



## Host-Microbiome Interaction in Fish

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The significance of the gut microbiome in fish and shellfish management, encompassing healthy growth and performance, is extensively acknowledged and researched for potential applications in aquaculture farming. The gut microbiome, integral to all animals, including fish, serves several beneficial functions, such as optimizing gastrointestinal development, synthesizing vitamins, enhancing nutrient absorption, and bolstering the immune system. It is often likened to an "extra organ" due to its pivotal role in intestinal development and regulation of physiological functions. Recent studies highlight its involvement in energy regulation, metabolic processes, and immune response. Understanding gut microbiome dynamics in cultured aquatic species is crucial for promoting animal health and productivity. Moreover, the gut microbiome serves as a valuable source of natural product discovery, with microbial communities associated with marine organisms yielding numerous bioactive compounds. Despite its importance, knowledge regarding host-microbiome interaction at cellular, genetic, and immunomodulatory levels is limited. Interaction among host, microbe, and

environment maintains gut homeostasis in fish and shellfish, with intrinsic factors, environmental influences, and the core microbial community all playing significant roles. This popular article aims to provide basic and brief insights into various aspects of host-microbiome interaction, focusing on immune system regulation, disease management, nutrient metabolism, gene expression, and overall health maintenance in aquatic species.

### INTRODUCTION

Microbiome communities, comprising a variety of microorganisms such as protists, yeasts, viruses, bacteria, and archaea, are commonly found not only in the digestive tract but also inhabit various other parts of fish and shellfish bodies, including the skin, gills, and muscular tissues. The population density and composition of these microbiome communities are influenced by environmental factors, as well as by seasons, host genetic factors, age, and diet (Diwan et al., 2023). Despite this variability, core microbial components, especially within the digestive tract, remain consistent across individuals of the same species, even under different rearing conditions. The diverse microbial species present in the gastrointestinal tract and



other bodily regions play crucial roles in maintaining physiological homeostasis and defending against pathogens. The specific functions of the digestive tract, its morphology, immunomodulation, and nutrient absorption are heavily influenced by the microbial composition present in fish and shellfish.

Research indicates that microbes play pivotal roles in modulating host physiology, health, and disease management across various organisms. Technological advancements, particularly in single-cell analysis such as genomics, transcriptomics, and spatial resolution, have significantly enhanced our understanding of the complexities involved in host-microbe interactions. While the significance of host-microbiome interactions in host development, immunity, metabolism, and pathways is well recognized, information regarding these interactions in fish and shellfish remains limited. Recent efforts have begun to explore these interactions, particularly in relation to physiological functions. Studies on hybrid fish have shown that host genetics-gut microbiome interactions contribute to dietary adaptation. Furthermore, investigations into the gut microbiome of fish have revealed its crucial role in various bodily functions, with microbial species acting as a "second genome" that regulates vital physiological processes. Both intrinsic and extrinsic factors, including feeding habits, influence the colonization of the fish gut microbiome community.

Emphasizing the importance of the holobiont concept, researchers have highlighted the necessity of understanding the interaction between hosts and their associated microbial communities. Together, these entities form a biological unit, constituting the holobiont concept.

Several studies have explored the functional roles of gut microbiome species and their interactions with hosts in both fish and shellfish. Ray et al. (2012) reported on the role of the gut microbiome in producing digestive enzymes and facilitating the digestion process. Other researchers have investigated various aspects, such as the production of vitamins, short-chain fatty acids, biofilm formation, and iron metabolism in the gut microbiome of both freshwater and marine fish (Nikouli et al., 2021). Li et al. (2022) conducted an in-depth analysis of growth performance in hybrid fish, examining the composition of microbiome species in the gut system as part of their study on host-microbiome interactions. However, studies assessing phenotypic variations in fish and shellfish and their correlations with gut microbiome composition are limited. Mushegian et al. (2019) delved into the genome of gut microbiome species to explore whether microbiome genes are involved in core microbiome selection preferences. Additionally, several researchers have investigated the role of host-gut microbiome interaction in managing various types of stress responses in fish.

### **MICROBIOME INTERACTION IN FISH**

When discussing the significance of holobiont research, it is imperative to inquire about the roles fulfilled by microbes in host organisms, leading to phenotypic and fitness effects. Similarly, understanding the mechanisms involved in host-microbiome interaction becomes crucial in comprehending the functions of holobionts (Simon et al., 2019). Despite numerous reports on the gut microbial composition of various finfish and shellfish, information concerning the functional properties of these microbes remains limited and poorly



elucidated. Previous studies have suggested that gut microbes can produce diverse digestive enzymes, implying their potential contribution to the hosts' digestive function (Ray et al., 2012). Furthermore, experimental evidence supports the production of vitamin B12 by fish gut microbes (Romero et al., 2014). Herbivorous fish species have been reported to produce short-chain fatty acids through the digestion of dietary fiber with the assistance of gut microbes. These acids not only fulfill a significant portion of the host's energy requirements but also aid in lowering pH levels in the gut, creating an environment less favorable for certain harmful pathogens, thus mitigating bacterial infections (Merrifield et al., 2015). The concept of a core microbiome species residing in the gut systems of fish and shellfish has garnered attention due to their specific functions within the body, which are generally unaffected by extrinsic or intrinsic factors. However, the existence of a core microbiome in the gut tract remains speculative, as some microbial species may deviate from this pattern, as observed in certain mammalian groups, including humans. This speculation also extends to fish and other aquaculture species and warrants further investigation. Xing et al. (2013), in their study on turbot fish microbiome composition, noted significant differences in bacterial abundance and functional analysis compared to other fish species, particularly in genes associated with the *Vibrio* genus, suggesting potential variances in metabolic potential among marine and freshwater fish microbiomes. Similarly, Li et al. (2022) explored microbial communities and host-microbial interactions in hybrid fish resulting from crossing herbivorous *Megalobrama amblycephala* (♀) with carnivorous *Culter*

*alburnus* (♂). They observed no substantial difference in growth rate between groups fed herbivorous and carnivorous diets during early developmental stages. The gut systems of these fishes exhibited a plethora of bacterial communities, with dominant groups such as *Acinetobacter*, *Gemmobacter*, *Microbacterium*, *Vibrio*, and *Aeromonas*. The abundance of other bacterial groups like Firmicutes, Actinobacteria, and Chloroflexi correlated with host growth levels. Spearman's correlation analysis revealed associations between differentially expressed homologous genes in the gut system and the dominant microbiome groups present, suggesting that host genetics-gut microbiota interactions contribute to dietary adaptation in hybrid fish. Thus, there is a pressing need for a comprehensive understanding of the core microbiome in the gut systems of various finfish and shellfish, along with their metagenomic functions, to draw definitive conclusions regarding such aspects.

To comprehend the interaction between hosts and their microbiomes, many researchers propose investigating the production of phenotypic traits and their correlation with gut microbiomes in fish or shellfish. Phenotypic variations in animals have been linked to the structural composition of the intestinal microbiome, as these microbiomes produce various biochemical compounds, including short-chain fatty acids, vitamins, and amino acids (Li et al., 2022). They also collaborate with the host intestinal immune system to hinder the invasion of exogenous pathogenic microorganisms. The animal host genome influences the selection of specific microbiome species, shaping the microbiome community in the gut system. Consequently, host genes play a crucial

role in designing the structural composition of the gut microbiome. Interactions between host genetics and gut microbiomes contribute to food digestion, physical development, and environmental adaptation. In studies focusing on host-microbiome interactions in zebrafish, Robinson et al. (2018) highlighted intra and extra-host factors that influence bacterial selection and adaptations in the digestive tract. These findings, supported by others, suggest that intestinal microbes significantly impact genetic evolution, growth, and development, not only in fish and shellfish but also in other animals. Evidence indicates that the gut microbiome profoundly influences brain function, including stress responses and behavior, transmitting signals to the brain through various pathways, such as the production of microbial metabolites and peptides, immune activation, and vagus nerve activation in the gut. Research demonstrates that, similar to mammals, the intestinal microbiome community affects the hypothalamic-pituitary-adrenal axis and stress response management in fish effectively (Ye et al., 2016).

Similarly, in gilthead sea bream, the intensity of growth performance relies on the presence and abundance of specific bacterial species in the gut. Studies have also noted distinct growth rates associated with bacterial species different abundances in fish intestines. Even in genetically selectively bred fish, distinct microbial species are observed in their intestinal tracts. In many organisms, including fish and shellfish, the intestine serves various functions, such as nutrient uptake, pathogen recognition, and regulation of intestinal microbiome composition. Structural changes in intestinal histology occur due to the intestine's multifunctional role, as

reported by several researchers. The influence of gut microbiome flora on various host functions and structural changes in the gastrointestinal tract has been extensively documented (Zhang et al., 2021; Martin et al., 2016). However, detailed investigations at the genetic expression and molecular levels are required to understand each physiological activity and its correlation with gut microbiome structure. The mechanism of interaction between hosts and their microbiome community is illustrated in Figure 1.

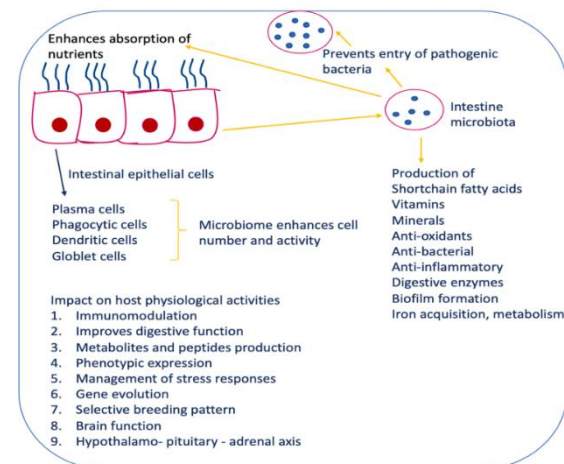


Fig. 1. Possible Mechanism of Host-microbiome Interaction

## GUT-MICROBIOME AND HOST HEALTH

The microbiome's pivotal role in host health is increasingly acknowledged, marking it as a significant realm within holobiont research aimed at preventing and treating diseases by restoring disturbed microbial communities (Diwan et al., 2021). Various researchers propose leveraging probiotics, prebiotics, synbiotics, and biofloc systems to modulate gut microbiota in fish and shellfish, thus curbing disease spread and fostering robust growth in aquaculture settings. Recent investigations underscore the criticality of gut microbiome-host interactions in



shaping intestinal mucosal development, maintenance, and functionality, alongside fortifying defenses against gastrointestinal pathogens and bolstering digestive processes through enzymatic and vitamin production (Sun et al., 2019). Probiotics exhibit multifaceted benefits, including immune stimulation, improved growth, enhanced feed utilization, and heightened disease resistance, while prebiotics, symbiotic, and biofloc technologies hold promise for augmenting fish immune status and overall production quality, though literature in this domain remains limited. Furthermore, the specific mechanisms through which probiotics and prebiotics confer mucosal benefits require deeper elucidation, emphasizing the need for future research to unravel these intricacies and optimize biotic interventions for bolstering immune function across key aquaculture species (Holt et al., 2020).

### CONCLUSION

The concept of hologenome and holobiont is vital for understanding organismal life, as it involves the intricate interaction between the host and its microbiome community. Disruptions in the gut microbiome composition, caused by various factors, can lead to physiological disturbances and impact organismal health. Further research is needed to strengthen this theory. Investigating the assembly and maintenance of core microbiomes in the gut system of fish and shellfish is crucial for future studies, particularly focusing on their functional aspects. Phenotypic trait production and its correlation with gut microbiomes require further exploration. Research on the animal genome's role in shaping microbiome composition is essential, especially concerning the gut microbiome's influence on brain function and behavior. Limited literature exists on

the correlation between host-microbiome interaction and selective breeding in fish and shellfish, necessitating more comprehensive research. Investigation into microbiomes associated with skin and other tissues and their interaction mechanisms is imperative. Recent breakthroughs in understanding gill microbe interactions reveal that fish microbiomes produce a specific antibody, IgT, in response to pathogenic microbes, similar to responses from mucosal gill microbes. Further research is needed to fully grasp host-microbe interactions and their genomic implications, as dysbiosis in gastrointestinal microbiome composition negatively impacts immune regulation and physiological processes, increasing susceptibility to infections and disease spread.

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