Small fish can help finding drugs to fight retina diseases

About 285 million people are visually impaired in the world. The arising of chronic eye diseases and ageing processes make more people at risk of blindness, 65% of visually impaired people being aged 50 or older.

Among the pathologies that lead to the loss of vision, retinal vascular diseases share a common feature: the abnormal growth of new blood vessels that, starting from the surface of the retina, invade the inner part of the eye and lead to severe ocular complications, including blindness.

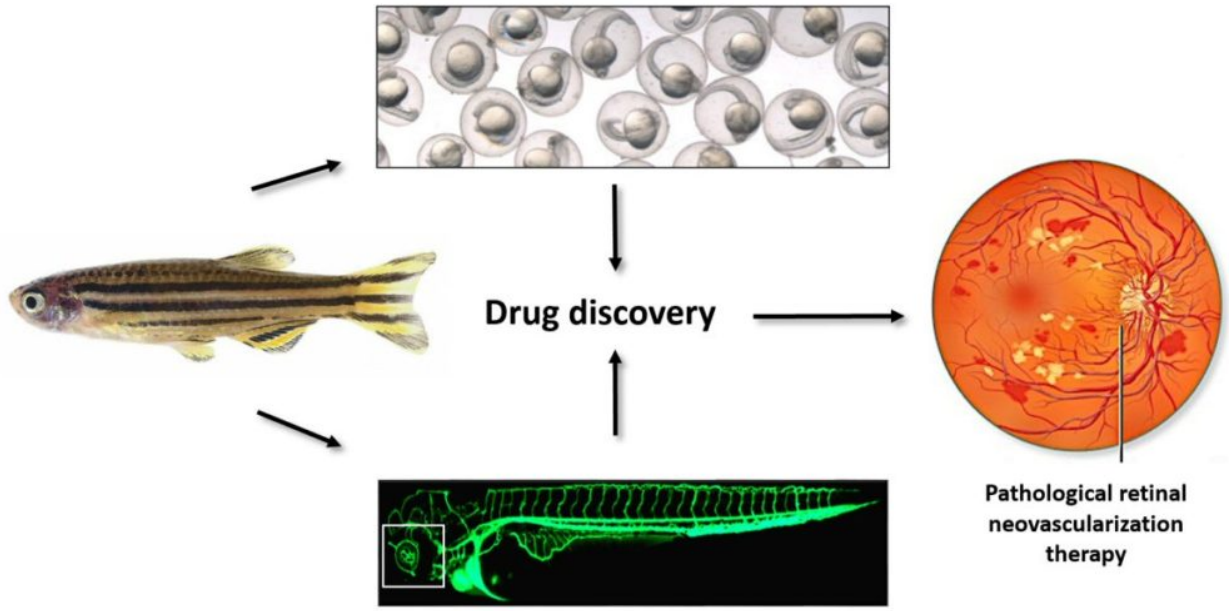

Fig. 1. Zebrafish as a tool for drug discovery in neovascular retinal diseases.

Preclinical and clinical evidences demonstrate that neovessel formation, also named pathological angiogenesis, is due to the aberrant production of high levels of proangiogenic factors in the eye. Among them, Vascular Endothelial Growth Factor (VEGF) appears to play a major role, leading to the hypothesis that anti-VEGF agents may arrest, or even reverse, the progression of angiogenesis-dependent eye diseases. On this basis, pharmacological approaches have been attempted to inhibit VEGF activity in pathological retinal angiogenesis. Indeed, the majority of patients under anti-VEGF therapy maintain vision, with approximately 30% of them showing a significant improvement. Nevertheless, adverse effects and resistance to treatment have been observed in these patients.

Due to the limitations of the current treatments, new experimental models of retinal

neovascularization are crucial for investigating novel anti-angiogenic strategies and bringing them to patients. The review article cited here highlights the importance of a small freshwater fish, named zebrafish, as a promising animal system for the screening of anti-angiogenic molecules to be employed for the treatment of angiogenesis-dependent eye diseases.

During the last 25 years, zebrafish has been largely used in developmental and biomedical research. Indeed, zebrafish offers several advantages when compared to classical animal models, including mice. For instance, zebrafish is a vertebrate with a rapid extra-uterine development, the fundamental biological and developmental processes being conserved between human and zebrafish embryos. Researchers can take advantages from the easy manipulation and the relative low cost of maintenance of this animal model. Furthermore, the possibility to set up large-scale screening of small molecules, including high-throughput screening of chemical compounds using robotic platforms, makes zebrafish embryo a useful model for the discovery and in vivo validation of new disease-driven therapeutic targets. Zebrafish combines the advantages of large-scale in vitro experiments with the biological significance of in vivo models, putative drugs being added directly to the water in which embryos are growing or can be injected in the embryonic blood stream. Moreover, the availability of transgenic zebrafish lines that express fluorescent reporter proteins in the vascular system allows the rapid in vivo visualization of the effect of the molecules under test on eye neovascularization.

Eye development in zebrafish starts very early during embryonic development and 3 day-old embryos already display a functional visual system. In addition, various models of retinopathy characterized by defects in blood vessels development have been established in zebrafish embryos and adults. Thus, due to its peculiar features, zebrafish represents an innovative model for large-scale screening of new angiogenesis inhibitors aimed to prevent eye neovascularization. As reviewed in this article, the successful testing of known anti-angiogenic compounds in zebrafish enforces this hypothesis.

In conclusion, the studies reviewed here support the concept that zebrafish embryo may represent a simple, cost-effective and rapid tool for the study of novel anti-angiogenic therapeutics and for the identification of genes associated with ocular vascular diseases that, in turn, may become targets for the development of new therapeutic approaches.

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