

Innovations

FALL/WINTER 2015

News + Highlights from

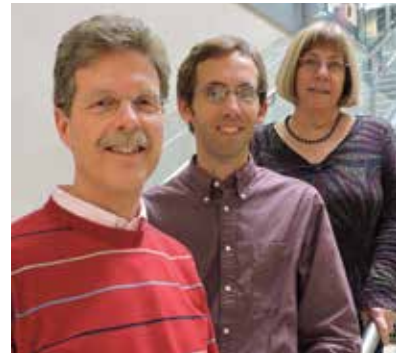
THE
University of Vermont
CANCER CENTER

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Getting Ahead of Breast Cancer: NCI Grant Funds UVM Research on Early-Stage Breast Cancer

Better technology and screening practices have led to the detection of more breast cancers in women—many of which fall into the broad category of early-stage cancer, including ductal carcinoma in situ (DCIS) and small invasive cancers confined to the breast. A question facing researchers now is why some of these early breast cancers remain idle while others progress. An interdisciplinary team of researchers at the University of Vermont (UVM) Cancer Center, with the support of a new, \$3.7 million federal grant from the National Cancer Institute (NCI), will be looking more closely for an answer to this question. By understanding how some cancers found through the screening process differ from cancers found in follow-up of symptoms, clues



From left: Donald Weaver, M.D., Brian Sprague, Ph.D., and Janet Stein, Ph.D.

may emerge about which screen-detected cancers may be most dangerous and which may likely remain idle.

Just as humans are influenced by their environments—we put on sweaters
continued on page 3

3-D Snapshot Determines Structure of DNA-Binding Protein Linked to Breast and Ovarian Cancers

Human bodies sustain thousands of attacks on DNA daily, however we have an army of DNA repair mechanisms designed to combat these assaults. Understanding the enzymes responsible for this repair process helps determine how and where cancer gets its foothold and flourishes, and helps to identify potential drug targets to inhibit cancer development.

University of Vermont Cancer Center structural biologist and X-ray crystallography expert **Sylvie Doublé, Ph.D.**, and postdoctoral fellow **Karl Zahn, Ph.D.**, recently determined the first crystal structures of an enzyme that

has entered the spotlight—human DNA polymerase theta or POLQ—as the only DNA polymerase overexpressed in certain breast and ovarian cancers. The researchers' findings were reported in a recent issue of the journal *Nature Structural & Molecular Biology*.

"This polymerase is known to serve a specialized role in repairing certain toxic double-strand breaks in the DNA, which can induce genomic instability if left unrepaired," shared Doublé. The visualization of the enzyme may provide key information for developing targeted approaches to certain breast and ovarian cancer development. ■

Advancing Cancer Research and Care The UVM Cancer Center

Since its founding in 1974, the University of Vermont (UVM) Cancer Center has been dedicated to advancing the prevention, detection, treatment, and survivorship of cancer. The physicians, scientists, caregivers and staff at the UVM Cancer Center are committed to providing state-of-the-art cancer diagnosis and treatment, delivering compassionate cancer care and support, providing education to patients and the community, and advancing innovative research from the laboratory to the patient. Through a unique partnership between the University of Vermont and the University of Vermont Medical Center, the UVM Cancer Center has built a team approach to science that brings patients the most advanced cancer care—right here in Vermont.

The UVM Cancer Center Leadership

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UVM Cancer Center
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Letter from the Directors

In the past six months researchers and clinicians at the UVM Cancer Center have made tremendous contributions to advancing cancer prevention, detection, treatment, and survivorship. From quality health improvements to disease prevention to building our understanding of the molecular mechanisms at work in cancer, their work is making a difference in the lives of cancer patients in Vermont and beyond.

Our UVM Cancer Center members are national leaders in improving the lives of cancer patients and their families. Just this year our collaborative teams of laboratory and behavioral scientists and physician investigators have made discoveries helping to inform national screening guidelines for mammography, answered important questions leading to better diagnostic care, demonstrated just how important exercise and diet are in preventing and surviving cancer, and uncovered new ways to prevent the spread of breast and prostate cancer.

We've also seen tremendous support and inspiration from our community. From children holding small fundraising events to larger community events, as well as support from individuals and local businesses, philanthropy has had a tremendous impact on our mission to reduce the burden of cancer in Vermont, northern New York and beyond.

We couldn't do all that we do here without the amazing faculty, staff, patients and supporters we consider part of our community. Enclosed are just a few highlights of their contributions.

Sincerely,

Gary Stein, Ph.D.
Director

Claire Verschraegen, M.D.
Deputy Director

News & Highlights

New Research Targets Prevention of Metastasis of Breast and Prostate Cancer

One concern for patients with breast and prostate cancer, especially in the case of the most aggressive forms of each, is the propensity of those tumor types to metastasize to bone. This complication makes treatment more difficult and often means a worse prognosis for a patient. New research, led by UVM Cancer Center researcher **Jane Lian, Ph.D.**, professor of biochemistry and Cancer Center research program director, is showing early indicators for finding a path toward a targeted therapy to prevent the spread of breast and prostate cancer to bone.

Small non-coding RNA, or miRNAs, are very small, unique molecules that play an important role in the regulation of cellular protein

levels in normal and tumor cells. In the world of cancer, miRNAs are being investigated in order to capitalize on their role in controlling tumor growth, spread, and even the start of cancer.

Lian's work shows a relationship between a particular protein associated with metastasis of breast tumors to bone, called RUNX2, and two specific miRNAs. This relationship provides a possible new target for controlling tumor cell growth in breast and preventing metastasis to other sites in the body. The work, featured recently in the journal *Cancer Research*, excites the UVM research team who will continue to investigate the therapeutic potential of the specific miRNAs in the prevention of breast and prostate cancer metastasis to bone.



Jane Lian, Ph.D.

In collaboration with **Chris Landry, Ph.D.**, UVM professor of chemistry, the team hopes to develop nanoparticle delivery mechanisms for the miRNAs—very small, yet effective, transportation methods to get the miRNAs to cancer sites to halt the progress of a cancer.

Lian shares, "It is early, but we've seen very promising results in small laboratory studies that we are headed in the right direction." Such research is part of a major shift in cancer research to individualized or precision medicine—developing targeted and effective treatment without unnecessary toxicity or side-effects for patients. ■

Getting Ahead of Breast Cancer *continued from page 1*

when it is cold, we sweat when it is hot—so too are cancerous lesions, or clusters of abnormal cells in our body that may progress into larger tumors. The tumor affects the body, but the body's microenvironment (the environment around cancer cells) also affects the tumor: it's a two way street. UVM Cancer Center researchers **Brian Sprague, Ph.D.**, assistant professor of surgery, **Janet Stein, Ph.D.**, professor of biochemistry and **Donald Weaver, M.D.**, professor of pathology and laboratory medicine, have joined forces to investigate this two-way communication between the tumor and its surroundings. The research team will be working to understand how the microenvironment of cancerous breast lesions impacts progression and tumor development.

Breast cancer is the most common cancer diagnosis among women and the majority of these cancers are detected by screening mammography. There is widespread concern that screening has led to substantial over-detection of early-stage breast cancer resulting in aggressive treatments for some breast cancers that would never have been life-threatening. This new research aims to identify just why some cancers progress and others don't—with the hope that women can safely be spared aggressive treatments, which carry their own risks and consequences.

The NCI grant recognizes and leverages strengths in interdisciplinary breast cancer research that exist at UVM, including a state-wide breast

cancer surveillance program, one of just six such programs nationally, as well as significant infrastructure and technology in place to tackle such a project. Other cancer centers nationally, including MD Anderson, Johns Hopkins, Stanford, Vanderbilt, UCLA, and Dartmouth, have been awarded sister grants through this collaborative NCI research program targeting similar objectives but in different tumor sites. Joining UVM in investigating the microenvironment of breast cancer is the University of California, San Francisco (UCSF).

The five-year study hopes to yield new information that will ultimately lead to better decision-making around screening and treatment of early breast cancers. ■

Research & Education

New Research Looks to Identify Risk for Blood Clots in Cancer Patients

Cancer and its treatments are well-recognized risk factors for venous thromboembolism (VTE), the third most common cardiovascular illness, which includes different forms of blood clots and is estimated to lead to nearly 300,000 deaths annually. Some blood clots are preventable, however treatment includes blood thinners which can increase the risk for bleeding. New findings from a study led by UVM Cancer Center researchers may help doctors better identify those cancer patients who are at increased risk of VTE.

For the first time, a UVM research team led by physician-scientists and UVM associate professors of medicine **Chris Holmes, M.D., Ph.D.**, and **Steven Ades, M.D.**, has linked the genetics of a tumor to the development of VTE in a patient with cancer. Through a large population study the research team uncovered a genetic link which could help clinicians identify cancer patients at a greater risk for blood clotting—allowing for an individualized approach to treatment which would prevent complications for both at-risk patients and those who may not be.

“No one has ever shown that the genetic mutations found in the tumor could actually link to a process such as forming blood clots in the patient’s body. We thought that tumor genetics would only tell us about risk of cancer spread and help us find cancer-specific therapies,” shared Holmes. She adds that patients with cancer have an overall risk of a blood clot of about twelve percent after starting

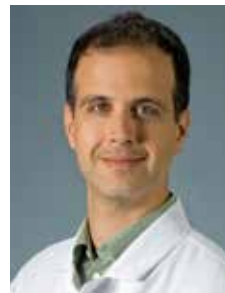
chemotherapy—encompassing a range from one percent to thirty percent, a huge range. For patients who develop a blood clot, they may suffer pain, swelling or shortness of breath during a critical time in their cancer treatment and have an increased one-month risk of dying. There is an identified need for better tools to predict who is at high risk and who may not need added intervention. Current risk models aren’t comprehensive, and this study, if validated in large trials, will allow for a personalized approach to treating individual risk for blood clots in cancer patients.

“Anything we can do to refine the decision-making means a better quality of life for patients with advanced cancer, and, importantly, lives saved,” said Holmes.

The UVM research team’s findings were published recently in the *Journal of Hemostasis and Thrombosis*. ■



Chris Holmes, M.D., Ph.D.



Steven Ades, M.D.

Skin Cancer Fast Facts

It is more common among people with fair skin, however, skin cancer CAN affect anyone. When skin cancers are found early, they are easily treated and usually curable. Here are some tips, from the National Cancer Institute, on finding skin cancers early:

- Talk to your health care provider if you notice changes on your skin that do not go away within one month.

PREVENTION TIP

Remember—do not use tanning beds, tanning booths or sunlamps—all emit harmful UV radiation. In fact, in Vermont and numerous other states, there are new laws banning tanning bed use for minors under age 18.

- Check the skin on all surfaces of your body, even in your mouth and on your scalp.
- Watch for a new mole or other new growth on your skin.
- Check for changes in the appearance of an old growth on the skin or scar.
- Watch for a patch of skin that is a different color and becomes darker or changes color.
- Watch for a sore that does not heal—it may bleed or form a crust.
- Check your nails for a dark band, Check with your doctor if you see changes, such as if the dark band begins to spread.

For more great information about skin cancer, including prevention tips, go to: www.cancer.gov/types/skin/anyone-can-get-skin-cancer.



Men's Health and Cancer Conference

Would men show up for a half-day to learn about and discuss their health? UVM Cancer Center physicians were certain they would, and so launched the inaugural Men's Health and Cancer Conference held on June 26, 2015. The half-day event, which drew 80 attendees, provided education around the prevention, detection, treatment and survivorship of common men's cancers and covered a range of related health topics.

Participants attended sessions on prostate cancer, colorectal cancer, lung cancer, nutrition, exercise and more. Small-group experiences allowed participants and experts the chance to engage in conversation about important health topics for men.

John Brumsted, M.D., Chief Executive Officer of the UVM Medical Center and Health Network, welcomed the audience and stressed the commitment that UVM Cancer Center physicians, nurses and staff have to education here in our community. He shared that it was not enough to just care for patients once they become ill. “We have a responsibility to help prevent illness and disease,” shared Brumsted.

The first annual event was hosted by the UVM Cancer Center and the UVM Division of Urology and made possible by generous support from the annual *Brovember* fundraising campaign for the UVM Cancer Center and philanthropic support from Leunig's Bistro on Church Street in Burlington. ■

Novel Approaches to Colorectal Cancer Treatment and Metastatic Bone Disease

The UVM Cancer Center has announced the first funded projects through its American Cancer Society (ACS) Institutional Research Grant (IRG). The ACS IRG, awarded to the UVM Cancer Center earlier this year, is designed to stimulate novel, interdisciplinary and translational cancer research at the UVM Cancer Center. Such research aims to bring scientific discovery from the laboratory to the benefit of patients in a collaborative approach.

UVM Cancer Center members **Jason Stumpff, Ph.D.**, UVM assistant professor of molecular physiology and biophysics, and **Christopher Anker, M.D.**, UVM assistant professor of radiology and a radiation oncologist at the UVM Medical Center, were competitively awarded funding from the IRG to pursue research on a new therapeutic target for colorectal cancer—one that may inhibit cancer cell growth.

In addition, the transdisciplinary team of **Jennifer Lisle, M.D.**, UVM associate professor of orthopedics, and **Jonathon Gordon, Ph.D.**, UVM assistant professor of biochemistry, has been selected as recipients of IRG funding for their proposed project, *Inhibition of Patient-Specific Marrow Stromal Cells That Mediate Tumor Growth and Metastatic Bone Disease*. The project's long-term goal is to identify more targeted treatment for breast and prostate cancer that metastasizes to bone.

Both projects aim to bring findings directly to patients here in Vermont to improve cancer outcomes and care locally and around the world. ■



Christopher Anker, M.D.



Jonathon Gordon, Ph.D.



Jennifer Lisle, M.D.



Jason Stumpff, Ph.D.

SAVE THE DATES!

For a full list of events visit www.VermontCancer.org

Men's Health & Cancer
2016 CONFERENCE

Friday, June 24, 2016

Women's Health & Cancer
CONFERENCE
2016

Friday, October 7, 2016

New Blood Clot Prevention Program

The hematology/oncology clinic at the University of Vermont Cancer Center has announced a new program aimed at preventing venous thromboembolism (VTE) without increasing bleed risk for patients with cancer. VTE is a prevalent cardiovascular disease which includes various types of blood clots and poses a particular risk for those who are undergoing certain cancer treatments. New research at the UVM Cancer Center has shown that genetic markers in tumors may indicate a greater risk for blood clots in some patients.

The new clinical intervention program, called VTE-PACC (VTE Prevention in the Ambulatory Cancer Clinic) launched in collaboration with the Jeffords Institute for Quality at the UVM Medical Center, officially started on October 1, 2015. The program will assess risk for clotting and bleeding for all patients beginning chemotherapy in the clinic. Patients found to be at high risk will be referred to the Thrombosis and Hemostasis Program at the UVM Cancer Center for follow-up.

This quality-health improvement effort will be studied and measured for impact on cancer deaths, quality of life, treatment processes and other cancer-related impacts by the VTE PACC team, which includes providers, nurses and researchers. The program also provides opportunities for potential research projects, including one already underway by this year's Lake Champlain Cancer Research Organization (LCCRO) fellow, **Dan Douce, M.D.**, who has looked at occurrence of VTE in patients here in Vermont to help assess risk and to set goals in reducing the number of patients who experience blood clots. ■

Skida Delivers Hats and Comfort to Patients

Patients and staff in the UVM Cancer Center's hematology and oncology clinic received a visit this summer from local business owner Corinne Prevot, who launched the headwear and accessory business Skida in 2008 while a high-school ski racer at Burke Mountain Academy. She continued to grow the business as a student at Middlebury College. Prevot, recognized by *Forbes* for her entrepreneurial achievement, has also proven herself to be a dedicated member of the Vermont community and has made giving back state-wide a priority.

Inspired by a friend whose wife was going through cancer treatment and had purchased a hat for her, Prevot applied her social outreach vision to starting the *Skida Plus One* program. The program allows customers to designate a local cancer clinic to receive one free hat, to be provided to a cancer patient, when making a purchase. Skida has generously donated many hats to cancer patients at the UVM Cancer Center and has donated over 500 hats to 10 cancer clinics across the country. Patients love the hats, which are particularly soft and comfortable during treatment that can leave skin highly sensitive.

Prevot shared, "I really believe giving back has to be a part of our business model." She also attended the 18th Annual Women's Health and Breast Cancer Conference in October 2015, where for every hat sold during the day, a hat was donated back to a cancer patient.

To learn more about the *Skida Plus One* program, please visit: www.shopskida.com/pages/skida-plus-one ■



Corinne Prevot, owner of Skida, third from right, with the UVM hematology/oncology team.

UVM Students Color Campus for Cancer Research

UVM students were busy this year—in addition to studies, athletics, and maybe some fun—they were fueling major efforts on the UVM campus to build awareness and raise funds for cancer research and education programs happening at the UVM Cancer Center. This past National Philanthropy day, the student government association at UVM asked fellow students to vote for a campus organization they felt had the biggest impact on their community. The winners were to be recipients of the 2015 senior class gift and the beneficiary of funds raised through the first annual *Catamount Color Run*.

In the end, there were five campus groups chosen by students, including the



ABOVE: UVM Men's hockey team, at *Rally Against Cancer*. TOP RIGHT: Runners at the *Catamount Color Run*.



"My brother was diagnosed with cancer at age 13—I am so glad I got to see what this amazing organization does for our community, especially one that we have right here on campus."

TAYLOR SULLIVAN
UVM student in the
Grossman School of Business

University of Vermont Cancer Center. At the May running event students could donate to one of five campus groups. Participants gave 389 gifts totaling \$3,813 to cancer research and education at the UVM Cancer Center!

At the same time students were running, more students and community members were cheering across campus at a UVM lacrosse game, one of eight UVM Athletics *Rally Against Cancer* events. Throughout the year, UVM athletes donned pink uniforms, socks and other accessories and rallied support for breast cancer research at the UVM

Cancer Center. This annual effort, hosted by UVM Athletics and sponsored by local business, Otter Creek Awnings and Vermont Custom Closets, engages the dedicated athletic community—students, athletes, coaches, and of course, fans, to build support for cutting-edge research in cancer prevention, detection, treatment and survivorship happening right here at UVM.

To learn more about the 2015-16 *Rally Against Cancer* efforts, including game dates/times, see the UVM Cancer Center event calendar at www.vermontcancer.org. ■

New UVM Cancer Center Community Advisory Board Announced

The UVM Cancer Center has a new arsenal of advocates who will help build awareness and support for the Center and the patients it serves. A group of 13 volunteers from the Chittenden County area have dedicated themselves to serving as ambassadors, advocates and fundraisers for the inaugural UVM Cancer Center Community Advisory Board.

Members of the board include: **Ginny Coolidge** of Shelburne, **Philip Daniels** of Williston, **John Evans** of South Burlington, **Patricia Fontaine** of Shelburne, **Sonja Fuller** of Burlington, **Kim Ireland** of Shelburne, **Anne Lezak** of Burlington, **Jeff Mullen** of Richmond, **Ernie Pomerleau** of Burlington, **Shelley Spillane** of Shelburne, **Lori Tarrant** of Colchester, **Tom Torti** of Essex, and **Todd Warren** of Essex.

Board members, at their first meeting, were enthusiastic about the ability to have an impact on the fight against cancer while supporting the greater Vermont community. Ginny Coolidge shared, "I want to see cancer be a thing of the past. Until it is, I want to do all I can to help cancer patients and their families."

"We can't do what we do without the support of our community," said UVM Cancer Center Director **Gary Stein, Ph.D.**, regarding the new board. "We are grateful to have the power and commitment of such a dynamic group join us in advancing cancer care and research here in Vermont."

To learn more about the UVM Cancer Center Community Advisory Board, visit www.vermontcancer.org. ■

The Courtyard at Given
4th Floor North
89 Beaumont Avenue
Burlington, VT 05405

Clinical Trials at the UVM Cancer Center

Clinical trials are critically important in establishing better cancer treatments and therapies, however, they also look to improve quality of life for cancer patients.

At the UVM Cancer Center there is a clinical trial underway called the BEAT (Behavioral weight loss and Exercise After Therapy) study. It provides breast cancer survivors who participate with an evidence-based weight loss and exercise intervention. Research has shown that exercise and a healthy lifestyle can reduce the risk of cancer recurrence. The primary goal of the study is to learn how to tailor better interventions for future breast cancer survivors here in Vermont and beyond.

BEAT study participant Shona Sladyk shares a bit about her experience in the trial:

“Never having considered myself to be overweight, I was taken aback when my doctor suggested I was eligible to take part in the BEAT study which has a high BMI as a prerequisite for participation as well as being a breast cancer survivor. I was hesitant to commit to a year of daily journaling of my food intake and regular exercise under the watchful eye of a nutritionist and physiotherapist, but after some thought I realized what a great opportunity this was for me and perhaps worth pursuing. I was right. One year later and 30 lbs. lighter, at the age of 55 I have never been in better shape, physically or mentally. The support I received both from the nutritionist and the group of fellow breast cancer survivors who met weekly was invaluable and I developed a regular exercise habit which continues to this day. As well as helping to prevent a recurrence of breast cancer, my cholesterol and BP stats



Shona Sladyk

were significantly reduced. I would highly recommend any cancer survivor to take part in a clinical study such as this given the opportunity.”

For more information about the BEAT study, or other trials at the UVM Cancer Center, please contact Karen Wilson, Clinical Research Supervisor, at (802) 656-4101 or Karen.M.Wilson@uvm.edu. ■