



HARBOR
TRANSCRIPT

Cold Spring Harbor Laboratory

CSHL

Amazing URPs!

CSHL's launch pad for gifted undergrads



PRESIDENT'S MESSAGE

To be a scientist requires passion and dedication to a way of working called the scientific method. It entails asking questions in a manner that involves embracing new ideas and abandoning dogma. It calls for careful strategic thinking even before experiments begin. Scientists, to be productive, need to develop a path for their research that will reveal coherence as it unfolds—step by step, over periods usually measured in many years, not months or days.

Today, research institutions like CSHL all over the country find themselves operating in an environment of short-term decision making due to an uncertain funding environment. Decisions are being made on the fly because Congress and the President have failed to agree on a national budget now for 5 years running. Moreover, in the last year vacillation has triggered automatic, indiscriminate, across-the-board cuts in everything the government supports, including scientific research that is a key economic driver.

Such indecision comes on top of an unprecedented decade of declining NIH budgets. The current malaise is also not good for our nation insofar as it results in widespread low morale, particularly among the new generation of American scientists who may not have a career in science. Eventually a lack of progress in science and medicine will imperil American world leadership.

The situation is serious and calls for resolution at the national level. In the meantime, Cold Spring Harbor Laboratory's position remains comparatively strong, in part because of the strength and foresight of our philanthropic benefactors. There are organizational reasons for our strength, too. We have a long history of attracting the best and the brightest who are strong competitors in the hunt for very limited federal grants. It is researchers like Professors Greg Hannon and Josh Huang, highlighted in the pages of this magazine, who have dedicated themselves to the highest standards and have achieved extraordinary results. These investigators are role models for up-and-coming scientists like the very talented undergraduate student you see on our cover, who worked at CSHL this summer.

As a nation we must make sure that today's undergraduates have the same opportunities as those of us who have had the good fortune to make major contributions to American science. Only by having a long-term vision will our society continue to be a pioneer in science.

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On the cover:

Alexis Tchaconas, a senior at Columbia University, was one of 27 gifted college students who took part in the Undergraduate Research Program in summer 2013. Her study of autism, performed in the lab of Professor Mike Wigler, was motivated by a family connection to the disorder.



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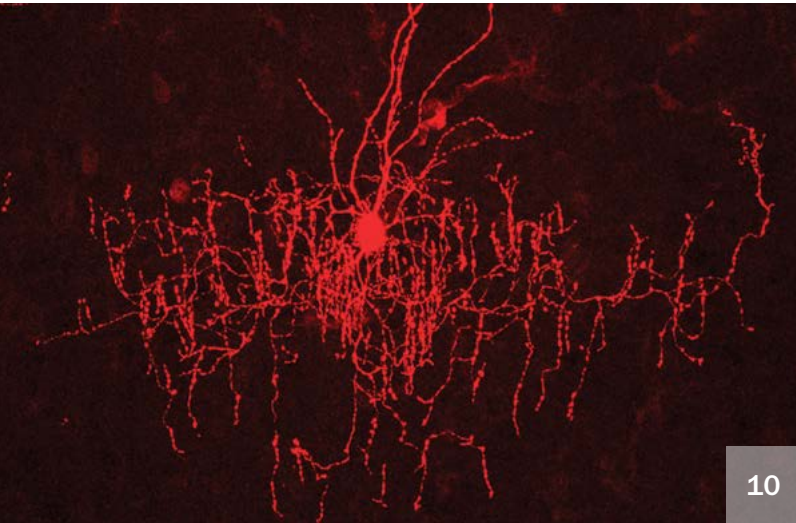
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Each cortical chandelier cell has veto power over the signal of hundreds of excitatory neurons



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Holding the line on rainforest loss



Genetic insights leading to higher yield may help governments prevent palm oil lands (right side) from moving further into the rainforest (left side).

Over the last decade, people around the globe have doubled their consumption of oils derived from the fruit of the oil palm tree. These relatives of the coconut palms more familiar to Americans have rapidly come to account for nearly 50% of edible oils used globally and are found in a vast diversity of commercial products ranging from chocolate to chewing gum to dishwashing detergent. The “palm” in Palmolive refers to the oil derived from this protean monocot.

It has become hard to *avoid* consuming products derived from the oil palm, and this helps to explain the plant’s reputation in some quarters as threat to the global environment. Fairly or not, commercial growers of the oil palm and Southeast Asian nations harboring the largest plantations have become anathema to Greenpeace, the World Wildlife Fund and some other environmental groups.

The rap is that the crop’s great commercial value encourages growers to sacrifice pristine tropical rainforest or drain peaty lowland swamps to make way for plantations, thus accelerating global warming and depriving forest creatures of habitat, including the endangered orangutan.

This past summer, scientists in Malaysia and the U.S., prominently including CSHL Professor and HHMI-GMBF

Investigator Rob Martienssen, published two papers in *Nature* revealing genetic secrets of the oil palm. The chief of these secrets is the identification of a long sought gene, dubbed *Shell*, that controls the plant’s oil yield. This new knowledge could lessen pressure on the rainforest by making it possible to produce more oil on less land.

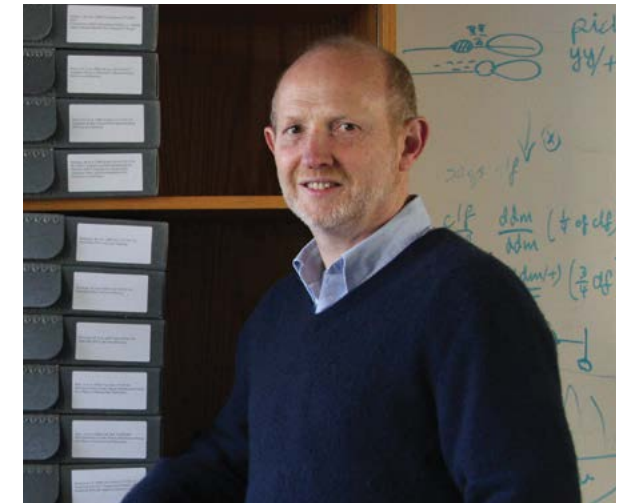
It is good news for every party to the debate. For growers, it means a clear path to higher yield and a solid basis for raising varieties bearing the highest-yielding fruit; for the governments of Malaysia and Indonesia, help in making the case for growers to observe existing moratoriums against further rainforest encroachment [see iPad extra]; and for conservationists, therefore, a basis for hope that pressure upon the forest and its denizens may now begin to recede.

Sequencing the oil palm genome was hard, “like assembling a huge jigsaw puzzle in which most of the pieces are identical,” Dr. Martienssen says. Oil palms come in only two species, one native to West Africa, the other to South America. The West African plant, the basis for today’s commercial crop, was the target of the project, which was funded by the Malaysian Palm Oil Board, a government agency. Martienssen began working with the MPOB on sequencing five years ago, in connection with his status

as scientific cofounder of St. Louis-based Orion Genomics (the other cofounder is CSHL Professor and gene sequencing expert Dick McCombie). Orion, which performed the assembly of the oil palm genome, is one of the 20-plus spin-offs seeded with technology and knowledge generated in CSHL labs.

Martienssen brought another vital asset to the project. He is among the foremost experts on epigenetics, a phenomenon first understood in plants. When living things reproduce, their offspring inherit the full complement of genes that defines their species. But in addition to their genes, plants, people, and all multicelled organisms inherit chemical marks that attach to their DNA, which influence how their genes are expressed. As Martienssen and others have shown, epigenetic anomalies can cause disease in plant offspring.

“The Malaysians had the great foresight,” Martienssen says, “to fund research that would lead to understanding” not only of the oil palm’s genome but also of epigenetic factors that cause costly defects in oil palm fruits. Plants



Professor Rob Martienssen

like commercially grown oil palms that are cloned are particularly susceptible to epigenetic errors.

While the epigenetics work continues, the completed genome sequencing project and the team’s identification of *Shell* shows growers why a hybrid variety can maximize oil yield. *Shell*’s secret is that it controls the thickness of the hard shell surrounding oil found in the fruit’s central kernel (see illustration, left).

Simple gene tests will make it possible for growers to find their high-yielders in the nursery, before committing to planting them and waiting 5–10 years before they fruit to discover their yield. “If we can get growers the seeds that will always give high yields, then we take a major step toward making this crop sustainable, by raising oil yield per unit of area planted,” Martienssen says.

It’s a win for science, for Malaysia, for growers, and, everyone hopes, for the forest and its creatures.

Peter Tarr



Fruits of West African oil palms, called *dura* (left), have thick shells and less oil inside, as well as a thinner pulp surrounding the shell, which is also oil-bearing. A mutant variety of the tree bearing fruit with no shell at all, called *pisifera*, is nearly sterile. But when these two varieties are crossed, a special kind of hybrid vigor (called single-gene heterosis, studied also by CSHL plant geneticist Zach Lippman) renders the offspring ideal. Their fruit (right) has “a shell thin enough to maximize oil yield, yet thick enough to ensure fertility,” Martienssen explains. This desired variety is called *tenera*.

My amazing 'URP' summer



The author (third from left) and 26 fellow URPs, class of '13

by Alexis Tchaconas
Columbia University Class of 2014

When I first arrived at Cold Spring Harbor Laboratory in early June, I knew this wouldn't be a typical summer. Even though I had worked in labs over past summers, never before had I completely immersed myself in science as I did during my 10 weeks as an "URP," a participant in the Undergraduate Research Program.

I was pleasantly surprised when I arrived and noticed all of the conspicuous artistic references to DNA throughout the campus, planted for the appreciation of biology lovers like myself. On our first tour of the grounds I marveled at the "Waltz of the Polypeptides," an arresting steel sculpture that unfurls itself across the hillside beside the Dolan building; and Beckman Lab's rectangular clock tower, each of its four sides adorned with one of the letters representing the DNA bases (A, T, C, G). As someone fascinated by genetics, I felt immediately at home in seeing these and other campus tributes to DNA.

Unlike most URPs, who are assigned to their faculty mentor after applying, I chose to reach out directly, to Dr. Michael Wigler, before applying. The Wigler lab uses quantitative

biology to investigate the mechanisms of genetic disorders like autism—an approach I wanted to learn more about. My interest was fueled by my personal connection to the disorder, as my older brother has autism.

I had just spent my junior year in college studying at the University of Oxford in the U.K., to better integrate my neuroscience major at Columbia University with my linguistics concentration. I have a great love of language and have come to appreciate its importance in science and medicine. But I also know that it is one of the things most commonly affected in autism, a disorder whose symptoms affect various aspects of social interaction. At Oxford I had the opportunity to conduct research on language impairment in Dr. Dianne Newbury's lab, where I was fascinated to learn that quantitative biology programs can scan sequencing data from an entire genome and find potential disease-causing mutations within minutes!

From that point on, I knew that I wanted my next research experience to be in quantitative biology—which is why I got in touch with Dr. Wigler. I remember our first interaction via e-mail; he responded within 5 minutes, encouraging me to submit an application for the URP program under his tutelage.

On my first day as an URP, Dr. Wigler was eager to welcome me as a member of his lab. After updating me on the lab's current work, he and I brainstormed project ideas that could be tackled during my 10 weeks at CSHL. Given that most genetic studies on autism have focused their analyses on DNA contained in the nucleus of cells—this is called nDNA, for nuclear DNA—we thought it would be worthwhile investigating another source of DNA, existing in the cell's plentiful energy-producing compartments called mitochondria.

DNA in mitochondria (mtDNA) is interesting in that it has a 5 to 15 times greater mutation rate compared to DNA found in the chromosomes. There would be plenty of material to study since multiple copies of mtDNA exist in each mitochondrion, and thousands of mitochondria can exist in a single cell.

The mitochondria, seen in this way, are a relatively understudied "hotspot" for genetic mutation. Autism is a neurodevelopmental disorder and mitochondria are highly expressed in nervous tissue, so mutations in mtDNA could alter energy production and thereby affect proper brain functioning. Furthermore, autism has a male bias—it affects far more males than females—and it so happens that males tend to have more mtDNA mutations than females.

Dr. Wigler and I designed a study to analyze mtDNA sequencing data from families whose DNA is sampled in the Simons Simplex Collection (SSC). These "simplex" families are ones with two or more children, only one of whom is diagnosed with autism. (This is in contrast to "multiplex" families, with more than one autistic child.) The objective of my project was to ascertain how often children with autism inherit mtDNA that is significantly different from their mothers' mtDNA, or inherit mtDNA in altered proportions.

After completing 10 weeks of URP research, I had made much progress in answering my research question—so much that I continued my project in the Wigler lab until I had to return to Columbia in late August. I can now offer this progress report: we have identified a bias for the emergence of new mtDNA mutations in children with autism, relative to their normal siblings. I am working on characterizing these mutations and analyzing more simplex families in additional data we've received from the SSC. The hope is that such work, beyond autism, could more broadly elucidate the biological mechanism of mitochondrial inheritance and its role in disease.

I will keep in contact with Dr. Wigler, as he has served as a nurturing mentor and an inspiring role model. And I will always have warm thoughts about CSHL and the URP program as a whole, which, outside of my research project, helped me learn more about what it means to be a scientist outside the lab and how to thrive in a scientific community.



URPs of yesteryear: (top) Alan Rein ('61) with Dr. A. Chovnick; (bottom) David Baltimore ('59) with Dr. B. Kaufmann

An historic incubator of young talent

Each year since 1959, CSHL's Undergraduate Research Program (URP) has offered up to 25 American and foreign undergraduate students a priceless opportunity to study side by side with some of the world's most distinguished scientists. The fully subsidized, 10-week summer program offers independent research projects in Cancer Biology, Neuroscience, Plant Biology, Cellular and Molecular Biology, Genetics, Bioinformatics and Genomics. A few of the notable alumni include Dr. Gerry Rubin (HHMI, Janelia Farm Research Campus), Dr. Alfred Goldberg (Harvard Medical School), Dr. Geraldine Seydoux (Johns Hopkins), Dr. Charles Gilbert (Rockefeller University), and Nobel laureate Dr. David Baltimore (California Institute of Technology).

Administered by the Watson School of Biological Sciences (WSBS), the URP course is designed to give students the skills and opportunity to conduct first-rate research. Applications are submitted online, and the deadline for the Summer 2014 program is January 15, 2014. For further information about the program, visit the webpage: cshl.edu/education/urp or send an email to urpadmin@cshl.edu.

Who gets to be an URP? Alexis' backstory



I grew up in East Northport, Long Island, and went to Commack High School, where I took advantage of the prestigious International Baccalaureate program and the school's phenomenal science research department. It was there that I got my first exposure to research and was encouraged to participate in nearby Stony Brook University's (SBU) biotechnology program the summer before my junior year. There I learned advanced biological laboratory techniques like polymerase chain reaction, or PCR, in

which you can greatly amplify tiny samples of DNA; and plasmid preparations, a way of purifying bacterial DNA.

Armed with these techniques, I returned for my junior year in high school and planned an investigation to explore a candidate gene that had been recently associated with autism: *contactin 4* (CNTN4). It is thought that having certain "risk" genes makes a person more susceptible to developing the illness. I began by searching public gene databases, where I found a version of this human gene in the roundworm, a simple model organism called *C. elegans*.

The summer before my senior year in high school, I was able to arrange with Dr. Lorna Role, chair of SBU's neurobiology department, to continue with this research in her lab as a Simons Foundation Summer Research Fellow. For this work I was named an Intel Science Talent Search semi-finalist, a New York State & Long Island Science Fair First-Place Winner, an Intel International Science & Engineering Fair (ISEF) Finalist, and a National Junior Science & Humanities Symposium (NJSHS) Finalist.

The following fall I entered Columbia University, where, during my first semester, I began researching in Dr. Martin Chalfie's neurobiology lab. I had already been lucky enough to have worked in my junior year in high school under the direction of Dr. Andrew Adesman, a developmental-behavioral pediatrician, with whom I co-authored a review article in *Current Opinion in Pediatrics*. Working with Dr. Chalfie on the clinical side of autism research confirmed my interest in a career as a physician-scientist.

It was at this point that I was accepted at the University of Oxford for my junior year of college—the experience that led me to write Dr. Wigler and apply for the URP program.

Once I graduate from Columbia this coming spring, I hope to pursue a 1-year research master's degree in the U.K. Ultimately, I hope to have both an M.D. and Ph.D., because I want to directly translate my findings at the bench to clinical applications at the bedside. It's the next step in what has already been an amazing journey, enabling me to merge a personal connection to autism and an intellectual interest in genetics into a lifelong effort to improve treatment, detection, and prognosis of people with autism.

Alexis Tchaconas
Columbia University Class of 2014

What mad pursuit!

A unique “sporting” event, the annual Plate Race has been a fixture of the summer Meetings & Courses program at the Laboratory since about 1983. What is a Plate Race? University of Oregon cell biologist and CSHL summer course instructor Dr. Bruce Bowerman describes it as follows: “It is a relay race in which each team member has to run one lap while carrying a stack of twenty 150mm stinky, used yeast plates (a petri dish containing a solid nutrient on which is grown yeast or bacteria). After completing the lap, each racer has to transfer the stack to the next team member, without dropping them. If you drop them, you have to go back to the beginning, get a new stack and start over!”

The race takes place on Bungtown Road in the heart of the CSHL campus and rapidly loops uphill in front of the Nichols building, and then downhill again, in a roughly 200m course. It’s really a symbol of the powerful, collaborative and enthusiastic learning experience that participants have in taking advanced summer courses at CSHL. So cheers to this year’s winning team, from the Gene Expression Course! With apologies to Francis Crick: What mad pursuit!

Edward Brydon

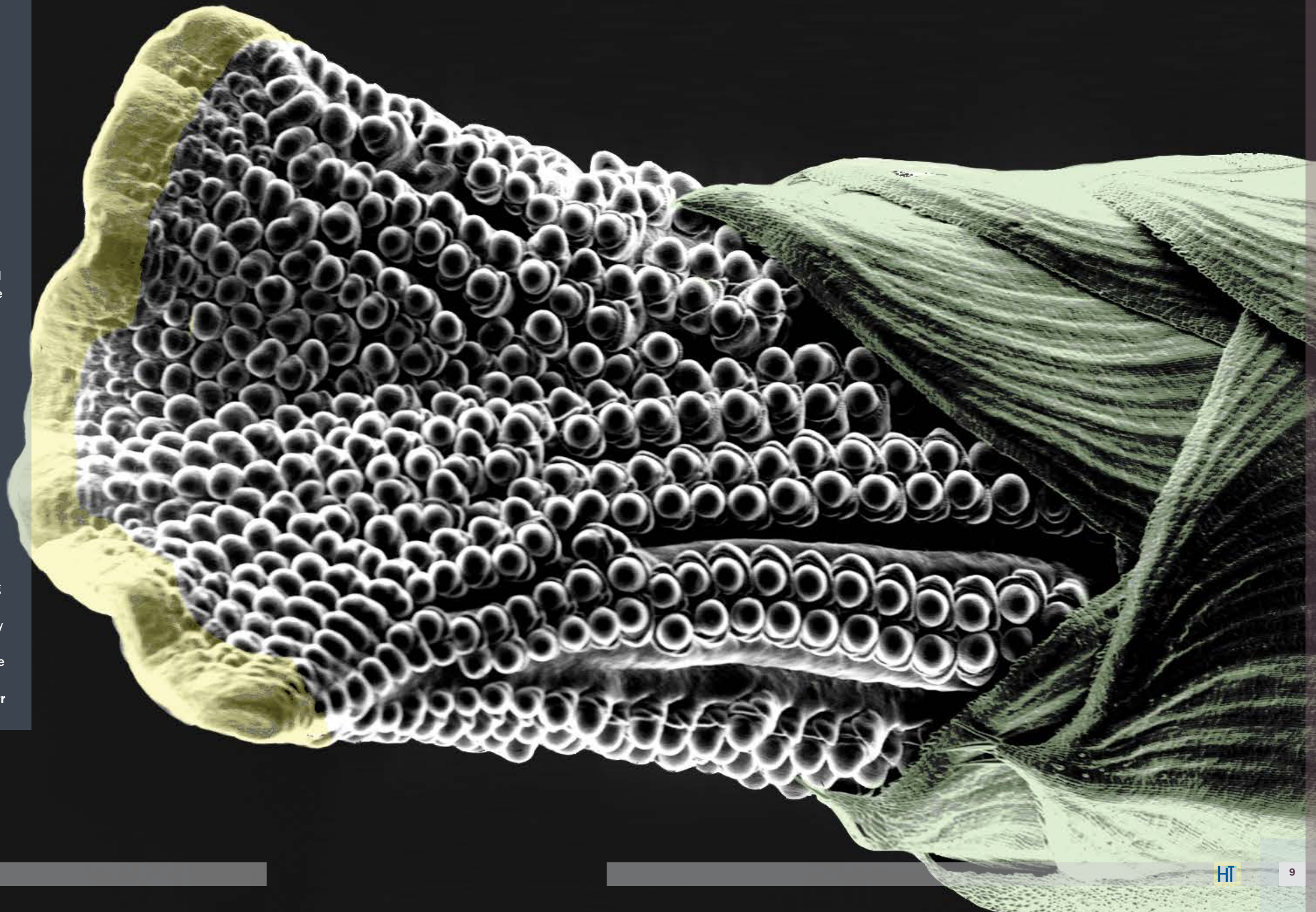
One experiment

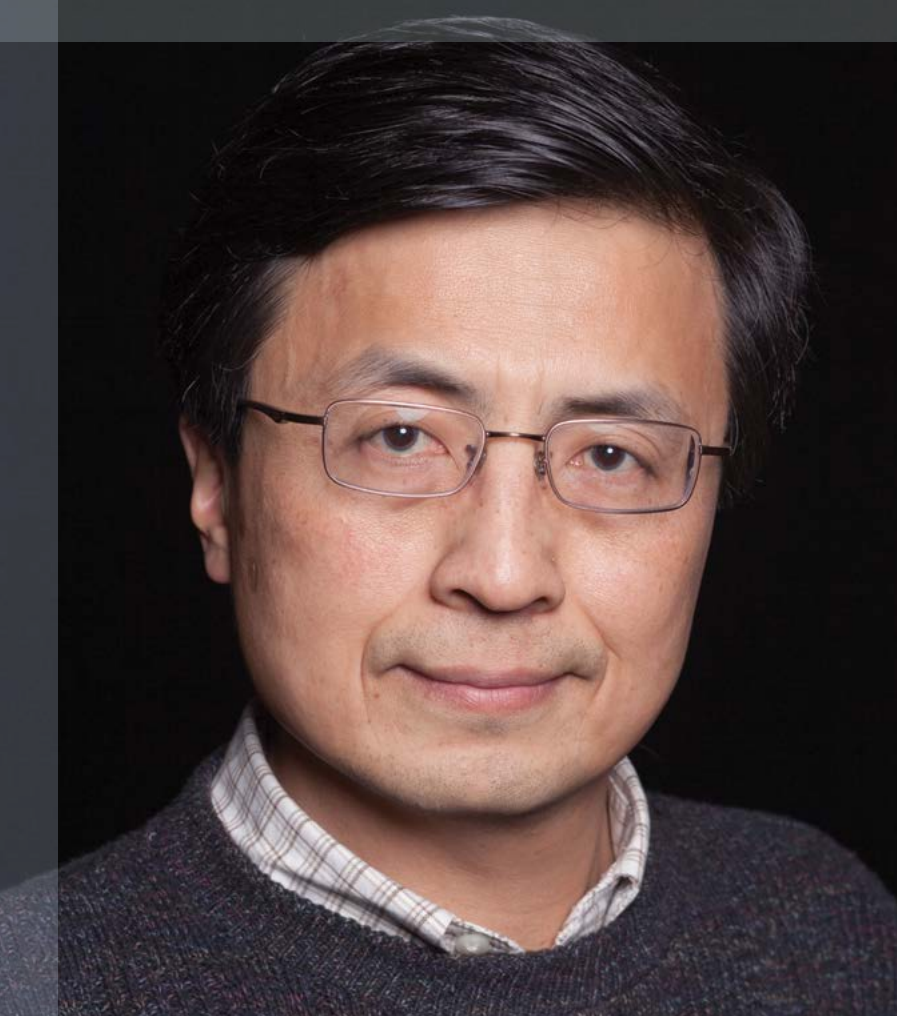
You're looking at an ear of corn, recently cut from the side of a five-foot-high maize plant (as corn is called nearly everywhere but in America). The ear, which we view through an electron microscope, is tiny, about a quarter of an inch in length and only just beginning to grow. Importantly, it's a mutant, and therefore just the kind of ear that Professor David Jackson and his lab love to study. For in mutants lay secrets of growth; and, as Jackson points out, in these secrets are clues about how to improve plants to adapt to a changing climate, or, as in the case of this mutant, clues about how to harness genetics to boost yield. The latter is critical as our planet's population continues its climb toward an expected 9 billion by 2050.

A mutated gene called *COMPACT PLANT2 (CT2)* renders this fruit of the maize plant flattened in shape, a phenomenon called fasciation. The husk, tinted green, has been pulled back to expose the developing, misshapen ear and its growing tip, tinted yellow, called the meristem. Normally conical in shape, the meristem, or stem-cell reservoir of the growing ear, is abnormally elongated. The bump-like baby kernels form a profusion of irregular, non-parallel rows, unlike the kernels of the prized varieties we eat, with their military-straight rows of succulent kernels.

In one recent experiment, the team demonstrated the significance of this ear's irregularity. Its genetic defect has caused stem cells in the meristem to proliferate abnormally. More seeds can mean greater yield; but here the process has spun out of control. In related research also published in 2013, Jackson and his former postdoctoral colleague Dr. Peter Bommert described another maize gene, *FASCIATED EAR 2 (FEA2)*, important in sending growth signals to the meristem. By making a weak version of *FEA2*, they created maize plants with significantly more kernels per ear. Happily, they were not fasciated or otherwise misshapen. The results could be even better when crosses are made with high-yielding commercial varieties.

Peter Tarr





RESEARCH PROFILE

Z. Josh Huang

Exploring the cerebral cortex

“An engineer will tell you that in order to understand how an electronic circuit works, you need to know the components. Well, that’s not too difficult if you know resistors, transistors, etc. But in the human brain, things are pretty murky. We are only just beginning to get a fix on the types of cells that it contains.”

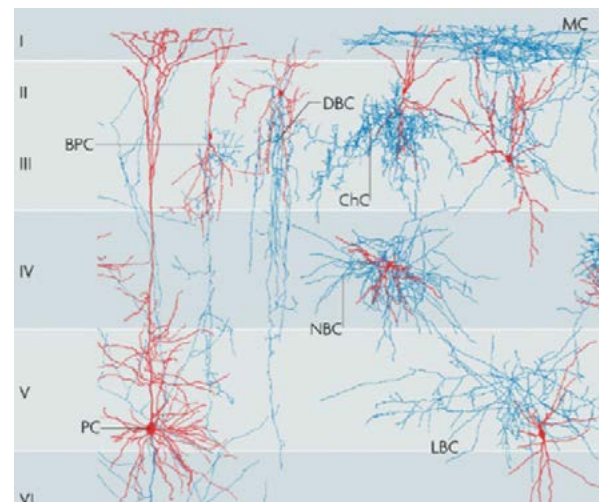
The speaker, Z. Josh Huang, is the Marie and Charles Robertson Professor of Neuroscience at Cold Spring Harbor Laboratory. He explores the magnificent and profoundly complex territory of the cerebral cortex. Accounting for about 80% of the human brain’s mass, the wrinkly cortex, the cerebrum’s outer layer, is the site of neural processing that gives rise (in *homo sapiens*) to species-defining qualities such as consciousness, memory,

attention, thought, and language. Over 3.5 billion years of life on Earth, says Huang, the human cerebral cortex is evolution’s “supreme achievement.”

It’s also a place where small-scale anomalies can have outsized, often tragic, consequences. Huang is studying the cortex, typically in mice, our mammalian relatives, to learn more about neuronal subtypes: how they originate, develop, and form functional circuits. This basic research crucially informs efforts to discover what goes wrong, for instance, in autism spectrum disorders such as Rett syndrome and in schizophrenia, both of which Huang studies with collaborators.

“Studying the structure and function of the cortex has been a big problem for a very long time,” says Huang. “It’s like being in the Amazonian jungle, surrounded by all kinds of trees and vines and other plants that are different but look similar. How do you keep from getting hopelessly lost? How do you make sense of it?” In 2011 his lab crowned five years of often frustrating effort with a great success: they delivered to the worldwide neuroscience community a series of genetically engineered mouse lines, each of which enables investigators to isolate, identify, and track in living animals one of a dozen distinct cortical cell subtypes.

All of the subtypes rendered visible in Huang’s engineered mice (the series continues to expand) are similar in one



Schematic of 6-layered mouse cerebral cortex. Cell labeled ‘PC’ (far left) is a pyramidal neuron, the most common excitatory cell type. Its dendrites (output channels, in red) cut across many layers. Inhibitory cells feature profuse axons (input channels, blue) whose reach is local, often confined to a single cortical layer.

important respect. All are inhibitory neurons, one of the two basic neuronal types. Inhibitory neurons are sometimes called GABAergic cells after the neurotransmitter (gamma aminobutyric acid, or GABA) that they release and that triggers inhibition. They have the crucial role of modulating circuits composed of the other basic neuronal type, excitatory cells, which dominate the cortex. Despite the inhibitory function they have in common, each GABA cell subtype is in some way distinct, and until dissemination of Huang’s mouse lines, they were impossible to study cortex-wide in a systematic and consistent manner.

“Our method brings the study of cortical cell types from out of the realm of art and into that of science, where everyone can be sure they are working on the same kind of cells,” Huang says. He likens his team’s achievement to the building of a GPS system for cortical inhibitory neurons, but better: “because GPS can only show you where you are, while in our mice you can observe how the cells got to where they are—you can see where they are born and how they migrate into their characteristic positions in the maturing cortex.”

Genetic handle

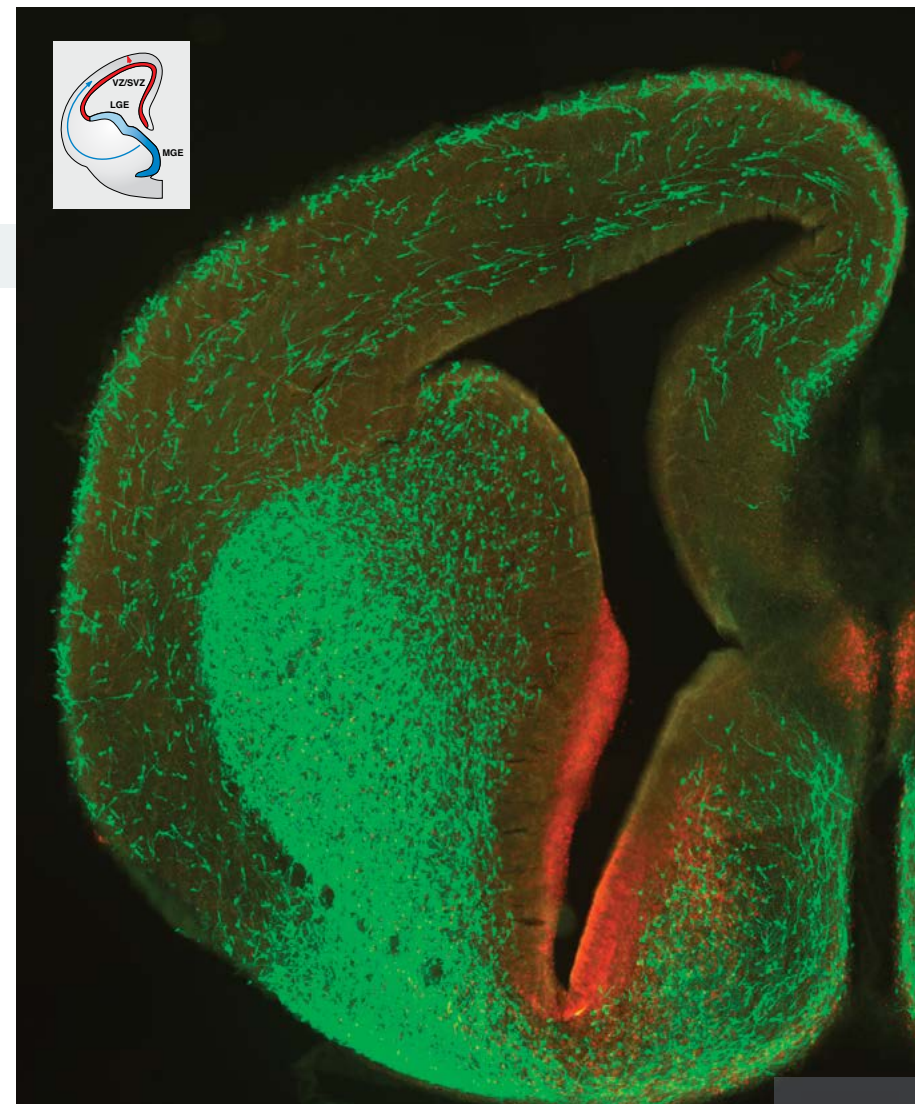
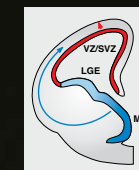
A native of Beijing who came to America in 1986, Huang appreciates the advantage of having grown up in the age of molecular biology. By the time he reached MIT as a postdoctoral researcher in 1995 after earning his Ph.D. at Brandeis, he knew he “wanted to build tools that would enable me to systematically study a problem that had been very difficult for classical neuroscience to address.” His GPS system for inhibitory neurons is precisely this kind of advance, for it provides a handle with which to tag or manipulate specific subtypes of neurons. Importantly, the handle is a genetic one. This makes it very powerful.

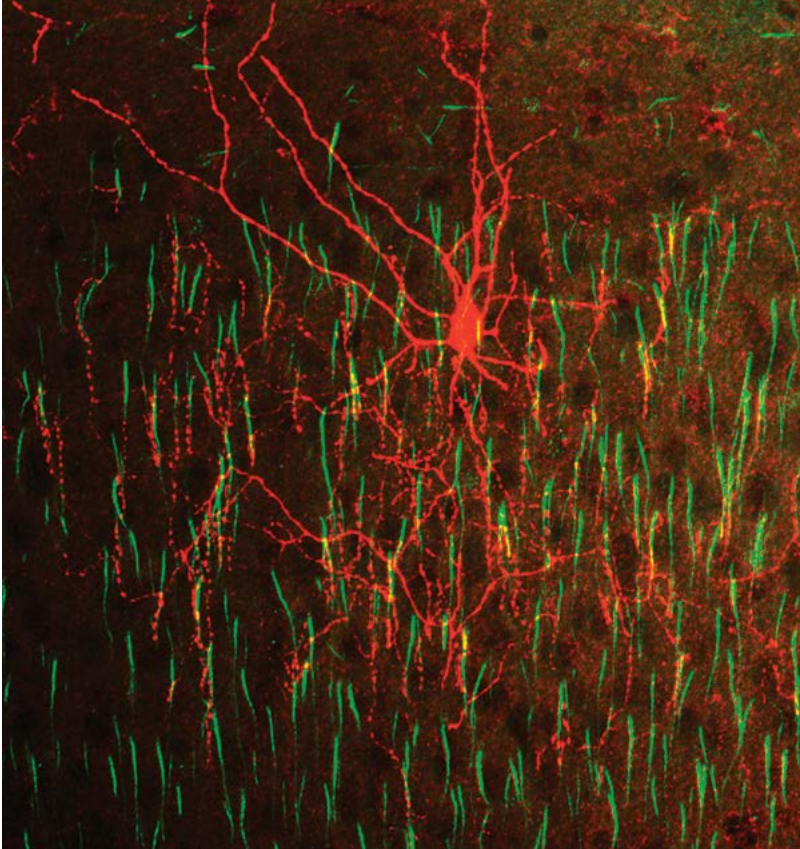
To explain why, Huang points out that the architecture of the human brain is fundamentally similar in

each individual. What makes each of us unique is partly a function of experience and how it tweaks nature’s basic design for the brain, by making some circuits as well as synapses between nerve cells stronger or weaker than others. Yet the underlying structural and functional similarity across individual brains is a product of the genetic program that guides brain development. “Genes provide the finest scalpels for circuit dissection,” he says.

In their GPS project—“a gene-based cell positioning system”—Huang’s team figured out how to genetically engineer mice in which a particular gene or genes of interest, ideally gene(s) expressed by a single subtype of inhibitory cell, becomes a place in the genome where a molecular

Migratory route of a GABA cell subtype. Only cells expressing the gene *Dlx5* glow green. It’s one of a family of regulatory genes switched on at various times in an inhibitory cell’s life—here, to regulate the young cell’s journey from its birthplace (area labeled MGE, inset) along a curving path (blue arrow, inset) into the cerebral cortex.





Master inhibitor: axons from a single chandelier cell (red) in the mouse cortex align precisely with green-labeled axon initial segments (AIS) emanating from many local excitatory neurons. By forming synapses at these points, one chandelier cell can halt or modulate signals coming from hundreds of excitatory cells.

tool can be attached. The tool might be a marker, like green fluorescent protein: in the animal bearing the modified gene, all brain cells expressing it will glow green. Or, one might splice in a gene that encodes a light-sensitive channelrhodopsin protein, so that any neuron expressing the protein can be activated or inactivated with a targeted beam of colored laser light.

Balancing inhibition and excitation

Neural circuits in the mature cortex depend on an exquisite balance between excitation and inhibition to function normally. “Keeping the balance is a very demanding task,” notes Huang. “This is because the balance is not static; cortical cells are constantly receiving inputs, and the balancing process is going on all the time, responding on a time scale in the range of tens of milliseconds [thousandths of a second].”

If inhibitory cells were not present in cortical circuits, the circuits would seize up, as in epilepsy, due to an overload of excitation. Because they supply needed balance on a dynamic basis, inhibitory cells can be thought of as rendering local groupings of excitatory cells functional.

Since they enable the observation of specific cell types in living animals, Huang’s technologies have opened a new window on disease processes. Some pathology in neuropsychiatric illnesses is assumed to be caused by errors in the way the cortex self-assembles; or by imbalances between excitation and inhibition that may originate in local circuitry in specific brain regions.

Huang and colleagues this past year solved a mystery about where in the brain a master-inhibitory cell type is born and how and when during development it navigates into the cortex. Called chandelier cells, each one of these rare gossamer structures “wires-up” to hundreds of excitatory cells, and acts as a kind of circuit breaker, capable of canceling out all of their input signals at once. Huang and Dr. David Lewis of the University of Pittsburgh are studying how schizophrenia pathology may be traceable to imbalances created by faulty or missing chandelier cells.

Recently, members of Huang’s team have made progress in developing a set of markers and tools for excitatory neurons (also called pyramidal cells). This will provide long-sought information about their diversity and functional organization. There are probably hundreds of excitatory cell subtypes in the cerebral cortex, Huang says, but no one knows how many or how they are distinguished functionally.

Unlike inhibitory cells, which tend to act locally and therefore have short axonal projections that can be traced with comparative ease, excitatory neurons project great distances, often across brain hemispheres and all the way down to the spinal cord, rendering them impossible to follow at high resolution in real time as they interact with distant cortical regions.

Yet these are “the real information processing streams and output channels in our brain, and, in a sense, inhibitory cells are there mainly to help these excitatory cells work properly,” Huang notes. “If we want to understand the cortex, we have to understand these cells. This will be a new chapter not just for my lab but for the entire field.”

Peter Tarr

Faculty & Friends



Double Helix Medals dinner

The 8th Double Helix Medals were awarded on November 4, 2013 to Innocence Project co-founders Peter Neufeld and Barry Scheck and “Good Morning America” co-host Robin Roberts, an advocate for breast and blood cancer research. Thanks to support from our Board of Trustees and many generous donors, the event raised \$3.7 million for CSHL research and education programs. Visit doublehelixmedals.cshl.edu for extras.

Four new trustees elected

The Laboratory’s governing body this year welcomed four new members with extraordinary academic and professional pedigrees: Dr. Cornelia I. Bargmann, Dr. Robert W. Lourie, Jeffrey E. Kelter and Thomas A. Saunders III.

Dr. Bargmann, a neuroscientist and winner of the 2013 Breakthrough Prize in Life Sciences, is the Torsten N. Wiesel Professor and codirector of the Shelby White and Leon Levy Center for Mind, Brain and Behavior at Rockefeller University.

Dr. Lourie, a former University of Virginia physics professor and market research expert, is the Head of Futures

Research at Renaissance Technologies LLC, an investment management company.

Real estate investment leader Jeffrey E. Kelter is founder and CEO of KTR Capital Partners, a private equity firm with expertise in all facets of real estate acquisitions, development, finance, operations and asset management.

Elected for a second time after having served on the CSHL Board from 1992–1998, Thomas A. Saunders III is an investment banker and philanthropist. Since 2000, he has been CEO of Ivor & Co., LLC, a privately owned investment firm.



Women's Partnership honors Elizabeth L. Watson

The 12th annual luncheon event honored Liz, who with husband Jim has lived and raised a family on the CSHL campus for 45 years. With master's degrees from the Columbia School of Architecture and Planning and the Palmer School of Long Island University, Mrs. Watson has authored two books about the Laboratory's history, landscapes and buildings.

The featured speaker on breast cancer prevention strategies was Camila Dos Santos, a postdoctoral fellow in the lab of Professor and Howard Hughes Medical Institute Investigator Gregory Hannon. A mother of two herself, Dr. Santos provided a personal perspective on her life as a scientist working to understand the impact of pregnancy on a woman's risk of developing breast cancer.

Teri Willey leads commercialization efforts

As Vice President, Business Development and Technology Transfer, Ms. Teri Willey now directs the Laboratory's commercialization and technology transfer activities, including patenting, licensing, company start-ups, and corporate partnerships and collaborations. She joins CSHL from Mount Sinai Medical Center, where she led technology transfer and business development efforts. Ms. Willey was founding Chief Executive and Executive Director, Cambridge Enterprise Ltd, University of Cambridge, UK, and was a cofounder and Managing Partner of ARCH Development Partners, a seed venture fund and spin-out from the University of Chicago and Argonne National Laboratory technologies.



John Maroney, who for the past 20 years has helped many CSHL investigators launch successful tech start-ups and negotiate licensing agreements to bring biomedical discoveries into the marketplace, will continue in his role as the Laboratory's general counsel. Mr. Maroney played a critical role in establishing the Broad Hollow Bioscience Park, a collaborative biotech incubator on the campus of SUNY Farmingdale that was the original home of LI cancer drug manufacturer OSI. "John has helped lay the foundation for Long Island to leverage the academic and clinical assets of its leading institutions, including CSHL, Stony Brook University, Brookhaven National Laboratory, Hofstra University and the North Shore-LIJ Health System," said President Bruce Stillman.

CSHL boasts four NARSAD winners

This year four CSHL postdoctoral researchers are among 200 awardees chosen from among 1199 applicants worldwide for the two-year, \$60,000 NARSAD grant award to help young scientists transition to work in laboratories they themselves direct. "On behalf of the entire faculty, let me say that we are proud of you, individually, and pleased that through your projects, the goal of CSHL's basic research program in neuroscience of understanding the biology underlying devastating disorders including schizophrenia and autism has been given an important boost," said President Stillman.



Three of the CSHL postdocs are studying autism and autism spectrum disorder (ASD); one is conducting research on schizophrenia. They are:

Sandra Ahrens, (Associate Professor Bo Li) who will use a mouse model to study a brain circuit called the thalamic reticular nucleus circuit and its dysfunction in schizophrenia. This circuit may have a critical role in cognitive functions such as attention.

Guy Horev, (Professor Alea Mills) who will assess brain development in mouse embryos with a genetic deletion that occurs in patients with autism, to pinpoint the genes that lead to autism-like impairment to see if rescuing the developmental impairment will correct the behavioral impairments.

Yongsu Kim, (Associate Professor Pavel Osten) who will explore how intranasal oxytocin works in the brain to improve social behavior in autism. He will use a mouse model of autism to describe which brain regions respond, and how this drug alters brain activity that leads to the observed improvement in social behavior.

Keerthi Krishnan, (Professor Josh Huang) who seeks to understand the genetic architecture of Rett syndrome, an autism spectrum disorder. She will use advanced genomic methods in a mouse model to trace molecular changes in a brain region-specific, cell type-specific manner during early development.

Professor Hannon selected for MERIT award

Professor Gregory Hannon has received the MERIT award of the National Institutes of Health National Institute of General Medical Sciences (NIGMS), recognizing highly productive scientists with extended funding for an existing research project grant. Hannon was selected for "his remarkable record of discoveries on how small RNA molecules regulate gene expression and help ensure that the genome is passed faithfully from parents to their offspring," said Michael Bender of NIGMS. "His work is likely to yield many additional insights into the biology of small RNAs, and also has the potential to lead to new, RNA-based treatments for cancer and other diseases."

Blavatnik Award goes to investigator Hodges

Dr. Emily Hodges is one of five finalists in the annual Regional Blavatnik Award for Young Scientists, celebrating the excellence of the most noteworthy postdoctoral scientists age 42 or under who work in New York, New Jersey, and Connecticut. Dr. Hodges will receive \$10,000 in unrestricted funds from the foundation. She received her Ph.D. from the Karolinska Institute in 2006 and after



Samuel Stuart



completing postdoctoral work on next-generation sequencing for targeted genomics under the mentorship of CSHL Professor Gregory Hannon, Hodges was promoted to CSHL Research Investigator. Her most recent work involves the use of epigenomic profiling to understand the role of DNA methylation in gene regulation and cell fate specification during development. Download the *Harbor Transcript* app to see a video about Dr. Hodges.



UNIVERSITY OF NOTRE DAME

Notre Dame establishes DNA Learning Center

Cold Spring Harbor Laboratory has partnered with the University of Notre Dame in a licensing agreement that shares the original mission of our DNA Learning Center (DNALC). “We encourage the spread of hands-on science centers devoted to modern biology education and preparing students and families to thrive in the gene age,” said David Micklos, the Executive Director of the CSHL center dedicated to public education. The center in Southbend, Indiana, will fulfill the vision of Notre Dame benefactors John and Heidi Passarelli, who saw firsthand how the DNALC was providing a superb participatory genetics education to children across the New York metro area. Through involvement in the DNALC Corporate Advisory Board, the Passarellis initiated the link to the University of Notre Dame. Celebrating its 25-year anniversary, CSHL’s DNA Learning Center has successfully collaborated with public school districts, private schools, departments of education, and universities, including the Republic of Singapore and Clemson University.

President’s Council on infectious disease

CSHL alumni headlined this year’s intellectual retreat for supporters who donate \$25,000 a year or more to help support CSHL Fellows, exceptionally talented young scientists who show the capacity for high-level, independent research. CalTech President Emeritus and Nobel laureate David Baltimore discussed new approaches for dealing with the AIDS pandemic. Dr. Baltimore is an alumnus of the CSHL Undergraduate Research Program who, as a Swarthmore College student, spent the summer of 1959 in the 10-week educational program on this campus. Dr. Niraj Tolia, who was part of the first graduating class of the Watson School of Biological Sciences in 2004, provided insights on developing a protective malaria vaccine. Dr. Tolia is now an assistant professor at Washington University School of Medicine. Other President’s Council speakers included Eckard Wimmer, Ph.D., Stony Brook University; Dr. Larry Barrett, Director of Plum Island Animal Disease Center; Jonathan Epstein, DVM, MPH, of EcoHealth Alliance; and Dr. Trevor Mundel, President, Global Health at the Gates Foundation.

Postdoc Christine Iok In Chio named a Damon Runyon Fellow

Christine Iok In Chio, Ph.D., a postdoctoral researcher, has been named a Damon Runyon Fellow. Dr. Chio works in the laboratory of Dr. David Tuveson, Deputy Director of Research at CSHL’s Cancer Center, Director of the Lustgarten Foundation Pancreatic Research Laboratory at CSHL and Director of Research for the Lustgarten Foundation. Dr. Chio’s research



focuses on pancreatic cancer, which is a particularly devastating and difficult-to-treat disease because of its ability to grow in conditions of high oxidative stress—conditions in which normal cells would not survive. She is evaluating the biological role of oxidative stress in pancreatic cancer development and progression, using mouse models of pancreatic cancer as well as human tumor samples. All 17 recipients of the prestigious, three-year Damon Runyon Fellowship award are outstanding postdoctoral scientists conducting basic and translational cancer research in the laboratories of leading senior investigators across the country.



With the installation of a commemorative engraved glass wall, we recognize the generous contributions of the donors who made possible the largest expansion in the history of the Cold Spring Harbor Laboratory. The six Hillside Laboratory buildings opened in 2009 allow CSHL to further its research and education mission well into the 21st century.

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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 orzelt@cschl.edu.

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Don't think science is for the masses?



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extras for
this issue!

Come for a drink, but stay for the science and mingle with 400 science enthusiasts at a monthly event in Brooklyn called the Secret Science Club. CSHL scientists are regular headliners. This summer, Assistant Professor Anne Churchland wowed the crowds discussing how the brain makes complex decisions. Associate Professor Zach

Lippman took to the stage earlier in the year, linking his latest tomato genetics research to big problems like world hunger. See their appearances for yourself on YouTube and watch for upcoming CSHL Secret Science Club appearances at the Bell House in 2014.

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