

FOX CHASE Forward

BROADENING THE CONVERSATION ABOUT CANCER | WINTER/SPRING 2022

*Artificial
Intelligence*

*Interdisciplinary
Research*

Epigenetics

*Nanoengineered
Stem Cells*

*From the Lab
to Patients*

Shaping the Future of Cancer Research

Fox Chase scientists are using cutting-edge
tools to advance cancer care



INVESTING IN OUR FUTURE

When I think about the future, I am excited about the possibilities. Fox Chase Cancer Center has long been a place of collegiality and collaboration, a place of discovery and delivery, a place I love. I know many of my colleagues share these same sentiments. But now we have opportunities before us that are potentially more life-changing than at any other time in my 30-plus years at this institution.

Our future will evolve through our commitment to outstanding science, our connection to our community, and our access to capital. We explore these themes in this special issue of *Forward*.

Compelling science has always been a cornerstone of Fox Chase. The discovery of the Philadelphia chromosome here provided evidence that cancer is genetic and led to the advent of targeted therapy. The identification

of the hepatitis B virus—a major cause of liver cancer—and development of the hepatitis B vaccine has saved millions of lives around the world. And the now-confirmed “two-hit” theory of cancer causation predicted the existence of tumor-suppressor genes that can restrain cancer cell growth. These milestones and many more make Fox Chase a national leader, and we continue to forge on.

In 2022, our researchers are using artificial intelligence to more accurately predict the 3D structures of proteins—a primary target for many drugs. We are employing nanoengineered stem cells to improve cancer drug delivery to increase the specificity and effectiveness of drug therapies. We are expanding the use of immunotherapy—a new frontier in cancer treatment that is helping patients for whom chemotherapy and radiation no longer work. While highly effective for some patients, many others have not responded to this new therapy. We are working to find out why, and to increase the number of patients who can benefit from it.

We are also studying the tumor microenvironment to better understand the relationship between cancer cells and the non-cancerous cells around them. These non-cancerous cells can provide nutrition to support cancer cells while deterring the body’s immune system from doing its job. We are exploring ways to interfere with how the microenvironment promotes cancer growth.

At the same time, we are engaging with our community to address health disparities and barriers to care, to understand why some groups are predisposed to certain cancers and have greater incidence and mortality rates, and to provide critical screening and education. We are also mentoring the next generation of scientists, reaching out as early as high school.

Backed by Temple University Health System and propelled by our own momentum, we are investing in our future: with funding, technology, equipment, infrastructure upgrades, and sheer dedication.

All of these things make this time exciting. With the talent and selfless commitment to excellence of our people—and the resources we now have—the future is ours.

I can’t wait to see what’s next.

Jonathan Chernoff, MD, PhD
CANCER CENTER DIRECTOR

FOX CHASE Forward

WINTER/SPRING 2022



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 of Fox Chase. One of the leading cancer research and treatment
 centers in the United States, Fox Chase was founded in 1904 as
 one of the nation's first cancer hospitals, and was among the
 first institutions to be designated a National Cancer Institute
 Comprehensive Cancer Center in 1974. Fox Chase joined Temple
 University Health System in 2012.

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FOX CHASE, WISTAR ANNOUNCE PHASE 1 CLINICAL TRIAL OF NEW ANTICANCER DRUG CANDIDATE

Fox Chase Cancer Center has opened an investigator-initiated, phase 1 clinical trial to evaluate the safety and efficacy of gamitrinib in patients with advanced cancer. Gamitrinib is a first-in-class, mitochondrial-targeted inhibitor of the molecular chaperone heat shock protein-90 (HSP90) that works by inhibiting tumor cell metabolism and survival.

Gamitrinib was developed at The Wistar Institute, an international biomedical research leader in cancer, immunology, infectious

“This innovative new trial of gamitrinib provides additional hope to our patients and is currently accruing.”

—ANTHONY J. OLSZANSKI, VICE CHAIR OF CLINICAL RESEARCH

disease, and vaccine development, and the two Philadelphia institutions are collaborating to bring this potential new therapy to patients.

The study is a single center, open-label, phase 1 clinical trial of weekly intravenous gamitrinib administration. It is designed to enroll 18 to 36 patients. The primary goal of the study is to determine safety and tolerability. It will be complemented by analyses to determine how gamitrinib is metabolized in humans, assess biochemical evidence of target engagement, and gauge early efficacy signals.



Anthony Olszanski is the principal Fox Chase investigator for a new drug trial being conducted with the Wistar Institute.

Anthony J. Olszanski, director of the Phase 1 Development Therapeutics Program and vice chair of clinical research at Fox Chase, is the principal investigator on the gamitrinib trial. “This innovative new trial of gamitrinib provides additional hope to our patients and is currently accruing. Gamitrinib represents an exciting new approach to treat cancer when other treatment options have been exhausted. We hope to make progress in this very first step toward a promising

new treatment for patients with advanced cancer, where there remains a high unmet need for new, effective therapies,” said Olszanski.

The laboratory of Dario C. Altieri, Wistar president and CEO, and director of the Ellen and Ronald Caplan Cancer Center, designed and developed the new drug candidate for clinical use. “It is a humbling moment to see what started as a research tool advance through preclinical development and now reach our patients.”

CRUCIAL ROLE FOR COMMON BRAIN TUMOR PROTEIN

Findings from a study conducted at Fox Chase Cancer Center could help pave the way for more effective treatment of aggressive brain tumors, researchers say.

The work was conducted by a team led by Zeng-jie Yang, an associate professor in the Cancer Signaling and Epigenetics research program. The project focused on glioblastomas, which are very malignant brain tumors for which treatment options are limited.

The most promising finding is that reducing nestin, a common molecular marker in cancer cells, in glioblastoma cells made them more sensitive to a particular class of drugs that disrupt proteins called tubulins. Yang's lab is currently working towards a method to target nestin, which would make these tubulin drugs more effective in treating glioblastomas.

Reducing nestin, a common molecular marker in cancer cells, in glioblastoma cells made them more sensitive to a particular class of drugs that disrupt proteins called tubulins.

Yang's team found that nestin is present at very high levels in glioblastomas. Yang, who is also a neurosurgeon, believes this research, which was published in *Molecular Cancer Research*, has immediate implications for

treatment. "During diagnosis, if a pathologist finds the tumor cells highly express nestin, it may mean that these cells are more resistant to the tubulin drugs, or conversely, if they do not express nestin, they may be more susceptible to the drugs," Yang said.

The collaborative environment at Fox Chase was instrumental in the success of this project, Yang said. Although his group found that they could prevent the growth of glioma cells by reducing nestin, the specific cause of this slowed growth was initially a puzzle.

That is until Tim J. Yen, a professor in the Cancer Signaling and Epigenetics research program, helped identify the molecular defects present in the nestin-deficient cells. With Yen's help, the team found that these cells did not properly form spindles, which are tubulin-derived structures that control cell division. The research team further demonstrated that nestin interacts with tubulins in this spindle, which led to the discovery that nestin makes glioblastomas sensitive to tubulin drugs.



STUART BRIERS

USING LIQUID BIOPSIES TO STUDY GENETIC VARIANTS IN BREAST CANCER TUMORS

In a study using liquid biopsies and tumor tissue biomarkers, researchers at Fox Chase Cancer Center found that PARP inhibitors and PD-1/PDL1 blocking immunotherapy could be considered an effective treatment in eligible inflammatory breast cancer patients.

Liquid biopsies, such as blood from cancer patients, have been used to study the genetic profile of primary tumors. Liquid biopsies

“The continuing study of liquid biopsies is very important because this is a noninvasive method that allows patients who cannot receive a standard biopsy to still have these genetic tests performed.”

—SANDRA V. FERNANDEZ,
BREAST CANCER TRANSLATIONAL
RESEARCH DISEASE GROUP

are much less invasive than specimens attained through tissue samples taken from tumors. They can provide information on the tumor, such as potential circulating tumor biomarkers, including cell-free DNA (cfDNA). Studies are ongoing to improve the sensitivity of this tool using high throughput next-generation sequencing.

“The patients we studied were in stages III and IV of inflammatory



breast cancer. We looked at the genetic variants of cell-free DNA, and we found a good match with the genetic variants we find in the tumor tissue,” said Sandra V. Fernandez, a research faculty member in the Breast Cancer Translational Research Disease Group at Fox Chase.

Fernandez conducted the study with a team of researchers at Fox Chase and other institutions and it was published in the *International Journal of Molecular Sciences*.

This work builds on previous studies at Fox Chase showing

that genomic profiles measured through cfDNA in the blood of breast cancer patients may provide a more effective way to track and treat cancer.

“The continuing study of liquid biopsies is very important because this is a noninvasive method that allows patients who cannot receive a standard biopsy to still have these genetic tests performed. It gives us the chance to observe genetic variants in these patients and identify the right treatment for specific mutations,” said Fernandez.

Shaping *the* Future of Cancer Research

Fox Chase scientists are using cutting-edge tools to advance cancer care



Fox Chase Cancer Center has a long history of groundbreaking research into the prevention, detection, and treatment of cancer, work that continues in 2022. Scientists at Fox Chase are harnessing a variety of cutting-edge tools and techniques—artificial intelligence, epigenetics, and nanoengineering, to name a few—to continue to unravel the inner workings of cancer.

This research is being facilitated by a renewed focus on interdisciplinary work involving faculty at Fox Chase and the Lewis Katz School of Medicine at Temple University. Fox Chase is part of the Temple University Health System. That synergy was underscored last year when Erica Golemis, Deputy Chief Science Officer at Fox Chase, was named chair of the newly created Department of Cancer & Cellular Biology at the Katz School of Medicine.

BY MARIAN DENNIS

ILLUSTRATIONS BY JACEY • PHOTOGRAPHY BY JOSEPH V. LABOLITO



“Dr. Golemis’ appointment is significant as we move toward greater integration with Temple Health,” said Jonathan Chernoff, Cancer Center Director at Fox Chase. “The formation of the Department of Cancer & Cellular Biology will help us to bring together researchers with associated interests and expertise from across the health system, capitalize on our strengths, create synergy of efforts, increase funding, promote diversity, and ultimately, raise the national profile of this program and our institutions.”

Fox Chase has long been focused on so-called bench to bedside approaches that implement basic research and bring it to the clinic to ultimately improve the lives of patients. This special section focuses on the groundbreaking work of just a few of the scientists at Fox Chase and Temple, work that will continue to change how cancer is prevented, detected, and treated.

Using Artificial Intelligence to Develop New Drugs

The Fox Chase Molecular Therapeutics research program has always embraced its mission to generate laboratory and clinical insights that improve the treatment of cancer, increase its effectiveness, and reduce treatment-associated morbidity. The program does this through a two-fold system of precision analysis of proteins associated with cancer and early and late-stage clinical trials.

With this in mind, the program has begun using a

new artificial intelligence technology called AlphaFold2 that was developed by DeepMind, a scientific discovery company. DeepMind is part of Alphabet, the parent company of Google. AlphaFold2 allows researchers to more accurately predict the 3D structures of proteins, one of the primary targets for, and a crucial ingredient in, many drugs.

“What DeepMind did is develop a deep-learning algorithm, a mathematical and computational algorithm that takes huge amounts of data and uses it to make predictions. The most common use for this is image recognition,” said Roland Dunbrack, director of the Molecular Modeling Facility.

Dunbrack said DeepMind has trained a neural network to take all of the 3D structures of proteins in the Protein Data Bank—about 180,000 structures and their sequences—and output a predicted structure of the protein in the form of three-dimensional coordinates.

“AlphaFold has been really transformative in two ways,” said John Karanicolas, co-leader of the Molecular Therapeutics research program at Fox Chase and director of the Moulder Center for Drug Discovery Research at the Temple University School of Pharmacy. “It used to be the case that if we were interested in the structure of some protein that had not yet been experimentally determined, we could make some predictions if it was very close to the structure of a protein that we already knew.”

AlphaFold, however, provides much more confident predictions about protein structures, Karanicolas added. “Instead of confidently knowing the structure of maybe a quarter of all human proteins, now we know the structure of about half or two thirds.”

In addition to allowing researchers to predict more structures, AlphaFold also has a 90% accuracy rate, as opposed to about 60% accuracy for predictions done manually, Dunbrack said. With the use of this technology, the Molecular Therapeutics Program can better assist researchers studying particular proteins.

Karanicolas said DeepMind provided the structures for many monomeric proteins, which are solo proteins, but it doesn’t give insight into how those proteins interact with one another. “By using AlphaFold ourselves, we can make predictions for how individual pairs of proteins can associate with one another—shedding light on their function—which could potentially lead to novel therapies.”



Swayam Prabha is investigating the use of nanoengineered stem cells to improve the effectiveness of cancer drugs.



Cihangir Duy is working on tools that could be used to attack dormant leukemia cells.

Nanoengineering Stem Cells to Improve Drug Delivery

When it comes to treating patients, every step of the process must be considered in order for a therapy to be effective. For example, without a feasible delivery method, a new drug can be rendered nearly useless.

Swayam Prabha, an associate professor of Cancer and Cellular Biology at the Katz School of Medicine, has been focusing her efforts on developing novel drug and gene delivery approaches to fulfill unmet needs in therapy, specifically through the use of nanoengineered stem cells.

Nanoengineering refers to the use of stem cells on the nanoscale, which is used to measure some of the smallest objects—one nanometer is one billionth of a meter. Over the last two decades, nanotechnology has been investigated for potential applications in the detection, diagnosis, and treatment of cancer and other conditions.

“My research is heavily focused on enhancing the specificity of cancer drugs. What happens with these drugs is that they are exposed to normal cells as well as tumor cells, which we are trying to avoid. So we use these ‘drones’ called mesenchymal stem cells,” said Prabha, who is also a member of the Molecular Therapeutics research program at Fox Chase.

Mesenchymal stem cells exist in almost all tissues and can be isolated from the bone marrow or fat tissue of patients. They can be successfully expanded in the lab, making it possible to use the patient’s own mesenchymal stem cells for treatment. Clinical-grade mesenchymal

stem cells are also commercially available. Prabha said this combination of individualized stem-cell therapy and state-of-the-art drug formulations fundamentally differs from currently used chemotherapy.

Prabha has published work showing that mesenchymal stem cells can be used for tumor-specific delivery of small molecular weight anticancer drugs by using nanoparticle-encapsulated forms of the drugs. Tumor-targeted drug delivery, she said, has the potential to improve how effective a cancer drug is and minimize its effect on the rest of the patient’s body.

“We were among the first ones to report from our study that these mesenchymal stem cells are actually working as Trojan horses and can sense and seek out tumors, delivering the anti-cancer drug just to the cancer. This not only reduces the side effects but also improves the effectiveness while only using low doses of the drug,” she said.

Prabha added that she and her colleagues have shown this approach to be very effective in lung tumor models in

“Basic research is fundamental to new drug discovery, because without it, our current study would not be where it is.”

—SIDDHARTH BALACHANDRAN
BLOOD CELL DEVELOPMENT AND FUNCTION
RESEARCH PROGRAM

mice. She is currently working on translational approaches to bring this new treatment method into the clinic for use in patients.

Prabha also initiated a new project to investigate a combination of radiotherapy and targeted delivery of nanoengineered agents to stimulate the immune system to fight cancer with Erica Golemis, Deputy Chief Science Officer; Hossein Borghaei, chief of the Division of Thoracic Medical Oncology; and Joshua Meyer, vice chair for translational research in the Department of Radiology, at Fox Chase. “We are excited about this work because it has the potential to overcome tumor-induced immunosuppressive mechanisms and result in improved treatment outcomes for patients diagnosed with lung cancer.”

Prabha and colleagues recently received \$500,000 in funding for two years from the Temple University Office of the Vice President for Research Catalytic Collaborative Funding Initiative to expand her work to involve more Fox Chase researchers.

Making Cancer ‘Catch’ *the* Flu

Fox Chase’s mission has always been to prevail over cancer through pioneering research, which is why scientists at the center are often examining biological processes outside of cancer for links that may lead to new therapies to treat the disease.

Siddharth Balachandran, co-leader of the Blood Cell Development and Function research program, is no stranger to this kind of work. Balachandran has been conducting research on viruses—specifically the influenza virus—and has uncovered what could be a potential therapy for patients with cancer.

When influenza infects the cells of the airways and the lungs, some of those cells die off and are replaced with new cells. More virulent strains of influenza, such as avian flu,

can cause a more severe form of cell death called necroptosis in which the cell ruptures, prompting a very potent immune response, Balachandran said.

His lab is particularly interested in how viruses such as influenza activate necroptosis. They are studying how necroptosis functions during acute viral infections to control pathogen spread and how this type of cell death can be leveraged for cancer immunotherapy.

“Immunotherapy is truly the next frontier in cancer treatment, and many patients who were unresponsive to chemotherapy and radiation are now responding to immunotherapy. The problem is that about 70% of patients still will not gain any lasting benefit from immunotherapy,” said Balachandran. “So the big question is, ‘How do we convert that 70% who are unresponsive to immunotherapy to being responsive?’”

Balachandran said these patients are not responding to immunotherapy because their immune systems do not recognize cancer as something dangerous and in need of eradication. He said an emerging idea is to find a way to selectively activate an inflammatory response within the cancer so that the immune system sees it as dangerous and responds appropriately.

“What we have fortunately stumbled upon in our lab is this highly inflammatory form of cell death that influenza activates. We came up with the idea that perhaps mimicking an influenza infection within a tumor might trick the immune system into now seeing the tumor as dangerous and in need of elimination,” said Balachandran.

His team is poised to publish a study describing the identification of a compound which does exactly this. The compound is an influenza mimetic, so it turns on a strong immune response when injected into tumors, enabling the host immune system to eradicate the tumor when paired with immunotherapy. Balachandran said the outlook for moving this study into clinical trials is positive because the compound tested is already being used in humans and has a well-established safety profile.

“The immediate translational potential of this work is an important aspect. Additionally, the odds of finding a compound like this in an average screen, where you’re simply looking for a compound capable of making immunotherapy work in the 70% of patients whose immune systems require such help, are close to zero. This is because you simply don’t know what to look for unless you’ve figured out how the immune system works in the first place,” said Balachandran.

“Without our prior research in the areas of viral infections, we would not have discovered that viruses activate necroptosis, and we therefore wouldn’t have been able to identify a compound which mimics virus infections and triggers on-demand necroptosis within tumors. In short, basic research is fundamental to new drug discovery, because without it, our current study would not be where it is.”

“Understanding epigenetic mechanisms *will* help us inform physicians on how to use new combinations of drugs *and* which drugs they may want to consider for certain patients.”

—JOHNATHAN WHETSTINE
DIRECTOR, CANCER EPIGENETICS INSTITUTE



Siddharth Balachandran is studying ways in which a compound that mimics a form of cell death activated by the influenza virus could be used to attack cancer.

Harnessing Epigenetics for Detection and Treatment

In 2021, Fox Chase furthered its already strong commitment to specialized research with the creation of the Cancer Epigenetics Institute. Epigenetics is used to understand how cancer cells react to their environments and discover ways to control those reactions. This new group is creating a locally based national hub for epigenetics study and collaboration, with a focus on reducing the morbidity and mortality associated with cancer by exploring biomarker research and therapeutic interventions.

The institute is headed by Johnathan Whetstine, who has already made discoveries that have expanded the field and have significant implications for understanding tumor variations and drug response. He also recently received a NIGMS R35 established investigator award for his contributions to understanding how epigenetics alters how DNA replicates and produces amplified oncogenes, which influences drug response and patient outcomes.

“Understanding epigenetic mechanisms will help us inform physicians on how to use new combinations of drugs and which drugs they may want to consider for certain patients,” said Whetstine. “If you know how to control epigenetic mechanisms or know how to look at these functions, you can determine if it’s been broken in tumors and how to leverage these insights into epigenetics to better use immunotherapy, conventional chemotherapy, and to leverage novel drug combinations.”

To further research on epigenetic mechanisms, the institute has recruited rising figures in the field, including Lu

Chen and Cihangir Duy, both of whom have made impressive strides in epigenetics research. Chen’s current role at Fox Chase involves research on how molecular details underlying RNA structure, localization, and modifications can be harnessed to combat cancer and other aging diseases. His lab currently focuses on the noncoding RNA component of telomerase—the “immortalization enzyme” for about 90% of cancers—and an aging hallmark whose dwindling level in stem cells contributes to stem cell aging.

Duy, whose work includes identifying drug survival mechanisms for new therapies, has been recognized with the W.W. Smith Charitable Trust Award as well as the V Scholar Award for promising research on the role of DNA methylation, a type of chemical reaction, in dormant leukemia cells. “There is an urgent need to understand the relapse mechanism in acute myeloid leukemia and the development of targeted treatments to improve outcome,” Duy wrote in a recent study.

In that study, Duy and colleagues found that leukemia cells that survive chemotherapy enter a dormant stage in which they stop growing and are able to recover from the stress produced by chemotherapy, allowing cancer to re-emerge. It was previously believed this stage was irreversible, but Duy said his team has uncovered more evidence of how this mechanism works, which could eventually lead to the development of targeted treatments.

“Chemotherapy mainly acts on proliferating cells; these dormant cells are protected from this chemotherapy. What we found was that these cells are simply in a senescent-like stage and are actually able to recover from this state. When they do, they become more aggressive,” Duy said in an interview.

“Senescence” refers to the process by which a cell ages and permanently stops dividing, but does not die. Duy

believes that inhibition of senescence pathways is crucial to impair survival of cancer cells after chemotherapy and will lead to improved remission rates for cancer patients.

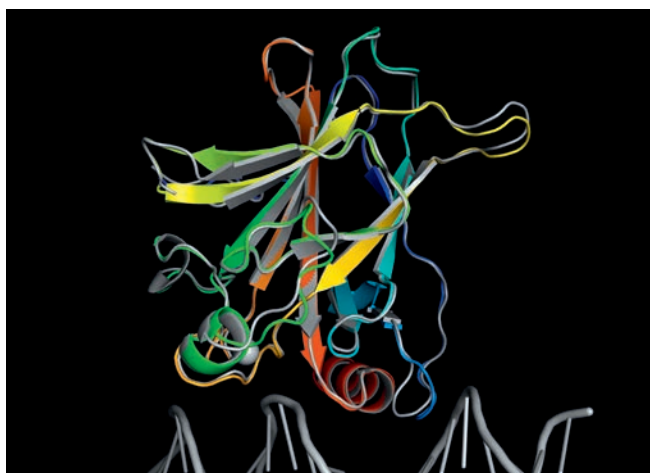
Colon Cancer Research: From *the* Lab to Patients

Taking research and translating it into tangible bedside therapies is an important goal for Fox Chase scientists and physicians. Margie Clapper, Deputy Scientific Director and co-leader of the Cancer Prevention and Control research program, and her lab staff are making significant headway towards this goal with a study focusing on early intervention in colon cancer.

“We’re conducting our first trial in high-risk subjects in the Risk Assessment Program at Fox Chase. As a basic research lab, we spend a great deal of time working with model systems, in particular mouse models. Based on our success in inhibiting colon tumors in mice, we are now testing this same strategy in a clinical trial in patients at Fox Chase,” said Clapper.

She is collaborating with Michael Hall, chair of the Department of Clinical Genetics and a member of the Risk Assessment Program at Fox Chase, to investigate the potential impact of aspirin and atorvastatin, the cholesterol-lowering drug, on the development of colon cancer in patients with Lynch syndrome. This syndrome is one of the most common hereditary cancer syndromes but remains under-recognized; carriers of DNA repair mutation have a high lifetime risk of developing colon cancer as well as other cancers.

Their study, funded by the Prevent Cancer Foundation, is truly interdisciplinary, including expertise from clinical



One of the most frequently mutated cancer genes encodes a protein whose structure was determined using both conventional methods and artificial intelligence. The methods produced nearly identical results.

“Based on our success in inhibiting colon tumors in mice, *we are now* testing this same strategy in a clinical trial in patients at Fox Chase.”

—MARGIE CLAPPER
DEPUTY SCIENTIFIC DIRECTOR

genetics, gastroenterology, hematology, clinical pathology, statistics, and molecular biology. Earlier findings from Clapper’s group indicate that atorvastatin dramatically decreases the formation of early colon lesions in mice when given before any evidence of polyps or cancer. If a polyp is already present, atorvastatin is only effective when given in combination with aspirin. The goal of the study is to determine if these drugs, in combination, can reduce the risk of colon cancer in humans with Lynch syndrome.

In this clinical trial, patients will take atorvastatin, with or without aspirin, for six weeks. Colon tissue will then be examined for markers associated with early transition to cancer, such as increased cell division and resistance to cell death. A larger clinical trial will then test whether atorvastatin alone or atorvastatin plus aspirin should be taken daily to reduce the risk of colon cancer and possibly help high-risk patients with Lynch syndrome.

“This study is very exciting because currently there is no therapy other than high-dose aspirin for patients with this particular disease, so there’s a great need for an effective preventive therapy,” said Clapper.

Fostering Breakthroughs at Pancreatic Cancer Institute

Tn 2017, Fox Chase launched The Marvin & Concetta Greenberg Pancreatic Cancer Institute with the aim of extending the lives of patients through breakthroughs in both early detection and treatment options. The institute, which is led by co-directors Edna Cukierman, a scientist, and Sanjay Reddy and Igor Astsaturov, who are both physicians, combines clinical and research expertise to allow Fox Chase to continue its role as a leader in pancreatic cancer detection and treatment. Fox Chase is the only cancer center in the Philadelphia region to be designated as both a Clinical and Academic Center of Excellence for Pancreatic Cancer

by the National Pancreas Foundation.

This clinical and research partnership has aided in much of the groundbreaking work being done for pancreatic cancer care. Cukierman, who is also a co-leader of the Cancer Signaling and Epigenetics research program, is among researchers there who have begun delving into new areas. Her focus has been on the effects of the tumor microenvironment, the tumor's "neighborhood," in the development and progression of cancer.

"It is no longer OK to just think about cancer as a bunch of cells that go through mutations and proliferate. It really is a reciprocal communication between the cancer cells and the non-cancerous cells," she said.

Cukierman added that the tumor microenvironment plays two major roles in cancer processes. The non-cancerous cells surrounding the tumor can not only provide nutrition for the tumor cells, but can also assist in deterring the immune system from fulfilling its role to eliminate cancer cells.

"The cells surrounding a tumor are very prominent in pancreatic cancer. We want to interfere with the way the microenvironment promotes the development and progression of cancer. We hope to use the natural tumor protection that the pancreas loses when cancer develops," said Cukierman.

She credits the multidisciplinary approach fostered by the institute with the significant breakthroughs in this area. The institute's main mission, she added, is to translate their pipeline of basic discoveries into the clinic.

"I cannot do my research without talking to physicians, surgeons, and population scientists regularly," Cukierman said. "We have been making huge differences from year to year and the only way we have been able to make these differences is by using a multidisciplinary approach."

Cell 'Antenna' Picks Up Signaling Pathways

In cancer research, the uncovering of new processes in familiar settings is not uncommon. Perhaps no one knows this better than Erica Golemis, Deputy Chief Science Officer at Fox Chase, whose work on the cell cilium has led to innovative insights into the function of cancer cells and cells in general.

The cilium, often referred to as the cell's antenna, is part of most non-cancerous cells in the body, with the exception of blood cells. The cilium protrudes from the cell surface



John Karanicolas is harnessing the power of artificial intelligence to help develop new drugs.

and works as a sensor, detecting fluid flow as well as small molecules. For many years, researchers were not sure what purpose the cilium served, but the work of Golemis has helped begin unraveling this puzzle.

"Cilia come and go through the cell cycle. They are there if the cell isn't growing and go away if the cell is growing. When it's present in non-proliferating cells, it acts as a receiver for classes of signals, including sonic hedgehog, the Wnt pathway, and others. These are growth factors that have relatively striking effects on the growth of cells and are linked to cancer biology," said Golemis.

Cilia, she added, are very important, particularly in the pancreas. There are signals traveling between the cancer cells and stromal cells that are dependent on cilia signaling through the sonic hedgehog protein. "Whether you have a cilium or not is going to affect how the drugs are working and whether a patient responds," she said.

Golemis and colleagues discovered this important function through the study of the protein Aurora-A kinase, a major drug target.

"Aurora is amplified in a lot of tumors and has many different cancer-specific functions. We were able to show that these drugs targeting Aurora-A also inhibited the cilia to resorb and targeted the mitotic function, which is how cells divide. It was suggesting that some drugs we were using in patients were having a very unexpected effect that could impact signaling pathways," said Golemis. "We extended those studies and it turned out that drugs that target epidermal growth factor receptor, which is one of the most targeted receptor tyrosine kinases in cancer, also affect ciliation."

Golemis said one of the open questions from these studies is whether some of the therapies being evaluated are working through this backdoor mechanism. "We and others are starting to realize that some targeted cancer drugs and chemotherapies change whether cells in the tumor microenvironment, the cells surrounding the tumor, have cilia. Understanding the effects of tumors and drugs on ciliation is potentially paradigm shifting." ♦

COMMUNITY: THE CORE OF CANCER RESEARCH TREATMENT



Research and services build on and better the lives of a diverse community

BY MARIAN DENNIS

At the core of cancer care is the community it serves, and without the community's active participation, interest, and feedback, the strides made in cancer care would be minimal, which is why community engagement has long been a priority at Fox Chase Cancer Center.

As a community hub for both cancer research and treatment, Fox Chase has been engaged in community outreach spanning across populations of all cancer types, ages, incomes, and backgrounds. This outreach has been pivotal in transforming lives, not only for those in the throes of a cancer diagnosis but for those looking for answers about prevention and risk.

ILLUSTRATION BY MARK SMITH



COMMUNITY CANCER SCREENING AND RESOURCES

In order to effectively research and treat cancer, Fox Chase emphasizes working with community members directly. Through offsite, bilingual cancer education and screening programs, Fox Chase brings high-quality information and services directly to neighborhoods throughout the Greater Philadelphia area and southern New Jersey.

One way Fox Chase is able to provide these services is through the Outreach Community Cancer Screening program, which operates a Mobile Screening Unit, an asset the center has used for more than 30 years. The unit, which is supported by *In Vino Vita*, a Fox Chase fundraising event, brings breast cancer screenings directly to community members. (See “*In Vino Vita* Raises Over \$1.5 Million,” page 31.)

“By using the mobile screening unit we reduce structural barriers such as location. We develop partnerships in multiple communities and then bring the unit to those sites. We also offer weekend screenings, which is helpful for working women. One of the main barriers we’ve identified through our community health needs assessment is a lack of access to preventive cancer services, specifically by medically underserved communities,” said Evelyn González, senior director of the Office of Community Outreach at Fox Chase.

“Nationally, cancer screening rates have been drastically reduced due to COVID, but our mobile screening unit continued to provide life-saving screenings throughout the pandemic.”

In addition to screenings, the Office of Community Outreach provides key information for cancer care through the Lippincott Resource and Education Center (REC), where professional health educators provide tailored, one-on-one assistance in person, over the phone, and via e-mail. Onsite, the REC provides vetted, evidence-based printed information, as well as computers and iPads so patients and caregivers can access online resources. Additionally, the staff connects patients to resources and programs at Fox Chase, as well as in their communities.

The Fox Chase monthly Virtual Patient and Community Education Series provides another avenue through which the center offers education to the public. These hour-long Zoom sessions feature Fox Chase clinicians, faculty, and staff who discuss a variety of topics related to cancer and the cancer experience. Topics span the continuum of care and have included clinical trials, nutrition, genetics and risk, skin cancer prevention, colorectal cancer screening, pain management, survivorship, yoga, mindfulness meditation, and many more.

One of the most important facets of community outreach for Fox Chase is its local partnerships, González

said. By working with community stakeholders, Fox Chase is better equipped to assist populations most in need of screening, information, and treatment. These partners include many entities, from local businesses to community based or government organizations.


“We really try to focus on disparate populations that either have a higher incidence rate or a higher mortality or morbidity rate,” said González. “We work with these groups to help them understand how they can reduce their risk factors or perhaps better understand the symptoms so they can identify when they’re having a problem and become more active in their healthcare. It could also include educating them on screening guidelines, which often change in ways that the general public is not generally aware of.”

These partnerships have also helped bolster another outreach program, the Patient-to-Patient Network. This program, which currently has over 200 volunteers, matches newly diagnosed cancer patients with cancer survivors who provide an additional layer of emotional support as patients navigate their new reality.

“This program is very successful and came about as a result of the community asking us to have that type of support for them. Sometimes you just want to talk to someone who has been in your shoes. The program was so well received that we started getting requests a couple of years later to implement this sort of support for caregivers,” said González.

With a similar structure, the program now includes a matching service for caregivers that links those with caregiving experience to those who are new to it. The Patient-to-Patient Network has now also been expanded to Temple University Hospital, which, like Fox Chase, is part of the Temple University Health System.

“Community really is at the core of cancer care. Without an active interest in the populations we serve, especially those most in need, we can’t even begin to understand some of the nuances involved in their care,” said González.



“Community really is at the core of cancer care. Without an active interest in the **POPULATIONS WE SERVE**, especially those most in need, we can’t even begin to understand some of the nuances involved in their care.”

—EVELYN GONZÁLEZ
OFFICE OF COMMUNITY OUTREACH



Evelyn González believes one of the most important facets of community outreach for Fox Chase is its local partnerships.

CREATING AN INTERNATIONAL NETWORK

Fox Chase researchers know that to understand how cancer affects certain populations, it is sometimes necessary to go beyond their own backyard and look further into the multidimensional factors affecting nearby, and farther flung, communities.

“There are unique risks, needs, and characteristics we must address, starting with the ability to accurately identify the problem through expanded research,” said Camille Ragin, a professor in the Cancer Prevention and Control research program and associate director of Diversity, Equity, and Inclusion.

In 2006 Ragin founded the African Caribbean Cancer

Consortium, which investigates and responds to increasing cancer vulnerability among African-descended populations worldwide. The group involves a diverse network of investigators in the United States, the Caribbean, and African countries.

“We know that when we look at Black communities in the United States, it is quite diverse. It consists of persons we refer to as African Americans who have descendants who were brought to the United States from the transatlantic slave trade,” said Ragin.

“Then we have Black individuals who are immigrants who have migrated from Africa or the Caribbean post-slavery. All of these subgroups, while they share a common ancestry in terms of genetics and culture, have distinct differences in behavior, culture, views, and attitudes. We believe these differences may play an important role in health and cancer prevention,” she said.

For more than a decade, Ragin has been working to eliminate cancer disparities among people of African ancestry. Since 2012, she has been engaged in the Cancer Prevention Project of Philadelphia (CAP3). This study heavily incorporates community engagement to create a model for population-based

health disparities research. It does this by recruiting individuals for a registry of cancer-free participants.

“This project was designed to allow us to be able to be more resourced with regard to epidemiological data on the social determinants of health, as well as bio specimens from underserved minorities, specifically persons of African ancestry,” said Ragin.

“We are trying to work together collaboratively to address cancer in all of these Black populations. But another important aspect to note is that doing these types of studies will inform and equip us better to know how to serve the Black populations in our catchment area, which we know is diverse,” she added.

Ragin said the CAP3 project has already helped support several studies at Fox Chase that have been focused around tobacco use and tobacco metabolism and how they relate to the development of head and neck cancer in Black

populations. “We’re comparing those individuals who have head and neck cancer with those who don’t. Those individuals who don’t have cancer have come from the CAP3 study.”

FOCUS ON UNDERSERVED COMMUNITIES

As Ragin and colleagues delve deeper into factors affecting cancer risk for African-descended populations, Grace Ma, associate dean for health disparities at the Lewis Katz School of Medicine at Temple University, has been working toward reducing cancer and health disparities among underserved Asian American and Pacific Islander communities. In 2000, Ma, who is also a member of the Cancer Prevention and Control research program at Fox Chase, established the Temple University Center for Asian Health, one of the first in the nation dedicated to reducing cancer and health disparities in this population.

“This started with a comprehensive needs assessment that I conducted in the late 1990s, and I found that there are multilevel barriers for people to have access to care and cancer



Grace Ma said her programs target Asians and Pacific Islanders who are low-income, blue-collar workers with limited English proficiency.

“We have this dynamic of co-learning from the community and the community learning from us, which is really the most effective way to conduct **HEALTH DISPARITIES RESEARCH** that leads to a long-term impact on advancing health equity at community and population levels.”

—GRACE MA
ASSOCIATE DEAN FOR HEALTH DISPARITIES

screening. There was also very low literacy related to cancer risks and prevention,” said Ma. “We have developed many culturally adapted and culturally and linguistically appropriate randomized controlled trials, and those trials are developed through rigorous design. Our target is low-income, blue-collar workers who have limited English proficiency.”

Ma, in partnership with community leaders, also co-founded the Asian Community Cancer Coalition and the Cancer Health Disparity Network, both the first of their kind in the northeastern United States, she said. She has mentored over 260 racial/ethnic minority junior faculty, postdoctoral fellows, doctoral, and master’s students, helping to create a diverse workforce of researchers in health disparities. Ma said this has not only allowed these individuals to understand the value of working with a community experiencing health disparities firsthand, but has also helped create a foundation for sustained community partnership.

FOSTERING **SCIENTIFIC CURIOSITY** AMONG THE COMMUNITY'S STUDENTS

As an institution focused on innovation in cancer care, Fox Chase Cancer Center recognizes the importance of engaging young populations in the community to foster a brighter future in cancer research. Although it offers graduate and postgraduate opportunities for students interested in cancer research, Fox Chase's dedication to encouraging young scientists begins much earlier.

One of the center's most robust offerings, the Immersion Science Program, offers high school students the opportunity to experience lab work firsthand and opens the door for many to the possibility of a future in science. The program was started in 2013 by Alana O'Reilly, associate professor in the Molecular Therapeutics research program, and Dara Ruiz-Whalen, who serves as the program's educational director.

"Dara and I started this program together to teach students how to be researchers before they enter labs. In our experience, we had previously taken kids from Philadelphia schools who don't have very strong STEM education," said O'Reilly. "We got them into a lab and, needless to say, they didn't do very well. They weren't familiar with the language, didn't know how to deal with the tools, and weren't accustomed to many other aspects of working in a lab."

With this in mind, they created an immersive course that allows students to participate in a research project that they design themselves. The focus of the course is on how diet impacts cancer, an

area of research that O'Reilly specializes in. Students are able to create their own projects based on a screen they perform at the beginning of the program and present their findings to their families and researchers at the end.

"A lot of students work on diseases that are of personal importance. We had about five child survivors of cancer who have been in the program, and most people work on a cancer their parents, relative, or grandparents have had," said O'Reilly. "So they get a lot of ownership of the health challenges in their family related to cancer and then become quite empowered to know that they can make a difference."

O'Reilly said the program has significantly transformed how researchers may look at cancer. She said what students may see as a cancer research problem may not be the same problem that would be identified by an experienced researcher who has gone through years of schooling and is in a lab being directed to work on a specific area.

"Our students come in as principal investigators from the second they walk in the door. Everything about it is designed to have an impact on their community. It's really flipping the hierarchy of scientific research upside down so that students come in and are in charge of the research," said O'Reilly.

"Giving all students an equitable platform to engage in research is key," said Ruiz-Whalen. "Our programs give participants a place to express themselves without fear and provides an outlet to support them in seeking answers to

questions that impact their loved ones or communities."

The Immersion Science Program also runs courses and programs for teachers to show them how to implement lab practices that allow students to participate in real-time research experiments. The program also welcomes postdoctoral researchers as well as area teachers to come into the program to teach the class based on their experiences. In many cases, these instructors choose a student to continue in their research lab.

O'Reilly said 76% of students who complete the program end up getting paid positions in research labs as undergraduates. In total, the program has welcomed 228 students since its inception and all but four have gone on to have careers in STEM.

The program has been so successful, in fact, that O'Reilly and Ruiz-Whalen recently received the prestigious Elizabeth W. Jones Award for Excellence in Education from the Genetics Society of America, which recognizes individuals or groups who have had significant, sustained impact on genetics education at any level.

She and Ruiz-Whalen are constantly working on ways to improve the program, O'Reilly said. Currently, they are working on efforts to understand how ancestral genetics contribute to cancer. "Students will work with Fox Chase, University of Pennsylvania, and Rutgers-Camden faculty to investigate how inherited genetic changes impact the development of particular cancers, with a focus on diseases that particularly affect the Philadelphia community."

"Our center has really been in the lead in terms of establishing the health disparity research infrastructure. This very robust, dynamic, sustained partnership—from academic, to clinical, to community—is very strong," said Ma. "Most importantly, though, the partners that have been working with us for the past 20 years are still working with

us. I think this research infrastructure is so valuable. We have this dynamic of co-learning from the community and the community learning from us, which is really the most effective way to conduct health disparities research that leads to a long-term impact on advancing health equity at community and population levels." ♦

Fox Chase Cancer Center is investing in enhancements that will benefit



Medical physics resident Troy Dos Santos using one of Fox Chase's new linear accelerators, a cutting-edge tool for radiation therapy.

patients and advance the overall mission of the center BY MARIAN DENNIS

BUILDING *for the* FUTURE



Fox Chase Cancer Center is poised to continue its leadership role in cancer care and research as investments from the Temple University Health System pave the way for new technology and other upgrades.

Funding from Temple has, and will continue to, fund the purchase of new state-of-the-art surgical, imaging, and basic research tools. Investments have included new patient rooms and upgraded ICU facilities; expansion of the urological clinic located in Rockledge, Pennsylvania; other infrastructure upgrades; and new technology, software, and equipment.

“We anticipate these enhancements to further elevate our capabilities and to accelerate the pace of cancer discovery and delivery. These considerable upgrades to our institution complement our greatest asset, the dedicated faculty and staff of Fox Chase,” said Joel Helmke, chief operating officer.

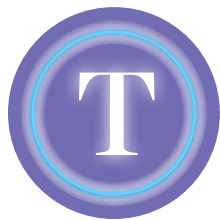
“Fox Chase researchers have done a phenomenal job doing high-impact research with older methodologies,” added David Wiest, scientific director of the Research Institute at Fox Chase. “I can only imagine the kind of research discoveries we will be able to produce when we’re working with the latest and greatest equipment, methodologies, and analysis tools that this kind of investment is going to bring to us.”

The following are among the dozens of recent and ongoing enhancements taking place at Fox Chase.

PHOTOGRAPHY BY JOSEPH V. LABOLITO



LINEAR ACCELERATORS



The arrival of new linear accelerators, known as linacs, has been an exciting new addition to Fox Chase's Department of Radiation Oncology. Linacs are the primary technology that radiation oncologists use to treat patients with external-beam radiation therapy. These state-of-the-art machines deliver high-energy X-rays and can be used to administer multiple therapies, including intensity modulated radiation therapy, image-guided radiation therapy, and stereotactic body radiosurgery. • "We're very excited about these new accelerators because they will enable us to continue to deliver the most sophisticated treatment to our patients," said Eric M. Horwitz, chair of the Department of Radiation Oncology. • The first of the new linacs is an Elekta Versa HD with Brainlab, which features additional hardware and software. The Elekta system includes the ExacTrac Dynamic system, a position-tracking tool that combines thermal-surface tracking with X-ray monitoring to deliver submillimeter precision during cancer treatment. • "It's always great to know that the health system is investing in Fox Chase Cancer Center, and specifically for our department, to bring in new, state-of-the-art equipment," Horwitz said. He added that these investments will allow his department to continue to provide excellent high-quality care for its patients and to continue to be in the forefront of the best possible ways to provide treatment.

Computerized Tomography Scanner

Fox Chase has obtained the latest in computerized tomography (CT) scanner technology through its acquisition of the new GE Revolution 256 Slice CT Scanner. A CT scanner is used to provide more detailed information about the body than X-rays are capable of giving. They use a combination of a series of X-ray images taken from different angles and use computer processing to create cross-sectional images, or slices, of parts of the body.

The GE 256 is a significant upgrade for the center. Helmke said it not only produces higher quality imaging, but can also help improve the patient experience.

"This machine is a leading-edge CT scanner that will significantly improve the speed of completing exams as well as the image resolution, while at the same time reducing the radiation dose a patient is exposed to," said Helmke.

Additionally, Helmke said the capabilities of the new machine allow it to produce images at two different

energies, which has been shown to be especially useful with cancer patients. It allows for the possibility of a diagnosis that may not have been seen before with previous CT scanners.

"This new technology is a great addition to the center and is just one more of the tools available for cancer diagnosis and treatment at Fox Chase," said Helmke.

Automated Microscope, Precise Imaging

The Molecular Therapeutics research program at Fox Chase recently acquired an ImageXpress Microscope, an automated microscope that allows more precise imaging of preserved and live cells. This technology can capture images of whole organisms, thick tissues, 2D and 3D models, and cellular or intracellular events.

The ImageXpress is equipped with high-speed laser autofocus, high-resolution digital camera, and a CRS Catalyst Express Plate loading robot. The unit has fluorescence and transmitted light capability, with environmental control, and is equipped with

MetaXpress Imaging and Analysis software and AcuityXpress Cellular Informatics software.

The device is part of the High Throughput Screening Facility at Fox Chase, which provides screening platforms and specialized instruments for more efficient experiments and higher screening capacity.

Mass Spectrometer Determines Identity of Molecules

Fox Chase will now also be using a new mass spectrometer called the Xevo TQ-XS. Mass spectrometry is an analytical tool used by researchers to measure the mass-to-charge ratio of molecules in a sample. It allows investigators to precisely determine the identity of molecules.

"You can take a protein and break it up into small fragments, and based on the mass of that fragment, tell whether that fragment is just amino acids or things have been added onto it. So you can measure what are called posttranslational modifications," said Wiest.

"Any time a cell wants to figure out what's outside and relay that information to the inside of a cell, it typically does that by moving phosphate or other chemical moieties around from one molecule to another inside the cell. This new machine can measure when those types of modifications are placed on proteins," he added.

Next-Generation Gene Sequencing

The genetic research facilities at Fox Chase are a key component of effective translational research. They have been structured to fulfill the needs of the center's multidisciplinary programs and enhance ongoing research by supplying information, reagents, and technical expertise not readily available to individual investigators.

Genetic researchers at Fox Chase are now able to utilize the Illumina NextSeq 2000 sequencing system.



The Da Vinci Xi surgical robot offers similar or better outcomes than conventional open surgery and is less invasive.

DAVINCI XI SURGICAL ROBOTS



ox Chase has also obtained two new Da Vinci Xi surgical robots for its operating rooms to assist in surgeries such as prostatectomies, which is removal of the prostate. Robotic-assisted laparoscopic surgery offers similar or better outcomes than conventional open surgery and is less invasive. Over 80% of modern prostatectomies are currently performed robotically. • This state-of-the-art equipment fea-

tures a small camera and specialized surgical instruments that are inserted into the patient's lower abdomen. The camera allows the surgeon to see the prostate and surrounding structures at a magnification of 10 times. • Because laparoscopy is a comparatively bloodless surgery, the surgeon has a clear view of the prostate and the vital surrounding structures, allowing for greater surgical precision. During the operation, the surgeon removes the prostate and surrounding pelvic lymph nodes through the small incisions. Recovery following robotic surgery typically involves one day in the hospital as opposed to several days for open surgeries.

The NextSeq 2000 uses advancements in optics, instrument design, and two-channel chemistry to increase output. This new platform provides expanded capabilities for researchers to conduct essential gene analysis.

Animal Facility Upgrades

The Laboratory Animal Facility (LAF) at Fox Chase plays a pivotal role in much of the research

conducted at the center. The LAF is responsible for the breeding, maintenance, and veterinary care of hundreds of unique, genetically modified mouse strains, which are required to support cutting-edge cancer research.

“Some of the investments have allowed us to really improve this facility and bring it into the 21st century. We’ve been able to bring back a wing of the facility that had been closed. We were also able to put in a new building automation system, which regulates temperature and humidity very carefully,” said Wiest, who serves as director of the LAF.

Now that renovations to the facility are nearly complete, the center can purchase new animal caging and racks. These cages are specifically designed to be self-contained, with a filtration unit attached that prevents pathogens from getting in or out. Wiest said the clean-ups and renovations will ultimately provide a clean mouse colony that will allow researchers to test how cancer will evolve in patients. ♦

BREAST SELF-EXAM LEADS TO UNEXPECTED FINDING

BY LEAH LAWRENCE

Ellie Moniz, 44, is a watercolor artist from the Philadelphia area who specializes in paintings of local cityscapes, landscapes, and coastal scenes. She had a history of fibroadenomas, a noncancerous type of mass, so she wasn't surprised when, in January of 2017, she felt a lump in her breast during a self-exam.

The next day she began the usual process of visiting her gynecologist for an examination. At that appointment, her gynecologist suggested she go see a surgeon to remove the growth.

A week later, a surgeon at a local hospital performed imaging to confirm that the mass was indeed a fibroadenoma. However, after the imaging, Moniz said she was called into an exam room, handed a packet of breast cancer information, and told she needed to undergo a biopsy. A week later, the diagnosis was confirmed.

"That is how I found out that I had cancer," Moniz said. She was only 39.

Moniz's physicians at that hospital recommended treatment with a lumpectomy and radiation therapy, but she decided to seek a second opinion at Fox Chase Cancer Center.

At Fox Chase, she underwent a PET scan and found that the

cancer had spread to her lymph nodes. "The news kept getting worse and worse, which was hard because I still felt fine," Moniz said.

She first met with surgical oncologist Elin Sigurdson, who explained the surgical options—a lumpectomy or mastectomy—and told Moniz what she thought the best surgical approach was. After that, Moniz met with medical

but Moniz's doctors told her there was still some micrometastases in the lymph nodes and she would need to undergo radiation therapy. Penny R. Anderson, chief of the Division of Breast and Gynecologic Radiation Oncology, and her team guided Moniz through 25 daily radiation treatments.

"From the time I first felt the

"I felt an immediate connection with my physicians at Fox Chase that went deeper than just being a patient."

—ELLIE MONIZ, BREAST CANCER SURVIVOR

oncologist Jennifer Winn and her physician assistant Zach Hasse.

"They were both amazingly supportive and took so much time out of their days to walk me through everything that was happening," Moniz said.

She was ultimately diagnosed with estrogen-receptor positive invasive ductal carcinoma and was started on chemotherapy. During chemo, her team helped her consider her surgical options, and she decided to undergo a double mastectomy without reconstruction.

The mastectomy was successful,

mass to the end of my radiation treatment was about one year," Moniz said. "By the end of 2017, I was told there was no evidence of disease and everything looked great."

Now, Moniz goes back to Fox Chase every six months for her checkups, and she has remained without evidence of disease for four years.

When Moniz was diagnosed, she and her husband had to tell their daughters, who were 7 and 9 at the time, that she was going to be sick for a while.

"They both helped me shave



my head when I started to lose my hair and were very supportive,” Moniz said. She needed her family’s support because when she started her chemotherapy she got very frail and sick. She could not stop vomiting.

“I ended up being admitted to the hospital for a week. That is when I became so close with Dr. Winn and Zach,” Moniz said. “They did everything they could to make me comfortable and worked

to tailor my treatment before my second round of chemotherapy to try to prevent my crazy nausea. From that point on, they were like family to me.”

They were so much like family that she is now working on ways to give back to them, and to Fox Chase, including donating some of her images to be used on greeting cards that the center can sell to raise money.

Moniz said it’s the least she can

do, because it’s hard to say how things would have gone if she hadn’t come to Fox Chase for a second opinion.

“I felt an immediate connection with my physicians at Fox Chase that went deeper than just being a patient,” Moniz said. “It felt like my doctors truly cared about my well-being and the well-being of my husband and kids. That, to me, was as important as the treatment I was getting.”

A ROUNDABOUT ROUTE TO A LEADERSHIP ROLE

BY SARAH JAYNE HUGHES

Some people grow up knowing they want to be a doctor, some even know the specialty they wish to practice, and others go into their career path in a more roundabout way.

Eric Horwitz, for example, wanted to be a veterinarian until high school. Then he received his undergraduate degree in history from the University of Pennsylvania. He went halfway through Albany Medical College in New York not knowing what type of doctor he wanted to be, but he knew one thing for sure: He did not want to be an oncologist.

“We get referred patients from all over the United States and even internationally because we are recognized as one of the main brachytherapy centers.”

—ERIC HORWITZ, CHAIR, DEPARTMENT OF RADIATION ONCOLOGY

But Horwitz has now been a radiation oncologist at Fox Chase Cancer Center for 25 years and is currently the chair of the Department of Radiation Oncology at both Fox Chase and the Lewis Katz School of Medicine at Temple University.

It was a required introduction to oncology course that changed his medical career. Ironically, Horwitz was assigned a project on

prostate-specific antigen, known as PSA, which he now works with regularly. “Back then PSA was a brand new tumor marker,” he said, one that could detect the likelihood that someone might have prostate cancer.

When it came time for a National Cancer Institute fellowship, one at the University of Michigan seemed perfect since his girlfriend at the time, now his wife, was getting a doctorate in clinical psychology there. The fellowship happened to be in radiation oncology and he kept comparing every med school rotation afterwards

to it. He always assumed he would soon find one that he liked better, but nothing ever topped it.

In 1997, Horwitz joined Fox Chase under the wing of the late Gerald “Gerry” E. Hanks, who Horwitz described as “one of the most renowned radiation oncologists in the world.” Added Horwitz, who is now the Gerald E. Hanks Endowed Chair in Radiation Oncology: “I have had the privilege

to basically take what Gerry built and grow it.”

Like his mentor, Horwitz is a trailblazer in the radiation oncology world and has been named one of *Philadelphia* magazine’s Top Doctors for 17 years in a row. He integrated the use of an MRI simulator into prostate cancer treatment planning for external radiation therapy, making Fox Chase one of the first centers in the world to do so. He also helped pioneer the use of high-dose-rate (HDR) prostate implants.

“I was actually hired to start a brachytherapy program for prostate cancer,” said Horwitz, referring to a form of radiation therapy in which radioactive pellets are placed directly into the tumor to target cancer cells.

He has since developed several advanced treatment programs using brachytherapy and HDR brachytherapy for prostate cancer, as well as intensity-modulated radiation therapy and image-guided radiation therapy. Fox Chase now has its own brachytherapy operating room and was the first in the northeastern United States to offer men with prostate cancer HDR implants.

“We get referred patients from all over the United States and even internationally because we are recognized as one of the main brachytherapy centers,” said Horwitz, who is a former president



of the American Brachytherapy Society. His influence in the field doesn't stop there.

"We are changing the training of the next generation of radiation oncologists. We want to, no pun intended, expose them to what radiation oncology really is," said Horwitz. "Six out of our seven residents who just graduated are now doing prostate brachytherapy somewhere in the United States. It is known as the Fox Chase way, and I want that to continue."

Horwitz has not just inspired the educational ambitions of his residents, but he and his wife, Judy Chasin, have also inspired their children's ambitions. Their daughter has a master's in education and their son is pursuing a

master's in architecture.

Horwitz has always been in demand over his 25 years as a practicing radiation oncologist. He has also seen many changes in the field. "When I was lecturing back in the early 2000s, people would say it was crazy to think that shorter courses of treatment would work better for patients. Now hypofractionated radiation therapy is the standard of care," said Horwitz.

In addition to pioneering cutting-edge treatment strategies, his philosophy is to have the latest technology to provide the most effective cancer care.

That viewpoint led in part to Fox Chase beginning the process of obtaining the next generation

of linear accelerators, also known as linacs, and other state-of-the-art technology to provide even more sophisticated care for cancer patients.

"The new generation of linacs will allow us to continue to provide excellent high-quality care for our patients and continue to push the envelope on the best possible ways to provide treatment for our patients," Horwitz said.

He added that this is part of the Fox Chase mission, to not just treat and ultimately cure cancer, but to offer the best possible care to the center's patients, one of the many reasons he loves his work. "It sounds like a total cliché, but it truly is a privilege to work at Fox Chase."

PLANTING THE SEEDS OF DISCOVERY

BY ANDREW BECKER

The National Cancer Institute invests more than \$2.5 billion annually in medical and scientific research. But even with such a significant amount, the agency is only able to fund about 20% of the applications it receives each year, and tens of thousands of researchers are left looking for other sources of support. It is not unusual for a researcher to apply several times before securing a government grant that provides seed money to support hiring lab staff, purchasing equipment, or getting a large-scale study into the field.

In cases where a grant application isn't successful, often the feedback is that the reviewers wanted to see preliminary results or other proof of concept before awarding funds. "Scientists in this situation are facing a version of the conundrum of the worker who finds entry-level job listings that require applicants to have meaningful experience in order to be considered," said Jonathan Chernoff, Cancer Center Director at Fox Chase Cancer Center.

Donors who provide pilot-stage funding enable a lab to test concepts and generate preliminary data before seeking a substantial grant to do a large-scale study. Foundations, corporations, and

generous individual donors like Don and Lauren Morel have an opportunity to make a major impact by supporting researchers at this stage.

Through nearly two decades of involvement at Fox Chase, the Morels have generously supported many different research and clinical initiatives. Don is a scientist and engineer by training,

community support programs. In 2017 they made a transformative leading gift to support pilot project funding as part of the annual *In Vino Vita* Benefit and Wine Auction, Fox Chase's signature fundraising event. The goal of the evening was to raise funds to support novel research ideas at the earliest stages of development.

With the gifts that the Morels

"Because of my background in science and industry, I know that the way to help worthy ideas evolve into innovations that benefit many people is to give researchers the resources they need to develop them."

—DON MOREL, FOX CHASE CANCER CENTER FOUNDATION BOARD OF DIRECTORS

and retired as the CEO of West Pharmaceutical Services Inc. in 2015. He is chair of the Fox Chase Cancer Center Foundation Board of Directors and serves on several corporate boards.

After a career as a telecommunications executive, Lauren is now vice president of the Morel Family Foundation, leading its

and others pledged that evening, Fox Chase created a new competitive pilot grant program. The first round of awards was announced in early 2018, and the second was awarded later in the year. There were 44 submissions from across the cancer center, of which 10 received two-year grants of \$150,000, for a total of \$1.5 million in initial



Neil Johnson, Molecular Therapeutics Research Program at Fox Chase.



Jeffrey Peterson, Cancer Signaling and Epigenetics Research Program at Fox Chase.



Vasily Studitsky, Cancer Signaling and Epigenetics Research Program at Fox Chase.



Raza Zaidi, Blood Cell Development and Function Research Program at Fox Chase and the Lewis Katz School of Medicine.

funding. Among the recipients are the labs of Neil Johnson, Jeffrey Peterson, Vasily Studitsky, and Raza Zaidi.

To date, the ten projects have yielded 12 publications in such high-profile peer reviewed journals as *Cancer Research*, *The Journal of Immunology*, and *Nature Communications*. They have also resulted in nine grants from outside organizations totaling more than \$5 million, including several from the National Institutes of Health and one from the Department of Defense.

“The review committee chose the

projects that seemed to have the highest potential, and seeing the initial return on that investment in terms of additional funding and publishing, it’s evident they chose very well,” Chernoff said.

Because the Morels’ 2017 gift was focused on the most promising ideas regardless of cancer type, it enabled progress on many fronts, including melanoma, acute myeloid leukemia, and liver, pancreatic, colorectal, and breast cancer.

Seeing the success of the first pilot projects they funded inspired them to make a second gift to support pilot research in 2021.

Work is now underway to hold a new competitive grants process that will be similar to the previous one. A committee of senior researchers led by Chernoff will review submissions in search of novel approaches that appear to have the greatest chance of broader success.

“Because of my background in science and industry, I know that the way to help worthy ideas evolve into innovations that benefit many people is to give researchers the resources they need to develop them,” Don said. “Lauren and I are happy to help make that possible.”

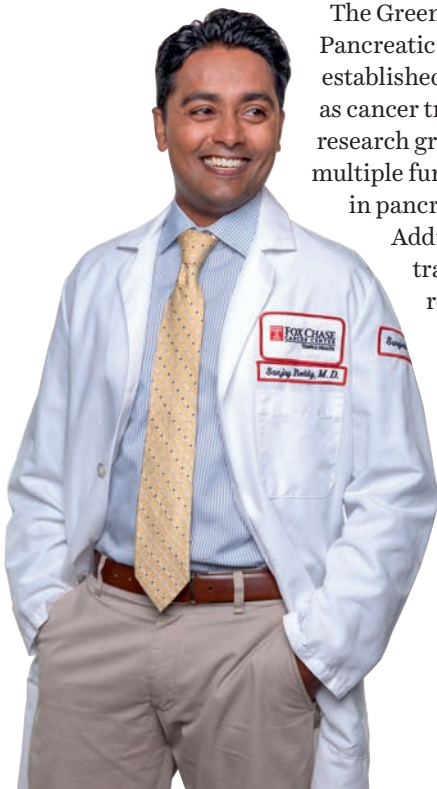
FOX CHASE RECOGNIZED FOR EXCELLENCE IN PANCREATIC CANCER

Fox Chase Cancer Center and the Marvin and Concetta Greenberg Pancreatic Cancer Institute were renewed as a Clinical Center of Excellence and named for the first time as an Academic Center of Excellence for Pancreatic Cancer by the National Pancreas Foundation. This distinction makes Fox Chase and the institute one of the few selected centers in the nation to hold this dual distinction.

“The process for this application was thorough. The foundation needs to see that we have true multidisciplinary care, not just that we have the clinical expertise but the academic backbone as well. Because of the Marvin and Concetta Greenberg Pancreatic Cancer Institute, we were able to highlight and showcase what we’ve done in the space of pancreatic research,” said Sanjay S. Reddy, who co-directs the institute with Igor Astsaturov and Edna Cukierman.

The Greenberg Pancreatic Institute has established the pancreatic cancer translational research group, which has multiple funded grants in pancreatic cancer.

Additionally, the translational research group also has worked to develop and built protocols that include clinical, basic science, and also population science, Reddy said.



RAGIN NAMED ASSOCIATE DIRECTOR OF DIVERSITY, EQUITY, AND INCLUSION

Fox Chase Cancer Center has appointed Camille Ragin, a professor in the Cancer Prevention and Control research program, associate director of Diversity, Equity, and Inclusion.

“We recognize the importance of welcoming diverse voices, valuing different skill sets and backgrounds, and celebrating the collective richness of our individuality. This appointment formalizes leadership to move us forward in this area,” said Jonathan Chernoff, Cancer Center Director at Fox Chase.

In this newly created role, Ragin will be responsible for enhancing

hiring practices to encourage diversity, facilitating more diverse leadership at all levels of the institution, providing training and education on race-related issues to the community, and facilitating collaboration among the Lewis Katz School of Medicine at Temple University, Temple University Health System, and Fox Chase on issues of diversity and inclusion.

Ragin has dedicated her career to understanding why Blacks have the highest incidence and death rates as well as the shortest survival for most cancers in comparison to all other racial and ethnic groups.

FOX CHASE RECEIVES TWO PATIENT EXPERIENCE AWARDS

Fox Chase Cancer Center has been recognized for excellence in patient care with two Press Ganey Awards, the Pinnacle of Excellence Award and the Guardian of Excellence Award.

Fox Chase was recognized for outstanding patient experience with the Guardian of Excellence Award, which recognizes organizations that have reached the 95th percentile for patient experience, employee or physician engagement, or clinical quality performance based on one year of data.

“There are a lot of ongoing patient projects that our nursing staff participates in that really solidify our place as an institution committed to patient experience,” said Anna Liza Rodriguez, chief nursing officer.

Fox Chase also received the Pinnacle of Excellence Award, which is given to the three top-performing organizations in each category. It recognizes institutions with consistently high levels of excellence in patient experience, employee engagement, physician engagement, or clinical quality performance.

IN VINO VITA RAISES OVER \$1.5 MILLION

In Vino Vita, Fox Chase Cancer Center’s signature fundraising event, which was held November 6, 2021, at the National Constitution Center, raised over \$1.5 million for cancer research, treatment, and prevention.

A highlight of the event was the presentation of the inaugural Fox Chase Corporate Philanthropy Award to West Pharmaceutical Services in recognition of their two decades of support for Fox Chase. The award was bestowed by J. Robert Beck, professor emeritus at Fox Chase, who co-chaired the event with his wife Maggie Beck.

“Through the years, their fundraising efforts have supported some of our highest priority initiatives and most promising research projects,” Beck said. “From melanoma, blood and pancreatic cancer research, to immunotherapy treatment, West has provided our scientists with remarkable opportunities to make a difference in the lives of cancer patients.”

Money from this year’s Special Pledge will fund a next-generation mobile screening unit that will build on Fox Chase’s three decades of experience as a leader in mobile cancer screening.

TWO RECEIVE DEPARTMENTAL AND DIVISION PROMOTIONS

Two clinical faculty members at Fox Chase Cancer Center recently received promotions. Margaret von Mehren, chief of the Division of Sarcoma Medical Oncology, was appointed vice chair of the Department of Hematology/

Oncology, and Iberia Romina Sosa was appointed the new chief of the Division of Hematology in the Department of Hematology/Oncology.

“Dr. von Mehren and I have worked together for almost five years. She exemplifies ‘quiet competence,’ that is to say, evaluating problems, proposing solutions, and getting results without drama,” said Martin J. Edelman, chair of the Department of Hematology/Oncology. She has been named one of *Philadelphia* magazine’s Top Doctors from 2006 through 2021.

In her new role, Sosa will focus on making sure the division is meeting the clinical needs of the cancer center and contributing to the advancement of research and innovation.

“Dr. Sosa has been a leader in both our clinical and research efforts in benign and malignant hematology,” Edelman said.



Iberia Romina Sosa (above) and Margaret von Mehren (below).

PHOTOS COURTESY OF FOX CHASE CANCER CENTER



Hossein Borghaei has been named one of three winners of the second annual Lung Cancer Heroes awards program,

a recognition of his national and international service to the lung cancer community.



Efrat Dotan has been appointed the vice chair of the National Cancer Institute’s Pancreas Task Force as part of the Gastrointestinal Steering Committee.



Linda Fleisher was recently recognized with the Lillie D. Shockney Lifetime Achievement Award from the Academy of

Oncology Nurse & Patient Navigators.



Jaye Gardiner has received an inaugural Black in Cancer post-doctoral fellowship, which is funded by Emerald Foundation

Inc. Gardiner will receive \$75,000 annually for three years, money that will fund her research into pancreatic ductal adenocarcinoma.



Shannon Lynch has received the American Cancer Society and Flatiron Health’s 2021 Real-World Data

Impact Award.



Delinda Pendleton has been named a Planetree Fellow in Person-Centered Care. The fellows program is operated

by Planetree International, a leading person-centered care advocacy and standard-setting organization.

BEATRICE MINTZ: A BASIC SCIENCE PIONEER

BY MARIAN DENNIS

Beatrice Mintz, a professor in the Cancer Biology Program at Fox Chase Cancer Center, left behind a 60-year legacy that is punctuated not only by her strides in basic science research but her lasting impact on those she worked with.

Mintz came to Fox Chase from the University of Chicago in 1960 to pursue research full-time. Her work at Fox Chase included several areas of science, including developmental genetics, gene-transfer technology, epigenetics, and the tumor micro-environment, which consists of normal cells and other components that surround tumor cells.

“When I came to Fox Chase, Bea was already past 70 and could easily have rested on her laurels, but she wanted to take on one more big challenge. After having done so much in developmental and stem cell biology, it was time, she said, to cure cancer,” recalled Jonathan Chernoff, Cancer Center Director at Fox Chase.

Mintz was known by colleagues for her innovative thinking and ability to pose the simplest, yet toughest questions. One of her most well-known experiments began with a simple query: How does a complex organism, with its diverse tissues and structures, arise from a single fertilized egg?

“To begin to address this problem, she combined early embryo cells of two genetically different mouse strains, creating ‘allophenic’ mice which contained multiple, genetically identifiable populations

of cells,” Chernoff said in an obituary for Mintz that was published in *The Cancer Letter*. “Using this approach, Bea demonstrated that just a handful of embryonic stem cells were able to generate a fully developed animal.”

Additionally, her work with manipulating mouse embryos led Mintz to address questions surrounding the tumor microenvironment, a field that is now being studied aggressively as an essential element in cancer development.

Mintz is responsible for developing many scientific tools and techniques that have changed how science is conducted. Among the

Skalka, senior advisor to the president and professor emerita at Fox Chase. “She was a fantastic scientist, a phenomenon unto herself.”

Among some of the highlights of a storied career is the list of recognitions and awards Mintz received. She was an elected member of the National Academy of Sciences since 1973 and an elected fellow of the American Association for the Advancement of Science since 1976.

Mintz was the first recipient of the Genetics Society of America Medal in 1981 and became an elected fellow of the American Academy of Arts and Sciences in 1982. In 1990, she was the first recipient

“She was truly one of a kind, one of the key scientific figures of the last 50 years.”

—JONATHAN CHERNOFF, CANCER CENTER DIRECTOR,
FOX CHASE CANCER CENTER

most important is her mouse model of malignant melanoma.

Although Mintz chose to work alone for most of her career, it did not diminish the admiration her colleagues had for her. Her high standards and tough criticisms defined her scientific career, but to those she did work with, she left a lasting impression.

“She was a private person, very reserved and strict with herself and her ideas for science, but if you got to know her personally, she was very warm,” said Anna Marie

of the Ernst Jung Gold Medal for Medicine, and in 1997, she was awarded the National Medal of Honor for Basic Research by the American Cancer Society.

Mintz passed away on January 3, 2022, at the age of 100. She is remembered not only as an inspirational researcher but as a pivotal figure in Fox Chase’s history.

“I, and my colleagues at Fox Chase, were privileged to know her. She was truly one of a kind, one of the key scientific figures of the last 50 years,” said Chernoff.





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