De novo Structure-Based Design of TEM-171 Beta-Lactamase Protein Inhibitors Using Integrated Deep Learning and Multi-Scale Simulations to Combat Bacterial Resistance

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The emergence of TEM-171 Beta-lactamase represents a significant threat to modern antimicrobial therapy due to its ability to hydrolyze an extended spectrum of Beta-lactam antibiotics. While traditional Beta-lactamase inhibitors like tazobactam show diminishing efficacy against this enzyme, no true systematic approach exists for developing targeted protein-based inhibitors. Here, I present an integrated computational pipeline for de novo protein design targeting TEM-171 Beta-lactamase, combining quantum-inspired diffusion models with evolutionary optimization. Beyond the immediate therapeutic application, the generalizable framework demonstrates development time per design and success rate much more efficient compared to in-vitro methods of generating stable protein-protein interfaces, overall establishing an effective pipeline for therapeutic protein development. These findings not only present a promising candidate for combating TEM-171-mediated resistance, but also provide a wider-scale methodology for addressing emerging therapeutic challenges, such as bacterial resistance as a whole, through rational protein design.

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