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Review

# Pathogen bacteria adhesion to skin mucus of fishes

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ABSTRACT

Fish are always in intimate contact with their environment; therefore they are permanently exposed to very vary external hazards (e.g. aerobic and anaerobic bacteria, viruses, parasites, pollutants). To fight off pathogenic microorganisms, the epidermis and its secretion, the mucus acts as a barrier between the fish and the environment. Fish are surrounded by a continuous layer of mucus which is the first physical, chemical and biological barrier from infection and the first site of interaction between fish's skin cells and pathogens. The mucus composition is very complex and includes numerous antibacterial factors secreted by fish's skin cells, such as immunoglobulins, agglutinins, lectins, lysins and lysozymes. These factors have a very important role to discriminate between pathogenic and commensal microorganisms and to protect fish from invading pathogens. Furthermore, the skin mucus represents an important portal of entry of pathogens since it induces the development of biofilms, and represents a favorable microenvironment for bacteria, the main disease agents for fish. The purpose of this review is to summarize the current knowledge of the interaction between bacteria and fish skin mucus, the adhesion mechanisms of pathogens and the major factors influencing pathogen adhesion to mucus. The better knowledge of the interaction between fish and their environment could inspire other new perspectives to study as well as to exploit the mucus properties for different purposes.



**Contents**



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## 1. Introduction

The innate immune system is the only defence weapon of invertebrates and a fundamental defence mechanism of fish. The bony fishes are derived from one of the earliest divergent vertebrate lineages to have both innate and acquired immune systems. The innate system also plays an instructive role in the acquired immune response and homeostasis (Magnadóttir, 2006). The innate immune system of fish is divided into physical barriers, cellular and humoral components although there are some important differences when comparing with other vertebrates (Uribe et al., 2011). Fish are considered to be an ideal model to study the underpinnings of immune systems precisely because of their phylogenetic position and the fact that their adaptive immune systems have not been elaborated to the extent seen in mammals (Magor and Magor, 2001). On the other hand, aquaculture industry demands better knowledge of immunity of farmed fish species. While most available studies focus on cellular and humoral components of fish immune system, less much attention has been focus on physical barriers.

The vertebrates immune system includes primary (organs in which lymphopoiesis takes place) and secondary (places of interaction between the different immune cells that have as mission provide a favorable environment for developing the immune response) lymphoid organs. One of the secondary organs is the MALT (mucous associated lymphoid tissue), which is the major lymphoid structure of the body. Since the majority of the infectious agents affects or initiates his process of infection in the mucous surfaces, the mucosal immune response plays a crucial role in the course of the infection (McNeilly et al., 2008). Skin, gill and gut are part of the fish mucosal immunity and constitute a large area (much greater than that of other vertebrates) for the possible invasion of pathogens. Among them particular interest (given its extension) has the GALT (Maaser and Kagnoff, 2002) while two very special fish organ, skin and gills, as organs implied in the first barrier to infection remains largely unknown (Ingram, 1980; Shephard, 1994; Ellis, 2001).

The layers of tegument of teleosts are the cuticle o mucus layer (with a very complex composition), which have bacteria forming the microbiota, the epidermis (scamous stratified epithelium with goblet cells) and dermis (with two layers, the hypodermis or stratum spongiosum, a frequent site of development of infectious processes and the innermost layer or stratum compactum) (Esteban, 2012). In fish the epidermal mucus is considered a key component of innate immunity it is produced primarily by epidermal goblet cells or mucus cells and is composed of water and gel-forming macromolecules including mucins and other glycoproteins (Ingram, 1980). Research on fish mucus has been undertaken for many decades. The origins of fish mucus, as well as the composition of different types of fish mucus have been well identified by many investigations using histological and biochemical techniques (Kerry, 1994; Al-Arifa et al., 2011; Bragadeeswaran et al., 2011). Conclusions of these studies show that the mucus insures many important biological functions that allow fishes to survive and to adapt to their environment (Balebona et al., 1995; Al-Arifa et al., 2011).

Recently, and using more precise and sophisticated techniques, many studies were reinterested on fish mucus for many objectives. Some studies tend to better understand the composition of fish mucus, their functions, and the effect of environmental circumstances on the mucus secretion (Al-Arifa et al., 2011), while others focused on biotechnological purposes such as possible uses of mucus in many other domains, such as to ameliorate conditions of fish cultures in farms (Hellio et al., 2002; Blanco et al., 2007).

The fish skin mucus is considered as a natural, physical, biochemical, dynamic, and semipermeable barrier that enables the exchange of nutrients, water, gases, odorants, hormones, and gametes (Esteban, 2012). Many fish species locally secrete adhesive mucus which is important for successful substrate attachment (Thomas and Hermans, 1985), whereas others may secrete antiadhesive mucus, which prevents colonization by fouling organisms (McKenzie and Grigovala, 1996). Mucus secretions may also contain toxins and lytic compounds to deter fouling organisms or predators (Bavington et al., 2004).

Mucus is considered predominantly on the general skin surface and gills, but also from the gut lining; indeed on all epidermal surfaces that mark the interface between the fish and external environment. Skin mucus can trap and immobilize pathogens before they can contact epithelial surfaces, because it is impermeant to most bacteria and many pathogens (Mayer, 2003; Cone, 2009). Furthermore, mucus is continuously secreted and replaced, which prevents the stable colonization of potential infectious microorganisms as well as invasion of metazoan parasites (Ingram, 1980; Ellis, 2001; Nagashima et al., 2003). Sometimes the mucus layer can be shed or digested, thus pathogens must move 'upstream' through the unstirred layers of mucus adhering to the cells on the epithelium surface or penetrate a mucus 'blanket' before it is shed (Cone, 2009).

Mucus is a complex fluid and its composition varies throughout the epithelial surface and among fish species. The composition and characteristics of skin mucus is very important for the maintenance of its immune functions (Cone, 2009). Furthermore, mucous cells and the compositions of the mucus they produce are influenced by endogenous factors (e.g. sex, developmental stage) and exogenous factors (such as stress, acid and infections) (Blackstock and Pickering, 1982; Zaccone et al., 1985).

The skin, gills, and intestine of most fishes are covered by a gel-forming molecule called mucus; the mucus of fishes is the site of contact direct of fish with their environment. Many functions are attributed to fish mucus, being noticeable among them its important role in the ionic and osmotic regulation, feeding, attachment, defence, cleaning, respiration, communication and reproduction (Kerry, 1994; Bavington et al., 2004). Furthermore, the fish mucus acts as the first barrier against an infection and it is the first site of interaction between fish cells and pathogens, being the first route for both aerobic and anaerobic bacteria to reach the fish cells. Thus, the mucus seems to have an important selective role to discriminate