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Vital A Fish: A Critical Review of Zebrafish Models in Disease Scenario and Case Reports Screens

Hayati Önemde Bir Balık: Hastalık Senaryolarında Zebra Balığı Modelinin Kullanıldığı Kritik Araştırmalar ve Vaka Raporlarının Taraması

Nurdan FİLİK

Süleyman Demirel University, Isparta, Turkey.

ABSTRACT

Virtually every major medical advance of the last century and at still has depended upon research with animals. Zebrafish's journey from the ocean to the laboratory leads to major scientific breakthroughs. Transparency structure of zebrafish helps in monitoring their internal structures and are permitting scientist to see effects of nano particles in fish. Their organs share the same main features as humans and so can be used to study human developmental processes. Zebrafish congruence 70% of their genes with humans, and 84% of ailment-depended genes have zebrafish congruence. The zebrafish embryos can also genetically modified. Certain fishes like zebrafish are able to regenerate damaged retinal nerve cells. Müller glial cells in retina of zebrafish can transform in response to injury and act like stem cells to regrow the retina and replace all damaged neurons. Though humans have the same exact Müller glial cell, they don't respond to damaged in the same way. Zebrafish are also very responsive to having their genomes edited. Zebrafish regenerate some tissue such as heart in during larval stage. In additionaly zebrafish are used as an animal model to study pharmocology – how drugs work and what they do to an organism's body. Aim of this review current knowledge of how these specialized structures and model organism by focusing on cellular behaviors and molecular mechanisms, highlighting findings from in vivo models and briefly discussing the recent advances in tissue cell culture and organoids. Review discusses the applications of human organoids models of disease on model organism and outlines the ailment treatments.

Keywords: Model organism, Zebrafish, Disease scenario, Case report screen, Diseases controlling.

ÖZ

Geçen yüzyılın ve halen de tıbbi gelişmelerin neredeyse tamamı hayvanlar üzerinde yapılan araştırmalara dayalıdır. Zebra balığının okyanustan laboratuvara olan yolculuğu büyük bilimsel buluşlara yol açar. Zebra balığının şeffaf yapısından dolayı iç organlarının izlenmesine yardımcı olur ve bilim adamlarının balıklardaki nano parçacıkların etkilerini görmesine olanak tanır. Organları insanlarla aynı temel özellikleri paylaşıyor ve bu nedenle insanın gelişim süreçlerini incelemek için kullanılabilir. Zebra balığı genlerinin %70'i insanlarla uyum gösterir ve hastalığa bağlı genlerin %84'ü zebra balığı uyumuna sahiptir. Zebra balığı embriyolarının genetiği de değiştirilebilir. Zebra balığı gibi bazı balıklar, hasar görmüş retina sinir hücrelerini yenileyebilir. Zebra balığının retinasındaki Müller galia hücreleri, yaralanmaya yanıt olarak dönüşebilir ve retinayı yeniden büyütmek ve tüm hasarlı nöronları değiştirmek için kök hücreler gibi davranabilir. İnsanlar aynı Müller galia hücresine sahip olsalar da, hasara aynı şekilde tepki vermezler. Zebra balığı aynı zamanda genomlarının düzenlenmesine de oldukça duyarlıdır. Zebra balığı larva döneminde kalp gibi bazı dokuları yeniler. Ayrıca zebra balığı, ilaçların nasıl çalıştığı ve organizmanın vücuduna yaptığı farmakolojik etkiyi incelemek için bir hayvan modeli olarak kullanılıyor. Bu derlemenin amacı, burada, hücresel davranışlara ve moleküler mekanizmalara odaklanarak, in vivo modellerden elde edilen bulguları vurgulayarak ve doku hücre kültürü ve organoidlerdeki son gelişmeleri kısaca tartışarak, bu özelleşmiş yapıların ve model organizmanın nasıl olduğuna dair mevcut bilgileri gözden geçirmektir. Derleme, insan organoid hastalık modellerinin model organizma üzerindeki uygulamalarını tartışmakta ve hastalık tedavilerinin ana hatlarının altını çizmektedir.

Anahtar Kelimeler: Model organizma, Zebra balığı, Hastalık senaryosu, Vaka raporu taraması, Hastalıkların kontrolü

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Sorumlu Yazar/Corresponding author: Nurdan Filik
E-mail: nurdanfilik@sdu.edu.tr

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Introduction

''Zebrafish are used as a model for typical and atypical human development. It is surprising how much we have in common with zebrafish'' says the NIH. In accompanying manuscript, outlined for using zebrafish models to research human ailments. The use of classical animal model systems and cell line in research during the late twentieth and early twenty-first centuries has been successful in major fields, such as improving of cellular signalling pathways, discovery drug targets and guiding design of candidate drugs for infectious disease (Klein et al., 2002). Model organisms that are produced under in vitro conditions and are easy to produce, have a short generation interval, have experimental advantages, are suitable for laboratory environments, and are used to investigate biological events, especially diseases (Kim et al., 2020).

In recent years, vertebrate model organisms have been frequently used in many studies in biological, genetic, pharmacological and toxicological fields (Kayhan et al., 2018). Selected species which as model organisms has been widely studied because of it is easy to maintain and propagate in laboratory and has certain experimental advantages. This models are non-human species used in the laboratory to help scientists understand biological processes (Jennings, 2011). Model organisms are used to create highly detailed genetic maps. Genetic maps are a visual representation of the location of different genes on a chromosome. Model organisms are widely used to study human diseases when human experiments are not possible or unethical. Research using animal models has been at the heart of many successes of modern medicine. They play important roles in fields such as neuroscience and infectious diseases, contributing much of the fundamental knowledge in fields such as human physiology and biochemistry (Fishmann, 1999; Sprague et al., 2007).

Escherichia coli, *Cavia porcellus*, T4 Phage virus, Phage lambda, Bacteriophage are other examples of model organisms (Pandey, 2011; Podlacha et al., 2021). Following the discovery that non-human creatures have very similar biological mechanisms to humans, it has been realized that we can have reliable ideas about the effects on humans by using newly produced technologies (vaccines, drugs, poisons, food, etc.) on other living creatures before humans. Also plays a key role in toxicology studies and drug screening (Swabe, 2002).

Of course, the creatures used when performing these tests cannot be chosen randomly; creatures that meet certain criteria must be selected. These creatures used in experiments and research are called "model organisms". A living being; It can be chosen as a model organism because it reproduces quickly, is easy to observe, is easy to care for, is widely available in sellers or in nature, or is similar to humans. The most famous model organism used in experiments is mice. There is even a laboratory mouse monument in Russia to show gratitude for the contributions of mice to science.

Recently, researchers have developed zebrafish models for human viral diseases, suffering new insights into molecular mechanisms of human viral agents as well as discovery of antiviral strategies. The zebrafish model has become model system for understanding host-virus interaction. Review of Liu et al., 2024 provides a comprehensive summary of use of zebrafish models in human viral research (Liu et al., 2024).

While mice are evolutionarily more similar to humans because they are mammals, Zebrafish (Danio rerio) have other advantages than just being transparent. One important advantage of zebrafish is that the adults are small and prefer to be housed in large groups. As a result, they require much less space and are cheaper to maintain than mice (Tarique et al. 2023). Zebrafish adults can lay hundreds of eggs every week which means that researchers have many them to work with. In addition, zebrafish development is rapid, so they reach their basic body structure within one day. Early zebrafish embryos are transparent, which makes it easy to visualise specific biological processes at minute details happening in real-time.

Zebrafish is animal model organism used extensively in developmental research. Althought it began to be used in the 1960s, it is only since the 1990s/2000s that it obtained a huge fame. The first to use this animal for research was George Streisinger, a tropical fish enthusiast at the University Oregon.

In this paper, 'model system' refers to a biological system, such as a type of cell, tissue, organ, organism, etc. that is studied to learn about a phenomenon of interest (Ankeny and Leonelli, 2011). In this review, we will review the recent findings made to elucidate the mechanisms involved in model organism. In addition to this, we will describe the neuronal structure and function of the fish, in order to further unravel how zebrafish plays a role in human diseases.

Zebrafish

The outher skin layer of the zebrafish larva forms a mosaic of mainly hexagonal cells showing a unique pattern of actin ridges.

Being easy to observe is also important in choosing a model organism. Although the adults of zebrafish are yellow-silver with blue stripes (jellyfish genes have resulted in colors such as pink, red, blue, yellow and orange that glow in dark), their offspring are transparent. Even if an experiment is carried out on internal organs, necessary observations can be made without the need to kill and open the animal. In this way, the results of the tests can be examined even while the embryo is developing. Zebrafish are excellent examples for genetic experiments and are frequently used because they can be seen from the outside at the cellular level to see what is going on inside fish.

Another reason why zebrafish are widely used in research is our detailed knowledge of their genomes and their genetic similarities to humans. Since their entire genome has been analyzed, zebrafish are one of the first stops for genetic researchers. Of course, this is not the only advantage. Human genome and zebrafish genome are 70% identical, and 84% of the genes that cause diseases in humans are also found in Zebrafish (McKie, 2013).

These surprisingly high genetic similarities, along with the other features we mentioned, make zebrafish a gem in genetic and medical research. Although many organisms can be used in certain experiments and in narrow areas, the convenience provided by zebrafish is increasing their prevalence of use, as can be seen from the graph below (Teame, et al. 2019).

On Case Report: Model Organism Zebrafish

Zebrafishes are important model organism for studying different biological processes. Information obtained from these studies helps scientist to understand disorders in humans, since many of these processes are similar in humans.

Zebrafish is a go to model organism for many experiments, particularly when studying development. One feature in particular can teach us a lot of about things like cellular communication and movement. The feature Posterior Lateral Line primordium (PLLp). The PLLp is a tight cluster of ~100 cells found behind the ear of a young zebrafish embryo. This cluster beraks away and migrates from the head to the tip of the tail. On its travels, it drops off cells that will become neuromasts, types of neurons that can sense movement in water. Scientists observed how cells in the PLLp would behave when they changed the tissues surrounding them. They found that the promordium cells weren’t able to properly coordinate their movements without there being overyling skin cells. The outermost cells of the primordium need to attach and wrap around skin cells in order to pull the cluster through the body (Calderon-Zavala, 2019; Pathak and Barresi, 2020; Yoshida, 2023).

Investigating the development of blood and lymhatic vessels in the zebrafish eye provides insights into human eye disorders and helps suggest potential avenues for treatment (Yang et al., 2016).

Zebrafish larvae are transparent and so make an excellent experimental model for neurodegenerative diseases, such as ALS. Jeremy Linsley, a postdoctoral scholar in Steve Finkbeiner’s laboratory, uses 3D reconstructions of labelled (red) motor neurons to study neurodegeneration in a live zebrafish larvae (Chia et al., 2022).

Transformation of heart from tube to organ needs orchestration of morphogenetic processes. Two structures critical for cardiac function, the cardiac valves and the trabecular network, are formed through extensive tissue morphogenesis endocardial cell migration, deadhesion and differentiation into fibroblast-like cells during valve formation, and cardiomyocyte delamination and apico-basal depolarization during trabeculation (Collins and Stainier, 2016). In the Priya Lab, they use zebrafish to study heart development. The basic layout and cellular makeup of the zebrafish heart are very similar to that of the human heart, and with their research they aim to understand the cell and tissue organisational principles that make a healthy, beating heart (Gunawan et al., 2021). Even in the case of ‘’heartbreak’’, zebrafish can recover through heart regeneration. Unlike humans, zebrafish form new cells called cardiomyocytes, generating heart contraction and enabling a robust comeback. Zebrafish studies provide precious insights for developmental and regenerative biology of heart and cardiovascular diseases treatment (Bournele and Beis, 2016).

Sciencist Norine VOISIN works with intellectually disabled patients who have also other symptoms such as morphological defects. Exome sequencing revealed that mutations in a gene called AFF3 are present in 11 patients with similar symptoms. Fortunately this gene is both present in human and zebrafish, which allowed Norine VOISIN to study its function directly in a laboratory. She suspected that accumulation of AFF3 protein causes bone malformations in patients. So how did she test her hypothesis? Zebrafish is a great model to study developmental diseases since it develops externally, very fast and its organs are transparent! This allows scientist to observe morphological defects at early stages in the development. In order to over Express a gene, one could inject mRNA directly at in Zebrafish eggs, or use morpholinos in order to knock down a spesific gene. Moreover, with CRISPR/Cas9 system it is possible to delete a region, include a spesific mutation or even insert a gene cassette in a desired location in the genome. Injecting human AFF3 mRNA into zebrafish embryos led to high expression of AFF3 protein from early stages of development. As she initally suspected. AFF3 protein accumulation caused developmental defects in zebrafish. So what is this AFF3 It is a member ALF protein family and it regulates transcription of certain genes through facilitating transcription elongation. In contrast to earlier studies on ALF proteins, Norine VOISIN's finding indicate that they are not redundant and might be associated with different developmental disorders (Voisin, 2019).

Worldwide visual ailments effect over 160 million people, of whom 37 million are blind. Major causes of eyes disorders are consist of cataracts, glaucoma, retinopathy and macular degeneration. Model organisms with similar physiology to humans are vital to understand underlying developmental processes, discovery causative genes for human visual disorders, and develop drug. Because of Zebrafish eye is so similar to a human eye, it's used to study human ocular development and diseases (Bibliowicz et al., 2011).

Hearing and balance scientists use the zebrafish for easy. Access to its sensory hair cells, located not only in their inner ear, like humans, but also along the length of their body. Hair cells help fish hear and balance upright in the water and also defect water flow (Nicolson, 2017).

In fact, research using zebrafish is everywhere in modern life, although we may not realize it. Examples of areas where zebrafish are used include development, genetics, immunity, behavior, physiology, and nutrition. They are a treasure trove for medical research. Areas of use include nervous disorders, infectious diseases, cardiovascular diseases, kidney diseases, diabetes, blindness, deafness, digestive disorders, hematopoiesis and muscle disorders (Teame, et al. 2019).

For example, it is hoped that the cell renewal abilities of zebrafish, which can even regenerate heart cells, can be transferred to humans (Major, et al. 2007). Likewise, it may be possible to transfer some features found in zebrafish to humans for the treatment of Alzheimer's disease. In fact, it is thought that the recent discovery that zebra fish can hibernate and protect themselves from the physiological effects of radiation may realize the idea of hibernating people when sending them to Mars or beyond (Biswas, 2021). Aside from the benefits of zebrafish to humans, they even help us unravel the evolutionary process. In studies conducted with mutant zebrafish, it was determined which genes may have played a role in the evolutionary transition from fin to limb (Hawkins, et al. 2021).

Although humans may appear to be extremely different than zebrafish, we are actually much more similar to them! In fact, 70% of human genes are found in zebrafish (Shrivastav, 2023). Moreover, zebrafish have two eyes, heart, brain, a mouth, spinal cord, muscle, kidney, pancreas, liver, intestine, blood, bile ducts, oesophagus, ear, nose, bone, teeth, and cartilage (Doiphode et al., 2021; Lin et al., 2022). Many of genes and critical pathways that are required to grow these features are highly conserved between humans and zebrafish (Dodd et al., 2000).

They have the amazing ability to heal the heart after various types of heart injuries. This ability is particularly interesting to scientists as they can produce new heart cells, which humans cannot! Scientists are looking in to this phenomenon as a means of mending our ‘’broken’’ hearts.

It is also a widely used model in pharmacological research. The drug 'verapamil', which is used against hypertension by causing the vessels to relax and the heart rate to decrease, was tested on zebrafish (Justis, 2020).

Conclusions

Transparent as a zebrafish. This suprising although undeniably true expression is not yet part of the common language. But to see how neurobiologists are fascinated by the case of this little vertebrate, it soon will be. Indeed, scientists see it as a model system for studying the transmission of information in the brain and spinal cord. Fluorescent markers present in the nervous system of the larva draw a colorful Picture looking like a Rorschach test (Gomes Da Silva Martinho, 2019).

Zebrafish is a common and useful scientific model organism for studies of brain disorders. Zebrafish models are used to stimulate the pathology of Alzheimer's disease, Parkinson's Disease, stroke, brain, epilepsy, multiple sclerosis or amyotrophic lateral sclerosis. This organism possesses numerous advantages: its development is very rapid, its genome has been fully sequenced, and it has a high physiological and genetic homology to humans (Han and Jiang, 2021). Drug discovery for Alzheimer's disease are complex due to the higher failure rate in drug process. Zebrafish is vital model for neurodegenerative and other research due to clearly visible forms. Cholinergic and glutaminergic pathways responsible for memory are present in zebrafish participate for transmission process. So, should be studying neurotoxic agents that induce dysfunction of memory neurons in zebrafish (Thawkar and Kaur, 2021).

Applying recent single-cell and labelling technologies to zebrafish, Saunders et al. generated a single-cell transcriptional atlas of 3.2 million cells from 1,812 developing zebrafish embryos, with 23 genetic perturbations across 19 timepoints (Li, 2024).

Most tissues in our faces, like our cheekbones, nose cartilage and teeth, were formed from a unique cell population called the neural crest. These cells are usuall in both their origin and their ability to from a huge range of anatomical structures. Despite their intriguing abilities, we still do not know all of the neural crest derivatives of now they form (Terrazas et al., 2017). In a new study, researchers provide significant insights into neural crest cells in zebrafish, revealling key factors involved in cell fate. The team achieved this by creating a new type of computational analysis called Constellations (Burton and Burgess, 2023). This tool helps visualise tissue changes and can predict the future of the cells as well as their developmental fate (Rocha et al., 2020).

Overall, comparing cortical and acortical rodent models with naturally acortical zebrafish reveals both distinct and overlapping contributions of neocortex and 'precortical' zebrafish telencephalic regions to brain functions. Albeit morphologically different, mammalian neocortex and fish pallium may possess more functional similarities than it is presently recognized, calling for further integrative research utilizing both cortical and acortical vertebrate model organisms (Zabegalov et al., 2024).

There are, of course, important differences between zebrafish and human metabolism. Also, as can be understood from the striking concepts here, this tiny organism accomplishes great things.

Researchers using zebrafish as a model organism to model human diseases should consider these major differences between zebrafish and humans and should consider that zebrafish cell and tissue physiology may not fully reflect mammalian and human physiology conditions and use caution when interpreting findings.

This paper will argue that model organisms are the key components of a unique and distinctively biological way of doing research. Although it is still in development, zebrafish model organism-based diagnosis and treatment crossing strategies will play an increasingly important role in treating vital diseases such as brain diseases.

Ocean tiny organism zebrafish is an important fish in the scientific platform and is frequently used as a vertebrate model organism in genetic and experimental research. It has many homologous genes with the human genome. For this reason, they can be used in experiments that cannot be investigated on humans.

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References

Ankeny, R. A., & Leonelli, S. (2011). What's so special about model organisms?. *Studies in History and Philosophy of Science* Part A, 42(2), 313-323. https://doi.org/10.1016/j.shpsa.2010.11.039.

Bibliowicz, J., Tittle, R. K., & Gross, J. M. (2011). Toward a better understanding of human eye disease: Insights from the zebrafish, Danio rerio. *Progress in molecular biology and translational science*, 100, 287-330. https://doi.org/10.1016/B978-0-12-384878-9.00007-8.

Biswas. J. (2021). Tiny zebrafish can help humans reach mars someday; here's how [New Study]. (21 Mayıs 2021). By Jeevan Biswas May 21, 2021 22:12 IST, Access of Date: 12.12.2021. *International Business Times*, https://www.ibtimes.co.in/tiny-zebrafish-can-help-humans-reach-mars-someday-heres-how-new-study-836571.

Bournele, D., & Beis, D. (2016). Zebrafish models of cardiovascular disease. *Heart failure reviews*, 21, 803-813. https://doi.org/10.1007/s10741-016-9579-y.

Burton, E. A., & Burgess, H. A. (2023). A critical review of zebrafish neurological disease models− 2. application: functional and neuroanatomical phenotyping strategies and chemical screens. *Oxford Open Neuroscience*, 2, kvac019. https://doi.org/10.1093/oons/kvac019.

Calderon-Zavala, A. (2019). Examining lateral line development through CXCL14 modulation of CXCL12-CXCR4 mediated gene expression in Danio rerio.

Chia, K., Klingseisen, A., Sieger, D., & Priller, J. (2022).

Zebrafish as a model organism for neurodegenerative disease. *Frontiers in Molecular Neuroscience*, 15, 940484.

Collins, M. M., & Stainier, D. Y. (2016). Organ function as a modulator of organ formation: lessons from zebrafish. *Current topics in developmental biology*, 117, 417-433. https://doi.org/10.1016/bs.ctdb.2015.10.017.

Dodd, A., Curtis, P. M., Williams, L. C., & Love, D. R. (2000). Zebrafish: bridging the gap between development and disease. *Human molecular genetics*, 9(16), 2443-2449. https://doi.org/10.1093/hmg/9.16.2443.

Doiphode, P., Bhosale, U., & Doiphode, P. (2021). Use of Laboratory Animals in Biomedical Research. *Medical Journal of Basic and Applied Research.*

Fishman, M. C. (1999). Zebrafish genetics: the enigma of arrival. *Proceedings of the National Academy of Sciences*, 96(19), 10554-10556. https://doi.org/10.1073/pnas.96.19.10554.

Gomes Da Silva Martinho, R. (2019). Genetic and functional analyses of the developing asymmetric zebrafish habenula (Doctoral dissertation, UCL (University College London)).

Gunawan, F., Priya, R., & Stainier, D. Y. (2021). Sculpting the heart: Cellular mechanisms shaping valves and trabeculae. *Current Opinion in Cell Biology*, 73, 26-34. https://doi.org/10.1016/j.ceb.2021.04.009.

Han, L., & Jiang, C. (2021). Evolution of blood–brain barrier in brain diseases and related systemic nanoscale brain-targeting drug delivery strategies. *Acta Pharmaceutica Sinica B*, 11(8), 2306-2325. https://doi.org/10.1016/j.apsb.2020.11.023.

Hawkins, M. B., Henke, K., & Harris, M. P. (2021). Latent developmental potential to form limb-like skeletal structures in zebrafish. *Cell*, 184(4), 899-911. doi: 10.1016/j.cell.2021.01.003.

Jennings, B. H. (2011). Drosophila–a versatile model in biology & medicine. *Materials today*, 14(5), 190-195. https://doi.org/10.1016/S1369-7021(11)70113-4.

Justis, B. S. (2020). Elucidating the Developmental Defects in Zebrafish Associated With the Cardiac Drug Verapamil. MSU Graduate Theses.

Kayhan, F., Kaymak, G., Duruel, H. E. E., & Kızılkaya, Ş. T. (2018). Biyolojik araştırmalarda zebra balığının (Danio rerio Hamilton, 1822) kullanılması ve önemi. *Gaziosmanpaşa Bilimsel Araştırma Dergisi*, 7(2), 38-45.

Kim, J., Koo, B. K., & Knoblich, J. A. (2020). Human organoids: model systems for human biology and medicine. *Nature Reviews Molecular Cell Biology*, 21(10), 571-584.

Klatt Shaw, D., & Mokalled, M. H. (2021). Efficient CRISPR/Cas9 mutagenesis for neurobehavioral screening in adult zebrafish. *G3*, 11(8), jkab089. https://doi.org/10.1093/g3journal/jkab089.

Klein, J., Fasshauer, M., Klein, H. H., Benito, M., & Kahn, C. R. (2002). Novel adipocyte lines from brown fat: a model system for the study of differentiation, energy metabolism, and insulin action. *Bioessays*, 24(4), 382-388. https://doi.org/10.1002/bies.10058.

Li, W. (2024). Single-cell atlas of mutant zebrafish embryos. *Nature Genetics*, 56(1), 9-9. https://doi.org/10.1038/s41588-023-01634-1.

Lin, J., Chen, Q., & Hu, J. (2022). Color Atlas of Zebrafish Histology and Cytology. *Springer Nature*.

Liu, J., Yuan, X., Fan, C., & Ma, G. (2024). Application of the zebrafish model in human viral research. *Virus Research*, 341, 199327. https://doi.org/10.1016/j.virusres.2024.199327.

Major, R. J., & Poss, K. D. (2007). Zebrafish heart regeneration as a model for cardiac tissue repair. *Drug Discovery Today: Disease Models*, 4(4), 219-225. doi: 10.1016/j.ddmod.2007.09.002.

McKie. R. (2013). How the diminutive zebrafish is having a big impact on medical research. (15 Eylül 2013). *The Guardian*. Sun 15 Sep 2013 08.00 CEST. Access of Date: 12.12.2023. https://www.theguardian.com/science/2013/sep/15/zebrafish-human-genes-project.

Nicolson, T. (2017). The genetics of hair-cell function in zebrafish. *Journal of neurogenetics*, 31(3), 102-112. https://doi.org/10.1080/01677063.2017.1342246.

Pandey, G. (2011). Model organism used in molecular biology or medical research. *International Research Journal of Pharmacy*, 2(11), 62-65.

Pathak, N. H., & Barresi, M. J. (2020). Zebrafish as a model to understand vertebrate development. In The Zebrafish in Biomedical Research (pp. 559-591). Academic Press. https://doi.org/10.1016/B978-0-12-812431-4.00045-2.

Podlacha, M., Grabowski, Ł., Kosznik-Kawśnicka, K., Zdrojewska, K., Stasiłojć, M., Węgrzyn, G., & Węgrzyn, A. (2021). Interactions of bacteriophages with animal and human organisms—safety issues in the light of phage therapy. *International Journal of Molecular Sciences*, 22(16), 8937. https://doi.org/10.3390/ijms22168937.

Rocha, M., Singh, N., Ahsan, K., Beiriger, A., & Prince, V. E. (2020). Neural crest development: insights from the zebrafish. *Developmental Dynamics*, 249(1), 88-111. https://doi.org/10.1002/dvdy.122.

Shrivastav, P. (2023). Zebrafish-A Promising Aspect Towards Heart Regeneration. *International Journal of Novel Research and Development,* 8 (1), 787-802.

Sprague, J., Bayraktaroglu, L., Bradford, Y., Conlin, T., Dunn, N., Fashena, D., ... & Westerfield, M. (2007). The zebrafish information network: the zebrafish model organism database provides expanded support for genotypes and phenotypes. *Nucleic acids research*, 36(suppl_1), D768-D772. https://doi.org/10.1093/nar/gkm956.

Swabe, J. (2002). Animals, disease and human society: human-animal relations and the rise of veterinary medicine. Routledge.

Tarique, I., Lu, T., & Tariq, M. (2023). Cellular activity of autophagy and multivesicular bodies in lens fiber cells during early lens development in rbm24a mutant of zebrafish: ultrastructure analysis. *Micron*, 169, 103446. https://doi.org/10.1016/j.micron.2023.103446.

Teame, T., Zhang, Z., Ran, C., Zhang, H., Yang, Y., Ding, Q., ... & Zhou, Z. (2019). The use of zebrafish (Danio rerio) as biomedical models. *Animal Frontiers*, 9(3), 68-77. doi: 10.1093/af/vfz020.

Terrazas, K., Dixon, J., Trainor, P. A., & Dixon, M. J. (2017). Rare syndromes of the head and face: mandibulofacial and acrofacial dysostoses. *Wiley Interdisciplinary Reviews: Developmental Biology*, 6(3), e263. https://doi.org/10.1002/wdev.263.

Thawkar, B. S., & Kaur, G. (2021). Zebrafish as a promising tool for modeling neurotoxin-induced Alzheimer's disease. *Neurotoxicity Research*, 39, 949-965.

Voisin, N. (2019). Identification Of New Genetic Causes Of Syndromic Intellectual Disability (Doctoral dissertation, Université de Lausanne, Faculté de biologie et médecine).

Yang, J. F., Walia, A., Huang, Y. H., Han, K. Y., Rosenblatt, M. I., Azar, D. T., & Chang, J. H. (2016). Understanding lymphangiogenesis in knockout models, the cornea, and ocular diseases for the development of therapeutic interventions. *Survey of ophthalmology*, 61(3), 272-296. https://doi.org/10.1016/j.survophthal.2015.12.004.

Yoshida, Y. (2023). Joint representation: Modeling a phenomenon with multiple biological systems. *Studies in History and Philosophy of Science*, 99, 67-76. https://doi.org/10.1016/j.shpsa.2023.03.002.

Zabegalov, K. N., Costa, F. V., Kolesnikova, T. O., de Abreu, M. S., Petersen, E. V., Yenkoyan, K. B., & Kalueff, A. V. (2024). Can we gain translational insights into the functional roles of cerebral cortex from acortical rodent and naturally acortical zebrafish models?. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 110964. https://doi.org/10.1016/j.pnpbp.2024.110964.