The zebrafish's growing impact on medical research

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Credit: University of Alabama at Birmingham

The National Institutes of Health website Clinicaltrials.gov estimates there are more than 48 million Americans currently enrolled in clinical or observational studies. While mice have traditionally been the other most commonly studied animal along with humans—mice and rats make up some 95 percent of animals used in research—the zebrafish has

become perhaps the fastest-growing segment of the research population.

Zebrafish, relatives of the minnow, are native to the Southeastern Himalayan region of Asia and are found in parts of India, Pakistan, Bangladesh, Nepal and Burma. They are a small fish, reaching about 2.5 inches in the wild and topping out around an inch and a half in aquariums. The first scientific study of zebrafish began nearly 40 years ago, but it has been in the past 10 that the use of zebrafish in research has boomed.

"There are approximately 20 researchers at the University of Alabama at Birmingham alone using zebrafish in their studies of human disease," said Susan Farmer, DVM, Ph.D., a veterinarian in UAB's Animal Resources Program and co-director of the UAB zebrafish research facility. "We have roughly 15,000 zebrafish on campus."

The fish are valuable for studies of a multitude of diseases, including cancer, heart disease, obesity, muscular dystrophy and narcolepsy. The reasons for their burgeoning popularity are varied. They are easy to care for and cost-effective. More importantly, they offer biological advantages that other research models cannot match.

One key is that, following fertilization, zebrafish embryos are transparent. Every facet of their rapid embryonic development can thus be observed by scientists.

"You can watch the body form over the course of a few days" Farmer said. "The eyes and most organs begin forming in the first 24-36 hours. Within five days, they are fully formed and swimming. It is an unparalleled system for studying the development of an organism from egg to maturity."

The cell physiology of a zebrafish is similar to that of humans, making

the fish a suitable model for many human diseases. Humans share some of the same molecular pathways—zebrafish get cataracts, for example. The zebrafish genome has been fully sequenced, so researchers can use gene editing techniques to better understand the role of individual genes on disease.

And it happens quickly.

A mouse might have a litter of 10 offspring that spend three weeks in the womb. A zebrafish will lay 100-500 eggs every week, and once fertilized, the eggs waste no time. The first cell division in the embryo occurs within 45 minutes of fertilization, so scientists can observe the effect of adding or deleting genes at the one-cell stage.

"Removing a gene at this early stage means the gene will not be present at all in the adult fish, giving researchers a tremendous opportunity to understand the effects of a single gene, an opportunity that is not possible with any other animal model of human disease," said Stephen Watts, Ph.D., professor in the Department of Biology at UAB and co-director of the zebrafish research facility.

Outside of the physiological advantages, zebrafish offer logistical benefits as well.

"They are small and don't require a great deal of space," Farmer said. "You can house a great many zebrafish in tanks similar to a home aquarium. They are also easy to care for."

UAB recently hosted a three-day seminar on how to care for zebrafish. Sponsored by the Zebrafish Husbandry Association, the event was run in conjunction with a program at Gadsden State Community College.

"The association is a grassroots group that was founded to train

laboratory technicians on the proper care of zebrafish," said Hugh Hammer, Ph.D., director of the Aquatic Science and Aquaculture Education and Development Center at Gadsden State. "We have a rigorous online training program, but also offer this hands-on seminar on topics such as required water quality, socialization, fertilization and feeding."

The seminar attracted more than 20 lab technicians from research institutions across the United States and Canada. Because zebrafish are not the only marine animal of interest to science, UAB will also host the eighth Aquatic Models of Human Disease Society international meeting in January 2017, directed by Peggy Biga, Ph.D., assistant professor of biology.

"There are UAB research projects looking at a variety of conditions in different species of fish," Farmer said. "Peter Verbeek, Ph.D., associate professor of anthropology, is using betta fish to study aggression. Mickie Powell, Ph.D., an assistant professor of biology, is looking at aging through the killifish, and Biga is using trout to study muscle biology."

"Zebrafish, or any fish for that matter, can't be used for all studies," Watts said. "They don't have lungs for example, or skin, and so have no utility for conditions or diseases of those organs. But we are just now beginning to tap into the potential knowledge that we can gain on human disease by the use of fish as models. We have a great deal more to learn, and this is a very exciting time for science."

Provided by University of Alabama at Birmingham