Breaking Through

2014 Annual Report to Our Donors

Michael Westphal is a champion marathoner.

Ever since his diagnosis nine years ago, Michael has been running a marathon against the debilitating condition known as Parkinson's disease. It's a long distance race, and he never gets any time off.

But the qualities that make him a champion—perseverance, endurance, and courage—allow him to break through the limits imposed by his disease every single day. The stakes couldn't be higher. Because Michael isn't just running for his own life.

He is running for all of us.

This report is dedicated to the donors, patients and scientists who *believe* and *make* breakthroughs possible.

Champions of Medical Breakthroughs

Not all champions are athletes. In fact, Merriam-Webster defines the word "champion" without even mentioning the concept of sports. A champion, the dictionary says, is a "warrior, fighter," or "a militant advocate or defender." And by these definitions, we encounter champions every day through the work of the MDI Biological Laboratory.

There are patients, like Michael Westphal and Alan Fidler, whose stories you will find in this report. They have both repeatedly shown the courage and determination of champions, fighting the challenges of Parkinson's and heart disease. Their commitment to breaking through the debilitating symptoms of their diseases in order to live fulfilling lives—to be there for their families—is inspiring. (Michael actually is also a champion athlete—a marathoner—but more on that in the following pages.)

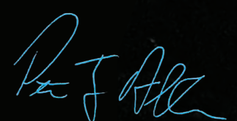
Then there are the scientists on our faculty, like Aric Rogers and Voot Yin, who come to work each day to fight the ravaging consequences of diseases like Parkinson's and heart disease. It requires the toughness and perseverance of champions to return to the bench each day to push the research a little bit farther. Contrary to the popular image, progress in science is rarely marked by a single, world-changing, "eureka" moment.

Rather, each new insight leads to another and another, until we finally achieve the breakthrough that the MDI Biological Lab seeks—to revolutionize human medicine by slowing down the aging process, and by enabling organs and body parts that have been damaged to regenerate.

What makes all this possible? You, our donors.

Without you, the MDI Biological Laboratory couldn't support the scientific experts and technical resources that make our transformative research possible. We couldn't pay for salaries, research supplies, or equipment.

Because of you, we are on the brink of making revolutionary improvements to human health. You are our champions of generosity, belief, and dedication. Thank you.



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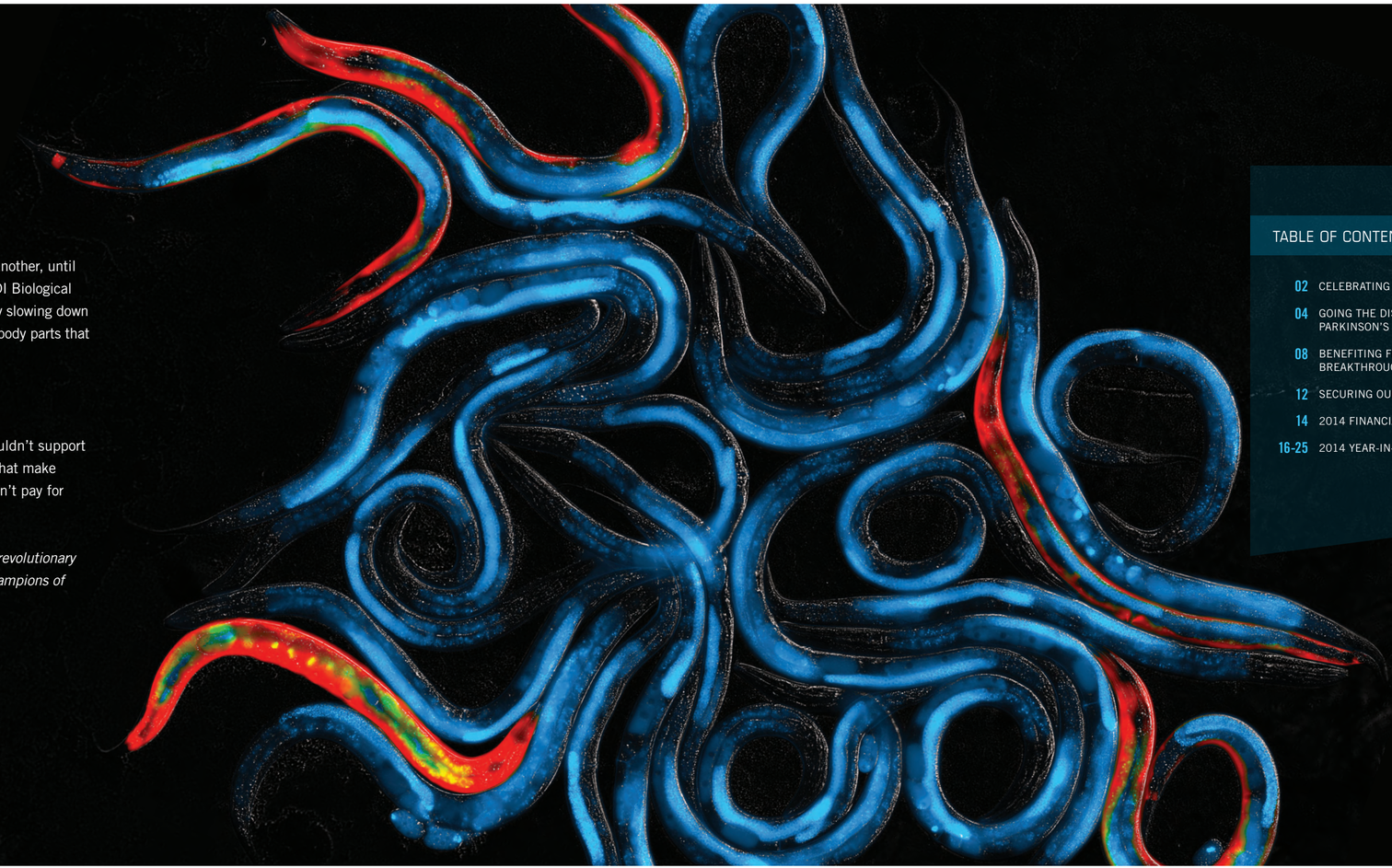

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"I'd sleep much better knowing that the smile on my little granddaughter's face will never be swept away by the consequences of Parkinson's."

Michael Westphal Going the Distance Against Parkinson's Disease

Michael is a born athlete. All through high school and college, he ran competitively—track and cross country—and he was known throughout his state of Maine as one of the best. After college, he continued to compete in long distance road races. He ran 14 marathons. And then he put competitive running aside for twenty years to focus on managing a growing business and raising two sons with his wife.

Unexpected diagnosis

Michael's vigorous physical condition made the bad news especially hard to believe. Nine years ago, at age 49, he was diagnosed with Parkinson's disease. Parkinson's is a degenerative, neurological disorder, affecting one million Americans and over four million individuals worldwide. The disease is age-related, striking most people at 50 or older. Symptoms include tremors, rigidity of the limbs and torso, slow movement or an inability to move, and impaired coordination. And they worsen slowly over time.

"My first reaction? I don't think I believed it," Michael remembers. My biggest fear was that in ten years, I'd be disabled, in a wheelchair. I decided early on that I wasn't going to lie down and take it. I'm a positive person. I didn't want people to feel sorry for me."

Michael took medications to control his symptoms to the extent possible, and spent the next seven years concentrating on his work. He and his crew (which includes both his sons, now ages 30 and 32) built three houses, and completed a number of other big projects. "My goal was to work as long as I could to save money for the time when I couldn't work anymore."

Determined to do what he always loved

Then, last year, he decided to take up running again. "I wanted to get more out of life than just working all the time," he says. He wasn't sure how he'd perform. "I knew I could run short distances, but I was surprised that I had the endurance to run long distances."

Michael was thrilled to find that he still has what it takes to exercise hard. But there's been a terrific bonus: he believes that running has improved his condition. "I have almost no symptoms and feel great when I'm running," he says. "Even during the rest of the day, I feel much more normal than I did before."

In fact, he felt so good that he decided to undertake a marathon. He began training—running up to 55 miles a week—for the 2015 "The Great Run," held each June on Great Cranberry Island. And he did it to raise funds for The Michael J. Fox Foundation for Parkinson's Research.

"Not everybody can run a marathon, but everybody should do what they can to further the cause they believe in. That's what I'm doing." Michael raised over $36,000 and completed the race in 3:32:56—a time that qualifies him to run the 2016 Boston Marathon.

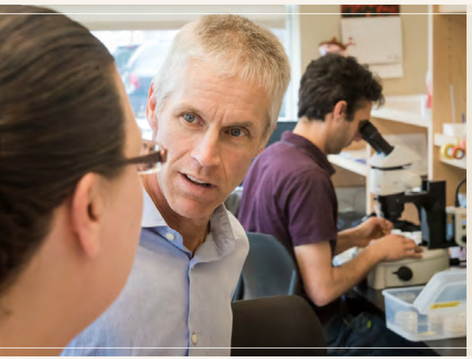
With the recent birth of his granddaughter, Maeve Grace, Michael has more motivation than ever for raising funds for Parkinson's research. About 15 percent of those with the disorder have a family history of Parkinson's. Four of Michael's close relatives—including his sister—have battled the disease.

"I'd sleep much better knowing that the smile on my little granddaughter's face will never be swept away by the consequences of Parkinson's," he says. "That's why I'm persevering to raise money."

The Rogers Lab fights against Parkinson's and other diseases

Meanwhile, across the bay at the MDI Biological Laboratory, Aric Rogers heads up a lab that is exploring why growing older causes certain individuals to succumb to degenerative diseases associated with aging—including Parkinson's disease.

Parkinson's, Alzheimer's, and Huntington's disease are all "diseases of aging," says Aric. "People live healthy for years—even if they have a genetic predisposition to one of these diseases. And then, late in life, something goes wrong with the genetic machinery that is tasked with keeping the cells clean and uncluttered. As a result, the cells of these individuals develop a dangerous build up of proteins—a different protein for each of these diseases—and lose their ability to function properly." And the disease takes over.



Michael Westphal owns his own carpentry business on Great Cranberry Island, off the coast of Mount Desert Island. Aric Rogers is a research scientist and assistant professor of regenerative biology at the MDI Biological Laboratory. They have something profound in common: they are both doing everything they can to fight the debilitating degenerative condition known as Parkinson's disease, each in his own way.

Aric's team is examining why—and searching for ways to prevent or slow down the failure of this "housekeeping" machinery that marks the onset of these diseases. Their approach to the problem is unusual in a couple of ways.

An innovative and expedient approach

First, they have chosen the tiny worm, *C. elegans,* as their research model, rather than more commonly used lab mice and rats.

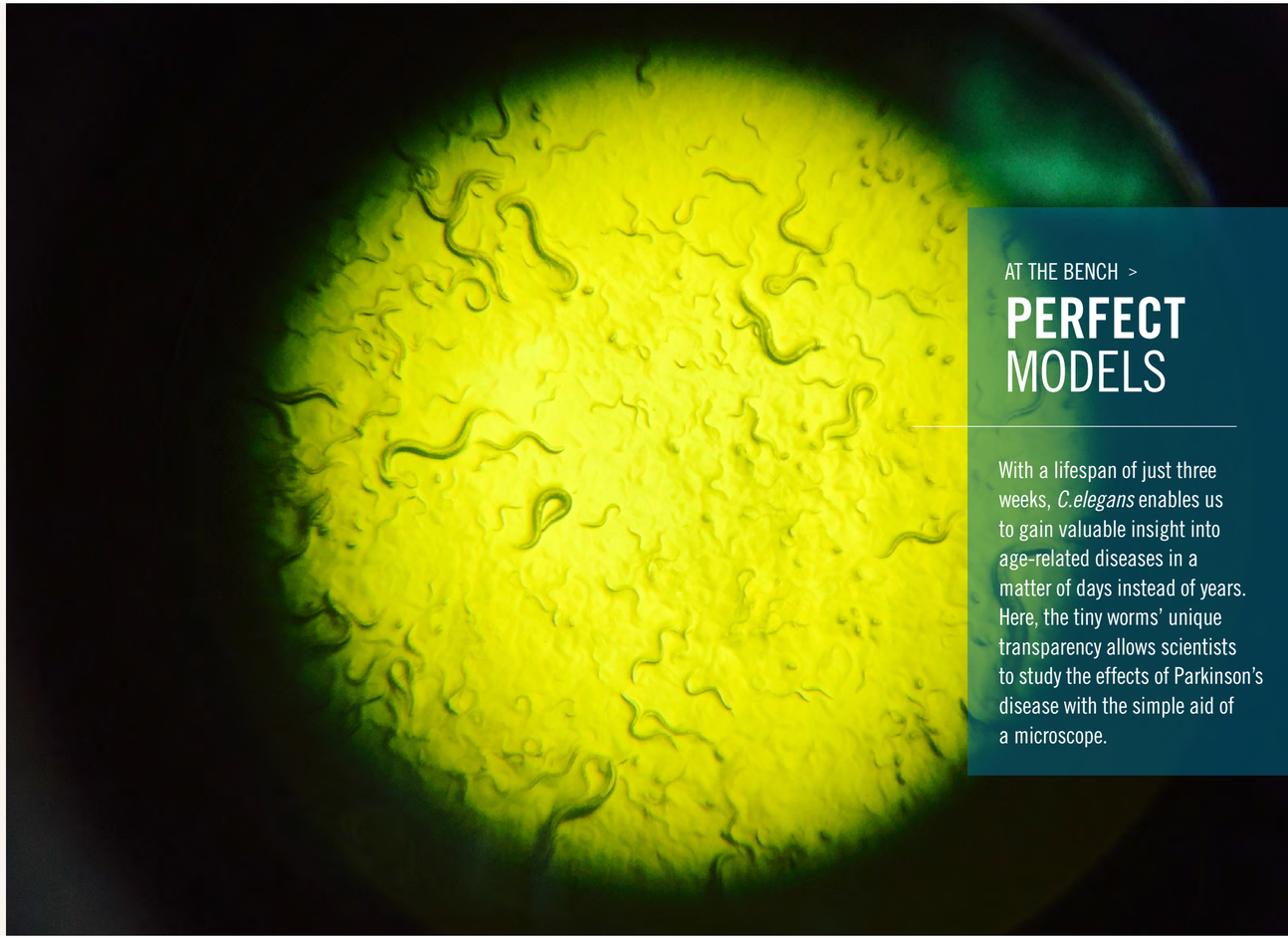
It may seem surprising to study a worm to learn about human aging and disease—but it's actually a perfect choice. It shares about half its genes with humans—including the mechanisms that are associated with keeping the cells clean and tidy. They live an entire lifetime in a matter of weeks—so the effects of aging on their cells can be studied quickly and easily. And they reproduce fast—each worm can make up to 300 worms in just a few days—so they are inexpensive and easily available.

The second trailblazing feature of Aric's approach: don't focus on eliminating the protein buildup in the cells. Instead concentrate on repairing the malfunctioning cell machinery so that it regains its ability to stop the protein buildup before it occurs. This will keep the cells healthy, longer—and help prevent the onset of all of these degenerative diseases of aging.

Based on their research so far, Aric and his colleagues believe that certain lifestyle changes have potential for strengthening cells that have been damaged in this way. They've seen that when cells are exposed to the temporary stress that comes with dietary restriction, exercise, or temperature change, for example, they respond by hunkering down to protect themselves—and in the process, they regain some of their efficiency. That's why Aric wasn't surprised to hear that Michael's Parkinson's symptoms have diminished with his increased physical training."

Aric's team is also exploring a variety of therapeutic compounds to do the job more effectively. "We're working to identify targets for new drugs that will reduce the effects of aging—including reducing the incidence of disease. That's the ultimate hope."

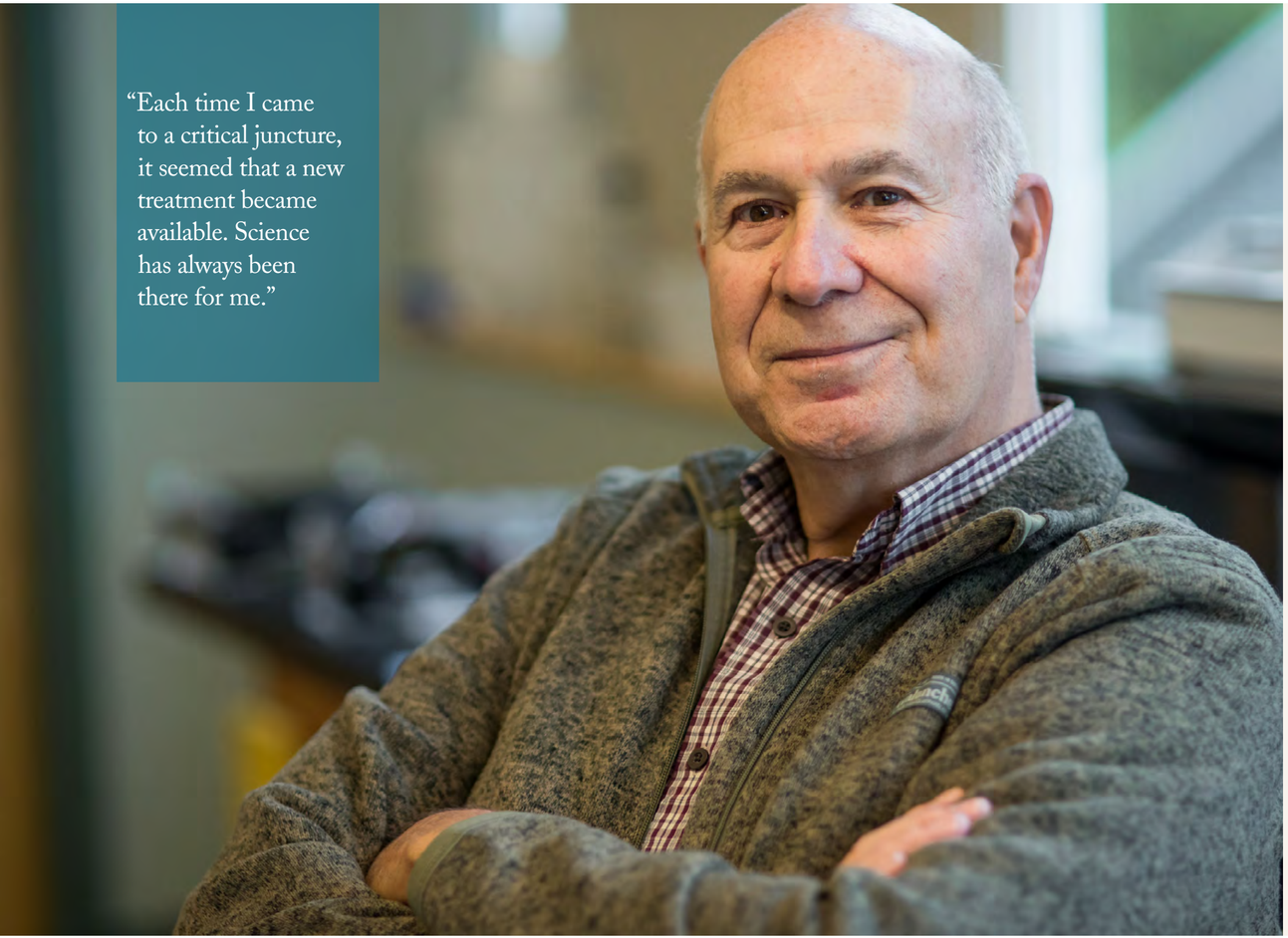
Michael Westphal, his family, and millions of others who deal with the pain, fear, and loss of Parkinson's and other degenerative diseases, are waiting.



AT THE BENCH >

PERFECT MODELS

With a lifespan of just three weeks, *C.elegans* enables us to gain valuable insight into age-related diseases in a matter of days instead of years. Here, the tiny worms' unique transparency allows scientists to study the effects of Parkinson's disease with the simple aid of a microscope.



Alan Fidler

Benefiting from Scientific Breakthroughs

Alan Fidler has battled heart disease for 35 years (and counting). He has undergone seven major surgeries and any number of less significant procedures and treatments. It began in 1980. Alan was 36 and healthy, working long days to launch a high-powered career as an engineer and executive at Polaroid. He had a wife and three young boys.

Out of the blue, he had a heart attack. “It wasn’t a terribly bad one—it was what they call a warning heart attack,” he recalls. “They did all the appropriate testing and risk analyses. I didn’t fit the profile—no high cholesterol or blood pressure, no family history of heart disease, nothing. I chalked it up to bad luck, started exercising more, went on the appropriate medications, and got on with my life.”

Neither he nor his doctors expected anything more to happen.

But three years later, they were all proved wrong. Alan suffered a massive heart attack. “I shouldn’t have lived through that one. I was closer to dead than alive.”

Emergency surgery revealed such extensive damage that the heart muscle could no longer beat symmetrically. Surgeons removed a significant portion of his heart and performed a quadruple bypass—an incredibly complex and dangerous surgery—and hoped for the best.

“I knew it was about as serious as it could get,” says Alan. “I remember saying goodbye to my wife and children.”

He kept the details of his struggle to himself, knowing that revealing his condition would sabotage his chances for professional success. “I was not going to let this thing define me.” He continued climbing Polaroid’s corporate ladder and raising his family.

But it wasn’t easy. It took a toll on Alan. Because the pumping ability of his heart was greatly reduced, he had to limit and monitor his activities. He watched his diet and took a lot of medications. He always wore a shirt in the pool to cover the frightening scar on his chest, and long pants to cover the scars on his legs where they took veins to use for his bypass surgery.

Perhaps even worse was the toll on his wife, who lost any semblance of security about the future, knowing that she had “a time bomb sleeping next to her each night.”

The following decades brought five more life-threatening surgeries for bypass repairs, electronic defibrillator implantation and subsequent repairs, surgical ablation, and defibrillator replacement. Alan is thankful that each procedure extended his life—but he’s all too aware that they are just Band-aids—not cures—for his heart disease.

“Heart damage is irrevocable—it can’t be fixed. For someone like me, there is nothing more that can be done,” says Alan.

But what if there were a way to stimulate the human heart to regrow or repair the damage caused by a heart attack?

The Yin lab: going way beyond the band-aid

Voot Yin, research scientist and assistant professor of regenerative biology at the MDI Biological Laboratory, and his colleagues are certain it's possible—because that ability has already been achieved in a variety of animals, over millions of years of evolution.

The zebrafish, for example, is a champion of regeneration. Cut off part of its tail, brain, spinal cord, pancreas—and yes, even its heart—and it will completely regenerate bone, nerves, muscle cells, and blood vessels, fully restoring both form and function.

Voot Yin, research scientist and assistant professor of regenerative biology, gives a simple explanation of a heart attack: "The arteries that provide oxygen to the heart muscle become clogged and the muscle, deprived of oxygen, begins to die. The major problem is that the human heart doesn't create new heart muscle to replace the damaged area." And in the U.S. alone—someone dies from a heart-disease related event every single minute.

"Why come up with the next great solution from scratch when the next great solution is already here?" asks Voot. He and his colleagues decided to study how zebrafish regenerate tissue, looking for ways to activate this process in humans. Since humans share 70 percent of their genes with zebrafish—including those the fish use for regeneration—it promised to be an expedient line of inquiry.

In 2012, when Voot and his colleagues identified a naturally occurring chemical that stimulates the genetic machinery of zebrafish to regenerate tissues two or three times faster, his team began exploring whether the substance might encourage regeneration in humans.

Subsequent research and testing have shown that this substance—potentially the basis for a new therapeutic drug—is stunningly effective at kickstarting the regrowth process—not only in zebrafish, but also in mammals who (like humans) don't naturally have the ability to regenerate damaged tissue. When this drug was administered for only four weeks to mice who suffered heart damage—just like the damage humans sustain from a heart attack—these animals showed a 200 percent improvement in heart function and a 50 percent reduction in scar tissue. The implications for human heart health are profound.

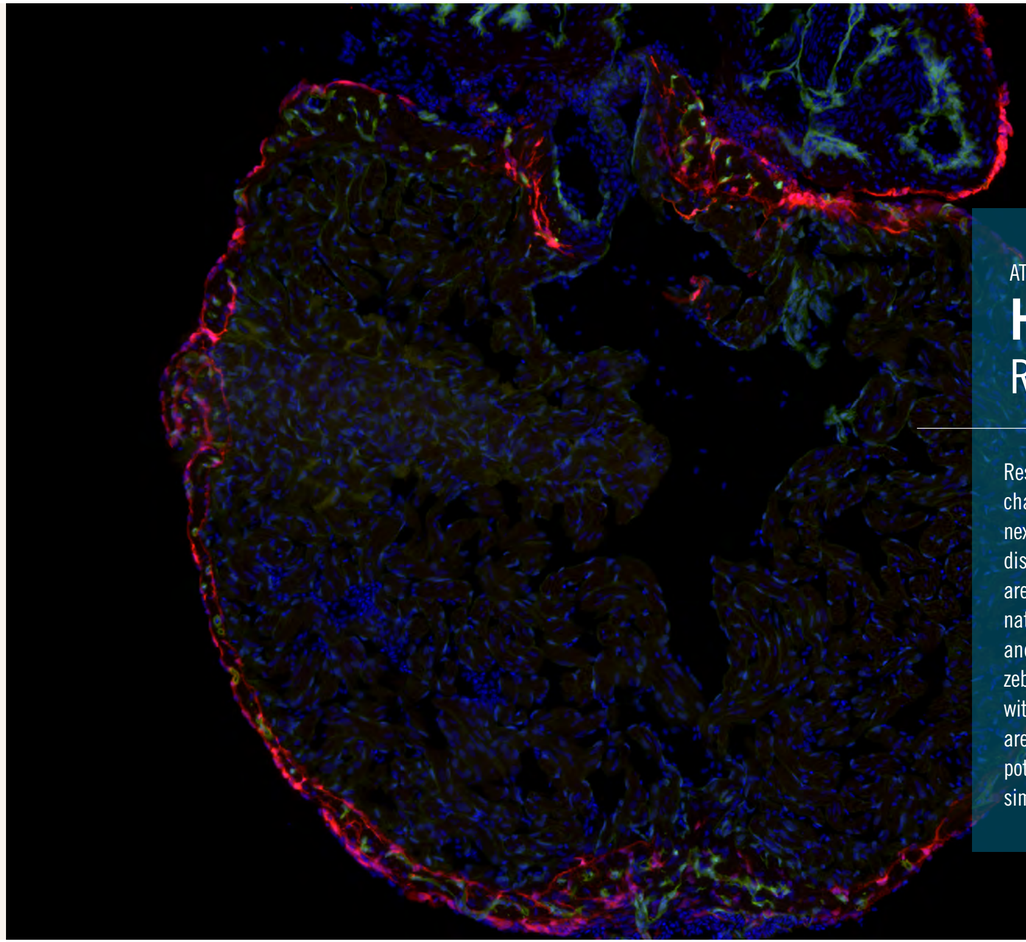
Particularly for someone like Alan. Voot believes that if drugs that stimulate heart regeneration were available at the time of his first heart attack, "Alan's life may have been completely different. He may never have experienced reduced heart function and his quality of life could have been improved."

Changing the future

For now, the testing of this drug will continue. Studies on adult pigs will follow the current mouse studies. And if those are successful, the researchers will move into human drug trials. If the drug works in humans, Voot believes that—with adequate funding for this research—it could be available for heart attack patients within ten years.

Alan is alive today because of the great leaps in medical science over the last 40 years. "Each time I came to a critical juncture, it seemed that a new treatment became available," he says. "Science has always been there for me."

But the next great innovation may be right around the corner, thanks to Voot's team and their zebrafish. "Alan's a great example of a person who has benefited by advances in scientific research and technological innovation," says Voot. "We're trying to push both of these frontiers so that we can help the future Alan Fidlers of the world.



AT THE BENCH >

HEART REGENERATION

Research scientist Voot Yin is championing what could be the next great solution for heart disease. Here, brightly colored areas depict the formation of naturally regenerating heart cells and blood vessels in a damaged zebrafish heart. Based on results with this model, Yin and his team are now exploring the ability of a potential new drug to stimulate similar repair in mammals.