

## Exploring the mechanism behind Alzheimer's Disease in adult Zebra fish

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**Background:** Zebrafish is emerging as an alternative vertebrate model for the study of memory dysfunction. Neuronal circuitries involved in learning and memory functions in Zebrafish are well characterized. With this model we can perform variety of behavior test, including learning and cognition, which has set a platform for use of this animal for behavioural pharmacology.

**Aim:** In this study we will establish the model of memory dysfunction by different methods like hypoxia-induced or chemical induced in adult Zebrafish and will try to uncover the mechanism behind memory dysfunction.

### Objective

1. To establish model of memory dysfunction in adult Zebrafish
2. To delineate the mechanism behind memory dysfunction in Zebrafish

### Material and Methods:

Adult Zebrafish (~3months old, maintained at 12 h light and 12 hr dark cycle) housed at our lab will be used for the study. Drugs like streptozotocin, reserpine, benzo- $\alpha$ -pyrene will be used to produce memory dysfunction in adult Zebrafish. Various parameters like behavioral (T-maze, Light and Dark chamber test), followed by biochemical and molecular analysis will be analysed.

### Expected Outcomes:

With this study we will be able to explore the new possible therapeutic target that will help us to delineate the pathology of this incapacitating disease Alzheimer's disease. And we will target the same with newer drugs to ameliorate the pathology behind this disease.

Zebrafish emerges as a model for translational research on human neurological disorders that is increasingly successful. The high degree of neurological and behavioral similarity of zebrafish to humans is evaluated in this study. This is highly validated for studying human neurodegenerative diseases as a strong vertebrate model. Zebrafish brain's neuroanatomic and neurochemical pathways have a strong similarity to the human brain. The parallels between physiological, emotional and social behavioral trends were also well known. It is important to note that zebrafish models have been successfully used to mimic Alzheimer's disease (AD) pathology as well as Tauopathy. Their relatively simple nervous system and the embryos' optical clarity allow for neurological imaging in real-time. The use of recent real-time imaging techniques to gain valuable insights into the neurodegeneration that occurs in AD is further elaborated here. Zebrafish is well adapted for Ca<sup>2+</sup> imaging, offering a greater

understanding of neuronal activity and axonal dystrophy in a non-invasive way of thinking. Three-dimensional visualization in zebrafish is a rapidly emerging technique that enables the whole organism to be visualized for an extensive functional and neurophysiological study in the state of disease in vivo. Appropriateness to high-throughput screening and human resemblance makes zebrafish an ideal model for screening neurospecific compounds. The zebrafish, instead Model can be decisive in bridging the gap between the bench and bedside. This fish is becoming an increasingly popular model for understanding AD with increased potential for neurodevelopment and neurodegeneration studies, which offers exciting research opportunities in the future.

Zebrafish may be used as a model for researching different pathologies of the disease in Alzheimer's disease.

Laser axotomy combined with time-lapse imaging and 3D imaging show fascinating details about zebrafish larvae degeneration / regeneration.

With this model, new approaches to treating Alzheimer's disease may be further uncovered.

How does zebrafish serve as an understanding model for Alzheimer's disease?

Can zebrafish real-time imagery address major breakthroughs in Alzheimer's research?

Could zebrafish bridge the void between clinical science and the discovery of neurospecific drugs?

The zebrafish is a prominent vertebrate model system for comprehensive analysis of the unique functions of genes during development and neurodegeneration along with their signaling pathways. Such studies were possible because the zebrafish has several distinct advantages over other models of the vertebrate.

Despite of the nature of their natural environment, it's much simpler to hold in a Laboratory to simulate conditions which are important to mammals. And you can grow zebrafish in a cost-effective manner. Their short 3-5-month generation times enhance the rate of experimental progress.

They exhibit external fertilization, and their pattern of development enables embryo evaluation and experimental manipulation. In addition, they have large clutch sizes varying from 200 to 300 per fish, ensuring a ready supply of animals for research work.

One of the peculiarities of zebrafish is Embryo's unrivaled optical clarity, allowing the visualization of individual genes (fluorescently coded or dyed) during the developmental cycle using non-invasive imaging techniques. This embryo openness also helps in genetic

engineering.

High-throughput screening of neuroactive compounds can be achieved quickly, due to the limited size of the larvae.

In a normal cellular environment, the introduction of transient manipulation of gene activities and their subsequent examination is very easy. The embryos are malevolent to genetic engineering by morpholino antisense oligonucleotide, mRNAs, transgenes and

techniques of genome editing like TALENS; CRISPR-Cas9.

The zebrafish have a neural structural organization of the vertebrate and their genome has several gene orthologies similar to those mutated in the disease of the human family Alzheimer (FAD). Scientists have recently upgraded the web tool for analyzing zebrafish genes using gene ontology in an interesting study, as the entire zebrafish genome was sequenced.