

HIGHLIGHTS OF THE YEAR

Research

Cancer

In October, Masaaki Hamaguchi and Michael Wigler published their discovery of a new tumor suppressor gene that is missing from or inactive in 60% of the breast cancer specimens they examined. The study is significant in part because it focused on sporadic (nonheritable) forms of breast cancer. Sporadic disease accounts for greater than 90% of all breast and other cancers.

Masaaki used a gene discovery method pioneered by Michael (called Representational Difference Analysis or RDA) for detecting the differences between the DNA of normal cells and breast tumors—differences that might contribute to tumor formation. This analysis, combined with other methods, enabled Masaaki to pinpoint a candidate tumor suppressor gene located on human chromosome 8. The gene was dubbed *DBC2*, for *deleted in breast cancer*. Subsequent analysis confirmed that the *DBC2* gene was either deleted, mutated, or silenced in many of the breast tumors or breast cancer cell lines Masaaki examined.

Importantly, restoring *DBC2* gene expression was sufficient to restrain the growth of breast cancer cells that lack *DBC2* expression. When expression of a mutated *DBC2* gene was induced in a breast cancer cell line, the cells continued to grow in an unrestrained manner. However, when expression of a normal *DBC2* gene was induced in the breast cancer cell line, the cells stopped growing. From a clinical standpoint, Mike Wigler thinks it would be difficult to restore a normal *DBC2* gene to cancer cells that lack it, say, by gene therapy. Instead, he believes identifying other proteins activated by the loss of *DBC2* expression in cancer cells, and inhibiting those proteins with new drugs, would be a promising therapeutic strategy.

By using genetically well-defined mouse models of cancer, Scott Lowe and his colleagues continue to reveal important information about the role of the *p53* tumor suppressor in programmed cell death ("apoptosis"), and how the alteration of specific downstream effectors in the *p53* pathway (e.g., Bcl2, Caspase-9) can unleash tumor growth and metastasis. Scott has developed powerful transgenic mouse models of lymphoma in which transplanted cells that are genetically predisposed to forming tumors are also labeled through their expression of a fluorescent protein. In this way, Scott and his colleagues can carry out whole-body fluorescence imaging of the mice to follow tumor formation and progression.

This year, such a study by Scott showed that among the many functions of *p53*, its action through Bcl2 and Caspase-9 to trigger the destruction of precancerous cells is *p53*'s principal tumor-suppressing function. This finding removes some of the complexity previously believed to underlie the role of *p53* in suppressing tumor formation, and significantly improves the theoretical framework necessary for developing rational cancer therapies.

Molecular Biology

By developing a method to correct defects in a complex process called RNA splicing, Adrian Krainer and Senior Fellow Luca Cartegni have moved a step closer to developing treatments for



Masaaki Hamaguchi



Adrian Krainer

a host of diseases as diverse as breast cancer, muscular dystrophy, and cystic fibrosis.

Mutations in DNA frequently cause errors in RNA splicing. Improperly spliced messenger RNA molecules can lead to the creation of altered proteins that fail to perform their duties properly, often resulting in disease. Many human diseases have been linked to defects in RNA splicing. Adrian's laboratory investigates this molecular editing process, which takes the information coded in genes and ultimately makes it available for building proteins. Adrian and Luca have devised a clever way to correct RNA-splicing defects implicated in breast cancer and spinal muscular atrophy (a neurodegenerative disease). In principle, the technique could correct RNA-splicing defects associated with any gene or disease.

For now, the method has been shown to work under the simplest of conditions—in test tubes with small segments of RNA.

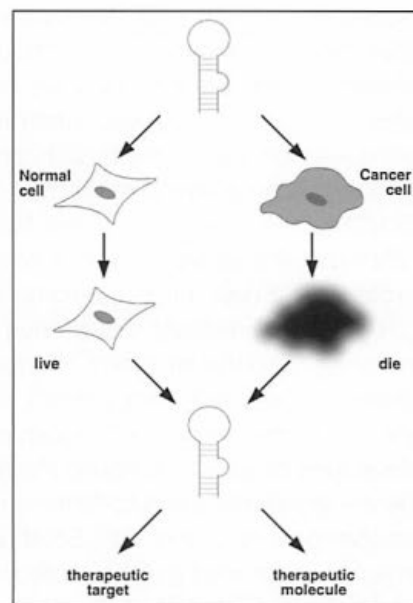
The next step is to adapt the technique for use in living cells. Adrian and Luca dubbed the method ESSENCE (for *Exon-Specific Splicing Enhancement by small Chimeric Effectors*). They are working to create ESSENCE designer splicing molecules that pass easily into cells and efficiently home in on the desired RNA-splicing targets. If such molecules can be developed, they may ultimately prove useful for treating a great diversity of human diseases.

RNA Interference

In the December 20 issue of the prestigious journal *Science*, the research of Greg Hannon, Shiv Grewal, and Rob Martienssen was recognized along with work from other institutions as the "Breakthrough of the Year" for 2002 among all the sciences. Collectively, the Breakthrough of the Year citation recognized the discovery that through a multifaceted process called RNA interference (RNAi), small RNA molecules can play a surprising variety of key roles in cells: They can inhibit translation of messenger RNA into protein, cause degradation of other messenger RNAs, and even initiate complete silencing of gene expression from the genome. The "Breakthrough of the Year" citation specifically characterized the work of Greg, Shiv, and Rob as "a crucial step" and as "the year's most stunning revelations."

Greg's lab has made a series of important and exciting discoveries concerning the properties and mechanisms of RNAi. Moreover, through detailed examination of the families of proteins involved in RNAi, Greg and his colleagues have uncovered a link between RNAi and the Fragile X syndrome, the most common developmental cause of mental impairment in humans. Finally, Greg's lab has developed methods for using RNAi to uncover genes that are involved in cancer.

Rob, Shiv, and their colleagues have revealed a previously undiscovered biological phenomenon, namely, that RNAi is required to establish specialized subregions within chromosomes in



Applications of RNAi

which genes are kept silent. This finding has profound implications for understanding how chromosome structure is regulated, and how specific active versus silent regions of chromosomes are determined and inherited. In addition, studies at Cold Spring Harbor Laboratory and elsewhere have shown that defects in the establishment or maintenance of silent chromosome architecture in the vicinity of tumor suppressor genes may contribute to cancer.

Neuroscience

Brain Imaging: By literally peering through a window into the brains of living mice, Karel Svoboda and his colleagues have caught a groundbreaking glimpse of adult brain cells forming new connections called synapses. Their study helps overturn a long-held tenet that the structure of the adult brain is largely fixed and sheds light on processes that underlie learning and memory.

Karel's lab has provided clear evidence that the brain can alter its wiring pattern in response to the outside world. Although the neuroscience community had begun to speculate that the architecture of the adult neocortex might be more dynamic than previously believed, definitive evidence was lacking, and neuroscience orthodoxy still held that brain architecture is relatively stable, limiting learning and recovery from injury.

Karel and his colleagues have demonstrated that new synapses are formed in the adult brain in response to new experience. Crucially, Karel has established that synapses form and dissolve in the neocortex continuously, perhaps through a "random sampling" process, and that sensory input stabilizes or makes permanent a subpopulation of particular synapses.

Receptor Trafficking: Evolution is an accidental tinkerer. It uses genes and segments of genes that are lying around in a genome, changes them at random or puts them together in myriad combinations, and auditions the new genes for new roles in the lives of the cell. Successful new genes are passed on efficiently to future generations. Two gene products, Ras and Rap, have well-defined, antagonistic growth-promoting and growth-inhibiting functions in nonneuronal cells which, when altered, can lead to cancer. Demonstrating the happenstance of evolution, this year, Roberto Malinow and Linda Van Aelst have discovered intriguing roles for Ras and Rap in cells of the nervous system.

Synaptic plasticity, or the ability of connections between neurons to

be shaped by experience, is believed to underlie several important aspects of brain development, learning, and memory. The most widely studied examples of synaptic plasticity are long-term potentiation (LTP), which strengthens the connections between neurons, and long-term depression (LTD), which weakens the connections between neurons.

Roberto's lab had previously shown that LTP results from the delivery of neurotransmitter receptor proteins called AMPA receptors to synapses. In new work, Roberto, Linda, and their colleagues have shown that Ras mediates this addition of AMPA receptors to synapses during LTP induction, whereas under

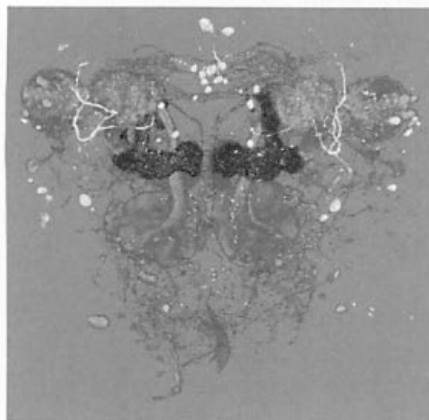


Linda Van Aelst



Roberto Malinow

conditions that induce LTD, Rap mediates the removal of AMPA receptors from synapses. Moreover, Roberto and Linda established a differential effect of Ras and Rap on different types of AMPA receptors. The resulting dynamics of AMPA receptor replacement at synapses is likely to be a principal mechanism of learning and memory.



Drosophila Brain

Learning and Memory: Tim Tully and Josh Dubnau together have taken two distinct yet complementary approaches to identifying genes that are involved in the formation of long-term memory in the fruit fly *Drosophila melanogaster*. Evolution and experimental evidence dictate that many of these genes are also involved in human memory. By using DNA microarray analysis, Tim, Josh, and their colleagues have identified 42 candidate memory genes. By using a behavioral screen for fruit flies with defective memory, they have identified 60 memory mutants. In his book *Time, Love, Memory*, Pulitzer Prize-winning author Jonathan Weiner called such mutants "Pavlov's Flies" (see below).

The separate approaches described above beautifully converged on an overlapping set of genes, reinforcing the notion that the genes are bona fide memory genes. Additional studies are required to determine the precise neurological functions of all of the candidate memory genes Tim and Josh have identified. Until then, the genes have been given names that correspond to those that Russian psychologist Ivan Pavlov (1849–1936) gave his famed Pavlov's Dogs, e.g., Norka, Laska, Tungus, Chingis Khan, Trezor, John, Jack, etc. (Tim uncovered some 40 such names during a 1992 visit to Pavlov's former residence in St. Petersburg, Russia.) Ultimately, comprehensive knowledge of how these numerous gene products act and interact should provide a solid foundation for understanding the processes of learning and memory.

Awards and Honors

Cold Spring Harbor Laboratory Assistant Professor Z. Josh Huang is one of 18 scientists in the nation named a Scholar in 2002 by the Pew Scholars Program in the Biomedical Sciences. The program, funded by the Pew Charitable Trusts, supports young investigators of outstanding promise in basic or clinical sciences relevant to the advancement of human health.



Z. Josh Huang

Karen Zito, a postdoctoral fellow in Karel Svoboda's lab, is one of 17 researchers named a 2002 Burroughs Wellcome Fund Career Awardee in the Biomedical Sciences. Each award provides a five-year, \$500,000 grant to support advanced postdoctoral training as well as the first years of faculty research.

Peter Gillespie, a postdoctoral fellow in Tatsuya Hirano's lab, has received a three-year, \$125,000 Postdoctoral Fellowship from the Jane Coffin Childs Memorial Fund for Medical Research. The fund was established in 1937 by the late Miss Alice S. Coffin and Mr. Starling W. Childs as a gift in trust to Yale University to support wide-ranging scientific inquiry into the causes and treatment of cancer.

Two Cold Spring Harbor Laboratory scientists received awards at the 93rd Annual Meeting of the American Association for Cancer Research (AACR) held in San Francisco in April. Scott

Lowe received a Sidney Kimmel Symposium for Cancer Research Scholars Award, and H. Guido Wendel, a postdoc in Scott's lab, was awarded an AACR-Amgen Fellowship in Translational Research. Scott and eight other early career scientists were selected for the Kimmel Symposium Award based on their receipt of highly competitive research grants from one of the following leading funders of cancer research: The Susan G. Komen Breast Cancer Foundation; the Cancer Research Foundation of America; the Damon Runyon Cancer Research Fund; the Leukemia & Lymphoma Society of America; the American Association for Cancer Research; or the Sidney Kimmel Foundation for Cancer Research. Scott is a CSHL Professor and Deputy Director of the CSHL Cancer Center. The AACR-Amgen Fellowship in Translational Research awarded to Guido is intended to foster cancer research throughout the world by scientists currently at the postdoctoral or clinical research fellow level.

DNA from the Beginning, a Web Site created by the multimedia group at the CSHL Dolan DNA Learning Center, is a winner of *Scientific American* magazine's 2002 Science and Technology Awards. *Scientific American's* editors reviewed thousands of sites and selected *DNA from the Beginning* as one of 50 of the most valuable science and technology resources for their readers. Other awards and commendations garnered by *DNA from the Beginning* include "Ten Cool Sites" (Exploratorium, San Francisco), "Best of the Web" (*Popular Science*), "BigChalk Best" (bigchalk.com), "The Webby Awards" (2000 nominee), "Top Rated Site" (MedExplorer), "Hotspot-Keysite" (*New Scientist*), "Selected Member" (Britannica Internet Guide), "Seal of Approval" (*Web Feet: The Internet Traveler's Desk Reference*), and "Digital Dozen" (The Eisenhower National Clearinghouse). *DNA from the Beginning* was made possible by a grant from the Josiah Macy Jr., Foundation.

Thomson-ISI, the Institute for Scientific Information, is an agency that tracks the impact of published research papers, mainly by counting the number of times a particular paper is cited by other scientists in the field. In January 2003, ISI ranked Cold Spring Harbor Laboratory as the number-one-cited institution in Molecular Biology and Genetics Papers for the past decade. This honor and distinction underscores the laboratory's mission to spread the details of our research to other scientists worldwide.

Cold Spring Harbor Laboratory President James D. Watson was again an award-winner, following the 2001 announcement that made him an Honorary Knight of the British Empire. This year, Jim was honored with the Gairdner Foundation Award of Merit for his work and dedication to genomics science, together with Francis S. Collins, Director of the National Human Genome Research Institute. The Gairdner Foundation, based in Toronto, is a nonprofit corporation devoted to the recognition of outstanding achievement in biomedical research worldwide. This year's awards focused on achievements in the field of genomics science.

Symposium

The 67th Cold Spring Harbor Symposium on Quantitative Biology was held May 29 through June 3, 2002. This year's Symposium, "The Cardiovascular System," was organized by David Stewart and myself. The Symposium addressed many aspects of cardiovascular science including normal heart and cardiovascular development and function, the failing heart, hypertension, atherosclerosis, vascular biology, angiogenesis, and tumor angiogenesis. The Symposium attracted 256 participants and featured 68 talks and 108 posters. Opening night speakers included Richard Harvey, Mark C. Fishman, Jonathan G. Seidman, and Rakesh K. Jain and the summary was presented by Christine Seidman. Richard Lifton delivered the annual Dorcas Cummings Memorial lecture, "Salt and Blood Pressure: New Insights from Human Genetic Studies" to a mixed audience of scientists and lay friends of the Laboratory.

Laboratory Senior Management Restructured

For more than eight years, Dr. Winship Herr served as the Assistant Director of Cold Spring Harbor Laboratory. During this period, the Laboratory's research program expanded considerably and, with the establishment of the Watson School of Biological Sciences in 1998, has become an accredited Ph.D. degree-granting institution.



Winship Herr

ably and, with the establishment of the Watson School of Biological Sciences in 1998, has become an accredited Ph.D. degree-granting institution. Winship led the formation of the Watson School and, along with his role as the Laboratory's Assistant Director, has been the inaugural Dean of the School since 1998. The parallel expansion of the Laboratory's research and academic programs has placed ever-increasing responsibilities on the roles of the Assistant Director and Dean. In August, Winship asked to step down as Assistant Director, to devote his efforts to the ever-expanding Watson School and his successful research program, to which I reluctantly agreed. During the past eight years, Winship has done a remarkable job in helping to both expand the Laboratory's research program and develop the highly successful Watson School. I thank him for his dedication and contributions as Assistant Director and am pleased that he will continue to play a senior leadership role at Cold Spring Harbor Laboratory as Dean of the Watson School of Biological Sciences.

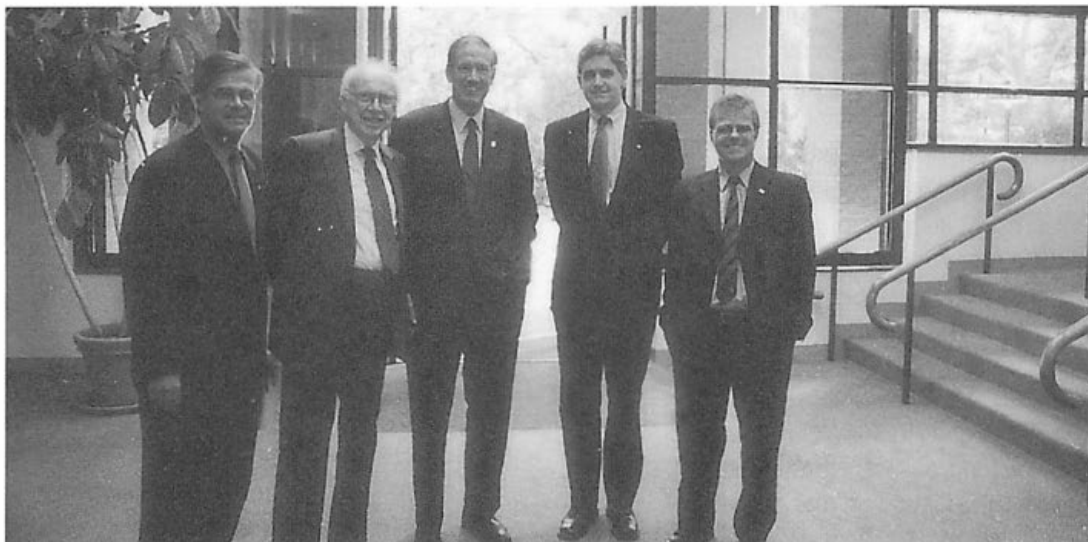
On August 1, 2002, Dr. Hollis Cline accepted the position of Associate Director for Research at Cold Spring Harbor Laboratory. Holly assumed the position following a reorganization of the research leadership of the Laboratory. As Associate Director for Research, Holly will have an important role in the future research directions of the Laboratory, as well as budget management for the research program and implementing the decisions made by the Laboratory administration. Holly is the Charles Robertson Professor at Cold Spring Harbor Laboratory and has made major contributions to the understanding of brain development and function. She is an outstanding neuroscientist who has already helped to expand the highly successful neuroscience program at the Laboratory. Her broad knowledge of neuroscience, coupled with an interest in cancer research, made her an obvious choice to help lead the Laboratory's research program.



Holly Cline

Governmental Achievements

New York Governor George Pataki, together with Nassau County's Senate Delegation of Dean Skelos, Charles Fuschillo, Kemp Hannon, Michael Balboni, and Carl Marcellino, made a ground-breaking announcement at Cold Spring Harbor Laboratory on Tuesday, September 24, 2002, by creating a biotechnology corridor on Long Island, called "Biotech Island." This new initiative, linking several institutions on Long Island, will create jobs, industry, financial improvements, educational opportunities, and a focus on research that will rival the rest of the nation, including Silicon Valley. With a \$48 million investment, and a \$20 million investment in Cold Spring Harbor's bioinformatics program, the New York State delegation made Cold Spring



Senator Dean Skelos, Jim Watson, Governor George Pataki, Bruce Stillman, Colin Goddard, CEO, OSI Pharmaceuticals

Harbor Laboratory a cornerstone for this initiative. Due to this effort, Long Island is now poised to become a center for biotechnology in the United States, and Cold Spring Harbor Laboratory has been identified as one of the key players in this exciting transformation.

The Women's Cancer Gene Initiative

In October, a delegation of researchers from Cold Spring Harbor Laboratory traveled to Washington to present to several New York legislators a new concept we call "The Women's Cancer Gene Initiative" for research in breast and ovarian cancer. This new program incorporates the many suc-



Congressman Steve Israel, Bruce Stillman

cesses of our breast cancer research program, combining Greg Hannon's new research developments in RNAi with the exciting cancer gene discovery research in Mike Wigler and Robert Lucito's laboratories, and the mouse models for cancer research in Scott Lowe's laboratory. The initiative was so well-received in Washington that two local representatives—Senator Hillary Rodham Clinton and Congressman Steve Israel—made visits in the following weeks to host press conferences and pledge their support to this exciting program. Representatives Peter King and Carolyn McCarthy also toured our Woodbury Cancer Genome Research Center, and spoke to researchers about their personal support of the program in Congress.



Senator Hillary Rodham Clinton, Scott Lowe

Banbury Center

It is not often that writers at *Sports Illustrated* contact the Banbury Center, but for a few giddy months at the beginning of 2002, Banbury was major news in the sports world. The March meeting on *Genetic Enhancement of Athletic Performance* examined the use of gene therapy in athletics. The World Anti-Doping Agency (WADA) is worried that athletes may use gene therapy to introduce "desirable" performance-promoting genes. The meeting was a fascinating mix of scientists, policy makers, and athletes, including Johann Koss, winner of four Olympic gold medals in speed skating.

Another highly topical meeting was prompted by the heightened awareness of the dangers of biological terrorism. *Microbial Forensics* was devoted to molecular fingerprints that will allow rapid identification of biowarfare agents and that could be used for tracing the source of the agents. The meeting was notable for the mix of scientists from academia and from government agencies—it also set a new record for the number of acronyms appearing in a program.

Robertson Research Fund

The Robertson Research Fund has been the primary in-house support for our scientists for nearly three decades. Since 1973, the Fund has grown from \$8 million to more than \$95 million. During 2002, Robertson funds supported cancer research in the labs of Gregory Hannon, Eli Hatchwell, Winship Herr, Tatsuya Hirano, Yuri Lazebnik, Bud Mishra, Michael Myers, and William Tansey; neurobiology research in the labs of Grigori Enikolopov, Josh Huang, Roberto Malinow, Jerry Yin, and Yi Zhong; and plant research in the lab of Robert Martienssen. Robertson funds also supported several new investigators, including Shiv Grewal, Alea Mills, Senthil Muthuswamy, Terrence Strick, David Jackson, Marja Timmermans, Carlos Brody, Lee Henry, Zach Mainen, and Tony Zador.

Cold Spring Harbor Laboratory Board of Trustees

Cold Spring Harbor Laboratory's Board of Trustees led the Laboratory through another exciting and eventful year, continuing to shape the direction and vision of this institution.

This year, the Board welcomed the addition of four new Trustees to its ranks: Titia de Lange, Ph.D., a professor of Cell Biology and Genetics at The Rockefeller University; Susan Lindquist, Ph.D., Director of the Whitehead Institute for Biomedical Research; Kristina Perkin Davison, Partner and cofounder of iEurope Capital, LLC; and Amy Goldman, an Agricultural Preservationist and author. Mrs. Evelyn Lauder was also elected to the Board as an Honorary Trustee.

Helen A. Dolan, William L. Matheson, Leon B. Polsky, and Mark Ptashne reached the end of their allotted terms as Trustees and were honored at the Board's November meeting for their outstanding service to the Laboratory. As noted in previous pages, we were saddened to learn in late 2002 of the death of William Matheson.



Helen A. Dolan



William L. Matheson



Mark Ptashne



Leon B. Polsky

Dolan DNA Learning Center

The Dolan DNA Learning Center (DNALC) significantly expanded its educational reach in 2002 by embarking on major agreements to license DNALC "know-how" in the United States and abroad. In the spring, the DNALC collaborated with North Shore–Long Island Jewish Research Institute (NS–LIJ) to open DNALC West to better serve students in western Nassau County and



CSHL Trustee Arthur Spiro, Bruce Stillman, Michael Dowling, CEO, NS–LIJ

New York City. This teaching laboratory, located adjacent to the NS-LIJ diagnostic laboratory in Lake Success, is managed and staffed by the DNALC and uses its teaching curricula. In the summer, the DNALC signed a three-year Memorandum of Understanding with the Ministry of Education (MOE) to support expansion of life sciences education in Singapore. The contract provides support for the DNALC and involves consultation and training of teachers. Initiated in the context of a national thrust to make biotechnology the "fourth pillar" of Singapore's future economy, the project revolves around the development of "sister" DNA centers at the Singapore Science Centre and National Institute of Education. In the fall, the DNALC entered into a licensing agreement with the Science EpiCenter of New London, Connecticut to develop a DNA Learning Center there to serve southern Connecticut. These licensing agreements, in addition to sponsored research by Carolina Biological Supply Company, and royalties on teaching kits and CDs, contributed about \$335,000 in revenue, or 14% of the 2002 operating income.

In September, the Dolan DNALC opened "The Genes We Share," the third major exhibition in the DNALC's history. The exhibit celebrates the 50th anniversary of the discovery of the DNA structure, which set the stage for the recent efforts to determine the entire DNA sequence of the human genome. As visitors explore the exhibition, they are encouraged to view the human genome as a record of our shared ancestry, an instruction manual for our bodies, and a source of information that can foreshadow a person's future health. Visitors are greeted in the front hall with photomurals that juxtapose New York "peoplescapes" with unique world populations, setting the stage for thinking about human similarities and differences. An interactive area in the main gallery encourages visitors to take stock of traits that make them unique, as well as anatomical, cellular, and molecular features they share with all people.

In another area, an interactive map of the world shows our shared ancestry in Africa, migration paths followed by humans over the past two million years, and environmental factors that account for some of our differences. Visitors then move into a recreation of a Neolithic cave, complete with paintings and the first reconstruction of an adult Neandertal skeleton. Visitors are asked to consider the anatomical, genetic, and behavioral changes that evolved to set humans apart from other primates. A final gallery focuses on the modern "gene age," moving from an eight-foot reconstruction of the original metal DNA model made by Watson and Crick in 1953 to a working DNA sequencer, which operates daily to sequence DNA submitted by student classes from around the United States.

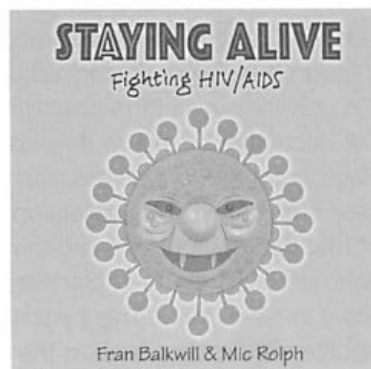
The November completion of *Your Genes, Your Health* (www.ygyh.org) marked the end of a five-year, \$1.3 million Web Site project funded by the Josiah Macy, Jr. Foundation. This multimedia guide provides up-to-date, engaging information on 15 common genetic disorders: Fragile X syndrome, Marfan syndrome, hemophilia, cystic fibrosis, Duchenne/Becker muscular dystrophy, phenylketonuria, Huntington disease, neurofibromatosis, sickle cell disease, hemochromatosis, Tay-Sachs disease, β -thalassemia, Down syndrome, Alzheimer disease, and polycystic kidney disease. Its companion site *DNA from the Beginning* (www.dnafb.org), an animated primer on genetics and molecular biology, was one of only 50 World Wide Web sites chosen by *Scientific American* for its 2002 SciTech Award (www.scientificamerican.com). The Macy-funded sites received more than 1.6 million visitors in 2002, accounting for 44% of the 3.8 million visitors to the *Gene Almanac* "portal."

CSHL Press

The Cold Spring Harbor Laboratory Press enjoyed another successful year. Twelve new books and two CDs were published and all four research journals grew in impact or circulation. But the most prominent—and ambitious—Press project of the year had true worldwide impact.

John Inglis, Executive Director of CSHL Press, was a member of a team of scientists and educators committed to developing effective, innovative, and sustainable HIV/AIDS prevention strategies for young people in South Africa and other vulnerable communities. Together, they prepared an important book entitled *Staying Alive: Fighting HIV/AIDS* that presents life-saving information in a direct, engaging, and age-appropriate manner to children aged 12 to 16. With funds from the National Institutes of Health, Oxford University, and Cold Spring Harbor Laboratory, 20,000 copies of *Staying Alive* were produced by the CSHL Press and distributed free of charge in three provinces of South Africa in July and August.

Staying Alive was written by Professor Frances Balkwill of Bart's Hospital Medical School, London, and illustrated by Mic Rolph. Balkwill and Rolph have previously collaborated on several highly successful children's books for CSHL Press, including *Enjoy Your Cells*, *Germ Zappers*, *Have A Nice DNA*, and *Gene Machines*. To gain a better understanding of the book's audience before creating *Staying Alive*, Balkwill and Rolph first visited schools, squatter camps, and orphanages in the provinces of Gauteng (Johannesburg) and Kwa-Zulu Natal (Durban), South Africa, where they met with students, teachers, medical scientists, and health professionals. The book resulting from these experiences incorporates artwork created by children during workshops conducted by Mic Rolph, as well as Rolph's own illustrations of the biology of HIV and how abstinence, faithfulness, and the use of condoms can reduce the spread of AIDS. With its lively graphics and direct language, *Staying Alive* gives explicit messages about the risks of disease, ways of preventing infection, the building of relationships based on mutual care, and the need for compassion and respect toward people living with HIV.



Staying Alive Book Cover

The available copies of the book are being distributed free of charge to educators and students from repositories in Gauteng, Kwa-Zulu Natal, and the Western Cape. Teachers, academics, and community activists have been recruited to conduct classroom exercises designed to evaluate the book's effectiveness and provide feedback for the development of future editions of *Staying Alive* and other teaching materials. The book-distribution tour included receptions in each province attended by local politicians and educators, as well as meetings with the South African Minister of Education, Dr. Kadar Asmal, the well-known satirist and AIDS educator, Pieter-Dirk Uys, participants in the Memory Box Project at the University of Cape Town, and representatives of Médecins Sans Frontières ("Doctors Without Borders"). During and after the tour, the creators of *Staying Alive* also received feedback from Christian missionaries, traditional healers, and even soccer clubs interested in helping fight the spread of AIDS in South Africa.

After completing this pilot phase of their project, the *Staying Alive* team received substantial funding from the Gates Foundation. With this support, a second edition of the book and related educational materials will be created in several South African languages and distributed on a much larger scale. In addition, a start will be made on addressing a newly identified need—a program that deepens science teachers' knowledge of the immune system and virus biology and increases their effectiveness as communicators of AIDS awareness.

CSHL Library and Archives

In 2002, the CSHL Library made great progress in its efforts to provide information electronically. On-line subscriptions to scientific journals, monographs, and reference materials have

increased significantly. InterLibrary Loan has seen an increased availability of articles in PDF format. This has facilitated the delivery of requested articles in a timely fashion. The Library has acquired several new electronic databases such as BioKnowledge Library from Proteome, FirstSearch that includes BasicBIOSIS and several full text databases, and Faculty of 1000 from BioMed Central. WebCat, the on-line catalog, now includes most of the titles in the Library's collection, including titles in video, electronic, and microfilm formats. The library has continued to participate in the BioInformation Synthesis Collaborative (BISC), which includes the libraries of The Rockefeller University, the American Museum of Natural History, Woods Hole Marine Biological Laboratory, and the New York Botanical Garden, which is developing several projects for interlibrary loan purposes.

The Archives have undergone tremendous growth and development. The James D. Watson Special Collection has been acquired and is beginning to be made available on our Web Site through the use of finding aids. The oral history project to document the Laboratory's history through the eyes of the scientists who worked and visited here has grown to 40 interviews and will ultimately be made available through our laboratory web page. The James D. Watson Photographic Archives are available on-line and the CSHL Symposium photo collection is also near completion. This collection contains a remarkable history of biology in the latter two thirds of the 20th century and into the new millennium. During this past year, a great deal of preparation has been made in planning the traveling exhibition "Seeking the Secret of Life: The DNA Story in New York." This exhibition will mark the 50th anniversary of the discovery of the DNA double helix and opened at the Science, Industry and Business Library of the New York Public Library in February, 2003.

New Major Gifts

The Laboratory was successful in continuing and commencing major campaigns, despite economic challenges in 2002. The campaigns to fund the Watson School of Biological Sciences, the Cancer Genome Research Center, the Women's Cancer Gene Initiative, and the Dolan DNA Learning Center all received substantial gift support. The philanthropic investments of our generous and supportive friends for the work of the educators and researchers at Cold Spring Harbor Laboratory allow us to remain at the forefront of biomedical knowledge. The announcement of New York State's commitment to the Laboratory of \$20 million by Governor George Pataki and the Long Island Senate team led by Senator Dean Skelos is a welcome recognition of the accomplishments at Cold Spring Harbor. Through this special commitment and generous private funding, the Laboratory is increasing the pace of research to control cancer and understand neurological diseases.

Watson School of Biological Sciences

Under the leadership of Dean Winship Herr, the Watson School of Biological Sciences continues to go from strength to strength. Not only has Winship introduced a strong graduate program, but the Watson School now effectively oversees all research-based education at the main laboratory campus, including the Undergraduate Research Program, the high school Partners for the Future Program, and Postdoctoral Fellow training.

Led by Honorary Trustee David L. Luke III, the first phase of the Watson School of Biological Sciences Campaign was completed this year, accomplishing an endowment of \$32 million as

a firm financial foundation for the Watson School. We are grateful for gifts from the William Stamps Farish Fund of \$300,000 and from the Estate of Elisabeth Sloan Livingston of \$2,200,000; and we appreciate gifts to build the Watson School's Innovative Education Fund, including the final payment of a challenge gift from an anonymous donor to match gifts of \$62,103 from the Seraph Foundation; and of \$10,000 from The William H. Donner Foundation; with further gifts to the Fund of \$50,000 from The G. Unger Vetelsen Foundation; of \$25,000 from Dr. and Mrs. Mark Ptashne; of \$10,000 from Mark and Karen Zoller; and of \$1,000 from the Packard Foundation; which collectively rounded out a solid campaign to provide funding for graduate student fellowships, lectureships, and courses.

A second phase of fund-raising is being commenced to allow an increase in the enrollment in the Watson School. This will enable the School to help fulfill the growing demand for researchers in the biological sciences. Laboratory Trustee Robert D. Lindsay is leading this phase. A gift of \$500,000 from the William Randolph Hearst Foundation has provided the base funding for a fellowship for disadvantaged students and is a welcome start to this important expansion of the School.

The Cancer Genome Research Center

Now in its first full-year in operation, the value of commitments to the Cancer Genome Research Center was evident, with the facilities underpinning many advances in cancer, neuroscience, and plant genomics research. We are grateful for major new contributions to the facility and its programs of \$2,500,000 from The Starr Foundation; of \$261,354 from the William and Maude Pritchard Charitable Trust; and of \$10,000 from Benjamin Development.

Dolan DNA Learning Center

Final gifts were made in support of "The Genes We Share" exhibit, which opened in September. We are grateful for a \$20,000 gift from the William Haseltine Foundation, the \$50,000 gift from the Richard Lounsbery Foundation, and the \$30,000 gift from Dr. Laurie Landeau, all of which helped to make "The Genes We Share" a success. Arrow Electronics also generously gave \$30,000.

Private Research Support

Private funding in 2002 advanced important research initiatives in cancer, neuroscience, and other areas. We gratefully acknowledge major gifts in the \$100,000 and above category, including for cancer research the Marks Family Foundation for \$500,000; The Miracle Foundation for \$100,000; The Breast Cancer Research Foundation/Lillian Goldman Trust for \$1,000,000; the Louis Morin Charitable Trust for \$105,000; The V Foundation for \$100,000, and for neuroscience research The McKnight Endowment Fund for Neuroscience for \$100,000; and Jeff Hawkins and Janet Strauss for \$100,000. We appreciate other support received from The Dana Foundation for \$100,000 and from Robert Gardner for \$100,000.

Breast Cancer Support

The generous support from local breast cancer groups again made a real difference in 2002, including from the Long Beach Breast Cancer Coalition; the Plainview–Old Bethpage Breast Cancer Coalition; the Elizabeth McFarland Fund; the Babylon Breast Cancer Coalition; and,

long-time supporters, 1 in 9: The Long Island Breast Cancer Action Coalition and Long Islanders Against Breast Cancer (LIABC). As in past years, we are indebted to the many individuals from local breast cancer groups working so hard to make it possible for Cold Spring Harbor Laboratory to continue its breast cancer research.

CSHL Planned Giving Advisory Board

The Cold Spring Harbor Laboratory Planned Giving Advisory Board—drawn from the financial services, accounting, and legal professions—consists of accountants, tax advisors, trust officers, bank officers, investment advisors, investment bankers, and lawyers, representing firms located on Long Island, in New York City, and in Connecticut. The Board was briefed on the Laboratory's activities and accomplishments in 2002. I appreciate the advice members provide in support of the Laboratory's goals.

President's Council

Members of the President's Council were once again invited to another successful one-day meeting at the Laboratory. This year's President's Council meeting explored the topic of "Human



Matt Ridley

Instincts and Evolutionary Psychology." Once again, our presenting scientists were engaging speakers and leaders in the field: famed science writer Dr. Matt Ridley, Dr. Richard Wrangham from Harvard University, Dr. Patricia Wright from Stony Brook University, and Dr. Randolph Nesse from the University of Michigan. The event began with tea at Ballybung, the home of Jim and Liz Watson. Guests were then invited to meet the Cold Spring Harbor Laboratory Fellows, Drs. Lee Henry and Terence Strick, followed by cocktails and then a discussion led by Matt Ridley on "Evolutionary Psychology of Instincts." The lectures continued on Saturday morning with discussions on "The Origins of Human Violence," "Parenting: Insights from Our Primate Cousins," and "Phobias and Depression." All who attended said it was, as always, a worthwhile learning experience.

Gavin Borden Visiting Fellows

The Gavin Borden Lecture series was named in memory of Gavin Borden, a publisher whose *Molecular Biology of the Cell* and other books made a lasting impression on many scientists, both old and new. This year, Sir John Gurdon, former Governor of the Wellcome Trust and former director of the Wellcome/CRC Institute of Cancer and Developmental Biology, delivered the eighth annual lecture titled, "Signal Factor Perception in Development" on March 25, 2002. The annual Gavin Borden Lecture was started by Jim Watson in 1995.



Sir John Gurdon

Building Projects

In addition to continuous up-dates to many of the Laboratory's facilities, Art Brings, the Laboratory's Chief Facilities Officer, and his team completed several major renovation and construction projects.

The first phase of a new project to provide additional student housing at Uplands Farm has begun. The completed project will provide high-quality, on-campus housing for up to 32 students upon completion.

Three rooms in the Carnegie Library were renovated and converted for use as the new Watson Archives, providing much-needed space and an area in which scholars and visitors may view previously inaccessible material.

Several key scientific facilities were completed during the year. Microscopy suites were constructed in the Beckman and Hershey Buildings and several core scientific facilities—Flow Cytometry, 2D Gel, and the Nucleic Acid Facilities—were relocated to newly expanded and renovated facilities.

Many of the Laboratory's administrative departments received upgrades to their offices as well. The Institutional Advancement department moved into renovated offices previously occupied by graduate students. The Nichols Building was virtually rebuilt from the ground up, providing the Accounting, Special Events, Technology Transfer, and Administrative departments with the top-quality facilities they require to efficiently manage the increased demands placed on them by the Laboratory's growth.

A team of craftsmen worked hard to prepare the Dolan DNA Learning Center for the opening of "The Genes We Share" exhibit on September 18. From installing each of the kiosks to wiring the lighting and computers, the team ensured that the exhibit was prepared for the crowds who have already come. The exhibit looked fantastic when it was highlighted in *The New York Times* and on *News 12 Long Island*.

Community Outreach

Traffic problems temporarily slowed down our runners and walkers, but 55 Laboratory employees still participated in the Cigna 5K Run/Walk for 1 in 9: The Long Island Breast Cancer Action Coalition at Eisenhower Park on August 8. All were happy to be there for a group that has been such a tremendous help to the Laboratory research for so many years. Overall, the event raised more than \$60,000 for the Laboratory.

Special Events

Public Lectures

After a successful first year, the *Harbor Lecture Series* doubled in size, featuring a total of six lectures this year, and proved it would become an annual favorite at the Laboratory.

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| May 5 | Michael Ruse, the Lucyle T. Werkmeister Professor of Philosophy at Florida State University: "Can a Darwinian be a Christian?—The Relationship between Science and Religion." |
| May 13 | Dr. Chung S. Yang, Professor at the Laboratory for Cancer Research at Rutgers and the Director of the Carcinogenesis and Prevention Program at the Cancer Institute of New Jersey: "Beneficial Health Effects of Tea: Evidence, Myth, and Perspectives." |



Bruce Stillman, Christopher Chyba, Edward Scolnick

- May 20 Elof Axel Carlson, Distinguished Teaching Professor in the Department of Biochemistry and Cell Biology at Stony Brook University: "Eugenics: When Science and Society Go Astray."
- June 14 Steven M. Block, a biophysicist at Stanford University; Christopher Chyba, co-director of Stanford's Center for International Security; and Edward M. Scolnick, CSHL Trustee and President of Merck Research Laboratories, and Executive Vice President for Science and Technology for Merck & Company, Inc.: "Bioterrorism: Protecting Our Country, Protecting Ourselves."
- October 1 Dr. Cynthia Kenyon, the Herbert Boyer Distinguished Professor of Biochemistry and Biophysics at the University of California, San Francisco: "Genetics of Aging and Longevity: The Search for the Fountain of Youth."
- October 8 Scott Lowe, CSHL Deputy Director of the Cancer Center: "Cancer: Mission Possible."

Other Lectures

As usual, Cold Spring Harbor Laboratory hosted the Huntington Hospital Lecture Series on cardiovascular health and related diseases in both the spring and fall in the Grace Auditorium.

The West Side School Lecture Program was again a hit with local, budding scientists in 4th through 6th grades. This year, five Cold Spring Harbor Laboratory professors—Tony Zador, Leemor Joshua-Tor, Alea Mills, Lee Henry, and Erik Vollbrecht—delivered lectures.

Concerts and Exhibits

The *Music of the Harbor Concert Series* was, as previously, a smashing success. All nine concerts were sold out between Meetings participants, CSHL Association members, and the general public. Co-sponsored by *Newsday*, the concert series featured old favorites such as jazz

guitarist Eric Johnson and off-the-beaten-path performances from people such as multipercussionist Joseph Gramley. The complete concert list included:

April 20	Ju-Young Baek, violinist
April 27	Alexander Fiterstein, clarinetist
May 4	Paavali Jumppanen, pianist
May 18	Courtenay Budd, soprano
September 14	Alpin Hong, pianist
September 21	Joseph Gramley, multipercussionist
September 28	Imani Woods, woodwind quintet
October 5	Eric Johnson, jazz guitarist and his band
October 12	John Kamitsuka, pianist



John Kamitsuka

One of Cold Spring Harbor Laboratory's own, Rachel von Roeschlaub, presented an art exhibit in the Bush Fireplace Room in June. von Roeschlaub is a self-taught artist who paints using a combination of aboriginal pointillism and American Folk Art. Her paintings are finished on modern mediums such as record albums, CDs, and natural paper. She also uses her experience as a technician at Cold Spring Harbor Laboratory to teach biotechnology professional development workshops. Last February, she taught a science workshop for Tibetan monks living in India. Proceeds from this art exhibition went toward promoting science education for the exiled Tibetans living in India.

Former photographer-in-residence, Doug Fogelson, returned to the Laboratory in July for a month-long exhibit of the photographs he took during "FotoLab I" in 2001. "Remember Far Away" was a visual memory and response to Fogelson's time spent at the Laboratory. It expressed sentiment—in some cases, through the use of manipulated images—inspired by photographs of the surroundings at the Cold Spring Harbor Laboratory campus. The exhibit also featured portraits of Dr. James Watson and myself.

Laboratory Employees

Long-term Service

The following employees celebrated milestone anniversaries in 2002.

30 Years	Terri Grodzicker
20 Years	Patricia Bird, Arthur Brings, David Micklos, Clifford Sutkevich
15 Years	Sadie Arana, Patricia Barker, Lisa Bianco, Joan Doxey, James Duffy, Julie Ehrlich, Edward Haab, John Inglis, Barbara Peters, Susan Rose, Stanley Schwarz, Inez Sialiano, Patricia Urena, Jan Witkowski

New Staff

Diane Fagiola has joined the Laboratory as Director of Development. Diane comes to CSHL from a position as Director of Fundraising for the Locust Valley Library.

Gerry Holler has joined the Laboratory as Director of Security. Gerry comes to CSHL from Photo Circuits, where he served as Assistant Director of Security.

Katie Raftery has joined the Laboratory as Director of Human Resources. Katie comes to CSHL from a position as Director of Human Resources for Ericsson Internet Applications.



Long-term Service Employees

First Row: Sadie Arana, Bruce Stillman, Bobbie Peters, Patty Bird, Terri Grodzicker, Inez Sialiano, Julie Ehrlich, Joan Doxey

Second Row: Pat Urena, Stanley Schwarz, Jim Watson, Clift Sutkevich, Lisa Bianco, Jan Witkowski, James Duffy, Pat Barker

Third Row: Dill Ayres, John Inglis, Dave Micklos

Promotions

On January 1, 2002, Lilian Gann was appointed Associate Dean of the Watson School of Biological Sciences. Lilian joined the Laboratory in March 1999 as Assistant Dean of the Watson School. Other promotions this year included Douglas Conklin to Research Investigator; Shivinder Grewal to Associate Professor; Gregory Hannon to Professor; Eli Hatchwell to Investigator; John Healy to Computer Scientist; David Jackson to Associate Professor; and Michael Zhang to Professor.

Departures

Michael Hengartner, Associate Professor, departed this year to take a position as Professor in the Institute of Molecular Biology at the University of Zürich.

Concluding Remarks

The breadth of our highly successful research and education programs is a testament to the people who work here and those who chose to support the Laboratory financially and otherwise. I am most fortunate to work at an institution that savors past accomplishments, yet does not rest on its laurels. We need to move forward, particularly in research that I believe will eventually help to control cancer, and at the same time invest in research on understanding the brain, one of the frontiers of modern biology that has a long way to go before we can comprehend how we learn, think, and behave. But the core of our future success will be securing the necessary funds to allow our scientists to do what they do best and not what grant reviewers think is best.

Bruce Stillman
Director