A Review on role of zebrafish in Huntington's disease

ABSTRACT

Treatment and effective therapies of most of the neurodegenerative disease are not available due to social and economic factors which makes it incurable. Huntington's disease is one of such disease. Huntington's disease (HD) is an inherited condition which leads to progressive degeneration of nerve cells may leads to cognitive, behavioral, and psychiatric symptoms. Discovery of zebrafish has filled the gap between in vitro and in vivo assays and makes the study of neuroscience easy with less complications. Zebrafish model has become a recent topic to focus on, as its utility in the study of neurological disease and role in improving screening methods makes the treatment and therapies more productive. Zebrafish hold many advanced functional genomics like human disease, the understanding of genetics, neurodegenerative disease and disorders and the discovery of therapeutics. It assess the mutant gene, etiology of human's disease, and it is role in the disease progression and allows the identification of relevant treatment for the same. This review highlights the role of the zebrafish in the Huntington's disease.

Keywords: Huntington's disease, zebrafish, neuroscience, neurodegenerative disease, therapeutics

1. INTRODUCTION

Huntington's disease (HD) is an autosomal dominant monogenic neurodegenerative disease which means that one person needs only one copy of defective gene to develop disorder that occurs due to the mutation in huntingtin or HTT gene. Mutation in HTT gene encodes abnormal trinucleotide that leads to glutamine (cag) expansion at the HTT protein amino terminal. A decline in the huntingtin cause abnormality in the normal pathogenesis (1). HD is one of the nine degenerative diseases characterized by the progressive deficit, mood alterations, involuntary movements, weight loss (even with the adequate dietary intake) and psychological symptoms (2). HD like the most neurodegenerative disease is incurable and fatal after 15-20 years of onset because its pathology evidence, the gradual and progressive death of medium spiny gamma-amino butyric acid (GABA) neurons of the striatum and selective death of the neurons found in the deep cerebral cortex (3).

Zebrafish, danio rerio belongs to the highly divergent genera cyprinid and family cyprinidae. Danio rerio, common carp (cyprinus carpio) and barbus(barbus intermedius), the genera danio and cyprinus separated 50 million years ago and cyprinus and cyprinus and barbus diverged 30 million years ago.(4) zebrafish has been proved to be a vertebrate model for the study of neurodegenerative disease, developmental biology, and gene function. The unique feature about the zebrafish is that it has all the main organs for metabolism (5). Popularity of zebrafish are not only that they are vertebrate, but they are more evolutionary alike to humans than invertebrates. Many studies revealed that in the zebrafish, HTT gene has 70% similarity with the human protein. These highlights make zebrafish a possibly reasonable living being to assess the effect of medications on the neuronal development and capacity (6). This survey intends to assess the plausibility of zebrafish as a framework for therapeutic aspect of Huntington's disease.

2. Behavioral Neuroscience of Zebrafish

Zebrafish, specifically, have been very much utilized in hereditary qualities, neuroscience, pharmacology, and toxicology (7). The following and continuous advance is to stretch out the zebrafish model to seek after inquiries of social neuroscience, an endeavor that requires substantial, dependable, and productive techniques for conduct appraisal(8). fish are effortlessly reared on a large scale and grow quickly,

diminishing the expense of trial and error and fundamentally expanding research throughput-possibly, more investigations can be run significantly quicker to respond to quite a few inquiries (Fig 1). Zebrafish has quickly turned into a noticeable model for concentrating on the atomic premise of vertebrate neurodevelopment. The logical capability of the zebrafish was found by George Streisinger. The unmistakable chorion of the zebrafish permits the nonstop representation of neuroanatomy; their quick turn of events and openness to hereditary investigation make the zebrafish a fantastic model framework for atomic and unthinking investigations of neurodevelopment. Since its presentation, numerous hereditary freaks have opened up, including assortments that can assist with deciding the atomic systems of neurobehavioral work. Zebrafish have been basic in the recognizable proof of an assortment of qualities influencing different parts of neural turn of events and capacity. Subsequently, the hereditary qualities and physiology of learning and memory are currently being all the more broadly concentrated in zebrafish (8, 9)

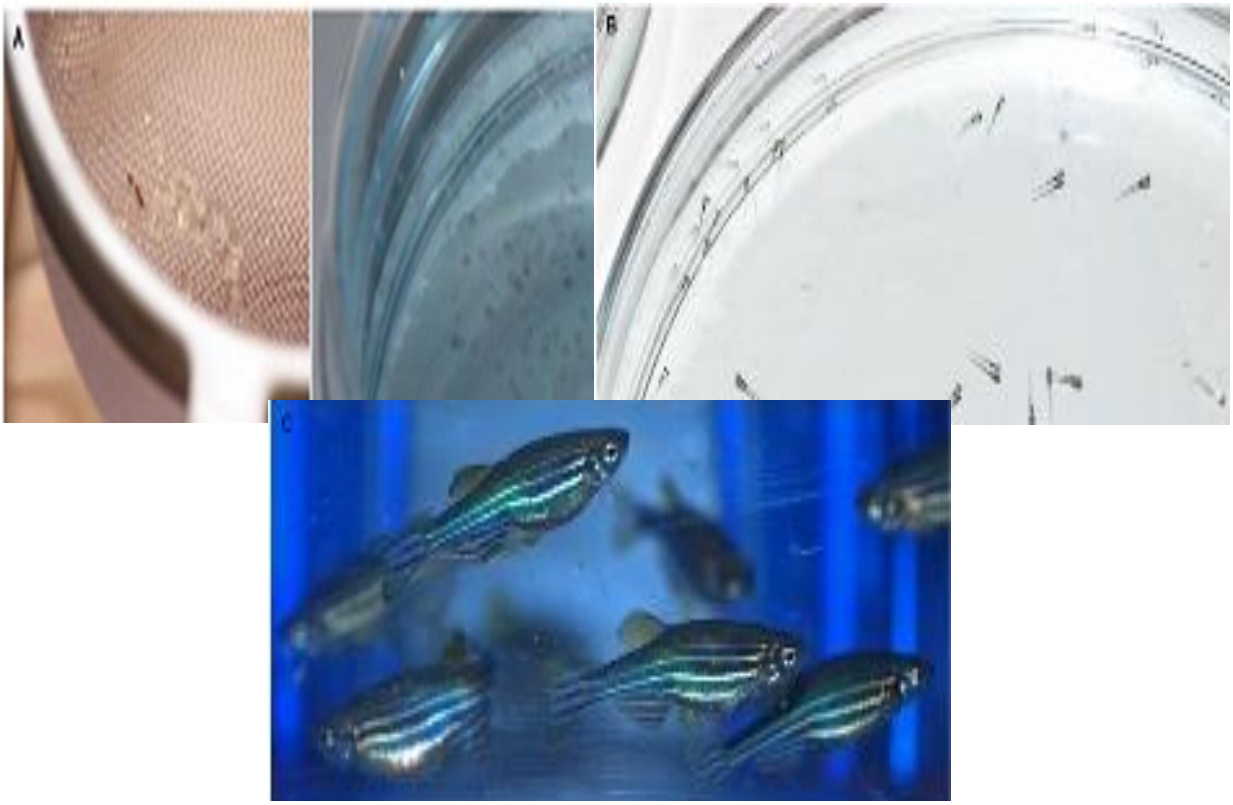

Figure 1: Represent images of Zebrafish at embryonic (A), Larval (B), and adult (C) stage (9) Neurol., June 2018 https://doi.org/10.3389/fneur.2018.00347

3. Dissemination year of the essential survey portraying a zebrafish model

Over the year zebrafish model were used to study various diseases especially the disorder related to CNS as show in Fig 2.

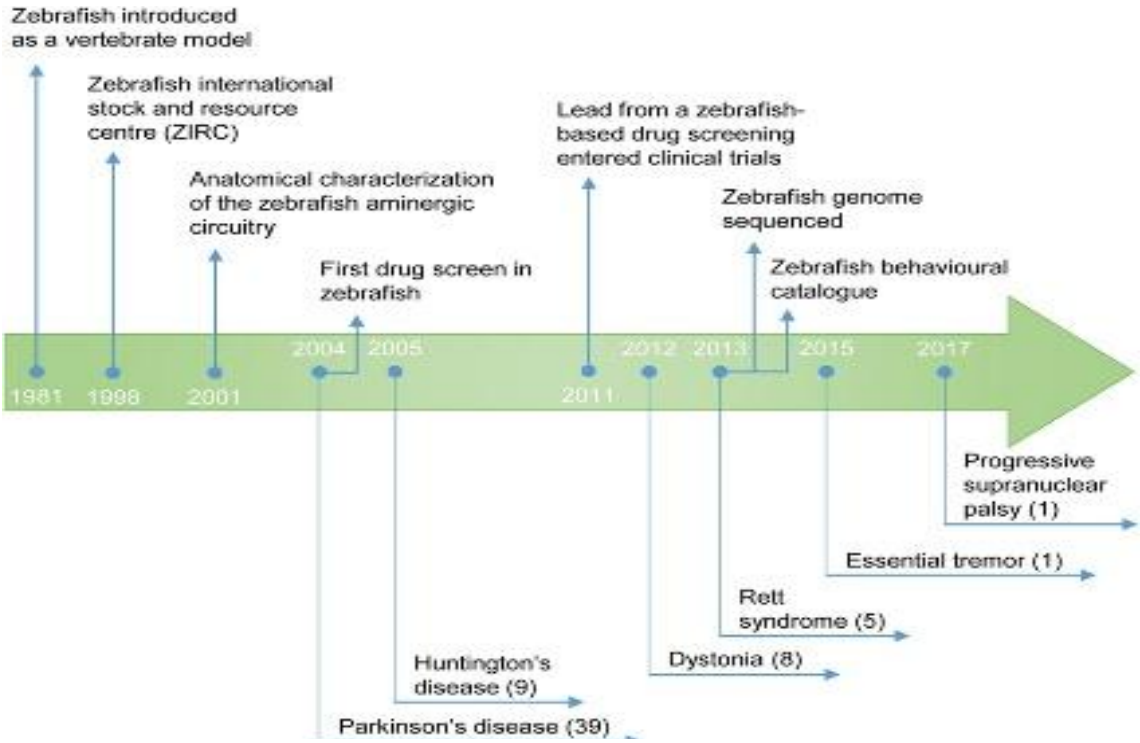

Fig 2: A plan of the use of zebrafish as a model for the examination of improvement issues and medicine exposure. The dissemination year of the essential survey portraying a zebrafish model of the improvement issue is highlighted (9)

4. Zebrafish Neurodegenerative Disorder Model

In zebrafish, the huntingtin (HTT) quality has been cloned and sequenced with a 3121 anticipated amino corrosive protein, which has 70% personality with the human peptide succession Knockdown of HTT utilizing morpholino innovation disturbed various elements of zebrafish improvement bringing about little head and eyes, deferred or paler pigmentation, and vapid hypochromic blood(10,11). In a different report, a 'Huntington's like' zebrafish was made by embedding mRNA of the N-terminal part of Htt with various length polyQ rehashes connected to a GFP-combination protein. The expanding polyQ length was related with an expansion in irregularities and apoptosis in the incipient organisms as soon as 24 hours p.f.(2) The incipient organisms containing the Q102-GFP created considerations in the cytoplasm, which expanded in size by consolidation of the solvent Q102 peptide prompting insoluble stores. These discoveries affirmed a past report where articulation of poly Q56 or more noteworthy displayed harmfulness and irregularities in the zebrafish incipient organisms with incorporation bodies framed in over 70% of incipient organisms (12, 13). These examinations additionally explored the impact of collection inhibitors which recommended that the avoidance of accumulation didn't decrease the harmful impact on the fish, inferring that the development of more modest middle totals was the fundamental driver of poisonousness (14). Hence, these models could be utilized to evaluate for novel mixtures for the treatment of HD by assessing either the anticipation of total development, improved freedom of totals, or the decrease in incipient organism demise (15-17). The zebrafish CNS is comparatively organized to that of different vertebrates and is customarily isolated into the climbing, slipping spinal cord, cranial nerves, motor spinal string, hindbrain, midbrain, Forebrain and tactile nerves. Human-related neurodegenerative infection proteins in zebrafish are homologous, featuring possibly saved sub-molecular cell works that can be effortlessly analyzed (2) as shown in tab. 1.

Disease	Protein	Human Gene	Zebrafish Gene	Amino Acid

				Similarity (%)
Huntington's Disease (2)	Huntingtin	HTT GeneID: 3064 Locus: 4q16.3 Protein length: 3144	htt GeneID: 30214 Chromosome: 1 Protein length: 3121	70

5. Huntington's Disease Treatment aspect

HD is an autosomal overwhelmingly acquired, trinucleotide rehash issue. The freak protein huntingtin (Htt) occupies an extended poly glutamine (poly Q) rehash at its N terminal locale (21, 22). Both additions of capacity and haplo insufficiency of the HD quality (likewise alluded to as IT15) appear to add to the advancement of this issue, yet the exact components prompting HD are still ineffectively perceived (23, 24). Aside from indicative treatment to deal with the development anomalies, no medications are accessible that can dial back the movement of HD. The zebrafish orthologue of HTT has been distinguished. Its prerequisite for zebrafish advancement and iron use has been uncovered through morpholino knockdown (25, 26).Despite the fact that deficiency of capacity of HTT didn't prompt specific neurodegeneration, misexpression of poly-Q extended HTT section causes protein total and neuronal passing. Curiously, sub-atomic chaperones can stifle the total arrangement and neuronal passing, and a few classes of little particle compounds including hostile to prion compounds have been approved to restrain poly-Q total development in zebrafish. These investigations show that zebrafish is a promising framework for demonstrating HD and for tracking down likely restorative treatment of HD (27, 28). Utilizing zebrafish as a model organic entity, logical progressions can be made in understanding the HD pathology/components with the expectation of creating likely treatments soon (29, 30).

6. CONCLUSION

Zebrafish have been widely utilized in the investigation of the CNS. All the more as of late, the utilization of zebrafish as a model of human CNS illnesses and for drug revelation has expanded. It helps in determining the outcome of reduced HTT gene expression in HD. Zebrafish modelling give a new direction in the molecular biology including the area of natural drug discovery, drug optimization, Nano medicine and regeneration medicine. Furthermore, the development attributes of zebrafish push the researchers to understand the etiology and the pathogenesis of the disease and hence it makes the way to find the optimal treatment for the disease and disorders. Thus, this makes the zebrafish a suitable organism to evaluate the therapeutic aspect of the drugs for neural development and neurological disorder.

Competing interests

Authors have declared that no competing interests exist

Ethical approval

Not Applicable

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