

A team approach to the many sides of cancer.

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UPMC CancerCenter
University of Pittsburgh Cancer Institute



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To us, nothing is more personal **than your care.**

Personalized medicine is a medical model defined by decisions and treatments that are customized to the individual patient. At the University of Pittsburgh Cancer Institute (UPCI) and UPMC CancerCenter, personalized medicine means being able to deliver the right therapy to the right patient at the right time.

With the advent of genomics, physician-researchers often can predict a patient's response and determine the best possible treatment strategy for that patient — which is the goal of personalized cancer medicine.

The benefits of personalized medicine may represent a true revolution in medical care by informing dramatically improved outcomes and quality of life, and through the avoidance of ineffective therapies.

We sequence complex sets of genes to predict how tumors will respond to treatment.



Dr. Yuri Nikiforov

Genomic medicine is the study of complex sets of genes and how those genes function within the cells and work together inside the body. The Human Genome Project, the first successful international research effort to sequence and map all of the genes of human beings — together known as the genome — identified approximately 25,000 genes in human DNA in 2003.

Now physician-researchers at UPCI and UPMC CancerCenter are using that genomic information to understand how genes interrelate to cause cancers to develop, grow, and metastasize, so that insight can be used to predict, treat, and, one day, prevent cancer.

Since November 2012, **Yuri Nikiforov, MD, PhD**, professor of pathology and director of the Division of Molecular and Genomic Pathology at UPCI, and his team have sequenced more than 400 tumors as part of a multigene testing strategy using Next Generation Sequencing (NGS).

This revolutionary genetic testing technology can sequence millions of nucleotides and identify more than 2,000 mutations in 50 critical genes overnight. NGS provides the opportunity to identify driver mutations underlying tumorigenesis — the formation of tumors — to establish novel therapeutic targets, optimize drug selection for intervention, and define markers for early tumor diagnosis.

“Using the older Sanger sequencing technology, we were able to look at only one mutation at a time,” says Dr. Nikiforov. “Now, using NGS, we can apply a personalized cancer mutation panel or PCMP looking for 2,800 markers to find any number of typical and atypical mutations. For example, in breast cancer alone there are multiple mutations within the tumor of a single patient.



Every cancer is unique; using NGS, we can decipher the code of the tumor and make some predictions about the tumor, how aggressive it is, how it will respond to certain therapies, and how best to treat it.”

This testing is limited to patients who were treated with conventional therapy but still experienced tumor growth. After the failed treatment, the patient’s tumor is sequenced and, if a mutation is found, a targeted chemotherapy that blocks the specific mutation can be administered to help stop tumor growth.

The goal of multigene testing is two-fold: first is to link as many patients as possible to clinical trials for their particular mutations and second is to create a database of the genetic profiles of the tumors that can be matched with the patients’ response or lack of response to different therapies.

After information from hundreds of patients is entered, researchers can analyze the data to predict the next generation of patient response. **James Lee, MD, PhD**, is the primary investigator on the multigene sequencing registry that holds the collected and analyzed data.

NGS profiling of tumors is one of the most active areas of research at universities throughout the country. However, UPCI and UPMC CancerCenter are among only a handful of U.S. academic centers offering this type of testing as a clinical tool for treatment decision-making. Eventually this testing will be offered for every tumor at its earliest phase if these initial studies are promising.

Revolutionary Concept in Medicine

The advent of NGS profiling has produced a radical and remarkable shift in the prevailing thinking about cancer. “Through NGS, we learned that mutations are not specific for certain cancer types; different kinds of cancers can have the same mutations,” says Dr. Nikiforov. So patients with certain mutations may benefit from chemotherapy drugs traditionally given for other cancers with the same mutations.

“We started to understand that it may be more important to know the mutational profile of a particular cancer than what type of cancer it is or which body part is affected,” Dr. Nikiforov explains. “Through information-sharing and collaboration, we hope to advance the clinical application of genomic science even faster.”

Proprietary Software Development

UPCI and UPMC

CancerCenter’s commitment to and investment in NGS technology goes further than simply purchasing the equipment and training lab personnel to operate it: They have invested in the development of proprietary software called Seq Reporter to interpret and analyze the massive amounts of data created by the sequencers. “Without the software, the information would just be a huge data dump. The file sizes are in the terabytes,” says Dr. Nikiforov. “Seq Reporter deciphers the data in line and converts it into analyzable data for clinical use.”

Investment in NGS Technology

UPCI and UPMC

CancerCenter’s gene sequencing lab features some of the most cutting-edge bench-top equipment on the market today. Among the sequencing technologies being used are:

- Life Technologies Ion Torrent™
- Life Technologies Ion-Proton™
- Illumina® MiSeq

We're using data from 10,000 sequenced tumors and the possibilities are limitless.



Dr. Adrian Lee

The University of Pittsburgh Cancer Institute (UPCI) is a key participant in The Cancer Genome Atlas (TCGA), a nationwide effort to advance personalized or precision cancer treatment by sequencing 500 tumors of 20 different cancer types for a total of 10,000 tumors. This massive collection of tumor data will provide the statistical power needed to produce a comprehensive genomic profile of each cancer, which is essential to identifying the best targets for drug development.

UPCI is the largest supplier of breast cancer samples to TCGA and has supplied more total tumor samples than any other academic institution in the country.

“Because UPMC, the University of Pittsburgh School of Medicine, and UPCI had a long-term vision for a Health Sciences Tumor Bank (HSTB) and invested in it years ago, we have been collecting tumor and blood samples,” says **Adrian V. Lee, PhD**, director of the Women’s Cancer Research Center at UPCI and Magee-Womens Research Institute. “Most tumor banks only collect tumor samples, but we have always collected both tumor and blood. Our collection techniques and high patient through-put make us an ideal contributor to TCGA.”

TCGA began as a three-year pilot project in 2006, with a \$50 million investment from the National Cancer Institute and National Human Genome Research Institute.

TCGA is among the largest, most comprehensive molecular phenotyping efforts ever undertaken for cancer.

The pilot proved that, with a common infrastructure, a national network of research and IT teams working on different but related projects, pooling their results and making them publicly available, could enable researchers

Different Approaches to Common Goals

A number of research teams are working on a variety of projects that share information and are interconnected through their relationship to TCGA's gigantic genomic database.

Among them:

- **Steffi Oesterreich, PhD,** and **George C. Tseng, ScD,** have identified a gene overexpressed in ovarian cancer.
- **Xinghua Lu, MD, PhD, MS,** is integrating multiple levels of data to create a pathway analysis to predict good or bad prognoses in breast cancer.
- **Takis Benos, PhD,** and his lab are analyzing omic, clinical, and other data to discover the molecular mechanisms underlying diseases and identify biologically relevant biomarkers.

around the world to make and validate important discoveries. Already, hundreds of scholarly papers have been published using the data.

"Basically, TCGA is becoming the dictionary for cancer," says Dr. Lee. "The project uses a rigorous system of quality controlled, high-quality tumor samples — only accepting samples comprising at least 70 percent tumor cells — and multiple data analysis sites. Then, TCGA makes all the data public on a website so that any IRB-approved researcher can download and use the data for their research studies."

UPCI also is using data available through TCGA in a novel way, Dr. Lee adds. "Although TCGA's database is public, the amount of data is so huge that most researchers couldn't process it themselves, so at UPCI, we decided to download the data into one central system, called the Pittsburgh Genome Resource Repository (PGRR)."

We're finding that cancer is much more complex than we ever realized and we are leveraging the power of computers to help us understand it.

TCGA's database already is accelerating our understanding of breast cancer at UPCI. Using the clinical and genomic data for 140 breast cancer patients, UPCI researchers have begun to ask questions about whether there is a molecular difference between premenopausal breast cancer and postmenopausal breast cancer that has led the team to submit a project to the National Institutes of Health to provide clinical trials for women with premenopausal breast cancer.

Mining the Data for Personalized Care

With so much data being generated through gene sequencing, there is great opportunity for offering precision medicine, but it also presents challenges because the appropriate computational systems are not in place to analyze all the data, according to Dr. Lee. "We're generating data much faster than we're creating knowledge," he says.

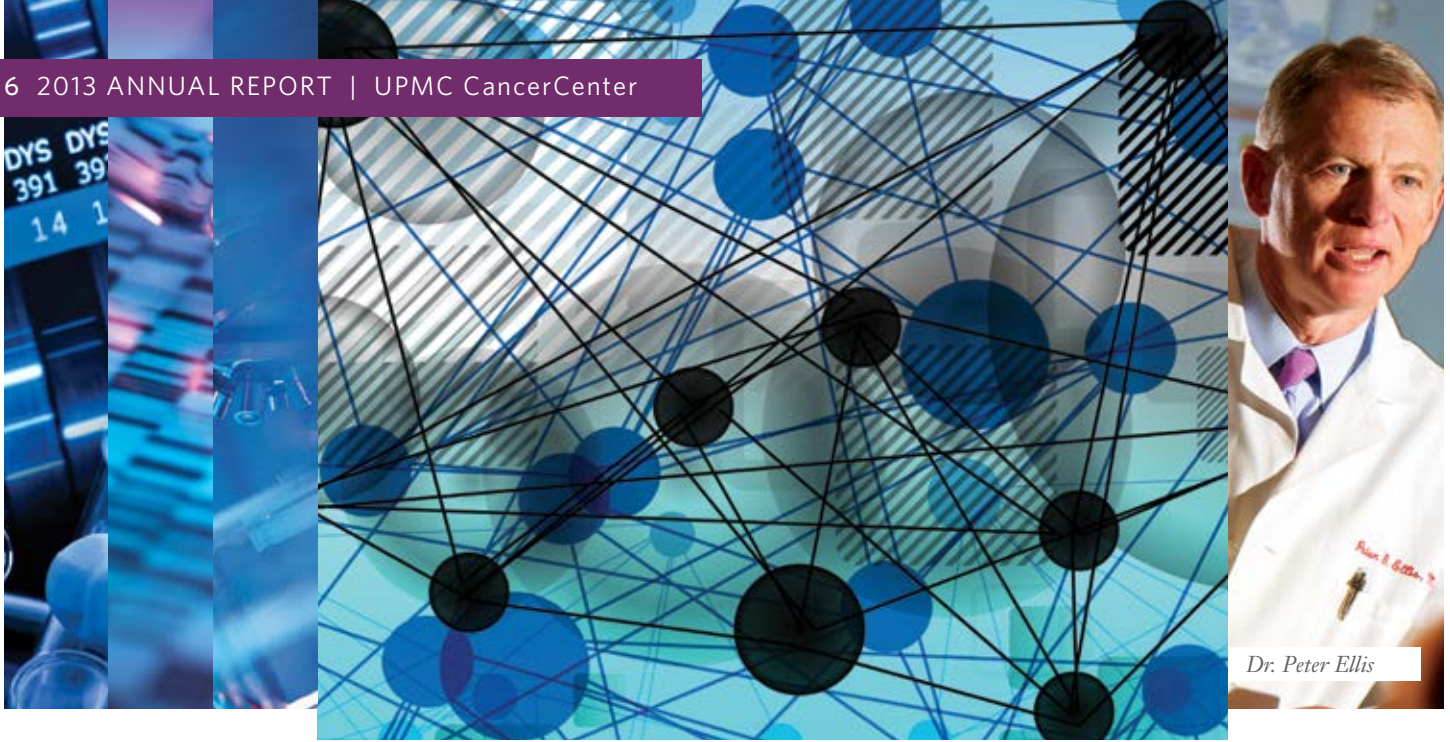
To enable clinicians and researchers to manage such huge datasets and perform complex analysis in a secure and traceable environment, UPMC CancerCenter, UPCI, and UPMC Enterprise Analytics partnered to develop and install an IT infrastructure. This infrastructure will serve as the foundation for UPCI's evolving efforts to make cancer discoveries that lead to the development of precision therapies and the delivery of personalized cancer care.

Next-generation discovery.

After Kathy Bilinsky, 64, was diagnosed with Stage 4 lung cancer, she went through six months of chemotherapy and the removal of her left lung, followed shortly by removal of her adrenal gland.

Not quite a year later, a CT scan revealed that the cancer had returned. Kathy was referred to nationally recognized lung cancer specialist **Mark Socinski, MD,** at Hillman Cancer Center, who sent her for six weeks of radiation therapy. At the same time, Dr. Socinski had ordered her tumor sample to be tested using Next Generation Sequencing (NGS) technology to possibly identify a genetic mutation causing her cancer. The test had found in Kathy's lung tumor the same mutation that causes renal cell or kidney cancer. Dr. Socinski prescribed Torisel (temsirolimus), an FDA-approved drug for treating kidney cancer, in addition to chemotherapy. Since April 2013, Kathy's scans have shown no additional tumor growth and she maintains an active lifestyle with her husband, Robert, four sons, and eight grandchildren.





Dr. Peter Ellis

Clinical Pathways:

Standards of care that ensure a higher standard of personalized medicine.

Clinical Pathways are disease-specific treatment regimens developed by teams of academic and clinical oncologists who regularly review the current literature and clinical practices to update Pathways for more than 90 percent of cancer types. Pathways help guide oncologists' decision-making to identify the most effective, least toxic treatment or, alternatively, a clinical trial for each patient's state and stage of disease, taking into account unique patient attributes, such as co-morbidities and biological markers or mutations.

An added advantage of Pathways is the ability to enable personalized care across large groups of patients. "In order for personalized medicine to be helpful to patients, it has to be evidence-based," says **Kathy Lokay**, senior vice president of commercial oncology services for UPMC's International and Commercial Services Division.

Pathways disease committees are physician-led. They meet regularly to review the evidence and prioritize therapy based on the best evidence for each person's state and stage of disease, as well as their biomarkers.

"Evidence-based biomarker predictions drive personalized medicine," adds **Peter Ellis, MD**, deputy director of clinical services for UPMC CancerCenter. "If a patient has an identifiable mutation that may predict a different outcome using a specific drug, and it's been studied, we mandate for that drug in Pathways. Because that standard of care is integrated into the Pathway, every patient with that same biomarker gets the appropriate personalized therapy and it continues to inform future standards of care."

Pathways are integrated into physicians' daily workflows through a secure web-based, real-time computer platform they use for decision support and for logging in each patient's unique attributes. The interactive interface allows physicians to follow the recommended Pathway or, due to individual patient circumstances or lab results, modify it. The computer platform also allows UPMC to measure adherence to Pathways and analyze data at the department, physician, and disease level on a monthly basis to ensure quality.

Medical oncology Pathways have been developed for 17 different cancers and radiation oncology Pathways for 18 cancers. UPMC CancerCenter now is embarking on surgical oncology Pathways, starting with breast cancer

and head and neck cancer. Each of the new surgical Pathways is being developed by a committee headed by one academic surgeon and one community surgeon.

Without Pathways, oncologists at other centers have only the guidelines published by the National Comprehensive Cancer Network (NCCN) and their own experience and literature review to rely on to devise treatment plans. Although the NCCN guidelines are evidence-based, they are extremely broad and often do not prioritize treatment based on unique patient attributes.

Pathways allow individual physicians to take advantage of the medical evidence, collective experience, and knowledge base of a panel of experts to make informed decisions about each patient.

According to Dr. Ellis, “Pathways are important to UPMC because they are the differentiators for our care — but they also better enable us to accrue patients to clinical trials and serve as excellent teaching tools for our fellows.”

And Pathways are constantly changing to leverage the newest scientific research and clinical experience being generated nationwide. Each Pathway is updated on a quarterly basis by a committee of experts from UPMC CancerCenter and other cancer centers around the country.

Also in development are Pathways for palliative or end-of-life care, and symptom management, in accordance with UPMC’s new models of care. These Pathways will aid in preventing unnecessary hospital admissions by alleviating symptoms that bring patients to the Emergency Department and ultimately improve the patient experience.

“Our goal is to preserve patients’ quality of life at home, so they don’t have to live their last days in a hospital intensive care unit, but also to allow patient-informed decision-making, realistic expectations, and advance care planning,” Lokay adds.

Pathways are being marketed externally to cancer centers through Via Oncology, an affiliate of UPMC’s International and Commercial Services Division. “The difference with UPMC’s program is that Pathways are marketed to cancer centers — not to insurance companies — so they are driven by patient outcomes rather than by profit or cost savings,” says Lokay.



Linda Macioce received the shock of her life in December 2009 when she was diagnosed with non-small cell lung cancer at age 49.

“I couldn’t even begin to wrap my head around the news,” she remembers. “I couldn’t quite understand how this had happened.”

Linda had never smoked and had no family history of lung cancer, but her prognosis was uncertain when a biopsy revealed that she had the Epidermal Growth Factor Receptor (EGFR) mutation. At the time, that diagnosis was grim, with typical life expectancies of only 12 months post-diagnosis.

Linda’s medical oncologist, **Mark Georgiadis, MD**, of UPMC CancerCenter at UPMC St. Margaret, used the Clinical Pathway for EGFR-positive lung cancer to determine her course of treatment. Beginning in January 2010, Linda was placed on Tarceva (erlotinib), a pill that works specifically to inhibit the EGFR mutation. For three years, the Tarceva held her cancer in check.

Linda did not experience any serious side effects from the drug and was able to maintain her normal lifestyle throughout her treatment. She has worked full-time at Allegheny County Children, Youth & Families, traveled to Las Vegas with her mom and sister, trekked to the Hoover Dam with Donny Osmond, and taken a road trip with her sister from Dallas to Memphis. Her travels have allowed her to build her collections of Native American pottery and Mexican folk art.

Linda had CT scans every three months for the entirety of her time on Tarceva. When the scans revealed that the cancer had begun to overpower the treatment in January 2013, Dr. Georgiadis decided to change her treatment plan. For the next year, Linda maintained a chemotherapy regimen of carboplatin, bevacizumab, and pemetrexed three weeks on, one week off.

A CT scan in January 2014 showed that the cancer was becoming more aggressive. Dr. Georgiadis worked with radiation oncologist **Ryan Smith, MD**, to develop an intense 10 rounds of radiation to try to shrink the lesion discovered on her lumbar spine.

Dr. Georgiadis and **Mark Socinski, MD**, a lung cancer specialist at Hillman Cancer Center, are currently working together to define a new treatment plan to keep the cancer under control.

Despite the relapse, Linda remains optimistic. “The Tarceva worked great for a long time,” she says. “I never expected to get three years out of it.” She is hopeful that the new treatment plan also will bring equally positive results.

Making hard-to-reach tumors easier to treat.

The newest-generation CyberKnife.



Dr. Dwight Heron

UPMC has long been known as a worldwide pioneer in stereotactic radiosurgery (SRS), which uses radiation to destroy — with pinpoint accuracy — tumors deep within hard-to-access areas of the body, such as the head, thorax, pelvis, and spine. The concept of radiosurgery began with Lars Leksell, a Swedish neurosurgeon, but was popularized mainly through ground-breaking research in Pittsburgh with the advent of the Gamma Knife® in 1987. Since then, UPMC has treated more than 13,000 patients using the Gamma Knife. This bloodless surgery is ideal for patients deemed poor surgical candidates due to co-morbidities, but has been found to be an effective alternative to traditional surgery for surgical candidates as well because the results have been so remarkable.

The original radiosurgery devices have evolved into the newest technologies, all of which are available through UPMC's SRS program, including the next generation of the CyberKnife®

UPMC was among the first centers in the world to use the CyberKnife and our unit, located at Mary Hillman Jennings Radiation Oncology Center at UPMC Shadyside, was recognized last year as the nation's busiest site and the world's fourth busiest for total procedures done using the device.

UPMC recently replaced its third-generation CyberKnife with an even more advanced and more powerful model — the M6™ — that can target areas of the body once considered unreachable. The CyberKnife M6 offers the best features of those two machines, with the added flexibility of a fully robotic arm, so that tumors in any part of the body can be treated.

Coming soon to UPMC's SRS program is another advancement — a multileaf collimator (MLC) — which will be the first offered on the CyberKnife. The device will manipulate the beam of radiation using continual image guidance to deliver a precise dose directly to the tumor

with sub-millimeter accuracy. The MLC also minimizes areas where too much radiation may be delivered to an overlapping area of the tumor or normal tissue to provide a more homogenous dose distribution.

“SRS has always been seen as a highly personalized treatment, because each patient’s radiation dose is literally sculpted to address the shape and placement of the individual tumor,” says **Dwight E. Heron, MD, FACRO, FACR**, director of radiation services. “Additional approaches to personalized medicine — such as advances in the field of metabolomics, which allows us to find out what’s happening inside the patient’s body on a cellular

level, and tumor profiling on an individual basis, looking at serum markers before and after a dose of radiation — help us predict therapeutic gain and prognosis. So we can now predict which patients will do well with radiosurgery. More importantly, in some cases we can predict those patients who are likely to not do well with radiosurgery alone, so we can formulate new treatment strategies to help improve their outcomes.”

The new M6 also offers a variety of improvements to the patient experience, including soothing environmental elements; faster, more effective treatments; and a frameless, non-invasive design to enhance comfort. The UPMC CyberKnife M6 will be the only model of its kind between Philadelphia and Columbus, Ohio.

CyberKnife M6 helping Lori Kacsur lead a normal life after breast cancer.

When **Lori Kacsur** of Kennedy Township found a lump in her breast in May 2010, she underwent a lumpectomy followed by chemotherapy and 35 sessions of radiation. After that, her scans were clear, and she thought she was out of the woods.

But about a year later, she was rushed to the hospital with appendicitis. And although the surgery was successful, a chest x-ray showed spots on her lungs and chest wall — metastasis of the breast cancer.

Lori underwent chemotherapy as part of a clinical trial to treat the cancer in her lungs.

A year later, an MRI revealed that Lori had developed several lesions on her brain. **Shannon Puhalla, MD**, Lori’s medical oncologist, sent her back to **Carol Scicutella, DO**, her original radiation oncologist at Heritage Valley Radiation Oncology, who successfully treated the lesions using whole-brain radiation. When a later scan showed that one lesion was particularly aggressive, Lori was referred to radiation oncologist **Steven Burton, MD**, and surgical oncologist **Johnathan Eng, MD**, for stereotactic radiosurgery (SRS).

Lori was one of the first patients to receive SRS using the new CyberKnife M6 at Mary Hillman Jennings Radiation Oncology



Center at UPMC Shadyside. “The first time you have the CyberKnife treatment, there’s a lot of anticipation,” she says. “But the procedure itself was nothing to be worried about.”

Lori had several CyberKnife treatments of between a half-hour to an hour each in October and November 2013. During the entire treatment process, Lori’s worst fear was that her memory would suffer as a result of the radiation. Thankfully, she never encountered that side effect.

After her first round of SRS, some of her lesions had completely disappeared, while several minor lesions and a single major lesion remained. Lori then received chemotherapy with carboplatin and avastin, and underwent an additional round of radiation therapy to her back prior to additional treatment with the CyberKnife.

Now 55, Lori has led a normal life since her diagnosis at 51, and her treatment plan has extended her time with her family. As a district administrator for a department store, she has continued to work 40 hours a week despite her condition. Few of her coworkers even know about her cancer, which is how she prefers it. Lori is very confident about the management of her cancer. “I know I am in good hands,” she remarks.

Cancer care that is specialized — and personalized.

SPORE Research Focusing on Gene-Based Treatment

The National Cancer Institute (NCI) has focused significant effort on increasing our understanding of cancer translational research — research that uses the established knowledge of human biology to develop and test the feasibility of cancer-related interventions and determines the biological basis for observations made in people with cancer or populations at risk for cancer.

One conduit for that research is the NCI-funded Specialized Programs of Research Excellence — or SPOREs — which are designed to enable the rapid and efficient movement, or translation, of basic scientific findings into clinical/applied settings and to discover new

approaches to the prevention, detection, diagnosis, and treatment of cancer. SPOREs are required to translate their findings to human populations within the five-year funding period. There are currently 62 active SPOREs located at academic centers in 23 states across the United States. The University of Pittsburgh Cancer Institute (UPCI) holds three of those SPOREs and collaborates on a fourth. SPORE grants are highly competitive, requiring institutions to document strong collaboration between eminent scientists and clinicians, as well as outstanding programs in translational research.



Dr. Jennifer Grandis

Renewed Head and Neck SPORE: Identifying targeted therapies.

Squamous cell carcinoma of the head and neck is a leading cause of cancer deaths worldwide. Because traditional therapies, such as surgery, radiation, and chemotherapy, are able to eradicate head and neck cancer in only 50 percent of cases, new approaches are needed.

“A primary research focus of our Head and Neck Cancer Program has been the identification of tumor or blood biomarkers that enable physicians to treat squamous cell carcinomas of the head and neck using personalized medicine targeted to the specific alterations in the patient’s tumor,” says **Jennifer R. Grandis, MD, FACS**, vice chair for research, University of Pittsburgh Department of Otolaryngology and leader of the UPCI Head and Neck Cancer Program. “Understanding the genetic, signaling, and immune alterations in head and neck cancer helps accelerate the development of new anticancer drugs that target novel pathways, and enables physicians to identify patients who will benefit from currently approved therapies.”

UPCI has received continuous funding from the NCI since 2002 for a SPORE in head and neck cancers, including the latest renewal of the SPORE that will run through 2015. The current SPORE aims to improve detection and treatment of head, neck, and oral cavity cancers, and to understand the mechanisms of susceptibility to these cancers.

The SPORE also contains funding for shared resources or cores, including a Histology/Tissue Banking Core, to ensure efficient use of tissue, blood, and body-fluid specimens of head and neck cancer patients to support the SPORE and other research, and a Biostatistics/ Informatics Core, to support all four of the research projects and the Histology/Tissue Banking Core.

The SPORE includes four major translational research projects, each of which highlights a personalized approach to treating head and neck cancer.

Project 1 is identifying genetic modulators of risk, prognosis, and response to therapy for head and neck cancer through a case-control study to identify single nucleotide polymorphisms (SNPs) associated with head and neck cancer risk, and a cohort study to identify SNPs associated with progression-free survival and treatment response with a focus on platinum-based therapy.

Project 2 is studying the effectiveness of targeting strategies aimed at blocking the epidermal growth factor receptor (EGFR), specifically using the monoclonal antibody cetuximab. Cetuximab is an effective therapy for advanced head and neck cancer, but not all patients respond to cetuximab. EGFR-expressing tumors typically result in poor survival rates and the presence of a modified EGFR protein is itself a predictor of a poor outcome.

Project 3 is studying whether the anti-tumor activity of cetuximab is influenced by its ability to trigger an EGFR-specific cellular immune response and by the escape mechanisms head and neck cancer cells use to avoid recognition and destruction by the body’s immune system. The results of this project will affect the clinical application of cetuximab-based immunotherapy on head and neck cancer patients by identifying predictive immune biomarkers of biological and clinical responses, which should optimize the selection of patients who are likely to benefit from it and contribute to the design of interventions to enhance its efficacy.

Project 4 is investigating the therapeutic benefits of co-targeting oncogenic pathways that are activated in the EGFR blockade setting when cetuximab has been administered. The study is examining mechanisms of resistance to EGFR targeting strategies and facilitating the design of therapies to enhance clinical response. In a Phase 2 clinical trial, patients who have been treated previously with cetuximab received a loading dose of the drug, followed one week later by dasatinib, an Src-family tyrosine kinase inhibitor, to determine dasatinib’s ability to enhance the clinical response to cetuximab.



Dr. John Kirkwood

Melanoma and Skin Cancer SPORE: Using genomics to advance treatment effectiveness.

The incidence of melanoma has increased significantly in the last decade, but no therapy has improved the overall survival rates for the majority of patients with unresectable metastatic disease. Each year, 9,000 people die of Stage 4 inoperable melanoma in the United States.

The University of Pittsburgh Cancer Institute (UPCI) Melanoma and Skin Cancer Program Specialized Program of Research Excellence (SPORE) recently was renewed for an additional five years and consists of four separate projects, each of which has a genomic basis.

Project 1 of the SPORE is nested within the adjuvant trial of interferon (IFN α) and the new agent ipilimumab that continues from the previous melanoma SPORE funding period. The new project compares high-dose interferon with two different dosages of ipilimumab, a checkpoint-blocking antibody that stimulates immune response. The goal is to identify biomarkers that classify the degree to which a patient may benefit from either drug, as well as predict which patients are at highest risk of recurrence and death. The trial is for patients with operable Stage 3 melanoma.

“This trial represents the zenith of our efforts to personalize the application of adjuvant therapy for melanoma, which we’ve led on an international basis since we conducted the first trial of interferon in Pittsburgh in 1985,” says **John M. Kirkwood, MD**, co-leader of the UPCI Melanoma Program, who is a medical oncologist specializing in melanoma and the principal investigator of the melanoma SPORE.

Both agents can be quite effective in treating melanoma, but both have side effects. Interferon causes flu-like symptoms and modest reversible decreases in blood count; ipilimumab, while less acutely toxic, can cause a host of dermatological, gastrointestinal, hepatic, endocrine, and glandular complications, so there is great potential value to using biomarkers that could predict which drug would prove to be most beneficial for which patients.

Project 2 centers on perhaps the ultimate form of personalized medicine — individualized vaccines — designed to provoke an immune response to tumor antigens to prevent the spread of metastatic melanoma. The trial is testing a novel dendritic cell-based vaccine, made of the patient’s own cells transfected with three tumor antigens and injected into the patient, as well as the addition of interferon in half of the patients to determine that drug’s benefit in boosting the body’s immune response. The analysis of several predictive biomarkers and prognostic biomarkers may identify patients who might benefit from immune-based approaches, as well as elucidate the mechanisms for that benefit.

Project 3 brings together the molecular anti-tumor therapy known as BRAF inhibitors and interferon, the established immunotherapy that has been the reference standard adjuvant treatment for the past 18 years. It seeks to find a safe and effective combination therapy to treat patients with metastatic melanoma with the BRAF mutation. This study will test the hypothesis that adding BRAF inhibitor to high-dose interferon (IFN α -2b) will enhance the therapeutic inhibitor efficacy of the interferon in patients with metastatic melanoma.

Project 4 will evaluate the application of an entirely novel approach to treating skin cancers through the delivery of chemotherapy and immune modifiers through the skin to kill accessible cutaneous lymphoma and in-transit melanoma cancer cells traveling through the dermal lymphatic system. The agents are delivered by a unique microneedle array device developed and produced at UPCI. This trial is currently in development and is expected to reach clinical testing to patients in 2014.

Dr. John Kirkwood is the principal investigator on the melanoma SPORE. The team consists of more than 30 investigators, including basic immunologists and molecular biologists, medical oncologists, dermatologists, surgeons, statisticians, bioinformatics specialists, and tissue bank and immunology lab physicians and staff, as well as patient advocates who consult about patient enrollment on the trials. This infrastructure was a key factor in enabling UPCI to secure and renew the SPORE — as was the quality of the science.



Dr. Mark Socinski

Lung Cancer SPORE: Improving detection and treatment.

In the United States, lung cancer accounts for more than 14 percent of all new cancers, and lung cancer death is more common than breast, prostate, and colorectal cancer death combined. Lung cancer has two forms — small cell and non-small cell — and together they represent the second most common cancer diagnosis in both men and women, behind only breast cancer in women and prostate cancer in men. Compounding the problem is that lung cancer is often not identified until the disease is in an advanced stage.

The University of Pittsburgh Cancer Institute (UPCI) has had a long-standing research commitment to lung cancer, as evidenced by its Lung Cancer SPORE, which is currently in its third five-year funding cycle.

“The continuation of the SPORE speaks to the credibility of the program and the strength of UPCI in conducting translational research on lung cancer,” says **Mark A. Socinski, MD**, a nationally recognized lung cancer specialist who serves as principal investigator on the UPCI Lung Cancer SPORE.

The overall goals of the UPCI Lung Cancer SPORE are to improve detection and treatment of lung cancer, and identify tobacco-exposed individuals at highest risk for developing lung cancer. There are four translational research projects in the SPORE:

Project 1 builds on the UPCI discovery that non-genomic estrogen receptor β (ER β) signaling through epidermal growth factor receptor (EGFR) is important in mediating the growth of primary non-small cell lung carcinomas. In the new study, the team is analyzing how estrogen receptors (ERs) and progesterone receptors (PRs) may be active in lung cancers and involved in lung cancer progression in both men and women. The team recently discovered in a lung cancer tissue microarray that ER β is a negative prognostic indicator, while PR is a positive prognostic indicator. The project will show if ERs and PRs predict outcome and response to anti-estrogens in lung cancer patients.

Project 2 extends upon UPCI research, which recently demonstrated that the active metabolite of vitamin D3 significantly inhibits the growth of lung cancer cells and antagonizes nuclear factor kB action, which has been connected to smoking-associated lung inflammation and cancer. Vitamin D supplementation seems to have potential to treat, delay, or prevent lung cancer; however, vitamin D is very potent and has a complicated metabolism, which makes it hard to dose. The project will evaluate whether supplementation with vitamin D3 corrects deficiency and will investigate its effects on inflammation and lung cancer risk.

Project 3 uses the blood and sputum samples from the Pittsburgh Lung Screening Study (PLuSS) to develop a biomarker panel looking for a pattern of certain enzymes present in lung cancer, then refine and validate a lung cancer risk prediction model based on those biomarkers. The goal is to improve prediction of lung cancer risk in tobacco-exposed populations by using genetic variations found in the blood and sputum, in combination with previously identified risk factors.

Project 4 tests a hypothesis that neutrophil elastase (NE) — which is secreted by white blood cells in the immune system — is a critical mediator of inflammation-associated, pro-cancer signaling in human lung cancer, and that interruption of its function may inhibit lung cancer with the K-ras mutation, which is resistant to other targeted therapies. The team is currently exploring a number of NE inhibitors in search of a suitable drug to test the validity of their hypothesis.



Dr. Robert Edwards

Ovarian SPORE: Harnessing the body's immune system to fight cancer.

Ovarian cancer is the fifth leading cause of cancer death in women. Although there have been slight improvements in progression-free survival after surgery and chemotherapy, survival rates remain poor for women with advanced ovarian cancer.

“Ovarian cancer is often detected much later than other types of solid tumors,” says **Robert Edwards, MD**, co-director of the UPCI Women’s Cancer Research Center, executive vice-chair of gynecologic services and director of the Ovarian Cancer Center of Excellence at Magee-Womens Hospital of UPMC. In fact, more than 75 percent of patients with ovarian cancer receive their diagnosis when their disease is advanced. Women with metastatic ovarian cancer have only about a 25 percent five-year survival rate. In contrast, women whose disease is caught at the earliest stage have five-year survival rates of more than 90 percent.

To reduce the prevalence of ovarian cancer and increase survival rates, the University of Pittsburgh Cancer Institute (UPCI) has partnered with Roswell Park Cancer Institute (RPCI) in Buffalo, N.Y., to form an Ovarian Cancer Specialized Program of Research Excellence (SPORE), one of only five ovarian cancer SPOREs in the country. Dr. Edwards serves as co-principal investigator on the SPORE with **Kunle Odunsi, MD, PhD**, director of the Center for Immunotherapy at RPCI. The UPCI-RPCI Ovarian Cancer SPORE will support individual translational research projects; developmental research, and career development synergistic programs; and supportive cores.

“The partnership between Roswell and UPCI is mutually beneficial in that it combines Roswell’s advanced science in ovarian cancer with UPCI and UPMC CancerCenter’s ability to accrue patients to the clinical trials,”

says Dr. Edwards. “UPMC CancerCenter’s high patient volumes will enable us to conduct the trials quickly, so we can help more patients while accelerating the science on ovarian cancer.”

Project 1 will test a novel therapeutic strategy to break indoleamine 2,3-dioxygenase (IDO)-mediated immune tolerance in ovarian cancer, while inducing anti-tumor-specific immunity in ovarian cancer patients in second remission. In this trial, ovarian cancer patients will be vaccinated in the hope that the vaccine will block the activity of this immune cell and prolong its ability to kill cancer cells.

Project 2 will test a combination strategy of mTOR inhibition and interleukin-21 for ex-vivo conditioning of antigen-stimulated CD8+ T cells for effector and memory-functional attributes; and whether the ex-vivo-generated cells produce durable immunity against ovarian tumors.

Project 3 will test whether autologous tumor-loaded type-1-polarized dendritic cells (α DC1s) will generate cytotoxic T lymphocyte cells (CTLs) capable of recognizing ovarian cancer when used both as a vaccine and for adoptive T cell therapy.

Project 4 is a population study that will determine the predictive significance of myeloid-derived suppressor cells (MDSCs), which have strong immunosuppressive properties in the long-term survival of ovarian cancer patients. The study will focus on the genetic pathways that regulate immune responses against cancer to predict who will most benefit from immunotherapy.



Josh on left, Alex on right.

Extras in film about cancer prove to be the real stars.

Several hematology-oncology patients and childhood cancer survivors from Children's Hospital of Pittsburgh of UPMC recently brought some realism to the set of a major motion picture filmed in Pittsburgh.

The patients appeared in "The Fault in Our Stars," a film based on the highly successful young adult novel by John Green. The story centers on the relationship between Hazel and Augustus, two teenagers dealing with cancer.

Among the patients serving as extras was Joshua Potter, a 19-year-old Children's patient from Perryopolis, Pa. Josh has had firsthand experience in playing a cancer patient because he has been one in real life — three separate times. Originally diagnosed with Burkitt's lymphoma at age nine and treated with intensive chemotherapy, he was in complete remission for five years until he was diagnosed with Ewing sarcoma of the pelvis as a teenager. Following an internal hemipelvectomy, which removed part of his pelvic bone, he did well for two years until he had a sarcoma recurrence in his lungs. He has finished radiation and will continue chemotherapy until spring 2014 if there is no evidence of disease progression.

Josh and several other current and former Children's cancer patients served as extras in a scene featuring

a support group for teens, which he said he thoroughly enjoyed. "It was a blast," he says.

The best part was getting to be with other kids who'd had cancer, because we had so much in common. I hadn't really met many other kids with cancer before.

Josh especially enjoyed the experience because he met and struck up a friendship with another Children's patient, Alex Murph, who'd had the same type of cancer, the same cancer doctor, and also was an Eagle Scout, like himself. The pair is in contact often, and Josh continues to keep up with the other kids through social media.

Josh is currently feeling good and working at a store that sells collectible model trains in Greensburg, Pa. "The Fault in Our Stars" is expected to open in theaters in June 2014. By then, Josh hopes to be done with chemotherapy and in remission once again.

Improving cancer care on a global scale.

Cancer hospital in Kazakhstan
being built with UPMC know-how.



Through its International and Commercial Services Division, UPMC is partnering with Nazerbayev University to begin development of a 300-bed cancer hospital with outpatient medical and radiation oncology, a research facility, and housing for family members to stay during their loved one's treatment.

"The new hospital will serve as the flagship location for a national cancer hospital system, using a similar model to the one we used for Hillman Cancer Center," says **Chuck Bogosta**, president of UPMC's International and Commercial Services Division and UPMC CancerCenter. "We are currently developing the cancer program's clinical activity, so the hospital can begin operations as soon as the facility is completed in 2016."

UPMC is working to develop strong relationships between Pittsburgh-based and Kazakhstan-based oncologists. During 2013, a number of surgeons from Kazakhstan came to Pittsburgh to observe UPMC processes, and UPMC CancerCenter physicians visited Kazakhstan to perform surgeries there.

Among them was **David Bartlett, MD**, vice chairman of surgical oncology and GI surgical services, who performed seven complex GI surgical oncology procedures over five days in summer 2013, including a major liver resection, a Whipple procedure, a laparoscopic colectomy, and a colorectal reconstruction. He was assisted by a UPMC anesthesiologist and a surgical nurse specialist.

Dr. Bartlett says he envisions UPMC professionals traveling to Kazakhstan on a regular basis to perform surgery on the most challenging cases following completion of the new hospital. "We hope to maintain a UPMC presence there and eventually do perfusions, investigational surgeries, and clinical trials." Currently, there are limited clinical trials available in Kazakhstan and partnering with UPMC CancerCenter will assist in providing more clinical trials for all cancer diseases.

The need for cancer care in Kazakhstan is extreme, as more than 30,000 new cases of cancer are detected annually, with more than half of all patients being diagnosed at a late stage.

In addition, because the country is so large and the existing cancer centers so few, patients must travel long distances to receive treatment. The new hospital should contribute to advancement in medical care, as well as to an increase in the number of patients with access to treatment.


Cancer screening is another area where Kazakhstan currently lacks resources. UPMC is starting a breast cancer screening program in the country, spearheaded by **Margarita Zuley, MD**, medical director of breast imaging at Magee-Womens Hospital of UPMC and associate professor of radiology at the University of Pittsburgh School of Medicine.

In addition, through the relationship, Kazakhstani patients with non-small cell lung cancers will gain access to next-generation gene sequencing through a genomics project headed by **Adam Brufsky, MD**, associate director for clinical investigations at the University of Pittsburgh Cancer Institute (UPCI), and **Mark Socinski, MD**, principal investigator on the UPCI Lung Cancer SPORE. The project will sequence genes for 50 patients and provide advice for targeted treatment for their particular mutations.



Putting out a strong message about not smoking.





As a National Cancer Institute (NCI)-designated Comprehensive Cancer Center (CCC), the University of Pittsburgh Cancer Institute (UPCI) has had a long-standing commitment to providing community outreach programs to educate the public about cancer and identify ways to reduce cancer risk, particularly among underserved populations in our region.

UPCI's underserved populations include African-Americans, the uninsured/underinsured, elderly, homeless, individuals residing in rural communities or transitional living centers, and the mentally or physically challenged.

Among the many programs offered by UPCI's Cancer Outreach Program are smoking awareness and cessation programs, which **Lyn Robertson, DrPh, RN, MSN**, UPCI associate director of Cancer Outreach, and her team take out into the communities through the innovative partnerships they have developed with local social services organizations, such as community centers, shelters, food banks, and businesses.

"Any time we do a cancer screening, we ask if the person is a smoker and inform him or her about the cancer risks associated with smoking and tobacco use," says Dr. Robertson. "Our mantra is prevention and early detection of cancer."

Dr. Robertson reports misperceptions among the underserved populations she assists, despite more than 50 years of Surgeon General reports and warnings and public awareness campaigns about smoking and cancer risk.

"There's been such a focus on smoking and lung cancer that some people think that's the only cancer associated with tobacco use," Dr. Robertson says. "They don't realize that tobacco use puts them at risk for other cancers, such as head and neck cancers, as well as a host of other

health issues, such as emphysema, chronic obstructive pulmonary disease (COPD), and heart disease. In addition, they don't always understand the risk their smoking presents to their children or grandchildren for developing asthma, ear infections, and respiratory problems due to exposure to second-hand smoke."

More people are trying to kick the habit, according to Dr. Robertson, whether at the urging of family members or because of societal pressures and legislation. "Many people will ask us, 'How can I quit?'" she says. "In some cases, residents in shelters and halfway houses ask how they can quit smoking at the same time as they're coming clean from drugs or alcohol, and we help them to develop a realistic plan, so that they can be successful. It is not always the best time to quit smoking when you are also in the midst of becoming sober or drug-free. So we work with them to develop a realistic timeframe."

The cancer outreach team has a number of options available to counsel community members who want to kick the habit. Resources include workbooks and contact information for established programs, such as the American Cancer Society's Quit for Life[®], American Lung Association's Not-On-Tobacco (NOT) program, and Pennsylvania Department of Health's PA Free Quitline, which includes coaching sessions and educational support. The team also can arrange nicotine replacement therapy, such as nicotine patches, gum, and lozenges at a reduced cost or free for those who qualify.



Educating kids about smoking starts in school.

Being out in the community often is an eye-opening experience for UPCI's Cancer Outreach team, as **Susan Radio, BSEd, MS**, community program educator, has discovered. She presents cancer-related messages to students in grades 1 through 9 throughout the region through the Healthy Choices for Students program.

Sadly, despite public awareness campaigns, Susan says that even kids at the middle school level report either having tried cigarettes or tobacco at least once or knowing kids who use tobacco and even drugs regularly, particularly in rural areas. "We teach students first and foremost why cigarettes are detrimental to the human body," Susan says. "We talk about the importance of making healthy choices at a young age. Kids are often told to stay away from tobacco, nicotine products, and other drugs, but not why they should stay away — so that's what we teach them."

Students at the high school level often already have developed tobacco habits and ask her how they can quit, Susan reports. "I help them enlist the help of a teacher or guidance counselor, or refer them to an appropriate program to help them quit."

But keeping kids from acquiring nicotine habits can be difficult, especially when new forms of tobacco continue to come onto the market. Besides mint-flavored nicotine pouches that appeal to youths, **Lyn Robertson, DrPHD, RN, MSN**, reports that nicotine gum, meant to help smokers quit, can be used by kids to get a nicotine buzz, as can nicotine-enriched water.

And a new type of smoking, called "vaping" — puffing on inhalers known as electronic cigarettes (e-cigarettes) or vape pens — is on the rise. The devices use batteries to heat a flavored liquid until it produces a vapor, which may contain varying levels of nicotine although no tobacco smoke is produced. "It is too early to say that e-cigarettes are safe," Dr. Robertson says.

These e-cigarettes were meant to help smokers quit, but that's not what we see happening in the community. They are becoming another way for kids to look cool, as though they're smoking.

"The problem is complex; we need to somehow get across that smoking is not acceptable or cool — that it's much cooler not to smoke. So these new nicotine delivery methods will have to be studied by researchers in the near future to learn their effects," says Dr. Robertson.



Our smoking-cessation research is igniting new ways to quit.

A number of UPCI researchers are undertaking projects to improve current smoking cessation resources to help smokers kick the habit more successfully. Among these projects:

Ellen Beckjord, PhD, assistant professor of psychology and a member of UPCI's Biobehavioral Medicine in Oncology Program, is receiving a KL2 award from the University of Pittsburgh to fund the development of a context-aware mobile application to aid in smoking cessation.

Currently in beta testing, the app, called QuitSmart, combines evidence-based behavioral science with machine learning technology to help smokers self-regulate and improve health behaviors.

Periodic prompts and responses help predict self-regulation failure (the urge to smoke). When a user reports an urge, he or she gets a real-time intervention based on his or her own preferences and motivators. When urge attributions are internal, a cognitive intervention is delivered; when an urge is external, a behavioral intervention is delivered. A varied menu of intervention options — such as progress charts — is offered, and users can input their own motivation enhancers, including photos and encouragements. Dr. Beckjord is working with a mentoring team consisting of **Dana Bovbjerg, PhD**; **Saul Shiffman, PhD**; and **David O. Wilson, MD**; as well as **Daniel Siewiorek** of Carnegie Mellon University's Human-Computer Interaction Institute and Virginia-based technical partner Vignet Corp.

Eric Donny, PhD, associate professor of psychology and a member of UPCI's Biobehavioral Medicine in Oncology Program, directs a major National Institutes of Health (NIH) U54 Specialized Center multisite grant studying the reduction of nicotine content in cigarettes as a product standard related to the Food and Drug Administration's new regulatory authority over tobacco products. The University of Pittsburgh is the coordinating institution for the Center grant.

The first clinical trial funded by the grant is the current 10-site, randomized, double-blind study exploring the behavior, biomarkers, and withdrawal symptoms of 840 smokers using cigarettes with varied lower levels of nicotine.

A second 10-site clinical trial of 1,250 smokers will compare the outcomes of participants who switch to reduced-nicotine content cigarettes immediately to those of participants who taper nicotine content gradually. A third study led by the University of Pittsburgh will compare the outcomes of participants who use low-nicotine cigarettes with or without a nicotine replacement patch; and a final study will look at the reactions to lower nicotine content cigarettes among smokers with schizophrenia.



Saul Shiffman, PhD, professor of psychology and a member of UPCI's Biobehavioral Medicine in Oncology Program, has been awarded a supplement to UPCI's Cancer Center Support Grant from the National Cancer Institute to conduct a trial for nondaily or intermittent smokers using low-nicotine cigarettes.

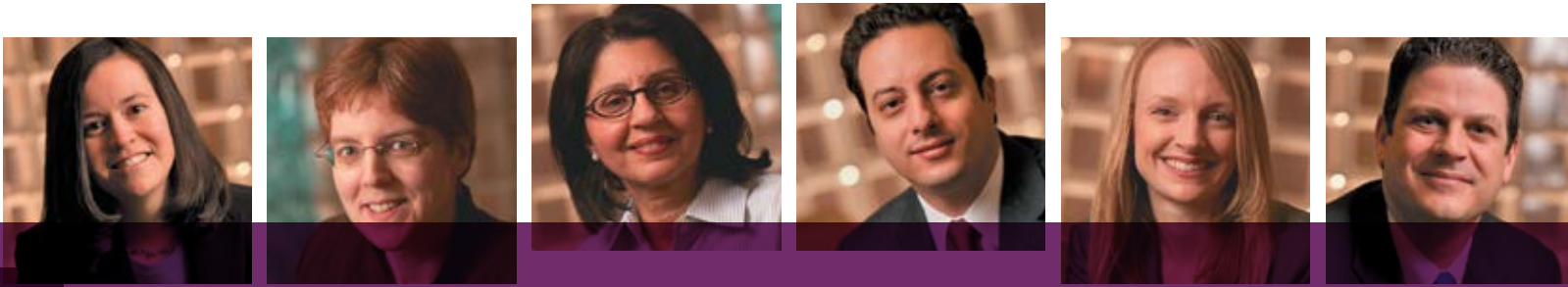
Studies show that one in three American smokers does not smoke every day, so they do not fit the typical nicotine-dependence model.

Low-nicotine cigarettes are posited as a way to help smokers cut down their nicotine dependence or quit altogether; however, because their smoking patterns essentially demonstrate that they don't need daily doses of nicotine, intermittent smokers may respond differently to low-nicotine cigarettes and, theoretically, could be encouraged to smoke more by using cigarettes with lower nicotine content. Dr. Shiffman also is the co-primary investigator on a study directed by **Hilary Tindle, MD, MPH**, assistant professor of medicine and member of the UPCI Biobehavioral Medicine in Oncology Program, which is exploring the surprisingly low success rates of intermittent smokers who try to quit smoking. Data collected in a previous research study suggests a strong link between smoking and specific situations or stimuli,

rather than on nicotine withdrawal. The study, funded through the University of Pittsburgh Department of Medicine and Department of Psychology, will explore whether intermittent use of nicotine replacement therapy — such as nicotine gum — can replace intermittent use of cigarettes and be an effective way for nondaily smokers to successfully quit altogether.

50th Anniversary of the Surgeon General's Report

January 2014 marked the 50th anniversary of Surgeon General's report that brought the negative health impact of tobacco into the public spotlight. To mark this golden anniversary a new Surgeon General's report reflecting our progress in the area of tobacco control and our understanding of the overwhelmingly negative effects of tobacco on human health was released. We are honored to have three University of Pittsburgh School of Medicine faculty serve as co-authors: **Hilary Tindle, MD**, **Steve Shapiro, MD**, and **Nancy Davidson, MD**.



Our employees lead by example by going smoke-free.

Beginning July 1, 2014, all UPMC employees — including nurses, physicians, volunteers, contractors, students, administrators, and support staff — will be required to refrain from smoking or using tobacco during their shifts, including breaks and meal times. UPMC adopted a Clean Air/Smoke- and Tobacco-Free Campus policy in 2007, and tobacco use currently is not permitted on any UPMC property by anyone, including patients, visitors, and employees. The ban on use during shifts will be an extension of the current policy.

“The prohibition of smoking and tobacco products is consistent with UPMC’s efforts as a health care system to promote healthy lifestyles and to provide the best possible care to our patients, but it’s even more important for the UPMC CancerCenter network to take a more aggressive stance, considering what we know about the relationship between tobacco and cancer,” says **Eric D. McIntosh**, human resources director for UPMC CancerCenter and a former smoker himself. “Cigarette smoking is inconsistent with the messages we deliver on making healthy choices and lowering cancer risk.”

Employees who smoke are always encouraged to quit, or at least cut down, and UPMC Health Plan has a number of tobacco-cessation resources to help them, including

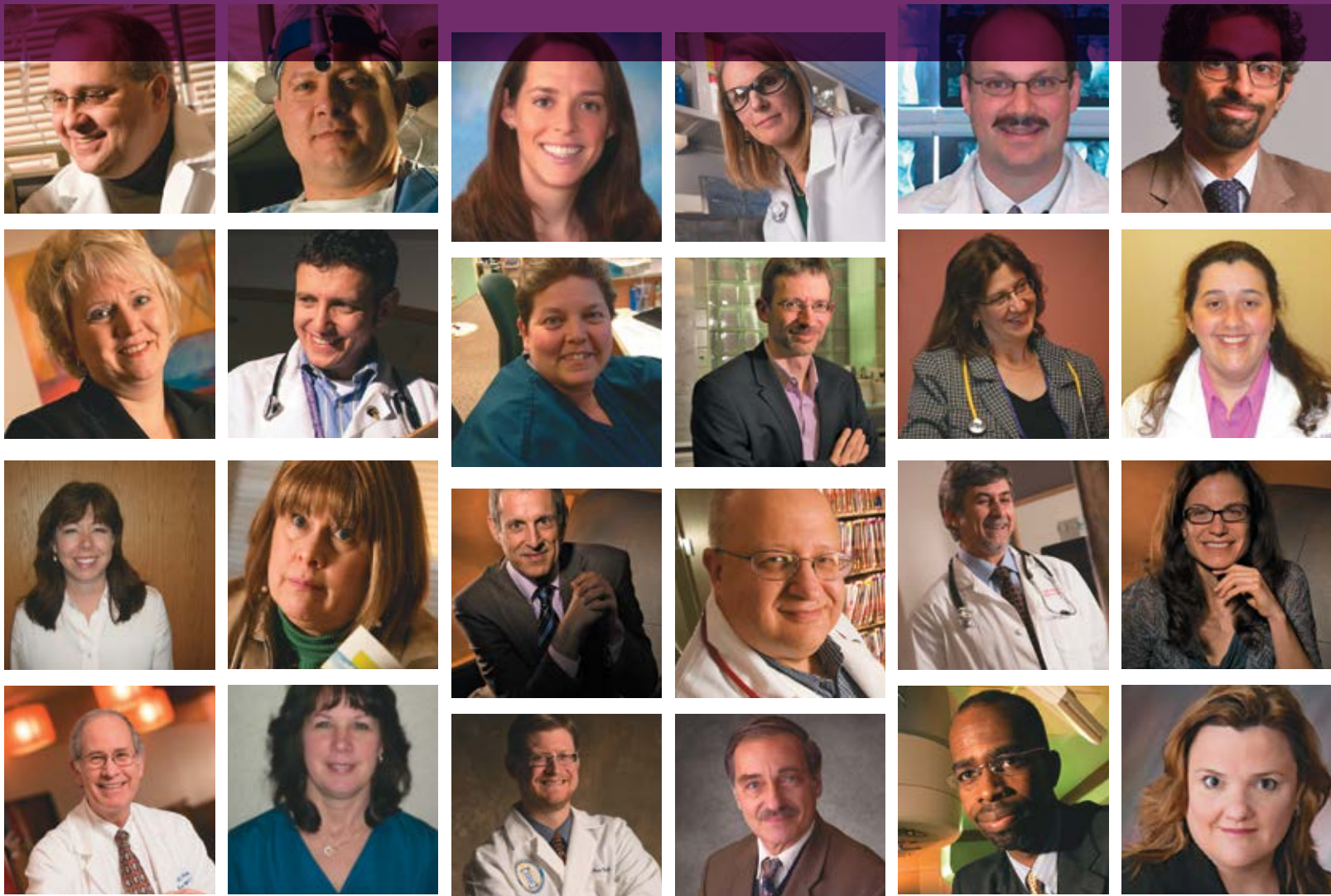
health coaches and counselors, an employee “Ready to Quit” program, and online programs. Employees also can get copay reimbursement for nicotine patches, gum, and tablets to help them kick the habit.

UPMC will still hire smokers and make smoking cessation programs available to them. New hires will be informed up front about the new policy.

Staff members are not required to quit, but they must comply with the ban on smoking and other tobacco use throughout their work day. “Our goal is to encourage people to quit, not penalize people for their habits,” Eric says. “But smoking really is in direct conflict with everything UPMC CancerCenter stands for. We are committed to maintaining a healthy environment for patients and visitors, and ensuring their experience with us is positive by reducing their exposure to tobacco products.”



UPMC CancerCenter employees soon will be practicing what they preach about tobacco use when UPMC puts into effect a systemwide ban on employee cigarette smoking and use of other types of tobacco products during the work day at all of its facilities.



As a pre-eminent cancer research center and one of the largest integrated community networks of cancer physicians, researchers, and health care specialists in the United States, UPMC CancerCenter and the University of Pittsburgh Cancer Institute (UPCI) have assembled a group of some of the most prominent experts in the country, and we continue to recruit new talent. With more than 40 locations, our patients have access to the most advanced, world-class cancer care, at a cancer center close to their homes. The goal of engaging new talent is to enhance our knowledge and expertise as an organization and help us to continuously improve cancer prevention and detection, discover new treatments, and advance our education and research missions.

Allow us to introduce some of our new physicians and researchers.

Colin Champ, MD

Radiation oncologist

Special expertise: the treatment of breast cancer and central nervous system malignancies, and clinical nutrition and exercise relating to cancer treatment

Medical school: Jefferson Medical College of Thomas Jefferson University, Philadelphia

Residency: radiation oncology, Thomas Jefferson University Hospital

Rushir Choksi, MD

Medical oncologist

Medical school: Wake Forest University School of Medicine, Winston-Salem, N.C.

Residency: internal medicine, UPMC

Fellowship: hematology/oncology, UPMC

Andy (David) Clump, MD, PhD

Radiation oncologist

Special expertise: head and neck malignancies and stereotactic radiosurgery

Medical school: West Virginia University School of Medicine

Residency: radiation oncology, UPMC

Madeleine Courtney-Brooks, MD, MPH

Assistant professor of gynecologic oncology

Special expertise: minimally invasive gynecologic oncology surgery, optimizing gynecologic oncology care for elderly patients, and quality of life at the end of life for gynecologic oncology patients

Medical school: Washington University School of Medicine, St. Louis, Mo.

Residency: obstetrics/gynecology, Magee-Womens Hospital of UPMC

Fellowship: gynecologic oncology, University of Virginia, Charlottesville

Laura M. De Castro, MD

Director of benign hematology, Institute for Transfusion Medicine and UPMC CancerCenter; director of clinical translational research, UPMC Sickle Cell Disease Research Center of Excellence

Special expertise: the impact of sickle cell disease on end-organ damage, psychosocial issues related to the disease, and development of novel treatments

Residency: internal medicine, Montefiore Medical Center in New York, N.Y.

Fellowship: hematology/oncology, Yale University School of Medicine

Ying Ding, PhD

Assistant professor, Department of Biostatistics, University of Pittsburgh

Special expertise: the design and analysis of biomarker studies and biomarker/subgroup identification; survival analysis, including semiparametric inference theory and method, and application of empirical process; comparative effectiveness research (CER) using Bayesian indirect and mixed treatment comparisons and meta-analysis of patient outcomes; and proteomics experiment design and network analysis

Doctorate: biostatistics, University of Michigan, Ann Arbor

Kathleen Dorritie, MD

Assistant professor of medicine, University of Pittsburgh School of Medicine

Special expertise: hematologic malignancies, stem cell transplantation, and the development of novel therapeutics for acute myeloid leukemia

Medical school: State University of New York Upstate Medical University, Syracuse, N.Y.

Residency: internal medicine, UPMC

Fellowship: hematology/oncology, UPMC

Melissa Hogg, MD

Assistant professor of surgery, University of Pittsburgh School of Medicine

Special expertise: gastrointestinal surgical oncology with a focus in minimally invasive treatment of benign and malignant diseases of the stomach, bile duct, and pancreas

Medical school: Northwestern University, Feinberg School of Medicine, Chicago

Residency: general surgery, McGaw Medical Center of Northwestern University

Fellowship: surgical oncology, University of Pittsburgh School of Medicine

Marilyn Huang, MD, MS

Assistant professor of gynecologic oncology

Special expertise: all gynecologic malignancies, hereditary gynecologic cancers, minimally invasive surgery, and Phase 1 clinical trials

Medical school: Eastern Virginia Medical School, Norfolk, Va.

Residency: New York-Presbyterian/Weill Cornell Medical Center

Fellowship: University of Texas MD Anderson Cancer Center, Houston

Annie Im, MD

Assistant professor of medicine, University of Pittsburgh School of Medicine

Special expertise: research of hematologic malignancies, such as leukemia, lymphoma, and myeloma; drug development; stem cell transplantation; and graft-versus-host disease

Medical school: State University of New York, Stony Brook School of Medicine, Stony Brook, N.Y.

Residency: internal medicine, UPMC

Fellowship: hematology/oncology, UPMC

Bruce L. Jacobs, MD, MPH

Urologic oncologist; assistant professor, University of Pittsburgh School of Medicine

Special expertise: minimally invasive and open surgery for prostate, kidney, bladder, and testicular cancer

Medical school: Vanderbilt University School of Medicine, Nashville, Tenn.

Master's degree: public health, University of Michigan School of Public Health, Ann Arbor

Residency: urology, University of Pittsburgh

Fellowship: health services research, laparoscopy/endourology, and urologic oncology, University of Michigan

Gregory J. Kato, MD

Professor of medicine, University of Pittsburgh School of Medicine; director, Adult Sickle Cell Center of Excellence, UPP Division of Hematology/Oncology

Special expertise: nonmalignant hematology, adult sickle cell disease, and early phase sickle cell clinical trials

Medical school: George Washington University School of Medicine and Health Sciences

Residency: Children's Hospital of Los Angeles

Fellowship: pediatric hematology/oncology, The Johns Hopkins Hospital

Brenda Kurland, PhD

Research associate professor, Department of Biostatistics, University of Pittsburgh

Special expertise: biostatistics and the design and analysis of clinical trials involving quantitative imaging, breast cancer, lung cancer, and functional imaging, specifically PET and breast MRI

Doctorate: biostatistics, University of Washington, Seattle

John Lech, DO

Hematologist/medical oncologist

Special expertise: the treatment of gastrointestinal malignancies and peritoneal carcinomas

Medical school: Lake Erie College of Osteopathic Medicine, Erie, Pa.

Residency: internal medicine, The Western Pennsylvania Hospital, Pittsburgh

Fellowship: hematology and oncology, The Western Pennsylvania Hospital, Temple University School of Medicine Clinical Campus, Pittsburgh

Carissa Low, PhD

Assistant professor of medicine, and assistant professor of psychology, University of Pittsburgh

Special expertise: bidirectional relationships between inflammation and patient-reported outcomes over the course of cancer treatments; development of interventions to reduce symptom burden and enhance quality of life in cancer patients

Doctorate: University of California, Los Angeles

Internship: clinical psychology, Western Psychiatric Institute and Clinic, Pittsburgh

Solomon Ofori-Acquah, PhD

Visiting associate professor of medicine and director, Center for Translational and International Hematology

Special expertise: sickle cell disease and acute chest syndrome, medical laboratory sciences specializing in hematology and blood transfusion

Medical school: Bromley College of Technology, Kent, England

Master's degree: biomolecular organization, Birkbeck College, University of London

Doctorate: molecular genetics, King's College School of Medicine and Dentistry, University of London

Javier Salgado, MD

Assistant professor of surgery, University of Pittsburgh School of Medicine

Special expertise: the treatment of colon and rectal cancer, inflammatory bowel disease (IBD), and other diseases of the colon and rectum

Medical school: Universidad Nacional de Cordoba, Argentina

Residency: general surgery, UPMC

Fellowship: minimally-invasive surgery, The Western Pennsylvania Hospital, Pittsburgh; colon and rectal surgery, Penn State Hershey Medical Center, Hershey, Pa.

Jack D. Schocker, MD

Radiation oncologist

Medical school: Hahnemann University, Philadelphia

Residency: Hahnemann Medical College and Hospital of Philadelphia

Alison Sehgal, MD

Assistant professor of medicine, University of Pittsburgh School of Medicine

Special expertise: allogeneic and autologous stem cell transplant, lymphoma, leukemia, and multiple myeloma

Medical school: Duke University School of Medicine, Durham, N.C.

Residency: internal medicine, University of Pennsylvania, Philadelphia

Fellowship: hematology/oncology, University of Pennsylvania, Philadelphia

Rajesh Sehgal, MBBS, MD, FACP

Hematologist/medical oncologist

Special expertise: solid tumors including breast, colon, and lung cancer, and blood disorders

Medical school: Government Medical College, Amritsar, India

Residency: internal medicine, McLaren Regional Medical Center, Flint, Mich.

Fellowship: hematology/oncology, UPMC

Felicia Snead, MD

Radiation oncologist

Special expertise: breast, central nervous system, and gastrointestinal cancers, and general radiation oncology

Medical school: Albert Einstein College of Medicine, Bronx, N.Y.

Residency: radiation oncology, New York Presbyterian Hospital, Columbia-Presbyterian Medical Center

Robert VanderWeele, MD, MS

Hematologist/medical oncologist

Special expertise: hematology and medical oncology

Medical school: Drexel University College of Medicine, Philadelphia

Residency: internal medicine, UPMC

Fellowship: hematology/oncology, UPMC

Joseph Wang, MD

Radiation oncologist

Special expertise: the treatment of all cancers, intensity modulated radiation therapy, and image-guided radiation therapy

Medical school: China Medical University, School of Medicine, Taichung, Taiwan.

Residency: anatomic pathology, Aultman Hospital, Northeastern Ohio Medical University, Rootstown, Ohio; radiation oncology, University of Iowa Hospitals and Clinics, Iowa City

Upwardly mobile.

Career advancement news.



Sally E. Carty, MD, FACS

Professor of surgery, chief of endocrine surgery, and director of the Endocrine Surgery Fellowship Program, University of Pittsburgh School of Medicine; co-director of the UPMC/UPCI Multidisciplinary Thyroid Center

Dr. Carty has been named president of the American Association of Endocrine Surgeons (AAES) after a year of serving as president-elect. The AAES is dedicated to the advancement of the science and art of endocrine surgery, which covers diseases of the thyroid, parathyroid, adrenal glands, and neuroendocrine pancreas. The theme of her year-long term is Education: Teach to Reach, which focuses on increasing the number of fellowships in endocrine surgery to keep pace with the increased national interest in this specialty.

“Nearly half of the academic institutions in the United States do not have an endocrine surgeon on staff, and this initiative will be working to change that,” she says.

Dr. Carty has been on the faculty of the University of Pittsburgh School of Medicine for more than 22 years, and has grown the program from two endocrine/breast surgeons to four full-time, dedicated endocrine surgeons, including an accredited fellowship which is in its eighth year. In her role with the AAES, she will be overseeing a new quality improvement and outcomes database, called the Collaborative Endocrine Surgery Quality Improvement Program (CESQIP). CESQIP enables clinicians from all surgical specialties who perform endocrine operations to receive ongoing performance feedback over a longer timespan than the National Surgical Quality Improvement Program (NSQIP) guidelines, which track outcomes for 30 days. Research shows complications from endocrine surgery typically take six months or more for accurate diagnosis. Dr. Carty is only the third female endocrine surgeon to head the AAES in its 33-year history.



Joseph P. Costantino, DrPH

Professor and director of
biostatistics at the University
of Pittsburgh Graduate
School of Public Health

Dr. Costantino has been appointed group statistician for the NRG Oncology Group, one of only four cooperative groups nationwide that will offer adult patients access to clinical trials through the newly configured National Clinical Trials Network of the National Cancer Institute (NCI).

NRG Oncology Group represents the merger of three separate adult cancer research groups — the National Surgical Adjuvant Breast and Bowel Program (NSABP), the Radiation Therapy Oncology Group (RTOG), and the Gynecology Oncology Group (GOG) — under the NCI's new structure, which is designed to stimulate infrastructure improvements, reduce data management costs among the groups, and streamline regulatory processes.

Dr. Costantino has been involved with the NSABP clinical trials cooperative group for more than 30 years, and has served as director of biostatistics since 2003. The NSABP is responsible for numerous landmark findings, including that tamoxifen reduced the risk of breast cancer recurrence by 50 percent; that lumpectomy with radiation is as effective as radical mastectomy; that breast cancer diagnosis could be reduced by 50 percent in high-risk women by prophylactic use of tamoxifen or raloxifene; and that the HER2-positive target drug Herceptin® could improve survival in women with HER2-positive breast cancer. The group also has conducted key sentinel node biopsy and whole-breast vs. partial-breast radiation therapy studies.

The \$45 million, five-year grant funding the biostatistics efforts for NRG Oncology began March 1, 2014, and will be housed at the University of Pittsburgh.

Circle of Hope

honors individuals, family foundations, and privately held companies that have made contributions of \$10,000 or more in a calendar year. This list recognizes those who were members in 2013.

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 Theresa L. Nimick-Whiteside, PhD
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Locations

★ 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 Jefferson Regional Radiation Oncology¹
- 6 Washington Health System Radiation Oncology¹
- 7 Uniontown Hospital Radiation Oncology¹
- 8 UPMC CancerCenter Radiation Oncology at UPMC East
- 9 Butler Health System Radiation Oncology¹
- 10 UPMC CancerCenter Radiation Oncology at UPMC Altoona

■ Medical Oncology Centers

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

- C Tony Teramana Medical Oncology³
- 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, Oakbrook Commons²
- 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 Butler Health System Medical Oncology¹

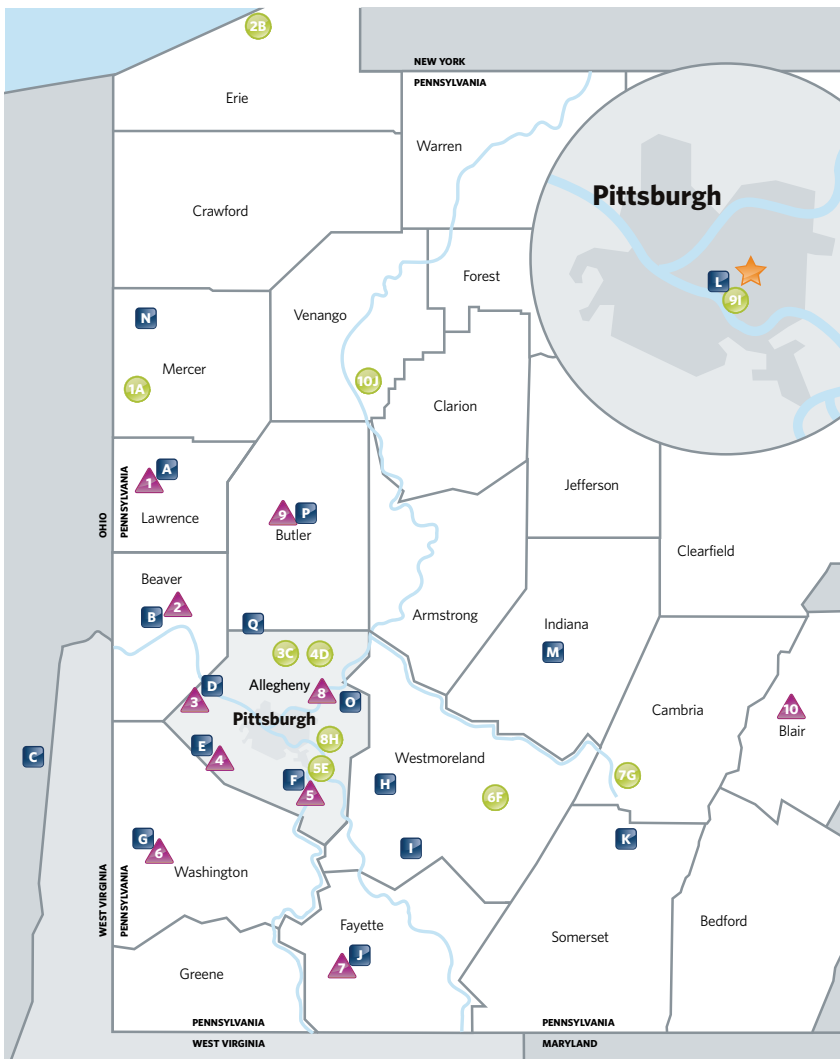
- Q UPMC CancerCenter Medical Oncology at UPMC Passavant-Cranberry

● 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, Natrona Heights
- 5E UPMC CancerCenter at UPMC McKeesport
- 6F Arnold Palmer Cancer Center²
- 7G John P. Murtha Regional Cancer Center⁴
- 8H UPMC CancerCenter at UPMC St. Margaret
- 9I UPMC CancerCenter at Magee-Womens Hospital of UPMC
- 10J UPMC CancerCenter at UPMC Northwest

▼ International

- 1 UPMC Beacon Hospital, Dublin, Ireland
- 2 UPMC Whitfield Cancer Centre, Waterford, Ireland
- 3 UPMC San Pietro FBF Advanced Radiotherapy Center, Rome, Italy
- 4 Partnership with the American Asian Medical Group (AAMG), Singapore



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¹In partnership with UPMC CancerCenter ²A partnership of Excelsa Health and UPMC CancerCenter
³A partnership of Trinity Health System and UPMC CancerCenter ⁴A partnership of UPMC CancerCenter and Memorial Medical Center





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