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Abstract

Functional Characterization Of Crocodylian Cathelicidins

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Abstract: Cathelicidins are one of the major classes of host defense peptides in vertebrates. These peptides display broad spectrum anti-infective properties against several pathogens and are also able to modulate host immune responses which makes them attractive candidates for novel therapeutics. A bioinformatics approach was used to identify novel cathelicidin sequences from the genomes of four crocodylian species. Based on certain physico-chemical parameters (such as charge, helicity and amphipathicity) combined with phylogenetic analysis, four cathelicidin peptides were selected for chemical synthesis and characterization. The antimicrobial and antibiofilm activity of the peptides was assessed *in vitro* and *in vivo* against several bacterial pathogens of medical importance using an organoid model of skin biofilm infection and a murine abscess model. The crocodylian cathelicidins showed broad and potent *in vitro* antimicrobial and antibiofilm activity against several species of bacteria. Notably, As-CATH8 and Gg-CATH5 showed good eradication capacity against *Staphyloccocus aureus* biofilms in an organoid model of biofilm infected skin, outperforming the human cathelicidin LL-37. As-CATH8 was also superior to LL-37 against bacterial abscesses arising from *S. aureus* and *Acinetobacter baumannii* in a murine model of high density bacterial infection. In this case, treatment with As-CATH8 significantly decreased the number of bacteria recovered from the abscess after three days and also reduced the abscess size. Overall, this work highlights the therapeutic potential of crocodylian cathelicidins against bacterial infections.