Breaking Through

Kidney Research at the MDI Biological Laboratory | SPRING 2019
Dear Friends,

Nearly a year ago I assumed the presidency of the MDI Biological Laboratory, which was then celebrating 120 years of discovery in cancer chemotherapy, environmental health, renal physiology and – in more recent years – regenerative biology and aging. My charge was to chart a new course while maintaining a connection with our past.

With the approach of my first anniversary, I am proud to say that we have established a clear direction for the future by focusing on four “pillars” that define the structure of the institution: faculty, visiting scientists, education and biotechnology.

I am delighted to announce that Iain A. Drummond, Ph.D., will assume the position of professor and senior scientist in October (see page 4), strengthening the first pillar. He offers an outstanding reputation as a research scientist and a focus on kidney regeneration that links our current research with our distinguished history of achievement in kidney physiology.

Drummond is one of four members of the federally funded (Re)Building a Kidney consortium who will conduct research at the laboratory this summer (see page 11). Their presence is the first step not only in revitalizing the visiting science program – the second pillar – but also in establishing the laboratory as a research center for the consortium, whose goal is to develop functional replacement kidney tissue.

After achieving a position of global leadership in regenerative biology and aging, we are now staking a claim to the unexplored territory at the interface of these disciplines with a new course and symposium (see page 14). These offerings join a rich schedule of research-oriented programs comprising the third pillar – education – and will serve as a template for the “Acadia conferences” planned for 2020 and beyond.

The final pillar – biotechnology – is focused on translating scientific discovery into new products and therapies. This year, two Germany-based life sciences companies will join the three biotechnology companies that are currently being incubated on campus (see page 14). Both are engaged in drug development, creating a valuable link for the laboratory with the international pharmaceutical industry.

Our success in strengthening the four pillars is due in large measure to your generosity. I am deeply grateful for your support of our vision to strengthen our research and educational programs. Thank you for continuing to be a source of inspiration for scientists around the world to work together to extend healthy human lifespan.

With heartfelt thanks,

Hernan Haller, M.D.
President
In October, Drummond, associate professor of medicine at Harvard Medical School, associate biologist in the Nephrology Division at Massachusetts General Hospital and director of the kidney program of the Harvard Stem Cell Institute, will become the MDI Biological Laboratory’s new senior scientist.

His vision calls for building on the institution’s distinguished reputation in kidney physiology and refining its focus on the regeneration of tissues and organs by establishing it as a center for research on the development of replacement kidney tissue and an artificial kidney.

“Regenerative medicine has reached an inflection point at which it will be able to take advantage of recent advances in tissue regeneration, stem cell biology and bioengineering to replace the kidney,” he says. “Because of the lab’s past history and its current expertise, it has a unique opportunity to lead this transformation.”

A major public health threat

It is a transformation that can’t come soon enough.

In recent years, chronic kidney disease (CKD) has emerged as a major public health threat among those age 60 and over due to diabetes, hypertension and cardiovascular disease, all of which can contribute to kidney damage and all of which are on the increase due to the aging of the world’s population (see page 6).

When kidneys fail, the typical treatment is dialysis, an expensive, time-consuming procedure in which the blood is cleansed by an external filtering device. The other option is transplantation, but only a fraction of the tens of thousands on transplant waiting lists receive donor kidneys because of a shortage of donors.

Which is why generating new kidney tissue has become the Holy Grail of nephrology, the branch of medicine specializing in the kidney.

“In the 20th century, scientists at the MDI Biological Laboratory drew on comparative biology to gain an understanding of the function of the human kidney,” Drummond says. “In the 21st century, we are still relying on comparative biology to study the kidney, but we can now use that knowledge to learn how to fabricate new kidney tissue that works.”

Like other kidney scientists, Drummond speaks reverentially of the era in which the laboratory was renowned for the contributions of renal physiologists like Homer W. Smith, D.Sc. (1895-1962), who identified how kidneys function, and E. K. Marshall Jr., M.D., Ph.D. (1889-1946), who demonstrated that secretion of wastes takes place in the renal tubules.

The (Re)Building a Kidney initiative

His approach toward reestablishing the institution’s preeminence in kidney research centers on a National Institutes of Health (NIH)-funded consortium, (Re)Building a Kidney (RBK), whose goal is to identify strategies to repair and regenerate nephrons—the key functional units of the kidney—and to engineer a biological artificial kidney.

That effort will get underway this summer when Drummond and three other RBK investigators will study kidney repair and regeneration as part of a visiting scientist program that has been revitalized by the new president, Hermann Haller, M.D., with support from the Salisbury Cove Research Fund (see page 11).

Though the many scientists in the RBK consortium are pursuing diverse, yet complementary, approaches,
The study of how such connections adults have kidney disease
Despite the focus on these "kidneys in a dish," however, Drummond remains committed to the institution’s tradition of looking to nature to gain an understanding of human health, just as Smith, Marshall and other renal physiologists once studied marine organisms such as the goosefish, dogfish and skate for insights into human kidney function.

He uses the common aquarium fish, the zebrafish, as a model to tackle one of the major challenges of building an artificial kidney: the need for connections to drain processed fluid from the organ. The study of how such connections develop in zebrafish offers insights into how to create them in artificial organs.

The challenge of building an artificial organ
The need for such "plumbing," however, represents only one of many challenges in building an artificial kidney. A famous comment from Homer W. Smith about kidney physiology — that it has "erred, more often than not, by attempts at oversimplification" — might equally apply to rebuilding a kidney.

The effort will involve coaxing stem cells to differentiate into more than 30 cell types, organizing them into an intricate organ-like structure, linking the organ to the circulatory system and generating the hundreds of thousands of nephrons that are needed (as opposed to the 100 or so that can now be grown in a dish).

Like Haller, who likens this effort to the Apollo space program, however, Drummond is optimistic — an optimism that has been buoyed by the recent discovery that human induced pluripotent stem cells (hiPSCs) are capable of spontaneously differentiating into different types of kidney cells and of self-assembling into nephrons.

"This is a time of great opportunity in regenerative medicine," Drummond says. "The technologies that we can bring to bear on repair and regeneration are the product of hundreds of years of scientific development. We can do so many things that we never could before. The challenge is to be bold — to not let the opportunity slip by."

A ‘little piece of nirvana’
Drummond believes a critical piece of achieving this goal will be to establish the MDI Biological Laboratory as a hub around which RBK scientists can convene. That vision is more than a little informed by nostalgia for the days when the laboratory was known not just for its science, but also as a place for socializing, a ‘little piece of nirvana’.
The fond memories associated with the MDI Biological Laboratory in the minds of many former visiting scientists are summed up by this quotation from Alfred P. Fishman, M.D. (1918-2010).

The spirit of collegiality fostered by the lab is what prompted these scientists to return year after year to what Fishman called a “summer nesting place for renal and comparative physiologists.” As a visiting scientist himself for more than 20 summers, it is a goal of Hermann Haller, M.D., the institution’s new president, to restore a robust visiting scientist program.

While times have changed since the halcyon 1950s era described by Fishman – few scientists now have the luxury of spending an entire summer at “the laboratory by the sea” – the need endures for a place for scientists to gather to exchange knowledge, collaborate and socialize. In this interview, Dr. Haller describes why this need may be greater now than ever.

Q. Why is it important to revitalize the visiting scientist program at the MDI Biological Laboratory?

A. Science is a team sport. Big things only get done when people work together in person. A robust visiting scientist program is essential to leveraging the strength of our faculty through the establishment of powerful research collaborations. By designing a visiting scientist program that promotes the kind of face-to-face activities that are essential to the advancement of science, including project collaborations, discussion of critical issues and the sharing of techniques and methods, everyone benefits. The example I like...
In a digital age, can’t such collaborations be achieved in other ways?

Q. No. We live in an era in which the time for conversation is a luxury. All scientists have tight schedules, but this is especially true of successful scientists. Typically, the opportunity to meet is limited to a day or two during conferences and the opportunity to collaborate in person is practically nil. By spending four to 10 weeks at the MDI Biological Laboratory this summer (see sidebar), the consortium will be working on research related to developing an artificial kidney as visiting scientists at the laboratory this summer (see sidebar).

Q. Why is the MDI Biological Laboratory suited to such a program?

A. We are one of the few independent research laboratories with a strong visiting scientist tradition. Indeed, we are renowned for the many important discoveries in renal physiology made here by visiting scientists in the 20th century. I want to revitalize this tradition—not only with regard to kidney regeneration, but for regenerative biology and aging research in general. The campus is uniquely suited to a visiting scientist program because of its natural beauty and tranquility: scientific discussions are more likely to lead to great ideas in a beautiful natural setting overlooking the Atlantic Ocean than in an urban conference room. Also, the design of the campus is conducive to the kind of personal interactions that lead to discovery. The courtyard is a natural meeting place that I intend to take advantage of for open-air lectures and lunch seminars, even an afternoon “science social.” The idea of a meeting place for science goes back to the agora of classical Athens, or in modern times to the Stazione Zoologica in Naples, which was the model for American research stations. But the MDI Biological Laboratory is one of the few independent research laboratories where the tradition lives on.

Q. What do you expect to happen when you get all these great minds together?

A. Collaborations, new ideas and scientific breakthroughs!

Research of New Visiting Scientists
Focuses on Aging and Kidney Regeneration

The 2019 summer visiting scientist program will host 15 visiting scientists from the United States and Germany. Six are new to the program and will be collaborating with President Hermann Haller, M.D., an internationally recognized nephrologist, on kidney research, including research on aging and kidney regeneration.

“Chronic kidney disease is among the most common diseases of the elderly,” Haller said. “Since our mission is to identify new regenerative medicine therapies to address the soaring incidence of age-related degenerative diseases, we are delighted that these renowned experts will be joining our roster of summer visiting scientists.”

Here are descriptions of the research of some of the new summer investigators:

Annette Melk, M.D., Ph.D., and Roland Schmitt, M.D., of Hannover Medical School in Hanover, Germany, will study cellular senescence, or the failure of cells to divide, a key driver of aging and age-related diseases. They will use kidney organoids to study cell regeneration, or small, three-dimensional “mini-organs,” to study and test senolytic drugs and to study stress-induced cellular senescence. They will also use zebrafish embryos to study how the toxins that accumulate in the body in chronic kidney disease contribute to cellular senescence. Both are looking forward to exchanging ideas on the study of aging with MDI Biological Laboratory faculty members.

Leif Oxburgh, D.V.M., Ph.D., of the University of Texas Southwestern Medical Center will use kidney organoids to study cell regeneration in the proximal tubule of the nephron, the functional unit of the kidney. Their research has implications for disease modeling and kidney replacement therapy. All are members of the federally-funded (Re)Building a Kidney (RBK) consortium of investigators.

Iain A. Drummond, Ph.D., of Harvard Medical School and Massachusetts General Hospital will study nephron regeneration in fish, which demonstrates a remarkable capacity to generate new nephrons. He will seek to identify the signals that trigger stem cells to make nephrons in a local population of kilifish. He will also collaborate with fellow members of the RBK consortium to determine if mechanisms discovered in fish can be used to generate functional replacement kidney tissue.
$1.2 Million Grant Awarded to Teach Data Literacy

Middle and high school students in Maine and New Hampshire will gain next-generation data literacy skills while also addressing a major public health threat through a new federally funded program spearheaded by the MDI Biological Laboratory in collaboration with Dartmouth College.

The laboratory will take a national lead in teaching data literacy to students and teachers though a five-year, $1.2 million SEPA (Science Education Partnership Award) grant from the National Institute of General Medical Sciences, an institute of the National Institutes of Health.

The goal is to establish a national learning model for STEM (science, technology, engineering and math) secondary school education in data literacy. The project will focus on the contamination of well water in Maine and New Hampshire by arsenic that leaches out of the bedrock.

Students will learn how to manage and analyze data about well water collected from their homes and to communicate their results to inform action at the local, regional and national levels. Arsenic in well water is a major public health problem in Maine and New Hampshire, where residents rely heavily on private wells.

“Students are more likely to expand their scientific inquiry skills and retain what they learn when the data have relevance,” said Jane E. Disney, Ph.D., senior staff scientist and director of education at the MDI Biological Laboratory. “The data they collect will be meaningful for them and their families, as well as for the larger community.”

The U.S. Environmental Protection Agency (EPA) has designated arsenic as the environmental contaminant with the biggest impact on human health. Long-term exposure, even at low levels, can lead to severe health problems, including cancer; diabetes; heart disease; and reproductive, developmental and cognitive problems.

The project will create student-teacher-scientist partnerships by recruiting scientist-mentors from the faculties of institutions of higher learning that participate in the federally funded Maine and New Hampshire INBRE (iDeA Network of Biomedical Research Excellence) programs, which promote biomedical education and research. Disney, principal investigator, will collaborate with Associate Director Bruce A. Stanton, Ph.D., a professor at the Geisel School of Medicine at Dartmouth in Hanover, N.H.

The project will examine data on arsenic contamination in well water as part of a federally funded program by the MDI Biological Laboratory.

COURSE SPOTLIGHT

The Colby INBRE Course: Taking the Cookie Cutter Out of STEM Education

It happens frequently in INBRE short courses: the students ask questions like “Is this the right answer?” or “Is this the result you were expecting?” only to be told that we don’t know the “right” answer until we do the experiment – that an unexpected answer, or an answer that reveals a hypothesis to be incorrect, may be the “right” answer.

This revelatory moment is when the students realize that, rather than engaging in a prescriptive lab experiment, they are engaging in scientific research. “They realize they are discovering things that have never been discovered before,” said Andrea R. Tilden, Ph.D., assistant professor and Maine INBRE director, with assistance from Joel H. Gruber, Ph.D., senior staff scientist and director of the computational biology and bioinformatics core, and Eli Hartig, a research assistant in the Coffman laboratory.

In addition to laboratory research, the course involved a hefty dose of bioinformatics, or the science of analyzing large volumes of biological data. “They are getting both – the intensive computational experience and the bench lab experience,” Tilden said. “It’s an opportunity they wouldn’t get anywhere else.”

As for the experiment, the results were unexpected. “I wasn’t anticipating that,” Coffman said. “But that’s what’s fun about these courses.”
New Life Sciences Companies Coming to Campus

MDI Biological Laboratory President Hermann Hailer, M.D., has announced that two Germany-based life sciences companies will establish a presence at the MDI Biological Laboratory in support of their expansion into the North American market.

- **Phenos GmbH** is a contract research organization with nearly 20 years of experience in using animal models for pharmaceutical testing. The company will work closely with research groups at the MDI Biological Laboratory using the zebrafish, a common aquarium fish, and C. elegans, a nematode worm, to test drug candidates. Phenos’ presence on campus will create a valuable link with the international pharmaceutical industry, Hailer said.

- **H+M Development** is developing a novel drug therapy for polycystic kidney disease, a genetic disorder that can lead to reduced kidney function and kidney failure. H+M will collaborate with MDI Biological Laboratory research groups on studies to gain a better understanding of the drug’s mechanism of action and to identify other potential applications, including for heart disease, diabetic kidney disease and diabetic neuropathy.

### Resetting the Aging Clock: Defining the Interface Between Aging and Regeneration

The MDI Biological Laboratory will take the lead in defining how aging is influenced by a decline in regenerative potential by convening a new course on the interface between aging and regeneration July 20 through Aug. 3.

Scientific thinking about aging has changed over the years. While it was once viewed as a “wearing out” process — occurring in the same way that a car or appliance wears out — that view has shifted over time to the idea that aging is a risk factor for age-related diseases such as Alzheimer’s, cancer, diabetes and heart disease.

In recent years, the thinking has changed again thanks to scientists like Arci Rogers, Ph.D., of the MDI Biological Laboratory whose research supports the idea that aging is the cause of — rather than a risk factor for — age-related diseases, and that the onset of these diseases can be delayed by manipulating the molecular pathways that govern aging.

Now the thinking is shifting yet again. Many scientists now view aging as a failure to regenerate — an idea that will be familiar to those who remember how quickly they healed when they were young. Indeed, aging can be thought of as “an accumulation of mini-wounds” in the words of faculty member Vicki P. Losick, Ph.D.

“The young heal wounds, mend bones and regrow tissues with ease, but these abilities are lost over time, leading to frailty, decay and age-related degenerative diseases,” said faculty member Voot Yin, Ph.D. “By gaining an understanding of why we lose regenerative ability, we will be able to develop therapies to reset the aging clock.”

The two-week research training course, “Immersion in Comparative Aging and Regenerative Biology (iCARB),” will be followed Oct. 4 through 6 by a National Institute on Aging-sponsored research program for visiting researchers, “Regenerative Biology (iCARB),” which will introduce participants to current research in comparative aging and regenerative biology.

The goal of the symposium is to catalyze interactions among scientists seeking to determine the determinants of regenerative capacity in diverse animal species and the causes of biological aging, and to develop strategies for applying what is learned from such research to improve human health.

Guest faculty and speakers for both events will include some of the most provocative thinkers in the fields of aging and regenerative biology. As part of the institution’s mission to promote scientific literacy and increase public engagement with science, the iCARB program will include lectures for the public by guest faculty and speakers.

For more information, please visit mdbl.org/events.

### Bodil M. Schmidt-Nielsen: ‘In Spite of It All, We Got Our Results’

This is the first in a series about women scientists at the MDI Biological Laboratory who have made significant contributions to science.

Bodil M. Schmidt-Nielsen, D.D.S., Ph.D. (1938-2005), was a comparative physiologist and former MDI Biological Laboratory board president whose research impacted on science and administration would last for more than three decades. She was the daughter of August Krogh, a Nobel Prize-winning physiologist from the University of Copenhagen known for the “Krogh Principle,” which states that among the diversity of animal species there is one that is ideally suited for use as an experimental model for any biological problem.

Schmidt-Nielsen — perhaps more than any other laboratory scientist — was guided by her father’s principle, which has served as a mainstay of the laboratory’s approach to research. She arrived in 1952, having been recruited by the famous kidney physiologist Homer W. Smith, D.Sc. Though she was renowned for studies with her then husband, Knut Schmidt-Nielsen, Ph.D., of kidney function in the kangaroo rat, which lives under arid desert conditions, her roster of animal models didn’t stop at rats. Over the years, she also used amoebas, beavers, camels, dogs, eels, fish, frogs, harbor seals, humans, insects, leeches, sea urchins, sharks, sheep, skates, tadpoles and toads.

Her accounts of her collecting expeditions offer a look back, notable women scientists at the MDI Biological Laboratory
In 1995, Jo Sollano was a graduate student at Columbia University Mailman School of Public Health. “I remember working really long hours for very little pay and feeling tremendous pressure to succeed. But I also remember how much I loved the work and how inspired I was by my mentor. It was a defining experience,” said Sollano.
Today, Sollano, M.P.H., Dr.P.H., is a biopharmaceutical consultant and member of the MDI Biological Laboratory’s board of trustees.

“As someone who has spent my entire career in the healthcare sector, and as a patient who has benefited from cutting-edge medical advances, I know firsthand the importance of basic research,” said Sollano. “But I also now how challenging it can be to succeed in science today, and this is why I want to do all I can to provide faculty and students at MDIBL with the resources they need to be successful.”

Combining her passion for education with her dedication to the research programs at the MDI Biological Laboratory, Sollano has established the Josephine A. Sollano Graduate Student Fellowship to support outstanding graduate students working with MDI Biological Laboratory faculty.

“Graduate and postdoctoral students are the lifeblood of any research lab,” said Dustin Urdzik, Ph.D., assistant professor at the MDI Biological Laboratory. “They are highly skilled and serve as our partners in conducting experiments, in developing new ideas and knowledge and in mentoring other students in the lab. We rely heavily upon them to help us reach our research goals.”

“I wanted to do something to help our early-career faculty and at the same time support meaningful educational experiences for students,” said Sollano. “Creating an endowed fellowship fund to support graduate students was the perfect solution.”

About Us

We are discovering new approaches to regenerative medicine by developing drugs that slow age-related degenerative diseases and activate our natural ability to heal. Our unique approach has identified potential therapies that could revolutionize the treatment of heart disease, muscular dystrophy and more. Through the Maine Center for Biomedical Innovation we are preparing students for 21st-century careers and equipping entrepreneurs with the knowledge and skills to turn discoveries into applications that improve human health and well-being.

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Are you interested in helping the MDI Biological Laboratory train the next generation of scientific leaders and further ground-breaking research, while also creating a legacy of philanthropic support? Good news! You can make a difference NOW and fund the discoveries of tomorrow by making a blended gift—an immediate gift of cash or appreciated assets combined with a future estate gift.

Blended gifts are ideally suited for donors like you who want to create a lasting legacy by allowing you to maximize the impact of your philanthropy. For example, making an initial cash gift allows you to establish a new endowment that could later be fully funded through a bequest or planned gift.

Gift planning can help you achieve multiple goals—whether it is minimizing your taxes, funding a grandchild’s education or ensuring an income stream for a loved one. There are many simple and flexible ways to include the MDI Biological Laboratory in your philanthropic plans.

For more information on how you can build a lasting legacy and provide transformative support, contact Michele Marks at 207.288.3605 or mmarks@mdibl.org.
THE HOMER SMITH COTTAGE ON SPRUCE POINT. the home of renowned kidney physiologist Homer W. Smith, D. Sci. (1895-1962), and his wife Margaret, was a centerpiece of daily life at the laboratory for more than 35 years.

The Smith Cottage is one of many historic structures on our campus whose visitors have made significant contributions to improving human and environmental health over the past 120 years.

With your help, we will continue to realize George B. Dorr’s vision to create a home on Mount Desert Island for men and women of science to study and learn from nature by restoring these historic cottages.

To contribute or learn more about our plans, contact Jeri Bowers at 207.288.3605 or jeri@mdibl.org.