Though there’s cutting-edge research happening there, don’t look for the Cardiovascular Research Institute of Vermont (CVRI) on a map of the University of Vermont campus: you won’t find it, and not because it’s housed elsewhere in the state. Like the circulatory system itself, which branches throughout the human body, supporting its components literally from head to toe, the CVRI has a subtle presence throughout dozens of laboratories, supporting research across a wide range of disciplines at the University. Through the work of its affiliates, it is at the forefront of cardiovascular research — not only in the United States, but worldwide.

In 2002, Burton Sobel, M.D., with an $8 million endowment in hand, formed a nonprofit cardiovascular research organization under the aegis of the College of Medicine’s Department of Medicine. The CVRI was subsequently formed in 2008. Its mission was generally outlined by a dedication to reductions in the incidence, morbidity, and mortality of heart and vascular diseases through improving prevention, diagnosis, and treatment. In July 2013, David Schneider, M.D., F.A.C.C., F.A.H.A., was appointed director, shortly after Dr. Sobel’s death. “Burt Sobel was a force, and the Cardiovascular Research Institute was really his baby to do cardiovascular research,” says Schneider. So as it has been rebirthed in this process there was a real direct effort to make the base less narrow. At the urging of the College’s dean, Rick Morin, that base has been redesigned “specifically to be broad, to reach out to many different areas and to different types of research and then to amplify that,” says Schneider. Today its reach extends across disciplines and research areas by providing funding and support to established senior investigators, as well as to those who are just beginning their careers. The CVRI encompasses the broadest possible definition of cardiovascular research, embracing everything from bench to translational research to clinical applications and including under its umbrella disciplines that range from cardiology to pharmacology, even psychology and engineering. While those who are associated with the CVRI are loosely referred to as “members,” there is no real membership per se, no application process or criteria other than the engagement in research that is related to cardiovascular health.

The first year of the revamped CVRI was outwardly quiet, but behind the scenes it was evolving and growing. That began with the formation of a board of directors, whose six members were chosen from across the University and appointed to three-year terms.
EXCELLENCE IN RESEARCH

Schneider first worked with Sobel while completing his cardiology fellowship at Washington University in St. Louis. That program was structured so that the first two years were spent on research and the second two involved clinical work, a translational approach that appeals to Schneider to this day. At Washington University Schneider analyzed the fibrinolytic system, which makes the proteins that dissolve blood clots that form in response to injury, and then looked at the balance between the activator and plasminogen activator inhibitor-1 (PAI-1) in patients who are diabetic or have other insulin-resistant states. Schneider’s research became fully translational when clinical trials were used to look at how insulin, glucose and fatty free acids affect the production of the protein.

“The research I’m involved in today and the research of the cardiology division are really designed to improve care,” says Schneider. “There’s some research that just understands how things work, but as a clinician, it makes sense that I try to always connect mine to the clinical side, and that’s what I’ve tried really hard to do throughout my career.”

When Sobel moved to UVM, where he’d accepted the E.L. Amidon Chair of Medicine, he invited Schneider to come along. Schneider arrived in Vermont in mid-1994, and once here, his interests broadened to include thrombosis and platelet function, in the hopes of identifying an individualized therapy for patients. Working with Professor of Biochemistry Paula Tracy, Ph.D., Schneider developed an assay that used flow cytometry to look at platelet function and activation; in the years since, his focus has remained on platelets and their functioning. He’s now getting started on a project with Associate Professor Kathleen Brummel-Ziedens, Ph.D., and Professor of Biochemistry Kenneth Mann, Ph.D., to find novel ways to characterize the risk of forming thrombin and causing platelet activation. Schneider believes they may have identified a new method to characterize platelet function. Brummel-Ziedens and Mann have been developing assays to better characterize an individual’s likelihood of developing blood clots. Together these may someday be useful tools to better target therapies to the individual. Some of that work has evolved because of proximity — Schneider’s lab is next door to Mann’s — which is the kind of naturally occurring relationship the CVRI board would like to see more of.

For Marilyn Cipolla, Ph.D., F.A.H.A., a professor in the Department of Biochemistry Paula Tracy, Ph.D., for patients. Working with Professor of Medicine David Schneider, M.D., has directed the Cardiovascular Research Institute of Vermont since 2013, and is seen here in his laboratory at UVM’s Colchester Research Facility.

Their first task was to generate a charter that laid out the governance, mission, and initiatives of the CVRI; that was adopted in January 2014, and for Schneider and his board, it wasn’t just an item on a checklist. “We really want to live our mission, which is fostering cardiovascular research,” says Schneider. “And the two prongs to that are highlighting the excellence in research that’s going on here and nurturing the next generation.”

“We REALLY WANT TO LIVE OUR MISSION, WHICH IS FOSTERING CARDIOVASCULAR RESEARCH … HIGHLIGHTING THE EXCELLENCE IN RESEARCH THAT’S GOING ON HERE AND NURTURING THE NEXT GENERATION.”

— David Schneider, M.D., F.A.C.C., F.A.H.A.

Schneider has in mind when he talks about the CVRI’s broad base; he also engages in interdisciplinary work that is one of its hallmarks, collaborating regularly with colleagues in other departments. For one project Bernstein conducted research with Alessandra Rellini, Ph.D., associate professor in the psychology department, on the vascular aspects of female sexual response, in an effort to determine whether they are related to broader indices of cardiovascular health. “We’re happy to have people who are in other colleges at UVM participate in the programming, be eligible for awards, and be part of the core culture that’s interested in cardiovascular sciences and its implications for human health.”

— Ira Bernstein, M.D.
INAUGURAL 2014–2015 GROUP
CARDIOVASCULAR RESEARCH INSTITUTE OF VERMONT

and its implications for human health,” says Bernstein.

The CVRI also recognizes what it calls Distinguished Investigators, those who are “performing sustained, impactful cardiovascular research,” with a five-year award. The current roster is made up of Philip Ades, M.D.; Joseph Brayden, Ph.D.; Martin LeWinter, M.D.; George Osol, M.D.; Russell Tracy, Ph.D.; and Kathleen Trybus, Ph.D. Their research interests span heart failure, vascular adaptation during pregnancy, thoracic aneurysms and coronary artery disease, genetics of heart disease, and weight loss in obese coronary patients, and their work is widely recognized on the international stage.

Along with the Distinguished Investigators initiative that came out of the CVRI charter, there is a concerted effort to support up-and-comers in cardiovascular research — the junior investigators, trainees, and others who are still in the early stages of their careers.

THE NEXT GENERATION

With travel awards, research seminars, and an Early Career Advisory Committee available to them, junior investigators who are affiliated with the CVRI have plenty of rich opportunities at their disposal.

“We’re here to support young researchers through money and exposure,” says board member Harold Dauerman, M.D., professor of medicine. Dauerman conducts clinical trial and registry research and has worked with the American Heart Association on quality improvement initiatives, and has also led national trials developing new technology and pharmacology for interventional cardiology procedures. He’s an active enroller in clinical trials at the College of Medicine and regularly instructs trainees in clinical trials and registries research, and says the ability to participate in a young researcher’s expenses early in his or her career is crucial. That support comes in the form of travel awards and is supplemented by exposure to cardiovascular experts from outside the university.

The travel awards were established to cover educational travel costs for anyone early in their career who is a primary presenting author of an abstract at a regional or national meeting. It’s an honor, and it also means that money that would otherwise have to be used for travel costs can be earmarked for research funding instead. Since July 2014, thirteen $2,000 awards have been made, sending assistant professors, postdoctoral fellows, residents in internal medicine, and graduate and medical students to among other meetings, the International Society for Stem Cell Research’s 2015 Annual Meeting in Stockholm; the Society for Reproductive Investigation’s 62nd Annual Scientific Meeting in San Francisco; and the American Heart Association’s Epidemiology, Prevention, Lifestyle and Cardiometabolic Risk 2015 Scientific Sessions in Baltimore. Katia Landry, a fourth-year medical student, received a travel award that allowed her to present her poster, “Association of Stroke Risk Biomarkers With Stroke Symptoms: The Reasons for Geographic and Racial Differences in Stroke (REGARDS) Cohort,” at the latter this spring. something she says would have been impossible for her to do otherwise, given the financial constraints of school loans.

The newly established Cardiovascular Research Institute seminars, meanwhile, bring nationally established cardiovascular investigators to UVM to not only expose UVM investigators to their work, but promote interaction with UVM junior investigators and trainees. Through the Sobel Visiting Professorship and the Albert Visiting Professorship, two world-renowned researchers are invited for an extended stay, allowing time for colloquia, grand rounds, and one-on-one meetings.

“YOU WANT YOUR TRAINEES TO HAVE THE OPPORTUNITY TO MEET PEOPLE WHO ARE LEADERS IN THEIR FIELD.”

— MARY CUSHMAN, M.D., M.Sc., F.A.H.A.
“I’m definitely interested in a research career, and I know that these next four years are going to be focused on learning how to be a strong clinician,” she says. “But I also want to stay connected to research and basic sciences. Being part of this committee will allow that.”

The committee is shepherded by Mary Cushman, M.D., M.Sc., F.A.H.A., director of the Thrombosis and Hemostasis Program, professor of medicine in the Hematology/Oncology Division, professor of pathology, and a CVRI board member for whom mentoring has long been a professional passion. She says that inviting early career individuals to dinners with visitors and to research and progress sessions — where they are welcome to present their work and get feedback — is important on several levels. “You want your trainees to have the opportunity to meet people who are leaders in their field,” says Cushman. “They might help them get their next job, or they could develop a collaboration. It also teaches them how to interact with scientists outside our institution.”

Cushman’s own work revolves around observations of substantial populations over time to identify risk factors for cardiovascular disease and stroke, particularly those related to genetic markers. As a steering committee member of the REGARDS (REasons for Geographic And Racial Differences in Stroke) study, now in its twelfth year, Cushman has helped enroll and follow 30,000 individuals nationwide. She’s also an active investigator in the Multi-Ethnic Study of Atherosclerosis (MESA), and has had continuous NIH funding for the efficient functioning of the heart’s for a feather in the cap of the university,” Warshaw says of such awards. Warshaw’s grant brings together private investigators from five institutions to study genetic mutations in cardiac contractile proteins. He was recently published in the inaugural issue of Science Advances for his findings on a critical protein that is responsible for the efficient functioning of the heart’s contractions. For Warshaw and Nelson and their colleagues who focus on elements of basic science, translational work is the only way to go.

“One of the big mandates is to try to move basic science into the clinics as quickly as possible,” says Warshaw. “The only way that will happen is if we have physicians and basic scientists communicating with each other and working hand in hand, both at the bench and at the bedside. And I think the Cardiovascular Research Institute is that connection.”

Nelson observes that the CVRI is the continuation of a long university tradition of outstanding cardiovascular research with premier investigators, many of whom received funding from the NIH’s National Heart, Lung and Blood Institute, and notes that any grant proposal review that considers environment has historically found that cardiovascular research is a particular strength of UVM and the College of Medicine. Looking ahead, Nelson would like to see a tenfold increase in the CVRI’s endowment, to allow the University to remain in the top ten percent of cardiovascular research areas.

“Ours is one instrument through which we can invest in the future by making things happen,” he says. “We need to be heavily investing in cutting-edge technology and people so we can keep the momentum going.”

Growth is continuing — as recently as March, the CVRI established a leadership council, composed of seven individuals who are community leaders, but not directly affiliated with UVM or the Medical Center. They will be tasked with highlighting CVRI-related activities and raising money to fund additional research. Schneider says he’d like the leadership council to create forums for investigators to talk about their work with the community at large — locally, and then regionally and beyond.

“I think many of the investigators within the University of Vermont are classic New England in that they tend to do hard work, and they’re oftentimes respected and acknowledged more when they get on a plane and go somewhere else,” says Schneider. So the leadership council’s first step will be to get the word out “to let people in Vermont be proud of what they have going on here.”

It’s nearly impossible to summarize the breadth of cardiovascular research that’s happening around UVM and the College of Medicine in a given day, the findings that are made at the microscopic and the clinical levels.