Design and Synthesis of Unprecedented Cyclic γ-AApeptides for Antimicrobial Development

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Antimicrobial peptides (AMP) have attracted increasing interest because they have the potential to be developed into a new generation of antibiotic agents, which circumvent emerging drug-resistance that occurs with conventional antibiotic treatment. Non-natural antimicrobial oligomeric peptidomimetics hold great promise due to their enhanced potency and *in vivo* stability. Here we report the design, synthesis, and evaluation γ-AApeptides based cyclic antimicrobial peptidomimetics. These cyclic γ-AApeptides show very potent broad-spectrum activities against fungi, and a series of clinically-relevant Gram-positive and Gram-negative bacteria, including pathogens that are unresponsive to most antibiotics. These results suggest cyclic antimicrobial γ-AApeptides that have the potential to emerge as a new class of novel antibiotic therapeutics. The findings will also shed further light on the design and optimization of other non-natural antimicrobial oligomers in the future.