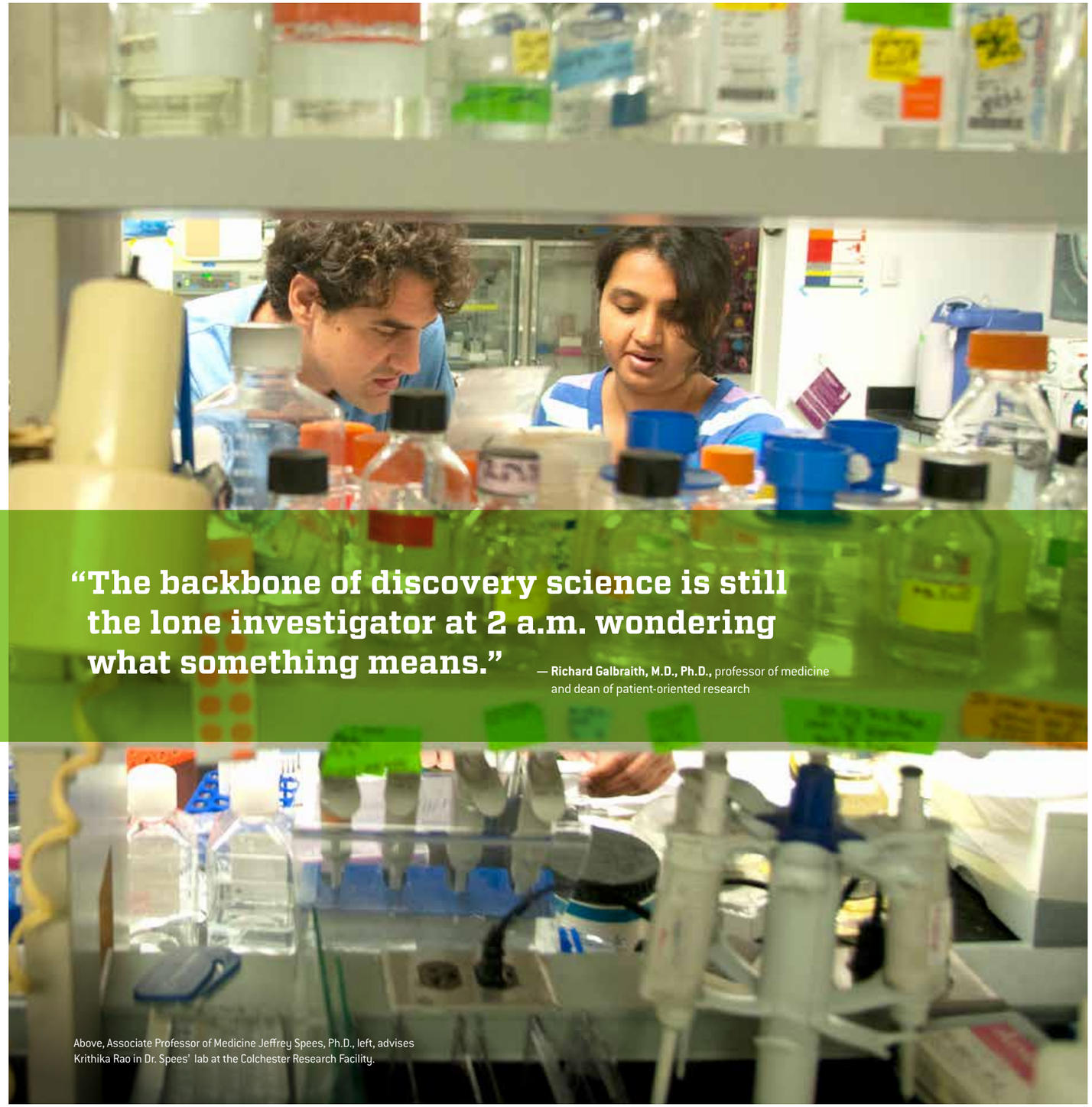

“The backbone of discovery science is still the lone investigator at 2 a.m. wondering what something means.”

— **Richard Galbraith, M.D., Ph.D.,** professor of medicine and dean of patient-oriented research

Above, Associate Professor of Medicine Jeffrey Spees, Ph.D., left, advises Krithika Rao in Dr. Spees’ lab at the Colchester Research Facility.

Making Scientists for the 21st Century

by **Erin Post**
photographs by **Alec Jacobson**

As the nature of scientific inquiry has become more interdisciplinary, and the range of job expectations for new scientists has radically changed, UVM has reshaped the pathways that lead promising students into careers in biomedical research.

It’s a question on the minds of research scientists the world over: When is that ‘aha’ moment going to happen? When will the pieces fall into place, leading to a new discovery that changes how we understand the biology of a human, treat disease, or care for patients?

“The backbone of discovery science is still the lone investigator at 2 a.m. wondering what something means,” says UVM Professor of Medicine Richard Galbraith, M.D., Ph.D., associate dean of patient-oriented research. What has changed is how that person fits into the larger whole. Interdisciplinary teams that look at questions from different angles are becoming more and more vital to scientific inquiry, says Galbraith, who is also the director of the UVM Center for Clinical and Translational Science. And with technology — especially the power of computers to analyze vast quantities of data — transforming what is knowable, scientists must be grounded in their discipline while also understanding its relevance to other fields.

To keep pace with this new reality, UVM and other institutions are re-thinking how they educate research scientists. Today, students entering a Ph.D. program affiliated with the College of Medicine choose from four programs that bring faculty together from multiple departments and colleges across the university — all under the administrative umbrella of the UVM Graduate College. Several programs have been restructured and combined to give students exposure to a wider variety of research, while a few new programs — clinical and translational science, and bioengineering — have been created to address relatively new fields. In all of these programs, students conduct their Ph.D. research with mentors who

have different areas of expertise, opening opportunities for innovation at the margins of what is known.

The reductionist approach — isolating one particular technique or biological process in the lab to understand how it works — has yielded great insights over the years, including vaccines and therapies responsible for saving many lives. But it has its limitations. What happens in a test tube doesn't necessarily hold when it is part of a larger system, notes Associate Professor of Molecular Physiology and Biophysics Chris Berger, Ph.D., director of graduate education at the College of Medicine. And then there's the realization that science doesn't end with what happens in the lab — politics and policy decisions, socioeconomic conditions, even the built environment affect health outcomes. "The world is more complex now," says Berger. "We need scientists who can connect the dots, and ask the right questions."

The message from federal agencies that set the research agenda, like the National Institutes of Health, has changed as well. It used to be that the success of an academic program was measured by how many Ph.D. students went on to tenure track faculty positions — essentially replacing the professors who retire. Now, with data indicating that employers outside of academia are snapping up students with biomedical training, the focus has shifted to also prepare students for jobs in biotech, government, publishing, teaching, and many other fields. According to the 2012 Biomedical Research Workforce Working Group Report from the NIH, less than half of Ph.D. graduates in the biomedical sciences go on to careers in academia, and about 30 percent of biomedical Ph.D.s work in the biotech and pharmaceutical industries. Young people today must be flexible as they enter a job market that can be fickle. Nevertheless, it's an exciting time to be working in science, says Mary Tierney, Ph.D., an associate professor with joint appointments in plant biology and microbiology and molecular genetics.

"People who are professional scientists now are extremely lucky," she says. "Science is opening up new ways to ask questions."

At the College of Medicine, four Ph.D. programs serve as pathways to careers in the biomedical sciences: Cellular, Molecular and Biomedical Sciences; Neuroscience Graduate Program; Clinical and Translational Science; and the Neuroscience Graduate Program.

"The world is more complex now. We need scientists who can connect the dots, and ask the right questions."

— Chris Berger, Ph.D., College of Medicine director of graduate education

At left: Chris Berger, Ph.D., director of graduate education, and Richard Galbraith, M.D., Ph.D., associate dean for patient-oriented research. Above, Professor of Microbiology & Molecular Genetics Nicholas Heintz, Ph.D., is director of the Cellular, Molecular, and Biomedical Sciences Graduate Program.

Cellular, Molecular and Biomedical Sciences

The most recent change in the graduate medical sciences at UVM is the merger of four College of Medicine graduate degree programs — microbiology and molecular genetics; molecular physiology and biophysics; biochemistry; and pharmacology — with cell and molecular biology. The new expanded program has a different name — cellular, molecular, and biomedical sciences — but a familiar acronym: CMB. Those three initials have stood for over 40 years for cell and molecular biology, the oldest cross-college graduate program at UVM.

"A lot of people see this as an opportunity to strengthen an already strong graduate program," says Mary Tierney, Ph.D., who served as the director of the new CMB program through the merger process. "The opportunity to provide more resources for our students was a major factor [in the decision to merge]."

As of July 1, 2013, Tierney handed leadership of the program to Nicholas Heintz, Ph.D., who will help guide the program as it grows and matures. The first 20 students in the new Cellular, Molecular, and Biomedical Sciences Program matriculated in the fall of 2012; they take a common core curriculum, but have the opportunity to rotate through several labs across the program prior to choosing their area of research focus. Preserving the distinct cultures of the individual departments — even with the merger — is important for the student experience, says Heintz, who is a professor of pathology with a joint appointment in microbiology and molecular genetics.

"This new structure gives us more flexibility. We provide students with as many opportunities as possible for rigorous training while still maintaining a personalized approach. That's very attractive for students," Heintz says.

Krithika Rao, a cellular and molecular biology student in her third year of study, came to UVM with a plan to research cell biology in injury after receiving her undergraduate degree in zoology and master's degree in applied biology at universities in India. She visited the lab of Jeffrey Spees, Ph.D., associate professor of medicine, and felt she'd found her place. He works at the leading edge of research on adult stem cells: One line of inquiry focuses on understanding the biology behind cardiac stem cells to determine possible therapeutic applications. Right now Rao is experimenting with mouse models of cardiac disease to pinpoint how stem cells from the heart may work to repair tissue damage if they are injected after a heart attack.

Congestive heart failure and heart attacks affect millions of people annually in the United States alone, so if cardiac stem cells prove to be therapeutically beneficial, the implications for patient care could be huge. With a publication in this September's *Stem Cells,* their research is already advancing knowledge in this emerging field.

"I decided I wanted to make a contribution to this field because it's so early," Rao says. "This is pretty unknown territory."

Neuroscience Graduate Program

For over 25 years, many graduate students interested in neuroscience studied under the banner of anatomy and neurobiology, while other students chose mentors in psychology, or biology. Although they received top notch training, they lacked a central hub for interdisciplinary study in neuroscience. That changed in 2006, with the formation of the Neuroscience Graduate Program (NGP). It started with five predoctoral students and one M.D./Ph.D. student, and today has grown to 24 Ph.D. students with 52 faculty members teaching in the program from 10 academic departments and four colleges across the University.

NGP Director and Professor of Neurological Sciences Rae Nishi, Ph.D., says the NGP benefitted at its founding from participation in the Carnegie Initiative on the Doctorate (CID), a nationwide program that looked at how to improve doctoral student training. A UVM committee she served on explored ways to structure the fledgling NGP so that students would be able to conduct research across disciplines and develop the communication skills to become stewards of the field. The program has been responsible for "breaking a lot of barriers down," says Nishi, in part because it brought faculty from different departments together in pursuit of a common goal.

"Science is becoming more interdisciplinary," she says. "We need specialists to collaborate; projects are stronger when you have all of this great expertise working together."

The NGP reflects this evolving reality. Students take several core science courses alongside medical students, while they choose electives that range from Toxicology to the Neurobiology of Learning and Memory. A new academic track created

Graduate student Nate Jebbett, in background above, worked with Upward Bound students this summer as they used multi-colored pipe cleaners to understand neuron construction.

COMMUNITY CONNECTIONS

Every summer, the Neuroscience Graduate Program (NGP) welcomes a cadre of SNURFs — Summer Neuroscience Undergraduate Research Fellows — to the medical campus. These eight to ten diverse undergraduates are selected from hundreds of applicants from across the country. They spend ten weeks attending lectures and conducting research with faculty members and NGP students, giving them valuable higher-level academic experience. And for neuroscience grad students, it's a chance to develop the teaching and communication skills necessary in a rapidly changing job market, says Rae Nishi, Ph.D.

"We should be preparing students for a number of different jobs," Nishi says. "I want to provide them with opportunities to do outreach."

NGP students connect with the wider community in a number of other ways. During Brain Awareness Week, students fan out to area elementary schools to conduct workshops, and they organize an annual Vermont Brain Bee for high school students. Another summer program brings Upward Bound students to campus for a series of classes that include one in brain science organized and taught by graduate students. Vanessa Ochoa, a NGP student who co-led one of Upward Bound classes, says her peers relish the chance to try their hand at running a classroom.

"I love to interact with students, and to inspire and mentor them," Ochoa says.

by the NGP and UVM's physical therapy program allows students to pursue both degrees, opening up exciting opportunities. Students are required to be a teaching assistant in at least two courses — setting an expectation for strong communication skills. Many NGP students work with undergraduates who come to campus for the Summer Neuroscience Undergraduate Research Fellowship Program (SNURF), which is funded by the National Science Foundation and the College of Medicine Office of Diversity and Inclusion. An essential feeder program for NGP, the success of SNURF is reflected in the diversity of the program — 21 percent of NGP students are from underrepresented minorities, compared to 5.6 percent of all grad students at UVM.

NGP students Vanessa Ochoa and Liana Merrill have honed their communication skills through these and other activities. Although both are spearheading important research — Ochoa works with Nishi researching neuroblastoma in children, and, with Margaret Vizzard, Ph.D., Merrill is focused on studying how the brain controls bladder function. Both students envision a future that also involves teaching. As a Mexican-American who is the first in her family to continue to professional school, Ochoa would like to work with minority students. Merrill hopes to teach at a liberal arts college or small university.

"Teaching is a lot of work but it is really rewarding to inspire someone who is younger than you," says Ochoa. Adds Merrill: "I feel like the outreach we do here is abundant. That makes us stand out from other programs."

Clinical and Translational Science

Graduate students in the Clinical and Translational Science (CTS) program bring with them expertise in a wide variety of subjects: The program attracts internists, audiologists, surgeons, and computer scientists, even lawyers and anthropologists. What unites them is a desire to apply their knowledge to health care in a research setting.

This was the case for Abigail Crocker, a faculty member in the mathematics and statistics department at UVM with a master's degree in biostatistics. She wanted to use her expertise to become an independent investigator, and in CTS found not only strong mentors, but a group of students who provided support and guidance.

"We learned a lot from talking to each other about how to systematically approach research studies," says Crocker, who defended her dissertation in April of 2013. "When you leave the program you should be an expert in the research process."

For a long time, students and faculty at UVM looking for this kind of mentoring sought it out through an informal network, says Benjamin Littenberg, M.D., Henry and Carleen Tufo Professor of Medicine and Professor of Nursing. In the mid-2000s, Littenberg found himself tapped to help transform this loose network into an academic program. Officially launched in 2008, CTS now includes a 75-credit Ph.D. program as well as a master's degree and certificate program. Doctoral students gain an understanding of their research as "part of a spectrum," Littenberg says, one that includes biomedical as well as ethical, legal, political, and social dimensions. "Students may come with experience at one part of the spectrum," says Alan Rubin, M.D., associate professor of medicine emeritus, "but they leave understanding how their research fits into a larger whole."

"It's interdisciplinary," says Rubin, who teaches CTS courses and is the program's liaison to the UVM Graduate College. "It causes curiosity and collaboration."

Crocker's work exemplifies this approach. She started by creating a mathematical model to help determine which babies of opioid-dependent mothers were likely to develop neonatal abstinence syndrome. Then, she looked into the breastfeeding habits of women struggling with opioid dependence. Despite clinical guidelines that recommend breastfeeding in this population, rates remain very low. Crocker wanted to find out why, and figure out ways to support these mothers. Working as a CTS post-doc with her mentor, Associate Dean for Primary Care Charles MacLean, M.D., she analyzed data using the state's all-payer health care claims database. In January 2014, she begins her new role as a research assistant professor in mathematics and statistics, in which she will expand on her student and post-doc work.

Bioengineering

"If you stand in the middle of campus, you could throw a rock to the College of Engineering, the College of Medicine, and the teaching hospital," says Bioengineering Graduate Program Director Jason Bates, Ph.D. "That is very unusual."

This physical proximity makes UVM particularly fertile ground for bioengineering, a discipline that stands at the intersection of fields. Launched about two years ago, the Ph.D. program now includes six students with mentors in the College of Medicine and the College of Engineering and Mathematical Sciences. Students apply quantitative engineering analysis to the study of biological systems, which may range from molecules all the way to populations.

"Bioengineers are in pretty big demand," says Bates, who is a professor of medicine and interim director of the School of Engineering. Recent advances in the development of artificial organs and tissues have grabbed headlines, while the ever-increasing volume of data humans produce has prompted new thinking about ways to leverage this information in health care. Bioengineering students at UVM are at the leading edge of much of this work.

M.D./Ph.D. student Joshua Pothen is working with a cross-disciplinary team of researchers — including pulmonologists Professor of Medicine Dan Weiss, M.D., Ph.D., Associate Professor of Medicine Matthew Poynter, Ph.D., and Bates — to create a computer model that predicts how cells in the lung respond to certain allergens. The goal is to understand why some people, particularly children, suffer from chronic asthma while others may have only a few attacks and recover. Because a computer model has the ability to simulate a complex system, it stands to capture the emergent behavior that comes from parts interacting as a whole. This knowledge can inform the direction bench research takes, allowing scientists to test big ideas before going to the lab. Huge advances in technology and data analysis have made this work possible, Pothen says, and bioengineers stand uniquely poised to make connections between computer modeling, lab research, and patient care.

"It takes someone who can connect the researcher and the clinician and say 'hey, you could use this,'" Pothen says.

With bioengineering faculty working on everything from tissue engineering and regenerative medicine to orthopaedic biomechanics and synthetic biology, collaboration is a part of everyday life. Faculty members hail from and work with the Advanced Computing Center, the Vermont Cancer Center, the Department of Rehabilitation and Movement Science, the Division of Cardiology and many other departments and programs across campus.

"[The program] brings engineering and medicine together in ways that wouldn't have happened otherwise," Bates says.

Like Pothen, students in all of the graduate medical science programs at UVM learn critical thinking, research, and teaching skills, and they leave prepared to enter a job market that is rapidly changing. Most important, they're also prepared to explore the unknown in science, and contribute new knowledge to their fields, says Chris Berger, Ph.D.

"New ideas come from synthesis, from thinking about a problem differently," Berger says. "That's where most scientific progress is made." And where the next generation of scientists emerge. VM

"Science is becoming more interdisciplinary. We need specialists to collaborate; projects are stronger when you have all of this great expertise working together."

— **Rae Nishi, Ph.D.,** Neuroscience Graduate Program Director and Professor of Neurological Sciences

Clockwise from above right, Rae Nishi, Ph.D., Professor of Neurological Sciences and director of the Neuroscience Graduate Program; graduate student Liana Merrill; graduate student Vanessa Ochoa (in lab coat) works with SNURF program participant Genelle Rankin; Abigail Crocker, Ph.D.'13 reviews data on her laptop with Associate Dean for Primary Care Charles MacLean, M.D.

At top, graduate student Joshua Pothen works with a cross-disciplinary team of mentors to create a computer model of lung cell response to allergens. Above, Professor of Medicine and Interim Director of the School of Engineering Jason Bates, Ph.D., is one of the mentors of Joshua Pothen and other students.