Understanding the role of fish microbiota in disease resistance and immune function

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Abstract

The interaction between fish and their relevant microbiota has been of significant concern in the study of aquatic biology, especially in its role in disease resistance and immune response. The microbiota, a community of bacteria, fungi, and viruses living on mucosal surfaces, including the skin, gills, and gut, is essential for physiological homeostasis and resistance to pathogen invasion. In recent years, discoveries in metagenomics and microbial ecology have shown that a balanced microbiota promotes immune responses by stimulating innate and adaptive immune systems, producing antimicrobial compounds, and regulating inflammatory pathways. On the other hand, microbial composition, usually affected by environmental stress, pollutants, or antibiotic excess, may result in dysbiosis, making them susceptible to infections and outbreaks of diseases. This paper will discuss the complex relationship between fish microbiota and immune responses, as well as the mechanisms by which microbial communities contribute to disease resistance. Also, it points to a new trend in microbiota modulation probiotics, prebiotics, and microbial transplantation as sustainable methods for enhancing fish health and aquaculture productivity. The study of these microbial-immune interactions holds great promise for improving fish welfare, promoting ecological stability, and developing novel disease management strategies in aquatic ecosystems.

Keywords: Fish microbiota, Disease resistance, Immune function, Microbial diversity, Host–Microbe interactions, Aquatic health, Probiotics and immunity

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Introduction

The fish microbiota is a complex association of microorganisms (mainly bacteria, archaea, fungi, and viruses) that colonize different mucosal surfaces of fish, including the skin, gills, and gastrointestinal tract. These microbial communities are vital to the biological system of the aquatic host and affect absorption, metabolism, and immunity. Specifically, the gut microbiota is a vast metabolic organ that supports digestion, vitamin production, and the creation of bioactive compounds essential to health (Xiong, Nie and Chen, 2018). Unlike animals living on land, fish are in constant contact with surrounding water, leading to dynamic interactions between environmental and host-associated microorganisms (Yukgehnaish *et al.*, 2020; Pravina, Radhika and Palappan, 2024). These microbial communities are determined by factors such as water temperature, salinity, diet, and farming conditions, and they constitute a delicate balance that is paramount for maintaining physiological and immunological stability (Gómez and Balcázar, 2008).

Fish microbiota is the first line of defense against invading pathogens, affecting colonization through competitive exclusion, antimicrobial metabolic product production, and immune response modulation (Gómez & Balcazar, 2008). SCFA produced by gut microbes enhances the antioxidative and immune functions of fish, resulting in resistance to disease (Li *et al.*, 2022). Additionally, commensal microbes induce mucosal immunity by enhancing the growth of immune cells and regulating cytokine production, thereby maintaining host homeostasis (Kelly and Salinas, 2017). Dysbiosis may also develop when this balance is disrupted, including through antibiotic use, stress, and poor water quality, exposing fish to vibriosis and enteritis (Medina-Félix *et al.*, 2023; Xue, 2024). The microbiotaimmune axis is thus a crucial determinant of the resistance to population collapse in fish in aquaculture.

Figure 1(a): Conceptual overview of fish microbiota and host interaction.

This figure (Figure 1(a)) demonstrates the interdependence among the fish host, its intestinal microbiota, the aquatic environment, and the immune system. The figure indicates that the gut microbiota is a pivotal mediator, connecting external environmental conditions—water quality, temperature, and nutrient availability — to the fish's internal physiological processes. Positive microbes in the intestines help digest and absorb nutrients, produce vital compounds, and support the immune system in identifying and counteracting the activity of pathogens. This balance may be disrupted by environmental stressors or pollutants, leading to dysbiosis and increased susceptibility to disease. On the other hand, a stable and diverse microbiota facilitates the function of fish mucosal barriers, modulates immunity, and supports homeostasis. This theoretical framework supports the role of microbiota-environment-host interaction as the basis of disease resistance and immune capabilities of aquatic organisms.

In recent studies, there has been increasing interest in the molecular communication between the microbiota and the host immune system to formulate sustainable aquaculture strategies. Research on animal species such as rainbow trout, zebrafish, and others indicates that probiotics can regulate gut microbiome composition and help overcome pathogenic infections more quickly (Rasmussen *et al.*, 2022; López Nadal *et al.*, 2020). Metagenomic methods have helped researchers map the diversity and functional potential of fish-associated microbiomes, revealing the presence of important microbial taxa that help regulate immune systems and nutrient metabolism (Yukgehnaish et al., 2020; Jessie Rani *et al.*, 2025). This abundance of data highlights the potential to improve fish health by controlling the microbiota through dietary interventions and ecological controls, thereby reducing the need for antibiotics in aquaculture systems.

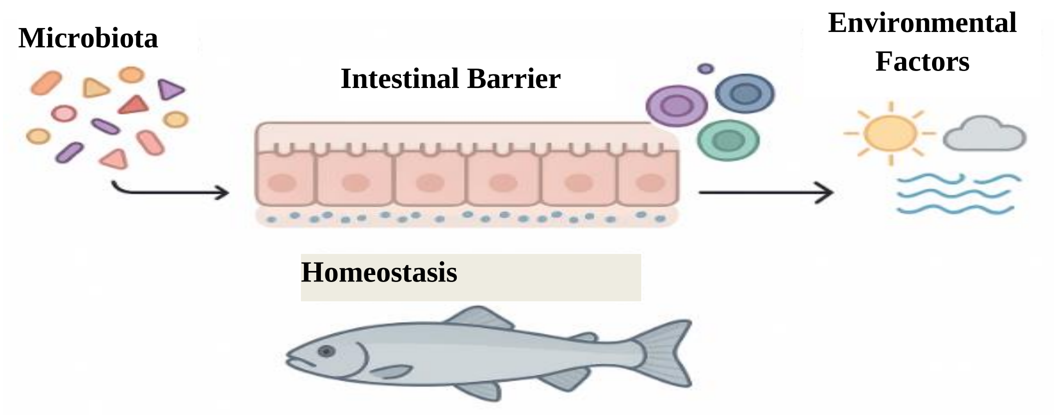

Figure 1(b): Architecture diagram of microbiota–immune system framework in fish.

This figure (Figure 1(b)) shows how all these interactions among microbial communities, the intestinal barrier, immune cells, and environmental factors can be combined to establish homeostasis in fish. The intestinal microbiota, which consists of various microorganisms, is in contact with the intestinal epithelial surface, which regulates the immune cell activity and ensures the host defense system. These interactions are also moderated by external environmental conditions, such as water quality, temperature, and salinity, which influence the equilibrium between beneficial and harmful microorganisms. Collectively, these elements form a whole microbiota-immune system that promotes physiological stability and disease resistance in aquatic life.

This paper is divided into several important sections to provide a clear picture of fish microbiota and its role in health and disease. The Introduction describes the fish microbiota and its role in immunity and disease resistance. The second part analyzes microbial interactions with pathogens and the defense mechanisms they employ. The third section describes the impact of the microbiota on the development and response of the immune system using the proposed computational model. The fourth part focuses on the environmental, dietary, and genetic influences on microbiota composition and their effects on performance indicators. The fifth part is dedicated to administering microbiota with probiotics and prebiotics to manage disease. Lastly, the Conclusion will summarize the important findings, implications for aquaculture, and future research directions.

Role of Fish Microbiota in Disease Resistance

The relationship between the fish microbiota and pathogenic bacteria involves a balance between microbial colonization and host defense mechanisms. Commensal microorganisms in a healthy fish inhabit ecological niches on the mucosal surfaces of the gut, gills, and skin, thereby inhibiting the settlement and growth of opportunistic pathogens (Gomez, Sunyer and Salinas, 2013). This can be described as colonization resistance and serves as a biological protective mechanism that prevents the establishment of infection by dangerous bacteria such as Vibrio anguillarum or Aeromonas hydrophila. Competition for nutrients and changes in mucosal conditions are also driven by the microbiota and create an adverse environment for pathogenic species (Yu *et al.*, 2021). The balance may be disrupted by environmental stress, antibiotics, or poor water quality, leading to dysbiosis, increased pathogen invasion, and systemic inflammation (de Bruijn *et al.*, 2018). Therefore, to prevent disease outbreaks in the aquaculture environment, it is important to preserve a stable microbial ecosystem. The protective effect of fish microbiota against disease is achieved through multiple interconnected pathways, including immune modulation, antimicrobial substance production, and maintenance of mucosal integrity. Some beneficial microorganisms also produce bacteriocins and organic acids, which directly kill pathogens.

In contrast, others produce metabolites, such as short-chain fatty acids, that enhance the host's antioxidative and immunological functions (Dawood, 2021). The microbiota also activates pattern recognition receptors, such as Toll-like receptors (TLRs), which promote the synthesis of antimicrobial peptides and mucins that amplify mucosal barriers (Yu, Yu, and Liu, 2025). Also, nutrigenomic research demonstrated that diet-induced changes in the microbiota can activate immune-related genes that regulate cytokine signaling and leukocyte proliferation (Martin & Król, 2017). Taken together, these mechanisms explain how microbial symbionts can coordinate extensive, interconnected immune defense mechanisms that make fish resistant to aquatic pathogens. Several empirical studies emphasize the importance of the microbiota in resistance to fish diseases. It has been shown that the intestinal microbiome of Cynoglossus semilaevis provides resistance against vibriosis through the growth of desirable bacteria and an anti-vibrial effect (Zhou *et al.*, 2022). Equally, (Liu *et al.*, 2022) found that dietary supplementation with an antimicrobial peptide in Ctenopharyngodon idellus improved intestinal morphology and stimulated immune gene expression, thereby increasing resistance to microbial-induced infections. Additionally, studies using multi-omics approaches have shown that mucosal immunity is activated by the microbiota, enabling teleosts to balance beneficial and harmful commensals and fight pathogens (Gomez, Sunyer and Salinas, 2013; Yu *et al.*, 2021). These results indicate that it is possible to harness microbiota-immune interactions through dietary control, probiotics, or microbiome development to achieve substantial disease resistance and enhanced fish welfare in aquaculture systems.

Role of Fish Microbiota in Immune Function

Influence of Fish Microbiota on the Development of the Immune System

The acquisition and maturation of the microbiota are closely associated with the development of the immune system in fish. Since the larval stage, microbial colonization initiates at mucosal surfaces (gut, gills, and skin), where microbial metabolites serve as important signals for immune tissue differentiation. Probiotic microbial species favor the growth of gut-associated lymphoid tissue (GALT), promote the differentiation of inflammatory macrophages, and balance pro-inflammatory and anti-inflammatory cytokines. This mechanism trains the immune system to distinguish between harmless microorganisms and hostile invaders. The essential role of the microbiota in immune ontogeny is demonstrated by the fact that, under hatchery conditions, sterile or antibiotic-treated fish have underdeveloped immune organs and downregulated immune gene expression. The community of microbes via bioactive factors such as short-chain fatty acids (SCFAs) provokes transcriptional factors such as the NF-KB and STAT pathways, which enhance gene expression associated with innate defense, phagocytic activity, and mucus secretion. In order to express this relationship mathematically, the developmental strength of the immune system (Id) can be declared as:

$$Id = \alpha M_c + \beta S_f + \gamma N_r \qquad (1)$$

In which M_c refers to microbial colonization index, S_f is the concentration of signaling metabolites (e.g., SCFAs), and the rate of gene response is normalized to N_r in immune tissues. The coefficients $\alpha, \beta, and\, \gamma$ reveal the proportional effect of each factor which was identified experimentally using metagenomic and transcriptomic datasets.

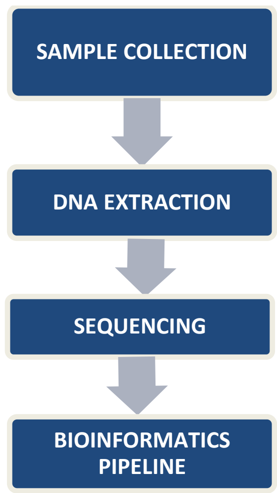

Figure 2: Experimental workflow for fish microbiota analysis.

This figure 2 shows the chronological order of events in the research of fish microbiota whereby; samples of fish are collected, DNA is extracted, the microbial genetic material is sequenced and finally bioinformatics analysis is done to identify and explain the microbial community structures and profiles of functionality.

Effects of Fish Microbiota on Pathogen Immune Response

After the immune system has developed, the microbiota becomes an active controller on host responses in the event of pathogenic interactions. The availability of balanced microbial community conditions the innate immune system such that when a pathogen is present the innate immune system is ready to recognize and get rid of the pathogen. The products of microbiota interplay with toll-like receptor (TLR), nucleotide-binding oligomerization domains (NOD), in epithelial and immune cells, resulting in activation of antimicrobial peptides, lysozymes and complement proteins. These reactions restrict the colonization of the pathogen and its transmission as well as the extension of inflammation that can destroy host tissues. To describe this, we will use a microbialimmune interaction model in which the strength of immune activation (I_a) is a dependent variable on the pathogen load (P) and microbiota stability (M_s):

$$I_a = \delta ln(P+1) + \kappa M_s - \eta D_b \ (2)$$

In this case, δ is the immune sensitivity to the load of pathogen, κ is the role played by the stability of the microbiota in defense, and ηD_b takes into consideration suppression of immunity due to dysbiosis. In the case of low D_b and high M_s, the immune system maintains the balance and eliminates pathogens quite effectively without provoking the chronic inflammation.

Specific Components of Fish Microbiota that Enhance Immune Function

Among the microbial community, some taxa have also been found to be major boosters of immune system. Generation Lactobacillus, Bacillus and Shewanella are known to produce exopolysaccharides, bacteriocins and enzymes that enhance mucosal barrier and trigger immunoglobulin generation. These microbes favor differentiation of T-like lymphocytes and macrophages with mucosal tolerance to commensals. Moreover, the metabolic products of these bacteria are the ligands of G-protein-coupled receptors in epithelial cells, which enhances cellular immunity and oxidative protection systems. In order to model this improving mechanism, it is possible to model the immune efficiency factor (E_f) as:

$$E_f = \frac{\sum_{i=1}^{n}(A_i \times M_i)}{R_i + \epsilon} \qquad (3)$$

with the A_i being the antimicrobial metabolite activity of species i, M_i being the relative abundance of that species, R_i being the pathogen resistance threshold and ϵ a non-zero constant to avoid dividing by zero. The more the E_f the more the immune resilience and less likely to be infected.

3.4 Proposed Algorithmic Model for Fish Microbiota–Immune Interaction

Algorithm 1: Fish microbiota–immune interaction model

Input: Microbiota composition M[], Pathogen concentration P, Gene response rate N_r

Output: Immune resilience index (IRI)

1. Initialize α, β, γ, δ, κ, η ← predefined constants

2. Compute microbial colonization index:

M_c = mean(relative_abundance(M))

3. Estimate signaling metabolite strength:

S_f = sum (metabolite_activity(M))

4. Calculate immune development score:

I_d = α*M_c + β*S_f + γ*N_r

5. Assess microbiota stability:

M_s = variance(M_c)$^{-1}$

6. Determine dysbiosis index:

D_b = 1 - M_s

7. Compute immune activation level:

I_a = δ*ln(P+1) + κ*M_s - η*D_b

8. Calculate final immune resilience index:

IRI = (I_d + I_a) / 2

9. Output IRI

This model predicts the interaction between microbial stability and metabolite activity to form immune resilience in a synergist manner. Combining the microbial dynamics, metabolic output, and the responses at the gene level, the algorithm would be useful in predicting the immune health and susceptibility within the aquaculture environment. These kinds of computational modeling assist in the management of precision to maintain the fish health and enhance resistance against the rising aquatic pathogens.

Factors Affecting Fish Microbiota

Environmental Factors that Can Alter Fish Microbiota Composition

Environmental factors like water temperature, salinity, pH, dissolved oxygen, and pollutant levels have a significant effect on the composition of fish microbiota. These parameters vary in natural ecosystems and aquaculture systems causing changes in the balance of the microbial communities, nutrients availability, and oxygen gradients that contribute to the growth of the microbes. As an example, warmer temperatures tend to promote the growth of opportunistic pathogens whereas low oxygen environment interferes with the normal metabolism of beneficial bacteria. The Environmental Sensitivity Index (ESI), which is the environmental effect on the stability of microbiota, can be expressed in the following way:

$$ESI = \frac{\sum_{i=1}^{n} \left| C_i - C_{i,ref} \right|}{n} \tag{4}$$

in which, C_i is the abundance of the microbial taxa i at altered conditions and $C_{i,ref}$ is the abundance of the microbial taxa i under optimal conditions and n is the total abundance of the microbial taxa being monitored. An increased ESI value shows the higher level of ecological stress and instability of microbiota.

Dietary Effect on Microbiota of Fish

The composition of the food is a prevailing factor in determining the amount and type of microbes in the gut and their metabolism in fish. High protein or vegetarian diets regulate the population of bacteria that produce fermentation, fatty acids and immune regulation. Additives like probiotics, prebiotics, amino acid supplements and others influence the microbial interactions by encouraging the growth of beneficial bacteria, and blocking harmful species. In order to assess the impact of the dietary factors, one can consider a Microbial Diversity Index (MDI):

$$MDI = -\sum_{i=1}^{n} p_i log(p_i) \tag{5}$$

p_i is the relative abundance of species i. Increase in MDI implies that the gut ecosystem is more diversified and stable to allow nutrient absorption and resistance to disease.

Genetics in Programming the Microbiota of Fish

Genetics of the host are also crucial in conditioning which species of microbes can colonize particular tissues. Microbial selection is influenced by genes that control mucosal secretions, immune receptors and epithelial integrity. The microbiota profile of closely related species or strains of fish varies due to genetic variation between fish species. This may be represented by the Genetic Influence Coefficient (GIC):

$$GIC = \frac{Cov(G,M)}{Var(G)} \quad (6)$$

$Cov(G,M)$ is the covariance between genotypic traits in the host and the abundance of the microbes and $Var(G)$ is the variance of the genetic factor.

Performance Evaluation

The microbial composition and diversity, as well as host-microbe correlations are evaluated using software tools like QIIME2, Mothur and R (vegan package). The standardized measures of performance, such as Shannon Diversity, BrayCurtis Dissimilarity, Network Stability Index (NSI), are used to measure performance. Performance assessment is a combination of such measurements which help to evaluate the extent to which environmental change, dietary inputs, and genetic characteristics together affect the microbiota balance. Using such analyses, aquaculture management can help to optimize the conditions to maintain a healthy microbial balance and enhance the resilience of fish to environmental and pathogenic stressors.

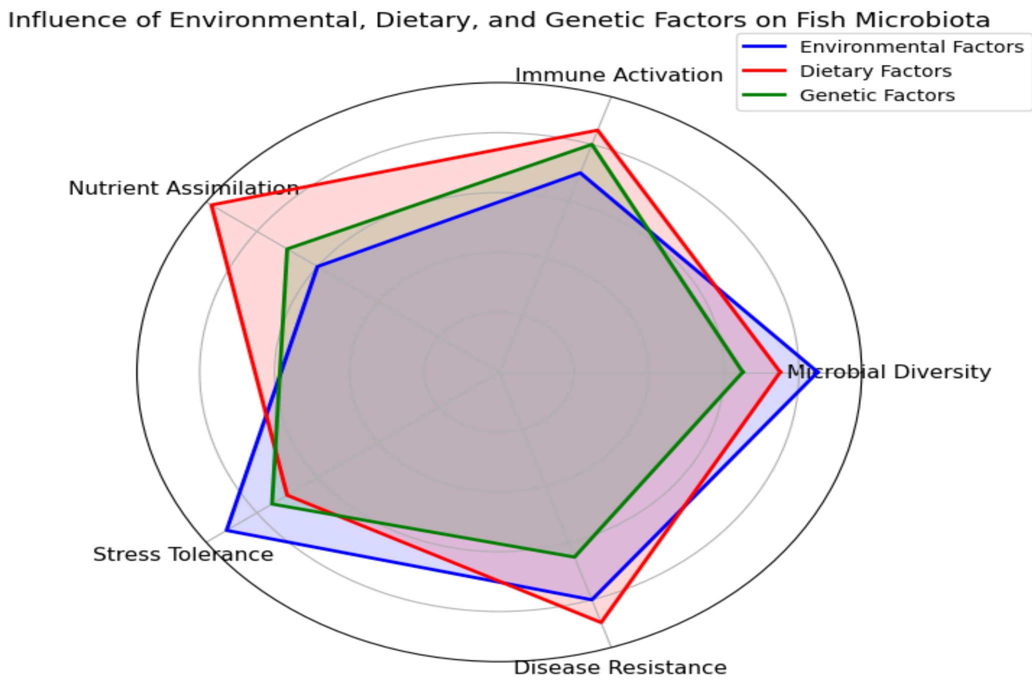

Figure 3: Influence of environmental, dietary, and genetic factors on fish microbiota performance metric.

This radar chart (Figure 3) shows multidimensional association between key determinants, which affect fish microbiota performance in aquatic ecosystems. The five most important measures, which are microbial diversity, immune activation, nutrient assimilation, stress tolerance and disease resistance are plotted as radial axes with each polygon corresponding to environmental, dietary and genetic factors respectively. The chart indicates that the environmental factors indicate higher contributions to microbial diversity and stress tolerance whereas the dietary influences dominate the nutrient assimilation and immune activation. Genetics, although neither extreme, have a considerable influence on the general stability of the microbes and the flexibility of the host. This comparative visualization gives an integrated view on the influence of external and intrinsic conditions on the overall fish health and immune competence as an integrated feature of establishing microbial equilibrium in dynamic aquatic environments.

Manipulating Fish Microbiota for Disease Management

Control of fish microbiota in the management of diseases has become one of the viable approaches in aquaculture, with emphasis on improving the natural microbial balance to increase disease resistance and health in general. Lactobacillus, Bacillus and Shewanella species are commonly used as probiotics to enhance the populations of beneficial bacteria that compete with the pathogenic bacteria in nutrients and adhesion sites as well as in stimulation of mucosal immunity and enhancing gut integrity in fish. Likewise, prebiotics like inulin, mannan oligosaccharides and 1,5- glucan can be used as selective energies that promote the growth of symbionic microbes that synthesize short chain fatty acids and antimicrobial peptides that assist in maintaining intestinal homeostasis. The microbial interventions have resulted in success in decreasing the rate of bacterial diseases such as vibriosis and aeromoniasis in fish such as the tilapia, carp, and salmon. Nonetheless, there are still difficulties because of host species variations, environmental factors and microbial flexibility which can frequently constrain predictable results. Also, regulatory gaps, strain non-specificity and short-term colonisation still present impediments to massive usage. In spite of the limitations, specific control of fish microbiota using probiotics and prebiotics remains a promising, environmentally friendly method of controlling the disease and immune-boosting in the context of contemporary aquacultural systems.

Conclusion

Fish microbiota is a field of study that has shown that it plays a basic role in ensuring the health of aquatic animals, especially in improving disease resistance and immune response. Bacterial communities that live in the gut and mucosal surfaces of fish serve as biological shields, and this prevents the colonization of the host by the pathogen and enables immune competence to develop due to continuous host-microbe interactions. The major conclusions demonstrate that a balanced microbiota allows the assimilation of nutrients, increases epithelial integrity, and both innate and adaptive immune responses, which are natural means of disease prevention. Knowledge of these microbial interactions has been applied in aquaculture through the development of new applications that include microbial-based diagnostics, microbial therapeutics, and personalised feeding systems that foster the growth of beneficial microbes. Future studies are required on clarifying the molecular mechanisms of hostmicrobiota crosstalk, in vitro development of species-specific microbial consortia, and combination of multi-omics protocols to streamline microbial management risks. Harnessing the opportunity of fish microbiota, therefore, offers a justifiable way of enhancing fish health, welfare, and productivity and minimizing antibiotic and chemical use. Microbiota-based interventions can be a stepping-stone towards sustainable and environmentally-friendly aquaculture systems that are able to sustain the increasing global demand of healthy aquatic food resources.

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