Precision Microbiome Stewardship: Moving Aquaculture from Transient Supplementation to Systemic Resilience

Till Röthig[1,*], Christian R. Voolstra[2], Haiwei Luo[3], André Billion[1], Thomas Wilke[1,4]

[1] Fraunhofer Institute for Molecular Biology and Applied Ecology IME, Branch for Bioresources, Giessen, Germany

[2] Department of Biology, University of Konstanz, Konstanz, Germany

[3] Simon F.S. Li Marine Science Laboratory and School of Life Sciences, The Chinese University of Hong Kong, Hong Kong SAR

[4] Institute of Zoology, Justus Liebig University Giessen, Giessen, Germany

[*] Correspondence:

Till Röthig, Fraunhofer Institute for Molecular Biology and Applied Ecology IME, Branch for Bioresources Ohlebergsweg 12, 35392 Gießen, Germany

Till.Roethig@ime.fraunhofer.de | +49 641 97219 213

ORCID: Röthig: 0000-0001-6359-8589, Voolstra: 0000-0003-4555-3795, Luo: 0000-0001-8452-6066, Billion: 0000-0002-5073-3347, Wilke: 0000-0001-8263-7758

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1 Introduction

Aquaculture now supplies more than half of all fish consumed globally[1] yet its continued expansion is constrained by infectious disease losses estimated at approximately USD 6 billion annually[2] and increasing antimicrobial resistance pressure[3,4]. The field has become increasingly effective at generating short-term microbiome-mediated benefits, but durable ecological integration, defined here as the persistence of beneficial microbes within the host and their functional embedding within the production system, remains largely unresolved. Over the last decade, targeted feed and water microbial treatments, including probiotics, prebiotics, and synbiotics have successfully enhanced innate immune responses, improved nutrient utilization, and elevated the overall welfare of various aquaculture species[5,6]. Despite these functional benefits, the dominant delivery model for microbial treatments remains largely supplemental. Many microbial treatments, regardless of strain origin, produce benefits mainly during repeated or continuous administration, while durable host association remains difficult to predict and is rarely validated post-dosing[7]. This continuous application approach is the supplementation bottleneck. While it optimizes temporary pathogen suppression and provides essential immune boosting, it often falls short of establishing structural and self-sustaining microbial resilience. This is the central controversy addressed here: aquaculture has scaled microbiome intervention commercially without yet establishing persistence, predictability, or resilience as the primary standards of evidence. The transition from pathogen control to resilience does not imply that previous probiotic therapies were misguided[6,8]. Rather, it proposes that disease resistance should be treated as one expected outcome of a functionally intact host-system microbiome, rather than the sole target of repeated therapeutic intervention. What remains underdeveloped is a stewardship framework that moves beyond treatment-period response toward a common management target: host-system microbial resilience. We argue that Precision Microbiome Stewardship — building on stewardship concepts established for medicine and ecosystem conservation[9,10] and extending them to aquatic production systems — must map intrinsic host constraints and extrinsic system levers, validate ecological integration rather than continuous supplementation alone, and use monitoring loops to detect dysbiotic trajectories before disease or production loss becomes visible.

Box 1 — Terminology box

- Microbial treatment: Use of live microbes, substrates, consortia or microbiome-directed practices to alter host or system microbiomes.
- Probiotic: Live microorganism administered to confer a host or system benefit.
- Pathogen-exclusion paradigm: Management strategy focused on preventing or suppressing pathogens, rather than building microbial resilience.
- Persistent associate: Administered or naturally occurring microbe detectable beyond dosing and associated with a reproducible niche.
- Resident microbiome: Microbial members reproducibly associated with a defined host tissue, mucosal surface, biofilm, biofilter or system compartment beyond transient environmental exposure.
- Resilient microbiome state: A community configuration that maintains function during perturbation or recovers function after perturbation, reducing transition into dysbiosis or opportunist dominance. A resident community is not automatically resilient; transient interventions can leave resilient legacy effects.
- Precision Microbiome Stewardship: Management framework that links host–system microbiome monitoring, evidence standards and targeted interventions to resilience outcomes.
- Microbiome Flux Model: Framework describing microbial exchange between host, water, feed, biofilms, biofilters and surfaces.
- Colonization resistance: Suppression of opportunists through niche occupation, resource competition or inhibitory interactions.
- Supplementation logic: Repeated microbial application aimed at treatment-period effects rather than durable ecological integration.

Scope note: This framework is bacteria-forward rather than bacteria-exclusive. Viromes, mycobiomes, resistomes and mucosal microbiomes of skin and gill are not addressed in detail but must be incorporated as evidence develops.

2 From Supplementation Logic to Ecological Residency

The aquaculture probiotic market is commercially established but relies on a supplementation model requiring repeated administration to maintain efficacy[7,11]. Precision Microbiome Stewardship addresses this by identifying persistent colonization, durable legacy effects and system-level microbial stabilization as complementary routes to resilience[12,13]. Of these, persistent colonization is the most tractable for intensive production contexts: the strain can be detected, its abundance monitored, and its presence linked directly to host performance, making validation, optimization and scale-up more feasible. Transient early-life exposures that leave durable legacy effects represent a complementary route that may be particularly relevant during developmental windows (i.e., larval and early juvenile stages) where microbiome assembly is most plastic but continuous supplementation is least practical. Importantly, long-term colonization is not guaranteed by host origin alone; allochthonous strains can achieve persistence under the right conditions, and host-derived strains frequently remain transient. Provenance alone is unlikely to be the determinative factor. Rather, evolutionary commitment to a host-associated lifestyle, evidenced by genomic signatures of host dependency, may provide a more tractable predictor of persistence potential. What remains missing is a predictive selection framework that identifies these signatures a priori rather than discovering persistence only empirically. Host residency is operationally defined in the framework below (Priority 3 MVD): detection of the administered candidate beyond the dosing period, or a persistent shift in microbiome trajectory attributable to the intervention.

This is the critical conceptual shift: trait-based screening is still largely aspirational, because it identifies candidates we hope will persist. Persistence-based screening, by contrast, treats persistence as a prediction to be tested. By first selecting for evolutionary genomic signatures of host dependency and then testing whether the candidate actually persists and confers benefit, we address the bottleneck of transient colonization directly rather than trying to work around it.

Coral microbiome research now provides a proof of concept for this logic. Rather than relying only on established functional screens such as pathogen inhibition, adhesion, safety traits or immune stimulation[8,14] and hoping for persistence, a recent preprint and companion study by Xie et al.[15,16] inverted the conventional logic. They selected first for evolutionary genomic signatures of emerging host dependency. Bacteria transitioning toward a host-associated lifestyle often exhibit two hallmarks: proliferation of insertion sequences (mobile genetic elements that drive genomic restructuring) and widespread pseudogenization that tightens host dependence. Applying this evolution-first screen to over 1,200 coral isolates identified *Ruegeria* MC10, a probiotic candidate associated with improved thermal stress tolerance in corals. Without continuous reapplication, MC10 remained detectable throughout an eight-month monitoring period that included a natural bleaching event. Nursery inoculation was sufficient to confer measurable thermal resilience during that event. This durable association was underpinned by a distinct functional profile: enhanced biofilm formation, siderophore-mediated iron chelation, and a host-responsive proteomic shift from motility to sessility. The value for aquaculture lies not in the strain itself, but in the transferable selection principle: persistence should be predicted before benefit is tested, not inferred retrospectively from repeated dosing success.

The evolution-first logic therefore generates a clear, testable hypothesis for aquaculture: candidates selected for host-dependency signatures are predicted to have a higher probability of durable colonization than candidates selected without explicit persistence criteria and should be tested for long-term host benefit under production conditions. Candidates lacking these signatures should be treated as lower-confidence persistence candidates until post-dosing persistence is directly tested; persistence may also arise through adhesion, biofilm formation, diet-supported niche availability or environmental reseeding.

Precision Microbiome Stewardship should complement established supplementation pipelines with an evolutionary genomics-driven approach that first identifies lineages with increased persistence potential. This reframes the order of candidate evaluation: first ask whether a candidate carries host-dependency signatures; then test whether it persists and what benefit its persistence confers. This makes host residency a testable design criterion rather than an assumed outcome. Evolution-guided candidate selection is one operational pillar of Precision Microbiome Stewardship, alongside host-system flux management, extrinsic habitat engineering, and monitoring-to-intervention loops.

3 The Microbiome Flux Model: Integrating Host and System

Host microbiomes in aquaculture do not exist in isolation. They are continuously shaped by the surrounding water column, surface biofilms, and feed inputs[17]. This bidirectional connectivity defines the Microbiome Flux Model (Fig. 1). Attempting to manage the host microbiome (intrinsic parameters) without simultaneously managing the system microbiome (extrinsic parameters) is operationally inefficient.

This environmental connectivity has direct management implications. In recirculating aquaculture systems (RAS), intensive disinfection and pathogen-exclusion practices can restrict the microbial colonizer pool and destabilize community assembly, without necessarily creating sterility, but reducing the diversity of potential colonizers and the ecological buffering capacity of the system[18]. Consequently, functionally mature biofilters and surface-associated communities should be viewed as microbial water-quality assets, not only as technical nitrification units or hygiene targets[18–20]. The objective is not to increase microbial load, but to manage selection pressures that limit opportunistic blooms and support predictable host–system microbial exchange.

Precision Microbiome Stewardship treats the surrounding water and system biofilms as managed assets rather than merely hygiene challenges. Tank material and surface chemistry represent plausible extrinsic microbiome levers: infrastructure shapes the microbial exposure landscape continuously and should not be treated as microbiologically inert. Direct microbial community effects of specific materials require dedicated validation[21]. Managing ecological selection pressures within the system may increase the probability that microbial flux supports, rather than disrupts, host-associated microbiome stability. However, host filtering, stochastic assembly, life stage, diet and system design will also shape outcomes.

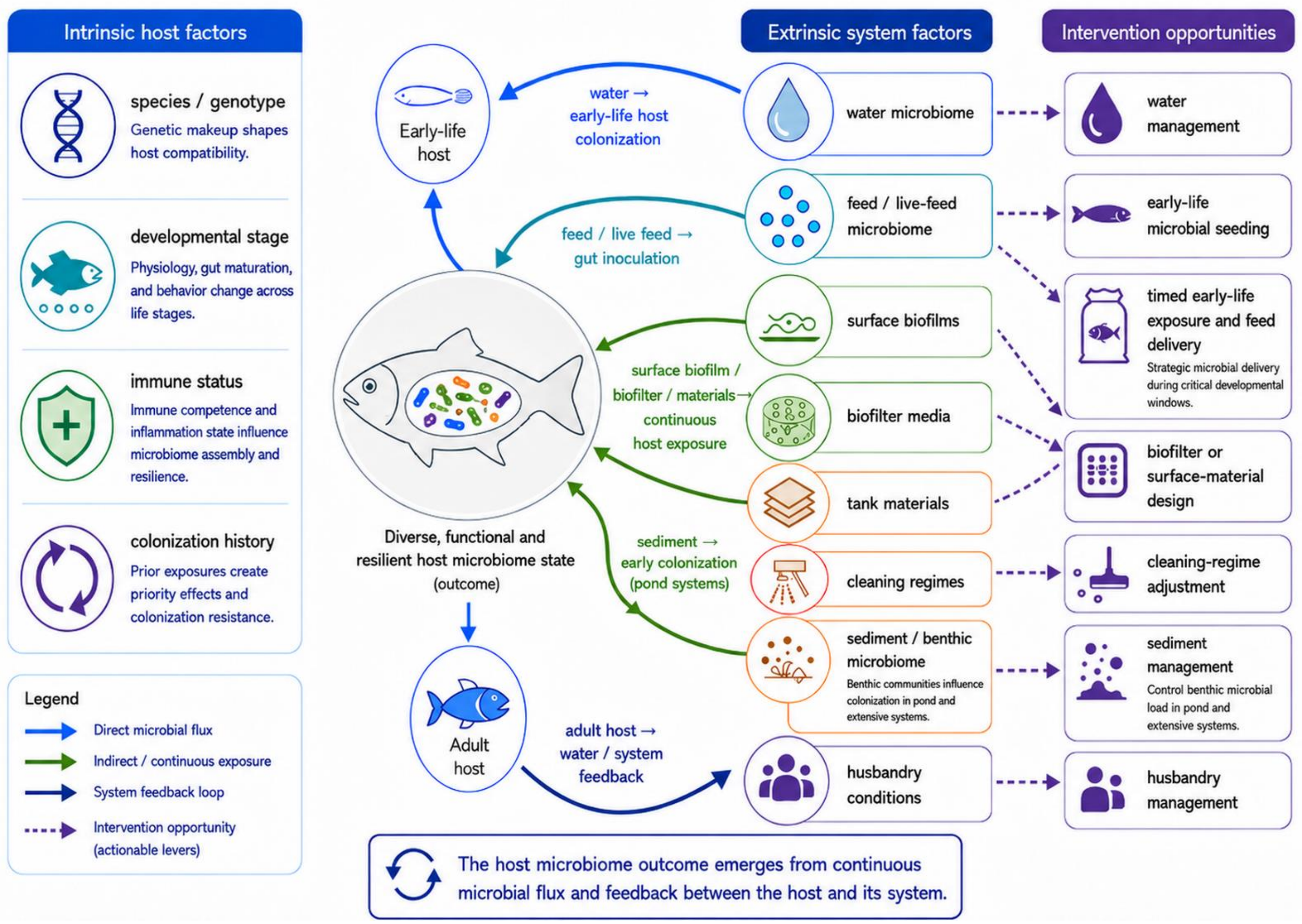

FIGURE 1 The Microbiome Flux Model. The host microbiome is shaped by continuous exchange between intrinsic host-side constraints (species and genotype, developmental stage, immune status,

colonization history) and extrinsic system-side intervention points (water microbiome, feed and live-feed microbiome, surface biofilms, biofilter media, tank materials, cleaning regimes, and husbandry conditions). Arrows indicate direct microbial flux (solid), bidirectional influence (dashed), and system feedback loops. Intervention opportunities are shown on the right.

4 Redefining the Target: Resilience and Animal Welfare

The traditional metric for evaluating microbial interventions has been the reduction of specific pathogen loads or overall mortality rates. However, modern microbiome research highlights that pathogen expansion often occurs in the context of disturbed host or environmental microbiomes, although dysbiosis may be a cause, consequence or correlate depending on the host, pathogen, life stage and production system[22]. Dysbiosis is characterized by a loss of microbial diversity, the depletion of beneficial commensals, and a compromised mucosal barrier[22]. These disruptions often precede clinical signs of disease.

If resilience is defined as the capacity of host and microbial system to absorb perturbations without transitioning into a disease state, then resilience must become the primary outcome variable. Durable resilience can arise through more than one route. Persistent host or system association by ecologically integrated candidates provides an active, ongoing relationship: the strain is detectable, its benefit continuously delivered, and its effect directly linkable to host performance. Transient early-life exposures can also leave lasting microbiome or immune legacy effects without organism maintenance[12,13], particularly during developmental windows when microbiome assembly is most plastic. For intensive production contexts, persistent colonization is the more predictable and scalable target; legacy-effect approaches are most relevant where early-life accessibility is high but long-term supplementation is impractical. Precision Microbiome Stewardship targets the evidence standard that distinguishes and validates both routes under production conditions. A resilient system is not pathogen-free; it is one in which microbial communities occupy niches, buffer disturbances, and limit opportunist expansion.

Environmental stressors can trigger dysbiosis in the water and host, allowing normally benign opportunistic bacteria to expand and become infectious[17,18,22,23]. Proactive microbiome resilience requires not only functional redundancy, but evidence for durable post-intervention effects: persistent host-adapted symbionts, stabilized resident communities, or lasting legacy effects after transient exposure. In principle, an evolution-primed probiotic that achieves stable host association may maintain resilience beyond the dosing period — as demonstrated in a coral host over eight months[15,16] — but this remains to be validated in fish and shrimp production systems. The management target should therefore be resilient microbiome trajectories (the capacity for functional recovery after disturbance) rather than static stability. Monitoring should detect departures from these trajectories toward dysbiosis before clinical disease or production losses appear[22]. This moves management upstream: not pathogen response, but prevention of the dysbiotic preconditions that enable outbreaks.

5 A Framework for Precision Microbiome Stewardship

Precision Microbiome Stewardship becomes operational when three elements are combined: first, a better candidate selection logic by selecting for evolutionary genomic signatures of host-compatible persistence rather than functional traits alone; second, recognition that both intrinsic host factors and extrinsic system factors shape the microbiome, making the production environment itself a stewardship lever; third, a shift in management target from disease prevention to active resilience building from reactive pathogen control toward robust aquaculture systems. We propose that these three advances together define the minimum conceptual threshold for Precision Microbiome Stewardship. By requiring post-intervention validation, including persistence, resident-community integration, durable legacy effects or system-level stabilization under production-realistic conditions, the industry can bridge the gap between laboratory potential and field performance. Baselines come first because without species-specific longitudinal reference data no intervention outcome can be causally interpreted; candidate selection and persistence validation follow, with system-integrated monitoring and closed-loop trials completing the framework. As detailed in Table 1, these priorities integrate host and system microbial flux into an actionable stewardship framework. Prediction is strongest in early-life and hatchery settings, where assembly dynamics have disproportionate effects on survival, and more variable and context-dependent in grow-out stages[24]. The analytical layer integrating these data streams could eventually function as a decision-support layer for the host–system microbiome: the limiting factor will not be algorithm choice, but data quality, sampling frequency, metadata standardization and interoperability across production systems.

TABLE 1 Operational priorities for transitioning from conventional probiotic supplementation to Precision Microbiome Stewardship in aquaculture. For each priority, the enabling function and the minimum viable demonstration required for field validation are specified.

Priority	Enabling Function	Minimum Viable Demonstration
1. Species-specific host microbiome baselines	Provides a calibration framework essential for the interpretation of intervention outcomes[24].	Longitudinal microbiome and health profiles in at least one commercially relevant host.
2. Host-compatible, persistence-validated candidate selection	Shifts candidate selection from trial-and-error to evolution-guided prediction. Screen for genomic hallmarks of host dependency and functional traits linked to persistence[15,16], combined with safety screening for virulence factors, antimicrobial resistance genes and mobile genetic elements[3,14].	Defined screening criteria applied to host-origin strains and validated against at least one non-candidate control; compared with commercial benchmarks.
3. Resident, persistent or legacy-effect validation	Bridges laboratory findings to commercial production reality.	Strain-resolved post-dosing detection by qPCR, barcoding or re-isolation, plus evidence of network association or functional activity; or, for legacy-effect approaches, a durable shift in microbiome trajectory, immune responsiveness or resilience outcome[12,13]. Amplicon shifts alone are insufficient.
4. System-integrated microbiome health indices	Makes monitoring data actionable for proactive intervention decisions[22,24].	Integrated host-system indicators (growth, FCR, survival, stress or mucosal markers, pathobiont load, water chemistry, organic load and biofilter recovery) predict resilience loss before clinical signs.
5. Closed-loop monitoring-to-intervention trials	Completes the stewardship framework through adaptive management.	Precision stewardship arm versus standard probiotic arm in a realistic production context.

6 Conclusions

The aquaculture sector has achieved commercial scale in microbiome intervention. However, it has not yet translated this scale into biological precision, because microbial products are still commonly selected and evaluated based on manufacturability, formulation stability, and short-term efficacy. The next step is not more supplementation of the same kind, but a change in evidence standards: persistence, ecological integration, and resilience must become the criteria by which microbiome-based interventions are evaluated. Formulation stability is not host compatibility and pathogen exclusion is not resilience. The goal is not to make aquaculture systems microbiologically cleaner, but microbiologically more resilient. In our view, the next generation of aquaculture microbiome interventions will be defined not by treatment-period effects, but by persistence, ecological integration, and resilience outcomes, collectively summarized as Precision Microbiome Stewardship.

Author Contributions

Till Röthig: Conceptualization, Writing – original draft, Writing – review and editing, Project administration, Visualization. Christian R. Voolstra: Conceptualization, Writing – original draft, Writing – review and editing, Visualization. Haiwei Luo: Conceptualization, Writing – review and editing. André Billion: Conceptualization, Writing – review and editing, Visualization. Thomas Wilke: Conceptualization, Writing – original draft, Writing – review and editing.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

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References

1. FAO. The State of World Fisheries and Aquaculture 2024. *State World Fish Aquac 2024*. Published online June 7, 2024. doi:10.4060/cd0683en
2. Maezono M, Nielsen R, Buchmann K, Nielsen M. The Current State of Knowledge of the Economic Impact of Diseases in Global Aquaculture. *Rev Aquac*. 2025;17(3):e70039. doi:10.1111/RAQ.70039
3. Watts JEM, Schreier HJ, Lanska L, Hale MS. The Rising Tide of Antimicrobial Resistance in Aquaculture: Sources, Sinks and Solutions. *Mar Drugs 2017, Vol 15, Page 158*. 2017;15(6):158. doi:10.3390/MD15060158
4. Caputo A, Bondad-Reantaso MG, Karunasagar I, et al. Antimicrobial resistance in aquaculture: A global analysis of literature and national action plans. *Rev Aquac*. 2023;15(2):568-578. doi:10.1111/RAQ.12741
5. Rajeev R, Adithya KK, Kiran GS, Selvin J. Healthy microbiome: a key to successful and sustainable shrimp aquaculture. *Rev Aquac*. 2021;13(1):238-258. doi:10.1111/RAQ.12471
6. El-Son MAM, Elbahnaswy S, Khormi MA, Aborasain AM, Abdelhaffez HH, Zahran E. Harnessing the fish gut microbiome and immune system to enhance disease resistance in aquaculture. *Fish Shellfish Immunol*. 2025;163:110394. doi:10.1016/J.FSI.2025.110394
7. Tayyab M, Zhao Y, Zhang Y. Microbiome engineering to enhance disease resistance in aquaculture: current strategies and future directions. *Front Microbiol*. 2025;16:1625265. doi:10.3389/FMICB.2025.1625265/XML
8. Merrifield DL, Dimitroglou A, Foey A, et al. The current status and future focus of probiotic and prebiotic applications for salmonids. *Aquaculture*. 2010;302(1-2):1-18. doi:10.1016/J.AQUACULTURE.2010.02.007
9. Jørgensen PS, Wernli D, Folke C, Carroll SP. Changing antibiotic resistance: sustainability transformation to a pro-microbial planet. *Curr Opin Environ Sustain*. 2017;25:66-76. doi:10.1016/J.COSUST.2017.07.008
10. Peixoto RS, Voolstra CR, Sweet M, et al. Harnessing the microbiome to prevent global

biodiversity loss. *Nat Microbiol 2022 711*. 2022;7(11):1726-1735. doi:10.1038/s41564-022-01173-1

11. Diwan AD, Harke SN, Gopalkrishna, Panche AN. Aquaculture industry prospective from gut microbiome of fish and shellfish: An overview. *J Anim Physiol Anim Nutr (Berl)*. 2022;106(2):441-469. doi:10.1111/JPN.13619

12. Giatsis C, Sipkema D, Ramiro-Garcia J, et al. Probiotic legacy effects on gut microbial assembly in tilapia larvae. *Sci Reports 2016 61*. 2016;6(1):33965-. doi:10.1038/srep33965

13. Dantan L, Carcassonne P, Degrémont L, et al. Microbial education plays a crucial role in harnessing the beneficial properties of microbiota for infectious disease protection in Crassostrea gigas. *Sci Reports 2024 141*. 2024;14(1):26914-. doi:10.1038/s41598-024-76096-4

14. Calcagnile M, Tredici SM, Alifano P. A comprehensive review on probiotics and their use in aquaculture: Biological control, efficacy, and safety through the genomics and wet methods. *Heliyon*. 2024;10(24):e40892. doi:10.1016/J.HELIYON.2024.E40892

15. Xie M, Xiang N, Liao T, et al. Evolutionary genomics predicts probiotic persistence in corals. *bioRxiv* [preprint]. Published online February 11, 2026:2025.06.16.659728. doi:10.1101/2025.06.16.659728

16. Xie M, Xu C, Xiang N, et al. Trait-based signatures associated with persistence and thermal benefit in a genomically decayed coral probiotic. *ISME J*. Published online May 7, 2026. doi:10.1093/ISMEJO/WRAG106

17. Chen CZ, Li P, Liu L, Li ZH. Exploring the interactions between the gut microbiome and the shifting surrounding aquatic environment in fisheries and aquaculture: A review. *Environ Res*. 2022;214:114202. doi:10.1016/J.ENVRES.2022.114202

18. Lorgen-Ritchie M, Uren Webster T, McMurtrie J, et al. Microbiomes in the context of developing sustainable intensified aquaculture. *Front Microbiol*. 2023;14:1200997. doi:10.3389/FMICB.2023.1200997/XML

19. Bartelme RP, McLellan SL, Newton RJ. Freshwater recirculating aquaculture system operations drive biofilter bacterial community shifts around a stable nitrifying consortium of ammonia-oxidizing archaea and comammox Nitrospira. *Front Microbiol*. 2017;8(JAN):241488. doi:10.3389/FMICB.2017.00101/TEXT

20. Almeida DB, Magalhães C, Sousa Z, et al. Microbial community dynamics in a hatchery recirculating aquaculture system (RAS) of sole (Solea senegalensis). *Aquaculture*. 2021;539:736592. doi:10.1016/J.AQUACULTURE.2021.736592

21. Bendag S, Barth A, Nitzsche J, Schubert P, Wilke T. Wood as Alternative Tank Construction Material in Sustainable Shrimp Aquaculture. *Aquac Res*. 2026;2026(1):8342238. doi:10.1155/ARE/8342238

22. Infante-Villamil S, Huerlimann R, Jerry DR. Microbiome diversity and dysbiosis in aquaculture. *Rev Aquac*. 2021;13(2):1077-1096. doi:10.1111/RAQ.12513

23. Kanika NH, Liaqat N, Chen H, et al. Fish gut microbiome and its application in aquaculture and biological conservation. *Front Microbiol*. 2024;15:1521048. doi:10.3389/FMICB.2024.1521048/XML

24. Shan X, Li K, Stadler P, et al. Microbiome determinants of productivity in aquaculture of whiteleg shrimp. *Appl Environ Microbiol*. 2025;91(5). doi:10.1128/AEM.02420-24