



1, 685, 210

The National Cancer Institute (NCI) estimates that 1,685,210 new cases of cancer will be diagnosed in the United States in 2016. University of Pittsburgh Cancer Institute (UPCI) and UPMC CancerCenter are focused on developing prevention and treatment approaches to reduce that number.



UPMC CancerCenter
University of Pittsburgh Cancer Institute

\$137,
062,
578

In FY 2015, UPCI received a total of \$137,062,578 in grants and other funding, enabling us to conduct innovative research that directly benefits our patients today and paves the way for the development of advanced treatment approaches in the future.



2 of 7

Researchers at UPCI discovered two of the seven viruses known to cause cancer in humans. Groundbreaking discoveries like this define our team at UPCI and UPMC CancerCenter. Our researchers and physicians have pioneered and refined some of the most advanced approaches to cancer prevention and treatment in practice today.



30 YEARS

OF CANCER LEADERSHIP

>40 +450 #12

UPMC CancerCenter maintains a growing network of more than 40 treatment facilities in the United States and elsewhere, making us one of the largest cancer networks in the world with more than 25,000 new patients per year.

Patients at UPMC CancerCenter have the opportunity to participate in clinical trials of the most advanced treatment approaches, some of which may not be available elsewhere. More than 450 clinical trials are in progress now through UPCI.

UPMC is currently ranked #12 (out of approximately 5,000) on the *U.S. News & World Report* Honor Roll of America's Best Hospitals.



Balancing FUTURE & PRESENT

THE UNIVERSITY OF PITTSBURGH CANCER INSTITUTE (UPCI) AND UPMC CANCERCENTER CELEBRATED A SIGNIFICANT MILESTONE IN 2015 THROUGH 2016, MARKING THE 30TH ANNIVERSARY OF THE INTRODUCTION OF WORLD-CLASS CANCER RESEARCH AND CARE IN PITTSBURGH.



Stanley M. Marks, M.D.
Stanley M. Marks, MD
 Chairman, UPMC CancerCenter

Nancy E. Davidson
Nancy E. Davidson, MD
 Director, University of Pittsburgh
 Cancer Institute

Since its founding in 1985 by Ronald B. Herberman, MD, UPCI has pioneered the study of these complex diseases that we call cancer, bringing novel discoveries to patients and new ideas to our fellow scientists. The partnership between UPMC CancerCenter and UPCI ensures that this balance between scholarship and clinical practice will continue to produce meaningful work that translates knowledge gained in the lab into practical application that benefits our patients here and everywhere.

so many in our region and beyond. Her influence and generosity allowed us to grow into what we are today: a cancer organization that attracts the best minds in research and the most capable, compassionate caregivers. We are grateful that her husband, Henry Hillman, continues her legacy.

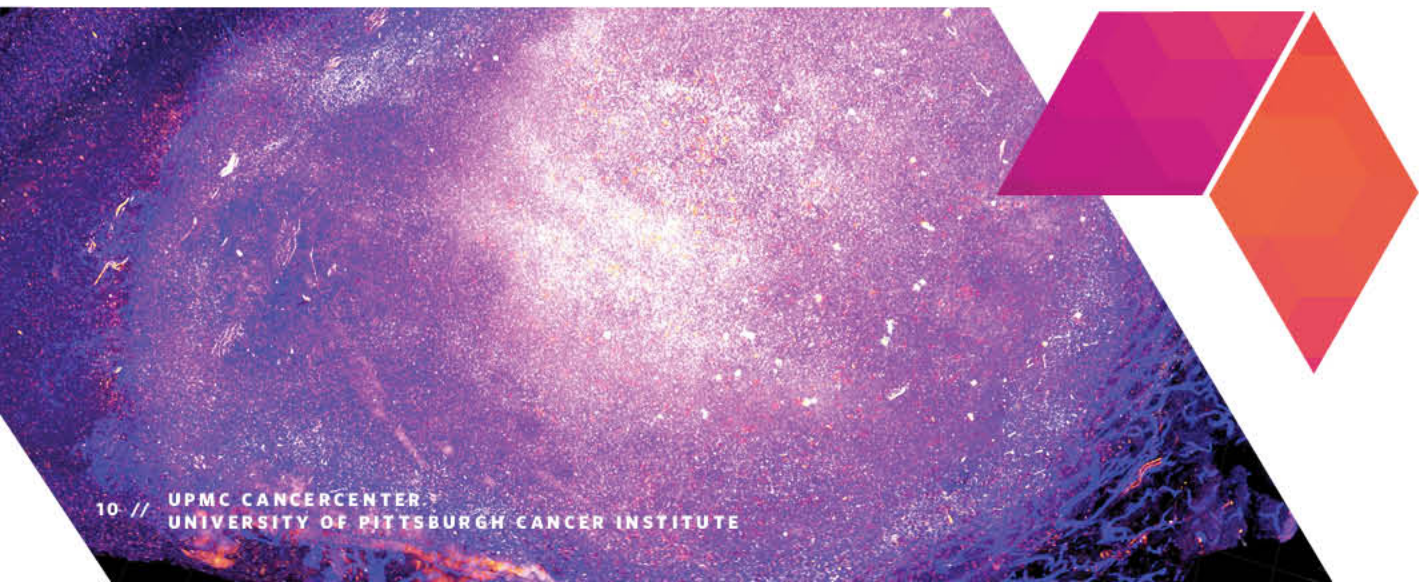
Every anniversary is an occasion for contemplation — a time to remember our past, and an opportunity to share our dreams for the future. This time can be bittersweet. In 2015, the National Cancer Institute (NCI) renewed our status as an NCI-designated Comprehensive Cancer Center, an elite designation that sets us apart in our region and the country. With this designation came the welcome news that the NCI also renewed our support grant, bringing \$25.6 million over five years to UPCI to maintain and expand our laboratory and clinical research infrastructure.

As we prepare for the next 30 years as a world leader in cancer research and care, UPCI and UPMC CancerCenter are poised to grow and change. Together we will draw upon our shared heritage to face the challenges of the future. As the relationship between medicine and computing continues to grow, so too will our dedication to innovative applications of bioinformatics and data-driven research and care. As we learn more about the possibilities contained within the genome, we will develop new ways to exploit our ever-growing knowledge to advance the science of precision medicine. As we better understand the complexities of the immune system, we will harness that knowledge to add immunotherapy to our armamentarium of anti-cancer approaches. An aging demographic presages a surge of new patients who will live longer; we will strive to care for this population using every resource.

But 2015 was also the year we lost one of our greatest champions, Elsie Hillman.

The importance of Mrs. Hillman's contributions over the years, from her philanthropic involvement in the birth of Hillman Cancer Center to her passionate support of our ongoing research and clinical efforts, cannot be overstated. By creating welcoming places and supporting people and their work, she improved the lives of

All of the elements are in place for progress at UPCI and UPMC CancerCenter to accelerate over the next thirty years — and for many more afterwards. Our growing team and our singular commitment to patient care and clinical practice, research, and education will ensure our continuing success. We are ready to build upon our legacy to improve health for all.





1985



With a grant from the Richard King Mellon Foundation and a team led by Ronald Herberman, MD, the University of Pittsburgh Cancer Institute is born.

1995



Gene therapy clinical trials begin at UPCI. Just a year later, we become the first in the nation to create and test a synthetic vaccine against cancer. UPMC CancerCenter is able to offer clinical trials to more and more patients over the years.

2015



UPCI and UPMC CancerCenter celebrate 30 years of groundbreaking research and comprehensive, compassionate patient care in Pittsburgh.

3 DECADES. 1 MISSION.

THIRTY YEARS AGO, WE WATCHED MICHAEL J. FOX GO BACK TO THE FUTURE IN A DELOREAN TIME MACHINE. "CALVIN & HOBBS" HIT THE COMICS PAGE, AND MICHAEL JORDAN WAS THE NBA'S ROOKIE OF THE YEAR. THE FDA APPROVED THE FIRST BLOOD TEST FOR AIDS. IN MANY WAYS, THINGS WERE LOOKING UP.

It was an optimistic time for cancer research and treatment as well — smoking had just been banned on all public transportation in the United States, and breast-conserving surgery was shown to be as effective as mastectomy. And 1985 was the year that Ronald B. Herberman, MD, came to Pittsburgh.

The University of Pittsburgh Cancer Institute (UPCI) and its partner, UPMC CancerCenter, came from modest beginnings. When Dr. Herberman arrived, the Richard King Mellon Foundation had just awarded a grant to start the Pittsburgh Cancer Institute. A handful

of dedicated scientists and leaders committed to applying that initial outlay into building an organization that would change the face of cancer, and, in 1985, UPCI was born. Within just five years, it received its designation as a National Cancer Institute (NCI) Comprehensive Cancer Center and was on its way to becoming one of the fastest-growing cancer institutes in the country.

Today, UPCI retains its NCI designation (still the only one in western Pennsylvania), reflecting its excellence in basic, translational, and clinical research. Its partnership with UPMC and the creation of UPMC CancerCenter helped spur the development of a network of more than 40 cancer centers, the largest of its kind in the nation.

EARLY ACCOMPLISHMENTS: THE 1980s

Born in 1940, Ronald B. Herberman was an immunologist, an oncologist, a researcher, and a professor of medicine and pathology. Before he came to Pittsburgh, he worked for the NCI.

In 1971, he led the NCI's cellular and tumor immunology group in the study of cell-mediated immune responses to tumors. This research led to the discovery of a new category of lymphocyte: the natural killer cells. Understanding the role of these cells in resisting cancer growth became his main focus.

In 1987, after Dr. Herberman had set the course of UPCI, he and his team developed the technology to produce activated natural killer cells and use them therapeutically. In this way, Pittsburgh

became a leader in cancer immunology — an area of inquiry that is transforming medicine and shaping the future of cancer research and treatment.

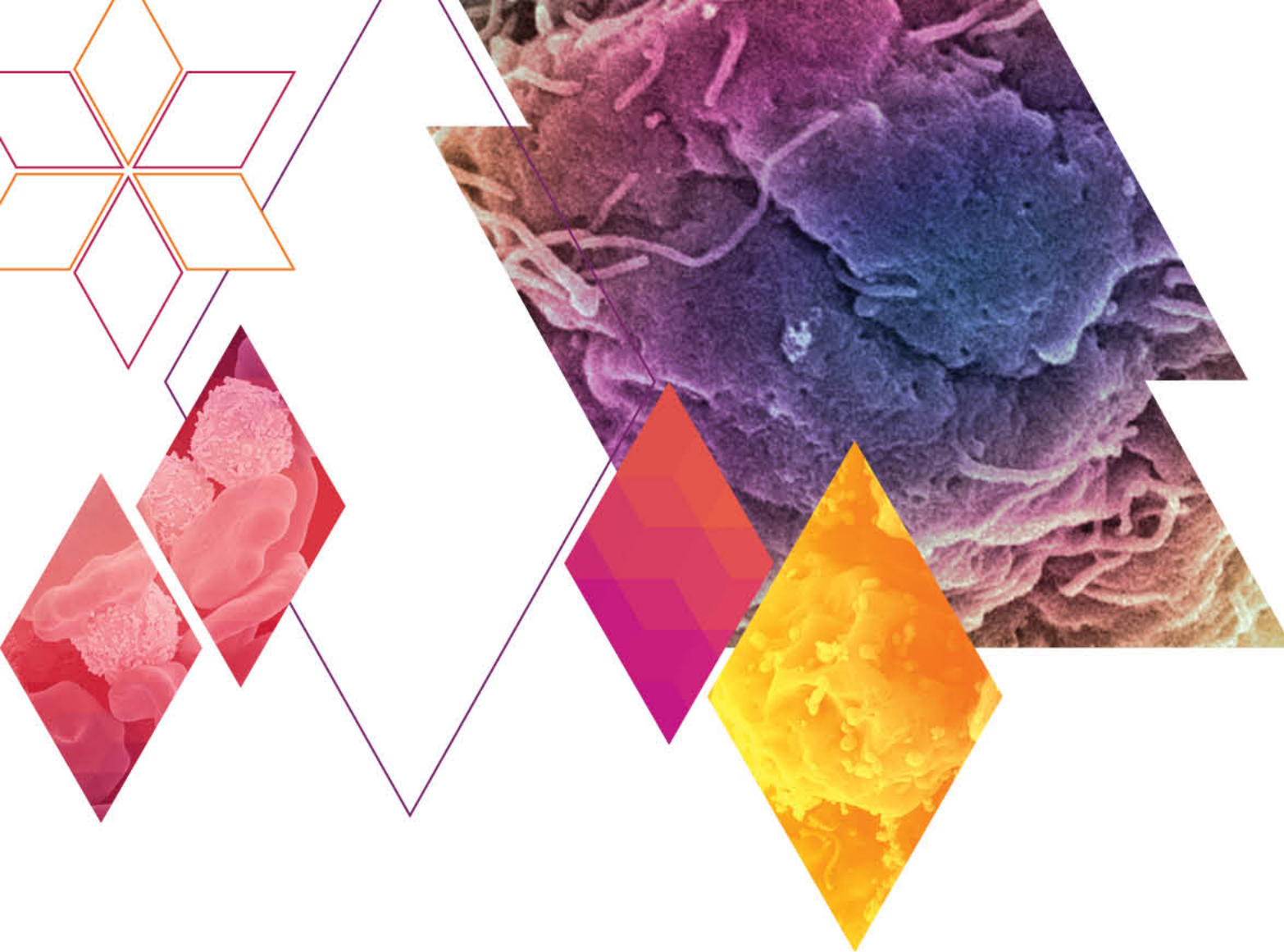
Over the course of his career, Dr. Herberman wrote or contributed to more than 700 publications, but his real legacy is the ongoing advancement of cancer research and treatment modalities in his adopted town.

A FOCUS ON GENETICS: THE 1990s

Our organization's roots in immunology set the tone for in-depth exploration of the molecular aspects of cancer genesis and therapy. The reasoning behind this approach was sound: if we can manipulate the smallest structures in the body to help them resist the development of cancer, and if we can exploit the body's own innate functions to strengthen the anti-cancer response, we may find ways to stop cancer before it begins.

As physicians, we know that preventing disease is better than curing it. It's usually more effective, too. UPCI and UPMC CancerCenter set their sights on becoming world leaders in a modern approach to cancer care.

In 1992, UPCI secured the NCI's authorization to conduct gene therapy clinical trials. We shared this distinction with just one other cancer center in the United States. Just a year later, UPCI became the first in the nation to create and test a synthetic vaccine, MUC-1, against cancer.



In 1995, our researchers created a computer program to accelerate the process of gene mapping, and, in 1996, UPCI scientists discovered a gene for inherited pancreatitis.

THE BIRTH OF HILLMAN CANCER CENTER: THE 2000s

Over the years, UPCI and its patient care partner, UPMC CancerCenter, continued to expand both in scope and in size. In 2001, volume doubled to more than 25,000 new patients per year at UPMC CancerCenter, making our institution one of the largest cancer networks in the United States. We were outgrowing our home at UPMC Shadyside.

In response, the Hillman Foundations, led by the late Elsie Hillman, gave our organizations a most astounding and generous gift: a significant investment in our mission and vision that enabled the construction of a state-of-the-art cancer center.

In 2002, the beautiful Hillman Cancer Center opened its doors to grateful patients, physicians, researchers, and thought leaders. The 350,000-square-foot facility, designed by the Pittsburgh architectural firm IKM, boasts five stories of technologically advanced laboratories, treatment spaces, offices, and patient facilities. Designed with the comfort of our patients in mind, its

proximity to UPMC Shadyside and its welcoming atmosphere firmly established it as a destination for cancer care and knowledge for people all over the world.

Over the course of a decade, the Hillmans and their foundations contributed approximately \$20M to our mission and aided in the recruitment of about 100 of the top scientists in oncology. Their generosity was instrumental in the growth of UPCI and UPMC CancerCenter. Today, Hillman Cancer Center is our flagship facility — a home for the clinical services of UPMC CancerCenter and the research of UPCI.

In 2007, UPCI became one of the top ten cancer institutes in the nation for funding. Accolades for our lung and skin cancer programs, among others, kept us in the spotlight.

In 2012, our organization marked another important development when Mario Lemieux, former ice hockey star and owner of the NHL's Pittsburgh Penguins, enlisted his charitable foundation to create the Mario Lemieux Center for Blood Cancers. This 24,000 square-foot clinic is located on the fourth floor of Hillman Cancer Center. Mr. Lemieux recovered from Hodgkin's lymphoma in the 1990s, and his experience inspired him to build a dedicated place where others could receive top-notch outpatient care.

INNOVATING FOR THE FUTURE

As we've grown, we've reinvested in the future of cancer care by applying thoughtful consideration to continuous improvement. UPMC CancerCenter oncologists pioneered the development of Via Oncology™ Pathways, an evidence-based, standards-rooted approach that ensures consistency of care regardless of network location. In 2008, we introduced our formal Pathways program for commercial use; as of today, five academic medical centers and 1,300 oncology providers nationwide have implemented this approach.

Our oncologists also developed and implemented centralized radiation oncology planning — another UPMC CancerCenter innovation that, through a commercial enterprise, is now available to other health care organizations around the world.

Our hub-and-spoke model of care has proven successful here at home and is catching the attention of other health care organizations. UPMC CancerCenter is now applying the model and its underlying operational philosophies to new and expanded cancer care facilities in other locations around the world. Ten years ago, we dedicated UPMC Whitfield Cancer Centre, near Waterford, Ireland. Since then, our leaders have worked with counterparts in Italy, Kazakhstan, Colombia, and elsewhere to share our clinical, technological, and managerial expertise and establish advanced care centers — centers that deliver the same excellent patient care as our hub. As we grow our global health care brand, we remain focused on our first mission: delivering the right care to the right patient, at the right time — every time.

AS ALWAYS, QUALITY FIRST

Our organizations understand the importance of growth, but we value quality above all. Our Volume to Value Initiative encapsulates this philosophy: as we've expanded, we've kept a sharp eye on the quality standards that have brought us to this leadership position. Fewer errors mean better outcomes, and that is always our goal.

As care continues to advance and more people live longer with cancer, our patient population will grow — and we will need to grow as well. Recruitment and talent development have always been important considerations; we are

confident in our ability to attract even more of the best minds in cancer research and care for many years to come. Our renewal as an NCI-Designated Comprehensive Cancer Center will aid tremendously in this endeavor.

Together, UPCI and UPMC CancerCenter make up one of the largest integrated cancer organizations in the United States. For 30 years, our experts have helped to define the nature of cancer care, using our growing body of knowledge to shepherd the science away from generalized treatments and toward a more personalized vision of precision medicine. By testing the limits of therapies that target the cellular and genetic origins of disease, we are able to strike a blow at the very core of cancer. Our work together as a complete cancer care destination has built a strong foundation for the next 30 years — and beyond.

2,000+

PHYSICIANS, RESEARCHERS,
AND STAFF MEMBERS

74,000

PEOPLE TREATED PER YEAR

5,000+

RESEARCH PUBLICATIONS PRODUCED
IN THE PAST FIVE YEARS



big DATA big DISCOVERIES

HOW BIOMEDICAL INFORMATICS IS CHANGING THE WAY WE ASK QUESTIONS AND FIND ANSWERS

It's difficult to remember a time before computers became commonplace in our lives. Not so very long ago, many of us spent long hours in the library, poring over research texts and plowing through periodicals. In the lab, we compiled our findings by hand and shared them with our colleagues on paper. Our memories and notes were the means by which we recognized patterns; tedious compilation took place before quantification could begin.

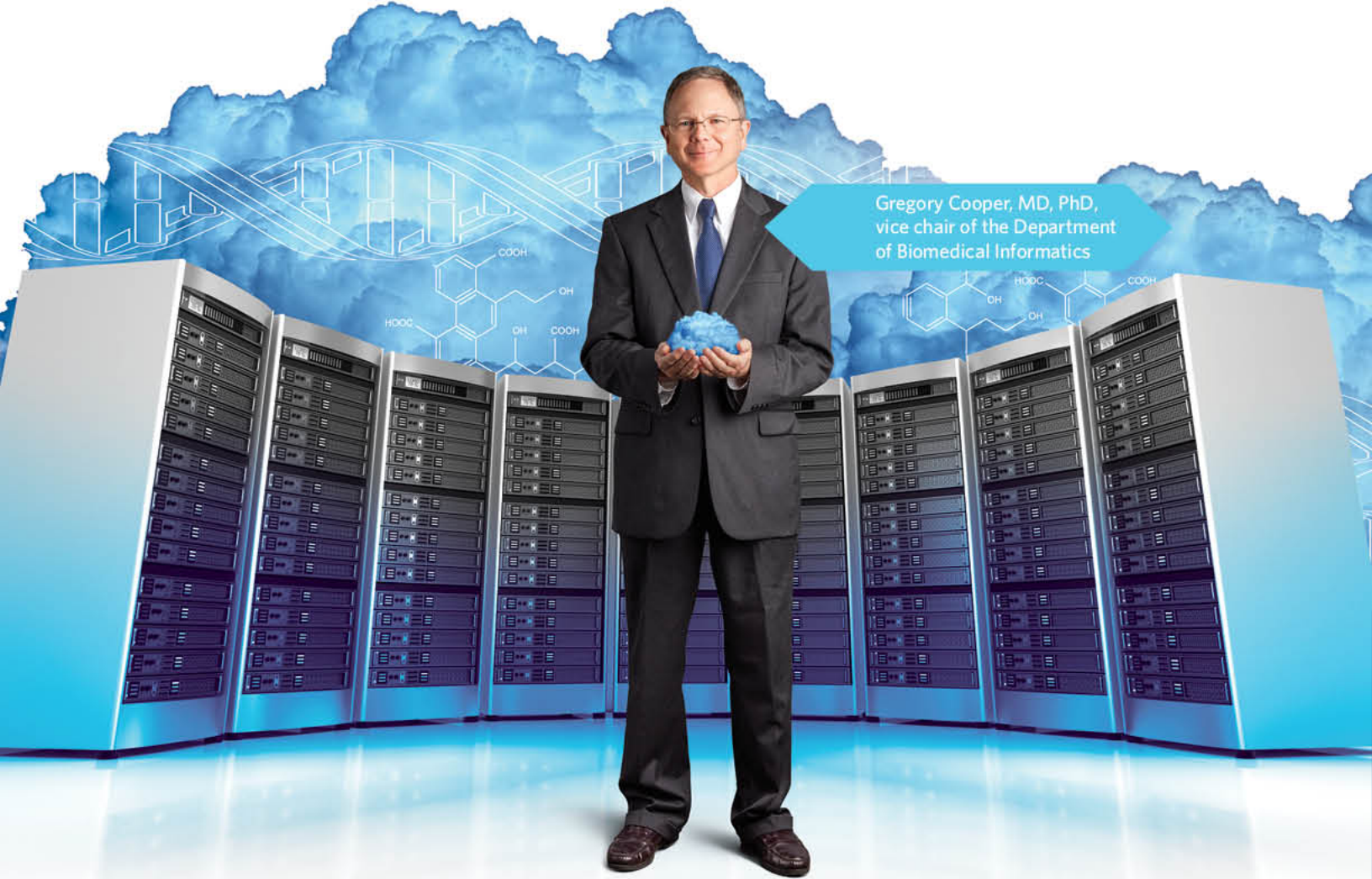
Today, we live and work in the digital age, and research institutions and health care systems have embraced information technology. The collaboration among researchers, software engineers, and statisticians, coupled with ever-evolving tools, has led to astonishing developments and advances in the field of

NIH allocates
\$656M
to create the
BD2K
INITIATIVE

biomedical informatics, exemplified by an enormous surge in large and complex datasets — electronic health records, digital images, and molecular analyses of genes, proteins, and metabolites.

The National Institutes of Health (NIH) understood that the informational explosion would require analysis and management, and, in 2012, it allocated \$656M to create the Big Data to Knowledge, or BD2K, initiative.

Modern computers and systems-based thinking are the tools that allow us to examine information in ways we'd never have dreamed possible just a few decades ago. Scientists from UPCI are among those who have been charged with making sense of big data.



Gregory Cooper, MD, PhD,
vice chair of the Department
of Biomedical Informatics

PITTSBURGH IS A BIOINFORMATICS POWERHOUSE

UPCI and UPMC CancerCenter have always been leaders in the integration of technology and medicine, and, in 2015, the NIH recognized this with a four-year, \$11M grant to lead a Center of Excellence for Big Data Computing. The University of Pittsburgh's Department of Biomedical Informatics is home to the funded organization, the Center for Causal Discovery (CCD) — an inaugural member of the BD2K initiative and one of only 11 such centers in the nation to receive this prestigious award.

THINKING OUTSIDE THE FILING CABINET

The creation of new tools and approaches to aid in the distillation of knowledge is the overarching mission of the CCD, but that seemingly simple mission belies the center's complex and multi-layered efforts. Each scientist in the group is dedicated to furthering the development and use of biomedical informatics tools to spark

the expansion of precision medicine and, ultimately, better patient care. Enabling an organized approach to digital research will lead to rapid translational benefits to human health.

"What was once a potpourri of collected data, experimental findings, and published materials is now growing into an accessible, useful body of knowledge that can more efficiently guide research," says Gregory Cooper, MD, PhD, vice chair of the Department of Biomedical Informatics and principal investigator leading the Center's involvement in the BD2K consortium. "Until now, our ability to make sense of data has lagged behind our ability to collect it."

"For cancer, we're focusing on personalized or precision medicine — applying the principles of causal discovery to individual patients' tumors and developing algorithms to discover the genomic changes that cause those cells to behave in ways that are cancerous," says Dr. Cooper. "If we can understand the driver behind the tumor, we have a better starting point for

understanding how to treat it. As we develop more treatments that are tailored to those cancer paths, we then can match up therapies that address those causes and have a better chance of therapeutic success."

WHAT DOES IT ALL MEAN?

The CCD provides biomedical and data scientists with the computational tools to analyze large datasets and develop insights about causal relationships that are novel, significant, and likely to be valid. Once such relationships are discovered, researchers can investigate them experimentally.

But how, exactly, do they do that? Dr. Cooper mentions the high-level theoretical knowledge that forms the foundation of this work — decision and probability theory, Bayesian statistics, and artificial intelligence. Clinical and high-throughput molecular data are the raw materials. Technically, the Center uses all of these ingredients to develop highly efficient causal discovery algorithms that researchers can apply to large and diverse biomedical datasets.

2015

The University of Pittsburgh's Department of Biomedical Informatics is leading Pittsburgh's involvement in BD2K.

\$11M

The NIH bestowed a four-year, \$11M grant to support our leadership of a Center of Excellence for Big Data Computing.

1 of 11

The Center for Causal Discovery is an inaugural member of the BD2K initiative and one of only 11 centers in the nation to receive this NIH grant.

Collaboration is a core aspect of the Big Data initiative. Dr. Cooper and his colleagues partner with researchers from Carnegie Mellon University and the Pittsburgh Supercomputing Center to develop algorithms, system architecture, and free, open-source software. Other collaborators include experts from Yale University, Harvard University, the University of Puerto Rico, California Institute of Technology, Rutgers University, Stanford University, and the University of Crete.

TRAINING THE NEXT GENERATION OF BIOINFORMATICS SPECIALISTS

The Department of Biomedical Informatics has always been committed to excellence, so it's not a surprise that the group drew the attention of the NIH. But no department can operate, discover, and innovate without keenly sharpened minds that are passionate about original thinking, which is why the department is dedicated to educating new scientists.

The department is home to the Biomedical Informatics Training Program, which teaches researchers and data scientists to design, implement, and evaluate new applications within the informatics domain. Now in its 25th year, the program's supporting grant from the NIH was renewed in 2015 to support the program for the next five years. The longevity of this support cements the organization's status as an incubator of ideas.

Rebecca Jacobson, MD, MS, is the director of the University of Pittsburgh Biomedical Informatics Training Program. In addition to guiding the next generation of scientists, she and her colleagues are involved in genomic and proteomic data mining, natural language processing, machine learning, and biosurveillance.

HOW WE HARVEST DATA FROM THE DEPTHS

Dr. Jacobson is currently the principal investigator on a \$3.9M NIH-sponsored project that extracts deep phenotypes from the electronic health records of cancer patients. "We're developing advanced analytic methods for extracting these phenotypes — the information that cancer researchers want — automatically," she says. "We're not going through each record manually but using software that applies natural language processing. This is a state-of-the-art approach for deep phenotyping; there's nothing else like it in the world."

Fostering thoughtful, efficient collaboration is another of her interests. Dr. Jacobson and her team spent a decade developing the

Text Information Extraction System (TIES), a language processing system that extracts de-identified information from academic journals, electronic health records, and other written data sources. The TIES software, an open-source tool, is now in use all over the world. "We freely share our tools and systems to advance the study of cancer," says Dr. Jacobson. Her group is now involved in a \$3.2M NIH-funded expansion of TIES to enhance access to tissue specimens for cancer research.

SCALING UP FOR THE NEXT BIG THING

The technology of TIES grew into another innovative approach to collaboration: the TIES Cancer Research Network (TCRN), a partnership that includes UPCI, Georgia Cancer Center, Roswell Park Cancer Institute, and the Abramson Cancer Center of the University of Pennsylvania.

Traditional research sharing methods required one institution to control the data and samples, which other groups could use within their own technology infrastructures. These centralized models are inefficient and impossible to scale to a national network. Established

to facilitate the sharing of data and biospecimens, TCRN uses advanced text processing to support large-scale research efforts across the entire network. Before, an institution may not have had access to enough cases to support a robust study — but now, several institutions can make use of aggregated data and tissue samples.

"Our work in this area will lead to more efficient, more productive collaboration that will foster discovery. The ramifications for patient care are vast," says Dr. Jacobson.

\$3.9M

The NIH has awarded the Biomedical Informatics Training Program a grant to develop analytic methods to extract deep phenotypes from electronic health records.

\$3.2M

An NIH grant supports the expansion of TIES, the Text Information Extraction System, an open-source software system that pulls cancer information from a variety of written sources.



Rebecca Jacobson, MD, MS

Going VIRAL

HOW TINY INFECTIOUS AGENTS CAN CAUSE BIG TROUBLE

Earth is home to billions and billions of viruses—at least 10^{31} , according to one of the latest estimates. As biological entities go, they outnumber every other living thing. Most are relatively harmless. Many, like those that cause the common cold, are pretty much ignored.

10^{31}
VIRUSES

IN
1994

Drs. Moore & Chang
discovered KSHV

IN
2008

Drs. Moore & Chang
discovered MCV

1 IN 5

cancers caused by
viruses

IN
2015

UPCI discovers protein
synthesis continues
during mitosis

JUST SEVEN VIRUSES ARE KNOWN TO CAUSE CANCER IN HUMANS. RESEARCHERS CURRENTLY BASED AT UPCI DISCOVERED TWO OF THOSE VIRUSES.

Patrick Moore, MD, MPH, and Yuan Chang, MD, are research partners (and spouses): Dr. Moore leads the Cancer Virology Program at UPCI, and Dr. Chang leads the program's molecular virology efforts. The programs overlap within their lab, which is dedicated to learning more about the viruses that cause cancer in humans — and how to use viruses as tools in the fight against cancer.

Compromised immunity or mutations can open the door to viruses that alter RNA and DNA or cause other sorts of cellular damage that, over time, lead to disease. For instance, human papilloma virus (HPV) is known to increase the risk for a wide variety of cancers, and human T-lymphotropic virus can lead to adult T-cell leukemia. Overall, infectious agents are responsible for more than one in five cancers worldwide.

WHERE DOES CANCER COME FROM?

The seven known cancer viruses take advantage of the patient's compromised immunity, and they target the same cellular pathways as those targeted by non-viral cancers. Specific mutations in specific pathways unlock the potential for oncogenesis. By exploring other potential pathways that these viruses may target, Dr. Moore and Dr. Chang hope to uncover different avenues of exploration. So what turns healthy cells into cancer cells, and why do tumors grow so rapidly?

In 1994, Dr. Moore and Dr. Chang discovered Kaposi's sarcoma-associated herpesvirus (KSHV), which causes Kaposi's sarcoma. This disease, characterized by cancer cells arising from endothelial cells — the cells that line lymphatic and blood vessels under the skin or in the mucous membranes — is particularly aggressive in patients with compromised immune systems. It is the most common malignancy associated with AIDS. This discovery allowed Dr. Moore and Dr. Chang to help uncover the links between immune signaling and cancer prevention. Scientists had worked for twenty years to

find an infectious agent for this disease, and the doctors' discovery capped off this quest while serving as a jumping-off point to explore general features of cancers.

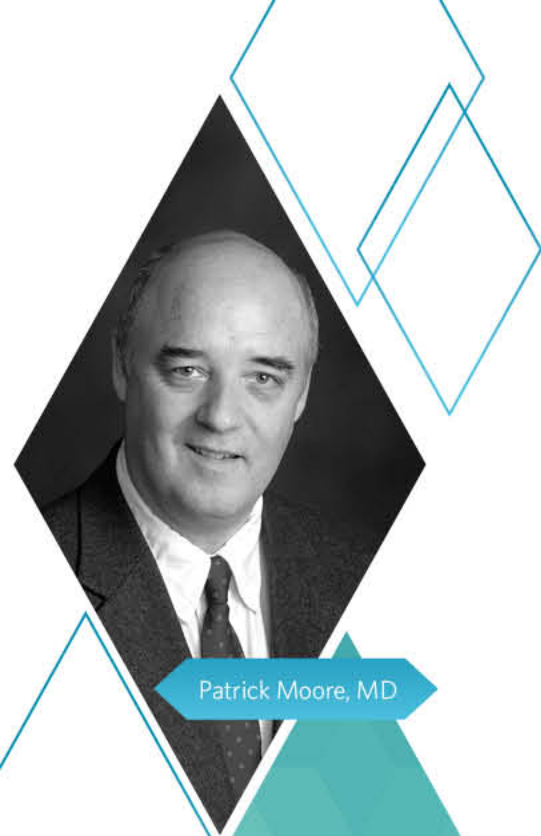
In 2008, Dr. Moore and Dr. Chang developed a bioinformatics technique called digital transcriptome subtraction, which makes possible the detection of novel pathogen transcripts through the computational subtraction of the host sequences. By removing the human DNA and running the extracted total RNA through a complex sequencing procedure, they identified Merkel cell polyomavirus (MCV), which causes about 80 percent of Merkel cell carcinomas — a rare skin cancer. With this discovery, they became the first team to identify two cancer-causing viruses, and UPCI solidified its reputation as a leader in viral oncology. The MCV virus exhibits a mutation when it is found in cancer cells, but, in healthy cells, it does not. Furthermore, inhibiting the production of MCV proteins causes MCV-infected Merkel carcinoma cells to die. This inhibition has no effect on malignant Merkel cells that are not infected. The identification of these aspects of MCV may lead to an immunological therapy that arrests its sometimes-oncogenic powers.

IT'S ALL IN THE PROTEINS.

The identification of tumor viruses presents opportunities for the development of advanced diagnostic techniques and, potentially, of vaccines. If a virus is already known to dysregulate the normal controls on protein expression, microbiological analysis may yield ways to exploit that tendency.

Scientists once thought that protein synthesis was suspended during mitosis, but, in 2015, scientists at UPCI discovered that cancer viruses change the way proteins are made — and that these changes continue during cell division.

Cap-dependent translation is a form of protein production that contributes to the proliferation of cancer cells. For decades, the belief persisted that cap-dependent translation stopped during mitosis. A protein called mTOR was thought to control the process on its own by inhibiting a gatekeeper protein, called 4E-BP1, that shuts off cap-dependent protein synthesis. For this reason, many cancer drugs target mTOR; reduced mTOR signaling should arrest cap-dependent translation and, therefore, cancer cell proliferation. The problem is that this doesn't always work.



Patrick Moore, MD

IN
2015

Drs. Moore & Chang
published their findings
on HPyV7



Yuan Chang, MD

When Dr. Moore and Dr. Chang discovered MCV, they still were unsure exactly how it caused Merkel cell carcinoma. Masahiro Shuda, PhD, a UPCI assistant professor, and his team examined the viral proteins and found one they called “small tumor protein,” or sT. This protein was determined to be responsible for enabling cell replication — and, when introduced into healthy cells, it turned them into cancer cells.

MCV sT triggers cap-dependent translation to enable tumor growth even in the presence of cancer drugs that inhibit mTOR signaling — and inhibiting sT stops cancer cells from replicating. The team discovered that another protein, CDK1, can substitute for mTOR to activate protein translation during cell division. Both mTOR and CDK1 work by inhibiting the gatekeeper, 4E-BP1, which shuts off cap-dependent protein synthesis. The proteins created during mitosis may act to preserve cancer cells.

These findings suggest that mitotic cap-dependent translation is generally sustained during mitosis by CDK1 phosphorylation of 4E-BP1 even when mTOR signaling is reduced. Our understanding of this control mechanism may someday lead to therapies that inhibit both mTOR- and CDK1-related protein synthesis.

NEW DEVELOPMENTS

The Cancer Virology Program continues to work toward identifying new pathogens, both by expanding upon previous discoveries and by combining information from the Human Genome Project with advanced sequencing technologies to

explore the hidden world of oncogenesis. The research of other Cancer Virology Program investigators, including Kathy Shair, PhD, who seeks to understand how the the Epstein-Barr virus causes nasopharyngeal carcinoma, and Saumendra Sarkar, PhD, who searches for immune pathways that control both viral infection and cancer cell growth, holds promise to broadly improve general cancer treatments. Genomic sequencing can also reveal unexpected relationships and underlying causes of other diseases.

In 2015, Dr. Moore and Dr. Chang published their findings regarding human polyomavirus 7 (HPyV7), which is related to the MCV family of viral agents. They discovered that this variant, which is usually harmless, is responsible for a dermatological disease in immunocompromised lung transplant patients.

“Our bodies play host to thousands of viruses that usually cause us no trouble at all — but under certain circumstances, like compromised immunity, mutations can occur that make those viruses very harmful. Now that we know HPyV7 is responsible for this skin disease, doctors can look for it in susceptible patients,” says Dr. Moore.

\$6.4M
GRANT

ONLY
60
PEOPLE
have won
the NCI
Outstanding
Investigator
Award

An NCI
Outstanding
Investigator:
Patrick S.
Moore, MD,
MPH

Last year, Dr. Moore received the Outstanding Investigator Award. This honor includes a seven-year, \$6.4M grant to support his work. With it, he and his team can continue investigating the link between viruses and cancer. The NCI has recognized just 60 people in the United States with this prestigious award.

The award will allow Dr. Moore and the experts of the Cancer Virology Program to conduct more intensive research into how MCV turns normal cells into cancer. They will also study how the virus that causes Kaposi sarcoma creates oncoproteins. Ultimately, they aim to identify new ways to find viruses that cause cancer in humans.

Dr. Moore is a Distinguished and American Cancer Society Professor and also holds the Pittsburgh Foundation Chair in Innovative Cancer Research at the University of Pittsburgh. Dr. Chang is also a Distinguished and American Cancer Society Professor and holds the UPMC Chair in Cancer Virology.



Peter Ellis, MD



Via Oncology™ Pathways: BLAZING TRAILS IN EVIDENCE-BASED PATIENT CARE

Protocols in medicine have been around for thousands of years. Early on, physicians followed the dictates of authority or tradition to treat their patients. As medicine developed into more of a science, clinicians observed that performing certain interventions in a certain order streamlined their practice and produced predictable outcomes that could be replicated. This notion of reproducibility is at the heart of every scientific endeavor; it's one of the pillars of the scientific method.

But the idea of a “cookbook” approach to medicine — the idea that experienced, sensitive physicians should follow a simple recipe to treat each patient — strikes many as wrong, and for good reason. Every patient is different, every presentation is different, and every case is unique. So how, then, can we justify the use of protocols?

The Pathways approach to care, first applied at UPMC CancerCenter in 2005, is driven by evidence-based results: if something works, it's worth doing again. This simple concept grew into a complex, protocol-based approach that begins with the physician. His or her experience, insight, and intuition shape and

direct the application of each protocol in response to the details of the patient's presentation. Pathways are the logical expression of evidence-based medicine. They begin with what is known and build upon that to result in an individualized approach to treatment that is rooted in proven best practices.

The Pathways approach ensures that the quality of care remains consistent across our extensive network. More than 95 percent of all patients seen at UPMC CancerCenter are on the medical oncology Pathway, and about 80 percent of our treatment decisions follow Pathway recommendations. The difference between those numbers is a sign of flexibility: no protocol can replace the insight of the physician.

“Pathways provide strong guidelines, but they always accommodate the practice of the art of medicine. We're pleased with our compliance rate.” — Peter Ellis, MD, deputy director, Clinical Services, UPMC CancerCenter • medical director, Via Oncology

In 2008, the approach grew into a company known as Via Oncology, which is affiliated with UPMC and UPCI. Via Oncology brings Pathways technology and support to five academic medical centers and approximately 1,300 oncologists all over the United States. Beginning as a simple paper-based tool for chemotherapy decision support, Pathways now operates as a web-based tool and covers more than 90 percent of cancer types and all major treatment modalities. Frequent updates and extensive expert reviews keep Pathways in line with best practices. Over the past year, UPCI and UPMC CancerCenter have participated in the development of new surgical oncology Pathways that ensure comprehensive consideration and evidence-based direction when this modality is recommended.

The Pathways approach continues to grow and change. Today, experts at UPCI, UPMC CancerCenter, and Via Oncology are working to incorporate more cancer types into the tool and to expand the scope to reflect changing approaches to palliative and end-of-life treatment. Defining the intent of therapy and the goals of care can help to decrease uncertainty and fear. By prompting the physician to invite thoughtful discussion of the patient's wishes at each stage of treatment, Pathways can ease the psychological burden of cancer on everyone involved.

We also continue to emphasize the importance of clinical trial participation by incorporating the recommendation of this choice as often as possible at the start of every appropriate Pathway. Only three to five percent of adult patients nationwide volunteer to participate in clinical trials, and, as a result, one in five studies fails to attract sufficient participation to evaluate the treatment. In Pittsburgh, adult participation rates are higher — UPCI estimates its rate at 13 percent. With Pathways, we hope to increase that number so we can accelerate the evaluation of new therapies and bring innovative developments to the general patient population that much more quickly.

Standardization often leads to increased efficiency; careful evaluation leads to individualized practice. With Pathways, UPCI and UPMC CancerCenter have combined these elements into a recipe for a more complete approach to compassionate, evidence-based treatment.

//2005//
THE PATHWAYS
APPROACH TO CARE IS
FIRST APPLIED AT UPMC
CANCERCENTER

MORE THAN
//95%//
OF ALL PATIENTS SEEN AT
UPMC CANCERCENTER
ARE ON THE MEDICAL
ONCOLOGY PATHWAY

ABOUT
//80%//
OF OUR TREATMENT
DECISIONS
FOLLOW PATHWAY
RECOMMENDATIONS

//2008//
PATHWAYS PROGRAM
IS COMMERCIALIZED AS
VIA ONCOLOGY



1 of 47
Comprehensive Cancer
Centers in the United States

In 2015
the National Cancer Institute
awarded the University of
Pittsburgh Cancer Institute
a rating of "outstanding."

IN ANY PROFESSION, THE
RECOGNITION OF ONE'S PEERS IS
THE HIGHEST OF HONORS. TO BE
REGARDED AS BEING AMONG THE
BEST IS TRULY MEANINGFUL ONLY
WHEN THOSE BESTOWING THE
HONOR ARE ALSO DOING THE HARD
WORK OF DEFINING EXCELLENCE.

\$25.6
MILLION GRANT

This grant supports the
infrastructure that lets us focus
on discovery and development.

In 2015, the National Cancer Institute recognized the University of Pittsburgh Cancer Institute as an NCI-designated Comprehensive Cancer Center and awarded us a rating of "outstanding." UPCI has been an NCI-designated Comprehensive Cancer Center since 1990, and our organization is one of just 47 such Comprehensive Cancer Centers in the United States.

This prestigious designation acknowledges the work we do every day — our efforts to contribute to the world's understanding of cancer, and our application of what we learn to delivering unparalleled patient care at UPMC CancerCenter. The NCI Comprehensive Cancer Center Grant recognizes our expertise and leadership across the full spectrum of cancer research, care, education and community outreach, and it supports our efforts to create an environment that fosters the growth of knowledge. With this grant, we are equipped to build the future of cancer care.



An Outstanding Achievement: OUR NCI COMPREHENSIVE CANCER CENTER GRANT

AN EXCEPTIONAL HONOR, WITH EXCEPTIONAL RESPONSIBILITIES

An extensive review process preceded our receipt of this NCI grant, which includes an award of \$25.6M over five years — a significant investment in the research infrastructure for UPCI and UPMC CancerCenter. Our researchers and physicians require access to state-of-the-art resources; this grant helps to ensure that they will always have the tools they need to perform at their highest level.

Being known as a Comprehensive Cancer Center comes with responsibilities. We take pride in our role as a model of excellence in every aspect of cancer, from basic science and translational research to clinical testing and beyond, into practice and community outreach and education. The entire continuum of what we consider "cancer science" is our sphere, and we are committed to building upon our reputation for outstanding achievement in each area. As the only NCI-designated Comprehensive Cancer Center in the region, UPCI and its partner, UPMC CancerCenter, are trusted to deliver innovative solutions to challenges that have existed ever since Hippocrates first described cancer more than two millennia ago.

Although our organizations cover the full spectrum of cancer research and care, UPCI and UPMC CancerCenter do have particular areas in which we excel. Our dedicated group of virology researchers is one of only a few in the nation formally studying the relationship between viruses and cancer. Our work on the immune system and immunologic approaches to cancer is also widely recognized. Our drug discovery team works at every stage of the continuum, from discovery of new compounds all the way through introduction of new agents in clinical trials. Our disease teams are experts on lung cancer, head and neck cancer, melanoma, and women's cancers. We excel at DNA repair and in the study of the biology of cancer. Our cancer center is truly exceptional.

THE SUPPORT WE NEED TO DREAM BIG

Organizations as large and comprehensive as UPCI and UPMC CancerCenter require substantial infrastructure support. Our work is facilitated by the ability to draw on more than a dozen specialized and fully equipped scientific facilities, each of which requires continual upgrading of scientific instrumentation and staffing by dedicated and skilled experts. From state-of-the-art diagnostic imaging equipment to tissue banks to DNA sequencers, animal care facilities and cellular products labs, and more, our research campus and clinical trial environments require tremendous financial support.

The buildings themselves are significant investments. They must house labs that manufacture pharmaceuticals or manipulate biological specimens in a highly controlled environment with special air quality systems and architectural finishes that meet regulatory requirements. And we want our labs to enable highly creative investigators to advance their work in a safe and supportive environment, never an inexpensive proposition.

More important than our physical facilities are the people of UPCI and UPMC CancerCenter. We attract the leading minds in cancer research, world-renowned physicians, and trainees who seek excellence in our academic programs. And each lab, office, classroom, and clinic requires extensive support from critical members of the extended cancer team, ranging from the people who run the business to the people who keep the facilities clean. Financial support is central to our ability to sustain our large community of cancer professionals and support staff.

The NCI Comprehensive Cancer Center Grant makes possible so much of our work, and we are eager to continue serving as one of our field's most respected organizations. We welcome the challenge of discovery, and we look forward to sharing our knowledge with the world in our continuing effort to eliminate cancer.



The Head and Neck Cancer SPORE: OUR ONGOING RESEARCH

In 1992, the NCI created a program to promote interdisciplinary research and shorten the time it takes to translate novel discoveries from bench to bedside. Funded by the NIH, these Specialized Programs of Research Excellence (SPOREs) are highly competitive — the NCI awards SPORE grants only to institutions that demonstrate close and productive collaboration between basic and translational scientists and clinicians. UPCI is host to several of these coveted grants, one of which is the Head and Neck Cancer SPORE.

**2015:
NCI
RENEWED
UPCI'S
SPORE
GRANT**

**\$10.9
MILLION
OVER 5
YEARS**

In 2015, the NCI renewed UPCI's Head and Neck Cancer SPORE grant for \$10.9M. This five-year award will allow our research scientists and clinicians to continue their interdisciplinary exploration of approaches to preventing, diagnosing, and treating cancers of the head, neck, and oral cavity. Understanding what makes people susceptible to these cancers is the key to advancements that will lead to better outcomes. Our partnership with UPMC CancerCenter ensures that the focus, as always, is on the ultimate goal: improving the health of our patients.

ANTIGENS AND ANTIBODIES

Robert Ferris, MD, PhD, is associate director for Translational Research, co-leader of the Cancer Immunology Program at UPCI, and chief of the Division of Head and Neck Oncologic Surgery at UPMC. He is particularly interested in applying the principles of immunotherapy to head and neck cancers. The SPORE group is also exploring the use of immunotherapy with radiation therapy to reduce or eliminate

chemotherapy, which, while often effective, can nevertheless cause many side effects for the patient.

The immune system recognizes cancer cells by their antigens. When T lymphocytes detect those antigens, they gear up to seek and destroy them. But the antigen-presenting dendritic cells also present an inhibitory signal, which can bind to a protein receptor (cytotoxic T lymphocyte-associated antigen 4, or CTLA-4), on the T lymphocyte. CTLA-4 is an immune system checkpoint: the inhibitory action will interrupt the immune system's mission and allow the cancer cells to survive. Several monoclonal antibodies (mAbs) can turn these inhibitory mechanisms off to allow the immune system to do its job.

Nearly all head and neck squamous cell carcinomas (HNSCCs) exhibit an overexpression of epidermal growth factor receptor (EGFR). Cetuximab is an anti-tumor mAb that inhibits EGFR, but it is only occasionally effective against HNSCCs. This is a puzzle: if this mAb targets that

growth factor, then it should work against all carcinomas that express high levels of EGFR — but most of the time, it doesn't.

Together with Dario Vignali, PhD, Dr. Ferris is co-leading a study within the SPORE that seeks to discover why cetuximab fails to trigger a T lymphocyte response in some patients but induces suppressive T lymphocytes in others. Their studies focus on the inhibitory aspect of the problem: how can targeting the checkpoint receptors enhance cetuximab's efficacy against HNSCCs?

"Our team has been a leader in this area for at least ten years," says Dr. Ferris. "Our head and neck program, combined with our work in immunotherapy and genomics, is one of the reasons for our ongoing SPORE support — in fact, it was funded upon the first submission. We're the only group in the United States working with cetuximab to define an immunological response to these cancers and bring a more curative approach to their management."

In keeping with the spirit of the SPORE, the research group at UPCI takes collaboration seriously. Along with David "Andy" Clump, MD, PhD, and Chris Bakkenist, PhD, Dr. Ferris is leading a study to evaluate the use of a combination of antibodies (cetuximab and nivolumab) with radiation therapy to treat head and neck cancers. This study is a cooperative project in conjunction with the Radiation Therapy Oncology Group, an NCI-funded organization. The team hopes to discover how integrating immunotherapy with standard radiation therapy may be able to improve survival for people with high-risk, locally advanced head and neck cancers.

The SPORE researchers are also testing the combination of cetuximab and radiation with ipilimumab, which more reliably binds to CTLA-4 to block inhibitory signals. The combination of an anti-tumor mAb with an anti-inhibitory receptor mAb may spark the development of the combination therapies of the future.



Robert Ferris, MD, PhD

STAT3

MUTATIONS ARE ASSOCIATED WITH HNSCC

MICRO-BUBBLE DELIVERY

OF STAT3 DECOY CAN DECREASE TUMOR BLOOD VESSELS

MUTATIONS AND MICROBUBBLES

Mutations in a protein known as signal transducer and activator of transcription 3 (STAT3) are known to play a role in a variety of diseases. Constitutive activation of the STAT3 transcription factor is associated with a variety of cancers, including HNSCCs. STAT3 binds to specific DNA sequences to control the transcription of genetic information from DNA to messenger RNA, and this makes it a target for therapy. By directly injecting a decoy oligonucleotide that targets STAT3 into an HNSCC tumor, we can decrease the expression of STAT3 target genes. But repeated injections are not ideal from anybody's perspective.

Chemical modification of the STAT3 decoy creates a more stable version that can be delivered intravenously, resulting in antiangiogenic activity — a decrease in the growth of new blood vessels that ultimately reduces tumor growth. And if IV delivery of this decoy can produce antiangiographic results, maximizing its concentration should be even more effective. In this case, more is more — the only thing missing is how to deliver it. But researchers in the SPORE are testing a promising new method.

In 2015, Flordeliza Villeneuve, MD, worked with Jennifer Grandis, MD, to investigate the potential of microbubble encapsulation of the STAT3 decoy, which will allow systemic delivery coupled with tumor-directed ultrasound to facilitate regional delivery. Site-directed ultrasound can be tuned to pop the microbubbles within the tumor, resulting in the release and delivery of the cyclic STAT3 decoy into the ultrasound-exposed tumor cells. This method can maximize selective cyclic STAT3 decoy accumulation in the area with highest tumor burden. For patients, this could someday mean a much less invasive course of treatment.



Halie Hudgins

When Cancer ISN'T CANCER

How reclassifying an indolent tumor gave a young woman a choice

Halie Hudgins received some unexpected news at her recent routine checkup: she had a nodule on her neck, and her doctor advised her to get it checked out.

A surprise of this sort is never welcome, but for Ms. Hudgins, it was a bit too familiar. Just a few years earlier, when she was a teenager, she'd had adenoid cystic carcinoma — cancer of the salivary gland. Now, it seemed, head and neck cancer was paying her another visit.

Ms. Hudgins went to a specialist for an ultrasound, and the study revealed a pair of masses on her thyroid. The one on the right wasn't very large, but the one on the left concerned the specialist. He ordered a biopsy, and it came back negative for cancer. Still, Halie was unsure. Because of her history, she figured she'd better get a second

opinion. She decided to visit Robert Ferris, MD, PhD, chief of Head and Neck Surgery at UPMC CancerCenter. He had treated her salivary gland cancer, and she trusted him.

Dr. Ferris was also suspicious of the negative biopsy; he ordered another, with ambiguous results. "He told me it may be cancer, or it may be benign," says Ms. Hudgins. "He said it was up in the air." Together, they discussed her options. She could have a full thyroidectomy, which would result in her having to take medication every day for the rest of her life. Because Ms. Hudgins was only 24 years old, she and Dr. Ferris were not particularly comfortable with that plan.

Alternatively, she could have a partial thyroidectomy. That could potentially eliminate the need for ongoing medical maintenance, but, with Halie's history, she could end up having to go back for a full

thyroidectomy later. Would it be better to treat the possible cancer aggressively from the start, or would it be prudent to take a more conservative approach?

The word itself — cancer — produces a visceral response in many people. For years, it wasn't spoken aloud. People whispered about the disease, and the patients it claimed were said to have died after "a long illness." Today, however, we do talk about cancer out in the open. Awareness efforts, walk-a-thons, and extensive coverage have brought cancer into the mainstream, but that awareness doesn't necessarily make people any less afraid. Cancer is a loaded word.

Ms. Hudgins was worried, but not inordinately so. She had already survived a malignant neoplasm. Her parents, too, were a bit less concerned this time (but only a

bit). Dr. Ferris told Ms. Hudgins that thyroid cancer, although not inconsequential, was generally much less of a threat to life than adenoid cystic carcinoma. But because he'd already treated her for cancer once, he wanted to be careful.

Dr. Ferris consulted his friend and colleague, Yuri Nikiforov, MD, PhD, a pathologist who also serves as the co-director of the Multidisciplinary Thyroid Center at UPMC. As co-leader of a project within the UPCI Head and Neck Cancer SPORE, Dr. Nikiforov studies the molecular-guided risk stratification of thyroid nodules and cancer. The project seeks to explain a striking disconnect: diagnoses of differentiated thyroid cancer have gone up more than three-fold over the past thirty years (faster than any other cancer in the world), but the mortality rate associated with these cancers remains low at approximately two percent.

Dr. Nikiforov and his group are using next-generation sequencing to identify novel mutations that correlate with less aggressive tumors. This approach also allows them to identify individuals with more aggressive disease. The team hopes that growing knowledge of the molecular genetics of thyroid cancer will reduce overdiagnosis and unnecessary surgeries.

Genetic testing can reveal a mutation of the RAS gene that correlates with a specific type of indolent tumor: encapsulated follicular variant of papillary thyroid carcinoma (EFVPTC). This non-progressing tumor type accounts for up to 20 percent of all thyroid cancers and, although it exhibits cellular behaviors that have traditionally been considered cancerous, it is not actually malignant. Dr. Nikiforov led a multi-year international study of more than 100 EFVPTCs that found not a single incidence of recurrence or other evidence of disease.

Dr. Nikiforov and his team proposed changing the name from EFVPTC to NIFTP — noninvasive follicular thyroid neoplasm with papillary-like nuclear features. The new name doesn't mention cancer, and these tumors do not require aggressive treatment. The reclassification marks the first time a cancer has been downgraded in nomenclature.

Dr. Nikiforov and Dr. Ferris determined that Ms. Hudgins has the RAS mutation that correlates with NIFTP, and this opens up the possibility of a lobectomy instead of a total thyroidectomy — a less aggressive course of treatment that would allow Ms. Hudgins to live her life without the burden of daily thyroid medication. But because her condition is still under investigation, the team is trying to match up features in Ms. Hudgins's and other patients' tumors with the new NIFTP classification. Ms. Hudgins and her physicians are still weighing her options, and a history of head and neck cancer may sway their decision toward thyroidectomy. NIFTP is still a very new designation, and a conservative approach may be the way to go. But even the possibility of avoiding a total thyroidectomy represents progress in reducing the extent of surgery for low-risk cancers—or for tumors that are being reclassified and may not be called "cancer" anymore.

"When I had salivary gland cancer, I was scared," says Ms. Hudgins. "I was young then. But this time, I'm not as frightened. I'm happy to have a doctor I'm familiar with, and to find out he specializes in this is just incredible."

Because of UPCI researchers and UPMC CancerCenter physicians, Ms. Hudgins now has options. She may choose to play it safe and have her thyroid removed, which eliminates the specter of cancer, or she and her doctors may decide that her condition meets the new criteria to a sufficient degree for a lobectomy. Either way, with or without medical maintenance, she'll be able to go about her life — caring for her dogs, looking forward to joining the Air Force, and eventually attending law school — with the peace of mind that comes with decisions based on solid knowledge. Advanced understanding of molecular genetics coupled with a subtle change in nomenclature have opened up a possibility for Ms. Hudgins that didn't exist before.

RAS
genetic mutation
correlates with
EFVPTC

20%
of EFVPTCs may be
reclassified as NIFTP



FIGHTING CANCER in a Challenging Environment

In medicine, prevention is preferable to a cure. To understand how to prevent a disease, we must first understand its origin — what causes it, and how it progresses.

Prevention is not new: for years, physicians have been advising their patients to quit smoking and watch what they eat. Controllable factors are important, but unavoidable exposure to environmental carcinogens also plays a large role in how cancer begins.

Many experts participate in the work of the UPCI Head and Neck Cancer SPORE, and together, they are advancing our knowledge of oncogenesis. Thomas Kensler, PhD, is participating in a Head and Neck Cancer SPORE project dedicated to the study of how diets rich in plants of the brassica genus can help humans fight disease. These cruciferous vegetables — broccoli in particular — show promise in the prevention of cancer.

"We have a good track record in this field, and a number of us have been working on the translational aspect of using the cytoprotective enzymes in broccoli to prevent, interrupt, or reverse the carcinogenic processes," says Dr. Kensler.

A significant portion of Dr. Kensler's research has taken place in China, where lax environmental controls in some cities have

rendered the air nearly unbreathable. By one estimate, breathing in these places has the same deleterious effects as smoking two packs of cigarettes a day. Poisonous air is powerful — no matter how many healthy habits a person has, there's little that can be done when carcinogens and toxins are in the air. But Dr. Kensler and his colleagues have discovered a work-around.

In his research, Dr. Kensler focuses on the biochemical and molecular mechanisms that spur cancer growth — and on finding ways to stop them. One means of protecting against toxicity is the induction of cytoprotective enzymes. He and his team are investigating the use of sulforaphane, the active phytochemical in broccoli, to activate a biological pathway that aids in detoxification. "No matter how early a tumor is diagnosed, ninety percent of the biological processes that led to its formation have already occurred," he says. "That ninety percent of the time is when we have an opportunity to prevent or slow the growth of the tumor."

To that end, a broccoli sprout-based delivery system of sulforaphane should fight against cancer development, even in the presence of environmental assaults. A study in a heavily polluted part of China confirmed that participants who drank a concentrated amount of broccoli sprout brew showed increased detoxification and elimination of air pollutants in their urine.



Thomas Kensler, PhD

An Outstanding Investigator: THOMAS KENSLER, PhD

In 2015, the NCI recognized Dr. Kensler's work in this area with its Outstanding Investigator Award, a prestigious honor that includes a seven-year grant for \$6.6M to enable continuing research. The NCI Outstanding Investigator Award is one of only 60 awarded in 2015, the first year of its existence. UPCI and UPMC CancerCenter congratulate Dr. Kensler on this award and look forward to the ongoing development of clinical applications for his work.



James Conner



Stanley Marks, MD

James Conner: A STORY OF VICTORY

At the very end of 2015, the Pittsburgh Panthers received some devastating news: their All-American running back and 2014 ACC Player of the Year, James Conner, had been diagnosed with Hodgkin's lymphoma.

James Conner himself was the one who made the announcement. A strong player, he'd broken Tony Dorsett's record for rushing yards in a bowl game just the year before — and yet here he was, tearfully explaining to his teammates and coaches that he was sick.

Tears do not equal weakness, of course. Mr. Conner said, "I choose to not fear cancer...I will play football again."

Mr. Conner began chemotherapy for his disease at the Mario Lemieux Center for Blood Cancers at UPMC CancerCenter. With Stanley Marks, MD, as his physician, he persevered through a grueling course of treatment, and he continued to work out with his team. Drills, the weight room, and team meetings remained part of his life during his battle with cancer.

Head coach Pat Narduzzi, his teammates, Dr. Marks, and Mr. Conner's family all knew him as a determined, mature person who always did his best and stuck it out no matter what the challenge, but even they were astounded at his dedication. He really was not going to allow cancer to change his life.

But his life did change. Already well known in the world of football and watched carefully by sports fans and journalists alike, Mr. Conner achieved a new level of prominence. Appearances on national television and in other mass media gave him the opportunity to share his story. He was able to raise \$400,000 for cancer research. He found ways, big and small, to share his strength with individuals who needed it. That's just the kind of person he is.

In May 2016, Mr. Conner received the news that he'd beaten Hodgkin's lymphoma. He'll return to the Pitt Panthers for another season, but he's already recorded perhaps the biggest victory of his career.

"This may sound crazy but in some ways I am grateful to cancer, because having it brought many great people into my life. I am grateful to Dr. Marks and the staff for saving my life. While I pray the cancer is gone forever, I know Dr. Marks will always be a part of my life."

"I was always happy I chose Pitt for football and my education. I never dreamed when I was 18 years old that this choice would save my life, because choosing Pitt meant I would get the best doctors in the country."

The Mario Lemieux Center for Blood Cancers

Over the course of its existence, the Mario Lemieux Center for Blood Cancers has made a difference in the lives of countless patients and their families. With its patient-focused design and welcoming atmosphere, the Center is a place where people can receive treatment that's comprehensive and convenient. Press Ganey has recorded our patient satisfaction ratings as very high, and that's due to the people who work here.

"We have a tremendous team, and the care they show for our patients is phenomenal." — Stanley Marks, MD

Remarkably, the Center is already outgrowing its home at Hillman Cancer Center, and UPMC CancerCenter is investigating options to expand so that we can continue to serve more patients. With ongoing support and an eye toward the future, we hope to go on making a difference for many years to come.



Steffi Oesterreich, PhD

PRECISION Medicine

The ability to understand the molecular biology of certain cancers can lead to ideas and insights, but it's the consolidation of knowledge about these fine details that creates the big picture.

In the past, researchers had no way of studying the genomic makeup of certain rare cancers — because they simply couldn't find enough of them to study. With the advent of big data, scientists can aggregate knowledge and begin to see patterns where they never could before.

Steffi Oesterreich, PhD, vice-chair of Precision and Translational Pharmacology in the department of Pharmacology and Chemical Biology, leads a lab that primarily studies breast cancer. She and her colleagues are investigating the role of estrogen receptors in the development of invasive lobular carcinoma, a less common disease that accounts for only about 15 percent of all breast cancers. Ductal carcinoma is well understood, but lobular is not. Because fewer people have this disease, it has not attracted much attention from researchers, and it has historically been difficult to study because of the lack of a data infrastructure.

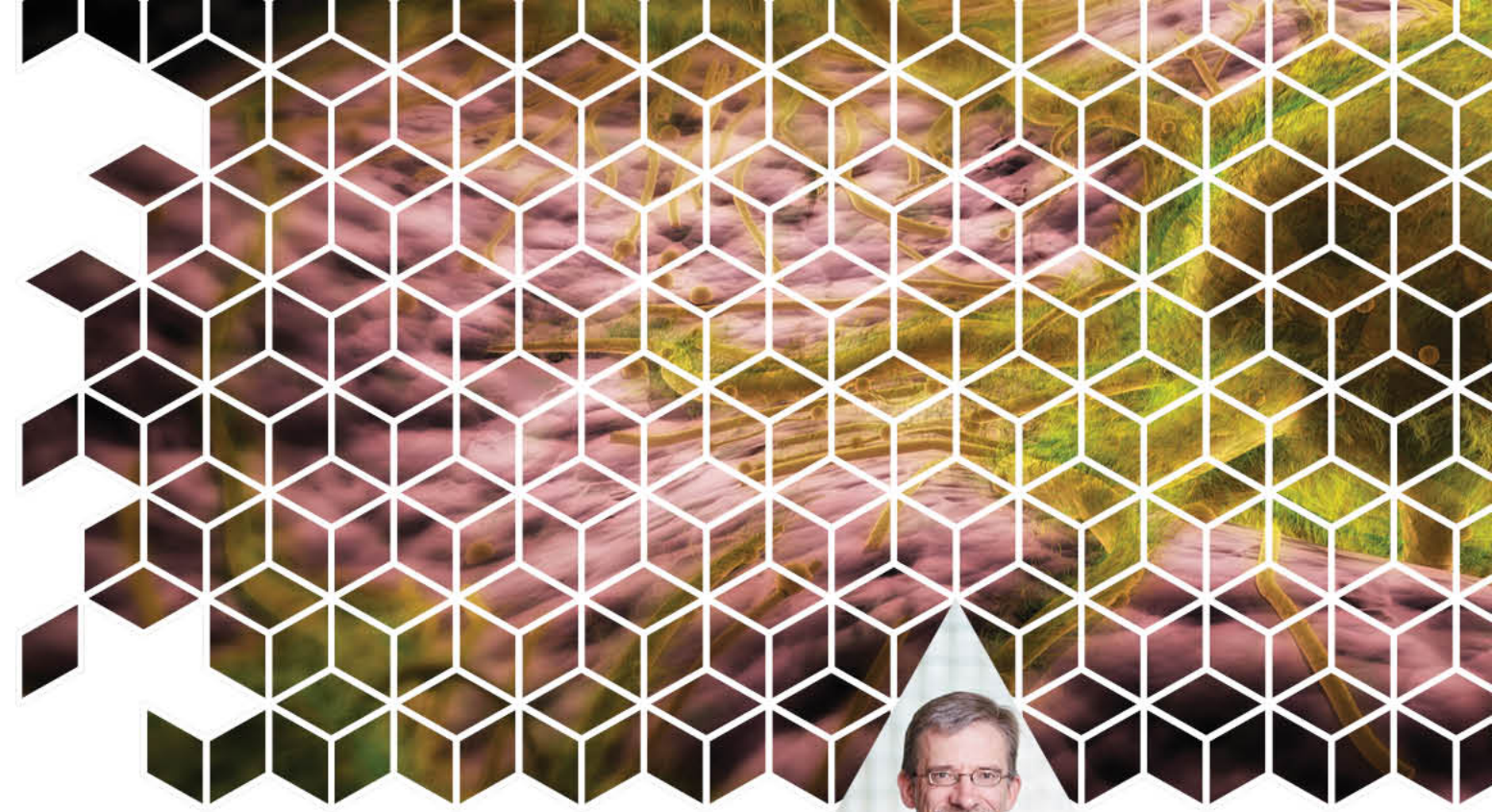
Invasive lobular carcinoma is known to be estrogen receptor-positive. The underlying difference in the molecular biology of invasive lobular

carcinoma is the aberrant expression of E-cadherin (CDH1), a gene that keeps cancer contained. When this gene is repressed, invasive lobular carcinoma may develop. Knowledge of this genetic predisposition, along with the cancer's estrogen receptor status, can lead to better detection.

Dr. Oesterreich and her team are now studying ways to apply their understanding of the role of estrogen receptors to the treatment of ovarian cancer.

Performing solid tumor biopsies for many types of breast cancers can be difficult. Dr. Oesterreich and her colleagues are investigating a liquid biopsy method, which reveals genetic biomarkers using a blood sample. By measuring the mutations associated with various types of breast cancer, physicians can track a patient's progress throughout treatment. And, by making this information available within a larger data infrastructure, scientists can advance the world's knowledge of the genetic bases of cancer development.

"What we've learned about genetic predisposition and estrogen receptors holds the potential for precision approaches to other cancers as well," says Dr. Oesterreich. "Knowledge like this is changing the way we're approaching cancer."



Adrian Lee, PhD

BIG DATA and Precision Medicine

Bioinformatics and the Big Data revolution have made possible the study of vast datasets, which turn up patterns and answers that had heretofore been hidden.

Sophisticated analytics allow us to mine data warehouses for genetic information and clinical histories that illuminate the road to more effective treatment.

Adrian Lee, PhD, is the director of the Women's Cancer Research Center at UPCI and director of the Institute for Precision Medicine at the University of Pittsburgh and UPMC. In addition to studying the hormonal regulation of breast cancer, he is part of the team that is working to implement the database infrastructure for precision genomic medicine.

New knowledge gleaned for data analytics can be used to personalize therapy for individual patients.

Physicians strive to understand and treat the individual differences in each patient's tumor, but they also look for patterns and commonality. With the advent of medical data analytics, each case can become part of a longer story.

"Collected data sets can help clinicians make predictions — for instance, a particular biomarker, like a genetic mutation, may point to a specific cause and individualized

treatment. Broader population-based markers, like cigarette smoking, may be associated with certain disease processes. Individual genomes and generalized markers can lead to the discovery of mutations or other changes that are associated with specific responses," says Dr. Lee.

"Personalized medicine is sort of a misnomer; medicine has always been personalized. What we're doing now is precision medicine."



Leading the NCI's TRANSFORMATION in Clinical Trials

FOR MANY OF THEIR CANCER PATIENTS, PHYSICIANS RELY ON TRADITIONAL STANDARDS OF CARE TO RECOMMEND TIME-TESTED TREATMENT THAT FOLLOWS A PREDICTABLE COURSE WITH FAIRLY PREDICTABLE OUTCOMES IN FAMILIAR PATTERNS.

But for other patients — those with unusual cancers or comorbidities, or factors that may make the standard course a less-than-ideal option — the road less traveled may be worth exploring. In some cases, physician-researchers and patients find themselves blazing new trails together by engaging in clinical trials.

The University of Pittsburgh Cancer Institute (UPCI) and UPMC CancerCenter are ideal partners in the practice of advanced medicine in a clinical trial environment. UPCI is home to visionary leaders in cancer research, and the vast UPMC CancerCenter network provides ample opportunity for our researchers to recruit patients for clinical trials.

UPMC CancerCenter pioneered the use of Pathways in the treatment of cancer, and in many cases, these decision-support

tools lead the way to proven treatments based upon historical evidence. But because a clinical trial of a new therapeutic approach can sometimes be the best option, we designed our program to begin with the suggestion that the physician investigate clinical trial options at the very start of the patient's cancer journey.

Clinical trials can lead to better care for all patients, and larger clinical trials that involve a network of sites can yield more meaningful data more quickly, particularly in the age of precision medicine and molecular targeting. UPCI has long been a leader in cooperative research. As a member of the California Cancer Consortium-Pittsburgh (CCC-P), a collaborative effort with three leading academic medical centers in California, we broadened our collective knowledge within a Phase I clinical trials research program supported by shared NCI grants. Edward Chu, MD, chief of the

Division of Hematology/Oncology and deputy director of UPCI, has led UPCI in its participation to ensure that patients will receive access to the latest cancer therapies and therapy combinations.

In 2014, Dr. Chu guided UPCI through the transformation of the NCI Experimental Therapeutics Program (NExT) from a series of separate institutions conducting early-phase cancer treatment trials into a consolidated, integrated program — the NCI Experimental Therapeutics-Clinical Trials Network (ET-CTN). Under Dr. Chu's leadership, our organization received an NCI ET-CTN with Phase I Emphasis grant, a \$4.25 million, five-year award to support first-in-human clinical testing of novel agents and combination regimens. Of note, UPCI was one of only 12 centers in the U.S. to receive this grant.

In 2015, the NCI decided to expand the early-phase clinical trials network to include the development of Phase II clinical trials. UPCI is only one of nine centers in the U.S. to have been awarded a grant from the NCI to support the conduct of Phase II clinical trials. For this effort, UPCI formed a strategic partnership with the Abramson Cancer Center (ACC) at the University of Pennsylvania to establish the Pennsylvania Cancer Consortium (PCC), which represents a collaborative effort between the two largest NCI-designated Comprehensive Cancer Centers

in the Commonwealth of Pennsylvania. The goal of this grant is to conduct Phase II clinical trials of novel agents or combination regimens with incorporation of translational correlative science. This effort is led by Weijing Sun, MD, principal investigator of Phase II Team operations and leader of the UPCI Phase II program; Ahmad Tarhini, MD, PhD, director of clinical science; and Jan Beumer, PharmD, PhD, director of translational science. The Phase II clinical trials will be conducted in solid tumors and hematologic malignancies, and several UPCI members serve on the disease site leadership team for this consortium.

*"By being part of the NCT-ETCTN network, we can offer access and availability to cutting-edge treatments our patients might not otherwise get."
— Edward Chu, MD*

UPCI is also the only center in Pennsylvania to receive a Lead Academic Participating Site (LAPS) grant under the NCI's new clinical trials network structure. Adam Brufsky, MD, PhD, associate director of Clinical Investigation and associate chief of the Division of Hematology/Oncology, is leading the transformation of the NCI National Clinical Trials Cooperative Group Program (CTCGP) into a consolidated, integrated program — the NCI National Clinical Trials Network (NCTN).

\$4.25
MILLION
FIVE
YEAR
AWARD

As one of only 30 institutions in the United States to receive a nearly \$5M LAPS grant, UPCI stands out as a leading academic research institution that is well positioned to attract higher levels of patient enrollment. The grant also recognizes our intellectual contribution and exceptional scientific leadership in the design and management of clinical trials. LAPS supports the institutional infrastructure required for large Phase III trials, which require extensive data management as well as patient care that is not normally covered by reimbursement.

“UPCI is one of only nine institutions to have won NCI grants within the new infrastructure to cover Phase I, Phase II, and Phase III trials. This will allow us to see our research through from beginning to end — from first-in-human studies all the way through therapeutic development and changing the standard of care. It can all happen here.” — Adam Brufsky, MD, PhD

From our initial NCI designation as a Comprehensive Cancer Center in 1990, though our involvement with the NCI-U01 Phase I Early Drug Development Program since 1999, and now as a Lead Academic Organization on NCI ET-CTN and NCTN, UPCI has been instrumental in pioneering new collaborative relationships and developing new research infrastructures within our discipline’s national research agency. Over the next years, our researchers and leaders will continue to break new ground in taking clinical trials beyond their earliest phases and into the future of cancer discovery and care.

ONE OF ONLY 30 INSTITUTIONS IN THE U.S.

\$5M LAPS GRANT



A BETTER CHANCE for Children with AML

Acute myeloid leukemia, or AML, is a disorder of hematopoiesis that arises from an abnormal transformation of stem cells in the bone marrow along with a reduced rate of malignant myeloid cell self-destruction. Myelodysplastic syndrome, or MDS, is also characterized by ineffective hematopoiesis; it is often thought of as being a preleukemic condition. Despite progress in the treatment of AML, approximately 40% of patients die from disease recurrence or treatment-related toxicities.

Cure rates for childhood cancers have improved dramatically over the past few decades, with mortality decreasing by more than 50 percent. Much of this progress may be due to the development of more effective chemotherapeutic agents and regimens. But some children are unable to benefit from traditional treatment approaches, and children who cannot undergo chemotherapy are not eligible for a stem cell transplant.

The chemotherapeutic induction period is intense; it destroys the majority of the cancer cells. After remission is achieved, intensification therapy wipes out any cancer cells that have survived. In practice, this approach is effective, but chemotherapy makes grueling demands on the body. For children with complications or poorly functioning organs, chemotherapy may not be an option.

Randy Windreich, MD, a pediatric hematologist/oncologist who conducts research and practices at Children’s Hospital of Pittsburgh of UPMC, has been working with Paul Szabolcs, MD, chief of the division of Blood and Marrow Transplantation and Cellular Therapies, to develop a reduced-intensity protocol for children who are not candidates for full-strength chemotherapy for AML and MDS. The protocol is less arduous for children who are too sick for traditional chemotherapy, but it sets the stage for a stem cell transplant that is potentially more successful.

Reduced-intensity conditioning regimens decrease the toxic effects that accompany severe myelosuppression, leading to decreased

transplant-related morbidity and mortality, but they can increase the risk of graft failure. The reduced-intensity prep under development at UPCI relies upon an immune-mediated process to strengthen the patient’s response to stem cell transplant. Chemosensitization is the key: G-CSF, a lab-created protein that stimulates the growth of white blood cells, enhances the safety and efficacy of the subsequent transplant.

Other researchers are exploring the use of chemosensitizers after stem cell transplant to make residual leukemia cells more susceptible to destruction, but Dr. Windreich and his group are pioneering a new approach that reverses the order: they administer the chemosensitizer before the transplant. AML blasts express many of the same adhesion molecules as normal hematopoietic stem cells, which allows them to interact with the bone marrow stroma. Priming with G-CSF during chemotherapy prior to transplant induces the proliferation of AML cells, rendering them more sensitive to the effects of chemotherapy. G-CSF is also a mobilizing agent; it disrupts the interaction between AML and bone marrow and causes AML cells to move from the bone marrow to the peripheral blood, making them more sensitive to chemotherapy effects.

**AML
ACCOUNTS
FOR ABOUT
20%
OF CHILDHOOD
LEUKEMIAS**

**40%
of pediatric
patients die
from AML
recurrence or
toxicity**

“This approach brings new hope to kids who wouldn’t have had this chance before. Children who in the past would not have been eligible for a life-saving stem cell transplant now have that opportunity,” says Dr. Windreich.

Clinical Trial Accrual: Meeting the Challenge

Clinical trials are always the first treatment consideration at UPMC CancerCenter: they help patients by increasing treatment options, they help physicians by permitting access to the latest therapies, and they help researchers by generating data that may, in turn, lead to new standards of care or uncover the need for more research. With all of these benefits, one would think patients would be eager to participate. Unfortunately, this is not the case.

Only three to five percent of adult patients with cancer nationwide will agree to participate in a clinical trial, and one fifth of all studies fail to attract enough participants to generate meaningful results. At UPCI and UPMC CancerCenter, patient participation is about 13 percent — but even with this advantage, clinical trials can suffer, and development can lag behind the urgent need for more effective therapies. Of course, the most important reason to boost participation is to improve individual patient care. Our physicians are sensitive to their patients’ need to feel safe in a clinical trial

environment, and we’re careful to stress that cutting-edge treatments may offer the best chance for a positive outcome without undue risk.

When a good idea gets stuck on the way from bench to bedside, it’s of no help to anyone. For this reason, we’re eager to find ways to encourage patients to participate and make it easier for physicians to identify clinical trials that match their patients’ needs. UPCI’s leadership in the reworking of NCI’s clinical trials programs is one way we’re accomplishing these goals.



Our INTERNATIONAL VISION

Those of us who are able to gain access to expert cancer care close to home are really very lucky.

We have quick, convenient access to world-class cancer care, and it's easy to forget that this is not the case for everybody around the world. In some areas, access to outstanding care (or adequate care, or any care at all) does not exist.

The people of UPCI and UPMC CancerCenter have always believed that everyone deserves access to high-quality care — care that's comprehensive and close to home. Many other health care organizations also believe in serving the needs of patients who live far away; they do this by developing relationships with separate hospitals that then send their patients away for treatment. But travel is a burden for patients and their families. We prefer to offer care where the patient is, not just where we are.

Ten years ago, UPMC CancerCenter embarked upon an ambitious campaign to extend our services into other regions around the world. Our first international location opened near Waterford, Ireland in 2006. Since then, we've expanded our vision and put into action our plans to establish

UPMC CancerCenter in other locations. Eventually, we hope to offer the full scope of our unique brand of cancer care to people in Italy, Kazakhstan, Colombia, Southeast Asia, and Russia.

Our hub-and-spoke model works well in western Pennsylvania, and we have proven that it is replicable. In international cities, we create the opportunity to offer our same outstanding care to people in the regions surrounding those cities. Thanks to our Pathways program, each patient is assured of receiving the same level of care and consideration as he or she would receive at any hub — from Waterford to Pittsburgh and beyond. Centralized radiation treatment planning through D3 Oncology Solutions, a UPMC spinoff company, ensures consistency.

With that said, UPMC CancerCenter is not a cookie-cutter operation. Patients do receive the same quality of care at any location, no matter how far it may be from Pittsburgh, but each international center provides customized care that is tailored to the needs of the surrounding population.



UPMC Whitfield Cancer Centre: A CASE STUDY IN INTERNATIONAL CANCER CARE

Some locations may require radiation oncology services to support an already existing medical oncology practice. Other locations may require a robust, fully developed program. By working closely with our partners, we're able to replicate the most appropriate elements of our flagship operation in a way that respects and fulfills their particular needs.

In developing markets, such as Myanmar, our approach is even more flexible — UPMC CancerCenter is able to provide necessary services with the same excellent quality while scaling our investment to the growth opportunity within the scope and timeframe of the region's economic development trajectory. This may take the form of a consulting agreement, or it may entail the creation of a new cancer care facility or practice. No matter what the form, the function always meets our standards.

During the implementation phases of our international ventures, physicians from the partner institution visit Pittsburgh to learn the unique approach that UPMC CancerCenter employs. Physicians from our organization also visit the new cancer center to lend assistance. As the venture matures, frequent visits and virtual meetings ensure adherence to our care models.

When it comes to health care management, survival and growth are inextricably linked. Our reputation is solid, and we are able to attract the best performers in cancer care practice and research from far and wide. If we are to thrive, however, we must grow — and our reputation must serve as our calling card in places where we have yet to establish a presence.

Recruitment and retention of high-performing physicians and researchers depend upon our leadership position. By expanding to serve patients in other countries, we burnish our reputation as a global influence and leader in the delivery of cancer care. In our professional capacity, we see the benefit of sharing our knowledge with colleagues in our sister cities. Rather than exporting our knowledge, we are expanding our understanding through the mutual exploration of novel therapies, Pathways-based care, and treatment approaches. We are establishing strong relationships with a give-and-take focused squarely on how we can help our patients.

In the beginning of our international journey, UPMC CancerCenter worked with organizations that sought us out—international partners who recognized our commitment to excellence and wanted to improve their own operations by establishing joint ventures. Today, we actively seek new opportunities to establish partnerships by developing relationships with physicians' groups. We also work with large international organizations and companies to identify co-marketing opportunities.

The additional capacity to generate revenue through international partnerships directly benefits our patient-care and research activities here in Pennsylvania. A bigger hospital means more resources to invest in our ongoing work — but our local region cannot support an operation large enough to foster growth on that scale. By establishing ourselves in global areas that need our services, we can generate the revenue we need for the future while serving patients and providing the best cancer care available anywhere.

Waterford, Ireland is not a small town: it is home to about 46,000 people, and the seaside city bustles with all the usual activity of a busy port. Art and history give Waterford its unique culture; multinational corporations like Bausch & Lomb and Hasbro make Waterford an important part of the economy. But, as big as Waterford is, the community didn't have a radiation oncology facility.

Waterford-area residents in need of radiation therapy had to travel 80 miles to Cork or 100 miles to Dublin to receive the care they needed. The burden of this journey — up to 200 miles roundtrip, five days a week, for multiple weeks — sharply limited or eliminated their access to treatment.

In October 2006, UPMC teamed up with Waterford officials to establish UPMC Whitfield Cancer Centre, a \$6M, state-of-the-art facility that offers radiation oncology services to people in and around Waterford. UPMC Whitfield is a joint venture of UPMC and Euro Care International, an Irish health care infrastructure development company. The cancer center is part of the Whitfield Clinic, a private hospital developed by Euro Care to address the scarcity of medical resources in this part of Ireland.

UPMC CancerCenter established UPMC Whitfield using its hub-and-spoke model. The Whitfield facility is linked to Hillman Cancer Center by a telecommunications network, and treatment plans are coordinated through our Pathways program to ensure consistently high quality. Medical physicists in Pittsburgh share information and expertise with their colleagues in Ireland to develop treatment approaches tailored to each individual patient.

Ten years ago, UPMC CancerCenter proved that the replication of a successful cancer care model in an international location was beneficial to all of the parties involved. We will build upon this success as we continue to expand our offerings in other cities in other countries.



OUR STEM CELL PROGRAM Is Growing



Warren Shlomchik, MD

UPCI AND UPMC CANCERCENTER EMBRACE THE CHANGES THAT HELP US GROW AS A RESEARCH AND CARE COMMUNITY. OUR OUTSTANDING REPUTATION HELPS US TO RECRUIT LEADERS WHO THEN CONTRIBUTE THEIR TALENTS TO OUR MISSION TO ENABLE US TO DEVELOP INTO AN EVEN MORE INNOVATIVE ORGANIZATION.

In 2015, we welcomed Warren Shlomchik, MD, who joined UPCI as director of Hematopoietic Malignancies. Dr. Shlomchik is a leading specialist in the field of stem cell transplantation and cell therapies and an expert in the immunologic mechanisms that contribute to graft-versus-host-disease, a complication that affects some stem cell transplant recipients. Dr. Shlomchik was previously at Yale Cancer Center at the Yale University School of Medicine.

Clinically, UPMC CancerCenter serves a large number of patients in its stem cell transplant program. Our high volume of approximately 200 transplants per year, performed by nine oncologists, places us among the busiest programs of this kind. Our commitment to comprehensive care compels us to offer our patients every opportunity to achieve better health — but the research arm of our program needed to become stronger to support a greater number of clinical trials.

Dr. Shlomchik's extensive experience and academic leadership make him a natural fit for UPCI. With his appointment, we look forward to building a more robust program of clinical trials along with a deeper program of basic science research on stem cell transplantation.

2015

WE WELCOMED WARREN SHLOMCHIK, MD, WHO JOINED UPCI AS DIRECTOR OF HEMATOPOIETIC MALIGNANCIES

200

TRANSPLANTS A YEAR PERFORMED BY

NINE

ONCOLOGISTS

CIRCLE OF HOPE

THE CIRCLE OF HOPE HONORS INDIVIDUALS, FAMILY FOUNDATIONS, AND PRIVATELY HELD COMPANIES THAT MAKE CONTRIBUTIONS OF \$10,000 OR MORE IN A CALENDAR YEAR. THIS LIST RECOGNIZES THOSE WHO WERE MEMBERS IN 2015.

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★ **UPMC SHADYSIDE CAMPUS**
Hillman Cancer Center
Mary Hillman Jennings Radiation
Oncology Center

▲ RADIATION ONCOLOGY CENTERS

- 1 Jameson Radiation Oncology¹
- 2 Heritage Valley Radiation Oncology, Beaver¹
- 3 Heritage Valley Radiation Oncology at UPMC West¹
- 4 UPMC/St. Clair Hospital Cancer Center¹
- 5 Washington Health System Radiation Oncology¹
- 6 Uniontown Hospital Radiation Oncology, Robert E. Eberly Pavilion¹
- 7 UPMC CancerCenter Radiation Oncology at UPMC East
- 8 John P. Murtha Regional Cancer Center³

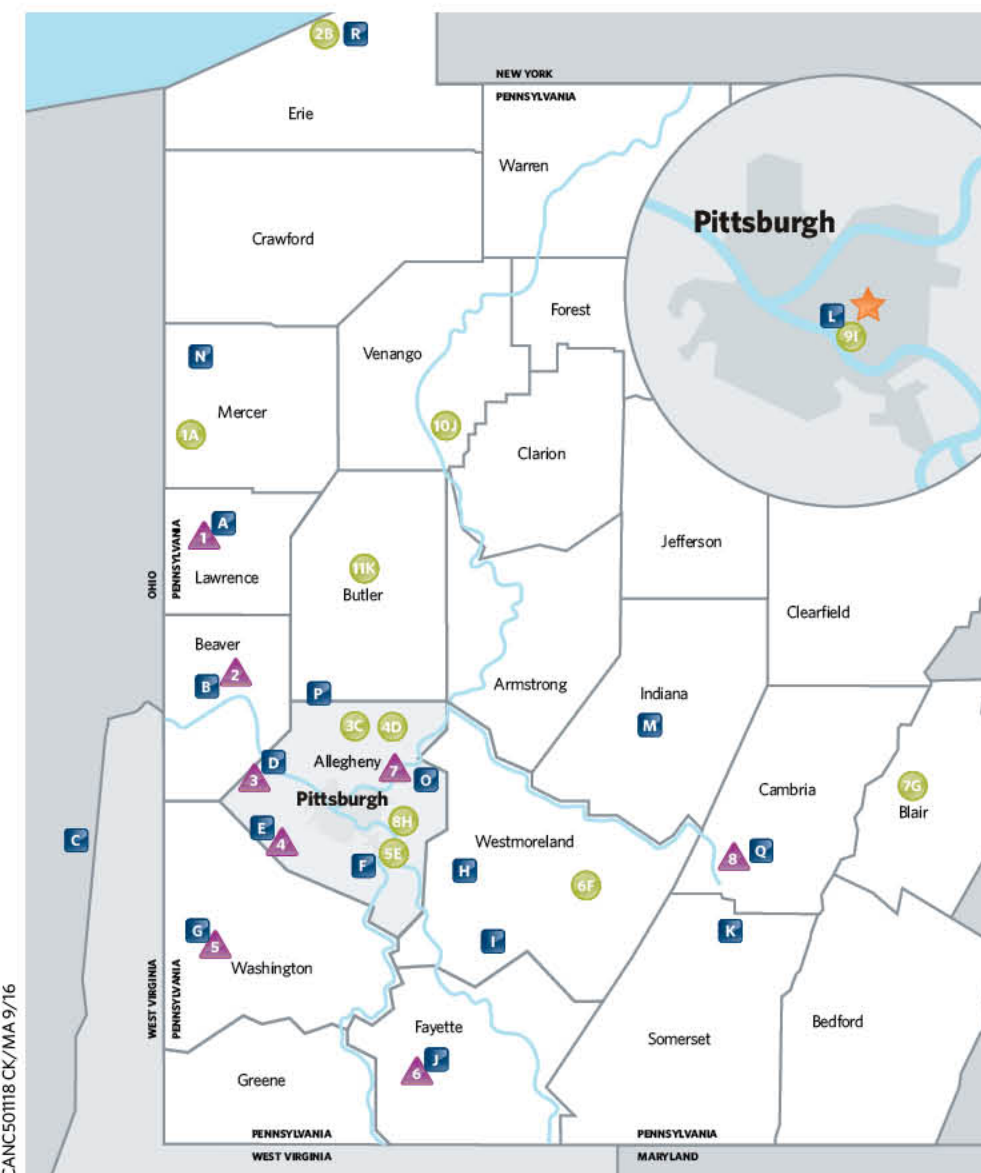
■ MEDICAL ONCOLOGY CENTERS

- A UPMC CancerCenter Medical Oncology, New Castle
- B UPMC CancerCenter Medical Oncology, Beaver

- C Trinity Tony Teramana Medical Oncology¹
- D UPMC CancerCenter Medical Oncology, Sewickley
- E UPMC CancerCenter Medical Oncology, Upper St. Clair
- F UPMC CancerCenter Medical Oncology, Jefferson
- G UPMC CancerCenter Medical Oncology, Washington
- H Arnold Palmer Medical Oncology, North Huntingdon²
- I Arnold Palmer Medical Oncology, Mt. Pleasant²
- J UPMC CancerCenter Medical Oncology, Uniontown
- K UPMC CancerCenter Medical Oncology, Windber
- L UPMC CancerCenter Medical Oncology at UPMC Mercy
- M UPMC CancerCenter Medical Oncology, Indiana
- N UPMC CancerCenter Medical Oncology, Greenville
- O UPMC CancerCenter Medical Oncology, Monroeville
- P UPMC CancerCenter Medical Oncology at UPMC Passavant-Cranberry
- Q UPMC CancerCenter Medical Oncology, Johnstown
- R UPMC CancerCenter Medical Oncology at UPMC Hamot

● DUAL CENTERS (RADIATION AND MEDICAL ONCOLOGY)

- 1A UPMC CancerCenter at UPMC Horizon
- 2B The Regional Cancer Center, Erie
- 3C UPMC CancerCenter at UPMC Passavant
- 4D UPMC CancerCenter at UPMC Natrona Heights
- 5E UPMC CancerCenter at UPMC McKeesport
- 6F Arnold Palmer Cancer Center²
- 7G UPMC CancerCenter at UPMC Altoona
- 8H UPMC CancerCenter at UPMC St. Margaret
- 9I UPMC CancerCenter at Magee-Womens Hospital of UPMC
- 10J UPMC CancerCenter at UPMC Northwest
- 11K Butler Health System Medical and Radiation Oncology¹



INTERNATIONAL LOCATIONS

UPMC San Pietro FBF
Advanced Radiotherapy Center
Rome, Italy

UPMC Whitfield Cancer Centre
Waterford, Ireland

Pinlon Hospital Radiotherapy Center
Myanmar, Burma

Hospital International de Colombia
Oncology Institute
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