# REVIEW ARTICLES

## Zebrafish approaches enhance the translational research tackle box

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**During the past few decades, zebrafish (*Danio rerio*) have been a workhorse for developmental biology and genetics. Concurrently, zebrafish have proved highly accessible and effective for translational research by providing a vertebrate animal model useful for gene discovery, disease modeling, chemical genetic screening, and other medically relevant studies. Key resources such as an annotated and complete genome sequence, and diverse tools for genetic manipulation continue to spur broad use of zebrafish. Thus, the purpose of this introductory review is to provide a window into the unique characteristics and diverse uses of zebrafish and to highlight in particular the increasing relevance of zebrafish as a translational animal model. This is accomplished by reviewing broad considerations of anatomic and physiological conservation, approaches for disease modeling and creation, general laboratory methods, genetic tools, genome conservation, and diverse opportunities for functional validation. Additional commentary throughout the review also guides the reader to the 4 new reviews found elsewhere in this special issue that showcase the many unique ways the zebrafish is improving understanding of renal regeneration, mitochondrial disease, dyslipidemia, and aging, for example. With many other possible approaches and a rapidly increasing number of medically relevant reports, zebrafish approaches enhance significantly the tools available for translational research and are actively improving the understanding of human disease. (Translational Research 2014;163:65–78)**

**Abbreviations:** cDNA = complementary DNA; dpf = days post fertilization; ISH = *in situ* hybridization; GFP = green fluorescent protein; KD = knockdown; KO = knockout; MO = morpholino; mRNA = messenger RNA; ZFIN = the Zebrafish Model Organism Database; ZIRC = Zebrafish International Resource Center

Technological innovation continues to expand disease-relevant information for both individuals and populations, and is facilitating broader and deeper associations of phenotypic and genotypic data. Coupled with the tremendous growth in access to animal genomes and the capacity to manipulate these genomes, the ability to create animal models of disease is historically unprecedented. Targeted transgenic approaches that have long been a mainstay for the mouse[1] but were largely inaccessible for many other relevant

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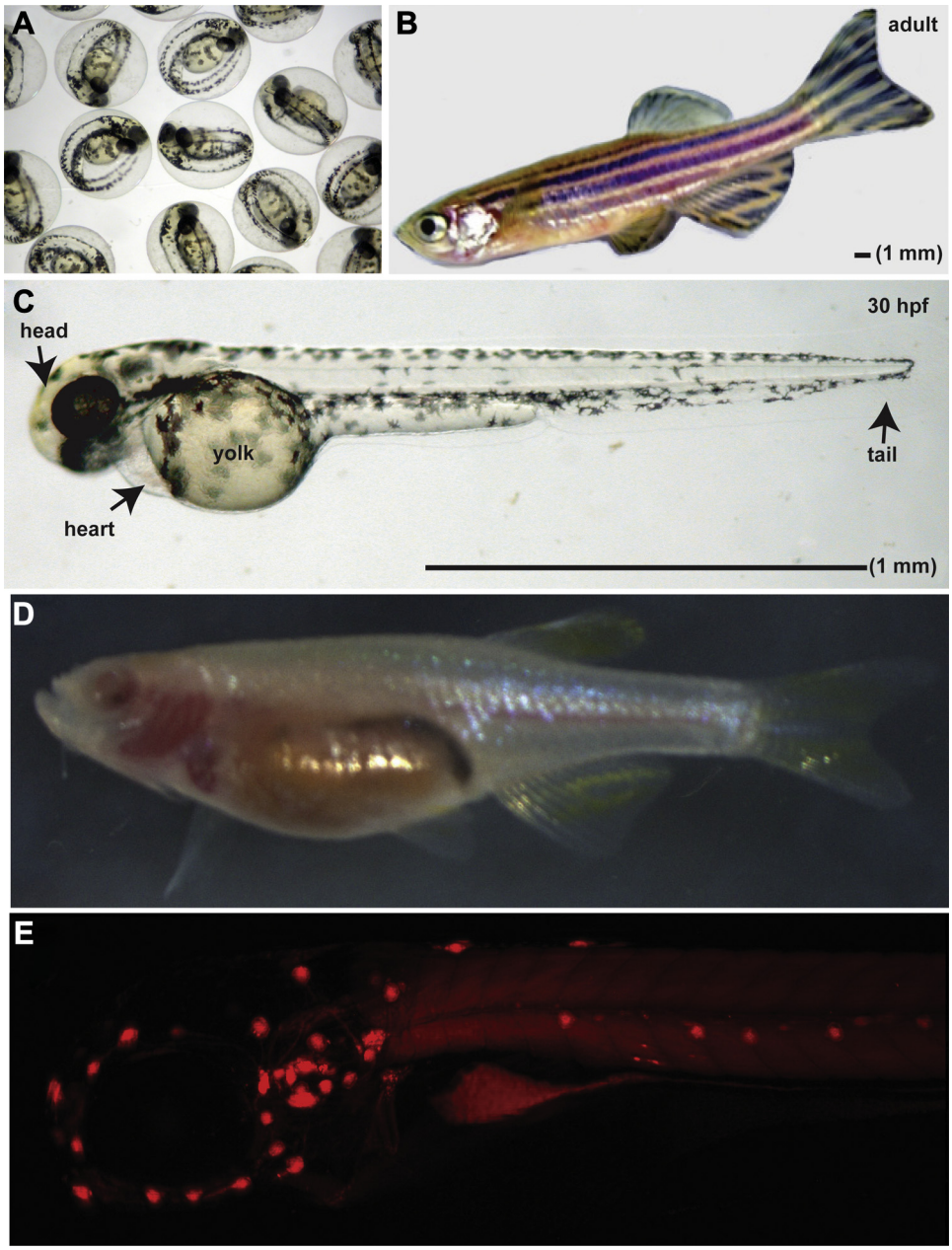


**Fig 1.** Selected images of zebrafish. (**A**) Clutch of 1 day post fertilization zebrafish embryos encapsulated by an embryonic shell, the chorion. (**B**) Adult zebrafish. (**C**) Zebrafish embryo at 30 hours postfertilization. (**D**) Sheer line of zebrafish (image courtesy of Henry G. Tomasiewicz). (**E**) Expression pattern of monomeric red fluorescent protein identifies neuromasts of zebrafish lateral line of an embryo 4 days post fertilization of a revertible protein trap gene-breaking transposon insertional mutant line[3] (image courtesy of Karl J. Clark and the Ekker lab). Bars (bottom right) of **B** and **C** indicate 1 mm to highlight relative differences in size of adult and embryonic zebrafish.

model species such as rat, are now possible.[2] As a result, animal models in nontraditional species that maintain a particularly relevant biomarker or model a specific pathology more closely than traditional models (eg, mouse or rat) are increasingly accessible and invaluable. One such model, the zebrafish (*Danio rerio*), highlighted in Fig 1,[3] is literally spawning a plethora of human disease models that reproduce disease processes reliably and hold distinct advantages that make them attractive. In addition, the use of these emerging animal models in translational research facilitates a deeper understanding of gene function through cross-species phylogenic investigations, shedding light on the natural evolution of species and structure/