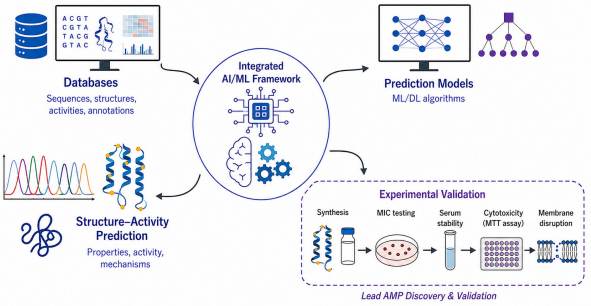
*Presenting Author

AN INTEGRATED AI-GUIDED PIPELINE FOR ANTIMICROBIAL PEPTIDE DISCOVERY AND OPTIMIZATION

Maryam Nawaz[1*], Ma Tianyue[1], Fahad Akhtar, Liu Hongyu[1], Amna Farooq, Heng Zheng[1#],
[1] *School of Life Science and Technology, China Pharmaceutical University, Nanjing 211100, PR China*
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Introduction

- Antimicrobial peptides represent a promising therapeutic space for addressing drug-resistant infections, yet their translation is constrained by the complex relationship between sequence, physicochemical properties, potency and host compatibility.
- Bridging computational prediction with experimentally validated function remains a key challenge in antimicrobial peptide discovery.



Our Laboratory Peptide Databases

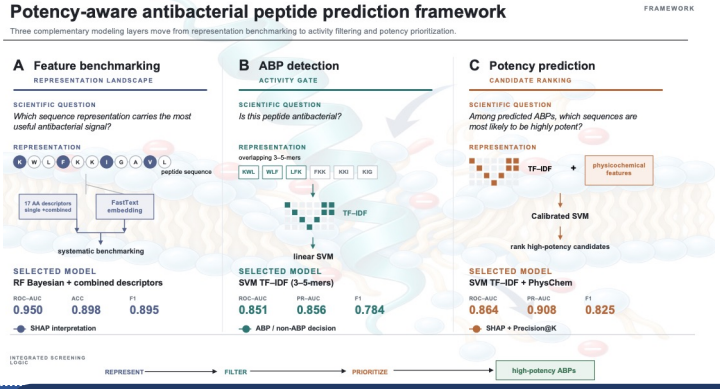
- To address these challenges, our lab integrates artificial intelligence (AI) with peptide biology to accelerate discovery, design, and validation.
- By leveraging AI-driven analyses of curated peptide datasets, we enable predictive modeling, hypothesis generation, and data-informed experimentation, advancing the development of next-generation peptide therapeutics.

DRAMP DRAVP DCTPep HORDB

Multi-Stage Computational Framework for Antibacterial Peptide Discovery

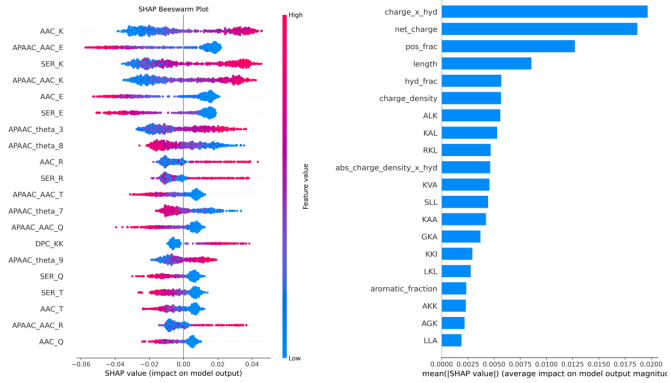
Computational prediction framework

- A multi-stage machine-learning pipeline was developed to benchmark peptide representations, classify antibacterial peptides, and predict antibacterial potency for candidate prioritization.



Model interpretation

- SHAP analysis identified the sequence and physicochemical features that contributed most strongly to antibacterial activity and potency predictions, highlighting the importance of charge, hydrophobicity, and amino-acid composition.

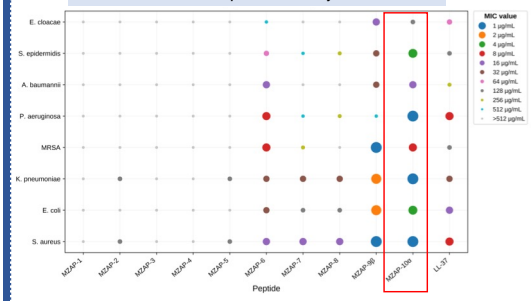


Computationally Guided Physicochemical Optimization of LL-37–Derived Novel Peptides

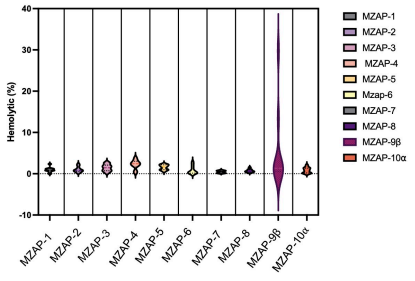
Experimental Validation

- Antibacterial activity was evaluated by MIC/MBC profiling across Gram-positive and Gram-negative pathogens.
- Lead candidates were further assessed for hemolysis, mammalian-cell compatibility, serum stability, and bacterial morphology.

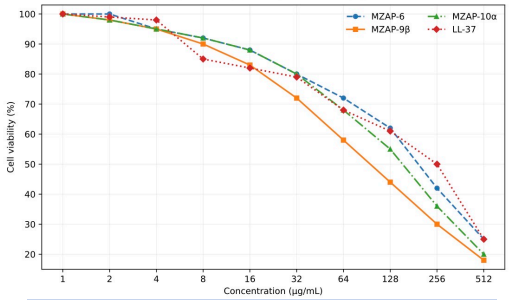
MZAP peptides Display Broad-Spectrum Antibacterial Activity with Strain-Dependent Variability



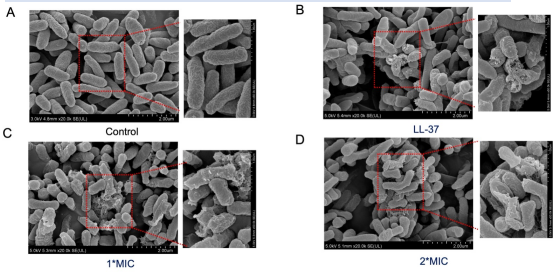
MZAP Peptides Exhibit Minimal Hemolytic Activity at Therapeutically Relevant Concentrations



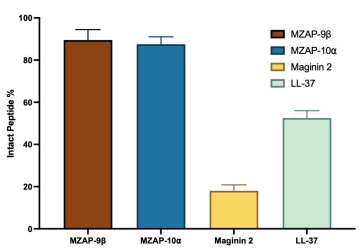
Selected MZAP peptides Maintain High Mammalian Cell (HEK-293T) Viability at Active Concentrations



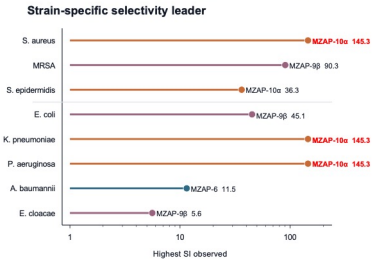
MZAP-10α Induces Concentration-Dependent Morphological Disruption of P.Aeruginosa cells



MZAP Peptides Show Enhanced Serum Stability Compared to LL-37



Selectivity Index Analysis Identifies MZAP-10α as the Most Balanced Antimicrobial Candidate



- ***MZAP-10α showed the most favorable overall balance of potency, stability, and host-cell compatibility.***

Conclusion

- Interpretable ML identified sequence and physicochemical features predictive of antibacterial potency.
- ML-guided prioritization coupled with experimental validation enabled efficient identification of active LL-37-derived peptides.
- MZAP-10α emerged as a lead candidate for further preclinical evaluation.
- The integrated computational–experimental workflow provides a data-informed framework for antimicrobial peptide discovery and optimization

Future Directions

- In vivo validation
- Mechanistic characterization
- Sequence optimization

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- Ma, T., et al., DRAMP 4.0: an open-access data repository dedicated to the clinical translation of antimicrobial peptides. Nucleic Acids Research, 2024.53(D1): p. D403-D410

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