



# THE NEW FACES OF GEISEL





What draws new faculty members to Geisel School of Medicine? They say it's the people, the opportunities, and the sense that Geisel is building upward momentum.

"People are, by far, our most vital asset," says Dean Wiley "Chip" Souba, M.D., Sc.D. "There is nothing more important than recruitment and retention of top faculty to ensure high quality teaching, research, and patient care."

The recruitment of top-notch researchers is a key part of Dean Souba's "20x20" strategic plan. More than 80% of recent additions to the clinical and basic science research faculty have brought NIH funding with them, and many have added to their funding since arriving at Geisel.

"I've been extremely impressed by the quality of our recent faculty recruits," says Duane Compton, Ph.D., the senior associate dean of research. "We are building upward momentum in the biomedical sciences, and I think young scientists can sense that."

There are many factors that have attracted these researchers here. For immunologist David Mullins, Ph.D., it was the ability to work closely with other scientists and physicians to move cancer vaccines into clinical trials. For psychiatrist Paul Holtzheimer, M.D., Geisel '99, it was the opportunity to build a mood-disorders clinic and collaborate with faculty across Dartmouth who are interested in developing better treatments for depression. For health economist Ellen Meara, Ph.D., it was the chance to add her expertise to the Dartmouth Institute for Health Policy and Clinical Practice.

The interests of these and other new faculty members are diverse, but they share a belief in the importance of working with other researchers and an excitement about taking advantage of opportunities across Dartmouth's professional schools and undergraduate departments.

According to Souba, that's not a coincidence. "We work hard to recruit faculty, students, and staff who are strong in terms of technical know-how and skills but also fit with our values and guiding principles," he says. "Those include valuing an interdisciplinary, team-based approach to solving big challenges."

*Dartmouth Medicine* sat down with nine new faculty members to find out more about their current work, their plans for the future, and why they chose to come to Geisel.



**Faculty recruitment is on the rise at Geisel. There were no new faculty recruits in fiscal year 2010, but there were nine new recruits in fiscal year 2011 and seven in just the first six months of fiscal year 2012.**

EXCEPT WHERE NOTED, ALL PHOTOGRAPHS WERE TAKEN BY MARK WASHBURN.



JON GILBERT FOX



“The environment here is very conducive to team science.”

David Mullins and Mary Jo Turk, researchers in the Department of Microbiology and Immunology, began working together even before Mullins arrived at Geisel in the fall of 2011.

**DAVID MULLINS, Ph.D.**

**Arrived at Geisel: August 2011**

**Came to Geisel from:**

**The University of Virginia**

**Graduate education: Ph.D. from Virginia Polytechnic Institute and State University**

**Current position: Assistant professor of microbiology and immunology**

I'm a tumor immunologist and basic scientist, but I've worked in translational research for some years trying to take the discoveries we make in our lab and put them forward into phase I clinical trials. I had gotten to know some of the basic researchers and clinicians at Dartmouth, and I think the environment here is very conducive to team science, which is what I think the future is for successful cancer research. It's also a wonderful environment for translational research.

I started working with Mary Jo Turk in immunology before I got here. Almost immediately after arriving we initiated collaborations with researchers in biochemistry, medicine, and microbiology and immunology. So we already have a very active collaborative research program up and running. The people here, at least in my experience, are very collaborative and collegial.

The focus of my research has been the development of vaccines for the treatment of metastatic cancers. The common misconception is that a vaccine must be given before disease. In fact, the vaccine stimulates an immune response and so we can actually vaccinate patients who already have metastatic disease. We had a program at the University of Virginia (UVA) where we had vaccinated over 700 patients with experimental vaccines and seen mixed results. The vaccines induced very large immune responses, but they didn't seem to have a lot of clinical effect.

My lab at UVA had identified what we thought was the defect in the vaccine paradigm, which is that the vaccines are inducing large numbers of circulating immune

cells but those cells aren't efficiently exiting circulation and infiltrating tumors that have metastasized. We work in melanoma. The CD8 T cells that we try to induce against melanoma innately try to infiltrate the skin. They've been programmed to believe the melanoma is in the skin, because that's where the melanoma rises. The problem, of course, is for a patient whose tumor metastasizes or moves, which is the lethal aspect of melanoma. Regardless of how much we enhanced the number of T cells, the T cells were still trying to go back to their site of origin, which is a skin tumor.

Our translational goal is to develop paradigms to modulate the tumor to make it receptive of T cells regardless of its location. In other words, we're working on developing treatments that would allow those T cells that were previously skin-homing melanoma cells to redirect and infiltrate a lung tumor and thereby control and eradicate that tumor.

One of the reasons we came here is the opportunity to do *in vitro* lab work and work with mice to model our hypotheses, and then to push these forward very quickly into clinical trial applications.

What I find here is that people are willing to give a little. They've been willing to step out of their safety zone and engage in meaningful and real collaborations. I think the tumor immunology program has already had a firm basis here, and we're poised to see some hopefully significant advances.

“A lot of my work is about unintended consequences...

We're trying to solve one problem, does it help or hurt something else?”

**Economist Ellen Meara, who has spent years studying the effects of changes in health policies, teaches an advanced undergraduate course on health-policy reform.**



I work at the intersection of topics that economists think about and the ones that health-services researchers think about. My past research has focused on things such as what changes in disability policy did for vulnerable populations, like people with substance-use disorders or mental-health disorders.

Currently I have two major research areas that are both funded by the National Institute on Drug Abuse. One is looking at the impact of parity legislation, which requires equivalent coverage for mental-health and substance-abuse treatment as for medical and surgical services. Did that, in fact, affect access to services for kids with behavioral-health needs?

In a second project, I'm using the fact that in 2003 and 2004 there was a very abrupt change in the use of antidepressants in pediatric populations—because of attention from the Food and Drug Administration—to assess how that change in treatment influenced academic outcomes, behavior, and substance use among those populations.

Since arriving here, I've launched some new research projects that are more traditional health economics, continuing an interest that I've had in past work. I'm looking at determinants and trends in medical spending over time. There are many initiatives going on here that look at the impact of various payment reforms—how payment reforms affect patterns of health-care use as well as outcomes.

A lot of my work is about the unintended conse-

quences of different policies. We're trying to solve one problem—does it help or hurt something else?

I work with clinicians a lot. For my work with mental health and substance abuse, I collaborate with psychiatrists who specialize in either child psychiatry or addiction psychiatry. And I've done a lot of work in the area of cancer research with clinicians.

I also teach health-policy reform. It's an advanced seminar for undergraduates who are doing a public-policy concentration. And with other faculty members I'm doing the health economics and policy sequence in the master's in health care delivery science program.

There is a great group of people here doing exciting work in health policy. There's a good mix of resources for myself and my husband, who is in the economics department at Dartmouth. It's been very welcoming.

**ELLEN MEARA, Ph.D.**

**Arrived at Geisel: August 2010**

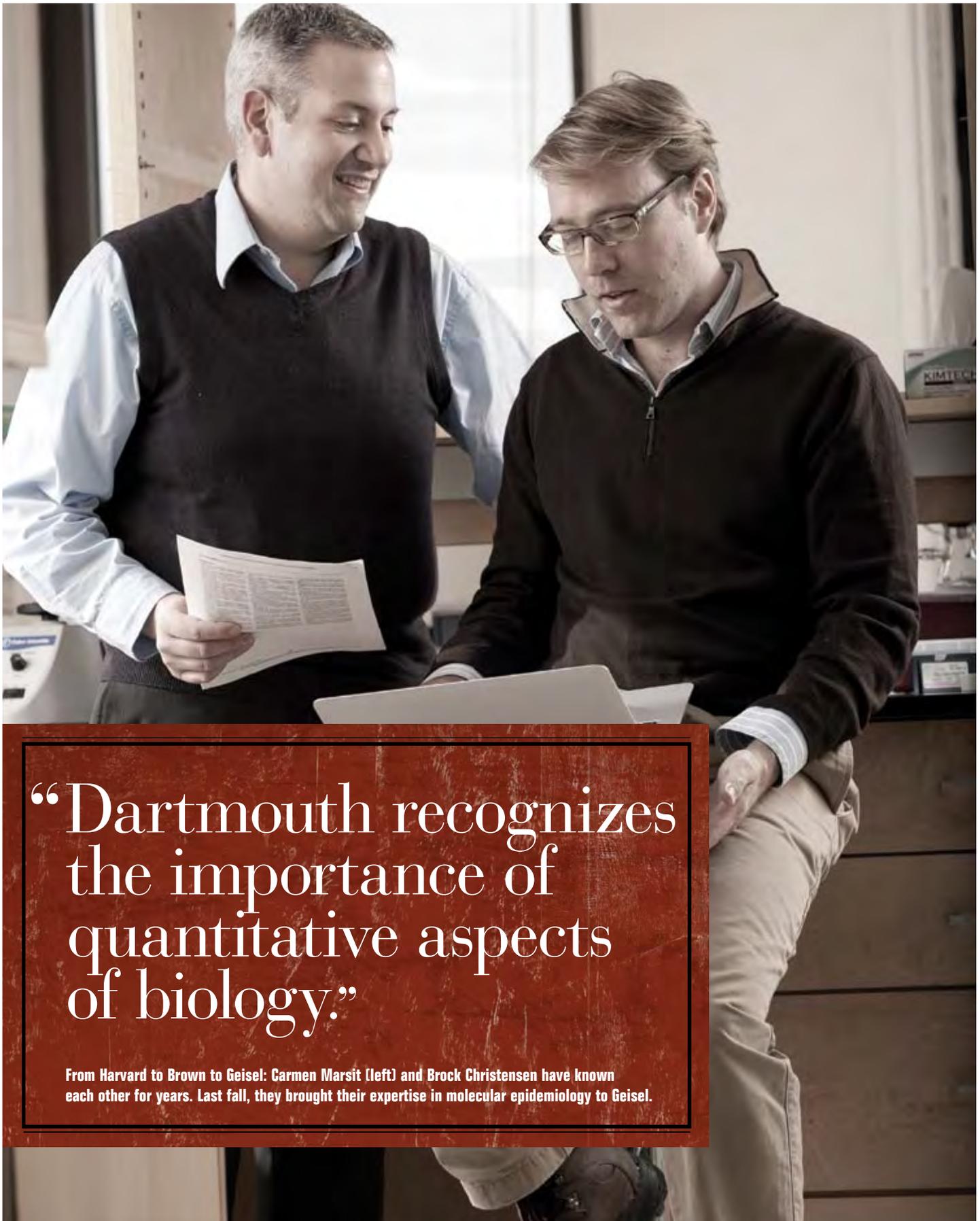
**Came to Geisel from:**

**Harvard Medical School**

**Graduate education:**

**Ph.D. from Harvard University**

**Current position: Associate professor of the Dartmouth Institute for Health Policy and Clinical Practice**



“Dartmouth recognizes the importance of quantitative aspects of biology.”

From Harvard to Brown to Geisel: Carmen Marsit (left) and Brock Christensen have known each other for years. Last fall, they brought their expertise in molecular epidemiology to Geisel.

A lot of epidemiology up to now has asked about the etiology of disease—the risk factors to get a disease. Less of it has been focused on how we can ask questions after a person has a disease, on how we can make some sort of impact on the clinical care of people. So I think that's sort of a new area the field can move into and that's somewhere I'd like to go.

The idea is to take biological markers and apply them to traditional epidemiological studies. Before, epidemiology was a black box. You had risk factors—you ask people about smoking and other lifestyle factors—and you had some kind of disease, and you looked to see where the associations were. Molecular epidemiology is filling in that black box to try to get at what might be happening. Now we can try to understand more about the biology of how exposures actually lead to diseases.

There have been links between secondhand smoke exposure and bladder cancer, but there hasn't been any biology there. A lot of people smoke, but not all of them get lung cancer, and it's not just genetics that determines who those people are. It may be that they have these epigenetic alterations that put them at risk. We're hoping that by looking at epigenetic mechanisms, we can get at some of those answers before we have to wait for people to get a disease.

A really interesting area of our research now is to try to develop blood-based epigenetic profiles that are associated with disease, particularly with cancers.

I wasn't classically trained as an epidemiologist. I was trained as a cancer biologist. So I learned all the basic cancer biology work and then applied that to a population setting. That's a different way to come into it, and it definitely requires a lot of collaboration. Just doing the epidemiology, getting the studies together, requires big interdisciplinary teams. So I definitely like to collaborate with a lot of people. I think it's more fun that way, because you also get a lot of different viewpoints on the questions. I look at it from this epigenetic, molecular viewpoint but then you have people who look at it from a socioenvironmental perspective or from the exposure route. By bringing all that together you can answer questions in a really interesting way.

This is a really nice research environment. There are a lot of resources here to take advantage of to move your research forward pretty rapidly. It seems like there is a real understanding of the need for collaboration. I think that's a really positive thing for Dartmouth, that they understand that this is the way science is moving and they're going to encourage it.

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If I had to call myself anything, I'd call myself a molecular epidemiologist.

For my thesis I worked on mesothelioma, which is related to asbestos exposure. Most of us in the Ph.D. program were training in biology but were in the setting of public health. So I learned molecular techniques and did all of the actual bench work that went into the papers that comprised my thesis. At the same time I had the opportunity to take epidemiology courses and biostatistics courses. Understanding the biology is very interesting to me, but of course I would be elated if I was able to actually have an impact at the level of public health.

The focus of my research has been epigenetics—specifically epigenetics in human cancers. Epigenetics is clearly very important in terms of helping explain the diversity and complexity of biology beyond just the genome itself. You have one genome that encodes all these different genes, but we also have 200-odd different cell types that have distinct functions. In order to extract from the single genome all of the different functions that make us work there needs to be a program, and part of that program is epigenetics.

Specifically, I study DNA methylation—which is a type of epigenetic mark that occurs on DNA—as well as microRNA expression. One major focus is trying to determine whether or not we can develop DNA methylation biomarkers that help us provide a more accurate prognosis for an individual who has just been diagnosed

with cancer. Another is to potentially use epigenetics and epigenetic biomarkers to understand whether or not a person's exposures may be contributing to precancerous alterations. If epigenetic biomarkers can indicate that an individual has an increased risk of acquiring disease in the future, they may be able to modify their behavior in a way that would reduce that risk.

One of the reasons I wanted to come here is because Dartmouth recognizes the importance of quantitative aspects of biology and pursues the training of individuals to tackle current and future problems. That investment is clear, and it aligns well with my goals and my needs as a researcher. Even though I have some quantitative background, I can't claim to know how to do all of these analyses myself, nor would I be able to. That's another huge plus of Dartmouth.

These are complicated problems. They require a lot of patients to study. Managing that epidemiological side is an enormous undertaking, but Dartmouth has an incredibly stellar track record of these types of studies.

One of the things that has impressed me about Dartmouth before I came here and since coming here is that people are incredibly willing to work with each other. There's an underappreciation of the necessity for collaborative science to make a translational impact. This is the type of research I'm going to do, so I need to be in a place where the environment is supportive of that. And this is definitely that place.

### **CARMEN MARSIT, Ph.D.**

**Arrived at Geisel: September 2011**  
**Came to Geisel from: Brown University**  
**Graduate education: Ph.D. from Harvard University**  
**Current position: Assistant professor of pharmacology and toxicology and of community and family medicine**

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### **BROCK CHRISTENSEN, Ph.D.**

**Arrived at Geisel: August 2011**  
**Came to Geisel from: Brown University**  
**Graduate education: Ph.D. from Harvard University**  
**Current position: Assistant professor of community and family medicine**



“There’s such expertise here in working with seriously mentally ill clients and a strong interest in expanding the work to adopt technology.”

**Lisa Marsch, an associate professor of psychiatry, came to Geisel to create the Dartmouth Center for Technology and Behavioral Health, part of the psychiatry department’s Psychiatric Research Center.**

**LISA MARSCH, Ph.D.**

**Arrived at Geisel: July 2011**

**Came to Geisel from: The National Development and Research Institutes, New York City**

**Graduate education: Ph.D. from the University of Vermont**

**Current position: Associate professor of psychiatry; director of the Dartmouth Center for Technology and Behavioral Health**

The Dartmouth Center for Technology and Behavioral Health is a new center. We just launched it. It’s housed here within the Psychiatric Research Center, which is part of the Department of Psychiatry. It’s funded by an NIH grant.

The center allows us to build up an infrastructure behind research we’ve been doing for a number of years—research that has been focused on developing, evaluating, and now disseminating technology-based interventions targeting behavioral health, particularly substance-use disorders but also mental-health issues. There are a number of effective behavioral treatments for addiction and mental-health issues, and there are a lot of challenges to delivering these types of interventions in any kind of widespread way. What we know works doesn’t always get into the hands of people who could benefit from it.

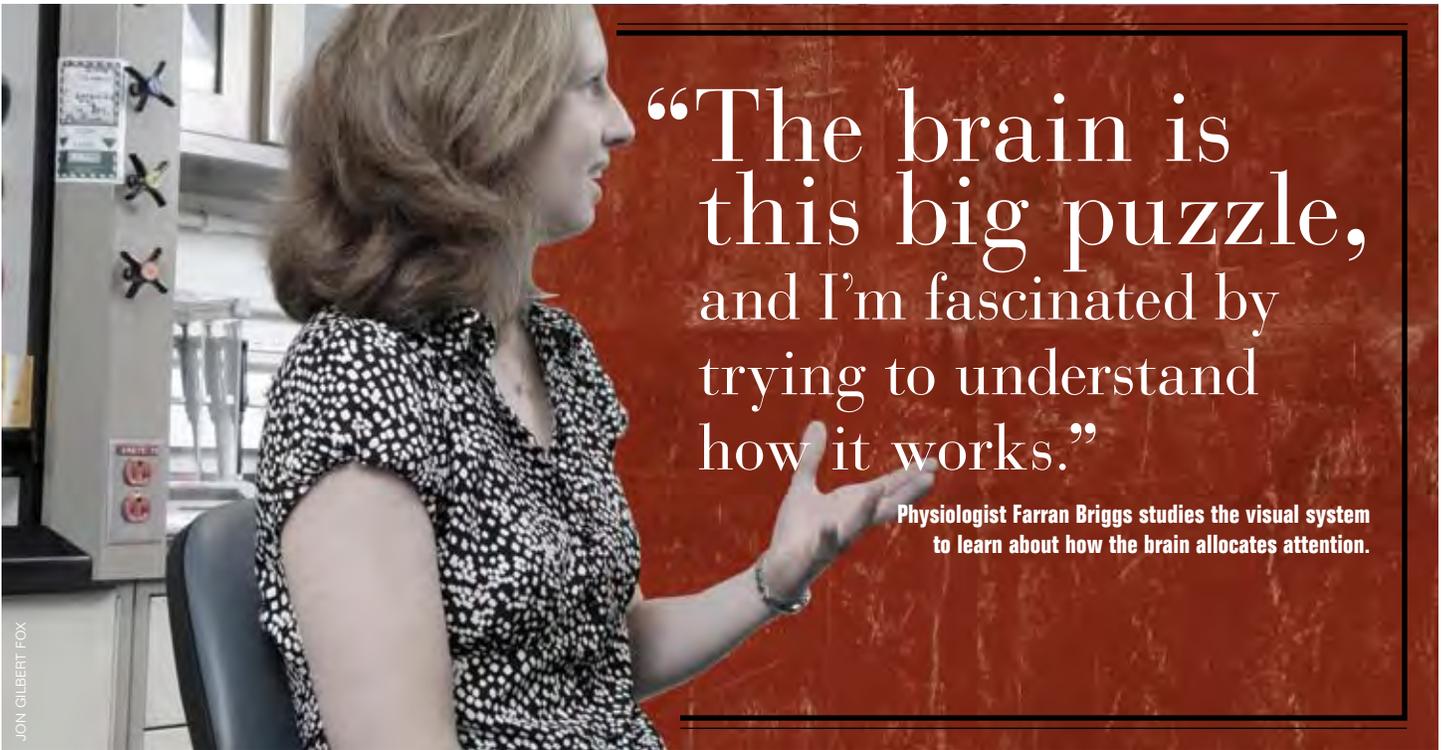
We have a whole array of activities focused on this type of research with a lot of different investigators. Some are focused more heavily on addiction, some on mental-health issues, and some on serious mental illness. And we’re thinking not only about how you optimally develop these tools but about how you optimally integrate them into care settings. How do you promote widespread dissemination? What’s going to have the biggest impact for different subpopulations?

To date a lot of our work has focused heavily on treatment, as well as on prevention. We have a whole array of activities focused on drug-abuse prevention, building up protective factors and reducing risk fac-

tors for drug use and other risk behaviors in children and adolescents. We have a number of investigators affiliated with the center doing work in smoking cessation, in diabetes management, working with seriously mentally ill patients, and working to use technology to promote reduction in HIV risk behavior. There is a really strong evidence base now to suggest that these things can work.

There’s an opportunity here at Dartmouth to enhance what we wanted to do with this research through collaborations with other groups, including the Psychiatric Research Center. There’s such expertise here in working with seriously mentally ill clients and a strong interest in expanding the work to adopt technology with those populations.

We have all of this beautiful data that shows us that these tools can work. What I’d really like to do now is scale up the work a bit by thinking about much larger demonstration projects in real-world settings, like large systems of care, especially in light of what’s happening in health care.



“The brain is this big puzzle, and I’m fascinated by trying to understand how it works.”

Physiologist Farran Briggs studies the visual system to learn about how the brain allocates attention.

JON GILBERT FOX

I took a psychology class in high school. We learned a little bit of neuroscience and I was just fascinated. I thought it was the coolest thing. When I came to Dartmouth as an undergrad, I tried to keep an open mind and take a variety of classes, but I think I always knew what I wanted to do. I was hooked. I wanted to run my own lab, do my own research.

There has been a lot of neuroscience work focused on the visual system. Vision is by far our strongest perceptual sense. We use it for everything. It’s highly developed, and in that sense it is somewhat easy to manipulate. We know a lot about the visual world. We can reduce visual stimuli into very simple entities, and we can use those to test how the brain encodes visual information. I think it is a very nice model for how the brain works.

I study visual attention, so I’m trying to understand the mechanisms that the brain uses to help a person allocate attention to a specific feature in a stimulus or a specific task that they’re doing. Our data indicates that attention can actually change neural activity at the subcellular level—the synaptic level. All previous studies of attention have been whole brain, like fMRI imaging, or looking at the activity of single neurons.

Now that we’ve found this interesting effect of attention at the synaptic level, we want to look at attention at a local circuit level. Does attention differentially modulate different neurons that are connected in a circuit in the primary visual cortex?

There are a lot of phenomena in the brain, and attention is a good example, where we’re very aware of our use of it but we really have almost no idea how the brain does it. Especially at the cellular, subcellular, or network level. So all of these studies are really aimed at trying to understand the neurophysiological changes and the network changes that underlie the phenomenon of attention. By extrapolation we could use that to try to build, for example, neurophysiologically accurate models of attention deficit.

I think Dartmouth is a very good fit for me. Probably the best thing about Dartmouth that I’ve encountered so far is the amazing possibility for collaboration with fantastic colleagues—at the Thayer School, in the psychology department, on the clinical side in neurology. Possibilities for exciting new research have sprung up all over.

I’ve been collaborating with a professor at Thayer. We have a couple of projects that we’re pretty excited about. We’re trying to develop some new and potentially exciting technology for small-scale brain recordings. I’ve also been working with some people in neurology, too, with the end goal of being able to use technology like this to measure brain activity. So there are a lot of applications for this stuff.

To me the brain is this big puzzle, and I’m fascinated by trying to understand how it works.

**FARRAN BRIGGS, Ph.D.**

**Arrived at Geisel: July 2011**

**Came to Geisel from: The University of California, Davis**

**Graduate education: Ph.D. from the University of California, San Diego**

**Current position: Assistant professor of physiology and neurobiology**

“It doesn’t feel like an internally competitive environment. It feels like an internally supportive environment.”

In the year that he has been at Geisel, physiologist Bryan Luikart has been impressed by the undergraduates—such as DC '12 Sarah Streeter—who have conducted research in his lab.

**BRYAN LUIKART, Ph.D.**

**Arrived at Geisel: January 2011**

**Came to Geisel from: Oregon Health and Science University**

**Graduate education: Ph.D. from the University of Texas Southwestern Medical Center**

**Current position: Assistant professor of physiology and neurobiology**

My research revolves around synapse formation and trying to understand how activity sculpts synaptic connectivity. I believe that it’s the way that activity changes connectivity between neurons that sort of sculpts our ability to respond to our environment and to learn to feel. It gives you both your cognitive and your affective being.

In one research focus I’m looking at a set of genes that we know for sure have a profound impact on synapse formation: the PTEN gene. If you take away PTEN, neurons tend to grow, and as they grow they form more excitatory synaptic connections with one another and likely make excitatory synaptic connections between other neurons that they normally wouldn’t be connected to at all.

About 10% to 20% of autism patients have macrocephaly, a large head. And in about 10% of those, mutations in PTEN have been found. We have a gene that we know can increase growth and increase synapse formation and we’re trying to understand the mechanisms whereby that happens. And one of the things we’re doing is we’re taking actual mutations that are found in humans that have the PTEN mutation and macrocephaly and we’re reintroducing those into the mouse neurons to see if we can find a neuron-specific mutation.

The other thing we’re looking at is microRNAs. This involves searching for new molecules and new mechanisms that regulate synapse formation. We’re studying the role of microRNAs in the way newborn

neurons grow up into the central nervous system. By finding microRNAs that will affect the growth and integration and then looking at the targets of those microRNAs—which genes they’re regulating—we find new genes that regulate synapse formation.

All major treatments for depression—including medications, things like rhythmic exercise, and treatments like electroconvulsive therapy—stimulate neurogenesis. The bottom line is that understanding neurogenesis, we hope, will give us some insight into the processes that are important for anti-depression.

The people here are really collegial. It doesn’t feel like an internally competitive environment. It feels like an internally supportive environment. If your thinking gets too focused and too narrow on what you do, you miss out on some potentially big discoveries. I like that at Dartmouth we’re small but we still have experts in a large array of areas, so you still have a lot of people to interact with.

The quality of the undergrads here and the fact that they’re really interested in research—that’s really nice. I don’t see that at other institutions. We have seven undergrads who come in and out of the lab right now, and they bring in a lot of enthusiasm and productivity. One was here full-time this last semester and he was able to make a significant enough contribution that most likely he’ll be published on the next paper that comes out of the lab.

“We know the cell division system is implicated in a lot of different kinds of cancers.”

**Assistant professor of biochemistry James Moseley, who studies the mechanics of cell division, says that the department has been very supportive of his efforts to establish his lab.**



I focus on cell division. My lab uses an organism called fission yeast. The cell division machinery is, for the most part, conserved between yeast and humans and everything in between. We know that the cell division system is implicated in a lot of different kinds of cancers. So hopefully by understanding it in this very simple system of fission yeast we can also understand what's going wrong in a lot of cancer cells.

The basic thing I'm interested in is how cells coordinate growth and division. It's one of the more basic questions in cell biology—how a cell divides and what it is that tells a cell to divide now.

A new cell is fairly small when it's newborn. It grows to a certain size and shape, and then it divides. A lot of the proteins that drive that growth have been known for a number of years. I'm interested in how those proteins communicate with the part of the cell that decides when to divide. People knew over 30 years ago that a lot of cell types would divide when they reach a certain size. But nobody has really known what the mechanisms are that measure size.

We found a group of proteins that all interact with each other and localize in the same place in the middle of cells, and their basic role is to promote division—they tell the cell it is time to divide. So then we looked at things that might regulate these proteins and we found a protein called Pom1. What Pom1 does is it inhibits these other proteins, and by doing that it inhibits cell division.

I was looking for an environment where people think about cell biology in the same way I do but also work on different problems and could provide different kinds of input. The Department of Biochemistry has been just a fantastic fit for me.

I've found the environment to be really supportive, which in my position, starting out a lab, is incredibly important. People in the department and the cancer center and the medical school have been really helpful in terms of getting grants, which is a tough first step. That has all gone really well for me, and I think a large part of that is the supportive environment here.

It's fun to be a part of a school like Dartmouth. Obviously it extends well beyond the sciences and the medical school. It's nice to think of yourself as part of something bigger than your lab and your department. On the Hanover campus we've got our small departments here and then I go over to the hospital and I'm reminded that I'm part of this huge thing. I think the overall size of it is a little deceptive sometimes. Dartmouth likes to promote the small school atmosphere, but the truth is, there is a lot of science and research being done on a fairly large level here, which is great.

**JAMES MOSELEY, Ph.D.**

**Arrived at Geisel: September 2010**

**Came to Geisel from:**

**Rockefeller University**

**Graduate education: Ph.D. from**

**Brandeis University**

**Current position: Assistant professor of biochemistry**

“Maybe we need to rethink how we approach depression in terms of clinical trials, animal models, and treatment development.”

Psychiatrist Paul Holtzheimer earned his M.D. at Geisel and returned last summer to head a mood disorders clinic.



**PAUL HOLTZHEIMER, M.D.**

**Arrived at Geisel:** July 2011

**Came to Geisel from:** Emory University

**Graduate education:** M.D. from Geisel School of Medicine

**Current position:** Associate professor of psychiatry and of surgery

I'd enjoyed Dartmouth and the academic atmosphere as a medical student, and the Dartmouth neuroscience section is quite strong. Dean Souba was a selling point as well. It was very clear that he wanted to see clinical neuroscience research expand. There was an opportunity to build something pretty significant that could rival the other places around the country and around the world—a place that could be a national and international center of excellence for the study of clinical research in mood disorders.

For many years, depression has been defined by a set of symptoms. One problem with that is, well, if we're talking about a number of different symptoms, and medications are going to be targeted toward a more specific system, then it may not be possible to reliably get decreases in all of those things. If depression really is about mood, then why aren't we just looking at mood?

Maybe we need to rethink how we approach this disorder in terms of clinical trials, animal models, and treatment development. One possibility is that depression be redefined as a core set of symptoms that make up the true illness.

A slightly more radical approach is to think of depression not as the state of being depressed but as the inability to regulate that state: the inability to come out of it, the inability to stop yourself from going into it. The state itself is not inherently abnormal. It's how that state is regulated over time.

Our current treatments for depression don't seem to keep people out of depression very well. We wanted to

look at that. So, in a recent study at Emory, we enrolled 10 patients with what we call standard depressive disorder and seven patients with bipolar II disorders and treated them with deep brain stimulation.

After two years of stimulation in the 12 patients that made it that far, we had a 58% remission rate and a 92% response rate. Remission in depression means essentially that your symptoms are gone. You have no significant symptoms of depression. You're essentially well. And response means you've had a 50% decrease in symptom severity, so it's a clinically significant drop.

Almost more important was that any patient that achieved remission at some point in the study had not had a relapse. So unlike other treatments for depression where you can get somebody well but then they relapse, these patients got well and didn't relapse.

On the clinical side, I often work with residents. They'll often do a lot of the data gathering and the initial thoughts about diagnosis and recommendations. Then we'll see the patient together and agree on a plan and get them back to the referring provider.

I always loved living in this area during medical school. It was my first time living in New England. I told my wife, who had never been here before, when we visited in mid-November, "If you like it in mid-November, you'll like it pretty much the rest of the year." ■