

BACK BASICS

From stem cells to yeast to neurons, basic scientists at the Medical School follow their curiosity wherever it leads. In this series of articles, a few of these scientists—undergraduates, graduate students, postdoctoral fellows, and faculty—share their discoveries and offer a glimpse of life in the biomedical sciences at Geisel.

MEDICINE'S BASIC FOUNDATION

By William Wickner, M.D.

THE LIFE SCIENCES ARE IN A PERIOD OF TREMENDOUS DISCOVERY. RESEARCH CARRIED OUT TODAY IS FORMING THE BEDROCK FOR CLINICAL ADVANCES AND FOR A BETTER UNDERSTANDING OF OURSELVES.

From 1800 B.C. to 1800 A.D. life expectancy—and many other aspects of human health—changed little. Even by the end of World War II little was known of how our cells work. But fundamental findings in chemistry and the physical sciences had provided the tools to learn more, and breakthroughs soon followed.

In 1948, DNA was found to be the genetic material. Just a few years later its structure was illuminated, and in the following decade its means of expression through RNA and protein synthesis was discovered. The advent of x-ray crystallography and electron microscopy revealed the structure of proteins and cells, leading to increasingly powerful means of genetic manipulation, sequence determination, and enzyme assay. This knowledge formed the foundation for countless pharmaceutical advances, from insulin to statins to a host of other medicines. Of equal importance, our understanding of the chemistry of our bodies has transformed our concepts of the human condition and of our place in the world.

Basic scientists at Dartmouth's medical school have made vital contributions to this progress. A very partial list includes Allan Munck's pioneering work on glucocorticoid receptors; E. Lucile Smith's studies of microbial electron transport; Elmer Pfefferkorn's illumination of how *Toxoplasma* triggers tryptophan starvation via interferon; Randolph Noelle's discovery of a ligand-receptor protein pair that has a central role in cellular immunity; the work of Jennifer Loros and Jay Dunlap to uncover the mechanisms of biological clocks; the investigation of cholesterol esterification and trafficking mechanisms by Ta-Yuan Chang; Ethan Dmitrovsky's studies of retinoid-induced proteasome activation and apoptosis; Charles Cole's discovery of the subunits of the nuclear pore; George O'Toole's work on the formation of biofilms by *Pseudomonas*; Gustav Lienhard's study of how insulin signaling regulates glucose transporters by controlling their membrane trafficking; Kendall Smith's identification of interleukin-2; Nancy Speck's discovery that a proto-oncogene is a transcriptional regulator of hematopoiesis; Miguel Marin-Padilla's studies of brain development; Duane Compton's illumination of the dynamics of the mitotic apparatus; Ronald Taylor's studies of cholera; Bernard Trumpower's isolation of functional components of the electron transport chain; the discovery of small regulatory RNAs by Victor Ambros; Heinz Valtin uncovering the role of vasopressin in diabetes insipidus; Charles Barlowe finding the receptors of protein traffic from the endoplasmic reticulum; and Lee Witters's discovery of the central role of AMP-activated protein kinase in the cell response to energy levels. The list could go on and on, and I apologize to the many faculty not mentioned here.

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These advances of the past 50 years have been recognized by an American Cancer Society Professorship, by the election of several faculty to the National Academy of Sciences, by an amazing number of coveted MERIT awards from the National Institutes of Health, and by many other honors. In the context of our small numbers, the Medical School's basic research enterprise is one of the top few in the country.

But the faculty hasn't done all this alone. Aspiring young scientists arrive as postdoctoral fellows or join our umbrella graduate programs (Molecular and Cellular Biology and the Program in Experimental and Molecular Medicine) in numbers comparable to the medical students, and they go on to join faculties around the world and to establish their own creative research careers.

The pathways between basic science and human disease run in both directions. For example, Nancy Speck's discovery that the oncogene that causes many human leukemias is a transcription factor that normally regulates hematopoiesis allowed a far better understanding of how normal cells differentiate. My own lab discovered and studied a large, six-subunit protein, called HOPS, that is essential for the fusion of yeast vacuole membranes. It is conserved from yeast to humans, but we study it in baker's yeast because of the ease of genetic and biochemical manipulation.

When my dear-departed mother asked me, "Are you curing or studying disease? Will you make a drug this way? Will it even help yeast to make better beer, wine, or bread?" I had to answer "No." But in an article published last year in *Nature*, another research group performed a screen to determine which of the 24,000 human genes are unnecessary for vegetative cell growth yet essential for the invasion of human cells by Marburg or Ebola viruses. Strikingly, just seven genes met these criteria, and those seven genes encode all six subunits for the human HOPS complex. It is a long way from our assays of HOPS to the development of an antiviral drug, but the path is now clear. Nancy Speck's research illustrates that studying human disease can lead to a better understanding of basic biology, and my lab's efforts show that studying basic biology provides the assays and fundamental knowledge needed to tackle human disease.

Dartmouth is small, and we pride ourselves on its intimacy. Just as the medical curriculum has grown to integrate the science of health-care delivery, so too should it ensure that all students understand the intimate, bidirectional relationship between fundamental scientific discovery and advances in medicine.

William Wickner, M.D., is the James C. Chilcott 1920 Distinguished Professor of Biochemistry.

FROM CALICO CATS TO CORD BLOOD

“Why does a skin cell stay a skin cell?” asks genetics researcher Patricia Ernst, Ph.D. “Why doesn’t it get confused . . . and turn into something else?” Why a cell, like a skin cell, keeps its identity has long fascinated Ernst. “When you become a skin cell, you decide to turn off neuron genes, blood genes, everything else—and that’s stable,” she says. “If it wasn’t stable it would be chaos.”

Skin cells keep their identity because of the way their genes are regulated. A classic example of gene regulation, which Ernst studied as a graduate student at UCLA, is the calico cat. A cat’s skin cells all have the same genes, but the expression of those genes determines whether a skin cell makes orange or black fur. In each skin cell, the choice of genes is permanent (a dominant orange or black color) and all the progeny from the cell create patches of skin of that color, creating the orange-and-black pattern calico cats are known for.

Learning about genetic regulation led Ernst to study the mixed lineage leukemia (*MLL*) gene. She soon plunged into leukemia research, with a focus on *MLL*, at Dana-Farber Cancer Institute. Now at Geisel, her lab focuses on the function of *MLL* in the development of hematopoietic stem cells, which are the source of all blood cell types. They can renew themselves and can differentiate into a variety of specific blood cells. In a normal hematopoietic stem cell, the proteins encoded by *MLL* regulate the expression of other genes, leading to the production of more blood stem cells, which in turn produce all the types of blood cells in the body—T cells, red blood cells, white blood cells, and others.

Ernst also studies *MLL*’s role in certain rare and deadly childhood and adult leukemias. In these leukemias, the chromosome where the *MLL* gene is located breaks and fuses with other chromosomes, leading to the production of abnormal proteins. These proteins turn on cancer-promoting genes within white blood cells, which eventually

causes leukemia. Ernst’s lab is figuring out how these abnormal proteins (called fusion proteins) work and how they differ in function compared to the normal *MLL* protein.

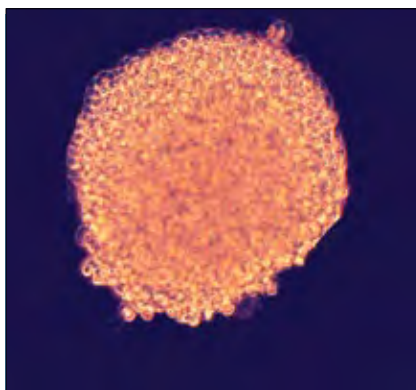
To better understand what *MLL* does in a cell, Ernst uses genetically engineered mice in which she can delete *MLL*. Ernst purifies normal hematopoietic stem cells from these mice, puts the cells in culture, turns on the gene that deletes *MLL*, and measures what happens to the cell. She can then determine what genes are controlled by *MLL*. One interesting finding is that *MLL* appears to suppress a large group of red blood cell genes. Ernst is working on the implications of this unexpected finding.

Ernst’s research follows a relatively new and controversial theory in cancer research that all cancers come from natural stem cells that convert to cancerous cells and proliferate. According to the theory, known as the stem cell theory of cancer, “the reason we’re so bad at treating cancer is that we’re trying to treat the tumor and not the stem cell before the tumor,” says Ernst. “So every time you kill the tumor cell, there’s that one little population cranking out new ones all the time.”

In her lab, then, Ernst is “teasing apart the really subtle difference” between how the *MLL* gene tells a hematopoietic stem cell to divide and grow, and stop when it is supposed to, versus *MLL*’s role in transforming a hematopoietic stem cell into a cancerous cell that keeps creating more cancer cells, doesn’t stop, and “wreaks havoc,” she says.

Another large part of Ernst’s research is to find a way, by manipulating the *MLL* molecular pathway, to make more human cord blood stem cells. These stem cells create umbilical cord blood; they also are self-renewing. Ernst’s hypothesis is that if the *MLL* pathway controls the self-renewing process, making the pathway more active might lead to the growth of more stem cells. “What’s really hard to do in a dish is to provide whatever signals it takes to keep this . . . happening,” she says. Cord blood stem cells have many potential uses for treating diseases of the heart and blood.

“We’re taking our mouse results and trying to extend them to the human cord blood situation,” says Ernst. It’s quite a long way from studying genetic principles in the calico cat.



A hematopoietic stem cell colony, which can be used to study the development of both normal blood cells and leukemia. Image courtesy of Erika Artinger, a graduate student in the lab of Patricia Ernst.

MARK WASHBURN



PATRICIA ERNST
ASSOCIATE PROFESSOR
DEPARTMENTS OF GENETICS AND OF
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WHY DOES *a* SKIN CELL
STAY *a* SKIN CELL?

PHILOSOPHY ON THE BRAIN

Allan Gulledge, Ph.D., an assistant professor of physiology and neurobiology, has always been fascinated with philosophical questions. “As early as middle school, I wondered how the brain could generate a conscious being that can learn, move and do things, and think,” he says. So it’s not surprising that his neuroscience research has focused on the neocortex, the wrinkly outer part of the human brain associated with higher thinking skills, such as perception, planning, and learning. “The ultimate question I’m asking is ‘How does the neocortex enable thought and perception?’” Gulledge says.

To get at that question—perhaps the most philosophical question that neuroscience asks—Gulledge studies several smaller questions, with the hope that the answers will eventually help build a complete picture of how the cells that make up the brain generate thought and perception. These building blocks include studying the type of neurons in the neocortex, how those neurons behave and communicate, and how signals from other parts of the brain change the way neurons in the neocortex function. The answers aren’t just philosophical. They’re critical to understanding and treating brain diseases that may involve the neocortex, such as depression, anxiety, and schizophrenia.

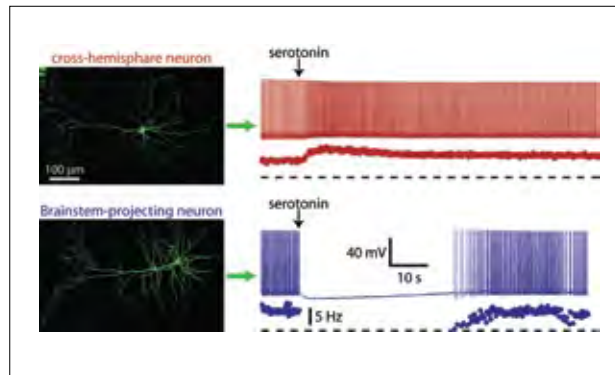
One component of Gulledge’s research is the study of the neurotransmitter serotonin, a chemical made in the lower part of the brain called the brain stem that can affect other parts of the brain, including the neocortex. Serotonin changes the way some neurons work, either exciting their electrical activity or suppressing it, depending on the neuron’s specific type of receptor. Some drugs used to treat schizophrenia and other diseases work by blocking the 2A receptor, which is an excitatory receptor. Gulledge and graduate student Daniel Avesar have studied a group of neurons in the neocortex that respond to serotonin. One type of these neurons—called colossal projection neurons—extends between the two halves, or hemispheres, of the brain, connecting them and facilitating communication between neurons in each half. Other neurons in the same area project down into the brain stem or other structures below the neocortex, including the thalamus. In a study published in March, Gulledge and Avesar found that the colossal projection neurons are functionally excited by serotonin through activation of the 2A receptor, while those that project downward are inhibited by serotonin acting at an inhibitory receptor, called the 1A receptor. Thus, serotonin excites cortical neurons that connect the two hemispheres, but suppresses the activity of neurons going to the brain stem and thalamus.

This distinction between the two groups of neurons was a novel finding and gave researchers a clue as to how antipsychotic drugs that block the 2A receptor may work. “We think that the neurons that project between the two brain hemispheres may be selectively involved in psychosis,” says Gulledge. Eventually, Gulledge hopes that this work will lead to new treatments that affect only the neurons involved in a disease, lessening side effects and increasing the impact on symptoms. And understanding more about the way neurons are affected by neurotransmitters will hopefully lead to a better understanding of how this delicately balanced system goes awry in brain diseases.

In a compelling twist, Gulledge also found that, in young mice, the neurons that project to the brain stem do express the excitatory 2A receptor, meaning that by the time the mice reach adulthood, something causes them to stop expressing those receptors. Gulledge is interested in the switch that changes the expression of receptors on those neurons. He says that one possibility suggested by the work of other labs and his own preliminary data is that early-life stress changes the expression of receptors in the brain stem projection neurons. And, he adds, “there is a potential that this change may be associated with an increased vulnerability to psychosis.”

Observing the intricately balanced, dynamic regulation of the neurons in the neocortex fascinates

Gulledge. “Cortical neurons change their behavior based on the many different chemicals released into the cortex,” he says. “Ultimately, we are looking at how all these signals interact to facilitate normal brain function.” Someday the results of these investigations may help Gulledge answer the more fundamental question that first intrigued him: How does the brain generate thought?



Electrical recordings (upper plots) and plots of firing frequency (lower plots) at right show the difference in the response of two types of neurons to serotonin. Serotonin excited the neuron that projects to the other hemisphere of the brain (top left), but it inhibited the neuron that projects to the brain stem (bottom left). Image courtesy of Allan Gulledge and Daniel Avesar.

ALLAN GULLEDGE
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MARK WASHBURN

A CURIOUS FINDING

In 2004, Henry Higgs, Ph.D., a professor of biochemistry, began studying a protein called INF2, despite the fact that, as he says, there was “absolutely no evidence that it might play an important role in anything.”

But Higgs was curious. He has long studied actins, filament-like proteins used by cells for any of a number of jobs. He compares actins to bricks, in that they can be used to assemble various structures. Previous research had predicted that INF2 was a type of protein called a formin, and formins are one of the major families of proteins that help assemble actin.

As Higgs and other members of his lab began examining INF2, they discovered what he thought were interesting biochemical and cellular properties, including that the protein is twice as big as researchers had predicted it would be from the gene that contains its blueprint. As they dug deeper, they found that half of the gene that encodes INF2 is located in what was thought of as the “desert” of the human genome, the portion of our DNA that typically does not encode proteins. It turned out that this section, however, actually did code for a protein sequence, making it something like an oasis within the desert. And, as Higgs soon found out, this oasis is associated with at least two diseases.

In 2009, Higgs's curiosity began to yield practical results. Harvard researcher Martin Pollak, M.D., called Higgs to talk about a discovery he had made regarding a disease of the kidneys called focal segmental glomerulosclerosis, or FSGS. Pollak had collected DNA from 93 families with a history of FSGS. In 11 of those families, he found mutations in the half of the *INF2* gene located in the oasis that were strongly linked to the disease—a more significant association than any that Pollak had found before.

Higgs and Pollak began working together, and with other researchers around the world who study families with FSGS. Soon they found mutations in the gene that encodes INF2 in about 15% of these patients.

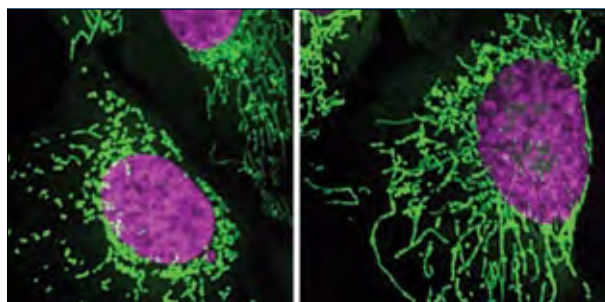
There was more to come. Late last year, a group of French researchers decided to look at whether INF2 has a role in the neurological malady Charcot-Marie-Tooth disease (CMT), an inherited neurological disorder. They had their suspicions, because a subset of CMT patients also have FSGS. They sequenced the DNA of patients with CMT and found INF2 mutations in 12 of 16 families. The mutations were in the same region as the mutations associated with FSGS but involved different amino acids and were predicted to have more severe consequences for the function of the INF2 protein.

Now Higgs had a connection between INF2 and neurological disease, because CMT is a type of peripheral neuropathy that affects, among others, the longest nerve in the body, the sciatic nerve, which runs from the lower spine to the feet. “The neuron that makes up this nerve has to spread its organelles, especially its mitochondria, very thinly along this long, narrow tube,” Higgs explains. “If the mitochondria don't spread out, they will not be able to provide energy along the nerve.” And that failure can result in some of the symptoms of CMT—weakness and numbness in the foot or leg, an abnormal gait, and foot drop (difficulty lifting the foot). Scientists know that some of the CMT-linked mutations they've already found involve the distribution of the mitochondria.

Before the connection to CMT, Higgs had been struggling to figure out what INF2 does in cells. “We were sort of stuck,” he says. Once he learned that INF2 was connected to CMT, he decided to look at what happens to mitochondria when the INF2 gene is mutated. “Sure enough, the mitochondria change,” says Higgs. “They get really long when you disable INF2 and they get really short when you overproduce INF2.”

Next, Higgs and his lab are going to look more closely at INF2's role in CMT and FSGS, and at how therapies may be able to help patients with the disorders. But there's an immediate implication for diagnosis. People who have family members with FSGS or CMT can be screened for the newly discovered mutations, which may help them get treatment earlier and slow the worsening of symptoms. In the longer term, research on INF2 may have significant implications for other neurological diseases, such as Parkinson's, Alzheimer's, and Huntington's.

“We think INF2 might be playing a vital role in mitochondrial dynamics,” says Higgs. “It's really cool how something we were looking at from a curious, basic-research standpoint ended up being a really important protein for these diseases.”



Depleting the protein INF2 affects the shape of mitochondria. In the human osteosarcoma cells shown above, the mitochondria (green) look normal in the control cell (left). The mitochondria of the cell that has low levels of INF2 (right) are much longer. Images provided by Farida Korobova.

JON GILBERT FOX



HENRY HIGGS
PROFESSOR
DEPARTMENT OF BIOCHEMISTRY

WE THINK INF2 MIGHT *be*
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MITOCHONDRIAL DYNAMICS.

KEEPING THE FAITH

As a child growing up in a Catholic household in Ciudad Juarez, Mexico, Yolanda Sanchez was so committed to public service that her parents thought she might become a nun. Today she can be found cloistered in a lab in the Department of Pharmacology and Toxicology rather than in a monastery, but she maintains that sense of commitment.

After finishing college at the University of Texas, El Paso, Sanchez decided to pursue a career in science. She was determined that her work would contribute to human health, so she wanted to focus on biomedical research that could lead directly to clinical applications. “I thought at the time—and I was wrong—that if it wasn’t really close to getting into humans, then it wasn’t really benefiting human health,” she says.

But during a postdoctoral fellowship, Sanchez reconsidered her stance on basic science. She began working with *Saccharomyces cerevisiae*, a species of yeast. Humans and yeast are very distant relatives; their evolutionary paths diverged more than one billion years ago. But they share genes in common, including some that are important for human health.

“I went back to that little yeast to study processes that go on in humans,” she says. “That’s when I decided that without basic research we would not have translational research.”

Using yeast, Sanchez studied cell cycle checkpoints. Cells face a constant barrage of threats to the integrity of their DNA. Everything from radiation to cigarette smoke can trigger DNA damage. But the cell cycle has checkpoints during which DNA damage can be repaired.

In 1996, Sanchez had a breakthrough. She cloned a gene, *Chk1*, that in both humans and yeast plays an essential role in allowing cells to repair DNA damage. If the DNA of a cell is damaged during the process of DNA replication, levels of Chk1—the protein encoded by *Chk1*—rise quickly, preventing the cell from going into mitosis and dividing. If DNA damage is not repaired, cells can accumulate mutations that allow them to become cancerous, so Chk1 and other checkpoint proteins play vital roles in the cell cycle.

Sanchez has continued to study checkpoint proteins, and in a new study she offers a very different understanding of *Chk1*. She investigated the possibility that in some situations *Chk1* actually promotes rather than prevents the development of cancer.

For this study, Sanchez used a mouse model of lung cancer that was developed by Ethan Dmitrovsky, M.D., the chair of Geisel’s Department of Pharmacology and Toxicology. In these mice, the protein cyclin E was overexpressed, which can cause DNA damage, and a genetic mutation meant that levels of activity of the Chk1 protein would be about 40% lower than normal. Typically, mice in which cyclin E is overexpressed would develop premalignant lesions within a month of birth and within six months about half of the mice would have tumors. But Sanchez found,

to her surprise, that inhibiting Chk1 delayed the development of tumors.

Three months after the mice were born, 44% of those with normal levels of Chk1 had developed lung tumors. But none of the mice in which Chk1 was inhibited had developed tumors at three months. At 10 months, 55% of the normal mice had tumors, compared to 21% of the Chk1-inhibited mice.

The most plausible explanation, Sanchez says, is that inhibiting Chk1 prevented cancer cells from being able to repair damage to their DNA. The results suggested that inhibiting Chk1 might be a way to slow the growth of tumors.

In similar studies, other researchers had suggested that Chk1 acts as a barrier to tumor growth, so Sanchez had expected to find the same thing. “I thought we were going to show that Chk1 was a barrier, and I was very surprised,” she says.

Sanchez notes that inhibitors of Chk1 combined with cytotoxic drugs are already being tested in clinical trials. Her research shows that using Chk1 inhibitors on their own might be a better approach, as it could potentially avoid the side effects associated with the cytotoxic drugs.

Sanchez knows that this finding—as significant as it is—will not lead overnight to longer lives for people with cancer. But she believes that this type of basic research is an essential step toward improved treatments. As the associate director for basic sciences at Dartmouth-Hitchcock’s Norris Cotton Cancer Center, Sanchez works to promote basic science and to convince others of the importance of basic research to feed translational research efforts, even if, at times, the immediate applications of

basic research are difficult to see.

“You can spend six months at the bench and get nothing,” she says. “If you can’t handle a variable schedule of reinforcement, you cannot be in science.” In other words, you have to have faith.



DAVID M. PHILLIPS/PHOTO RESEARCHERS, INC.

The study of *Saccharomyces cerevisiae*, or baker’s yeast, has led to insights into human health. Yolanda Sanchez has used this species of yeast to investigate cell cycle checkpoint proteins.

YOLANDA SANCHEZ
ASSOCIATE PROFESSOR
DEPARTMENT OF PHARMACOLOGY
AND TOXICOLOGY

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MAIR WASHBURN

THINKING INDEPENDENTLY, TOGETHER

Ruth and Lilian Kabeche would like to dispel the rumor that they are attached at the hip. True, they're sisters, and both are graduate students in the Department of Biochemistry. Yes, they both work on the fourth floor of Remsen, and you may often see them eating lunch together. And, well, they do share an apartment in Hanover.

But when it comes to science, they love to be out on their own.

"Science keeps you on your toes," says Ruth, who is now in her third year at Geisel and is the younger of the sisters. "You have to think for yourself. Of course, you need help from your P.I. [principal investigator], but you have to come up with ideas and you have to . . . come up with something that no one else has ever done."

Lilian, a fifth-year graduate student, agrees. "I like trying to find the answers to something," she says. "You know something that no one else knows, and you are the expert on what you do."

As a member of the lab run by Duane Compton, Ph.D., a professor of biochemistry, Lilian is helping to piece together the process by which chromosomes are shared between dividing cells. Tumor cells often missegregate their chromosomes—meaning that one cell will end up with more chromosomes than the other cell—which

complicates the treatment of cancer. In a recent journal article, Lilian outlined the role of a protein that, when overexpressed, promotes chromosome missegregation.

Just down the hall from the Compton lab, Ruth studies the relationship between cell growth and cell division as a member of the lab of James Moseley, Ph.D., an assistant professor of biochemistry. She has helped to pinpoint the function of a previously unidentified protein in fission yeast, which led to her first scientific publication. "What is great about what I'm doing is that no one is working on it in my model organism," she says. "No one has ever looked at it, and we found it."

Despite their intellectual independence, Lilian and Ruth agree that it's nice to have someone to talk to when work in the lab doesn't go as well as hoped.

"We're sisters before anything else, so it's nice to have someone here that understands what you're going through," Ruth says.

381

number of graduate students at Geisel



SCOTT ACHS

SCIENCE *keeps* YOU
on YOUR TOES...

Ruth (left) and Lilian Kabeche are sisters and graduate students in the Department of Biochemistry.



ADAPTING TO NEW HABITATS

Over the past 30 years, a new species has carved out a niche for itself within a well-established and competitive ecosystem. The species was rarely spotted before the 1950s, but it began to proliferate rapidly in the 1980s and continues to grow today.

The species, postdoctoral researchers—or postdocs, as scientists refer to them—can now be found at just about any institution home to scientific research. Postdocs are closely related to both graduate students and faculty researchers, but they have distinctive traits of their own. And the relatively recent increase in postdoc positions means that in some ways their role in the scientific community is still evolving.

As a postdoc, evolutionary biologist, and president of the Dartmouth Postdoctoral Association, Salvador Almagro-Moreno, Ph.D., has both a professional and personal interest in examining how species survive—and sometimes thrive—in new environments.

Working in the lab run by Ronald Taylor, Ph.D., a professor of microbiology and immunology, Almagro-Moreno studies *Vibrio cholerae*, the bacterium that causes cholera. In the developing world, *V. cholerae* is the cause of millions of cases of disease and more than 100,000 deaths each year. Almagro-Moreno was recently part of a collaboration that found *V. cholerae* in the waters of the Great Bay Estuary in New Hampshire. The strains identified there were nonvirulent, meaning they cannot cause cholera, but Almagro-Moreno says that it would not take very much for a nonvirulent strain to become a threat to human health. He has studied the mechanisms by which the bacterium is able to colonize the human intestine and become toxic, which may help scientists figure out how to prevent cholera.

“By understanding how it evolves and how it behaves in the natural environment, I think we can come up with some different approaches to targeting it,” he says.

The warming of northern ocean waters due to climate change means that more strains—potentially including virulent strains—may find these waters hospitable. “The warmer the waters, the more it can spread,” Almagro-Moreno says.

Almagro-Moreno arrived at Dartmouth in 2010 and is likely to spend a couple more years here. But when he leaves he won’t have earned a degree, and there won’t be any numbers after his name associating him with Dartmouth, despite the fact that he may spend more time here than most undergraduates.

But while they are not students, postdocs are not always considered full-fledged professionals, either. Postdocs are often regarded as a transition between graduate school and a long-term position, but, Almagro-Moreno says, “You might spend four or five years here. That’s not a transition.”

At some large universities, Almagro-Moreno says, the role of postdocs is more clearly defined than at Dartmouth because of their large numbers. But he has found some advantages to being at Dartmouth



POSTDOCS *are an* INTRINSIC PART *of the* RESEARCH *that* GOES *on* HERE.

Postdoc Salvador Almagro-Moreno in his natural environment, Ronald Taylor's lab in the Department of Microbiology and Immunology.

as well. “You don’t just feel like a cog in a big machine,” he says. “We are an intrinsic part of the research that goes on here.”

Many postdocs go on to faculty positions, but not every postdoc remains in academic science for the long haul, which is why the Dartmouth Postdoctoral Association holds informational sessions and trainings that help prepare postdocs for alternative careers. Almagro-Moreno would like to see more of these sessions offered for postdocs, even if he has no doubt about his own long-term career goals.

“This is what I want to do,” he says. “I’ll do whatever it takes.”

THE SCIENTISTS OF TOMORROW (AND TODAY)



As a freshman, Ilenna Jones spent five months conducting research with Jason Moore, Ph.D., a professor of genetics. As part of Moore's research program, Jones investigated interactions between different genes to find clues to the biology of Alzheimer's disease.

Now a sophomore, Jones says that her time working with Moore, gave her an appreciation of the "detective work needed to bridge the gap between statistical findings and biological explanation."

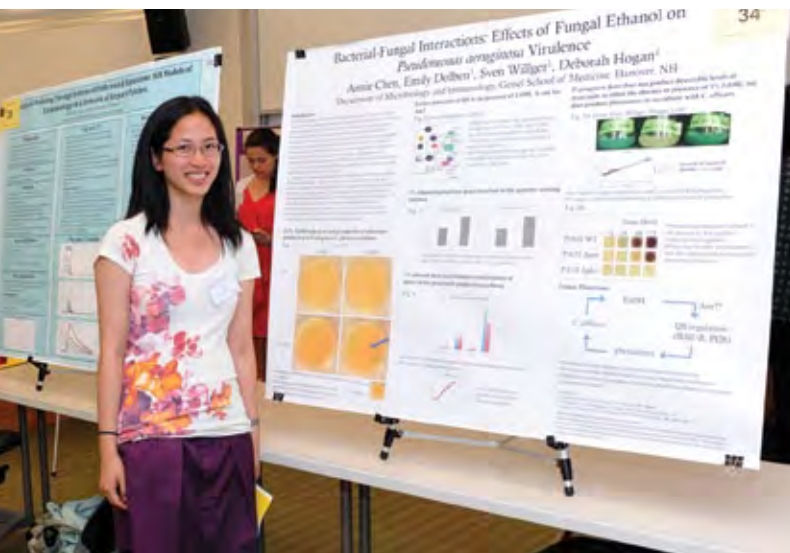
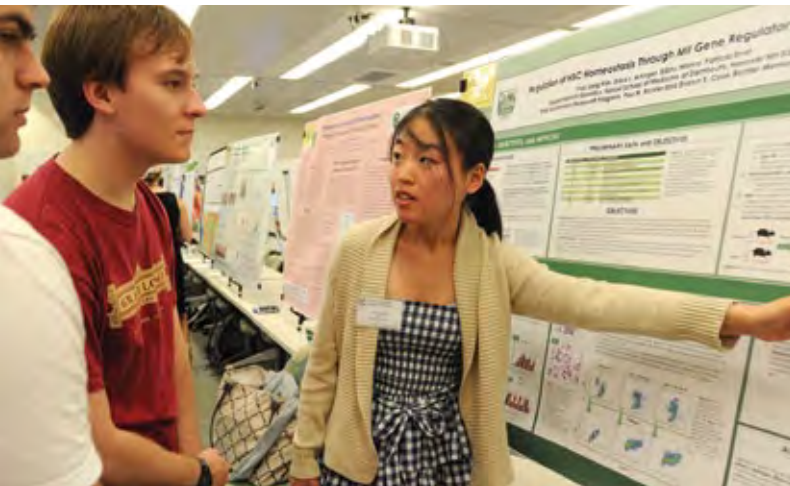
The summer after her freshman year at Dartmouth College, Annie Chen started working in the lab of Deborah Hogan, Ph.D., an associate professor of microbiology and immunology at Geisel. More than two years later, Chen continues to work in the lab, where she is now doing a senior honors thesis on interactions between the bacterium *Pseudomonas aeruginosa* and the fungus *Candida albicans*, research that has implications for the understanding and treatment of cystic fibrosis.

"It has been a great learning experience," Chen says. "Not only have I learned various microbiology techniques, but I have also learned how to think more like a scientist."

Yoo Jung Kim, a Dartmouth junior, started working with a Geisel professor at the beginning of her freshman year. She is now a James O. Freedman Presidential Scholar, which will help support her time in the lab this year. Under the mentorship of Patricia Ernst, Ph.D., an associate professor of genetics, Kim conducts research on a gene involved in the development of leukemia.

Kim has found herself intrigued not just by the science but by the process of conducting research. "I am fascinated by experimental design," she says. "Since there's no direct way of observing all the complex events that are occurring at the molecular level, we have to be able to infer what's happening from data from well-constructed experiments."

Kim, Jones, and Chen all currently plan to pursue graduate degrees in science or medicine (or both) when they graduate from Dartmouth.



Many Dartmouth undergraduates gain research experience by working with Geisel faculty. Ilenna Jones (opposite page), Yoo Jung Kim (top), and Annie Chen were among the undergraduates who presented findings from their research at the Karen E. Wetterhahn Science Symposium in May.

UNDERGRADUATES AT GEISEL

Dartmouth's Office of Undergraduate Advising and Research helps students find opportunities to conduct research, often in Medical School labs. In the past academic year more than 100 undergraduates spent time working with Geisel faculty as part of the following programs:

39

worked closely with
GEISEL FACULTY
as **James O. Freedman**
Presidential Scholars

32

were awarded
Sophomore
Science
Scholarships

to spend about **10 hours a week** conducting research with a Geisel faculty mentor.

5

spent time in Geisel labs as Junior Science Scholars.

received **RESEARCH GRANTS** independent research under Geisel faculty member as part of a senior

27

to carry out the supervision of a during a leave term or honors thesis.

WERE AWARDED
FUNDING

to work part time in a Geisel lab as part of the Women in Science Project.

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