Novel Method To Identify the Optimal Antimicrobial Peptide in a Combination Matrix, Using Anoplin as an Example

Microbial resistance is an increasing health concern and a true danger to human well-being. A worldwide search for new compounds is ongoing, and antimicrobial peptides are promising lead candidates for tomorrow’s antibiotics. The decapeptide anoplin (GLLKRIKTLL-NH₂) is an especially interesting candidate because of its small size as well as its antimicrobial and nonhemolytic properties. Optimization of the properties of an antimicrobial peptide such as anoplin requires multidimensional searching in a complex chemical space. Typically, such optimization is performed by labor-intensive and costly trial-and-error methods. In this study, we show the benefit of fractional factorial design for identification of the optimal antimicrobial peptide in a combination matrix. We synthesized and analyzed a training set of 12 anoplin analogs, representative of 64 analogs in total. Using MIC, hemolysis, and high-performance liquid chromatography retention time data, we constructed analysis-of-variance models that describe the relationship between these properties and the structural characteristics of the analogs. We show that the mathematical models derived from the training set data can be used to predict the properties of other analogs in the chemical space. Hence, this method provides an efficient means of identification of the optimal peptide in the searched chemical space.

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