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Genomic Insights into Hypoxia Tolerance Mechanisms in *Channa* spp.

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Abstract The study summarizes the current genomic results on how Channa fish adapt to hypoxia. We performed high-quality genome assembly and transcriptome analysis on *Channa asiatica*. The results showed that it has more gene families related to oxygen binding and transport. When it is exposed to air, many pathways related to oxidative stress are activated. This shows that it has the genetic ability to adapt to hypoxia and also reveals some of the molecular mechanisms. We also studied gene expression in the liver of *Channa striatus* under long-term hypoxia. We found that many genes involved in transcription, translation, signal transduction, electron transport and immune response were activated. Several transcripts related to hypoxia tolerance were also identified, such as heat shock protein 90 and fatty acid binding protein, and we also obtained their complete sequences. These research results provide important genomic and transcriptome resources, which will help us to better understand how Channa fish adapt to low oxygen environments. At the same time, it also lays a foundation for future research on hypoxia tolerance breeding and ecological adaptation.

Keywords Channa genus; Hypoxia tolerance; Genomics; Transcriptome; Molecular mechanism

1 Introduction

Snakehead (*Channa genus*) is an important freshwater fish. Snakehead has high economic value, a wide distribution range, and can adapt to various harsh environments, so many ecological people and fish farmers have always paid attention to them. Especially in Southeast Asia and South Asia, snakehead is not only a common ingredient on people's tables, but also an important role in maintaining the ecological balance in water. One of the biggest characteristics of snakehead is its strong tolerance to hypoxia. They can survive in water with extremely low oxygen content. This is very interesting to scientists because they want to know how snakehead survives in such conditions. From this perspective, studying snakehead helps us understand the mechanism of fish adaptation to the environment, and it is also of reference value for improving artificial breeding methods and coping with problems such as hypoxia in water bodies. Such research is even more important today as global climate change intensifies and water quality deteriorates.

In recent years, with the advancement of genomic and transcriptomic technologies, scientists can study the hypoxia tolerance mechanism of Channa in more depth. For example, the genome assembly and analysis of *Channa asiatica* found that some gene families related to oxygen transport in its body have increased. In hypoxic environments, their cells also activate many pathways related to antioxidants. Another example is the study on *Channa striatus*. Researchers analyzed its liver gene expression under long-term hypoxic conditions. They found that many genes related to gene expression regulation, signal transduction, energy metabolism and immune response had significant changes. This shows that this fish can adapt to hypoxia through a series of gene regulation.

This study summarizes the current research results on the hypoxia tolerance mechanism of snakehead carp. We hope to have a clearer understanding of how snakehead carp survive in hypoxic environments from the genetic and molecular levels. At the same time, we explore the role of these research results in ecological protection and aquaculture. By collating and analyzing the latest sequencing data and functional gene information, we hope that this article can provide some help for subsequent research and practical applications.

2 Hypoxia in Aquatic Ecosystems

2.1 Definition and types of hypoxia (acute vs chronic, diel cycles)

Hypoxia refers to the lack of oxygen in the water, which affects the respiration of organisms. Generally, when the dissolved oxygen concentration is lower than 2 mg/L, it is considered to be an oxygen-deficient state (Díaz, 2001; Wu, 2002; Vaquer-Sunyer and Duarte, 2008; Conley et al., 2009). According to the time when hypoxia occurs and the duration of hypoxia, it can be divided into three main types: acute, chronic and diurnal (Wu, 2002; Conley et al., 2009; Friedrich et al., 2013; Fennel and Testa, 2019; Roman et al., 2019). Acute hypoxia is sudden and usually lasts only a few hours to a few days. It is easy to occur when a storm or a large amount of organic matter suddenly enters the water (Friedrich et al., 2013; Dugener et al., 2023). Chronic hypoxia lasts for a long time, sometimes for weeks, months or even longer, and is common in lakes, estuaries or bays that are easily polluted (Wu, 2002; Conley et al., 2009; Jenny et al., 2016). There is also a diurnal periodic hypoxia. It is characterized by more oxygen in the water during the day and less oxygen at night. This is because plants photosynthesize more during the day, and plant and animal respiration dominates at night, consuming oxygen. This situation is more common in shallow lakes, wetlands and small rivers (Friedrich et al., 2013; Gobler and Baumann, 2016; Roman et al., 2019; Carter et al., 2021).

2.2 Natural and anthropogenic drivers of hypoxia in freshwater systems

The causes of freshwater hypoxia can be divided into two categories: natural and anthropogenic. Natural causes include water stratification (such as thermal stratification or salt stratification), slow water flow, too much naturally fallen leaves or plant and animal debris, and rising temperatures (Grantham et al., 2004; Conley et al., 2009; Rabalais et al., 2010; Friedrich et al., 2013; Fennel and Testa, 2019; Dugener et al., 2023; Chen et al., 2024). There are even more anthropogenic factors. For example, nitrogen and phosphorus from fertilizers in farmland enter the water, sewage from factories and domestic use, and pollution caused by urban expansion can all cause water bodies to become eutrophic (Díaz, 2001; Conley et al., 2009; Rabalais et al., 2010; Díaz and Rosenberg, 2011; Jenny et al., 2016; Lu et al., 2018). Eutrophication can cause algae to grow in large quantities. When the algae die, they consume a lot of oxygen during the decomposition process, leading to hypoxia (Conley et al., 2009; Rabalais et al., 2010; Jenny et al., 2016). Global warming will make water stratification more obvious, reduce oxygen exchange between bottom water and air, and make hypoxia more serious (Grantham et al., 2004; Rabalais et al., 2010; Ni et al., 2019; Chen et al., 2024). Extreme weather will also have an impact. For example, heavy rains or droughts will change the law of water flow, thereby affecting the distribution of oxygen (Ziegler et al., 2021; Dugener et al., 2023; Chen et al., 2024).

2.3 Biological consequences of hypoxia in fish

Hypoxia has a great impact on fish, including physiological reactions, behavioral changes, growth and development, and the entire population structure. In terms of physiology, fish will breathe faster, their heart rate will change, their hemoglobin will increase, and their metabolism will decrease when they are hypoxic. If the situation is serious, they may even enter an anaerobic metabolic state (Burnett, 1997; Wu, 2002; Wu et al., 2003; Abdel-Tawwab et al., 2019; Roman et al., 2019). Behaviorally, fish may swim to areas with high oxygen content, reduce activity, eat less, or even escape from hypoxic waters (Wu, 2002; Ekau et al., 2009; Brandt et al., 2023; Luczkovich et al., 2024).

Fish at different developmental stages also respond differently to hypoxia. Embryos and small fish are usually more susceptible to the effects, such as slow growth, deformities, and even increased mortality (Wu, 2002; Wu et al., 2003; Abdel-Tawwab et al., 2019). Long-term or repeated hypoxia can also affect fish reproduction, such as hormone disorders, weakened immunity, and a significant decrease in population size (Wu, 2002; Wu et al., 2003; Abdel-Tawwab et al., 2019; Zhan et al., 2023). From an ecological perspective, hypoxia can change the composition of fish populations. Some fish that are more tolerant to hypoxia will become more numerous, while those that are intolerant may decrease or even disappear (Wu, 2002; Vaquer-Sunyer and Duarte, 2008; Ekau et al., 2009; Levin et al., 2009).

2.4 Comparison with other teleost fish responses

Different species of bony fish respond very differently to hypoxia. Most bony fish breathe through gills and have a high oxygen demand, so they are very sensitive to hypoxia (Wu, 2002; Vaquer-Sunyer and Duarte, 2008; Ekau et al., 2009; Abdel-Tawwab et al., 2019). The Channa genus (such as the black snakehead) is special because they have evolved special respiratory organs to help them survive in hypoxic environments (Wu, 2002; Zhan et al., 2023). At the molecular level, most fish have HIF signaling pathways that help fish regulate their bodies in low-oxygen environments. However, HIF gene expression, regulation, and metabolic strategies are not exactly the same in different fish (Wu, 2002; Nie et al., 2019; Lee et al., 2023; Zhan et al., 2023). Some fish also adapt to low oxygen environments by changing their behavior (such as swimming away from hypoxic waters) or making physiological adjustments (regulating the type of hemoglobin, etc.) (Burnett, 1997; Wu, 2002; Ekau et al., 2009; Roman et al., 2019; Brandt et al., 2023; Zhan et al., 2023).

3 Overview of Channa spp. and Their Hypoxia Tolerance

3.1 Taxonomy and distribution of key Channa species

Channa, also known as snakehead fish, belongs to the Channa family and is a freshwater fish that can breathe using air. Channa fish are mainly found in South Asia, Southeast Asia, and southern China. There are several representative species, such as *Channa striata*, *Channa marulius*, and *Channa asiatica*. *C. striata* and *C. marulius* are the most widely distributed and valuable fish. *C. striata* is commonly found in ponds, rice fields, and swamps in India, Bangladesh, Southeast Asia, and southern China. *C. marulius* mainly lives in rivers and lakes in the Indian subcontinent and Southeast Asia (Mohapatra et al., 2017; Zhou et al., 2024). These fish have a strong ability to adapt to the environment and can survive in places where the oxygen content in the water varies greatly.

3.2 Behavioral and physiological adaptations

Fish of the genus Channa are famous for their ability to survive in low-oxygen environments. They have specialized auxiliary respiratory organs, such as swim bladders or suprabranchial organs, that help them breathe air directly. When there is too little oxygen in the water, they will swim to the surface, inhale through their mouths, and then exchange gases with their suprabranchial organs, so that they can maintain the oxygen needed by the body (Mohapatra et al., 2013; Zhou et al., 2024) (Figure 1). Fish like *C. striata* will burrow into the mud to "hibernate" when there is extreme lack of oxygen or drought, slowing down the body's metabolic rate and thus reducing energy and oxygen consumption (Mohapatra et al., 2013). At the molecular level, studies have found that they will activate some "antioxidant response pathways" when they are hypoxic, such as increasing the expression of genes such as heat shock protein (hsp90β) and lactate dehydrogenase. These changes can help cells better cope with hypoxia (Mohapatra et al., 2013; 2017; Zhou et al., 2024).

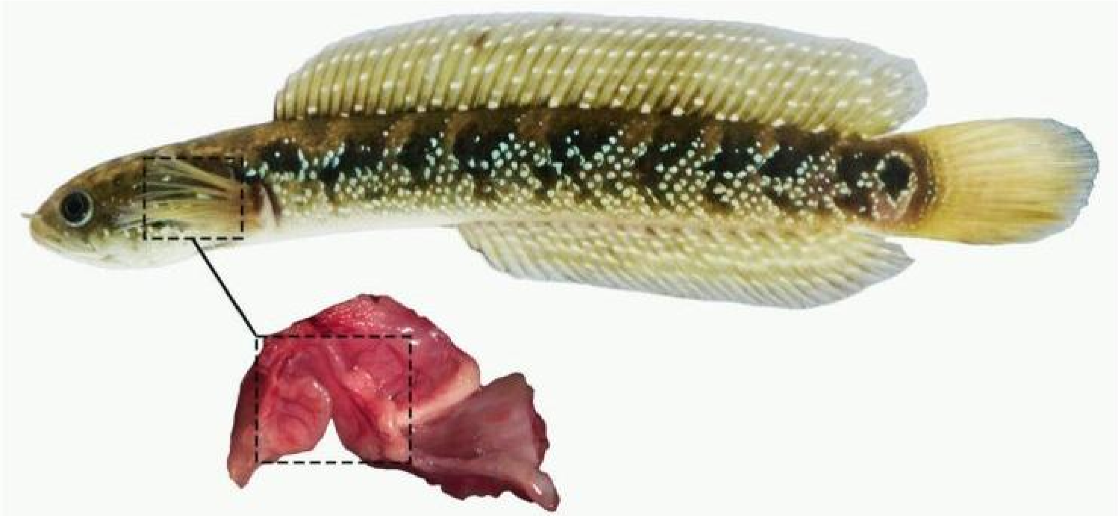

Figure 1 A typical photograph of *C. asiatica*. The picture in the box shows the suprabranchial organ (Adopted from Zhou et al., 2024)

3.3 Ecological niches and survival strategies under hypoxic conditions

Channa fish play a special role in the ecosystem. Because they can survive in water with extremely low oxygen content, Channa fish have an advantage over other fish in terms of survival. In addition to relying on air breathing to adapt to low oxygen, Channa fish also adjust their behavioral habits (such as moving less or burrowing into the mud to hibernate) and change their metabolic methods (such as stronger anaerobic metabolism) to cope with sudden or long-term hypoxia (Mohapatra et al., 2013; 2017). Zhou et al. (2024) studied the genome and transcriptome of this fish and found that fish such as *C. asiatica* have added many genes related to oxygen transport during evolution. Under hypoxic conditions, they also activate many antioxidant and stress response pathways. These mechanisms provide a stable genetic basis for their "anti-hypoxia" ability.

4 Genomic Resources for Channa spp.

4.1 Current genomic databases and sequencing efforts

In recent years, great progress has been made in the genome research of Channa fish. The research content includes whole genome sequencing, transcriptome sequencing, and mitochondrial genome sequencing. Now many species have completed high-quality genome assembly, such as *Channa argus*, *Channa asiatica*, *Channa maculata*, and *Channa striata*. These genomes use a combination of multiple sequencing technologies, such as PacBio, Hi-C, Nanopore, and Illumina, which can make the genome assembly more complete and accurate (Ou et al., 2021; Zhou et al., 2022; Dai et al., 2024; Sun et al., 2024; Zhou et al., 2024). The genome size of C. argus is 712.14 Mb, the scaffold N50 reaches 28.08 Mb, and the BUSCO completeness is also very high, with 98.6%. It also annotated 21 643 protein-coding genes (Sun et al., 2024). The assembly of *C. asiatica* is also of high quality, with a genome size of 722 Mb and 23 chromosomes. It is also combined with transcriptome data to find many genes related to hypoxia tolerance (Zhou et al., 2024). Transcriptome sequencing has also been used in many aspects, such as studying the respiratory organs, immune response, sex determination, body color changes, etc. of fish, which has greatly enriched the genetic information resources of the Channa genus (Jiang et al., 2016; Chen et al., 2018; Sun et al., 2023; Chen et al., 2024; Jin et al., 2025). Mitochondrial genomes have also been sequenced a lot, covering more than a dozen Channa species. These data are very helpful for species classification, kinship and population genetics studies (Liu et al., 2020; Meng and Zhang, 2016; Li et al., 2018; Zhu et al., 2018; Alam et al., 2019; Chandhini et al., 2019; He et al., 2019; Wang et al., 2023; Xu et al., 2024).

4.2 Quality and completeness of available genome assemblies

The quality of the genomes of Channa fish is now much better than before. For example, the latest assembly of C. argus used PacBio HiFi and Hi-C technology, with a scaffold N50 of 28.08 Mb and a BUSCO completeness of 98.6%, which is much better than the results of the early Illumina technology (when contig N50 was only 81.4 kb and scaffold N50 was 4.5 Mb) (Xu et al., 2017; Zhou et al., 2022; Dai et al., 2024; Sun et al., 2024). The genome assemblies of *C. maculata* and *C. asiatica* have also reached the chromosome level, with their contig N50 and scaffold N50 exceeding 10 Mb, and BUSCO completeness is generally above 96% (Ou et al., 2021; Zhou et al., 2022; Zhou et al., 2024). Some studies have also evaluated the annotation completeness, repetitive sequence ratio, gene family expansion and other aspects of these genomes, and the results show that these genomes have high research value (Ou et al., 2021; Zhou et al., 2022; Dai et al., 2024; Sun et al., 2024; Zhou et al., 2024). Some early assembly versions, especially those using only short-read technology, still have some problems, such as poor continuity and incomplete annotation (Jiang et al., 2016; Xu et al., 2017; Liu et al., 2020). The quality of the mitochondrial genome is also very good and the annotations are also very complete, which provides very reliable data support for subsequent evolutionary and population studies (Meng and Zhang, 2016; Li et al., 2018; Zhu et al., 2018; Alam et al., 2019; Chandhini et al., 2019; He et al., 2019; Liu et al., 2020; Wang et al., 2023; Xu et al., 2024).

4.3 Comparative genomic insights across Channa and other air-breathing fish

Channa fish are fish that can breathe air, and their genomic data provide new clues to the question of "how fish adapt to low oxygen". Studies on C. asiatica have found that some of its gene families responsible for oxygen binding and transport have increased, and multiple antioxidant pathways are activated in low-oxygen environments (Zhou et al., 2024). The genome of *C. argus* has also been compared with other air-breathing fishes, such as climbing perch (*Anabas testudineus*), catfish (*Clarias magur*), and loach (*Misgurnus anguillicaudatus*). These comparisons revealed key differences, such as differences in respiratory organ development, gas exchange efficiency, and ion transport functional genes (Jiang et al., 2016; Luo et al., 2016; Sun et al., 2024; Zhou et al., 2024). Channa and other hypoxia-tolerant fishes also have many differences in chromosome structure, gene family expansion, and positive selection genes, which indicates that they have different adaptive strategies in the face of hypoxia (Luo et al., 2016; Ou et al., 2021; Prazdnikov, 2023; Sun et al., 2024; Zhou et al., 2024). Comparative studies of mitochondrial genomes have also found that there are many differences in evolutionary relationships and genetic characteristics between different Channa species and between them and other air-breathing fish (Meng and Zhang, 2016; Li et al., 2018; Zhu et al., 2018; Alam et al., 2019; Chandhini et al., 2019; He et al., 2019; Liu et al., 2020; Wang et al., 2023; Xu et al., 2024).

5 Key Gene Families Involved in Hypoxia Response

5.1 HIF (Hypoxia-Inducible Factor) pathway genes

The HIF pathway is one of the most important mechanisms for fish to cope with hypoxic environments, and the HIF pathway also plays a key role in Channa fish. Zhou et al. (2024) studied the genome and transcriptome of C. asiatica and found that in hypoxic environments, the number of gene families related to oxygen binding and transport in their bodies increased, which shows that the related genes in the HIF pathway play an important role in adapting to low oxygen environments. The study also found that when Channa fish are exposed to air or low oxygen environments, the HIF pathway will activate a series of antioxidant-related signaling pathways, further proving the core position and role of the HIF pathway in fish tolerance to hypoxia.

5.2 Heat Shock Proteins (HSPs) and oxidative stress response genes

When Channa fish face hypoxia, the expression of heat shock protein (HSP90) and some antioxidant genes will increase significantly. Mohapatra et al. (2017) found the complete cDNA sequence of HSP90 when studying the liver of *C. striatus* and confirmed that its content was significantly upregulated under hypoxic conditions. HSP90 can help cells process damaged proteins and protect cells from damage. In addition to HSPs, some antioxidant genes such as fatty acid binding protein (FABP) will also be activated. These genes can help cells maintain their normal state and fight oxidative stress together.

5.3 Metabolic reprogramming genes

In a hypoxic environment, Channa fish will maintain energy supply by adjusting their own metabolism. This adjustment is also called "metabolic reprogramming". In the absence of oxygen, genes such as glycolytic enzymes and lactate dehydrogenase will be activated, helping fish to obtain energy through anaerobic metabolism instead of relying solely on oxygen for breathing (Mohapatra et al., 2017; Zhou et al., 2024). This change allows Channa fish to survive in an environment with low oxygen.

5.4 Ion transport and osmoregulation genes

In addition to metabolic changes, ion transport and osmotic pressure regulation are also critical. The latest whole-genome study found that in the respiratory organs such as the gills and suprabranchial organs of Channa fish, some MAPK pathway genes (such as mapk8, mapk12 and mapk14) will undergo significant changes in hypoxia (Sun et al., 2024). These genes are not only involved in how cells respond to stress, but also help regulate ion concentrations and balance water in the body to maintain the normal state of the body.

5.5 Functional annotations and expression profiles under hypoxic stress

Through high-quality genome and transcriptome analysis, researchers have made detailed functional annotations for many hypoxia-related genes in Channa fish. In the genome of *C. asiatica*, about 96.6% of protein-coding genes have been clearly annotated. These genes are involved in many important functions, such as oxygen transport, antioxidant response, metabolic regulation and ion regulation (Zhou et al., 2024). Under hypoxic conditions, these genes are activated together to form a complex molecular response network, helping fish to better adapt to low oxygen environments (Mohapatra et al., 2017; Sun et al., 2024; Zhou et al., 2024).

6 Transcriptomic and Epigenetic Modulations

6.1 Differential gene expression under normoxia vs hypoxia (RNA-seq data)

In recent years, with the development of high-throughput sequencing technology, scientists have made great progress in the study of gene expression in Channa fish under hypoxia. Taking *Channa asiatica* as an example, genome and transcriptome analysis found that the number of genes responsible for oxygen transport in this fish has increased. When it is exposed to air, that is, in a hypoxic environment, multiple antioxidant pathways in the body will be activated (Zhou et al., 2024) (Figure 2). In the study of *Channa striatus*, scientists used suppression subtractive hybridization (SSH) and EST sequencing technology to find 130 transcripts in its liver that were significantly increased in hypoxia. These genes are related to processes such as transcription, translation, signal transduction, energy conversion, and immune response. Genes such as heat shock protein 90 (HSP90), prefoldin, and fatty acid binding protein have significantly increased expression in hypoxic environments. This suggests that they may be important for fish's tolerance to hypoxia (Mohapatra et al., 2017).

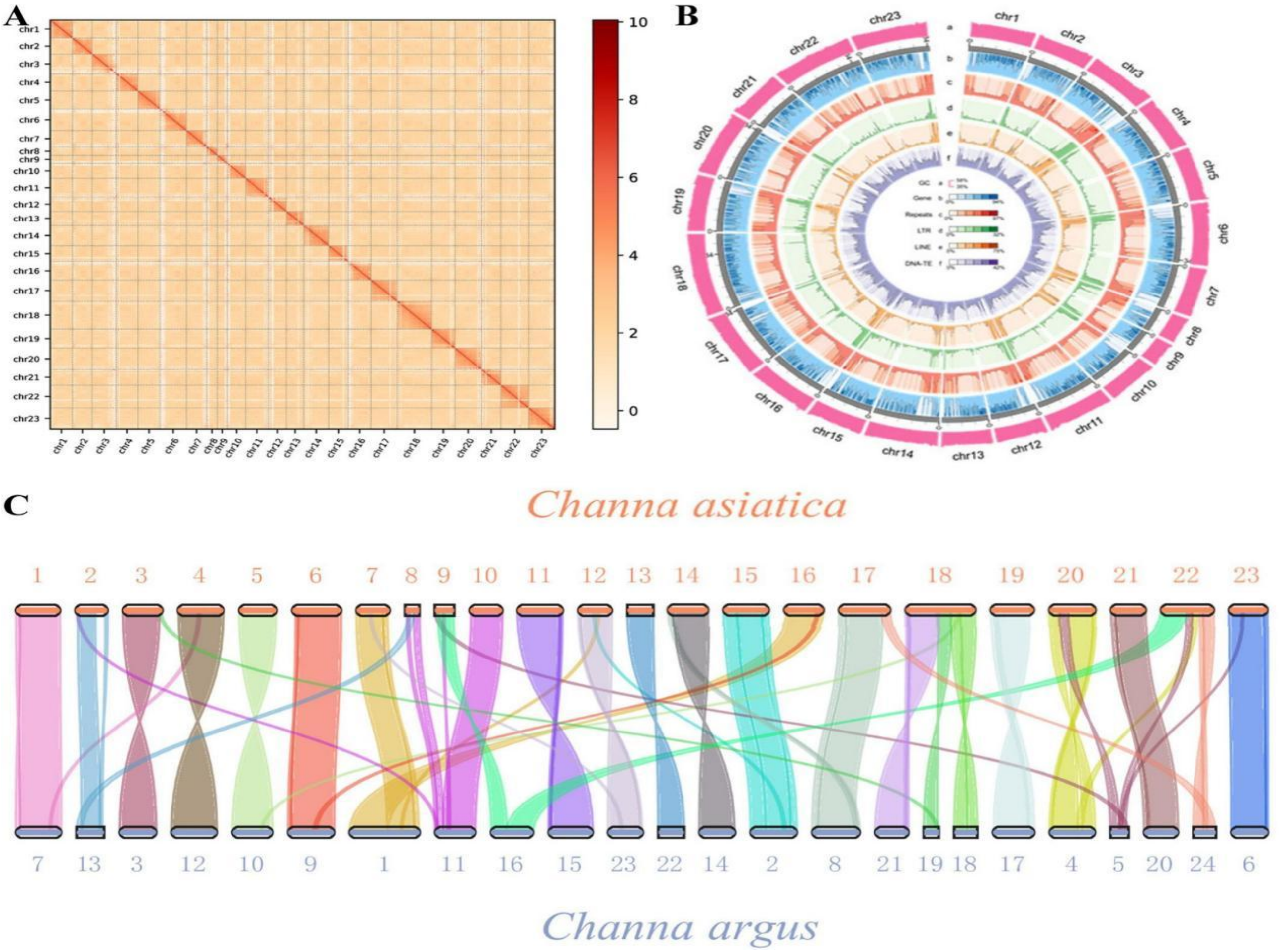

Figure 2 Genome assembly and gene annotation of *C. asiatica*. (A) A heatmap of chromosomal interactions in *C. asiatica*. The blocks represent the 23 pseudochromosomes. The colour bar illuminates the contact density from yellow (low) to red (high). (B) Circos plot of distribution of the genomic elements in *C. asiatica* from the outer circle to the inner circle: (a) GC content of the genome; (b) gene distribution; (c) tandem repeats (TRPs); (d) long terminal repeats (LTRs); (e) long interspersed nuclear elements (LINEs); (f) short interspersed nuclear elements (SINEs). (C) Synteny between genomes of *C. asiatica* and *C. argus*. The number in the figure represents the chromosome identity for each species (Adopted from Zhou et al., 2024)

6.2 Epigenetic changes

Although there are not many epigenetic studies on Channa fish, there is some evidence that regulatory methods such as DNA methylation and histone modification also affect hypoxia response. Some whole-genome methylation analyses found that under hypoxic conditions, methylation changes occurred in the promoter regions of some genes that control energy metabolism and oxygen transport. This change affects gene expression.

Acetylation and demethylation modifications on histones may also affect whether these genes are "on" or "off". In this way, cells can regulate how they respond to hypoxia.

6.3 miRNA and long non-coding RNA roles in hypoxia regulation

In addition to protein-coding genes, non-coding RNA is also involved in the hypoxia response of Channa fish. Among them, miRNA and lncRNA are the two most studied. miRNA can directly affect the stability and translation of hypoxia-related mRNA. In other words, they can control whether certain genes should be expressed and how much they should be expressed. In the absence of oxygen, the expression of some miRNAs will increase, thereby helping cells reduce death and enhance energy metabolism. Long non-coding RNA (lncRNA) can also regulate the gene network related to hypoxia by interacting with some transcription factors or chromatin regulatory proteins. Although research in this area has just begun, some results have shown that these non-coding RNAs are also important for the hypoxia tolerance of Channa fish.

7 Comparative Genomics and Evolutionary Perspectives

7.1 Adaptive evolution of hypoxia-related genes in Channa spp.

In recent years, scientists have released a lot of high-quality genomic data, which also allows us to understand more clearly how fish in the Channa genus adapt to hypoxic environments. Whole-genome analysis of *Channa asiatica* found that the number of gene families responsible for oxygen binding and transport in its body has increased significantly. This expansion may be one of the reasons why it can survive in a hypoxic environment. Transcriptome studies further showed that when it is exposed to air, that is, when facing an extremely low oxygen environment, many antioxidant pathways in its body will be activated. This shows that it relies on regulating multiple molecular pathways to cope with hypoxia (Zhou et al., 2024). Similar situations have been found in *Channa striatus*. Researchers found that when it is under long-term hypoxia, many genes related to transcription, signal transduction, energy conversion, and immunity in its liver are mobilized. This shows that its regulatory mechanism is also very complex (Mohapatra et al., 2017).

7.2 Positive selection and gene family expansions

The increase in the number of gene families and positive selection are two important ways in the evolution of fish tolerance to hypoxia. In the genome of *Channa asiatica*, studies have found that the number of genes related to oxygen transport, such as hemoglobin and myoglobin, has increased. This may allow it to carry oxygen better in anoxic environments and enhance its antioxidant capacity (Zhou et al., 2024). Transcriptome studies have also found that in hypoxia, the expression levels of genes such as HSP90, prefoldin and fatty acid binding protein will increase. Some genes may have also experienced positive selection, that is, they have become more useful in order to adapt to the environment (Mohapatra et al., 2017). These results show that the hypoxia adaptability of the Channa genus is not just based on "more genes", but more importantly, these genes have become more effective and more suitable.

7.3 Phylogenetic comparisons with hypoxia-sensitive and tolerant fishes

Comparing the Channa genus with some other fish can better understand the special features of Channa fish. In 2024, Zhou et al. (2024) compared the genomes of *Channa asiatica* with those of 12 other fish species and found that the gene family related to hypoxia in *Channa asiatica* was significantly expanded compared with many hypoxia "sensitive" fish (such as zebrafish). At the gene expression level, the gene pathways activated by *Channa striatus* in hypoxia have many similarities with those of "tolerant" fish such as crucian carp, including the activation of some antioxidant responses, energy metabolism regulation, and molecular chaperones (Mohapatra et al., 2017).

8 Case Study: Genomic Insights into Hypoxia Adaptation in Channa striata

8.1 Experimental design: hypoxia exposure and sampling strategy

When studying how Channa striata (blackhead fish) adapt to hypoxia, the researchers designed a laboratory simulation. They placed the fish in an environment with hypoxia for a long time to see how the fish responded. At specific time points, the researchers took liver samples from the fish for molecular analysis. To understand which genes changed under hypoxia, they used suppression subtractive hybridization (SSH) technology to construct an enriched cDNA library from hypoxia. Then, they sequenced and analyzed these libraries (Mohapatra et al., 2017).

8.2 Omics analysis results (transcriptomics, metabolomics if applicable)

Through SSH technology, the researchers obtained a total of 130 different transcripts. The results of BLAST analysis showed that 58% of them were known genes, 18% were genes that had not been studied in depth, and 24% were completely unknown sequences. These known genes are involved in multiple important pathways, such as transcription, translation, signal transduction, electron transport, immune response, reproduction, and cell transport. Further analysis revealed that in hypoxic liver tissue, the expression levels of 11 known genes, 1 uncharacterized gene, and 1 unknown gene were significantly increased. The study also used RACE technology to obtain the full-length cDNA sequences of HSP90 and CSHL-338 (an uncharacterized gene). In addition, they also obtained the complete sequences of prefoldin and FABP (fatty acid binding protein) from the SSH library. These genes are upregulated in hypoxic environments (Mohapatra et al., 2017).

8.3 Key findings: upregulated genes, novel pathways, or regulatory networks

This study found that Channa striata mobilizes many genes to cope with environmental stress when hypoxic. Among them, HSP90, prefoldin, and FABP performed the most prominently, and their expression levels increased significantly when hypoxia occurred. These genes may play a key role in helping cells fold proteins, cope with stress, and regulate energy. Some unknown or uncharacterized genes were also upregulated, which may indicate that there are some hypoxia response mechanisms in fish that we do not yet understand.

8.4 Discussion of physiological relevance and potential aquaculture applications

These research results not only allow us to understand more clearly how Channa striata copes with hypoxia, but also provide useful information for its application in aquaculture. Genes such as HSP90 and FABP that are upregulated in hypoxia help maintain cell stability, improve fish resistance, and improve energy utilization. This genetic response is very important for some high-density farms or water environments with unstable oxygen. In the future, molecular breeding and other technologies can be used to select Channa striata strains that are more resistant to hypoxia to improve aquaculture production and stress resistance. Genes that have not been fully studied may also become new molecular markers or regulatory targets, providing directions for subsequent breeding and biotechnology development (Mohapatra et al., 2017).

9 Applications and Future Directions

9.1 Use of genomic biomarkers in selective breeding for hypoxia tolerance

With the release of more and more high-quality genomes of Channa fish, such as *Channa asiatica* and *Channa striatus*, researchers have found many genetic markers related to hypoxia tolerance. These markers include SNPs, amplified gene families, and expression patterns of some key genes, which have begun to play a role in molecular breeding. In the genome of C. asiatica, the number of genes responsible for oxygen binding and transport has increased. These genes can be used as "molecular markers" to determine which fish are more tolerant to hypoxia, which helps to select stronger varieties (Zhou et al., 2024). Transcriptome analysis also found that many oxidative stress pathways are activated in hypoxic environments. Gene expression data in these pathways can also be used to screen individuals in advance and predict their performance (Mohapatra et al., 2017; Zhou et al., 2024). Using these molecular markers, breeding efficiency can be improved, making selection faster and more accurate.

9.2 Genetic engineering and CRISPR opportunities

Gene editing technologies such as CRISPR/Cas9 have brought new opportunities to study and improve the hypoxia tolerance of Channa fish. Scientists can use these tools to directly knock out or enhance some key genes, such as HSP90 or FABP, to see what role they play in dealing with hypoxia (Mohapatra et al., 2017). In the future, genomic and transcriptomic data can be combined to select candidate genes with clear functions and then precisely modified by CRISPR. This will make it possible to breed new fish species that are more tolerant to hypoxia and bring breeding into a new stage of "directed improvement".

9.3 Integrating genomics with physiological and ecological modeling

It is actually difficult to explain the complex biological phenomenon of hypoxia tolerance based on a single type of omics data. Future research needs to integrate data from different fields such as genomics, transcriptome, physiology, and ecology. Gene expression can be analyzed together with fish respiration and behavioral changes, so that different fish species can be more realistically predicted in aquaculture environments (Mohapatra et al., 2017; Zhou et al., 2024). Ecological modeling can also play a role. It can help us understand how genotype and environment affect each other, and can also provide references for species protection and water ecological restoration.

9.4 Gaps in current knowledge and recommendations for future research

Although there have been many advances, there are still many gaps in the research on hypoxia tolerance of Channa fish that need to be filled. Many candidate genes have only been found to be expressed more, but we don’t know how they work specifically because there is still a lack of genetic manipulation and actual performance verification (Mohapatra et al., 2017). Although many molecular markers have been found, they have not been widely used in real breeding work. There is currently a lack of large-scale fish experiments and commercial cases. The integration method of different omics data is not mature. There is currently no standard process for modeling, and it is difficult to conduct cross-disciplinary collaborative research. In the future, it is recommended to start from several aspects: first, strengthen the editing and verification of gene functions; second, promote the actual use of these molecular markers in breeding; third, develop better data integration methods and model tools. Only in this way can we comprehensively improve our understanding and application capabilities of the hypoxia tolerance mechanism of Channa fish (Mohapatra et al., 2017; Zhou et al., 2024).

10 Conclusion

This review summarizes the recent progress in genomic research on the hypoxia tolerance mechanism of Channa fish. The study found that *Channa asiatica* has increased the number of gene families related to oxygen binding and transport during its evolution. This gene expansion may be an important reason for its ability to adapt to hypoxic environments. When faced with hypoxia, *Channa asiatica* also activates many antioxidant-related molecular pathways, indicating that it adapts to oxygen-deficient environments through gene regulation mechanisms at multiple levels. For *Channa striatus*, researchers found through transcriptome analysis of the liver that the expression levels of many genes increased under hypoxic conditions. These genes are involved in transcription, translation, signal transduction, electron transport and immune response, especially heat shock proteins, prefoldin and fatty acid binding proteins, which are significantly upregulated under hypoxia. These findings further help us understand how fish survive hypoxia.

These research results not only deepen our understanding of the hypoxia tolerance mechanism of *Channa asiatica* fish, but also provide useful information for protecting aquatic organisms and improving aquaculture. Finding these key genes and regulatory methods will help us select fish species that are more adaptable to the environment, thereby improving breeding efficiency and reducing environmental risks.

As sequencing technology becomes more advanced and multi-omics combined analysis becomes more mature, we will have the hope of further understanding how the complex traits of "non-model fish" come from. This will be of great help to future molecular breeding, genetic improvement, and aquatic resource protection, and can also provide stronger technical support for the sustainable development of aquaculture.

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Conflict of Interest Disclosure

The authors affirm that this research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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