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Role of antimicrobial peptide in fish immunity

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Introduction

Antimicrobial peptides (AMPs) are an important component of innate immunity across all classes of life ranging from prokaryotes to higher animals. Being a key component of innate immunity, AMPs are produced in the sites which are at high risk of pathogen invasion. The main advantage of AMPs possesses broad spectrum antimicrobial activity and can function without memory and specificity, against bacteria, fungi, virus and even parasites. They also exhibit diverse biological functions such as immunomodulation, neutralization of endotoxin and induction of angiogenesis, wound healing, antitumor in addition to its antimicrobial activity. AMPs generally consist of 10 to 50 amino acids and most of them are cationic in nature with a net charge of +2 to +9, although some anionic (negatively charged) AMPs have also been discovered. They are divided into several subgroups such as anionic, cationic α-helical, cationic β-sheet and extended cationic AMPs based on the amino acid sequences, net charge and structure. An attractive feature of AMPs is the attack on microbial membranes and rapid killing action reducing the chances of developing resistance by the microbes. Further, AMPs have also been recognized as one of the promising alternatives to antibiotics as they are effective against multi-drug resistant bacteria. Till date, many AMPs have been identified from different sources including fish. Being an aquatic animal, fish survive in an environment loaded with saprophytic and pathogenic microbes. Since the adaptive immune system in fish is less developed, they rely more on their innate immune system to shield themselves from the attack of pathogenic microbes. This indicates that fish must produce numerous non-specific antimicrobial molecules which play critical roles in maintaining its health.

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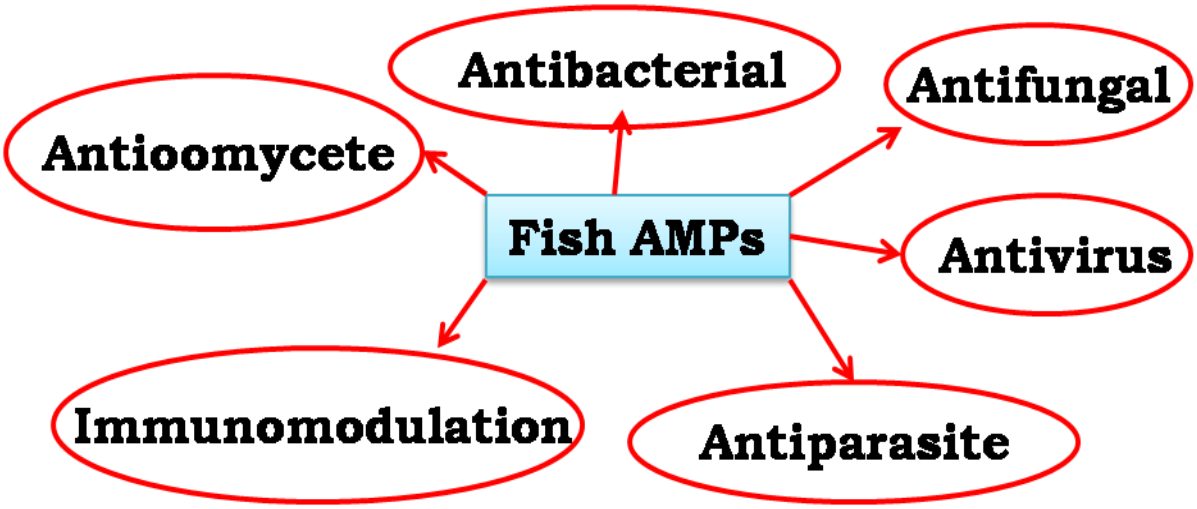

Different functions of fish antimicrobial peptide

AMPs of fish

Fish produces all major classes of AMPs similar to mammals in addition to a specific class called piscidins. Fish AMPs exhibit immunomodulatory functions and broad-spectrum antimicrobial activity against both fish and animal pathogens. AMPs derived from fish and their functions are discussed below;

i) Piscidins: They are a family of linear amphipathic AMPs with potent antimicrobial activity against a variety of microorganisms. They are active against bacteria, fungi, water molds, virus and parasites. They are mainly produced in gill, skin, and intestine and also found in head-kidney and spleen. Expression of piscidin gene can be induced by stimuli like presence of bacterial or bacterial cell component such as LPS. Piscidins have immunomodulatory functions and are able to modulate the expression of pro-inflammatory and other immune-related genes.

ii) Defensins: These are the cysteine rich cationic AMPs which are active against both Gram-negative and -positive bacteria and fish specific viruses. They exhibit chemotactic activity and can stimulate antimicrobial activity in phagocytes. It is constitutively expressed in early developmental stages as a part of the defense system. Its expression can also be induced by stimuli like LPS, β-glucans and peptidoglycan.

iii) Hepcidin: These are cysteine-rich peptides with antimicrobial activity against a wide variety of fish pathogens at the low micromolar range. It has the ability to modulate the expression of different immune-related genes in fish. Its expression can be detected as early as in the

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fertilized egg and can also be induced by exposure to both Gram-positive and Gram-negative bacteria, fungi and viruses. It also acts as iron regulator and may also serve as pleiotropic sensor for other divalent metals.

iv) Cathelicidin: Fish cathelicidins have variable antimicrobial activity depending on its source. Some cathelicidin has activity against only Gram-negative bacteria while others are active against both Gram-negative and positive bacteria and even fungus. Its expression is observed as early as in embryonic stage suggesting its role in immunity. Expression can be induced by bacteria, bacterial DNA and oomycetes. The immunomodulatory activity has been demonstrated in Atlantic salmon cathelicidins.

v) Histone-derived proteins: These are the fragments of proteins derived from histones with broad-spectrum activity against fish pathogens including water molds and parasitic dinoflagellate. They are expressed in fish skin, and found in other tissues, such as gill, spleen and the gut and can be induced under stress conditions.

Conclusion

Production of different classes of AMPs in fish right from early developmental stage to adult is indicative of its importance in defense mechanism. Presence of these peptides in the sites such as skin and gills which forms the physical barrier also indicates that AMPs play a role to prevent the entry of the pathogens. As fish rely heavily on innate immunity, the non specific bioactive molecules including AMPs are crucial to keep its body guarded from the pathogenic microorganisms and maintain its health. Further, fish has been recognized as a good source of AMPs having broad spectrum activity against not only fish pathogens but also human pathogens. AMPs are also considered as a unique candidate to fight against antibiotic resistance due to its membrane disruption ability and rapid killing action. Therefore, fish AMPs can be expolored to discover new AMPs for development of novel therapeutic agents.

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