PHARMALOGOS

DEPARTMENT OF PHARMACOLOGY - NEWS LETTER

An Official Publication of

DEVAKI AMMA MEMORIAL COLLEGE OF PHARMACY

(Affiliated to Kerala University of Health Sciences, Thrissur and Approved by AICTE & PCI, New Delhi)

Chelembra, Pulliparamba P.O., Malappuram (Dt)- 673 634, Kerala.

Website: www.devakiammamemorial.org E-mail: devakiammapharmacycollege@gmail.com

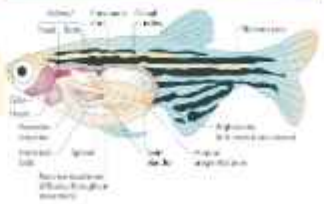
Volume: 03 Issue: 01 September 2019

ISSUE HIGHLIGHTS

ZEBRAFISH: AN ALTERNATIVE MODEL FOR HUMAN DISEASE

Animal experimentation has an important role in scientific evolution. Although some models have been replaced by alternative methods, scientific research still needs animal models for development, reliability and legitimacy of science. The use of Zebrafish *(Danio rerio)* as an experimental model has grown rapidly for biomedical research.

Zebrafish



The Zebrafish *(Danio rerio)* is atropical fresh water teleostei, belonging to the Cyprinidae family. This species is characterized by small size, adult measures about 4-5 cm, have a cylindrical body, and a distinct color pattern alternating light and dark horizontal stripes. Exhibit sexual dimorphism: males are thinner and generally golden in the ventral region, females are more rounded and silvery, mainly in the ventral region, which is most evident in the period close to the spawn. Females may spawn every 2-3 days and a single spawn may contain hundred eggs. The spawn may contain 200 eggs from a single female; the fry grow quickly and can reach sexual maturity within 2-3 months. The natural habitat of the Zebrafish is in South Asia, Ganges and Brahmaputra rivers basins, in northeastern India, Bangladesh, Nepal and northern Myanmar.

In the remembrance of

Sri. K.V. Sankaranarayanan

(01.01.1948 - 12.07.2013)

Founder, Devaki Amma Memorial Institutions

Animal experimentation

Biomedical research relies on the use of animal models to understand the pathogenesis of human and animal diseases to develop and test new therapies. A number of factors must be considered for the use of experimental models; in addition to significant evolutionary proximity and anatomical similarities, it should be considered as the approach of cellular processes. The use of animals in scientific research has generated great discussions in recent years and there has been growing concerns related to bioethics and animal welfare. Now a days the scientific community has been growing interest in alternative methods aimed at reducing the use of animals in experiments as these represent a high cost in research, since they must be contained, fed and kept healthy for scientific purpose. Alternative methods correspond approximately 90% of biomedical research and include mathematical and computational models, advanced tissue and cell cultures, and scanning technology.

Advantages and Disadvantages of Zebrafish in Biomedical Research

The Danio rerio has emerged as an excellent model for research in different areas, among them pharmacogenetics, neurology and embryology. The main reasons are the easy access to all stages of development, the optical clarity of embryos and larvae that allows view in great-time development, in addition to high genetic, easily manipulated and homologous physiology with humans, especially in the central nervous system.

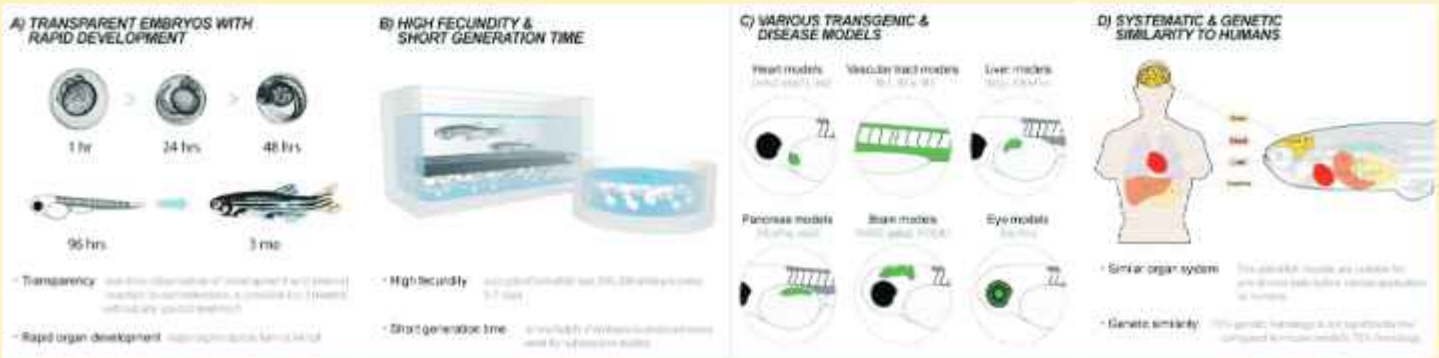
Its small size enables high storage, does not need large infrastructure facilities, as in mouse animal houses. The cost of using Zebrafish is less than the mouse; per year, creating mice is about three times larger compared to the Zebrafish.

The generation time of the species is short (three months), and you can create many copies in a limited space (100 adults in a tank of 8-12 L). Another advantage is the rapid reproduction and abundant (for a single spawn, the female produces about 100 eggs), and high (80-85%) homology to human gene.

The transparency of the Zebrafish embryo facilitates the studies in genetic development programs, because it is possible to monitor and manipulate its development without difficulties. Furthermore, rapid development shows, breaks in less than three days and become mature in 90 days, which makes the search more rapid. The drugs readily diffuse across the skin and gills and penetrate orally after 72 hours after fertilization, not requiring active application of drugs.

Lack of knowledge about the genetics of their lineages is a limitation of this experimental model and still, the strains that are known are not standardized, in contrasted, species such as the mouse.

Model a human disease in fish



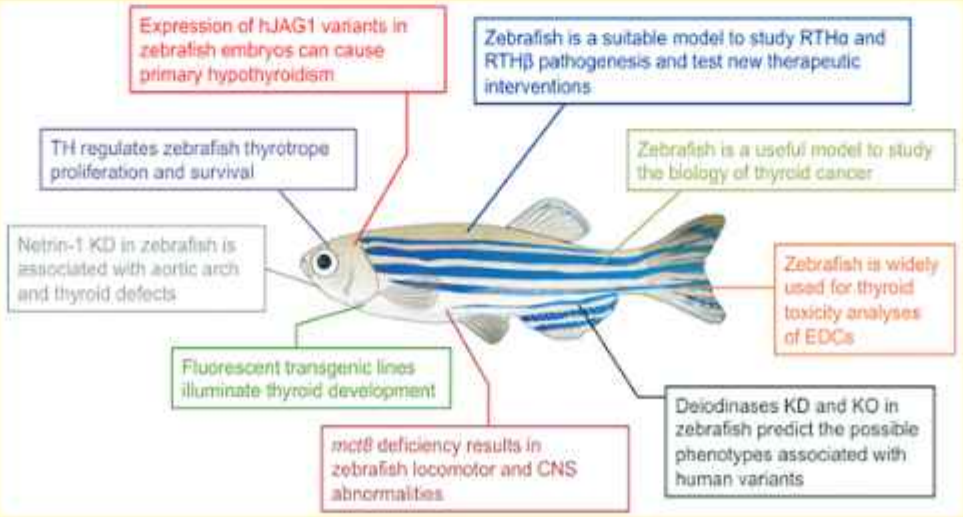
Although humans may appear to be extremely different than Zebrafish, we are actually much more similar to them than you might think. In fact, 70% of human genes are found in Zebrafish. Moreover, Zebrafish have two eyes, a mouth, brain, spinal cord, intestine, pancreas, liver, bile ducts, kidney, esophagus, heart, ear, nose, muscle, blood, bone, cartilage, and teeth. The generation of a knock-out of the dystrophin gene in Zebrafish has been shown to closely resemble the severity and progression of the human disease Duchenne muscular dystrophy. Patients with Duchenne muscular dystrophy been found to carry mutations in dystrophin and demonstrate childhood muscle weakness that gets progressively worse. In both humans and the Zebrafish model, the loss of dystrophin gradually leads to necrotic muscle fibers that are replaced by inflammatory cells, fibrosis, and abnormally sized muscle fibers. Many of the genes and critical pathways that are required to grow these features are highly conserved between humans and Zebrafish. Thus, any type of disease that causes changes in these body parts in humans could theoretically be modeled in Zebrafish.

Zebrafish as an alternative method of mice

While mice are evolutionarily more similar to humans because they are mammals, Zebrafish have several advantages over their furry competitors. One important advantage of Zebrafish is that the adults are small and prefer to be housed in large groups, or "shoals". As a result, they require much less space and are cheaper to maintain than mice.

Another advantage is that adult Zebrafish breed readily (approximately every 10 days) and can produce as many as 50 to 300 eggs at a time. This is quite different from mice as they generally produce litters of one to 10 pups and can only bear approximately three litters in their lifetime.

Scientific experiments are generally repeated multiple times in order to prove that the results are accurate, so having an animal that can produce a large number of offspring over and over is helpful. Zebrafish embryos are also laid and fertilized externally, which allows them to be easily manipulated in a variety of ways. In vitro fertilization can be performed if necessary. The one-cell-stage fertilized eggs can be easily injected with DNA or RNA to permanently modify their genetic makeup in order to generate transgenic or knock-out Zebrafish lines. Working with mice in this way is much more complicated. Mouse embryos develop inside the mother, and to access and manipulate them the mother would have to be sacrificed. To keep the embryos alive after fertilizing or injecting them, they would need to be transplanted into another female mouse, as well.



Applications in Biomedical Research: Neurology

The use of adult and larvae Zebrafish in neuroscience has increased in recent decades because of the similarity of physiology and genetics to human, and the ease of handling and similarity of the central nervous system. The morphology of the brain of mammals and Zebrafish is similar, including macro-organization of the brain. As in other vertebrates, the Zebrafish central nervous system is formed outside the neural plate, in an ectodermal epithelium layer on the dorsal side of the embryo. Another example is the similarity Habenula, Epithalamus core located in the brain, which regulates the serotonin and dopamine, which have close correlation with the neurochemical disorders of depression. Clinical depression is strongly correlated with genetic factors, environmental stress, and neurochemical disorders, and it seems to play similar function phenotypes in Zebrafish.

The gene, grs357, of Zebrafish, with a mutation of the glucocorticoid receptor demonstrates an increase in glucocorticoid levels that induces abnormal behavior, such as reduced mobility and smoothly, that resemble the phenotypes observed in human clinical depression. Based on a research referencing the Zebrafish as a highly social species, which prefers to swim in shoals, it was considered that it would be possible to use it in studies of autism spectrum disorder, a dysfunction of human development that affects the ability of communication and socialization. Some drugs are clinically effective in some symptoms of autism, but do not reduce other symptoms. For example, risperidone, an antipsychotic, effective to treat irritability, it does not reduce the symptoms of social impairment and repetitive / obsessive behaviors in humans and appears to have similar effects in Zebrafish; this indicates that there is high sensitivity to drugs relevant for the disease.

There are some Zebrafish genes related neurodegenerative diseases in humans and manipulation of these genes that can facilitate the understanding of the genetic mechanisms causing the pathogenesis (Lee; Freeman, 2014). Regarding neurodegenerative diseases in humans, describe a Zebrafish gene homologous to the transmembrane protein of ATP13A2 that plays an important role in embryonic development. This protein has been associated with Parkinson's disease; mutations in TP13A2 were observed in several cases of Parkinson's disease. Two homologous genes have been found in the Danio rerio with the same functions of the human protein, neurogenesis in the embryo.

Toxicology

The development of toxicological studies in Zebrafish has offered several advantages to the tracking of a large number of drug compounds and toxicological studies. The neurotoxicity of Plumbum (Pb) in Zebrafish embryos changed the behavior of individuals as adults, these results showed that exposure to Pb caused deficits in learning and memory, indicating that this exposure persists into adolescence and in adulthood and affects mental development. The growth retardation was observed during the development of Zebrafish embryos exposed to teratogens, occurring deformations on the yolk sac and tail. The Anthracyclines (widely used in chemotherapy treatments, but in the long run can cause cardiac toxicity) suggest toxic effects on the developing of the Zebrafish embryogenesis, and changes in gene expression and hatching.

Cardiovascular

The Danio rerio has also been used as a model for cardiovascular disease, congenital heart defects to arrhythmias and cardiomyopathy. myloidosis is a disease in which bone marrow cells produce amyloid, an abnormal protein substance that accumulates in various organs, including the heart, causing damage to the heart muscle. Zebrafish treated with amyloidosis developed cardiac dysfunction and apoptosis of cells. The cardiac amyloidosis is

characterized by a low systolic blood pressure, coinciding with the contractile dysfunction found in Zebrafish, the same as in humans.

Regenerative Medicine

The research of Zebrafish has become a bridge between the cell and the biological development due to its rapid development. The Zebrafish fully regenerates the heart muscle within a few weeks; therefore it has been used in studies on regeneration. This species, as a model for heart damage, provides a means to guide the search cell types and pathways that may assist in the recovery of regeneration of cardiac patients. The Zebrafish has a number of features that make it an excellent model for research on aging: many descendants and their short lifespan relative to other mammals, the Zebrafish takes only 30-40 minutes to their embryo be observed and manipulated, 72 hours to become larvae and 90 days is an adult; the rapid growth rate coupled with its longevity is a possible relationship to research.

Mr. Deepak V. S.
IV Sem. M. Pharm

FDA APPROVED DRUGS IN PAST 6 MONTHS

The following database contains a list of new drugs approved by Food and Drug Administration (FDA) for sale in the United States. Drug information is as follows.

BRAND NAME	DRUG	MANUFACTURER	TREATMENT	APPROVED MONTH
Keytruda	Pembrolizumab	Merck	Esophageal cancer	July 2019
Dupixent	Dupilumab	Regeneron Pharmaceuticals	Chronic Rhinosinusities	June 2019
Bavencio	Avelumab	Merck and Pfizer	First line treatment of Renal cell carcinoma	May 2019
Cyramza	Ramucirumab	Eli Lilly	Hepatocellular carcinoma	May 2019
Piqray	Alpelisib	Novartis	Metastatic breast cancer	May 2019
Ruzurgi	Amifampridine	Jacobus Pharmaceuticals	Myasthenic syndrome in pediatrics	May 2019
Venclexta	Venetoclax	Genentech and Abbvie	Lymphotic leukemia	May 2019
Vyndaqel	Tafamidis meglumine	Fold Rx Pharmaceuticals	Cardiomyopathy	May 2019
Balversa	Erdafitinib	Janssen Oncology	Metastatic urothelial carcinoma	April 2019
Dovato	Dolutegravir and Lamivudine	Viiv Healthcare	HIV-1 infection	April 2019
Duobrii	Halobetasol propionate and tazarotene	Ortho dermatologics	Plaque psoriasis	April 2019

BRAND NAME	DRUG	MANUFACTURER	TREATMENT	APPROVED MONTH
Evenity	Romosozumab-aqqg	Amgen	Osteoporosis in postmenopausal women	April 2019
Keytruda	Pembrolizumab	Merck	Renal cell carcinoma	April 2019
Cimzia	Certolizumab pegol	UCB	Non-radiographic axial spondyloarthritis	March 2019
Jatenzo	Testosterone undecanoate	Clarus Therapeutics	Deficiency or absence of endogenous testosterone	March 2019
Mavenclad	cladribine	Merck	Relapsing multiple sclerosis	March 2019
Mayzent	Siponimod	Novartis	Relapsing multiple sclerosis	March 2019
Egaten	Triclabendazole	Novartis	Fascioliasis	February 2019
Herceptin Hylecta	Trastuzumab and hyaluronidase	Halozyme	HER2-overexpressing breast cancer	February 2019

Ms. Krishna Priya P. G.
II Sem. M. Pharm

DEPARTMENT HIGHLIGHTS

INVITED SPEAKERS

Dr. A. Suresh, Professor and Head presented a seminar on title "REFRESHMENT AND MOTIVATION OF MEDICAL PROFESSIONALS" in a Medical Professional Meet organized by BAGEO Pharmaceuticals Pvt Ltd, Le Poshe Hotel, Kodaikanal on 26th March, 2019.

Dr. E. Tamil jothi, Associate Professor presented a seminar on title "Emerging Technology - Zebrafish" in International Conference on Development in Pharmaceutical Sciences organized by Scient Institute of Pharmacy, Hyderabad on 16th March, 2019.

SEMINAR/CONFERENCE ATTENDED

Dr. A. Suresh, Professor and Head, Amritha C. K., Deepak V.S., P. Prajitha, Sreelakshmi S.S., T. Savitha IV Semester M.Pharm (Pharmacology) Students attended International Conference on "CURRENT TRENDS IN HERBAL DRUGS AND PHARMA INDUSTRY" organized by College of Pharmaceutical Sciences, Govt. Medical College, Thiruvananthapuram on 29th and 30th March, 2019.

Mrs. Saheera K. M., Asst. Professor attended PCI Sponsored First continuing education programme on "New paradigms in teaching - learning process" organized by Al Shifa College of Pharmacy, Perunthalmanna on 25th - 27th March, 2019.

Mr. S. Venkatesh, Asst. Professor attended on International Conference on "CHEMICAL SCIENCES AND NANOMATERIALS" organized by Department of Chemistry, School of Advanced Sciences, Vellore Institute of Technology on 7th - 9th March, 2019.

Aiswarya Babu K., Krishna Priya P. G., Mumtaz P., II Semester M.Pharm (Pharmacology) Students attended "Symposium II about glimpses of the Indian pharmaceutical industry from global perspective to local reality" organized by National College of Pharmacy, Kozhikode on 7th January, 2019.

PAPER PRESENTATION

Mr. S. Venkatesh, Asst. Professor presented a research entitled "Anti-venom activity of ethanolic extract of leaves of Ampelocissus araneosa" in International Conference on "CHEMICAL SCIENCES AND NANOMATERIALS" organized by Department of Chemistry, School of Advanced Sciences, Vellore Institute of Technology on 7th - 9th March, 2019.

The Destination for Excellence

Courses Offered

	Ph.D.	
	Pharm. D.	
	M.Pharm.	M. Ed.
M. Arch.	B. Pharm.	B. Ed.
B. Arch.	D.Pharm.	D.Ed. (TTC)

For Admission details Contact: **9847 77 33 77, 9847 82 20 80**

DEVAKI AMMA MEMORIAL INSTITUTIONS

CHELEMBRA, Near Calicut University, Pulliparamba P.O., Malappuram Dt. Pin -673634, Kerala.
Phone: 0483 - 2891623, 2890695, 2891330

DG COLLEGE OF ARCHITECTURE | DEVAKI AMMA MEMORIAL COLLEGE OF PHARMACY | DEVAKI AMMA MEMORIAL TEACHER EDUCATION COLLEGE | DEVAKI AMMA MEMORIAL TEACHER TRAINING INSTITUTE

Printed @ Fine Offset - 9061380231