


Research Perspective

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Molecular Breeding Techniques for Disease Resistance in Common Carp: Current Advances and Future Prospects

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Abstract The fatty acid composition of aquaculture fish is of great importance in enhancing their nutritional value and human health. With the development of the aquaculture industry, researchers are increasingly focusing on how to optimize the fatty acid composition of fish through genetic and biochemical strategies. This study aims to explore the correlation between the fatty acid composition of aquaculture fish and human health. The study found that the fatty acid profiles of different fish are influenced by their diets, with marine fish generally having higher levels of n-3 polyunsaturated fatty acids such as EPA and DHA, compared to freshwater fish. The type of feed used significantly affects the nutritional value of the fish, with sustainable feeds often resulting in lower levels of EPA and DHA. Selective breeding has shown potential to increase the levels of beneficial fatty acids in fish muscle, and alternative lipid sources such as microalgae and genetically modified crops may serve as future sources of essential fatty acids. The study indicates that both genetic and biochemical strategies can effectively enhance the fatty acid composition of aquaculture fish, thereby improving their nutritional value, which is significant for the prevention of cardiovascular diseases. This research aims to provide theoretical basis and practical guidance for future studies and practical applications.

Keywords Aquaculture fish; Fatty acid composition; Human health; Genetic strategies; Biochemical strategies

1 Introduction

Common carp (*Cyprinus carpio* L.) is one of the most widely cultivated fish species globally, valued for its adaptability to diverse environmental conditions and its significant role in aquaculture. Originating from Asia, common carp has been introduced to various parts of the world, becoming a staple in both commercial and subsistence fisheries. The species is known for its robust growth rates and ability to thrive in a range of aquatic habitats, making it a crucial component of freshwater aquaculture systems (Jeney et al., 2011). Disease resistance in common carp is of paramount importance due to the substantial economic losses caused by infectious diseases (Verma et al., 2021). Among the most significant pathogens affecting common carp are Cyprinid herpesvirus-3 (CyHV-3), also known as koi herpesvirus (KHV), and *Aeromonas hydrophila*. CyHV-3 is notorious for causing high mortality rates in both ornamental and food production carp, with outbreaks leading to severe economic impacts on the aquaculture industry (Rakus et al., 2012). Similarly, *Aeromonas hydrophila* is a bacterial pathogen that can cause significant morbidity and mortality in carp populations, further underscoring the need for disease-resistant strains (Jeney et al., 2011).

Recent studies have highlighted the genetic basis of disease resistance in common carp, identifying specific genes and alleles associated with increased resistance to these pathogens. For instance, polymorphisms in the major histocompatibility (MH) class II B genes have been linked to varying levels of resistance to CyHV-3, suggesting that these genetic markers could be utilized in selective breeding programs to enhance disease resistance (Rakus et al., 2009). Additionally, differential gene expression analyses have provided insights into the immune responses of carp lines with varying susceptibility to CyHV-3, revealing potential targets for genetic improvement (Rakus et al., 2012).

This study aims to integrate the latest advancements in molecular breeding techniques to enhance disease resistance in carp. By synthesizing recent research findings, it summarizes genetic markers and molecular

pathways associated with disease resistance in carp and evaluates the effectiveness of different breeding strategies. The study also discusses future prospects and challenges. By providing a comprehensive review of the current state of molecular breeding for disease resistance in carp, this study aims to inform future studies and guide the development of more resilient aquaculture systems.

2 Overview of Disease Resistance in Common Carp

2.1 Major diseases affecting common carp

Common carp (*Cyprinus carpio* L.) are susceptible to a variety of diseases that can significantly impact aquaculture productivity. Among the most notable diseases are those caused by bacterial pathogens such as *Aeromonas hydrophila*, which leads to motile aeromonad septicaemia (MAS) (Jeney et al., 2011; Liu et al., 2014), and viral infections like Cyprinid herpesvirus-3 (CyHV-3), also known as koi herpesvirus (KHV) (Palaikostas et al., 2018a; Palaikostas et al., 2019). Additionally, carp are affected by various parasites, mainly including *Dactylogyrus*, *Trichodina*, and copepod parasites (Obaid et al., 2021). These diseases can lead to high mortality rates and cause substantial economic losses in carp farming.

2.2 Traditional breeding approaches

Traditional breeding approaches for disease resistance in common carp have primarily involved selective breeding, crossbreeding, and hybridization. Selective breeding has been used to enhance resistance to specific diseases, such as dropsy, through long-term selection programs. Crossbreeding and hybridization have also been employed to combine desirable traits from different strains, leading to improved growth rates and disease resistance (Vandeputte et al., 2003). For instance, through selective breeding, Krasnodar common carp have enhanced resistance to dropsy disease, resulting in strains with higher survival and growth rates.

2.3 Limitations of conventional methods

Despite the successes of traditional breeding methods, there are several limitations. Conventional breeding approaches often require long timeframes to achieve significant genetic improvements and may not always result in the desired level of disease resistance. Additionally, the genetic basis of disease resistance is complex and influenced by multiple genes, making it challenging to achieve consistent results through traditional methods alone (Vandeputte et al., 2003). Furthermore, environmental factors can introduce biases in heritability estimates, complicating the selection process (Vandeputte et al., 2003). The need for more precise and efficient breeding techniques has led to the exploration of molecular breeding methods, which offer the potential to overcome these limitations and accelerate the development of disease-resistant common carp.

3 Marker-Assisted Selection (MAS)

3.1 Principles and applications of MAS

Marker-Assisted Selection (MAS) is a molecular breeding technique that utilizes DNA markers to select for desirable traits in organisms, such as disease resistance in common carp. The primary principle of MAS is to identify and use molecular markers that are closely linked to genes of interest, thereby enabling the selection of individuals carrying these genes without the need for phenotypic screening. This approach significantly accelerates the breeding process by allowing early and accurate selection of desirable traits (Banu et al., 2017; Eze, 2019).

MAS has been successfully applied in various breeding programs, particularly for traits with simple inheritance patterns. For instance, in crop plants, MAS has been used to introgress resistance genes into elite cultivars, thereby enhancing disease resistance and improving overall crop performance (Eze, 2019). Similarly, in nematode resistance breeding, MAS has facilitated the rapid and objective identification of resistant plant accessions, streamlining the breeding process (Banu et al., 2017).

3.2 Advantages over traditional methods

MAS offers several advantages over traditional breeding methods. Firstly, it reduces the time and resources required for breeding by enabling early selection of desirable traits. Traditional breeding often involves lengthy and labor-intensive processes of phenotypic screening, which can be bypassed using MAS (Banu et al., 2017; Eze,

2019). MAS enhances the precision of breeding programs. By using molecular markers, breeders can accurately select for specific genes, reducing the risk of losing desirable traits during the breeding process. This precision is particularly beneficial for traits with simple inheritance patterns, where the linkage between markers and genes is strong (Eze, 2019).

Moreover, MAS can be integrated with high-throughput genotyping platforms, further accelerating the breeding process and enabling the handling of large populations. This integration opens new avenues for molecular-based resistance breeding, making it more efficient and effective (Banu et al., 2017).

3.3 Case studies

Eze (2019) discussed how MAS (Marker-Assisted Selection) can use molecular genetic markers as criteria for selecting desirable traits, thereby accelerating the breeding process and improving accuracy and efficiency. MAS is particularly suitable for selecting traits that are difficult to measure, have low heritability, or are recessive. Through MAS, traits such as growth rate, disease resistance, and meat quality can be improved more quickly. The study conducted a cohabitation model experiment to compare the survival rates and virus transmission abilities of different types of carp when faced with CyHV-3 virus infection. The results showed that disease-resistant fish not only had higher survival rates after virus infection but also had a lower capacity to transmit the virus. This implies that disease-resistant fish have a significant advantage in reducing virus spread and infection. These findings are of great importance for disease control and fish breeding in aquaculture.

4. Quantitative Trait Loci (QTL) Mapping

4.1 Identification of QTLs linked to disease resistance

Quantitative Trait Loci (QTL) mapping is a powerful tool for identifying genetic regions associated with disease resistance. In common carp, significant progress has been made in identifying QTLs linked to resistance against various pathogens. For instance, a genome-wide significant QTL affecting resistance to Koi Herpesvirus (KHV) was identified on linkage group 44, explaining approximately 7% of the additive genetic variance. This QTL region includes the TRIM25 gene, which was identified as a promising candidate gene for resistance due to a putative premature stop mutation (Palaiokostas et al., 2018a). Additionally, QTL mapping has been extensively used in plants to study complex disease resistance, providing insights into the number of resistance loci involved, their interactions, and their race-specificity.

4.2 Use of QTLs in breeding programs

The identification of QTLs linked to disease resistance has significant implications for breeding programs. Marker-assisted selection (MAS) can be employed to incorporate these valuable traits into breeding lines, enhancing disease resistance in future generations. For example, DNA markers tightly linked to quantitative resistance loci (QRLs) controlling quantitative disease resistance (QDR) can be used for MAS to incorporate these traits into crops such as wheat, barley, common bean, tomato, and pepper (Clair et al., 2010). In the context of common carp, incorporating QTLs linked to KHV resistance into breeding programs could reduce morbidity and economic losses in carp farming (Palaiokostas et al., 2018a).

4.3 Case studies

The study by Jia et al. (2021) provides valuable insights into the use of Quantitative Trait Loci (QTL) mapping for identifying genetic markers associated with disease resistance. By integrating transcriptome data and focusing on immune-related pathways and genes, the study elucidates how QTL mapping can precisely locate key genetic loci that contribute to resistance against CyHV-3 (Figure 1). This approach enables selective breeding of carp strains with enhanced disease resistance, thereby improving the efficiency of aquaculture.

Figure 1 illustrates the application of QTL (Quantitative Trait Loci) mapping technology in breeding disease-resistant carp. The experiment compared the daily mortality rates and pathological changes between disease-resistant and non-resistant carp strains after infection with the CyHV-3 virus, verifying the effectiveness of resistance genes in reducing viral infection and transmission. The experimental results indicated that the

disease-resistant strains had significantly lower mortality rates and pathological damage compared to the non-resistant strains, demonstrating the presence and function of resistance genes. This figure shows that QTL mapping technology can effectively identify and select resistance genes, thereby enhancing the disease resistance of carp. This provides empirical support for the application of molecular breeding techniques in aquaculture.

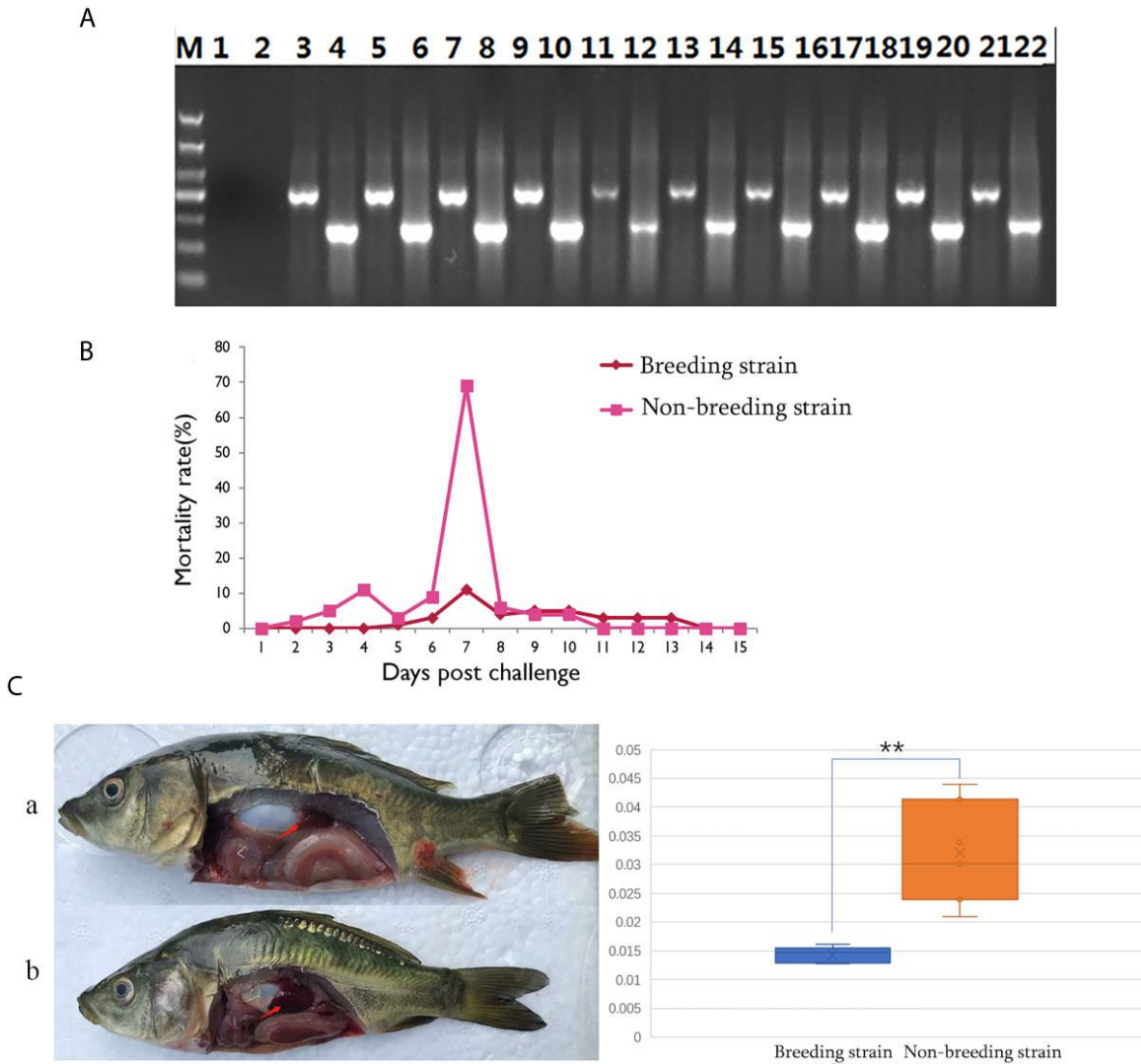


Figure 1 Differential appearance of general mortality and pathology between fish from the breeding and non-breeding strains (Adopted from Jia et al., 2021)

Image caption: (A) The PCR validation of the CyHV-3 virus genes TK and Sph. Lane 1-2 represents the negative control, and afterwards, lane 3-22 represents the result for tested 10 virus infected fish. (B) Comparison of daily mortality between the breeding and non-breeding strains. (C) The degree of swelling trunk kidney was limited in the survivors from the breeding strain (a) compared with the markedly enlarged trunk kidney observed in fish from the non-breeding strain (b). The arrow indicates the trunk kidney region. “***” means the very significant difference ($p < 0.01$) between current compared two groups (Adapted from Jia et al., 2021)

5 Genomic Selection (GS)

5.1 Overview of genomic selection

Genomic Selection (GS) is a modern breeding technique that utilizes genome-wide genetic information to predict the breeding values of individuals. This method has gained attention in aquaculture due to its potential to enhance the accuracy of selection and accelerate genetic gains compared to traditional pedigree-based selection methods. GS involves the use of dense genetic markers spread across the genome to capture the genetic architecture of traits of interest, allowing for more precise selection of breeding candidates (Palaiokostas et al., 2018b; Palaiokostas et al., 2019).

5.2 Benefits in improving disease resistance

The application of GS in aquaculture, particularly in common carp, has shown significant promise in improving disease resistance. One of the primary benefits of GS is its ability to increase the accuracy of selecting individuals with desirable traits, such as resistance to diseases like Koi Herpesvirus (KHV). Studies have demonstrated that GS can enhance prediction accuracy by 8%-18% over traditional methods, thereby improving the efficiency of breeding programs aimed at disease resistance (Palaiokostas et al., 2019). Additionally, GS allows for the simultaneous improvement of multiple traits, such as disease resistance and growth rate, which is crucial for maintaining overall productivity in aquaculture (Palaiokostas et al., 2018b; Lin et al., 2020).

5.3 Case studies

Several case studies highlight the successful application of GS in improving disease resistance in common carp and other aquaculture species:

1) Koi Herpesvirus Resistance in Common Carp: A study involving 1,425 common carp juveniles challenged with KHV utilized Restriction Site-Associated DNA sequencing (RAD-seq) to genotype the population. The study identified a significant Quantitative Trait Locus (QTL) on linkage group 44, explaining approximately 7% of the additive genetic variance for KHV resistance. The TRIM25 gene was identified as a promising candidate within this QTL region, suggesting its potential role in enhancing disease resistance through GS (Palaiokostas et al., 2018a).

2) Juvenile Growth Rate in Common Carp: Another study on common carp focused on juvenile growth rate as a polygenic production trait. Using RAD sequencing, the study constructed a medium-density genetic map and tested GS, resulting in an 18% improvement in prediction accuracy over pedigree-based methods. This case illustrates the broader applicability of GS beyond disease resistance, highlighting its potential to enhance economically important traits in common carp breeding programs (Palaiokostas et al., 2018b). These case studies collectively demonstrate the efficacy of GS in improving disease resistance and other key traits in aquaculture, paving the way for more resilient and productive breeding programs.

6 CRISPR/Cas9 and Gene Editing

6.1 Mechanism of CRISPR/Cas9

The CRISPR/Cas9 system, derived from the adaptive immune system of bacteria, has emerged as a powerful tool for genome editing. The mechanism involves two key components: the Cas9 protein, which acts as a molecular scissor, and a guide RNA (gRNA) that directs Cas9 to a specific location in the genome. The gRNA binds to a complementary DNA sequence, and the Cas9 protein induces a double-strand break at this site. The cell's natural repair mechanisms then take over, either through non-homologous end joining (NHEJ) or homology-directed repair (HDR), allowing for targeted insertions, deletions, or modifications of genes (Mushtaq et al., 2019; Ahmad et al., 2020; Islam et al., 2020).

6.2 Applications in developing disease-resistant strains

CRISPR/Cas9 has been extensively utilized in developing disease-resistant strains across various species, including plants, livestock, and aquaculture species like common carp. In plants, CRISPR/Cas9 has been used to knock out susceptibility genes or to introduce resistance genes, thereby enhancing resistance to bacterial, viral, and fungal pathogens (Mushtaq et al., 2019; Ahmad et al., 2020). In livestock, CRISPR/Cas9 has facilitated the insertion of disease resistance genes such as NRAMP1 in cattle for tuberculosis resistance and the deletion of the CD163 gene in pigs for resistance to porcine reproductive and respiratory syndrome (PRRS) (Islam et al., 2020). In common carp, CRISPR/Cas9 has been employed to target genes related to bone development and muscle growth, demonstrating its potential for genetic improvement in aquaculture (Zhong et al., 2016).

6.3 Case studies

CRISPR/Cas9 has many successful applications in developing disease-resistant strains. For example, the study by Dorfman et al. (2024) conducted a detailed analysis of different strains of carp exposed to the CyHV-3 virus. It was found that disease-resistant strains not only had higher survival rates but also significantly reduced the viral

load in the water (Figure 2). In common carp, CRISPR/Cas9 has been used to disrupt the *sp7* and *myostatin* genes, leading to severe skeletal defects and increased muscle cell growth, respectively, demonstrating the efficiency of this system in modifying the genome of common carp and its potential in aquaculture genetic research and breeding (Zhong et al., 2016).

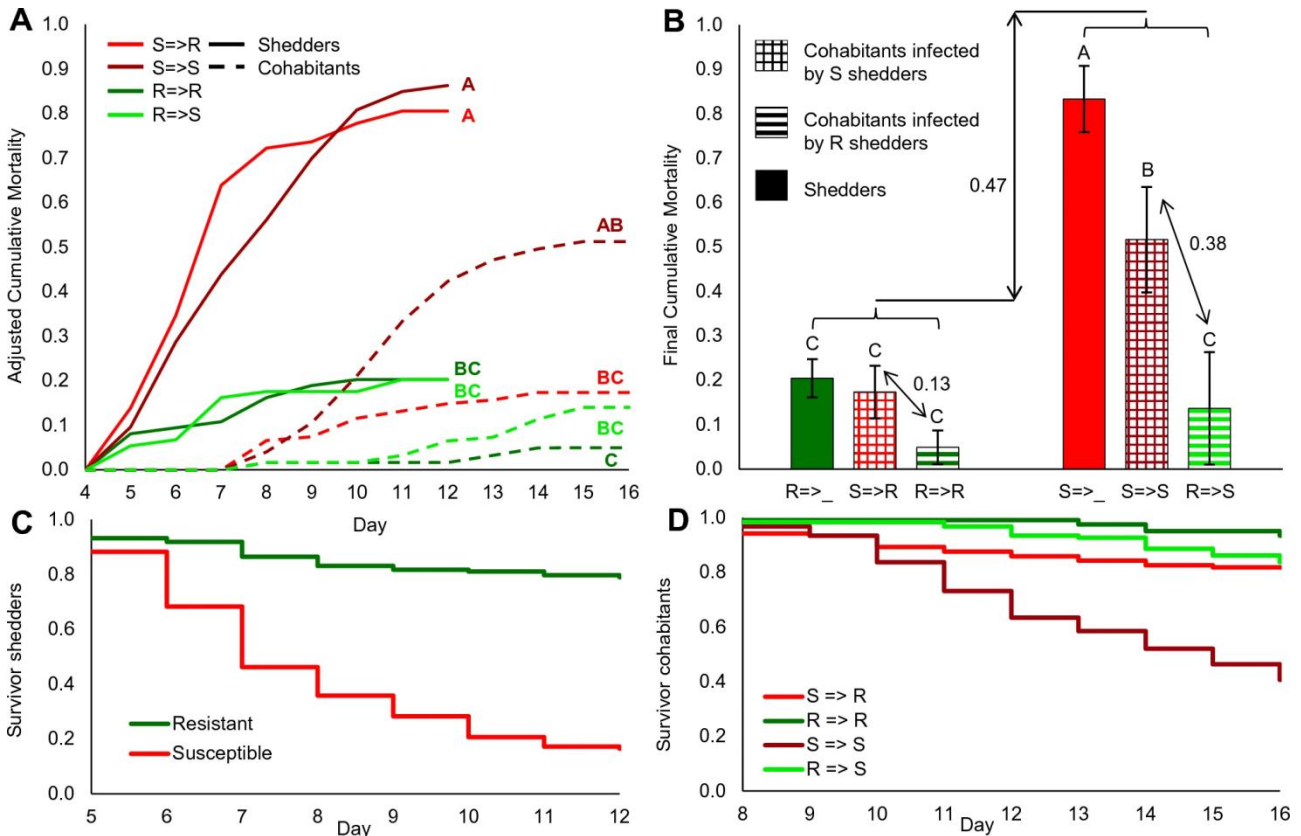


Figure 2 Cumulative mortality of experimental groups (Adopted from Dorfman et al., 2024)
 Image caption: (A) Mean cumulative mortality by days (adjusted to start day) for shedders (full lines) and cohabitants (dashed lines). (B) Final mean cumulative mortalities and standard errors for resistant (left bars) and susceptible (right bars) categories. (C) shedders, right censored to day 12 and (D) cohabitants, right censored to day 16. Note that survival analyses results are similar to mortality analyses presented in (A) (Adapted from Dorfman et al., 2024)

Figure 2 from Dorfman et al. (2024) shows the cumulative mortality rates during the experiment for different treatment groups (resistant and susceptible shedders and their cohabitants), averaged over four replicates. The results demonstrate that improving disease resistance in common carp through molecular breeding techniques, such as CRISPR/Cas9, is not only feasible but also effective. The final cumulative mortality rate of resistant shedders was significantly lower than that of susceptible shedders, confirming the presence and effect of resistance genes. Specifically, the cumulative mortality rate for susceptible shedders was 83%, while for resistant shedders it was only 20%. This outcome validates that resistant carp have a higher survival rate when facing CyHV-3 virus. By selecting and introducing resistance genes through molecular breeding techniques like CRISPR/Cas9, the survival rate and overall disease resistance of carp against viral infections are significantly enhanced. These findings provide strong support and scientific evidence for the application of molecular breeding in aquaculture.

7 Transcriptomics and Proteomics

7.1 Role of transcriptomics in understanding disease response

Transcriptomics has played a pivotal role in elucidating the molecular mechanisms underlying disease resistance in common carp. By analyzing the transcriptome of CyHV-3-resistant strains, researchers have identified key immune-related genes and pathways that contribute to the fish's ability to combat infections. For instance,

integrative transcriptomic analysis has revealed that the resistance to CyHV-3 in common carp involves specific innate immune mechanisms, including autophagy, phagocytosis, cytotoxicity, and virus blockage by lectins and mucin 3 (MUC3) (Jia et al., 2020; Jia et al., 2021). Additionally, transcriptome analysis of common carp infected with *Aphanomyces invadans* has highlighted the importance of efficient antigen processing, enhanced phagocytosis, and increased leukocyte recruitment in disease resistance (Verma et al., 2020). These findings underscore the significance of transcriptomics in identifying immune pathways and potential genetic markers for breeding disease-resistant carp.

7.2 Proteomic approaches to identify disease resistance markers

Proteomics complements transcriptomics by providing insights into the protein-level changes associated with disease resistance. Proteomic studies have identified several proteins and pathways that are crucial for the immune response in common carp. For example, the identification of single nucleotide polymorphisms (SNPs) in immune response genes, such as TLRs and MyD88, has facilitated the development of genetic markers for mapping innate immune response genes (Kongchum et al., 2010). Moreover, the characterization of proteins involved in the immune response, such as CD40 and CD154, has revealed their significant roles in resistance to viral infections like grass carp reovirus (GCRV) (Lu et al., 2018). These proteomic approaches are essential for identifying disease resistance markers that can be used in selective breeding programs to enhance the resilience of common carp to various pathogens.

7.3 Case studies

Transcriptomics and proteomics have extensive applications in understanding and enhancing disease resistance in common carp.

Resistance to *Aphanomyces invadans*: Transcriptome analysis of common carp infected with *A. invadans* revealed that efficient antigen processing, enhanced phagocytosis, and increased leukocyte recruitment contribute to the fish's resistance to this pathogen (Verma et al., 2020). The study identified 5,288 differentially expressed genes (DEGs) and 731 genes involved in 21 immune pathways through RNA sequencing of head kidney samples from infected and uninfected carp (Figure 3). The findings highlight the carp's ability to efficiently process and present antigens, enhance phagocytosis, recognize pathogen-associated molecular patterns, and recruit leukocytes to the infection site. This systematic understanding of disease resistance mechanisms at the molecular level is of great value for developing disease management strategies.

Figure 3 in the study by Verma et al. (2021) shows that 12 days post-infection (dpi), no gross lesions were observed in both the experimental and control groups of common carp. However, histopathological examination revealed mild degeneration of muscle fibers and the presence of hyphae at the injection site in the infected fish. By 12 dpi, granulomas had formed around the hyphae, indicating that the immune response helped to combat the infection. This figure emphasizes the effectiveness of the carp's immune response in controlling the pathogen and preventing extensive tissue damage, highlighting the role of granuloma formation in disease resistance.

Transcriptomics and proteomics are powerful tools for understanding the molecular basis of disease resistance in common carp. By identifying key immune pathways and genetic markers, these approaches pave the way for the development of disease-resistant carp strains through selective breeding programs.

8 Challenges and Future Directions

8.1 Genetic diversity and inbreeding

One of the primary challenges in molecular breeding for disease resistance in common carp is maintaining genetic diversity while avoiding inbreeding. Inbreeding can lead to a reduction in genetic variability, which is crucial for the adaptability and long-term survival of the species. Studies have shown that different strains of common carp exhibit varying levels of resistance to diseases such as *Aeromonas hydrophila* and *Cyprinid herpesvirus-3* (CyHV-3) (Jeney et al., 2011). The use of genetically diverse strains, such as the Tata and Szarvas 15 domesticated strains, has been effective in producing families with higher resistance to diseases (Jeney et al., 2011). However,

continuous monitoring and management of genetic diversity are essential to prevent inbreeding depression and ensure the sustainability of breeding programs.

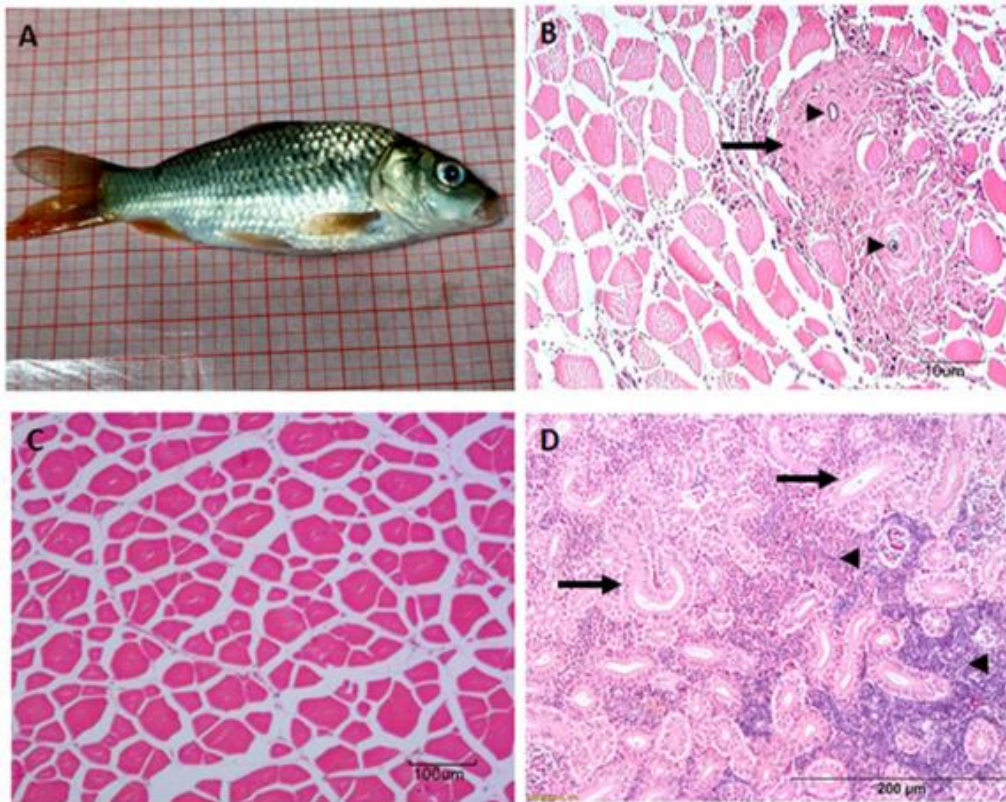


Figure 3 Common carp injected with zoospores of *A. invadans* (Adopted from Verma et al., 2021)

Image caption: (A) No gross lesions observed 12 days post-infection (dpi); (B) Section of muscle from experimentally infected common carp showing granuloma (arrow) around the oomycete hyphae (arrowheads) at 12 dpi; (C) Section of muscle tissue from the control common carp injected with autoclaved pond water, showing normal muscle fibers; (D) Head kidney of experimentally infected common carp at 12 dpi showing normal architecture, i.e., haematopoietic tissue (arrowhead) and renal tubules (arrows), similar to the control group (Adapted from Verma et al., 2021)

8.2 Ethical and regulatory issues

The application of molecular breeding techniques raises several ethical and regulatory concerns. The use of genetic markers and selective breeding for disease resistance must comply with national and international regulations to ensure the welfare of the fish and the safety of the environment. For instance, the World Organization for Animal Health has listed Koi herpesvirus as a notifiable disease, necessitating strict regulatory measures for its control (Palaiokostas et al., 2018a; Jia et al., 2020). Ethical considerations also include the potential impact of genetically modified organisms (GMOs) on natural ecosystems and the need for transparent communication with stakeholders, including consumers and environmental groups.

8.3 Technical limitations and costs

The implementation of molecular breeding techniques involves significant technical challenges and costs. High-throughput sequencing technologies, such as Restriction Site-Associated DNA sequencing (RADseq), and genome-wide association studies (GWAS) are essential for identifying quantitative trait loci (QTL) and genetic markers associated with disease resistance (Palaiokostas et al., 2018a; Jia et al., 2020). However, these technologies require substantial financial investment and technical expertise. Additionally, the development and validation of single nucleotide polymorphism (SNP) markers for immune response genes are time-consuming and resource-intensive (Kongchum et al., 2010). The cost-effectiveness of these techniques must be evaluated to ensure their feasibility for large-scale breeding programs.

8.4 Environmental and ecological considerations

The release of genetically selected or modified common carp into natural water bodies poses potential environmental and ecological risks. The introduction of disease-resistant strains could disrupt local ecosystems and affect the genetic makeup of wild populations. Studies have highlighted the importance of understanding the ecological impact of breeding programs and the need for comprehensive risk assessments (Palaiokostas et al., 2019). Moreover, the potential for horizontal gene transfer and the spread of resistance genes to other species must be carefully monitored. Sustainable breeding practices should aim to balance the benefits of disease resistance with the preservation of natural biodiversity and ecosystem health.

9 Concluding Remarks

Molecular breeding techniques have shown significant promise in enhancing disease resistance in common carp (*Cyprinus carpio*). Key findings from recent studies highlight the role of major histocompatibility complex (MHC) genes, particularly MHC class II α and II β alleles, in conferring resistance to pathogens such as *Aeromonas hydrophila* and *Cyprinid herpesvirus-3* (CyHV-3). Integrative transcriptomic analyses have revealed that specific immune mechanisms, including autophagy, phagocytosis, and virus blockage by lectins and mucin 3, are crucial for resistance to CyHV-3. Additionally, genomic selection and quantitative trait locus (QTL) mapping have identified significant genetic markers and candidate genes, such as TRIM25 and various toll-like receptors (TLRs), that are associated with enhanced disease resistance.

Molecular breeding is pivotal in aquaculture for several reasons. Firstly, it offers a sustainable alternative to antibiotics and vaccines, which can have environmental and health repercussions. By selecting for disease-resistant traits, molecular breeding reduces the incidence of infectious diseases, thereby improving fish health and survival rates. This is particularly important for economically significant species like common carp, which are susceptible to devastating diseases such as CyHV-3 and *Aeromonas hydrophila* infections. Moreover, molecular breeding techniques, including genomic selection and QTL mapping, enable precise and efficient identification of desirable traits, accelerating the breeding process and enhancing genetic gain.

Future research should focus on expanding the genetic databases and refining molecular tools to further enhance the accuracy and efficiency of breeding programs. Key recommendations include:

- 1) Expanding Genetic Studies: Conduct comprehensive genome-wide association studies (GWAS) and QTL mapping to identify additional genetic markers and candidate genes associated with disease resistance
- 2) Integrative Approaches: Utilize integrative transcriptomic and proteomic analyses to uncover the complex immune mechanisms underlying disease resistance and to identify novel targets for genetic selection.
- 3) Genomic Selection: Implement and optimize genomic selection techniques across diverse carp populations to ensure broad applicability and to maximize genetic gain.
- 4) Cross-Breeding Programs: Develop cross-breeding programs that combine resistant strains from different genetic backgrounds to enhance overall disease resistance and genetic diversity.
- 5) Environmental Considerations: Investigate the interaction between genetic resistance and environmental factors to develop holistic breeding strategies that consider both genetic and ecological aspects.

By following these recommendations, the aquaculture industry can significantly improve the resilience and productivity of common carp, ensuring sustainable and profitable fish farming practices.

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Conflict of Interest Disclosure

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Reference

- Ahmad S., Wei X., Sheng Z., Hu P., and Tang S., 2020, CRISPR/Cas9 for development of disease resistance in plants: recent progress limitations and future prospects, *Briefings in Functional Genomics*, 19(1): 26-39.
<https://doi.org/10.1093/bfpg/elz041>
- Banu J., Meena K., Selvi C., and Manickam S., 2017, Molecular marker-assisted selection for nematode resistance in crop plants, *Journal of Entomology and Zoology Studies*, 5: 1307-1311.
- Clair D., 2010, Quantitative disease resistance and quantitative resistance Loci in breeding, *Annual Review of Phytopathology*, 48: 247-68.
<https://doi.org/10.1146/annurev-phyto-080508-081904>
- Eze F., 2019, "Marker-assisted selection in fish: a review", *Asian Journal of Fisheries and Aquatic Research*, 3(4): 1-11.
<https://doi.org/10.9734/ajfar/2019/v3i430038>
- Islam M., Rony S., Rahman M., Çınar M., Villena J., Uddin M., and Kitazawa H., 2020, Improvement of disease resistance in livestock: application of immunogenomics and CRISPR/Cas9 technology, *Animals : an Open Access Journal from MDPI*, 10(12): 2236.
<https://doi.org/10.3390/ani10122236>
- Jeney G., Ardó L., Rónyai A., Bercsényi M., and Jeney Z., 2011, Resistance of genetically different common carp *Cyprinus carpio* L., families against experimental bacterial challenge with *Aeromonas hydrophila*, *Journal of Fish Diseases*, 34(1): 65-70.
<https://doi.org/10.1111/j.1365-2761.2010.01211.x>
- Jia Z., Chen L., Yanlong G., Shengwen L., Peng W., Li C., Zhang Y., Hu X., Zhou Z., Shi L., and Xu P., 2020, Genetic mapping of Koi herpesvirus resistance (KHVR) in Mirror carp (*Cyprinus carpio*) revealed genes and molecular mechanisms of disease resistance, *Aquaculture*, 519: 734850.
<https://doi.org/10.1016/j.aquaculture.2019.734850>
- Jia Z., Wu N., Jiang X., Li H., Sun J., Shi M., Li C., Ge Y., Hu X., Ye W., Tang Y., Shan J., Cheng Y., Xia X., and Shi L., 2020, Integrative transcriptomic analysis reveals the immune mechanism for a cyhv-3-resistant common carp strain, *Frontiers in Immunology*, 12: 687151.
<https://doi.org/10.3389/fimmu.2021.687151>
- Jia Z., Wu N., Jiang X., Li H., Sun J., Shi M., Li C., Ge Y., Hu X., Ye W., Tang Y., Shan J., Cheng Y., Xia X., and Shi L., 2021, Integrative transcriptomic analysis reveals the immune mechanism for a CyHV-3-resistant common carp strain, *Frontiers in Immunology*, 12: 687151.
<https://doi.org/10.3389/fimmu.2021.687151>
- Kongchum P., Palti Y., Hallerman E., Hulata G., and David L., 2010, SNP discovery and development of genetic markers for mapping innate immune response genes in common carp (*Cyprinus carpio*), *Fish and Shellfish Immunology*, 29(2): 356-361.
<https://doi.org/10.1016/j.fsi.2010.04.013>
- Lin Z., Hosoya S., Sato M., Mizuno N., Kobayashi Y., Ito T., and Kikuchi K., 2020, Genomic selection for heterobothriosis resistance concurrent with body size in the tiger pufferfish *Takifugu rubripes*, *Scientific Reports*, 10(1): 19976.
<https://doi.org/10.1038/s41598-020-77069-z>
- Liu J., Liu Z., Zhao X., and Wang C., 2014, MHC class II α alleles associated with resistance to *Aeromonas hydrophila* in purse red common carp *Cyprinus carpio Linnaeus*, *Journal of fish diseases*, 37(6): 571-575.
<https://doi.org/10.1111/jfd.12131>
- Lu X., Chen Y., Cui Z., Zhang X., Lu L., Li S., Xia X., Nie P., and Zhang Y., 2018, Characterization of grass carp CD40 and CD154 genes and the association between their polymorphisms and resistance to grass carp reovirus, *Fish and Shellfish Immunology*, 81: 304-308.
<https://doi.org/10.1016/j.fsi.2018.07.037>
- Mushtaq M., Sakina A., Wani S., Shikari A., Tripathi P., Zaid A., Galla A., Abdelrahman M., Sharma M., Singh A., and Salgotra R., 2019, Harnessing genome editing techniques to engineer disease resistance in plants, *Frontiers in Plant Science*, 10: 550.
<https://doi.org/10.3389/fpls.2019.00550>
- Ortega F., and Lopez-Vizcon C., 2012, Application of molecular marker-assisted selection (MAS) for disease resistance in a practical potato breeding programme, *Potato Research*, 55: 1-13.
<https://doi.org/10.1007/s11540-011-9202-5>
- Obaid H., Hussein N., Obed T., and Boundenga L., 2021, Common Carp (*Cyprinus carpio*) parasites diversity and prevalence in Erbil aquacultures: gills, skin and intestinal infections, *The Iranian Journal of Veterinary Science and Technology*, 13: 34-41.
<https://doi.org/10.22067/IJVST.2021.64304.0>
- Palaiokostas C., Kocour M., Prchal M., and Houston R., 2018b, Accuracy of genomic evaluations of juvenile growth rate in common carp (*Cyprinus carpio*) using genotyping by sequencing, *Frontiers in Genetics*, 9: 350926.
<https://doi.org/10.3389/fgene.2018.00082>
- Palaiokostas C., Robledo D., Veselý T., Prchal M., Pokorová D., Piačková V., Pojezdal E., Kocour M., and Houston R., 2018a, Mapping and sequencing of a significant quantitative trait locus affecting resistance to koi herpesvirus in Common Carp, *G3: Genes|Genomes|Genetics*, 8: 3507-3513.
<https://doi.org/10.1534/g3.118.200593>
- Palaiokostas C., Veselý T., Kocour M., Prchal M., Pokorová D., Piačková V., Pojezdal E., and Houston R., 2019, Optimizing genomic prediction of host resistance to koi herpesvirus disease in carp, *Frontiers in Genetics*, 10: 543.
<https://doi.org/10.3389/fgene.2019.00543>

- Rakus K., Imazarow I., Adamek M., Palmeira L., Kawana Y., Hirono I., Kondo H., Matras M., Steinhagen D., Flasz B., Brogden G., Vanderplasschen A., and Aoki T., 2012, Gene expression analysis of common carp (*Cyprinus carpio* L.) lines during *Cyprinid herpesvirus 3* infection yields insights into differential immune responses, *Developmental and Comparative Immunology*, 37(1): 65-76.
<https://doi.org/10.1016/j.dci.2011.12.006>
- Rakus K., Wiegertjes G., Adamek M., S' i A., Lepa A., and Imazarow I., 2009, Resistance of common carp (*Cyprinus carpio* L.) to *Cyprinid herpesvirus-3* is influenced by major histocompatibility (MH) class II B gene polymorphism, *Fish and Shellfish Immunology*, 26(5): 737-743.
<https://doi.org/10.1016/j.fsi.2009.03.001>
- Vandeputte M., 2003, Selective breeding of quantitative traits in the common carp (*Cyprinus carpio*): a review, *Aquatic Living Resources*, 16: 399-407.
[https://doi.org/10.1016/S0990-7440\(03\)00056-1](https://doi.org/10.1016/S0990-7440(03)00056-1)
- Verma D., Peruzza L., Peruzza L., Trusch F., Trusch F., Yadav M., R., Shubin S., Morgan K., Mohindra V., Hauton C., West P., Pradhan P., and Sood N., 2020, Transcriptome analysis reveals immune pathways underlying resistance in the common carp *Cyprinus carpio* against the oomycete *Aphanomyces invadans*, *Genomics*, 113(1): 944-956.
<https://doi.org/10.1016/j.ygeno.2020.10.028>
- Zhong Z., Niu P., Wang M., Huang G., Xu S., Sun Y., Xu X., Hou Y., Sun X., Yan Y., and Wang H., 2016, Targeted disruption of *sp7* and *myostatin* with CRISPR-Cas9 results in severe bone defects and more muscular cells in common carp, *Scientific Reports*, 6(1): 22953.
<https://doi.org/10.1038/srep22953>



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