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Editorial

ZEBRA FISH AS A PRECLINICAL MODEL FOR NATURAL DRUG

Wen Li*

Department of Pharmacy, New Bulgarian University, Bulgaria

EDITORIAL

Early life stage studies with zebra fish were utilised to determine toxicity of compounds from natural bloom extract on their embryolarval development, and zebra fish have been employed as a preclinical model for identification of numerous natural compounds found on natural products. Zebrafish embryos are almost transparent, allowing researchers to view the development of interior components with ease. Because zebrafish eggs are fertilised and develop outside of their mothers' bodies, they are an excellent model organism for studying early development. The genetic structure of zebrafish is comparable to that of humans. As a toxicology model, zebrafish has the potential to reveal the pathways of developmental toxicity due to their similarity with those of mammals. Zebrafish therefore, provides a sound basis for the risk assessment of drug administration in humans.

Embryonic and larval development The *Danio rerio* (zebrafish) is becoming more popular as a toxicological model for rapid in vivo tests and developmental toxicity assays. The zebrafish's high genetic homology to mammals, robust phenotypes, and high-throughput genetic and chemical screening have made it a powerful tool for evaluating in vivo toxicity. New genome editing technologies including as CRISPR/Cas9, ZFN, and TALEN make it a good model for study of human genetic illnesses. This review examines recent studies that have used zebrafish as an experimental model, comparing it to other in vivo and in vitro models, and presenting zebrafish as a powerful vertebrate tool for assessing drug toxicity and efficacy in order to facilitate a more extensive, easy, and comprehensive understanding of new generation drugs.

Initially, zebrafish was used as a model system in the early 1970s, when it was chosen to build

the first vertebrate assay capable of forward genetic screening. Zebrafish were virtually exclusively utilised to examine organ development over the next 30 years. This led to the identification of an unusually large number of genes involved in vertebrate pathways, paving the door for the zebrafish to become a useful model for human disease and pharmacological research. The potential to use zebrafish assays in medium-to-high-throughput screening mode for pharmacology investigations is appealing because the zebrafish is a small (5 cm for an adult and 5 mm for 7 days post-fertilization (dpf) larvae) and robust fish that is easy to maintain thanks to their high density.

Previously, zebrafish were employed to assess the toxicity of agrochemical chemicals, but their use for toxicity testing of pharmaceutical substances has expanded dramatically. In zebrafish larvae, an *in vivo* toxicity study can be completed in a week; similar mammalian studies were necessary due to the shorter time frame. Toxicology investigations frequently reveal consequences that necessitate further inquiry to explain, which is both costly and time consuming. Screening tools for potential off-target effects on the cardiac system, as well as other systems such as the central nervous system, the digestive tract, auditory and visual functions, pro-convulsant potential, and bone formation, exist and are being further developed in zebrafish. As a result, zebrafish technology should be taken into consideration.

Key facts

- The use of zebrafish (*Danio rerio*) as a model organism began in the 1960s.
- The zebrafish is a Tropical fish native to Southeast Asia.
- The zebrafish is about 2.5 cm to 4 cm long.
- In its larval stages it is transparent and as it matures to an adult it develops stripes that run along the length of the body and look blue in colour.
- Males are slender and torpedo-shaped usually with a pink or yellow tinge.
- Females tend to be less pink than the males and are fatter due to the eggs they carry.
- Zebrafish have already been used to help unlock a number of the biological processes behind muscular dystrophy, and are an important model for understanding the mechanisms of development and diseases such as cancer.
- The complete genome sequence of the zebrafish was published in 2013.

- Its genome is 1,505,581,940 base pairs? in length and contains 26,247 protein-coding

Benefits of the zebrafish

- The zebrafish is small and robust.
- They are cheaper to maintain than mice.
- Break of daylight triggers mating in zebrafish (many other fish only lay eggs in the dark).
- Zebrafish produce hundreds of offspring at weekly intervals providing scientists with an ample supply of embryos to study.
- They grow at an extremely fast rate, developing as much in a day as a human embryo develops in one month.
- Zebrafish embryos are nearly transparent which allows researchers to easily examine the development of internal structures. Every blood vessel in a living zebrafish embryo can be seen using just a low-power microscope.
- As zebrafish eggs are fertilised and develop outside the mother's body it is an ideal model organism for studying early development.
- Zebrafish have a similar genetic structure to humans. They share 70 per cent of genes with us.
- 84 percent of genes known to be associated with human disease have a zebrafish counterpart.
- As a vertebrate, the zebrafish has the same major organs and tissues as humans. Their muscle, blood, kidney and eyes share many features with human systems.
- Zebrafish have the unique ability to repair heart muscle. For example, if part of their heart is removed they can grow it back in a matter of weeks. Scientists are working to find out the specific factors involved in this process to see if this will help us to develop ways of repairing the heart in humans with heart failure or who have suffered heart attacks.
- The zebrafish genome has been fully sequenced to a very high quality. This has enabled scientists to create mutations? in more than 14,000 genes to study their function.

Correspondence Author:

Wen Li *

Department of Pharmacy, New Bulgarian University, Bulgaria

E-mail: liw@gmail.com

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