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Abstract

Antimicrobial Peptides Derived from the Genome Mining of Animals Living in Pathogenic Environments †

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Antimicrobial peptides (AMPs) have been used on animals for millions of years. However, AMPs lack any specific consensus amino-acid sequences that are associated with biological activity, although most of them maintain certain common features, such as containing a positive charge and relatively hydrophobic and amphipathic structure. With the increasing number of genomes sequenced and available in the public domain, one alternative methodology to obtain novel AMPs is to analyse genes and proteins from genomic databases to predict and identify amino acid sequences that share similarities and molecular features with natural bioactive peptides. Cathelicidins are found in varying numbers in numerous different vertebrate species. A remarkable degree of molecular diversity has been noted within this gene family. However, a well-conserved feature across evolutionary distant species is an N-terminal cathelin-domain. Using this domain, we have found novel cathelicidins from the genome mining of vertebrates from avian, aquatic and terrestrial environments. The in silico structural analysis of the peptides indicated that all of them were alpha helical, had a positive net charge, with a hydrophobicity around 50% and a Boman index between 1.33 kcal/mol and 3.64 kcal/mol. We have derived 12 peptides from different animals and have studied their in vitro antimicrobial activity, together with the haemolytic activity as a measure of their potential toxicity. All peptides showed remarkably antimicrobial activity and lower toxicity. We believe that newly characterized molecules from several species have inspired molecular designs for the creation of therapeutics, and will continue to do so as more are discovered, because these are based on antimicrobial strategies that have proven efficacious over millennia. Every species harbours a unique, specific collection of antimicrobial peptides, tuned to defend the organism against microorganisms that it will predictably encounter. Therefore, a more detailed analysis of antimicrobial peptides structure and function from pathogen-resistant species will aid our understanding of antimicrobial peptides recognition and neutralization of pathogens, yielding a potentially large number of effective therapeutics. We hope that our preliminary investigation with these novel peptides could provide novel treatment opportunities based on antimicrobial peptides.

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