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Influence of adding terminal tags on the structural and antimicrobial properties of the peptide caerin 1.1

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ABSTRACT

Aquaculture is threatened by severe bacterial and viral outbreaks which can cause massive mortality and limit productivity. Antimicrobial peptides are a promising tool for the control of infectious diseases; however, their use in the aquaculture sector has been poorly explored. Recombinant production of peptides is an interesting alternative to their chemical synthesis, which has still important challenges to address. Although extra amino acid tags are usually added to the ends of recombinant proteins to enhance their stability and facilitate their purification or their translational processing, the effect of these tags on the function and the stability of antimicrobial peptides is completely unknown. This is particularly important in the case of the short cationic antimicrobial peptide caerin, originally isolated from frog skin secretions, and other peptides which bioactivity has been directly related with its ability to adopt an amphipathic alpha-helical structure upon interaction with the microbial membranes. Caerin has demonstrated bactericidal activity against several important human pathogens, however its antimicrobial activity over usual aquaculture pathogens remains practically unexplored. In the present work, we have studied the effect of adding the terminal tag polyhistidine (6xHis) and the 2A peptide from the foot and mouth disease virus (FMDV-2A) to the N- or the C- terminus of caerin on its activity against a collection of bacterial and viral pathogens common to aquaculture species. In addition, the antimicrobial activity of a peptide composed of two tandem consecutive caerin sequences has been investigated. We have concluded that the addition of terminal tags to caerin causes a drastic reduction of its antiviral activity against the studied viruses and that the effect of the added tags on the bactericidal activity of the peptide depends of the target bacterial species. However, caerin with a 6xHis extension at its N terminus maintains or increases its antimicrobial activity against most of the fish pathogenic bacteria tested. According to our data, there is only a moderate agreement between the theoretical predictions obtained from *in silico* models and the experimental observations. This information is essential for the rational design of strategies to aim the recombinant production of caerin and other antimicrobial peptides, which can be used as anti-infective agents in aquaculture.

1. Introduction

The aquaculture sector has grown rapidly over the past decades, reaching 53% of the world fish production in 2018 (http://www.fao.org/state-of-fisheries-aquaculture). Aquaculture, however, still has *big challenges to face, such as* severe bacterial and viral *outbreaks,* which produce high mortality and reduction in productivity (Toranzo et al., 2005). Although vaccination and the use of antibiotics are extended practices to prevent infections, the high cost of vaccines and their inefficiency at early development stages of fishe or in invertebrates, which lack an adaptative inmune system, as well as the concerns raisen against the abusive use of antibiotics, have revealed the need of

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