A GOLD MINE OF A FISH

An exciting development in the search to find a cure for cancer is taking place in a Portland State University lab. Read this article to find out more.

Research on these amazing fish may hold answers for us all.

A key to unlocking a cure for cancer may someday be swimming in an aquarium in a campus laboratory built specially for assistant biology professor Jason Podrabsky.

Hundreds of fish inhabit the tight quarters, made even tighter by Podrabsky’s small crew of graduate students, who squeeze past each other in the warm humidity to reach for pipettes, claim space in front of the microscope, or collect and label lidded glass dishes containing fish eggs. And of course they feed the fish, which swim in carefully controlled conditions in row upon row of aquariums stacked on a system of tall metal shelves.

These are no ordinary fish. The killifish, a native of Venezuela, possess a particular talent for surviving in an unforgivingly harsh environment. They live in mud puddles that can heat to as high as 113 degrees Fahrenheit, then dry up completely. When the puddles dry, the fish die, but their fertilized eggs live on.

In an early stage of development, the egg embryos go dormant, encasing themselves in a hard protective shell that seals in all moisture. They stay this way throughout the hot, dry summer, waiting in the cracked earth. Then, when the infrequent rains come and the dusty depressions become ponds once again, the embryos emerge from their state of suspended animation to become adult fish and start the cycle anew.
In Podrabsky’s lab, these embryos look like tiny glass beads, which roll freely and clink together when you tip their glass dish. But look at one under a microscope and you’ll see a large eye and the very beginnings of a body that will eventually become a spotted and rather flashy-looking adult. Some 4,000 of these embryos are produced in the lab every week.

What interests Podrabsky is the mechanism within each embryo’s cell that tells it to go dormant and form a hard shell. It’s called gene expression. Under certain conditions, some of the cell’s genes are “switched on” to make more of a specific protein. Genes can also turn off the production of other proteins to produce another result. In the case of the killifish, environmental factors trigger a kind of gene expression that allows the fish embryos to live without water for months or perhaps years at a time.

Not much is known about how factors such as temperature differences, exposure to light, changes in oxygen levels, or dehydration cause the embryos to do certain things. Podrabsky is working to find those answers with funding help from the National Science Foundation.

Although killifish use their adaptive talents in a novel way, gene “expression” is a common trait among all living things.

“All organisms have it, including us. All of us are looking for ways to adapt in our environment,” says Podrabsky, who earned his bachelor’s degree in biology at Oregon State University and his doctorate at University of Colorado in Boulder.

And that’s why his research may offer insights into the causes of and possible cures for cancer and other diseases. Cancer is a disease in which the mechanics of cell growth and functioning are thrown off kilter, often by an environmental trigger. In a sense, cells lose the ability to adapt to their environment. Excessive exposure to sunlight can trigger skin cancer, for example. Exposure to the chemical benzene has been identified as a possible trigger for leukemia. Environmental factors may be the only explanation for why one person develops cancer while his or her twin sibling doesn’t.

Part of Podrabsky’s research involves the environment in which the killifish live. “We can put the embryos in a higher incubation temperature to cause them to bypass their dormant phase, for example, or we can expose them to light. We also look at other ways in which they won’t break dormancy,” he says.

One characteristic of all embryos is that they grow rapidly from a single cell. The cell divides, then divides again, doubling continuously until it reaches a certain point. Then the rapid development phase stops. The cells are programmed to stop dividing so that other phases of development—such as building of the skeleton, nervous system and organs—can take the forefront. Cancer cells are immune to the negative regulators that halt cell growth. They divide uncontrollably.
“These killifish embryos have the ability to globally shut down or regulate cell proliferation and metabolism. If we can figure that out, we can address cell proliferation in cancers,” Podrabsky says.

Each type of tissue in the human body has its own unique types of cells, each with its own set of cues telling it to grow or not grow. So studying a liver cell won’t tell you much about colon cancer, for example.

“But in these embryos,” Podrabsky explains, “everything is shutting down. We are looking for this master controller that could act in any cell at any one time.”

Podrabsky says that if he can find the genes responsible for cell proliferation, he will pursue National Institutes of Health funding for cancer research. While he is working on that problem, the American Heart Association has given him funding to study another: the effects of oxygen deprivation.

While adult killifish have to have oxygen, early embryos and embryos that are in their dormant phase can go 90 days without it. If we can understand the differences at the cellular level between the heart of an embryo and that of an adult, Podrabsky says, we will gain a better understanding of how to survive heart attacks and strokes.

When a person has a heart attack, for example, the heart is deprived of oxygen. Some heart cells will die as a result, but other cells will survive the low-oxygen event only to die when oxygenated blood flows back into the area, Podrabsky explains.

“So it’s not a given that a heart attack victim will survive after they’ve been stabilized. Much of the damage happens when blood is reintroduced,” he says.

The killifish embryos Podrabsky is studying don’t have that problem. They can go for extended periods of time without oxygen and suffer no ill effects when oxygen is reintroduced. Is it their genes or the environment?

One theory holds that the heart cells that die when they are reexposed to oxygen do so because they are programmed to self destruct. This phenomenon of programmed cell death, called “apoptosis,” is inherent in all healthy cells. Under normal conditions, cells die off to make room for new cells or to make way for a new phase in the organism’s development.

“Every cell in your body is ready to commit suicide if given the right signals,” Podrabsky says.

For example, humans are born with fingers instead of paddle-like fins because the cells that form the webbing between the fingers kill themselves off during embryonic development. One reason cancer is such a lethal disease is that cancer cells have lost this ability to self destruct.

So why would a heart cell choose to do away with itself instead of taking advantage of a new chance at life in the form of oxygen-rich blood?
Podrabsky is hoping that the killifish, whose embryonic hearts make that choice to live, will provide an answer.

“These fish are a gold mine,” he says.

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Notes on my thoughts, reactions and questions as I read:

1. Describe what makes killifish embryos important to scientists and different from other embryos.

Important:

Different:
2. Use the Venn diagram below to show the similarities and differences between the use of the killifish in cancer research and heart research.

Kilifish Use in Research

Cancer Research

Heart Research

Similarities

3. How does the author feel about this research project? **Use evidence** from the text to support your answer.
4. The article states that Podrabsky is waiting for funding help from the National Science Foundation. **Use evidence** from the text, to make at least **two predictions** of what is likely to happen if this funding becomes available.

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5. This article was written for the Portland State University Magazine. What does the author want the reader to know or do after reading it?
6. Identify two quotes from Professor Podrabsky, one that uses technical language and one that uses figurative language (personification, simile, metaphor, etc.). Explain the effect of each quote.

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