OMICS International
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Bhusnure O G et al., J Develop Drugs 2015, 4:4
http://dx.doi.org/10.4172/2329-6631.C1.011

4th International Summit on

GMP, GCP & Quality Control

October 26-28, 2015 Hyderabad, India

Zebrafish as a model system for drug target screening and validation

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From ancient times to today, drug discovery transitioned from serendipity to rationality over its long history. Drugs are a physician's most powerful weapon to combat disease. The discovery of new drug targets is the basis of new drug development and examination of new drug mechanisms. Proper drug target selection and validation are crucial to the discovery of new drugs. Zebrafish have recently entered the fray as a model animal for some human diseases. The fish are more affordable, easier to keep, and faster to raise than mammals, giving a higher-throughput system. Zebrafish being a non-mammalian, drugs can also be tested for toxicity and their potential therapeutic activity against the target more easily than in mammals. Perhaps, surprisingly, genes that cause disease in zebrafish are similar to those in humans, for example in angiogenesis, inflammation and insulin regulation. Presently, the research using zebrafish is expanding into areas such as pharmacology, clinical research as a disease model and interestingly in drug discovery. The use of zebrafish in pharmaceutical research and discovery and drug development is mainly target screening, target identification, target validation, morpholino oligonucleotide screens, assay development for drug discovery, physiology based drug discovery, Quantitative Structure-Activity Relationship (QSAR) and Structure-Activity Relationships (SAR) study and drug toxicity study. In last few years, the use of zebrafish (Danio rerio) in scientific research is growing very rapidly. Initially, it was popular as a model of vertebrate development because zebrafish embryos are transparent and also develop rapidly. The zebrafish embryo has become an important vertebrate model for assessing drug effects. It is well suited for studies in genetics, embryology, development, and cell biology. Zebrafish embryos exhibit unique characteristics, including ease of maintenance and drug administration, short reproductive cycle, and transparency that permits visual assessment of developing cells and organs. Compounds on various organs, including the heart, brain, intestine, pancreas, cartilage, liver, and kidney, were observed in the transparent animals without complicated processing, demonstrating the efficiency of toxicity assays using zebrafish embryos. The use of animal models allows researchers to investigate disease states in ways which would be inaccessible in a human patient, performing procedures on the non-human animal that imply a level of harm that would not be considered ethical to inflict on a human. Using zebrafish, it is possible to obtain results quickly at lower costs. "Reducing failures early in the development is far more important than filling a pipeline with poorly chosen late-stage products likely to fail, and fail expensively" says Szymkowski.

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