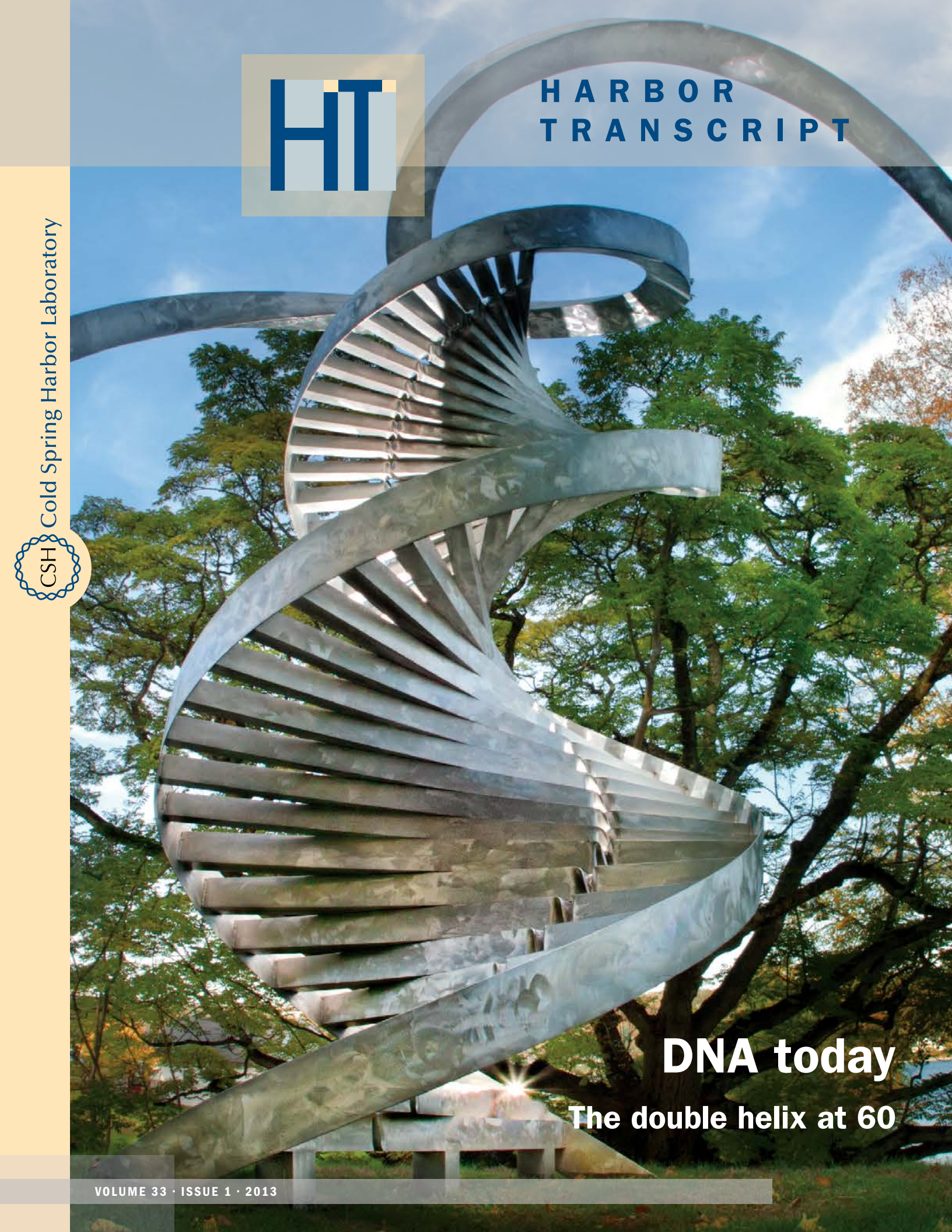


HARBOR TRANSCRIPT

Cold Spring Harbor Laboratory

CSH

DNA today

The double helix at 60

VOLUME 33 · ISSUE 1 · 2013

Cold Spring Harbor Laboratory

PRESIDENT'S MESSAGE

Congratulations to Jim Watson on the 60th anniversary of the discovery of the double helix structure of DNA and to both Jim and his wife Liz on their 45 years of dedication to Cold Spring Harbor Laboratory. That CSHL continues to lead the global field of molecular biology and genetics is a testament to Jim's foresight. Under his auspices, the Lab has enhanced its excellence in basic research and is rated one of the world's top research institutions. Increasingly, our basic research is paying huge dividends in treating diseases such as cancer and neurological disorders.

As we celebrate the 10th graduating class of the Watson School of Biological Sciences, it is clear that Jim's mark on the field of scientific education is no less significant. The Ph.D. program that bears the Watson name trains scientists to have an impact on both science and society. This dual objective resonates throughout our educational programs, from the CSHL Meetings & Courses to the Banbury Conference Center, the CSHL Press and the DNA Learning Center.

We were proud to invite our neighbors to an Open House this spring. So many people drive past our campus daily without fully grasping the significance of what our people contribute to science and medicine. It's important that we take every opportunity to remind the public that research makes a difference. What we do at CSHL has an impact on some of the biggest issues of the 21st century, like healthcare, the environment, agriculture, and clean energy.

This *Harbor Transcript* provides a snapshot of our many varied programs that I hope you will share with your own neighbors and help us open the doors of CSHL to more friends. (The *HT* is also available electronically via the CSHL website and as an interactive iPad app.) Research at CSHL has made a difference to many who suffer from disease, and our work is also contributing to the economic well-being of Long Island and the nation.

The future of federal funding for research is in a state of limbo as our elected officials continue to grapple with federal deficits. We can't expect public funding without greater public awareness that research really does matter. I hope you will use this *Harbor Transcript* to promote our research with your own friends and neighbors. As Jim Watson will attest, the last 60 years have yielded great advances in the history of biology, setting the stage for even bigger breakthroughs that will undoubtedly change the world for the better.

Harbor Transcript

Volume 33, Issue 1, 2013

Harbor Transcript is published by the Department of Public Affairs of Cold Spring Harbor Laboratory.

Public Affairs
One Bungtown Road
Cold Spring Harbor, NY 11724

516.367.8455
pubaff@cshl.edu

www.cshl.edu

V.P. Communications:
Dagnia Zeidlickis
Managing Editor:
Phil Renna
Science Writers:
Edward Brydon
Peter Tarr
Design & Layout:
Margot Bennett
Photography:
Constance Brukin: front cover, 1, 4–5, 6–7, 10, 15;
Charles Camarda: inside front cover;
Courtesy David Spector: 1, 10, 12;
Courtesy Erkan Karakas: 1, 10–11;
Courtesy CSHL Archives: 2–3;
Leonard McCombe 1970: 2;
Joan James 1979: 2;
New York Times 1980: 2;
Ed Campodonico 1990 & 1993: 3;
Daniel Goodrich 1991: 3;
Watson Family 1997: 3;
Ross Meurer 2013: 3;
R.I. Kumaran & Zsolt Lazar: lower right 12;
Melanie Eckersley-Maslin & Zsolt Lazar:13;
Courtesy Howard Hughes Medical Center: 14;
Courtesy Duke University: 14;
Philip Renna: 16;
Edward Brydon: 14, back cover
Illustration:
James Duffy: 11;
Catherine Dougherty: inside back cover

Jim & Liz celebrate 45 years

1968

In the living room of Jacob Bronowski, La Jolla, an hour before Jim and Liz married. "On a Monday, Jim called and said, 'Come out and marry me on Thursday!'"

1970

Jim in lean times, in his unadorned office, 2nd floor, Nichols. "I didn't take a salary for six years."

1974

It was LIBA chair Ed Pulling and his wife Lucy (below) who introduced the Watsons to Charles Robertson (right), who provided the endowment seeding future growth.

1978

1979

Hershey dedication: "From the right, you have the famous 'trio' — Luria, Delbrück and Hershey."

Jim: People say I "made" the Lab what it is today. I don't think I created it; I inherited it this way. It was the presence that [Max] Delbrück gave the Lab — the feeling that we were a non-pompous, non-necktie, informal institution. Delbrück was reacting against the sternness and strictness of German academic society. I thought I was maintaining the Lab, or strengthening it. The Symposium, for instance, already existed. We just created more symposia and more meetings. I had a blueprint already in front of me. Did I want to make Cold Spring Harbor different? We were *already* different, from Harvard, from Caltech. The problem I faced was that the Laboratory might fail [financially]. It didn't fit into the pattern by which institutions succeed. That's why the assistance of Ed Pulling [Long Island Biological Association chairman and first fundraiser for the modern Lab] was so important. If we hadn't gotten the [Charles] Robertson gift [in 1973], I'd still be a member of the Harvard faculty!

Liz: When we got the endowment — the Robertson gift — Jim's first move was to buy the marina across the harbor. Walter Page, who headed the Board, didn't think that was a good idea. So Jim resigned — he just stood up at a meeting and resigned. I remember that day — Rufus and Duncan were romping around in the grass at Osterhout, where we then lived and brought up the boys. And Jim came bursting through the shrubs and greenery, saying, "I quit!"

Jim: I told the Board if we didn't save the harbor, I didn't see a future for the Lab, and I was resigning as of that moment, and walked out of the room. About half an hour later they asked me to come back — they would buy the marina. It was the same with the land now occupied by the Hillside campus. If we hadn't acquired that I would have quit again, because I would have seen the Lab as being totally constrained. Being Director is an unusual position. You've got to think 20 years ahead. My experiences at the University of Cambridge and Harvard told me how great institutions behave and what they need.

1980

"We fixed up Davenport House and created this music room, where we had a concert series that went on for three years."

Liz: This is a campus like no other. Jim was aware of what Cambridge was like — styles changed, but it didn't. We started by fixing up all of the fallen-down buildings. Everything here was traditional. And most of the buildings weren't used at all. We have been very lucky in our choice of architects, and in being introduced to Charles Moore, whose firm has designed every single thing contextually.

Jim: You ask about highlights of 45 years. The highlights for us were when something was accomplished. My chief pleasure has been in being with people who are doing things! Not just smart people, but people who want to *accomplish* something. There's a real difference. Looking back, the main conclusion is: as a pair, Liz and I, we did a lot!

1990

With Francis Crick and Lita Annenberg Hazen, the founding donor of the CSHL Neuroscience program, at the Symposium on the Brain.

1991

"Ah, the day we dedicated the Hazen Tower!," with CSHL trustee Bayard Clarkson, M.D.

1993

"Jim knew nothing beforehand about the bronze DNA sculpture. He was very pleased."

At home earlier this year.

2013

1997

Rufus (standing) and Duncan with their parents.

Marking an epochal discovery

On February 28, 1953, Francis Crick and James Watson strolled into the *Eagle*, their local pub in Cambridge, England, and announced to all and sundry present they had "discovered the secret of life." They had solved the structure of DNA, heralding the dawn of a new age in molecular biology and genomics.

Starting February 28, 2013, Cold Spring Harbor Laboratory hosted a 4-day meeting on the 60-year anniversary of that momentous day, a celebration of the announcement that changed the nature of biological research, and a future-looking survey of work yet to be done.

In fact CSHL had played its own role in the dissemination of the discovery. After the publication of Watson and Crick's landmark manuscript in *Nature* earlier in 1953, Watson was invited to present the paper at that summer's Quantitative Biology symposium, focusing on "Viruses."

It was the first presentation of the paper to the global research community, forever associating CSHL with the double helix, and of course with Watson, who would move to the Laboratory to become its director in 1968 (while, for the time, retaining his professorship at Harvard).

To commemorate the occasion, the CSHL bar in the Blackford building, *Winship's*, was redecorated to look like a replica of the *Eagle*, including an authentic-looking sign outside the bar and photographs from the period decorating its interior walls. On entering the bar, Watson was clearly taken with it, and walked around nodding his approval and commenting on the photographs here and there.

The meeting itself, "From Base Pair to Body Plan," was organized by Alex Gann, Dean of the Watson School of Biological Sciences, and Professor Rob Martienssen, with help from Meetings & Courses Executive Director David Stewart.

Nobel Prize winners Christiane Nüsslein-Volhard, Elizabeth Blackburn, Carol Greider, Craig Mello and Sir John Gurdon, as well as many other notable scientists, were among those attending.

While the meeting was held as a celebration, it was "as much about looking forward as looking back," said Stewart.

Speakers detailed the progress of their current research and some speculated on where it was going. It was, as Stewart noted, "a modern scientific meeting, where a lot of new ideas were discussed."

There were many lively debates, something that again quite clearly pleased Watson, who is known for his vigorous and unapologetic discourse.

Even within the forward-looking theme of the meeting there was time enough for a one-hour session late on Saturday afternoon that saw Watson, Sydney Brenner, Matthew Meselson and Walter Gilbert take the podium for some reminiscing. Speaking for about 10 minutes each, they recalled the heady days surrounding the announcement of the structure and the atmosphere in the years immediately following it.

"Someone should pay us to sit in a room and talk about this for a week," said Meselson, only slightly tongue-in-cheek. "I'm serious, because in a few years we'll be gone and so will these stories and details of research."

On March 1st a Gala at Oheka Castle on Long Island capped the anniversary celebration. Over 300 scientists and friends of CSHL attended the event feting Watson and the discovery of the double helix structure of DNA.

Edward Brydon

Top: Christiane Nüsslein-Volhard

Above: Sir John B. Gurdon

Left: From left to right; Sydney Brenner, James Watson, Giorgio Bernardi, Walter Schaffner and Walter Gilbert

Watson School 2013 graduates

Megan Bodnar

Saya Ebbesen

Joseph Calarco

Eyal Gruntman

The Watson School of Biological Sciences, which administers the Ph.D. program of Cold Spring Harbor Laboratory, continues to turn out top-class students.

Megan Bodnar

Starr Centennial Fellow
The dynamics of pluripotency genes upon differentiation of mouse embryonic stem cells

Megan's interest lies in understanding how gene expression is regulated in early embryonic development. For her doctoral work in David Spector's laboratory she focused on several genes related to an embryonic stem cell's potential to become many different cell types. By looking closely at the movement of these genes within the cell nucleus, she was able to identify the DNA elements that allowed the two copies of each gene to "find" each other during differentiation. As Megan pursues a postdoctoral position, she says she feels "very lucky to have been exposed to a wide variety of people and scientific disciplines over such a short period of time."

Joseph Calarco

David Koch Fellow, NSERC Scholar
A system to study chromatin dynamics through pollen development

In Rob Martienssen's laboratory Joe studied the "tagging" of DNA by methylation, a process that he says is "one of the most well studied yet still misunderstood." His major breakthrough came when he was able to show that some of these tags are retained during the sexual reproduction of plant germ cells, unlike their complete genome-wide erasure in mammalian sperm cells. Joe is heading out to Stanford this summer to begin postdoctoral studies.

Saya Ebbesen

Starr Centennial Fellow, NIGMS - NIH Trainee
RNAi mouse models of breast cancer tumor suppressor genes

"The lack of hierarchy, strong sense of community, and the integrated research-centered lifestyle" drew Saya to the Watson School. Under the mentorship of Scott Lowe she pursued the development of new mouse models of breast cancer that integrate RNA interference (RNAi) technology. In the course of her studies she found that in one mouse model of poor-prognosis breast cancer, the continued absence of a tumor suppressor gene is required for sustained growth of established mouse mammary tumors.

Eyal Gruntman

Elisabeth Sloan Livingston Fellow
Integration properties of Kenyon cells in the Drosophila melanogaster *mushroom bodies*

Eyal came from Israel to study at CSHL where, he said, "experiencing a four-season year for the first time in my life was a lot of fun." His studies in Glenn Turner's laboratory were concerned with the sense of smell, known as olfaction. Working with the fruit fly *Drosophila melanogaster*, his work focused on looking at a particular set of cells, Kenyon cells, in an area of the brain called the mushroom body. These cells receive different input impulses from the olfactory cells and are required in turn to trigger a "spike" or output impulse. Eyal moves on to a postdoctoral position at HHMI's Janelia Farm.

Paloma Guzzardo

Felix Schlesinger

Maria Pineda

Petr Znamenskiy

Paloma Guzzardo

Leslie C. Quick, Jr. Fellow, William Randolph Hearst Foundation Scholar, NIGMS - NIH Trainee
Identification and characterization of novel components of the Drosophila *piRNA pathway*

In Greg Hannon's laboratory small RNAs are the unifying research topic. Paloma's studies were concerned with a particular class of small RNAs known as the PIWI-interacting RNAs, or piRNAs, which are known to be important for maintaining genome integrity in the germline. In a large-scale approach, Paloma was part of a team that searched the whole genome of the fruit fly and found more than 80 genes that could be involved in piRNA production and their mechanism of action. Paloma is planning to do a postdoc in Europe but CSHL is such a special place and close-knit community that she was moved to say "I am positive that no other institute will be quite like it."

Maria Pineda

CSHL Women's Partnership for Science Student, William Randolph Hearst Foundation Scholar
Substrate specificity of receptor tyrosine kinases is critical for selective signaling

It was her interest in drug discovery that led Maria to join Raffaella Sordella's laboratory, which focuses on cancer research. In her thesis work Maria aimed to gain an understanding of how genetic mutations in proteins called receptor tyrosine kinases (RTKs) affect treatment response and survival differences in lung tumors. Supporting the idea that biological functions are the result of complex interconnected networks, she found that certain RTKs modify a single target protein such as SOCS3 in different ways. On her future plans Maria said "I want to pursue opportunities that will combine my skills in science and business while having a major impact in healthcare."

Felix Schlesinger

Crick-Clay Fellow
Discovery and classification of transcription at cis*-regulatory elements*

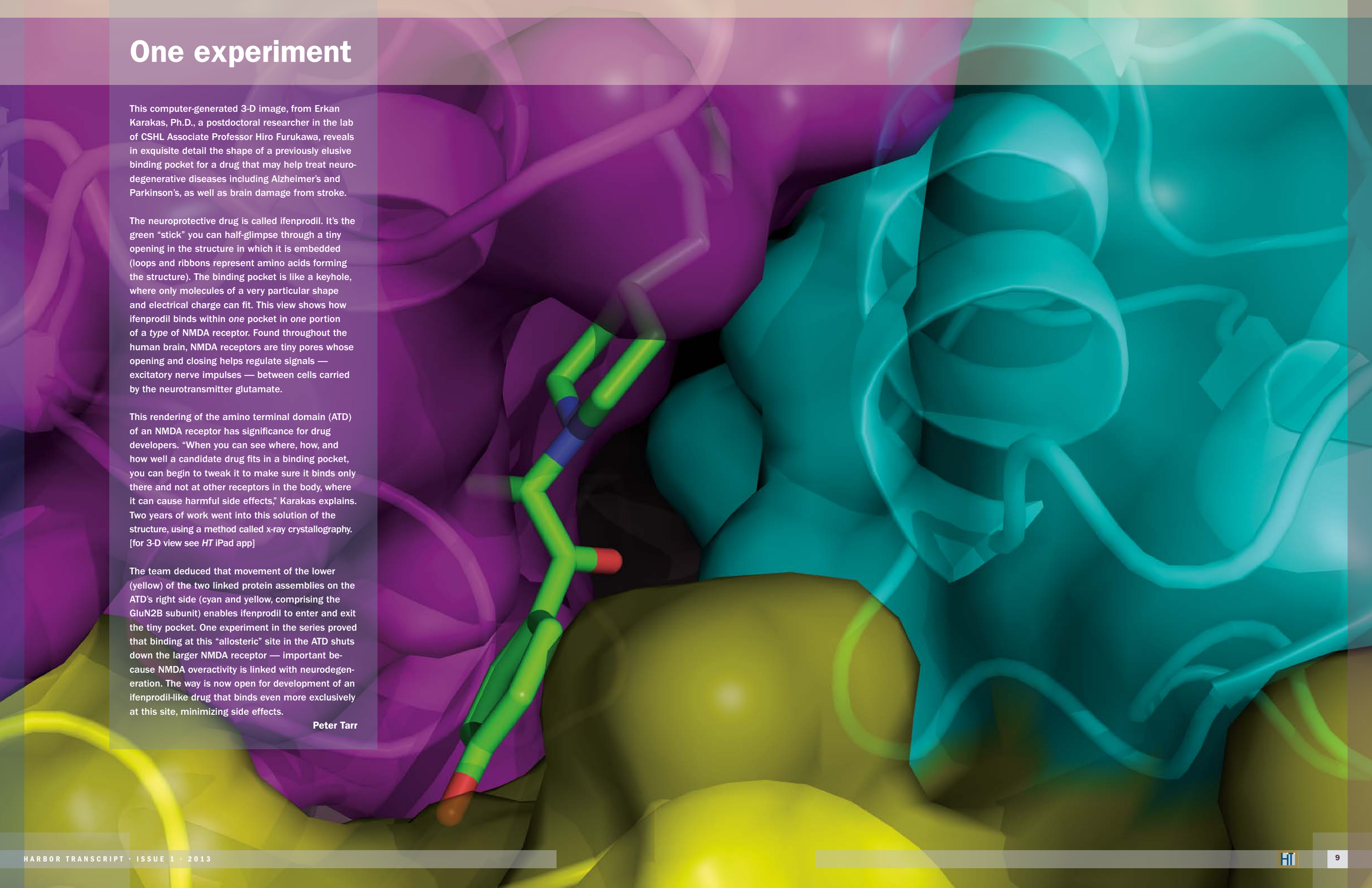
Felix's overall goal during his thesis studies in Thomas Gingeras' laboratory was to better understand how gene regulation is encoded in the human genome. Using computational analyses in a bioinformatics approach, he developed methods for the identification of novel non-protein-coding RNAs and clues to their regulation. His work formed part of the massive collective effort known as the Encyclopedia of DNA elements (ENCODE). Felix is joining Illumina as a Bioinformatics Scientist, but will miss "the great scientific discussion at the CSHL bar after meetings and seminars."

Petr Znamenskiy

David and Fanny Luke Fellow
Role of corticostriatal projections in auditory discrimination

Petr's research in the laboratory of Professor Tony Zador focused on determining the connections between the auditory cortex and other parts of the brain. "The auditory cortex provides a map of sound frequency, and these connections may be important in making judgments about the properties of sounds, e.g., pitch." Petr now moves on to a postdoc at the University of Basel, Switzerland, but will miss the people and camaraderie of CSHL and the Marks building in particular.

One experiment



This computer-generated 3-D image, from Erkan Karakas, Ph.D., a postdoctoral researcher in the lab of CSHL Associate Professor Hiro Furukawa, reveals in exquisite detail the shape of a previously elusive binding pocket for a drug that may help treat neurodegenerative diseases including Alzheimer's and Parkinson's, as well as brain damage from stroke.

The neuroprotective drug is called ifenprodil. It's the green "stick" you can half-glimpse through a tiny opening in the structure in which it is embedded (loops and ribbons represent amino acids forming the structure). The binding pocket is like a keyhole, where only molecules of a very particular shape and electrical charge can fit. This view shows how ifenprodil binds within *one* pocket in *one* portion of a *type* of NMDA receptor. Found throughout the human brain, NMDA receptors are tiny pores whose opening and closing helps regulate signals — excitatory nerve impulses — between cells carried by the neurotransmitter glutamate.

This rendering of the amino terminal domain (ATD) of an NMDA receptor has significance for drug developers. "When you can see where, how, and how well a candidate drug fits in a binding pocket, you can begin to tweak it to make sure it binds only there and not at other receptors in the body, where it can cause harmful side effects," Karakas explains. Two years of work went into this solution of the structure, using a method called x-ray crystallography. [for 3-D view see *HT* iPad app]

The team deduced that movement of the lower (yellow) of the two linked protein assemblies on the ATD's right side (cyan and yellow, comprising the GluN2B subunit) enables ifenprodil to enter and exit the tiny pocket. One experiment in the series proved that binding at this "allosteric" site in the ATD shuts down the larger NMDA receptor — important because NMDA overactivity is linked with neurodegeneration. The way is now open for development of an ifenprodil-like drug that binds even more exclusively at this site, minimizing side effects.

Peter Tarr

RESEARCH PROFILE

David L. Spector

A journey into the nucleus

Molecular biology is a young science — so young that many of today's leading researchers have had a hand in the discoveries that shape the areas in which they specialize. Professor David L. Spector of Cold Spring Harbor Laboratory is one such scientist.

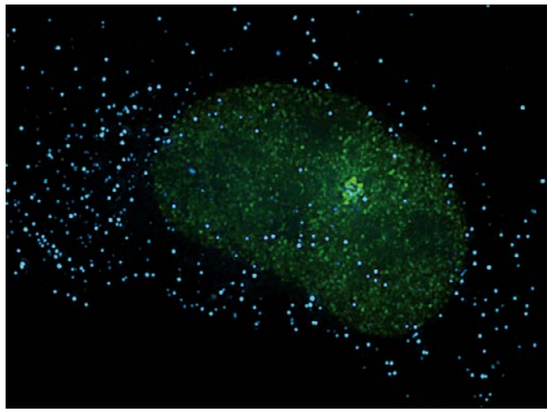
Spector is an enthusiast. To hear him relate a story of discovery in which he and his team have been involved is to be swept up in a tale of suspense, for he tells these stories as if they were mystery thrillers. And, although he probably doesn't realize it, he has the winning custom of discussing the various molecular actors in experiments as if they were people — *dramatis personae* — rather than submicroscopic proteins and nucleic acids.

Spector, who in addition to heading his own lab group holds the demanding position of Director of Research at CSHL, is one of the foremost authorities on the cell nucleus. As depicted on the facing page, the nucleus is almost like a cell within a cell. It's the command center where the genetic material — DNA, the stuff of the genome — resides, and where perhaps the most important activity in all of biology takes place. It's where a variety of tiny molecular machines copy information encoded in the double helix to single-stranded "messenger" molecules made of RNA.

Many of these messenger-RNAs exit the nucleus through tiny pores and migrate to structures in the cell called ribosomes, where they serve as templates for the manufacture of proteins. Proteins are the incredibly diverse class of molecules that do the work and, indeed, form the very structures of the cells and organs of living things.

Spector's lab was the first to visualize this central process — referred to rather dauntingly as "the central dogma of molecular biology" — as it actually unfolds in live cells. In 2004 they released time-lapse movies to the world showing how the expression of a single gene cluster led to the production of RNAs, which, upon leaving the nucleus, were processed by ribosomes to generate proteins that migrated to cellular organelles called peroxisomes.

At the time it was a technological *tour de force*, and over the years, with updates reflecting new technologies, the system he and his team developed to make it possible



Visualizing gene expression: active genes (green cluster) spur production of proteins targeting peroxisomes (blue).

has continued to be useful in labs around the world. But the pace of discovery in biology is relentless, and today, less than a decade later, both Spector and his field have moved, in a real sense, a world beyond the central dogma. The world of their science now reveals how that dogma (DNA → RNA → protein) does not, after all, describe the fate of many expressed genes in the nuclei of our cells. Alas, many RNAs are *not* messages carrying instructions for protein synthesis. But what *do* they do?

A busy, beautiful world

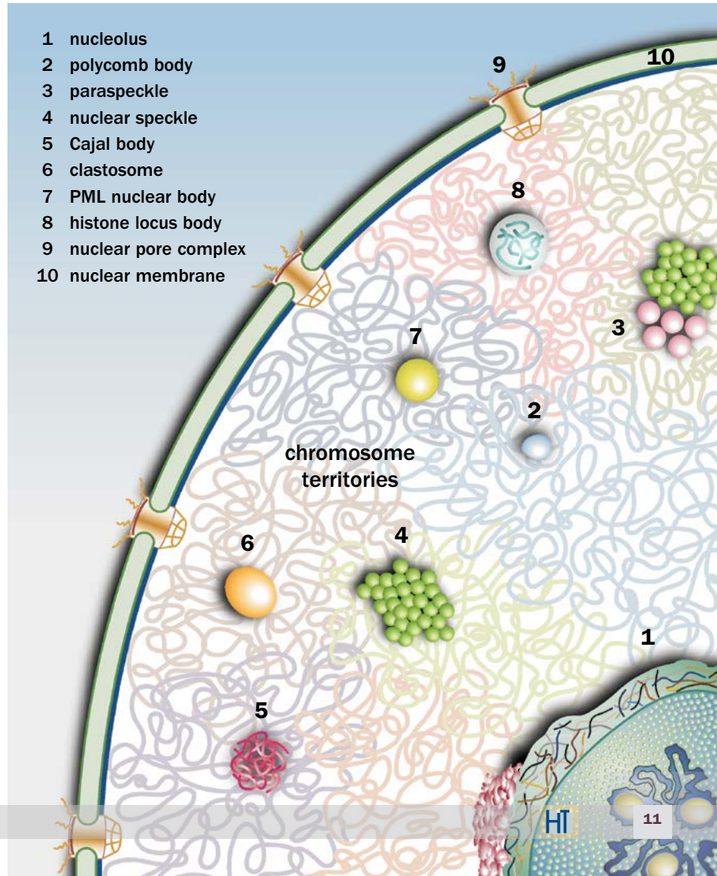
"What most non-scientists don't know," Spector says, "is that there's a lot more to the cell nucleus than DNA." Much of his career has been devoted to characterizing and learning about how various structures — "nuclear bodies" — discovered inside the nucleus perform a variety of functions. As Spector's career has progressed, the nucleus gradually has been revealed, in part by his own research, as a world within the world of the cell — complex, beautiful, dynamic, and very, very busy.

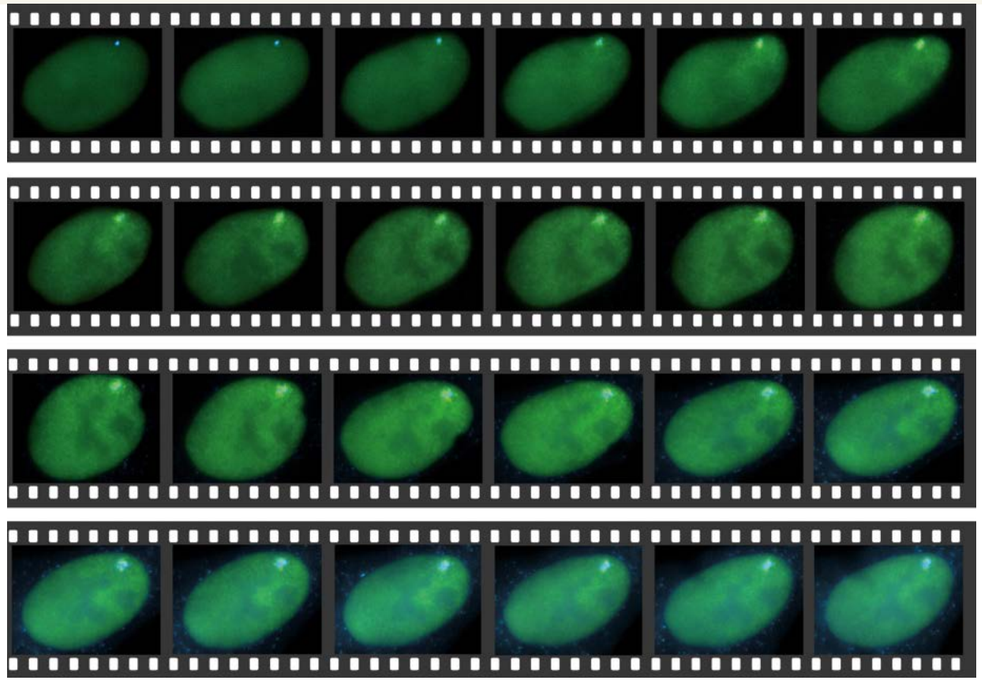
A native New Yorker whose interest in biology was piqued by a City College professor who taught him how to use an electron microscope, Spector became fascinated in a kind of algae called dinoflagellates. By the time he finished his doctoral research at Rutgers University,was nearly ready to publish what proved the first textbook on the tiny marine organisms, responsible for red tides and harmful algal "blooms." By the early 1980s Spector had transferred his attention to mammalian cells, and specifically, to the process by which RNA messages carrying the genetic code are spliced — edited — by fleets of specialized proteins inside the cell nucleus.

At the Baylor College of Medicine, Spector in his first academic appointment headed a group looking at these proteins, called splicing factors. Initially, using antibodies derived from people with autoimmune disorders, it was possible to examine how splicing factors localized in the nucleus and to study their relationship to specific nuclear bodies. "For me, this was the entrée to trying to correlate structures in the nucleus with their functions," Spector explains. Ever since, this has been the central theme of his work. He carries this part of his work forward using super-resolution imaging approaches.

Not long after arriving at Cold Spring Harbor Laboratory in 1985 — hired over a luncheon with then-Director Jim Watson ("who ended the meal by asking, 'When can you start?,' which I have to say was pretty cool!") — Spector soon collaborated with another new hire, Adrian Krainer, and future Nobelist Richard Roberts on projects relating

The cell nucleus is a world within the larger world of the cell (whose watery cytoplasm, here shaded blue, surrounds it). The nucleus is bound by a double membrane and contains, at various times in the cell cycle, up to 10 nuclear bodies. But most of the nucleus is a 'sea of chromatin' — chromosomes containing the genome and the proteins that pack them. Chromosome territories often overlap to facilitate gene expression.





Spector's real-time visualization system clearly marks 'locus' of a switched-on gene (blue dot). Locus grows in size as the DNA 'decompacts,' so as to be accessible to machinery that copies its 'message' to RNA. Green background color changes as proteins are recruited from the nucleus to take part in the process.

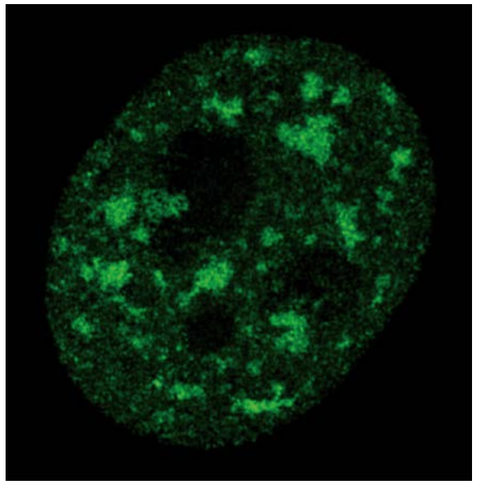
to the splicing machinery. Gradually, Spector's focus turned to the broader machinery involved in gene expression.

Two technological advances, the introduction of GFP, or green fluorescent protein, and the use of a bacterial DNA sequence called the lac operator array, made it possible by the late '90s for Spector to make visible both genes and their products, in a novel way. The visualization systems his lab designed were "inducible": by providing a drug, one could switch on what amounted to "a designer gene," and watch what happens in real time.

Movies 'worth a million words'

One thing that happens is a process called decompaction, in which tightly bundled DNA becomes much more loosely packed, making it possible for specialized protein complexes to attach to the DNA and initiate the process of gene expression. Spector, who also directs the Microscopy Shared Resource at CSHL, has always maintained a keen interest in techniques of visualization, reminding us that "you will find things in continuous imaging, i.e., in 'movie' form, that you can't detect and often cannot imagine from fixed-cell studies." If a static picture is worth a thousand words, he says, "a movie is worth a million."

Spector's live-cell imaging work helped him realize that there is a good deal more plasticity in the structure and positioning of nuclear components than he was at first willing to believe. This proved "one of the most unexpected findings in my career," reminding him how "plasticity is actually a good thing, enabling biological systems to respond to a wider range of conditions than if they were rigid or fixed and providing them with an evolutionary advantage."



Green areas show distribution of nuclear speckles in a single nucleus. These bodies store and assemble splicing factors that 'edit' RNA messages.

Research in the years since the "gene expression" movie was made has shed light on the varied functions that nuclear bodies perform. Spector has become keenly interested in the possibility that they may serve as prognostic or diagnostic markers in disease. His interest in nuclear bodies, moreover, intersects with an interest he shares with other CSHL lab leaders including Gregory Hannon and Thomas Gingeras: in types of RNAs that *don't* serve as templates for protein synthesis. "One current project in my lab focuses on a specific non-coding RNA (ncRNA) that localizes to bodies in the nucleus called nuclear speckles," Spector notes. "We're studying its role in breast cancer metastasis."

Another line of work linking the lab's interest in the nucleus with disease has grown out of inquiries relating the spatial position of nuclear bodies to the manner in which genes are expressed and regulated. Among the critical facts that have come to light: sometimes a protein will migrate from a nuclear body to "find" a gene sequence in the nucleus, to which it binds to perform a specific role — say, help switch the gene on or off. Other times, it appears that genes or RNAs actually *move to* areas occupied by certain nuclear bodies, so as to avail themselves of something inside needed for their regulation.

In contrast to what Spector and others long believed, it now appears that chromosomes occupy "neighborhoods" in the nucleus which overlap to some extent. This facilitates interactions between genes located on different chromosomes and provides the basis for gene interactions and translocations that can result in various forms of cancer.

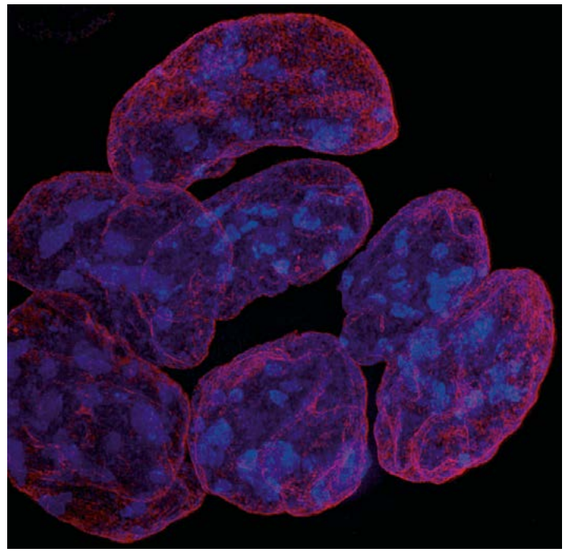
It's not far-fetched, Spector acknowledges, to think of the nucleus as a sea of chromatin — the protein-plus-DNA bundles that "pack" the chromosomes into the tiny nuclear space; and at various locations in that chromatin sea are 10 or more types of nuclear bodies, whose contents and position in nuclear space at a given moment facilitate the critical processes by which: genes are expressed; RNAs are trafficked; and proteins move in and out of nuclear structures. A busy picture, indeed.

Insights into disease

A recent area of excitement in the Spector lab centers around studies utilizing mouse embryonic stem cells. "We're very interested in understanding the regulatory mechanisms that are engaged to keep these remarkable cells in the pluripotent state as well as those influencing their differentiation to different cell types." Studies focusing on gene positioning and expression levels in the nucleus, as well as differential expression of ncRNAs, are providing exciting new hints as to how these processes may be regulated.

In turn, says Spector, this raises the larger question of "how do genes 'know' they're making RNA at the right level?" It's a question of great importance across the full gamut of diseases that are caused in whole or part by gene misregulation, from cancer to diabetes to disorders of the brain. It is, too, a superb example of the value of basic research. For Spector and his team, a specific interest in the microscopic world of the cell nucleus has led to inquires of this kind, with the broadest of consequences for human health.

Peter Tarr



Mouse embryonic stem cells (nuclei shown here) may hold clues to causes and means of addressing genetic illness.

Faculty & Friends

Open House brings new friends

You didn't need to have a Ph.D. to enjoy the Open House held at CSHL on March 23. Of course, that was the whole idea: a day for the local community to gather at the Laboratory and learn from its faculty, postdoctoral fellows, students, and staff what actually happens at the cutting edge of biological research. In addition to representatives of CSHL's research and educational programs, members of administrative departments like Technology Transfer as well as CSHL Association directors were on hand to share information with 500+ visitors. Interactive demonstrations, posters, and videos made for an informal fair-like atmosphere. Highlights included campus tours and 5-minute science sound byte talks presented by postdocs and Ph.D. candidates at the Watson School — see images and videos on the iPad app!

WSBS confers honorary degrees

In celebration of the 10th graduating class of the Watson School of Biological Sciences (WSBS), honorary degrees were presented to Jack E. Dixon, Ph.D., and Brigid L.M. Hogan, Ph.D., F.R.S.

Dr. Dixon is Vice President and Chief Scientific Officer of the Howard Hughes Medical Institute and Distinguished Professor at the University of California, San Diego. He earned his Ph.D. in chemistry from the University of California, Santa Barbara. A member of the Institute of Medicine and National Academy of Sciences, Dixon has had a distinguished scientific career focused on protein tyrosine phosphatases that govern a key biochemical reaction called phosphorylation, and which play a central role in signaling between cells.

Dr. Hogan is Professor and Chair of the Department of Cell Biology at Duke University. She earned her Ph.D. in biochemistry at the University of Cambridge. A developmental biologist, she is noted for her contributions to stem cell research and transgenic technology and techniques. Dr. Hogan's work on transgenic mice led her to teach the Molecular Embryology of the Mouse course at CSHL and edit the first two editions of *Manipulating the Mouse Embryo: A Laboratory Manual*, considered the "bible" of mammalian embryo manipulation techniques.

Professor Hannon elected to U.S. National Academy of Sciences

Gregory Hannon, Ph.D., a CSHL Professor and an Investigator of the Howard Hughes Medical Institute, was elected to the National Academy of Sciences (NAS), one of the highest honors conferred upon scientists in America. The body was formed by an act of Congress, signed by President Abraham Lincoln in 1863 at the height of the Civil War, calling upon the NAS to provide independent advice to the government on matters related to science and technology. Hannon is recognized the world over as among the foremost authorities on small RNA biology and RNA interference. RNAi, as it's called, is a natural cellular mechanism implicated in genome defense, in which small RNA molecules act to regulate gene expression. It has been used to hunt for cancer genes, to stop viral infections, and most recently, for treating diseases in clinical trials.

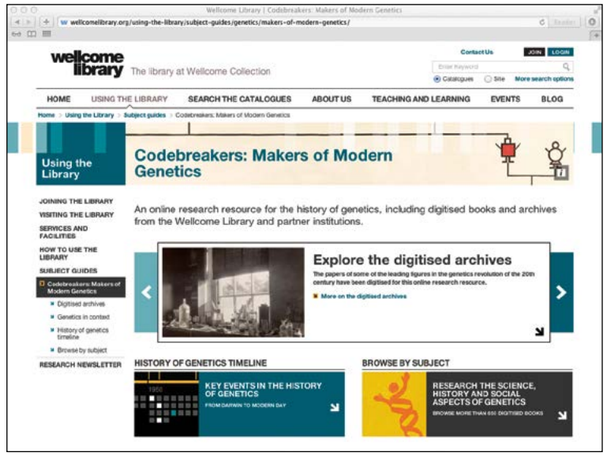
Hannon's lab strives to understand the biology of cancer cells, with a focus on breast and pancreatic cancer, and on the biological mechanisms of resistance to targeted cancer treatments.

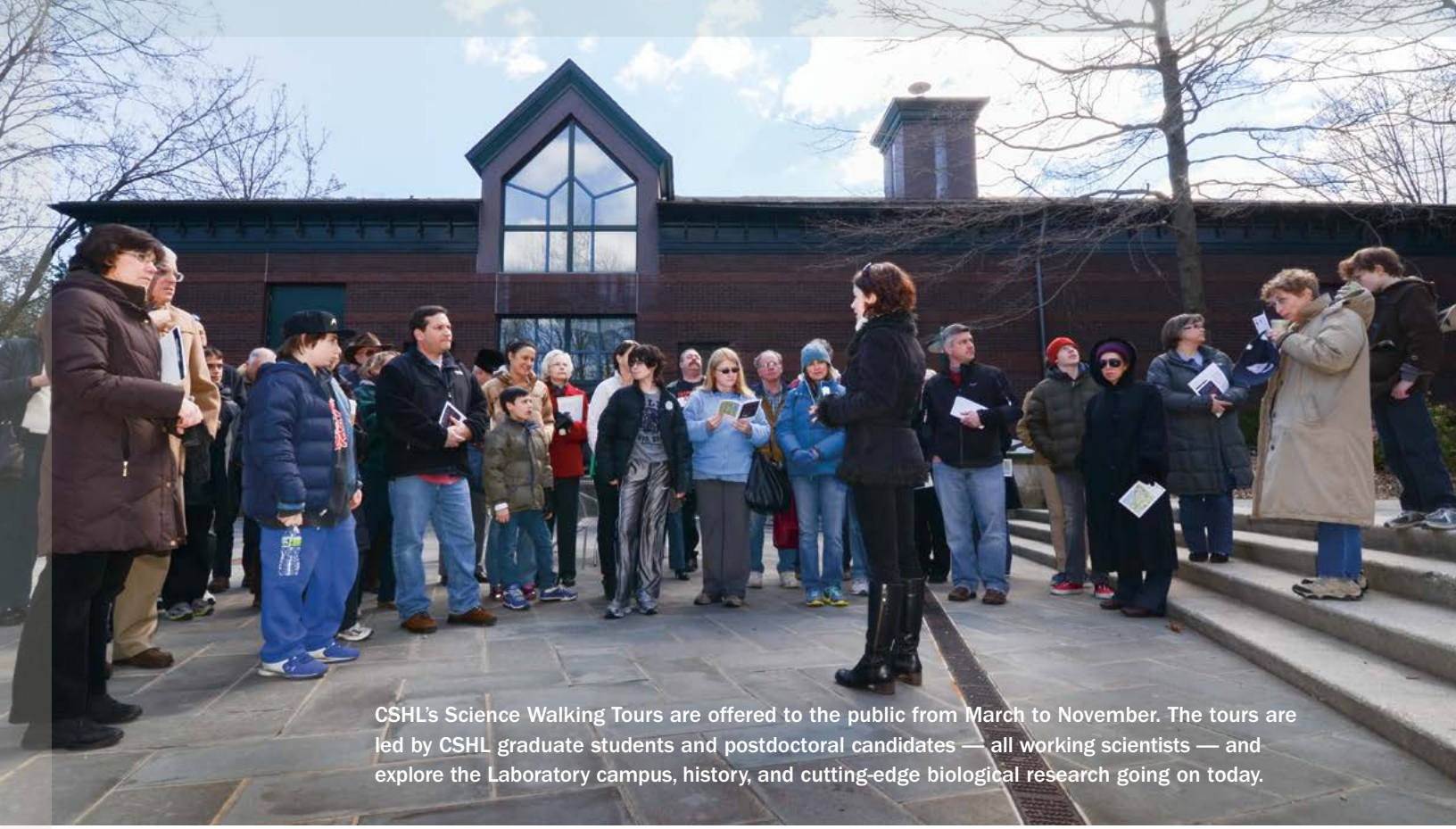
Professor Joshua-Tor elected AAAS Fellow

CSHL Professor and HHMI Investigator Leemor Joshua-Tor, Ph.D., has been named a Fellow of the American Association for the Advancement of Science (AAAS). Election is an honor bestowed upon AAAS members by their peers in recognition of their scientifically or socially distinguished efforts to advance science or its applications. As a member of the Section of Biological Sciences, Joshua-Tor was cited for contributions to the field of nucleic-acid enzymes, particularly in the fields of RNA interference and DNA replication. Her lab studies the molecular basis of cell regulatory processes by using the tools of structural biology and biochemistry to examine proteins and protein complexes associated with these processes. Efforts largely center on nucleic-acid regulation including the process of RNA interference (RNAi) and DNA replication initiation in papillomaviruses. Joshua-Tor was the Dean of CSHL's Watson School of Biosciences from 2007–2012 and is a member of the National Institutes of Health (NIH) external working group on the future biomedical workforce.

CSHL contributes to online *Codebreakers* archive

Francis Crick's preliminary sketches of the double helix. James Watson's February 1953 letter to Max Delbrück reporting that he has "a very pretty model" for DNA. Rosalind Franklin's famed x-ray diffraction "photo 51." These and a million other primary-source documents telling the amazing story of the biological revolutions of the 1950s and 1960s are now freely available to the public on the World Wide Web thanks to an effort led by the Wellcome Library of Great Britain. Entitled *Codebreakers: Makers of Modern Genetics*, the portal provides access to first-hand notes, letters, sketches, lectures, photographs and essays from the circle of brilliant minds responsible for uncovering the structure of DNA. CSHL's Library & Archives collections, which include the papers of Nobel laureates James Watson and Sydney Brenner among others, are a key source for *Codebreakers*. "CSHL was very happy to participate in the project with partners Churchill Archives Centre Cambridge, the University of Glasgow, King's College London and University College London," says Ludmila Pollock, Executive Director of CSHL's Library & Archives.





CSHL's Science Walking Tours are offered to the public from March to November. The tours are led by CSHL graduate students and postdoctoral candidates — all working scientists — and explore the Laboratory campus, history, and cutting-edge biological research going on today.

Cold Spring Harbor Laboratory Board of Trustees

CSHL Association

CSHL Association comprises some 1000 neighbors and friends of the Laboratory who contribute to the Annual Fund, an essential source of unrestricted support for outstanding young scientists. 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 Karen Orzel, Director, Annual Giving and Donor Relations, at 516.367.6886 or orzel@cshl.edu.

CSH 78th Cold Spring Harbor Symposium on Quantitative Biology

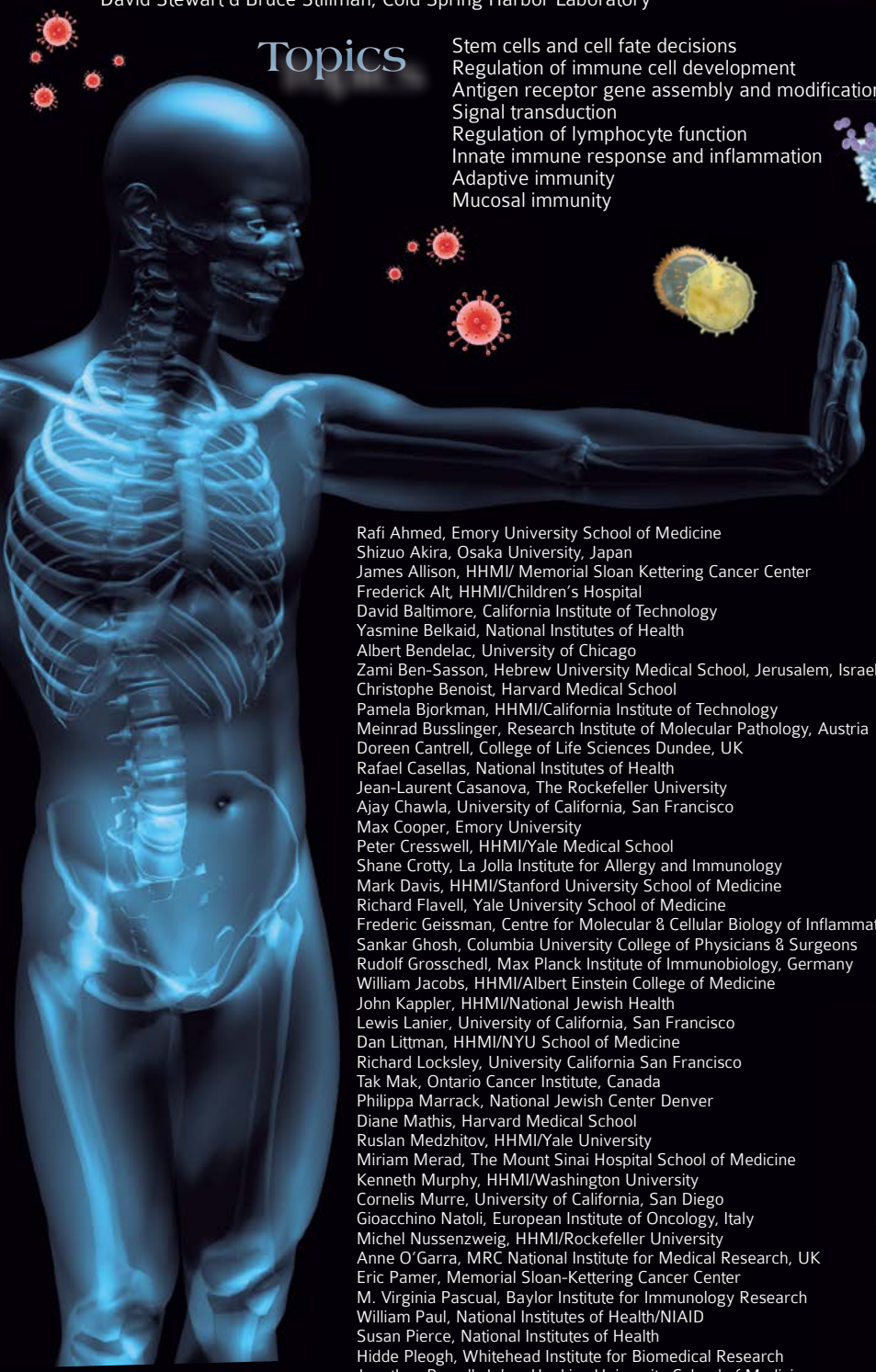
Immunity & Tolerance

May 29 - June 3, 2013

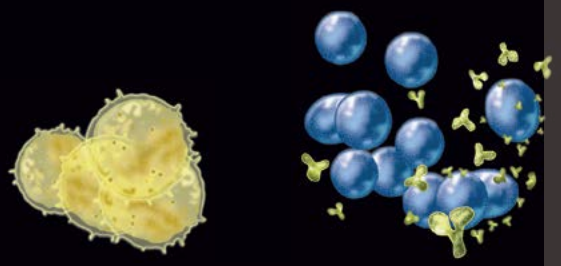
Organized by:
Michel Nussenzweig, HHMI / The Rockefeller University
Anne O'Garra, MRC National Institute for Medical Research, UK
Stephen Smale, University of California, Los Angeles School of Medicine
David Stewart & Bruce Stillman, Cold Spring Harbor Laboratory

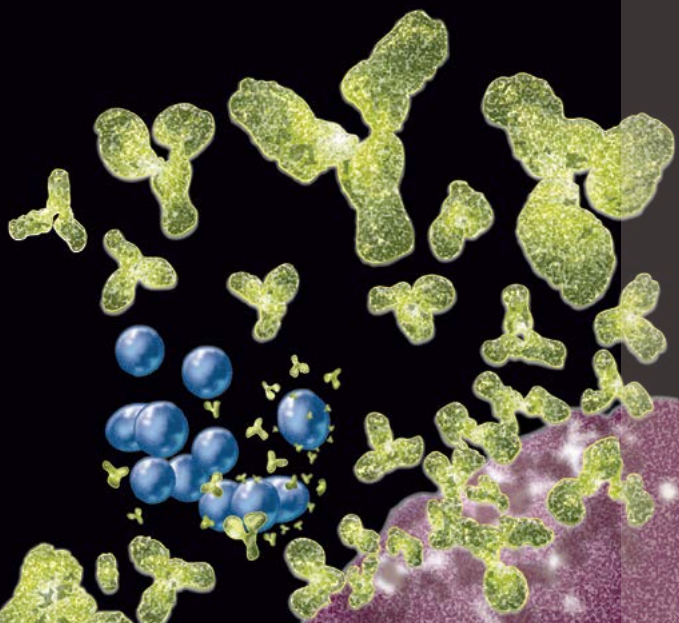
Topics

Stem cells and cell fate decisions
Regulation of immune cell development
Antigen receptor gene assembly and modification
Signal transduction
Regulation of lymphocyte function
Innate immune response and inflammation
Adaptive immunity
Mucosal immunity
Organ-specific immunity
Immune regulation and tolerance
Autoimmunity and allergy
Immunity and cancer
Pathogen–immune system interactions
Vaccine development
Novel strategies to engineer/harness immunity



Rafi Ahmed, Emory University School of Medicine
Shizuo Akira, Osaka University, Japan
James Allison, HHMI/ Memorial Sloan Kettering Cancer Center
Frederick Alt, HHMI/Children's Hospital
David Baltimore, California Institute of Technology
Yasmine Belkaid, National Institutes of Health
Albert Bendelac, University of Chicago
Zami Ben-Sasson, Hebrew University Medical School, Jerusalem, Israel
Christophe Benoist, Harvard Medical School
Pamela Bjorkman, HHMI/California Institute of Technology
Meinrad Busslinger, Research Institute of Molecular Pathology, Austria
Doreen Cantrell, College of Life Sciences Dundee, UK
Rafael Casellas, National Institutes of Health
Jean-Laurent Casanova, The Rockefeller University
Ajay Chawla, University of California, San Francisco
Max Cooper, Emory University
Peter Cresswell, HHMI/Yale Medical School
Shane Crotty, La Jolla Institute for Allergy and Immunology
Mark Davis, HHMI/Stanford University School of Medicine
Richard Flavell, Yale University School of Medicine
Frederic Geissman, Centre for Molecular & Cellular Biology of Inflammation
Sankar Ghosh, Columbia University College of Physicians & Surgeons
Rudolf Grosschedl, Max Planck Institute of Immunobiology, Germany
William Jacobs, HHMI/Albert Einstein College of Medicine
John Kappler, HHMI/National Jewish Health
Lewis Lanier, University of California, San Francisco
Dan Littman, HHMI/NYU School of Medicine
Richard Locksley, University California San Francisco
Tak Mak, Ontario Cancer Institute, Canada
Philippa Marrack, National Jewish Center Denver
Diane Mathis, Harvard Medical School
Ruslan Medzhitov, HHMI/Yale University
Miriam Merad, The Mount Sinai Hospital School of Medicine
Kenneth Murphy, HHMI/Washington University
Cornelis Murre, University of California, San Diego
Gioacchino Natoli, European Institute of Oncology, Italy
Michel Nussenzweig, HHMI/Rockefeller University
Anne O'Garra, MRC National Institute for Medical Research, UK
Eric Pamer, Memorial Sloan-Kettering Cancer Center
M. Virginia Pascual, Baylor Institute for Immunology Research
William Paul, National Institutes of Health/NIAID
Susan Pierce, National Institutes of Health
Hidde Pleogh, Whitehead Institute for Biomedical Research
Jonathan Powell, Johns Hopkins University School of Medicine
Fiona Powrie, University of Oxford, UK
Cristina Rada, MRC Laboratory of Molecular Biology, UK
Klaus Rajewsky, Harvard Medical School
Anjana Rao, La Jolla Institute for Allergy & Immunology
Lalita Ramakrishnan, University of Washington
David Raulet, University of California, Berkeley
Jeffrey Ravetch, The Rockefeller University
Ellen Rothenberg, California Institute of Technology
Alexander Rudensky, Memorial Sloan Kettering Cancer Center
Federica Sallusto, Institute for Research in Biomedicine, Switzerland
David Schatz, HHMI/Yale Medical School
Robert Schreiber, Washington University School of Medicine
Harinder Singh, Genentech
Stephen Smale, UCLA School of Medicine
Tadatsugu Taniguchi, University of Tokyo, Japan
Alexander Tarakhovsky, The Rockefeller University
Craig Thompson, Memorial Sloan Kettering Cancer Center
Carola Vinuesa, Australian National University, Australia
Ulrich von Andrian, Harvard Medical School
Harald von Boehmer, Dana-Farber Cancer Institute
Bruce Walker, Ragon Institute of MGH, MIT and Harvard
Hedda Wardemann, Max Planck Institute for Infection Biology, Germany
Art Weiss, HHMI/ University of California, San Francisco
Irving Weissman, Stanford University
Wayne Yokoyama, HHMI/Washington University





Registration, abstract submission and further information:
http://www.cshl.edu/meetings ♦ email: meetings@cshl.edu
phone: 516-367-8346 ♦ fax: 516-367-8845

Image credit: James Duffy & James Whitaker
Poster credit: Catherine Dougherty

Cold Spring Harbor Laboratory
Cold Spring Harbor, NY 11724

NYC ♥ STEM

City schools chancellor at Spring Break DNA Science Camp

Download the *CSHL Harbor Transcript* iPad app to view extras for this issue!

New York City Department of Education Chancellor Dennis M. Walcott paid a visit to the Harlem DNA Lab on March 29. He was visiting students participating in the first Spring Break DNA Science Camp. Dave Micklos, Executive Director of the DNA Learning Center (DNALC), was there to brief him. Of the 80 students who applied, 30 enthusiastic and precocious young girls and boys, whose families hail from 17 different countries, were selected to learn how to manipulate and perform experiments with DNA. All 5 boroughs were represented, as were schools from the full spectrum of those found in NYC. The Harlem DNA Lab is situated in the John S. Roberts Educational Complex (J.H.S. 45). It is directly administered by the DNALC and funded through the Office of School Programs and Partnerships (OSPP) at the NYC Department of Education.

Visit www.cshl.edu to sign up for our monthly email newsletter.