



Under the direction of biomedical engineer Richard Price (center), graduate students Andrew Thin, Alex Matthew, and Natasha Sheybani (l to r), are developing critical technology for a groundbreaking clinical trial.

Tackling Cancer Through Team Science

Breast Cancer Clinical Trial is First of Its Kind in the World

For patients suffering from metastatic breast cancer, where the disease has spread throughout the body, the survival rate is only 22%. These women and men face ongoing treatment for the rest of their lives, often with harsh side effects. Although treatable, there is no cure for metastatic disease.

The University of Virginia Health System is working to change that, and has launched a clinical trial that uses groundbreaking focused ultrasound technology to target metastatic breast cancer and make tumors responsive to immunotherapy—without surgery. The study is the first in the world to combine focused ultrasound and immunotherapy to treat breast cancer in humans. If successful, this clinical trial will provide new hope for patients diagnosed with this late stage of breast cancer.

While immunotherapy has proven effective at treating some cancers, such as melanoma, breast cancer is typically considered immunologically silent. As breast cancer grows, it produces certain proteins and antigens that allow it to evade recognition by the immune system. The breast cancer cells are not recognized as invasive, so the immune system doesn't attack them.

“Breast cancer cells can ride under the radar of the body's immune system so that it is tolerated and allowed to grow,” explains the study's co-investigator David Brenin, MD, chief of breast cancer surgery at UVA and co-director of the UVA Breast Care Program.

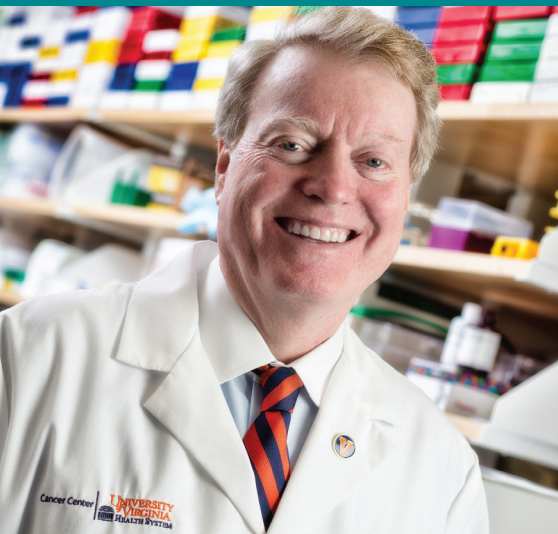
Each patient in the trial will undergo focused ultrasound, a non-invasive procedure that directs multiple soundwaves to a single point

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INVESTING IN

Philanthropy in Action at UVA Cancer Center

THE LEADERSHIP CORNER



For the UVA Cancer Center, 2017 was a year of momentum. We're currently the only cancer center in Virginia nationally ranked by the *U.S. News & World Report*, and we're among the top three percent of cancer centers in the nation. For the fifth consecutive year, *Becker's Hospital Review* has named UVA Cancer Center to its list of 100 hospitals and health systems with great oncology programs. UVA was the only health system in Virginia on that list.

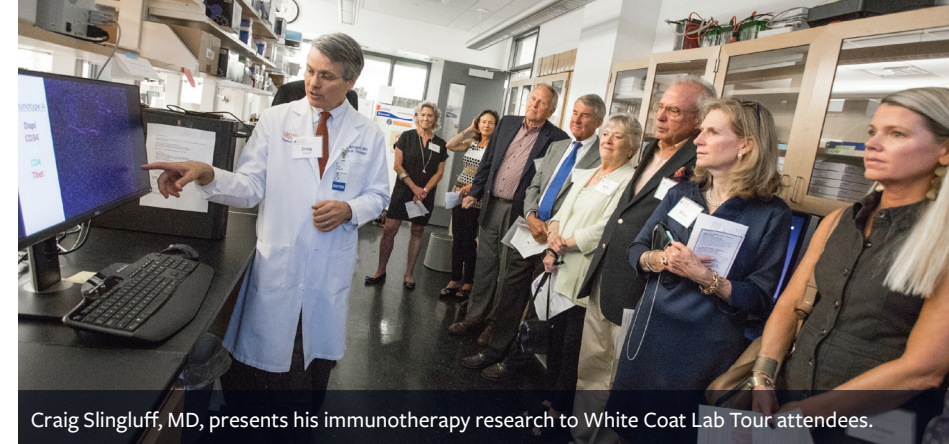
In the lab, our research spans basic discovery to starting the first gene therapy clinical trial in Virginia. We're diagnosing cancer sooner and treating it more effectively thanks to specialized screenings offered by our high-risk breast

and ovarian cancer program and high-risk pancreatic cancer program.

Just as importantly, some of the greatest minds in cancer research have chosen UVA as their new home. Karen Ballen, MD; Francine Garrett-Bakelman, MD, PhD; Bob Klesges, PhD; Daniel "Trey" Lee, MD; and Lawrence G. Lum, MD, DSc., are invaluable additions to our team.

Conquering this disease is a group effort, and it starts in the labs, in the clinics, and in the community. Thank you for being a part of it. I can't wait to see what 2018 will bring.

-Tom Loughran Jr., MD
Director, UVA Cancer Center



Craig Slingluff, MD, presents his immunotherapy research to White Coat Lab Tour attendees.

Behind the Scenes

Lab Tours Reveal Latest in Cancer Discoveries

The latest cancer treatments and discoveries, from innovative immunotherapy clinical trials to earlier cancer detection methods, can all be traced back to one origin: the lab.

This fall, friends and supporters of UVA Cancer Center gathered for a series of behind-the-scenes lab tours and presentations at the Carter-Harrison Research Building. Attendees heard about the latest advances in cancer research at UVA, and were able to see firsthand the technology and techniques that make life-changing breakthroughs possible.

Several researchers at UVA are at the forefront of immunotherapy research, which uses the body's own immune system to fight cancer and is revolutionizing the way doctors approach cancer treatment.

Drs. David Brenin and Patrick Dillon are partnering with biomedical engineer Richard Price, PhD, and pathologist

Timothy Bullock, PhD, to use focused ultrasound technology to target breast cancer. For more on their lab, see cover story.

Craig Slingluff, MD, and his team, are conducting clinical trials that utilize immunotherapy through vaccination to combat melanoma and other cancers. Meanwhile, Daniel "Trey" Lee, MD, the head of UVA's pediatric transplant program, and his team are developing immunotherapies that drastically improve transplant outcomes. Lawrence Lum, MD, shared the latest details of his immunotherapy methods and research, which spotlight infusions as having the potential to destroy cancer cells in various parts of the body, and possibly even target immune-related diseases beyond cancer—all on an outpatient basis.

The lab of Chip Landen, MD, is pioneering a two-pronged approach to combat ovarian cancer. Their strategy includes the development of a non-invasive, early

detection test that can be performed as part of a woman's regular annual exam, and increasing sensitivity to chemotherapy to prevent recurrence caused by cells becoming chemoresistant.

Todd Bauer, MD, and Kim Kelly, PhD, both are researching new tools that can identify cancer earlier. Bauer studies the fundamental processes that cause pancreatic cancer, allowing his team to focus on personalized, combination patient therapies. In a separate lab, Kelly uses functional proteomics to detect novel markers of disease for early detection and targeted therapies.

Karen Ballen, MD, oversees UVA's adult bone marrow transplant program, and both she and UVA Cancer Center Director Tom Loughran, MD, are doing leukemia-specific research. Ballen and her team offer advanced care for leukemia patients, while Loughran and his team are examining why normally dormant LGL leukemia cells can abruptly become active and multiply, causing life-threatening symptoms in patients.

"As both a physician and a researcher, I have really become humbled seeing my own research directly impact our patients," Loughran says. "Our researchers focus on the patient and patient outcomes, and being able to share that insight as well as the latest discoveries taking place in our labs with an incredible group of supporters—many of whom are cancer survivors—was nothing short of inspiring."

Research Legacy

A Quest to Help Others

Former cancer patient Bob Tanner always kept a handwritten note in his wallet that read, "I would like my legacy to be a celebration of life by helping to alleviate the pain and suffering of people in general!"

Today, that vision is coming true. Before pancreatic cancer claimed Tanner's life, he pledged \$3 million to support UVA cancer research through the Robert Edison and Hermie Tillman Tanner

Medical Research Fund. The fund, which honors Tanner and his late wife Hermie, generates annual, ongoing support for innovative cancer research.

At a recent White Coat Lab Tour event, Tanner's close friend and former financial adviser visited, for the first time, the labs of some of UVA's leading cancer researchers. That firsthand experience gave her a glimpse into the groundbreaking work that Tanner's gift will make possible:

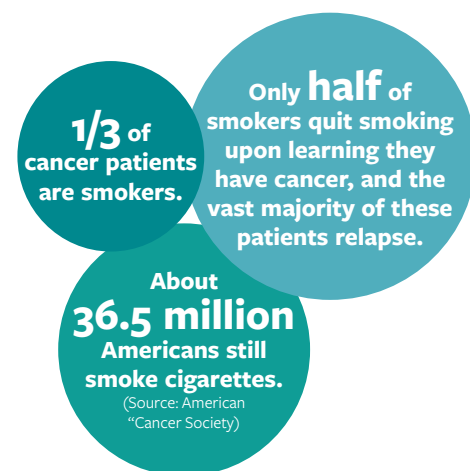
"It was inspiring to see all of the research taking place. Not a lot of people know how much research is going on and how it can affect lives for many years to come. Bob Tanner was an individual who wanted to support medicine because he knew that he could make a difference in many lives."

In the coming months, income from the Tanner Fund will support cancer research related to tobacco use. The research will be led by new UVA recruit Bob Klesges, PhD, and his colleagues. Klesges, a professor of public health sciences, co-directs UVA's Center for Addiction and Prevention. This multidisciplinary group works to assess health risk behaviors and develop effective interventions and policies for communities aimed at reducing cancer risk.

"Of all high-risk medical populations, no group needs to quit smoking more

than cancer patients and survivors," says Klesges. "Quitting, even after a cancer diagnosis, increases treatment outcomes, reduces treatment complications, and decreases mortality. UVA researchers have developed, and are testing, innovative methods to achieve smoking cessation with cancer survivors. Additional research is sorely needed to treat arguably the most important behavior change that cancer patients and survivors need to make."

Through his vision and support, Bob Tanner has created a legacy of cancer research, driven by his desire to alleviate pain and suffering. The fund bearing his name will give generations of researchers the resources to develop new ways to treat—and perhaps even prevent—cancer.



Bob Klesges, PhD, co-directs UVA's Center for Addiction and Prevention. Klesges is collaborating on research with colleagues in Virginia and beyond.

The Cynthia and Mark Lorenzoni Volunteer Service Award

In 1983, Cynthia and Mark Lorenzoni started what is now the largest all-women's race in Virginia, the Charlottesville Women's Four Miler. Since 1993, the race has raised more than \$4 million for the UVA Breast Care Center.

After more than 35 years, the W4M has become more than just a race—it is a community celebration that highlights the

very best of Charlottesville. This is in large part thanks to the commitment and generosity of the Lorenzonis.

To honor them, the UVA Cancer Center has created the **Cynthia and Mark Lorenzoni Volunteer Service Award**, to be given to an outstanding volunteer at UVA Cancer Center starting in 2018. The award is intended to recognize an individual who has volunteered for UVA Cancer Center over a sustained period of time, and made positive contributions to both the advancement and image of UVA Cancer Center.



Runners line up at the 2017 Women's Four Miler.

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INVESTING IN HOPE

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inside the body—in this case, the site of the breast tumor. As these beams of ultrasound energy come together with pinpoint accuracy, they produce heat that damages diseased tissue. Brenin and his collaborators will determine the correct thermal dose to damage, but not completely ablate, the breast cancer cells. They hope the ablation will attract white blood cells to the tumor.



(From l to r) Patrick Dillon, MD, Richard Price, PhD, and David Brenin, MD.

Each patient also will receive infusions of an immunotherapy drug to block the protective function of the breast cancer proteins and trigger a brisk immune system response. Researchers hope the medication will interfere with the protective functions of the tumor markers, allowing cancer-killing immune cells to recognize and attack the invasive cells.

“Those immune cells hopefully will educate the T-cells, or cancer-killing cells, to recognize the proteins or antigens of the breast cancer,” says UVA hematologist/

oncologist Patrick Dillon, MD, principal investigator for the clinical trial. “Then, we hope they will destroy any cancer cells in the local site within the breast, but also circulate throughout the rest of the body, recognizing and destroying cancer cells that have deposited in distant sites such as the bones, lungs, or liver. The use of focused ultrasound acts almost like a vaccine in educating the immune system or stimulating a systemic immune response.”

This clinical trial is truly a cross-Grounds collaboration, with roots in basic scientific research. Brenin and Dillon partnered with biomedical engineer Richard Price, PhD, research director of the UVA Focused Ultrasound Center, and Tim Bullock, PhD, a basic science researcher specializing in immunotherapy and focused ultrasound, to develop the study. This team-based approach, involving scientists from different disciplines working together, is only possible at academic medical centers like UVA—and offers the best chance to make progress for cancer patients.

“There will be challenges, but at the end of the day, this has potential to affect millions of people with cancer,” says Price. “UVA has been a leader in unlocking the many positive benefits of focused ultrasound. This study allows us to magnify our expertise in the field and provides an opportunity to differentiate the institution.”

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