

Review

Integrating Multi-Omics in Aquaculture: From Genetic Gains to Sustainable Aquaculture

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Abstract

In recent years, aquaculture, a critical pillar of global food security, has faced challenges including germplasm resource degradation, frequent disease outbreaks, and insufficient environmental adaptability. To address these issues, omics technologies—centered on genomics, transcriptomics, and related fields—are driving the transformation of aquaculture toward precision and intelligence by establishing a three-dimensional “genotype–phenotype–environment” knowledge network. In this review, we outline foundational applications of omics in aquaculture and highlight the characteristics and current applications of distinct omics approaches. Furthermore, we summarize three core application domains of omics in aquaculture: (1) genetic breeding via genomic selection (GS), gene editing, and multi-omics molecular dissection of economic traits; (2) disease prevention through host–pathogen interaction studies and microbial engineering; and (3) environmental assessment through multi-omics characterization of biological and ecological responses. Additionally, we identify challenges in applying omics technologies to aquatic breeding and database development. Overall, this review aims to provide aquaculture practitioners with actionable insights by enhancing understanding of omics-driven innovations in sustainable aquaculture advancement.

Keywords: aquaculture; omics; breeding; immunology; environment

Key Contribution: This review systematically synthesizes how genomics, transcriptomics, epigenomics, proteomics, metabolomics, and metagenomics drive precision breeding, disease prevention, and environmental management in aquaculture, and highlights an integrated “genotype–phenotype–environment” framework connecting genomic selection, gene editing, host–pathogen interactions, microbial engineering, and omics-enabled ecosystem assessment.

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1. Introduction

As the fastest-growing animal protein production sector, aquatic animal products possess valuable nutritional properties that address various forms of malnutrition by providing high-quality nutrients and moderate energy, thereby helping to reduce food and nutritional insecurity [1]. According to Food and Agriculture Organization of the

United Nations (FAO) data, global aquaculture production has expanded at an annual rate of 2.5–8.3% over the past two decades, with aquatic animal products accounting for 20% of the total animal protein supplied per capita and represent 14.56% of the global animal protein supply, benefiting a population of 3.2 billion people, which exceeds 40% of the global population. In 2022, global aquaculture production reached a historic high of 130.9 million tons, where aquatic animal production surpassed capture fisheries for the first time in history, reaching an estimated 91 million tons. The future importance of aquaculture for human diets is evident.

Despite these significant achievements, the sector still faces major challenges from rising disease outbreaks, genetic resource degradation, and environmental overload, all of which threaten the industry's sustainable development [2]. Traditional experience-driven aquaculture practices demonstrate significant limitations in addressing rapidly evolving pathogens and compound environmental stressors. The limitations of conventional approaches are further exacerbated by the lack of robust genetic and genomic resources tailored to address these emerging challenges. Additionally, the overreliance on chemical-based disease management and the inadequate understanding of host–pathogen interactions hinder the development of sustainable and resilient aquaculture systems [3]. These issues underscore the urgent need for innovative, science-driven solutions that integrate advanced biotechnological tools and ecological principles to ensure the long-term viability of the industry.

Over the past three decades, the application of omics technologies has rapidly advanced the development of aquaculture, particularly by increasing breeding efficiency and reducing the environmental footprint [4]. With the continued development and convergence of genomic, transcriptomic, epigenomic, proteomic, metabolomic, microbiome, and phenomic approaches, aquaculture is increasingly shifting toward data-intensive and integrative biological research. These technologies are now being used not only to dissect the genetic basis of economically important traits [5], but also to improve genomic selection [6], resolve host–pathogen interactions [7], characterize nutritional and physiological states [8], evaluate responses to environmental and climate-related stressors [9], and assess microbial and ecosystem processes relevant to production [10]. More importantly, multi-omics integration provides a means to connect genetic variation, molecular regulation, phenotype, microbiota, and environmental conditions, thereby supporting more informed decisions in breeding, health management, feeding, and production system optimization.

This review summarizes the current status and challenges of omics applications in aquaculture, aiming to explore the co-evolution patterns among technological chains, biological mechanisms, and industrial application scenarios (Figure 1). Key explorations include: (1) germplasm resource development and breeding, (2) disease diagnosis and prevention, and (3) ecological assessment. We then propose a set of priorities for future research.

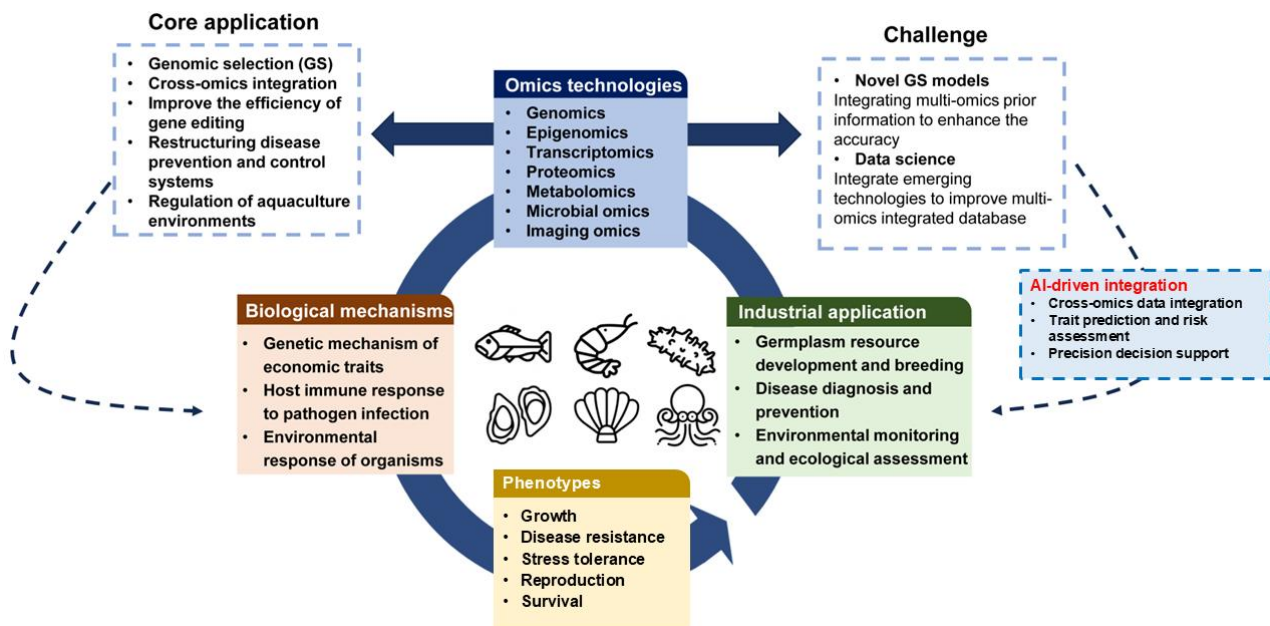


Figure 1. Omics applications in aquaculture.

2. Omics Foundations for Aquaculture Research and Breeding

2.1. Genomics Provides the Infrastructure for Aquaculture Genetic Resources and Trait-Oriented Breeding

Genomics provides the basic framework for linking aquatic germplasm resources with economically important traits, including growth, disease resistance, reproductive performance, feed efficiency, environmental tolerance, and adaptation to farming systems. In aquaculture, genome resources are not only used to describe species evolution or genome structure, but also serve as essential tools for germplasm evaluation, marker discovery, genome-wide association studies (GWAS), genomic selection (GS), and candidate gene identification. This role is particularly relevant to aquatic species, many of which show high fecundity, large effective population sizes, high heterozygosity, diverse reproductive strategies, and relatively short domestication histories.

The zebrafish genome project, initiated in 2001 by the Wellcome Sanger Institute using Sanger sequencing, represented one of the earliest large-scale genomic efforts in aquatic organisms [11]. In 2002, the genome sequencing and assembly of Japanese pufferfish was completed using a whole-genome shotgun strategy, marking an important milestone in aquatic genomics [12]. Since 2010, reference genomes have been progressively generated for representative species across major aquaculture groups, including fish, mollusks, crustaceans, and echinoderms [13–17]. These resources have greatly promoted studies of genome evolution, whole-genome duplication, sex determination, trait diversification, and ecological adaptation in aquatic species [18,19]. More importantly, they have provided the genomic coordinates needed to investigate the genetic basis of aquaculture traits.

Early genome assemblies of aquatic species mainly relied on second-generation sequencing and paired-end libraries, and many of them remained at the scaffold level with limited continuity. This restricted their use in chromosome-scale trait mapping, structural variation analysis, and comparative genomics. The integration of long-read sequencing, optical mapping, and Hi-C technologies has greatly improved genome continuity and chromosomal anchoring, making chromosome-level assemblies increasingly common in aquaculture species (Table 1). These improved assemblies provide a more accurate genomic context for interpreting genetic variation, transcriptomic

profiles, epigenomic signals, and chromatin architecture, thereby facilitating the dissection of economically important traits and complex inheritance patterns. For example, in golden pompano, high-quality female and male chromosome-level genomes generated by integrating second- and third-generation sequencing with chromosome-scale scaffolding approaches provided improved genome accuracy and continuity, thereby enabling reliable QTL mapping and GWAS to identify candidate genes associated with sex determination, including *Hsd17b1*, *Mical2*, and *Lmx1a*, as well as growth-related SNP loci and the candidate gene *gpsstr1* [20]. Similarly, in gibel carp, second- and third-generation sequencing combined with Hi-C technology were used to assemble two high-quality haploid genomes of a novel double-triploid individual, revealing recombination events between homologous chromosomes from paternal genome sets [21]. Together, these studies indicate that chromosome-level genome assemblies are shifting aquaculture genomics from descriptive reference construction toward mechanistic interpretation of trait architecture, reproductive complexity, and germplasm evolution.

Table 1. Telomere-to-telomere genome and chromosome-level genome of aquaculture species.

Latin Name	Common Name	Genome Size (Mb)	Contig N50 (Mb)	Scaffold N50 (Mb)	Reference
Telomere-to-telomere genome					
<i>Larimichthys crocea</i>	Large yellow croaker	716.87	31.75		[22]
<i>Protosalanx chinensis</i>	Asian icefish	380.76	14		[23]
<i>Acanthopagrus schlegelii</i>	Blackhead seabream	714.98	31.8		[24]
<i>Procypris rabaudi</i>	Rock carp	~1640	32.36		[25]
<i>Cyprinus carpio</i>	Koi carp	1555.86	30.45		[26]
<i>Ctenopharyngodon idella</i>	Grass carp	890.92	35.87		[27]
<i>Lateolabrax maculatus</i>	Chinese sea bass	632.75	27.95		[28]
<i>Lates calcarifer</i>	Asian sea bass	614.19	26.57		[29]
<i>Epinephelus lanceolatus</i>	Giant grouper	~1030	44.38		[30]
<i>Mastacembelus armatus</i>	Zig-zag eel	600.1			[31]
<i>Clarias gariepinus</i>	African catfish	969.62	33.71		[32]
<i>Triplophysa yaopeizhii</i>		671.58	26.04		[33]
Chromosome-level genomes of fishes					
<i>Carassius gibelio</i>	Qihe gibel carp	~1607	28.97	29.84	[34]
<i>Platichthys stellatus</i>	Starry flounder	643.56	10.00	26.19	[35]
<i>Barbodes Wynaadensis</i>	Yellow-shelled fish	~1760	33.53		[36]
<i>Rhabdosargus sarba</i>	Goldlined seabream	764.59	30.5	33.98	[37]
<i>Rhomboplites aurorubens</i>	Vermilion Snapper	987.5		41.3	[38]
<i>Sinocyclocheilus jii</i>		~1750	35.34		[39]
<i>Parachromis managuensis</i>	Jaguar guapote	888.60	5.14	38.19	[40]
<i>Clarias fuscus</i>	Hong Kong catfish	982.84	36.16	37.66	[41]
<i>Scomberomorus guttatus</i>	Indo-Pacific king mackerel	797.66	8.84	32.90	[42]
<i>Larimichthys polyactis</i>	Small yellow croaker	677.35	25.99	28.51	[43]
<i>Micropterus salmoides</i>	Largemouth bass	~964	1.23	36.48	[44]
Chromosome-level genomes of crustaceans					
<i>Cherax quadricarinatus</i>	Redclaw crayfish	~5260	0.14		[45]
<i>Paralithodes platypus</i>	Blue king crab	~5250	0.15	51.15	[46]
<i>Oratosquilla oratoria</i>	Japanese mantis shrimp	~2970	1.66	65.98	[47]
<i>Macrobrachium rosenbergii</i>	Giant freshwater prawn	~2960	0.64	55.76	[48]
<i>Eriocheir sinensis</i>	Chinese mitten crab	~1770		17.13	[49]
<i>Macrobrachium nipponense</i>	Oriental river prawn	~4500	0.23	86.8	[50]
Chromosome-level genomes of mollusks					

<i>Hyotissa hyotis</i>	Giant honeycomb oyster	~3390	0.80	177.18	[51]
<i>Chaetoderma</i> sp.	Chaetoderma worm	~2450	1.06	141.46	[52]
<i>Corbicula fluminalis</i>	Asian clam	~1140	31.93	58.80	[53]
<i>Rapana venosa</i>	Veined rapa whelk	~2300	0.43	64.63	[54]
<i>Panopea generosa</i>	Pacific geoduck	~1470	1.6	73.8	[55]
<i>Crassostrea gigas</i>	Pacific oyster	586.8	3.1	60	[56]
Chromosome-level genomes of echinoderms					
<i>Colochirus anceps</i>	Sea cucumber	2238.33	15.09		[57]
<i>Amphiura filiformis</i>	Brittle star	~1570	3.2	68.8	[58]
<i>Asterias amurensis</i>	Amur starfish	~480	10.85	23.34	[59]
<i>Ophiura sarsii vadicola</i>	Sars' brittle star	~1270	2.44	66.91	[60]
<i>Paracentrotus lividus</i>	Purple sea urchin	927.4		41	[61]
<i>Helicidaris tuberculata</i>	Helmet urchin	~1060			
Chromosome-level genomes of algae					
<i>Euglena gracilis</i>	Euglena	~2370	0.69	1.12	[62]
<i>Bracteacoccus bullatus</i>		68.85		1.07	[63]
<i>Bracteacoccus minor</i>		65.99		3.07	[63]
<i>Tetraselmis helgolandica</i>		309.6	1.65	27.96	[64]
<i>Saccharina japonica</i>	Japanese kelp	516.11	0.49	16.24	[65]
<i>Haematococcus pluvialis</i>	Green microalga	316.0	0.30	0.94	[66]

Note: Table 1 summarizes recently published high-quality genome assemblies of representative aquatic species, including telomere-to-telomere (T2T) genomes and chromosome-level genomes of fishes, crustaceans, mollusks, echinoderms, and algae. Relevant studies were identified through searches of Web of Science, PubMed, and Google Scholar using combinations of keywords such as “aquaculture”, “aquatic species”, “telomere-to-telomere genome”, “T2T genome”, “chromosome-level genome”, and “genome assembly”. Studies published mainly between 2021 and 2025 were considered, with priority given to recent assemblies of representative aquaculture or aquatic species with chromosome-level or T2T completeness and available assembly quality metrics, including genome size, Contig N50, and/or Scaffold N50. The table was compiled to provide representative examples of recent advances in high-quality aquatic genome resources rather than an exhaustive catalogue of all published assemblies.

With the continuous optimization of third-generation sequencing technologies and assembly algorithms, the integration of highly accurate long reads, ultra-long reads, and chromosome conformation capture data now enables the construction of complete, gapless, telomere-to-telomere (T2T) genomes [67]. Compared with conventional chromosome-level assemblies, T2T genomes can better resolve telomeric regions, centromeres, repetitive sequences, segmental duplications, and other complex genomic regions. These regions may contain structural variants, duplicated genes, or regulatory elements related to adaptation, fertility, immunity, and other aquaculture-relevant traits. Although the number of completed T2T genomes in aquaculture species remains limited compared with model organisms, their value is becoming increasingly evident. For species with high heterozygosity, recent genome duplication, polyploid backgrounds, or abundant repetitive sequences, T2T genomes provide a more complete basis for genetic diversity assessment, trait-associated variant discovery, and germplasm resource optimization.

However, even a complete reference genome from a single individual cannot fully represent the genetic diversity of an aquaculture species. Many aquatic organisms retain substantial wild genetic variation and population structure, and breeding populations are often derived from different geographic origins or founder stocks. Therefore, reliance on a single linear reference genome may introduce reference bias and underestimate important genetic variants. Pan-genomes address this limitation by integrating genome

sequences from multiple individuals, populations, species, or closely related taxa into a broader reference framework. Compared with a single reference genome, a pan-genome can provide a more comprehensive catalog of genetic variation, especially structural variants such as presence–absence variations (PAVs), copy number variations (CNVs), inversions, and lineage-specific sequences. Pan-genome research in aquaculture species is still developing, but existing studies have already shown its potential. In the Mediterranean mussel, pan-genome analysis revealed extensive gene presence–absence variation and showed that the dispensable genome was associated with broad environmental adaptability [18]. In cichlids, eight long-read genome assemblies were integrated to construct a pan-genome graph, revealing that approximately 4.73% to 9.86% of the assembled sequence length among species consisted of structural variants [68]. The study further suggested that transposable elements may contribute to adaptive processes such as retinal development, sex determination, and body coloration. These findings indicate that pan-genome approaches can capture genetic variation that may be missed by a single-reference strategy and may be especially useful for aquaculture species with high genetic diversity, local adaptation, and complex domestication backgrounds.

The practical value of genome resources depends on whether genomic variation can be efficiently measured in large breeding populations. With the availability of reference genomes and the accumulation of population genomic data, genotyping technologies have become widely used in aquaculture. Whole-genome sequencing and resequencing have been applied to genetic marker discovery, population structure analysis, selective sweep detection, GWAS, and trait improvement. These approaches have contributed to the identification of variants associated with disease resistance [69], feed conversion efficiency [70,71], growth performance [72,73], reproductive traits [74,75], and environmental stress tolerance [76,77].

Because aquaculture breeding programs often involve large numbers of individuals and families, efficient and cost-effective genotyping platforms are essential. SNP arrays have been developed for many high-value aquaculture species [78–82]. These arrays usually contain tens of thousands to hundreds of thousands of high-confidence SNP markers and provide useful tools for genetic linkage mapping, GWAS, GS, parentage assignment, inbreeding control, and germplasm management. Compared with whole-genome resequencing, SNP arrays are more standardized and convenient for routine breeding applications, especially when stable breeding populations and target traits have already been established. Genotyping-by-sequencing (GBS) approaches provide another flexible strategy for large-scale genotyping, particularly in species with limited genomic resources or in breeding programs that require lower-cost marker discovery [83]. Representative methods include restriction site-associated DNA sequencing (RAD-seq) and low-coverage whole-genome sequencing (lcWGS). In Pacific oyster, lcWGS combined with genotype imputation was successfully used for population-scale genotyping, providing accurate information for population structure and genetic diversity analyses while reducing sequencing costs [84]. Similar applications have been reported in salmon [85], swimming crab [86], and shrimp [87], demonstrating the broad utility of GBS approaches in aquaculture genetics and breeding.

Overall, reference genomes, T2T genomes, pan-genomes, and scalable genotyping platforms have shifted aquaculture genomics from resource construction toward trait-oriented genetic management. These tools support the assessment of genetic diversity, the identification of trait-associated variants, the optimization of breeding populations, and the implementation of genomic selection. Nevertheless, several limitations remain. Genome quality and annotation completeness are still uneven across aquaculture taxa; phenotypic and environmental records are often less standardized than genomic data; rapid linkage disequilibrium decay in some aquatic populations may reduce the efficiency

of marker-based prediction; and structural variants detected by T2T or pan-genome approaches are not yet routinely incorporated into GWAS or GS models. Future progress will require closer integration of genome resources with transcriptomic, epigenomic, phenotypic, and environmental data, so that genomic variation can be more effectively translated into breeding decisions and sustainable aquaculture practices.

2.2. Regulatory, Functional, and Microbial Omics Link Environmental Cues with Aquaculture Phenotypes

While genomics provides the genetic background for aquaculture traits, regulatory, functional, and microbial omics explain how this background is expressed under farming conditions. Aquatic animals are continuously exposed to changing temperature, salinity, oxygen availability, diet composition, stocking density, pollutants, and pathogen pressure. These factors often affect growth, reproduction, immunity, stress tolerance, and product quality through regulatory and physiological changes rather than through changes in DNA sequence itself. Therefore, epigenomics, transcriptomics, proteomics, metabolomics, and microbial omics form a connected framework for interpreting how environmental cues are translated into aquaculture phenotypes.

Epigenomics provides one layer for understanding this regulatory plasticity. DNA methylation, chromatin accessibility, histone modifications, and non-coding RNAs can regulate gene expression without altering the genetic sequence [88]. In aquaculture, this is particularly relevant because many economically important traits are sensitive to environmental and nutritional conditions. For example, dietary components can influence the methylation status of growth-related genes and thereby affect muscle development and growth performance [89,90]. Epigenetic markers have also been used to investigate sex differentiation and may contribute to monosex breeding strategies in species where sex control has economic value [91,92]. Under environmental stress, changes in DNA methylation or chromatin state can reflect regulatory responses to temperature shifts [93,94] or pollutant challenges [95,96]. Because epigenetic responses may occur more rapidly than stable genetic changes, they may help explain short-term acclimation and environmental sensitivity in farmed populations.

A further implication of epigenomics is its possible role in transgenerational plasticity. In some cases, environmentally induced epigenetic marks in gametes may transmit information about parental conditions to offspring, suggesting a mechanism by which the broodstock environment can influence progeny performance [97]. This has practical relevance for broodstock management, early-life conditioning, and stress-resilience breeding. However, many epigenetic associations reported in aquaculture remain correlative. Their stability, heritability, and causal contribution to complex traits still require validation. Epigenomics is therefore most informative when combined with genomic, transcriptomic, phenotypic, and environmental data.

Transcriptomics captures the next layer of regulation by measuring mRNA expression under defined physiological, pathological, or environmental conditions [98,99]. Compared with genomics, which identifies genetic potential, transcriptomics shows how this potential is expressed in response to farming conditions. Bulk RNA-seq remains widely used in aquaculture because it can identify differentially expressed genes and pathways related to growth, nutrition, immunity, reproduction, and environmental adaptation. For example, transcriptomic analysis of fish gills under salinity stress has revealed changes in ion transport and immune-related genes, providing insight into osmoregulatory adaptation [100]. Similarly, transcriptome profiling in oysters after pathogen infection has helped identify immune pathways and candidate defense genes involved in host responses [101]. These studies are useful for discovering candidate genes,

but tissue-level RNA-seq averages signals from mixed cell populations and therefore cannot fully resolve cell-specific mechanisms.

Single-cell RNA sequencing addresses this limitation by measuring gene expression at the level of individual cells or nuclei [102]. This is important in aquaculture because many key processes, including immune defense, stress response, tissue regeneration, and gonadal development, depend on specialized or rare cell populations. In disease-related studies, scRNA-seq can identify pathogen-responsive cell types and distinguish immune cell states within the same tissue. Representative examples include the analysis of liver cell heterogeneity in Atlantic salmon after pathogen challenge [103], heterogeneous hemocyte responses in Pacific white shrimp during white spot syndrome virus infection, and leukocyte responses in flounder after vaccination with an inactivated pathogen [104]. These studies suggest that host defense in aquaculture species is shaped not only by immune pathway activation but also by the organization and functional differentiation of specific cell populations.

Single-cell approaches are also useful for understanding how aquatic animals respond to abiotic stress. Environmental stressors such as temperature, hypoxia, salinity, nitrite, heavy metals, and microplastics often act through tissue-specific and cell-type-specific processes. Studies of oyster gills and hemocytes under copper exposure revealed distinct stress-responsive cell populations and detoxification programs [105,106]. In shrimp, scRNA-seq helped characterize hemocyte responses to nitrite stress [107]. In scallop, single-cell transcriptomic profiling of heart tissue revealed heterogeneous responses to heat stress [108], while studies in crucian carp gills identified cell-specific responses of the interlamellar cell mass under hypoxia [109]. These examples show that cellular heterogeneity is an important part of environmental adaptation in aquaculture species.

In addition to stress biology, scRNA-seq has been used to construct cell atlases for immune and developmental studies. Cell atlases of immune tissues in cartilaginous and bony fishes have provided information on the conservation and diversification of vertebrate immune systems [110]. In large yellow croaker, scRNA-seq was used to trace the developmental trajectory of spermatogenic cells during the reproductive cycle, revealing cellular heterogeneity during spermatogenesis [111]. Additional immune and developmental atlases have been reported in turbot, tilapia, crucian carp, crustaceans, mandarin fish, *Procambarus clarkii*, bay scallop, and mud crab (Table 2). These resources provide a cellular basis for studying immunity, reproduction, development, and species-specific adaptation in cultured aquatic organisms.

Table 2. scRNA-seq and snRNA-seq studies in major aquaculture species.

Latin Name	Common Name	Tissue	Research Contents	References
<i>Salmo salar</i> L.	Atlantic salmon	liver	biotic stress, <i>Aeromonas salmonicida</i>	[103]
<i>Salmo trutta fario</i>	Brown trout	head kidney	biotic stress, <i>Aeromonas salmonicida</i>	[112]
<i>Larimichthys crocea</i>	Large yellow croaker	gill	biotic stress, parasitic	[113]
<i>Leiocassis longirostris</i>	Chinese longsnout catfish	skin	biotic stress, <i>Aeromonas hydrophila</i>	[114]
<i>Lates calcarifer</i>	Asian Seabass	hemocytes	biotic stress, scale-drop disease virus	[115]
<i>Odontobutis potamomophila</i>	Freshwater dark sleeper	head kidney	biotic stress, <i>Aeromonas veronii</i>	[116]
<i>Litopenaeus vannamei</i>	Shrimp	hemocytes	biotic stress, white spot syndrome virus	[117]
<i>Paralichthys olivaceus</i>	Flounder	head kidney	biotic stress, <i>Edwardsiella tarda</i>	[104]

<i>Carassius auratus</i>	Crucian carp	head kidney	biotic stress, <i>Rahnella aquatilis</i>	[118]
<i>Eriocheir sinensis</i>	Crab	hemocyte	biotic stress, <i>Spiroplasma eriocheiris</i>	[119]
<i>Crassostrea hongkongensis</i>	Oyster	hemocytes	abiotic stress, Cu	[106]
<i>Crassostrea hongkongensis</i>	Oyster	gill	abiotic stress, Cu	[105]
<i>Penaeus monodon</i>	Black Tiger Shrimp	hepatopancreas, haemocytes	abiotic stress, ammonia	[120]
<i>Penaeus vannamei</i>	Shrimp	hemocytes	abiotic stress, nitrite	[107]
<i>Scophthalmus maximus</i>	Turbot	gut	abiotic stress, nitrite	[121]
<i>Oreochromis niloticus</i>	Tilapia	head kidney	abiotic stress, high-salinity	[122]
<i>Exopalaemon carinicauda</i>	Ridgetail white prawn	gill	abiotic stress, high pH	[123]
<i>Oreochromis niloticus</i>	Tilapia	gill	abiotic stress, microplastics and nanoplastics	[124]
<i>Argopecten irradians</i>	Bay scallop,	heart	abiotic stress, heat	[108]
<i>Litopenaeus vannamei</i>	Pacific white shrimp	hepatopancreas	abiotic stress, cold	[125]
<i>Eleutheronema tetradactylum</i>	Threadfin fish	gill	abiotic stress, hypoxia	[126]
<i>Carassius auratus</i>	Crucian carp	gill	abiotic stress, hypoxia	[109]
<i>Acipenser dabryanus</i>	Yangtze sturgeon	multi-tissue	evolution and development	[127]
<i>Chiloscyllium plagiosum</i>	White-spotted bamboo shark	spleen, liver, kidney		
<i>Danio rerio</i>	Zebrafish	head kidney	evolution and development	[110]
<i>Cynoglossus semilaevis</i>	Chinese tongue sole	head kidney		
<i>Procambarus clarkii</i>	Red swamp crayfish	hepatopancreas	evolution and development	[128]
<i>Ictalurus punctatus</i>	Channel catfish	spleen	evolution and development	[129]
<i>Ictalurus punctatus</i>	Channel catfish	spleen	evolution and development	[130]
<i>Micropterus salmoides</i>	Perciform fish	head kidney	evolution and development	[131]
<i>Scophthalmus maximus</i>	Turbot	multi-tissue	evolution and development	[132]
<i>Lampetra morii</i>	Lamprey	gills, intestines, blood	evolution and development	[133]
<i>Siniperca chuatsi</i>	Mandarin fish	ovary	evolution and development	[134]
<i>Siniperca chuatsi</i>	Mandarin fish	ovary	evolution and development	[135]
<i>Litopenaeus vannamei</i>	Shrimp	hemocyte	evolution and development	[136]
<i>Penaeus vannamei</i>	Shrimp	hemocytes	evolution and development	[137]
<i>Marsupenaeus japonicus</i>	Shrimp	hemocyte	evolution and development	[138]
<i>Argopecten irradians</i>	Scallop	gonad	evolution and development	[139]
<i>Mizuhopecten yessoensis</i>	Scallop	adductor muscles	evolution and development	[140]
<i>Tridacna crocea</i>	Giant clam	siphonal mantle	evolution and development	[141]
<i>Crassostrea gigas</i>	Oyster	gonad	evolution and development	[142]
<i>Crassostrea gigas</i>	Oyster	lophotrochozoan larvae	evolution and development	[143]
<i>Crassostrea gigas</i>	Oyster	hemocyte	evolution and development	[144]
<i>Procambarus clarkii</i> , <i>Penaeus japonicus</i> , <i>Penaeus monodon</i> , <i>Penaeus vannamei</i>	Crustaceans	hemocyte	evolution and development	[145]
<i>Tegillarca granosa</i>	Blood clams	hemocyte	evolution and development	[146]
<i>Lytechinus variegatus</i>	Sea urchin	embryo	evolution and development	[147]
<i>Heliocidaris crassispina</i>	Sea Urchin	embryo	evolution and development	[148]

Note: Table 2 summarizes representative applications of single-cell transcriptomic approaches in aquatic species, covering studies of biotic stress, abiotic stress, and evolution and development across different tissues and cell types. Relevant studies were identified through searches of Web of Science, PubMed, and Google Scholar using combinations of keywords such as “aquaculture”, “aquatic species”, “single-cell RNA sequencing”, “single-cell transcriptomics”, “scRNA-seq”, “biotic stress”, “abiotic stress”, “immune response”, and “development”. Studies published mainly between 2021 and 2026 were considered, with priority given to recent studies applying single-cell transcriptomic technologies to representative aquaculture or aquatic species and providing clear information on the investigated tissues, experimental conditions, and biological questions. The table was compiled to illustrate representative advances and major application areas of single-cell transcriptomics in aquatic research rather than to provide an exhaustive catalogue of all published studies.

Spatial transcriptomics further extends transcriptomic analysis by preserving the spatial organization of gene expression within tissues [149]. This is relevant to aquaculture because mucosal immunity, tissue lesions, gonadal development, and pathogen invasion often occur in defined tissue microenvironments. Spatial transcriptomic studies have identified tissue-region-specific expression patterns in Atlantic salmon skin [150] and developmental signaling domains during zebrafish embryogenesis [151]. Although applications in aquaculture remain limited, early studies in model and commercially important species indicate that spatial transcriptomics can help connect gene expression with tissue architecture, improving the interpretation of localized disease responses, developmental patterning, and environmental stress effects [152–154].

Proteomics and metabolomics provide functional information that cannot be fully inferred from transcriptomic data alone. Protein abundance, post-translational modifications, enzyme activity, and metabolite composition are closer to physiological performance and phenotypic outcomes. This is especially important in aquaculture, where growth rate, feed utilization, immunity, stress tolerance, and product quality are often shaped by rapid physiological responses to diet and environmental conditions. Proteomics, based on methods such as liquid chromatography–tandem mass spectrometry (LC-MS/MS) and two-dimensional electrophoresis (2-DE), has been used to analyze protein expression, modifications, and interaction networks [155]. In aquaculture species, proteomic studies have contributed to the characterization of shrimp antiviral proteins involved in responses to WSSV [156], the evaluation of dietary effects such as changes in cytoskeleton-related proteins after linseed oil supplementation [157], and the identification of proteins associated with hypoxia tolerance and iron homeostasis [158]. These studies help verify whether transcriptional changes are translated into functional protein-level responses.

Metabolomics focuses on small-molecule metabolites, including amino acids, lipids, organic acids, and other biochemical intermediates, using nuclear magnetic resonance (NMR), GC-MS, or LC-MS platforms [159]. Because metabolites are close to physiological endpoints, metabolomics is useful for monitoring energy metabolism, nutritional status, stress responses, and health condition in farmed aquatic animals. For example, metabolomic studies have revealed lactate accumulation and impaired ATP synthesis in fish muscle under hypoxia [160], as well as lipid metabolic reprogramming during thermal adaptation in Bleeker’s stone loach [161]. Metabolomics has also been used to guide fishmeal replacement strategies by evaluating amino acid and lipid metabolic pathways [162], and to assess pollutant-induced metabolic disruption in tissues such as the hepatopancreas [163]. Together, proteomics and metabolomics serve as functional validation layers that connect molecular regulation with aquaculture performance.

Microbial omics adds another dimension because aquatic animals live in direct contact with microbe-rich environments. Microorganisms are not only commensal components of the host intestine but also active members of water, sediment, biofilters, feed residues, and pathogen reservoirs. Therefore, 16S rRNA sequencing, metagenomics, and related approaches are useful for studying the links among host health, pathogen dynamics, water quality, and farming stability [164]. In host-associated studies, microbiome analysis has helped identify microbial taxa related to nutrition, immunity, and disease resistance. By characterizing intestinal microbial communities, researchers can develop microbiome-targeted probiotics or microbial management strategies to improve host health and aquaculture performance [165,166].

Microbial omics is also important for disease prevention. In shrimp acute hepatopancreatic necrosis disease (AHPND), microbiome studies have shown that the overgrowth of pathogenic bacteria is associated with disruption of the intestinal microbial community [167]. Probiotic supplementation may help restore microbial balance, improve antioxidant capacity, enrich short-chain fatty acid-producing bacteria, and enhance intestinal barrier function and protein utilization [168,169]. Integrated microbiome–metabolome analysis further suggests that microbial metabolites can regulate host lipid metabolism and other physiological processes, indicating that microbes affect aquaculture animals not only through community composition but also through metabolic interactions. Beyond the host intestine, microbial omics has direct relevance to aquaculture system management. In recirculating aquaculture systems (RAS), microbial communities in biofilters determine ammonia oxidation, nitrite removal, and nitrogen cycling efficiency. Monitoring functional groups such as nitrifying bacteria can guide biofilter management and improve water quality stability [170,171]. This expands aquaculture omics from a host-centered perspective to a host–microbe–environment framework. Such a framework is useful for disease prevention, probiotic development, precision feeding, and RAS management. However, microbial communities are highly sensitive to diet, water source, stocking density, season, antibiotics, and farming practices. Future studies should therefore emphasize functional validation, standardized sampling, and causal links between microbial shifts and aquaculture outcomes.

Imaging omics further extends multi-omics analysis from molecular and microbial profiles to production-scale phenotyping. In aquaculture, many important traits, such as growth, behavior, stress response, disease status, body composition, and product quality, are difficult to measure continuously using conventional methods. Imaging omics, mainly based on computer vision and deep learning, provides a non-invasive approach for extracting quantitative phenotypic information from images or videos [172]. Its general workflow includes image acquisition and standardization, image segmentation, feature extraction and selection, and model construction and validation. These approaches have been applied to health monitoring, behavioral analysis, phenotypic measurement, and disease-related trait assessment in aquatic organisms. For example, Xu [173] investigated behavioral responses of sturgeon, perch, and carp under different experimental conditions and observed changes in movement trajectories, activity levels, spatial distribution, and swimming velocity. Such behavioral indicators can provide useful information for detecting abnormal ammonia levels. Imaging-based approaches have also been used for real-time monitoring of aquaculture environments [174] and for rapid quality assessment in seafood processing, such as estimating fat-to-muscle ratios [175]. Therefore, imaging omics provides an important phenotypic feedback layer for linking molecular regulation, environmental variation, and measurable aquaculture performance.

Taken together, regulatory, functional, microbial, and imaging omics bridge the gap between genetic potential and production performance. Epigenomics explains how environmental signals may be recorded in regulatory states; transcriptomics reveals

tissue-, cell-, and spatially resolved gene expression responses; proteomics and metabolomics verify functional outputs at the protein and biochemical levels; microbial omics places host physiology within the broader host–microbe–environment system; and imaging omics provides non-invasive, high-throughput phenotypic feedback under practical aquaculture conditions. Integrating these layers with genomic resources, ecological assessment, and standardized phenotypic records will be essential for developing predictive and intervention-oriented strategies in precision aquaculture.

3. Applied Omics for Precision Aquaculture and Production Improvement

3.1. Genomic Selection Breeding

Traditional breeding methodologies that rely on genealogical records for breeding value estimation fail to account for Mendelian sampling effects, leading to imprecise quantification of true genetic relationships between individuals [176]. In certain family-based breeding schemes, this limitation may restrict the proportion of genetic variation effectively captured, thereby reducing the accuracy and efficiency of genetic improvement. To overcome this limitation, Meuwissen et al. (2001) pioneered genomic-based assessment of molecular relatedness, thereby eliminating biases inherent in pedigree-based estimations and substantially enhancing breeding value prediction accuracy [177]. Consequently, GS—employing genome-wide markers to calculate genomic estimated breeding values (GEBVs)—has emerged as a transformative selective breeding strategy. This methodology enables precise evaluation of candidate population breeding values, thereby accelerating genetic progress through reduced generational intervals.

The genomic best linear unbiased prediction (GBLUP) model represents a widely adopted GS approach that computes GEBVs by constructing genomic relationship matrices derived from genome-wide molecular markers. Notably, SNP-based genomic prediction has become a cornerstone technology in aquatic animal breeding programs, demonstrating successful implementation across multiple commercial species. In 2014, Ødegård et al. [178] pioneered one of the early studies GS study in aquaculture species. Their work systematically evaluated identity-by-descent (IBD-GS) and GBLUP models across varying densities (1–220k) of genome-wide SNP markers, comparing their predictive accuracy against conventional pedigree-based approaches. Results demonstrated that GS models significantly outperformed pedigree-based methods, achieving relative accuracy improvements of 15–52%. Subsequent research has expanded GS applications across diverse aquaculture taxa, with the majority of studies focused on finfish, followed by mollusks and crustaceans. In aquaculture fishes such as European seabass [179], Nile tilapia [180], and groupers (*Epinephelus* spp.) [181], the priority traits for GS research have centered on growth performance (body length, weight), carcass quality, and disease resistance. Similarly, GS has been extensively employed in shellfish breeding programs, particularly for Pacific oysters [182], Eastern oyster [183,184], and scallops [185], targeting morphometric traits (shell length, width, height, wet weight), immunity, and environmental resilience. Research on crustacean GS focused on penaeid shrimp species, such as Chinese shrimp [186] and Pacific white shrimp [187]. While GS has gained widespread adoption in aquatic breeding programs to rapidly identify parental stocks with superior breeding values, the distinctive biological characteristics of aquatic organisms—particularly their habitat adaptation mechanisms and reproductive strategies—pose operational constraints on GS implementation and may ultimately affect the accuracy and operational efficiency of selection.

Genotype-by-environment interactions (G×E) serve as crucial determinants of phenotypic variation, significantly impacting the reliability of genomic predictions and the outcomes of breeding programs. G×E can reduce the accuracy of genetic evaluation and consequently limit genetic gain. In Pacific white shrimp, simulation results showed

that the loss of genetic gain under pedigree-based selection ranged from 9.4% to 38.9% as G×E increased, whereas genomic selection substantially mitigated this loss under the evaluated breeding scenarios [188]. Quantifying environmental effects on phenotypic development to enhance GS efficacy remains a critical challenge in aquatic breeding. Terrestrial crop research typically employs two G×E paradigms: (1) Applying differential treatments (e.g., irrigation gradients, fertilization regimes) within single regions to monitor genotypic response patterns and identify adaptive genotypes, or (2) cultivating identical genotypes under controlled environments (greenhouses, phytotrons) while recording phenotypic data (yield, stress resistance) alongside environmental variables (temperature, precipitation, soil fertility) to develop statistical models quantifying G×E effects. However, continuous environmental and phenotypic data collection remains challenging for open-water species across extended temporal scales. Consequently, although limited G×E studies have been investigated in aquaculture breeding, large-scale and standardized studies remain limited, and current research predominantly focuses on relatively easily measurable traits, such as survival rate [189]. Encouragingly, breakthrough progress in G×E studies has been achieved in intensively farmed aquatic species. A representative case involved the comprehensive analysis of 8976 rainbow trout [190] across four aquaculture regions, where researchers elucidated the tripartite interactions among genotypes, phenotypic traits (harvest weight), and environmental variables (harvest age, water temperature, dissolved oxygen levels, and photoperiod). The investigation revealed that body mass variation in rainbow trout was strongly associated with cumulative thermal units (day-degrees) and photoperiod, demonstrating significant genotype-by-environment interactions.

In addition to genotype–environment interactions, the accuracy of GS is influenced by multiple factors including reference population size, genetic marker density, linkage disequilibrium (LD) magnitude, population structure complexity, and trait heritability. Aquatic species, particularly wild populations, are characterized by large effective populations, rapid generational turnover, high fecundity, and panmictic breeding strategies—biological traits that collectively drive rapid LD decay. Commercial species such as shrimp [191], oysters [192], scallops [193], and sea cucumbers [194] exhibit particularly short LD spans. Compared to the high LD levels in livestock and crops, lower LD levels in aquaculture breeding make it difficult to capture association effects between SNP markers and QTL, greatly increasing the difficulty of GS.

Notably, most GS research in aquaculture has primarily employed cross-validation strategies to estimate genomic prediction accuracy, with limited studies evaluating the practical benefits of GS implementation in farmed aquatic species [195]. This methodological constraint arises from two key factors. First, small-bodied invertebrate species (e.g., oyster) necessitate sacrificing parental organisms for genotype and gonad sampling during breeding, which reversing the conventional “selection-first” GS workflow into a “post-breeding genomic evaluation” and significantly increasing temporal and labor costs in breeding programs. Developing non-lethal genotyping methods for live specimens therefore becomes crucial for accelerating practical GS implementation in these aquaculture species. Second, the less controllable behavioral patterns of aquatic organisms pose challenges in maintaining candidate individual within designated spatial–temporal parameters following genotype–phenotype data collection. However, for large finfish species in aquaculture, this issue can be effectively resolved through physical tagging on fins.

3.2. Resolution of a Multi-Omics Regulatory Network for Economic Traits

Multi-omics economic trait research systematically elucidates the genetic and molecular regulatory mechanisms underlying economic traits in aquaculture species through the integration of multi-level biomolecular data (i.e., genomic, epigenomic, transcriptomic, proteomic, and metabolomic data). Compared to conventional single-omics approaches, the primary advantage lies in cross-hierarchical integration across the genotype-to-phenotype continuum.

3.2.1. Genome–Transcriptome

Genome–transcriptome integration not only enables localization of key trait-associated genes but also reveals their dynamic regulatory mechanisms. Two core strategies dominate this approach:

(1) From genomic localization to transcriptional validation: a GWAS identifies trait related SNP loci, coupled with transcriptomic screening of differentially expressed genes (DEGs) in individuals with extreme traits. For instance, a GWAS conducted on 234 Japanese grenadier anchovy specimens for growth traits, identifying two critical genes (*bmp8a*, *uqcrfs1*). Subsequent comparative transcriptomics of extreme-size groups validated these genes in brain and muscle tissues, respectively, ultimately reconstructing an mTORC1-associated growth regulatory pathway [196].

(2) Linking genomic SNPs with expression profiles: eQTL mapping identifies genetic loci associated with variation in gene expression, and integration with phenotypic data can further facilitate the construction of trait-associated gene regulatory networks. For instance, Huang et al. through eQTL mapping of 78 yellow drum under *Vibrio* challenge, identifying seven regulatory loci controlling the zinc-finger protein *yd23210* associated with pathogen resistance [197]. In addition, the convergence of single-cell technologies with genomic integration demonstrates expanding potential in applying single-cell eQTL to resolve complex mechanisms like resistance-associated cellular heterogeneity and rare cell subpopulation regulation. Integrating bulk RNA-seq with scRNA-seq through deconvolution methods enables cellular-resolution eQTL analysis [198,199], thereby significantly reducing the costs of single-cell eQTL studies and making their application in aquaculture species possible.

3.2.2. Epigenome–Transcriptome

The epigenome, encompassing DNA methylation, histone modifications, and chromatin conformation, serves as a “regulatory gate” for gene expression by controlling chromatin accessibility to determine transcriptional potential. This regulatory tier exhibits upstream–downstream coordination with the transcriptome (mRNA dynamics): epigenetic modifications may mediate relatively persistent regulatory responses to environmental signals (e.g., pathogen infection, thermal stress), while the transcriptome reflects real-time execution states of gene activation/silencing. For example, the researchers identified a set of major transcription factors that play a key role in the regulation of cold-elicited transcriptional responses in tilapia by combined RNA-seq and ATAC-seq analysis [200]. Their integrated analysis suggests coordinated regulatory relationships among environmental signals, epigenetic regulation, and transcriptional response, thereby providing the molecular foundations for the adaptability and plasticity of economic traits.

3.2.3. Transcriptome–Proteome

Integrated transcriptomic and proteomic analysis can improve the robustness of candidate gene identification. As an intermediate layer (mRNA abundance), the transcriptome may exhibit “expression decoupling” from the functional execution layer

(protein levels) due to translational suppression or post-translational modifications. Thus, cross-omics analysis can provide complementary evidence for identifying biologically relevant candidate genes and reduce uncertainty associated with single-omics analyses. For example, the stress-responsive up-regulation of fish disease resistance gene mRNAs requires validation through translation efficiency and phosphorylation modifications of their protein products [201].

3.2.4. Transcriptome/Proteome–Metabolome

The metabolome provides complementary information on downstream metabolic states associated with transcriptomic and proteomic changes. Metabolites not only represent end products of upstream gene expression but also regulate epigenetic/transcriptional states through feedback mechanisms. Integrated “transcriptome/proteome–metabolome” analysis can help identify coordinated metabolic pathways and associations linking molecular changes to phenotypic functions. For example, the coordination of energy supply and ammonia excretion through enhanced glycolysis and tricarboxylic acid cycle strategies under high ammonia stress in Pacific white shrimp was elucidated by combined transcriptomic and metabolomic analyses [202]. This multidimensional approach provides complementary evidence for interpreting potential links between gene expression and metabolic phenotypes.

3.3. Synergistic Innovation of Gene Editing and Multi-Omics Validation Systems

Gene editing technology refers to bioengineering methods that enable precise modifications of an organism’s DNA sequence to alter genetic traits for desired functions or characteristics [203]. Its robust applications span both forward genetics and reverse genetics, serving as critical validation tools for phenotype-to-gene omics inference and synergizing with multi-omics validation systems to advance aquatic breeding industries. Current mainstream gene editing tools include CRISPR-Cas9, TALENs (Transcription Activator-Like Effector Nucleases), and ZFNs (Zinc Finger Nucleases). CRISPR-Cas9 dominates aquaculture research due to its operational simplicity and cost-effectiveness.

Precise gene editing relies on both technological innovation and strategic integration with omics approaches, which are inseparable in gene function analysis and biological mechanism exploration. Omics technologies serve as critical tools for identifying editing targets, while post-editing omics analyses enable functional investigation of downstream effects. This synergistic combination has been applied across medical, pharmaceutical, ecological safety, agricultural/food security, and animal model development fields. In aquaculture research, studies aimed to address [204–206] intermuscular bones (IBs) by performing scRNA-seq on wild zebrafish caudal muscle to identify candidate genes. Through CRISPR knockout and phenotypic observation, they identified *runx2b* as the master gene controlling IBs formation. Subsequent scRNA-seq analysis of edited zebrafish revealed near-complete osteoblast depletion, with enrichment analysis implicating TGF- β /BMP signaling in IB development. Building on this mechanistic understanding, the team successfully edited *runx2b* in blunt snout bream and grass carp, successfully inducing fish with reduced or absent intermuscular bones.

However, broader application of gene editing in aquaculture still faces important technical and translational challenges. Mosaicism, off-target or unintended on-target effects, and pleiotropic consequences may compromise editing reliability and require careful molecular and phenotypic validation. In addition, ecological risk, animal welfare, regulatory requirements, and consumer acceptance should be considered before gene-edited aquatic animals are deployed at commercial scale.

The application of gene editing integrated with multi-omics remains relatively limited in aquaculture species, partly due to the lack of well-annotated genomes, efficient

editing systems, and standardized functional validation pipelines in many farmed species. Future studies could establish an iterative framework of “omics-based target discovery–gene editing validation–multi-omics assessment”, enabling more reliable functional characterization of candidate genes and systematic evaluation of downstream and potential off-target effects. Such an integrated strategy may accelerate the translation of molecular discoveries into economically important traits, including growth, disease resistance, stress tolerance, and reproductive performance.

3.4. Restructuring Disease Prevention and Control Systems

Water serves as the primordial environment for pathogen survival, and outbreaks of pathogenic bacteria in aquatic systems are characterized by considerable uncertainty and uncontrollability. Guided by omics-driven approaches, the restructuring of disease prevention and control systems can effectively address emerging or sudden disease challenges through systematic, multi-level optimization of existing strategies, methodologies, technologies, and management frameworks. This comprehensive approach enhances preparedness for pathogen outbreaks in aquatic environments while mitigating economic losses.

3.4.1. Omics Atlas of Pathogen–Host Interactions

Integrated omics analyses facilitate systematic and comprehensive elucidation of pathogenic mechanisms. In aquaculture species, white feces syndrome (WFS) in shrimp is a multifactorial gastrointestinal syndrome associated with disruption of the intestinal ecosystem. Through microbiome and metabolome profiling, Huang et al. demonstrated that WFS is caused by a specific gut microbial dysbiosis, involving the enrichment of ten bacterial genera and the depletion of others. This microbial imbalance leads to impaired lipoic acid and mineral absorption [207]. Furthermore, multi-omics approaches have been applied to study pathogenic mechanisms in diverse systems, including *Edwardsiella tarda* infections in crucian carp [208], Singapore grouper iridovirus infections in dusky grouper [209], hepatic tumor disease in common dab [210], and *Streptococcus iniae* infection in tilapia [211]. Beyond bacterial and viral infections, omics approaches have also been increasingly applied to parasitic and polymicrobial diseases, broadening our understanding of diverse host–pathogen interactions in aquaculture species [212,213].

3.4.2. Microbiome-Informed Probiotic Strategies

Microbiome-informed probiotic interventions offer promising strategies for disease prevention and health management in aquaculture. Conventional supplementation with natural or functionally selected probiotic strains can modulate host-associated microbial communities, whereas microbiome engineering more specifically involves deliberate manipulation of community structure or function, such as through designed microbial consortia or genetically engineered microorganisms. By optimizing the intestinal microbial communities of aquatic species, probiotics not only suppress pathogenic microorganisms but also enhance immune responses, providing an eco-friendly and safe alternative. For instance, Jager et al. demonstrated the beneficial effects of the seaweed *Gracilaria* on bacterial communities through microbiome analysis of abalone effluent and *Gracilaria* cultivation systems [214]. Li et al. further investigated how functionally selected probiotics influence fish metabolism and immunity to improve host health [215]. Tanpichai et al. showed that oral administration of the probiotic *Bacillus subtilis* in Asian sea bass increased intestinal microbial richness and diversity while boosting immune capacity [216]. Similarly, Phan et al. confirmed that a lactic acid bacteria strain improves growth, survival, and health in Pacific white shrimp through microbiome modulation [217]. Although the widespread application of microbiome technologies significantly aids

in discovering and developing beneficial strains, practical implementation requires further validation of probiotic efficacy, application methods, and performance in complex aquatic environments to better support sustainable aquaculture development.

For practical application, probiotic and microbiome-based interventions require strain-level identification and safety evaluation, particularly regarding antimicrobial resistance genes, potential pathogenicity, and environmental persistence. These considerations become especially important for designed microbial consortia and genetically engineered microorganisms, which require more rigorous biosafety assessment before field application.

3.5. Regulation of Aquaculture Environments

With the rapid global transition of aquaculture toward intensification and intelligence, the ecological functional profiling of aquatic microbiomes and omics-based monitoring technologies for RAS have emerged as critical domains for optimizing aquaculture environments and enhancing sustainability. Microbial community analysis techniques—using high-throughput sequencing (e.g., 16S/18S rRNA) and metabolomics—can accurately characterize the dynamic distribution and functionality of nitrifying bacteria, denitrifying bacteria and probiotics in aquaculture systems [218,219]. In RAS, integrated multi-omics monitoring systems is expected to significantly refine aquaculture management: metagenomics tracks microbial composition in water [220], while metabolomics dynamically evaluates ecosystem stability by detecting small-molecule metabolites (e.g., organic acids) from cultured organisms [221]. Furthermore, proteomics technology provides a molecular level basis for optimizing the efficacy of biofilters by resolving the activities of key functional proteins of algae in the aquaculture ecosystem [222].

Although multi-omics techniques have been applied to aquaculture ecological assessment, there are still some technical difficulties. The core challenge in technological implementation lies in bridging the gap between vast omics data and real-time environmental regulation. While industry leaders such as Norway's AKVA Group have pioneered an intelligent RAS integrated with IoT-enabled sensors (e.g., pH, dissolved oxygen, temperature) and AI-driven feeding optimization (<https://www.akvagroup.com/land-based/technology-solutions/ras/>; accessed on 17 August 2026), current frameworks remain limited in leveraging omics data for ecological assessment: On one hand, high-throughput sequencing workflows, encompassing sample processing and data analysis, introduce delays ranging from hours to days, failing to meet the millisecond-level real-time adjustment demands of the RAS. On the other hand, functional redundancy within microbial communities and the highly nonlinear dynamics of environmental responses amplify prediction error rates in existing artificial intelligence (AI) models, particularly under disruptive scenarios such as abrupt salinity fluctuations or extreme temperature events. Additional barriers include cost and standardization gaps. Omics-integrated systems remain prohibitively expensive for small-to-medium farms, while the absence of global standardized microbiome databases and monitoring protocols hinders scalability. Although the international organization for standardization (ISO/TC234) is leading efforts to establish such guidelines (<https://www.iso.org/committee/541071.html>; accessed on 17 August 2026), their practical implementation will require years of coordinated effort.

Looking to the future, the integration of synthetic biology and digital twin technologies holds promise for overcoming current limitations. By using CRISPR gene editing to design highly efficient denitrifying bacterial strains, the pollutant treatment capacity of biofilters could be significantly enhanced. Meanwhile, digital twin systems, by constructing virtual aquaculture environments, can simulate the succession trajectories of

microbial communities under varying temperatures and feeding strategies, allowing preemptive testing of regulatory solutions. Concurrently, rapid advancements in low-cost, portable omics devices—such as Oxford Nanopore’s MinION sequencer (<https://nanoporetech.com/products/sequence/minion>; accessed on 17 August 2026)—enable preliminary microbial identification in complex environments within short timeframes, making on-site, point-of-care testing feasible. In summary, with the iterative advancement of AI algorithms and the deep convergence of “omics-AI-IoT” technologies, aquaculture environmental management will transition from traditional experience-driven approaches to data-driven precision models. This paradigm shift will enable the full harnessing of ecological service functions within aquatic microbiomes, unlocking their maximal potential for sustainable aquaculture practices.

4. Methodological Innovation and Challenge

4.1. Novel GS Approaches Integrating Multi-Omics Data

Currently, the majority of GS studies in aquaculture species are conducted using the GBLUP method. However, in its standard formulation, GBLUP models additive genomic breeding values as random effects with a covariance structure determined by the genomic relationship matrix, which is constructed from genome-wide markers. Under common parameterizations, this formulation assumes a common variance structure for marker effects and primarily captures additive genetic effects unless non-additive effects are explicitly incorporated. Such simplifying assumptions may limit prediction accuracy when complex traits are influenced by heterogeneous marker effects, dominance, epistasis, or other features of genetic architecture. In reality, genomic regions can differ substantially in their functional relevance and contribution to phenotypic variation because of differences in gene content, regulatory activity, and expression patterns. However, conventional genomic prediction models generally rely on genome-wide marker information without explicitly accounting for such functional heterogeneity among genomic regions or marker categories. This limitation may reduce their ability to accurately predict complex traits [223].

To address these limitations, various advanced methodologies have been developed, including Bayesian approaches (BayesA, BayesB, and BayesC), weighted GBLUP (WGBLUP), weighted single-step GBLUP (WssGBLUP), and trait-specific marker-derived relationship matrices (TABLUP) [224]. These methods incorporate prior biological knowledge, such as the presence of major genes or QTLs influencing target traits. By assigning differential weights or larger effect sizes to SNPs in high LD with causal mutations or associated with QTLs, these enhanced models improve the accuracy of GEBVs compared to conventional GBLUP. Recent advancements in multi-omics research have accumulated substantial biological prior information, including the genomic positions of protein-coding genes (PCGs), regulatory elements of PCGs, GWAS results for key traits, and gene interaction networks. Emerging evidence demonstrates that systematic integration of these biological priors into GS models can effectively enhance prediction accuracy. Collectively, the integration of multi-omics data into GS frameworks represents a paradigm shift in precision breeding, particularly for complex traits influenced by intricate genetic and regulatory networks.

Current applications of GS strategies incorporating prior biological information have achieved notable successes in livestock and crop breeding. For milk fatty acid-related traits, the integration of GWAS results through weighted GBLUP improved prediction accuracy by an average of 38% in Dutch cattle populations, 23% in Danish herds, and 13% in Chinese populations compared to conventional GBLUP [225]. In sheep breeding, incorporating resequencing-based GWAS prior information significantly enhanced GS accuracy for eight economically important traits (six meat-related and two wool-related

traits) [226]. Wu et al. demonstrated that integrating genomic deleterious mutation information identified through comparative genomic analysis into yield trait predictions for potatoes resulted in a 24.7% accuracy improvement over standard models [227]. In aquaculture [228], the EU Horizon 2020 project AQUA-FAANG (“Advancing European Aquaculture by Genome Functional Annotation”) represents a landmark initiative in aquaculture genomics, systematically characterizing the functional architecture of genomes for six major European farmed fish species. By performing comprehensive functional annotations across diverse tissues and developmental stages, the project has prioritized genetic variants linked to regulatory elements and candidate genes within QTLs and other regions of interest. This foundational work provides critical resources to refine aquaculture GS strategies, enabling more accurate prediction of genetic merit for complex traits across populations and generations.

4.2. Critical Considerations and Bottlenecks in Aquaculture Multi-Omics Integration

The rapid expansion of omics technologies has greatly increased the molecular and phenotypic information available for aquaculture research, but the accumulation of additional data layers does not necessarily lead to better biological interpretation or more effective breeding and management decisions. A critical issue is that different omics platforms capture fundamentally different types of biological information and differ in their stability, context dependence, analytical maturity, and proximity to measurable phenotypes [229]. Genomic variation is relatively stable and heritable, making it particularly suitable for population-scale genetic evaluation and selection [184], whereas epigenomic, transcriptomic, proteomic, metabolomic, microbial, and imaging-derived features are generally more dynamic and responsive to physiological and environmental conditions [230]. This distinction is especially important in aquaculture, where temperature, salinity, diet, stocking density, developmental stage, microbial exposure, and other farming conditions can simultaneously influence multiple molecular and phenotypic layers [231]. Therefore, the value of an omics platform should not be judged by its position in a presumed molecular hierarchy, but by whether it provides reliable and non-redundant information for the biological question or production objective being addressed.

The design and utility of multi-omics also differ across aquaculture taxa and production systems. In finfish, established pedigrees, individual tagging, and repeated non-lethal sampling make it comparatively feasible to link genomic information with longitudinal phenotypes [232]. In many crustaceans and bivalves, high fecundity, communal rearing, small body size, and difficulties in tracking individuals can weaken genotype–phenotype matching and make family- or population-level designs more practical [233]. Production systems impose another layer of contrast: RAS provides relatively controlled conditions for repeated sampling and environmental attribution, whereas in biofloc systems the microbial community is itself part of the production process and should be analyzed together with the host [219]. By contrast, ponds and open mariculture receive substantial external environmental and microbial inputs, making spatial replication and environmental metadata particularly important for distinguishing host-associated signals from site- or season-specific effects.

These differences make multi-omics integration more difficult than simply combining additional data layers. Molecular layers operate on different temporal and spatial scales, and genomic variation, transcriptional responses, protein abundance, metabolites, microbial communities, and imaging-derived phenotypes may not reach their most informative states at the same sampling time. Integration is further weakened when different omics are generated from different individuals, tissues, developmental stages, or experimental batches, because apparent cross-omics correlations may then

reflect sampling structure rather than biological regulation [234]. This problem is especially relevant to aquaculture experiments, where family relatedness, tank effects, diet, water quality, and shared environmental exposure can generate correlated responses across multiple data layers. In addition, multi-omics datasets differ markedly in dimensionality, sparsity, dynamic range, and missing-value structure [235], while sample sizes in aquaculture studies are often relatively small compared with the number of measured features. Under such conditions, simple feature concatenation, pathway overlap, or correlation-based network construction can produce statistically convincing but biologically unstable associations [236].

Effective aquaculture multi-omics should therefore be question-driven rather than layer-driven. Omics data should preferably be collected from matched biological units at biologically justified time points, accompanied by standardized phenotypic and environmental metadata, and analyzed using models that account for family structure, tank effects, and other major sources of biological dependence. Candidate molecular signatures should also be validated across independent populations, seasons, diets, or farming environments before they are considered useful for breeding or management. From a practical perspective, the most valuable molecular features are not necessarily those showing the strongest statistical differences, but those that retain predictive or mechanistic value under heterogeneous production conditions. In this context, genomics is likely to remain central for inherited selection, whereas transcriptomic, proteomic, metabolomic, microbial, and imaging information may provide greater added value for resolving genotype-by-environment interactions, identifying physiological biomarkers, diagnosing health or nutritional states, and providing dynamic phenotypic feedback for precision management. Multi-omics integration should therefore be judged by whether an additional omics layer improves biological interpretation, prediction, or intervention beyond genomic, phenotypic, and environmental information alone, rather than by the number of data layers included.

4.3. Progress and Challenges in Aquaculture Data Science

With the accumulation of vast omics data, the construction of aquaculture-specific databases has progressively improved. Table 3 summarizes the current status of omics database development for common aquaculture species. In fish database development, Fish10K [237] was initiated by BGI in 2019, aiming to sample, sequence, assemble, and analyze the genomes of 10,000 representative fish species over a decade. The AQUA-FAANG project [228] has collected the genomes of six commercially important fish species—Atlantic salmon, rainbow trout, common carp, gilthead sea bream, European sea bass, and turbot—along with functional genomic annotation datasets primarily comprising RNA-seq, ATAC-seq, and ChIP-seq data. These multi-omics annotations cover information from embryonic development, tissue-specific expression, and immune challenges (viral and vibrio). The FishCODE project (<http://bioinfo.iuh.ac.cn/fishcode>; accessed on 17 August 2026) has compiled extensive multi-omics data for 35 fish species, encompassing 11,216 samples derived from 540 sets of genomic, transcriptomic, and methylomic datasets. The integrated information includes transcript structure and expression, gene methylation levels, as well as protein-related data such as domains, subcellular localization. Furthermore, the resource provides functional annotations like best-matched proteins (Swiss-Prot), associated SNP loci (47,111,018), orthologous genes, phylogenetic trees, and GO/KEGG annotations. FishDB [238], the first fish multi-omics database, integrates 233 fish genomes, 201 fish transcriptomes, 5841 mitochondrial genomes, and non-coding RNA information (e.g., miRNA, piRNA, lncRNA). In addition, several fish omics databases focusing on the collection of a single omics type have been developed. Examples include the fish gene expression and transcriptome database

FishGET [239], the single-cell transcriptome database FishSCT [240], and the spatial transcriptome database FishSED [241]. iFish [242] is a recently published comprehensive multi-omics resource for fish, integrating genomic, transcriptomic (including bulk RNA-seq, scRNA-seq, and miRNA-seq), epigenomic, and proteomic data from 88 fish species. Building on these data, iFish enables in-depth functional analyses, such as gene annotation, transcription factor identification, regulatory network construction, and cross-species comparisons, serving as a powerful platform for genetic research in fish.

Table 3. Omics databases of major aquatic species.

Species	Database Name	Data Type	Creation Time	Website
Fish	Fish10K	genome	2019	https://db.cngb.org/datamart/animal/DATAani16/ ; accessed on 17 August 2026
	AQUA-FAANG	genome, bulk transcriptome, epigenome, metagenome, proteome	2020	https://data.faang.org/projects/AQUA-FAANG ; accessed on 17 August 2026
	FishDB	genome, bulk transcriptome, mitochondrial genome, miRNA, piRNA, lncRNA, UTR, CDS	2020	https://fishdb.sinica.edu.tw/eng/fishquer.php ; accessed on 17 August 2026
	FishSCT	single-cell transcriptome	2023	http://bioinfo.iuh.ac.cn/fishsct ; accessed on 17 August 2026
	FishSED	spatial transcriptome	2023	http://bioinfo.iuh.ac.cn/fishsed ; accessed on 17 August 2026
	FishCODE	genome, bulk transcriptomic, and epigenetics	2024	http://bioinfo.iuh.ac.cn/fishcode ; accessed on 17 August 2026
Mollusc	iFish	genome, bulk transcriptomic, single-cell transcriptome, microRNA, epigenetics, proteomics, transcription factors	2025	https://gonglab.hzau.edu.cn/iFish/ ; accessed on 17 August 2026
	MODB	mitochondrial genomes	2021	http://modb.ytu.edu.cn/ ; accessed on 17 August 2026
	MolluscDB	genome, bulk transcriptome	2021	http://mgb.biocloud.net/home ; accessed on 17 August 2026
	MolluscDB 2.0	mtGenome, single cell transcriptome, proteome, epigenome, metagenome	2024	http://mgb.biocloud.net/home ; accessed on 17 August 2026
Crustacean;	ShrimpGPAT	gene and protein sequence	2014	https://ngdc.cncb.ac.cn/databasecommons/database/id/4758 ; accessed on 17 August 2026
	CrusTF	transcription factor	2017	http://qinlab.sls.cuhk.edu.hk/CrusTF ; accessed on 19 August 2026
	CrustyBase	bulk transcriptome	2020	https://crustybase.org ; accessed on 17 August 2026
	CrusTome	bulk transcriptome	2022	https://invertome.github.io/ ; accessed on 17 August 2026
Echinoderm	EchinoBase	genome	2017	https://www.echinobase.org/echinobase/ ; accessed on 17 August 2026

Algae (freshwater)	FWAlgaeDB	genome	2023	http://www.fwalagedb.com/#/home ; accessed on 17 August 2026
Comprehensive	AquaMine v1.2	genome, genomic variant, bulk transcriptome	2024	https://aquamine.rnet.missouri.edu/aquamine/begin.do ; accessed on 17 August 2026

Note: Table 3 summarizes representative omics databases and data resources for aquatic organisms, including fishes, mollusks, crustaceans, echinoderms, freshwater algae, and comprehensive aquatic databases. Relevant resources were identified through searches of Web of Science, PubMed, and Google Scholar using combinations of keywords such as “aquaculture database”, “aquatic species database”, “fish database”, “mollusk database”, “crustacean database”, “echinoderm database”, “genome database”, “transcriptome database”, “single-cell database”, and “multi-omics database”. Databases established or substantially updated between 2014 and 2025 were considered, with priority given to publicly accessible resources that provide curated omics datasets for aquatic species, including genomic, transcriptomic, single-cell transcriptomic, spatial transcriptomic, epigenomic, proteomic, metagenomic, and other functional genomic data. The table was compiled to provide representative examples of major aquatic omics resources rather than an exhaustive catalogue of all available databases.

For mollusks, MolluscDB [243] collects omics data from 22 species that represent eight major classes of mollusks, including 7 species represented by genome sequences and 15 by transcriptome assemblies. This resource is designed to support research into molluscan phylogeny, gene family evolution, and genes associated with biomineralization. MODB [244] is the first dedicated database for molluscan mitochondrial genomes, providing a comprehensive collection of 616 mitochondrial genomes spanning species across seven taxonomic classes of mollusks. It is noteworthy that the recently released MolluscDB 2.0 [245] is the most comprehensive multi-omics resource to date, encompassing genomic, bulk transcriptomic, single-cell transcriptomic, proteomic, epigenomic, and metagenomic data for 1450 species across eight mollusk classes.

In crustacean databases, ShrimpGPAT [246] compiles gene and protein sequences from six shrimp species and eight other decapod crustaceans, providing functional annotation tools for shrimp researchers. CrusTF [247] is a dedicated resource built to advance the study of crustacean transcriptional regulation. By mining 170 transcriptomes, it has cataloged 131,941 TFs from 63 families. CrustyBase [248] combines ten crustacean transcriptome datasets and allows users to upload new RNA-seq datasets. CrusTome [249] integrates transcriptomic data from 189 crustacean species across multiple tissues. CRUSTADB [250] is a recently published integrated multi-omics resource for crustaceans, featuring 33 high-quality genomes (including 14 decapod species) across classes like Malacostraca and Branchiopoda, 297 transcriptomes from 28 reference-genome species, and 312 mitochondrial genomes; it also includes 789 Gb of resequencing data from 100 samples covering 10 decapod species.

Other aquaculture species databases have been reported. Examples include EchinoDB v2.0 [251] or EchinoBase [252], which focus on genomic and transcriptomic data from echinoderms, and FWAlgaeDB [253], which is dedicated to genomic data from algae. Notably, the comprehensive genome database AquaMine v1.2 has been released. It integrates genome assemblies and gene annotations for aquatic eumetazoan species of significant importance to U.S. aquaculture and fisheries, comprising genomic data and genomic variant data from 37 aquatic species alongside transcriptomic datasets for a subset of them [254].

While progress has been made in constructing databases for aquaculture species, substantial data imbalance and fragmentation remain. Major challenges include

incomplete genome annotation for many farmed species compared with model organisms such as zebrafish, as well as limited cross-omics integration, with most existing databases covering only one or a few data layers. With the rapid development of high-throughput sequencing, computer vision, cloud computing, and artificial intelligence (AI), future aquaculture research will increasingly require integrated repositories linking genomic, molecular, phenotypic, environmental, and production data, supported by a unified framework of data ecosystems, computational architectures, and algorithmic collaboration. Beyond conventional data integration, emerging AI approaches may further transform multi-omics analysis from retrospective association toward predictive and adaptive modeling [255]. Foundation models could facilitate transferable representation learning across species and omics layers, which is particularly valuable for aquaculture species with limited training data, whereas graph neural networks offer a natural framework for modeling relationships among genes, proteins, metabolites, microbes, environmental factors, and phenotypes [255]. Large language models may complement these approaches by linking multi-omics signals with dispersed biological knowledge and assisting knowledge-guided interpretation. More importantly, integration of multi-omics data with real-time environmental sensors and imaging systems could support digital twins of aquaculture systems, enabling dynamic simulation of disease risk, nutritional responses, and environmental interventions. However, the practical value of these AI-driven systems will depend not only on predictive performance but also on explainability, cross-species transferability, and validation under heterogeneous farming conditions. Explainable AI will therefore be particularly important for distinguishing biologically meaningful drivers from dataset-specific correlations and translating complex multi-omics predictions into reliable breeding and farm management decisions.

5. Conclusions

Multi-omics is expanding the scope of aquaculture research from the characterization of individual molecular layers toward a more integrated understanding of how genotype, physiological state, microbiota, and environment jointly shape production traits. Its value, however, will depend less on the continued accumulation of omics datasets than on whether these data can be translated into robust biological knowledge and practical decisions. Greater attention is therefore needed to standardized phenotyping and environmental metadata, matched and longitudinal sampling, and independent validation across populations and farming conditions. These efforts are particularly important for distinguishing reproducible signals from context-dependent associations and for determining when additional omics layers provide information beyond conventional genomic, phenotypic, or environmental measurements. At the same time, routine application will require lower analytical costs, interoperable data resources, and appropriate data governance. For technologies involving gene editing, microbiome manipulation, or other interventions with potential ecological consequences, biosecurity, animal welfare, environmental risk, and regulatory considerations must also be incorporated into their development. With these foundations in place, multi-omics can move beyond descriptive integration and become a practical framework for connecting biological mechanisms with selective breeding, health management, and environmental assessment in aquaculture.

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