Enhancing Aquatic Animal Resilience to Environmental Stressors via Gene and Metabolic Regulation

Nahavandi R.[1*]; Abbaspour Anbi A.[2]; Pourmozaffar S.[3]

Received: August 2025 Accepted: November 2025

Abstract

Environmental stressors such as temperature fluctuations, hypoxia, pollution, and osmotic imbalances significantly impact the physiology, growth, and survival of aquatic animals. This review summarizes current knowledge on how gene regulation and metabolic adaptation work together to enhance resilience in aquatic species. Gene regulatory mechanisms—including transcriptional control, epigenetic modifications, and post-transcriptional adjustments—enable precise and dynamic responses to environmental changes. Metabolic reprogramming simultaneously modulates energy use, antioxidant production, and osmotic balance, forming an integrated defense against cellular and systemic damage. Recent biotechnological advances, such as CRISPR-based genome editing, omics-driven selective breeding, and nutrigenomic feed strategies, offer new opportunities to improve stress resilience in aquaculture species. However, challenges remain due to multi-stressor complexity, genetic diversity, environmental variability, and regulatory and ethical constraints. Future research should integrate multi-omics approaches with real-time environmental monitoring to identify robust biomarkers and optimize interventions. Responsible application of molecular and metabolic insights through interdisciplinary efforts will be key to sustainable aquaculture, strengthening aquatic animal resilience under climate change and anthropogenic pressures while safeguarding ecosystem health and food security.

Keywords: Environmental stressors, Gene regulation, Metabolic regulation, Aquatic animal resilience, Biotechnological interventions

1-Animal Science Research Institute of Iran (ASRI), Agricultural Research, Education and Extension Organization (AREEO), Karaj, Iran
2-National Artemia Research Center, Iranian Fisheries Science Research Institute (IFSRI), Agricultural Research, Education and Extension Organization (AREEO), Urmia, Iran
3-Persian Gulf Mollusks Research Station, Persian Gulf and Oman Sea Ecology Research Center, Iranian Fisheries Sciences Research Institute, Agricultural Research, Education and Extension Organization (AREEO), Bandar Lengeh, Iran
*Corresponding author' Email: Rezanahavandi91@gmail.com

Introduction

Environmental stresses such as temperature fluctuations, hypoxia, pollution, and salinity changes are major threats to aquatic animals, impacting their survival, growth, and reproduction. These pressures are intensifying due to global climate change and increasing anthropogenic pollution. Aquatic organisms have developed complex physiological and molecular mechanisms to sense, respond to, and mitigate the harmful effects of these environmental stressors (Wannas and Mohammed, 2025). Understanding these natural defense strategies, particularly at the gene expression and metabolic regulation levels, is crucial for advancing sustainable aquaculture and conservation efforts. Gene regulation plays a vital role in the acclimation and adaptation processes to environmental stresses (Pelletier *et al*., 2020). Specific genes encoding heat shock proteins, antioxidant enzymes, and metabolic enzymes are differentially expressed in response to stress, allowing organisms to maintain cellular homeostasis and protect vital functions. Moreover, epigenetic modifications dynamically influence stress-responsive gene expression, enhancing phenotypic plasticity in aquatic populations (Vieira *et al*., 2025). Metabolic regulation complements gene expression changes by adjusting energy production, antioxidant defenses, and biosynthetic pathways necessary for survival under stress conditions. For example, shifts from aerobic to anaerobic metabolism may occur under hypoxia, while antioxidant metabolites increase to counteract oxidative damage induced by thermal or chemical stress (Jin *et al*., 2025). Integrating knowledge of gene and metabolic regulation mechanisms can provide innovative avenues to improve stress resistance. Emerging biotechnologies, including gene editing and omics-based nutritional strategies, have the potential to enhance the resilience of aquaculture species to environmental challenges (XU and Wang, 2022). This review outlines the current understanding of molecular and metabolic responses to environmental stresses in aquatic animals, highlights recent advances in gene and metabolic regulation research, and discusses applications for stress resistance improvement.

Environmental stresses affecting aquatic animals

Aquatic animals inhabit environments characterized by a delicate balance of physical, chemical, and biological factors essential for their survival and development. However, these ecosystems are increasingly subjected to a wide range of environmental stressors, threatening the health, survival, and performance of aquatic species (Martyniuk *et al*., 2025). Understanding the nature, sources, and biological impacts of these stressors is fundamental to advancing the resilience of aquatic animals through molecular and metabolic regulation (Hu *et al*., 2024).

Temperature stress

Temperature is one of the most critical environmental parameters influencing aquatic organisms. Rapid global climate change has resulted in increased frequency and intensity of thermal fluctuations, including heatwaves and cold spells, which disrupt physiological homeostasis (Zhang *et al*., 2025). Elevated temperatures can accelerate metabolic rates, leading to increased oxygen demand while reducing oxygen solubility in water, creating a complex challenge for aquatic animals. This can impair growth, reproduction, immune responses, and increase mortality rates. Conversely, exposure to cold stress slows down biochemical reactions and can cause cellular damage through ice formation in some species (Kendrick *et al*., 2019).

Hypoxia

Hypoxia, or low dissolved oxygen levels in water, is a widespread issue caused by eutrophication, stratification, and increased organic matter decomposition. Oxygen depletion triggers a cascade of physiological stress responses in aquatic animals, forcing them to switch from aerobic to less efficient anaerobic metabolism. This shift results in energy deficits, accumulation of toxic metabolic byproducts, and oxidative stress upon reoxygenation. Prolonged hypoxia compromises immune functions and increases susceptibility to diseases (Rojas *et al*., 2025).

Pollution and toxicants

Aquatic environments are increasingly contaminated by pollutants such as heavy metals (e.g., mercury, cadmium), pesticides, hydrocarbons, and pharmaceuticals. These toxicants can accumulate in tissues and disrupt cellular function by inducing oxidative stress, damaging DNA, proteins, and lipids, thereby impairing physiological processes (Yang *et al*., 2025). Sub-lethal exposure can alter behavior, feeding, and reproduction, while chronic toxicity leads to population declines. The combined effects of multiple pollutants often produce synergistic or additive impacts enhancing the severity of stress (Carrier-Belleau *et al*., 2021).

Salinity and pH fluctuations

Fluctuations in salinity and pH levels, often resulting from freshwater inflow alterations, pollution, or acid rain, challenge osmoregulation and acid-base balance in aquatic organisms. Osmoregulatory organs work harder to maintain ion homeostasis under fluctuating salinity, which can be energetically costly and reduce growth efficiency. Similarly, pH changes impact enzyme activity, ion transport, and can provoke stress responses impacting overall fitness (XU and Wang, 2022).

Multiple and cumulative stressors

In natural and cultured environments, aquatic animals are rarely exposed to isolated stressors. Instead, multiple stressors interact in complex ways, sometimes amplifying each other's effects and pushing organisms beyond their tolerance thresholds. For example, the combination of increased temperature and hypoxia can synergistically elevate oxidative damage and metabolic disruption. Understanding these interactions is imperative for realistic assessments of aquatic animal resilience (Villar-Argaiz *et al*., 2018).

Gene regulation mechanisms

Gene regulation is fundamental to how aquatic animals respond, acclimate, and adapt to environmental stresses. The complex interaction between environmental cues and the genome results in dynamic changes in gene expression profiles, allowing organisms to maintain homeostasis and enhance survival under adverse conditions (Liu *et al*., 2022). Understanding these regulatory mechanisms at molecular, epigenetic, and transcriptional levels provides insight into biological resilience and offers pathways for enhancing stress tolerance in aquaculture species (XU and Wang, 2022).

Transcriptional regulation in stress responses

One of the primary modes of gene regulation involves transcriptional changes triggered by stress signaling pathways. Environmental stressors such as temperature fluctuations, hypoxia, and pollutants induce the activation of stress-responsive transcription factors (e.g., heat shock factors (HSFs), nuclear factor erythroid 2–related factor 2 (Nrf2), and hypoxia-inducible factors (HIFs) (Liu *et al.,* 2025). These factors bind to specific gene promoter regions, inducing or repressing expression of target genes that are involved in protective processes. For instance, heat shock proteins (HSPs) are among the most studied products of stress-induced gene activation (Liu *et al*., 2024). These molecular chaperones aid in protein folding, prevent aggregation of denatured proteins, and promote cellular repair mechanisms. Similarly, antioxidant enzymes such as superoxide dismutase (SOD) and catalase are transcriptionally upregulated to combat oxidative stress generated by environmental insults (Liu *et al*., 2022).

Epigenetic modifications

In addition to direct transcriptional control, epigenetic regulation plays a crucial role in mediating gene expression changes in response to environmental stress without altering the DNA sequence. Mechanisms such as DNA methylation, histone modifications, and non-coding RNAs influence chromatin structure and gene accessibility (Lu *et al*., 2025). DNA methylation, particularly at promoter regions, generally suppresses gene expression. In aquatic organisms, stress conditions have been shown to induce hypomethylation of genes critical for stress resistance, thereby increasing their expression. Intriguingly, some epigenetic alterations have been reported to be heritable across generations, suggesting a mechanism of transgenerational acclimatization or adaptation (Li *et al*., 2024).

Post-transcriptional and post-translational regulation

Gene regulation extends beyond transcription to post-transcriptional processes including mRNA splicing, stability, transport, and translation efficiency. Environmental stress can modulate these layers, further refining the cellular response. For example, microRNAs (miRNAs) have emerged as key regulators by targeting messenger RNAs for degradation or translational repression in stress contexts (Pashay *et al*., 2025). Post-translational modifications such as phosphorylation and ubiquitination also modulate protein activity, localization, and degradation. These dynamic modifications enable rapid cellular adjustments in response to changing environmental conditions (Bari *et al.,* 2025).

Integration of gene regulatory networks

Environmental stress responses in aquatic animals involve coordinated regulation across numerous genes, forming complex gene regulatory networks. Systems biology approaches have been applied to understand these networks, revealing co-regulated gene modules that work synergistically to execute stress response programs (Liu *et al*., 2025). For example, pathways involved in energy metabolism, immune responses, and apoptosis are tightly regulated to balance cell survival and damage control. Understanding these networks not only elucidates fundamental biological processes but also helps identify candidate genes and pathways for genetic improvement and biotechnological interventions aimed at enhancing aquatic animal resilience (Ge *et al.,* 2022).

Metabolic regulation

Metabolism encompasses the complex biochemical processes that sustain life by converting nutrients into energy and cellular building blocks. In aquatic animals, metabolic regulation plays a pivotal role in responding and adapting to environmental stresses such as temperature fluctuations, hypoxia, pollution, and osmotic changes (Yang *et al.,* 2023). These stressors impose energetic constraints and necessitate dynamic metabolic adjustments to maintain cellular homeostasis, support critical physiological functions, and ensure survival under adverse conditions (Sun *et al*., 2024).

Metabolic responses to temperature stress

Temperature profoundly influences enzymatic activities, membrane fluidity, and overall metabolic rate in aquatic ectotherms. As environmental temperatures rise, metabolic rates generally increase exponentially, elevating oxygen consumption and energy demand. However, thermal stress can disrupt mitochondrial function, leading to increased production of reactive oxygen species (ROS) and oxidative damage. To counteract these effects, aquatic animals often shift their metabolic pathways to optimize energy production while minimizing oxidative stress. For example, enhanced glycolysis and altered lipid metabolism have been observed under heat stress, alongside upregulation of antioxidant systems to detoxify ROS. Conversely, cold stress slows metabolic reactions, reduces ATP production, and impairs biosynthesis, necessitating metabolic downregulation or remodeling. Some species accumulate cryoprotectants like glycerol or antifreeze proteins, adjusting carbohydrate and lipid metabolism to protect cells from freezing-induced damage (XU and Wang, 2022).

Oxygen availability and metabolic adaptation

Hypoxia is a critical environmental stressor that limits aerobic respiration, forcing aquatic animals to employ alternative metabolic strategies. Transitioning from aerobic to anaerobic metabolism reduces ATP yield but sustains vital functions during oxygen scarcity. Anaerobic pathways generate lactate or other metabolites such as succinate and alanine, which must be efficiently cleared or converted when oxygen becomes available again. Moreover, chronic hypoxia induces long-term metabolic reprogramming, including changes in carbohydrate and lipid metabolism, mitochondrial biogenesis, and antioxidant defenses. For example, increased reliance on glycolytic enzymes and shifts in Krebs cycle enzyme activities have been documented in several fish and mollusk species, reflecting efforts to balance energy supply and oxidative damage under low oxygen (Rubalcaba *et al.*, 2020).

Metabolic regulation of osmotic stress

Aquatic organisms constantly regulate internal osmolarity to cope with fluctuating salinity. Osmotic stress leads to significant energy expenditures to power ion transporters and maintain cellular volume (Hu *et al*., 2024).

These energetic demands prompt changes in ATP turnover and substrate utilization. Compatible osmolytes such as taurine, betaine, and free amino acids accumulate to stabilize proteins and membranes (Mkulo *et al*., 2025). Metabolic pathways associated with amino acid metabolism and ion transport are modulated in response to salinity changes, ensuring ionic equilibrium while minimizing energetic costs. Shifts in nitrogen metabolism also reflect the need to detoxify ammonia efficiently, crucial under altered water chemistry (Jin *et al*., 2022).

Oxidative stress and antioxidant metabolism

Environmental stressors increase production of ROS, which can damage DNA, proteins, and lipids. To maintain redox balance, aquatic animals regulate the synthesis and activity of key antioxidant enzymes like superoxide dismutase, catalase, and glutathione peroxidase. Metabolic pathways provide reducing equivalents (NADPH) through the pentose phosphate pathway and maintain glutathione pools essential for detoxification. Activation of redox-sensitive signaling pathways triggers metabolic adjustments to mitigate oxidative damage. These include modulation of mitochondrial respiration efficiency, repair mechanisms, and metabolic repression during severe stress (Zhang *et al*., 2025).

Integration of gene and metabolic regulation

Metabolic regulation is tightly coupled with gene expression alterations. Stress-induced transcriptional changes modulate enzyme levels, transporter proteins, and signaling mediators that coordinate metabolic shifts. The interplay between genetic and metabolic controls enables aquatic animals to tailor their physiological responses to the specific nature, intensity, and duration of environmental challenges (Jin *et al*., 2022).

Applications in aquaculture and environmental conservation

Understanding metabolic regulation under stress has practical implications for aquaculture. Optimizing dietary formulations to support metabolic resilience, employing metabolic biomarkers for early stress detection, and selecting genotypes with favorable metabolic profiles are promising strategies. Advanced omics technologies enable detailed mapping of metabolic pathways and identification of key regulatory nodes, facilitating targeted interventions to enhance stress tolerance (Wannas and Mohammed, 2025).

Biotechnological approaches to enhance resistance

Environmental stresses impose severe challenges to aquatic animals, particularly within aquaculture industries striving for sustainability amid climate change and environmental degradation. Conventional breeding and management practices, while invaluable, are often insufficient to rapidly address these multifaceted stressors. Biotechnology offers innovative tools and methods to enhance the resilience of aquatic species by directly manipulating genetic, epigenetic, and metabolic pathways that underlie stress resistance. This section reviews cutting-edge biotechnological approaches applied or promising for aquaculture enhancement, emphasizing gene editing, omics-based strategies, and nutrigenomics (Jie *et al*., 2024).

Gene editing technologies

The advent of precise genome editing tools, notably CRISPR-Cas9, has revolutionized the capacity to enhance desirable traits in aquatic animals with unprecedented accuracy and efficiency. This technology allows targeted modification of stress-responsive genes to boost tolerance against thermal extremes, hypoxia, pathogens, and pollutants (Liang *et al*., 2024). Research demonstrates successful knockout or overexpression of key genes such as heat shock proteins, antioxidant enzymes, and immune receptors in species including tilapia, shrimp, and salmon. For instance, modifying heat shock transcription factors can enhance thermal tolerance by upregulating protective chaperones Similarly, editing hypoxia-inducible factor genes modulates adaptation to low oxygen environments. Despite promising results, challenges remain, i.ncluding off-target effects, delivery methods, and regulatory acceptance. Advances in base editing and prime editing promise even more refined genomic interventions with minimal undesired alterations (Liu *et al*., 2022).

Genomic and transcriptomic approaches

High-throughput sequencing technologies, including whole-genome sequencing, RNA-seq, and epigenome mapping, allow unprecedented insights into the molecular basis of stress resistance. Integrating these omics datasets enables identification of candidate genes, regulatory elements, and pathways associated with environmental resilience. Marker-assisted and genomic selection methods use these molecular markers to accelerate breeding programs by selecting broodstock with superior stress tolerance without the time-consuming phenotypic screening. Additionally, transcriptomic profiling during stress exposure reveals dynamic expression patterns that inform targeted interventions. Epigenetic modifications, characterized through methylome and histone modification profiling, offer another layer for improving resilience. Artificially manipulating epigenetic marks through epigenome editing or environmental conditioning holds potential but needs further exploration (Ge *et al.,* 2022).

Nutrigenomics and metabolomics

Nutrigenomics examines interactions between nutrition and gene expression, providing powerful strategies to enhance metabolic resilience and immune function in aquatic animals. Customized diets supplemented with functional nutrients such as omega-3 fatty acids, antioxidants, amino acids, and prebiotics modulate gene expression profiles to mitigate stress effects. Metabolomics, the comprehensive study of metabolites, complements nutrigenomics by revealing shifts in metabolic pathways under stress and dietary modulation. This information guides formulation of feeds that optimize energy metabolism, antioxidant defenses, and osmoregulation, improving overall fitness and productivity. Feed additives such as nano-encapsulated compounds and bioactive peptides are emerging to enhance delivery and efficacy of these functional nutrients, enabling more precise metabolic regulation (Li *et al*., 2024).

RNA interference and functional genomics

RNA interference (RNAi) technology offers a gene-silencing approach to transiently reduce expression of deleterious genes or pathogens in aquatic animals. This method has been explored for antiviral, antibacterial, and anti-parasitic applications to reduce disease-related stress. Combined with functional genomic assays, RNAi expedites validation of gene functions in stress response, improving the identification of molecular targets for genetic and nutritional interventions (Liu *et al*., 2022).

Challenges and ethical considerations

While biotechnological approaches hold significant promise, responsible development and deployment are essential. Regulatory frameworks, environmental risk assessments, and public acceptance strongly influence adoption. Ethical concerns regarding genetic modifications, especially in open aquatic systems, require transparent stakeholder engagement and rigorous biosafety protocols. The integration of multidisciplinary research, including molecular biology, nutrition, ecology, and socioeconomics, will optimize the sustainable use of biotechnologies to enhance aquatic animal resilience (XU and Wang, 2022).

Challenges and future directions

Environmental stress resistance in aquatic animals is a multifaceted biological phenomenon shaped by complex interactions among genetics, metabolism, physiology, and the surrounding ecosystem. Despite significant advances in understanding gene and metabolic regulation mechanisms, substantial challenges hinder the full realization of these insights into practical applications for aquaculture and conservation (Bai *et al*., 2025).

Complexity and multifactorial nature of stress responses

One of the foremost challenges is the inherent complexity of stress responses. Environmental stressors rarely act in isolation; rather, organisms encounter multiple, simultaneous stressors such as thermal fluctuations, hypoxia, pollution, and salinity changes. These stressors often interact synergistically or antagonistically, complicating the prediction of organismal outcomes. The gene regulatory and metabolic networks mediating these responses are highly interconnected, nonlinear, and context-dependent, making it difficult to pinpoint universal biomarkers or targets for intervention. Future research must adopt integrative systems biology approaches that combine genomics, transcriptomics, proteomics, metabolomics, and phenomics data to create comprehensive models of stress resilience. Incorporating environmental and ecological variables into these models will enable better simulation of real-world scenarios and identification of critical regulatory hubs (Liu *et al*., 2022).

Genetic and epigenetic diversity

The genetic diversity within and among aquatic species influences variability in stress tolerance, yet this diversity is often underappreciated in current studies. Epigenetic modifications add another layer of variability and potential heritability in stress response traits. Harnessing this diversity in breeding programs requires high-resolution genomic information and sophisticated selection tools (Ignatz *et al*., 2025).

The challenge lies in balancing genetic gains for stress resistance with the maintenance of overall biodiversity and avoiding inadvertent negative consequences such as reduced fitness under non-stress conditions. Advances in genome-wide association studies (GWAS), epigenome editing, and functional genomics will be crucial for identifying beneficial alleles and epigenetic marks responsible for resilience (Liu *et al*., 2022).

Translating molecular insights into phenotypic outcomes

Another critical obstacle is translating molecular and metabolic findings into measurable phenotypic improvements under commercial aquaculture settings. Laboratory and experimental conditions often do not replicate the complex, variable environments experienced by cultured aquatic animals. High-throughput phenotyping technologies, combined with precision aquaculture tools like sensors and environmental monitoring, must be integrated to validate candidate genes, pathways, and metabolic traits under realistic stress exposures. Developing reliable biomarkers for early stress detection and resilience prediction will enhance selective breeding and management (Li *et al*., 2024).

Technological limitations and ethical considerations

While gene editing and omics technologies offer unprecedented potential, they face technological, regulatory, and ethical challenges. Precise gene editing techniques suffer from limitations such as off-target effects, mosaicism, and delivery hurdles, particularly in aquatic species with complex reproductive cycles (Huang *et al*., 2025). Ethical concerns regarding genetic modifications, potential ecological impacts, and public acceptance require transparent governance frameworks. Addressing these issues demands multidisciplinary collaboration among molecular biologists, ethicists, policymakers, and industry stakeholders. Engaging the public through science communication and participatory decision-making will be crucial for the responsible development and deployment of biotechnologies (Zhu *et al*., 2024).

Environmental variability and climate change

The accelerating pace of climate change introduces unprecedented environmental variability, challenging the adaptive capacities of aquatic animals. Predicting the combined effects of rising temperatures, ocean acidification, hypoxia, and emerging pollutants is a daunting task due to complex feedback loops and novel stressor combinations. Future studies should prioritize long-term, multi-generational experiments that assess adaptive plasticity, transgenerational epigenetic inheritance, and evolutionary potential. Integrating climate models with molecular and ecological data will inform conservation and management strategies that enhance resilience at population and ecosystem levels (XU and Wang, 2022).

Nutritional and metabolic interventions

Though nutrigenomics and metabolomics have elucidated potential dietary interventions to improve stress resistance, practical applications remain limited. Issues related to nutrient bioavailability, interactions among feed components, and variability in individual metabolic responses constrain widespread use (Jakiul *et al*., 2024). Future research should focus on precision nutrition tailored to genetic backgrounds and environmental contexts to optimize feed formulations. Advances in feed additive technologies, such as microencapsulation, probiotics, and immune stimulants, will enable targeted delivery of metabolic modulators (Okoli *et al*., 2022).

Data integration and computational modeling

The vast volume and heterogeneity of data generated by multi-omics and environmental studies pose enormous challenges for data integration, analysis, and interpretation. Developing interoperable databases, standardized protocols, and advanced bioinformatics tools is imperative for extracting actionable knowledge. Machine learning and artificial intelligence hold promise for deciphering complex datasets and predicting stress outcomes. However, algorithms must be transparent, validated, and coupled with mechanistic understanding to guide empirical research effectively (Morabito *et al*., 2025).

Future directions: Toward sustainable aquaculture

Looking forward, the field should embrace a holistic approach that merges molecular, ecological, nutritional, and socio-economic perspectives to enhance aquatic animal resilience sustainably. Some promising avenues include:

- Combining gene editing with selective breeding to stack multiple beneficial traits (Yang *et al*., 2025).
- Exploiting epigenetic modifications to induce rapid acclimatization or adaptation.
- Developing integrative biomarkers for multi-stressor resistance.
- Leveraging environmental DNA (eDNA) monitoring for ecosystem health and species resilience (Naya-Català *et al*., 2023).
- Applying precision aquaculture tools for real-time stress management and optimized husbandry.
- Promoting interdisciplinary collaborations among academia, industry, and policy makers.
- Addressing socio-economic and ethical implications to foster equitable and responsible aquaculture development (Ruben *et al*., 2025).

Implementing these strategies will require continuous innovation, robust regulatory frameworks, and global cooperation to meet the dual challenges of food security and environmental stewardship in aquatic systems.

Conclusion

Advancing resistance to environmental stresses in aquatic animals through the intricate interplay of gene and metabolic regulation represents a pivotal frontier in sustainable aquaculture and biodiversity conservation. The multifactorial nature of stressors such as temperature extremes, hypoxia, pollution, and osmotic variations necessitates comprehensive understanding at molecular, cellular, and systemic levels. Gene regulation mechanisms, encompassing transcriptional activation, epigenetic modifications, and post-transcriptional controls, orchestrate adaptive responses that enable aquatic species to maintain homeostasis and mitigate damage. Complementarily, metabolic adaptations dynamically reshape energy production, antioxidant defense, and osmotic balance, underpinning physiological resilience under adverse conditions. The emergence of sophisticated biotechnological approaches—including genome editing, omics-driven breeding, and nutrigenomic interventions—offers unprecedented opportunities to enhance aquatic animal robustness. However, these advances are tempered by challenges related to the complexity of stress responses, genetic and epigenetic variability, and the translation of molecular insights into phenotypic traits under realistic environmental contexts. Regulatory frameworks, ethical considerations, and public acceptance further influence the trajectory of biotechnological applications. Looking forward, integrative systems biology combining multi-omics data with environmental monitoring, together with precision aquaculture tools, holds promise for optimizing stress resistance strategies. Emphasizing interdisciplinary collaboration, transparent governance, and equitable technology deployment will be essential to harness these innovations responsibly. Ultimately, bridging fundamental molecular understanding with applied aquaculture practice will play a critical role in addressing climate change impacts, ensuring food security, and preserving aquatic ecosystem health in an increasingly uncertain world.

References

Bai, L., Sun, G., Li, J., Sun, J., Wu, Z., Li, C., Ma, R. and Meng, Y., 2025. Metabolic response and adaption to chronic hypoxia of triploid rainbow trout by the crosstalk between the liver and muscle, *Aquaculture*, 602, ISSN 0044-8486, https://doi.org/10.1016/j.aquaculture.2025.742333.

Bari, S.M., Fuad, M., Hossain, M.J., Ahammad, I., Begum, M. and Uddin Helal, M.M., 2025. A meta-analysis of public RNA-Seq data identifies conserved stress responses in rainbow trout. *BMC Genomics,* 26, 999. https://doi.org/10.1186/s12864-025-12127-2.

Carrier-Belleau, C., Drolet, D., McKindsey, C.W. and Archambault, P., 2021. Environmental stressors, complex interactions and marine benthic communities' responses. *Scientific Reports*, 18, 11(**1**), 4194. DOI:10.1038/s41598-021-83533-1.

PMID: 33603048; PMCID: PMC7892560.

Ge, J., Lin, Y.H., Araneda, C. and Wang, Q., 2022. Editorial: Genetic adaption and metabolic response of aquatic animals to diverse water environment parameters. *Frontiers in Physiology*, 18,13, 1092413. DOI:10.3389/fphys.2022.1092413. PMID: 36467677; PMCID: PMC9716266.

Hu, J., Yang, J. and Liao, H., 2024. Progress on stress resistance breeding in fish. *Reproduction and Breeding*, 4, 4, pp. 267-278, ISSN 2667-0712, https://doi.org/10.1016/j.repbre.2024.09.004.

Hu, W., Yi Cao, Y., Liu, Q., Yuan, C. and Hu, Z., 2024. Effect of salinity on the physiological response and transcriptome of spotted seabass (*Lateolabrax maculatus*), *Marine Pollution Bulletin*, 203, 116432, ISSN 0025-326X, https://doi.org/10.1016/j.marpolbul.2024.116432.

Huang, S., Jiang, S., Jiang, S., Jianhua, H., Yang, L., Jianzhi, S., Erchao, L., Zhou, F. and Li, Y., 2025. Omics analysis of *Penaeus monodon* in response to salinity changes. *Stress Biology*, 5, 17. https://doi.org/10.1007/s44154-024-00207-4.

Ignatz, E.H., Allen, M.S., Hall, J.R., Sandrelli, R.M., Fast, M.D., Perry, G.M.L., Rise, M.L. and Gamperl, A.K., 2025. Application of genomic tools to study and potentially improve the upper thermal tolerance of farmed Atlantic salmon (*Salmo salar*). *BMC Genomics*, 26, 294. https://doi.org/10.1186/s12864-025-11482-4.

Jakiul Islam, Md., Puebla, O. and Kunzmann, A., 2024. Nutritional mitigation of heatwave stress in European seabass, *Dicentrarchus labrax*: Metabolic, cellular, and molecular responses, *Aquaculture Reports*, 36, 102168, ISSN 2352-5134. https://doi.org/10.1016/j.aqrep. 102168.

Jie, Hu., Yang, J. and Liao, H., 2024. Progress on stress resistance breeding in fish. *Reproduction and Breeding*, 4, 4, pp. 267-278, ISSN 2667-0712, https://doi.org/10.1016/j.repbre.2024.09.004.

Jin, X., Wang, X., Tse, W.K.F. and Shi, Y., 2022. Editorial: Homeostasis and physiological regulation in the aquatic animal during osmotic stress. *Frontiers in Physiology*, 8, 13, 977185. DOI:10.3389/fphys.2022.977185. PMID:36003653; PMCID: PMC9393640.

Jin, M., Zheng, A., Mkulo, E.M., Wang, L., Zhang, H., Tang, B., Zhou, H., Wang, B., Huang, J. and Wang, Z., 2025. Metabolomics-Based Analysis of Adaptive Mechanism of *Eleutheronema tetradactylum* to Low-Temperature Stress. *Animals (Basel)*,19, 15(**8**),1174. DOI:10.3390/ani15081174. PMID:40282008; PMCID:PMC12024119.

Kendrick, G.A., Nowicki, R.J., Olsen, Y.S., Strydom, S., Fraser, M.W., Sinclair, E.A., Statton, J., Hovey, R.K., Thomson, J.A., Burkholder, D.A., McMahon, K.M., Kilminster, K., Hetzel, Y., Fourqurean, J.W., Heithaus, M.R. and Orth, R.J.,2019. A Systematic Review of How Multiple Stressors from an Extreme Event Drove Ecosystem-Wide Loss of Resilience in an Iconic Seagrass Community.

Frontiers in Marine Science, 6, 455. DOI:10.3389/fmars.2019.00455.

Li, Y., Li, Y.F., Campinho, M.A. and Fuentes, J., 2024. Editorial: Endocrine regulation and physiological adaptation of stress response in aquatic organisms. *Frontiers in Physiology*, 8, 15, 1406986. DOI:10.3389/fphys.2024.1406986. PMID: 38651046; PMCID: PMC11033506.

Liang, C., Lu Y., and Mai, R., 2024. CRISPR-Cas9 mediated gene editing in tilapia: enhancing growth rates and disease resistance, *Genomics and Applied Biology*, 15(**2**), pp. 99-106. DOI: 10.5376/gab.2024.15.0012.

Liu, Z., Zhou, T. and Gao, D., 2022. Genetic and epigenetic regulation of growth, reproduction, disease resistance and stress responses in aquaculture. *Frontiers in Genetics*, 2, 13, 994471. DOI:10.3389/fgene.2022.994471. PMID:36406125; PMCID: PMC9666392.

Liu, Y., Liang, Z., Li, Y., Zhu, W., Feng, B., Xu, W., Fu, J., Wei, P., Luo, M. and Dong, Z., 2024. Integrated transcriptome and microRNA analysis reveals molecular responses to high-temperature stress in the liver of American shad (*Alosa sapidissima*). *BMC Genomics*, 25, 656. https://doi.org/10.1186/s12864-024-10567-w.

Liu, Q., Zou, X., Zhao, M., Guan, Q., Xuan, Z., Liu, L. and Gao. Z., 2025. Integrated transcriptome and metabolome analysis of liver reveals unsynchronized growth mechanisms in blunt-snout bream (*Megalobrama amblycephala*). *BMC Genomics*, 26(**1**), 30. https://doi.org/10.1186/s12864-025-11208-6.

Lu, G., Wang, J., Luo, M. and Wang, C., 2025. Epigenetic mechanisms and applications in aquaculture and fisheries, with perspectives on technology and analysis, *Aquaculture and Fisheries*, pp. 1-12. ISSN:2468-550X, https://doi.org/10.1016/j.aaf.2025.10.002.

Martyniuk, C.J., Li, E. and Rise, M.L., 2025. Editorial: Environmental stressors and aquatic animal immune system function. *Frontier in Immunology*, 16, 1610969. DOI:10.3389/fimmu.2025.1610969. PMID:40666522; PMCID:PMC12259446.

Mkulo, E.M., Iddrisu, L., Yohana, M.A., Zheng, A., Zhong, J., Jin, M., Danso, F., Wang, L., Zhang, H., Tang, B., Zhou, H., Amoah, K., Huang, J., Wang, B. and Wang, Z., 2025. Exploring salinity adaptation in teleost fish, focusing on omics perspectives on osmoregulation and gut microbiota. *Frontiers in Marine Science*, 12, 1559871. DOI:10.3389/fmars.2025.1559871.

Morabito, A., De Simone, G., Pastorelli, R., Brunelli, L. and Ferrario, M., 2025. Algorithms and tools for data-driven omics integration to achieve multilayer biological insights: a narrative review. *Journal of Translational Medicine*, 10, 23(**1**), 425. DOI:10.1186/s12967-025-06446-x. PMID: 40211300; PMCID: PMC11987215.

Naya-Català, F., Belenguer, A., Montero, D., Torrecillas, S., Soriano, B., Calduch-Giner, J., Llorens, C., Fontanillas, R., Sarih, S., Zamorano, M.j., Izqierdo, M and Perez-Sancehz, J., 2023. Broodstock nutritional programming differentially affects the hepatic transcriptome and genome-wide DNA methylome of farmed gilthead sea bream (*Sparus aurata*) depending on genetic background. *BMC Genomics*, 24, 670. https://doi.org/10.1186/s12864-023-09759-7.

Okoli, A.S., Blix, T., Myhr, A.I., Xu, W. and Xu, X., 2022. Sustainable use of CRISPR/Cas in fish aquaculture: the biosafety perspective. *Transgenic Research*, 31(**1**), pp. 1-21. DOI:10.1007/s11248-021-00274-7. PMID:34304349; PMCID:PMC8821480.

Pashay Ahi, E., Lindeza, A.S., Antti Miettinen, A. and Primmer, C.R., 2025. Transcriptional responses to changing environments: insights from salmonids. *Reviews in Fish Biology and Fisheries,* 35, pp. 681-706. DOI:10.1007/s11160-025-09928-9.

Pelletier, M.C., Ebersole, J., Mulvaney, K., Rashleigh, B., Gutierrez, M.N., Chintala, M., Kuhn, A., Molina, M., Bagley, M. and Lane, C., 2020. Resilience of aquatic systems: Review and management implications. *Aquatic Sciences*, 28, 82(**2**), pp. 1-44. DOI:10.1007/s00027-020-00717-z. PMID:32489242; PMCID:PMC7265686.

Rojas, I., de Mello, M.M.M., Zanuzzo, F.S., Sandrelli, R.M., Peroni, E.d.F.C., Hall, J.R., Rise, M.L., Urbinati, E.C. and Gamperl, A.K., 2025. Chronic hypoxia has differential effects on constitutive and antigen-stimulated immune function in Atlantic salmon (*Salmo salar*). *Frontiers in Immunology*, 16, 1545754. DOI:10.3389/fimmu.2025.1545754.

Rubalcaba, J.G., Verberk, W.C.E.P., Hendriks, A.J., Saris, B. and Woods, H.A., 2020. Oxygen limitation may affect the temperature and size dependence of metabolism in aquatic ectotherms. *Proceedings of the National Academy Sciences of the United States of America*, 15, 117(**50**), 31963-31968. DOI:10.1073/pnas.2003292117. PMID: 33257544; PMCID: PMC7749359.

Ruben, M.O., Akinsanola, A.B., Okon, M.E., Shitu, T. and Jagunna, I.I., 2025. Emerging challenges in aquaculture: Current perspectives and human health implications. *Veterinary World*, 18(**1**), 15-28. DOI:10.14202/vetworld.2025.15-28. PMID:40041520; PMCID:PMC11873385.

Sun, X., Chen, Y.L., Xin, F. and Zhang, S., 2024. Transcriptome-wide identification and analysis reveals m6A regulation of metabolic reprogramming in shrimp (*Marsupenaeus japonicus*) under virus infection. *BMC Genomics*, 25, 1103. https://doi.org/10.1186/s12864-024-11032-4.

Vieira, R.S.F., Venâncio, C.A.S. and Félix, L.M., 2025. Behavioral, metabolic, and biochemical alterations caused by an acute stress event in a zebrafish larvae model. *Fish Physiology and Biochemistry*, 51(**1**), 25. DOI:10.1007/s10695-024-01421-7. PMID:39673016; PMCID:PMC11645430.

Villar-Argaiz, M., Medina-Sánchez, J.M., Biddanda, B.A. and Carrillo, P., 2018. Predominant Non-Additive Effects of Multiple Stressors on Autotroph C: N: P Ratios Propagate in Freshwater and Marine Food Webs. *Frontiers in Microbiology*, 9, 69. DOI:10.3389/fmicb.2018.00069.

Wannas, A.K., and Mohammed, S.H., 2025. The role of environmental stress in fish health: A review. *GSC Biological and Pharmaceutical Sciences*, 32(**01**), pp. 17-27.

https://doi.org/10.30574/gscbps.2025.32.2.0304.

Xu, W. and Wang, L., 2022. Editorial: The physiological and molecular response of aquatic animals to environmental stresses. *Frontiers in Physiology*, 25, 13, 987004. DOI:10.3389/fphys.2022.987004. PMID: 36091395; PMCID: PMC9454087.

Yang, S., Li, D., Feng, L., Zhang, C., Xi, D., Liu,H., Yan, C., Xu, Z., Zhang,Y., Li, Y., Yan, T., He, Z., Wu, J., Gong,Q., Huang,X. and Du, X., 2023. Transcriptome analysis reveals the high temperature induced damage is a significant factor affecting the osmotic function of gill tissue in Siberian sturgeon (*Acipenser baerii*). *BMC Genomics,* 24, 2. https://doi.org/10.1186/s12864-022-08969-9.

Yang, Y., Liu, Y., Liu, W., Han, L., Yuan, F., Wang, J., Wu, S., Sun, Y. and Han, S., 2025. Multi-omics-based study on metabolic-physiological response to heat stress in rainbow trout (*Oncorhynchus mykiss*). *Comparative Biochemistry and Physiology Part A: Molecular and Integrative Physiology*, 308, 111903. DOI:10.1016/j.cbpa.2025.111903. PMID:40639437.

Yang, Z., Fu, G., Lee, M., Yeo, S., Yue, G.H., 2025. Genes for editing to improve economic traits in aquaculture fish species, *Aquaculture and Fisheries*, 10, 1, pp. 1-18. ISSN:2468-550X, https://doi.org/10.1016/j.aaf.2024.05.005.

Zhang, Y., Xiang, P., and Fu, S., 2025. The responses of stress tolerance, physiological performance and energy metabolism to acclimation temperature between tropical and temperate fish species. *Frontiers in Marine Science,* 12 https://doi.org/10.3389/fmars.2025.1593656.

Zhu, M., Sumana, S.L., Abdullateef, M.M., Falayi, O.C., Shui, Y., Zhang, C., Zhu, J. and Su, S., 2024. CRISPR/Cas9 Technology for Enhancing Desirable Traits of Fish Species in Aquaculture. *International Journal Molecular Sciences*, 27, 25(**17**), 9299. DOI:10.3390/ijms25179299. PMID:39273247; PMCID:PMC11395652.