THE SEARCH

The Jackson Laboratory

A tale of two coasts

A day in the life of a doc
It is brain surgery

Blood warrior
Nick Boynton, t1d and the NHL

Westward ho!
The Jackson Laboratory—West

50 years back to the future
Where genetic medicine begins

The Jackson Laboratory: Leading the search for tomorrow's cures

Vol. 2 No. 2


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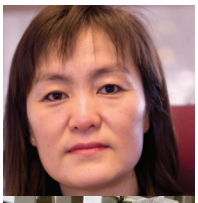
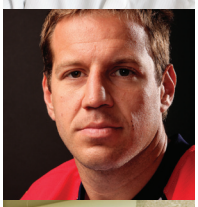
THE SEARCH Vol. 2 No. 2





How do you maintain a new facility with super-stringent sterility standards? With the latest equipment and technology, of course. The Jackson Laboratory—West employs a Space-Age looking Vaporized Hydrogen Peroxide (VHP) machine, which works as a sort of antibiotic humidifier, to decontaminate equipment and spaces not reachable by other means. It's all part of the effort to ensure the highest quality mice and services for our West Coast customers.

Photograph by William Foster

Cover photography by William Foster

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The Search

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Mission statement

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

Our researchers

218 Ph.D.s, M.D.s, and D.V.M.s, including:

38 Professors

42 Research Scientists and Research Associates

50 Postdoctoral Associates

18 Emeritus Scientists

21 Adjunct Scientists

17 Visiting Investigators

6 Affiliated Scientists

Editor's message

The year 2009 marks several significant anniversaries for The Jackson Laboratory. While they celebrate past accomplishments, all of the anniversaries are notable for how they also point us to the future.

For the 50th consecutive year, we will welcome an impressive group of researchers to the Short Course on Medical and Experimental Mammalian Genetics this summer. The Short Course will conclude with a public symposium exploring the future of genetics and health with luminaries in the field including two Nobel laureates. It will be moderated by National Public Radio science correspondent Joe Palca. See page 25 for more details.

It was also 50 years ago that the Mouse Mutant Resource (MMR) officially began its quest to identify and develop naturally occurring mutations in mice that prove useful for human disease research. Over the years these mice have contributed to research for a variety of human diseases not only at The Jackson Laboratory but in laboratories around the world. (For more, see News & Notes.)

Exactly 100 years ago, Jackson Laboratory founder Clarence Cook "C.C." Little developed the first inbred strain of laboratory mouse, an innovation that helped launch the Laboratory and revolutionized biomedical research for the century to come.

Coincidentally, this year is the 200th anniversary of the birth of naturalist Charles Darwin, whose theory of natural selection laid the foundation for modern evolutionary theory and genetics, and the 150th anniversary of the publication of his book, *On the Origin of Species*.

The year 2009 is full of accomplishments to remember and celebrate in the realm of genetics. At The Jackson Laboratory, we are intent on building on this rich past to create a future of better human health.

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

News & Notes

Mouse Mutant Resource turns 50

It is difficult to overstate the scientific value of the Laboratory's Mouse Mutant Resource (MMR) program. Now entering its 50th year, the program has built a unique repository of naturally occurring mutations that has greatly assisted research into a wide variety of human diseases, including obesity, diabetes, heart disease, neurological disorders and more.

"People have genetic disorders because of mutations—something that has gone wrong in their chromosomes," says Muriel Davisson, Ph.D., a Jackson Laboratory professor whose research over the last 37 years has relied heavily on naturally occurring lab mouse mutations. "Through the MMR, we're discovering [disease] models that occur through the same spontaneous processes that occur in people."

New technologies that allow researchers to develop targeted mutations can supplement, but not replace, the spontaneous mutants.

"These are complementary strategies that need to be sustained on a parallel basis," says Davisson. "Each comes with its own advantages."

Challenge gift to attract, support new faculty

Geneticist and author Weslie Janeway of New York has made a $1 million "challenge gift" to the Laboratory for the recruitment and support of new scientists working to understand the genetic basis of human disease. The challenge gift is intended to encourage $1 million in matching gifts from other donors.

"A secure funding base is necessary to attract outstanding researchers," says Janeway, a Laboratory trustee. "This represents the best possible investment in the future of The Jackson Laboratory."

The gift arrives as the Laboratory embarks on a five-year strategic plan to expand its faculty to 45 principal investigators from the current 38 by 2014.

"Mrs. Janeway's generous gift will help us attract bright young faculty with new ideas and approaches to enhance our genetics research at the Laboratory," says Richard Woychik, Ph.D., president and CEO of the Laboratory.

Stem cell technologies attract grant funding

The Jackson Laboratory recently received a $12,500 seed grant from the Maine Technology Institute to investigate new stem cell technologies.

In theory, stem cells can adapt and grow into any kind of tissue in the body. Using them to repair pancreas damage might reverse type 1 diabetes, or putting them to work regrowing heart tissue could restore function after a heart attack. Recent progress has yielded a way to convert adult cells into embryonic-like stem cells, potentially eliminating a wide range of ethical and technical problems associated with using embryonic stem cells.

Anne Greenlee, Ph.D., and Michael Wiles, Ph.D., will lead the project to see if the adult cells, called induced pluripotent stem (iPS) cells, do indeed function as embryonic stem cells would. According to Greenlee, "This will be an important step in establishing whether iPS cells could someday be harvested from an individual patient and used as a kind of 'replacement parts kit' for that patient's own diseased tissues."

Laboratory ranked second for postdocs

The Jackson Laboratory is among the nation's top institutions for scientists in the postdoctoral phase of their careers. The Laboratory was voted No. 2 in a poll of postdocs conducted by *The Scientist*, a magazine for

News & Notes

people working in the life sciences, up from the No. 9 spot in 2008.

After completing their Ph.D.s, most young scientists find a postdoctoral research position under the mentorship of a principal investigator, a kind of apprenticeship before setting up their own laboratories. Jackson postdocs participating in the survey cited training, mentoring and funding as the institution's greatest workplace strengths. The results of the survey were published in the March edition of *The Scientist*.

In November, The Jackson Laboratory was also listed among the top 20 in *The Scientist's* "Best Places to Work in Academia" poll.

See our new video

A new eight-minute video documents how genetics research at The Jackson Laboratory is contributing to a future of personalized medicine, in which health care will be tailored to the unique genetic makeup of each individual. The video, produced by AirStream Pictures of Gorham, Maine, in collaboration with the Laboratory, is available upon request as a DVD and is also on the Laboratory's website at www.jax.org. To watch it online, click on the "Watch video" link below "Advances in human health." To request a DVD, call the Communications Office at 207-288-6051, or email pubinfo@jax.org.

Former Jackson researchers highlighted in *The Scientist*

Genetics and molecular biology are now so intertwined that it's easy to forget that not long ago they were regarded as two separate topics. In 1980 it was unusual for a molecular biologist to want to work at The Jackson Laboratory, long a pre-eminent hub for genetics research. But as profiled in the February issue of *The Scientist*, Nancy Jenkins, Ph.D., and her husband/collaborator Neal Copeland, Ph.D., were among the first to bring modern molecular biology techniques to bear on genetics problems, building a formidable list of contributions to human disease research based on their work at the Laboratory.

Jenkins and Copeland used viruses that carry RNA, known as retroviruses, as their primary tools. Retroviruses produce DNA in the host cells, which then integrates into the host's genome, sometimes producing disease-causing mutations. Jenkins and Copeland used retroviruses to identify and clone genes, with a particular focus on cancer-causing genes, and their work at the Laboratory throughout the 1980s greatly improved genetics research techniques. They now work at Singapore's Institute of Molecular and Cell Biology, but their time at the Laboratory remains why they are described as "the founders of modern mouse genetics."

Jackson Laboratory researchers seek root causes of lupus

Systemic lupus erythematosus (SLE) in humans is a chronic, multigenic autoimmune disease characterized by a wide spectrum of clinical abnormalities. SLE affects more than 2 million Americans—90 percent of them women—with symptoms that include joint pain, extreme fatigue and renal disease. The cause of SLE is not well understood.

The primary job of the immune system is to identify and vanquish potentially dangerous infectious pathogens. Autoimmune diseases develop when the immune system instead unleashes this potent defense system against the individual's own tissues, with predictably severe consequences.

In a recent paper (*Proceedings of the National Academy of Sciences*, February 3, 2009), researchers led by Jackson Laboratory Professor Derry Roopenian, Ph.D., and Postdoctoral Associate Jason Bubier, Ph.D.,

present evidence for a possible root cause of lupus and hope for better therapies. They focused on interleukin 21 (IL-21), an important component of immune system signaling. However, IL-21 produced in overabundance by individuals susceptible to SLE can cause the defense mechanism to misfire and produce antibodies that attack the individual's own tissues.

"The findings provide a strong clue towards understanding how SLE occurs and a clear indication of the importance of interleukin 21 signaling in lupus-like diseases," says Roopenian. "They suggest that interrupting interleukin 21 signaling events may prove to be an effective therapeutic option for human SLE."

Study: Calorie restriction helps only obese mice live longer

A small but dedicated group of people eats very little in a quest to live longer. Research in a variety of laboratory animals and even a recent human study indicated that caloric restriction improves longevity. But does a calorie-restricted diet actually lengthen your life? Probably not, unless you're already overweight, say scientists at the University of Southern California and North Texas Health Science Center.

The scientists studied two strains of JAX® Mice from The Jackson Laboratory to see whether subjecting them to a low-calorie diet prolonged their life span by lowering the rate of metabolism. The C57BL/6J mouse tends to gain weight throughout its lifetime, while the DBA/2J mouse stays lean.

The results, recently published in the *Journal of Nutrition*, showed that while calorie restriction did lower the metabolic rate in both strains, there was no effect on the life span of the DBA mice when compared to DBA mice that were allowed to eat as much as they wanted. The "dieting" C57BL mice did live longer than their free-feeding peers, but the researchers attributed that to the diet's returning the animals to a state of balance between their energy intake and energy expenditure.

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.

Rebecca O'Donnell

An epic bike ride for diabetes

A young woman described by her mother as "one tough kid" will raise money this summer for diabetes research at The Jackson Laboratory by cycling cross-country, a trek of 4,300 miles. Rebecca O'Donnell, 16, was diagnosed with type 1 diabetes at age 9. Ever since, she and her family have been participating in local fundraisers for diabetes research. This year, the Mount Desert Island High School junior is organizing her own fundraising adventure, a three-month ride from California to Maine. It begins at The Jackson Laboratory—West in Sacramento in early June and ends at The Jackson Laboratory in Bar Harbor in late August.

"The more we fundraise, the sooner we'll get to a cure," Rebecca says.

Joining her on the ride will be her 12-year-old brother, James, her father, Mike, and her mother, Deb, who will take a sabbatical from her position as a facilities engineer at the Laboratory.

See the O'Donnell family's progress on their blog at rebeccasride.blogspot.com.

A day in the life of a doc

by Joyce Peterson Photography by Ned Johnston

Every principal investigator, or P.I., as the lead scientist of a research group is known, writes the grant proposals for the funding that keeps his or her lab functioning and prepares research papers for submission to scientific journals. P.I.s plan and run the experiments that lead to new discoveries, serve on institutional committees and manage the day-to-day operations of their labs. Many have young families, with all the responsibilities: child care, meals, gymnastics meets, help with homework. None has enough hours in the day.

8:15 a.m.

Assistant Professor Kyuson Yun, Ph.D., a cancer researcher at The Jackson Laboratory, strides into her first-floor office, energetic and chatty. "The last two nights I've been getting home at midnight," she says, as if to apologize for starting her day later than usual.

Yun hangs her coat up and sits at her computer. She scans her electronic calendar for the day's appointments and then triages the emails that have accumulated overnight.

8:56 a.m.

Yun is waiting for a phone call from a foundation grant officer, "to see what I need to do to get my project funded," she explains. In the meantime she's got a travel agency on another line on her phone to nail down lodging plans for an upcoming conference on tumor microenvironments.

9:17 a.m.

Ted Duffy, Ph.D., manager of the Laboratory's Flow Cytometry Service, comes to Yun's office to consult with her on procedures that need to be completed before the lab can proceed with one of the day's experiments.

The Yun lab focuses on two kinds of brain cancers: medulloblastomas, the most common pediatric brain tumor, and glioblastomas, the most aggressive form of brain cancer, which is currently incurable. The lab investigates the role of cancer stem cells in those tumors.

Just as normal stem cells develop into different kinds of cells that make up a healthy body, cancer stem cells give rise to all the other cell types found in cancer. The experiments in Yun's lab involve isolating and targeting cancer stem cells in mouse models of brain cancer, the first steps in developing potential new treatments for cancer patients.

"I hope it's a good day.

It's possible that this mouse has only a very small tumor in the spinal cord that's causing the paralysis, which won't allow us to do the study that we need to do."

9:25 a.m.

After speaking to Duffy, who will sort medulloblastoma cells so that they can identify the cancer stem cells, Yun prowls the hallways in search of Seungbum Choi, the graduate student in her laboratory. "We've got to get going on this," she says.

Though her seven-days-a-week work schedule has no time for a formal exercise program, a recent pedometer test shows she can rack up five miles a day just dashing around the Laboratory. Choi, who is from Seoul, South Korea, and is in the second year of a Ph.D. program at the University of Maine, appears moments later, and they both head into the lab.

9:30 a.m.

P.I.s are managers as well as innovators, and each has a distinctive leadership style. Yun is a coach: part teacher, part cheerleader-motivator. When she assigns tasks, she takes time to explain why they're important.

"I've been working in Kyuson's lab for about eight months now," Choi says. "She's always here for us, and for students it's really important to be close to your advisor."

Bob Chaplin, a local middle-school science teacher who has a part-time research internship in Yun's lab, has arrived. Choi is his mentor, and Chaplin will be pitching in to help with the medulloblastoma project.

Kyuson Yun discusses the morning's work with Bob Chaplin.

*It **is** brain surgery. Kyuson Yun and Seungbum Choi suit up.*

Yun gathers her laboratory staff around her like a coach in a pregame huddle and explains the shifts in the day's schedule. "What do we do in this lab? Multitask!"

Choi moves to the front of the lab to a hooded procedure area, where he gowns and gloves up and proceeds to collect medulloblastoma cells. In the meantime Yun is discussing her own experiment with research assistant Ben Low.

"This is the moment I've been waiting for," Yun says, swiveling on Low's desk chair. "We've been watching this very special mouse, which has three cancer gene mutations and is the only one we've managed to breed so far. It has some paralysis in its left leg, so it may have a brain tumor."

She pauses a moment. "I hope it's a good day. It's possible that this mouse has only a very small tumor in the spinal cord that's causing the paralysis, which won't allow us to do the study that we need to do." Then she gets up and goes to help Choi.

On occasion, Yun shows a mischievous side. Chaplin says, "She tells me things to say in Korean to Choi. I don't know what I'm saying to him, but whatever it is sure gets his attention!"

11:17 a.m.

Now that Choi has passed the tumor cells to Duffy, there's time for the "journal club" discussion originally scheduled for 10:00 this morning. This is a weekly meeting in which Choi reports on recent scientific papers on cancer stem cells and other relevant fields that Yun has assigned him to read.

Teaching, she has said, is one of her most important roles. "I'm here to make sure that what they're working on is helping them to meet their goals as scientists," she says.

Yun received her B.S. in biology from Caltech in 1989 and her Ph.D. in biology from Caltech in 1997. She came to the Laboratory from Dartmouth College, where she was an instructor in the Department of Genetics.

Kyuson Yun spends dinner time with sons Tommy (left) and Andy.

She was born in South Korea well after her father fled North Korea during the Korean War. He brought his family to California when Kyuson, who spoke no English, was 13. Her brother is an astrophysicist. (Perhaps their childhood arguments were along the lines of "It's not rocket science" and "It's not brain surgery.")

12:05 p.m.

At the monthly scientific faculty luncheon, Yun gets in the buffet line beside Associate Professor Judy Blake, an expert in bioinformatics, and the two chat as they carry their trays into the conference room. Professor David Serreze is at the front of the room, setting up for the talk he'll present on type 1 diabetes.

"There's such a collegial environment here," Yun comments later. "Everybody wants to see you succeed, and they provide so much help along the way."

1:00 p.m.

On the agenda for the weekly Yun lab meeting is a presentation by Low on the proper use of nomenclature—the very specific letters and numbers that designate a gene. Yun sits at the end of the table, facing the screen, arms folded, attentively watching and occasionally checking in with the other members of the group to make sure they understand the concepts Low is explaining.

2:51 p.m.

Scrolling through the latest batch of emails, Yun sees a note from Ted Duffy that the cells have been sorted and would be delivered shortly to her lab. She calls Choi's extension.

3:00 p.m.

Choi hastily walks towards the Research Animal Facility. Yun leaves her lab heading in the same direction as Choi. "I'm the technician for my graduate student—isn't that great? Ha!" Yun jokes about multitasking, but her actual working style is highly focused on one undertaking at a time. She will spend the next two hours helping Choi inject into mice the four kinds of cells from the morning's medulloblastoma cell sorting.

6:10 p.m.

Yun, her husband, David Gallup, and young sons, Andy and Tommy, live at the top of a wooded street less than a mile from the Laboratory. At the stove in the large kitchen-living room rimmed with wide windows, Yun gently probes a fish fillet with a spatula. She seems more relaxed, her voice softer than when she's at work. She moves efficiently, but without hurry.

The boys, ages 10 and 12, bound into the kitchen and onto their dad in a bear-hug scrum. What's it like to have such a busy mom? "She's away a lot," says Tommy, punctuating his words by jumping up and down, "but it's great when she's home!"

Yun later says she could not do her job without her husband's dedication to caring for their family. "When we were in San Francisco, he was growing his business and I was the one who was home with the kids. Now he's semi-retired, so he's able to be home with Andy and Tommy. I'm really lucky."

7:38 p.m.

After dinner, Yun is back at the Laboratory, settling at her desk to work on a grant proposal. On her door she has stuck a pink card that reads: "Granting, Grumpy, Go away." New researchers receive start-up funding from The Jackson Laboratory, but after three years she must assemble enough public and private funding to support her lab's ongoing operations.

Where does Yun get the energy to get through these long days? "I'm very impatient, and there is so much to do," she answers. "I don't have the patience to say I can wait until tomorrow for answers.

"Also, a lot of caffeine. Ha!"

On a deeper level, Yun is highly motivated to find a cure for cancer. "Cancer has had a big impact on the world and on my family," she says. "My father died from lung cancer, and my older brother had a sarcoma when he was in his mid-20s. Helping to cure cancer—that would be exciting and worthy of the sacrifice I ask from my family. That keeps me going."

11:45 p.m.

Back home and ready for bed, Yun picks up a book she recently bought for her kids. "I've found that reading children's books is very relaxing," she says, "and at the same time I can make sure the books are suitable for my sons."

Multitasking to the end, she opens the book and starts to read.

Watch Kyuson Yun talk more about her research and motivations at www.jax.org/thesearch/kyuson-yun.

Westward ho!

—By Tom Walsh

—Photography by William Foster

Willie Sutton had a very good reason for robbing banks.

"That's where the money is," the legendary stickup artist once told a reporter.

That same bulletproof logic underpins the recent relocation and major expansion of The Jackson Laboratory—West, the California satellite facility of the Bar Harbor, Maine-based Laboratory.

"Just look at all the East Coast biomedical research that goes on between Maine and the Research Triangle area of North Carolina, which includes all the medical centers in Boston, the New York-New Jersey area and the National Institutes of Health centers around Washington," says Jackson Laboratory President and CEO Richard Woychik, Ph.D. "All that represents only half of the biomedical research that goes on in California. The West Coast biomedical research community is an exciting community, and we're becoming a bigger part of it."

For the last eight years, The Jackson Laboratory has met the needs of its growing mix of academic

and pharmaceutical customers in California and other Western states through a leased facility in West Sacramento. Earlier this year, those operations were moved a few miles into newly renovated space designed to maximize quality and accommodate growing demand for a wide range of products and services. That $40 million investment also saw JAX—West's headcount double from a staff of 40 to about 80.

The new facility will expedite maintenance and delivery of a wider variety of JAX® Mice & Services' lab mice to researchers in academic and commercial laboratories, including strains that were once trucked cross-country. That can be a stressful journey for a mouse, spanning four time zones and 3,287 miles, 40 miles farther than the distance between Bar Harbor and Paris.

"We can now provide mice to West Coast researchers on shorter notice," says Charles Hewett, Ph.D., The Jackson Laboratory's vice president and chief operating officer. "We now have the capability of providing many of our most popular mice within 24 to 48 hours, versus eight to 10 days. This capability also lowers the cost per mouse by as much as 25 percent."

Sandy Paige, the new facility's senior director, says the JAX—West expansion represents "a serious commitment to better meeting the needs of researchers in this hotbed of scientific research.

"What all this means to us is that we have an expanded, growing and vibrant West Coast presence," Paige says. "We're now better positioned to collaborate in basic research with the California research community, which is an important sector in what is the world's fifth largest economy. California is home to the largest concentration of mouse-based research in the world. California-based research is consistently at the top of the list for National Institutes of Health grants, by far.

Beyond providing lab mice required for testing new drugs and devising new treatment strategies for a wide range of human diseases, JAX—West can perform such research on a contract basis for clients that don't have—or don't want to have—their own in-house research centers stocked with laboratory mice.

"Creating a vivarium, constructing and maintaining laboratory space, and having the staff required to do complex biomedical research represents a huge investment," Hewett says. "A lot of these companies would prefer to just turn this process on when they need it and turn it off when they don't. We can do that for them."

For more than two years, Seattle-based Qwell Pharmaceuticals has been developing therapeutic compounds for human cancers, and autoimmune and inflammatory diseases, in collaboration with JAX—West. Those ongoing studies, says Qwell President Roger Anderson, are going well.

The JAX—West expansion represents "a serious commitment to better meeting the needs of researchers in this hotbed of scientific research."

–Sandy Paige

"I first met with the staff eight months before Qwell began its first study with JAX—West," Anderson says. "The knowledge and professionalism of the staff was without question. All of the study directors were extremely skilled and helpful in crafting study plans, and deadlines were always met. Proposals were always very specific, with well-defined parameters.

"All of our studies, and there have been a number, have been executed per plan," Anderson says. "Project updates were provided on a regular basis. Communication throughout the program has been excellent, and the presentations of study results have been straightforward, clear and concise."

Space within the new facility has been set aside for development of seminar rooms and other venues for educational programming. Just as the Laboratory's Bar Harbor campus has become something of a biomedical mecca for scientists eager to share the insights of their front-line genetics research, the Sacramento facility may one day serve the same role for West Coast researchers. The first such event is a two-day special symposium at the Hyatt Regency Sacramento, to be held on May 5-6 in conjunction with the formal ribbon-cutting ceremony for JAX—West.

BLOOD WARRIOR

By Tom Walsh

Photography courtesy of the Florida Panthers

Nick Boynton and the Florida Panthers were having a terrible night.

The Boston Bruins, Boynton's former team, had scored 48 seconds into the game and never looked back. A burly defenseman with 10 years' experience in professional hockey, Boynton also happens to be a type 1, insulin-dependent diabetic. The bad feeling on this night had nothing to do with his blood sugar, though. With the final minutes ticking down, the Panthers were behind 6-1, a blowout by National Hockey League standards. Boynton was not amused.

With just over four minutes left, Boston right-winger Blake Wheeler picked off yet another errant Panthers' pass and sped across the blue line, one-on-none, toward Panthers goalie Craig Anderson. A breakaway goal here would make the score 7-1.

Boynton had seen enough. In a burst of speed, he found himself only a stride behind Wheeler as the Bruins winger was winding up to shoot. Boynton wrapped the blade of his stick around Wheeler's midsection and yanked him to the ice. Two minutes, hooking.

It was a minor penalty that brought Boynton's penalty minutes for the season to 83, 30 minutes more than any of his teammates. Boynton skated slowly to the penalty box. His blatant hooking penalty had made sure there would be no seventh goal. Enough was enough.

As Panthers Coach Peter DeBoer met with reporters after the game in the press room—"It was just ugly," he tells them—Boynton was back in the visitor's locker room, checking his blood sugar and fiddling with his insulin pump.

"I switched to an insulin pump three or four years ago," Boynton says. "It's been a big help…. I take the pump off during the game while I'm playing, and I test my blood sugar and put it back on at intermission and correct myself if need be. Usually, I'm working so hard, and it's pretty physical activity, so my sugar stays pretty level."

Boynton's diabetes wasn't diagnosed until he was 20, long after he began playing hockey. The news, he says, "came as a bit of a shock."

"I was really, really sick for two or three months," he says. "My doctor misdiagnosed me as type 2 and put me on pills. The pills didn't work, and I kept losing weight. I probably lost 35 pounds and actually saw doctors here in Boston, and they finally diagnosed me correctly as type 1. I was worried it was something else."

After his diagnosis, Boynton's doctors suggested that he take some time off from hockey.

"I just got to Boston and was trying out, trying to make the team, so I didn't take any time off," he says. "That was probably a bit of a mistake; I should have gotten a better handle on it before I did physical activity. But it didn't discourage me at all, and it hasn't stopped me from doing anything."

Despite his diabetes, year-round training has allowed Boynton to endure the quick energy bursts required for an all-out, on-ice, 40-second shift.

"It doesn't really ever stop me," he says. "There's a handful of times in a season when I go low and I may miss a shift here and there because I need to if I get a little light-headed or whatever. It's a very physically intense sport, but the diabetes hasn't been a problem. You train the same way in the summer, for minute-on sprints and a minute off, and the diabetes hasn't really affected that at all."

When Boynton meets with young athletes who are type 1 diabetics, he encourages them to pursue their athletic goals.

"I advise them to check their sugar often and to find a routine, with their doctor, that works for them," he says. "It shouldn't stop them from doing anything. I've been fortunate and have played professional for 10 years now, and the diabetes hasn't been a factor in me playing or not playing.

"It's a scary disease, but, as long as you have a good doctor and you're in control, it's something that can be managed and managed well."

Boynton's great-grandmother died from complications of diabetes. His two young daughters, ages 1 and 3, have been screened but don't show signs of the chronic, lifelong disease. "Nothing so far, and hopefully it stays that way," Boynton says. "If it were to happen, I'm well prepared, I guess, to help them."

Hear Nick Boynton speak about living with type 1 diabetes at www.jax.org/thesearch/nick-boynton.

Diabetes:
Investigating a "geneticist's nightmare"

Jackson Laboratory scientists are busy amassing the biomolecular insights essential to heading off the growing, global scourge of diabetes.

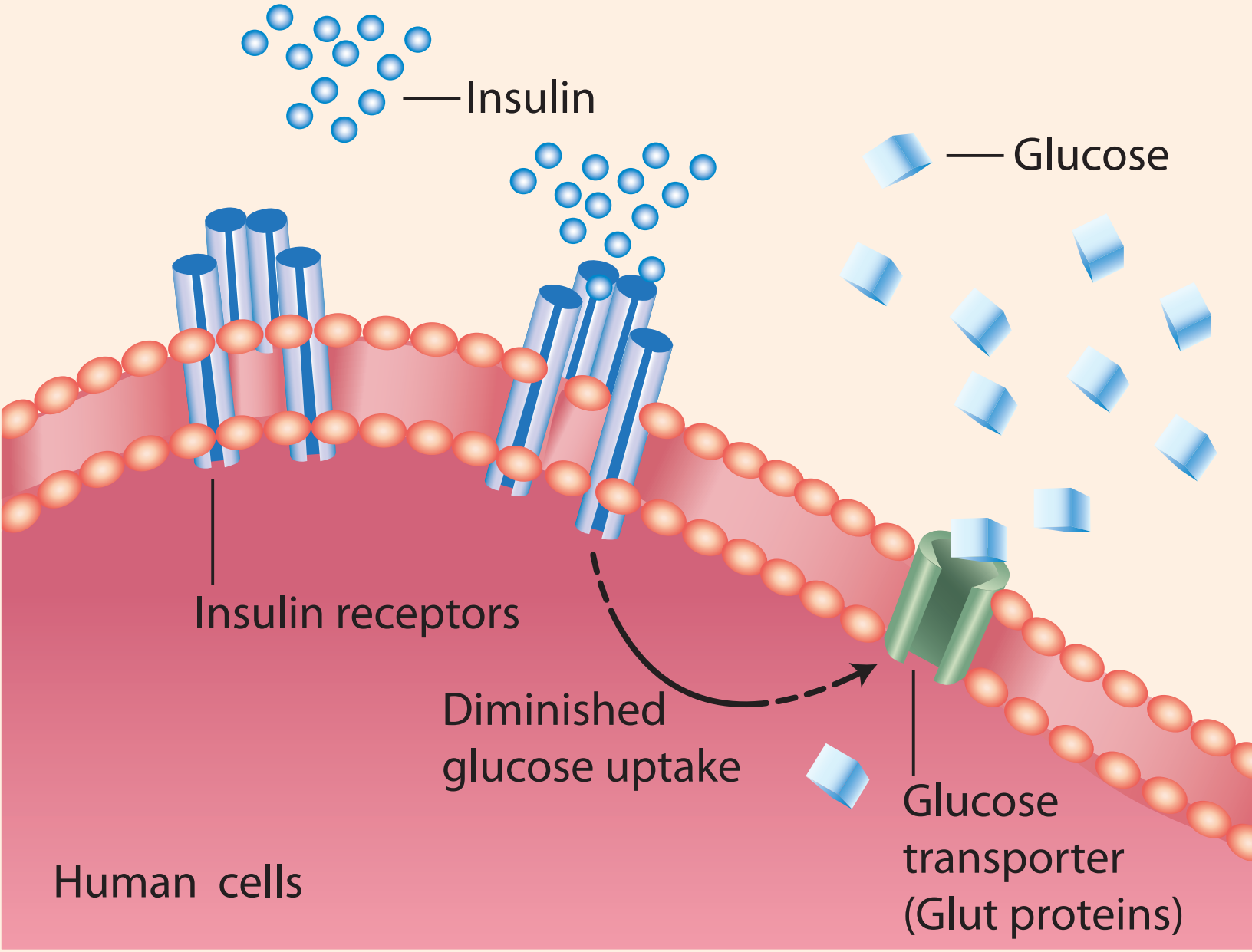
This serious, lifelong metabolic disorder impacts how the body converts digested food into the fuel required for energy and growth. In the United States, where the rate of diabetes has doubled over the last 10 years, diabetes is now an epidemic. More than 23 million Americans have the disease, with about 1.6 million new cases being diagnosed each year.

The least common—and most serious—form of diabetes is an autoimmune disease. In type 1 diabetes, the body's immune system attacks and destroys cells within the pancreas that produce insulin, the hormone required to deliver blood sugar to the cells. Type 1 diabetics require daily insulin injections. Also known as "juvenile" diabetes, this life-threatening disease is most commonly diagnosed in children and young adults.

After studying type 1 diabetes at The Jackson Laboratory for 25 years, David Serreze, Ph.D., describes the disease as "a geneticist's nightmare" by virtue of its complexity.

"Type 1 diabetes involves many, many interactive genes, with 30 to 40 contributing to the disease," he says. "The highest incidence is among people of northern European extraction, especially those from Finland. As the world becomes a more international place, what happens when a Finn marries a Brazilian in terms of the genomes of their children getting more and more complicated? As these different genetic combinations can contribute to diabetes, the reality of a heterogeneous human population is nightmare number one."

Type 2 diabetes affects more than 90 percent of people with diabetes. For reasons largely



While type 1 diabetes affects the pancreatic cells that produce insulin, people with type 2 diabetes don't properly process the insulin they produce. When insulin binds with receptors on a cell, a transportation mechanism moves to the outside of the cell and, in essence, opens a door for glucose to enter the cell via glucose transporters. Type 2 diabetes disrupts the cell's ability to respond to insulin, making it much more difficult for glucose to enter cells.

unknown, type 2 diabetics are unable to effectively use the insulin their bodies produce. This insulin resistance interferes with the conversion of blood sugar into energy, putting type 2 diabetics at greater risk for heart disease, high blood pressure, stroke, kidney disease, nerve damage, amputations and blindness. Should they live long enough, type 2 diabetics eventually become insulin dependent, as are type 1 diabetics.

The role of genetics in the ongoing epidemic of type 2 diabetes is a complex puzzle complicated by the role that genetics plays in another public health epidemic: obesity. The interaction of many genes is associated with the clinical reality that, while about 7 percent of people who are obese develop type 2 diabetes, about 90 percent of those with type 2 diabetes are obese.

"This suggests that, in type 2 diabetics, obesity genes interact with diabetes susceptibility genes to produce the obese/diabetic phenotype that some have termed 'diabesity,'" says Jürgen Naggert, Ph.D., a Jackson Laboratory professor. "Obesity genes alone would only lead to obesity, while diabetes susceptibility genes alone may not cause this overt phenotype."

For more on type 1 diabetes, visit www.jax.org/diabetes.

5 aues

tions...

Rachael Hageman, Postdoctoral Associate, The Jackson Laboratory

Q: Did you study biology as an undergraduate?

A: No, I began as an engineering major, then switched to math. I have always liked a challenge, solving hard problems. I also liked pursuing subjects that not many women study. We need more female role models in math and the sciences.

Q: How did you bridge the gap between math and biology?

A: My graduate school mentor at Case Western Reserve [Daniella Calvetti] was exploring biological applications, modeling metabolic processes with differential equations. She met [Jackson Laboratory Professor] Gary Churchill at a conference. He liked what we were doing and thought it could apply to genetics.

Q: Is that connection the reason you chose the Laboratory for your postdoc?

A: I actually pursued other options and was accepted at other institutions. What grabbed me here was the excellent mentoring they do for postdocs. And we're an important part of the research community, which wasn't always true at other places. (See page 5 for more about the postdoctoral program.)

Q: What are you working on now, and what would you like to do moving forward?

A: I recently received an NIH grant—I'm taking a systems biology approach to understanding the effects of genetic drug targets on HDL metabolism and atherosclerosis. I am working on it with [Research Scientist] Ron Korstanje, who handles the data gathering in the lab while I perform the analyses. In the future I think I'd like to continue my research at a university, but the grant here is for three years, so we'll see where that takes me.

Q: How do you spend your time outside of your work?

A: I run, bike and hike, and it's wonderful to be able to go play in Acadia National Park. I love to be outside and this is a beautiful area to explore.

See interview highlights with Rachael at www.jax.org/thesearch/5questions

Pictured are Lori Petronis (left) and Shelly Meeusen, Ph.D. (right).

Given the vast differences in their backgrounds, Shelly Meeusen, Ph.D., and Lori Petronis have virtually nothing in common.

Nonetheless, these two high-energy professional women recently proved themselves essential to improving and expanding The Jackson Laboratory's presence on the West Coast.

Meeusen and Petronis were instrumental in the yearlong process of relocating The Jackson Laboratory—West into an enlarged and newly remodeled facility in Sacramento, Calif. While Petronis orchestrated the physical relocation of mice and the teams of animal care technicians who support them into the larger facility, Meeusen helped smooth the transition of *in vivo* operations into new research space.

With no previous experience at JAX—West, Petronis arrived in early December and designed, led and participated in the team efforts that accomplished everything from unpacking truckloads of mouse cages and water bottles to cleaning and stocking new mouse colony production rooms.

Petronis' total immersion into the relocation effort meant leaving her husband, Chuck, and their 15-year-old son, Scott, behind in Maine after volunteering for a three-month tour of duty in California.

"I have been fortunate to work with some great mentors, and I wanted to give some of that back to others," she says, now back in Maine with her family. "The JAX—West project was one of the great opportunities I have been given. It is only once in a lifetime you can say you gave 100 percent and feel you have helped in making a difference."

As study director in *In Vivo* Research Services, Meeusen works with client collaborators in designing and directing research studies on therapeutic agents and analyzing data and reports. Throughout the transition to the new

A tale of two coasts

By Tom Walsh

Photography by William Foster

facility, she helped ensure that the move didn't disrupt the continuity of those research studies or jeopardize the quality of the data being collected for a growing array of *In Vivo* clients.

"I worked on customer relations and growing our client base," Meeusen says. "By offering new services and new disease models, we've been building a solid base of repeat customers for the larger facility."

Meeusen is among the JAX—West staffers who were inspired by Petronis' infectious, must-do attitude. "Lori ran circles around the rest of us in terms of the heavy lifting for the transition," she says.

The two women's selfless efforts in smoothing the transition didn't go unnoticed, or unappreciated, by The Jackson Laboratory's Senior Management Team.

"Lori is a natural leader and manager," says Charles Hewett, Ph.D., The Jackson Laboratory's vice president and chief operating officer. "She intuitively understands how to organize a team and motivate and coach people.

"Shelly," he says, "inspires customer confidence in JAX® Mice & Services' ability to reliably carry out customer experiments. She is a versatile scientist and continual learner."

Petronis is from Maine, born in Bar Harbor and raised in nearby Ellsworth, where she graduated in 1987 from Ellsworth High School.

Meeusen was born in Milwaukee, but grew up in many places. Her father's academic and professional careers bounced their family back and forth between California and the Midwest. A self-described "bio-brat," she's a 2003 graduate of the University of California, Davis, where she earned a doctorate in biochemistry and molecular biology.

In 2001, Petronis left a job waiting tables and began working for The Jackson Laboratory in Bar Harbor as an animal care trainee, tending to the needs of colonies of laboratory mice. Eight years and countless promotions later, she was recently selected to lead the Laboratory's custom breeding operations on both coasts.

"This is bigger than anything I have ever thought I could be part of," she says. "I'm thankful every day to have been given the opportunity to say that I am part of the hope created by biomedical discovery."

In 2007, Meeusen left her job at the University of California, Davis Medical Center, where she studied stem cells linked to cerebral palsy, to sign on as associate study director for The Jackson Laboratory—West. Within a year she was promoted to study director in *In Vivo* Research Services.

"My role at JAX allows me to very directly make a significant impact on improving the quality of human life and human health," Meeusen says.

"Toward the end of graduate school, my best friend was diagnosed with end-stage colon cancer. It had spread through his liver and was inoperable. He was barely 30 when he died. He was a huge part of me, and that's when I really wanted to change direction and do work that would have a direct impact on human health."

50 years back to the future

by Luther Young

Personalized medicine. Genetics and health. While these have only recently become hot topics in laboratories, clinics and news media around the world, the merging of genetics with medicine has drawn special attention at The Jackson Laboratory for two weeks every summer for 50 years.

The dedication and vision of the "father of genetic medicine," Victor McKusick, M.D., launched the Short Course on Medical and Experimental Mammalian Genetics in 1960 and has kept it going strong since. Sadly, it won't be McKusick who rings the starting bell outside the Laboratory's C.C. Little Auditorium the morning of July 20, 2009. Another hand will open the 50th annual session of the Short Course, the world's most prestigious genetics education course.

The beloved Johns Hopkins University physician and pioneering geneticist died on July 22, 2008, at age 86. In an era in which the remarkable similarities between mouse and human genetics remained largely unexplored, McKusick saw into the future and established one of the first clinics for patients with inherited disease conditions.

"It seemed to me that [The Jackson Laboratory] did the same thing that we did [in the clinic], namely, identify deviant phenotypes [traits] and try to determine whether these are genetic; if so, how they are inherited, what is the basic defect, and what can one do about them," he recalled in an oral history interview in 1998.

The goals of McKusick's legacy course, known to the biomedical community as the "Bar Harbor Course," remained steadfastly the same at the time of his death. As an enduring collaboration between The Jackson Laboratory and Johns Hopkins, the Short

Photo above: Short Course participants, 1965

...the Short Course has paralleled and influenced

the evolution of modern genetic science over the last half century.

Course has paralleled and influenced the evolution of modern genetic science over the last half century.

"The Short Course continues to be one of the most effective means of teaching how to integrate the power of the mouse and human clinical genetics to better understand the mechanisms of human disease," says Richard Woychik, Ph.D., president and CEO of The Jackson Laboratory.

The roster of lecturers reads like a Who's Who of the biomedical community. Under McKusick's guidance, they came to Bar Harbor under a long-standing formula of equally dividing courses among speakers from The Jackson Laboratory, Hopkins and other prominent academic and research institutions. Faculty has grown from 28 in 1960 to 55 last year, with a total of 638 through 2008.

The 45 students who gathered in 1960 primarily included medical students and academic physicians. By 2008, the mix of 121 students included researchers from pharmaceutical and technology companies, faculty from dental and veterinary schools, and graduate students. Total student participation through 2008 numbered 4,754.

This year's course will convene under the co-direction of The Jackson Laboratory's Patsy Nishina, Ph.D., and Jürgen Naggert, Ph.D., with David Valle, M.D., and Aravinda Chakravarti, Ph.D., from the Johns Hopkins School of Medicine. Valle heads the distinguished Hopkins faculty representation, and he will step in to present McKusick's tour-de-force, 45-minute lecture the first day of class on the history of medical genetics.

The event also offers opportunities to enjoy Acadia National Park and other areas of Downeast Maine. A Maine native, McKusick once observed: "It didn't hurt that we would be meeting on the Maine coast." More important than sightseeing, the Short Course allows students to converse one-on-one with the very scientists who wrote the textbooks these students read in school.

What will medicine look like 50 years from now?

Some of the world's leading scientists will attempt to answer that tantalizing question at a daylong symposium July 31 sponsored by The Jackson Laboratory. The symposium, Biomedical Science and Medicine in the Next 50 Years, will cap this year's Short Course on Medical and Experimental Mammalian Genetics.

Luminaries such as Nobel Laureates Richard Axel and Mario Capecchi, former National Institutes of Health Director Elias Zerhouni, Rudolf Jaenisch, Janet Rowley and more will discuss the future of genetics research and medicine, including cancer, neurogenetics, stem cells, public policy and individualized medicine. The agenda also includes panel discussions about the presentations, moderated by National Public Radio science correspondent Joe Palca. A reception, dinner and lecture by Massachusetts Institute of Technology genome researcher Eric Lander at the Bar Harbor Club will culminate the symposium.

A limited number of tickets are available to the public. For information on the symposium, visit courses.jax.org/2009/50th_symposium.

[A Minute to understanding]

in vivo

[in-ˈvē-(ˌ)vō]

***in vivo*: in the living body of a plant or animal**

DNA, RNA and proteins—important molecules we know from high school biology class—are not static fragments unto themselves, but instead are dynamic components of a greater whole. They form a breathtakingly complicated mosaic of systems, networks, and biological checks and balances.

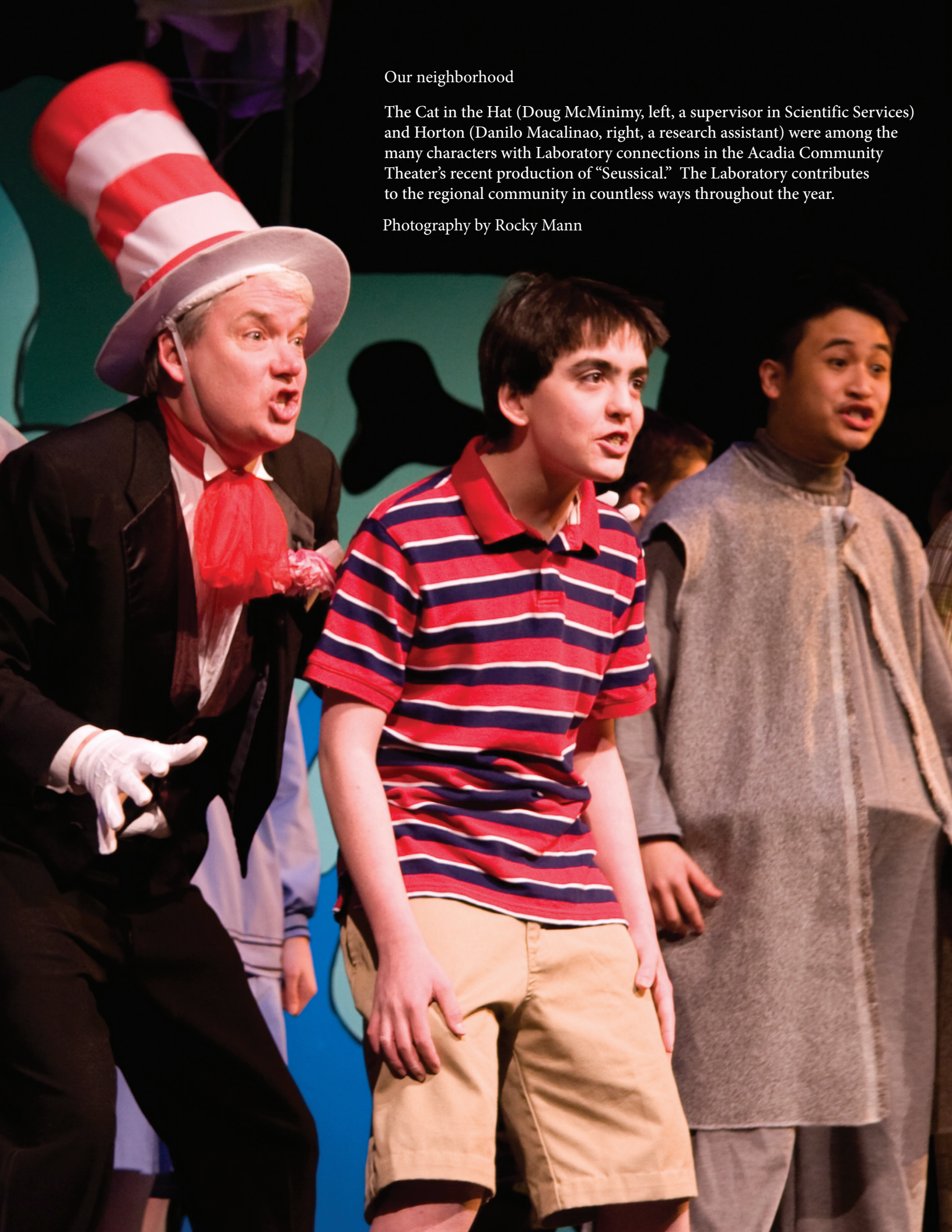
Progress in biomedicine, then, requires more than studying individual components in test tubes or Petri dishes. That's where *in vivo* research comes into play. *In vivo* is a Latin term for "within the living." To see how a drug or therapy actually works, we need to see what it does as part of a whole organism.

But before we test something new in ourselves through clinical trials, we need to get a better handle on how it works and whether it might cause harmful side effects. The best surrogate model available is the mouse. *In vivo* research using mice is becoming more useful and applicable to human health all the time, especially as we learn more about human and mouse genetics and genomics.

Our neighborhood

The Cat in the Hat (Doug McMinimy, left, a supervisor in Scientific Services) and Horton (Danilo Macalinao, right, a research assistant) were among the many characters with Laboratory connections in the Acadia Community Theater's recent production of "Seussical." The Laboratory contributes to the regional community in countless ways throughout the year.

Photography by Rocky Mann



The Jackson Laboratory
Leading the search for tomorrow's cures

600 Main Street
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When Rebecca O'Donnell (second from right) heads off with her family on a California-to-Maine bike ride to support diabetes research at The Jackson Laboratory (see news item, page 7), it won't be her first cross-country trip by bicycle. Thirteen years ago, when she was three, she was cargo as her parents, Mike and Deb O'Donnell (far left and far right), towed her more than 4,000 miles in a kid trailer. This time the trio will be joined by Rebecca's younger brother, James (second from left).