FISH TANKS AND DIABETES DISCOVERIES: 
THE ZEBRAFISH RESEARCH LAB

WITH STRIPED FISH DARTING BACK AND FORTH INSIDE ROWS OF FISH TANKS ARRAYED ON METAL SHELVES, this might almost be mistaken for an unusual pet store. But these fish are no pets. They are critical components of research that could revolutionize the treatment of diabetes.

This is the zebrafish lab of Raghu Mirmira, MD, PhD, who joined the University of Chicago Medicine faculty last year and added his extensive research portfolio to the Kovler Diabetes Center scientific team.

Mirmira conducts research across multiple platforms, from cells in petri dishes to zebrafish to mice to humans. “We translate across this disparate group of organisms with the goal that central ideas we might discover in lower systems have a pipeline to move into humans,” Mirmira explained.

And zebrafish, says research assistant professor Ryan M. Anderson, PhD, who oversees this lab, are diabetes research superstars.

They are an ideal species for studying the central focus of diabetes research: the beta cell, which produces insulin. Zebrafish can regenerate beta cells. Investigating how they do so holds great promise in exploring ways to treat, and potentially cure, type 1 diabetes.

Moreover, their embryonic development—the period when they initially make beta cells—indicates new avenues of research.

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RYAN M. ANDERSON, RESEARCH ASSISTANT PROFESSOR, IN THE ZEBRAFISH LAB HE OVERSEES
cells, along with other parts of the body—is especially easy to study.

For one thing, zebrafish eggs and embryos are nearly transparent. “You can look through the shell and see the embryo. You can look through the skin of embryo, and see the internal organs,” Anderson said.

For another, researchers can observe the formation of the pancreas and beta cells during development without changing the processes’ natural course.

“If you want to study the development of a mouse embryo, you would have to remove it from the mother,” Anderson pointed out. “Once you do that, you’re altering conditions.” But zebrafish embryos normally grow from eggs hatched in water. When scientists watch them develop in a petri dish, they are seeing exactly what happens in nature.

Rounding out their impressive research qualities, zebrafish are inexpensive to maintain, and reproduce and grow so quickly that researchers can conduct multiple rounds of experiments at high speed.

And though it’s not a scientific requirement, zebrafish embryos are beautiful—at least to Anderson, who switched to zebrafish from studying mouse embryos. “I was lured into studying zebrafish by the beauty of the embryos,” he said. “There is most certainly an aesthetic attraction.”

The view under the microscope is especially dramatic because in order to make the development process even easier to see, the lab genetically engineers the fish to highlight the pancreas and beta cells fluorescent green and red.

Anderson began working with zebrafish during his fellowship, when he was studying the remarkable ability of the zebrafish pancreas to repair itself. He genetically engineered a strain of zebrafish with beta cells that were designed to be sensitive to a common antibiotic. He was able to destroy their beta cells, and thus induce an artificial form of diabetes complete with blood sugar spikes, simply by adding the antibiotic to their tank water.

Then he removed the antibiotic—and the fish grew new beta cells. The new beta cells began producing insulin. With their insulin restored, the fish did what for now humans can only dream of: they recovered from diabetes.

Whole new avenues of research opened. “What are the ways they do this? Where do the new beta cells come from? What are the genetic or molecular pathways involved? We can genetically engineer the zebrafish to find new ways to increase this and understand it better, and we can look for new drugs that will enhance regeneration.”

Mirmira’s team is using these genetically engineered zebrafish to answer those questions and to test drugs that might be able to protect beta cells from damage or coax them to regenerate. The lab has just gotten a new grant from the National Institutes of Health (NIH) for studies on a genetic pathway involved in beta cell regeneration and replication.

This work is highly promising. To Anderson, it also remains visually amazing. Even after years of working with them, when he looks through a fluorescence microscope and sees those bright red-stained beta cells bubble up inside a glowing green pancreas, he is struck by the sight.

“They’re a little hypnotic,” he said. “I still find myself staring at them.”

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