Bioinformatics at the Heart of Research
**Team Science**

> Scientific discovery in the biological and biomedical sciences is brimming with breakthroughs, opening new frontiers at a pace never witnessed before. The fact that science today is so nimble and quick is partly due to advances in technology that impose fewer limits on the rate of discovery. Another factor is that complex scientific research projects are increasingly accomplished by larger groups of researchers. This seems to defy common sense: Ever larger groups of people are performing ever more complex work in ever more productive fashion. It’s a minor miracle, made possible by a fundamental change in the way scientific work has come to be organized at this moment of profound technological innovation.

Historical images of reclusive scientists toiling alone in a remote laboratories are for the most part just that — history. The contemporary scientist is an interactive leader of and participant in a multidisciplinary team, who constantly searches far and wide for the optimal combination of expertise, tools and funding to make his or her project a success. Just glance at the long list of authors in many contemporary scientific papers. The message is clear: Teamwork today is indispensable.

Technological advances have enabled, and in many cases demanded, closer collaboration and interaction between investigators separated by geographic and institutional boundaries. Where traditionally, research initiatives were led by one principal investigator, now multiple investigators contribute synergistically to projects, sharing success and credit. Some researchers today may not have an independent faculty position. Nonetheless, they are essential for the successful execution of projects and need to be recognized appropriately for their contributions. This new way of doing research also necessitates new models for supporting research, something we have not yet achieved at the institutional level.

The fundamentally new face that research presents across the life sciences today is exemplified in the integration of quantitative biology. The subfield of bioinformatics is at the very heart of today’s biomedical revolution, providing computational and mathematical analysis of complex data sets. It is the cornerstone for the recent explosion of discoveries and is a discipline that is represented in most scientific research projects at CSHL. Even cancer researchers like me use the products of bioinformatics research via the use of databases. Geneticists can’t map genes without it. Molecular biologists can’t find the function of a gene without it. Neuroscientists can’t understand the brain without it. Plant biologists can’t know their favorite plant without it. (Learn more on page 2.)

The idea of collaborative effort, while new to some, is not new to CSHL. It has historically reached out to investigators, research institutions and clinical centers around the world, and remains at the heart of global dialogue on biomedical research. CSHL has purposefully nurtured the collaborative spirit on our campus, a spirit that is fundamentally reflected in campus design. This year, we are working hard to complete and fund our Hillside Campus expansion. Expected to be ready for occupancy in 2009, it will be a research center that will physically intertwine quantitative biologists with those studying human genetics, cancer and neurobiology. By creating buildings that encourage the mingling of scientists with varied expertise — but a common scientific mission — CSHL will advance research in diseases such as autism, schizophrenia and cancer.

We’ve moved decisively from an age of “silo” science to a way of doing science characterized by multidisciplinarity, collaboration and interactivity. The complexity that attends the resulting “network effects” can be expected to yield scientific insights of unprecedented subtlety and richness.
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Contents

p. 2 » Math, Statistics and Computing:
The Heart of Contemporary Biology
How math, statistics and computing define the latest disciplines in the life sciences: bioinformatics, computational biology and quantitative biology.
Peter Tarr

p. 5 » Awards
Kudos to CSHL faculty, postdoctoral students, scientific journals, educational programs and the Hillside Campus expansion project!

p. 6 » Fighting Malaria with DNA Barcoding
CSHL’s Banbury Center brings DNA barcoding technology to the fight against malaria.
John Connolly

p. 8 » 2007 Double Helix Medals Award Dinner
New Yorkers at their best: The 2007 Double Helix Medals Dinner celebrates biomedical science and philanthropy.
Jim Bono

p. 12 » Science Is Star Trek; Law School Is Trivial Pursuit
How biology and CSHL shaped the career of biotech industry pioneer Karen Talmadge, Ph.D.
Kiryn Haslinger

p. 14 » Members Only
A peek at CSHL President’s Council members getting hands-on exposure to RNA interference, with top investigators and Nobel laureates as instructors.
Gayle Quaglia

p. 16 » Research Locally, Share Globally
Renovation and expansion of facilities at CSHL will bring new library and archives resources to investigators and students on campus and online around the world.
Gayle Quaglia

p. 17 » Lab Notes
The Harbor Transcript’s editor-in-chief invites you to a new feature!

back cover » Upcoming Events/CSHL Association

Front Cover: Bioinformatics, computational biology and quantitative biology provide the muscle for today’s biomedical breakthroughs. © www.medi-mation.com
Math, Statistics and Computing

The Heart of Contemporary Biology
What roles do math, statistics and computing play in biological research?

Ask the principal investigator of virtually any research group at Cold Spring Harbor Laboratory (CSHL), and the response will be the same: They aren’t accessories to biological research; they’re embedded inextricably — part of the very structure of experimentation throughout the life sciences today.

“Absolutely essential,” says CSHL Professor Nicholas Tonks, speaking of statistical and computational methods integrated into the design and execution of experiments, as well as the subsequent analysis of data in labs everywhere. “These are some of the key technologies that will enable us to make progress over the next couple of years in lots of areas, such as cancer, neurological diseases like Alzheimer’s and Parkinson’s, neuropsychiatric illnesses like schizophrenia and autism, and all aspects of plant biology and genetics.”

Given the universality of the acknowledgment, it’s ironic that these vital math-based disciplines — all about quantification and precision — are referred to by a fuzzy assortment of names: bioinformatics, computational biology and quantitative biology.

Tool Makers and Tool Users

Mathematicians and computer scientists are making diverse contributions to the great enterprise of understanding life. Their insights are helping biologists who design and make tools for experimentation, as well as aiding biologists who are end users of those tools. CSHL has made seminal contributions in both areas, with tool makers in literally dozens of labs devising new capabilities that their colleagues are putting to novel uses in areas ranging from cancer genomics to neurobiology to plant genetics.

Strictly speaking, “bioinformatics” refers to the activity of gathering, manipulating, interpreting and making accessible the masses of data that experimenters generate. The much-celebrated HapMap (which describes the common patterns of human DNA sequence variation) and Gramene (which describes the comparative mapping of grasses) genome databases developed by CSHL Professor Lincoln Stein and colleagues are outstanding examples of tools that have enabled work in labs around the world.

In contrast, those who employ information science, or informatics, tools to experimentally test biological hypotheses are “computational biologists.” These days, experimenters often design their experiments in close cooperation with informatics experts. The quantitative dimension is thus woven into the very fabric of contemporary biology.

At the heart of the informatics revolution is the suite of technologies and techniques that made possible the sequencing of the human genome. The Human Genome Project spurred the development of gene-sequencing machines and the computer software capable of stitching together the thousands of independently sequenced DNA segments into a continuous, comprehensive “human reference genome,” some three billion nucleotides in length. At CSHL, Professor W. Richard McCombie and colleagues are working to fine-tune the most powerful and cost-effective elaboration of gene-sequencing technology to date, a generation of commercial machines and new software “that in the not-too-distant future is going to make it possible,” McCombie says, “to map mutations in model organisms by simply sequencing their full genomes and comparing them, one to another.” Full-genome sequencing, until now, has been prohibitively expensive.

Probing the Opaque Origins of Disease

Functional genomics describes the effort to probe genomes to obtain fundamental insights about the relationship between structure and function, and about the opaque origins of the dysfunctions that cause disease. It’s a new science rooted in the stunning capabilities of informatics. To the layperson, this informatics
engine is a kind of “black box,” a compendium of sophisticated mathematical procedures, called algorithms, that direct powerful computers to extract bits of meaning from statistical chaos.

Postage-stamp-size glass and silicon slides, or “chips,” called microarrays, spotted with hundreds, thousands, tens of thousands and now millions of distinct DNA or RNA fragments, enable scientists to conduct highly repetitive experiments in “massively parallel” fashion. Entire genomes, including the human genome, can be “assayed” rapidly for gene expression patterns that begin to reveal the connection between disease pathologies and the way genes operate in specific tissues of specific individuals.

Related technologies have enabled computational biologists like CSHL Professor Michael Zhang to correlate gene expression levels with epigenetic events, molecular modifications of DNA that occur across the genome. These changes can have the effect of “turning up” or “turning down” specific genes. CSHL Professor Adrian Krainer has collaborated with Zhang to probe irregularities in the sites at which precursor messenger-RNA is spliced. They want to use epigenetic data to predict splicing events and to understand the role alternative splicing may play in causing a devastating genetic illness called spinal muscular atrophy.

An Alphabet Soup of Innovation

Over the last decade, CSHL Professor Michael Wigler and CSHL Assistant Professor Robert Lucito have pioneered new ways of employing microarrays and advanced statistical tools to peer into the functional properties of genes. An assortment of state-of-the-art probes with alphabet-soup names like RDA, ROMA and CGH have had a profound impact on genome science worldwide. Wigler and CSHL Assistant Professor Jonathan Sebat recently employed one of these techniques to investigate autism, and in so doing have stirred the debate on what causes the disease. Using CGH (comparative genome hybridization), an assay that builds on the fundamental fact that any single strand of DNA or RNA will bind to its molecular “complement” upon contact, Wigler, Sebat and colleagues have conducted experiments linking the propensity to develop autism with variations in the number of copies of specific genes possessed by an individual.

The insight that gene copy-number can vary from person to person or even cell to cell is not new, but the ability to link copy-number variations (CNVs) with individual risk for a specific disease like autism or cancer is potentially revolutionary. CSHL Senior Computer Scientists Alexander Krasnitz and Lakshmi Muthuswamy are informatics experts in the Wigler lab who have been involved in the new work on autism and cancer. “After the data are acquired,” Krasnitz explains, “they undergo various stages of processing. We begin with microarray experiments, which yield an image that is scanned and processed statistically. Various areas of the image are identified with various locations in the genome.”

The “image” to which Krasnitz refers looks like a collection of densely packed red and green dots. These correspond to separate readouts of the particular sample under study (dyed “red”) and portions of the reference-version of the human genome (dyed “green”). “By comparing those two channels, we determine the relative copy number of genes we’re interested in at particular locations in the genome,” Krasnitz says.

This is only the beginning of a process, Muthuswamy points out, that also involves trying to account for possible irregularities introduced by the experiment itself, and then trying to determine which of the signals read off the arrays are true, and which are false. The details boggle the mind and involve further parsing of “coherent noise” from “incoherent noise.” But the overall purpose of the exercise, Muthuswamy says, “is to distinguish signal from noise, so you can arrive at true information about the relative number of gene copies in a given tissue sample versus the reference genome.”

“The key discipline in all of this is statistics,” Krasnitz stresses. In the specific example of efforts of the Wigler and Sebat labs to employ CGH and novel algorithms to interpret data scanned from microarrays, the revelation that much of autism might be caused by spontaneous gene mutations — and not, as current consensus holds, by comparatively minor contributions of many genes acting in concert — is a potential game-changer in the quest for effective autism treatments. It’s one of literally dozens of efforts under way at CSHL in which complex statistical and computer tools are helping get to the bottom of major diseases afflicting people everywhere. Peter Tarr
Winter/Spring 2008

**HHMI Grant for Precollege Education**

CSHL is the only New York metro area institution awarded a five-year grant for its precollege science education programs from Howard Hughes Medical Institute (HHMI). This grant has enabled CSHL to open a DNA Learning Center in a Harlem public school, which will not only train local urban teachers but give the students an opportunity to participate in real laboratory DNA experiments. As one of only 31 precollege grants awarded by HHMI, CSHL’s program will be a model for how research institutions can interact with large school systems and transform science education for urban students.

**Gregory Hannon Wins Paul Marks Medal**

Gregory Hannon, Cold Spring Harbor Laboratory (CSHL) professor and Howard Hughes Medical Institute (HHMI) investigator, was awarded the Memorial Sloan-Kettering Cancer Center’s 2007 Paul Marks Prize for cancer research. Hannon, along with two other investigators under the age of 45, received a medal and a share of a $150,000 cash award. The Paul Marks Medal is awarded to young investigators who are already leaders in their respective fields and who have made significant contributions to the basic understanding and treatment of cancer.

**Pathway to Independence Award**

Alexei Aravin, a CSHL postdoctoral fellow in Gregory Hannon’s laboratory, was awarded the K99 Path to Independence Award from the National Institute of Child Health and Human Development. A new award given by the National Institutes of Health (NIH), it provides funding for one to two years of mentored postdoctoral research and three to five years of independent research. Aravin is the second CSHL researcher in Hannon’s laboratory to receive this prestigious award this year; José Silva received one earlier in the year.

**CSHL in Top One Percent of “Highly Cited Papers”**

CSHL ranks among the most published and cited institutions according to a study released by Thomson Scientific’s *Essential Science Indicators*. The analysis placed CSHL in the top one percent of papers cited most by molecular biology and genetics researchers from 2002–2006. According to the ranking, CSHL research was the third most-cited research institution during the five-year period. With nearly 11,000 total citations, CSHL ranked sixth among its peers, placing CSHL research teams among the elite in molecular biology and genetics. In addition, *Genes and Development*, a publication of CSHL Press, ranked sixth in the category of journals that publish high-impact research in molecular biology and genetics. As for individual researchers, CSHL Professor and HHMI Investigator Gregory Hannon was identified as having contributed at least eight high-impact reports during the same period of time.

**Joan’s Legacy**

Raffaella Sordella, a CSHL assistant professor, was awarded $100,000 by Joan’s Legacy: The Joan Scarangello Foundation to Conquer Lung Cancer. The two-year grant will fund CSHL’s pioneering lung cancer research involving a new class of genetic mutations that appear to be a trigger in non-small cell lung cancer, the leading cause of cancer deaths in the U.S. The Joan’s Legacy grant awarded to Sordella is part of a $1.2 million grant designated by the foundation for 12 researchers conducting innovative projects at nationally recognized institutions. This is the second time Joan’s Legacy has awarded a grant to a CSHL researcher; in 2005 David Mu received one that enabled his 2007 discovery of three new genes that cause lung cancer.

**NYS Grant for Hillside Campus**

This past January Empire State Development announced a $2 million grant to purchase new equipment for the Hillside Campus facilities project. The grant reaffirms New York State’s commitment to encouraging the growth of the local biotech industry and recognizes CSHL’s long history of research discoveries that improve the human condition. The Hillside Campus will bring 40 new scientists to CSHL. It is estimated that for each scientific job created at CSHL, five additional jobs are created to support that scientist’s work. This grant is in addition to the $380,933 awarded to CSHL by the Empire State Stem Cell Board as part of New York State’s multiyear stem cell research program earlier that month. These funds will support the work of CSHL’s Patrick Paddison, Linda Van Aelst, Grigori Enikolopov and Marja Timmermans.
Fighting Malaria with DNA Barcoding
Each year, malaria infects at least 500 million people, killing between one and three million, the vast majority of whom are children under the age of five. Intervention has been hampered by the existence of about 3,500 species of mosquitoes that spread the disease and respond differently to intervention. By spearheading a technique for identifying species, CSHL's Banbury Center has played a unique role in efforts to eradicate the disease. The technique, called DNA barcoding, is a triumph for "big picture" science — the hallmark of Cold Spring Harbor Laboratory's Banbury Center for 30 years.

DNA barcoding was developed by Paul Herbert at the University of Guelph in 2003 as a research tool for the field of taxonomy (the science of naming organisms). The technique centers on a gene called cytochrome c oxidase I (COI). COI is the perfect gene for differentiating organisms — it's found in every member of the animal kingdom, it's short and therefore manageable, and it's located in mitochondria, making it easily accessible to researchers. What makes it especially useful, however, is that COI is unique in every species on the planet. Even though all creatures share a copy of the COI gene, that copy is different in each species.

The Alfred P. Sloan Foundation, known for promoting new areas of biological research, decided that barcoding was an important initiative that justified further development. Jesse Ausubel, the Sloan Foundation program officer who took on the project, contacted Witkowski about a workshop to explore the promises (and pitfalls) of DNA barcoding. That discussion proved fruitful. On March 9, 2003, the Banbury Center partnered with the Sloan Foundation and brought together a distinguished group of researchers from Europe and North America to explore Taxonomy and DNA.

The group devised many potential applications for DNA barcoding, of which the Mosquito Barcoding Initiative (MBI) is the example with the highest profile. The MBI was subsequently adopted by London’s Natural History Museum and has already had a substantial impact on malarial research. Three hundred ninety mosquito species have been barcoded, and 27 new species have been identified. Not all mosquitoes carry malaria, and some are considerably more virulent than others, but the use of DNA barcoding has made it easier to identify and target the most lethal species.

A case in point is Anopheles oswaldoi, which was known to carry malaria in northern Brazil but for unknown reasons was benign in the southern regions of the country. By using DNA barcoding, researchers were able to establish that the A. oswaldoi was not one but four different species — only one of which carries malaria. By controlling the spread of that carrier, researchers can effectively control the spread of the disease.

During the next two years, the MBI aims to barcode 80 percent of the world’s mosquitoes, which may be carriers of lethal diseases such as West Nile virus and dengue fever, in addition to malaria.

DNA barcoding is also being piloted in fields as varied as customs control (to target the illegal transportation of wildlife) and aviation administration (to identify which birds strike planes most often). Among the items currently under discussion is a proposal to add multigene capabilities to barcoders. This would add flexibility to the technique and make it possible to also study vegetation. This places major ecological issues, such as the management of biodiversity, on the barcoding radar. In short, an entirely new field of scientific inquiry has taken shape. “As a consequence of these meetings,” Witkowski reflects, “a whole ‘industry’ of barcoding has developed and is being used widely throughout the world.”

The success of the DNA barcoding meeting owes much to the approach of the “Banbury Style.” Witkowski organizes up to 24 meetings each year, which span the gamut of molecular, neural and biomedical research. Although topics vary widely, the meetings share one purpose — the advancement of breakthrough science. Banbury Center meetings are intended to forge new ground in intellectual inquiry by critically assessing the often-controversial state of play in the field under review. Witkowski has the unenviable responsibility of making this happen. Toward this end, he outlines a few simple rules. “The first,” he says, “is the size of the group. It’s small enough that everybody has to contribute. You’re conspicuous if you don’t speak up and take part. But it’s also a sufficiently large number to ensure an interesting mix of experts.”

Because of Banbury’s role in leading science innovation, the focus is on policy implementation. The limited number of participants — between 24 and 36 — is large enough to ensure a good range of opinion, but not so large that opinions get lost in the cacophony.

For this concept to work, however, it is important to have the right mix of scientists, and diversity is critical. “With every meeting I do, somebody calls to ask why they’ve been invited. They see the title of the meeting; they even see a description of what the meeting is about, and they still can’t understand why they’ve been invited. And that, I think, is a rather good thing to happen.” explains Witkowski.

Cognitive diversity, which refers to different styles of thinking, is decisive in engendering the mix of ideas from which ingenuity prospers. Every Banbury meeting brings together opinion leaders from diverse fields to innovate. Attendees at the “Taxonomy and DNA” meeting in 2003 had backgrounds in bioinformatics, ecology, evolution, genetics, microbiology, molecular biology, neurobiology, oceanography, taxonomy, telecommunications and zoology.

This harks back to the founding of the Banbury Center, which was introduced as a conference center in 1977. The center was donated to CSHL by Charles Robertson, a philanthropist from Lloyd Harbor, N.Y. Through the Banbury Center Robertson hoped “to win the big prize.” There are few prizes bigger than the eradication of malaria, and this recipe for “big picture” science has made Banbury a focal point of scientific communication. On June 14, 1977, when Nobel laureate Francis Crick gave the dedicatory address there, he spoke of the free exchange of opinions and information, and of the importance of communication to fostering new ideas. This has been the “Banbury Style” ever since. John Connolly
2007 Double Helix Medals Award Dinner

raises millions for CSHL research
New Yorkers are often stereotyped as hard-driving, uncaring and aloof, but the Double Helix Medals Dinner completely shatters that myth.

On November 8, 2007, some of the most generous people in New York City came to the Mandarin Oriental Hotel along Columbus Circle. They gathered at this picturesque venue overlooking Central Park for the second Double Helix Medals Dinner to support Cold Spring Harbor Laboratory (CSHL) and to honor David H. Koch, Dr. Richard Axel and Dr. Michael Wigler.

The Double Helix Medal refers to the unique structure of the DNA molecule, which carries all of life’s information. The term “Double Helix” was selected because the structure is central to all biological research and is at the heart of the work performed at CSHL. Today, under the leadership of President Bruce Stillman, Ph.D., more than 400 scientists conduct groundbreaking research to help us understand and treat cancer, autism, schizophrenia, Parkinson’s disease and other causes of human suffering.

“As an institution, Cold Spring Harbor Laboratory has long been recognized for its excellence in biological and biomedical science research,” Stillman said during the awards ceremony. “It is therefore fitting that we recognize individuals who have dedicated their lives to conducting or supporting genetics research that will improve the health of people everywhere.”

Hundreds of friends and supporters celebrated at the black-tie gala as the event’s master of ceremony, Phil Donahue, seamlessly navigated through the evening with sophistication and a healthy dose of self-deprecating humor.

Honorary CSHL trustee Evelyn Lauder of The Estée Lauder Companies Inc., graciously presented Double Helix Medals to Nobel laureate Dr. Richard Axel and Dr. Michael Wigler, CSHL professor. The two friends and research colleagues collaborated to discover cotransformation, a novel gene transfer technique that permits the introduction of virtually any gene into any cell, leading to numerous novel therapies that benefit mankind.

Hillie Mahoney, one of CSHL’s most benevolent supporters, presented the Double Helix Medal to David H. Koch, co-owner and executive vice president of Koch Industries, the largest privately held company in America. A CSHL trustee from 1992 to 1998, Koch has personally pledged and contributed more than $400 million to organizations and programs that further cancer research, enhance medical centers, support educational institutions, and sustain art and cultural institutions.

Koch’s speech touched everyone at the dinner. His passion for finding a prostate cancer cure was felt throughout the room. As he described how he and his three brothers had been diagnosed with prostate cancer, his eyes welled up with emotion, and he stressed his determination to protect his two young sons from contracting this disease. “It is their well-being that is a powerful incentive to continue to support prostate cancer research,” Koch said.

Thanks to David Koch and all of the supporters of the Double Helix Medals Dinner that evening, CSHL raised $3.1 million to continue our mission to prevail over cancers, neurological diseases and other forms of human suffering.

Please visit our special Web site dedicated to the Double Helix Medals, where you can see pictures and videos of the event, the honorees and our generous supporters: http://doublehelixmedals.cshl.edu

Jim Bono
2007
Double Helix
Medals Award Dinner

Violinist Jourdan Urbach

Drs. Paul and Joan Marks; Dr. and Mrs. Michael Wigler

Dr. Bruce Stillman and Julia Koch; Lisa Kennedy DiCicco, Michael Kennedy, Elenora Kennedy
**Science Is *Star Trek*; Law School Is Trivial Pursuit**

**Cold Spring Harbor alumna **

**Karen Talmadge** talks about making it in science and society

> John Fiddes and Karen Talmadge’s first Christmas together at CSHL in their apartment above the Hershey Laboratory in 1982.

**HT:** Why study biology?

**KT:** I am fascinated the most by medical sciences — the nexus of chemistry and biology. That’s where things are so elegant and powerful, with direct application to our daily lives. The structure of DNA is the epitome of why one should absolutely love molecular biology. The matching DNA base pairs allow one DNA strand to dictate the sequence of the other, and allow the strands to unzip to be copied for cellular processes or reproduction. The power of that simple chemistry to explain the complexity of genes!

**HT:** You were at Cold Spring Harbor Laboratory as a postdoc in the 1980s. How did it happen that you and your husband John Fiddes worked as scientists at CSHL?

**KT:** I began my graduate work at Harvard during the time that recombinant DNA techniques were being developed and becoming controversial. I was in the lab of Wally Gilbert, who proposed building a P3 facility (to provide a high level of protection) for recombinant DNA research. Groups outside the university expressed safety concerns, and Wally encouraged me to help coordinate our department’s response to the community.

That introduced me to a host of issues related to science and society, which I thought were fascinating. As I finished my Ph.D. and began my postdoctoral studies, also with Wally, I decided to pursue this area by going to Columbia Law School. I loved it! It was the most fun I had ever had in a classroom. But, I quickly realized that I didn’t want to be an attorney.
To me, law school was the best game of Trivial Pursuit you could ever play. But science is Star Trek. It’s the search of the unknown. It’s finding out what’s new. In science, we haven’t created the rules. We’re finding out about the universe. We’re finding out about things that are fundamentally independent of us, which we can observe and bring into our own understanding and knowledge to advance society in meaningful ways.

I said, “I’ve got to go back to science.” My husband, John, a staff scientist at CSHL at the time, suggested, “Why don’t you postdoc here?”

**HT:** What made CSHL different?

**KT:** It’s different because of the special nature of the campus and the collection of scientists. The strength of CSHL was always to recognize good science, important science, and to bring together people who were at the top of their game doing research that was basic and yet very relevant to health.

During the summer, scientists from all over the world would gather for the courses — with world-renowned faculty attracting young scientists like me, along with experienced scientists seeking new research avenues. The intellectual fervor and fermentation of that time! Every two weeks a new course would begin. There’d be a whole new group of people when you’d come down to the lawn from the lab, and you’d join their happy hour and have a conversation that would change your experiment within minutes!

During the long winter, you worked with the community of scientists at the Lab, who brought their disparate scientific interests to create a bubbling broth — a fantastic stew of scientific progress and scientific focus. It was a truly formative time for me.

**HT:** Later in your career, you co-founded a medical device company called Kyphon, which was bought by Medtronic for $4.2 billion in November 2007.

**KT:** I left Cold Spring Harbor Laboratory to join a biotech company. My role morphed when some of my early interest in science and society reappeared. I became responsible for both the research and the operations of a diabetes and obesity subsidiary, and I had a business role interacting with Pfizer, which had funded this subsidiary.

All of the information I had gathered from science, law school and business was there when one day — 10 years after joining the biotech company — I met an orthopedic surgeon with a new concept for treating fractures of the spine. His proposed procedure was elegant and straightforward: Inflate appropriate balloons inside crushed bone to restore anatomy; remove the balloons and maintain the restored anatomy with a standard biocompatible plastic polymer. When I looked into the clinical literature, I also saw a tremendous need for this in patients, so I left the biotech company to pursue it with him.

It was difficult to persuade people to invest, but we finally opened the doors of Kyphon in 1996. Last year, we had 1,300 employees operating in more than 45 countries. This growth attracted the interest of the biggest medical device company in the world — Medtronic.

**HT:** What about your interest in diabetes? You mentioned it in your work in biotech and you have also shown a very personal philanthropic interest in this disease.

**KT:** John and I diagnosed our daughter’s Type 1 diabetes when she was only 2 years old. My background in diabetes, from my work at Harvard (producing insulin in bacteria), and my diabetes and obesity role at the biotech company taught me about the burden of diabetes, which I now witness every day at home. That’s why I’ve volunteered for the American Diabetes Association for 15 years, currently serving in multiple roles, including as a member of its Research Foundation board of directors.

**HT:** How did your time at CSHL influence your career?

**KT:** At Harvard and Cold Spring Harbor Laboratory, your mentors and your peers are not going to accept sloppy thinking. They challenge you, and you ultimately become your own worst critic, with a goal of having answers before anyone asks the questions. You welcome criticism. You welcome new thinking. You expand, learn and grow because of it. This is why I was willing to start a company to change the way we treat spinal fractures, and how I was able to accept and address the initial skepticism.

*Interview conducted, condensed and edited by Kiryn Haslinger*
RNA interference (RNAi) was discovered by accident through attempts to intensify the color of purple petunias. The unexpected result of adding an extra copy of a pigment gene to the DNA of a light purple petunia plant was light purple petals with white stripes. The experiment had accidentally triggered the plants to produce double stranded RNA and suppress, instead of augment, the gene for pigment. RNAi research today shows incredible promise for the development of new drugs to combat a wide range of human diseases.
Imagine listening to a world-renowned scientist, even a Nobel laureate, talk about the most recent discovery of RNA interference (RNAi) over a drink. Now, imagine the two of you are involved in an RNAi experiment together. This, and more, is what members of Cold Spring Harbor Laboratory’s (CSHL) President’s Council enjoyed at their 13th annual meeting, “The RNAi Revolution.”

Members of the council, who make contributions to CSHL of $25,000 or more annually, are invited by the president, Dr. Bruce Stillman, to participate in a special two-day symposium showcasing cutting-edge science. This year’s symposium illuminated the power of RNAi, a mechanism that regulates the expression of genes so that genetic messages are not translated into proteins. It could allow scientists to inhibit genes that give rise to diseases such as cancer. The 2007 meeting was co-chaired by Jane and John H. Friedman, of Easton Capital, an investment group focused primarily on science and health, who are longtime friends of CSHL and patrons of both art and science; Dr. William A. Haseltine, founder and former chairman of Human Genome Sciences, chairman of Haseltine Global Health LLC, and president of the Haseltine Foundation for Medical Sciences and the Arts; and George F. Ohrstrom, president of the Ohrstrom Foundation, which is dedicated to education, civic affairs, conservation, medical research and art.

Members were briefed on “The ABC’s of RNAi” by Nobel laureate Sydney Brenner. They also listened to lectures and watched demonstrations at the Dolan DNA Learning Center (DNALC). Guest lecturers were David Micklos, executive director, DNALC; Bruce Nash, assistant director for science, DNALC; Marja Timmermans, associate professor, CSHL; Gregory Hannon, CSHL professor and Howard Hughes Medical Institute investigator; and Phillip Sharp, Nobel laureate and institute professor, Center for Cancer Research, Massachusetts Institute of Technology.

The annual contributions of the President’s Council, which total more than $500,000, support the Cold Spring Harbor Fellows, a group of outstanding postdoctoral scientists who demonstrate the capacity for independent, high-level biomedical research. Long-time CSHL supporter and honorary trustee, Mary D. Lindsay, a member of the President’s Council since its inception in 1994, described her experience: “As a reward for our generosity, the council was invited to spend a weekend at the Lab learning about RNAi. I witnessed RNAi in action ... I examined worms that had genes turned off by feeding the worms double-stranded RNA. It was mind-boggling.”

Joan Tilney, who joined the President’s Council in 2007, was also delighted with the event. “Participating in the President’s Council weekend was like a homecoming for me. My husband, Bob Olney, and I were involved in the Lab during the ’60s and ’70s when we lived in Cold Spring Harbor. My husband eventually became treasurer of the CSHL Board of Trustees. In October, I traveled from my home in Maine to join the President’s Council for this tremendously stimulating meeting. The money raised by the council goes to support the exceptionally talented scientists in the fellows program, and I feel very blessed to be involved.”

For more information about the President’s Council, contact Kiryn Haslinger at (516) 367-8841 or haslinge@cshl.edu.

Gayle Quaglia
Promoting education for scientists and nonscientists alike is an integral part of Cold Spring Harbor Laboratory’s (CSHL) mission. The next chapter toward fulfilling that mission is marked by the current expansion of the CSHL Library and Archives, which will enable broad access to the unique and ever-expanding collection of materials for studying the history of molecular biology, genetics, genomics and biotechnology.

The groundbreaking for the expansion began in the fall of 2007 with a ceremony hosted by CSHL President Bruce Stillman. With nearly 100 friends and guests in attendance, Stillman explained that “Cold Spring Harbor Laboratory holds a very important place in the history of genetics and continues to be positioned at the leading edge of molecular genetics research. The expansion of the library and the use of modern technology will provide us with even more opportunities to share knowledge and experience with scientists, students and the general public around the world.”

For decades, the CSHL Library and Archives has collected materials that document scientific research, including the collections of several notable scientists. According to Mila Pollock, executive director of the CSHL Library and Archives, “Dedicated to the idea that historical research material provides the foundation for future discoveries, CSHL set out to find the best way to acquire, preserve and disseminate research information to a worldwide audience.”

The library and its archives already contain more than 2,000 books on genetics and an extensive archival collection of original documents and reprints — an unparalleled storehouse of knowledge. In 2006, CSHL received a generous gift from the pioneering biotechnology firm Genentech to establish the Genentech Center for the History of Molecular Biology and Biotechnology. The center aims to preserve the history of important scientific research in molecular biology and biotechnology through the acquisition of new collections, scholarly research, historic meetings and online dissemination.

In addition to digitizing scientific materials to allow computer access from anywhere in the world, research suites are being incorporated into the library, complete with computers and fax machines, for the use of resident and visiting scientists. The expanded facility will be home to the personal material of four Nobel laureates: James Watson, Sydney Brenner, Alfred Hershey and Barbara McClintock, as well as the extensive collection of prominent molecular biologist Norton Zinder.

“This provides the means for key documents that witnessed the historic transformation of genetics research into molecular genetics to be accessible worldwide,” Dr. James Watson said at the event.

The library expansion is made possible by the generous support of CSHL donors, the Josiah Macy, Jr. Foundation, Genentech Inc. and, in particular, the vision and commitment of Waclaw Szybalski, professor emeritus of oncology at the McArdle Laboratory for Cancer Research at the University of Wisconsin–Madison.

At the groundbreaking ceremony, Szybalski recounted his time in the CSHL Library in the 1950s, saying, “I have always had a fondness for libraries and firmly believe in the expansion of the CSHL Library so that others may benefit from the work being done here.” The library expansion project is expected to be completed at the end of 2008. Gayle Quaglia
» As the editor-in-chief of the Cold Spring Harbor Laboratory (CSHL) Harbor Transcript, I have the pleasure of interacting daily with the CSHL community of more than 1,000 scientists, educators, administrators and many others, who all work to make our institution so powerful. “Lab Notes” is a new feature of the Harbor Transcript that gives you the opportunity to interact with the CSHL community, too.

Let us know what you’re thinking!

- Comment on Harbor Transcript articles you’ve read.
- Ask about recent CSHL discoveries that you may have heard about in the news or seen in our press releases, which are posted regularly on our Web site at www.cshl.edu/pressroom.
- Challenge us to explain something that you don’t understand about genetics and molecular biology.
- Do you have a question about cancer research?
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- Any follow-up questions to the bioinformatics article in this edition?
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- Share your ideas for future Harbor Transcript stories.
- Give us your perspective on the importance of science today.

I will publish notes we receive from you, along with responses from the experts in the CSHL community — our scientists, staff and students!

Please send your notes to me at pubaff@cshl.edu or by postal mail at:

Dagnia Zeidlickis
Cold Spring Harbor Laboratory
Department of Public Affairs
1 Bungtown Road
Cold Spring Harbor, NY 11724

Best,

[Signature]
CSHL Association

The Cold Spring Harbor Laboratory Association comprises some 1,000 neighbors and friends who contribute to the Annual Fund, an essential source of unrestricted support for outstanding young scientists and their promising, early-stage research projects. Association members get to know CSHL scientists at lectures, concerts, dinners and other social events that support the Laboratory. Membership levels start at $100 per year. For more information, please contact Diane Fagiola, director of development, at 516-367-8471 or fagiola@cshl.edu

Upcoming Events

To celebrate the 10th annual Jazz at the Lab, CSHL spices up this year’s event with The Lab goes Latin! Come join us for a night of dinner and dancing at the Nature Conservancy in Cold Spring Harbor.

The Lab goes Latin! is a critical fundraiser for the Laboratory’s annual fund, which provides unrestricted resources for biomedical research in cancer and neurological disorders including autism, Alzheimer’s and Parkinson’s disease. Tickets start at $350 per person; we hope to see you on May 10!

For more information, please call Diane Fagiola at 516-367-8471.