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Production of specifically targeted antimicrobial peptides with predicted properties facilitated by AI-driven validation

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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]. However, broad-spectrum AMPs can disrupt the host's beneficial microbiota and potentially have a cytotoxic effect, highlighting the need for more selective antimicrobial agents.

The main goal of this study is the development of Specifically Targeted AntiMicrobial Peptides (STAMPs) as a strategy to address this challenge and develop a safer and more effective alternative to antibiotics while minimizing the chances of developing resistance [3].

In order to achieve this goal we employ a hybrid peptide strategy to combine a broad-spectrum AMP with a targeting peptide domain to enhance specificity. This allows us to design novel peptides that provide targeted activity while maintaining safety and efficacy.

The structure and properties of new peptides, such as MIC and activity levels, is predicted in silico using a machine learning algorithm based on the data from DBAASP that contains known AMP sequences and working concentrations. This approach makes the process of STAMP development significantly more time and cost-effective by allowing to obtain preliminary results before the peptides are produced and tested [4]. 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.

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 streamline the STAMP development process through validation of antimicrobial properties of new peptides before they are tested experimentally, which will significantly reduce timelines of the experiment.

References

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