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Mucosal immunity and probiotics in fish

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ABSTRACT

Teleost mucosal immunity has become the subject of unprecedented research studies in recent years because of its diversity and defining characteristics. Its immune repertoire is governed by the mucosa-associated lymphoid tissues (MALT) which are divided into gut-associated lymphoid tissues (GALT), skin-associated lymphoid tissues (SALT), and gill-associated lymphoid tissues (GIALT). The direct contact with its immediate environment makes the mucosal surfaces of fish susceptible to a wide variety of pathogens. The inherent immunocompetent cells and factors in the mucosal surfaces together with the commensal microbiota have pivotal role against pathogens. Immunomodulation is a popular prophylactic strategy in teleost and probiotics possess this beneficial feature. Most of the studies on the immunomodulatory properties of probiotics in fish mainly discussed their impacts on systemic immunity. In contrast, few of these studies discussed the immunomodulatory features of probiotics in mucosal surfaces and are concentrated on the influences in the gut. Significant attention should be devoted in understanding the relationship of mucosal immunity and probiotics as the present knowledge is limited and are mostly based on extrapolations of studies in humans and terrestrial vertebrates. In the course of the advancement of mucosal immunity and probiotics, new perspectives in probiotics research, *e.g.*, probiogenomics have emerged. This review affirms the relevance of probiotics in the mucosal immunity of fish by revisiting and bridging the current knowledge on teleost mucosal immunity, mucosal microbiota and immunomodulation of mucosal surfaces by probiotics. Expanding the knowledge of immunomodulatory properties of probiotics especially on mucosal immunity is essential in advancing the use of probiotics as a sustainable and viable strategy for successful fish husbandry.

1. Introduction

The aquatic environment harbors a wide array of biological, physical and chemical hazards. The constant exposure of fish to their environment typifies the importance of mucosal epithelia as a main organ of defense. The mucosal immune system of the fish is characterized by diverse and unique repertoire of innate and adaptive immune cells and molecules. They are orchestrated in the presence of antigenic factors such as bacteria or viruses to prompt specific and robust responses. In addition, the associated commensal microorganisms that are lining the mucosal surfaces serve as a biological reinforcement in protecting these surfaces against pathogens. An exceptional and interesting mechanism governs the maintenance of homeostasis between the immune-rich mucosal surfaces and their associated microbiota. Manipulation of the mucosal surfaces including their inherent and adherent factors have become key and emerging mode of disease control specifically in aquaculture where outbreak is a longstanding issue [1–5] Table 1.

Immunostimulants, vaccines and probiotics are believed to be ideal and effective disease control strategies that foster sustainability in aquaculture. The popularity of these alternatives was brought forth when call for reduction on the use of antibiotics and for the development of an eco-friendly industry arose. Antibiotics have been the conventional and popular bacterial control agents in aquaculture for almost three decades until evidences were presented on their risks to the consumers and environment [6,7]. The use of probiotics is regarded as a very promising strategy and their wide acceptance for use in aquaculture is evidently shown in the number of research studies published over the last ten years [8–11]. The ability of probiotics in modulating the immunity of the host has revolutionized the application of probiotics on a wider scale. The immunomodulatory features of probiotics presents two interesting scientific domains: ***i***) the properties of probiotics reveal

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Table 1
Immunological influences of probiotics on the mucosa-associated lymphatic tissues (MALT) of the fish.

MALT	Key findings	Probiotics used	Origin of probiotics	Fish species under study (Age[a]; administration strategy[b])	References
Gut-associated lymphoid tissues (GALT)	Increased T-cells and acidophilic granulocytes; Lowered transcription of pro-inflammatory cytokines	*Lactobacillus delbrueckii* ssp. *delbrueckii* (AS13B)	host gut	*Dicentrarchus labrax* (LV, *nm*; LF)	[3]
	Lowered lactate dehydrogenase activity and caspase-3 during *V. anguillarum* infection	*Pseudomonas* sp. *(GP21)* and *Psychrobacter* sp *(GP12)*	host microbiota	*Gadus morhua* (JV, 300–400 g; IV)	[29]
	Increased expression of chemokines but no change with the interleukins	*Pseudomonas* sp. *(GP21)* and *Psychrobacter* sp *(GP12)*	host microbiota	*G. morhua* (JV, 300–400 g; IV)	[27]
	Increased villi height; Increased population of intraepithelial lymphocytes and acidophilic granulocytes	*Lactobacillus rhamnosus* GG (ATCC 53103)	human intestine	*Oreochromis niloticus* (JV, 30–50 g; FF)	[5]
	No pronounced effect on gut integrity and leukocyte level	*Pediococcus acidilactici*	commercial[c]	*O. niloticus* (JV, ~175 g; FF)	[89]
	Elevated intraepithelial leukocytes; Influenced goblet cell population; Upregulated *tnfα* expression	*P. acidilactici*	commercial[c]	*O. niloticus* (JV, ~9 g; FF)	[90]
	Modulated expression of *il1β*, *tgfβ* and *tnfα*	*Bacillus subtilis C-3102*	commercial[d]	*O.niloticus* × *Oreochromis aureus* hybrid (JV, ~1 g; FF)	[97]
	Increased level of leukocytes infiltration, number of goblet cells and villi height	*Bacillus cereus* var. *toyoi*	soil isolate	*Oncorhynchus mykiss* (JV; FF)	[91]
	Increased lysozyme activity of the mucus	*B. subtilis*	host digestive tract	*O. mykiss* (JV, ~30 g; FF)	[96]
	Increased phagocytic activity of the mucosal leukocytes	*Lactococcus lactis* subsp. *lactis* CLFP 100, *Leuconostoc mesenteroides* CLFP 196, and *Lactobacillus sakei* CLFP 202	intestine of healthy salmonids	*O. mykiss* (JV, ~50 g; FF)	[93]
	Influenced expression of *il8* during feeding and during infection	*Lactobacillus plantarum*	host origin	*O. mykiss* (JV, ~26 g; FF)	[22]
	Unchanged pro-inflammatory cytokine expression	*Carnobacterium maltaromaticum* B26 and *C. divergens* B33	host intestine	*O. mykiss* (JV, ~300 g; IV)	[76]
	Increased microvilli length	*P. acidilactici*	commercial[c]	*O. mykiss* (JV, ~100 g; FF)	[92]
	Increased mucosal fold length and infiltration of epithelial leukocytes	*P. acidilactici* (*administered with short chain fructooligosaccharides*)	commercial[c]	*Salmo salar* (JV, ~250 g; FF)	[103]
	Alleviated epithelial cell damage caused by the pathogens	*Carnobacterium divergens*	Arctic charr gut	*S. salar* (JV, ~73 g; IV)	[94]
	Pronounced abundance leukocyte-like cells in the intestinal epithelium; Prevented the damaging effect of *Aeromonas salmonicida*	*L. delbrueckii* subsp. *lactis*	culture collection strain	*S. salar* (JV, ~140 g; IV)	[95]
	Increased population of Ig^+ and acidophilic granulocytes	*Lactobacillus fructivorans* (AS17B) *L. plantarum*	host gut human feces	*Sparus aurata* (LV, *nm*; LF)	[4]
	Influenced the expression of *il8*, *casp1*, *actb*, *ocln*, *cox2* and *tf*	*B. subtilis* (administered with inulin and microalgae)	culture collection strain	*S. aurata* (JV, ~50 g; FF)	[99]
Skin-associated lymphoid tissues (SALT)	Increased myeloperoxidase activity, lysozyme activity and total protein content of the mucus	*Bacillus amyloliquefaciens* FPTB16	fermented fish product	*Catla catla* (JV, 20–30 g; FF)	[107]
	Mitigated *V. anguillarum*-induced apoptosis; Modulated the expression of immune-related genes	*Pseudomonas* sp. (GP21)	host microbiota	*G. morhua* (JV, 300–400 g; IV)	[106]
	Increased protein content of mucus	*Lactobacillus casei*	commercial[e]	*Poecilopsis gracilis* (LV, ~47 mg; LF)	[105]
Gill-associated lymphoid tissues (GIALT)	Influenced *defb* expression in the gills	*Pseudomonas* sp. (GP21)	host microbiota	*G. morhua* (JV, ~150 g; RW)	[57]
	Maintained gill structure and promoted regenerative gill filaments during pesticide exposure	*B. subtilis*, *L. lactis* and *Saccharomyces cerevisiae*	culture collection strain	*Labeo rohita* (JV, ~7.5 g; FF)	[108]

nm = not mentioned.
additional note: the weight shown in the table is the initial weight of the fish or the weight of the fish where mucosal cells were isolated for *in vitro* studies.
[a] Age of fish: **LV** = larvae; **JV** = juvenile.
[b] Administration strategy: **RW** = rearing water; **FF** = formulated feed; **LF** = live feed; **IV** = *in vitro*.
[c] Added as Bactocell®.
[d] Added as Calsporin®.
[e] Added as Yakult®.