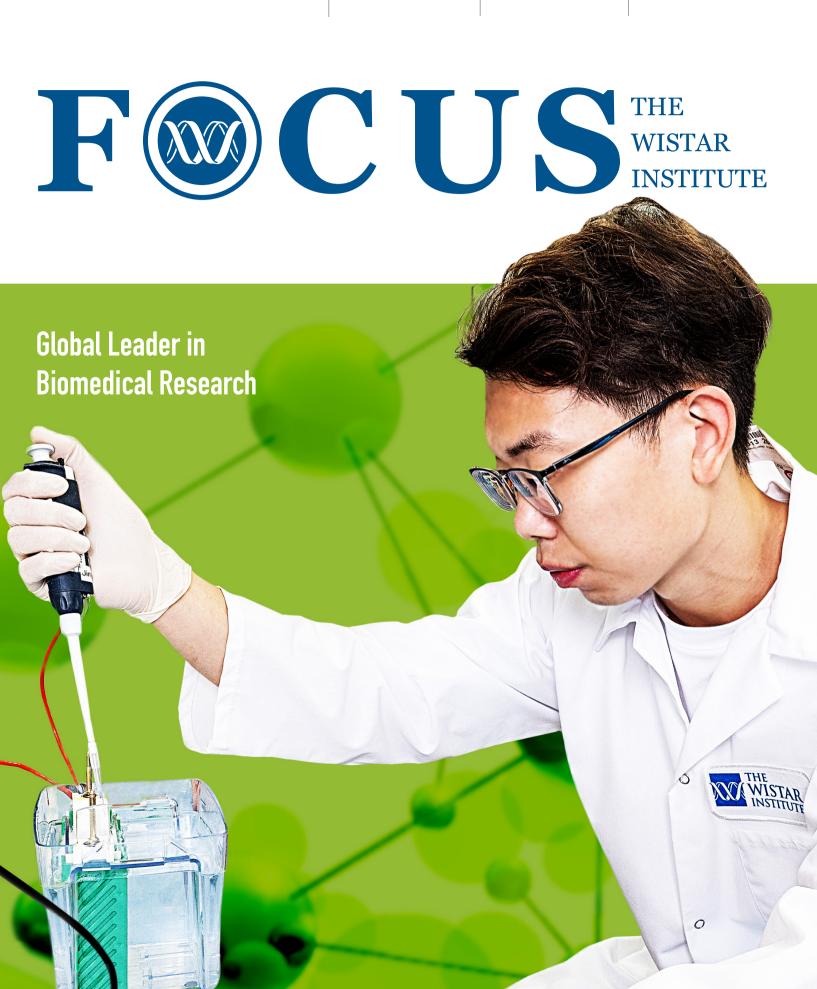
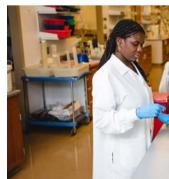
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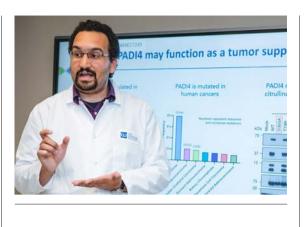












CEO PROFILE

Dario C. Altieri

RESEARCHER PROFILE

Up Close with Vaccine Researcher Amelia Escolano



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ACCOMPLISHMENTS

On the High-Risk, High-Reward High Wire:

How do you describe what you do to somebody who is not a scientist?

When I get in the car to drive to work in the morning, there are a few people in the car with me. There is a copy of me that is the scientist who does laboratory work. There is a copy of me that serves as an administrator, and there is a copy of me that leads other scientists. With all these iterations of me, one thing has remained constant: the passion to discover, the idea of a quest, the idea of asking questions and getting answers has always been a thrill.

Why do you think collaboration is so important to advancing the collective body of knowledge for Wistar scientists?

My professional interest is cancer research. Great progress has been made, but a lot of work remains to be done. I always say that there is no I in cancer research. There is only we. The problems are too complex. The disease is too diverse, so different, that none of us is smart enough to figure it out by ourselves.

What experimentation would make sense? What technologies do we want to bring to the table? For Wistar, collaboration is one of our core values.

Collaboration is about sharing, parking the egos outside of the building and coming to the table with humility. As scientists, we work better when we share ideas or concepts.

You have said this "once-in-a-century pandemic has taught Wistar the critical need to be nimble." How do you translate that lesson into specific action for the future?

Wistar remained open throughout the pandemic. I came to Wistar every day. We were designated by the governor as a life-sustaining business, and we were at the forefront. Think back to the end of 2020. That was the worst. We did not have vaccines. We did not have antivirals. Our testing was spotty at best, and we were being confronted with a completely new virus. The idea of being nimble was to turn on a dime, leverage 130 years of history in immunology and vaccine development, and



apply that to better understand what was going on with SARS-CoV-2.

As a result of that focus, Wistar scientists made a significant contribution. We have a vaccine candidate that is being co-developed with another vaccine platform. And we are advancing second-generation neutralizing antibodies against SARS-CoV-2. Wistar science helped show the world the inherent value of science for all of humankind. We should not waste this time. We need to reflect on what happened and how we can be better for the next one because the next one is coming.



People have said that Wistar science "punches above its weight" when you compare the size and scale of the organization with others. What do you attribute this to?

We are small when compared with the behemoths in our sector. Wistar includes 334 staff on payroll and 32 labs. What's Wistar's superpower? I think there are two. One is the freedom to discover. The scientists who come here have complete free range to ask why and pursue that why. They can study what they want. They can apply whatever technology they feel is relevant to solve one problem, to address one question. That generates innovation, and that is one very important aspect that makes us punch way above our weight. In the health sector, the SCImago Institution Rankings (SIR) places Wistar in the top 1 percentile for innovation

among the world's leading academic and research-related institutions. There's a reason we rank so high in innovation.

We are intentional about creating a culture of innovation. When scientists join Wistar, they can apply their curiosity, their desire to solve a problem in whatever project that they think is important. Nobody's telling scientists what to work on, how to do it, or what problem to solve. That's one aspect, complete freedom.

The other one is what we were discussing before, collaboration. Coming together in science multiplies the output and creates an incredible multiplier effect. It's always a lot more than the sum of the parts.

What does success in 2023 look like to you?

We just completed a five-year strategic plan that started in 2021. We are in the midst of a transformational philanthropic campaign. Every philanthropic donation, every dollar that comes into Wistar, goes to science.

In 2023, we continue on our path of attracting great scientists to Wistar, encouraging strong collaboration and inspiring our donors by sharing how their investment generates new knowledge that ultimately results in new cures.





Wistar assistant professor Dr. Amelia Escolano received the 2022 National Institute of Health's New Innovator Award and was chosen to join the 2022 cohort of Pew Scholars. Both highly regarded honors speak to the distinctive research she and her team have chosen to undertake and her innovative approach to pressing biomedical research challenges. The funding and resources will support her research pursuing novel vaccine approaches to viruses that mutate. This research will provide the basis to design universal vaccines for mutating viruses.

Viruses that rapidly mutate pose a significant global health challenge. These viruses are diverse with multiple variants, making it difficult for existing vaccination strategies to provide broad and long-lasting protection without boosters. Dr. Escolano intends

to enhance vaccines by designing novel sequential immunization protocols. Sequential immunization involves a series of injections with different immunogens, gradually introducing mutations to antibodies to help them neutralize broadly against viruses.

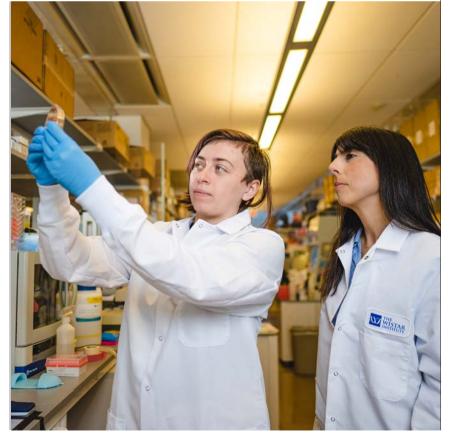
In conjunction with developing sequential immunization strategies, Dr. Escolano is tracking immune cell interactions upon repeated vaccination to help further fine tune universal vaccine success and efficacy. Ultimately, this research could translate into long term protection against some of the world's deadliest viruses and diseases that mutate frequently in humans, including HIV, influenza, and SARS-CoV-2.

With her focus on developing universal vaccines that adapt to mutating viruses, Dr. Escolano offered a glimpse into her life as a Wistar principal investigator.

What were some of the professional challenges you experienced running your own lab?

When I moved into the lab, I worried about recruiting people and equipping my lab. Getting a lab up and running takes immense planning. During my transition to Wistar I felt stressed, but I never felt lost. Wistar was very supportive in every way possible. I never felt I didn't know what to do or whom to ask for help.





What do you find most gratifying about your work here at Wistar?

I love the independence to decide what direction to take my research and how to handle it. I have the freedom to decide if and with whom I want to collaborate.

Things I like about scientific research are thinking, creating, coming up with new ideas, and placing your experiments in context with other innovative science. That's why I really enjoy the grant writing process – it is a moment for reflection and creativity. Now there are several very interesting projects running in the lab with great students working on them. I get to see the results, troubleshoot if necessary, and then discuss how to move forward. And that's a lot of fun. I also enjoy discussing science with other researchers to see how we can combine our skills, resources, expertise, and come up with new collaborations.





How would you describe your leadership style as a scientist?

My previous mentors and supervisors were very good to me and I'm trying to emulate that with my students. I say my door is always open. I hope they feel confident and comfortable about coming and sharing with me.

I want them to enjoy their work and inspire them to think outside the box because that's what a scientist does.

I encourage my students to spend time thinking about their results and what they mean and then come to me to discuss.

The views expressed are those of the author(s) and do not necessarily reflect the views of The Pew Charitable Trusts.

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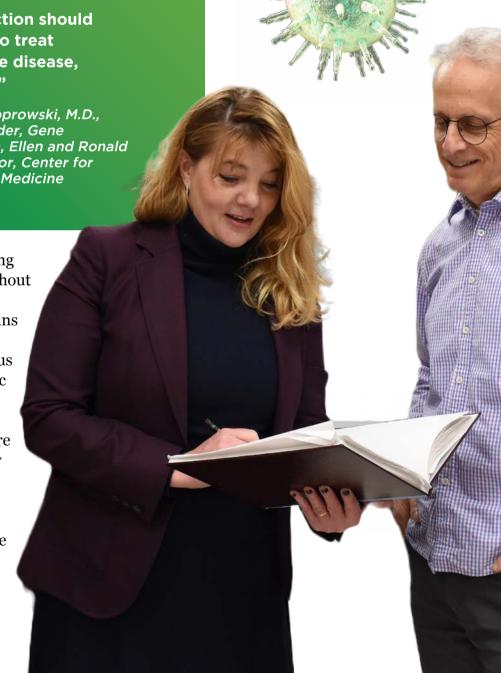
For the full feature go to wistar.org.

Linking *Epstein-Barr Virus*and Multiple Sclerosis

"Eliminating EBV latent infection should be a safe and effective way to treat EBV cancers and autoimmune disease, especially multiple sclerosis,"

- Paul Lieberman, Ph.D., Hilary Koprowski, M.D., Endowed Professor; program leader, Gene Expression & Regulation Program, Ellen and Ronald Caplan Cancer Center; and director, Center for Chemical Biology & Translational Medicine

Epstein-Barr virus (EBV) is a lifelong infection that affects people throughout the world. EBV targets the immune system's B-cells and typically remains silent in immune system memory cells. Though infection with the virus largely shows no symptoms, specific biological and environmental conditions can enable the virus to cause more serious diseases like rare cancers, which occur at particularly high rates in immunosuppressed individuals. Recent research found a connection between EBV and the neurodegenerative disease, multiple sclerosis (MS). We talked with Dr. Samantha Soldan, staff scientist in Wistar's Lieberman lab about how EBV can trigger MS and potential therapeutic solutions that can be developed with this knowledge.



What do we know about the progression of MS in humans?

Multiple sclerosis is a common disorder that causes damage to the protective covering around brain nerves, especially in young adults, and affects more than one million individuals in the U.S. alone. MS is often a disabling disease. The clinical progression of MS is variable and unpredictable with several distinct disease progressions.

In addition, studies have shown environmental factors (including EBV infection) that contribute to one's risk of developing MS often occur many years before clinical onset. Collectively, these complex interactions among genetic, immunologic, and environmental risk factors make identifying disease-contributing agents and designing preventative measures and effective therapies for MS very challenging.

How does EBV trigger MS? Can you explain these processes?

Today, we know very little about how EBV triggers disease in a small percentage of those who are infected. For MS and many autoimmune diseases, we can identify inflammatory and autoreactive immune responses and characterize immune responses to infectious agents and antigens that trigger an immune response in patients. However, understanding

Left: Samantha Soldan, Ph.D., staff scientist in the Lieberman Lab Right: Paul Lieberman, Ph.D. what sets immune cells on an autoreactive and inflammatory path before the patient is symptomatic is a difficult task.

There are several theories as to how EBV may be both a trigger and a driver of MS, and we believe it is likely that EBV is involved in the pathogenesis of MS.

What are some potential therapies that could arise out of understanding the role of EBV in MS?

In recent years, therapies depleting B-cells have proven to be tremendously beneficial in MS. While EBV primarily infects B-cells, these B-cell depletion therapies eliminate cells regardless of whether they are infected by EBV, making it difficult to determine if any of the clinical benefit derived from these drugs is related to their effects on the virus.

There are several EBV specific therapies in development that have the potential to present new, effective options for patients with MS. These include vaccines, cell-based immunotherapies, and EBV specific antivirals.

Where is Wistar research headed regarding MS and EBV?

We are working to better understand the role that EBV plays in the development of MS. Our current research focuses on characterizing virus-host interactions and maintenance of EBV latency in EBV infected B-cells from MS patients as compared to healthy patients. We are also testing EBV-specific antiviral therapies, including the EBNA1 inhibitor developed in the Lieberman lab, to determine its potential as a therapeutic agent for use in MS.

For the full feature go to wistar.org.

Dr. Heather Steinman Makes Maximum Impact

Heather A. Steinman Ph.D., M.B.A., joined The Wistar Institute as vice president for business development and executive director of technology transfer in October 2014. Dr. Steinman was hired into a newly created position to forge strategic partnerships with industry, nonprofit, and local academic institutions and advance Wistar's growing pipeline of biomedical research discoveries.

Dr. Steinman leads and oversees the implementation of Wistar's intellectual property strategy and all technology commercialization activities.

When you talk to non-scientists, how do you describe what you do?

I am the facilitator and translator of scientific discoveries into products through our partners, which include startup companies, entrepreneurs, biotech, biopharma, contract research organizations – anybody who's working in the life sciences space. Wistar works purely on biomedical research and cancer, infectious disease, and immunology. We look to see how we can move those findings outside of the laboratory into the realm of broader society.

As the translator, I work with our scientists and trainees to understand what they're working on in the lab – the fundamental biology for how a cell works, how cancer starts, how it progresses, how you can detect cancer, every

aspect of biomedical research. I try to help make the connection between what they're doing in the lab and what other companies or stakeholders in the life sciences arena are working on. I try to find out where there's synergy and where there's overlap between what we do on the basic research side and what companies do on the product development side to move something that might take 10, 15, 20 years to turn into a new therapy. It all starts from a Wistar lab, so I have the fun of seeing what people are working on and help break down any communication barriers that might exist between an academic scientist and an industry scientist and the whole life sciences chain.

What do you look for when you're pursuing a new strategic partnership?



I start with the scientist. Everything begins with what the scientist is working on and what they would like to do and how far they would like to advance their discovery. There might be instances where people really aren't interested in making a drug so they're not going to start a whole new drug discovery program. In that case, I'm going to look for partners that already have similar programs and might be a good fit. Quite honestly, if there's not a good fit between the scientist and the external party, nothing will come of your relationship.

Since you can't do science one-sided, there needs to be an exchange and a good relationship between the two. You want to make sure that there's a good fit between the personalities and

an alignment of interests. At Wistar, we tend to do everything that will benefit not only the scientists but help advance the program. It's customized. We can do that here.

Wistar takes great pride in being nimble. How does your approach to business development reinforce that strength?

Being nimble is an incredible asset that a lot of institutions lack. Here's the great advantage: imagine that in most places they're evaluating a technology and figuring out how that technology can be advanced to the next stage so it can be externalized in some way and further developed. You're normally limited to one particular discovery or project or asset within one investigator's laboratory, within a department, within a larger organization. At Wistar, at any given moment, I can look across the entire Institute and figure out how we can recombine or combine in new ways, different technologies, different platforms. We can make various combinations to advance our discoveries quicker even further.

We don't have the political barriers that a lot of organizations do. Everything is focused on collaboration, so all your time is spent on the science and figuring out how that science can advance. It is just so awesome to see in real-time how different investigators collaborating together can create new data that's going to help me figure out where it fits in the broader world.

I think that is really special, and people don't necessarily recognize that because we don't communicate it; we don't tell people how we go about doing things. You just see the end products of our licensing partners or startups and you hope that products will be there 15 to 20 years down the road.





Wistar Drs. Rahul Shinde and Mohamed Abdel-Mohsen are investigating the role the gut microbiome plays in cancer and infectious diseases.

The gut microbiome is a combination of microbes that may include bacteria and fungus and thrives in your gut. Below are some science snapshots of research published in 2022 by the Shinde and Abdel-Mohsen labs as they uncover answers from the gut by examining biological systems from the inside out.

"The successful outcome of this research may form the basis for gut bacteriabased therapies or diet-based therapies to improve the survival as well as the quality of life of pancreatic cancer patients."



Pursuing improved therapeutics for pancreatic cancer

Rahul S. Shinde, D.V.M.,
Ph.D., is working on
understanding the gut
microbiome and identifying
potential targets for cancer
therapies. He was recently
awarded the Pancreatic
Cancer Action Network Career
Development Award to drive
forward his foundational
research to inform potential
supplementary therapies for
pancreatic cancer.

In one of Dr. Shinde's recent papers, his team reported that a metabolite derived from a gut microbe called trimethylamine N-oxide (abbreviated TMAO) boosts immunity against tumors by triggering immune activation in pancreatic cancer. This study offers evidence that targeting TMAO production in the gut microbiome could improve the efficacy of immune checkpoint blockade (ICB) therapy for the disease.

Dr. Shinde says, "This study can create a new paradigm for discovering novel gut microbial metabolites influencing anti-tumor immunity and inform innovative treatment strategies for highly lethal and hard-totreat pancreatic cancer."

This work is supported by the NIH, the W. W. Smith Charitable Trust, the 2022 Pancreatic Cancer Action Network Career Development Award Grant Number "22-20-SHIN", the Tobin-Kestenbaum families, as well as the Caspar Wistar Fellowship Program at The Wistar Institute.

"The gut microbiome is being recognized as a very important contributor to overall health and conversely in association with many diseases. For long COVID, this is an opportunity to understand the disease and how gut microbial translocation is likely a major contributor of these symptoms."

Launching investigations into long COVID

Persistent, recurrent, or even new symptoms at least three months after acute COVID-19 infection can be called long COVID.

There are a lot of potential mechanisms that might be contributing to it, including microbial translocation – some disruption in the gut and/or the lung that leads microbes to translocate which causes inflammation.



In a recent publication, Dr. Mohamed Abdel-Mohsen, and collaborators looked at markers of microbial translocation and found that individuals with long COVID have a higher level of markers of gut barrier permeability and fungal translocation compared to individuals who are fully recovered. This level of fungal translocation correlates with more inflammation and a higher number of symptoms wherein this individual suffers from lower quality of life. They also found that this mechanism is targetable with a small molecule inhibitor. These new findings could be important in the development of treatments for the persistent, long-term effects of SARS-CoV-2 on the body. "Persistent and recurrent symptoms have also been reported for SARS-CoV-1, MERS, polio, and many other infections. Understanding mechanisms that contribute to this postacute infection sequela will be a very important factor moving forward for SARS-CoV2 as well as for a plethora of existing and emerging infections," shares Dr. Abdel-Mohsen.

This research was supported by The Campbell Foundation, Commonwealth of Pennsylvania COVID-19 funding, and the NIH.



For the full feature go to wistar.org.

Training Next Gen **Scientists**

Public-Private Partnerships Advancing Equity in STEM-based Careers

The Hubert J.P. Schoemaker **Education and Training Center** continues to broaden and expand focused programs that teach highdemand scientific skills for people interested in life science careers.

Wistar Launches Quality Science Pathway Certification Program

The Quality Science Pathway Apprenticeship (QSPA) is a no-charge certification program and provides onthe-job training and instruction for career opportunities in the biotechnology and pharmaceutical industries. Critical to various industry careers, quality science ensures that the safety and efficacy of life science products and outputs meet the sector standards and needs throughout the research and development cycle, including clinical trials and production stages. Wistar began accepting applications for their first class in fall 2022.



"The QSPA enables Wistar to meet its strategic education goals by creating an innovative public-private partnership that aligns workforce needs constraining the regional biotechnology industry with a novel STEM work-based learning and training model that provides career pathways to traditionally underserved populations – ultimately advancing diversity, equity, and inclusion in the life sciences."

- David Zuzga, Ph.D.

Associate Dean of Biomedical Studies

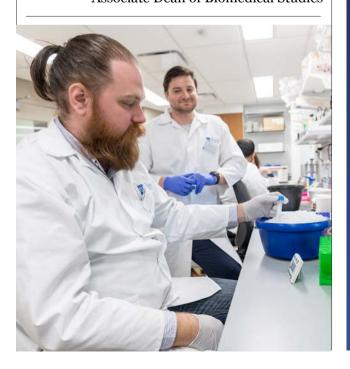
Undertaking Undergrads

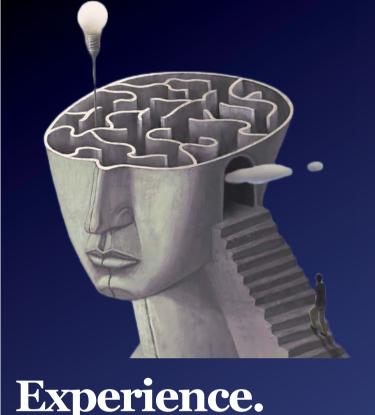
Starting in summer 2023, The Wistar Institute will launch its own National Science Foundation Research Experiences for Undergraduates (REU) Site, Understanding the Rules of Life: The Molecular Basis of Cellular Phenotypes. The REU program is actively recruiting students across the nation from underserved or underrepresented backgrounds and will provide them with an immersive laboratory experience and support to continue into successful life science graduate careers.

"This REU program will establish a national footprint. Our goal is that this REU becomes an ongoing Wistar program, raising the visibility of the collaborative graduate programs we offer. We want to see our participants pursue advanced degrees and perhaps return to the Institute for graduate training."

- David Zuzga, Ph.D.

Associate Dean of Biomedical Studies





Experience. Explore. Excite.

Do you ever wonder what happens inside a lab?

Here's your chance to wander through a Wistar lab. Wistar's Virtual Tours will take you through the tissue culture room tucked into a corner of Dr. Montaner's HIV research lab, to learning about the stateof-the-science advanced instrumentation Wistar scientists use. Throughout your journey, encounter various scientific topics as well as meet the ambitious researchers that propel Wistar science.

Welcome to Wistar!

To embark on a tour from the comfort of your computer or digital device, please visit: wistar.org/VirtualTours

Wistar 2022

This timeline summarizes some of the major accomplishments made possible by the dedicated and innovative scientists, staff, and donors committed to advancing biomedical research, early-stage discoveries and cures.

January

- Wistar and Stanford
 Medicine initiates a
 phase 2 clinical study of VK-2019
 in patients with Epstein-Barr
 Virus-positive nasopharyngeal
 carcinoma and lymphoma who
 have had their symptoms recur or
 progress following therapy.
- Wistar scientists publish in Nature Communications on a potential pathway for developing therapeutics that target Epstein-Barr virus
- Wistar scientist identified that damaged "ghost" mitochondria are found to drive tumor progression.
- Wistar hosts U.S. Assistant Secretary of Commerce for Economic Development Alejandra Y. Castillo for the announcement of a major national grant in support of locally driven STEM education programs.

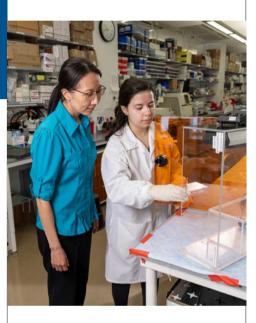
February

- A paper in the journal *Cell*Reports highlights work of
 Wistar scientists who developed
 a more targeted vaccine for
 SARS-CoV-2 that shows stronger,
 broader, and more durable
 protection in a single low dose. A
 key advantage of the novel vaccine
 is its potential to be stored at
 room temperature.
- Wistar researchers develop an immunogen that produces Tier-2 neutralizing antibodies, which may offer a promising step toward an HIV vaccine.



March

 Wistar's prestigious NCIdesignated cancer center is named the Ellen and Ronald Caplan Cancer Center recognizing The Caplan Family's \$10 million gift. It is one of only a few named biomedical research cancer centers in the country.



April

- Wistar receives a
 PAsmart grant from the
 Pennsylvania Department of
 Labor and Industry to on-board
 more apprentices and create
 additional pre-apprenticeships.
- Wistar scientists identified proteins in EBV-infected cells that decreased expression of genes linked to the spread of the virus, a fresh direction for EBV research.
- Wistar researchers identify a mutation associated with scarring of the lungs, revealing a useful diagnostic tool and target for gene therapy.

June

- Pennsylvania
 Department of Labor
 and Industry Secretary Jennifer
 Berrier and State Senator
 Vincent Hughes toured The
 Wistar Institute.
- Dr. Amelia Escolano, assistant professor in The Wistar Institute's Vaccine & Immunotherapy Center, joins the 2022 cohort of Pew Scholars.
- Wistar launches the Bold Science
 // Global Impact Campaign to
 rechart the future of health.
 Philanthropic support of the
 Campaign will fund the expansion
 of the Ellen and Ronald Caplan
 Cancer Center and the Vaccine &
 Immunotherapy Center, as well
 as the creation of a new Center for
 Advanced Therapeutics and the
 Hubert J.P. Shoemaker Education
 and Training Center.



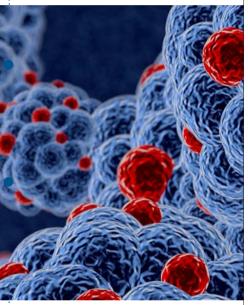
• Wistar scientists identified that inhibiting therapeutic target KDM5A re-activates an immune response against tumors.



- Wistar, a global center for conducting groundbreaking HIV research, hosted the first globalstreaming of Wistar's annual Jonathan Lax Award Lecture.
- Wistar receives a transformational \$20M gift from an anonymous donor to create a new Center for Advanced Therapeutics.
- SCImago Institution Rankings (SIR) ranked Wistar in the 1st percentile for innovation and in the 8th percentile for research. Wistar research teams published 103 collaborative manuscripts in journals on research and discoveries advancing the body of knowledge in cancer research, immunotherapy, and vaccines.



- A Wistar-led collaboration funded by DARPA and JPEO-CBRND advances to clinical trials. It is studying the rapid pre-clinical development of DNA-encoded SARs-CoV-2 monoclonal antibodies to prevent COVID-19.
- Wistar scientists reveal new function of enzyme ADAR1,



linking it to age-related diseases via a role independent of RNAediting during aging.

- Wistar director of operations Pete Scarpati is featured in *Blueprint* Vol. IV 2022.
- Wistar Institute Chief Financial Officer (CFO) Joseph Trainor, C.P.A., is chosen as one of the *Philadelphia Business Journal's* 2022 CFOs of the Year.





August

- NCI grants a Cancer
 Center Support Grant Merit
 Extension Award totaling more
 than \$5 million to The Wistar
 Institute's Ellen and Ronald
 Caplan Cancer Center.
- The Pancreatic Cancer Action Network announced that Rahul S. Shinde, D.V.M., Ph.D., received the Pancreatic Cancer Action Network Career Development Award.



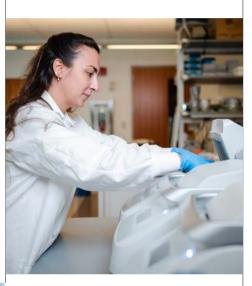
September

- Wistar researchers
 and collaborators
 at Jubilant Therapeutics Inc.
 discovered that inhibiting protein
 arginine deiminase 4 (PAD4) in
 neutrophils halts tumor growth.
- Wistar scientists identify key biomarkers that reliably predict response to immune checkpoint inhibitor therapy for melanoma.
- Wistar and ChristianaCare's
 Helen F. Graham Cancer Center &
 Research Institute mark a decade
 of collaboration to expedite the
 pipeline of cancer interventions
 from bench to bedside. The
 National Cancer Institute (NCI)
 describes the collaboration—the
 only one of its kind between
 an NCI-designated research



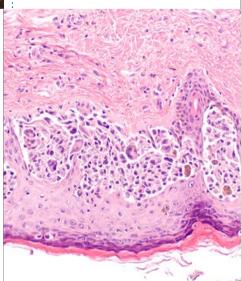
center and an independent academic community cancer—as "extraordinary and innovative."

• A \$1 million grant awarded by Pew Charitable Trusts now helps Wistar recruit a world-class researcher to lead the new Center for Advanced Therapeutics and put into use the Center's new drug discovery platform. Wistar scientists alongside national and international collaborators distinguish a specific gene signature indicative of mitochondrial reprogramming in tumors that correlates with poor patient outcome.



October

The National Institutes of Health honors Amelia Escolano, Ph.D., assistant professor in Wistar's Vaccine & Immunotherapy Center, with its 2022 Director's New Innovator Award.



 Think tank Heartland Forward ranks Wistar among top 3 in the nation for innovation, research, and tech transfer.

November

Wistar's 2022 Helen
Dean King Award is presented
to Nobel Prize winner Dr.
Carolyn Bertozzi of Stanford
University in recognition of her
outstanding biomedical research
on understanding how sugars that
coat our cells impact diseases.

December

The National Science
Foundation (NSF) granted
a Research Experiences for
Undergraduates (REU) grant to
The Wistar Institute's Hubert
J.P. Schoemaker Education and
Training Center totaling more than
\$400,000 for three years.





• The Wistar Institute's Biomedical Technician Training (BTT) preapprenticeship program was voted the BioBuzz 2022 Workforce Champion of the Year.



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2023, THE WISTAR INSTITUTE



WAITING IN THE WINGS...

Women & Science Virtual Event:

Tropical Medicine Catalyzing Equity in the Vaccine Sciences

Featuring distinguished speaker Dr. Maria Elena Bottazzi

Thursday, Apr. 27, 2023 5:00 p.m. to 6:00 p.m.

Dr. Bottazzi is an internationally recognized tropical and emerging disease vaccinologist, global health advocate, and cocreator of a patent-free, open science COVID-19 vaccine technology that led to the development of Corbevax in India and IndoVac in Indonesia – COVID-19 vaccines suitable for global access.



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