteins possess strong antimicrobial properties that make them promising candidates for the development of new antimicrobial agents. The molecular docking studies have provided evidence that these proteins can bind to the cell membranes of pathogens and disrupt their integrity, leading to cell death. The analysis of the biochemical properties and conserved motifs of the histone proteins has provided insights into the factors that contribute to their antimicrobial activity.

## FUTURE PROSPECTS

The findings of our study suggest that archaeobacterial histone proteins possess promising antimicrobial properties that could be explored for the development of new therapeutic agents. However, to validate these findings and further explore the potential of these proteins, experimental studies are required. These could include in vitro and in vivo assays to assess the antimicrobial activity of the histone proteins against a range of bacterial and fungal pathogens.

## REFERENCES

Singh, A., Kar, S. K., Modak, S. B., Chaturvedi, M. M., & Purohit, J. S. (2021). Extra-nuclear histones: origin, significance and perspectives. *Molecular and Cellular Biochemistry*, 477(2), 507–524. <https://doi.org/10.1007/s11010-021-04300-4>