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Immuno-modulation in fishes against parasitic infections: A review

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Abstract

Parasites are the opportunist organisms that attack on varied number of fish species and lead to various physiological and anatomical changes in them. It is well documented that fish parasites are associated with the alterations in haematological, biochemical and histopathological changes in fish communities all over the world. By acing as secondary pathogens, they have been linked with the imunomodulation in fishes. This review presents a thorough literature citing the various instances of immunomodulations in fishes against parasites.

Keywords: Parasites, infections, fish, immuno-modulation

Introduction

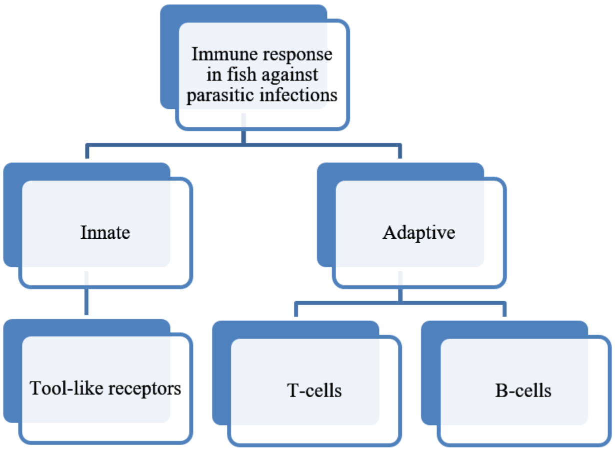
The parasitic infestations are known as exemplary opportunism shown by the some organisms in varied number of fish species around the world. Their primary purpose being derivation of nutrition from the hosts, without caring about their wellbeing. Parasitic infections are maximum in the world and known not only to cause various physiological dysfunctions but also lead to alterations in the immune system of host fishes. Immuno-modulation signifies an induced alteration in the immune system of an organism, the host, by the opportunist pathogen to its desired level. In fishes, Immuno-modulation is well documented against the parasitic infections.

Fish parasites as immune-modulators

Parasites secrete certain substances perhaps for their own benefit which are known to modulate the secretion of host immune factors. Role of host genotype in response to the transcriptome levels expressed by parasite was investigated by Pawluk (2018) [25] using RNA-seq. Significant differences in gene expression were observed. Results suggested that the genetic background plays an important role in the transcriptome response to parasites. Scharsack (2004) [30], analysed the leukocytes isolated from the head kidney and peripheral blood of 3-spined sticklebacks *Gasterosteus aculeatus* infected with the tapeworm *Schistocephalus solidus* using flow cytometry during. Although the body weight of parasites increased continuously throughout their observation period (98 days), but the proportions of granulocytes increased in blood and head kidney only up to certain period of post- infection (63 days). This reflected the ability of *S. solidus* to damage the host's immune response while developing in the body cavity of *G. aculeatus*. Similarly higher respiratory-burst reaction upon phagocytosis of zymosan particles *in vitro* was observed in leucocytes of head kidney from sticklebacks infected with *S. solidus*, Kurtz (2004) [14, 30]. In another study conducted by Barber (2001) [1], *S. solidus*-infected *G. aculeatus* was reported to show increased counts of total white blood cells. Hoole and Arme (1982) [11] studied the roach *Rutilus rutilus* infected with the cestode *Ligula intestinalis*. Parasites were found to survive apparently unharmed, as long as the host is alive, despite the presence of a host cellular immune-response. Nie and Hoole (2000) [20] tested the granulocyte responses in fish towards *Bothriocephalus acheilognathi*. Formation of lamellipodia at the anterior cell-pole and small tails at the posterior cell-pole of granulocytes was observed on adding this parasite extract. Reduced polarization was reported in the head kidney granulocytes in infected carp. In gudgeon, *Gobio gobio* infected with *Ligula intestinalis*, absorbtion of protective host proteins occurs onto the surface of the parasite, Hoole and Arme (1983) [12]. Suppression in the proliferation of splenic lymphocytes occurs in presence of *L. intestinalis* extracts, Taylor and Hoole (1994) [39]. Rohlenova (2011) reported the immunosuppressive role of 11-ketotestosterone on fish immunity measured by complement activity in parasite infected fishes.

Responsiveness of fish immune system against parasites

Immune system plays a primary role in protecting an organism against infections and thus minimizing fitness costs of infected ones, Rohlenová *et al*. (2011) [28]. In fishes, physiology as well as immunity is influenced by seasonal variations, pathogen interactions and parasites. Parasites act as influential operators of evolutionary process. The genetic variations both in host and in parasite populations co-evolve as a result of parasite virulence and host resistance. Fish shows innate as well as adaptive immune responses towards parasitic infestations



Innate response begins with the recognition of pathogen-associated molecular patterns (PAMPs) by pathogen recognizing receptors (PRRs). In addition to Toll-like receptors (TLRs), some molecules are also capable of functioning as PAMPs in fish against some fish parasites. TLRs play a crucial role in cell–cell interaction and in signalling. C-type lectins, characterised of having C-type lectin receptors (CLRs) with carbohydrate recognition domains (CRDs), McGreal (2004) [20] are known for their capability in recognizing specific pathogen-associated carbohydrate structures. Transmembrane proteins present on dendritic cells and macrophages also produce or secrete few CLRs, Cambi and Figdor (2005) [9]; Medzhitov (2007) [21]. These specific lectin–carbohydrate interactions have been found for several fish parasites, such as *I. multifiliis*, Xu (2001) [45], *Glugea plecoglossi*, Kim (1999) [13], *Gyrodactylus derjavivni*, Buchmann (2001) [6]; Buchmann and Lindenstrøm (2002) [7] and *Hetrobothrium okamotoi*, Tsutsui (2003) [42]. Inflammatory responses are shown by TLRs and few NLRs (NOD-like receptors). Activation of tissue-resident macrophages by these receptors, results in the production of inflammatory cytokines, including tumour-necrosis factor (TNF), interleukin-1b (IL-1β) and IL-6. Cytokines produced activate hepatocytes to produce acute-phase proteins (APPs) which in turn activate complement and pathogen opsonisation occurs due to phagocytosis by macrophages and neutrophils. Adaptive immunity in fish expresses by the production of T-cells and B-cells. Fish B-cells chain rearrangement and allelic exclusion, Miller (1998) [22]. IgM tetramer is the most common immunoglobulin in serum of teleosts, Solem and Stenvik (2006) [34]. IgD, IgT and IgZ also found in few fishes Randelli (2008) [37].

Table 1: Fish immune response exhibited for parasitic remediation

Host fish	Parasite involved	Remediation effect shown by host in response to parasite	Reference
Oncorhynchus mykiss	*Gyrodactylus derjavini*	Induction of interleukin β expresion	Lindenstrom (2003)
Salmo salar	*Gyrodactylus salaris*	Upregulation in Mc1-1 (related to IL 1 β)	Matejusova (2006)
Paralichthys olivaceus	*Neoheterobothrium hirame*	Upregulation in the expression levels of several immune-regulated genes	Matsuyama (2007) [19]
Dicentrarchus labrax	*Diplectanum aequans*	Upregulation in cytokines	Faliex (2008) [10]
Oncorhynchus mykiss	*Discocotyle sagittata*	High antibody titres	Rubio-Godoy (2003) [29]
Carp	*Dactylogyrus vastator*	Extensive proliferation and hyperplasia of gill epithelia reduced parasite burdens	Wunder (1929) [44]
Tench	*D. macracanthus*	Proliferation of gill epithelia reduced parasite burdens	Wilde (1935) [43]
Oncorhynchus mykiss	*Gyrodactylus derjavini*	Release of cytokines leading to decrease of the ectoparasite population	Buchmann (1999) [4]
Carp	*Gyrodactylus* sp	Production of IL-1 like factors which inturn induces hyperplasia	Singel (1986)
Japanese flounder	*Neobenedenia girellae*	Growth suppression of N. girellae	Bondad-Reantaso (1995) [2]
Rainbow trout	*Gyrodactylus*	Production of IL-1 like factors	Buchmann and Bresciani (1998) [3]

Prophylactic and therapeutic measures for disease prevention in fishes caused by parasites

1. Prevention of parasitic diseases in natural water bodies

Water is a precondition for life, including the parasites as well. Many infectious diseases directly depend on water bodies for their spread and transmission or as a habitat for intermediate or final hosts, Lv (2013) [17]. Presence of environmental pathogens, low resistance of the fish stock and unsatisfactory water environment act as the major causes for fish disease outbreak. Pathogens are found in all natural water bodies, but healthy fishes have adequate resistance against them. Fish becomes vulnerable to those pathogens whenever there occurs huge increase in pathogen number and fish is not able to cope with the increased pathogens. External factor especially water quality change increases the risk of pathogenic infestation.

Some preventive measures for controlling parasitic diseases are:

- Preventing water deterioration
- Use of hygienic food
- Avoiding overfeeding
- Removing fish carcasses promptly from fish ponds
- Maintaining suitable stocking density
- Avoiding the use of trash fish for feeding
- Disinfecting fish ponds and gears

2. Vaccines used in parasitic diseases

Combating fish diseases has become a great challenge in aquaculture. The most important disease management strategy used to maintain animal health worldwide is vaccination. Use of vaccination in fish cultures has reduced the antibiotic usage and thus prevented the antibiotic resistance in aquaculture.

Vaccines are available for some economically important bacterial and only few vaccines for viral diseases and no vaccine has been developed for fish parasites and fungus. Limited understanding of fish immunology, unlicensed vaccines, high cost and stressful administration methods are some important limitations in the development of fish vaccines, Muktar *et al*. (2016) [23]. As per Sommerset (2005) [35] no parasite vaccines were commercially available till that date.

3. Therapeutic agents for parasitic diseases

Benzimidazoles and Praziquantel drugs are commonly administered against helminth worms. Buchmann and Bjerregaard (1990) [5] studied the activity of mebendazole against *Pseudodactylogyrus bini* and *P. anguillae* infecting eels. In *in vitro* conditions, *P. anguillae* was found more resistant than *P. bini*, but reverse was observed in *in vivo* situation. They further suggested that the effect may be due to protective tissue reactions around *P. bini* occurring in latter case. The metacercariae of eye flukes in the lens of rainbow trout can be treated to some extend by incorporating praziquantel drugs in feed, Bylund and Sumari (1981) [8]. Immersion treatment of praziquantel was used by Plumb and Rogers, (1990) [24] in channel catfish against eye flukes and yellow grubs. Efficacy of praziquantel and ivermectin injections and immersion treatments in praziquantel and trichlorfon was tested by Lorio (1989) [16] against yellow grubs in channel catfish. Praziquantel (injections and immersion) and ivermectin injections were found effective but not 100% efficient. No action was found by trichlorfon. Praziquantel was found superior than ivermectin. Apart from all this niclosamide and nitroscanate are commonly used against Gyrodactylosis. Several antihelmintics were tested by Taraschewski *et al*. (1988) [37-38] against worms in eels. Among all these, levamisole by immersion was considered to me most suitable.

Efficacy of nitroimidazoles against the parasitic diseases of fish was reported by Tojo and Santamarina (1998) [41]. Protozoan infestations are usually treated using three drugs: *amprolium*, Herwig (1979) Schmahl (1989) [31] and Stoskopf (1993) [36]; *Bithionol*, Tojo and Santamarina (1998) [41] and *toltrazuril*, Schmahl (1989) [31], Schnlah (1989) [32] and Stoskopf (1993) [36]. Toltrazuril is widely used for the treating parasitoses of fish, has been recommended for the treatment of various microsporidian and myxosporidian infections, Schnlah *et al*. (1989) [32].

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