

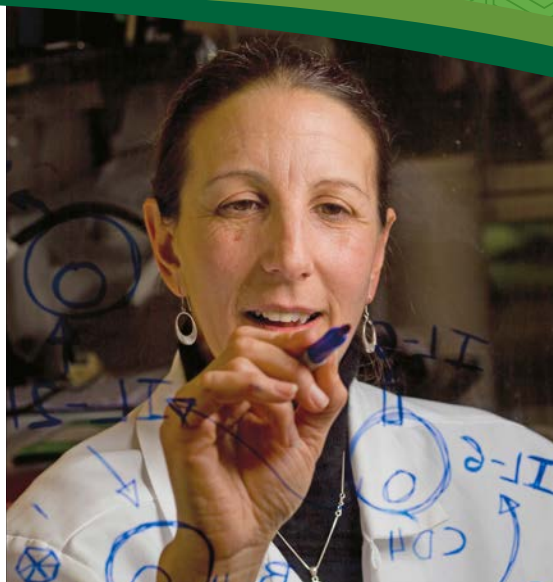
Innovations

NEWS & HIGHLIGHTS WINTER/SPRING 2019

Overcoming Chemoresistance

About 40,000 women die each year from breast cancer in the United States due to a resistance to chemotherapy drugs known as *chemoresistance*. Chemotherapy is still one of the most effective and widely used means of treating breast cancer. More than one third of breast cancer patients are dependent on chemotherapy as the only available treatment, including those who are diagnosed with metastatic cancer: “We recognized a clear, unmet need to challenge chemoresistance in breast cancer patients,” shared UVM Cancer Center researcher and UVM Larner College of Medicine Professor of Immunobiology Medicine, **Mercedes Rincón, PhD**. In order to address the significant challenge of chemoresistance in breast cancer patients, Rincón and her team began investigating a cellular mechanism that impacts the way chemotherapy reaches and kills cancer cells.

Recently, Rincón and her team earned a highly competitive translational research grant from the National Cancer Institute. This specific category of federal funding is designated for innovative cancer research that promises to directly impact patient care, bringing discovery from the lab to patients. Rincón will use the funding to pursue novel research that looks to inform a new therapy for breast cancer that aims to interfere with cancer cells’ resistance to chemotherapy. She explains that pumps found in some cancer cells work to expel the chemotherapy drug, protecting the cancer cell from death. In her preliminary research she observed these pumps, called ABC transporters, use large quantities of energy, in the form of Adenosine triphosphate, or ATP, produced by mitochondria, the “engine” of cells. Rincón’s team proposed that limiting the energy produced by mitochondria would hinder the pump mechanism, possibly allowing the chemotherapy



Mercedes Rincón, PhD

drug to reach the cancer cell more effectively.

The research team observed that some cancer cells have lost a molecule, called MCJ, that serves as a brake for mitochondrial production of ATP. As a result of this finding, they observed that the mitochondria of those MCJ-deficient cancer cells produces more energy, maintaining more active drug pumps that allow a cell to resist chemotherapy more effectively. Rincón and her team have developed new compounds that mimic MCJ and restore MCJ function in those cells that have lost it. The MCJ mimicking compounds act as alternative brakes for the mitochondria, reducing the ATP, or energy, available to the cellular pumps, thus, allowing chemotherapy drugs to more effectively act on the cancer cell.

Rincón’s research continues, supported by the exciting finding that these MCJ mimetics could be used as therapeutics in breast cancer patients to overcome chemoresistance to standard chemotherapeutic drugs. ■

THE
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*Produced by Creative Services
 at The University of Vermont
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Annual UVM Cancer Center retreat

About the University of Vermont Cancer Center

The University of Vermont Cancer Center is a national leader in cancer research. Our members work collaboratively with experts around the world to improve the lives of cancer patients here in Vermont and beyond. The UVM

Cancer Center brings together more than 200 scientists, clinician-researchers, nurses, staff and community members dedicated to advancing knowledge to reduce the burden of cancer for individuals, families and communities. Research partnerships across the University of Vermont's many academic departments as well as nearly all clinical departments at the UVM Medical Center are expediting discovery and bringing advanced care to patients.

**YOU made a
 DIFFERENCE**



2018



**WOMEN'S
 HEALTH
 & CANCER
 CONFERENCE**

The 2018 Women's Health and Cancer Conference, hosted by the UVM Cancer Center, brought nearly 900 cancer survivors, health care professionals, caregivers, cancer researchers, and members of the general public together for an impactful day of learning. Thank you to all the supporters who help keep this annual event free and open to the public.



ELEANOR B. DANIELS
 FUND

THE VICTORIA BUFFUM FUND at the UVM CANCER CENTER



SEVEN DAYS
 sevendaysvt.com



SAVE THE DATE: 22nd Annual Women's Health and Cancer Conference, Friday, October 4, 2019

Ahern Receives Grant to Study Phthalates and Childhood Cancer Risk

International research collaborations led by University of Vermont Cancer Center member **Thomas Ahern, PhD, MPH**, Assistant Professor of Surgery at the UVM Larner College of Medicine, have been recognized with a nationally competitive grant from the St. Baldrick's Foundation. The award will support investigation of phthalate exposure and childhood cancers. St. Baldrick's, the largest private funder of childhood cancer research, recently announced 76 grants totaling more than \$19.1 million to support physician-scientists studying innovative treatment options in the pediatric cancer space.

Ahern's ongoing research in the area of phthalates, a common category of chemicals added to many everyday products and some common medications, led his team to question whether phthalate exposure in utero or during childhood increases the risk of childhood cancer. The research team, which includes partners from Aarhus University in Denmark, has successfully examined Danish pharmacy records and cancer incidence data to study possible health effects of phthalates. This strategic approach capitalizes on the intensive exposure to phthalates posed by some medications to those who take them regularly. The results could indicate whether



Thomas Ahern, PhD, MPH

prolonged exposure impacts cancer risk, and could therefore be used to inform important policy to protect consumers, especially children, from phthalate exposure and prevent future cancers from occurring.

Ahern and his team are one of 76 research projects around the globe receiving funding this year from St. Baldrick's. "At St. Baldrick's, we focus on funding research that has the best potential of giving kids the healthy childhoods they deserve," said Kathleen Ruddy, CEO of the St. Baldrick's Foundation. "I'm proud to say that we have now funded more than a quarter billion dollars since 2005 to support lifesaving childhood cancer research." ■

Mesothelioma Research Uncovers New Clues to the Disease's Development

Asbestos exposure is widely known to cause human disease, including the deadly cancer mesothelioma—although researchers aren't sure why. While asbestos is inhaled into the lungs, mesothelioma develops in physically remote mesothelial cells throughout the body. No successful methods exist for early detection of exposure to asbestos. New research published by UVM Cancer Center researcher **Arti Shukla, PhD**, in *The FASEB Journal*, may have unlocked the first piece of this puzzle.

"Our findings suggest that cells in one region of the body are capable of sending messages to



Arti Shukla, PhD

cells in a distant location, and can cause significant genetic changes," said Shukla, Associate Professor of Pathology and Laboratory Medicine at the University of Vermont Larner College of Medicine. "This

communication from injured or diseased cells to healthy cells has the potential to initiate changes that might lead to cancer or other diseases."

The team's discovery has implications for how asbestos exposure may cause cancer by sending exosomes, or fluid-filled, cell-derived cavities,

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MESOTHELIOMA CONTINUED FROM PAGE 3

that detrimentally alter the genetics of cells. The study also points to the remarkable potential of these exosomes and the proteins they contain to act as biomarkers, indicating the development or progression of asbestos-related disease.

“These intriguing findings go a good ways toward explaining the conundrum of how a pulmonary irritant triggers distant effects,” said Thoru Pederson, PhD, editor-in-chief of *The FASEB Journal*. “They also add to the burgeoning array of studies that link exosome-based communication to pathogenic events.”

This research was supported financially by the U.S. Department of Defense and the National Institute of Environmental Health Sciences, at the National Institutes of Health. ■

“OUR FINDINGS SUGGEST THAT CELLS IN ONE REGION OF THE BODY ARE CAPABLE OF SENDING MESSAGES TO CELLS IN A DISTANT LOCATION, AND CAN CAUSE SIGNIFICANT GENETIC CHANGES.” —ARTI SHUKLA, PhD

(This article was adapted from a press release produced by Todd Bentsen, Director of Communications, FASEB.)

Clinical Trials Q&A with Dr. Alissa Thomas

Dr. Alissa Thomas is a neuro-oncologist at The University of Vermont Cancer Center and UVM Assistant Professor of Neurology who specializes in the treatment of brain tumors, CNS lymphoma, and neurologic complications of cancer.



Alissa Thomas, MD

She works with a team of physicians from neurosurgery, radiation oncology, radiology, and pathology, as well as specialists in nutrition, social work, palliative care, clinical research, physical therapy, occupational therapy, child life, speech therapy, and nursing to provide comprehensive cancer care for patients with brain tumors.

As part of her commitment to provide the best care for patients, Dr. Thomas is actively involved in clinical trials. Her research focuses on neuro-oncology, particularly vaccine therapy and immunotherapy for gliomas.

Q: As a physician who treats cancer patients, can you share the impact clinical trials have for patients here in our region?

AT: Clinical trials are the greatest tool we have to advance the way we treat cancer. For patients who have cancer, participation in a clinical

trial may give access to new medications or treatments that are otherwise not available. Clinical trials are one of the sources of hope for better treatments for cancer.

Q: What is one major misconception people might have about clinical trials?

AT: I just came from a national meeting about clinical trial design and cancer research and the biggest message was that clinical trials are patient-centric. I think sometimes people see clinical trials as just research for research's sake. In our current health care system there are many challenges, but I think that the physicians, researchers, and others involved in clinical trials truly have the patient at heart and a genuine hope that we can improve patients' outcomes.

Q: Can you share an example of a current trial you are involved with at the UVM Cancer Center?

AT: At the UVM Cancer Center we have several different kinds of clinical trials. We have a number of clinical trials that are testing new drugs to try to treat cancer, and many of these studies are national clinical trials that we participate in as one of many sites across the country. We also have a large number of clinical trials that are designed and developed by clinical researchers at UVM and many of these studies have a goal of improving quality of life through better management of symptoms and side effects. ■



NORTHERN NEW ENGLAND
CLINICAL & TRANSLATIONAL
RESEARCH NETWORK

Four members of the UVM Cancer Center have been awarded grants from the Northern New England Clinical & Translational Research Network (NNE-CTR Net), a partnership of the University of Vermont and Maine Medical Research Institute funded by a \$20 million National Institutes of Health grant to advance research that addresses the unique health needs of northern New England—including cancer.



Jessica Heath, MD, UVM Assistant Professor of Pediatrics has been funded for her work which looks to inform the development of improved treatments for certain childhood leukemias

that are more easily administered to pediatric patients. Leukemia patients who live in rural locations, such as northern New England, may have particular difficulty completing intensive chemotherapy regimens that require very frequent travel to and from the clinic. It would be especially beneficial to these populations to further the development of effective oral medications, or intravenous medicines that can be given less frequently. Dr. Heath's proposal will prioritize the study of such medicines in leukemia.



Robert Gramling, MD, the UVM Holly and Bob Miller Chair of Palliative Medicine, is joined by collaborators at Maine Medical Research Institute, Alexa Craig, MD and Paul Han, MD, MA,

MPH for their project, "Northern New England Palliative Care Teleconsult Research Laboratory." The proposed project will conduct innovative

research to expand access to palliative care for underserved rural communities in Vermont and Maine using telehealth technology. The project will focus on patients with advanced-stage cancer and heart failure, and on optimizing telemedicine-based physician/patient communication of complex information.

Janet Stein, PhD, UVM Cancer Center Associate Director for Basic and Translational Science, and UVM Professor of Biochemistry, and

Nicholas Farina, PhD, postdoctoral student in biochemistry, have been funded for their research, "Discovering the Potential of tsRNA as Breast Cancer Biomarkers and Therapeutic Targets." The project looks to address distance and travel as a challenge to cancer screening by investigating the development of a blood-based test for breast cancer that can be performed by physicians in rural areas. The test may also provide a way to monitor response to various treatments without the patients traveling to a cancer treatment center, often a long distance from their homes. Further, a simple blood draw is far less stressful and costly than some other screening options. ■



RESEARCH SYMPOSIUM



UVM Cancer Center members gather with invited guests; pictured: Alison Landrey, MD; Gary Stein, PhD; Brian Sprague, PhD; Marie Wood, MD; Electra Paskett, PhD, The Ohio State Comprehensive Cancer Center; Tracy Onega, PhD, Norris Cotton Cancer Center; Chip Cole, PhD; Jean Harvey, PhD, RD; and Christie Befort, PhD, University of Kansas Cancer Center.

The UVM Cancer Center welcomed national experts to its annual Clinical and Translational Research Symposium. The 2018 symposium focus, "Cancer Control in a Rural Environment," addressed the unique challenges faced by Vermonters and other rural communities at all stages of the cancer spectrum, from screening and prevention to treatment and survivorship. Participants tackled topics including tobacco use, prostate cancer screening, and lifestyle intervention research happening at UVM, as well as case studies from Appalachia, the Midwest, and the Northeast on cancer care in rural populations.

AWARDS

The UVM Larner College of Medicine hosted its second annual Dean's Celebration of Excellence in Research Awards event this fall, a two-day event to highlight research being conducted by junior faculty, senior faculty, postdoctoral trainees, and graduate students at the University and the UVM Larner College of Medicine. Of the 15 awards given, nine were recognized contributions of UVM Cancer Center members as researchers and mentors across the following categories:

FACULTY AWARDS

Rising Star New Investigator:

Thomas Ahern, PhD, Assistant Professor of Surgery

Mid-Career Investigator:

Brian Sprague, PhD, Associate Professor of Surgery

Research Laureate:

Jason Bates, PhD, Professor of Medicine

UVM Health Network Medical Group Junior Researcher of the Year:

Christopher Anker, MD, Associate Professor of Radiation Oncology

STUDENT AWARDS

Junior Graduate Student:

Alex Thompson for "Mutations in the Kinesin Motor Protein KIF22 Cause Defects in Skeletal Development." Thompson's mentor is UVM Cancer Center member and Assistant Professor of Molecular Physiology and Biophysics **Jason Stumpff, PhD**.

Senior Graduate Student:

Christopher Dustin for "DUOX1-dependent IL-33 secretion from the airway epithelium involves positive feedback signaling through activation of IL-33R/ST2." Dustin's mentor is UVM Cancer Center member and Professor of Pathology & Laboratory Medicine **Albert Van der Vliet, PhD**.

Postdoctoral Fellow:

Kirsten Tracy, PhD for "Mitotically associated long non-coding RNA MANCR affects genomic stability in breast cancer." Tracy's mentor is UVM Cancer Center research program leader and Professor of Biochemistry **Jane Lian, PhD**.

Trainee Award for Outstanding Research Publication:

Jamie Abbott for "Substrate interaction defects in histidyl-tRNA synthetase linked to dominant axonal peripheral neuropathy." Abbott's mentor is UVM Cancer Center member and Professor of Biochemistry **Christopher Francklyn, PhD**. ■

Michael Kenney, RN, Receives "DAISY" Award from UVM Medical Center

This honor recognizes excellence in nursing care based on patient nominations.

Michael Kenney, RN

of Richmond, Vermont, a nurse working at the UVM Medical Center and UVM Cancer

Center, has received a "DAISY" Award, which recognizes nurses

who provide care to patients and their families with great

clinical skill and extraordinary compassion. The patient who nominated Kenney for the award had just started chemotherapy and was feeling overwhelmed, according to the nomination letter.

"I am used to being the caretaker in the world, and it's hard to have roles reversed, but Michael made me feel safe and like I was in good hands," the patient wrote.

Good nursing requires not only technical skills but compassion—a combination of the head and the heart, Kenney says. Whenever he can, he tries to drop-in and connect with patients. "I feel it really improves care when we can have that time to sit and explain," he says.

The DAISY Award is a nationwide program that started in 1999 to honor nurses at the Seattle Cancer Care Alliance who cared for a young father named Patrick Barnes. DAISY stands for diseases attacking the immune system, which was the cause of Barnes' death. Today, more than 3,300 healthcare facilities and nursing schools in all 50 states and 18 other countries honor nurses with the DAISY Award.

Patients can nominate a nurse any time by visiting www.uvmhealth.org/medcenterdaisy or sending an email to DaisyAward@UVMhealth.org. ■



Michael Kenney, RN, with Kate Fitzpatrick, RN, Chief Nursing Officer

Buffum Fund Expands Support

The annual Women’s Health and Cancer Conference recently received an exciting investment in its future from partners with a shared vision. The goal of the free, all-day conference is to empower the community around cancer prevention, detection, treatment and survivorship.

Tom and Melissa Gauntlett of Shelburne, Vermont, recently made a three-year commitment as Presenting Supporters for the event in the name of **The Victoria Buffum Fund**. The conference, which hosts nearly 1,000 individuals and more than 80 interactive sessions, relies on philanthropy to ensure that access for all remains free.



Tom and Melissa Gauntlett with Dean Rick Page, MD

The Victoria Buffum Fund at the UVM Cancer Center funds initiatives that support patients, families, and caregivers as they navigate cancer treatment. “Vicki” Buffum touched the lives of many during her own cancer journey, and established the Buffum Fund in 2002. Tom Gauntlett, Vicki’s brother, is excited about the conference’s alignment with his sister’s vision for the fund.

“We have a tremendous responsibility to provide support and education to lessen the burden of cancer for those in our region,” shared Gary Stein, PhD, Director of the UVM Cancer Center. “We are incredibly grateful to the Gauntletts and The Victoria Buffum Fund for helping us to advance this goal.” ■



Service to Our Cancer Community

The community impact of two local businesses, **Leunig’s Bistro & Café** and **Farrell Distributing**, extends far beyond excellent service. The UVM Cancer Center, and the patients and families it serves, have been the grateful beneficiaries of decades-long fundraising efforts by these businesses whose leaders, employees, and patrons consistently strive to give back to their communities.

Recognizing many personal and community ties to cancer, the two organizations initiated fundraising efforts over 17 years ago for breast cancer research and patient care at the UVM Cancer Center. In total, the two organizations and their many partners, through wine and beverage sales and successful events, such as *Wine, Wellness and Song*, have raised nearly \$500,000 for ongoing cancer patient support and research initiatives.

These efforts have supported cancer prevention and screening programs and have advanced targeted breast cancer research projects. The UVM Cancer Center recognizes the ongoing support of these two distinguished community icons and the many businesses and individuals who have joined them in supporting their local cancer community. ■

UVM Athletics is once again “Rallying Against Cancer,” raising awareness and funds for the UVM Cancer Center at select events. This year, the teams are switching from a focus on “pink” to the use of lavender as a way to be more inclusive of all cancers. Last year, donations to the UVM Cancer Center totaled \$11,000 thanks to fan pledges and the efforts of sponsor Vermont Custom Closets.



YOUR SUPPORT MATTERS!

Pictured (L to R): Todd and Beth Warren, owners of Vermont Custom Closets and sponsors of the UVM Athletics Rally Against Cancer program; Gary Stein, PhD, Director of the UVM Cancer Center; Rally Catamount (UVM Mascot); Marie Wood, MD, UVM Cancer Center oncologist and Associate Director for Cancer Control and Population Health Sciences; and Jeff Shulman, Director of UVM Athletics

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Clinical Trial News

The American Society for Radiation Oncology (ASTRO) is the world's largest radiation oncology society, with more than 10,000 members, including radiation oncologists at the UVM Cancer Center. Below are two exciting clinical trial updates, recently presented at ASTRO's 60th Annual Meeting. We are proud to say that the UVM Cancer Center and our patients participated in both of these important projects.

Combined therapy including pelvic lymph node radiation provides significant benefit for prostate cancer patients

The first report of a large international clinical trial shows that, for men who show signs of prostate cancer after surgical removal of their prostates, extending radiation therapy to the pelvic lymph nodes combined with adding short-term hormone therapy to standard treatment can extend the amount of time before their cancer spreads. The findings were so encouraging—exceeding rigorous threshold criteria—that the results were released by the research team ahead of schedule. To read the full report, visit astro.org.

Did you know? Clinical trials provide advanced treatment options for patients through new approaches to surgery, chemotherapy, and radiation, but also by looking to improve quality of life, cancer prevention, and survivorship outcomes.

To learn more about clinical trials or to see a full listing of open clinical trials at the UVM Cancer Center, please visit vermontcancer.org or call us at **(802) 656-4414**.

Radiation therapy cuts low risk of recurrence by nearly three-fourths for patients with “good risk” breast cancer

A subset of patients with low-risk breast cancer is highly unlikely to see cancer return following breast conservation surgery but can lower that risk even further with radiation therapy, finds a new long-term clinical trial report. These 12-year follow-up data are the only prospective, randomized trial to compare recurrence outcomes after treatment for low-risk ductal carcinoma in situ (DCIS). To read the full report, visit astro.org.



Members of the UVM Cancer Center Clinical Trials Office