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Review Article

A Review of Zebrafish as an Alternative Animal Model and Its Benefits over Other Animal Models in Various Disease Conditions

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Abstract

The zebrafish (Danio rerio) model has been exponentially adopted because it is a small tropical freshwater fish with crucial genetic, anatomical, and physiological homology with humans. Therefore, zebrafish constitute an excellent experimental model for behavioral, genetic, and toxicological studies that unravel the mechanisms of various human diseases. The zebrafish is a vertebrate, as it shares many organs with humans, including the blood, muscles, kidneys, and eyes. Genome organization and the pathways involved in controlling signal transduction appear to be highly conserved between zebrafish and humans, and therefore zebrafish may be used for modeling human diseases. The zebrafish genome has been sequenced, allowing scientists to study the functions of more than 14,000 genes by inducing mutations in those genes. Zebrafish have a special ability to repair their heart muscle, and scientists are attempting to determine the specific factors involved in this process to help people with heart problems. This review focuses on the use of zebrafish as a potential alternative model and its advantages over other animal models for conducting biomedical research on various human disease conditions.

Keywords: Zebra fish, alternative model, human disease, biomedical research.

INTRODUCTION

The tropical freshwater fish known as the zebrafish (Danio rerio), formerly known as the Brachydanio rerio, is primarily found in Southeast Asia. The species can frequently be found in slowly moving water [1]. Zebrafish are typically found near the bottom of the water in their natural habitat to reduce attack by predators. Due to these species' high rates of fecundity and fertility, it has frequently been used as animal model in a variety of research studies. Zebrafish are currently thought to be an appropriate model to study development, genetics, immunity, behavior, physiology, and nutrition. Because of their varied diets and omnivorous feeding habits (euryphagous), zebrafish are classified as omnivores. Various dietary feeds in various amounts are used by researchers during experimental trials. The ingredients are used in the same proportions for both adult and larval zebrafish. Additionally, some laboratories use a variety of feeds and feeding schedules to elevate zebrafish, sometimes without performing a systematic evaluation [2].

Danio rerio possesses 70% of human genes, as revealed by the zebrafish genome sequence, which also revealed that mice, humans, and other animals share 12719 genes in common. As a result, when human disease-causing genes are introduced into zebrafish

embryos, the growing fish eventually develop the same disease [3]. So the potential model for human diseases and new drug screening is done by the zebrafish model [4]. The species has therefore been extensively used in research aimed at the treatment of genetic disorders like depression, schizophrenia, and Parkinson's disease. The physiology and morphology of the animal also share many similarities with that of humans, including the presence of multiple hematopoietic cells (erythrocytes, myeloid cells, band T lymphocytes, etc.), the central nervous system, the skeletal system complex, and the cardiovascular system [5]. Zebrafish are considered to be a good model because they have many major organs that are very similar to their human counterparts, including the kidney, pancreas, adipose tissue, and skeletal muscles. In a large number of labs, zebrafish are used to study a variety of human illnesses, including those related to the nervous system, cancer, infectious diseases, cardiovascular disease, kidney disease, diabetes, blindness, deafness, digestive diseases, hematopoiesis [6].

TAXONOMY OF ZEBRAFISH

Species : D. rerio
Class : Actinopterygii
Order : Cypriniformes
Family : Cyprinidae
Phylum : Chordata
Genus : Danio
Kingdom : Animalia [7]

REPRODUCTION OF ZEBRAFISH

The zebrafish's development and fertilization are external processes. Without any parental supervision, reproduction is carried out in small groups by scattering the eggs beneath the soil. Although sexual maturity usually occurs between ten and twelve weeks of age, it is recommended that reproduction begins at six months to achieve good reproduction results and higher-quality embryos [8]. A distinct characteristic of this species is its small size; the adult is about 4-5 cm long, has a cylindrical body, and alternates light and dark horizontal stripes. exhibit sexual dimorphism, with males being more rounded and typically golden in the ventral region and females being thinner and more silvery overall. This is most noticeable in the time leading up to spawning. Because the females are asynchronous, Every two to three days, females may spawn multiple times per day, and each spawn can produce up to 100 eggs. The spawn may come from a single female and contain 200 eggs. The fry grows quickly and can become sexually mature in two to three months [9].

ADVANTAGE OF THE ZEBRAFISH MODEL OVER OTHER ANIMAL MODELS

Zebrafish are superior to rodent models in many ways for the study of vertebrate development and disease. A single clutch can contain hundreds of embryos, and the optical clarity of the developing embryo allows for real-time imaging at the organism level [10] Zebrafish (Danio rerio) have become increasingly popular as experimental models in biomedical research. These animal models are probably not the first that comes to mind when thinking about animals used in medical research. The fact that this species' embryos can develop outside the mother's body and are transparent is one of the most common reasons why researchers around the world are becoming more and more interested in this small tropical freshwater fish. This is a fantastic benefit that enables researchers to thoroughly study the development of vertebrate embryos without the need for invasive procedures. Another advantage is that zebrafish can lay 200–300 fertilized eggs per week, with embryogenesis finishing in just 72 hours [11]. In addition to having a high genetic similarity to humans, especially in the central nervous system, and being easily manipulable, due to its tiny size, it can store a lot of data and doesn't require a lot of infrastructures, unlike the animal houses needed for mice. Zebrafish are less expensive to use than mice, and producing mice cost more annually than zebrafish [12]. One of the challenges with using animals is easily stressed, certain human behaviors cannot be fully utilized or trusted in these circumstances so the researchers make use of zebrafish models. The zebrafish were discovered during the search for new experimental models to reduce, improve, and replace the use of animal models.

Zebrafish is another animal model in human and animal vaccination analysis.

The benefits of using the zebrafish model for vaccination tests are Zebrafish have additional biological advantages over other vertebrates, such as high fecundity, external fertilization, optical transparency, and rapid development. A highly developed immune system that is notably similar to the human immune system is also present in zebrafish. It reveals that the majority of the molecules and signaling pathways involved in the immune response in mammals should exist and function similarly in fish. Because fish are susceptible to infections by gram-negative and gram-positive bacteria, protozoa, viruses, fungi, and mycobacteria, the presence of components of innate and adaptive immunity in fish enables research into infectious processes [13].

Zebrafish as an alternative animal model for cancer

Zebrafish are amenable to genetic manipulation. The usefulness of forward genetics in identifying new cancer markers is demonstrated. Both spontaneous mutations and transgenetics that mimic the mutations found in human cancers have been used to create cancer models. The zebrafish's transparent body makes it easy to examine cancer cells over time as well as how the environment reacts to them, such as through angiogenesis and inflammation. It is possible to identify cancer cells and transplant them into zebrafish. Zebrafish embryos are useful for pharmacological

screening, and they are small and simple to keep. Proto-oncogenes that are misregulated in human disease were overexpressed to produce leukemia models in zebrafish [14].

Zebrafish as an alternative animal model for epilepsy

Zebrafish demonstrate many neurological similarities to humans and have known homologs for 85% of the recognized epilepsy genes found in people. Genetic engineering is very easy to do with zebrafish. Drugs are directly absorbed by zebrafish embryos from their bathing medium. Zebrafish are easy to maintain in large populations, so it is necessary to screen for genes that decrease seizure susceptibility or increase seizure susceptibility [15].

Zebrafish as an alternative animal model for diabetes mellitus

Zebrafish were used for a variety of developmental studies and organogenesis, including the morphogenesis of the pancreas. Zebrafish research explains how extrinsic signaling molecules like FGF, retinoic acid, and Shh affect intrinsic transcriptional programs[16]. Zebrafish are now a useful alternative model to study the onset of diabetes mellitus and its treatment modalities. Zebrafish become hyperglycemic when exposed to high glucose levels, and they develop retinopathies when their blood sugar levels are persistently high [17]. Zebrafish were raised on high-calorie, high-fat diets, which activated metabolic pathways similar to those in humans and affected obesity and obesity-related diseases. Zebrafish submerged in a 111 mM high-glucose solution showed decreased amounts of mRNA for insulin receptors in muscle and an increase of 41% in froctosamine levels in the eyes [18]. By overfeeding a high-calorie diet in Zebrafish, researchers also created a model of type 2 diabetes mellitus in these organisms. In both zebrafish and humans, the gene expression profiles of the pancreas reveal a common pathway for the onset of type 2 diabetes mellitus. Studies on the association between age and type 2 diabetes mellitus have revealed that younger zebrafish (4 to 11 months old) develop hyperglycemia more slowly than older zebrafish with rapidly increasing glucose concentrations [19]. Immersion of adult zebrafish in a 1% glucose solution for 24 hr resulted in an increased blood glucose level of up to 400 mg/dL. The two transgenic models of insulin resistance include skeletal muscle insulin resistance produced by transgenic expression of the IGF-I receptor in skeletal muscle. In the second model, insulin resistance was attained via liver-specific knockdown of the insulin receptor gene using CRISPR/Cas9 [20].

Zebrafish as an alternative animal model for Nonalcoholic Fatty Liver Disease and Other Liver Disorders:

The cellular makeup, genetics, and function of the zebrafish liver are similar to those of the human liver. As a result of this observation, the detailed embryology and genetics involved in the development of the human liver, as well as liver disorders and potential treatments for liver diseases, were studied using zebrafish liver, The development of liver tumors in zebrafish using carcinogenic substances and comparison with gene expression in tumors of human livers first highlighted the significance of zebrafish as a suitable biomedical model. Zebrafish exposed to 6% fructose develop hepatic steatosis in a manner resembling the signs and symptoms seen in people who consume a lot of carbohydrates by using different feeding techniques [21]. Zebrafish overfeeding accelerated the carcinogenic process and caused fatty liver development. In the oncogenic and overfed zebrafish, the hormone leptin, which causes obesity, was also unregulated [22].

Zebrafish as an alternative animal model for Cardiotoxicity:

One of the major concerns in drug development is cardiotoxicity. Studies have shown that the mechanisms by which cardiotoxic agents cause toxic effects in zebrafish embryos are similar to those in humans. Clomipramine and terfenadine treatments impaired cardiac functions, caused hemorrhaging, caused edema, stopped the heartbeat, and ultimately led to the death of zebrafish. Small molecules that regulate heart rate were tested using a transgenic zebrafish model by researchers [23].

Zebrafish as an alternative animal model for Lipid-related Diseases:

The suitability of the zebrafish to study lipid-related diseases is due to its similarities with mammals in lipid absorption, processing, and metabolism [24]. Zebrafish are an effective atherosclerosis model, enabling the examination of lesion development, lipid deposition, and various cellular level alterations in the vascular wall, as well as in vivo macrophage lipid deposition. Zebrafish are used in the study of obesity because their melanocortin system responds to leptin and their energy homeostasis is similar to that of mammals, including mammals' modulation of their fat content. SREBP (sterol-regulatory element-binding protein) and LXR (liver X receptor) systems, which were found to be similar in mammals, are shared transcriptional regulators of the metabolism of cholesterol in zebrafish. The phenotypes of the mutant fish genes resemble those of human pathologies.

Zebrafish as an alternative animal model for Tumorigenesis

As a vertebrate model, a variety of fish has been used to study the tumors brought on by environmental carcinogens. Zebrafish were discovered to be the variety that was preferred for studying the processes of embryogenesis, organogenesis, and tumorigenesis [25]. The tumor suppressor genes (TSGs) and orthologous oncogenes are similar in zebrafish and

humans, and the chemically induced tumors in zebrafish and humans are found to be more similar histopathologically. Zebrafish and humans' hepatic gene expression studies revealed that different gene expression profiles at various tumor aggressiveness stages were conserved between these two phylogenetically distinct species [26].

Zebrafish as an alternative animal model for kidney disorders

Zebrafish are freshwater fish, and their kidneys play an important role in maintaining osmoregulation and excreting water. However, zebrafish and mammalian kidneys share many functional similarities, which makes them superior models for research on the kidneys. To study processes like glomerular filtration, renal tubular clearance, polycystic kidney disease (PKD), nephronophthisis, and acute kidney injury (AKI), zebrafish can be a useful organism [27].

CONCLUSION

Zebrafish are a leading animal model for biomedical investigation. Zebrafish research on mutagenesis, carcinogenesis and genome sequencing can aid in the development of new drugs for humans. A potential model for various diseases and drug testing is the zebrafish. Research on organogenesis and embryogenesis is aided by zebrafish. Additionally, it aids in the creation of various genetic research tools. Zebrafish models are used as an alternative to animal models and have advantages over them for conducting biomedical research on a variety of human disease conditions.

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