International Journal of Medical and Health Research
www.medicalsciencejournal.com
ISSN: 2454-9142
Received: 30-12-2024, Accepted: 29-01-2025, Published: 13-02-2025
Volume 11, Issue 1, 2025, Page No. 38-44

The zebrafish genome: Unveiling human disease mechanisms and drug target

Asmita Mitra, Biswadeep Das
Department of Biotechnology, Kalinga Institute of Industrial Technology, Bhubaneswar, Odisha, India

Abstract
The zebrafish (*Danio rerio*) has emerged as a key model organism in biomedical research, considerably improving our understanding of human disease mechanisms and medication discovery. This study investigates the structural and functional similarities between the zebrafish and human genomes, revealing that roughly 70% of human protein-coding genes are zebrafish counterparts. These genetic connections enable zebrafish to effectively model human disorders, providing important insights into gene function, developmental biology, and disease etiology. Zebrafish offer distinct advantages, such as rapid development, transparent embryos, and high-throughput screening (HTS) capabilities, which allow for real-time observation of genetic, molecular, and physiological processes. Researchers can use modern techniques like CRISPR/Cas9 to generate precise genetic models of human disease states ranging from neurological illnesses to malignancies. Zebrafish also play an important part in drug discovery, providing for fast screening of drug candidates as well as cost-effective assessments of toxicity and efficacy. Zebrafish incorporation into personalized medicine enhances individualized therapeutic research by allowing for the study of patient-specific genetic alterations. This study emphasizes the importance of zebrafish in translational research, where their genetic and physiological parallels to humans, combined with their flexibility in high-throughput applications, make them an invaluable tool for understanding disease pathways and speeding up medication development.

Keywords: Zebrafish, disease mechanisms, genetic similarity, developmental biology, drug discovery, high-throughput screening, CRISPR/Cas9, personalized medicine, translational research

Introduction

The zebrafish, *Danio rerio,* has emerged as a fast increasing and extremely significant model organism in the field of vertebrate developmental biology. Since its introduction as a modern experimental model in the early 1980s, researchers have gained valuable insights into vertebrate development. The zebrafish has a variety of traits that make it an excellent organism for researching development in both normal and abnormal settings. Because of its strong genetic and molecular similarities to other vertebrates, including humans, findings in zebrafish development are frequently directly applicable to human biology. This review will emphasize the benefits of using zebrafish as a model system and present instances of how zebrafish research has increased our understanding of human biology.

One of the key reasons why zebrafish are so useful in developmental biology studies is their unusual accessibility during early development. Unlike mammals, zebrafish embryos develop externally, making them visible from the moment of fertilization. Scientists can examine developmental events in real time because the zebrafish embryo and its surrounding chorion, or protective membrane, are transparent. The quick rate of zebrafish development adds to their visual accessibility; embryos hatch within two days of fertilization, and larvae begin feeding independently within five days. During the essential first five days, zebrafish establish all of their major organ systems, which begin to operate shortly after. Zebrafish are a popular model for researching organogenesis, brain development, and cardiovascular development because to their rapid and obvious development.

Furthermore, zebrafish are particularly advantageous because they may breed all year round. Female zebrafish can produce hundreds of embryos per week, providing researchers with a steady and plentiful supply of material for study. The enormous number of children is especially useful for genetic mapping research, which require large sample sizes. Furthermore, zebrafish are easy to keep in high-density tank systems, which take up much less room and cost less than the facilities required to house mammals such as mice or rats. These characteristics make zebrafish an appealing option for researchers seeking to conduct large-scale genetic screens or developmental tests.

Recent technological improvements have increased the potential of zebrafish as a model organism. Innovative imaging tools have enabled scientists to view cellular and molecular processes in unprecedented detail. Furthermore, genetic techniques like CRISPR-Cas9 gene editing have allowed researchers to precisely change specific genes, boosting study into gene function and the molecular pathways underlying development and illness. The capacity to view developmental processes in real time, combined with strong genetic tools, has created new pathways for research in developmental biology, particularly in the study of congenital disorders, cancer, and other problems that affect human development [1, 2, 8].

Fig 1: An image of a zebrafish

Source: https://www.yourgenome.org/theme/model-organisms-the-zebrafish/#:~:text=They%20share%2070%20per%20cent,many%20features%20with%20human%20systems.

Research objectives

- To explore the genomic structure and evolutionary significance of the zebrafish.
- To investigate the role of zebrafish in elucidating the molecular mechanisms of human diseases.
- To examine the application of zebrafish in drug discovery and development.

Research methodology

The purpose of this study was to use secondary data analysis to examine how zebrafish (*Danio rerio*) may be used to better understand human disease mechanisms and medication discovery. Three primary goals, each concentrating on different facets of zebrafish as a model organism, served as the framework for the study. In order to accomplish these goals, we gathered and examined information from earlier research that was published in peer-reviewed journals, Research Gate, academia, Google Scholar, Sodhganga, and Research articles. This allowed us to provide a thorough overview of the genetic, molecular, and therapeutic uses of zebrafish.

This work provides a thorough grasp of how human disease mechanisms and medication discovery relate to the zebrafish model. We made contributions to the larger area of biomedical research by using this study to establish links between zebrafish genetic traits, illness modeling, and the medication development process.

The genomic structure and evolutionary significance of the zebrafish

The genetic structure of the zebrafish (*Danio rerio*) provides exceptional insights into vertebrate biology, owing to structural and functional parallels with the human genome. This similarity is especially significant in the study of human genetics, as roughly 70% of protein-coding human genes have counterparts in the zebrafish genome. Furthermore, zebrafish orthologs exist for 84% of human disease-associated genes. Because of this genetic correspondence, zebrafish are an important model for investigating a wide range of biological processes and disease mechanisms, with the zebrafish genome providing pertinent insights into human health and disease.

One of the most distinguishing properties of the zebrafish genome is its chromosomal conservation with humans, known as syntenic correspondence. In other words, genes that are on the same chromosomes in zebrafish are frequently found on the same chromosomes in humans. This preservation of chromosomal order enables researchers to examine zebrafish genetic activities in a context that is directly relevant to human genetics. Zebrafish's synteny makes them ideal for mapping human genes to their zebrafish counterparts and investigating their functions in development and disease.

Another distinguishing feature of the zebrafish genome is its low number of pseudogenes when compared to humans. Pseudogenes are non-functional DNA segments that mimic functioning genes but lack the ability to encode proteins. Humans have roughly 13,000 pseudogenes, but zebrafish have only 154. This simplified genomic organization is likely to simplify gene functional analysis by reducing the number of pseudogenes to consider when interpreting genetic investigations. This reduction in genomic complexity may also help to improve the effectiveness of genetic manipulations and gene function studies in zebrafish, allowing researchers to better understand the roles of specific genes in development and disease.

Furthermore, the time of DNA replication in zebrafish is closely related to transcriptional activity and epigenetic changes, mirroring similar processes seen in other vertebrates, including humans. In zebrafish, DNA replication control is critical to embryonic development because it maintains appropriate gene expression. Researchers can get significant insights into the molecular mechanisms that drive developmental changes by investigating replication timing in zebrafish, as well as how these processes are regulated at the genetic and epigenetic levels. The relationship between replication time, transcriptional activity, and epigenetic changes in zebrafish is a critical field of study for understanding how genes are activated or repressed at various stages of development [3, 4, 5, 6, 7].

Evolutionary significance

Zebrafish's evolutionary value as a model organism stems from their rapid development and the variety of genetic modification tools accessible for use with them. Zebrafish have evolved a genome that preserves many essential biological activities shared by vertebrates, making them an important tool for studying vertebrate biology and evolution. Their ability to develop quickly and exhibit a wide range of biological processes enables scientists to explore how evolutionary adaptations have affected vertebrate physiology. The conservation of essential genetic pathways, such as those involved in organ development and function, emphasizes the zebrafish's importance in understanding how these systems arose in more complex vertebrates, including humans. As a result, zebrafish have emerged as an essential model for studying evolutionary biology and the genetic basis of species variety.

Developmental Biology

One of the most convincing arguments for utilizing zebrafish in developmental biology research is their capacity to develop quickly, allowing researchers to monitor developmental processes in real time. Zebrafish embryos develop soon after fertilization, and within hours, they show early signs of cell division, organ creation, and differentiation. This offers a rare opportunity to observe these essential processes as they occur. Because of their translucent embryos, scientists can directly study cellular processes including as migration, division, and differentiation without using invasive procedures. This makes zebrafish ideal for researching organogenesis (the production of organs) and cellular differentiation, in which certain cells take on discrete tasks to produce tissues and organs. Furthermore, the capacity to modify genes and see their effects on development in real time has resulted in substantial advances in fields such as brain development, cardiovascular development, and gene expression regulation. As a result, zebrafish serve as an effective model for studying not only normal developmental processes, but also the diseases that might result when these processes fail [6, 7].

Comparative genomics

Zebrafish and humans have a high degree of genetic similarity, making them ideal for comparative genomics, which is the study of genetic similarities and differences between species. Zebrafish have orthologs for around 70% of human protein-coding genes, making them a valuable system for studying the evolution of gene functions. By comparing the zebrafish genome to those of humans and other vertebrates, researchers can uncover key genes implicated in disease processes and gain insight into the molecular pathways that underpin diverse illnesses. Such comparative studies have already uncovered numerous conserved genomic pathways involved in diseases such as cancer, neurological disorders, and cardiovascular issues. Furthermore, zebrafish are a good model for studying evolutionary adaptations since they share many of the same important biological activities as humans while simultaneously exhibiting distinct variances. These distinctions provide a unique viewpoint on how specific genes or pathways have developed to fulfill the needs of various animals over time. By finding these evolutionary adaptations, scientists can gain a greater understanding of how vertebrates evolved to deal with various environmental stressors, as well as how these adaptations may be linked to specific human qualities or disorders [4].

Zebrafish: A Model Organism for Human Diseases

Zebrafish have evolved as an effective and adaptable model organism for researching human diseases, providing researchers with a unique platform to investigate the genetic basis of diverse ailments and test prospective treatment strategies. This is partly owing to the zebrafish's strong genetic similarities to humans, as well as its ease of genetic manipulation. In recent years, zebrafish have gained popularity in biomedical research, particularly in understanding disease mechanisms at the genetic and cellular levels, as well as medication discovery. The capacity to build and study illness models in zebrafish has given us vital insights into human health and opened up new paths for drug development.

Advantages as a model organism

One of the primary advantages of using zebrafish as a model organism is how easily their genomes can be changed. Advanced genetic techniques, including as CRISPR/Cas9 and the Tol2 transposon system, have enabled precise gene editing in zebrafish, allowing the development of extremely specialized disease models that closely resemble human diseases. These techniques enable researchers to add mutations or cure genetic abnormalities, allowing them to explore how these genetic changes influence disease development. This capacity to precisely change genes has been helpful in the development of zebrafish models that mimic human genetic illnesses, allowing for a better understanding of the molecular pathways underlying these conditions. By analyzing the effects of these genetic alterations in real time, researchers can discover new therapeutic targets and investigate prospective treatments.

Another advantage of employing zebrafish is that they are ideal for large-scale phenotypic screening. Zebrafish embryos develop externally and are transparent, allowing researchers to study the morphological and behavioral changes caused by genetic abnormalities. Large-scale genetic screening in zebrafish have identified a number of mutant phenotypes that are similar to human clinical diseases. These screens have yielded crucial information about the genetic basis of diseases like cancer, heart disease, and neurological disorders. By investigating how certain genetic abnormalities impact zebrafish growth and physiology, researchers can find disease pathways and evaluate therapeutic therapies.

Furthermore, zebrafish have substantial advantages in drug discovery. Their physiological processes are extremely comparable to those of humans, making them an ideal model for evaluating pharmaceutical substances. The transparent embryos enable researchers to track the impact of medications on development and organ function in real time, offering quick input on efficacy and toxicity. This makes zebrafish an excellent platform for screening a large number of drug candidates and identifying interesting chemicals that could be developed into therapeutic treatments. In reality, some medications that were discovered to be successful in zebrafish models have advanced to clinical trials, demonstrating the importance of zebrafish in the drug development pipeline [3, 4, 5, 8].

Research Applications

Zebrafish models have helped us gain a better knowledge of many human diseases. For example, in cancer research, zebrafish have been used to model carcinogenesis and test anti-cancer medications. Researchers may produce cancer-like circumstances in zebrafish by adding certain genetic mutations or environmental variables, which allows them to study tumor formation and spread. This has revealed new information about how cancers grow and spread, as well as identified new medication targets for cancer treatment.

Zebrafish have shown to be an essential tool in cardiovascular research, helping to investigate heart development and function. The transparency of zebrafish embryos enables researchers to view the growth of the heart and blood arteries in real time, providing a unique window into cardiac development. This has resulted in the discovery of genes involved in heart creation, as well as a platform for investigating congenital heart anomalies and evaluating possible heart disease treatments.

Zebrafish are an excellent model for studying neurological illnesses, particularly neurodegenerative ones. Their rudimentary nervous system and transparent bodies let researchers can monitor neural development, degeneration, and healing. This has made zebrafish a valuable model for researching disorders like Alzheimer's and Parkinson's, allowing researchers to analyze the molecular pathways underlying brain cell death and test possible medications for delaying or reversing neurodegeneration [4, 9, 10, 11].

The role of zebrafish in elucidating the molecular mechanisms of human diseases

Zebrafish as a model organism in biomedical research

Similarities in Genetics and Manipulation: Due to their striking genetic resemblance to humans, zebrafish are extremely important in scientific research. roughly 80% of the genes associated with human disorders have comparable orthologs in zebrafish, and roughly 70% of zebrafish genes are identical to those in humans. Zebrafish are good models for researching genetic mutations, disease progression, and therapeutic interventions because of their genetic overlap, which enables researchers to develop models that closely resemble human situations. Advanced genetic editing technologies like CRISPR/Cas9 and the Tol2 transposon system have significantly improved the ability to precisely modify the zebrafish genome. Scientists may insert particular mutations into the zebrafish genome thanks to these techniques, which enable precise genetic changes. In this way, scientists can mimic human genetic conditions like muscular dystrophy, Alzheimer's disease, and cystic fibrosis. These models offer a useful platform for evaluating possible treatment approaches and offer a clearer knowledge of how particular genetic changes contribute to disease mechanisms. Additionally, the zebrafish's transparent embryos and quick development allow for the real-time observation of the direct impacts of genetic changes, which facilitates the investigation of gene functions throughout early development and illness onset. The zebrafish is an essential model organism in illness research because of its genetic similarities, robust manipulation capabilities, and real-time observation [3, 12, 13].

Investigating the Pathophysiology of Disease: Because of their transparent embryos, which enable researchers to watch illness progression and developmental processes in real time, zebrafish are very useful for investigating disease pathogenesis. This transparency offers a unique chance to track the effects of mutations on tissue growth, cellular behavior, and organ formation over the course of a person's life. Scientists can monitor disease progression at different stages thanks to the zebrafish's quick and external development, which gives them real-time insights into how environmental influences or genetic abnormalities affect the development of diseases. Mutants that have symptoms similar to human diseases have been found using extensive genetic screening in zebrafish. Finding the genetic pathways underlying diseases including cancer, heart disease, and developmental problems has been made possible thanks in large part to these screens. Zebrafish, for instance, have been used to simulate muscular dystrophy, a hereditary condition marked by the degradation of muscles. Researchers can study the development and progression of the disease by causing mutations in genes linked to muscle function. This allows them to test prospective treatment medicines and gain a clearer knowledge of the mechanisms at work.

Furthermore, zebrafish models are useful for researching infectious disorders because they provide a dynamic environment for analyzing host-pathogen interactions. Because zebrafish allow researchers to see firsthand how infections interact with the human immune system, they have been utilized to study diseases like tuberculosis (TB). The zebrafish's transparent body allows researchers to track pathogen behavior and immunological reactions in real time, including how the germs alter host cell functions or avoid immune detection. This capacity aids in the identification of possible treatment targets and improves our comprehension of disease mechanisms, especially in relation to chronic infections. In addition to offering important insights into microbial pathogenesis, the zebrafish's capacity to imitate infectious disorders enables the quick testing of immune-modulating and antimicrobial medications. This real-time monitoring of the pathogen's and host's behavior during infection offers a crucial tool for creating novel treatments to fight infectious diseases [12, 13, 14].

Identifying Therapeutic Targets: In addition to being helpful for comprehending disease causes, the zebrafish model is essential for medication testing and discovery. The high-throughput screening of possible medicinal substances is made possible by the ability to quickly produce huge numbers of genetically engineered zebrafish. By evaluating medications' safety and effectiveness in vivo, researchers can get important information that can guide clinical trials.

For example, research has shown that zebrafish can be used to test novel medications on particular genetic abnormalities associated with diseases like as metabolic disorders and cancer. The knowledge gathered from these investigations is essential for creating tailored treatments that target the molecular causes of human illnesses [3, 12, 13].

The application of zebrafish in drug discovery and development

The unique biological traits of zebrafish, along with the potential of functional genomics and high-throughput screening (HTS) technologies, have made them indispensable in drug discovery and development. The zebrafish model has significantly advanced personalized medical techniques, improved drug testing procedures, and helped discover new therapeutic targets. Researchers can monitor drug efficacy and toxicity, expedite the preclinical stages of drug discovery, and more efficiently investigate treatment possibilities by utilizing the biological advantages of zebrafish and new technology advancements.

Zebrafish Benefits for Drug Discovery

Particularly for extensive screening and drug testing, zebrafish provide a number of strong benefits over conventional mammalian models. Their cost-effectiveness is one of the biggest advantages. Compared to mammalian models, zebrafish are comparatively cheap to keep and breed, and each mating can result in hundreds of embryos. Because of this high rate of reproduction, scientists can conduct comprehensive drug screenings—which necessitate huge sample sizes in order to produce statistically meaningful results—without having to pay the exorbitant fees associated with mammalian research. Zebrafish embryos' transparency, which permits real-time observation of interior activities, is a crucial benefit. Because it enables researchers to observe how medications impact individual organs and systems during early development without invasive procedures, this transparency is especially beneficial in the drug discovery process. The accuracy of medication toxicity and efficacy evaluations is improved by the ability to immediately see drug effects on organogenesis, blood flow, and neural development in zebrafish embryos by real-time imaging. Extremely susceptible to genetic modification, such as CRISPR/Cas9 gene editing methods. This capacity to precisely alter genes makes it easier to create illness models that closely resemble real-world situations. This helps researchers understand how genes function in biological systems and evaluate the impact of drugs on certain genetic alterations.

By facilitating in-depth investigations of gene function, target identification, and validation, functional genomics methods have completely transformed the use of zebrafish in drug discovery. Forward and reverse genetics are two crucial methods that are essential for determining the genes and pathways involved in different disease processes. By causing random mutations and tracking the resulting symptoms, forward genetics can identify genes linked to human diseases that were previously unknown. By examining mutations that result in particular disease characteristics in zebrafish, researchers can find possible treatment targets.

On the other hand, reverse genetics allows researchers to target individual genes for deletion or mutation, making it easier to examine how certain genes operate and how they relate to disease. In this context, the potent gene editing tool CRISPR/Cas9 technology has had a particularly significant influence. Because CRISPR/Cas9 makes it possible to precisely modify zebrafish DNA, researchers can accurately mimic human genetic abnormalities in the zebrafish model. This accuracy in gene editing aids in both verifying therapeutic targets and assisting researchers in determining the genetic roots of disorders. Drug development for illnesses with known genetic causes can be advanced by scientists by developing zebrafish models that replicate particular human genetic mutations and examining the effectiveness of medications intended to target those abnormalities [15, 16, 17, 18, 19].

High-Throughput Screening (HTS) for Zebrafish Models

High-throughput screening (HTS) technologies have revolutionized drug development by allowing for the quick testing of thousands of chemicals in zebrafish models. This method is critical for identifying beneficial molecules early in the drug development process, hence shortening the road from research to viable treatments. Automated screening platforms, such as ARQiv-HTS, represent a significant advance in HTS. These platforms enable researchers to test thousands of zebrafish embryos at once, employing modern imaging and quantification techniques to assess medication impacts on diverse phenotypes. For example, ARQiv-HTS can evaluate nearly half a million transgenic zebrafish larvae in a single session, providing a scalable and effective method for monitoring a wide range of biological reactions to medications. The automation and large capacity of such platforms allow researchers to test many compounds in a cost-effective and time-efficient manner, which is critical for narrowing down drug candidates early in the drug development pipeline.

Another significant feature of zebrafish HTS is phenotypic drug screening, which allows researchers to monitor the impact of pharmacological molecules on living creatures in real time. This method provides crucial insights into drug efficacy and toxicity by evaluating phenotypic changes in entire organisms rather than isolated cells. As a result, phenotypic screening in zebrafish frequently detects both therapeutic advantages and potential side effects of compounds considerably sooner than previous approaches, enhancing the overall safety and efficacy of medication candidates. By monitoring how these substances affect complex physiological systems, researchers acquire insights that are frequently more relevant to human biology than *in vitro* methods [15, 20, 21].

Identifying Novel Drug Targets using Zebrafish Models

The combination of functional genomics and HTS in zebrafish models has sped the discovery of new therapeutic targets, as zebrafish genetics allow for quick alteration and screening. Zebrafish genetic screenings have identified mutations associated to a variety of human diseases, directly aiding target validation by exposing particular pathways and molecular targets involved in disease processes. This target identification is critical for drug discovery since it narrows the potential processes that medicines should target. Mutations found in zebrafish that are linked to human ailments, for example, have led to the discovery of genes and pathways directly implicated in disease pathology, presenting clear targets for therapeutic intervention.

Furthermore, zebrafish are excellent disease models because they provide an in vivo environment that mimics a variety of human ailments, including cancer, cardiovascular disease, and neurological problems. illness models in zebrafish are useful because they allow researchers to watch illness progression and test potential therapies in a living organism with complex systems similar to those in humans. This feature is especially useful since it offers information on how possible pharmaceuticals interact with numerous biological systems, thereby ensuring that therapeutic results are delivered without undesired side effects. The ability to create zebrafish models of human diseases and then test drugs in these models greatly advances our understanding of how drugs interact with living systems, making zebrafish an invaluable tool for identifying and validating drug targets early in the drug discovery process [15, 16, 17, 22].

Using Zebrafish Models to Advance Personalized Medicine

Zebrafish models have also shown promise for the progress of personalized medicine, particularly in terms of providing individualized therapeutic insights based on specific patient data. By adding patient-specific genetic mutations into zebrafish models, researchers can analyze treatment reactions in a manner that is tailored to the genetic profile of particular patients. These patient-derived models help researchers understand how certain genetic backgrounds may influence drug efficacy or resistance, allowing them to develop treatment regimens that are more appropriate for specific patient populations. The use of zebrafish in this context promotes the creation of more effective, individualized treatments, indicating a move toward more personalized methods to drug discovery.

Furthermore, zebrafish are extremely effective in predictive toxicology, allowing researchers to examine possible toxicities in drug candidates before they enter clinical trials. Studies have demonstrated that zebrafish can anticipate toxicity liabilities with more than 80% accuracy, which is equivalent to more established mammalian models. Zebrafish's quick life cycle and translucent embryos enable for the easy detection of toxic effects in organs and tissues, typically within days. This capacity allows researchers to detect and remove compounds with significant toxicity risks early in the drug development process, thereby improving drug safety and minimizing the likelihood of late-stage clinical trial failures. Thus, zebrafish predictive toxicology is a crucial step in the early safety assessment of new drug candidates, making a substantial contribution to personalized medicine by identifying safer medications that are more matched to individual patient needs [17].

Discussion

The zebrafish model has proven beneficial in biomedical research, providing insights into genetic, developmental, and disease-related mechanisms similar to human biology. Zebrafish's utility stems mostly from its genetic resemblance to humans, since around 70% of human protein-coding genes have a zebrafish homologue. This genetic alignment makes zebrafish an effective tool for investigating the genetic and molecular basis of many illnesses. Rapid development, transparency during embryogenesis, and accessibility of genetic manipulation are all significant advantages, providing unique real-time insights into gene function and disease progression. The zebrafish model, in particular, allows researchers to explore organogenesis, cellular differentiation, and disease etiology with greater speed and clarity than mammalian models.

Zebrafish's high-throughput screening (HTS) capabilities enable quick testing of therapeutic candidates, resulting in the identification of interesting molecules. Researchers can use modern techniques like CRISPR/Cas9 to produce precise genetic abnormalities in zebrafish, resulting in models for diseases including muscular dystrophy, Alzheimer's disease, and numerous malignancies. This functional genomics method not only improves our understanding of gene-disease interactions, but it also speeds up the identification of therapeutic targets and medication candidates. Furthermore, the cost-effectiveness and ease of zebrafish upkeep make them a viable option for large-scale screenings, potentially replacing or supplementing mammalian models in early drug discovery.

Conclusion

zebrafish offer a reliable, efficient, and cost-effective model for investigating human illnesses and medication discovery. Zebrafish are indispensable for translational research due to their genetic and developmental parallels with humans, as well as their simplicity of use in genetic manipulation and real-time observation. The model has provided valuable insights into disease molecular pathways, as well as accelerated drug development through high-throughput screenings and personalized medicine applications. Zebrafish research will play an increasingly important role in understanding complicated disease causes and creating new therapeutics as modern genomes and imaging technologies are integrated. This model organism has enormous potential for contributing to personalized medicine by offering patient-specific models that can lead individualized therapeutic methods, emphasizing zebrafish's vital role in the future of biomedical science and drug development.

References

1. Veldman MB, Lin S. Zebrafish as a developmental model organism for pediatric research. Pediatr Res [Internet],2008:64(5):470–6. Available from: https://www.nature.com/doifinder/10.1203/PDR.0b013e318186e609
2. Choe S-K, Kim C-H. Zebrafish: A powerful model for genetics and genomics. Int J Mol Sci [Internet],2023:24(9):8169. Available from: https://www.mdpi.com/1422-0067/24/9/8169
3. Biobide. Zebrafish model for human disease, 2024. Available from: https://biobide.com/zebrafish-model-for-human-disease
4. Sci. news. Zebrafish genome found strikingly similar to humans, 2013. Available from: https://www.sci.news/genetics/article01036.html
5. Martínez M. Zebrafish as a translatable model system, 2021. Available from: https://www.zeclinics.com/blog/zebrafish-as-a-translatable-model-system/
6. Siefert JC, Georgescu C, Wren JD, Koren A, Sansam CL. DNA replication timing during development anticipates transcriptional programs and parallels enhancer activation. Genome Res [Internet],2017:27(8):1406–16. Available from: http://genome.cshlp.org/lookup/doi/10.1101/gr.218602.116
7. Kaaij LJT, van der Weide RH, Ketting RF, de Wit E. Systemic loss and gain of chromatin architecture throughout zebrafish development. Cell Rep [Internet],2018:24(1):1-10.e4. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2211124718308982
8. Hong T, Park J, Song G, Lim W. Brief guidelines for zebrafish embryotoxicity tests. Mol Cells [Internet],2024:47(8):100090. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1016847824001158
9. Al-Thani HF, Shurbaji S, Yalcin HC. Zebrafish as a model for anticancer nanomedicine studies. Pharmaceuticals [Internet],2021:14(7):625. Available from: https://www.mdpi.com/1424-8247/14/7/625
10. Hason M, Bartůněk P. Zebrafish models of cancer—new insights on modeling human cancer in a non-mammalian vertebrate. Genes (Basel) [Internet],2019:10(11):935. Available from: https://www.mdpi.com/2073-4425/10/11/935
11. Shen Y, Sheng R, Guo R. Application of zebrafish as a model for anti-cancer activity evaluation and toxicity testing of natural products. Pharmaceuticals [Internet],2023:16(6):827. Available from: https://www.mdpi.com/1424-8247/16/6/827
12. Phillips JB, Westerfield M. Zebrafish models in translational research: tipping the scales toward advancements in human health. Dis Model Mech [Internet],2014:7(7):739–43. Available from: https://journals.biologists.com/dmm/article/7/7/739/3691/Zebrafish-models-in-translational-research-tipping
13. Choi T-Y, Choi T-I, Lee Y-R, Choe S-K, Kim C-H. Zebrafish as an animal model for biomedical research. Exp Mol Med [Internet],2021:53(3):310–7. Available from: https://www.nature.com/articles/s12276-021-00571-5
14. Varela M, Meijer AH. A fresh look at mycobacterial pathogenicity with the zebrafish host model. Mol Microbiol [Internet],2022:117(3):661–9. Available from: https://onlinelibrary.wiley.com/doi/10.1111/mmi.14838
15. Dash SN, Patnaik L. Flight for fish in drug discovery: a review of zebrafish-based screening of molecules. Biol Lett [Internet], 2023, 19(8). Available from: https://royalsocietypublishing.org/doi/10.1098/rsbl.2022.0541
16. Zon LI, Peterson RT. In vivo drug discovery in the zebrafish. Nat Rev Drug Discov [Internet],2005:4(1):35–44. Available from: https://www.nature.com/articles/nrd1606
17. Cornet C, Di Donato V, Terriente J. Combining zebrafish and CRISPR/Cas9: toward a more efficient drug discovery pipeline. Front Pharmacol [Internet], 2018, 9. Available from:

https://www.frontiersin.org/article/10.3389/fphar.2018.00703/full
18. Cassar S, Adatto I, Freeman JL, Gamse JT, Iturria I, Lawrence C, *et al*. Use of zebrafish in drug discovery toxicology. Chem Res Toxicol, 2020.
19. Stern HM, Zon LI. Cancer genetics and drug discovery in the zebrafish. Nature Reviews Cancer, 2003.
20. White DT, Eroglu AU, Wang G, Zhang L, Sengupta S, Ding D, *et al*. ARQiv-HTS, a versatile whole-organism screening platform enabling *in vivo* drug discovery at high-throughput rates. Nat Protoc [Internet],2016:11(12):2432–53. Available from: https://www.nature.com/articles/nprot.2016.142
21. Lubin A, Otterstrom J, Hoade Y, Bjedov I, Stead E, Whelan M, *et al*. A versatile automated high-throughput drug screening platform for zebrafish embryos [Internet], 2020. Available from: http://biorxiv.org/lookup/doi/10.1101/2020.12.16.423108
22. Angom RS, Nakka NMR. Zebrafish as a model for cardiovascular and metabolic disease: the future of precision medicine. Biomedicines [Internet],2024:12(3):693. Available from: https://www.mdpi.com/2227-9059/12/3/693