COLD SPRING HARBOR LABORATORY
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CSH

HARBOR TRANSCRIPT

Messages in maize

What plant genes teach us about development

COLD SPRING
HARBOR LABORATORY

PRESIDENT'S MESSAGE

Before a large gathering of the Laboratory's most committed friends, we dedicated the new Hillside Laboratories this past June. Our keynote speaker, Nobel laureate and CSHL alumnus Phillip A. Sharp, remarked that we had added another precious jewel to the crown of research in this country. In early fall, as the first groups of scientists began moving into their new homes within the six-building complex, we initiated a process that will culminate in an expansion of active research space by 40 percent, and of research staff by 20 percent.

While impressive, these numbers don't do justice to the possibilities that the Hillside Laboratories represent. Two hundred new research personnel will be the catalyst for new levels of insight the nature of which we can't predict today, the product of more superb minds working together on major problems of common interest.

I am particularly sanguine about what we shall discover at Cold Spring Harbor Laboratory in the coming years because of our commitment to collaboration, across labs and across disciplines. The Hillside complex was planned with team science in mind. Its design is ingenious. The process began with the hypothesis that we could encourage interdisciplinary scientific collaboration and innovation through architectural and landscape design.

The significance of the architectural accomplishment will be measured over a period of many years. Taking aim at what Phil Sharp called "the greatest scientific challenges of our time," our ever more formidable research staff will engage in projects that span the disciplines, from molecular and cell biology to genomics to quantitative biology. Working together, they will forge fundamental new understandings about how to halt metastatic and drug-resistant tumors in their tracks, and how to accurately diagnose and more effectively treat neurodevelopmental disorders such as autism, bipolar depression and schizophrenia. We stand today at the threshold of these exciting developments.

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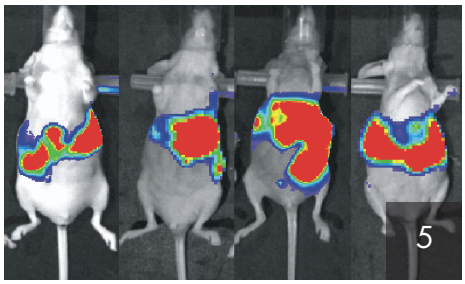
FEATURES

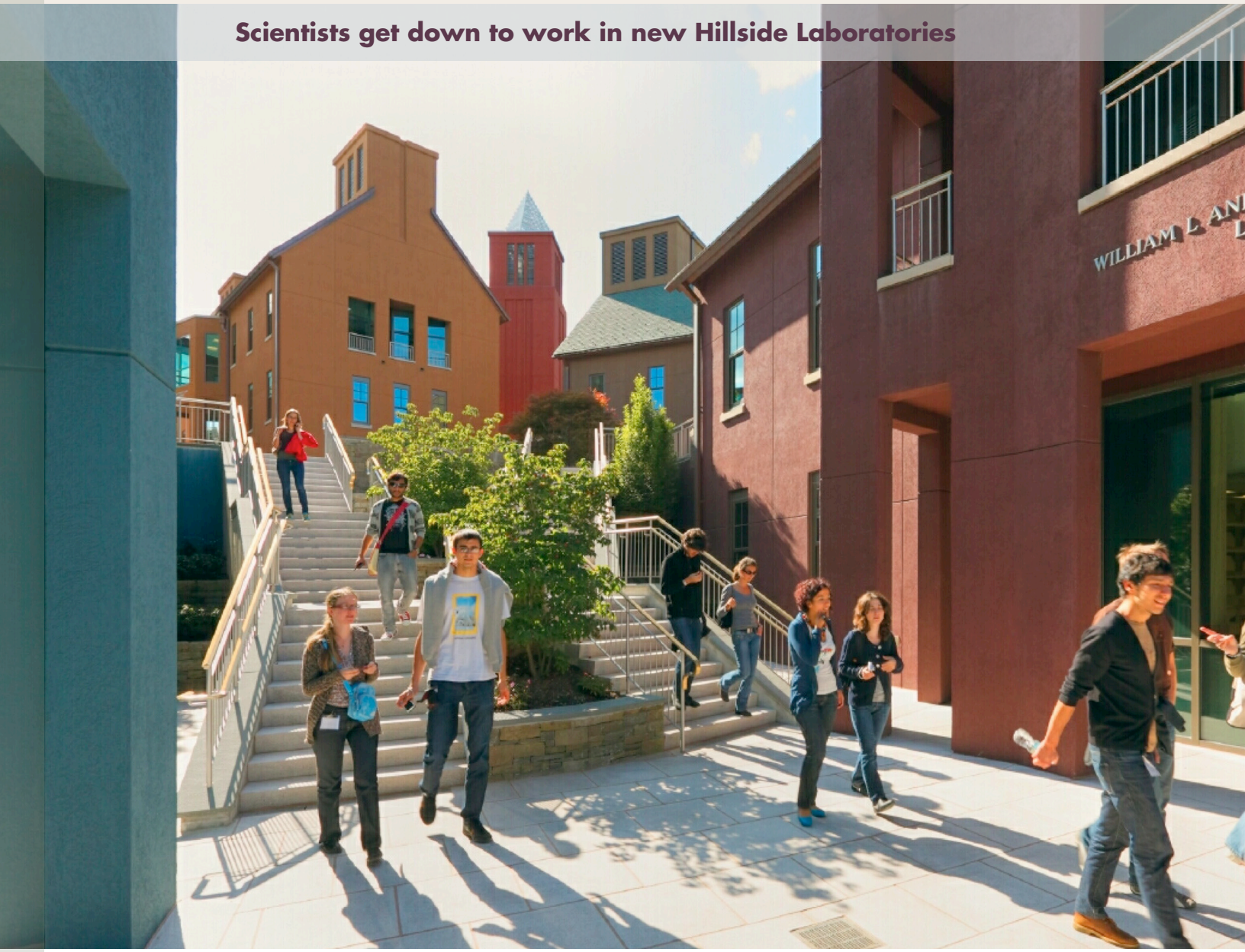


FACULTY & FRIENDS

On the cover:
In the Uplands Farm greenhouse, Prof. David Jackson (center) discusses maize genetics with members of his lab, Morgan Xu and Tara Zadrozny.

Crown jewels

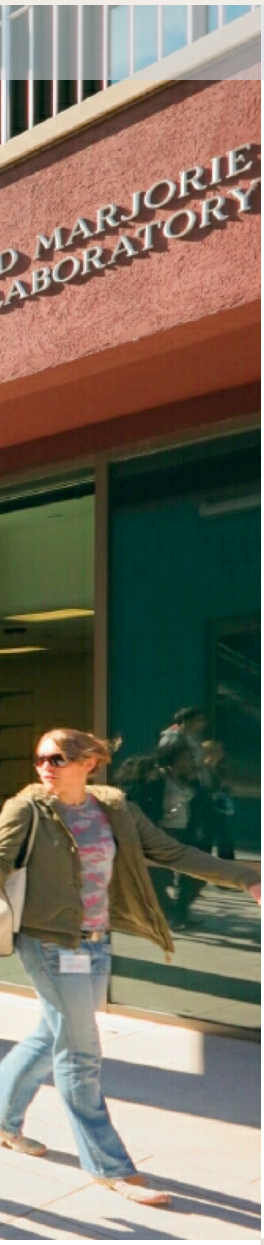
Scientists get down to work in new Hillside Laboratories



It is a conception so pleasing to the eye, so consonant with the surroundings, that it is hard to believe its importance to the future of research. The Hillside Laboratories, formally dedicated in June before hundreds of staff, supporters and friends of Cold Spring Harbor Laboratory, have instantly provided the institution with 40 percent more space for research. When the buildings are fully occupied, the Laboratory's staff will total 1200, a doubling over the last decade. The 200 high-tech jobs created by the Hillside project represent the largest expansion in CSHL's 119-year history.

At the dedication ceremony, a beaming President Bruce Stillman said, "This expansion will allow Cold Spring Harbor Laboratory to do more of what it has always done best: perform pioneering research at the leading edge of biological science, particularly in the areas of cancer and neuroscience, but also in the emerging field of quantitative biology."

CSHL Board Chairman Eduardo Mestre added, "An important goal for the design of the Hillside Laboratories was to encourage collaboration among scientists and foster the progress of scientific discovery, while preserving the historic appeal of CSHL's picturesque campus. Looking at this beautiful complex, I believe we have succeeded."



The Hillside Laboratories are an architectural marvel. As the *New York Times* astutely observed in a June 24th article: "Visitors to the Cold Spring Harbor Laboratory looking for the new state-of-the-art 100,000-square-foot science lab might be excused for asking, 'Where is it?'" What is distinctive about the design, by Centerbrook Architects and Planners LLP, reflects what is distinctive about Cold Spring Harbor Laboratory as a whole. It would be hard to identify another state-of-the-art scientific research facility of similar size that fosters so palpable a sense of intimacy.

The complex reflects an abiding interest in human scale and eco-friendly expansion. The six new buildings are actually outcroppings of a single interconnected structure with an infrastructure that is integrated beneath ground level. Nestled within the hillside, the buildings are connected at various elevations and share a common utility grid that makes them 30 percent more energy efficient than prevailing standards for laboratory facilities.

"These buildings remind me that Cold Spring Harbor Laboratory continues to be the most beautiful place in the world to do science," observed Chancellor Emeritus James D. Watson in his dedication remarks. He added that the Hillside complex was "a reaffirmation of the desire of the Laboratory and those people who support it and love it to remain a significant force in the acquisition of knowledge toward the betterment of the human condition."

Chief architect William Grover, who has made his mark in structures from one end of CSHL's historic campus to the other, has commented that he has "always liked buildings with narrow spaces between them that frame views." Eschewing "big, grand interior dramatic spaces," Grover and his team seized the opportunity "to make outdoor spaces that were as interesting as indoor spaces."

Science on the Hillside

- **The Donald Everett Axinn Laboratory:** research on the neurobiological roots of mental illness
- **The Nancy and Frederick DeMatteis Laboratory:** research on the genetic basis of human diseases, including autism, cancer, and schizophrenia
- **The David H. Koch Laboratory:** home to a newly established Center for Quantitative Biology and CSHL core computing facility
- **The William L. and Marjorie A. Matheson Laboratory:** research on the tumor microenvironment and metastasis
- **The Leslie and Jean Quick Laboratory:** research on new therapeutic strategies for treating cancer
- **The Wendt Family Laboratory:** research on neurodevelopment and the wiring of complex circuits in the brain

People exchanging ideas in natural and informal settings — faculty, students and postdocs, often mingling with visitors taking part in Meetings & Courses — are an essential feature of daily life at the Laboratory, a continuing source of intellectual ferment. The Hillside complex provides another memorable setting for impromptu gatherings of this type — a plaza at the entry level of the six new buildings dotted with tables and benches that command breathtaking vistas across the harbor. Meantime, the new complex seen from the harbor's eastern shore blends in almost seamlessly, appearing more like a hilltop village than a vital outpost in efforts to improve treatments for cancer and discover neural pathways implicated in devastating neurodevelopmental illnesses such autism and schizophrenia.

The Hillside Laboratories were designed, engineered and built by Long Islanders — some 250 project contractors, consultants and craftsmen. The project was made possible by the generous contributions of private donors, philanthropic foundations and the New York State 'Gen*NY*sis' initiative, which provided a grant of $20 million. A capital campaign raised over $200 million to support construction, recruitment of new investigators, equipment for new research projects and endowment for research and graduate education. The project was also supported by a bond issued with the Nassau County Industrial Development Authority. **Peter Tarr**

Teaming up against cancer

Finding cancer's genetic drivers

Genetically speaking, cancer cells are a mess. Their DNA is ravaged by mutations, some of which spawn cancer by driving the cells to grow and divide abnormally. Other mutations pile up as cells bypass built-in restraints and error-checking mechanisms and careen into chaos. Cells in human pancreatic and colorectal tumors, for example, contain an average of 60 altered genes.

In 2006, a massive multi-institutional project got under way in the United States to analyze hundreds of samples from patients with different tumor types. The object was to compile an atlas of the cancer genome. At around the same time, a coalition of scientists at Cold Spring Harbor Laboratory began tackling cancer's murky genetics with a different approach.

"Cataloging every mutation in a tumor will help construct a detailed genetic fingerprint of each patient's cancer," says Scott Lowe, the architect of the CSHL strategy. "But we also need to annotate this list with functional information."

Lowe and the other CSHL scientists are, in other words, finding out which of the mutated genes actually cause cancer ("drivers") as opposed to those that have no effect on cancer ("passengers"). These investigators are charting how mutated genes work in tandem to let tumors thrive and develop resistance to drugs. Importantly, they are also searching for mutations that, if targeted by drugs, could halt cancer.

Not only might this provide leads for more effective therapies. It could also help doctors predict the course of a patient's disease and anticipate drug resistance. And it has great potential for helping them choose better options among existing treatments.

The CSHL approach, dubbed "integrative oncogenomics," is essentially a rapid, large-scale dragnet for genes that are deleted in human cancers. These genes are suspected of functioning as tumor suppressors — a class of genes that inhibit the activity of tumor-promoting oncogenes, which are multiplied in cancer. Suspect genes are then evaluated for their ability to trigger cancer in mice.

In a pilot experiment last year, Lowe and members of four other CSHL labs whittled down a candidate list of 360 genes that are frequently missing — deleted — in samples of human liver cancer. They confirmed 13 of them as tumor suppressors. In understanding the genetic causes of liver cancer, the fifth most common type of cancer worldwide and one of the deadliest, these findings are a treasure trove.


1


2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> "Each group in this collaboration brought something unique and critical to the table."
>
> Scott Lowe

Fine-tuning a cancer mouse model

The CSHL approach has coalesced and evolved around Lowe's push to establish useful animal models for cancer. "Tumors that grow in animals are much more realistic than cancer cells growing in a Petri dish, and are a better system for ferreting out cancer-driving genetic changes," explains Lars Zender, formerly a Clinical Fellow and mouse expert in Lowe's lab, and who is currently on the front lines as a practicing oncologist in Germany.

1 Scott Lowe
2 Scott Powers
3 Mike Wigler
4 Greg Hannon
5 Richard McCombie

Lowe's group first shortened the amount of time it took to induce cancer in mice from the year or more taken by standard techniques to two months, a record. Their approach was to introduce two cancer-causing mutations — one that switched on an oncogene and another that switched off a tumor suppressor — into liver stem cells harvested from mouse embryos.

"The effect is like jamming on a car's accelerator while cutting off its brakes," explains Lowe. When transplanted into an adult mouse, the mutant cells embed themselves in the liver to create a "mosaic" animal, and quickly produce tumors similar to those seen in humans. This innovation set the scene for a multi-group collaboration.

Piecing together a unique gene screen

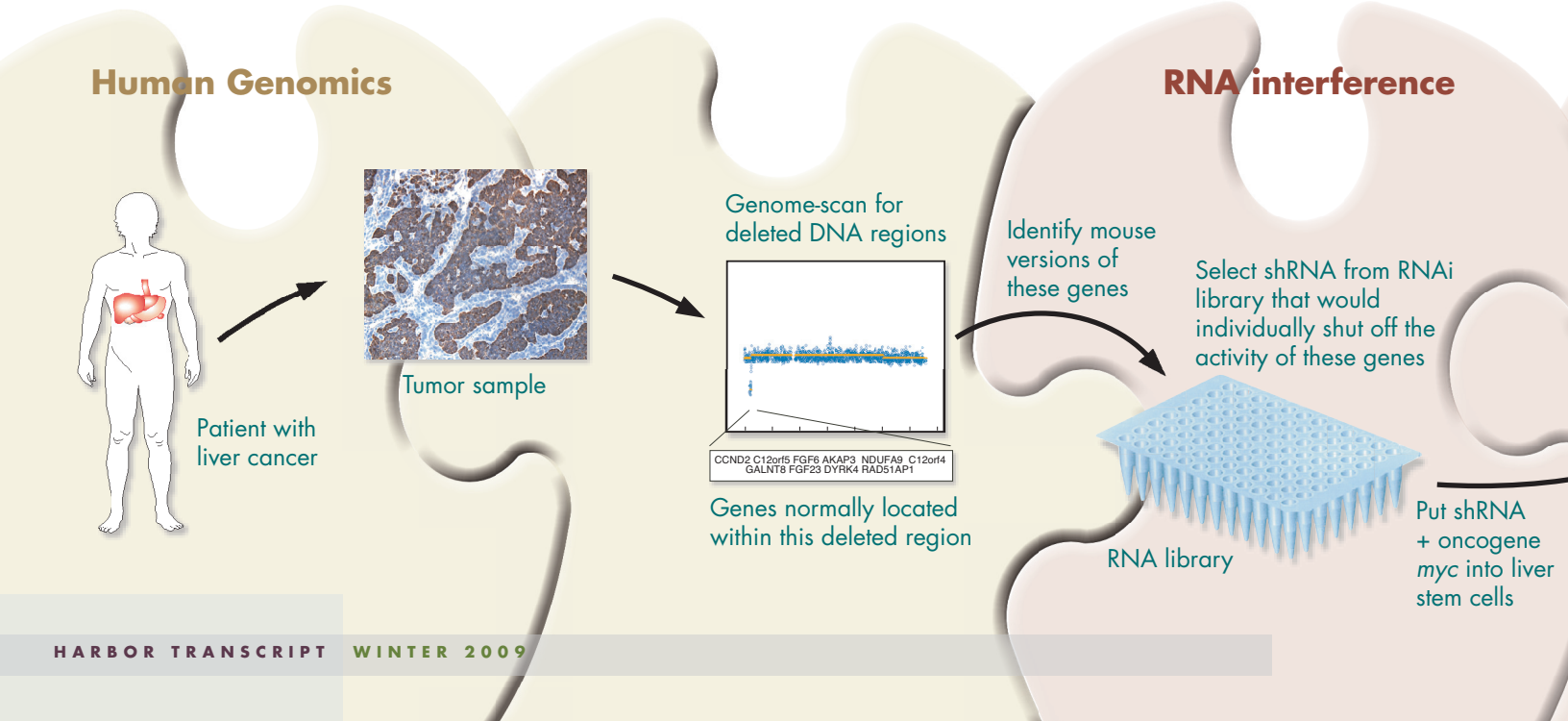
To take a closer look at the genetic landscape of the mouse tumors, Lowe's team enlisted help from CSHL's Mike Wigler and Rob Lucito, co-inventors of a genome-scanning technique called ROMA. This method enables researchers to identify segments of DNA deleted or abnormally multiplied in cancer cells.

The group found a genetic alteration in the mouse tumors that was identical to an alteration that Scott Powers, another CSHL researcher, had previously identified in human liver cancer. Lowe and Powers immediately began to collaborate. Their initial idea for a side-by-side comparison study between human and mouse tumors eventually stalled, Powers recalls. But he got over his disappointment when Lowe pitched him a broader and much more exciting idea when they met one evening at the coffee bar in Blackford Hall, a favorite hangout on the CSHL campus.

Instead of comparing genetic alterations in mouse and human tumors, Lowe proposed using ROMA to first gather data on genomic alterations that occur in human cancers and then mimicking these alterations in mice to see which of them caused cancer. "Of course, in retrospect, it is clear that this is a much more straightforward and widely applicable approach to testing which altered genes are cancerous," Powers remarks.

The final piece of technology needed to make this idea work came from another CSHL researcher, Greg Hannon. Hannon had created a collection of short, hairpin-shaped RNA (shRNA) molecules, which, via a cellular mechanism called RNA interference (RNAi), suppress the activity of specific genes. Because each shRNA molecule is tagged with a unique molecular "barcode," researchers using Hannon's shRNA "library" to screen the activity of a multitude of genes at once can still keep track of shRNA molecules that trigger a particular change.

The CSHL team first used shRNA to switch off one suspected tumor suppressor and induce liver cancer in mice. This proved that shRNA, which had thus far only been tested on cells grown in lab dishes, could also work in mice. With this proof-of-principle in hand, the team was ready to ramp up the scale of their experiment and screen hundreds of genes for tumor-suppressing activity.



Stimulus for collaboration

The importance of CSHL's innovative team approach to cancer genetics has been recognized by the federal government. The American Recovery and Reinvestment Act (ARRA) of 2009 awarded CSHL $4.75 million to set up a facility to analyze the wealth of data generated by human cancer genome projects. The aim is to discover cancer pathways and establish a new set of cancer biomarkers. Scientists will use both RNAi-based tools and another strategy developed by Scott Powers that uses molecules called cDNAs to validate candidate genes in mouse models for various types of cancer. Another aim is to discover and validate a new generation of cancer drugs with which doctors will be able to target a patient's specific constellation of mutations.

Powers used his expertise in analyzing cancer genomes to first identify DNA regions that were recurrently deleted in more than 100 human liver cancer samples. With software developed by Alex Krasnitz, a computational scientist in Wigler's group, Powers then picked out the regions likeliest to be the locations of deleted tumor suppressor genes, and compiled a list of the 360 genes that normally reside at these sites.

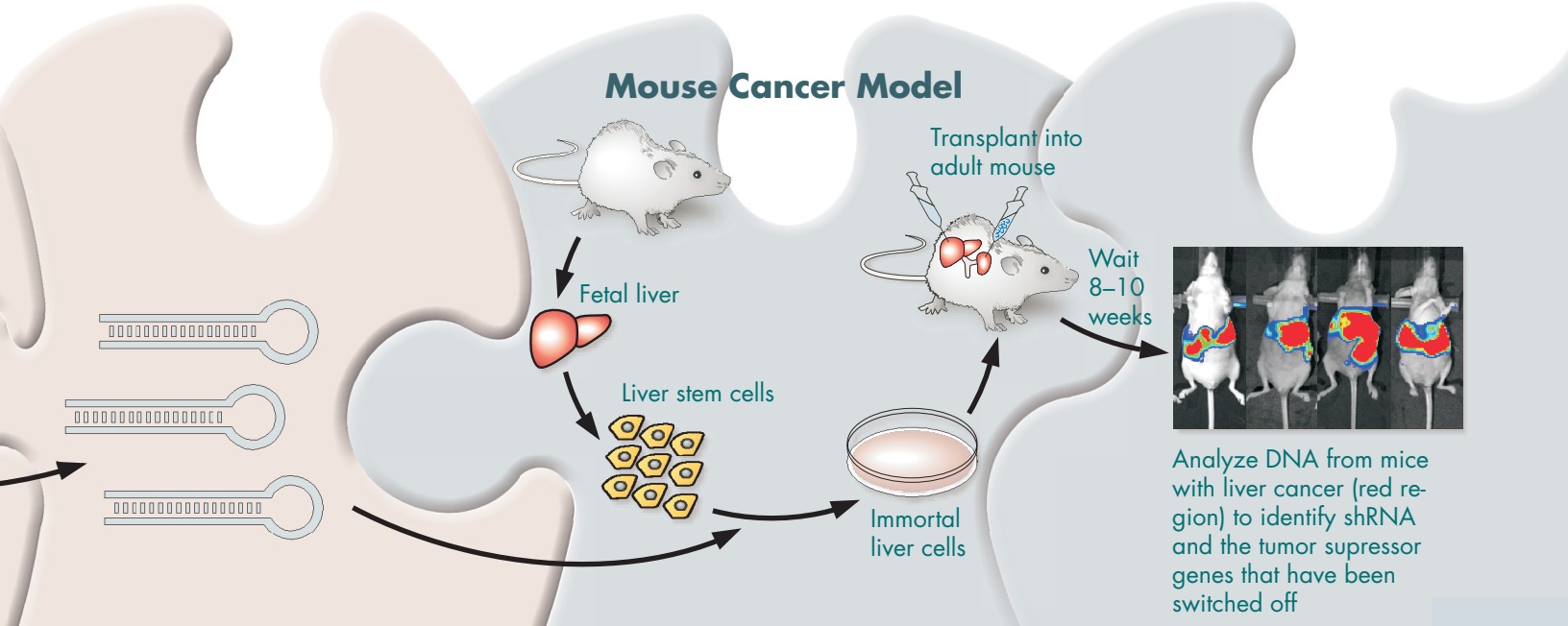
Selecting shRNAs from Hannon's library, Zender and his labmates Wen Xue and Johannes Zuber then systematically knocked out each of the 360 genes in mice that had also been engineered to overproduce a protein called Myc encoded by an oncogene. This painstaking work produced results within a month. Liver tumors appeared in mice in which a tumor suppressor gene had been turned off by a shRNA.

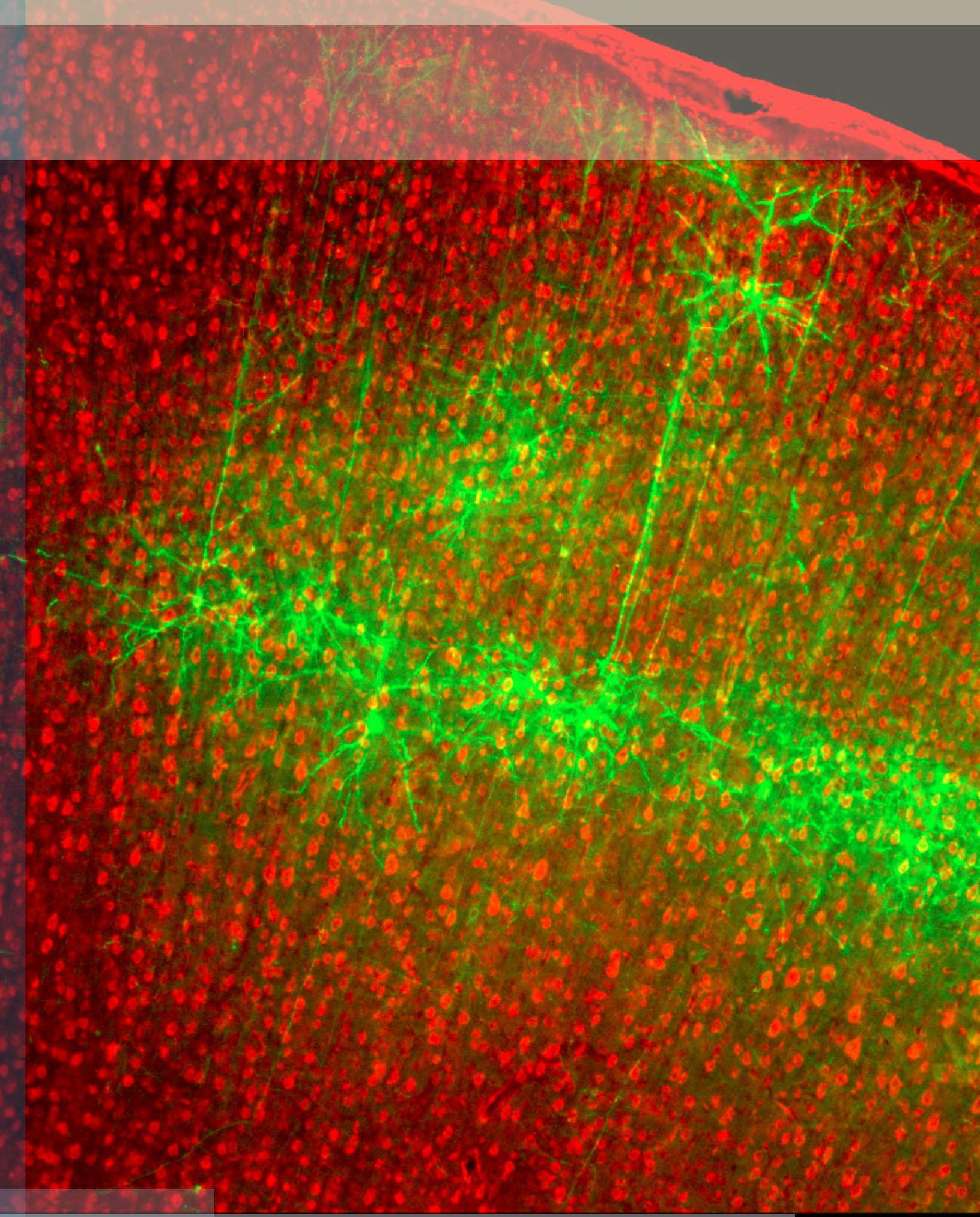
A rich pay-off

The researchers extracted DNA from the tumors and analyzed it with help from another CSHL scientist, Richard McCombie. The exciting result: the identification of 13 tumor suppressor genes, most of which had yet to even be linked to cancer. "We wouldn't have guessed their relationship to cancer if we hadn't followed this approach," says Lowe. Published in *Cell*, a leading journal, the paper describing this first "RNAi-based screen" in animals quickly rose to the top of the scientific community's must-read list.

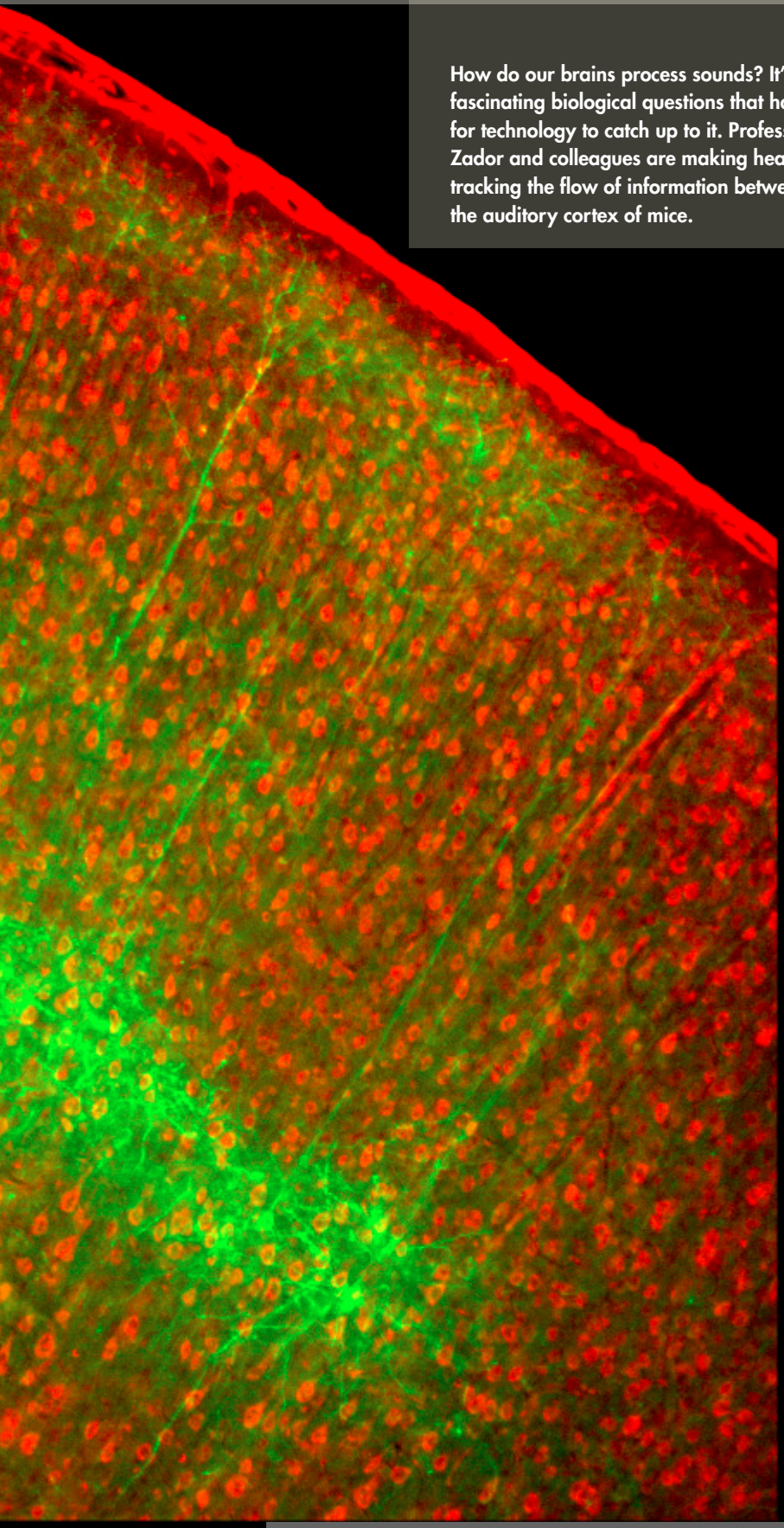
CSHL's oncogenomics approach is a major step forward in the international effort to understand cancer. Now, researchers can rapidly filter genomic information to pick up only those genes that affect cancer development in living animals, and focus follow-up studies on those that might be most useful clinically.

"Each group in this collaboration brought something unique and critical to the table," says Lowe. CSHL President Bruce Stillman concurs. "On their own, each of the five labs involved in this work is doing groundbreaking research. Their various areas of expertise, brought to bear on a single problem, demonstrates the power of team science." **Hema Bashyam**





One experiment



How do our brains process sounds? It's one of many fascinating biological questions that has had to wait for technology to catch up to it. Professor Anthony Zador and colleagues are making headway by tracking the flow of information between neurons in the auditory cortex of mice.

Crammed into the region are scores of neuronal subsets that differ in genetic type, function and point of origin in the brain. The conventional method of recording nerve impulses — via implanted electrodes — can't discriminate between neuronal types. This makes it impossible to know how each group responds to a sound cue.

Zador solved the problem by "tagging" neuronal groups with channelrhodopsin-2 (ChR2), a light-sensing protein from green algae that causes neurons to fire an impulse when exposed to a flash of light. In one experiment, postdoc Susana Lima hitched ChR2 to a green fluorescent dye, packed it into a harmless virus, and injected it into a mouse's right auditory cortex. By entering nerve endings and traveling through cable-like axons to their point of origin, the virus marked a group of neurons (green cells in the image) that originated on the far side of the brain. By gauging their response to a flash of light, the team could determine if these left-brain neurons fired impulses into the right brain when the mouse heard a particular sound. **Hema Bashyam**

RESEARCH PROFILE

David Jackson

Studies in plant genetics are teaching us about how organisms develop

It's a late summer afternoon and many members of the faculty at Cold Spring Harbor Laboratory are busy at their computers or huddled over experiments in fluorescent-lit laboratories. David Jackson and several of his postdocs are no less engrossed in their work, yet we find them outdoors on this beautiful day, in the middle of a sun-drenched field just up the road, beyond the mudflats of the lower harbor. They are carefully examining specimens of *Zea mays* — maize, a.k.a. corn — planted in long, ruler-straight rows.

Jackson, a member of the CSHL faculty for a dozen years and a professor since 2006, studies genes that influence the shapes that plants take. Finding odd-looking ears and tassels in maize – respectively, the plant's female and male floral structures, or inflorescences — has proven a productive jumping-off point. Each year, in fact, Jackson and a few members of his team make pilgrimages to vast corn-growing regions of the American Midwest and Mexico, looking for maize mutants that are the products of natural variation.

Learning from mutations is a time-honored procedure in plant research, and one with immense implications for genetics. "Going all the way back to Mendel, plant breeding has led the way in our efforts to understand the secrets of development and the underlying principles of inheritance," Jackson observes. Perhaps the most famous of CSHL's plant breeders was Barbara McClintock, who grew corn next to Carnegie Library in the 1930s and '40s en route to her Nobel-winning discovery of bits of DNA that propagated themselves, seemingly at random, across the chromosomes — what she called "jumping genes" and others later called transposons.

Technology has dramatically changed what happens after interesting specimens are gathered from the field. "Until recently, we've been very focused on finding interesting genes, one by one," says Jackson. For example, a gene in corn called *TILLERED1*. In 2007, Jackson discovered that it encodes a protein that regulates other genes, which turn out to be responsible for how and when branching takes place. *TILLERED1* was notable because Jackson's team found that it responds to light, suggesting one way in which plants adjust to environmental conditions.

Like many of the discoveries his lab is making, the *TILLERED1* insights have potentially interesting applications in agriculture. Those possibilities can be expected to multiply as new tools, especially new imaging technologies and very fast gene sequencers, "are now enabling us to see how groups of genes work together," according to Jackson.

Gene interactions play a fundamental developmental role in all organisms. Jackson's work on plant architecture therefore is only an aspect of a diverse body of work that has also provided insights about how developmental signals are propagated in plants, particularly in the inflorescences that give rise to the seeds valued by agriculturalists and upon which billions of the planet's hungry people depend.

'Taking things to pieces'

Dave Jackson loved nature as a child, and could often be found hiking the English countryside on the outskirts

of Lancaster, in the northwest, where he grew up. He took inspiration from his father, an engineer with a big workshop at home. "In the basement there were tools everywhere and we used to fix things — or, in my case, take them to pieces and not be able to fix them again," Jackson remembers. "I always wanted to know how things worked."

He was an undergraduate at the University of Leeds in the mid-1980s, interested in biotechnology, although not specifically in plants until hearing a talk at the Royal Society, at which the doctoral thesis of a student named Robert Martienssen was discussed. Ten years later, Martienssen would be instrumental in bringing Dave Jackson to CSHL, following Jackson's Ph.D. at John Innes Institute, the center of plant genetics research in England, and a fruitful period of postdoctoral research at U.C. Berkeley.

At Berkeley, Jackson became involved in work on a maize gene called *KNOTTED1*. His mentor, Sarah Hake, had succeeded in showing the gene was involved in development of the maize plant, but also

> "Going all the way back to Mendel, plant breeding has led the way in our efforts to understand the secrets of development and the underlying principles of inheritance."
>
> David Jackson

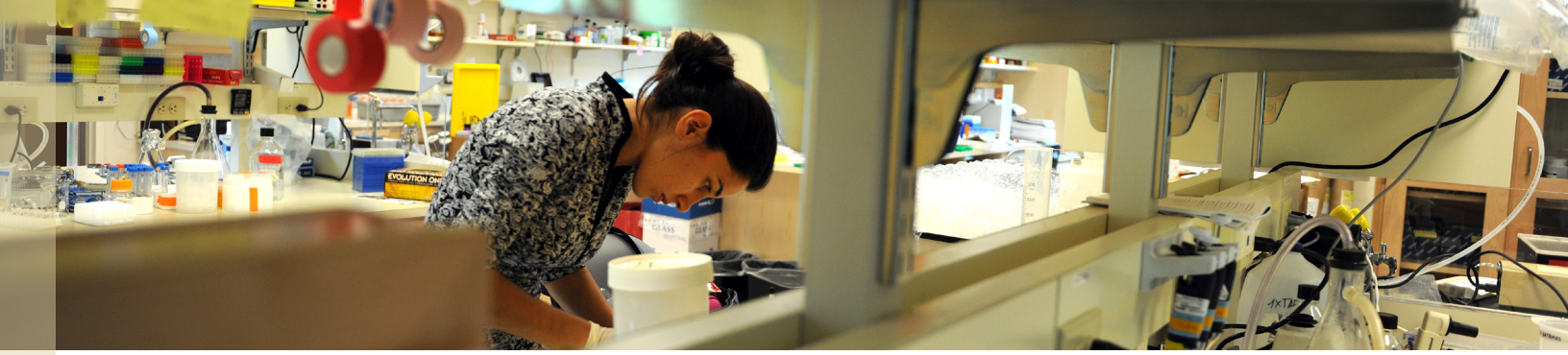
that it acted, in a manner not yet understood, as a signal. In its developmental role, *KNOTTED1* was a transcription factor that encoded a protein, KN1, which moved into the cell nucleus to regulate other genes. What made it interesting, says Jackson, was its separate role in signaling between cells. He wanted to study that role.

This work continued after Jackson was brought to Cold Spring Harbor Laboratory by Martienssen and Winship Herr, the founding dean of CSHL's Watson School of

Channels of communication

Since 2005, Jackson and colleagues have made some interesting discoveries about those tiny conduits, the plasmodesmata. They've revealed that the KN1 protein, encoded by *KNOTTED1*, has not two but at least three potential destinations in plant stem cells located in meristems. A portion of the KN1 protein's structure called a homeodomain enables it to bind specific DNA sequences, accounting for its function as a regulator of developmental genes. KN1 can also bind to its own RNA and enter plasmodesmata, acting as a signal. And when it interacts with a protein called MBP2C, it becomes anchored in the cytoplasm, preventing it from acting as a signal (presumably in response to a developmental cue).

This spring, Jackson led a team that discovered a gene called *GAT1* that instructs cells to produce a protein found mainly in meristems. The protein, an antioxidant, relieves cellular stress; its impact in meristem cells is to improve the flow of traffic through the tiny plasmodesmata. It's a mechanism, says Jackson, by which the channels change their structure in response to environmental cues as development unfolds.



Biological Sciences, in 1997. In tracing the path of the KN1 signal, Jackson's attention was drawn to tiny channels called plasmodesmata which connect plant cells. These minuscule conduits — numbering in the hundreds or thousands in each cell — carry nutrients between cells and serve as pathways for viruses.

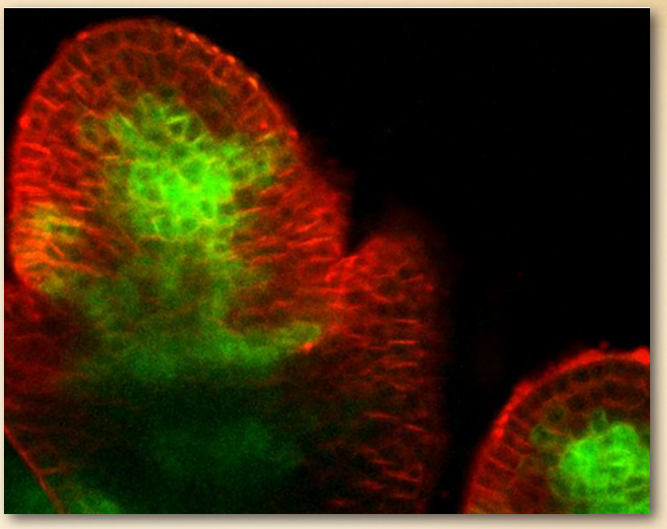
Inside the meristem

His work in the intervening years has brought to light new knowledge about the plasmodesmata, particularly about their previously unrecognized importance in signaling. Using maize and another plant, a cress called *Arabidopsis*, as models, Jackson and colleagues have focused on communities of stem cells in plants called meristems, situated at the growing tips of shoots and roots. In maize, the shoot meristem, which gives rise to leaves and flowers (tassels and ears), is a niche containing hundreds of stem cells. It's where *KNOTTED1* expresses the protein KN1. It's also where a gene called *RAMOSA3* is expressed, a gene first identified, by Jackson, several years ago.

RAMOSA3 is remarkable because it encodes an enzyme that has proved to have a very important role in maize development — it controls branching in inflorescences. What makes this extraordinary is the fact that the encoded enzyme was known previously for a very ordinary function: the removal of phosphate groups from sugar molecules. "The fact that this gene could be controlling something so important as plant morphology was really incredible," says Jackson. "But now we're doing the interesting part: trying to figure out how this thing is working — how this ordinary enzyme gained such a vital function. Finding something unexpected like this is what keeps us going in science." **Peter Tarr**

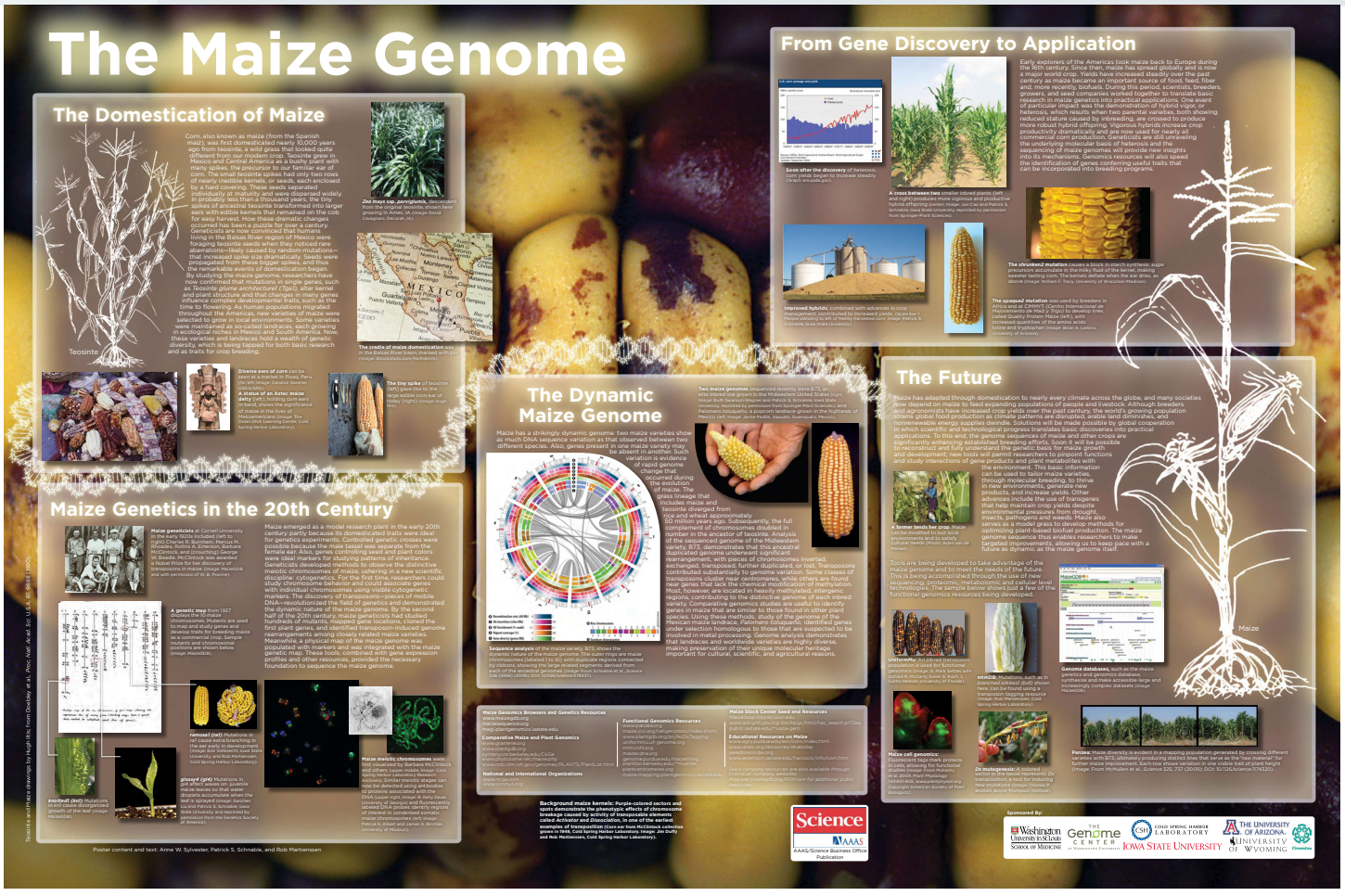
Creating new imaging tools

Jackson and colleagues have made important contributions to the broader research community by developing genetic tools that provide the means with which to observe processes not previously seen in living plants. Under an NSF grant, Jackson is creating 100 maize plant lines that express fluorescent proteins across the full spectrum of cellular "compartments." These have yielded images that are not only beautiful to behold but also productive of new knowledge about how plant cells work. The recent *Science* poster on the maize genome (see p. 13) includes a Jackson image (below) revealing proteins called expansins (green) being expressed in the wall of maize meristem cells (red) just as those cells prepare to grow out into new organs.



Maize milestone

A major multi-institutional effort in which three CSHL scientists played important roles culminated in late November with publication in *Science* of a reference genome for maize. (Part of an accompanying informational poster is reproduced below.) Doreen Ware, Rob Martienssen and Richard McCombie were co-principal investigators on the project, which Ware calls "a landmark." Ware's lab focused on annotation of the genome, the rough equivalent of an extensive reference manual that will help guide future research. Ware also co-led a parallel effort simultaneously reported in *Science* to generate the first haplotype map of maize. The HapMap gauges diversity in the maize genome by comparing 27 distinct maize lines with the reference version; it sheds new light on subjects ranging from the evolution of maize and other plants to the adaptation of maize to environmental changes, including global warming.



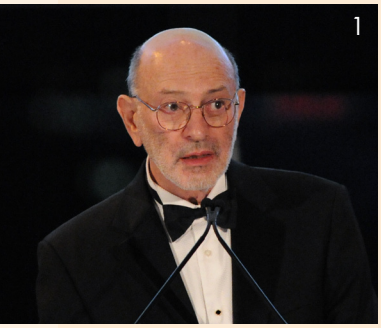
Courtesy AAAS

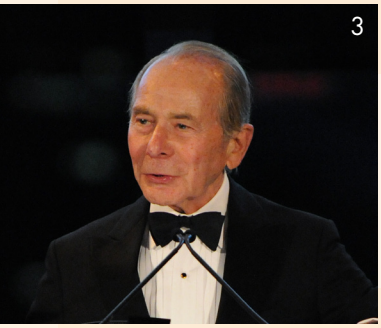
Faculty & Friends

4th Double Helix Medals

In November, CSHL awarded Double Helix Medals to four extraordinary people who have positively influenced human health by conducting groundbreaking research or raising awareness and funds for research.

"Driven by passion, intellect and vision, our recipients have boldly participated in the fight to find cures for diseases that plague us," said President Bruce Stillman at the 2009 gala.





1 Stanley Cohen
2 Herb Boyer
3 Maurice "Hank" Greenberg
4 Kathryn Davis

The event raised $3.1 million to strengthen and expand research and education programs at CSHL. Medals for Scientific Research were presented to **Herbert W. Boyer, Ph.D.** and **Stanley N. Cohen, M.D.** who co-discovered recombinant DNA, thereby launching the biotechnology revolution and leading to synthetic human insulin for diabetes, as well as growth hormones, cancer treatments and more. This seminal discovery was the basis for Dr. Boyer's founding of Genentech in 1976.

Kathryn W. Davis was honored for Humanitarianism. A lifelong philanthropist, Ms. Davis and her family established CSHL's Davis Chair in Human Genetics to focus on uncovering the roots of genetic disorders. She also founded the Kathryn W. Davis RNAi Research Center at the Laboratory to support the understanding of how the RNAi machinery might be programmed to turn off genes that lead to cancer and other disorders.

Maurice "Hank" Greenberg was presented with the medal for Corporate Philanthropy. Mr. Greenberg's $100 million commitment to the Starr Cancer Consortium has strengthened cancer research and collaboration among five area institutions — Weill-Cornell Medical College, Rockefeller University, Memorial Sloan-Kettering Cancer Center, the Broad Institute and Cold Spring Harbor Laboratory.

Chairs for the event were Mr. and Mrs. Eli Broad, Mr. and Mrs. Christopher Davis, Ms. Florence A. Davis, Mr. and Mrs. Edward E. Matthews and Dr. Richard H. Scheller. For more details and images from the event, visit http://doublehelixmedals.cshl.edu. **Denise Lenci**

Timmermans named a CSHL Professor

Marja Timmermans, Ph.D., was promoted in October to full professor. Timmermans uses *Arabidopsis* and maize as model organisms to study the role of small regulatory RNA molecules as potential signals. She and her colleagues also seek to elucidate mechanisms that distinguish "indeterminate" stem cells in plants from cells that are undergoing differentiation.

Two fellowships for Adam Kepecs

CSHL Assistant Professor Adam Kepecs received two important fellowships in 2009. In February, he was named a Research Fellow of the Alfred P. Sloan Foundation; and in July he won a Klingenstein Fellowship in the Neurosciences. The Sloan Research Fellowship provides a two-year grant to stimulate fundamental research by early-career scientists of outstanding promise. The Klingenstein Fellowship, which provides funding over three years, supports young investigators engaged in basic and clinical neuroscience research. Kepecs' research is concerned with the neurobiological principles by which the brain makes decisions.

Lin He named a MacArthur Fellow

Lin He, a former CSHL Fellow, has been named a MacArthur Fellow by the John D. and Catherine T. MacArthur Foundation. She was honored for advancing our understanding of the role of microRNAs in the development of cancer and laying the groundwork for future cancer treatments. The MacArthur Fellowship is a five-year grant to individuals who show exceptional creativity in their work. Dr. He was a postdoctoral fellow at the Laboratory from 2003–07, prior to becoming an assistant professor of molecular and cell biology at the University of California, Berkeley, in 2008.

Hassana Oyibo selected for first Abrams Award

Hassana Oyibo, a member of the Watson School of Biological Sciences entering class of 2007, has been named the first recipient of the Abrams Charitable Trust Award. Oyibo is conducting her Ph.D. research in the laboratory of Tony Zador on mapping brain circuitry involved in attention.

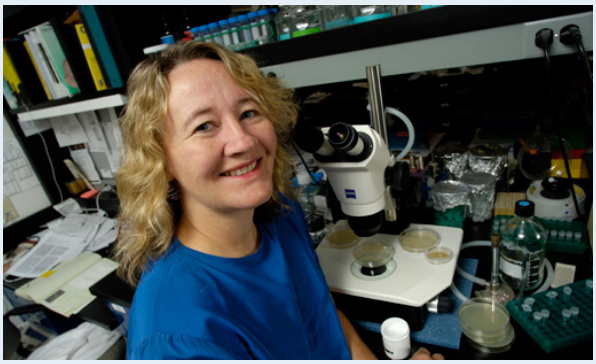
President's Council tackles legal, ethical challenges of genome science

Those who conceived and planned the effort to sequence the human genome realized the epochal project would raise profound ethical and legal questions. In October, Bruce Stillman convened a meeting of the President's Council devoted to exploring some of these issues as they have played out since publication of the reference version of the human genome in 2003. The Council, which meets twice yearly, is composed of individuals whose contributions support the Cold Spring Harbor Laboratory Fellows, a group of young scientists of exceptional promise. (Carol Greider, co-recipient of a 2009 Nobel Prize [see p. 16] was among the first of the CSHL Fellows.)

Peter Neufeld's remarks before the Council served to throw into dramatic relief one way in which genome science has already affected society. An attorney, Neufeld is co-founder and -director of The Innocence Project, which began as an effort to exonerate the wrongfully convicted, making use of DNA evidence. The Project has blossomed into an effort to identify and address the systemic causes of wrongful convictions. Others who addressed the Council included David Botstein, a geneticist and CSHL Scientific Trustee; Esther Dyson, whose own genome was among the first sequenced in the Personal Genome Project; Elaine Mardis, Co-Director of The Genome Center, Washington University School of Medicine; Dr. Philip Marshall of WebMD Health Services; and CSHL Assistant Professor Gurinder "Mickey" Atwal.

Peter Neufeld

Faculty & Friends



A Nobel for Carol Greider

Former CSHL Fellow Carol Greider, along with her colleagues Elizabeth Blackburn and Jack Szostak, won the 2009 Nobel Prize for Physiology or Medicine for discovering how chromosomes are protected in cell division by telomeres and the enzyme telomerase. During her fellowship from 1988–1990, Dr. Greider identified the key mechanism by which telomerase adds DNA to the ends of chromosomes. She continued her research career as a member of the CSHL faculty from 1990–97 and is currently Daniel Nathans Professor and Director of Molecular Biology and Genetics at the Institute for Basic Biomedical Sciences at Johns Hopkins School of Medicine.

A four-star charity, eight times (in a row)

For the eighth year running, CSHL received a 4-star rating for sound financial practices from Charity Navigator, an impartial monitor of U.S. charitable organizations. "Cold Spring Harbor Laboratory consistently executes its mission in a fiscally responsible way, and outperforms most other charities in America," said Ken Burger, Charity Navigator's president and CEO.

Trustee Charles Sawyers honored with Lasker Award

Charles L. Sawyers, M.D., Chair of the Human Oncology and Pathogenesis Program at Memorial Sloan-Kettering Cancer Center and a Scientific Trustee of CSHL, in September received the 2009 Lasker-DeBakey Clinical Medical Research Award. Dr. Sawyers and two colleagues were recognized for their groundbreaking work on the treatment of chronic myeloid leukemia (CML). Their research has led to the development of drugs that have rendered CML a manageable condition for most patients. The Lasker Award is one of the nation's most prestigious honors for biomedical research. Seventy-nine Lasker laureates have received the Nobel Prize, including 30 in the last two decades.

Transformative NIH grants awarded to Partha Mitra and Josh Dubnau

Two CSHL neuroscientists are among an elite group of only 42 researchers nationwide to receive special five-year grants for transformative research from the National Institutes of Health (NIH). This is the first year the NIH has offered "Transformative R01" grants, which were devised to encourage "exceptionally innovative, high-risk, original and/or unconventional research that has the potential to create new or challenge existing scientific paradigms." Professor Partha Mitra will use his grant to produce the first brain-wide circuit diagram for the mouse, and using this as reference, attempt to determine alterations in the corresponding circuits of mouse models of neuropsychiatric disorders. Assistant Professor Josh Dubnau's "transformative" project will study how the conversion of genetic information — its translation from RNA to protein — is regulated in neurons.

Partha Mitra

Josh Dubnau

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CSHL Association

CSHL Association comprises some 1,000 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 Diane Fagiola, Director of Development, at 516.367.8471 or fagiola@cshl.edu.

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