

Third Quarter 2023

Highlighting  
Wistar people

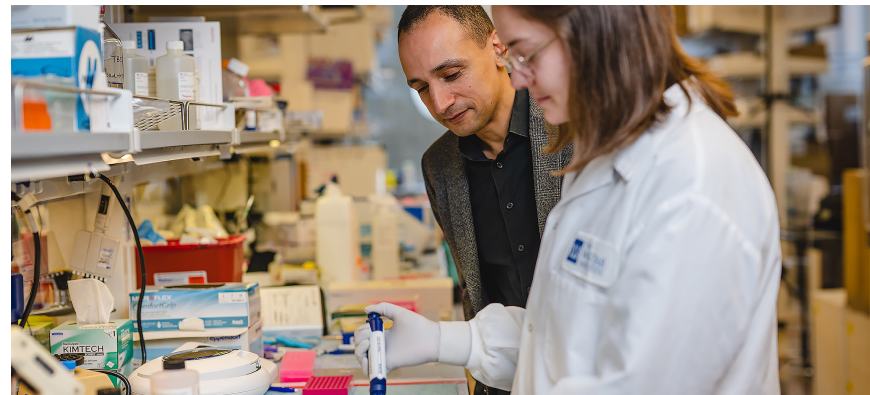
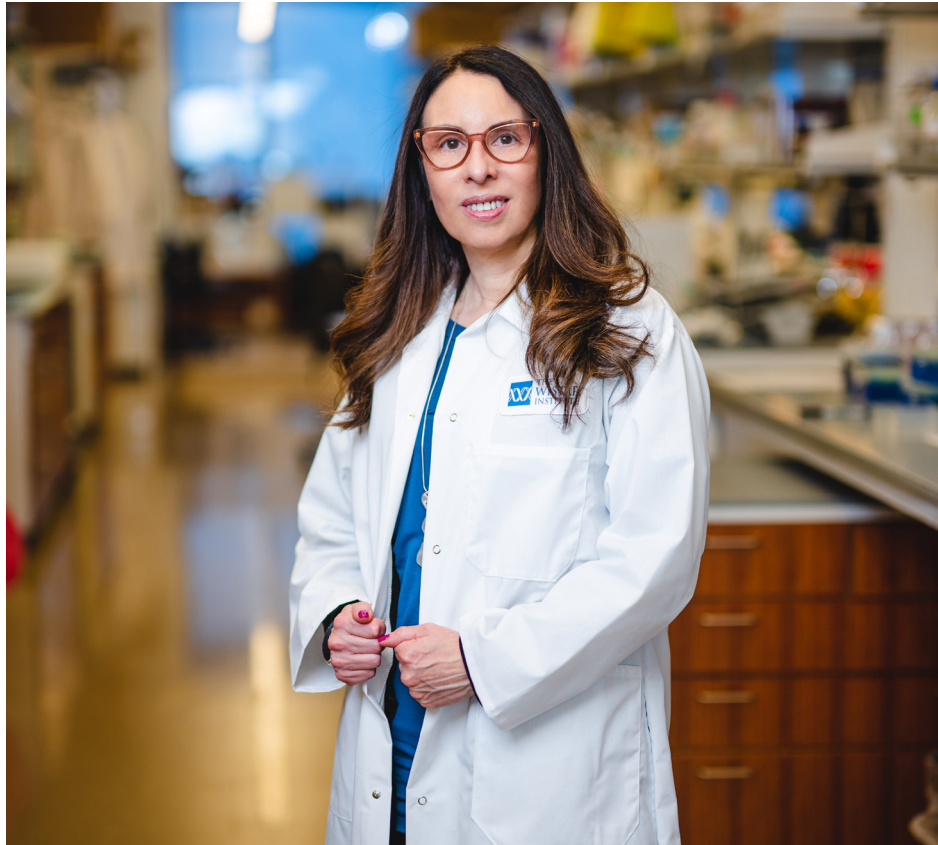
Understanding  
Wistar science

Celebrating  
Wistar successes

# FOCUS

THE  
WISTAR  
INSTITUTE





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# Navigating a path to success

*In cancer research and drug development, persistence is key*



**What do you think has been the most seminal or important breakthrough in cancer treatment in recent years?**

The best answer is immunotherapy. We have been speculating for decades that the immune system doesn't work when it comes to cancer – that cancer is a disease of the aging because of a less vibrant, less responsive immune system. It turns out all those assumptions are wrong, and the reason is science: great research discovered the fact that tumor cells are smart, and they engineer all sorts of mechanisms to block the immune system's ability to recognize and fight a tumor. It was the launching of new drugs called immune checkpoint inhibitors that removed those barriers and allowed the immune system to fight the cancer and provide a positive response for patients.

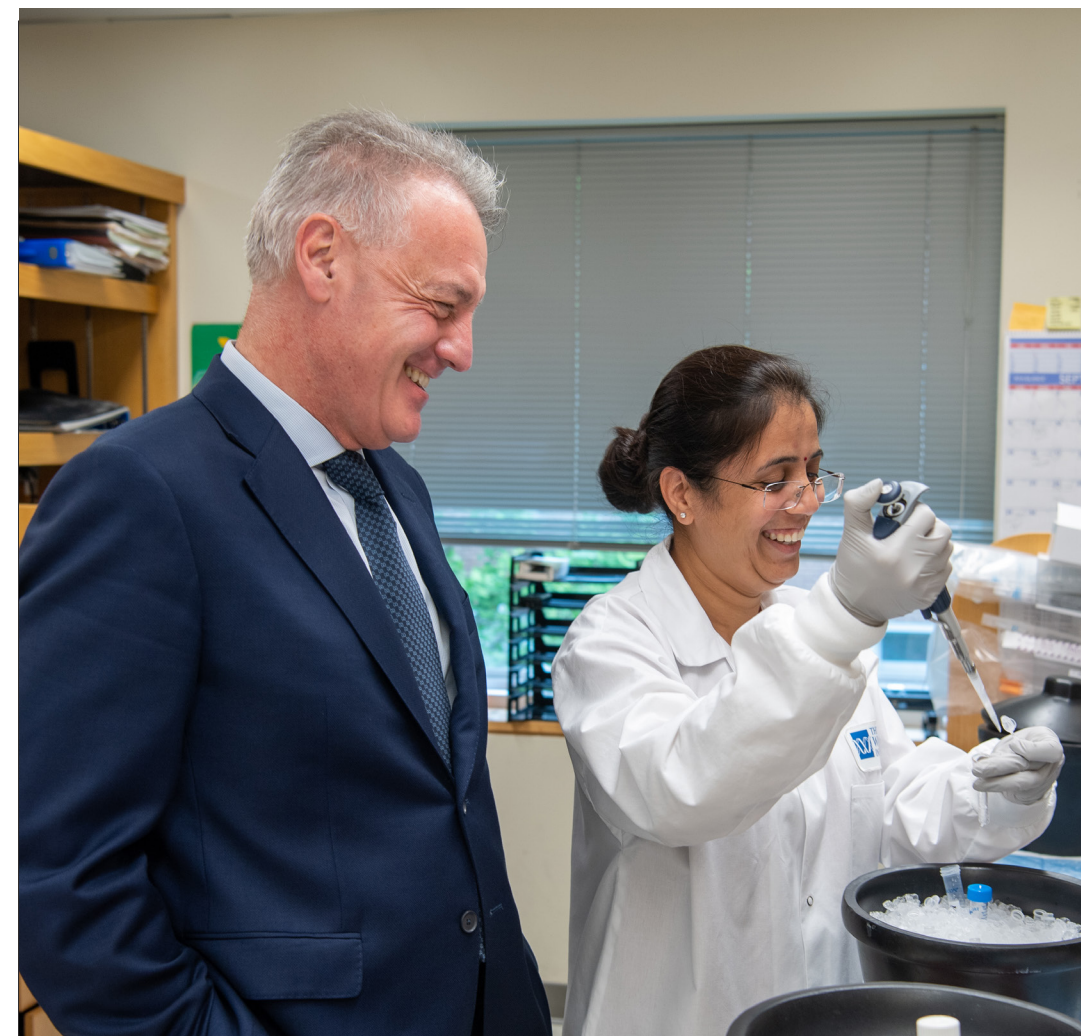
**Do you think there's going to be a time when site-specific cancers can be treated more like a chronic disease?**

I do. For a long time we've been looking for the magic bullet: a miraculous cure that suddenly melts the tumor away. The reality has been that we have gotten better at keeping the disease at bay. Even people with advanced

disease now live a lot longer than in the past, even to a level that would have been unthinkable a few years ago. I think that seems to be the trend: we'll get better and better at formulating first line treatment with fewer side effects, and we also have a second line treatment that may keep the patients going.

**The process of getting a drug to market can be lengthy. Is there anything you would change in terms of getting drugs to market safely?**

This is a process that I've lived personally for the past 13 or so years. The process can take decades, and unfortunately, the oncology space is one with the highest rates of failure. To their credit, the US Food and Drug Administration has relaxed some of the requirements for early-stage evaluation of new oncology indications. But what could be done to accelerate the process? I think my answer is twofold. One is practical, and the other one is philosophical. The practical is the need to provide more funding for those mechanisms. You hit what people call the valley of death – the gap between discovery and early-stage clinical trials. There is funding for early-stage discovery, there is funding for early-stage clinical trials, but bridging the gap between those two is very, very difficult. The philosophical answer—and this is my own personal view—is that we as a community have become very, very risk averse. Places like Wistar—freestanding, fiercely independent research institutions—they're more willing and prepared to take risks.



**You mentioned your personal experience with bringing a drug to market – tell us more about that.**

It's truly been a journey. The steps of oncology development are complex, they are multi-layered, and like Murphy's Law, anything that can go wrong will go wrong. But I have to say that it's been an incredible experience because I got to meet truly amazing people that are so passionate, so committed, to making a difference. There are tons of reasons why something might not work right, but sometimes we have to close our eyes and say, OK, we're going to give it a try anyway.

**Is there a quality or attitude that you look for when a new potential scientist walks through the door?**

Resilience. Persistence. Stubbornness. Someone who is a self-starter, somebody that is driven by internal passion and has the desire to succeed through excellence and really wants to make a contribution. Also, the ability to go around obstacles, navigate complex waters, be sensible in decision-making and work and learn from others. Those are the things that, in my experience, make a successful scientist. In addition to being smart, of course.

# Targeting critical pathways:

## How the Villanueva lab works to tackle treatment resistant melanoma

*In the last 15 years, the worldwide melanoma research community has made tremendous strides unlocking the biology of the disease and coming up with nearly 15 approved treatments for the fastest growing, most aggressive form of skin cancer. Despite significant progress, however, nearly half of all melanoma tumors either evade existing pharmacological therapies completely, or respond initially, but soon become resistant. Jessie Villanueva, Ph.D., and her lab at The Wistar Institute are working toward a strategy that blocks melanoma's critical pathways and contributes to the development of new treatments for patients who currently have few therapeutic options.*

### Tell us about your team's research in Wistar's Melanoma Research Center.

We have been focusing on a particular type of melanoma with mutations in a gene called NRAS (neuroblastoma ras viral oncogene homolog). NRAS is a small protein, but one that plays a big role in regulating key cellular processes such as cell division. All cells have NRAS – the gene signals to cells when to grow, and when to stop growing. But when it is mutated, the gene stays persistently on, signaling cancer cells to keep growing. The challenge is that there are no drugs available yet to directly target mutated NRAS.

### How does melanoma develop?

Exposure to ultraviolet radiation from the sun—or tanning beds—leads to changes in the DNA, which are the molecules that contain the genetic information in our bodies. When those genes become damaged, they contribute to cancer.



Jessie Villanueva, Ph.D., associate professor, Molecular & Cellular Oncogenesis Program with The Wistar Institute Melanoma Research Center and associate director for Diversity, Equity and Inclusion, Ellen and Ronald Caplan Cancer Center

Melanoma originates in a specialized type of skin cell called a melanocyte that produces melanin, the pigment that gives color to the skin. Melanocytes normally grow in a slow and controlled manner, but with certain environmental cues, such as excessive UV exposure, they accumulate genetic alterations, start proliferating at higher rates, and lead to the skin cancer known as melanoma.

### Who is at increased risk for melanoma?

Anyone can get melanoma. Risk factors include fair skin, light-color or red hair, light-color eyes, individuals who burn easily when exposed to the sun or have many freckles or moles. Family history of melanoma—especially in a first-degree relative such as a parent or sibling—increases one's risk of developing melanoma. This could be attributed to genetics or family lifestyle habits, such as spending considerable time outdoors. That said, it is a complete misconception that people with dark skin don't need to protect themselves from UV rays. For those with darker skin, melanoma tends to present on the palms of the hands, soles of the feet or nails. These type of tumors, called acral melanoma, are rare but highly aggressive and in urgent need of effective therapies.

### What is on the research horizon in the fight against melanoma?

We are extremely optimistic and excited about new targets, new immunotherapies, and mRNA vaccines. We expect to have

combination therapies that are more effective, more durable, less toxic and hopefully less likely to lead to treatment resistance. We also expect that the identification of molecular markers will help to determine which patients are likely to respond to specific treatments.

### How does diversity drive discovery in biomedical research?

At Wistar, we tackle scientific needs affecting communities both locally and around the globe. Then, diversity of experience is key to remain at the forefront of biomedical research. Diversity also fosters global collaboration. Discoveries by our highly diverse team of Wistar scientists representing nearly 25 different nationalities have led to the development of vaccines and monoclonal antibodies, as well as the identification of genes associated with different types of cancer.



Researchers with The Wistar Institute Melanoma Research Center encourage you to educate, prevent and protect yourself from the fastest growing and most aggressive form of skin cancer. Know your family history; limit exposure to UV rays from the sun and tanning beds; wear protective clothing, sunscreen and sunglasses; and check your skin monthly for the ABCDs:



Asymmetry



Border



Color



Diameter

## Homecoming: How one Wistar scientist is on a *quest to bring antique microscopes back home.*

On the second floor of the Wistar building, behind a nondescript office door that can be found just adjacent to a working lab, sits history. It's not the history of Wistar itself, an organization that is rich with it, or of its buildings or research discoveries. Instead, it is the collection of a Wistar Principal Investigator named Italo Tempera – a collection that happens to be the very reason he is here, in this lab, studying the effects of Epstein-Barr virus.

Microscopes. More than a dozen antique microscopes are arranged across one side of his u-shaped desk, most of them brass, glinting in the sunlight that streams through the window. There are various sizes and configurations, some with knobs and various adjusters, and one can't help but wonder: were any of these used in a

groundbreaking discovery – something that changed the path of medicine? “I think that was one of the things that drove me over to science,” Tempera explains, gesturing toward the collection.

***“Thanks to these microscopes and people who made them, we were able to really have some of the most important scientific breakthroughs in the world. Because we could see a world that didn't exist – we could only imagine diseases.”***

Tempera's interest in microscopes started early, in 8th or 9th grade, when his family bought a microscope that he found fascinating. That draw toward a world of the unknown, toward things too small to see with the naked eye, eventually led him to earn his Ph.D. and join Wistar.

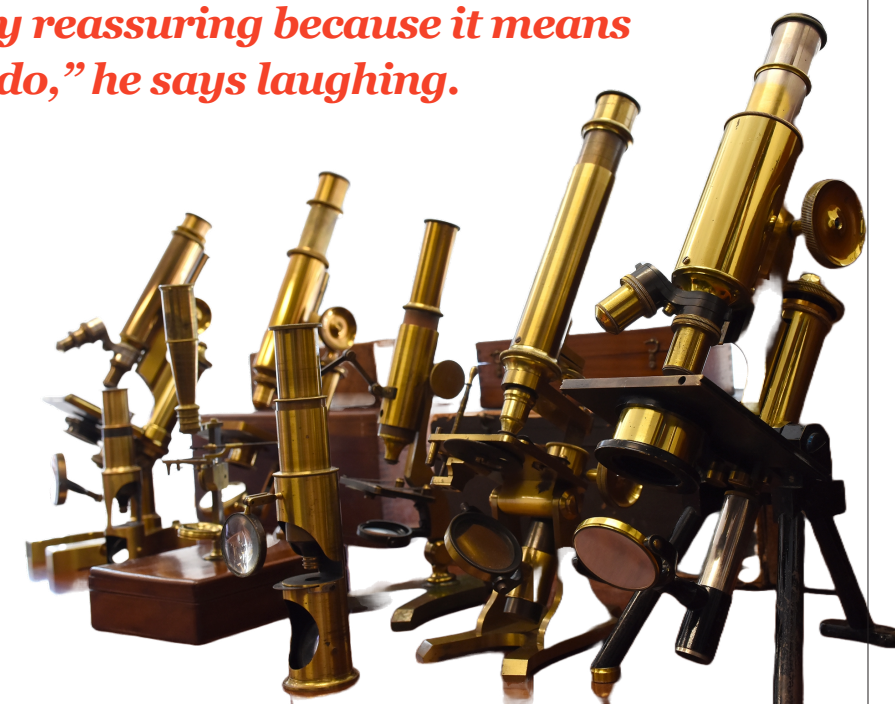
After purchasing one small microscope that he says was “cheap,” he started hunting for others. When the pandemic hit, with a bit more time on his hands and looking for a distraction, his collection began to grow.



***“The more you get, the more you learn... You discover communities, and it's very reassuring because it means you are not the only weirdo,” he says laughing.***

Some of his microscopes were originally sold by merchants in Philadelphia, who imported them from manufacturers in France, England, and Germany. Over time, they were purchased and made their way to other locations outside of the city, or even the state.

In some ways, that path mirrors the one that Tempera took: from University of Rome, he came to Wistar as a visiting scientist, working with Paul Lieberman for several months.





After returning home to Italy to complete his Ph.D., he returned to Wistar for a fellowship, and then eventually was brought on as a Principal Investigator. “There was an opportunity to come back, and ... this is a place that you can be inspired by brilliant people.”

Today, Tempera studies how the Epstein-Barr virus – a common virus carried by approximately 90 percent of the world’s population – can cause certain cancers in individuals who are immunocompromised. His goal is to understand the viral genes that ultimately lead to EBV-associated cancers and develop therapies that can treat the disease.

That world of unseen genes, and the research that Tempera undertakes, is only made possible

by the development of the microscopes that he collects.

Tempera’s oldest microscope is one from 1840. Mounted to a wooden box that serves as its base, the microscope is fairly rudimentary, with a small clip to hold samples, a selection of lenses to change magnification, and a mirror to help focus light. Inside the box is a perfectly intact instruction pamphlet along with several additional lenses, as if it were a time capsule.

Some of the later microscopes are like works of art, with exposed engineering elements plainly visible, similar to the interior of a fine watch. Gear mechanisms alter the height, apertures can be used to adjust light, and lens adjustments can be made through



a series of arms that swing in and out of the mechanism. “It’s fun to see the ingenuity that has been put into these tools.”

Over time, Tempera has become more particular about what he purchases, but he’s always on the hunt for microscopes that originated from Philadelphia. “I like the idea that they’re coming from this area,” he explains. “I like this idea that these microscopes may have been used by someone at the University of Pennsylvania.”

Now, perched on his desk overlooking Penn’s campus nearly 175 years later, the microscopes are finally home.

# Advancing an HIV Cure with Deeper Community Engagement

To make their research more inclusive and collaborative Dr. Montaner and stakeholders—within Wistar and outside Wistar—developed a more equitable and collaborative standard to advance HIV cure-directed research: the community engagement group, or CEG model. A CEG composed of a three-part structure:



***“It is time for a new model of community engagement, one that builds a deeper trust and bond among all key players and moves beyond inequities, power dynamics, and cultural differences. We needed something more equitable and collaborative. I believe that such a model brings us organically closer to an HIV cure,”*** said Luis Montaner, D.V.M., D.Phil., vice president for scientific operations, Herbert Kean, M.D., Family Professor, director, HIV-1 Immunopathogenesis Laboratory, and leader, HIV Research Program, Vaccine & Immunotherapy Center at The Wistar Institute.

An internationally recognized leader in HIV cure-focused research, Dr. Luis Montaner leads a team of outstanding scientists at Wistar. The Montaner HIV cure-directed research program has long held ties with community partner organizations and advocacy groups, federal HIV/AIDS organizations, and major academic science groups here and beyond.

a Community Advisory Board (CAB), Community nonprofit organizations, and researchers.

When Dr. Montaner joined Wistar in 1997, he was intentional in meeting the people of the Philadelphia local community living with and at-risk for HIV as well as the people supporting them. Through time, bonds strengthened. Dr. Montaner and his colleagues applied their combined experience and connections to rethink the Community Advisory Board (CAB) model.

***“Unlike isolated advisory board models, where researchers propose ideas and the board reacts and offers advice, the CEG model is a collaborative working unit at every stage of the process,”*** said Dr. Montaner. ***“Community engagement groups are a valuable resource for scientists because they have broader reach and deeper credibility within the community.”***

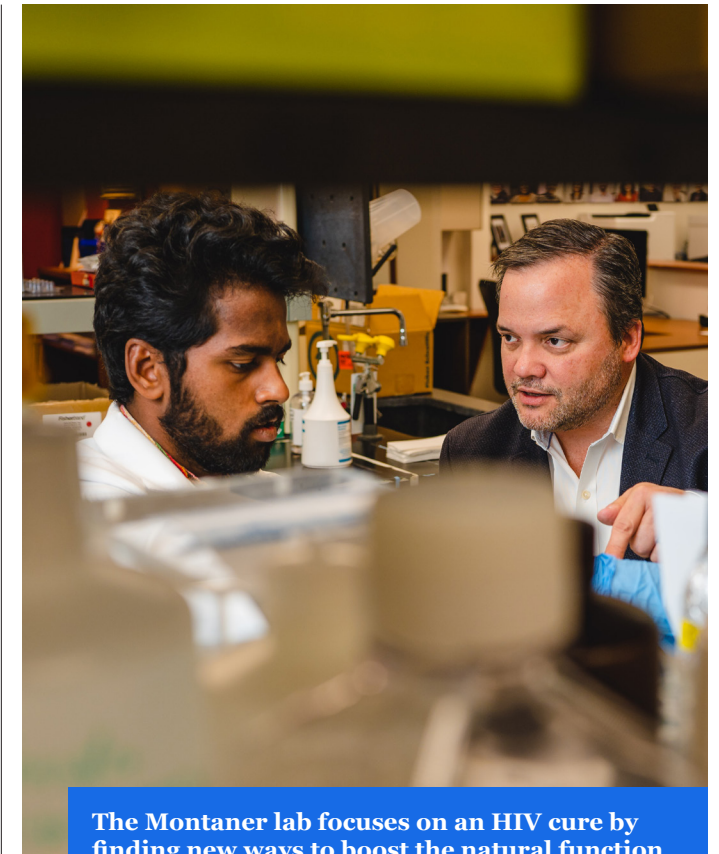
Dr. Montaner and team recently published a report detailing the decades-long relationship between HIV researchers at Wistar and Philadelphia FIGHT, a federally qualified health center (FQHC), and a nonprofit AIDS services organization, clinic, and advocacy group. The collaboration led to the establishment of the BEAT-HIV Community Engagement Group or CEG. The report documents specific projects, lessons learned, along with the challenges faced by the CEG since its start. Importantly, it also provides a roadmap for others to follow.

“Projects are developed in partnership,” Dr. Montaner said. “Above all, working under a more inclusive community engagement group model fosters greater trust when communicating with otherwise hard to reach persons living with HIV in our community.”

What was once a life-threatening disease is now a chronic condition when managed with antiretroviral therapy (ART). But there are still 1.2 million people living with HIV.\* Dr. Montaner and his collaborators are aware of – and have contributed to – many advances made in HIV research during the last forty plus years but the work can always be refined.

Read the case study combining Wistar scientists, Philadelphia FIGHT and a CAB under a CEG model, entitled “Community engagement group model in basic and biomedical research: lessons learned from the BEAT-HIV Delaney Collaboratory towards an HIV-1 cure,” published June 8, 2023 in the journal *Research Involvement and Engagement*.

\* Centers for Disease Control and Prevention



The Montaner lab focuses on an HIV cure by finding new ways to boost the natural function of the immune system to combat infection or viral-associated disease.



***“This is a unique, dynamic model because we all work together. We (the community) work in unison with researchers and Philadelphia FIGHT and it’s a brilliant thing. In my eyes, the scientists with collaborators dream up the roadmap to implement cure research. And then the community makes the dream its own. Scientists’ dreams don’t come to light because they can’t take that injection, they can’t take that pill. You need health clinics and services to help organizations. Then you need us. I don’t see how we can fail.”*** – William B. Carter

# Up Close with Wistar Researcher Maureen Murphy, Ph.D.



*Ira Brind Endowed Professor Maureen Murphy, Ph.D., studies the genetics of the p53 tumor suppressor protein, focusing on genetic variants of p53 that exist in populations of African descent and Ashkenazi Jewish descent. The variants of p53 she studies produce a lesser functioning protein, so these people are predisposed to cancer and usually develop several independent tumors in a variety of tissues in early adulthood.*

## Why did you come to Wistar?

The Wistar Institute was the most appealing because of its distinctive culture of collaboration.

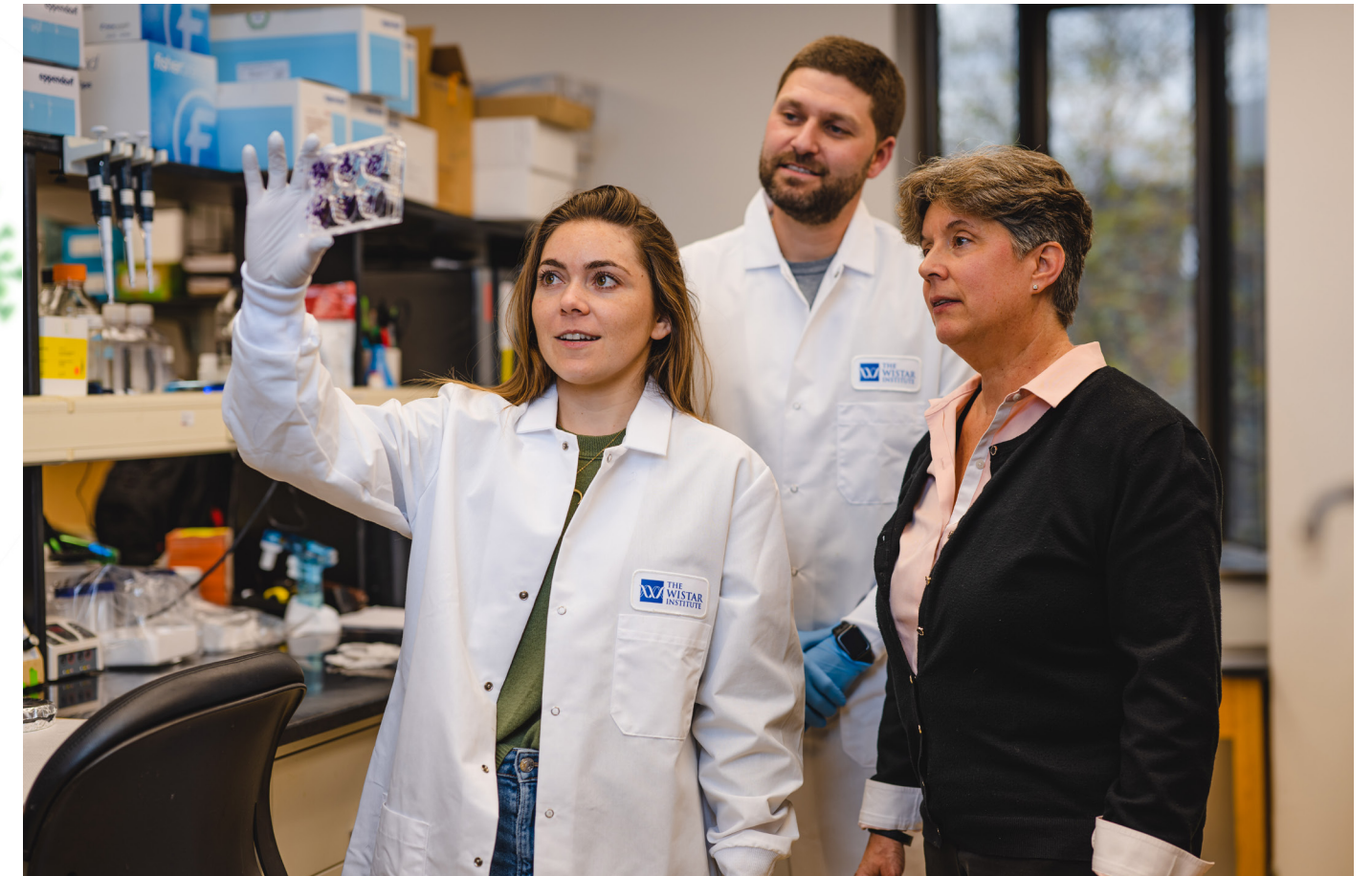
We share a common goal every day when we walk through the door: to reduce the burden of human disease.

I had looked all over the United States for a cancer center director who is an inspirational leader as well as being an exceptional scientist who understands the importance of collaboration. It's rare to find leaders that do all of this well. I picked Wistar because Wistar's president and CEO Dr. Dario Altieri is a leader who embodies all of these traits. I'm sure others are out there, but they are rare.

## What do you think makes Wistar unique?

When I met some of the Wistar scientists, their passion for their research is remarkable. You just want to be around that kind of passion.

We are all cogs in a wheel, and we respect the importance of every single cog. When there's a major Wistar discovery, I can guarantee you that the people who are our security guards, who run our facilities, who work in our administration, they all feel part of that success. So there's a common goal, a family sort of aura, and everyone feels responsible for all of our success; that is what makes Wistar different.

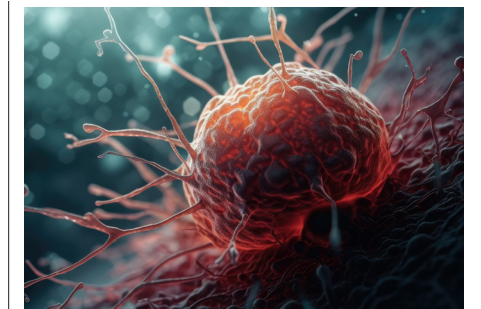


## What's the future of research?

I am passionate about personalized medicine and machine learning. We are getting more and more big data sets and gene expression data from tumors. We use machine learning to make sense out of huge amounts of data. It's no longer enough that we are smart enough to come up with novel hypotheses. Now we need to use machine learning algorithms to help us generate those hypotheses, and we can use machine learning to test different hypotheses over and over and over again to come up with one that I can then test. So I think when it comes to making sense out of chaos, machine learning is key.

## What are you telling students and current scientists about expanding their skill sets in that area?

When you're a scientist, find out what techniques you love and become the best at that. You will become more marketable.





# The Transformative Power of Philanthropy

## Meet Wistar's New Development Team



**Michael Criscuolo**  
Vice President of Development,  
The Wistar Institute  
mcriscuolo@wistar.org

**Meet Michael Criscuolo, The Wistar Institute's recently appointed Vice President of Development.** With more than two decades of success leading development teams and exceeding goals on capital and programmatic campaigns, Michael has taken the lead role in supporting Wistar's fundraising strategy. Since joining Wistar, Michael has dedicated the last few months to building a new development team eager to work with Wistar donors and prospective donors to advance Wistar's mission of early-stage discovery in biomedical research.

The new team comprises an experienced group of professionals that are devoted to helping Wistar advance its mission with the support of philanthropic contributions from all sectors. "We're really excited to give everyone an opportunity to get to know our outstanding team and demonstrate the great work that goes on at Wistar," said Criscuolo. "We hope to meet many of you in person soon."

*"Every philanthropic donation, every dollar that comes into Wistar, goes to science. That support enables Wistar to attract talented scientists, pursue collaborations, perform groundbreaking research, and ultimately produce new cures."*  
- Wistar CEO Dario C. Altieri, M.D.



**Dara Lieberman**  
Manager of  
Foundation  
Relations,  
Stewardship, &  
Acquisition

**(dlieberson@wistar.org)** Perhaps the most familiar face on the team, Dara joined Wistar's Development team in 2019 taking on an increasingly expansive role. Her knowledge and expertise in the foundation and grant arena have resulted in significant contributions to support Wistar scientists and their mission-critical research.



**Brittany McCrimmon**  
Director of  
Development

**(bmerimmon@wistar.org)** Brittany has nearly 15 years of expertise in hospital fundraising at Main Line Health. This knowledgeable, dedicated professional fundraiser has a keen eye for strategy and an impressive track record of securing major gifts working with a team that successfully raised nearly \$80 million for a host of capital and programmatic campaigns.



**Lynn A. Keily**  
Development  
Operations  
Associate

**(lkeily@wistar.org)** Lynn brings to the team more than 20 years of experience in the nonprofit sector, most recently at Bryn Mawr Hospital. Lynn is playing a mission-critical role optimizing Wistar's fundraising infrastructure – from budgets to database and everything in between, Lynn is ensuring Wistar's development operations run smoothly and efficiently.

*"Collaboration is key to achieving philanthropic success," Criscuolo explained. "By working together with our donors and prospective donors, we can create opportunities for scientific growth, accelerate discoveries, and help build healthier communities throughout the world."*

# Wistar welcomes three new members to its Board of Trustees

The Wistar Institute recently welcomed three new members to its Board of Trustees. Wistar is excited to have their experience and expertise on the Board and we look forward to working with them to help further advance biomedical research, early stage discoveries and cures.



**Squire Servance**  
An influential and driven business executive, Squire Servance brings to the Board an extensive knowledge of the life sciences industry through his leadership of Syridex Bio, an impact-driven, life sciences-focused investment firm geared towards investing in therapies that accelerate global health equity.



**Joy Taylor**  
Joy Taylor, CEO of EastEdge Consulting Services, is an accomplished executive and entrepreneur, and offers the Board more than 25 years of cross-functional experience in operations, change management, and executive leadership, specifically in the life sciences sector.



**Sozi Tulante**  
A respected legal scholar and strategist, Sozi Tulante joins the Board with an extensive background in corporate and intellectual property law, policy matters, regulatory issues, and a record of building and leading diverse and sophisticated teams. He is currently General Counsel of Form Energy.

## Dr. Alex Price Joins Wistar as Assistant Professor in the Gene Expression and Regulation Program

Alex Price, Ph.D., recently joined The Wistar Institute's Ellen and Ronald Caplan Cancer Center as assistant professor in the Gene Expression and Regulation Program. Dr. Price's research focuses on the genomic mechanisms of viruses – specifically, how viruses regulate and exploit RNA transcription and

processing. His work aims to identify and exploit therapeutic targets in viruses' transcriptional machinery to combat disease. "I'm thrilled to have the opportunity to launch the Price Lab at Wistar," said Dr. Price. "Between Wistar's reputation for scientific excellence and the Institute's state-of-the-science research facilities, I have every confidence in establishing a productive, collaborative laboratory here." Price earned his Bachelor of Science degree in Genetics and Cell Biology at Washington State University. In 2016, he received a Ph.D. in Molecular Genetics and Microbiology from Duke University. Price did his postdoctoral research in affiliation with the University of Pennsylvania and the Children's Hospital of Philadelphia.



# Media Roundup

The Wistar Institute's groundbreaking research, innovative scientists, and diverse training programs have been featured in a number of news articles, TV segments and radio shows this year. Here is a selection of some of the more recent media coverage featuring Wistar.



**Boosting the cell and gene therapy workforce with a skilled, localized approach**

*The program's structure helps solve one of the key challenges of training regenerative medicine technicians that a nationalized curriculum likely wouldn't account for — the varying techniques and skills required by each drug developer to create individual products.*



**Wistar Research: New Insight into How Cancer Metastasizes to the Brain**

**Wistar Institute Appoints Sozi Tulante to Board of Trustees**

**Philly Department of Commerce Pushing Hard to Support City's Life Science Growth**



**Philly High Schoolers Work on Published HIV Research**



**Fifth Person Potentially 'Cured' of HIV**

*"Before these types of cases, we did not know that a cure was possible," said Luis J. Montaner, D.V.M., D.Phil., a disease expert at the Wistar Institute in Philadelphia who studies the mechanisms of conditions such as HIV, cancer, COVID-19 and emerging viral infections.*



**Breakthrough Discovery Could Lead to New Treatments for Brain Metastases**



**Philly's Biotech Scene Needs More Local Money — Now**



**Why viral reservoirs are a prime suspect for long COVID sleuths.**

*At the Wistar Institute, Abdel-Mohsen has found evidence that fungi, which should reside in the lungs and gut, are leaking into the bloodstream of some people with long COVID.*



**These Philly high schoolers helped with a new study of a possible treatment for HIV**

*The results of the students' experiments were so useful that they have now been included in a new published study from the research center in West Philadelphia.*



**Friends and scientists reunite at the Wistar Institute**



*Friends Dr. Maria Elena Bottazzi and Dr. Jessie Villanueva reunited during Wistar's Women & Science event on April 27th.*



**CBS3 Spotlights Wistar High School Training of Next-gen Scientists**



**Wistar, Pennsylvania Biotechnology Center and Blumberg Institute Partner to Accelerate Philly Life Sciences**

*"We have two incubators that really have a blueprint for success, speed-to-market know-how, and a network that we think could benefit both Blumberg and Wistar." – Louis P. Kassa III, CEO of Pennsylvania Biotechnology Center (PABC)*



**Philadelphia life sciences jobs being filled more by women than men, study finds**

*Willis credits local training and apprentice programs such as those run by the Wistar Institute ... with helping expose girls to the life sciences field while they are in middle school and high school.*



**Wistar's Biomedical Technical Training Program Featured on Fox 29 Good Day Philadelphia.**

*The students have the opportunity to work alongside world-reknown medical researchers at The Wistar Institute.*

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**WAITING IN THE WINGS...**

## Women & Science Event

**Helen Dean King Award  
Ceremony Honoring  
Cori Bargmann, Ph.D.**

**November 16, 2023  
6:00 to 8:00 p.m**

Dr. Bargmann is Torsten N. Wiesel Professor and head of the Lulu and Anthony Wang Laboratory of Neural Circuits and Behavior at The Rockefeller University. She has focused her life's work on exploring the genetic and neural circuit mechanisms of behavior, pursuing answers to the question: how do genes influence decisions?

## Thank You, Wistar Donors!

The Wistar Institute is the nation's first nonprofit biomedical research organization. And since its earliest days, philanthropy has played a key role in advancing Wistar science and its breakthrough discoveries. If you want to learn more about how you can support Wistar science, **visit [wistar.org/give-join](https://wistar.org/give-join)**.

The Wistar Institute is a 501(c)(3), tax ID# 23-6434390, and all gifts are tax deductible to the full extent allowed by law.

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2023, THE WISTAR INSTITUTE



A Cancer Center Designated by the  
National Cancer Institute

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