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Exploring small cationic peptides of different origin as potential antimicrobial agents in aquaculture

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ABSTRACT

Antimicrobial peptides (AMPs) form part of the innate immune response, which is of vital importance in fish, especially in eggs and early larval stages. Compared to antibiotics, AMPs show action against a wider spectrum of pathogens, including viruses, fungi and parasites, are more friendly to the environment, and do not seem to generate resistance in bacteria. Thus, we have tested *in vitro* the potential use of several synthetic peptides as antimicrobial agents in aquaculture: frog Caerin1.1, European sea bass Dicentracin (Dic) and NK-lysin peptides (NKLPs) and sole NKLP27. Our results demonstrate that the highest bactericidal activity against both human and fish pathogens was obtained with Caerin1.1 followed by sea bass Dic and NKLPs, having the sea bass NKLP20.2 none to negligible activity. Interestingly, *Aeromonas salmonicida* was refractory to all the fish peptides tested. Regarding the antiviral activity, synthetic peptides were able to inhibit the viral infection of nodavirus (NNV), viral septicaemia haemorrhagic virus (VHSV), infectious pancreatic necrosis virus (IPNV) and spring viremia carp virus (SVCV), which are some of the most devastating virus for aquaculture. However, their effectiveness was highly dependent on the type of virus. Strikingly, IPNV resulted the most resistant virus since Caeerin1.1 and sea bass NKLP20.2 were unable to reduce its titre and the other peptides tested only reduced it to values in the 43–78% range. These data demonstrate that synthetic peptides have great antibacterial and antiviral *in vitro* activity against important fish pathogens and point to their use as potential therapeutic agents in aquaculture.

1. Introduction

Discovery, design and application of antimicrobial peptides (AMPs) as therapeutic agents is one of the research fashion topics in medicine and animal production. These small peptides are called to replace antibiotics since they can act against a wide range of pathogens and their particular mode of action, involving more than one mechanism, seem to hamper the acquisition of resistance by the target bacteria, as usually happens with traditional antibiotics. For this reason, since the discovery of the first bacterial AMP gramicidin in 1939, the plant purothionin in 1941 and the animal defensin in 1956, lots and lots of AMPs have been identified and proposed as novel drug candidates [1,2]. To integrate and facilitate their study several AMP databases have been generated being the dbAMP (dbAMP, http://csb.cse.yzu.edu.tw/dbAMP/) one of the largest, with more than 4300 experimentally verified AMPs and more than twice potential candidates awaiting further biological characterization.

AMPs are gene encoded defense molecules, produced by members of all kingdoms of life with a major function for lysis of a wide range of pathogens, being the antibacterial activity the most evaluated and best-known characteristic of these peptides. In animals, they are synthetized in the ribosomes and usually traduced to immature pre-pro-peptides with less than 10 kDa, which are then cleaved to release the mature peptides. Most AMPs share some common properties, such as short length of 10–50 amino acids, cationic nature with +2 to +11 net charge, amphipathicity and a high proportion of hydrophobic residues [1–3]. They can be classified according to their amino acid composition into cationic and non-cationic, or to their secondary structure into α-

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