
AI-Generated Fluorescent Antimicrobial Peptides: From De Novo Design to Mode-of-Action Elucidation

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Résumé

Fluorescent probes for detecting pathogenic bacteria have emerged as promising tools for the clinical diagnosis of infectious diseases. Their design is typically based on bacteria-targeting antibiotics or antimicrobial peptides (AMPs). To date, however, most of these probes have relied on a limited repertoire of naturally occurring AMPs, while the vast sequence space of linear peptides of comparable length ($> 10^4$) remains largely unexplored. In this context, artificial intelligence (AI) approaches offer a powerful alternative to traditional screening methods by enabling the rational design of molecular structures with tailored properties (1). In this study, we investigate the feasibility of leveraging explainable AI models to design bacteria-targeting fluorescent probes, thereby expanding the toolkit for infectious disease diagnostics. Ten selected peptides were synthesized, evaluated for their activity against a panel of model bacteria, and their mode of action was investigated using a combination of biophysical and chemical approaches. The lead peptide exhibited a low-micromolar MIC against Gram-positive bacteria, including *Staphylococcus aureus*. Finally, the peptides were labelled with a red fluorophore to generate bright fluorescent probes, which will be further optimized as tools for the clinical detection of bacteria.

Références : _

K. Pikalyova, et al. *J. Chem. Inf. Model.* **2026**, *66*, 744

Mots-Clés: Fluorescent probes, Antimicrobial peptides, Artificial intelligence

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