The Jackson Laboratory

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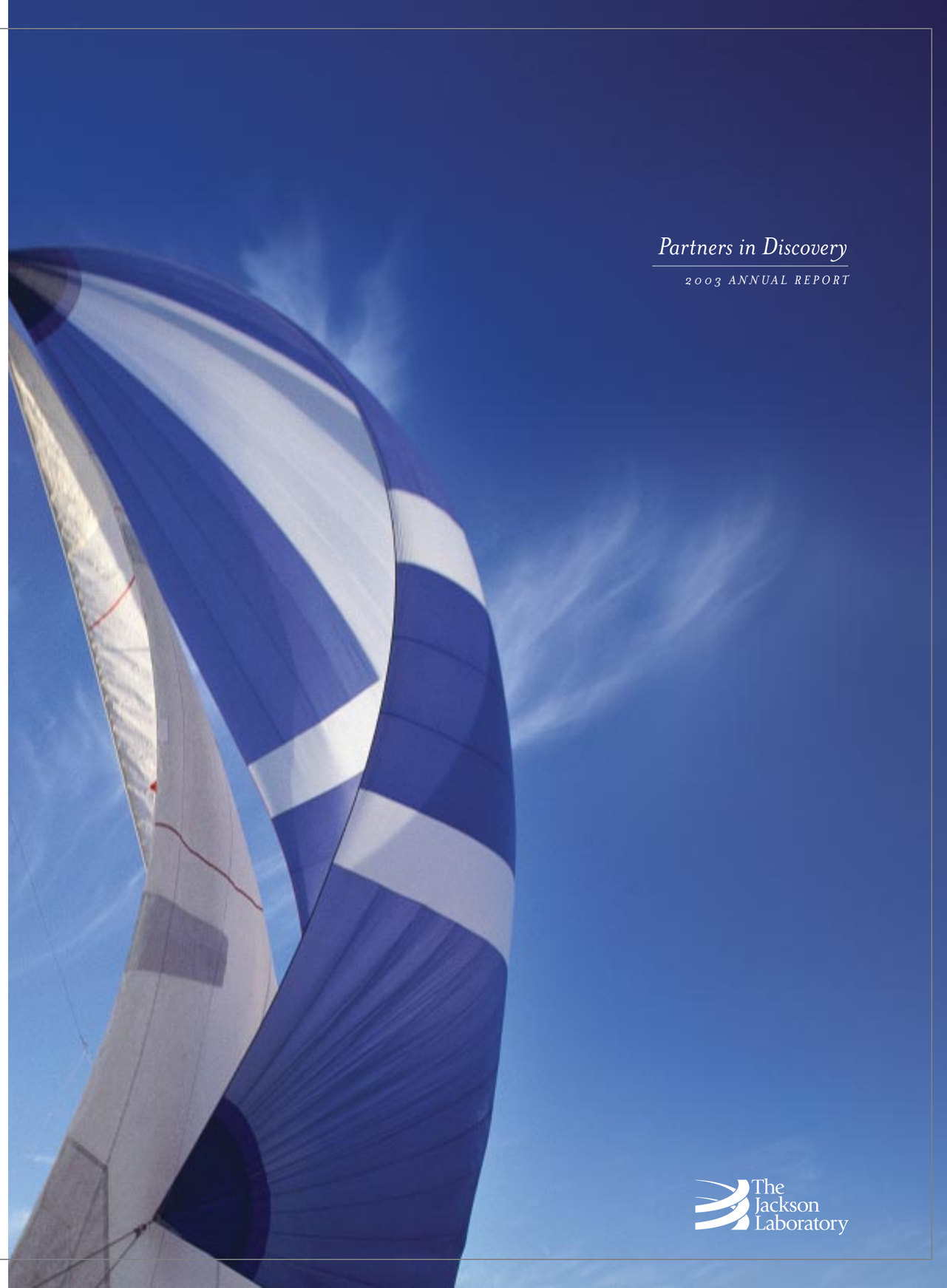
(207) 288-6000
www.jax.org
www.jacksonlaboratory.org

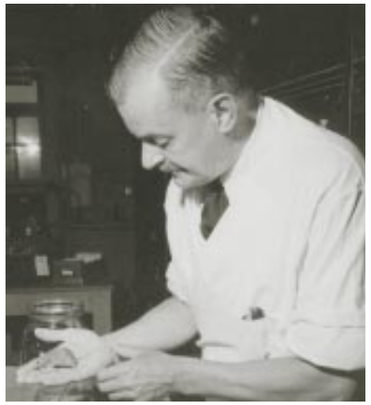


Partners in Discovery

2003 ANNUAL REPORT

The Jackson Laboratory

Clarence Little



Partnerships launch discoveries.

It was back in 1929 when Dr. Clarence C. Little, a Harvard-trained geneticist, started the Laboratory with a small group of highly dedicated scientists who were passionate about bringing scientific rigor to the emerging field of cancer genetics research.

As the first director of The Jackson Laboratory, Little's bold vision for generating and using genetically pure stocks of mice not only had an immediate impact on beginning to define heritable factors that predispose to cancer, but also contributed in an important way to launching a whole new experimental paradigm in biomedical research—one that involved using genetics approaches in the mouse to better understand the genes that define human biology and disease.

We have come a long way over these last 75 years. The entire genetic code from both humans and mice has now been determined, and the mouse has become one of the best-recognized model organisms for studying human biology and disease. Dr. George Snell's mouse genetics work on tissue transplantation was the basis for awarding him the Nobel Prize in 1980. Any patient who receives a heart, kidney, liver, or tissue transplant is the beneficiary of the experiments that Dr. Snell conducted here at The Jackson Laboratory. Additionally, *Nature*, one of the premier scientific journals, recently declared that 17 Nobel prizes and countless biomedical advances can be traced to The Jackson Laboratory and its genetically defined mice. The Laboratory has become one of the world's preeminent institutions for scientific contributions and resources in the field of mouse genetics research.

Little's vision alone, however, was not enough to launch a new organization that would prove to be so influential in the worldwide scientific community. Little had the interest and financial support of three very influential non-scientists: Edsel Ford, Roscoe Jackson, and George Dorr. Ford and Jackson were automotive tycoons who summered here on Mount Desert Island, and Dorr was heir to a private fortune. Ford and Jackson provided the financial resources; Dorr donated the first 13 acres of land on which to build the Laboratory. (At the same time, Dorr was organizing the gifts of private land that would become Acadia National Park.) Together, these three individuals formed a partnership with Dr. Little that made it possible to do things that no one of these individuals could have accomplished on his own.

So it is with The Jackson Laboratory and its partners in discovery. Donors over the past decades supported the development of the infrastructure that has made the research and educational programs at the Laboratory possible. Today's donors both facilitate the work at our Laboratory in Bar Harbor and actually enable the research that is conducted at thousands of research institutions around the world. That happens in three ways. >

"There is great and growing opportunity to make real and lasting contributions to increase knowledge of the origin, nature, and eventual delay or prevention of the most subtle and entrenched causes of human suffering and death. It is a great, progressive scientific evolution. Those of us in contact with that opportunity and certain of what increased stability and support can accomplish directly and without waste are bound to offer to others the chance to share it."

— CLARENCE COOK LITTLE, Sc.D.

First, the kind of fundamental research conducted at The Jackson Laboratory is making significant contributions to understanding mammalian biology and human disease at the molecular level. These contributions are the basis of the diagnostics, treatments, and even cures that will be developed here in Bar Harbor as well as at other institutions worldwide.

Second, we build the databases for the genetics and biology of the laboratory mouse that biomedical researchers everywhere can access freely, and each year we provide about 2 million genetically defined mice to thousands of laboratories.

And third, we teach the scientists of today, tomorrow, and the future. The Jackson Laboratory has long held courses, conferences, and training programs that are filled to capacity with scientists from around the world. Additionally, our research staff trains new scientists who are postdoctoral associates—the scientific equivalent of a medical intern. Recently, we joined with the University of Maine to actively participate in Ph.D. programs. And with the generosity of some of our partners, we are able to provide a number of innovative educational opportunities for high school and college students, year-round and in our historic Summer Student Program. We even reach out to primary school pupils to inspire them to think of science as a career.

The task is far from over and we need your help. Our web site (www.jax.org) details some of the exciting discoveries the researchers at The Jackson Laboratory are making, but it remains sobering how much work still needs to be done. We need more individuals who will partner with our research scientists here at the Laboratory to find cures for the devastating disorders that continue to impact our lives. Too many of our friends and family members continue to be severely impacted and die from disorders that need new drug therapies and treatments. We must continue to inspire hope, because I believe that cures can be found.

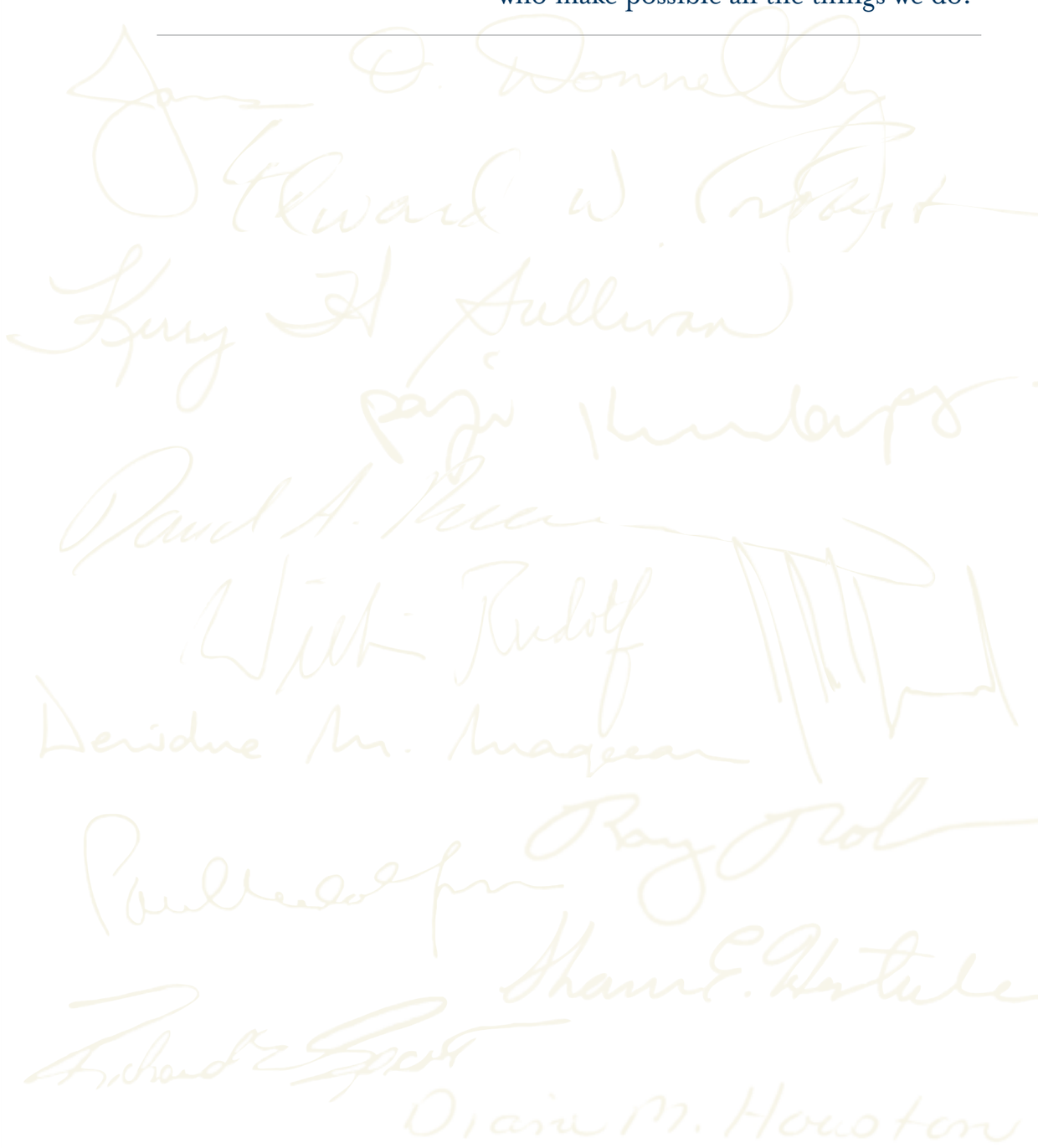
For years, we have shared those discoveries with you in annual reports. This year, you will still find scientific information on each page and in the Year in Review section. But in this edition, we focused on giving voice to some of our current partners so they can tell you in their own words why they support basic research at the Laboratory. All of us at The Jackson Laboratory are grateful for their support, and we embrace their partnership to help us achieve our mission.

For without these partners in discovery, there could be no discovery. And without basic research, there would be scant drug development and hope for new therapies.

THE IMPROVEMENTS IN HUMAN LIFE
BEGIN WITH BASIC RESEARCH,
AND THAT BEGINS WITH YOU.

Richard Woychik, Ph.D.

This year we honor those
who make possible all the things we do.



"The way to make new discoveries is to take risks and fund the exciting ideas, not the safe ones."

RICHARD SPROTT, Ph.D.

"The way to make new discoveries is to take risks and fund the exciting ideas, not the safe ones," explained Richard Sprott, Ph.D., executive director of The Ellison Medical Foundation.

One of the foundation's main focus areas is aging. "But our primary objective is not just making people live longer," he said. "We want to fund research the conventional funding agencies will reject, either because the researcher is unknown or because the researcher has an idea that seems unconventional. We want to drive the science to understand the [aging] processes. That understanding will lead others to a way of curing diseases."

Dr. Sprott knows about aging, mouse models for human disease, and The Jackson Laboratory. He first came to the Laboratory for a postdoctoral fellowship in behavior genetics. After a time in academia, he returned to Bar Harbor in 1969 as a principal investigator, studying single gene influences on behavior and the interaction of aging variables with those genes. Dr. Sprott then moved to the National Institute on Aging, directing the Institute's programs on the biology of aging. For much of his career, he focused on developing animal models for aging research. Now, he funds other researchers through The Ellison Medical Foundation.

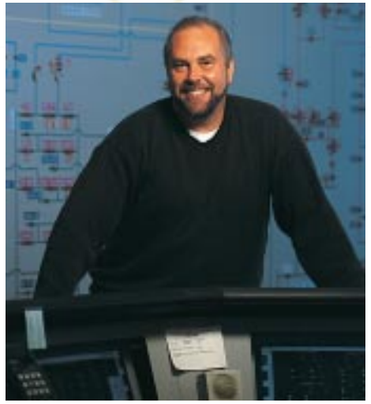
"We are not outcome-driven," Dr. Sprott said on a recent visit to the Laboratory. He was vacationing in the area and came by to visit and see the building he helped fund—a building devoted to mouse models. "But I do measure success by things like I heard today, when one of your young researchers mentioned she is studying a mouse model of aging from that new facility.

"That's how we measure success—by seeing how funding something that is new can drive discoveries in the science of aging."

Research Scientist Kenneth Johnson's research benefits from collaboration with a scientist from the National Institute on Deafness and Other Communication Disorders (NIDCD). "In our studies of hearing loss, we've been successfully collaborating with former Postdoctoral Associate Konrad Noben-Trauth of the NIDCD's intramural program," Dr. Johnson said. "Through this collaboration, we've been enabled to draw upon each other's strengths and resources." With Research Scientist Qing Yin Zheng, Drs. Johnson and Noben-Trauth demonstrated for the first time that age-related hearing loss (AHL) in certain inbred mouse strains is caused by a polymorphism in a gene called *Cdh23*. "A better understanding of the genes and molecular mechanisms underlying AHL will contribute to the development of diagnostics, preventive interventions, and therapies," Dr. Johnson said.

"This information exchange will save years of research to get results and cures."

RAY ROBINSON



Like many partners in discovery, for 43-year-old Ray Robinson, his support is personal.

"I was only 10 when my mom went to the hospital for cancer treatment," he recalled. "We lived on our farm in Saskatchewan. That morning I was out hunting, trying to get my first mallard duck with my pellet gun. Although I took longer than I wanted, I was successful. I remember racing all the way home. I got there just in time to show my mother my prize and wish her well just as she got into the car to leave for the hospital."

Last year, when Mr. Robinson, now the chief operating officer of Bangor Hydro-Electric Company, was going into the hospital for cancer surgery, his mother came to visit. She gave her son a replica of the mallard he had brought her years earlier as she left for treatment. After 33 years, she still remembered the day in the special way mothers remember things about their children.

Now, mother and son share something else: both survived cancer. That gives Mr. Robinson a personal interest in the research of The Jackson Laboratory, which is one of eight basic research facilities on the National Cancer Institute's list of 61 Cancer Centers. "I don't know if my cancer is inherited or not, but my mother survived uterine cancer and mine was testicular. I think there might be a relationship," he said. In fact, while not every type of cancer is inherited from a parent, every cancer is "genetic"—the result of mutations in the DNA of cells that lead to the growth of tumors and other cancer symptoms.

But he also supports the Laboratory simply because he feels the research and services will leverage his donations. "When I visited the Laboratory, I was particularly impressed with the bioinformatics databases that are available without charge to any scientist. This information exchange will save years of research to get results and cures."

Associate Staff Scientist Joel Graber was drawn to The Jackson Laboratory by opportunities for collaboration with scientists performing bench work. His partnership with Director of Research Barbara Knowles has proven most fruitful. "The opportunity for collaboration is a large part of the reason I'm here at The Jackson Laboratory. Barbara and I have been working together extensively. Her lab is testing experimentally the things that I'm investigating computationally," explained Dr. Graber. "We're both interested in the same phenomena, although we see results differently, providing each other with challenging new perspectives." Although Dr. Graber has been with the Laboratory for only a year, his collaboration is already paying off. "We have joint projects nearing publication, and a broad set of problems to investigate from here."

Partners in Discovery

2002-2003

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Kids' Science Night welcomes children from the Bar Harbor area as well as visitors to the state for a night of science and fun. Here, Research Associate Carlisle Landel helps a young visitor try on protective gear used in the Cryopreservation Laboratory.

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† *Deceased*

"Supporting basic research enables the research of scientists at other institutions as well."

DIANE HOUSTON

"My relationship with the Laboratory started when I was a little girl," recalled Diane Houston.

It was the summer her family vacationed in Bar Harbor. They attended the Summer Visitor Program at The Jackson Laboratory one afternoon.

Years later, Mrs. Houston and her husband, Thomas (at left), visited Bar Harbor, and she attended the Summer Visitor Program for the second time. "Ever since that trip," she explained, "I have had a fascination with the Laboratory and an appreciation for the research conducted there." She put her name on the Laboratory's mailing list and followed the research and other activities of the institution.

About 10 years ago, she and her husband became partners in discovery by helping to fund the Laboratory's research. In addition to contributing to the Annual Fund, the Houstons send donations in memory of friends and family members throughout the year. "It seems most of the people we know die from cancer, diabetes, or heart disease," Mrs. Houston said. "Whenever that happens, we make a donation to the Laboratory in the person's memory. It seems a fitting tribute to help find a cure for the disease that took the life of someone we know or love.

"We are not wealthy and cannot give to many charities," she explained. "But supporting basic research is very effective since it enables the research of scientists at other institutions as well." While research is her focus, she also mentioned the importance of the educational programs at The Jackson Laboratory.

The Houstons retired quite young. They plan to visit Bar Harbor again one August, to celebrate their wedding anniversary. The trip will, of course, include another visit to the Summer Visitor Program at The Jackson Laboratory.

Staff Scientists Jürgen Naggert and Patsy Nishina are engaged in a vital collaboration with three laboratories headed by Ronald Krauss, M.D., Children's Hospital Oakland Research Institute; Paul Hopkins, M.D., M.S.P.H., University of Utah; and Jurg Ott, Ph.D., Rockefeller University. "We are each doing a portion of the project to clone the human gene for ATHS," explained Dr. Naggert. The ATHS gene predisposes individuals to atherosclerosis, the major cause of heart disease in the U.S. "We simply couldn't do the project if we didn't have these collaborators."

"The economic and social benefits of this research are expected to be extremely high."

DEIRDRE M. MAGEEAN, Ph.D.

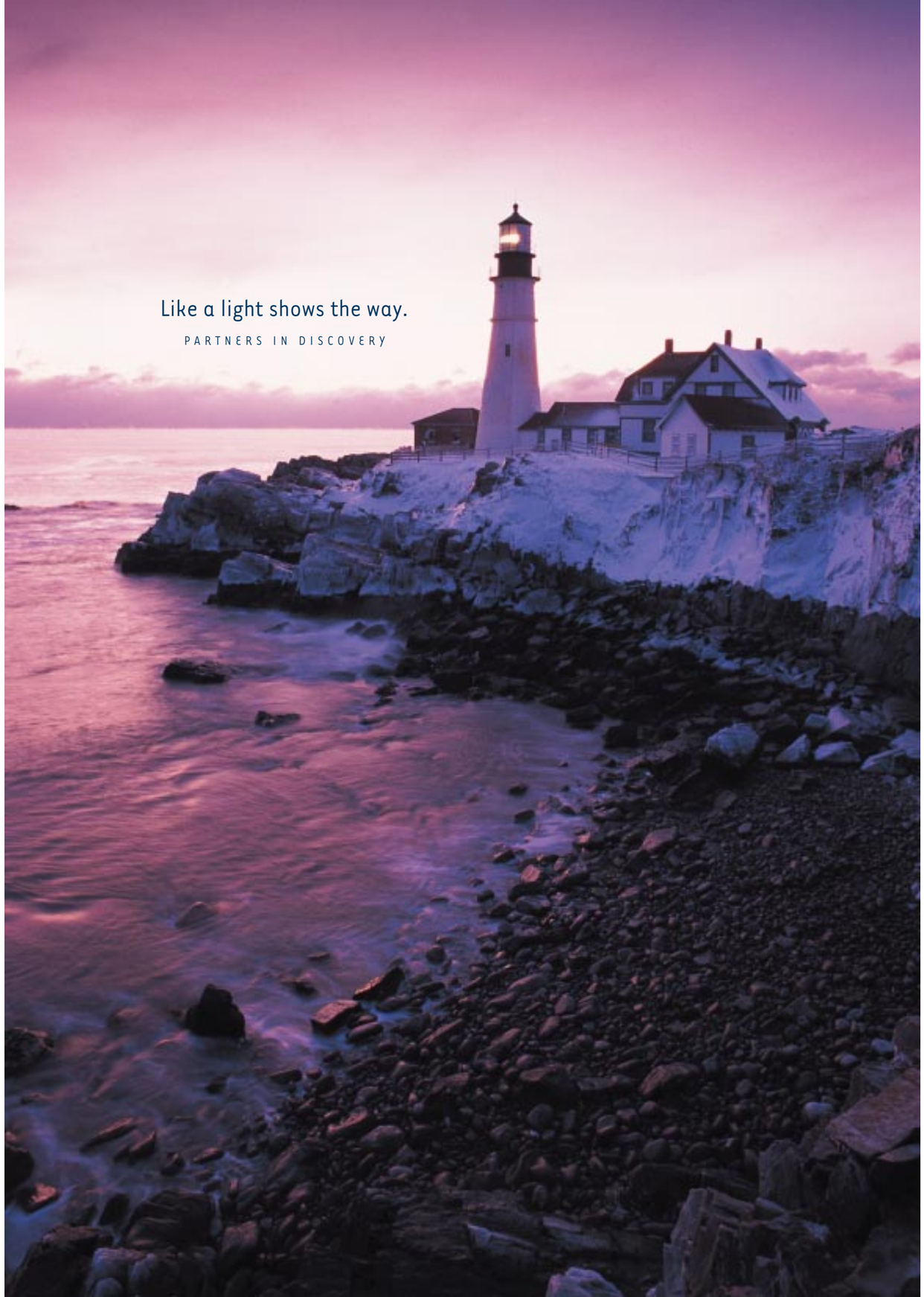
One of The Jackson Laboratory's innovative partnerships with other Maine institutions this year is the creation of the Institute for Molecular Biophysics.

The Jackson Laboratory, the University of Maine, and the Maine Medical Center Research Institute have jointly established the Institute for Molecular Biophysics, with The Jackson Laboratory serving as its headquarters. The Institute will bring together biologists, physicists, computational scientists, engineers, and chemists to develop tools that will generate future breakthroughs in biomedical research. "By assembling partners that bring expertise, then working together to achieve a synergism, we can accomplish things that no one partner could alone," Dr. Rick Woychik, Jackson Laboratory director, commented.

In May 2003, the National Science Foundation (NSF) launched the Institute with a $6 million grant, which garnered a commitment of $3 million in matching funds from the state of Maine. "The economic and social benefits of this research are expected to be extremely high," said Deirdre Mageean, Ph.D., director, Margaret Chase Smith Center for Public Policy, University of Maine. "Better understanding of structure-function relationships on a molecular and cellular level will open the way for the treatment of gene-based disabilities and diseases. It will also lead to the development of more effective drugs, biological homeland defense, and advances in ecological and environmental sciences."

"We want to launch first-rate programs that have the highest visibility and that can attract the world's best investigators," said Dr. Woychik. Toward this end, the stated objective of the NSF grant is to create a nationally recognized interdisciplinary center for biophysical research and graduate education. Principal investigators for the Institute are Michael Grunze, Ph.D., from the University of Maine; Barbara Knowles, Ph.D., from The Jackson Laboratory; and Thomas Maciag, Ph.D., from the Maine Medical Center Research Institute.

A long-standing partnership with Dr. Clifford Rosen of the Maine Center for Osteoporosis Research and Education has resulted in a valuable collaboration for Research Scientist Leah Rae Donahue. "The collaboration that I have with Cliff grew out of my graduate work at the University of Maine," Dr. Donahue said. "Cliff was the chairman of my master's thesis committee and encouraged me to pursue a Ph.D." When Dr. Donahue came to The Jackson Laboratory to work on her Ph.D. project with Senior Staff Scientist Wes Beamer, she immediately involved Dr. Rosen, which is how his association with the Laboratory began. "Cliff's expertise in endocrinology and my knowledge of nutrition are mutually beneficial, and Cliff's ability to extrapolate research to human clinical studies is a great advantage in bone genetics and models of skeletal disease," Dr. Donahue said.



With the mouse as our partner,
we can treat the cause instead of the symptoms.

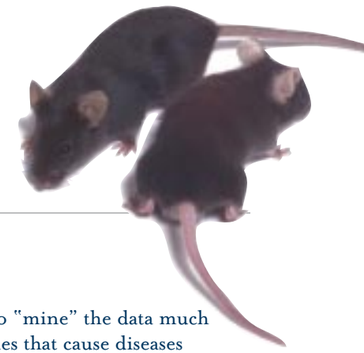
THE MOUSE

"The early group of workers on the staff of The Jackson Laboratory at once recognized that no fundamental progress toward the solution of the role of heredity in cancer could be made without a thorough and complete investigation of the heredity of the mouse." — CLARENCE COOK LITTLE, Sc.D.

Nine scientists came to Bar Harbor, Maine, soon after the completion of The Jackson Laboratory's construction in 1930, and dedicated themselves to the vexing problem of cancer. Just two years earlier, Sir Alexander Fleming, Ph.D., had discovered the first antibiotic. Dr. Fleming's discovery, coupled with advances in diagnostics and surgery, boosted life expectancy almost 30 years by the year 2000. Decades later, as Dr. Little and his colleagues posited, research with mice is demonstrating how to improve those numbers much further, yielding breakthroughs in cancer and myriad other diseases—building on the vision of the Laboratory's founders.

Asthma. Lupus. Spina bifida. Alzheimer's disease. SARS. Diabetes. Influenza. Psoriasis. Heart disease. Glaucoma. Parkinson's disease. Life-threatening allergies. Anthrax. ALS. Obesity. Huntington's disease. Smallpox. Fetal alcohol syndrome. AIDS. Cancer. A glance through this year's science news articles shows that each of these disorders is being investigated in mouse models all over the world, with new information emerging about genes, disease onset, vaccines, or possible treatments. Every major university, medical school, and pharmaceutical company utilizes laboratory mice—in fact, 90 percent of all research mammals in use today are mice. The Jackson Laboratory offers the world's largest collection of mouse models, as well as unparalleled genetics information and resources that draw from focused expertise in mouse genetics.

In December 2002, *The New York Times* stated: "The mecca of the mouse world is The Jackson Laboratory in Bar Harbor, Maine." From the original scientific staff of nine, the Laboratory has grown to 179 doctoral-level scientists investigating an array of diseases and innovating new mouse models. This is the world's largest assemblage of mammalian genetics researchers. Moreover, when young scientists seek to learn mouse genetics and biology, they come to Bar Harbor, where the training program is growing rapidly to accommodate them.



Mice partner with Jackson Laboratory scientists every day, enabling every finding and launching new research directions. Researchers from a wide range of biomedical fields have gravitated to the mouse because of its close genetic and physiological similarities to humans, as well as the ease with which its genome can be manipulated and analyzed.

This year saw the momentous publication of the mouse genome—a genetic "blueprint" of the mouse. We now know that 99 percent of a mouse's genes have counterparts in the human genome. As such, comparing the human genome with the mouse genome will allow scientists to gain the fullest understanding of how genes operate and interact to cause disease. In short, scientists have been provided the means to optimize drug discovery and therapeutic interventions.

Francis Collins, Ph.D., director of the National Human Genome Research Institute, called the unveiling of the mouse genome "a tremendously exciting and defining moment for biomedical research." Dr. Collins has predicted that by 2040, comprehensive, genomics-based health care will be the norm. Such individualized preventive medicine will be based upon the understanding that disease susceptibility is reflected in personal genetic profiles.

At present, Jackson Laboratory scientists are integrating the mouse genome with the wealth of biological information in the Laboratory's publicly available databases. This will help researchers at the Laboratory and elsewhere to "mine" the data much more effectively to find genes that cause diseases in both mice and humans. As Dr. Rick Woychik, director of The Jackson Laboratory, explained, "Now that we have the template for the mouse, the timelines for biomedical research will be vastly accelerated. Investigators sit in front of a keyboard to do real experimentation rather than having to sit at a laboratory bench and do their own sequencing. It opens up a whole new era of investigation." From a computer mouse to thousands of mouse models, The Jackson Laboratory and mice are broadening the horizons of human disease research together.

Jackson Laboratory researchers pursue projects in areas that include:

- CANCER
- DEVELOPMENT AND AGING
- IMMUNE SYSTEM
  — *lupus, type 1 diabetes, transplant rejection*
- BLOOD DISORDERS AND CARDIOVASCULAR DISEASE
- NEUROLOGICAL DISORDERS
  — *Alzheimer's disease, ALS, Down syndrome*
- SENSORY DISORDERS
  — *glaucoma, deafness, macular degeneration*
- METABOLIC DISEASES
  — *obesity, type 2 diabetes*

As part of his research program in epilepsy, Senior Staff Scientist Wayne Frankel collaborates with H. Steve White, Ph.D., professor of pharmacology and toxicology, University of Utah. "We are working on seizure-threshold models," Dr. Frankel said, "that is, mice that may be more prone or more resistant to epilepsy. Steve taught me everything I know about testing anti-seizure drugs and the best ways to assess seizure threshold in mice. We wouldn't be doing this work without him." Dr. Frankel brings his extensive knowledge of the genetics of epilepsy to the project. "If we can determine the genes that lead a mouse to be more resistant to seizures, that could yield promising therapeutic targets because that would be a case where the genetic mutation actually helps the individual." Low seizure-threshold mice, by contrast, would serve as excellent epileptic models for testing such interventions.

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Robert Cooke, science writer for Newsday, has been coming to Press Week at The Jackson Laboratory for more than 20 years. Alicia Chang is new to science writing. The Brown University student was the Laboratory's first science writing Summer Student.

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"I realized the profound social and economic implications of genetics research..."

DAVID BRANCACCIO

Spending a summer at The Jackson Laboratory proved to be a pivotal experience for David Brancaccio.

The former host and senior editor of *Marketplace,* heard daily on public radio stations across the United States, moved to public television in 2003 and is co-host of the PBS series *NOW with Bill Moyers.* Mr. Brancaccio's love for journalism emerged while he was a high school participant in the Laboratory's Summer Student Program.

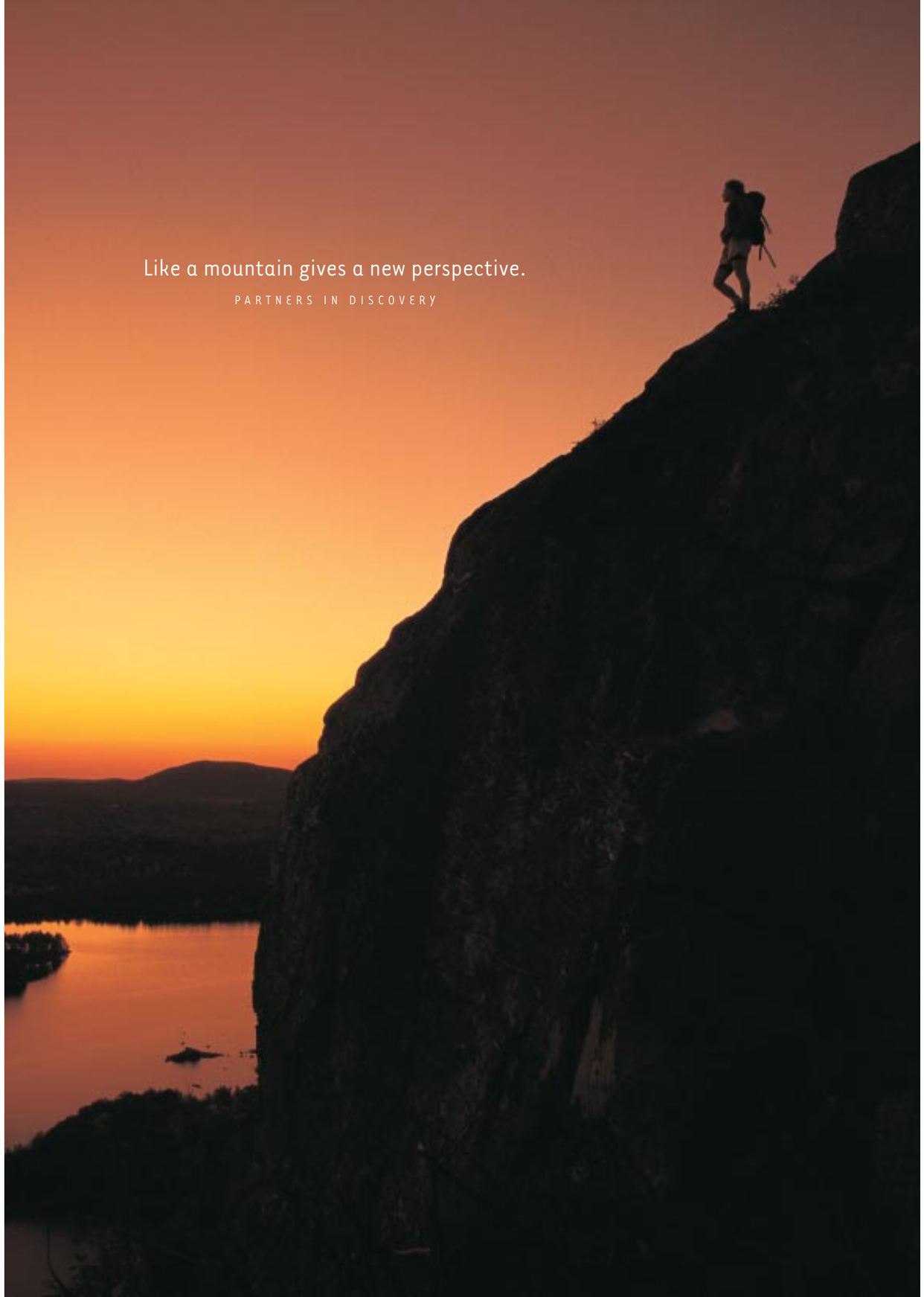
"Of the participants that summer, I may not have had the strongest science project, but I made two very important discoveries," said Mr. Brancaccio. "I realized the profound social and economic implications of genetics research, and the fact that someone had to take the role of translating and mixing the cultures."

He said The Jackson Laboratory is one of the unique institutions that accepts its role in society and carries understanding well beyond narrow scientific constituencies. "I find it exhilarating to discover an institution where people recognize and accept that role and acknowledge the various stakeholders. That is especially true for an institution like the Laboratory, on the forefront of science. That makes it a powerful social force." He continued, "The world needs trusted intermediaries to inform and educate society about the role and implications of science."

To continue that flow of information to the public, The Jackson Laboratory has a wide range of educational and public outreach programs. For example, the Laboratory hosts an annual Press Week, linking top science journalists and researchers from around the world.

In 2003, at the urging of Mr. Brancaccio, the Laboratory brought on its first summer student in a science-writing role. "I have a deep interest in seeing that the world learns more about science and its far-reaching social, governmental, and economic ramifications," he explained. "We simply cannot get enough of this kind of partnership. We need to educate the world."

Senior Staff Scientist Thomas Gridley recently collaborated with Hiroshi Hamada, M.D., D.M.Sc., and his laboratory at Osaka University, Japan. "We found that an evolutionarily conserved communication system between cells, the Notch signaling pathway, helps determine the difference between the left and right sides of a developing mouse embryo," Dr. Gridley said. Generation of left-right asymmetry is an integral part of the establishment of the vertebrate body plan. In humans, mutations in genes encoding components of the Notch signaling pathway are found in one type of cancer and in three inherited disease syndromes.



"My contacts with The Jackson Laboratory have been my primary source of knowledge about mice and mouse genetics."

DAVID VALLE, M.D.

After nearly 30 years of coming to the world-renowned Short Course on Medical and Experimental Mammalian Genetics, David Valle, M.D., said he "...cannot overestimate the importance of the Short Course.

"I teach medical students all year, but the preparation for the Short Course is the most focused teaching activity I do," Dr. Valle said. "Teachers always learn more than the students and the preparation for the course is of enormous benefit to my own education."

Dr. Valle (at right), a pediatrician who heads the Predoctoral Training Program in Human Genetics and the Center for Inherited Disease Research at The Johns Hopkins University School of Medicine, studies clinical, biochemical, molecular, and therapeutic aspects of human genetic diseases. His research is at the interface between human genetics and mouse genetics, and ranges from clinical activities with patients to basic research with mouse models of human disease. "My contacts with The Jackson Laboratory have been my primary source of knowledge about mice and mouse genetics," he explained. "I make mouse models of the human conditions I study. The Laboratory provides an outstanding intellectual environment." He first attended the Short Course nearly 30 years ago and became one of the co-organizers in 1992. Now in its 44th year, the Annual Short Course on Medical and Experimental Mammalian Genetics has always been a partnership between The Jackson Laboratory and The Johns Hopkins University.

The Short Course concept was the idea of Victor McKusick, M.D. (at left), who went on to become physician-in-chief and William Osler Professor of Medicine at The Johns Hopkins University School of Medicine, and founder of Hopkins' Center for Medical Genetics.

Dr. McKusick co-founded the Short Course with John Fuller, Ph.D., then assistant director for training at The Jackson Laboratory, in 1960. McKusick is still co-organizer of the program that has trained, literally, thousands of geneticists.

Senior Staff Scientist Jane Barker seeks to innovate treatments for a rare, devastating disease called MPS VII or Sly syndrome. Children born with this genetic disorder experience mental retardation, abnormal facial features, bone deformities, cardiac valve defects, and loss of vision and hearing. Ultimately, the disease is fatal. A mouse model of Sly syndrome first discovered at The Jackson Laboratory in 1989 closely mimics the human disease. "Our mice have problems with their bones—they're shorter—and we've always wondered if the treatment we give them will help alleviate those problems," Dr. Barker said. "[Senior Staff Scientist] Wes Beamer, who studies bone biology, has helped us to show that our treatments do help with the mice's bone structure. We hope to collaborate with Jackson scientists Ken Johnson and Bo Chang on assessing the mice's hearing and eyesight after treatment, as well."

"The circle of hope starts right here in Bar Harbor."

JAMES DONNELLY

James Donnelly is unique. He came to Maine "from away," a term natives of the state apply to anyone who was not born in Maine, and became a state representative for part of Maine's northernmost region, rural Aroostook County.

During his eight years in the state legislature, Mr. Donnelly began his partnership with The Jackson Laboratory—a partnership that endures in his new role as regional vice president of Machias Savings Bank.

"I learned about the Laboratory while on the Appropriations Committee and later as House minority leader," he explained. "The legislature was looking at ways the state could invest in research and development to stimulate the economy. In Maine, that means The Jackson Laboratory. The Laboratory is so successful, I decided to sponsor a tax-credit program and co-sponsor a bond issue to stimulate research and development throughout the state." Now his interests in research at the Laboratory are more personal.

On an August afternoon, Mr. Donnelly and his wife, Melissa, brought their three sons to the Fun with Science session at the Laboratory. More than ever, the research at the Laboratory has family implications for him. "There is a history of breast cancer in my dad's family," he said. "Now, my mom started chemotherapy for breast cancer late in August 2003. The true importance of the research being done at the Laboratory has hit home for me in a way that it had not before my mother's illness.

"The circle of hope starts right here in Bar Harbor," Mr. Donnelly commented. "I'm tickled to have the Laboratory in my backyard and happy to support everything the institution does. I measure the success of my partnership with The Jackson Laboratory by the breakthroughs I read about in the news. There were some major ones this year." The Laboratory has made great discoveries in breast cancer, as far back as the first paper published by the staff in an issue of the journal *Science,* more than 70 years ago.

Collaboration between the laboratories of Staff Scientist Simon John, a Howard Hughes Medical Institute associate investigator, and Senior Staff Scientist John Schimenti, led Research Scientist Richard Smith to the discovery of an important mouse model of human eye disease. "In the course of screening mice for eye defects, I came across a mouse that had an unusual eye appearance, suggesting it might have glaucoma," Dr. Smith explained. "From a single mouse, we have derived a new colony of mice with multiple defects, including developmental glaucoma, retinal vascular anomalies, and multifocal vascular stroke." The responsible gene has been isolated and these mice are now a valuable model for both congenital glaucoma and stroke.

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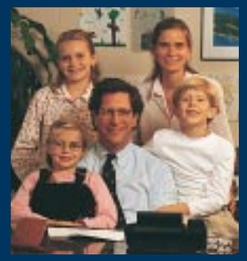

Alan MacEwan, Esq., joined The Jackson Laboratory Corporation in 2002 and almost immediately began working to increase awareness of the institution. He now chairs the Laboratory's Maine CEO Business Roundtable. Here, he and his wife, Holly, share a moment with their children: Ellie, younger daughter Louisa, and Graham.

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"...I was amazed at the outstanding scientists from all around the world whom I met at The Jackson Laboratory."

RAJU S. KUCHERLAPATI, Ph.D.

"The Jackson Laboratory gives so much to so many researchers, so I teach there as my way of giving something back to the Lab," said Raju S. Kucherlapati, Ph.D., scientific director of the Harvard Medical School—Partners Healthcare Center for Genetics and Genomics in Boston.

"When I was just starting out as a postdoc at Yale, I was working in the laboratory of Dr. Francis Ruddle," he recalled. "Dr. Ruddle was teaching in the Short Course at The Jackson Laboratory in 1972 or 1973. That was long before there was a dedicated training laboratory in Bar Harbor, and Dr. Ruddle brought me along to set up the temporary training laboratory. That was my first trip to Bar Harbor and I was amazed at the outstanding scientists from all around the world whom I met at The Jackson Laboratory."

Now the Paul C. Cabot Professor of Genetics and professor of medicine at the Harvard Medical School, Dr. Kucherlapati comes back to Bar Harbor and teaches a variety of courses at The Jackson Laboratory each summer. He often speaks about his recent research contributions, including his participation in mapping and sequencing of the human genome.

Dr. Kucherlapati recently served as a member of the National Advisory Committee for Human Genome Research at the National Institutes of Health. He is also a board member of three public companies. "I have met so many diverse scientists over the years during my trips to The Jackson Laboratory, and I have done collaborative work with many of them," he said.

The Animal Health and Husbandry Research Program is performing studies to determine the amount of floor space needed by laboratory mice. "We are studying several parameters of health and well-being, including testosterone levels as a measure of stress," explained Research Scientist Abigail Smith. "This study is performed in collaboration with Dr. Cameron Muir of Brock University, Ontario, Canada, who is one of the world's experts on interpretation of murine urinary testosterone assays." Studies completed so far have revealed that testosterone levels are unrelated to housing density even in very crowded conditions. The results of these experiments will be used to support space recommendations in the seventh revision of the *Guide for the Care and Use of Laboratory Animals*.

"I want this relationship to continue making great strides—especially in cancer research—for the rest of this century."

EDWARD W. PROBERT

When he steps down as chief executive officer of the Fannie E. Rippel Foundation at the end of 2003, Edward W. Probert is hopeful that his legacy will include a continuation of the partnership that exists between the foundation and The Jackson Laboratory. "I want this relationship to continue making great strides—especially in cancer research—for the rest of this century," Edward Probert said.

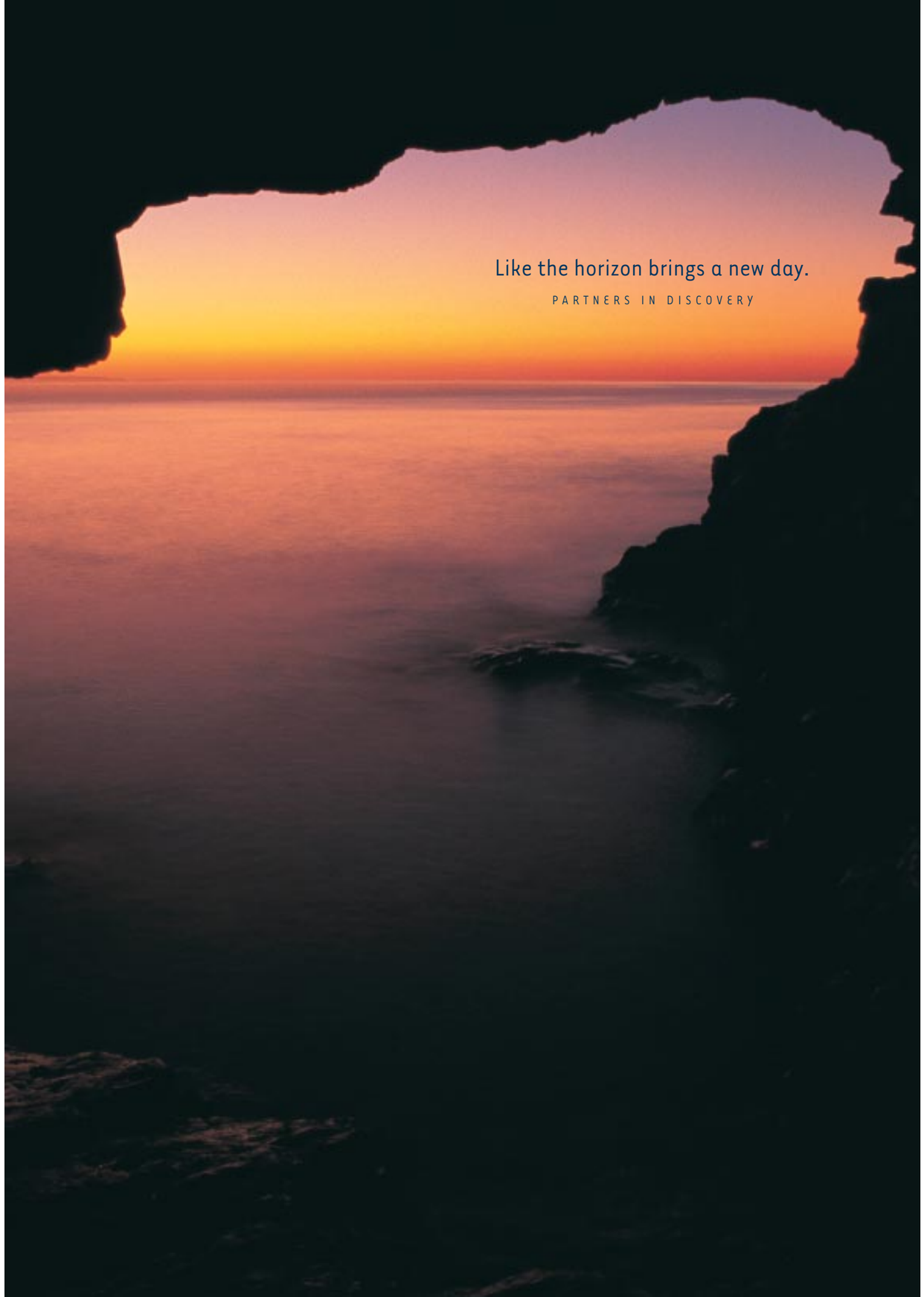
"For a foundation like ours, without a scientific advisory board, the credentials of the Laboratory have been important factors in our grant-making decisions," Mr. Probert said. Those credentials include the National Cancer Institute's designation of The Jackson Laboratory as a Cancer Center. Another factor the Rippel Foundation considers important is the level of success the Laboratory has achieved in applying for research grants from the National Institutes of Health. Recognizing that research grants do not pay for buildings and equipment, the Rippel Foundation provided funding for the Genetics Resources Building and for four mouse breeding rooms.

"Some of our funding supports scientists who are making new models of human cancer and other diseases. And some of our funds are allocated to the production facilities where these models are bred for other research facilities to use," Mr. Probert explained. That way, the foundation's donations enable the Laboratory to fulfill its mission to conduct research and enable the research of others.

In addition to cancer, the Rippel Foundation supports initiatives that further understanding of heart disease and also address the needs and issues affecting women and the elderly.

Cancer research is more than an academic subject for Mr. Probert, a cancer survivor who was diagnosed some 13 years ago. Mr. Probert describes The Jackson Laboratory as "… the kind of institution one does not want to overlook."

Staff Scientist Gary Churchill has a valued collaborator at The Jackson Laboratory: Senior Staff Scientist Beverly Paigen. "We work on inherited traits like cholesterol and blood pressure," he said. "She runs the lab and mouse components, and I do statistical analyses. The two of us working together have found genes in a way that neither of us could do alone. Also, we collaborate with Haralambos Gavras, M.D., from the Whitaker Cardiovascular Institute at Boston University School of Medicine," Dr. Churchill continued. "So that's a mouse biologist, a statistician, and a human biologist. Together, we've recently found a salt-sensitive human blood pressure gene that could have implications for treatment of this disorder."



"...I have come to believe fervently in the importance of basic research."

WILLIAM RUDOLF

"If I had to pick one thing that fuels my excitement about The Jackson Laboratory, it is the satisfaction I get from knowing that I am making an investment to advance human health for future generations," said William Rudolf.

The process of his investing in the future has an interesting history. For decades, Mr. Rudolf has spent summers with his wife, Edith (at right), and their two children on a lake near Bar Harbor. Among their neighbors is another summer family, Drs. Kenneth and Beverly Paigen. Some 30 years ago, the Paigens were summer researchers at The Jackson Laboratory, and the Rudolf children were in the Laboratory's Summer Student Program. Today, Paul Rudolf and his sister, Margaret Coffey, are both physicians.

In 1989, Ken Paigen became director of The Jackson Laboratory, and on the weekend following his confirmation, the Laboratory was partially destroyed by fire. Mr. Rudolf immediately phoned his neighbor. "I called to ask if there was anything I could do. Ken asked me to join the Board of Governing Trustees and I agreed," he recalled. "As a result, I have come to believe fervently in the importance of basic research. Almost all advances in medicine and human health come from basic research, and this is not truly appreciated."

About 10 years ago, the Rudolfs hosted a small reception to give a dozen of their neighbors some exposure to basic science. That reception is now an annual summer event that draws about 75 people from towns up to an hour away.

The Laboratory keeps growing, which Mr. Rudolf considers another benefit. "It is nonpolluting and provides jobs for the Maine economy. It exposes Maine elementary, high school, and college students to science throughout the year. In addition, The Jackson Laboratory has a structured summer program to educate young scientists from all over the country."

Collaborations happen through scientists talking to other scientists about their work. Director of Research Barbara Knowles, through talks with Dr. Joe Verdi at Maine Medical Center Research Institute (MMCRI), realized that his work, and that of Research Associate Mimi de Vries, nicely dovetailed. She put the two scientists in contact, and Dr. de Vries is now the principal investigator of one of four projects in the initial phase of the establishment of a Center of Biomedical Research Excellence in Stem Cell Biology and Regenerative Medicine. "This collaboration will allow the flow of information between The Jackson Laboratory and MMCRI in an effort to determine the underlying pathways determining stem cell development," Dr. de Vries said.

"The Laboratory allows scientists freedom to ask—and hopefully answer—interesting, novel questions...."

PAUL M. RUDOLF, M.D., J.D.

Paul M. Rudolf, M.D., J.D., chief medical officer in the Office of Policy at the Food and Drug Administration, began his scientific career in 1973 when he attended the Summer Student Program at The Jackson Laboratory.

"It was my first exposure to scientific research and to other students who were interested in science," he recalled. "Based on my experience that summer, I decided to do more research, and eventually went to medical school."

He recently joined the Corporation of The Jackson Laboratory, and said he measures the success of the institution "in terms of its creativity in developing new relationships with other partners in academia and industry and in terms of novel approaches to educating both scientists and non-scientists about science."

Such creativity comes from the structure of governance of the Laboratory, according to Dr. Rudolf. "The Laboratory allows scientists freedom to ask—and hopefully answer—interesting, novel questions without being driven by a herd mentality seen so often in large academic institutions, where a department or division director determines the research program."

His area of medical expertise is adult endocrinology, so he follows the research developments in obesity and diabetes. "However," he said, "I believe the Laboratory has much more to offer than just its research."

Dr. Rudolph joined his father, William, on the board of The Jackson Laboratory in 2003.

Staff Scientist David Serreze maintains an "extremely fruitful collaboration" in type 1 diabetes with three scientists at Albert Einstein College of Medicine: Teresa DiLorenzo, Ph.D.; Stanley Nathenson, M.D.; and Marshall Horwitz, M.D. "The biochemistry is done at Albert Einstein College of Medicine," Dr. Serreze explained, "and The Jackson Laboratory has the genetic tools and resources. Marrying these two makes the work possible." In a July 2003 paper, these partners identified a protein called IGRP that is targeted by immune cells during the early stages of type 1 diabetes. They proposed that an immune attack targeting IGRP and the resulting inflammation of the islets may be the first destructive stage of the disease. Therefore, IGRP could be a potential new target for diagnosis and treatment. In an interview with Reuters Health, colleague Teresa DiLorenzo, Ph.D., suggested clinical partnership possibilities to come: "This is generating a fair amount of excitement in the field, so we're not going to be alone in these human studies. We should know, hopefully within the next year, whether [IGRP] is a relevant target in humans."

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This family is part of The Jackson Laboratory family. Peggy Kotter works in Institutional Relations. John Craigo is in charge of occupational physical therapy and worker ergonomics. With sons Max (left) and Ethan, they capture the warmth of Indian summer at Indian Point, a few miles from the Laboratory.

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"I look to seeing new therapies for ALS and muscular dystrophy tested this year."

SHARON HESTERLEE, Ph.D.

The biggest public exposure of the Muscular Dystrophy Association (MDA) is during its Labor Day weekend telethon. Host Jerry Lewis raises tens of millions of dollars each year, which the MDA invests in research to cure neuromuscular disorders.

Much of the research sponsored by the MDA is focused on target identification—finding the point in the disease process that can respond favorably to drugs or other types of therapy, explained Sharon Hesterlee, Ph.D., director of Research Development at MDA. "For many of the diseases we are beyond exploring the basic mechanisms," she said, referring to the search for cures her organization supports.

One of the roles The Jackson Laboratory plays is as a central repository of mice, particularly strains that are unprofitable for commercial breeders. In fact, Jackson Laboratory researchers found the world's first animal model for muscular dystrophy in the early 1950s. Today, The Jackson Laboratory has more genetically pure strains of mice than any other source in the world. The MDA provides funding through grants to individual researchers that helps to maintain some of those mice that model human neuromuscular diseases.

Those diseases represent many genetic variations, noted Bob Mackle, MDA director of Public Information. "So our researchers need mice with many genetic variations. But the different models have to be standardized. More mouse models mean more tests of therapies—pharmaceuticals, stem cells, and even gene therapy."

"Our researchers have been supplied with mice through The Jackson Laboratory for more than a decade," Dr. Hesterlee continued. "It is very cost-effective and the researchers appreciate the services of the Laboratory."

The partnership resulting in the availability of specialized mice for research into neuromuscular disease is meaningful only if it improves human life. Dr. Hesterlee seems confident. "I look to seeing new therapies for amyotrophic lateral sclerosis and muscular dystrophy tested this year," she said.

For many years, Senior Staff Scientist Leonard Shultz has brought his expertise in immunodeficiency to collaborations involving such diseases as cancer, diabetes, anemia, and AIDS. This year, he received a grant from the Muscular Dystrophy Association to work with Dale Greiner, Ph.D., University of Massachusetts Medical School, and Emanuela Gussoni, Ph.D., Children's Hospital of Boston and Harvard Medical School. Dr. Shultz's immunodeficient mouse model can accept stem cell grafts; with further genetic modifications, the mice can become susceptible to muscular dystrophy. The research team hopes that stem cell therapy will allow the muscular dystrophy mouse models to generate normal muscle cells. "These models serve as a bridge between animal experimentation and clinical trials of stem cell therapy," Dr. Shultz said.

"We hope to see improvement in student achievement by funding the teacher training and mentoring components."

KERRY HERLIHY SULLIVAN

It seems fitting that a foundation created by the man whose Balfour class rings are synonymous with graduation partnered with The Jackson Laboratory to boost graduation rates in rural Maine. The late Lloyd Balfour wanted to see his foundation benefit institutions furthering education. Fleet National Bank serves as sole trustee of the L.G. Balfour Foundation.

In addition to the institutions specified in Mr. Balfour's will, the trustee funds innovative programs that help improve access to quality education for underserved populations, from elementary schools through universities.

The Balfour Foundation recently announced a $230,000 grant for "Mastering Science," an innovative educational program that will pair University of Maine science teachers-in-training with Jackson Laboratory scientists in a content-rich, research-based, graduate-level training program. The teacher candidates will gain hands-on experience in working with high school students interning at The Jackson Laboratory. This collaboration, launched in May with a grant from the Howard Hughes Medical Institute, will also include a statewide mentoring network for teachers throughout Maine and eventually New England.

"Many of our grants have focused on urban populations. This grant allows the Balfour Foundation to fund efforts to improve quality science education in Maine and throughout all of New England," explained Kerry Herlihy Sullivan, director, Charitable Asset Division, Foundation & Philanthropic Services, which is the Fleet unit that administers the trust. Fleet National Bank has a long history of supporting education through its own charitable organization, the FleetBoston Financial Foundation, in addition to the trusts it administers.

"National research shows a strong correlation between student achievement in math and science and teaching quality," said Ms. Sullivan. "We hope to see improvement in student achievement by funding the teacher training and mentoring components."

Senior Staff Scientist John Schimenti has collaborated with 17 postdoctoral associates during his career, training the emerging scientists to establish their own laboratories or pursue other avenues in biotechnology and related areas. "Generally," he explained, "postdocs are discouraged from continuing collaborations with their former mentors, because they need to show independence. But I'm currently finishing up projects with Antonio Planchart and Jeremy Ward, who are now assistant professors at Bates and Middlebury colleges, respectively." Other recent, former postdocs include Dieter Naf, who worked on a cancer biology database at the Laboratory before taking a position at the National Cancer Institute; Neal Goodwin, who started a biotech company called Phenome Systems; Doug Pittman, who is now an assistant professor at the Medical College of Ohio; and Brian Libby, who is pursuing a degree in patent law in Maine.

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Dean Booher, D.D.S., is a longtime supporter of The Jackson Laboratory. His son, Brian, is a network systems administrator at the Laboratory. Christopher Booher enjoys an afternoon at the soccer field in Bar Harbor, Maine, with his father and grandfather.

Our Silent Partners

ANONYMOUS

Many donors prefer anonymity. Some merely wish to retain privacy; sometimes it is in the terms of an estate. Regardless of the reason, these partners in discovery prefer no public acknowledgement, yet they deserve our thanks.

For example, an anonymous gift enabled The Jackson Laboratory to install a Beowulf Cluster—a method of bringing enormous computing power to the Laboratory without an enormous supercomputer. The concept originated about 10 years ago when two technicians at Goddard Space Flight Center connected 16 ordinary processors by an ordinary Ethernet. They named the configuration "Beowulf" after the classic poem.

Thanks to the generosity of these anonymous donors, Beowulf is slaying computational monsters at The Jackson Laboratory with the dispatch its namesake showed against the mythical monster, Grendel.

"One scientist came in and asked if we could compare 2.5 million DNA sequences against the genome," said Charles Donnelly, manager of Computational Biology Resource Applications at the Laboratory. "That would have taken a year and a half on a single server. The Beowulf Cluster completed the comparison in 10 days." The Laboratory's cluster consists of 32 personal computers that host 64 CPUs. Installed in November 2002, the system has been operating nonstop since that time.

No other funding source existed for this powerful research tool, but anonymous donors grasped the importance of the new technology, becoming partners in discoveries previously not possible at The Jackson Laboratory.

According to Staff Scientist Carol Bult, integrating genomic and genetic approaches to understanding key biological processes is a unique aspect of research at The Jackson Laboratory. "My group collaborates with the laboratory of Dr. Tim O'Brien to combine computational and wet bench research methodologies to understanding the regulation of genes that are key to early mammalian development," Dr. Bult explained. "Tim and I are leveraging the availability of the mouse and human genome sequences and using comparative sequence approaches to identify potential regulatory elements in the mouse genome." Dr. Bult said recent results suggest they are converging on a computational method that can be used to identify sequences that regulate genes involved in specific developmental processes they want to study.

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Philanthropy

Fiscal Year 2002-2003

FROM THE CHAIR OF THE BOARD OF GOVERNING TRUSTEES

In the past year, we reached two significant milestones in our philanthropic efforts.

First, our annual support, on which we depend to fund the operating budget, surpassed our goal, despite a difficult economic climate. This in itself is a significant philanthropic achievement.

Second, I am pleased to report that the private or "silent" phase of our new capital campaign—the Campaign for Discovery—has been a resounding success. With the support of 100 percent of the Board of Governing Trustees, and approaching 100 percent of the Corporation, we have received commitments for more than $46 million toward our $85 million goal. We have received heart-warming gifts, both large and small. Many stretched to make substantial gifts so that the Campaign would be a success.

The purpose of the Campaign is to fund construction of a new state-of-the-art research building and associated infrastructure, including additional space for research animals, special projects, and endowment. These elements are critical if we are to remain a vigorous, world-class institution making fundamental contributions to the diagnosis, treatment, and prevention of genetic diseases. We have now launched the "public" phase of the Campaign, in which we will seek new sources of support outside our immediate family of friends. This new support is essential to the success of the Campaign, and to our ability to bring the Laboratory's full capabilities to bear on the biomedical questions of importance to people everywhere.

What is incredible is that the goal of conquering genetic disease—the dream of many past generations—appears finally to be within our grasp. In the foreseeable future, researchers will discover therapies and will likely be able to prevent many of the dreaded diseases of our time: cancer, heart disease, diabetes, and neurological afflictions.

In this great, worldwide endeavor, The Jackson Laboratory will play a unique and critical role. I do not use those words lightly. Nowhere else in the world is there such a confluence of knowledge, resources, expertise, and scientific talent built around the mouse and mouse genomics. Our own research is world-class. And through our mouse resources—we ship millions of animals each year to thousands of labs near and far—we empower the world's researchers in virtually every state and in virtually every country in which cutting-edge research is under way. As the mouse is the world's best hope for genetic research, we provide hope to the world.

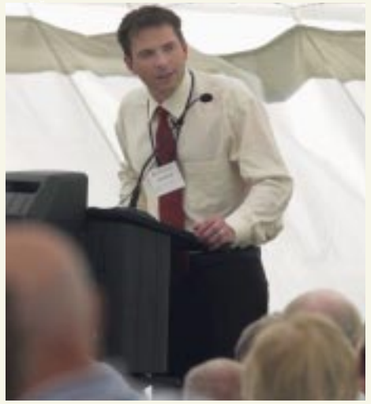
We are grateful beyond words for the support of our donors, whose names are listed in the pages throughout the report. To those who have yet to participate, we extend a warm invitation to join us on our voyage of discovery.

Donald Stern

Donald A. Stern, Esq.

"Today virtually no advance occurs in disease research without the use of The Jackson Laboratory's managed resources…"

JAMES ALLEN HEYWOOD: THE CASE FOR EXPANSION—NEW PARTNERSHIPS AND NEW CURES



James Allen Heywood, d'Arbeloff founding director of the ALS Therapy Development Foundation (ALS-TDF), Cambridge, Mass., presented the keynote address at the luncheon formally launching the new capital campaign of The Jackson Laboratory. The effort—Campaign for Discovery—will greatly enhance the research capacity at the Laboratory. The following are excerpts of the speech during which Mr. Heywood explained to luncheon guests why he is a partner with The Jackson Laboratory, and made the case for supporting the expansion plan.

Six years ago, my brother was an architect and builder. Today, my brother, Stephen, would physically remind you of Stephen Hawking, the famous physicist who also has amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease). Both use a computer to talk and drive a wheelchair with buttons mounted on the headrest. My brother is 34 years old and unable to feed or care for himself.

Why haven't we cured this disease?

The current amount of spending is totally inadequate to the task. Biological and disease research provides the greatest opportunity to improve the human condition. Perhaps more importantly, I believe such research is also the most effective way to maintain international leadership both economically and morally. What a beautiful thing it would be for cures for the world's diseases to be the United States' chief export. Better human health generates more stable governments and supports democracy. There is a great future possible if we invest wisely to build that future. So let's spend more.

But first, let's spend better.

At ALS-TDF we do one experiment and we do it on an assembly line. We simply test drugs in the mouse model of ALS to see which drugs make the mice live longer. Our drug discovery program provides a sense of what is possible when one focuses on a single problem and then runs a scaled program to address it. Over the last 10 years, all ALS scientists have only published 40 drug studies in mice. In the last two years, we have completed more than 90. My brother and other patients are now taking a drug discovered in our lab using this process, and two of our drugs are now entering trial at the University of California, San Francisco. The work we do is not inventive or new.

In the words of our external research vice president, "We just do the obvious at high speed."

It all comes down to focusing on the question of what has the best chance of making a difference in Stephen's life and the lives of other ALS patients, and then building a scaled program to implement it. I do not know if these drugs will extend my brother's life, but I do know that they make mice live longer and that's the best chance he has.

Which brings me back to The Jackson Laboratory.

How is it that a small organization like ALS-TDF that spends $3 million a year on research can so cost-effectively test new drugs? We do it by partnering with an institution that shares our values: strategic focus, knowledge management, and large-scale science.

I believe the significant future advances and successes in science will come from institutions that apply these approaches. Think about the vision that The Jackson Laboratory displayed in recognizing how valuable a resource it would be to provide the world with a repository of mouse models and information. It did not just remain a vision—you built it.

Where does a researcher turn to evaluate a disease in a mouse model? Or to find comprehensive knowledge about that model? What if a scientist needs to generate hundreds of new models for human disease in a single center and then actually scale a program to cost-effectively deliver them? The Jackson Laboratory makes this all possible. It took strategic vision to recognize that these would be critical things for the advancement of science and disease research.

Today virtually no advance occurs in disease research without the use of The Jackson Laboratory's managed resources—though rarely do you get the credit you deserve. I will give you that credit. ALS-TDF would not be where we are today without The Jackson Laboratory.

I have a vision for a future where strategic plans to improve human health are built and implemented. Where we mine the vast scientific knowledge we have compiled and build large-scale programs to deliver tangible improvements in human health. I believe that The Jackson Laboratory and organizations like ALS-TDF are a key part of that future.

I believe that The Jackson Laboratory is uniquely positioned to be a large part of a new way of approaching science. Let's take the expertise you have and apply it to the vast therapy development gap we are attempting to fill at ALS-TDF. As partners, we can help transform the orchard of scientific ideas into concrete opportunities to improve human health and eradicate disease.

I also have a challenge for all [who can become partners in discovery]. Help The Jackson Laboratory fund it. Creating the strategy, building the knowledge-management processes, and then starting these large-scale projects will be expensive. It will require significant philanthropic resources. The government will follow. The foundations will follow. You must help Jackson and ALS-TDF lead.

THERE IS GREAT OPPORTUNITY HERE TO DO HUMAN GOOD. LET'S START NOW.

Spinal muscular atrophy (SMA) is the number-one genetic killer of children under the age of two. One in every 40 people carries the gene that causes SMA; any child of two carriers has a one in four chance of developing the disease. Associate Staff Scientist Gregory Cox investigates a very rare form of SMA called SMARD1 (spinal muscular atrophy with respiratory distress type 1). Researchers in Germany recently discovered the human gene that causes SMARD1 by studying six unrelated families affected by the disease. "I had already cloned a genetic mutation called neuromuscular degeneration *(nmd)* in mice," Dr. Cox explained. "The German scientists were able to pinpoint the human gene very quickly when they heard about the mouse gene we'd found, by comparing our mouse's gene to genes in the families they were studying. Essentially, it's the same gene in mice and humans that causes SMARD1. In fact, our *nmd* mice develop the same motor neuron disease as children with SMARD1, so analysis of these mice may provide information directly relevant to the human disease."

The Year in Review

FOLLOWING IS A SUMMARY OF NEWSMAKING EVENTS AT THE JACKSON LABORATORY

Scientific News

The international scientific journal *Nature* released a landmark paper on a new draft sequence of the mouse genome and its implications for understanding the human genome. Jackson Laboratory Senior Staff Scientist Wayne Frankel and Staff Scientist Carol Bult were among the more than 200 scientists credited on the *Nature* mouse genome paper.

The results of Staff Scientist Susan Ackerman's team's work, published in *Nature,* provide a genetic model of neurodegeneration mediated by oxidative stress. The harlequin mouse provides the first model for studying the role of oxidative stress on aberrant cell cycle reentry and subsequent death of neurons.

To date, amyotrophic lateral sclerosis is the one neurodegenerative disorder known to be caused by oxidative damage to neurons. However, oxidative stress has been identified as a possible cause of several later-onset neurodegenerative diseases, and there are also indications that the diseased neurons of Alzheimer's patients duplicate their DNA.

While studying mice with a mutant gene whose counterpart causes inherited glaucoma in humans, Jackson Laboratory researchers, led by Staff Scientist Simon W.M. John, associate investigator of the Howard Hughes Medical Institute, have discovered a second gene mutation that worsens the structural eye defect that causes this type of glaucoma. The newly discovered gene mutation affects production of L-DOPA. The researchers suggest that it might be feasible to prevent glaucoma by administering L-DOPA, which is used in treating Parkinson's disease.

Scientists at The Jackson Laboratory, in conjunction with collaborators at the Albert Einstein College of Medicine, discovered a way to protect insulin producing cells from the immune responses that cause type 1 diabetes. In the May issue of *Diabetes,* the team led by Staff Scientist David Serreze reported that diabetes development is inhibited in non-obese diabetic mice that have been genetically engineered to express adenovirus-derived immunological shielding proteins in insulin producing cells of the pancreas.

Originally identified in human adenoid tissue as a cause of respiratory diseases, adenoviruses make several proteins that thwart the immune process from destroying them, without diminishing the system's ability to fight other invaders.

The researchers' findings might ultimately lead to a way that would protect engrafted pancreatic beta cells from being destroyed by the immunological processes that cause type 1 diabetes, and thus allow them to reverse disease without putting patients on immunosuppressive drugs.

Biology of Reproduction, a leading journal in the field of reproductive sciences, has named Jackson Laboratory Senior Staff Scientist John J. Eppig as Editor in Chief, and Adjunct Senior Staff Scientist Mary Ann Handel as Assistant Editor in Chief.

Summer Student Charles Kircher of Biddeford, Maine, was one of 11 high school students from New England in the regional finals of the Siemens Westinghouse Competition in Math, Science and Technology, held at the Massachusetts Institute of Technology (MIT) on Nov. 8-9, 2002.

Staff Scientists Jürgen Naggert and Patsy Nishina maintain partnerships with numerous families affected by the diseases they study. By testing affected individuals and family members across generations, the scientists can narrow the search for disease-causing genes. "In the case of Alström syndrome," Dr. Nishina said, "we started out working with French-Acadian families, and now we are in contact with families of many ethnicities throughout the world. They are true collaborators," she stressed. "And our Senior Professional Assistant Jan Marshall started a nonprofit support foundation that arose from these studies—an international community of families whose loved ones have Alström syndrome."

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† *Deceased*

Mark Kandutsch, M.D., has a nearly lifelong connection to The Jackson Laboratory. He is the Laboratory's consulting physician. His father is on the Emeritus staff. On a fall afternoon in Bar Harbor, Mark and Lauri Braley-Kandutsch share the changing color of the leaves with their son, Gabriel.

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Financial

The Jackson Laboratory was awarded a $539,779 science education grant by the Howard Hughes Medical Institute. The three-year grant will fund research internships for high school students and for student teachers-in-training enrolled in the University of Maine's new Master of Science in Teaching program.

The National Science Foundation has awarded a $6 million grant to the University of Maine, The Jackson Laboratory, and Maine Medical Center Research Institute to establish the Institute for Molecular Biophysics. The funds will be used to establish a research partnership among the three institutions and conduct interdisciplinary work leading to better treatment of genetic diseases.

A $2.6 million grant from the National Science Foundation will support a new Genomics Ph.D. program at the University of Maine, The Jackson Laboratory, and Maine Medical Center Research Institute.

As of July 1, 2003, research and training grants awarded to The Jackson Laboratory total more than $60 million, up $4 million from a year earlier.

Bond Issue

In June 2003, the voters of the state of Maine approved a $70 million dollar bond with $20 million going to the Maine Biomedical Research Coalition. Of that, The Jackson Laboratory will garner approximately $14 million.

Partnerships and Awards

Collaboration between The Jackson Laboratory and VisualSonics will leverage the use of high-resolution imaging to enhance development of small animal phenotyping.

Australian-born Senior Staff Scientist Emeritus Wesley Kingston Whitten, B.V.S.c., D.Sc., was named as a recipient of the Centenary Medal for his service to science. This most prestigious award is given to those who have contributed to the betterment of Australian society during the first 100 years of federation, and to those who continue to extend their contribution into the next century.

Maine Governor John E. Baldacci presented The Jackson Laboratory with one of six 2003 Governor's Awards for demonstrating a consistently high level of commitment to its community, employees, and manufacturing or service excellence.

As part of his studies in neurodevelopment, research partnerships in The Jackson Laboratory community have proven most rewarding for Associate Staff Scientist Robert Burgess. "Since arriving at Jackson two years ago I have been actively involved in two internal collaborations," Dr. Burgess said. The first, with Associate Staff Scientist Timothy O'Brien, examined the mammalian ortholog of a gene that affects nerve terminal morphology in *C. elegans* and drosophila. "This study has resulted in a paper that is now accepted for publication in *Molecular and Cellular Biology*," explained Dr. Burgess. The second collaboration, with Staff Scientist Susan Ackerman, examined the role of the RCM gene in motor axon pathfinding, and led to the discovery of a novel gene that may direct this process. "We are nearing submission of the results obtained with Sue, and my lab is now pursuing the new gene in a project that received funding from the Edward Mallinckrodt, Jr. Foundation."

Financial Summary

Revenues & Expenses *(in millions)*	FY2003	FY2002	FY2001	FY2000
Revenue—Operating				
Public Support, including program grants & contracts	$57.8	50.2	37.7	32.6
JAX Research Systems	$55.6	46.3	39.2	34.2
Contributions & Bequests—Operating*	$1.1	4.3	3.7	1.6
Other	$4.0	3.0	1.4	1.0
SUBTOTAL, OPERATING REVENUE	*$118.5*	*103.8*	*82.0*	*69.4*
Revenue—Non-Operating				
Construction Grants	$6.2	5.2	1.8	1.7
Contributions & Bequests—Capital*	$3.9	2.1	0.9	3.7
Endowment & Investment**	$(1.3)	(1.1)	(0.6)	13.6
Other	$(6.2)			
SUBTOTAL, NON-OPERATING REVENUE	*$2.6*	*6.2*	*2.1*	*19.0*
TOTAL REVENUE	*$121.1*	*110.0*	*84.1*	*88.4*
Expenses				
Research Program	$63.7	54.0	43.2	36.6
Training Program	$1.9	1.4	1.7	1.3
JAX Research Systems	$51.1	44.7	36.8	30.5
Development***	$0.4	1.0	1.0	0.7
Public Information	$0.7	0.7	0.5	0.4
SUBTOTAL, EXPENSES	*$117.8*	*101.8*	*83.2*	*69.5*
Changes in Reserves				
Operating Reserve	$0.7	2.0	0.9	1.9
Realized & Unrealized Gains	$0.3	(1.1)	(2.5)	12.0
Endowment & Plant	$1.6	7.3	2.5	5.0
SUBTOTAL, CHANGES IN RESERVES	*$2.6*	*8.2*	*0.9*	*18.9*
TOTAL EXPENSES & CHANGES IN RESERVES	*$120.4*	*110.0*	*84.1*	*88.4*

Assets & Fund Balances	FY2003	FY2002	FY2001	FY2000
Assets				
Land, Buildings & Equipment (Net)	$125.3	108.7	97.6	89.9
Bond Assets Held by Trustee	$15.7	4.7	7.0	8.3
Other Assets	$45.5	30.9	24.4	25.5
Endowment Fund	$50.3	49.4	50.4	52.8
Contributions Receivable	$3.7	1.3	0.8	1.3
TOTAL ASSETS	*$240.5*	*195.0*	*180.2*	*177.8*
Liabilities & Fund Balances				
Unrestricted	$114.1	115.5	110.1	110.7
Temporarily Restricted	$18.3	15.1	12.4	11.4
Permanently Restricted	$6.7	6.0	5.9	5.9
Current Liabilities	$30.7	23.4	16.7	15.5
Long-Term Bond Payable	$70.7	35.0	35.1	34.3
TOTAL LIABILITIES & FUND BALANCES	*$240.5*	*195.0*	*180.2*	*177.8*

**Contributions and bequests identified here pertain only to revenue received (cash and pledge payments) during each fiscal year.*
***Attributable to realized and unrealized gains and losses on investments as of May 31.*
****Development costs total less than 1 percent of the annual operating budget.*

Funding

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Public Support

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Department of Energy
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National Aeronautics and Space Administration
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National Center for Research Resources
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National Heart, Lung, and Blood Institute
National Human Genome Research Institute
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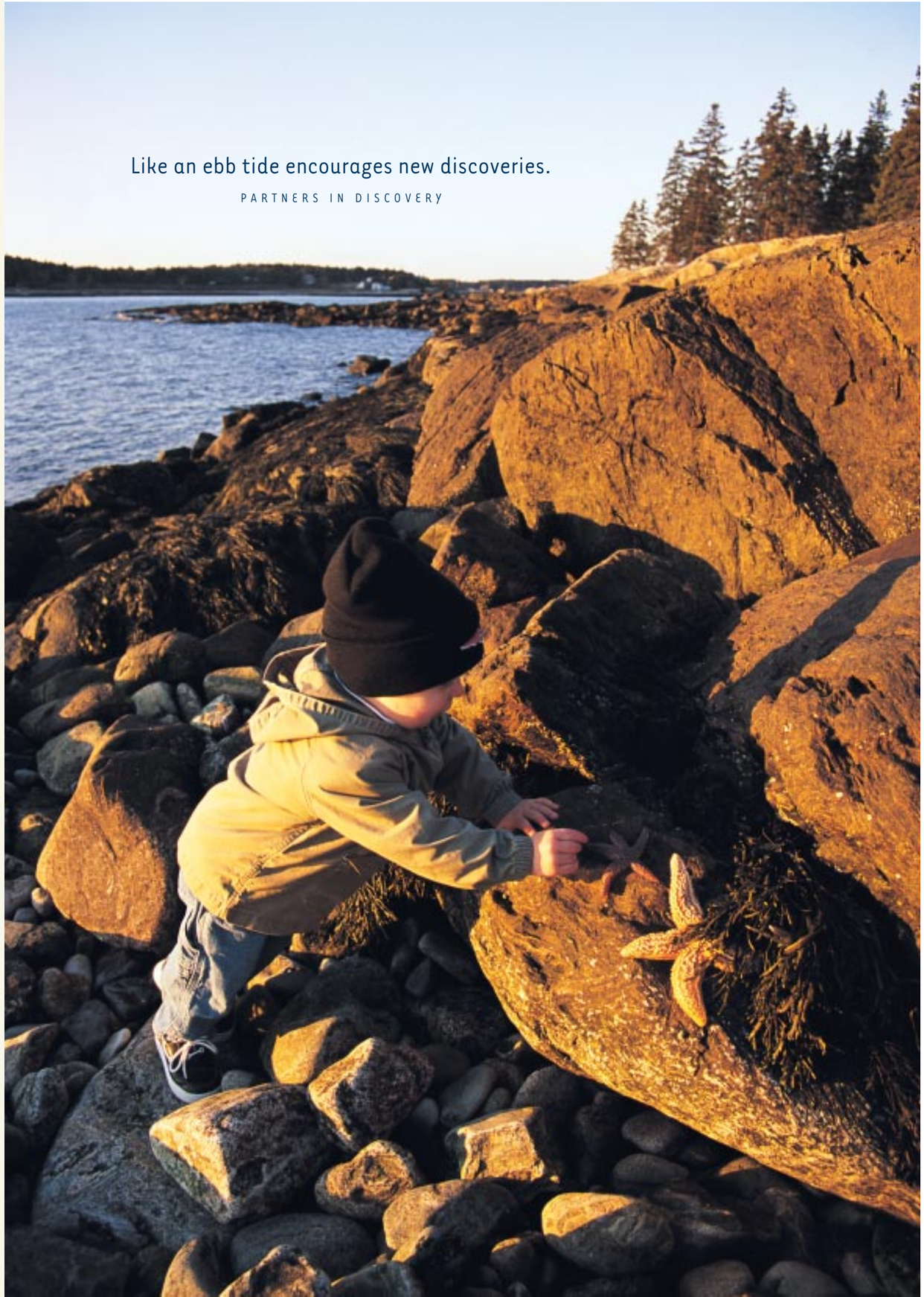
NHLBI Program for Genomic Applications



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