



2005 Annual Report



New Horizons on the Research Landscape

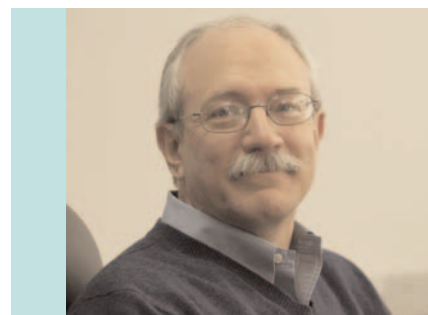
From the Director: *What's on the horizon*

In 2004, the National Institutes of Health completed the Congressionally mandated doubling of its budget. But in 2005, NIH funding was flat, and this is a trend we expect to see for the coming years. Accordingly, the Laboratory is both actively seeking new funding sources and engaging in new research efforts in order to continue our growth and success.

As the NIH places an increasing emphasis on translational research—that is, bringing discoveries from the bench to the bedside—several Laboratory investigators are working directly with drug companies to expedite development of new treatments. Pharmaceutical and biotech companies have a growing need for JAX® Mice & Services. Also, the Laboratory has launched a couple of innovative partnerships with clinical organizations over the past year. The first of these is with Eastern Maine Healthcare Systems and the University of Maine to deliver new and better treatments for cancer and other chronic diseases. The second involves a collaboration with the School of Medicine at the University of Vermont.

Federal and private research funding sources are also increasingly focused on multidisciplinary and collaborative efforts, and here too the Laboratory has made much progress over the past several years. The groundbreaking Institute for Molecular Biophysics brings together the University of Maine, The Jackson Laboratory, the Maine Medical Center Research Institute and the University of Heidelberg. This year \$1.9 million in combined National Science Foundation and W.M. Keck Foundation funding brought the world's most powerful light microscope to the Laboratory—the only 4Pi confocal laser scanning microscope in the Americas—along with other instrumentation and programs.

The governor and legislature of the state of Maine, in light of The Jackson Laboratory's growth trajectory and success in securing outside funding, have continued to push for state funding for biomedical research. In November 2005, voters approved Governor John Baldacci's \$20 million economic development bond package, of which The Jackson Laboratory's share—about \$5 million—will go toward building the Laboratory's information technology infrastructure.



Every American research institution today faces challenges. Yet after working with our Board of Scientific Overseers, Board of Governing Trustees and Corporation over the past year on a stringent analysis of our operations and development of a 5-year strategic plan, we believe that The Jackson Laboratory is well positioned to succeed in the future: free from the constraints of academic institutions or for-profit ventures; endowed with a dynamic, collaborative research staff focused on tomorrow's medicine; and providing vital research resources to the worldwide biomedical research community.

A handwritten signature in blue ink that reads "R. Woychik".

Richard P. Woychik, Ph.D.

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Conquering the challenges of translation



Since the human and mouse genomes were sequenced a few years ago, researchers have been able to use the mouse genome as a kind of “translation dictionary” to find the genes that cause human diseases. Increasingly, this ability allows Jackson Laboratory researchers to turn discoveries in basic research into potential new treatments—a process known as translational research.

New strategies to block leukemias

Shaoguang Li, M.D., Ph.D.

When Dr. Shaoguang Li completed medical school in Shenyang, China, in 1983, he came to a painful conclusion. “My cancer patients, including young children, were suffering, and I did not have enough ways to help them,” said the soft-spoken scientist. Dr. Li decided that the only way to make a real difference in his patients’ lives was to conduct research in the genetics of cancer.

In an unusual switch from bedside to bench, Dr. Li did his Ph.D. studies in Immunology and Oncology (at the Chinese Academy of Medical Sciences, Beijing), and in Cell and Molecular Biology (at Tulane University in New Orleans), had postdoctoral training at the Harvard Medical School Center for Blood Research, and came to The Jackson Laboratory in 2001 as an associate staff scientist.

Since Dr. Li’s arrival in Bar Harbor, his lab has made several major breakthroughs in approaches to treating chronic myelogenous leukemia (CML) and B-cell acute lymphoblastic leukemia (B-ALL, the type of leukemia that predominantly strikes children). Both cancers belong to the most common group of blood malignancies known as Philadelphia chromosome-positive leukemias.

In CML and B-ALL, enzymes that should regulate the growth and development of white blood cells go awry, resulting in uncontrolled growth of the cells, which in turn can accumulate in organs and cause damage. In 2001, the Swiss-based pharmaceutical company Novartis developed Gleevec, a drug in a new class known as small-molecule kinase inhibitors that fight cancer by blocking an errant enzyme. It proved effective against one phase of CML, but not the advanced phase or against B-ALL. In some patients, it seems CML can develop a resistance to Gleevec.

Dr. Li and his team developed an accurate mouse model of this category of Philadelphia chromosome-positive leukemias and, in research published in the journal *Nature Genetics*, announced success with blocking a different group of kinases used by cancer than the kinase addressed by Gleevec. Major support for these groundbreaking studies has been provided by the Linda Tallen and David Paul Kane Educational and Research Foundation. The researchers discovered that the errant gene activates three additional enzymes that lead to B-ALL leukemia. One of these enzymes may also be involved when CML patients no longer respond to Gleevec.

“When combined with Gleevec, this other kinase inhibitor may provide more effective treatment in later phases of CML,” said Dr. Li. “So we really need to find a combined drug therapy.” The Li lab is already working with pharmaceutical companies to bring the new discoveries to patients, demonstrating the power of translational research.



The Li lab is working with pharmaceutical companies to bring new discoveries to patients. This progress demonstrates the power of translational research.

The Li lab is now developing additional mouse models representing all the members of the Philadelphia chromosome-positive leukemias, in an effort to make available a range of targeted therapies for this category of cancer. *“The more options doctors have to help their cancer patients, the better,” Dr. Li said with a smile.*

The “humanized” mouse vs. disease

Leonard D. Shultz, Ph.D.

What if new treatments for blood diseases or AIDS could be thoroughly tested for safety and effectiveness without putting individuals at risk? A mouse model with immune reactions that closely mimic those of humans may soon achieve this bold goal.

The mouse with a “humanized” immune system is the work of Senior Staff Scientist Leonard Shultz, together with collaborators at St. Jude Children’s Research Hospital and the University of Tennessee, both in Memphis, the EMD Lexigen Research Center, Billerica, Mass., and the University of Massachusetts, Worcester.

To develop the mouse model, Dr. Shultz explained, the researchers started with mice born with virtually no immune system. “Most people have heard of the ‘boy-in-a-bubble’ syndrome,” he noted, “in which a baby is born with a very impaired immune system and is therefore highly vulnerable to infections. There are actually close to 100 of these inherited primary immune deficiency diseases in humans, and several mouse strains model these diseases.” Dr. Shultz and his collaborators started out by crossing mice with several of these hereditary immune deficiencies to arrive at a strain whose mouse-immunity is virtually canceled out.

The next and most extraordinary step essentially gives the mouse a human immune system. Hematopoietic stem cells (HSCs) are produced in the bone marrow and are the origin of all red and white blood cells and various parts of the immune system. The researchers successfully introduced human HSCs into the mouse, which then mounts an immune response like the human donor’s, not its mouse ancestors.

With the dizzying name of NOD.Cg-Prkdcscid Il2rgtm1Wjl/Sz, the new mouse will be a valuable tool for studying how stem cells give rise to the various parts of the immune system, including T lymphocytes; how immune cells kill cancer cells and fight infections; and how immune cells respond to radiation and chemotherapy, which are two major treatments for many cancers, the researchers said. It will also enable the study of the HIV (AIDS) virus in a model that mimics the human immune system better than any previously constructed.

“One reason The Jackson Laboratory is unique,” Dr. Shultz commented, “is our ability to develop new mouse models and send them out into the research world where they can make a difference in human health. I get every bit as much satisfaction from another investigator’s success, if he or she has used a mouse I helped to develop, as from my own lab’s discoveries.”



Above: The “humanized” mouse model in the hands of Dr. Leonard Shultz.

A bone health revolution

Clifford Rosen, M.D.

“This is really exciting,” said Dr. Clifford Rosen, with his customary enthusiasm. “We found an almost 30 percent increase in bone density with sequential use of the drugs.”

Dr. Rosen is a senior staff scientist at The Jackson Laboratory and director of the Maine Center for Osteoporosis Research and Education at St. Joseph Hospital in Bangor. In 2005 he and his colleagues published their findings in the *New England Journal of Medicine*: In clinical trials, two well-known treatments for osteoporosis are much more effective when patients receive them sequentially.

In the trials, postmenopausal women in Bangor, New York, Philadelphia and Minneapolis who took a bone-building drug (parathyroid hormone or PTH) for one year, followed by a year on a standard drug that fights bone loss (alendronate), experienced greater increases in bone density than has been reported from any other drug regimen. Bone density is the standard predictor of fracture risk associated with osteoporosis.

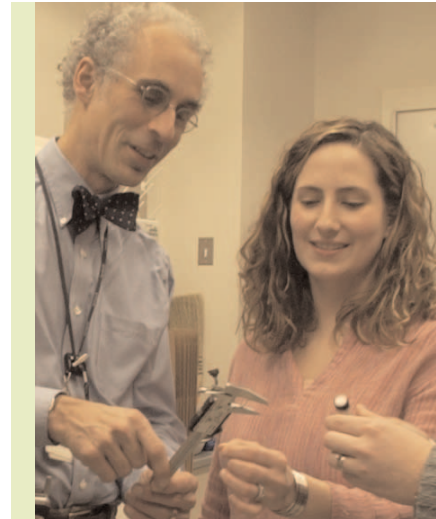
“We’re looking at ways to maximally optimize our use of osteoporosis drugs,” he continued. “PTH is a very powerful drug and it works, but it has to be given in the right way. If you give patients PTH only for a year and don’t follow up with any other treatment, they’re going to lose a lot of the bone mass they gained in that first year. And since it’s a very expensive treatment—some \$7,800 a year—it’s really critical to follow it up with another form of therapy that will continue to consolidate the bone mass gains.”

In 2003, Dr. Rosen and colleagues published research findings that administering both PTH and alendronate simultaneously does not increase bone density.

According to Dr. Rosen, the clinical trials both demonstrate the value of translational research and show that the ideal of individualized medicine—based on each individual’s own genetic makeup—is becoming reality. “Our clinical research with PTH began with animal studies more than 10 years ago with Dr. Wesley Beamer at The Jackson Laboratory and colleagues at other institutions,” he said, “looking at the role of PTH in building bone in mice and rats. We have found that some mouse strains respond spectacularly to PTH, building lots of bone mass, and some don’t. And lo and behold, among the women in our recent study, some experienced a huge increase in bone density—100 percent or more—while others had no response.”

The new research suggests the potential for identifying in advance those patients most likely to benefit from PTH treatment. “It would save a lot of money, and a lot of patient inconvenience,” Dr. Rosen noted.

“This is the first thinking in the bone field about tailoring pharmacology to patients’ genetic makeup, and it’s very promising.”



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Above: Dr. Clifford Rosen and Research Assistant Lindsay Horton taking a mouse bone measurement.

2005 Research Highlights

EPILEPSY **Absence epilepsy findings:** In her studies of absence epilepsy—a generalized form of epilepsy most commonly diagnosed in children and characterized by brief losses of consciousness—RESEARCH SCIENTIST VERITY LETTS and colleagues at The Jackson Laboratory discovered that a complex balance of closely associated proteins expressed in the brain work together to suppress seizures. Dr. Letts’ findings, in collaboration with SENIOR STAFF SCIENTIST WAYNE FRANKEL, were published in the January 25, 2005, issue of the *Proceedings of the National Academy of Sciences*.

ASTHMA **Multiple genes involved in asthma:** New findings on genetic components of asthma were reported in January 2005 by a research team based at Brigham and Women’s Hospital and Harvard Medical School, and included Jackson Laboratory SENIOR STAFF SCIENTIST GARY CHURCHILL. The research team found that wheezing—a key physiological component of asthma—requires the interaction of genes in several locations. The work, involving multiple independent verifications, demonstrated the complexity of the genetic predisposition to asthma.

GLAUCOMA **Study of glaucoma turns up possible new treatment for neurodegenerative diseases:** In a discovery that could point to new treatments for a wide range of neurodegenerative diseases, SENIOR STAFF SCIENTIST SIMON JOHN and researchers in his laboratory have found that high-dose radiation and bone marrow transfer treatments on glaucoma-susceptible mice completely blocked the development of glaucoma, by preventing neurodegeneration. The research paper, published in March 2005 in the *Proceedings of the National Academy of Sciences*, is the first to suggest that high-dose radiation together with bone marrow transfer—treatments in use today for human patients with leukemia and other cancers—could potentially treat other neurodegenerative diseases such as Alzheimer’s disease and Parkinson’s disease, though Dr. John cautions that extensive research would be required to advance this idea.



From left: Research Scientist Verity Letts; Senior Staff Scientist Gary Churchill; Senior Staff Scientist Wayne Frankel; Senior Staff Scientist and Howard Hughes Medical Institute Investigator Simon W.M. John.

HEART DISEASE **Mouse gene turned on by fatty food linked to human heart-disease gene:** There is more evidence linking a high-fat diet to heart disease: An international research team has identified a gene in mice that interacts with environmental factors such as diet to influence atherosclerosis susceptibility. As reported in *Nature Genetics* in March 2005, the team, based in SENIOR STAFF SCIENTIST BEVERLY PAIGEN’S lab and jointly led by RESEARCH SCIENTIST XIAOSONG WANG of The Jackson Laboratory and Dr. Jacob Lagercranz of Sweden’s Karolinska Institute, found that *Ox40l* is a gene that makes C57BL/6J mice susceptible to high-fat-diet-induced atherosclerosis. “Thirty percent of the

calories in our mouse diet were fat-based—the American Heart Association’s recommended limit,” explained Dr. Wang. “Unfortunately, the average American’s fat calorie intake exceeds this limit.”

**CEREBRAL
HEMORRHAGE &
PORENCEPHALY**

Genetic defect linked to cerebral hemorrhage and porencephaly:

An international team led by DR. DOUGLAS GOULD, a postdoctoral fellow at The Jackson Laboratory, and Jackson Laboratory SENIOR STAFF SCIENTIST SIMON W.M. JOHN, discovered a genetic defect that weakens blood vessels in the brain, making an infant much more vulnerable to hemorrhaging. Their research, published in the May 19, 2005, issue of the journal *Science*, may have significant implications for preventing the disease in humans.

TYPE 1 DIABETES

Possible target to prevent type 1 diabetes found:

A multi-institution team including SENIOR STAFF SCIENTIST LEONARD SHULTZ identified an enzyme that appears to be necessary for the development of type 1 diabetes. This discovery could lead to development of a pharmaceutical that prevents the destruction of the islet cells that produce insulin. The research was conducted using mice bred by The Jackson Laboratory specifically as models of human diabetes.

ALS

Early motor changes in ALS mice pave way for testing candidate drugs:

Mice that recreate the symptoms of ALS (amyotrophic lateral sclerosis, also known as Lou Gehrig’s disease) in the laboratory display an early, subtle change in their walking gait that should help investigators find new treatments for ALS. In a report published online in the journal *Muscle & Nerve*, Jackson Laboratory researchers including ASSOCIATE STAFF SCIENTIST GREGORY COX AND RESEARCH SCIENTIST KEVIN SEBURN, funded by The ALS Association, demonstrate that treadmill performance falters long before overt symptoms appear, in mice that have symptoms similar to ALS. The early and subtle loss of motor function should help scientists to target crucial aspects of ALS much sooner in the disease process using mice that model the disease.



From left: Associate Staff Scientist Robert Burgess leading a talk; Staff Scientist Carol Bult; Associate Staff Scientist Gregory Cox; Vice President and Chief Operating Officer Chuck Hewett with Research Scientist Kevin Seburn.

DEVELOPMENT

Non-coding RNA has major role in controlling development:

An international consortium of genome research institutes and investigators, including Jackson Laboratory STAFF SCIENTISTS CAROL J. BULT AND MARTIN RINGWALD, has reported significant new breakthroughs in understanding how the genes in mammals are controlled. According to Dr. Bult, “The studies provide unprecedented insights into both the dynamic nature of the genome and the importance of genome organization on its function. The data will serve as a basis for discovery for many years.”

The new explorers



In 2005: The Jackson Laboratory recruited three new investigators as part of a major research expansion effort; young members of the scientific staff made headlines; and extraordinary new research and education collaborations started changing “how science gets done” in Maine.

New directions, new investigators

Kevin Mills came to The Jackson Laboratory in January 2005, fresh from a postdoctoral stint at Harvard Medical School. Kyuson Yun arrived from Dartmouth a little less than a year later and is just launching her research program. (A third associate staff scientist, Dr. Zhong-wei Zhang, has agreed to join the Laboratory and will move his laboratory to Bar Harbor in mid-2006.) These talented young researchers may be just beginning their work as principal investigators, but already their achievements and interests help demonstrate the outstanding resources available at the Laboratory and the potential for leveraging future discoveries.

Kevin Mills, Ph.D.

Initially, Dr. Mills' research focused on serious injuries to the genetic material, known as DNA double-strand breaks, and on the intricate mechanisms that cells possess to fix them. When those repair mechanisms fail, the affected cell could be transformed into a cancer cell. What Dr. Mills could not have predicted were the new directions his work with mouse models of DNA repair malfunctions would quickly take, thanks to two cutting-edge tools at The Jackson Laboratory.

Dr. Mills is among the first researchers in the world to see chromosomes through the new 4Pi microscope, which provides the world's highest resolution light microscopy images. For the first time, it's possible to see, in three dimensions and fine detail, the architecture of the cell nucleus, where chromosomes reside. Ultimately Dr. Mills expects to use the 4Pi to learn how chromosome surfaces interact and how their physical structure may contribute to genetic instability in tumor models.

In another approach, Dr. Mills is using microarray techniques developed and used at the Laboratory to compare gene expression between normal cells and tumor cells. Using a mouse model that is deficient in DNA double-strand break repair, Mills has found significant overexpression of a gene in B-cell lymphoma cells, a discovery that may ultimately have implications for B-cell lymphoma treatment in humans.

Mills still hopes to pursue basic research into DNA double-strand break repair mechanisms, but he recognizes that the new discoveries may change his priorities for a while. Pulling out a chart showing the overexpression data, he lists experiment after experiment that he wants to do to expand upon it and characterize the effects of the protein.

"You can grind away for a long time without much happening, then in one day your career might change on a dime," he said. "There could be years of work"—he pointed to a wavy line showing the overexpression of the gene—"based on that one finding."



Dr. Kevin Mills cites “the mouse resources, the community of mouse researchers and the thriving expertise, together with unique technological resources” as the reasons he came to The Jackson Laboratory.

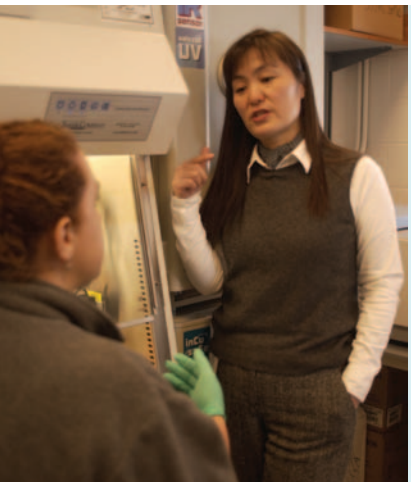
Kyuson Yun, Ph.D.

Dr. Yun's research focus has been neural stem cells and neurodevelopment. She is particularly interested in the role of transcription factors—proteins that regulate gene expression—in generating and maintaining neural stem cells. But at the Laboratory she also plans to work with a different kind of stem cell: tumor stem cells. First isolated only a few years ago, recent research suggests that they play a critical role in developing and maintaining tumors.

Having already isolated tumor stem cells from a mouse model of brain tumors, Dr. Yun will use the resources available to her at the Laboratory to characterize them at cellular and molecular levels. She will also use a genetically manipulated mouse model to test her hypothesis that destroying tumor stem cells is both necessary and sufficient to abolish existing tumors in animals.

Tumor stem cells represent a new frontier for research, and Dr. Yun's work at The Jackson Laboratory is full of promise, even if it leads her in directions quite different from those she envisions at the moment.

“The tumor stem cells are slow-dividing, and are therefore able to survive therapies that target the quickly dividing cancer cells,” she said. “If a small number of these surviving cells can initiate tumors, that may explain the recurrence of cancer when the tumor appears to have been eliminated by chemotherapy.”



Top: Associate Staff Scientist Kyuson Yun talking with Adrienne Buckley, a member of her new lab team.

Staff Scientist and newly appointed Howard Hughes Medical Institute Investigator Susan L. Ackerman.

Opening worlds of possibility

Susan L. Ackerman, Ph.D.

In March 2005, Jackson Laboratory Staff Scientist Susan L. Ackerman was named a Howard Hughes Medical Institute (HHMI) investigator, one of the top distinctions in American biomedical research.

Dr. Ackerman is one of 43 scientists selected, through a nationwide competition, from more than 300 exceptional nominees working at American universities, medical schools and institutes. The HHMI investigator program is designed to spur scientific discovery by funding the nation's most talented and innovative scientists. As one of two HHMI investigators at the Laboratory (the only two in Maine), she joins Dr. Simon W. M. John, a pioneer in the study of glaucoma.

Dr. Ackerman is exploiting the power of mouse genetics to provide a whole new view of the molecular and genetic mechanisms of neurodegeneration, such as that underlying Alzheimer's disease, Parkinson's disease and motor neuron disease.

“Every Jackson Laboratory principal investigator is here because he or she has a passion for exploring new avenues of research,” Dr. Ackerman said. “But we also need to spend a lot of time seeking funding from public and private sources. This support from the Howard Hughes Medical Institute really helps to free up our laboratory to focus on our research goals.”

Research and Education Collaborations in Maine

Maine is a big state with a small, mostly rural population and no large academic research institutions. But The Jackson Laboratory is working with the many centers of biomedical research and academic excellence spread across the state to create “virtual” research institutions that can compete successfully for public and private funding.



THE INSTITUTE FOR MOLECULAR BIOPHYSICS “is an interdisciplinary leap into the future,” said Dr. Barbara B. Knowles, Jackson Laboratory vice president for education, training and external scientific collaborations. The University of Maine program, based at the Laboratory and in collaboration with the Maine Medical Center Research Institute and the University of Heidelberg, was founded to bring together physicists, geneticists, engineers and others to some of today’s most challenging biological questions. The IMB is already a worldwide leader in microscopy: With the only 4Pi confocal laser scanning microscope in the U.S., IMB scientists are able to focus on living cells with higher magnification and resolution than ever before.

MAINE INSTITUTE FOR HUMAN GENETICS AND HEALTH: In his January 2005 “State of the State” address, Maine Governor John Baldacci announced a new public-private partnership aimed at translating breakthroughs in basic genetics research into treatments for the chronic diseases that most adversely impact Mainers, while strengthening the advanced biomedical research workforce in northern Maine. In collaboration with the University of Maine, the Institute, to be located in Brewer, will be a subsidiary of Eastern Maine Healthcare Systems. Scientists at the University of Maine and the Laboratory will channel promising new discoveries in mouse and model organism genetics to the new Institute.

GRADUATE SCHOOL OF BIOMEDICAL SCIENCES: In collaboration with The Jackson Laboratory and other nonprofit research institutes in the state, the University of Maine is launching a Graduate School of Biomedical Sciences to prepare Maine students for jobs of the future. The new program will offer a doctoral degree in biomedical sciences with concentrations in molecular and cellular biology, neuroscience, biomedical engineering and functional genomics.

More 2005 Highlights

- MICE & SERVICES** **JAX[®] Mice, citizen of the world:** During 2005, JAX[®] Mice & Services enabled more scientists than ever before to take advantage of the Laboratory's unique mouse models and innovative mouse-related research services. According to Jackson Laboratory VICE PRESIDENT AND CHIEF OPERATING OFFICER CHUCK HEWETT, "As a result of both expanding its reach and operating more productively than ever, JAX[®] Mice & Services supported more external research than ever before and contributed \$24.3 million in surplus to support the Laboratory's current and future activities."
- AGING** **A major boost for aging research:** With a normal life span of about two years, mice are in many ways the ideal model for aging research. Some of the longest-lived mice on record have come from Jackson Laboratory colonies developed by SENIOR STAFF SCIENTIST DAVID HARRISON, one of the nation's leading investigators in the genetics of aging and longevity. This year the Laboratory was awarded a new, five-year institutional grant from the National Institute on Aging totaling \$3.6 million, and designating the Laboratory as a Nathan Shock Center of Excellence in Basic Biology of Aging to support aging research nationwide. Principal investigators are DR. HARRISON AND SENIOR STAFF SCIENTIST BEVERLY PAIGEN, who studies a wide range of aging-related diseases such as heart disease, hypertension and gallstones.
- ENABLING** **Investment in Jackson resources:** Recognizing The Jackson Laboratory's leading role in developing the tools, technologies and skills to improve the efficiency of mouse-based research around the world, the Howard Hughes Medical Institute awarded the Laboratory \$1,960,000 for resource development work. The funds will support innovations in cryopreservation (freezing mouse embryos, sperm and other reproductive tissue), embryonic stem cell technology and mouse colony management.
- EDUCATION** **Training the next generation of scientists:** Funding for Jackson Laboratory education and training programs included support from the National Science Foundation for college students participating in the historic Summer Student Program; a National Cancer Institute grant supporting research experiences for undergraduate students; and a \$442,000 gift from the A.K. Watson Charitable Trust to support Jackson Laboratory postdoctoral fellows.
- COLLABORATION** **Jackson researcher heads new open-access journal:** In January 2005, the Public Library of Science (PLOS) in San Francisco announced the launch of *PLoS Genetics*, an international open access, peer-reviewed journal. Jackson Laboratory SENIOR STAFF SCIENTIST WAYNE FRANKEL was appointed editor-in-chief of the new journal, which began accepting submissions in January and commenced publication in July 2005. *PLoS Genetics* aims to address genetics and genomics research with a breadth that includes human studies as well as research on all model organisms. "Papers published in *PLoS Genetics* are chosen most importantly for their ability to drive the field forward," Dr. Frankel said.

BOND **Maine economic development bond approved:** In November 2005, Maine voters approved Governor John Baldacci's \$20 million economic development bond package, of which The Jackson Laboratory's share—about \$5 million—will go toward building the Laboratory's information technology infrastructure.

AWARDS **Jackson Laboratory Emeritus Scientist Douglas Coleman wins Gairdner Award:** In April 2005, Jackson Laboratory **SENIOR STAFF SCIENTIST EMERITUS DOUGLAS COLEMAN** learned he would be one of six scientists to receive the 2005 Gairdner Foundation Award. The prestigious awards, established by Toronto businessman James Gairdner, have been presented since 1959 to honor achievement in medical science. Canadian-born Dr. Coleman, a resident of Lamoine, Maine, was recognized "for contributions to our understanding of obesity and particularly for the discovery of the adipose (fat) tissue hormone, leptin." Other 2005 recipients include Dr. Jeffrey Friedman of Rockefeller University, whose discovery of leptin expanded upon Dr. Coleman's research. The awards, which carry a \$30,000 cash value, were formally presented at a ceremony in Toronto in October. Of the 273 Gairdner winners, 64 have subsequently won the Nobel Prize.

Jackson Laboratory employee video wins national award: A video created by and for **JACKSON LABORATORY EMPLOYEES**, celebrating the institution's 75th anniversary, has won the American Business Awards' Stevie Award in the category of Employee Relations/Recognition. Internal Laboratory Relations Director Joanne Harris and Foundations Officer Nessa Reifsnyder, the film's director and writer, were in New York to accept the award at a ceremony on June 6.

International Silver Fern Award to two Jackson researchers: Jackson Laboratory **SENIOR STAFF SCIENTISTS LEONARD D. SHULTZ AND JOHN P. SUNDBERG** were awarded the Silver Fern Award for their outstanding work in laboratory animal medicine, for developing mouse models for many human diseases. The award was presented at the 2005 meeting of the Australian & New Zealand Society for Laboratory Animal Science meeting in Fremantle, Western Australia.

Jackson Laboratory 2004 annual report named to international top 100: The 2005 AR100 Award Show, which recognizes the top 100 annual reports internationally, included The Jackson Laboratory's 2004 Annual Report. The report, designed by Ariel Creative of Rockport, Maine, celebrated the Laboratory's 75-year history. Each year the winning reports are reproduced in the AR100 Award Show Book. Some past winners include Samsung Group, Charles Schwab, Harley Davidson, Microsoft and the Progressive Corporation.

2005 Financial Summary

Revenue and Expenses	FY 2005	FY 2004
<i>(in millions)</i>		
Operating Revenue		
Public Sector	\$58.9	58.6
Private Sector	\$6.1	4.8
Resource Income	\$69.6	62.2
Other Revenue	\$2.6	2.4
SUBTOTAL, OPERATING REVENUE	\$137.2	128.0
Operating Expense		
Research	\$49.5	46.4
JAX Research Systems	\$38.2	38.8
Genetic Resources	\$9.6	12.2
Training and Education	\$2.1	2.0
Institutional Support	\$21.3	23.6
SUBTOTAL, OPERATING EXPENSE	\$120.7	123.0
INCREASE (DECREASE) IN NET ASSETS FROM OPERATING ACTIVITIES	\$16.5	5.0
Construction, Endowment and Other Non-Operating Activities		
Construction Grants	\$13.8	7.8
Contributions for Plant and Endowment	\$1.3	4.5
Long-Term Investment Return, net of amount utilized	\$2.3	6.7
Other Non-Operating Changes	(\$6.3)	4.3
INCREASE (DECREASE) IN NET ASSETS FROM NON-OPERATING ACTIVITIES	\$11.1	23.3
INCREASE (DECREASE) IN NET ASSETS	\$27.6	28.3

	FY 2005	FY 2004
<i>(in millions)</i>		
Assets		
Land, Buildings and Equipment (net)	\$149.4	134.9
Bond Assets Held by Trustee	\$0.8	6.4
Current Assets	\$73.1	57.7
Other Assets	\$2.3	3.3
Endowment Fund	\$59.9	57.3
Contributions Receivable	\$2.7	4.5
TOTAL ASSETS	\$288.2	264.1
Liabilities and Fund Balances		
Current Liabilities	\$29.7	31.9
Bonds Payable, net	\$63.5	64.7
Fund Balances		
Unrestricted	\$169.3	140.4
Temporarily Restricted	\$18.3	19.9
Permanently Restricted	\$7.4	7.2
TOTAL LIABILITIES AND FUND BALANCES	\$288.2	264.1

Please Note:

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



On behalf of everyone at The Jackson Laboratory, we are honored to recognize the generosity of those who support our work. Thank you for making the achievements highlighted in this report possible.

Philanthropic Support Annual Fund Gifts

6/1/04 – 5/31/05

The Annual Fund for Fiscal Year 2005 (June 1, 2004, to May 31, 2005) exceeded its goal of \$890,000, with a total \$926,227 raised. We extend our sincere appreciation to our long-standing, loyal supporters and all our new friends, who value basic biomedical research and its importance to improving human health.

Discovery Club

\$50,000 +

Ms. Sigrid Berwind
Berwind Corporation

21st Century Club

\$25,000 - \$49,999

The Shelby Cullom Davis
Foundation
Fraternal Order of Eagles
TransporTech, LLC

The Jackson Club

\$10,000 - \$24,999

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The Cotswold Foundation
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Don Peter Liu, Ph.D.
Cathleen M. Lutz, Ph.D.
Anthony Nicholson, B.V.S.c., Ph.D.
Anne E. Peaston, Ph.D.
Janice Pendola, Ph.D.
Petko Petkov, Ph.D.
Stephanie Pretel, Ph.D.
Raymond Robledo, Ph.D.
Kenneth E. Sahr, Ph.D.
Tali Shalom-Barak, D.V.M.
You-Qiang Su, Ph.D.
Robert Taft, Ph.D.
Shrijay Vijayan
Michael Wiles, Ph.D.
Rong Yuan, Ph.D.

Affiliated Scientists

Peggy Danneman, V.M.D., M.S.
Senior Director, Laboratory Animal
Health Services
James Fahey, D.V.M.
Chief, Diagnostic Services
Jon Geiger, Ph.D.
Director, Educational Programs
Allison Kitten, Ph.D.
Product Manager
John Macauley, Ph.D.
Senior Director, Courses and
Conferences
Barbara Tennent, Ph.D.
Senior Director, Scientific Program
Development
Ray Vonder Haar, Ph.D.
Senior Manager, Quality Control
& Services

Administrative Staff

Richard P. Woychik, Ph.D., Director
Muriel T. Davisson, Ph.D., Director,
Genetic Resources
Charles E. Hewett, Ph.D., Vice
President and Chief Operating
Officer
Barbara B. Knowles, Ph.D., Vice
President for Education, Training and
External Scientific Collaborations

*Our mission is to improve
the quality of human life
through discoveries arising
from our own genetic research
and by enabling the research
and education of others.*

The Jackson Laboratory is a National Cancer Institute (NCI) designated Cancer Center. For information on the latest cancer treatments, and information about clinical trials, call the NCI Cancer hotline at 1.800.4.CANCER or visit www.nci.nih.gov.



We are pleased to announce that Charity Navigator, America's premier independent evaluator of charities (www.charitynavigator.org), has awarded The Jackson Laboratory its highest rating of four stars. This is the Laboratory's third consecutive four-star rating.

CREDITS

RESEARCH AND WRITING: Joyce Peterson, Public Information Manager;
Mark Wanner, Public Information Representative

EDITING: Carol Lamb, Assistant to the Vice President for Advancement;
Nessa Reifsnnyder, Foundations Officer

REVIEW: Janet Braga, Corporate Giving Director/New York Region Officer;
Cheryl Callnan, Annual Giving and Development Services Manager

DATA COLLECTION AND REVIEW: Penny Fox, Information Records Specialist;
Ronald Sucey, Budgets and Planning Director

CONCEPT, DESIGN, AND PRODUCTION: Karan Cushman, Ariel Creative

PHOTOGRAPHY AND ARTIFACTS: Peter Travers; additional photos by Stanton Short,
Photography and Conference Services Supervisor; Kimball Wade, Multi-Media Technician

THE JACKSON LABORATORY

600 Main Street
Bar Harbor, ME 04609
207-288-6000

www.jax.org