



Summer 2022

FOCUS

ON THE W I S T A R I N S T I T U T E

TRANSFORMATION

AT WISTAR

Tower
JTE
in 1972

Bold Science // Global Impact

IN THIS ISSUE: **Advancing Science** // **Expanding Education** // **Cultivating Collaborations**

CONTENTS

- 03 Letter from the President & CEO
- 04 A Focus on the Ambitious Transformation of The Wistar Institute
- 06 Scientists Drive Innovation at Wistar's Ellen and Ronald Caplan Cancer Center
- 09 What's New and Next with BEAT-HIV
- 10 Advancing Scientific Enterprise at Wistar's Vaccine & Immunotherapy Center
- 12 Unraveling the Enigmas of Melanoma
- 14 Inspiration, Mentoring, and a Philanthropic Commitment
- 16 Supporting Science Across Borders with Student Exchange
- 18 Expanding Education at Wistar
- 19 Fighting Breast Cancer Disparities Through Collaboration
- 22 Wistar-ChristianaCare Spring 2022 Grand Rounds Seminars
- 23 Global Voices for HIV Advocacy and Cure Research Come Together at Wistar's 26th Annual Jonathan Lax Lecture

THERE IS NO BETTER TIME THAN NOW

Over the course of 130 years, The Wistar Institute's groundbreaking discoveries in the life sciences have forged a distinguished and impactful history known and respected worldwide. We've pursued biomedical breakthroughs that spur innovation, challenge dogmas, create new knowledge, and, ultimately, save lives.

So now, with great enthusiasm, I announce Wistar's next five years. Wistar is embarking on a \$75M **Bold Science // Global Impact** Capital Campaign to accelerate progress in the most challenging — and promising — areas of research.

The roadmap encompasses the Institute's core strengths in cancer, immunology, and vaccine creation. It pushes the boundaries of knowledge and combines our research expertise with the most advanced technological approaches, where artificial intelligence and computational biology merge with high tech equipment to propel the biomedical breakthroughs of tomorrow.

To attain this transformative stage of innovation we are guided by the same strategic imperatives that are the core values of our organization: drive lifesaving innovation in biomedical research; expand our impact in the education and training of the next generation of trailblazing innovators; and establish powerful collaborations with other academic institutions, industry, government, and the private sector across the street and around the world.

In these pages, you will read the stories — Wistar snapshots — that make up our mantra and mission: **Bold Science // Global Impact**.

Wistar is and has always been about the science. Every day, our scientists pursue answers and solutions to humanity's most complex problems. Wistar is poised at a convergence: a renewed, public hope and trust in what science can achieve and the measureless ability of our scientists enabled to pursue their own curiosity. That ability will create the medicines of the future and save millions of lives.



DARIO C. ALTIERI, M.D.

President & CEO

Director, Ellen and Ronald Caplan Cancer Center

Robert and Penny Fox Distinguished Professor

The Wistar Institute

A Focus on the Ambitious Transformation of The Wistar Institute

WISTAR'S **BOLD SCIENCE // GLOBAL IMPACT** CAPITAL CAMPAIGN HAS BOLSTERED OUR FIVE-YEAR ROADMAP FOR ACCELERATING PROGRESS IN BIOMEDICAL RESEARCH AND THE TRAINING OF TOMORROW'S OUTSTANDING WORLD-CLASS INNOVATORS.



Ronald Caplan and Dario Altieri

The pandemic further stressed the critical need to have the scientific freedom, capacity, and agility to address global health crises. **Bold Science // Global Impact** is our Institute-wide commitment to take bold action now so we can continue to push forward with purposeful discoveries that have the power to transform the life science industry and rechart the course of human health. It will prioritize growth and innovation in three areas: science and technology, education and life sciences, and strategic partnerships.

This ambitious goal would not be possible without the dedicated participation of our science collaborators, our Board of Trustees, and our donors, who support our vision with their substantial philanthropic investment. Since the initiation of its silent phase which began in the fall of 2021, this Campaign has already raised over half of its \$75 million goal, including an anonymous \$20 million gift to create a new center of collaborative research.



From left to right, Elizabeth Anderson, Eric Rugart, Pauline Rugart and David Anderson; Vanessa Atkins and Anne Schoemaker; Sharon Kestenbaum and Rick and Ruth Horowitz.

Specifically, **Bold Science // Global Impact** will fund the expansion of these existing Wistar Centers:



THE WISTAR INSTITUTE

The recently renamed **Ellen and Ronald Caplan Cancer Center** will advance fundamental and translational cancer research into next-generation therapeutics by recruiting new leaders who will focus on treatment resistance, metabolic and cellular reprogramming, cancer systems biology, and personalized anticancer strategies.



THE WISTAR INSTITUTE

The **Vaccine & Immunotherapy Center** will strengthen our capacity to support pandemic preparedness as well as fast-track advances in drug development – including innovative platforms for novel drug candidates to halt disease resistance, advance diagnostics, and accelerate discovery of personalized treatment strategies.

The Campaign will also support the creation of two interdisciplinary centers:



THE WISTAR INSTITUTE

The **Hubert J.P. Schoemaker Education and Training Center** will augment education and mentorship opportunities for current and aspiring researchers with distinct programs that will create career opportunities and foster a diverse life science talent pipeline. Within the new Center, the Institute's flagship training program was renamed the **Fox Biomedical Research Technician (BRT) Apprenticeship** and will serve more students and partners across the state.



THE WISTAR INSTITUTE

Coming to fruition this fall, the **Center for Advanced Therapeutics** will integrate computational biology, artificial intelligence, and structural biology with next-generation sequencing technologies and groundbreaking immunotherapy research. The Center aims to tailor medicines to radically alter disease by harnessing the immune system in truly novel ways. ●

The **Bold Science // Global Impact** Capital Campaign was officially announced and celebrated the evening before Wistar's June Board of Trustees meeting. Take a journey into the vision of the Campaign in this issue of FOCUS to learn more about how Wistar is investing in biomedical advances to save lives.

Scientists Drive Innovation at Wistar's Ellen and Ronald Caplan Cancer Center

WISTAR CONTINUES TO BE A DYNAMIC ENVIRONMENT PREPARED TO TACKLE BIOMEDICAL CHALLENGES IN A COLLABORATIVE, INNOVATIVE, AND INCLUSIVE CULTURE. READ MORE ABOUT OUR CAPLAN CANCER CENTER COMMITMENT TO SCIENTIFIC CAREER DEVELOPMENT, A DIVERSE RESEARCH COMMUNITY, AND HOW PREVIOUSLY INTRODUCED RECRUITS ARE SETTLING IN AND ADVANCING IMPACTFUL SCIENCE.

ENHANCING CAREERS AND EXPANDING DIVERSITY

Italo Tempera, Ph.D.

Associate Director for Cancer Research Career Enhancement

Tempera was a postdoctoral fellow at Wistar and returned as an associate professor in the Gene Expression and Regulation Program in 2020. His research focuses on epigenetic mechanisms behind Epstein-Barr Virus (EBV). He was recently named associate director for Cancer Research Career Enhancement.

Tempera considers the time he spent at Wistar to be formative. With its very collaborative introductory environment, Wistar is an "... opportunity for our students not only to learn about our science but to get in contact with scientists."

Furthermore, he outlines what he would like to accomplish in his new role. "We're outstanding scientists and we have excellent mentors. The opportunities for our trainees to do an internship with different departments is something we want to push forward, and we want to expand the



Cancer Biology Ph.D. program that we have now with Saint Joseph's University."

He shares that Wistar gave him the opportunity to grow as a scientist and advance in his research career. "When someone asks what was one of the most important aspects of a scientist's pre- or post-doctoral training, my goal is for the trainee to think back and reply that being at Wistar has made all the difference."

Jessie Villanueva, Ph.D.

Associate Director for Diversity, Equity, and Inclusion

Villanueva joined Wistar first as a postdoctoral fellow and then was appointed assistant professor in the Molecular and Cellular Oncogenesis Program. Her work aims to identify targets for therapy to treat melanoma.

"Diversity leads to innovation and scientific excellence. New discoveries and scientific breakthroughs often rely on collaborations, and diverse teams are more creative and resourceful," she shares.





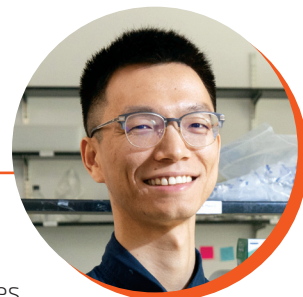
For her new role, Villanueva aims to lead and inspire everyone at Wistar to integrate inclusion, diversity, and equity into all facets of the Institute. “Our goal is to continue fostering an inclusive community where everyone can develop to their full potential while contributing to Wistar’s mission of scientific discoveries.” To accomplish this, she plans to work with leaders and stakeholders across the Institute to identify challenges and areas for improvement and propose strategies to address them.

“Diversity supports Wistar’s mission,” Villanueva asserts. She elaborates that many of the Institute’s scientific breakthroughs are largely impactful for biomedical sciences and human health, and these discoveries rely on “... outstanding scientists, trainees and staff with diverse backgrounds and skills who support Wistar’s goals wholeheartedly.”

ADVANCING IMPACTFUL SCIENCE

Nan Zhang, Ph.D.

Assistant Professor, Immunology, Microenvironment & Metastasis Program



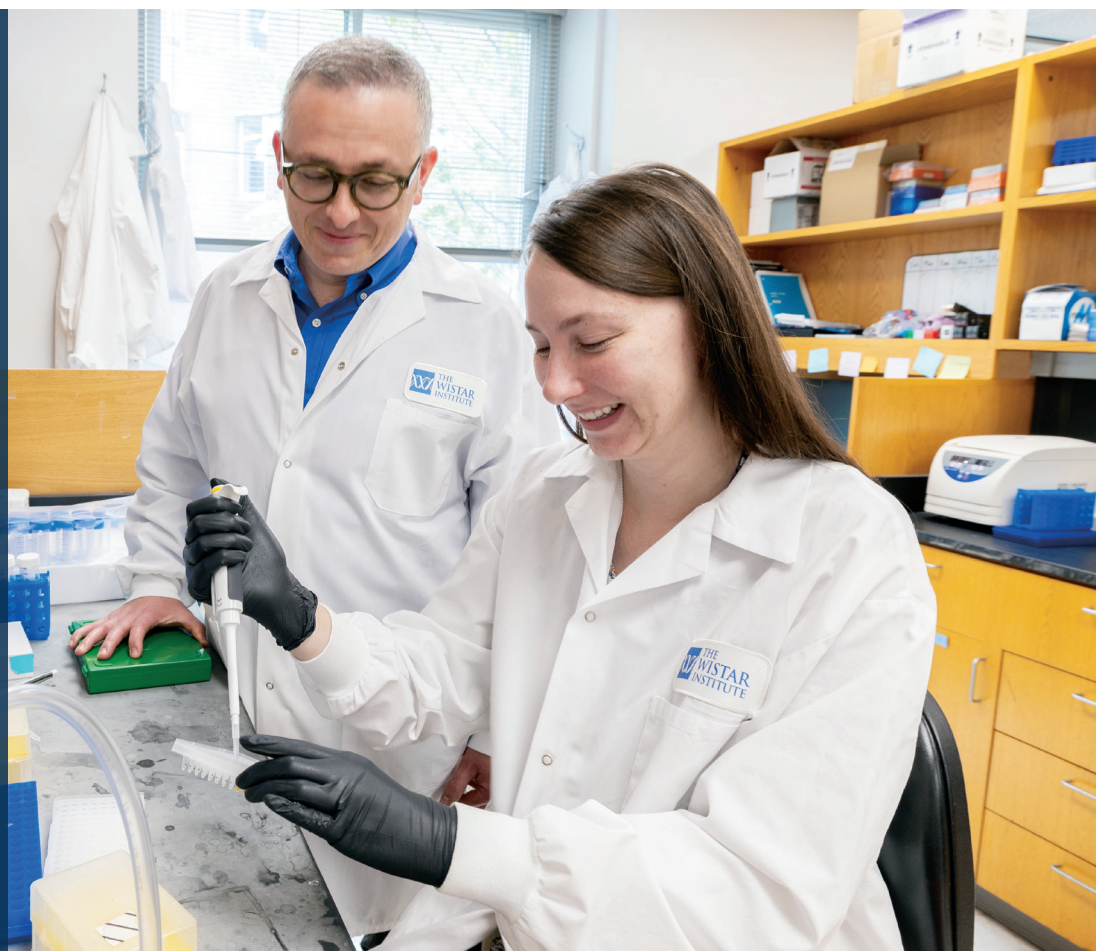
Zhang joined Wistar in September 2021 as an assistant professor and currently researches how immune cells play a role in tumor growth in abdominal cancers.

“Studying disease was always one of my passions,” Zhang shares as he describes both a personal and professional draw to cancer research. He began his career studying the immune system — particularly macrophages, a special population of white blood cells that removes unwanted materials in the body like harmful microorganisms or dead cells.

Upon completion of his postdoctoral position, Zhang felt that cancer in the peritoneal space — the area of the body encompassing the abdomen and the organs within it —

“When someone asks what was one of the most important aspects of a scientist’s pre- or post-doctoral training, my goal is for the trainee to think back and reply that being at Wistar has made all the difference.”

ITALO TEMPERA, Ph.D.



would be a great direction to pursue for his future career because of its unique complexity and how it's less understood relative to other focus areas for cancer research. This is what he works on now at Wistar.

Immersed in the Institute's world class techniques, resources, and renowned scientists, Zhang continues to push forward his research to tackle how to use specialized cells called macrophages to combat tumors as a checkpoint therapy for cancer. He is also investigating immunological questions about the microenvironment of the peritoneal space and how this knowledge can help inform therapeutics and treatment development.

He shares, "Wistar is competitive, and the support in the Institute for junior faculty is great. We have meetings every week and this is an environment I really wanted for my career and research."



"Wistar is competitive, and the support in the Institute for junior faculty is great. We have meetings every week and this is an environment I really wanted for my career and research."

NAN ZHANG, Ph.D.

Noam Auslander, Ph.D.

Assistant Professor, Molecular & Cellular Oncogenesis Program



Auslander joined Wistar in June 2021 as an assistant professor and conducts her research at the intersection of computer science and biological science. She uses machine learning to investigate genetic factors underpinning cancer evolution to improve diagnostics and therapeutics.

"I work on cancer and viruses. Both are complex and have high mutation rates. As a computational scientist, it's very interesting because there are a lot of computational challenges that can be investigated," Auslander comments.



She joined The Wistar Institute because of its reputation and expertise, particularly in researching both cancer and viruses. She shares her experience during her first year, "It's a small institute with a lot of opportunities to collaborate. It's a very good environment and people are very helpful and supportive."

Simultaneous to establishing and expanding her lab group, Auslander is currently looking into improving clinical prognosis to cancer and other diseases by uncovering unknown infectious agents and therapeutic biomarkers. To accomplish this, her lab applies the power of advanced computational platforms to very intricate and complex biomedical data to make these predictors of treatment responses more biologically interpretable. She says, "My main focus at the moment is to train my growing lab and develop frameworks to identify new viruses and eventually new microbiomes in cancer." ●

What's New and Next with BEAT-HIV

The BEAT-HIV Collaboratory is a consortium of more than 100 top HIV researchers working with nonprofit, industry, and government collaborators, to progress their experimentation of various immunotherapies for human immunodeficiency virus (HIV). The Collaboratory focuses on three goals: investigate how HIV hides in the body, strengthen the immune system against the virus, and develop HIV “killer cells” to combat the disease. Wistar’s **Dr. Luis Montaner** is a BEAT-HIV principal investigator and project leader and focuses his laboratory’s research on immune system-based studies toward an HIV cure.



“We want to broaden participation and accelerate the pace of research within and between research focus areas.”

LUIS MONTANER, D.V.M., D.PHIL.

Vice President, Scientific Operations and Associate Director for Shared Resources, Ellen and Ronald Caplan Cancer Center

The BEAT-HIV Annual Meeting was held in April of this year and brought together a true collaborative — with a total of 101 members from 41 institutions and 10 industry partners. Furthermore, this dynamic group published more than 100 member publications from August 2021 to April 2022. The meeting reviewed progress in basic and clinical research, including presentations from Wistar Drs. Montaner, Abdel-Mohsen, Kulp, and Claiborne. The consortium also discussed research priorities for the next year and positioning BEAT-HIV as a resource to promote community engagement and access to a new generation of HIV cure investigators. The meeting concluded with an independent program review by the Scientific Advisory Board (SAB). ●

Advancing Scientific Enterprise

WISTAR'S VACCINE & IMMUNOTHERAPY CENTER

With just over a year at The Wistar Institute under their respective scientific belts, innovator-scientists **Amelia Escolano, Ph.D.**, and **Daniel Claiborne, Ph.D.**, have been pushing the scientific envelope in Wistar laboratories using mouse models to pursue basic research and potential therapies for one of the toughest problems in medicine: HIV.

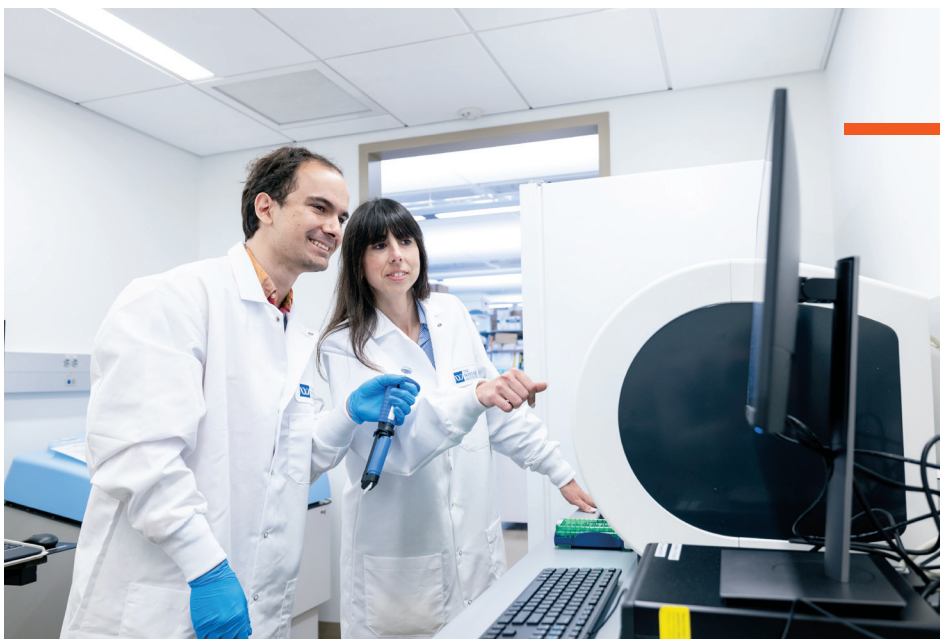
In line with the priorities of Wistar's **Bold Science // Global Impact** Strategic Plan to advance the scientific enterprise at the Institute, they are making their mark as the newest members of The Vaccine & Immunotherapy Center (VIC) at The Wistar Institute.

Escolano joined Wistar from Rockefeller University, where she was a postdoctoral fellow. With a background in inflammatory diseases, Escolano began her postdoctoral work focusing on vaccine design. There, she was one of the first researchers to use a mouse model called immunoglobulin knock-in mice for HIV vaccine research. Escolano's expertise with this mouse model, along with her experience developing sequential immunization protocols, make her a valuable addition to the VIC team.

A knock-in mouse is a mouse that has a specific DNA fragment inserted into a particular position on the mouse's genome. In the case of immunoglobulin knock-in mice, genes that make antibodies are inserted into the genome. Escolano and her lab then use the mice to test whether their immunogen designs — proteins that induce an immune response, like in vaccines — activate the mouse's B cells to produce those antibodies that fight disease.

"These mice are used to see how we can activate those B cells and how we can make them evolve to become broadly neutralizing antibodies," said Escolano.

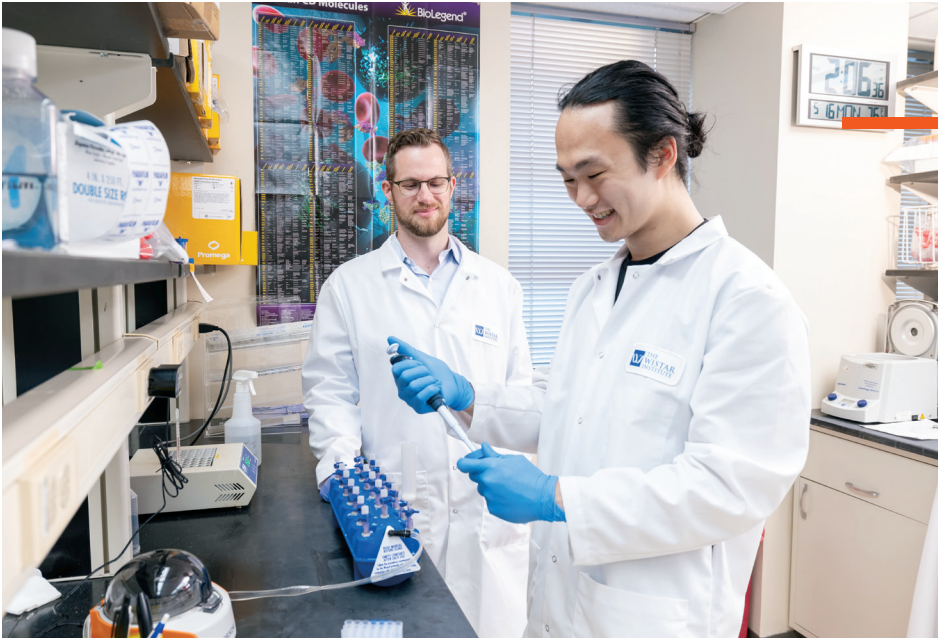
"Making antibodies evolve" is Escolano's area of research, specifically designing a sequential immunization protocol to induce neutralizing antibodies against HIV. Sequential immunization involves a first injection with one immunogen, then a subsequent injection with a slightly different immunogen, and so on. The purpose is to gradually introduce mutations on the antibodies which make them evolve to neutralize against HIV more effectively so that the result is a potent and broadly



“

"After my postdoctoral fellowship, I was looking for a place that was collaborative. I wanted to be in a top scientific environment where I knew people and I could interact with them easily. At Wistar, I found exactly what I was seeking."

AMELIA ESCOLANO, Ph.D.



“

“Wistar is building a diverse group that works well together. I think there’s a lot of purpose and intelligence behind how they’re building this group and I feel very lucky to be a part of it.”

DANIEL CLAIBORNE, Ph.D.

neutralizing antibody. This sophisticated form of antibody is necessary to combat HIV and other viruses that mutate quickly and form many different strains.

“Here at Wistar, I’m continuing my efforts to design these types of sequential immunization protocols and make them work in model systems and eventually in humans,” said Escolano.

Ultimately, she and her lab hope to answer the question of why some vaccines induce protection for years, while others only offer protection for months. With this knowledge, scientists will be able to design vaccines that induce protection for a long time — potentially even a lifetime.

Claiborne came to the VIC as a Caspar Wistar Fellow. This fellowship is awarded to early-stage investigators with outstanding research records who, as Claiborne puts it, “have unique angles on things.” His distinct expertise is using humanized mouse models to research T-cell dysfunction, specifically in pursuit of therapies that could cure HIV. “At the same time Wistar was just starting a humanized mouse program, I came in with knowledge on how to use that model well,” Claiborne shares.

In the context of vaccinology and immunology research, a humanized mouse is a mouse that is engineered to have a human immune system. Claiborne is a proponent of this model because it can be more readily translated to clinical settings. “I’m a basic scientist, but it’s always important to

think about how this is going to advance human health,” he said. “In humanized mice, you can use authentic strains of HIV, which facilitates the translatability of anything you’re doing that’s a therapeutic intervention.”

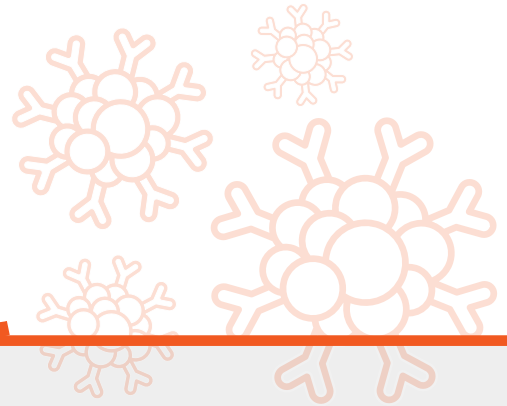
In his own research, Claiborne is using humanized mice to try to answer the question of how T cells, a type of white blood cell, become dysfunctional when they see their target over and over again, like in chronic HIV or cancer. “Functional exhaustion” turns off T cells and protects them from becoming overactivated — a state in which T cells could kill you. However, when it comes to certain therapies for HIV and cancer, such as CAR T-cell therapies, T cells that turn off ruin the efficacy of the treatment.

In CAR T-cell therapies, T cells are removed from a patient’s blood. Then, a specific receptor is added to the T cells that helps them find the target the patient’s body needs to fight. The T cells — now called “chimeric antigen receptor” or “CAR” T cells — are injected back into the patient. However, these cells are only effective as long as they continue to find and fight that target. Researchers found that when CAR T cells encounter the same antigen repeatedly and do not clear it, as with HIV, they self-regulate and turn off. Claiborne and his lab are investigating how this process begins.

“At the end of the day, we’re trying to figure out how T cells start to go down that path of functional exhaustion so we can stop that from happening,” said Claiborne. “That would have implications for all CAR T-cell therapies.” ●

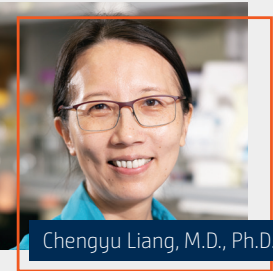
Melanoma

UNRAVELING THE ENIGMAS OF



Meenhard Herlyn, D.V.M., D.Sc.

Meenhard Herlyn, D.V.M., D.Sc., is known internationally as one of the fathers of melanoma research. As the founder of The Wistar Institute Melanoma Research Center, he has led the way with breakthrough discoveries about this mysterious and hard-to-treat cancer. A highlight of his work includes building Wistar's collection of patient-derived xenografts — a groundbreaking tool that allows tumor cells to be implanted into models for melanoma research.



Chengyu Liang, M.D., Ph.D.

Now, a new generation of melanoma researchers are building on that foundation. This up-and-coming-scientific force includes **Chengyu Liang, M.D., Ph.D.**, a rising star in studying how UV exposure damages cells.

"Dr. Herlyn is a great mentor and a great scientist," Liang said. "He established the platform, the foundation, that has been indispensable not only for Wistar melanoma research, but for the entire melanoma research field."

BUILDING A BETTER MODEL

"One of the guiding forces in our research has been to mimic human disease, to figure out what makes cells become cancer, and to use this knowledge for new strategies to develop therapies," Herlyn said.

One of these strategies involves the use of artificial skin. Lab-grown skin had previously been developed for wound healing. Using this existing technology, Herlyn pioneered its application to melanoma research. Herlyn's team was the first to use artificial skin to grow and study melanocytes — normal pigment cells — which they have used to understand how cancer cells form and how to make treatment more effective.

"We wanted to really know what tumor cells do, and to understand that, we first need to know what normal cells do and where the tumor cells come from," he explained.

Herlyn joined Wistar in 1976 and spent the early years of his career focused on developing monoclonal antibody treatments, a breakthrough drug that mimics or enhances the immune system's natural disease-fighting activity to attack cancer cells.

One of Herlyn's frequent collaborators during this time was his wife, Wistar scientist Dr. Dorothee Herlyn, who is now retired. "She was the immunologist of the family," he said. Together, they helped develop a number of monoclonal antibody molecules,

some of which are still used in cancer therapies today.

Herlyn is also behind Wistar's patient-derived xenograft program which supports a collection of patient cancer tissues. These samples can be implanted into genetically altered mice to more closely mimic conditions in the human body. It's a powerful tool scientists can use to conduct cancer experiments and test new treatments under conditions that more closely mimic the disease in humans.

"We now have more than 500 tumors from patients," Herlyn said. "These come directly from the patient and are implanted without ever being cultured, making them much more like real life tumors."

THE “SUNSCREEN GENE” AND MELANOMA

Dr. Liang didn't set out to study melanoma. Originally trained as a medical doctor, she became a research scientist with the mission of improving patient outcomes. Her drive to understand cancer and develop better treatments became more personal after her mother passed away following a two-year battle with cancer.

“When someone you love has cancer, you're trying to find answers. Why did this person have cancer? Why is this treatment not helping?” she said. “Eventually, that drove me to get my Ph.D. in medical science. I wanted to know more.”

Liang initially focused her research on tumor virology, studying how viruses cause cancer. During her research, she encountered a gene called UVRAG that piqued her interest in melanoma.

Previous work had found that this gene seemed to be involved in protecting skin cells from UV radiation, but the mechanism behind it was unclear. Liang's team showed how the gene repaired DNA damage from UV radiation, and that disrupting the gene could increase a person's risk of melanoma and other skin cancers. They nicknamed UVRAG the “sunscreen gene.”

The finding sparked many questions about how UV radiation causes genetic mutations that lead to cancer. “The question we asked is, ‘What makes melanoma melanoma?’” she said.

One thing that sets melanoma apart is its extremely high rate of genetic mutations — much higher than other cancers. “It's in the skin, which is where the body interconnects with

the environment and UV radiation, so in a way, that's not surprising,” she explained.

Liang's recent research has focused on identifying signs of DNA-repair deficiency as an early sign of damage that can trigger melanoma-driving mutations. “If we can find genetic signs that can predict this process, we might be able to catch the disease much earlier,” she noted.



“The question we asked is, ‘What makes melanoma melanoma?’”

CHENGYU LIANG, M.D., Ph.D.

CULTURING COLLABORATION

Herlyn not only laid the groundwork for Liang and fellow cancer researchers. He also serves as a leader and mentor who is generous with his knowledge and support, Liang said. “He's like a big dictionary of melanoma,” she described. “When you have a question, he can always share something instructive.”

This philosophy of collaboration, Herlyn shared, has been a driving force in his work. “One of the major strengths at Wistar has been our flexibility and our ability to look for

collaborators,” he pointed out. “My approach has always been to look for the best people I could work with.”

This has included a longtime collaboration with oncologists, pathologists, and other clinical colleagues at the University of Pennsylvania as well as other institutions. “I've always believed strongly in a good connection between the laboratory and the clinician,” he said.

Herlyn also helped found the Society for Melanoma Research, the first ever medical conference dedicated to bringing together researchers, clinicians, and patients to share knowledge about melanoma. Liang emphasized that with such a complex and unique disease, it's critical for scientists to work together to find new diagnostic tools and treatments.

“There's still a lot of mystery,” she stated. “Despite all the tremendous progress we have made in the melanoma field, I think we are still at the tip of the iceberg.” ●



Anne Schoemaker spoke to Wistar about her investment in Wistar science education and the creation of the *Hubert J.P. Schoemaker Education and Training Center* to build upon the values she shared with her late husband to inspire and mentor future generations of scientists.

Above, Anne Schoemaker with her late husband Dr. Hubert J.P. Schoemaker.

Inspiration, Mentoring, and a Philanthropic Commitment

You and your husband have had a rich history of supporting education and training. What do education and investing in future generations of scientists mean to your family?

Hubert never wasted a minute reinforcing his belief that education enables a life of possibility. There was no time in our family life that we did not discuss the importance of education around the dinner table. It was a value Hubert inculcated in our children through quiet discussion, sometimes raucous argument, and constant reinforcement. “With a good education, life is full of possibility; without one, your choices will be far fewer.” This quote, excerpted from a note he wrote encouraging one of our children to get on with their college applications, was a familiar refrain in our home.

As a youngster, Hubert was not an especially good student. In part due to his dyslexia, his performance in school was only average, and he showed no particular interest in science. His potential could so easily have remained untapped, and a brilliant intellect and keen scientific mind undiscovered but for an educational course correction that would change everything. As he began college, his passion for learning was set alight. He raced through his undergraduate degree at the University of Notre Dame and graduate studies at MIT in record time, his affinity for science fully revealed in the process. He credited the unleashing of his potential to the faculty and mentors who invested in him and the environment in which he was privileged to study. This experience heavily influenced the value he placed on mentoring young

scientists in the workplace and executives in industry, something for which he was well-known.

Education is the engine of possibility. It generates the spark that lights the flame, that creates the energy that fuels the imagination, and drives humanity forward. Hubert's scientific achievements and contributions to improving human health could easily have remained unrealized without the education and training he received. Our family is honored to help ensure that future generations of scientific leaders and their discoveries will not be lost, and that hidden talent, wherever it is found, can be encouraged to express itself fully. Frankly, there is no initiative to which Hubert's name could be attached that would have greater significance for him or us.

It's so wonderful that you are an alumna of Wistar and have consistently been involved with the Institute. What is special about Wistar as a place to create an education center?

Wistar has always lived at the cutting edge of translational science — long before that phrase became part of the biomedical lexicon. Its breakthrough discoveries in cancer, infectious diseases, immunology, and vaccine development and their impact on human health are clear examples of this ethos. At Wistar, the more traditional boundaries of basic scientific research have always been somewhat muted. Interdisciplinary collaborations occur spontaneously, and the environment for extending Wistar's excellence into other areas is fertile. Leveraging Wistar's intellectual capital to inspire, educate,

train, and mentor the next generation of technicians and scientists is an ambition that can be achieved here, and the growth of the biotechnology industry in this region and Wistar's planned expansion demands that we do so.

What goals do you have for the Hubert J.P. Schoemaker Education and Training Center?

Creating an education and training program at Wistar is not a new idea. Dr. William Wunner, seeing an opportunity to provide a path forward in science for young students—particularly those from under-represented populations—initiated the Biomedical Technician Training (BTT) Program at Wistar many years ago. This program and others developed subsequently, have inspired many students to pursue careers in science and graduate study thanks to the unique experiences they had at Wistar.

The success of BTT and other programs begged many questions: How might they be expanded to reach more students? How can they relate to one another? And how would both existing and new programs align with Wistar's mission and its role in the research community? The Center concept evolved into a holistic, all-encompassing vision for leveraging Wistar's intellectual capital to add broader value to the Institute, the City of Philadelphia, the scientific community, and the biotechnology industry. Creating a Center under whose auspices all education and training activities could be developed, enhanced, and expanded will unify and solidify Wistar's purpose in this initiative. Providing a continuum of

educational programs that address the needs of under-resourced students can create a pipeline of talent for the life sciences industry. From highly trained technicians to future researchers, it will support Wistar's growth and the regional economy. From Philadelphia to the far corners of the globe, the Center can provide education, training, and mentorship opportunities in ways that are unique to the Institute and take full advantage of its culture and scientific excellence.

What impacts do you think this Center will have on STEM education?

If we successfully develop programs along a continuum of educational needs and consolidate them within the Center, I believe it will significantly impact STEM education, certainly regionally. Under the exceptional leadership of Drs. Kristy Shuda McGuire and David Zuzga, the growing number of partnerships and collaborations cultivated over the past year alone would predict success. Further, the Center can export the programs it develops virtually anywhere, so the potential reach is unlimited in some respects. Whether high school, two-year college, or college programs oriented toward students who have been without access to career-building opportunities; doctoral programs; or postdoctoral fellowships for young scientists aspiring to bolster their career in research and run their own labs, the ways the Center's programs can support STEM education and provide training opportunities are numerous. ●

Supporting Science Across Borders with Student Exchange

Nestled in Northern Italy, the city of Bologna is one filled with medieval architecture, sprawling city squares, and a culture of scientific excellence. The University of Bologna is considered the oldest university in the western world and asserts a reputation as a leading institution for biomedical education in Italy and around the globe. In 2020, The Wistar Institute kickstarted a Ph.D. exchange program with the University of Bologna for budding scientists in cell and molecular biology. Exchange students travel to Philadelphia and complete their thesis over the course of three years at the Institute while being supervised by a Wistar principal investigator and immersed in a collaborative, supportive research environment.

Ilan Kirkel, an exchange student in Wistar's Gardini lab, who presented a research proposal to University of Bologna faculty and was invited to Wistar by **Alessandro Gardini, Ph.D.**, said, "I looked online, and it just seemed like the most unbelievable place with so many opportunities. I thought, 'Count me in! I'll see you in November!'" Ilan is currently researching biological machinery involved in regulating the process of transcription. Specific transcription complex subunits are potentially linked to the repair of DNA breaks, which is an important activity that affects the functioning of cells and Ilan seeks to understand these regulatory processes.

Exchange student **Davide Maestri** is working in the lab of **Italo Tempera, Ph.D.**, on understanding the mechanism underpinning Epstein-Barr Virus (EBV) latency in hosts. EBV latency could present differently in immunocompetent versus immunocompromised individuals and these differences could be linked to tumor formation, making the latency mechanism a potential effective target to treat EBV-associated tumors. "What attracted me to this exchange program was the possibility of incredible professional growth. I've always wanted to expand my "research horizons" to cancer research and genomics and after reading the projects that were ongoing in the Tempera Lab, I thought it would be a perfect match for me," Davide states.

An exchange student in the lab of **Rugang Zhang, Ph.D., Simona Lombardi** is focusing on the epigenetics of cancer. "I always dreamt about being a researcher and this program was the perfect opportunity for me to achieve my goal. I remember my joy when I found the lab that could best match me at the Institute," Simona recalls. Her Ph.D. thesis project is about investigating epigenetic alterations involved in endometrial cancer and revealing potential therapeutic targets for more effective cancer treatments.

Learning in a Creative and Nurturing Environment

Students in **The Wistar Institute and University of Bologna Ph.D. Exchange Program in Cell and Molecular Biology** have been in Philadelphia kickstarting their science. In addition to settling in and starting their research, these students have been immersed in an innovative atmosphere unique to Wistar that is focused on learning and career building.

"I feel academically liberated," Ilan divulges. "It's wonderful to be surrounded by so many driven and intelligent people. At Wistar, you can tackle problems from almost every single angle. For example, I just participated in Wistar's Life

"Day after day, I am more convinced that the choice I made for my Ph.D. program has been the best one. I believe that a Ph.D. is a fundamental step in our growth as researchers, and we must choose it carefully and find a place that nurtures and feeds our passion even more."

SIMONA LOMBARDI

Science Innovations course where we gave a 'shark tank' style biotechnology pitch to investors and it exposed me to the business side of life sciences."

Simona, who joined Wistar in late 2020, affirms, "Day after day, I am more convinced that the choice I made for my Ph.D. program has been the best one. I believe that a Ph.D. is a fundamental step in our growth as researchers, and we must choose it carefully and find a place that nurtures and feeds our passion even more."

Davide provides a perspective as one of the students who has been at Wistar the longest, adding, "I've been here a year and a half now, and this has been one of the best experiences in my life so far! I had the opportunity to work in close contact with highly competent and humble people who are always ready to help me with my experiments."

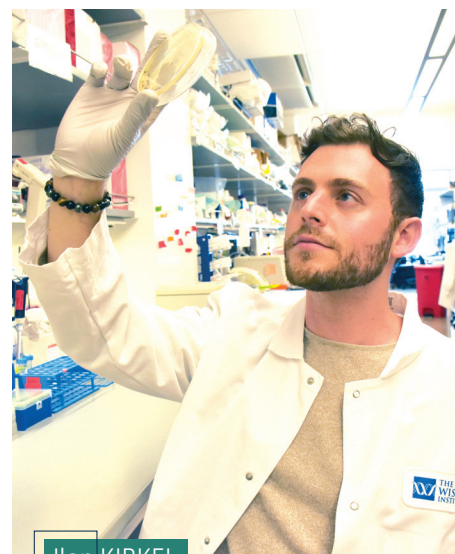
A Future of Internationally Reaching, Impactful Science

Looking forward, the exchange students will continue to craft their thesis projects and investigate the endless mysteries that the life sciences field poses to researchers.

Davide intends to pursue a career in academia. He details, "I still have another year and a half in front of me here at Wistar that I hope will be as scientifically stimulating as the first half of my exchange." After his thesis defense, he would like to remain in the U.S. and start a post-doctoral position. Simona is also planning on staying in the U.S. after finishing this program and pursuing her scientific questions even further. "I am determined to continue my career in the field of cancer research," she states.

"A Ph.D. crystallizes as time goes on," says Ilan. "Being at Wistar and seeing cutting edge research and utilizing state-of-the-art resources helped me realize I can do so much." He feels prepared to quickly move into an academic research position after completing his degree but is staying open to the diverse career opportunities to be pursued in the life sciences. "Three years is a bit of time for me to think and see what else I can accomplish."

With promising talent and a degree program that addresses the creative, collaborative, and global nature of successful STEM research careers, the Institute is excited to continue supporting these Ph.D. students as they discover, innovate, and impact. ●



Ilan KIRKEL



Davide MAESTRI



Simona LOMBARDI



Expanding Education at Wistar

The Wistar Institute is committed to investing in all stages of the STEM pipeline to allow for bolder research ideas and bigger scientific impact. These fruitful efforts are exemplified through the continued success of the Institute's education and training programs.

Through a PAsmart Grant awarded to Wistar by the Pennsylvania Department of Labor and Industry and a grant from the National Science Foundation, the **Hubert J.P. Schoemaker Education and Training Center** is on-ramping more students and collaborators to amplify the impact of Wistar programs on the Pennsylvania life science workforce.

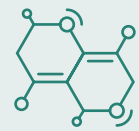
Particularly, Wistar's **Biomedical Technician Training Program (BTT)** has been accelerated into a single summer and is expanding to include students from community colleges across Philadelphia, Montgomery, Bucks, Delaware, and Chester Counties in Pennsylvania and Camden County in New Jersey. Between 2021 and 2024, the Center is increasing the BTT summer cohort from a dozen to over twenty participants. Additionally, Wistar will add more industry collaborators to host internships for BTT students after the completion of their two-week Wistar laboratory training orientation. In Fall 2022, the Center will also start a new BTT cohort for adult learners to enter the life science workforce.

With this expansion of the BTT Program, which serves as a state-registered pre-apprenticeship, Wistar will also increase the size of its **Fox Biomedical Research Technician (BRT) Apprenticeship** – the first non-traditional apprenticeship in biomedical research registered by the Pennsylvania Department of Industry and Labor. The Center will recruit new life science companies who will serve as pre-apprenticeship training sites and employers in the group apprenticeship. A potential high school pre-apprenticeship program is also being explored.

"In this growing Pennsylvania life-science industry, the talent pipeline is vital for cultivating the next generation of leaders in biomedical science," shared **Kristy Shuda McGuire, Ph.D.**, Wistar Dean of Biomedical Studies. "This is an opportunity that can only happen through diverse, inclusive education and training programs in collaboration with government and industry partners in the life-science sector." ●

2021 Stats from Wistar's flagship Biomedical Technician Training (BTT) Program

181



students have completed the BTT Program (**50%** underrepresented minorities and **70%** women)

64.4%



BTT students continued education and **46.3%** obtained related positions within 1 year of completing the Program.

100%



of 2021 cohort of accelerated BTT participants continued education and/or obtained laboratory positions

Fighting Breast Cancer Disparities Through Collaboration

A DECADE-LONG COLLABORATION BETWEEN WISTAR AND CHRISTIANACARE IS LEADING TO NEW DISCOVERIES AND BETTER TREATMENT FOR TRIPLE-NEGATIVE BREAST CANCER PATIENTS.



Dario C. Altieri, M.D., president, CEO, and director of the Ellen and Ronald Cancer Center at The Wistar Institute, and **Nicholas J. Petrelli, M.D.**, Bank of America endowed medical director of the Helen F. Graham Cancer Center & Research Institute at ChristianaCare, formed a collaboration between the two institutions that would expedite the pipeline of cancer interventions from bench to bedside.

"We had the patients, and they had the world-class science," said Petrelli. "We felt that this was a great opportunity between an NCI-designated, basic science, research center and an NCI community cancer center. This relationship is unique in cancer research."

This collaboration has yielded more than a dozen translational cancer research papers to date and advanced research discoveries made in Wistar labs into early clinical trials at ChristianaCare. One of the newest projects to come from this collaboration is a population health study on treating triple-negative breast cancer.

RESEARCHING TRIPLE-NEGATIVE BREAST CANCER

Triple-negative breast cancer is an aggressive form of breast cancer with few treatment options. It's more than twice as common in Black women as in white women, and Black women have a 40% higher mortality rate^[1,2]. These factors are what led **Zachary Schug, Ph.D.**, an assistant



Nicholas J. Petrelli, M.D., FACS

professor in the Molecular and Cellular Oncogenesis Program at Wistar's Ellen and Ronald Caplan Cancer Center; **Jennifer Sims-Mourtada, Ph.D.**, lead scientist and director of Translational Breast Cancer Research at ChristianaCare's Helen F. Graham Center & Research Institute; and **Scott Siegel, Ph.D., MHCDS**, director of population health research at ChristianaCare to join forces.

Siegel says, "Disparities in breast cancer are the result of multiple interacting factors operating at different scales, so if we're going to do something meaningful, we can't take a silo-based approach and focus on one key variable. We really do need to look across this spectrum."



Zachary Schug, Ph.D.

ALCOHOL AND BREAST CANCER

Schug, Sims-Mourtada, and Siegel share three intersecting research interests: breast cancer, health disparities, and investigating the connection between alcohol and cancer – truly *the* linking factor in the context of this project.

As a molecular and cellular biologist, Schug examines the problem of alcohol and breast cancer at the "smallest" level of the three researchers. His research has shown that breast tumors feed on a breakdown product of alcohol called acetate, which they use to grow and fight the body's immune responses. How and why the breast cancer cells use acetate in this way are questions Schug continues to pursue. However, it's important for him to make his work clinically meaningful as quickly as possible.

"Instead of just focusing on individual tumor cells and trying to do things at a molecular level, we wanted to ask more broad questions," Schug explains, "and that's where Scott and Jen come in with what they're doing."



Jennifer Sims-Mourtada, Ph.D.

GENETICS AND ALCOHOL METABOLISM

Sims-Mourtada is a translational breast cancer researcher who studies how gene expression regulates and alters the progression of breast cancer. Her work intersects neatly with Schug's because she is investigating whether race-based differences at the genetic level affect how many alcohol-metabolizing enzymes are produced in breast cancer stem cells.

"We have some data that show that a certain isoform of enzyme is overexpressed in tumors from Black women, and a possible reason for this could be some kind of genetic factor," said Sims-Mourtada.

Specifically, there are reports from alcohol use disorder research suggesting the existence of tiny genetic variations called single nucleotide polymorphisms (SNPs) that may be involved in alcohol metabolism. Sims-Mourtada is working on identifying SNPs that might cause an alcohol-metabolizing gene to become overactive or underactive in individuals of differing races which, combined with the individual's alcohol use, could increase tumor growth.



Scott Siegel, Ph.D., MHCDS

ALCOHOL-RELATED ENVIRONMENTS AND BEHAVIORS

Siegel looks at the problem of triple-negative breast cancer at a population level. His research focuses on identifying modifiable risk factors for cancer—i.e., whether people’s cancers can be affected by where they live and what they do.

“My contribution to this project is to collect behavioral data on patients. Then we can relate these variables to the processes Jennifer and Zach are looking at, including the enzymes that metabolize alcohol and ultimately the metabolites,” said Siegel.

In examining prevalence of triple-negative breast cancer within ChristianaCare’s home state of Delaware, he found that the areas that have the highest rates of this cancer also have the highest rates of alcohol use disorder and the highest density of alcohol retail stores. The collaboration will help to dig into the biology and genetics that may belie this correlation.

THE RESEARCH PROJECT

The researchers plan to recruit 1,000 women with breast cancer, 500 Black and 500 white. They will biopsy the women’s tumors, which Sims-Mourtada will use to examine differences in gene expression by race. They will also take blood, which Schug will analyze for levels of ethanol and acetate in order to assess the patient’s drinking level, as well as nutrients to get a sense of the patient’s diet. Finally, the researchers will collect extensive patient reported data – including lifestyle, environmental, and socioeconomic factors – which Siegel will assess to determine how the patient’s behaviors and environment relate to what is happening inside their body.

“I think it’s a unique approach to be looking at this multi-level analysis. We’re not just taking into consideration the neighborhood or the behavior, but how those influence what actually happens biologically and genetically,” said Sims-Mourtada.

IMPACTING PATIENTS, PROVIDERS, AND COMMUNITIES

At a patient level, the researchers are hoping to identify biomarkers that would not only indicate risk of developing triple-negative breast cancer but also help detect the cancer sooner than is currently possible via conventional methods.

“Triple-negative breast cancer may start earlier in life before mammography is recommended or develop between screenings. To be able to do a blood test the way one could do a cholesterol test for heart disease, maybe we can see cancer developing sooner,” said Siegel.

The researchers also want to uncover risk factors that healthcare providers can use to educate patients and steer them toward behaviors that match their individual risk level. Alcohol consumption won’t necessarily increase cancer risk for everyone. But it will for some, and those individuals should be informed. With just gentle nudges from a physician, simple changes in alcohol consumption

“

“We had the patients, and they had the world-class science. We felt that this was a great opportunity between an NCI-designated, basic science, research center and an NCI community cancer center. This relationship is unique in cancer research.”

**NICHOLAS J. PETRELLI,
M.D., FACS**

could save lives by reducing the probability of breast cancer in certain high-risk individuals.

At a community level, identifying where rates of risk for triple-negative cancer are highest could mean more targeted outreach. To be able to use public health resources in the areas where they could make the biggest impact could amplify effects on many lives.

A LASTING COLLABORATION

Wistar and ChristianaCare's joint efforts have repeatedly yielded a two-way benefit: basic scientists learn directly from clinicians about the issues clinicians are seeing at the bedside, and the clinicians learn from the scientists about the challenges scientists face as they are trying to solve problems in the quest for therapeutic solutions.

"We will be publishing in basic science journals, but we will also be changing how we practice in the cancer center, potentially how we do our community outreach, and possibly prevent loss of life as a result of this research," said Siegel.

"It really has been a special marriage made in heaven," said Petrelli, "and I see it continuing for a long time." ●

SOURCES

1. McCarthy, A. M., Friebel-Klingner, T., Ehsan, S., He, W., Welch, M., Chen, J., Kontos, D., Domchek, S. M., Conant, E. F., Semine, A., Hughes, K., Bardia, A., Lehman, C., & Armstrong, K. (2021). Relationship of established risk factors with breast cancer subtypes. *Cancer Medicine*, 10(18), 6456–6467. <https://doi.org/10.1002/cam4.4158>

2. Cancer of the Breast (Female) – Cancer Stat Facts. Chart Death Rate per 100,000 Persons by Race/Ethnicity: Female Breast Cancer. (2018). SEER. <https://seer.cancer.gov/statfacts/html/breast.html>

Wistar-ChristianaCare Spring 2022 Grand Rounds Seminars

This spring, Wistar hosted lectures for Wistar researchers featuring ChristianaCare physicians on the latest innovations in cancer care and treatments. This series helps promote creative collaboration between Wistar scientists and Christiana health care professionals. Below are highlights from three sessions that ran once a month during Spring 2022:

Lindsay B. Romak, M.D., Radiation Oncology, "Emerging Techniques in Radiation Oncology"

Dr. Romak walked the audience through the progress of radiation oncology methods that have been used to treat cancers. She suggested opportunities for future collaboration with Wistar investigators — specifically harnessing the Institute's expertise in cancer immunology — including how to optimize radiation's impact on the immune system by assessing different timings, doses, and tumor sites.

Mary V. Iacocca, M.D., Pathology, "Selected Topics in Pathologic Handling of Cancer Specimens"

Dr. Iacocca reviewed various methods to process cancer specimens, including histological processing and case studies involving flow cytometry, sentinel lymph node processing, tissue collection via next generation sequencing, and imaging breast specimens. Wistar researchers were able to compare Christiana's methods and how to best perform advanced procedures to deliver clinically relevant data.

Jamal G. Misleh, M.D., Hematology/Oncology, "Diagnosis and Treatment of Acute Myeloid Leukemia"

Dr. Misleh discussed different types of leukemia, recurrent genetic abnormalities and mutations in acute myeloid leukemia, diagnostic methods like bone marrow aspiration, and standard treatment options. He highlighted some challenges in treating this unique disease, which provides opportunity for collaboration with Wistar scientists to drive advancements in clinical medicine for acute myeloid leukemia.



INTERNATIONAL IMPACT

Global Voices for HIV Advocacy and Cure Research Come Together at Wistar's 26th Annual Jonathan Lax Lecture



The Wistar Institute continuously innovates ways of amplifying its global reach. From international research collaborations to educational and industry partnerships around the world, the Institute extends its impact across several countries. This year, The Wistar Institute hosted the Annual Jonathan Lax Memorial Award Lecture virtually, bringing together HIV scientists and activists on a global stage. Celebrating 26 years of continuous HIV research collaboration, the event was streamed on June 28, 2022, and saw attendees from North and South America, Europe, Africa, and Asia.

The event opened with a music video by Moses "Supercharger" Nsubuga, HIV Outreach and HIV Cure Research Advocate and musician from Uganda and the Stigmaless Band performing their song "Optimistic", setting a positive and engaging tone that reminded everyone of the work towards a common goal of HIV cures that prevent, control, and treat the virus.

The keynote speaker delivering the Lax Lecture was **Mike McCune, M.D., Ph.D.**, head of the HIV Frontiers Initiative and Biotechnology Accelerator Programs of the Bill & Melinda Gates Foundation, who emphasized the scientific progress toward curative interventions for HIV for all parts of the world. He highlighted efforts toward the development of gene therapies and "single shot" vaccine candidates and looking forward to clinical trials.

McCune shared his view of an ideal HIV cure: available in an outpatient clinic; given in one shot—like a vaccine—and durable for over three years; can prevent or control infection; and affordable for resource limited nations. Also, McCune mentioned creating an affordable home testing kit, similar to COVID-19 test kits, for people to monitor the disease.

McCune shared, "We need to have a long-term vision and we need to have steps along the way that show we're moving towards it."

The event also hosted a panel centered around the question "What does an HIV cure mean to you?". The global community discussion included Moses "Supercharger" from Uganda; Philister Adhiambo, Community Liaison Officer and HIV Cure Advocate from Kenya; and Michael Louella, Community Engagement Project Manager of the defeatHIV collaborative in the U.S. They all agreed that research can move forward if it prioritizes the community. Their strong perspectives came from the realities they see every day in their communities: participation in cure-directed studies, of being female with HIV/AIDS, living with HIV/AIDS in low- and middle-income countries outside the U.S., remaining on antiretrovirals for decades not knowing the toll it takes on their bodies, and stigmatized people that lost opportunities because they were HIV positive.

"26 years ago, we set out to make a difference in HIV/AIDS treatment strategies through the most cutting-edge research, done shoulder-to-shoulder with clinicians, advocates, and people living with HIV/AIDS in Philadelphia," said **Luis Montaner, D.V.M., D.Phil.**, Herbert Kean, M.D., Family Endowed Chair Professor, leader of the HIV Research Program at The Wistar Institute, and co-principal investigator of the BEAT-HIV Delaney Collaboratory. "Our program has now grown beyond the region and country to gain a network across the globe. Our mission hasn't changed, but we have grown into a global center to report the most groundbreaking HIV cure research together with community input."

McCune stated, "Now is the time to move forward. Solving these challenges is not going to happen overnight, but it's starting now."

FOLLOW US ON TWITTER
@TheWistarLIKE US ON FACEBOOK
Search "The Wistar Institute"CONNECT WITH US ON LINKEDIN
Search "The Wistar Institute"CONNECT WITH US ON YOUTUBE
Search "The Wistar Institute"**PANCREATIC CANCER IS
PRIMED TO BECOME AN
IMMUNOLOGIC DISEASE****Wednesday, September 14, 2022**
5:00 p.m. to 6:00 p.m.
*Virtual Event***WOMEN & SCIENCE HELEN
DEAN KING AWARD CEREMONY****"What the Sugar Coating on Your
Cells is Trying to Tell You"****Thursday, November 17, 2022**
5:00 p.m. to 6:00 p.m.
Virtual Event

LEARN MORE:

wistar.org/womenandscience**EDITORIAL STAFF****Darien Sutton**

Associate Director, Communications & Marketing

Chloe Tenn, M.S.

External Relations Science Writer

Markisha Evans

Digital Marketing Specialist

DESIGN BY IMOGEN DESIGN

COVER IMAGE BY JEFFREY TOTARO

The Wistar Institute is an equal opportunity/affirmative action employer. It is the policy of the Institute to provide equal employment opportunities to all individuals regardless of race, citizenship, ethnicity, color, creed, religion, marital status, national origin, ancestry, sex, age, veteran status, mental or physical disability (including HIV and AIDS), pregnancy, caregiver status, domestic or sexual violence victim status, sexual orientation, gender identity and expression, or on the basis of genetic information, or any other characteristic protected by federal, state, or local law, with respect to all terms and conditions of employment.

To contact the editor, call 215-898-3945 or email
comm-marketing@wistar.org.

Email kjohnson@wistar.org for address changes.

© 2022, THE WISTAR INSTITUTE

The Wistar Institute is a National Cancer
Institute-designated Cancer Center.