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Zebra fish, a great tool for drug development

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Abstract

The traditional “target-based” drug discovery approach involves in vitro biochemical and cell-based assays followed by in vivo animal tests before ultimately trials in humans. Typically more than 99% of drug leads identified in the early in vitro screening fail in the later in vivo studies and clinical trials. As result, developing a new drug typically takes 15 years and costs 1.2 billion US dollars before it reaches the market. The challenge for traditional “target-based” drug discovery could be overcome by zebrafish “phenotype-based” approach. Based on the hypothesis that a small molecule that selectively targets a signaling pathway involved in embryonic patterning should phenocopy genetic mutations in that pathway, we discovered several highly selective small molecule modulators of signaling pathways in the zebrafish phenotype-based screening recently. For instance, we have developed exclusively selective inhibitor of bone morphogenetic protein signaling, DMH1, based on the fact that fish embryos treated with DMH1 would pheno-copy dorsalized morphology seen in BMP signaling mutant fish. In addition, we have discovered a highly specific VEGF receptor 2 inhibitor (DMH4), Wnt/β-catenin inhibitor (Windorphen) and a new group of Hedgehog pathway inhibitor (Eggmanones). Our research demonstrates that zebrafish phenotype-based approach is an efficient way for drug development.

Biography

Jijun Hao obtained his Ph.D.degree in biochemistry and molecular biology from University of Leeds (UK) in 2003, which was followed by postdoctoral training in the fields of chemical genetic and stem cell biology at Vanderbilt University Medical Center. In 2010, He was appointed as a Research Assistant Professor at the Division of Cardiovascular Medicine in Vanderbilt University. Currently Hao is an assistant professor at Western University of Health Sciences. He has published 13 peer-reviewed articles and three book chapters, and filed three patents.