HARBOR TRANSCRIPT

3D SCIENCE!

Cold Spring Harbor Laboratory

CSHL shapes the future

Discovery in 3D

VOLUME 37 · ISSUE 1 · 2017

Cold Spring Harbor Laboratory

PRESIDENT'S MESSAGE

At the end of 2016, we completed a multi-year 125th Anniversary Capital Campaign that raised $278 million for Cold Spring Harbor Laboratory (CSHL), including much needed endowment funds for research. During this time, we raised an additional $180 million in philanthropic research and education support. Thus, philanthropy continues to propel us forward into exciting new areas of discovery. These funds put into motion forces that allow CSHL to continue to shape the future of life science.

In this magazine, Campaign Committee members share their personal connection to the Lab. Thank you to the committee, led by the indomitable Marilyn Simons. Together with Board Chairman Jamie Nicholls, Marilyn led the effort to secure 60% of campaign contributions from current, honorary and former trustees. Notably, planned gifts from many long-time friends—now Helix Society members—were extremely meaningful and significant to our success.

Read about the most innovative ideas for cancer treatment and diagnosis being pursued by CSHL's new National Cancer Institute-designated Cancer Center Director David Tuveson, M.D., Ph.D. Having held that position for 25 years, I asked David to take over so that I can focus on my role as CSHL President and CEO. David is a pioneer in 3D cancer models called organoids that are changing our perspective on this disease.

In the "One Experiment" feature, see in 3D how Dr. Mikala Egeblad envisions a way to stop metastasis in breast cancer patients. And, learn about a serendipitous collaboration between two labs that joined forces to make important advances in the autism spectrum disorder Rett syndrome.

It's clear that CSHL is a multi-faceted institution. Technology is now allowing our scientists to visualize and study biology in multiple dimensions. The campaign to which so many so generously contributed gives us the means to capitalize fully on that power. The endowment unleashes that power forever.

So grab the 3D glasses on the right and explore the next pages. Please take another look at the magazine cover. It serves to remind how CSHL is shaping the next generation of cancer therapy. From part of the genome that some used to call "junk DNA," Director of Research David Spector identified a non-coding RNA that he's developed into a drug target for breast cancer.

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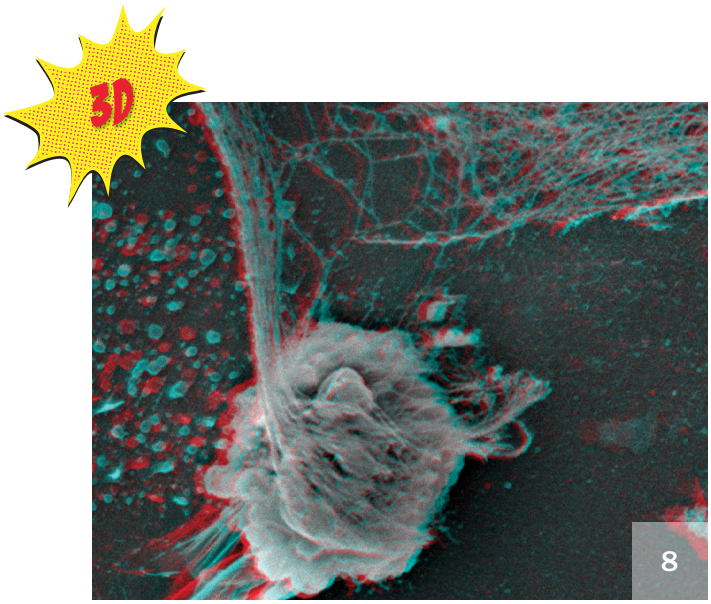

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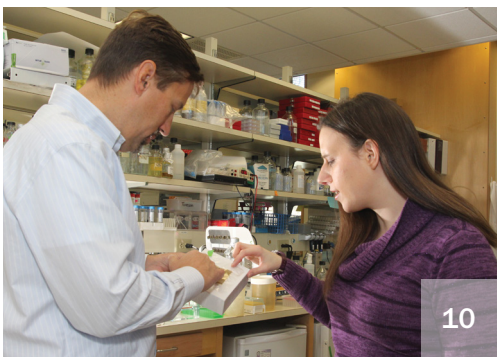
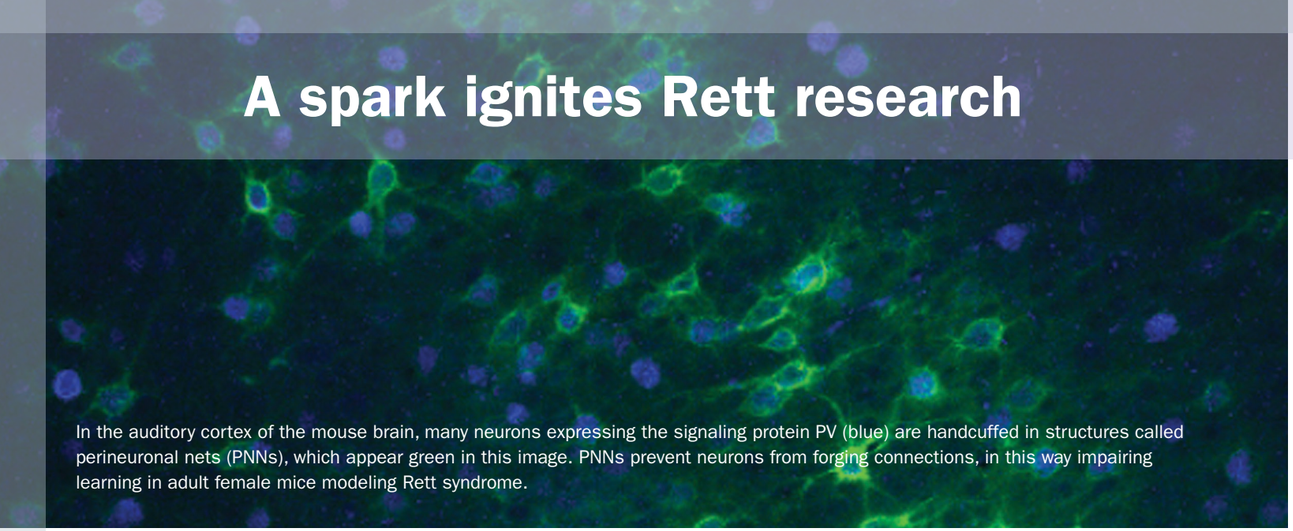


FEATURES

FACULTY & FRIENDS

On the cover and on the web:
The clumpy, bulbous appearance of this organoid from the Spector lab reflects the aggressive nature of the breast cancer subtype it was grown from. After 6 days of treatment with antisense technology that knocks down a long non-coding RNA called MaTAR20, the cancer shrank and lost its branched appearance, suggesting loss of metastatic potential. See for yourself at http://bit.ly/2dkEHbi

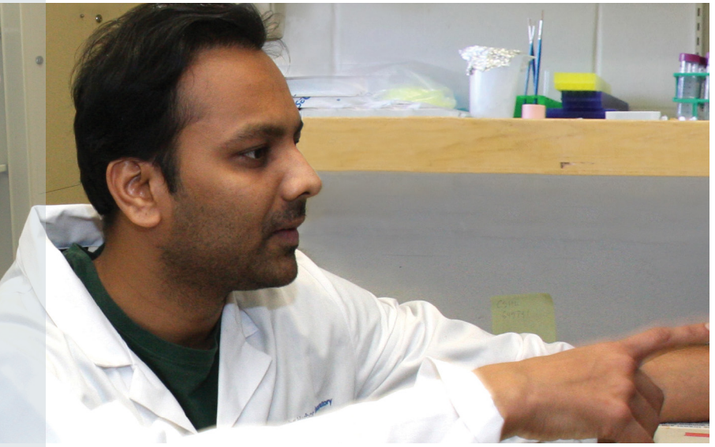
A spark ignites Rett research



In the auditory cortex of the mouse brain, many neurons expressing the signaling protein PV (blue) are handcuffed in structures called perineuronal nets (PNNs), which appear green in this image. PNNs prevent neurons from forging connections, in this way impairing learning in adult female mice modeling Rett syndrome.

Without traditional departmental silos keeping them apart, and encouraged by "everyone's-invited" lectures and an informal, non-hierarchical campus culture, the 600 research scientists at Cold Spring Harbor Laboratory are constantly trading ideas.

Often, sparks fly.



Experiments led by Dr. "Nava" Krishnan in the Tonks lab suggest some Rett symptoms may be reversible.

Case in point: In 2012, Keerthi Krishnan, a postdoc in the neuroscience labs of Professor Josh Huang and Associate Professor Stephen Shea, had a chance conversation with Navasona Krishnan, a postdoc in Professor Nick Tonks' lab. She talked about an experiment involving a mouse model of Rett syndrome—a devastating neurodevelopmental condition often grouped with the autism spectrum disorders.

Keerthi and "Nava," despite having the same family name, were unrelated. In terms of specialty, they were as distant as scientific "cousins" could be. Keerthi studied brain circuits and animal behavior; Nava was a protein biochemist focused on signaling pathways in cells.

"It's a really cool thing, being at Cold Spring Harbor, where something like this can happen," says Shea. "We have creative, intellectually curious people here, and a very free atmosphere that encourages scientists like Keerthi and Nava to find common points of interest. It's a big part of why I like being at the Lab."

In their casual conversation, Keerthi mentioned something that Nava couldn't stop thinking about. "When you delete *Mecp2* in brain cells, mice become obese. They develop resistance to leptin, the hormone that sends a signal when you've had enough to eat," Nava remembers.

Mecp2 is the mouse version of a gene that, when severely mutated or missing, causes Rett in people. Within minutes of the conversation, Tonks recalls, "Nava burst into my office and said, 'Have you ever heard of Rett syndrome and *Mecp2*? Should we look at this?'"

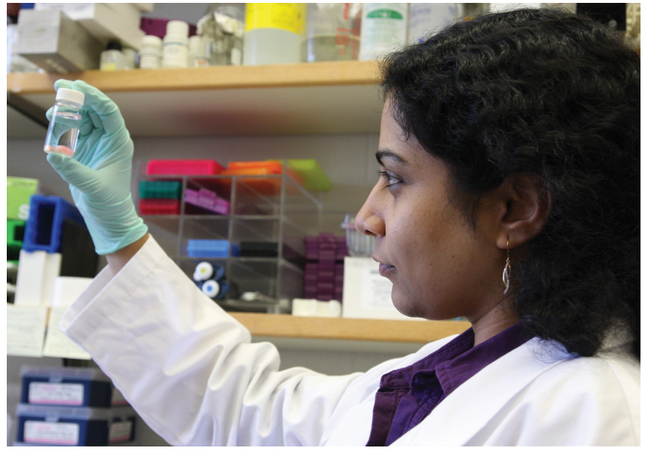
Tonks' reply—"absolutely!"—calls for some history. In 1988, he purified a protein called PTP1B. It was the first-discovered member of a "superfamily" of enzymes called PTPs (protein tyrosine phosphatases) that have the vital job of removing phosphate groups from other proteins. Adding and removing phosphates is a basic means by which signals are sent within and between cells.

Nava (now a Research Investigator in the lab) knew from Tonks that PTP1B is an important "negative regulator" of leptin, as well as insulin, the hormone that controls the way we regulate glucose. Drugs that inhibit PTP1B were identified 20 years ago, with the hope they would be next-generation treatments for obesity and diabetes.

For technical reasons those compounds were not taken further by the pharmaceutical industry (although new inhibitors are now in clinical development). In the Tonks lab, Nava had these compounds at his disposal, and soon started to test them in the "Rett" mice with which Keerthi was working. He was intrigued by the relationship between the absence of *Mecp2* and the inability of the animals to regulate their metabolism.

Keerthi and Steve Shea, meanwhile, focused on the biology behind a behavior observed in the mouse model of Rett. It seemed that mice lacking *Mecp2* could not perform a classic behavioral test that involved an adult female learning to retrieve distressed newborns.

A healthy adult female learns quickly to gather scattered pups into a compact, secure nest—even if they aren't her own and she's never cared for offspring. But females lacking *Mecp2* can't gather distressed pups, no matter how often they have the chance to learn. Why?



Dr. Keerthi Krishnan led research in the Shea lab revealing mechanisms underlying learning impairments in Rett syndrome.

Both labs' Rett projects produced exciting results, revealing (in Shea's lab) anomalies in neural circuits in the brain's auditory cortex that inhibit plasticity, and hence, the ability to learn, in the adult females lacking *Mecp2*; and (in Tonks' lab) the promise of PTP1B inhibitors in reversing symptoms of Rett syndrome.

In early experiments, Nava discovered that PTP1B inhibitors had a beneficial impact when given to frail male mice missing *Mecp2*. Males have only one copy of the gene, which is located on the X chromosome, and when it's missing they don't survive very long. (In the human disorder, 9 in 10 patients are female for this reason.) Male mice treated with PTP1B inhibitors lived nearly twice as long. Females missing *Mecp2* generally fare better; having two "Xs," they have two copies of the gene and can survive with a single working copy. Would PTP1B inhibitors ameliorate Rett-like symptoms in female mice? If so, this might be an approach to treat Rett patients.

Tests with three different PTP1B inhibitors in female "Rett" mice resulted in improvements in Rett-like impairments, including a paw-clasping behavior and the ability of the mice to remain on a rotating wheel. These effects, Nava and Tonks believe, are due to the release of a molecular "brake." Using the inhibitors to reduce PTP1B activity restores a key metabolic signaling pathway. By inhibiting PTP1B—which Nava had shown is overly abundant in mice lacking *Mecp2*—the experimenters effectively "took their foot off the brake," opening a cellular pathway through which leptin and insulin signals are normally sent. Meanwhile in the Shea lab, Keerthi (who has since joined the faculty at University of Tennessee) and postdoc Billy Lau linked the inability of female "Rett" mice to learn pup retrieval to an impairment of plasticity in neurons in the auditory cortex—cells that process the squeals made by distressed pups. They traced the pathology to neurons that release a signaling protein called parvalbumin (PV). Loss of *Mecp2* leads to elevated PV levels and the handcuffing of PV neurons within structures called perineuronal nets (PNNs). These structures prevent neurons from connecting. Forging new connections is a key part of how learning occurs in the brain.

These experiments, stemming from a casual conversation between postdocs in different fields, have led to progress in understanding Rett pathology and advancing a new treatment concept. "The critical point," observes Tonks, "is the diversity of research that's done at CSHL, that allowed Nava to listen to someone in another field talk about a problem and come away with an idea that launched a project. Cold Spring Harbor is a melting pot of people from different backgrounds, different expertise, widely different areas, and you never know where the next idea is going to come from!"

Peter Tarr

A capital achievement

A 3D rendering of the renovated Demerec Laboratory, new home to the Center for Therapeutics Research.

"CSHL is a national treasure and a remarkable center for scientific excellence, education and talent. The 125th Capital Campaign is key in the Board's long-term mission to match the institution's scientific preeminence with the financial strength to pursue pioneering research, regardless of the federal funding environment. Seventy percent of the gifts raised support the endowment, funding vital research and education in perpetuity with a powerful and lasting impact on the Laboratory's success."

Jamie C. Nicholls,
Chairman of the CSHL Board

"Right now we are the guardians of this institution and we want to build it, we want to help it continue in the future. I hope that it will be around in 250 years, still continuing to make big breakthroughs and making the world a better place for humanity."

Marilyn H. Simons, Ph.D.
Vice Chairman of the CSHL Board of Trustees
and 125th Anniversary Campaign Chair

In celebration of Cold Spring Harbor Laboratory's 125-year anniversary in 2015, the Board of Trustees set a challenge to raise $250 million to continue the Laboratory's leadership in biology far into the future. Led by Marilyn Simons, Vice Chairman of the Board, the Campaign Committee raised $278 million by the end of 2016.

Thank you to all who generously supported this campaign, especially the Campaign Committee: Dill Ayres, David Boies, Casey Cogut, Kristina Davison, Jeff Kelter, Laurie Landeau, Howard Morgan, Jamie C. Nicholls, George Sard, Marilyn Simons, Dinakar Singh, Bruce Stillman, Paul Taubman, and Roy Zuckerberg. Here's how your contributions are helping:

Investing in discovery

"The bulk of the Capital Campaign endows research, the excellence of which is the bedrock of our reputation," explains CSHL President Bruce Stillman. "The cost of doing research has skyrocketed since the dawn of the genome era. As the government's contribution has declined over the last decade, a second factor has come into play.

Today, the amount of money an investigator can expect from a government grant is frozen. Our investigators are receiving less money to perform work that costs much more to do. This is seriously eroding the ability of scientists to plan ambitious and innovative programs."

The Pre-Clinical Experimental Therapeutics facility is gearing up to test drug targets with the latest imaging technologies.

“Today, in collaboration with top hospitals and clinical centers, scientists at the Lab are building on that expertise to develop effective treatments for the toughest cancers.”

Roy J. Zuckerberg
CSHL Board Trustee

A robust endowment allows for strategic growth of CSHL’s scientific agenda.

$136 million endows the President’s Fund, providing flexibility to the Laboratory’s leadership to facilitate the most innovative, high-risk/high-reward research. Funds will be directed to transform basic discovery and technology advances into patient-specific treatments for debilitating diseases.

$105 million supports the Cancer Therapeutics Initiative to integrate world-class cancer genetics with cancer metabolism and to test and validate the efficacy of novel drugs and drug combinations using the latest imaging technologies. $22 million builds and equips the Pre-Clinical Experimental Therapeutics Facility—a drug-target testing and imaging center. A $25 million New York State grant renovates the existing 1953 Demerec Laboratory as the home for a new Center for Therapeutics Research—a nexus of biology, chemistry and medicine that will not only discover drug targets but transform them into next-generation therapies.

Opening new doors to students

With teaching facilities in Cold Spring Harbor, Lake Success, and Harlem, the DNA Learning Center (DNALC) currently serves over 30,000 middle and high school students annually, providing field trip labs, in-school instruction and camp programs. A flagship facility in New York City will allow for exponential growth in the number of students and teachers CSHL can serve.

$25 million expands the reach of hands-on laboratory experiences to New York City’s public and private schools.

“I am thrilled to help provide thousands more students each year, especially those from low-achieving schools, with opportunities to do real scientific experiments that will help develop critical thinking skills.”

Laurie J. Landeau, V.M.D.
CSHL Board Trustee r

DNALC students benefit from hands-on lab experiences.

$2 million builds the Nicholls Biondi Pavillion, a dedicated space for scientific poster expositions that are key to scientific conferences at CSHL. Additional funds support advanced technology courses and the Ph.D. program.

Philanthropy empowers the risk-taking and innovation in biological research and education that have and will continue to make CSHL unique in its contributions to the health and well-being of our society.

Dagnia Zeidlickis

One experiment

Cancer is infamous for repurposing molecules and mechanisms our body routinely uses to sustain itself. This remarkable 3D image, made by CSHL's expert electron microscopist Stephen Hearn, dramatically captures one such mechanism, spider web-like structures made of DNA and studded with toxic enzymes. Normally, these webs are cast out into extracellular space by white blood cells called neutrophils—like the one in the lower left of this image. The webs snag and digest invaders such as bacteria and viruses.

Using a separate visualization technique called intravital imaging that she developed, Associate Professor Mikala Egeblad recently discovered that the lattice-like structures—appropriately dubbed neutrophil extracellular traps (NETs)—also serve the dark side. In their ceaseless struggle to gain advantage, cancer cells in the vicinity of neutrophils are able to emit signals that cause the neutrophils to release their NETs, even in the absence of a local infection. In mouse models of triple-negative breast cancer, a very aggressive subtype, Egeblad's team linked cancer cells' hijacking of NETs with metastasis. She hypothesizes that malignant cells mobilize the NETs to chew away at scaffolding that supports tissue—in say a lung or bone, where the resulting holes and crevices can be colonized, metastatic outposts fit for occupancy.

With Michael Goldberg of Dana Farber Cancer Institute, Egeblad has figured out a way to hitch a NET-digesting drug called DNase to tiny spheres called nanoparticles. Used to clear NETs in cystic fibrosis, DNase is FDA-approved to be delivered through an inhaler. Attaching the drug to nanoparticles increases its stability, and when delivered in a mouse model of triple-negative breast cancer this version reduced and in some cases prevented metastasis to the lung. The team is optimizing the drug, while thinking carefully about which patients might benefit from it and when to administer it in relation to chemotherapy, which depresses the immune system and thus requires any approach to target these ethereal lattices—usually helpful but sometimes harmful—to be confined to metastatic hotspots.

Peter Tarr

RESEARCH PROFILE

David Tuveson

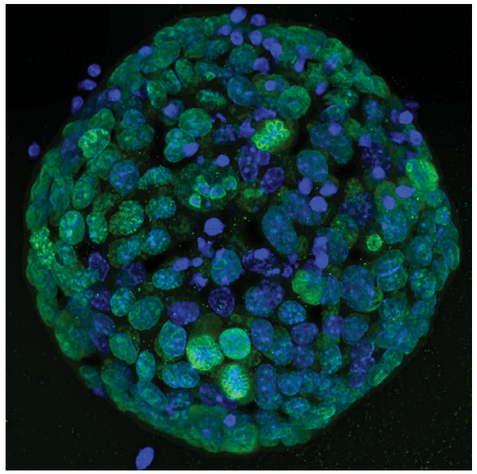
In his lab atop CSHL's Hillside campus, and in a sparkling new preclinical animal experimentation facility in nearby Woodbury, David Tuveson, M.D., Ph.D., and his large team are relentlessly testing new treatment approaches in mice and in three-dimensional cellular models of pancreatic cancer.

The 3D models, which take the form of tiny spheres called organoids, are derived from pancreatic tissue in mice and people. "Organoid technology provides us with the opportunity to learn what we were not previously able to learn about pancreatic cancer," Tuveson says. "These clumps of cells are telling us for the first time how the biology of the tumor is changing from its earliest beginnings through later stages of development, and this, in turn, is presenting new targets for therapy. Observations like this are what enable our science to move forward."

Tuveson, the Roy J. Zuckerberg Professor of Cancer Research at Cold Spring Harbor Laboratory and the recently appointed director of CSHL's National Cancer Institute-designated Cancer Center [see page 13], is also Research Director of the Long Island-based Lustgarten Foundation, the nation's largest philanthropic funder of pancreatic cancer research. He has spent his entire career fighting the illness, one of the few common cancers for which there is still no effective treatment. Half of newly diagnosed patients live only 6 months. Just 8 percent survive 5 years.

Pancreatic cancer is difficult for well-known reasons. Notorious for being "silent" in its initial (and presumably treatable) stages, it is usually diagnosed late—often at Stage 4, after it has begun to spread. Pancreas cancers are hard to see, sprouting in a part of the body that is not observed in routine physical exams. Worse, pancreas tumors are embedded in a mass of extraordinarily dense tissue called stroma, making them hard for chemotherapy to reach.

Tuveson compares pancreatic cancer to an oatmeal-raisin cookie, where the raisins are the cancer cells. Not only is the "oatmeal"—the stromal tissue surrounding the cancer cells—denser than in other cancer types; some of its non-cancerous component cells promote tumor survival and growth. In important research published earlier this year, Tuveson's team demonstrated that a cell type in pancreatic stroma, called fibroblasts, comes in at least two varieties. One type seeds the stroma; the other secretes interleukin 6 (IL-6), an immune signaling molecule associated with cancer proliferation.



Organoids are hollow spheres that grow from samples of pancreatic tissue, enabling Tuveson's team to faithfully recapitulate the full course of pancreatic cancer and test new diagnostics and therapies in the lab.

Dr. Christine Chio, a postdoctoral investigator in the Tuveson lab, is working on a novel drug therapy that kills pancreatic cancer cells by reducing their antioxidant levels.

"This finding underscores that stroma is not homogeneous in pancreatic cancer," Tuveson notes, "and this provides an opportunity to develop therapeutic agents that target specific fibroblast populations." It's only one of several hopeful developments in the lab that could lead to new treatments and diagnostics.

'I hated disease'

A native Chicagoan, Tuveson grew up outside Ann Arbor, Michigan, where, he says, "I was always interested in life—things that flew in the air, crawled on the ground, swam in the water. I just loved looking at nature and touching it."

He attended MIT, where he majored in chemistry, and turned to biology as a postgraduate because "I just hated disease—and not because members of my family were sick. It was just the dismay that the beautiful intricacy of biology could collapse with the snap of your fingers. Disease seemed to me counter to the care that was taken by nature to create life in the first place."

He earned a medical degree at Johns Hopkins, then studied for a Ph.D. under physician-researcher Douglas Fearon, who "pretty much taught me the scientific method." Now that Fearon has also joined the CSHL faculty, the two are actively collaborating in pancreatic cancer research.

Tuveson realized during his clinical training that "the disease nobody had any answers for was cancer—and the patients who seemed to have the worst luck of all were pancreatic cancer patients."

His postdoctoral project under Tyler Jacks at MIT was to develop the first animal model of the illness. He made good progress, and took the model with him to his first faculty job, at the University of Pennsylvania. He later moved to the University of Cambridge, in the U.K., where studies with the mouse model "made clear it was very difficult to get drugs into pancreas tumors," he recalls. This is when his focus began to turn to the "oatmeal-raisin cookie" problem.

After 6 years in England, Tuveson was persuaded by CSHL President Bruce Stillman and by the Lustgarten Foundation to come back to the U.S. "Cold Spring Harbor was perfect—someplace filled with brilliant basic scientists where I could think, as I was able to do in Cambridge," Tuveson says. He was particularly heartened by discussions with Stillman, Jim Watson and faculty about the Lab's evolving attitude toward translational cancer research. His interest in this branch of research—in which insights obtained in basic research are applied in experiments with clinical implications—stemmed from progress he was making with models of pancreatic cancer.

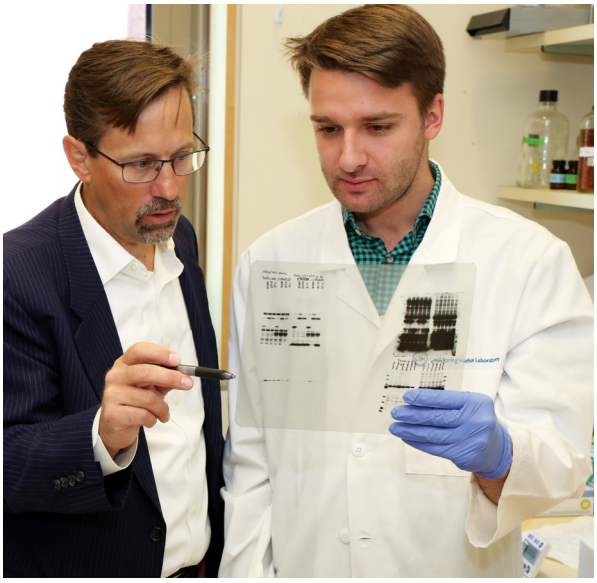
Members of the Tuveson lab help increase public awareness at the Lustgarten Foundation's annual Long Island Pancreatic Cancer Research Walk.

World Pancreatic Cancer Day provides another occasion for Lab members to educate the public about one of the most lethal cancers.

Not just animal models. While still in Cambridge, then continuing in his new lab at CSHL, Tuveson and collaborator Hans Clevers, president of the Royal Netherlands Academy of Arts and Sciences, developed a method to grow pancreatic tissue in the form of hollow spheres called organoids.

Pancreatic cancer cells had always been hard to grow in culture, slowing research. Until the advent of organoids, scientists had to rely on cells grown in flat culture dishes and depended on samples from genetically engineered mice, which take a year to generate. Organoids, which grow in a 3D medium, develop in days.

In addition to enabling researchers to observe pancreatic cancer from its beginnings, pancreatic organoids have special value in "in vivo" experiments. Once the spheres grow to a certain size, they can be transplanted into mice, where they faithfully recapitulate the course of the illness in people. Extrapolating from the new knowledge gained in organoids to preclinical experiments "is really the foundation of our laboratory," Tuveson says.



Dr. Tuveson conferring with Georgi Yordanov, a Watson School grad student in his lab.

One of Tuveson's insights while still at Cambridge centered on the role of antioxidants in pancreatic cancer. This work, taken up by postdoc Christine Chio in his CSHL lab, has led to another new therapeutic idea. Chio has led experiments showing how reducing antioxidant levels in cancer cells provides a powerful way to get the cancer, in her words, "to burn itself out."

This work stems from Tuveson's research on Nrf2, a master regulator of the delicate oxidant-antioxidant balance in cells. Chio is testing combination therapies to reduce antioxidants in cancer cells while leaving healthy cells unharmed. Her team is learning that some of these combinations work better than others and is trying to optimize the approach.

Another team, led by Tuveson lab postdoc Danielle Engle, is finding ways to detect pancreas tumors while they're still small and treatable. "Current technology shows us tumors that are golf ball-sized," says Tuveson. "I would love to have a way of seeing them when they're the size of blueberries or grapes." Tuveson hopes Engle and her team will devise "a dipstick test," *i.e.*, one that can be given routinely at trivial cost to people at their annual physical exam. Early signs of abnormality would call for a more expensive and detailed anatomical examination of the pancreas with functional MRI scans.

"Our lab has a remarkable amount of freedom to find answers," Tuveson reflects. "Strong support from Bruce Stillman and the very generous contributions made by Lustgarten allow us to be fearless as we pursue things we think important. Waking up every morning, I can't wait to get to the lab to see the results of the previous day's experiments. The science we're doing is so exciting. This is the best time I've ever had as a scientist!"

Peter Tarr

Taking center stage

In November 2016 Dr. David Tuveson was named Director of the Laboratory's National Cancer Institute (NCI)-designated Cancer Center. "What a privilege," he later commented. "I feel as if I have been asked to come in and take the baton of the New York Philharmonic! For the last 25 years Bruce Stillman has ensured the Center's greatness by appointing rising stars. Our opportunity is to continue to excel in discovery science while translating our insights into diagnostics and therapies to defeat cancer."

Of Tuveson's three predecessors, Stillman has shaped the Cancer Center as it exists today, having guided it through five NCI sponsorship renewals. During this time, basic research has revealed cancer's genetic roots, making possible a first generation of targeted therapies.

Tracing cancer's roots in aberrant genes and cellular signals fulfills a vision that launched the modern era of cancer research at CSHL. Soon after becoming Director in 1968, James D. Watson committed the Laboratory to tumor virus study, in 1971 securing a key NCI grant. In the 1980s, research grew to include the study of cellular oncogenes, cell growth and cell-cycle control. NCI cancer center designation came in 1987. Watson, the Center's first director, yielded to Richard Roberts in 1988. In 1992, Stillman took the reins.

Under Stillman, the Hillside Campus, which opened in 2009, enabled growth of the cancer program. In 2015, he piloted a strategic affiliation with Northwell Health to accelerate the translation of basic research to the clinic.

"Basic science has been our underpinning," explains Tuveson. "Proof-of-concept experiments in animal models have prepared the way for our current opportunity of testing therapies to interrupt cancer progression. Our new relationship with Northwell Health will spur unique collaborations in which basic scientists will work closely with practicing physicians to get tumor samples and also get involved in designing clinical trials."

Basic insights won't only be leading to experiments in mouse models "but also in patients who *have* cancer. It's going to be meaningful and productive and I hope many of our scientists will get to participate in that, while they continue to pursue the fundamental research that they are world leaders in."

Peter Tarr

Watson School 2017 Ph.D.s

Brittany N. Cazakoff

University of Saskatchewan

Edward and Martha Gerry Fellow

NSERC Scholar

I made it! There were a few snags, but the reward for moving forward—the incredible opportunity to work in a place so passionate about discovery—vastly outweighed the setbacks. I've grown immeasurably as a scientist, learning to perform rigorous experimentation. I also had the pleasure to talk with researchers from around the world and explore fields well beyond my own imagining. I would like to thank everyone who made this such a fantastic journey.

M. Joaquina Delás Vives

Universidad Politécnica de Valencia

Boehringer Ingelheim Fonds Fellow

"la Caixa" Fellow

When I first heard about CSHL, it was described as a "monastery of science." The Lab has lived up to that and more. Everyone who comes here shares that deep scientific excitement which convinced me to join the Watson School of Biological Sciences in the first place. I am very aware how special this place is, not only because of the ambitious research projects we get to attempt as graduate students, but also because of the thought-provoking discussions it encourages.

Abram Handly-Santana

University of California, Santa Cruz

William Randolph Hearst Foundation Scholar

When I first came to New York, I was immediately accosted by the hurricanes, snowstorms, and frigid weather I never would have encountered had I stayed in sunny California. And yet, I've never regretted coming here. CSHL is a peculiar village of science where collaboration is encouraged, and it was an enthusiasm for such an environment that led me to join the laboratory of David Tuveson. There, with friends at my side, I gained the passion and tenacity required to do great science.

Justus M. Kebschull

University of Cambridge

Boehringer Ingelheim Fonds Fellow

David and Fanny Luke Fellow

I had the good fortune to work in Tony Zador's lab on the groundbreaking (and somewhat crazy) idea of using DNA sequencing to map brain connectivity. I could not have wished for a better project or mentor. Through the Watson School program, I forged countless friendships, and even had the opportunity to co-found the first CSHL Boat Club, which I am sure will carry on putting students into rowboats for years to come. All that remains to be said now is "Thank you. I won't forget."

Matthew Sungmin Koh

University of California, Berkeley

George A. and Marjorie H. Anderson Fellow

There is something exciting and different about the way that CSHL's community views the world. It's here that you learn there is no scientific problem that cannot be solved with the right mix of tenacity and cleverness. Working in a stimulating environment with so many brilliant people has caused a small amount of that magic—that confident outlook, both humbling and empowering at the same time—to rub off on me. I will carry it with me forever.

Maria Nattestad

University of the Pacific

Genentech Foundation Fellow

John and Amy Phelan Student

I started my time at CSHL with a focus on cancer genomics and ended with a passion for creating methods for data exploration. I am grateful for the flexibility and support the Watson School has given me to develop my interests wherever they lead. CSHL has been my home, my small town, my tight-knit little community of brilliant people. As I step out into the world, I'll be taking with me a bit of the wisdom and memories this place has to offer.

Annabel Romero Hernandez

Instituto Politécnico Nacional

Gonzalo Río Arronte Fellow

Genentech Foundation Fellow

Starr Centennial Scholar

I did my thesis research in Hiro Furukawa's laboratory, where I had the opportunity to study—at the molecular level—a class of receptors that are fundamental for learning and memory. With this project, I was able to answer previously unanswered questions—the essence of being a scientist. Even as my journey at the Watson School ends here, I'm taking with me all the knowledge and good memories that will help me to succeed in the new scientific adventures to come.

Charles J. Underwood

University of Oxford

William R. Miller Fellow

I joined Rob Martienssen's lab to study epigenetics—"inheritance above the DNA sequence"—in plants. I reveled at the chance to develop and test my own ideas, and gradually became an independent scientist. Thanks to the flexibility of the Watson School program, I was able to collaborate and even "follow my nose" for exciting findings. As a result, I discovered two approaches to speed up crop breeding and hope to continue bettering the plant/biotech industry.

Faculty & Friends

Trinity College President elected Trustee

Dr. Joanne Berger-Sweeney, president and professor of neuroscience at Trinity College, has joined the CSHL Board of Trustees. Before becoming president of Trinity in 2014, Dr. Berger-Sweeney taught and ran a neuroscience laboratory at Wellesley College for over 15 years, and served as the dean of the School of Arts and Sciences at Tufts University. She earned her M.P.H. from the University of California, Berkeley, and her Ph.D. in neurotoxicology from the Johns Hopkins School of Public Health. "Her leadership at premier academic institutions in the United States, as well as her experience and accomplishments as a research scientist, make Dr. Berger-Sweeney uniquely qualified to contribute to our governing body," says CSHL Chairman Jamie C. Nicholls. Welcome, Dr. Berger-Sweeney!

Silicon Valley & CSHL reward star students

Even the most famous of scientists don't often get true star treatment—but shouldn't they? Elevating scientists to star status is one of the goals of the Breakthrough Prize, founded by Silicon Valley giants including billionaire tech investor Yuri Milner, Facebook's Mark Zuckerberg, Google's Sergey Brin, and 23andMe's Anne Wojcicki. Launched in 2014, the yearly award show is a mix of science and Hollywood that has earned it a reputation as the "Oscars of science." With the help of CSHL's DNA Learning Center (DNALC), Breakthrough is showing students worldwide that their work can really make a difference, too. At the December 2016 award show, Breakthrough Junior Challenge awards went to high school seniors Deanna See of Singapore and Antonella Masini of Peru, who will help lift others at their schools into scientific excellence with a DNALC-led lab redesign valued at $100K.

Nobelist honored by WSBS

At its 14th Commencement Convocation, the Watson School of Biological Sciences presented an honorary degree to a scientist who is already a CSHL alum: Nobel laureate Carol Greider. She was recruited in 1988 as one of the first CSHL Fellows, a program designed to give outstanding young scientists who have just finished their Ph.D. the opportunity to pursue their own scientific questions. Greider thrived in this position, and began to uncover the health implications of her co-discovery of telomerase, for which she shared a Nobel Prize in 2009. That major discovery was made by studying a tiny pond organism called *Tetrahymena*, a point Greider brought up during a scientific lecture that she gave at CSHL earlier this year. "Discoveries often come from unlikely places. Curiosity-driven research provides unexpected understandings that may have important implications in health," she said, adding with a smile, "I know you all know this already."

New faculty: David McCandlish

All of us are mutants, in a sense. While mutations that cause disease tend to get the most attention, there are many mutations within each of our genomes that cause no harm. This distinction fascinates the newest addition to the Simons Center

for Quantitative Biology, Assistant Professor David McCandlish, who comes to CSHL after completing a Ph.D. at Duke University and postdoctoral work at the University of Pennsylvania. Using computational tools, he is searching for differences between the many harmful and benign mutations in our genomes. He hopes to uncover ways to predict which mutations fall into which category—a topic that is relevant to the problem of antibiotic resistance—and ultimately use this knowledge to guide the development of a new generation of drugs.

Banbury tradition with a new twist

As the new head of CSHL's Banbury Center, Rebecca Leshan has the title of "Director"—but "connector" would be as appropriate. A Ph.D. from the University of Michigan with postdoctoral experience at Rockefeller University and an ambassadorial role representing U.K. science in the U.S., Leshan succeeds Jan Witkowski, Ph.D.

"It has been a great privilege and pleasure to have been director for the past 30 years, a period of great change in biomedical research," says Witkowski. "The success of the Banbury Center shows that small, by-invitation-only meetings are vital, even in the age of the Internet," he adds. Witkowski's remarkable ability to connect the right people at the right times has been key. The Innocence Project, which has used DNA evidence to free over 300 wrongfully convicted people, is just one example of the innovations generated by the Lab's meeting place for science policy.

"Now more than ever, the inspiring discussions that happen at the Banbury blackboard will be crucial to science worldwide," says Leshan. "I am thrilled to continue the Banbury tradition while forging bold, new ways to advance science and humanity."

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.

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