

# We're living longer, but are we living better?

Today more people are growing old than ever before. And that means more of us—young and old—are living with debilitating injuries, organ damage, or diseases.

The past century was a period of extraordinary progress in medical science. Discoveries, including vaccines, antibiotics, more effective cancer therapies, and improved treatments for traumatic injuries, have enabled us to escape many dangerous health threats that once proved fatal.

But while these therapies allow us to live with injuries and degenerative diseases, they rarely fully repair or cure them. Today, we can survive catastrophic injuries, but can we recover our quality of life?

And as we grow older, we become increasingly susceptible to chronic illnesses and degenerative diseases. Frightening conditions like Alzheimer's, Parkinson's, heart disease, diabetes, kidney disease, and cancer all occur more frequently as we age.

How can we look forward to our golden years, facing the very real possibility of severe mental or physical disability?

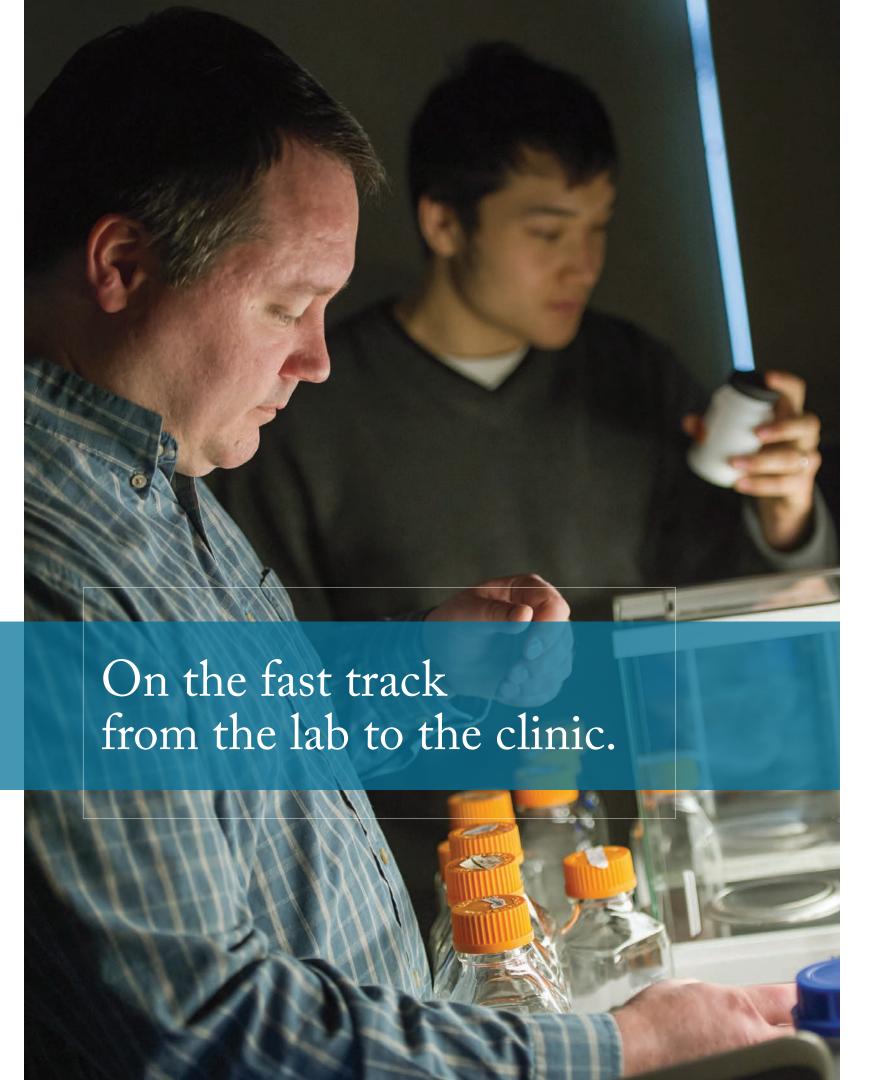


# The future could look very different.

Imagine your children and grandchildren living in a world where the crushing consequences of traumatic injuries can be fully reversed, where degenerative conditions like Alzheimer's and heart disease are routinely cured.

Imagine yourself in your seventies, eighties, or nineties, physically strong, active, and free of chronic disease. Your health is so robust that you are unlikely to succumb to a serious illness, but if you do, effective remedies are readily available.

With your help, and the revolutionary work of the scientists at the MDI Biological Laboratory, that promising future can be here sooner than you think—for you, your children, and your grandchildren.



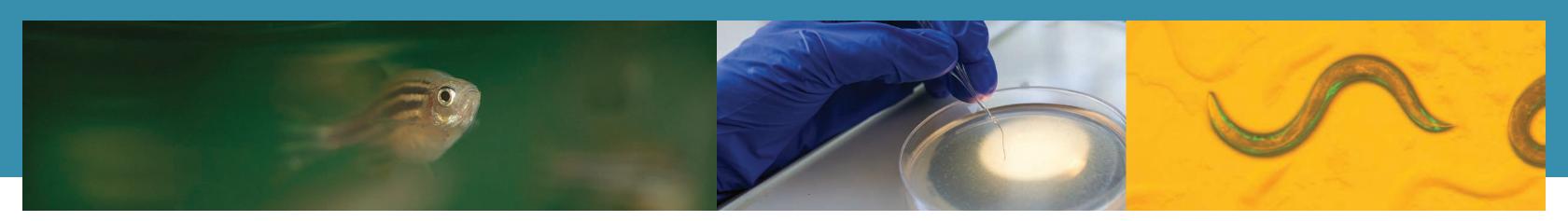
### We are different.

The MDI Biological Laboratory may look like a typical cutting-edge, biomedical research institution, but we are driven by a passion to get health-preserving discoveries into the hands of physicians and their patients faster than ever before. And that means we've made some unusual choices.

We believe that medical science must move beyond simply treating the symptoms of disease and disability. As the population ages, baby boomers are reaching their sixties and seventies and the incidence of degenerative and age-related illnesses is rapidly accelerating. Unless something changes, we will soon be confronting a major health crisis.

That's why everything we do in our laboratories is for one purpose only: to develop groundbreaking new treatments that dramatically improve human health and quality of life.

We're lean and agile, so we can adapt quickly to new or unexpected findings. We're collaborative and open to unconventional ways of looking at problems—in fact, we embrace out-of-the-box thinking, because we know it's the best way to generate new breakthroughs.



# Our lab tools and methods are different, too.

Small rodents are the models of choice in the vast majority of labs in the U.S. Rodents are critical to medical research, but are they always the best choice?

"If you are trying to understand how organs repair and regenerate, you can't study that in a mammal—because mammals can't regenerate most of their organs," says the president of the MDI Biological Laboratory, Kevin Strange, Ph.D.

**We know you can't solve every problem with the same tool.** When we investigate a pressing human health problem, we carefully examine its characteristics and variables. Only then do we choose the model species—from a diverse array of choices—that is best suited for our research.

Take the zebrafish, for example. This common aquarium fish has the ability to regenerate its body parts—limbs, organs, nerves, skin—whenever they are damaged. And humans share the very same fundamental genetic machinery that controls their ability to do it. That's why everything we learn about the healing process in zebrafish has direct implications for humans, making it an ideal model to help us develop our own potential to repair and regenerate lost and damaged body parts.

Or take the tiny nematode worm, *C. elegans*. It's an excellent research tool for learning about genetic factors that influence length of life because nearly half its genes have human matches—including the genes that impact longevity. And since it lives for only a few weeks, we can quickly see the effects of our experiments on its lifespan. As with the zebrafish, our discoveries in *C. elegans* are applicable to understanding a wide range of human health issues.

The laboratory models we choose are not only ideally suited for our particular experiments. With their short lifespans, low cost, and simple maintenance requirements, they also yield results faster and at far less expense than widely used rodent models.

## Being different has advantages.

#### It takes audacity to pursue an unconventional approach in biomedical research.

But we do it because we believe that solving the mysteries of regeneration and longevity is the key to preventing and curing countless diseases, to restoring function after traumatic injury, and to slowing or reversing the degenerative changes that occur as we age. And our approach—asking big questions, bringing new perspectives to problem-solving, and using unconventional research models—is designed to find the fastest, most efficient path possible from the lab to the clinic.

Because we don't have a moment to waste.

And neither do you.



The zebrafish has amazing powers of regeneration. Cut off part of its tail, brain, spinal cord, pancreas—even its heart—and it completely regenerates bone, nerves, and blood vessels, fully restoring both form and function. Voot Yin's team is studying how zebrafish do this, looking for ways to activate this seemingly miraculous repair process in people.

We share 70 percent of our genes with zebrafish—including the genetic machinery that gets switched on to activate the regrowth process when necessary. But in people, that switch is stuck in the "off" position. Voot wants to find a way to flip that switch "on" in the event of an injury or degenerative disease—when someone suffers a heart attack, for example.

In the summer of 2012, Voot took a giant step toward that goal. He identified a naturally occurring chemical that, when administered to a zebrafish, doubles or triples its rate of regeneration. Voot suspected this substance might have potential for encouraging regeneration in humans.

To test his hypothesis, he altered the zebrafish's genes to make it mimic the human reaction to heart damage—in other words, he forced its regeneration switch into the off position. Then it responded to injury just as human hearts do—no repair, no regeneration. Next, he injected the new substance into the zebrafish. The result was astonishing. The switch flipped back on and the zebrafish regained the power to heal its heart.

Within weeks of this discovery, Voot and the MDI Biological Laboratory had spun off the Laboratory's first biotechnology company, Novo Biosciences, to find out if this substance could also turn the power of regeneration on in humans. Since the company's founding, testing has shown that the substance has a profound effect on the restoration of heart function in mammals following a heart attack.

Our goal? To speed the development of this chemical substance and others like it, creating drug therapies to improve our ability to regenerate and repair damage to our bodies.



Just down the stairs from Voot's lab, where scientists are exploring how to boost our ability to heal the damage caused by aging and disease, Aric Rogers' team is taking a different approach. Rather than looking for ways to treat existing disease and damage, he is investigating approaches that will prevent those diseases from occurring in the first place.

His research focuses on *C. elegans*, a tiny nematode worm about one millimeter long. Its natural habitat is soil and it is very easy and inexpensive to raise in the lab. It is an ideal subject for aging research because it shares nearly half its genes with humans—including those that are associated with longevity. And since it lives only two to three weeks, studies on *C. elegans* can quickly identify new ways to prolong lifespan.

Aric's team found that altering various features in this tiny worm's environment can trigger changes in the way its genes are activated. Certain of these genetic changes in turn can increase its lifespan up to ten times. Modifying its diet is one of the most effective ways to influence the genetic machinery that controls its lifespan.

Aric is exploring how changing the nematode's diet alters its lifespan. And since we share the relevant genes, how can we use this knowledge to develop therapies that slow aging in humans?

It sounds like the stuff of science fiction, but it's within our reach: drug therapies that increase lifespan and optimize health, delaying or even eliminating the onset of age-related diseases.



Most of us know someone who has suffered from the pain and disability of nerve damage. It has many varied causes, including diabetes and cancer treatment using chemotherapy. Its symptoms can be truly debilitating, ranging from numbness or intense pain to loss of physical coordination and mobility. Worst of all, nerve damage caused by chemotherapy may force the termination of life-saving treatment.

Sandra Rieger's team is pioneering the development of drug therapies to lessen or cure such nerve damage. Her research focuses on three-day-old zebrafish because they possess the ability to repair damaged nerves just as healthy humans do—and since they are transparent, the process they use to do this can be observed as it happens.

Her experiments revealed that nerve regeneration in zebrafish is triggered when cells surrounding damaged nerves release hydrogen peroxide—the same common chemical we use for cleaning cuts or scrapes. Could a simple chemical like hydrogen peroxide help stimulate the repair of nerves damaged by disease or chemotherapy?

Sandra and her team are using cancer chemotherapy drugs to cause nerve damage in zebrafish—just as they do in humans. Then they test a variety of chemicals on them to identify new drugs that prevent nerve damage or stimulate nerve regeneration.

Next steps? Testing these drugs in mammalian models. If Sandra has similar success in mammals, we may soon see drug treatments that prevent or alleviate nerve damage caused by chemotherapy treatments.



# On the origin of the MDI Biological Laboratory

#### Building on the foundation of modern biology

Darwin's *On the Origin of Species* was published in 1859, inspiring scientists to go into the field to study, compare, and learn basic biology from a diverse range of organisms. MDI Biological Laboratory was founded in 1898 as a summer research facility to provide this opportunity. Its location on the rocky Maine shore offered access to countless marine animal species.

Building on the knowledge gained here during these early years, our scientists narrowed their research focus to important health issues beginning in the 1920s. Milestone discoveries in kidney function and the health impacts of environmental toxins like DDT and oil spills were some of the highlights of the work conducted by our summer scientists during the last century.

The common thread through all our research has always been our commitment to choosing the model that best matches each problem under investigation.

Goosefish, sand dollars, sea urchins, nematode worms, dogfish sharks, zebrafish, and salamanders (to name just a few) have each fit the bill at one time or another, always with the goal of finding relevant results as efficiently, quickly, and inexpensively as possible.

"The MDI Biological Laboratory is having stunning success, even in the face of the worst funding climate in the history of modern biomedical science.

Now is the time to build on that success and boldly expand the institution—to take big steps toward improving human health."

- Kevin Strange, Ph.D., president, MDI Biological Laboratory



# Visionary leadership

After nearly twenty-five years at premier academic medical institutions—Harvard Medical School, Boston Children's Hospital, and most recently, Vanderbilt University School of Medicine where he served as director of research in critical care and anesthesiology—Kevin Strange was looking for a different kind of challenge. So in 2009, he came to Bar Harbor to lead the MDI Biological Laboratory. "Large academic institutions can fall into the trap of putting too much emphasis on knowledge for knowledge's sake. I came here to build an institution that is focused on solving problems."

Kevin brings new energy to the MDI Biological Laboratory with his vision of building a research and development institution with a laser-like focus on finding solutions to serious health problems—and doing it faster and for far less money than is typically the case at large institutions.

His creative strategies and forceful advocacy have brought millions of dollars of new funding and brilliant experts in regenerative and aging biology to the institution. Together they have already made discoveries that promise to have a significant impact on human health issues like heart disease, Alzheimer's, and wound healing. In 2013, the National Institutes of Health designated the MDI Biological Laboratory as a Center of Biomedical Research Excellence in regenerative and aging biology and medicine.

And we are just getting started.

"Kevin's outstanding scientific accomplishments are equally matched by his ability to quickly transform vision into reality. It is indeed unusual to have vision combined with strategic, scientific, and administrative strengths in a research institution's leader."

 Peter Allen, M.D., chair, board of trustees, MDI Biological Laboratory; Murray F. Brennan chair in surgery, Memorial Sloan Kettering Cancer Center



# Who are we today?

#### Scientists at the leading edge of human health research

Today, in the early 21st century, the pressure to find treatments and cures is fast increasing as the number of people living with devastating injuries and diseases reaches new heights. Fortunately, advances in genetics and technology have also accelerated, enabling trailblazing new research into healing injuries, eliminating diseases, and prolonging healthy life.

The MDI Biological Laboratory is at the leading edge of this important work—and we have redefined ourselves to get there.

No longer just a summertime enterprise with a broad range of scientific interests, we are now a rising biomedical research institution focusing on regenerative and aging biology and medicine. Our education and research facilities have also grown, most recently with the opening of two state-of-the-art, environmentally responsible laboratory buildings.

We have outstanding faculty who chose to come here because they believe that our unconventional approach is the quickest path from research to cures.

**Our latest endorsement?** The MDI Biological Laboratory is designated by the National Institutes of Health as a Center of Biomedical Research Excellence—a highly competitive award that brings with it a grant of \$13 million to propel our growth as a world-class research institution.

#### Educators making a real world difference

The MDI Biological Laboratory trains over 350 students each year through our courses and conferences. Our public outreach activities reach hundreds more. Like our laboratory research, our education and outreach programs focus on achieving workable solutions to real-world problems.

Our students range from high schoolers to practicing physicians, scientists, teachers, and members of the public. In addition to scientific training, we teach problem solving and communication skills. We engage our students in authentic research experiences that they can take back to their workplaces and classrooms. We educate the public about the critical importance of science to our country's economy and security. And we excel at bringing diverse groups of stakeholders together to find common ground and collaborate on solving human and environmental sustainability problems.

Perhaps most importantly, we encourage out-of-the-box thinking, entrepreneurship, and partnership building.

Our goal is to help make better doctors, inspire current and budding scientists, and develop a science and technology workforce that is ideally equipped for success in the 21st century.

# Although we've accomplished so much, our future depends on you.

It's tougher than ever to pay for scientific research. Most research funding comes from two sources—corporations and government. And in this post-recession economic climate, both sources have been cut back dramatically. They have become much more cautious about funding the kind of high-risk, high-reward research that has the greatest potential for critical scientific breakthroughs—the kind of research we do at the MDI Biological Laboratory.

Without outside funding, we simply will not have the resources to sustain and grow our work in regenerative medicine and aging biology. We need you to be bolder and dream bigger than the corporations and government agencies that have traditionally funded biomedical research.



## ... now and in the future.

At the MDI Biological Laboratory, we know exactly how to speed up the rate of our important discoveries and quickly move them from the lab into the hands of physicians and their patients. **With your generous help, we will:** 

#### Recruit four world-class scientists

We will increase our research capacity by adding four new research groups led by top experts in regenerative and aging biology and medicine. These labs will be staffed with gifted, highly qualified postdoctoral scholars, graduate students, and lab assistants.

#### • Expand our scientific core facilities and resources

To attract and retain the best scientists and accelerate their research efforts, we need to provide them with cutting-edge tools. We must expand our microscopy, bioinformatics, and drug development facilities and update them on a regular basis as new technologies are developed.

#### Build a state-of-the-art student training laboratory

A new, fully equipped lab designed especially for teaching and hands-on learning will enhance the quality and scope of our education programs.



Help us make what sounds like science fiction become science fact.

Please join us.
Invest in a better future
for you, your children,
and generations to come.



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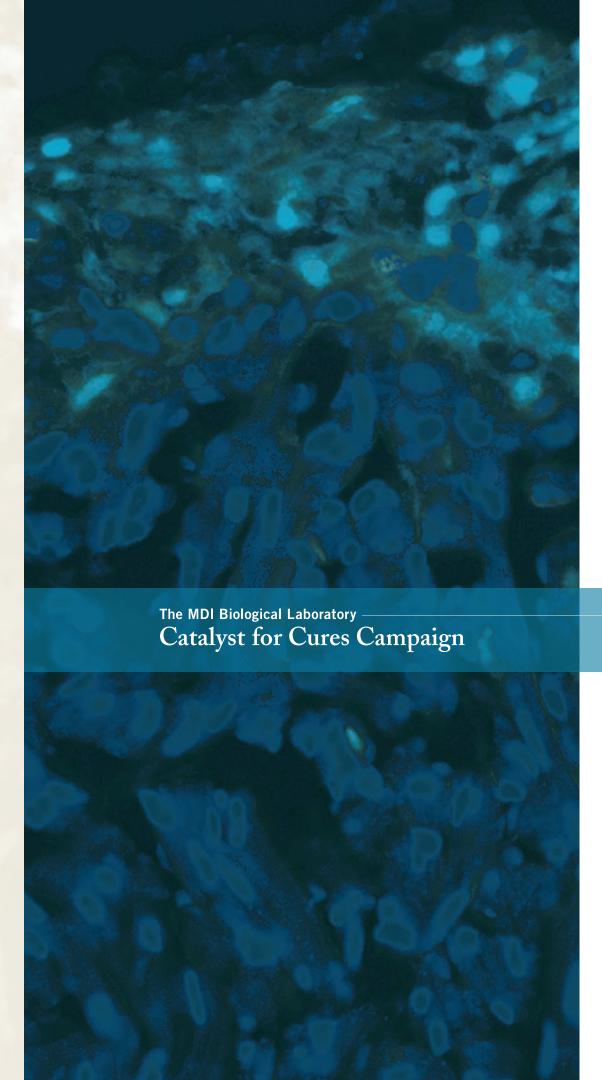
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