

**PRODUCTION OF ANTIMICROBIAL PEPTIDES WITH PREDICTED
PROPERTIES ENABLED THROUGH AI-DRIVEN DISCOVERY**

Vera Shaniavskaia (ITMO University), **Al-Abbass Mohamed** (ITMO University), **Georgy Otinov** (ITMO University)

Supervisor – Head of Laboratory, Dr. Elena Koshel (ITMO University)

Introduction: The emerging problem of multidrug resistance in microorganisms has significantly lowered the effectiveness of standard antibiotic treatments. Antimicrobial peptides (AMPs) are a promising alternative as they have a broad-spectrum activity and lower likelihood of developing resistance due to their dual mechanism of function that both targets bacterial membranes and triggers immune response [1].

Despite several advantages of AMPs over traditional antibiotics, their widespread usage is limited by several issues, such as susceptibility to proteolytic degradation in physiological conditions, off-target toxicity and high production cost. Stability and specificity can be improved with structural modifications, while the cost of production could be lowered by the development of genetically engineered microbial expression systems [2].

Main part: The main goal of this study is to design and produce safe and effective drug candidates that could become an alternative to traditional antibiotics while lowering the chances of developing resistance.

In order to achieve this goal we examined the amino acid sequences of known AMPs using sequence alignment methods and identified conserved motifs and residues responsible for specific functions. This allows us to design novel peptides that merge the properties of different AMPs, providing targeted activity while maintaining safety and efficacy.

The structure and properties of new peptides is predicted *in silico* using a machine learning algorithm, an approach that makes the process of AMP development significantly more time and cost-effective [3]. Designed sequences of potential drug candidates are cloned into pET303CT/His and pET15b vectors using restriction-ligation method. Expressed recombinant peptides are purified and empirically assessed to determine their antimicrobial activity to ensure effectiveness, and hemolytic activity to rule out non-specific killing.

Conclusion: Proposed approach allows for the development of safer, more stable antimicrobial peptides with predicted activity with the additional advantage of reduced cost enabled by expression through bacterial vectors. Incorporation of artificial intelligence promises to notably facilitate this process, which in turn will speed up the transition of designed AMPs into clinical trials.

References:

1. Magana M, Pushpanathan M, Santos AL, et al. The value of antimicrobial peptides in the age of resistance. *Lancet Infect Dis.* 2020. doi:10.1016/s1473-3099(20)30327-3.
2. Bucataru C, Ciobanasu C. Antimicrobial peptides: Opportunities and challenges in overcoming resistance. *Microbiol Res.* 2024;286:127822. doi:10.1016/j.micres.2024.127822.
3. Wan F, Wong F, Collins JJ, et al. Machine learning for antimicrobial peptide identification and design. *Nat Rev Bioeng.* 2024;2:392-407. doi:10.1038/s44222-024-00152-x.