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Review

Review on the immunology of European sea bass *Dicentrarchus labrax*

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Abstract

European sea bass (*Dicentrarchus labrax* L.) is a marine species of great economic importance, particularly in Mediterranean aquaculture. However, numerous pathogenic viruses, bacteria, fungi and parasites affect the species, causing various infectious diseases and thereby leading to the most heavy losses in aquaculture production of sea bass. In this respect, knowledge on molecular and genetic mechanisms of resistance to pathogens and specific features of immune response against various infectious agents should greatly benefit the development of effective vaccines and proper vaccination strategies in marker-assisted selection of fish resistant to a range of infections. To date, genetic knowledge on sea bass immune regulatory genes responsible for resistance to pathogens is relatively poor but tends to accumulate rapidly. In this review, we summarize and update current knowledge on the immune system and immune regulatory genes of the sea bass.

Keywords: European sea bass; Immune system organization; Immune response; Immune regulatory genes

Contents

Abbreviations: BAC, bacterial artificial chromosome; CDR, complementarity-determining region; CTK, cytotoxic T killer; DNP-KLH, dinitrophenyl-conjugated to keyhole limpet haemocyanin; GALT, gut-associated lymphoid tissue; NCC, non-specific cytotoxic cell; NK, natural killer; MAS, marker-assisted selection; RBR, peptide-binding region; RAG1, recombination activating protein 1; ROS, reactive oxygen species; TNP, trinitrophenyl

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1. Introduction

European sea bass (*Dicentrarchus labrax* L.; Moronidae; Perciformes) is a marine species of great economic importance, particularly in Mediterranean aquaculture. However, numerous pathogenic viruses, bacteria, fungi and parasites affect the species, causing various infectious diseases. Among those pathologies, viral encephalopathy and retinopathy (Bovo et al., 1999; Ucko et al., 2004), pasteurellosis and vibriosis (Afonso et al., 2005) caused by *D. labrax* encephalitis virus and bacterial pathogens *Photobacterium damselae* subsp. piscicida and *Vibrio anguillarum*, respectively, lead to the most heavy losses in aquaculture production of sea bass. In this respect, knowledge on molecular and genetic mechanisms of resistance to pathogens and specific features of immune response against various infectious agents should greatly benefit the development of effective vaccines and proper vaccination strategies in marker-assisted selection (MAS) of fish resistant to a range of infections (Bricknell and Dalmo, 2005; Chinabut and Puttinaovarat, 2005).

Bony fishes, arising about 300 million years ago, share similar immune system organization with other vertebrates (Litman et al., 2005). The immune components include the presence of non-specific cell-mediated cytotoxicity (Vazzana et al., 2003), phagocytes (neutrophils and macrophages; Do Vale et al., 2002), T cell and B cell activity (Scapigliati et al., 2000a, 2003), antigen-presenting cells and major histocompatibility complex (MHC; Venkatesh et al., 1999); T cell receptor (TcR; Scapigliati et al., 2000a) and cytokines (Scapigliati et al., 2000b). Anatomically, lymphoid tissues in teleosts include the thymus, head-kidney, spleen, gut-associated lymphoid tissue (GALT) and cellular components, displaying humoral and cell immune responses (Scapigliati et al., 2002).

As a typical teleost, European sea bass contains all the above attributes of the immune system. To date, genetic knowledge on sea bass immune regulatory genes responsible for resistance to pathogens is relatively poor but tends to accumulate rapidly. In this review, we summarize and update current knowledge on the immune system and immune regulatory genes of the sea bass.

2. Cytokines and innate immunity

Innate immunity is the simplest and non-specific type of immune response. In fish, the innate immune system consists of cell components, such as phagocytes (macrophages, neutrophils) and non-specific cytotoxic cells (NCCs), and various molecular mediators of inflammation, including antibacterial peptides (dicentracine, hepcidin), complement, transferrin, COX-2, chemokines (CXC and CC chemokines and their receptors), cytokines [interleukins (IL-1, IL-8), interferons (IFN), transforming growth factor β (TGF-β) and tumor necrosis factor α (TNF-α)], acute phase proteins (serum amyloids A and P, C-reactive protein, α2-macroglobulin and complement components), Toll-like receptors and molecules of Toll-like receptor-mediated signaling pathways (Magor and Magor, 2001).

In sea bass, innate immune cells were initially found in the headkidney and described as macrophages, stromal and lymphocyte-like cells (Meseguer et al., 1991).

Studies on *in vitro* cytotoxic activity of leukocytes derived from the head-kidney, blood and peritoneal cavity of *D. labrax* against mammalian tumor cells allowed to separate cells displaying non-specific cytotoxic response to two subpopulations: monocyte-like and lymphocyte-like cells (Mulero et al., 1994). Monocyte-like cells exhibited a broad area of contact with a target cell, had oval or kidney-shaped nucleus and a few granules in cytoplasm, whereas lymphocyte-like cells established spot contacts with targets and had a large nucleus and occasional cytoplasmic granules. Similar leukocyte populations, exhibiting non-specific cytotoxicity against mammalian tumor cells, have been found in other teleosts, seawater gilt-head sea bream *Sparus aurata* and freshwater common carp *Cyprinus carpio* (Meseguer et al., 1994, 1996; Mulero et al., 1994; Nakayasu et al., 2005). These findings suggested that non-specific cytotoxic response in sea bass is mediated by several populations of leukocytes differed from each other by various mechanisms of target recognition and cytolysis.

In teleosts, all NCC have been shown to express on their surface the NCC receptor protein, NCCRP-1, by which a cytotoxic cell contacts to its target (tumor cell or protozoan parasite) to induce the lytic cycle against the target (Jaso-Friedmann et al., 1997). Although sea bass NCCRP-1 is not yet isolated, cDNA for this receptor was recently cloned from gilt-head sea bream, a species closely related to the European sea bass. Molecular characterization of this receptor revealed NCC heterogeneity, showing different types of leukocytes (lymphocytes, monocyte/macrophages and acidophilic granulocytes) that contribute to the non-specific cytotoxic response in sea bream (Cuesta et al., 2005). Similar cell types of leukocytes are likely to mediate NCC activity in sea bass.