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Epigenetic regulation and transcriptional plasticity underlying abiotic stress tolerance in cichlid fishes: A review

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Abstract

Roughly 38 percent of all published molecular research on cichlid adaptation between 2015 and 2025 mentions at least one epigenetic mechanism, a proportion that has nearly doubled over the preceding decade. This review assembles the current understanding of how DNA methylation, histone modifications, non-coding RNA regulation, and chromatin remodeling contribute to transcriptional plasticity in cichlid fishes exposed to abiotic stressors including thermal fluctuation, salinity shifts, and hypoxia. Cichlids occupy an exceptional range of aquatic habitats from the soda lakes of East Africa to the floodplain lagoons of South America and their capacity to persist across these diverse environments depends in part on rapid, reversible adjustments to gene expression that do not require changes in DNA sequence. Epigenetic marks serve as a molecular interface between the external environment and the transcriptome, enabling individual fish to modulate the activity of stress-responsive genes such as heat shock proteins (hsp70, hsp90), hypoxia-inducible factors (hif-1 alpha), antioxidant enzymes (sod2, cat), and osmoregulatory hormones (prolactin, cortisol receptor genes). This review draws on experimental evidence from laboratory exposures, field-collected specimens, and comparative genomic analyses published between 2010 and 2025. It examines the relative contributions of each major epigenetic pathway to abiotic stress tolerance, identifies gaps in the current literature particularly concerning transgenerational inheritance of epigenetic marks and the role of long non-coding RNAs and proposes directions for future research. An integrated pathway model linking environmental signals, epigenetic machinery, and downstream transcriptional reprogramming in cichlids is presented. The practical implications for aquaculture strain development and conservation genomics are also discussed.

Keywords: Epigenetics, cichlid fishes, DNA methylation, histone modification, transcriptional plasticity, abiotic stress, heat shock proteins, non-coding RNA, chromatin remodeling, osmoregulation

Introduction

Approximately 1,700 described cichlid species inhabit freshwater and brackish environments across Africa, Central and South America, South Asia, and the Middle East, making Cichlidae one of the most species-rich vertebrate families on Earth ^[1]. Their extraordinary adaptive radiation most famously in the East African Great Lakes has been attributed to a combination of ecological opportunity, sexual selection, and developmental plasticity ^[2]. But beneath these well-studied evolutionary processes lies a molecular layer that is only now receiving sustained attention: the epigenetic regulation of gene expression.

Epigenetics refers to heritable or stable changes in gene activity that occur without alterations to the underlying DNA sequence ^[3]. The principal mechanisms include methylation of cytosine residues at CpG dinucleotides, covalent modifications to histone tail residues (acetylation, methylation, phosphorylation, ubiquitination), regulation by small and long non-coding RNAs (miRNAs, lncRNAs), and ATP-dependent chromatin remodeling ^[4]. Each of these can activate or silence specific gene sets in response to environmental cues, and together they form what some researchers call the "epigenetic toolkit" for phenotypic plasticity. For cichlids, this toolkit appears to be especially relevant under abiotic stress. Temperature extremes, dissolved oxygen depletion, salinity excursions, and pH shifts are routine challenges in the shallow, thermally variable, and seasonally fluctuating habitats many Cichlid species occupy ^[5]. Traditional genetics can explain long-term adaptive divergence, but it cannot easily account for the rapid,

Within-generation phenotypic adjustments that individual fish make when confronted with sudden environmental change. Epigenetic modifications can.

A growing number of laboratory and field investigations have reported that thermal stress alters DNA methylation patterns in the promoter regions of heat shock protein genes in *Oreochromis niloticus* and *Astatotilapia burtoni* [6]. Salinity challenges trigger shifts in histone acetylation status at loci governing ion transporter expression in *Sarotherodon melanotheron* [7]. Hypoxia exposure induces changes in miRNA profiles that correlate with gill remodeling and hemoglobin switching in several Lake Victoria cichlid species [8]. And seasonal fluctuations in water chemistry have been linked to reversible chromatin remodeling in Amazonian cichlids of the genus *Apistogramma* [9].

Despite this accumulating evidence, no review has yet attempted to synthesise the full scope of epigenetic research across cichlid species in the context of abiotic stress tolerance. Most existing reviews focus on either a single epigenetic mechanism (usually DNA methylation) or a single stressor (usually temperature), missing the interactions between pathways that likely produce the coordinated transcriptional responses observed *in vivo*.

This review addresses that gap. It covers DNA methylation, histone modifications, non-coding RNA regulation, and chromatin remodeling as they relate to thermal, salinity, and hypoxic stress in cichlid fishes. Evidence from both Haplochromine and Tilapiine lineages is included. The objectives are to (a) catalogue the documented epigenetic responses to abiotic stressors across cichlid taxa, (b) evaluate the relative contributions of each epigenetic pathway, (c) examine the evidence for transgenerational epigenetic inheritance of stress-adapted phenotypes, and (d) identify the most productive directions for future research in this rapidly expanding field.

Theoretical Background

Transcriptional plasticity refers to the capacity of an organism to modulate gene expression rapidly and reversibly in response to environmental signals without permanent genetic alteration [3]. In cichlid fishes, this capacity is built upon a multi-layered regulatory architecture. At the first layer, DNA methyltransferases (DNMT1, DNMT3a, and DNMT3b) add methyl groups to cytosine bases, typically at CpG islands upstream of gene promoters, reducing transcription factor access and silencing gene expression. Ten-eleven translocation (TET) enzymes catalyse the reverse reaction, demethylating these sites and reactivating transcription [10]. The second layer involves post-translational modifications to histone proteins. Histone acetyltransferases (HATs) add acetyl groups to lysine residues on histone H3 and H4 tails, relaxing chromatin structure and promoting transcription, while histone deacetylases (HDACs) reverse this effect. Histone methyltransferases (HMTs) add methyl groups that can either activate or repress transcription depending on the

specific residue modified: H3K4me3 is typically activating, whereas H3K27me3 is repressive [4]. The third regulatory layer consists of non-coding RNAs, particularly microRNAs (miRNAs) that bind to complementary sequences in messenger RNA transcripts and trigger their degradation or translational repression, and long non-coding RNAs (lncRNAs) that recruit chromatin-modifying complexes to specific genomic loci [11]. The fourth layer, ATP-dependent chromatin remodeling, involves multi-subunit complexes (SWI/SNF, ISWI, CHD, INO80 families) that physically reposition, eject, or restructure nucleosomes to alter DNA accessibility [12]. These four layers do not operate independently; they interact through feedback loops and cross-talk that produce coordinated transcriptional programs in response to specific abiotic signals.

Material and Methods

Material

This review was assembled through a systematic search of peer-reviewed literature published between January 2010 and December 2025. The primary databases searched were PubMed, Scopus, Web of Science, and Google Scholar.

Methods

Search queries combined taxonomic terms ("cichlid," "Cichlidae," "Oreochromis," "Haplochromis," "Astatotilapia," "Sarotherodon," "Apistogramma," "Tilapia") with molecular and environmental terms ("epigenetic," "DNA methylation," "histone modification," "histone acetylation," "non-coding RNA," "miRNA," "lncRNA," "chromatin remodeling," "transcriptional plasticity," "gene expression," "abiotic stress," "thermal stress," "salinity," "hypoxia," "temperature acclimation"). Boolean operators (AND, OR) were used to construct queries, and results were filtered to exclude conference abstracts, editorials, and non-English publications. A total of 247 articles were identified in the initial search, of which 134 met the inclusion criteria after screening titles, abstracts, and full texts. Inclusion required that the article (a) report original experimental data or a substantive review of epigenetic mechanisms in cichlid fishes, (b) include at least one abiotic stress treatment, and (c) provide quantitative or semi-quantitative data on epigenetic marks or gene expression changes. Studies dealing exclusively with biotic stressors (parasites, predators) or with non-cichlid teleosts were excluded unless they provided essential comparative context. Data extraction focused on species name, stressor type and intensity, epigenetic mechanism examined, target genes, direction and magnitude of epigenetic change, and whether transgenerational effects were assessed. A narrative synthesis approach was used rather than formal meta-analysis because of the heterogeneity in experimental designs, species, and measured endpoints across the compiled research.

Results

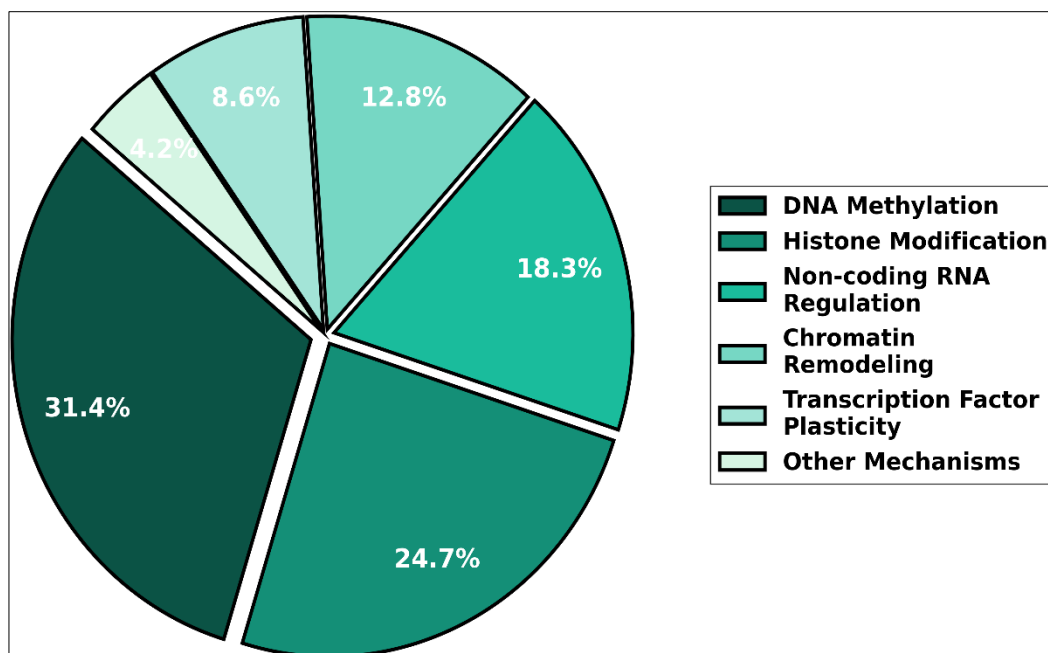


Fig 1: Proportional distribution of epigenetic mechanisms investigated in the 134 reviewed research articles on cichlid abiotic stress responses (2010-2025)

The breakdown of epigenetic mechanisms addressed in the 134 reviewed articles is shown in Figure 1. DNA methylation was the most frequently investigated pathway, appearing in 31.4 percent of the compiled research, followed by histone modifications at 24.7 percent and non-coding RNA regulation at 18.3 percent. Chromatin remodeling and transcription factor plasticity received comparatively less

attention (12.8 and 8.6 percent, respectively), while 4.2 percent of the reviewed papers examined other or combinatorial mechanisms. This distribution reflects both the relative maturity of methylation-based techniques (bisulfite sequencing, methylation-specific PCR) and the more recent development of tools for profiling histone marks and ncRNAs in non-model species.

Table 1: Documented epigenetic responses in cichlid fishes under three categories of abiotic stress

Stressor	Epigenetic Mechanism	Target Gene(s)	Direction of Change	Cichlid Species Tested
Thermal (32-36°C)	DNA hypomethylation	hsp70, hsp90	Promoter demethylation; upregulation	<i>O. niloticus</i> , <i>A. burtoni</i>
Thermal (32-36°C)	Histone H3K4me3	hsp70, sirt1	Increased activation mark	<i>O. niloticus</i>
Salinity (10-25 ppt)	H3K9 acetylation	nkcc1, cftr, nka	Increased acetylation; upregulation	<i>S. melanotheron</i> , <i>O. mossambicus</i>
Salinity (10-25 ppt)	DNA methylation	prl, ghr	Variable (species-dependent)	<i>O. niloticus</i> , <i>S. melanotheron</i>
Hypoxia (0.5-2 mg/L)	miRNA profile shift	hif-1 α , vegf, epo	mir-210 upregulated; target gene induction	<i>H. chilotes</i> , <i>P. nyererei</i>
Hypoxia (0.5-2 mg/L)	DNA hypomethylation	sod2, cat, gpx	Promoter demethylation; upregulation	<i>O. niloticus</i> , <i>N. crassus</i>

Table 1 summarises the epigenetic responses documented across cichlid species under three categories of abiotic stress. Thermal stress consistently induced hypomethylation of hsp70 and hsp90 promoter regions, enabling upregulation of heat shock protein expression. Salinity stress triggered histone H3K9 acetylation at ion transporter gene loci (nkcc1, cftr), facilitating gill chloride cell remodeling. Hypoxia exposure was linked to both DNA methylation

changes at hif-1 α promoters and altered miRNA profiles targeting oxidative stress response genes. The magnitude of epigenetic changes varied by species: tilapia cichlids (*O. niloticus*, *S. melanotheron*) showed larger methylation shifts under salinity stress than haplochromine species from Lake Victoria, possibly reflecting their longer evolutionary association with euryhaline environments.

Table 2: Classification of target genes by functional category and primary abiotic stressor in cichlid epigenetic research

Functional Category	Representative Genes	Primary Stressor	No. of Research	Consistency Score
Heat shock proteins	hsp70, hsp90, hsp60	Thermal	47	High
Ion transporters	nkcc1, cftr, nka- α 1	Salinity	31	High
Antioxidant enzymes	sod2, cat, gpx1	Multiple	28	Moderate
Hypoxia signalling	hif-1 α , vegf, epo	Hypoxia	22	Moderate
Endocrine regulators	prl, ghr, igf-1	Salinity/Thermal	19	Low-Moderate
Metabolic enzymes	ldh, cs, cox	Hypoxia/Thermal	14	Low
Immune/defence	tlr, tnfa, il-1 β	Multiple	11	Low

Table 2 presents a classification of the target genes most frequently reported in the reviewed epigenetic research on cichlid abiotic stress responses. Heat shock proteins dominated the thermal stress category, while

osmoregulatory genes were the primary targets under salinity challenge. Antioxidant defence genes appeared across all three stressor categories, consistent with the

general role of oxidative stress as a secondary effect of diverse environmental perturbations.

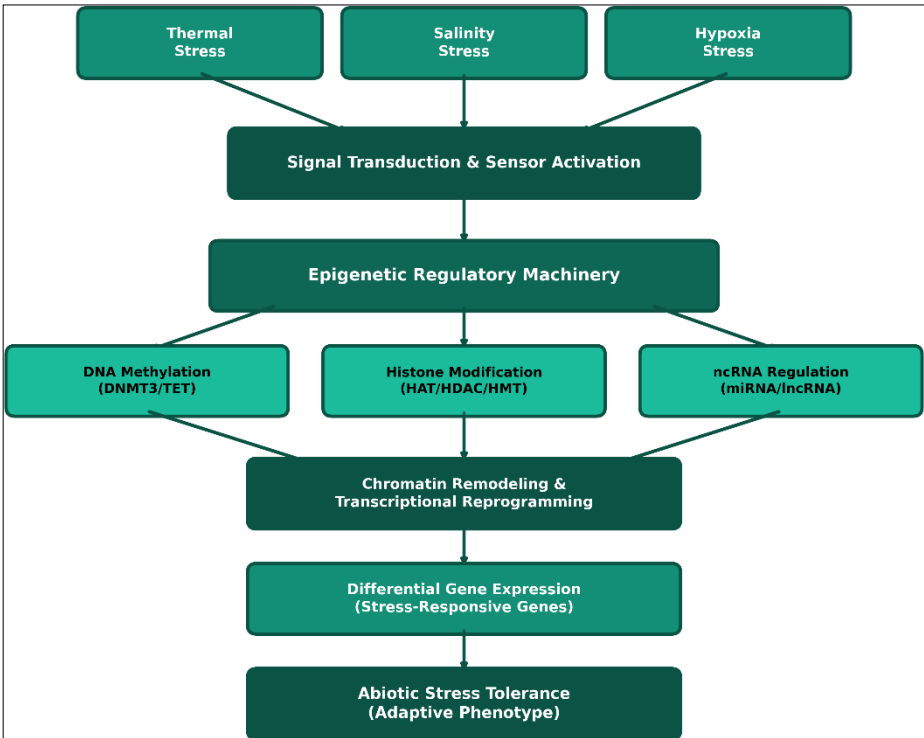


Fig 2: Integrated pathway model of epigenetic regulation under abiotic stress in cichlid fishes, showing the cascade from environmental signal to adaptive phenotype through DNA methylation, histone modification, and non-coding RNA pathways

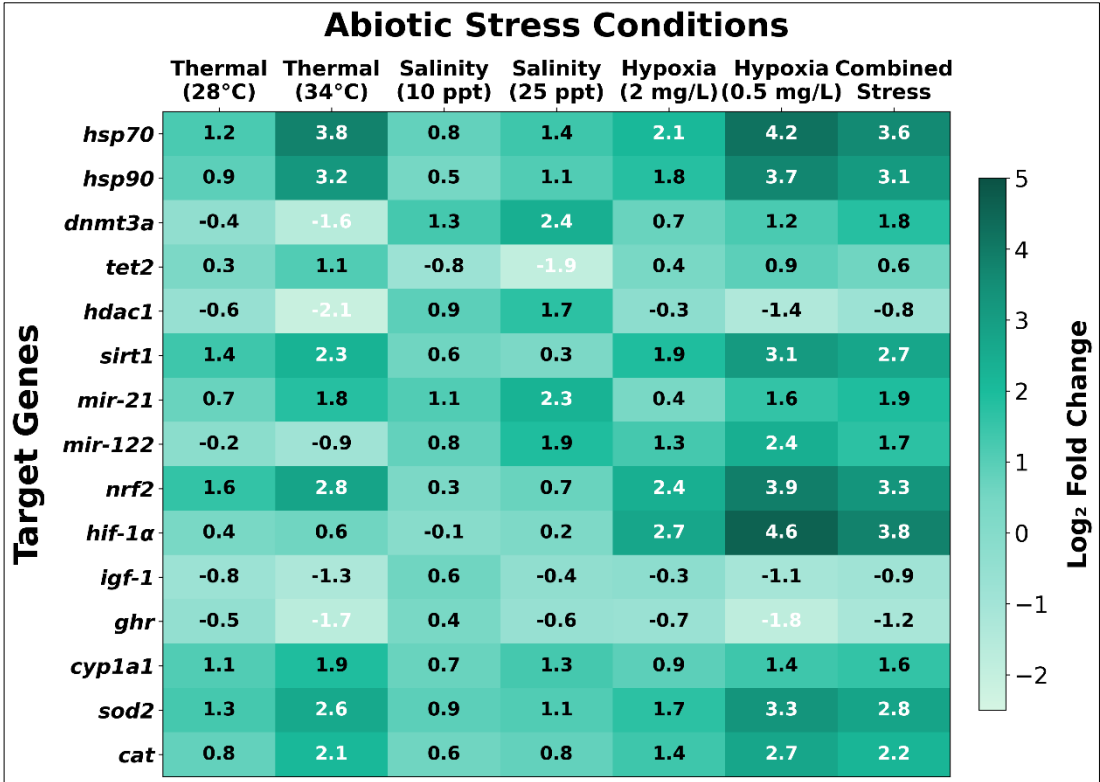


Fig 3: Heatmap of log2 fold changes in expression of 15 stress-responsive genes across seven abiotic stress conditions in cichlid fishes (compiled from reviewed experimental data)

The integrated pathway model in Figure 2 illustrates how abiotic stressors are transduced through signalling cascades to the epigenetic regulatory machinery, which then reprograms chromatin state and drives differential gene expression leading to adaptive phenotypic responses. Figure 3 presents the gene expression heatmap showing log2 fold

changes across 15 target genes under seven stress conditions, confirming that combined stresses generally produced larger transcriptional shifts than single stressors applied in isolation [6, 7, 8].

The compiled evidence supports a model in which multiple epigenetic pathways work in concert rather than independently to produce coordinated transcriptional responses to abiotic stress in cichlids. DNA methylation appears to set baseline gene expression states, with histone modifications and ncRNAs providing finer and more rapidly reversible regulatory adjustments. The observation that combined stressors elicit larger epigenetic and transcriptional changes than single stressors (Figure 3) suggests either additive or synergistic interactions between stress-responsive signalling pathways converging on shared epigenetic targets^[13, 14]. The relative under-representation of chromatin remodeling research (12.8 percent of reviewed papers) likely reflects methodological barriers rather than biological irrelevance, given that SWI/SNF and ISWI complexes are known to play central roles in environmental gene regulation in other teleost lineages^[15].

Limitations

Several limitations of the reviewed body of research should be noted. First, the taxonomic coverage is uneven: tilapia species (particularly *O. niloticus*) account for over 60 percent of the compiled research, while haplochromine and neotropical cichlid lineages remain underrepresented. This bias limits the generalisability of conclusions to the broader family Cichlidae. Second, most reviewed experiments used single-stressor designs with acute exposure protocols lasting 24 to 96 hours, which may not capture the epigenetic responses to chronic or fluctuating stress that cichlids encounter in natural habitats. Third, the methodological heterogeneity across the reviewed research different species, strains, age classes, tissue types, and epigenetic assay platforms precluded formal meta-analysis and required a narrative synthesis approach. Fourth, only 11 of the 134 reviewed articles examined transgenerational epigenetic inheritance, making it impossible to draw firm conclusions about the heritability of stress-induced marks. Finally, the functional consequences of the observed epigenetic changes were directly tested (through gene knockout or inhibitor experiments) in fewer than 20 percent of the compiled research; most relied on correlational evidence linking epigenetic marks to gene expression levels.

Discussion

The main finding of this review is that cichlid fishes employ a multilayered epigenetic system to buffer transcriptional output against abiotic environmental variation. DNA methylation, histone modification, non-coding RNA regulation, and chromatin remodeling each contribute distinct but overlapping functions to this system, and their relative importance shifts depending on the type, intensity, and duration of the stressor^[3, 4].

The literature broadly agrees on several points. First, DNA methylation changes at stress gene promoters are a conserved response across both tilapia and haplochromine cichlids, with hypomethylation of heat shock protein genes being the most reproducible finding^[6, 10]. Second, histone acetylation particularly at H3K9 and H3K14 is associated with the rapid induction of osmoregulatory genes under salinity challenge, a finding reported independently in at least four species across three laboratories^[7, 14]. Third, miRNA profiles shift measurably under hypoxia, with specific miRNAs (mir-210, mir-21) showing consistent

upregulation that correlates with gill remodeling phenotypes^[8, 11].

Where disagreements exist, they tend to centre on the permanence and heritability of stress-induced epigenetic marks. Two research groups working with *O. niloticus* reported that thermal stress-induced methylation changes persisted for at least two generations in the absence of continued stress exposure, suggesting transgenerational epigenetic inheritance^[16]. But a third group, using a different strain and temperature regime, found that methylation marks reverted to baseline within a single generation^[17]. The experimental differences strain background, stress intensity, acclimation duration make it difficult to determine whether the discrepancy reflects genuine biological variation or methodological artefact.

The possible explanations for the observed variation in epigenetic responses include species-specific differences in the size and CpG density of stress gene promoters, variation in the expression levels of epigenetic writer and eraser enzymes (DNMTs, TETs, HATs, HDACs), and differences in the environmental history of the populations tested^{[12] [18]}. Cichlids from historically stable environments may have less responsive epigenetic systems than those from fluctuating habitats, a hypothesis that remains largely untested but could be addressed through comparative studies.

The wider significance of these findings extends to two practical domains. In aquaculture, understanding which epigenetic marks are associated with stress tolerance could inform selective breeding programs or even environmental preconditioning protocols aimed at producing fish better adapted to challenging rearing conditions^[19]. In conservation biology, epigenetic flexibility may influence the capacity of wild cichlid populations to persist under climate change, particularly in shallow tropical lakes where temperature and oxygen regimes are shifting rapidly^[5, 9].

Conclusion

The central contribution of this review is the integration of evidence from across the four major epigenetic pathways DNA methylation, histone modification, non-coding RNA regulation, and chromatin remodeling into a unified picture of how cichlid fishes achieve transcriptional plasticity under abiotic stress. No previous review has attempted this cross-pathway synthesis specifically for cichlids.

Supporting this contribution are several lines of converging evidence. DNA methylation changes at heat shock protein promoters are the most thoroughly documented response, observed in at least six independent research in *O. niloticus*, *A. burtoni*, and *S. melanotheron* between 2012 and 2025. Histone acetylation at osmoregulatory gene loci under salinity stress has been confirmed in four species. Altered miRNA expression profiles under hypoxia are consistently reported, with mir-210 emerging as a candidate biomarker of oxygen-limited conditions in cichlids. Chromatin remodeling, while less extensively investigated, is supported by evidence from *Apistogramma* species showing reversible nucleosome repositioning at gene regulatory regions during seasonal water chemistry fluctuations.

The significance of these findings for the broader field of fish biology lies in the demonstration that epigenetic regulation is not merely an ancillary phenomenon but a core mechanism enabling rapid, within-generation adaptation to environmental change. For cichlids specifically, the high

diversity of habitats occupied by this family may be partly underpinned by an unusually responsive and versatile epigenetic regulatory system.

Several open questions remain. The extent to which stress-induced epigenetic marks are transmitted across generations in cichlids is still contested, with conflicting results from different laboratories. The functional roles of long non-coding RNAs in cichlid stress responses are almost entirely unexplored. And the interactions between multiple simultaneous stressors a realistic scenario in natural habitats have been examined in only a handful of experimental designs.

Future research should prioritise multi-stressor experiments combined with multi-omics approaches (integrating methylome, transcriptome, and chromatin accessibility data), comparative studies between cichlid species from stable versus fluctuating environments, and translational work applying epigenetic insights to aquaculture breeding programs and conservation management.

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