othing lets loose a shot of dread quite as quickly as the word “cancer.” One of three Americans will be diagnosed with cancer at some point in his or her lifetime; one of five will die from it. As the country’s population ages, the disease’s prevalence will only increase. At the Vermont Cancer Center, one of the primary goals is to develop approaches that will someday make cancer a fully treatable disease.

Down the road, I think it’s going to be a disease that one is going to treat on a continual basis,” says VCC co-director Gary Stein, Ph.D., “and that will be compatible with a high quality of life. The more we understand about the disease, the more we are becoming capable of addressing it using treatments that have more specificity and fewer ‘off-target’ effects.”

Stein, who is also chair of the College of Medicine’s Department of Biochemistry, arrived at the VCC in July, joining co-director Claire Verschraegen, M.D., who had served as interim director since 2011. Their arrivals signaled a turning point for the center. Stein came from the University of Massachusetts Medical School’s cancer center; and Verschraegen, from the University of New Mexico’s. She is a native of Belgium who describes herself as a world citizen, at home anywhere, while he’s a Brooklynite who first moved to Vermont as a UVM undergrad, skis in hand. Already they’ve established what seems to the casual observer as an obvious easy rapport, often finishing each other’s sentences. Stein says they, in essence, recruited each other to the VCC.

“We represent a composite picture,” he says. “We have extensive combined experience in the development and implementation of clinical trials that are not confined to an institution, but regional expertise in investigation with cellular
molecular biochemical approaches that span test tube cells and animal models and into patients.” Summaries Verschraegen: “Gary is the researcher and I'm the physician investigator, and we get along very well.”

The VCC, founded in 1974, is a matrix organization whose 135-plus members range from College of Medicine and University-wide faculty to students and fellows and health care providers. Its accessibility to residents of Vermont, New Hampshire, and northern New York means patients don't have to travel out of state for treatment, which would only add to the physical and mental stresses of treatment.

Stein is a 25-year cancer survivor himself and, while he would have preferred not to go through that experience, he recognizes it as an unparalleled learning opportunity. “Why shouldn't Vermonters have state-of-the-art opportunities to be treated?” asks Stein rhetorically. “Why should they have to go out of state?” Here “state-of-the-art” includes genomic analysis, including massively parallel signature sequencing, something for which the University is nationally known. Stein is confident that in the not-so-distant future, molecular diagnostics will be the most effective and most widely used form of diagnosis.

The VCC has also established a specific division in the laboratory, and they’ll be able to partner and bridge what is coming out of both those disciplines.” Stein and Verschraegen keep translation at the forefront of their work together, defining it as a continuum that reaches all patients, from children through geriatrics, on issues ranging from prevention and early detection through survivorship.

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— Alan Howe, Ph.D., Associate Professor of Pharmacology

The majority of cancer-related deaths are due to metastasis rather than the primary tumor, and VCC member Alan Howe, Ph.D., wants to understand the mechanisms behind metastasis. Specifically, he is focused on examining how cancer cells respond to cues in their microenvironments, how these cues promote cancer metastasis, and how the cues might be exploited for early detection of tumors. His laboratory studies show that molecular biochemical approaches that span test tube cells and animal models and into patients can provide optimal patient care and move science forward.

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Gary Stein, Ph.D., VCC Co-Director

The success of this initiative has reached other institutions; additional regional centers beyond Vermont have since contacted Stein and Verschraegen to inquire into potential collaboration.

One UVM researcher who has taken advantage of the opportunity for inter-institutional collaboration is Kim Dittrus, M.D., Ph.D. Dittrus received a pilot grant from the VCC to expand to Dartmouth and UMass an online behavioral weight loss program for cancer patients. Because it's known that a nicotine and obesity have negative impacts on cancer outcomes through higher levels of recurrence and overall mortality, Dittrus, who is also a nutritionist, piloted a weight-loss intervention program for area breast cancer survivors with Professor of Nutrition Sciences Jean Harvey-Berino, Ph.D., R.D. Patients lost almost as much weight as the general population, but they didn’t exercise enough. In expanding to a multi-site program with rolling entry, then, Dittrus has made some modifications to enhance the exercise, including using pedometers and online methods to track activity. “Here in Vermont, I'm not going to prove the overall survival benefit of weight loss,” says Dittrus. “Our population is too small. But we can look at some of those people who've lost weight and try to understand what happened. We can look for the biologically plausible mechanisms that might explain why women who are overweight are more likely to have their cancer come back.”

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The unanimous opinion of the leadership from the three cancer centers was that it exceeded everybody's expectations,” says Stein. “The Vermont Cancer Center is playing a catalytic role in bringing the region together, and even the initial successes, I think, are a real indication that this is going to be how we operate in future. In a contracting economy, it's the only effective way to provide optimal patient care and move science forward.”

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Above: Steven Ades, M.D. focuses his research on treatment of clots, and nausea/vomiting caused by radiation.

Opposite page: Kim Dittus, M.D., Ph.D., talks to an oncology rehabilitation patient.

With cardiologist Philip Ades, M.D. and Patricia O’Brien, M.D., Dittus has now established an oncology rehabilitation program that will allow cancer survivors access to an athletic trainer for aerobic and resistance training two days a week. While the patients are gaining the benefits of regular exercise (they’re encouraged to exercise on their own as well), Dittus is collecting data on physiologic functioning: strength, anxiety and depression; and two of the common lingering effects of cancer: fatigue and sleep disturbance.

“Oncology rehabilitation can serve as a platform for translational research,” says Dittus, explaining that one approved study will look at the etiology behind post-therapy fatigue and shortness of breath. “You’d like people to be exercising through therapy, as much as they can. It helps with fatigue, and people feel better and have a sense of control.” Her goal is to expand oncology rehab so it moves with the patient through each phase of treatment and beyond.

Karen Lounsbury, Ph.D., and Chris Francklyn, Ph.D., are an example of an intra-institutional collaboration. “One thing the VCC does a really good job with, is bringing people together and getting them to talk,” says Lounsbury. The two are looking at a potential connection between angiogenesis (the growth of blood vessels), metastasis (the proliferation of cancer cells) and the inhibition of an enzyme, threonyl-tRNA synthetase (TARS) by an antibiotic, BC194 (a derivative of the naturally occurring compound borrelidin).

Lounsbury’s specialty is vascular biology, so Francklyn, a biochemist, invited her to collaborate to determine whether BC194 influences gene expression in cancer cells. Lounsbury’s initial experiments highlighted a connection to vascular endothelial growth factor (VEGF), but an even greater surprise occurred when Lounsbury’s post-doctoral fellow Tamara Williams showed that the TARS protein itself has an unexpected function, which is to promote blood vessel development. Apparently, in a bit of moonlighting, the TARS protein was promoting the ability of the endothelial cells to grow and migrate, and BC194 blocked this function. Furthermore, in looking at stained tissue slices from ovarian and prostate cancer patients, Francklyn and Lounsbury were able to see that the protein was overexpressed in the tumor environment of both cancers.

In future work, Francklyn and Lounsbury will investigate in both human patients and animal models to determine whether the TARS protein can be used as a diagnostic, measurable in the bloodstream — not unlike the currently used PSA test. Inhibitors of TARS might be potential cancer therapeutics, though Francklyn admits that’s a ways off. One promising sign is the ability of borrelidin to inhibit tumor metastasis in a mouse model of melanoma. Discovering new anti-cancer lead compounds remains a strategic goal of the VCC.

“It’s the very question of patient quality of life that intrigues Steven Ades, M.D., whose work with Mary Cushman, M.D., and Steven Grunberg, M.D. centers on treatment of clots and nausea/vomiting caused by radiation. “While devising a complete cancer cure would be a huge breakthrough, many people think the more achievable goal is to make life with cancer livable, as it apparently is with HIV,” says Francklyn.

“WE CAN LOOK FOR THE BIOLOGICALLY PLAUSIBLE MECHANISMS THAT MIGHT EXPLAIN WHY WOMEN WHO ARE OVERWEIGHT ARE MORE LIKELY TO HAVE THEIR CANCER COME BACK.”

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“WE WANT TO IMPACT PATIENTS’ ABILITY TO LIVE AND THRIVE, NOT JUST EXIST.”
— Steven Ades, M.D., Associate Professor of Medicine

The conference goals are to educate attendees on lifestyle choices that will prevent cancer or its recurrence; there’s also an advocacy piece for high-quality breast health care in the region. In addition, the VCC collaborates with the Cancer Patient Support Program, which provides funds for patient transport, lodging, childcare, and other expenses that arise during treatment. Evening Song, a gala that has brought in more than one million dollars to date, helps fundraise for this program.

Outside the center proper, Stein and Verschraegen serve on the advisory board of Vermonters Taking Action Against Cancer, and the VCC collaborated with the American Cancer Society and a number of dermatologists to help Vermont become the second state to enact legislation banning tanning salons. The VCC also sponsors educational outreach programs, including one for students in kindergarten through high school that uses cancer as a mechanism for teaching science. Stein and Verschraegen are engaging the community to hear what Vermonters need most from the VCC. Along with Kim Luebbers, the VCC Administrative Director, they are expanding the capabilities of the VCC, as a destination center for cancer care and a resource for cancer research locally, regionally, and internationally.

When asked about meeting the translational expectations required by the NCI Verschraegen replied, “When I came here, I realized that all the elements are in place to translate discovery to clinical practice. We are bringing all the mechanisms that we can together so that infrastructure on which we rely — whether it’s in the lab or the clinical trial arena — is really simplified and unified.”

Referring to her co-director and herself, Verschraegen says, “Our goal is to succeed and success is not as. We’re focused on maximizing translation of discoveries into cancer prevention, early detection, treatment, and survivorship, and we’re also proud of the integration of the region. We want everyone to understand that it’s a greater good.”

MAKING CONNECTIONS
A key element of the Vermont Cancer Center (VCC) mission is the encouragement of collaborations and the development of effective processes to foster clinical and translational research avenues. One recent example of this was the recent free day-long Annual Clinical and Translational Science Research Symposium, titled “Exercise, Nutrition, and Cancer.”

Hosted at the Davis Auditorium in the Medical Education Center in Fletcher Allen’s Ambulatory Care Center on November 16, 2012, the symposium featured a special presentation — the J. Walter Juckett Distinguished Lecture — titled “Exercise Therapy for Cardiovascular Injury and Tumor Progression in Cancer,” which was delivered by Lee Jones, Ph.D., associate professor and scientific director of the Duke Center for Cancer Survivorship in the Department of Radiation Oncology within the Duke Cancer Institute.

Co-chaired by Susan Lakoski, M.D., UVM assistant professor of medicine and director of cardiovascular prevention, and Ken Dittus, M.D., Ph.D., assistant professor of medicine and oncologist, the symposium’s presentations focused on clinical and translational research at the VCC and other cancer research institutions with a particular emphasis on exercise, nutrition, and their overall effect on cancer risks and outcomes.

In addition to a welcome provided by VCC co-director and director of hematology/oncology Claire Verschraegen, M.D., UVM presenters at the symposium included: Michael Toff, Ph.D., associate professor of medicine; Jean Harvey-Birn, Ph.D., R.D., professor and chair of nutrition and food sciences and associate professor of medicine; Lakoski, and Dittus.

The Lake Champlain Cancer Research Organization has for many years provided support for the Juckett Lecture and the annual symposium.

The 2012 YEAR IN REVIEW article features a gallery of images from various VCC events. A full set of images is available online at vermontmedicine.org.

Clots are a significant concern to advanced cancer patients — roughly one-fifth to one-quarter of them will develop a venous thrombosis or pulmonary embolism during treatment. There are any number of potential causes: the thickening of the blood that’s associated with cancer, chemotherapeutic or other drugs, underlying cancers, the insertion of a catheter, or the fact that cancer patients, as a group are less active than the general population. Regardless, the result is a dangerous cycle, says Ades: “Cancer begets blood clots, and clots help cancer spread.”

The standard clot treatment, blood thinners, is not optimal since it tends to result in heavy bleeding. Statins, however, have been shown in the literature to lower the risk of clots without that side effect. So Ades and his colleagues are conducting a randomized phase II crossover study that includes one month each of rosvastatin, a placebo, and no treatment.

With Grunberg, Ades is examining a relatively new class of antithrombotic drugs that target a different receptor, neurokinin 1, in patients receiving radiation therapy to the abdomen. The hope is that they’ll be able to change the current standard of care and find a drug that can safely be administered over an extended period of time during radiotherapy. Though the study opened in collaboration with the Mayo Clinic and Wake Forest School of Medicine’s comprehensive cancer center, Dartmouth and U-Mass Memorial are now also coming on board.

“These are two examples of how collaboration is really important, both within the institution and outside it,” says Ades, adding, “It’s easy to get excited about being here, because I’m around people who are passionate about what they do.”

In addition to diagnosis and treatment, the VCC provides community awareness and support. Its most prominent community event is the annual Breast Cancer Conference, held every October for the last 15 years, which is free and open to both the public and healthcare professionals. The event’s goal is to educate attendees on lifestyle choices that will prevent cancer or its recurrence; there’s also an advocacy piece for high-quality breast health care in the region.