A Universal Automated Algorithm for the Generation of Potent Antimicrobial Peptides

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Recently, antibiotics, one of the greatest advancements in modern science, have been losing their effectiveness because of the rise of antibiotic resistant bacteria. Diseases such as Methicillin-resistant Staphylococcus aureus (MRSA) are capable of causing infection and illness comparable to the pre-antibiotic era. One promising alternative to combat antibiotic resistant bacteria such as MRSA is antimicrobial peptides (AMPs), small natural proteins that typically inhibit growth of bacteria in the concentration range of single to hundreds of micromolar. Here, a universal method for creating novel, synthetic AMPs with single micromolar minimum inhibitory concentrations against any target bacteria has been developed. The method consists of two parts: (i) a Markov model that generates AMPs with local similarities to those in existing databases and (ii) a scoring algorithm that selects the best peptides from the Markov designed AMPs. The scoring algorithm was validated using databases of AMPs against two target bacteria, Staphylococcus aureus and Mycobacterium tuberculosis. The entire AMP design process has been validated by generating an AMP against S. aureus with a MIC of 4.7 μM. A discussion is given detailing successes and limitations of the method, as well as goals for future work.