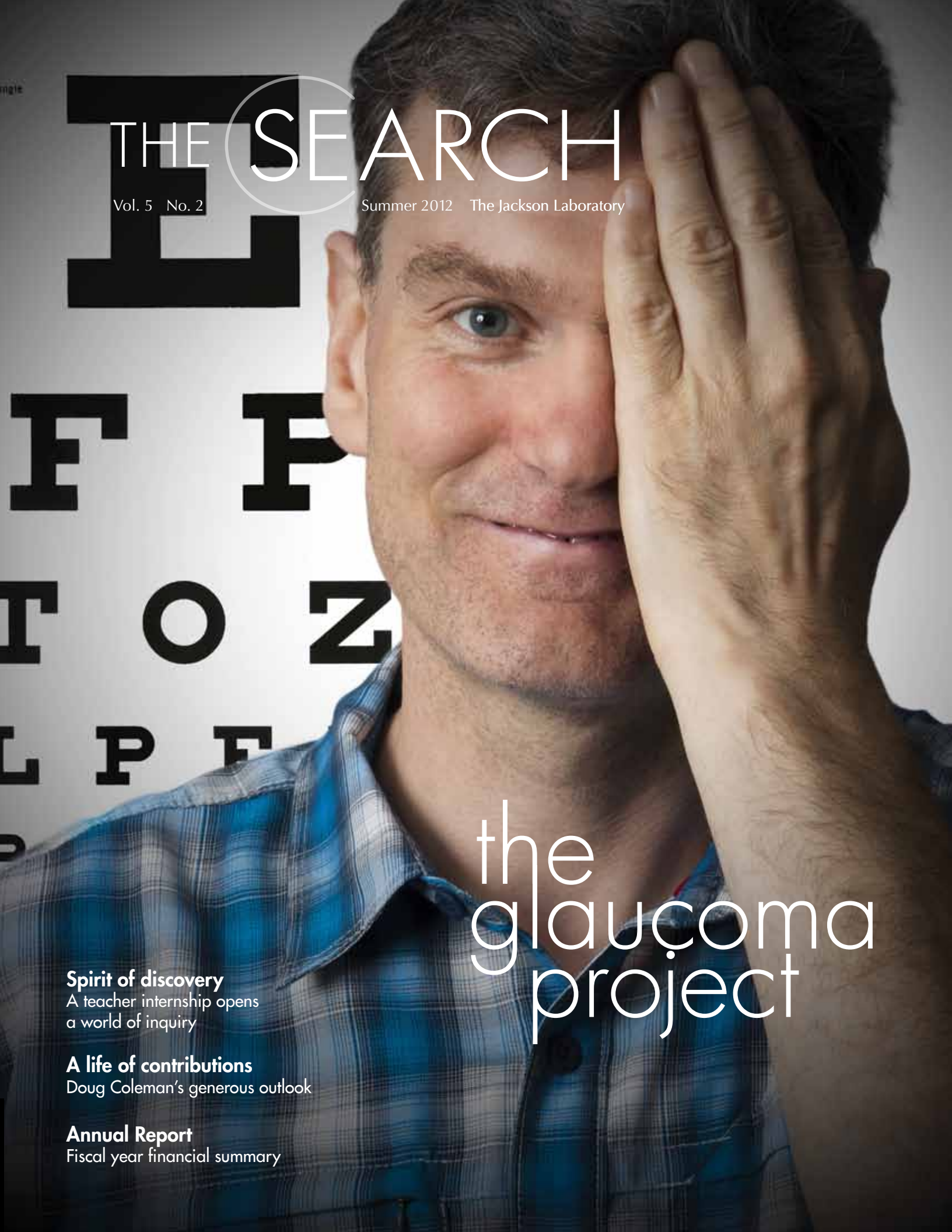

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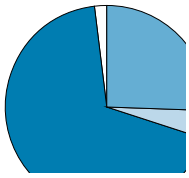

Annual Report

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The Jackson Laboratory for Genomic Medicine's unique auditorium façade is shown here in an architectural rendering. The building will be completed in 2014, but researchers and staff are already starting to work in temporary facilities on the University of Connecticut Health Center campus in Farmington, Conn.

Rendering courtesy of Centerbrook Architects and Planners

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Cover photo of Simon John, Ph.D., by Françoise Gervais

The Search

Editor: Mark Wanner

Art Director: Barbara Kaegi

Copy Editor: Carol Lamb

Web Editor: Joseph Blanchette

Contributors: Joyce Peterson, Barry Teater, Mark Wanner

Photographers: Françoise Gervais, Jennifer Torrance, Rogier van Bakel

The Jackson Laboratory

President and Chief Executive Officer: Edison Liu, M.D.

Vice President for Advancement and External Relations: Michael Hyde

Director of Communications: Barry Teater

Mission

We discover the genetic basis for preventing, treating and curing human disease, and we enable research and education for the global biomedical community.

Vision

Our mouse models and genetics research lead the world to solutions for cancer and other complex and intractable diseases.

Research programs

Cancers: brain, leukemia, lung, lymphoma, mammary, ovarian; cancer initiation and progression; cancer detection and therapies

Computational biology and bioinformatics: mouse genome informatics, comparative genomics

Developmental and reproductive biology: birth defects, Down syndrome, sex determination, aging, osteoporosis

Immunology: HIV-AIDS, autoimmunity, immune system disorders, lupus, tissue transplant rejection

Metabolic diseases: atherosclerosis, diabetes, hypertension, obesity

Neurobiology: blindness, cerebellar disorders, deafness, epilepsy, glaucoma, macular degeneration, neurodegenerative diseases

Printed August 2012

The Jackson Laboratory

Leading the search for tomorrow's cures

Editor's message

Q: "So, when are you moving to Connecticut?"

A: "We're not! In fact, we're expanding in Maine."

Given the excitement around the establishment of The Jackson Laboratory for Genomic Medicine in Farmington, Conn., it's not surprising that some people wrongly assume it involves a move to Connecticut.

It's true that JAX Genomic Medicine represents a significant expansion of the Laboratory's research capabilities as well as its physical presence in a new state. But work continues at the headquarters campus in Bar Harbor, Maine, as it has for 83 years, and at the Laboratory's JAX—West facility in Sacramento, Calif. Plans call for growing the workforce in Maine and in California, and recent technological advances are making mammalian genetics research more important than ever to progress in clinical medicine.

Indeed, the Laboratory is looking to add another facility in Maine even as it begins work on the Connecticut site. The planned purchase of a large vacant facility in neighboring Ellsworth, 20 miles from Bar Harbor, will increase the Laboratory's ability to serve the biomedical research community.

At the turn of this new century, the Laboratory was a prestigious but specialized research institution with a single campus. Within the next few years, it will have a much larger presence in every way: four locations in three states, and an increasing role in human genomics research and personalized medicine. While it's impossible to predict the details, it's safe to say that our work will provide vital contributions to medical care and patient health.

Subscribe to our free electronic newsletter, JAX eNews, at www.jax.org/subscribe

News & Notes

The Jackson Laboratory for Genomic Medicine update

The first part of 2012 has been marked by swift progress at The Jackson Laboratory for Genomic Medicine in Farmington, Conn. Planning for the permanent facility is well along, as the dramatic architectural rendering on the inside front cover shows. Groundbreaking for the 173,000-square-foot facility is scheduled for January 2013 on the campus of the University of Connecticut Health Center. The new building will be ready for occupancy in late 2014. In the interim, the newly hired faculty and staff have established interim quarters.

Recruitment has accelerated, and several administrators and faculty members have already begun their work in the interim facility.

Yu-Hui Rogers, site director

Yu-Hui Rogers, M.S., a genomics researcher and experienced scientific administrator, will be in charge of operations and all aspects of research support at JAX Genomic Medicine, including finance, human resources, information technology, facilities and scientific services. She began work in July.

Yu-Hui Rogers, M.S.

Jeffrey Chuang, Ph.D.

Jeffrey Chuang, associate professor

Jeffrey Chuang, Ph.D., comes to JAX Genomic Medicine from Boston College. Chuang is a computational biologist who investigates gene regulation, molecular evolution and high-throughput lipidomics, the study of cellular lipid pathways. He began work in August.

Frank McKeon, professor, and Wa Xian, assistant professor

Frank McKeon, Ph.D., came to JAX Genomic Medicine in July with his colleague and partner Wa Xian, Ph.D. McKeon previously held positions at Harvard Medical School and the Genome Institute of Singapore and will serve as director of quantitative cell biology in addition to his faculty position. He and Xian research stem cell maintenance and pathways through which stem cells may contribute to early stages of cancer development.

Administration

Several administrative positions have also been filled. Senior Human Resources Manager Carol O'Brien will be in charge of HR functions; Nicholas Trafford is the new computer network engineer; and Tammy Brink will serve as the assistant to Site Director Yu-Hui Rogers.

News & Notes

Edison Liu elected to Foundation for NIH Board of Directors

The Foundation for the National Institutes of Health (FNIH) elected Jackson Laboratory President and CEO Edison Liu, M.D., to its Board of Directors for a term beginning June 19, 2012. Liu was the scientific director of the National Cancer Institute's Division of Clinical Sciences before serving for 10 years as founding director of the Genome Institute of Singapore.

"To know Ed is to admire and respect him," says Martin J. Murphy, Ph.D., FNIH board member. "This is a great day for the National Institutes of Health and its Foundation, but most of all it's a great day for patients."

Liu's research has focused on the functional genomics of human cancers, particularly breast cancer, uncovering new oncogenes, and investigating the genomics of cancer biology. "As a member of the Foundation for the National Institutes of Health, I'm looking forward to working with the private sector to build support for the medical breakthroughs we need to address critical public health issues in our nation and around the world," says Liu.

Summer Student Program welcomes top student researchers

These days, getting into The Jackson Laboratory's Summer Student Program is about as competitive as being accepted by an Ivy League college or university. The 39 students in the 2012 program were selected from more than 600 applicants. This year's students come from 17 U.S. states and Israel.

Now in its 88th year, the renowned program welcomes students to campus for a summer of biomedical research. Each student conducts an independent research project under the mentorship of a Laboratory scientist and presents their work at the conclusion of the program. In addition to working on their research projects, the students participate in outdoor activities throughout the summer, including hiking, sea kayaking, white-water rafting, camping trips and nature cruises.

The Summer Student Program experience has helped to inspire many successful careers in science and medicine, including those of three Nobel Laureates: Howard Temin, David Baltimore and Jack Szostak.

Laboratory's expansion covered by *Nature*

The Jackson Laboratory for Genomic Medicine is a vital part of a large-scale effort by the state of Connecticut to expand nonprofit and academic biomedical research in the state. Assistant Editor Karen Kaplan of *Nature Careers*, published by one of the world's most influential scientific journals, covered the development of the new institute in "Gains and losses," a trend story posted online on May 30, 2012.

Connecticut is facing contraction of its corporate pharmaceutical and biotech companies. At the same time, the Laboratory, the University of Connecticut and Yale University are all expanding in the field.

"At a time when most of American higher education is facing serious financial hardships and public institutions are reeling from budget cuts, The Jackson Laboratory, UConn, Yale and the state of Connecticut are partnering to focus on a new field of science: genomic medicine," says Jackson Laboratory Vice President for Advancement Mike Hyde.

Doug Coleman, Ph.D.

Researchers find link between maturation and life span

An intriguing clue to longevity lurks in the sexual maturation timetable of female mammals, Jackson Laboratory researchers and their collaborators report.

Research Scientist Rong Yuan, Ph.D., has led investigation into the role of a hormone, IGF1, in longevity. He found mouse strains with lower circulating levels of IGF1 at six months of age tend to live longer than strains with relatively higher levels. Further inquiry, published in the *Proceedings of the National Academy of Sciences* on May 7, reveals that females with low IGF1 levels also reach sexual maturity at a significantly later age. "This suggests a genetically regulated tradeoff—delayed reproduction but longer life—that is at least partially mediated by IGF1," Yuan says.

Given that a high level of IGF1 in humans has been shown to lead to earlier age of menarche (onset of menstruation), it may also affect human longevity. Further research into IGF1's role in both development and longevity will yield insight into the aging process.

Laboratory among 'Best Places to Work in Academia'

The Jackson Laboratory has again been voted among the top 15 "Best Places to Work in Academia" in the world for 2012. The poll was conducted by *The Scientist*, a magazine for people working in the life sciences, and published in the August 2012 issue. Topping the list was J. David Gladstone Institutes, a biomedical research facility in San Francisco.

The Laboratory was ranked No. 11 of 25 top worldwide academic research institutions (up from No. 13 in 2011), placing just ahead of the Cleveland Clinic and Boston Children's Hospital. Readers participating in the survey cited the Laboratory's infrastructure and environment as well as peer interactions as the institution's greatest workplace strengths.

The Search is partially underwritten by the generous support of Walter and Dorsey Cabot on behalf of family members confronting cancer and the millions of others challenged by genetic diseases.

The Cabots invite readers of *The Search* to share their experiences with other readers. If you have a story related to the work of the Laboratory, please contact the editor at mark.wanner@jax.org.

Awards dinner honorees

At its annual awards dinner on July 13, 2012, The Jackson Laboratory honored a longtime researcher and philanthropist; a respected physician and Laboratory supporter; and a pioneering mouse geneticist and environmental activist.

Professor Emeritus Douglas Coleman, Ph.D., received the Award for Philanthropy for his ongoing support of research and education at the Laboratory. Coleman's 40-year research career focused on finding the genetic causes of obesity and type 2 diabetes. (See feature on page 20.)

The Award for Distinguished Service was presented to neurologist Robert Holtzman, M.D., who began his association with the Laboratory as a 14-year-old summer student in 1956. Holtzman chairs the New York Chapter of The National Council, the Laboratory's network of supporters, and has hosted numerous chapter dinners and receptions on behalf of the Laboratory.

The Award for Scientific Achievement went to geneticist Beverly Paigen, Ph.D., who joined the Laboratory in 1989. Paigen is recognized as a pioneer in using mice to study heart disease. She was an early adopter of computational biology and statistical genetics in her research and has been active in developing and presenting educational programs.

the glaucoma project

By Joyce Peterson
Photography by Françoise Gervais

Mimi de Vries, Ph.D., stands back from the whiteboard on which she has just drawn an elaborate organizational chart, full of boxes, lines and arrows, of the Simon W. M. John laboratory. The John lab's perennially sunny manager smiles pensively. "And it all has to run like clockwork."

The unique organization of the John lab—with several research scientists operating independent but interconnected projects with their own teams of technicians and postdocs, in collaboration with a team of engineers from Purdue University—could be the secret behind the group's extraordinary success. It's a kind of Manhattan Project to develop weapons against the complex group of diseases known collectively as glaucoma.

Glaucoma, a leading cause of blindness, affects more than 4 million Americans, at least half of whom don't even know they have the disease. Current treatments target intraocular pressure (IOP) elevation, the best-known risk factor for glaucoma. However, blindness-inducing damage to retinal ganglion cells and the optic nerve can occur in patients with normal IOP.

As the leader of this "Glaucoma Project," John himself combines the visionary intensity of the Manhattan Project's lead scientist, J. Robert Oppenheimer, with down-to-earth logistical precision. "Current treatments aren't adequate," he says in his clipped Welsh accent. "They're all aimed at lowering the IOP, and they're not effective in all patients. If we can identify the genes that are associated with the risk of developing glaucoma, this would suggest new pathways and targets for treatment."

A Jackson Laboratory professor and Howard Hughes Medical Institute (HHMI) investigator, John is also one of only eight researchers in the nation to receive a Collaborative Innovation Award from HHMI. These awards are intended to fund interdisciplinary, collaborative and "potentially transformative" research.

John is mounting his war on glaucoma on multiple fronts, deploying specialized teams to find new ways of detecting the disease earlier—before symptoms develop—and to invent better treatment strategies for preventing blindness due to glaucoma. The strategy is paying off: In just the past year the John lab has reported important breakthroughs in several aspects of glaucoma.

Using a mouse model that reliably develops the disease as most humans do, in late middle age (around 12-18 months for a mouse), the researchers demonstrated a new analysis technique that detects early stages of glaucoma, and actually mitigated the disease by targeting some of the molecular events in those early stages. In other research they showed that a form of RNA granules known as stress granules—key players in basic cell processes—can affect eye development, leading to juvenile cataracts and glaucoma in humans and mice. And they discovered a gene implicated in an acute and severe form of glaucoma known as angle-closure glaucoma.

Most recently, in March the John lab demonstrated that a single, targeted X-ray treatment of an individual eye in young, glaucoma-prone mice provided that eye with apparently lifelong and complete protection from glaucoma. This work also implicated monocytes, a type of immune cell not seriously considered in previous glaucoma research, as important initiators of damage. The radiation treatments prevent monocytes from entering the eye, which may explain the mechanism of protection. Further research in other animal models to assess protection as well as safety and efficacy is necessary before attempting human treatments, but this work raises the possibility of using highly controlled localized radiation—or perhaps another therapy that blocks monocytes—to prevent human glaucoma.

Organizing for success

The John lab has multiple projects going on at the same time, some "front of the eye" (studying the genetics and biology of IOP) and some "back of the eye" (investigating the neurodegeneration in glaucoma). Each needs high-level expertise for day-to-day management,

At a lab meeting, Simon John, Ph.D., works with Purdue's Art Chlebowski, Ph.D., who is at the Laboratory to develop miniature sensors to monitor eye pressure.

"We've brought in fresh B.A. or B.S. graduates: talented, energetic young people who are motivated to go on to medical, graduate or veterinary school but who first want to take a couple of years to work in a lab to gain more research experience."

—Gareth Howell, Ph.D.

so the usual model of one principal investigator managing several postdocs won't work. John determined that in addition to training postdocs he needed to hire from a category called research scientists—Ph.D.s who had already completed their postdoc stints and were thus ready to run research projects with more autonomy.

In so doing, John is providing valuable support for the careers of several young research scientists: Gareth Howell, Ph.D., Sai Nair, Ph.D., and Krish Kizhatil, Ph.D. It's a tough world out there for Ph.D. researchers. Setting up a new lab at any U.S. research institution and becoming a principal investigator means securing National Institutes of Health funding for basic research. With the average age for a biomedical researcher's first so-called R01 grant now 42, that's a long road to travel.

Howell, whose work focuses on neurodegeneration and genomic sequencing, met John about 10 years ago, when he was a postdoc in another laboratory. Now that Howell is ready to set up his own laboratory as a principal investigator, he says John gave him the mentorship, training and background he needs to succeed, as well as a boost thanks to John's own prestige in the field.

"Simon is so well respected a mouse geneticist and glaucoma researcher that people are always keen to work with him," Howell says, noting that this leads to many invitations from other institutions to give seminars or collaborate.

The unusual structure of the John lab also gave Howell hands-on management experience. "In the last five years we've brought in fresh B.A. or B.S. graduates: talented, energetic young people who are motivated to go on to medical, graduate or veterinary school but who first want to take a couple of years to work in a lab to gain more research experience. The first few of those students have now moved on to some of the best programs in the country."

Howell has been overseeing the daily activities of two of these "pre-grad" research assistants, Catherine Braine and Katharine MacNicoll. "That gave me great experience in running a lab and organizing projects, and that gives me a huge advantage now that I'm ready to set up my own lab."

John's most important training, Howell says, "though it may sound corny, is in how to do good science—how to think critically, to look at the experiments and the data and go that extra mile to make sure you've done enough. The diseases we work on are complex so you can't use just a few samples to get the answer. Most of all, [he shows] how to be a leader in the field by thinking about what's needed and how to get that done."

When John was himself a postdoc, he too had a remarkable mentor: 2007 Nobel Laureate Oliver Smithies, D.Phil., Weatherspoon Eminent Distinguished Professor at the University of North Carolina School of Medicine.

"What a joy to have Simon as a postdoctoral fellow," Smithies says. "He was as unstoppable as a tank, and always full of adventure. Not content with studying the genetics of blood pressure in mice, he decided—completely as a result of his own imagination and drive—to study the genetics of intraocular pressure. And now he is a world authority on glaucoma. I regard it as one of my greatest achievements to have had him in training."

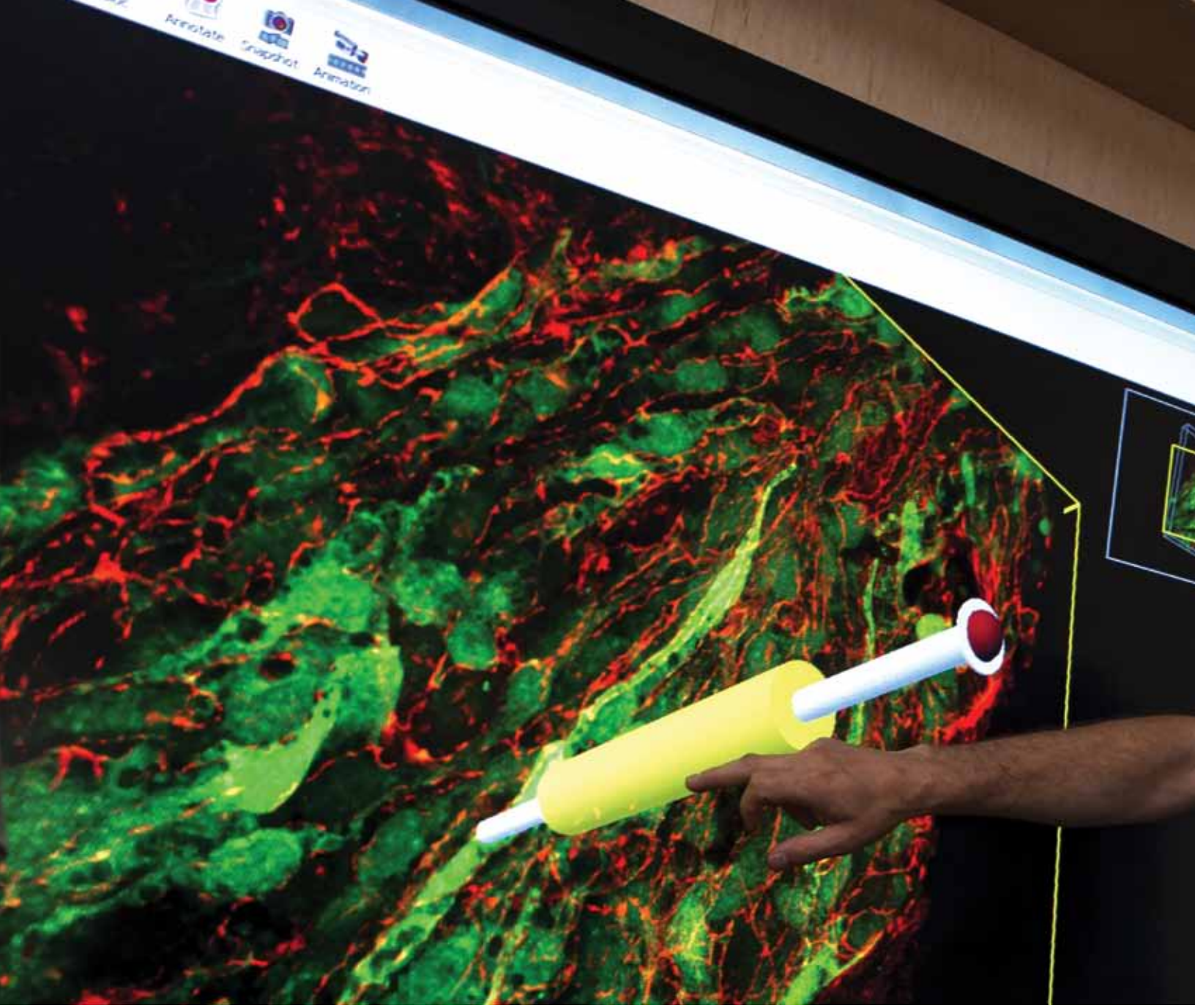
Mischievously, the British-born Smithies adds, "[He is] as unstoppable as a tank, and almost as impenetrable in his accent."

Engineering better research tools

John, who earned his Ph.D. in biology from McGill University in Montreal, came to The Jackson Laboratory in 1995, fresh from being a postdoc in Smithies' lab, with a plan to continue his research in glaucoma. Recognizing the need for a way to measure the IOP of a mouse eye, he invented the first procedure for precise IOP measurements and has continued to refine it.

Since then the John lab has innovated many other research tools, including a database system that most Jackson Laboratory scientists, and many others, depend on. The HHMI Collaborative Innovation

Gareth Howell (right) gained valuable experience mentoring research assistants in the John lab. Here he works with Katharine MacNicoll.



Award was used to develop yet another tool: miniaturized sensors to detect changes in IOP.

Pedro P. Irazoqui, Ph.D., a Purdue University associate professor of biomedical engineering and electrical and computer engineering, is starting a sabbatical term on the Laboratory's campus. Irazoqui and Purdue electrical engineer Bill Chappell, Ph.D., are John's collaborators on the project.

Irazoqui says his first encounter with John was by telephone. "I was on a beach in Spain, vacationing with my wife and son, and my phone rang. It was Simon John, this crazy Welshman, and at first I couldn't understand him for the life of me!" John had read a Purdue press release about Irazoqui's development of an implantable device to go in the human eye, and wanted to know if a mouse-sized version was possible. "I said sure, but it will take a lot of time and money."

Irazoqui describes his ensuing collaboration with John as "extraordinarily productive." The project has led to the invention of a new class of small, implantable tools powered by WiFi. The miniature wireless devices have the potential to transform research capabilities and medical practices.

"The difference between Simon and all the other biologists and doctors I work with is that most of them just want me to build them a widget, but they don't really want to know how it works," Irazoqui says. "Simon actually wants to understand the engineering, but even more importantly, he actually contributes to it.

"He's a good rock climber, too," Irazoqui adds with a smile. "I think that's a prerequisite to working with Simon." Across from the office he occupies, a window is plastered with photos of John lab members scaling impossibly steep-looking rock faces in nearby Acadia National Park.

In fact, John deeply values the time he spends with members of his lab rock-climbing, kayaking, hiking and socializing. "I see them as a team—even as an extended family," he says. "When I invite someone to join our lab, I want it to be the start of a lifelong relationship."

John says the vision and mission of his lab, the reason for hiring the best young researchers and advancing their careers, for developing new research tools and reaching out to collaborators, is simple.

"I'm driven to make a contribution, to help patients and society. And that keeps getting stronger."

Simon John, Margaret Ryan and Jeff Merchant discuss an image of a retina using the Laboratory's new display technology.

By Meg Haskell

Photography by Françoise Gervais

Spirit of discovery

The students in Brad LaRoche's 6th-grade science class at the Camden-Rockport Middle School have a lot of questions. Some of them are posted on a bulletin board in the classroom:

"I always ask them. 'What other questions do you have after you answer that one?'" LaRoche says. "That's the best way to open up their curiosity about the world."

LaRoche, 52, has been teaching middle school science for 15 years. He grew up in Searsmont, Maine, a small town just inland from Belfast, and graduated from the University of Maine in 1981 with a degree in Recreation and Park Management. He worked as a park ranger, educating visitors to the Boston Harbor Islands National Park, before becoming a school teacher.

It's a background that has fueled his lifelong love of nature and energized his enthusiasm for sharing it with others. His transition to the classroom was a natural next step.

In 2009, LaRoche participated in the semester-long Research Internship program for classroom teachers at The Jackson Laboratory. His school freed him up from January through May, a hard call for any school district, but made easier thanks to a Laboratory stipend provided to working teachers who take part in the program. The salary may then be used by the school to hire a classroom substitute. The program is supported by the Howard Hughes Medical Institute, the Arthur Vining Davis Foundations and Jane's Trust.

LaRoche lived in a small house near the Bar Harbor campus and put in a regular work week at the Laboratory.

"They teamed me up with Tom Chase, who worked in Lenny Shultz's lab," LaRoche recalls. "He was studying cures for heart disease in mice with muscular dystrophy."

The mice in Chase's study exhibited surprising strength in their heart muscles, despite having been specially bred to lack a key enzyme for healing breaks in muscle tissue. For five months, LaRoche immersed himself in the hands-on workings of the lab, examining mouse muscle fiber cells for their regenerative ability in response to a variety of conditions.

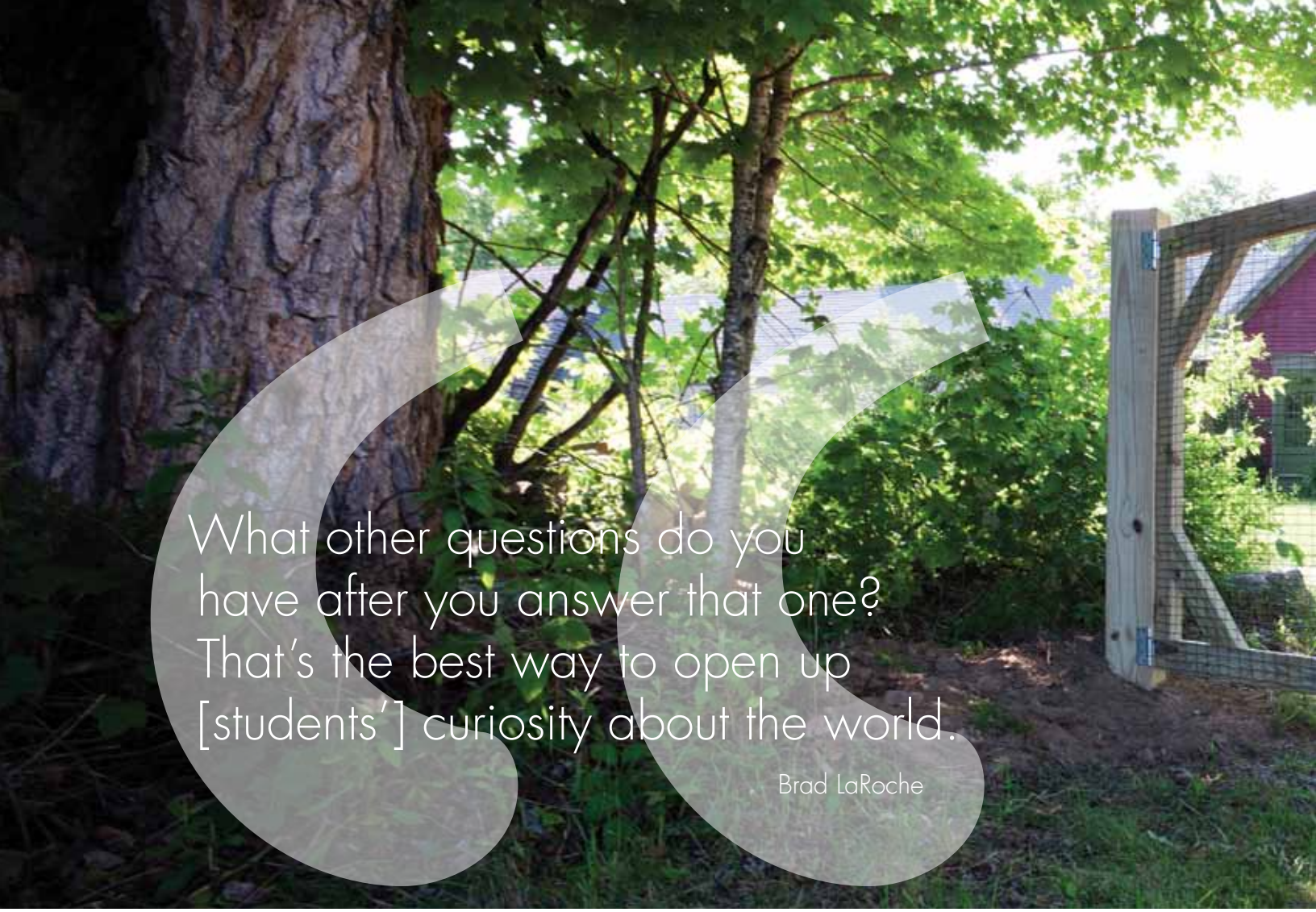
"I did everything that the research called for," LaRoche says. "The last month I was there, I was walking around the lab, looking at all these high-level scientists and Ph.D.s from around the world and feeling amazed that I was having the chance to work with them."

LaRoche is one of 10 public school science teachers in Maine who have taken part in the Laboratory's Research Internship program since it started in 2004. Another 17 participants have come from the Master of Science in Teaching program at the University of Maine that prepares aspiring teachers to tackle the challenges of teaching in the STEM fields of science, technology, engineering and math.

Professor Molly Schauffler of the University of Maine Department of Earth Sciences coordinates a weekly seminar at the Laboratory in which the interns learn to prepare a five-day, research-based classroom science lesson. They also learn about students' common science misconceptions.

"For instance, many high school students believe that elephant cells are bigger than mouse

Brad LaRoche enjoys spending time outdoors at his home in scenic Searsmont, Maine.



cells," Schauffler says. "Or that cells always look like a fried egg, because that's how they're usually drawn in textbooks." Inaccurate ideas like this can undermine a student's long-term progress in science, but a well prepared teacher can identify and dismantle student misconceptions, she says.

According to Schauffler, most of those who participate in the Research Internship are looking to improve their own understanding of the scientific process, as well as to give themselves a competitive edge in the teaching market.

"What attracts them most of all is the enrichment experience," she says. "A school wouldn't dream of hiring a basketball coach who had never played the game, but it is not uncommon at all for them to hire science teachers who have never done real science."

The Laboratory has supported as many as six interns each spring, says Lisa John, who manages educational outreach programming. The overarching goal of the program is to equip teachers with a deep understanding of the scientific process, first by helping them develop a project proposal, then by allowing them to work closely with a scientist mentor to carry out their project during the semester.

Nationally, public education standards call for classroom teachers to have a stronger preparation in research theory and practice, John says, and to teach basic scientific principles beginning early in a student's educational life.

"This is an area we really need to strengthen in our schools," she states. "And the template is one that can be applied from second grade through graduate school."

The Research Internship is one of several Jackson Laboratory educational programs aimed at promoting an interest in science among young people. High school and college undergraduate students can take part in on-campus internships

LaRoche's time at the Laboratory taught him that inquiry opens up the world of science for his students.

during the school year and in the summer, while younger students benefit from age-appropriate, in-class science activities. The Laboratory hosts the Maine State Science Fair and is represented on the state's STEM (Science, Technology, Engineering and Mathematics) education advisory board.

The Internship Program for educators creates a "multiplier effect" in reaching students, as teachers return to their classrooms with a new enthusiasm for laboratory science and fresh tools for passing it on to their students.

The five participants in the 2012 class of interns studied mouse models for the genetic basis for congenital diaphramatic hernia and liver fibrosis; neuromuscular junction defects in a family of disorders known as Charcot-Marie-Tooth disease; the effect on fertility of chromosome crossover timing during reproductive cell division; and a new technique for scanning the brain's prefrontal cortex.

In the future, Lisa John says, the Laboratory may develop an online component to the program to allow more participation without demanding interns' on-site presence for a full semester. But the goal will remain the same: to provide a deep immersion in the hands-on practice of laboratory science.

At the Camden-Rockport Middle School, Brad LaRoche says his experience at the Laboratory "changed who I am as a teacher." He wishes more public school teachers would take advantage of the internship opportunity.

"I can see now that the question drives everything in science," he says. "If we don't allow students to direct their own learning, they won't learn as much. But if we have a culture of encouraging students to ask questions, we can drive tremendous change in public and private education in this country."

5 ques

tions...

Rob Taft, Ph.D., Scientific Director, Reproductive Sciences R&D, The Jackson Laboratory

Q: Did you always have an interest in science?

A: Not directly. I grew up on a dairy farm in northeast Ohio, and figured I'd end up there. I got my bachelor's degree from The Ohio State University in dairy science, but all along I expected I'd go back to the farm and milk cows for a living.

Q: What changed your outlook?

A: I took graduate-level courses in reproductive biology as an undergraduate at OSU, and I found them very interesting. Still, I went back and farmed for a year after I graduated but developed repetitive motion injuries in my arms and hands. I figured 21 was too young to be having these problems on the farm.

Q: So you went back to school?

A: Well, I can't remember life without liquid nitrogen tanks—reproductive technologies were already a part of farming. I went on to get a master's at OSU and my Ph.D. in reproductive biology at West Virginia University, still working with cattle. WVU was a great program, a real team environment where you had to pool resources and work together. It shaped how I wanted to work in my professional life.

Q: Cattle to mice is a pretty big jump. Why did you change?

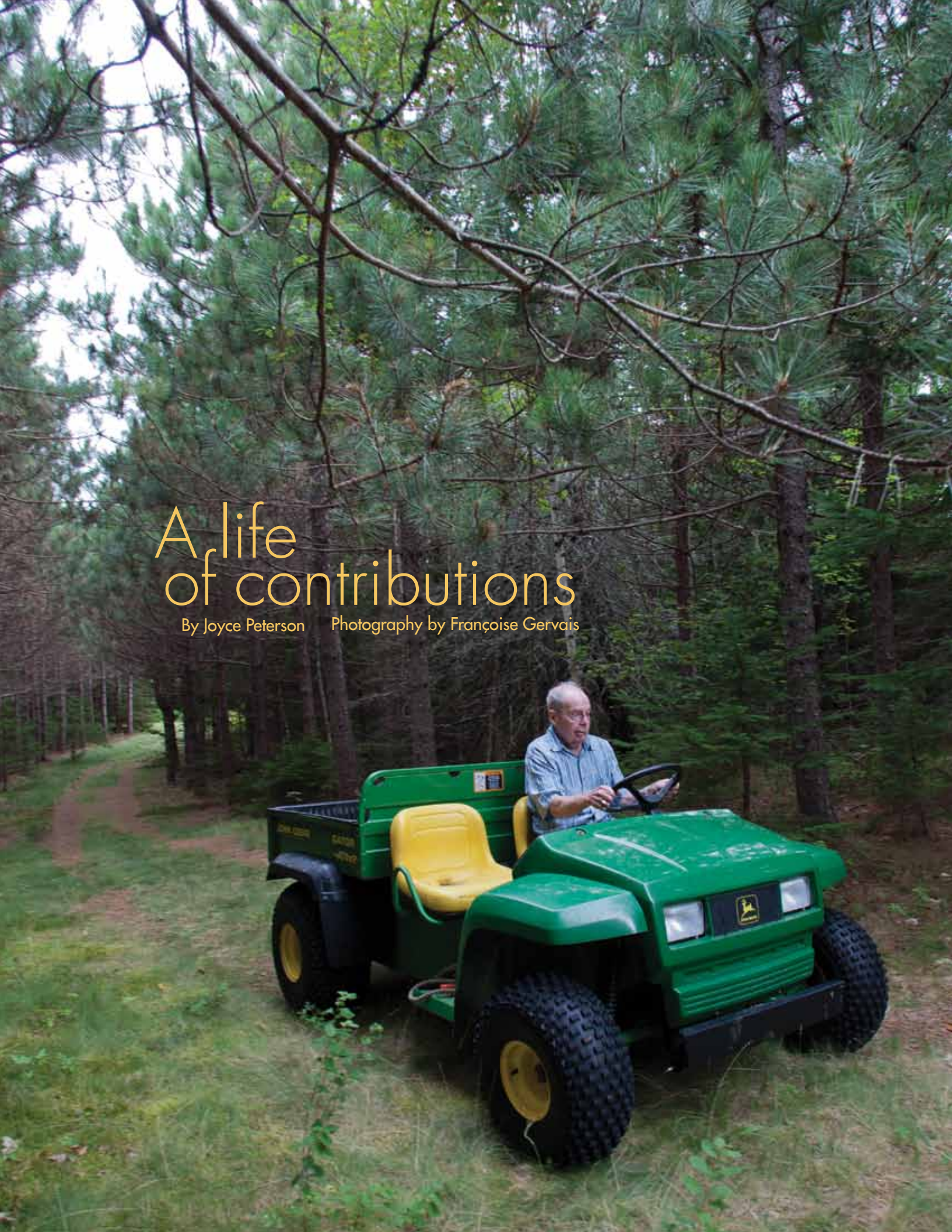
A: I became very interested in research into egg development, which led me to the Laboratory to work with John Eppig for my postdoc. I went on from there to manage the reproductive sciences group. I enjoy integrating basic science with practical applications, and to scale those applications so they benefit the global research community.

Q: That sounds like a big job. What do you like to do when you're not at work?

A: Home improvement. I enjoy building things and have been gradually converting an unfinished log cabin to a finished log cabin. I like making visible progress—that's very gratifying—and my wife's very patient!

A life of contributions

By Joyce Peterson Photography by Françoise Gervais



Jackson Laboratory Professor Emeritus Douglas Coleman, Ph.D., is wrapping up his Friday morning workout on a stationary bicycle in the Laboratory's employee fitness center. It is fitting that he is a familiar face at the facility because it was named in his honor last year.

Glancing out the window at the brilliant summer sunshine and green mountains surrounding the Laboratory, Coleman tells Janet Anker, another morning work-out regular on the bike next to him, that he's on his way to his weekly volunteer duties at the Wild Gardens of Acadia. "The 'Wild Ladies' will be waiting for me," he says with a smile, a fond reference to the Gardens' organizers, his longtime friends. Coleman volunteers in honor of his late wife, Beverly, who had worked on the gardens for more than 25 years.

Now 81, the retired scientist is more active than most people half his age. When not working with the "Wild Ladies," he spends most mornings outdoors on the scenic waterfront land of his home in Lamoine, Maine, a few miles north of the Laboratory along Frenchman Bay. He travels the world, already making plans for a passenger-boat trip to the fjords of Norway after a recent trip to Holland.

"I plunged into retirement with the same enthusiasm that I had for research," Coleman wrote recently in an autobiographical profile. "My love of the outdoors and concern for the environment led me to become actively interested in forest management, land protection, conservation and other ecological issues. I've spent long hours each day rehabilitating our woodlot, making recreational trails that the public, especially students, are encouraged to use for both recreational and educational purposes. In all things science as well as environment, I've tried to leave things better than I found them."

Canadian-born Coleman was the only son of parents who had little formal education. "I was encouraged to excel in school," he recalls. He became interested in biochemistry while an undergraduate at McMaster University and earned his Ph.D. from the University of Wisconsin in 1958. Faced with several career options, Coleman decided to join The Jackson Laboratory's scientific staff as a research scientist working with, among others, George Snell, who would go on to win the 1980 Nobel Prize.

"This decision was transformative," he says. "The Jackson Laboratory had fascinating genetic disease models, interactive colleagues and Acadia National Park as a backyard."

Since his retirement in 1997, Coleman has accumulated some of the highest honors of the scientific world, primarily for his pioneering contributions to understanding the genetic components of obesity.

In the 1970s, Coleman conducted a landmark series of experiments that led him to propose the existence of a "satiety factor" that would account for obesity and type 2 diabetes among certain mice in The Jackson Laboratory's colonies. Later, armed with new tools such as gene mapping, Rockefeller University Professor and Howard Hughes Medical Institute Investigator Jeffrey Friedman would identify that factor as leptin, a hormone that regulates appetite and body weight.

The scientists' work showed that chemical and genetic factors—not just willpower and eating habits—are involved in obesity. Their discoveries provided a window into the genetic complexities of obesity and offered the first possibilities for pharmaceutical treatments for the rare cases of human obesity that are specifically due to defects in leptin processing.

Doug Coleman, Ph.D., drives through a wood lot where he and his wife planted red pine.

"I do not care for honors or awards; they embarrass me." —Doug Coleman, Ph.D.

Coleman and Friedman shared the 2009 Shaw Prize in Life Science and Medicine, widely regarded as the "Nobel of the East," as well as the 2010 Albert Lasker Basic Medical Research Award, the top American prize in biomedical research. Coleman himself won the 1977 Claude Bernard Medal of the European Diabetes Federation, the McMaster University Distinguished Alumni Award in 1999, and the 2005 Gairdner Foundation International Award. He was elected to the National Academy of Sciences in 1998.

Well known among his Jackson Laboratory colleagues and friends for his modesty and plainspoken honesty, Coleman shuns the limelight that now shines on him. "I do not care for honors or awards," he says. "They embarrass me."

Coleman has created yet another post-retirement role for himself: philanthropist. With his share of the $1 million Shaw Prize award, Coleman established two $100,000 endowments at The Jackson Laboratory to support research and education. The Douglas Coleman Research Fund supports Laboratory investigators, with preference given to early-career scientists who are studying obesity and diabetes. The Beverly Coleman Memorial Fund supports young students and educational programs.

"I never expected all these accolades," Coleman says, "and my two sons are already financially stable. So I wanted to make a contribution to future scientists." In July Coleman received The Jackson Laboratory's Philanthropy Award in recognition of his generous donations.

It's somewhat ironic that what may be Coleman's greatest research contribution is only peripherally related to the work that garnered all the awards. His longtime friend and colleague, Professor Emeritus Ed Leiter, Ph.D., a renowned authority in type 2 diabetes, points out that Coleman was the first to recognize the importance of genetic background in understanding diseases.

Before he came to The Jackson Laboratory, Leiter reviewed a paper by Coleman and others showing that the same mutation led to different effects in different strains of mice. Leiter says that paper, now widely hailed as a hallmark in genetics, established the influence of "modifier genes," other genes that enhance or reduce the effect of a specific mutation. "Since then searching for genetic modifier genes has been a mainstay of Jackson Laboratory research," he says.

Science dominated much of Coleman's life, but today it is just one of many interests. "I'm glad my career was when it was," he reflects. He enjoyed the hands-on, almost artisanal aspects of 20th century research. "We had to synthesize our own reagents. To me this proved you were a real chemist, what we were trained for. Today everything comes in a kit!"

And unlike today's researchers, who spend most of their time seeking grant funding to support their work, he notes, "Ed (Leiter) and I, and our peers, had the luxury of spending full time at the bench doing our research ourselves, not delegating it to others. Grants were easy to get and were not hard to write."

The Jackson Laboratory provided Coleman with a close-knit environment that was very different from the university setting he was trained in. "Here it was more like a family, with people from different disciplines interacting every day," he says. "I came here as a biochemist and got into biochemical genetics, and became a jack-of-all-trades. I'd never find another group of colleagues like this anywhere else."

In looking back over his career, he likes to quote Louis Pasteur, who said, "Luck favors the prepared mind." Says Coleman: "My mind was prepared by many mentors at The Jackson Laboratory."

Coleman, chatting with friend Janet Anker, makes regular use of the fitness center named in his honor.

The Jackson Laboratory
Leading the search for tomorrow's cures

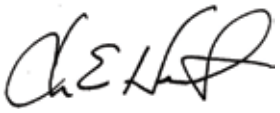
In 2011 The Jackson Laboratory transitioned from its traditional June 1 – May 31 fiscal year to one based on the calendar year. Therefore, FY2012 will run from January 1, 2012, through December 31, 2012. The change left a seven-month "partial year," which ran from June 1, 2011, through December 31, 2011. The financial data opposite this page covers this seven-month period.

While short, the partial year was an exceptionally eventful and positive time for the Laboratory. Of particular significance was the naming of Edison Liu, M.D., as president and CEO on August 25, after an extensive international search. Two months later, the Connecticut legislature approved funding for a new Jackson Laboratory research institute in Farmington, Conn., now known as The Jackson Laboratory for Genomic Medicine.

Several other important awards and transitions punctuated the partial year:

- Leo Holt succeeded Brian Wruble as chair of the Board of Trustees in August.
- Two of the larger grants in Laboratory history, announced in September, funded important collaborative research projects. The Mouse Genome Informatics database program received $25.1 million, and the Laboratory received more than $33 million to play a key role in the second phase of the Knockout Mouse Project, an international effort to disrupt the function of individual genes across the mouse genome.
- The Laboratory was named among the "Best Places to Work in Academia" and "Best Places to Work in Maine" for 2011.
- Professor Simon John, Ph.D., published work about a technique to detect the early stages of glaucoma in mice and ways to target molecular events and block the disease in those early stages.

The groundwork laid in the partial year provided a foundation for continued growth and progress for the Laboratory as we seek better understanding of human genetic diseases and better ways to treat, cure or prevent them.



Charles E. Hewett, Ph.D.

Executive Vice President

Financials

Note: PFY 2011 totals are for the period 6/1/11 – 12/31/11.
FY 2011 totals are for the period 6/1/10 – 5/31/11.

Statement of Activity

Revenue and Expenses *(in millions)*	PFY 2011	FY 2011
Operating Revenue		
Government Support	33.8	56.8
Private Gifts and Grants	5.8	10.4
JAX® Mice & Services	89.9	144.4
Other Revenue	2.3	3.1
Subtotal Operating Revenue	**131.8**	**214.7**
Operating Expenses		
Research	38.2	69.3
JAX® Mice & Services	51.1	83.5
Training and Education	1.9	2.9
Institutional Support	19.4	26.4
Subtotal Operating Expenses	**110.6**	**182.1**
Increase in Net Assets From Operating Activities	**21.2**	**32.6**
Non-Operating Financial Support (Expense)		
Construction Grants	1.6	4.3
Contributions for Plant and Endowment	0.5	2.6
Long-Term Investments Return, Net of Amount Utilized	(6.2)	10.1
Realized and Unrealized Loss on Interest Rate Swaps	(3.5)	(0.3)
Other Non-Operating Changes	(1.9)	0.3
Increase (Decrease) in Net Assets From Non-Operating Activities	**(9.5)**	**17.0**
Increase (Decrease) in Net Assets	**11.7**	**49.6**

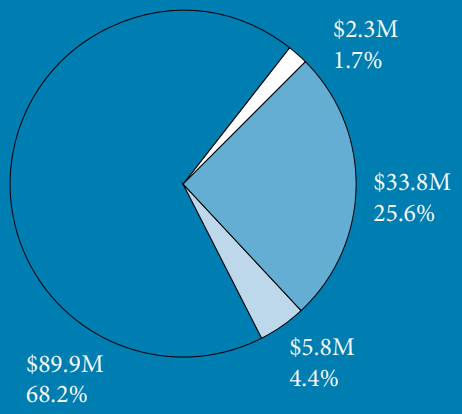
Statement of Financial Position

	PFY 2011	FY 2011
Assets		
Land, Buildings and Equipment (Net)	216.6	209.2
Current Assets	132.7	112.8
Other Assets	12.5	16.0
Endowment Fund	80.8	87.5
Contributions Receivable	2.8	3.6
Total Assets	**445.4**	**427.9**
Liabilities and Fund Balances		
Current Liabilities	50.1	43.5
Bonds Payable, Net	77.9	79.9
Fund Balances	**317.4**	**305.7**
Total Liabilities and Fund Balances	**445.4**	**429.1**

1. The Jackson Laboratory receives operating revenue from several sources including public sector support in the form of federal grants, private sector support in the form of private foundation grants and philanthropic contributions, and resource revenue in the form of cost and fees collected for JAX® Mice & Services. Federal grants are typically awarded competitively for multiple years and cover direct costs and a portion of indirect costs for research and education efforts. State grants are typically restricted to purchasing equipment or supporting efforts to expand research. Other operating revenue includes conference fees, interest income, endowment income dedicated to operating costs and miscellaneous fees.
2. The Laboratory's operating expense is shown by major program and shared services costs. Direct personnel, facility, scientific services, animal health and other direct costs are shown under the program costs. Indirect costs of services that support all of the programs such as administrative support, Human Resources, Information Technology, Advancement and Fiscal Services are shown as institutional support costs.
3. Non-operating activity includes grants and gifts restricted to construction costs or endowment, earnings on the endowment above the amount stipulated to be used to support research and education each year, unrealized changes in the value of interest rate hedges, and non-recurring costs.

2011 Partial Year Financial Data

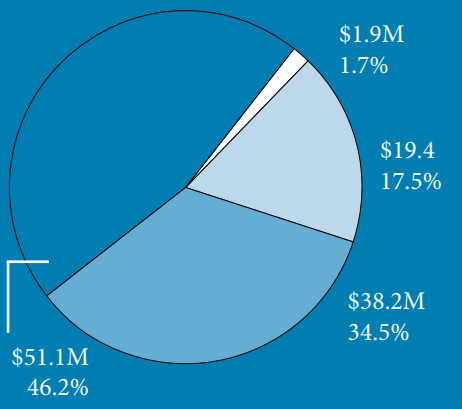
Operating Revenue PFY 11



Total Operating Revenue
PFY 11 $131.8M

- JAX® Mice & Services
- Government Support
- Private Gifts and Grants
- Other Revenue

Operating Expenses PFY 11



Total Expenses Revenue
PFY 11 $110.6M

- JAX® Mice & Services
- Research
- Institutional Support
- Training and Education

Beyond the news

It's well recognized that our genes serve as the starting point for our development and health through life. But they don't determine our fate. What we encounter along the way (our environment) and what we do (our behavior) have profound effects on us as well. But what underlies behavior itself?

Assistant Professor Elissa Chesler, Ph.D., is working to find out. The rapid progress in research technologies and capabilities, such as whole genome sequencing and large-scale data analysis, provides an unprecedented opportunity to identify the genes associated with behaviors and neurological disorders. In a recent review article in *Neurotherapeutics*, Chesler provides a detailed overview of how research in the field, including her own, is benefiting from the recent advances.

Elissa Chesler, Ph.D.

The same biological mechanism may underlie disorders that frequently occur together, while at the same time different mechanisms may give rise to similar behaviors, so challenges still abound. Newly developed mouse models are proving to be vital tools in the research process. Researchers are able to control their genetics with far more precision, in turn making behavior research more accurate and effective.

The genes identified through mouse model research provide vital insight into human behavior genetics, including the discovery of genes not previously identified as important to human neurobehavioral research. The knowledge gained is vital to refining mental illness diagnostic categories and improving treatment of neurological and psychiatric disease.

Bubier JA, Chesler EJ 2012. Accelerating Discovery for Complex Neurological and Behavioral Disorders Through Systems Genetics and Integrative Genomics in the Laboratory Mouse. Neurotherapeutics. 9(2): 338–348.

Our neighborhood

Team Flower Power from the Laboratory takes to the track in Ellsworth, Maine's, Relay for Life on June 1, 2012. Team members annually raise money for cancer research and this year dedicated their efforts to a colleague's fight against cancer.

Photograph by Françoise Gervais

The Jackson Laboratory

Leading the search for tomorrow's cures

600 Main Street
Bar Harbor, ME 04609-1500

A budding scientist examines bacterial colonies that arose from a swab of his classroom's rug. The Jackson Laboratory's second-grade bacteriology course brought the fundamentals of microbiology to Mount Desert Elementary School in spring 2012.

Photograph by Rogier van Bakel