Discovery of indolicidin derived antimicrobials by diastereomeric optimization

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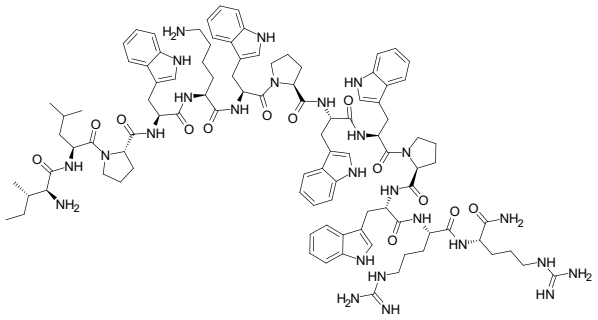
Antimicrobial peptides (AMPs) are regarded as reliable resources for anti-bacteria agents[1]. Indolicicin (ILPWKWPWWPWRR-NH_2) is a linear AMP displaying moderate and broad antibacterial activities towards gram-negative bacteria. However, severe hemolysis and limited antibacterial ability are the obstacles in therapeutical application[2]. As a result, discovering indolicidin analogues with increasing anti-bacteria efficiency and hemolytic safety has arose wide attention as a feasible method.



Recently, several interesting works in our group confirmed that diastereomeric optimization is an available strategy to modify peptides bioactivities and lead to optimized AMPs. Siriwardena *et al.* demonstrated stereochemical purity plays a critical role in the properties of AMPs[3]. Stereorandomization preserves antibacterial effect and decrease hemolysis. Personne *et al.* introduced D-residues in a α-helical linear undecapeptide to obtain stereoisomeric analogues with improved antibacterial effect and reduced toxicity[4]. Based on these works, diastereomeric optimization might provide a promising method to obtain effective and safe indolicidin derivatives. This project focuses on replacing the L amino acids with D amino acids to obtain diastereomeric indolicidin analogues. Preferred peptides will be tested at further biological and pharmaceutical experiments to investigate cellular mechanism and drug-like property.

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