UPMC HILLMAN CANCER CENTER

CANCER INSIGHTS

WINTER 2018

Inside This Edition

Introduction

We are pleased to present you with this issue of *Cancer Insights.*

As one of the largest integrated cancer networks in the United States, UPMC Hillman Cancer Center is committed to delivering quality patient care and participating in groundbreaking research. With more than 500 clinical trials and more than 2,000 physicians, researchers, and staff, we are advancing the latest research discoveries, driving clinical innovation, and pioneering new therapies to ensure that patients receive the best care possible.

In this issue of *Cancer Insights,* we highlight three areas in which we are translating innovative bench research into cutting-edge care at the bedside.

Circulating Cell-Free DNA and Breast Cancer Biopsies: The Liquid Approach — An overview of how this approach is impacting clinical practice and providing a better understanding of aspects of basic cancer biology, disease progression, and response to treatment modalities.

Melanoma Immunotherapy and the Microbiome — A look at how the microbiome influences the development of certain malignances but may also play a role in how an individual reacts to various therapeutic regimens.

Naïve T Cell Depletion and Chronic Graft-versus-Host Disease: New Research and Clinical Trials — An update on research and clinical trials in the area of naïve T cell depletion.

We are extremely proud of the research and clinical activities at UPMC Hillman Cancer Center and our plans for continued growth. We look forward to keeping you up-to-date on our progress and developments in future issues of *Cancer Insights.*

For more information about our program, please visit **UPMCPhysicianResources.com/Cancer**.

Robert L. Ferris, MD, PhD
Director, UPMC Hillman Cancer Center
Co-Principal Investigator, University of Pittsburgh SPORE Grant

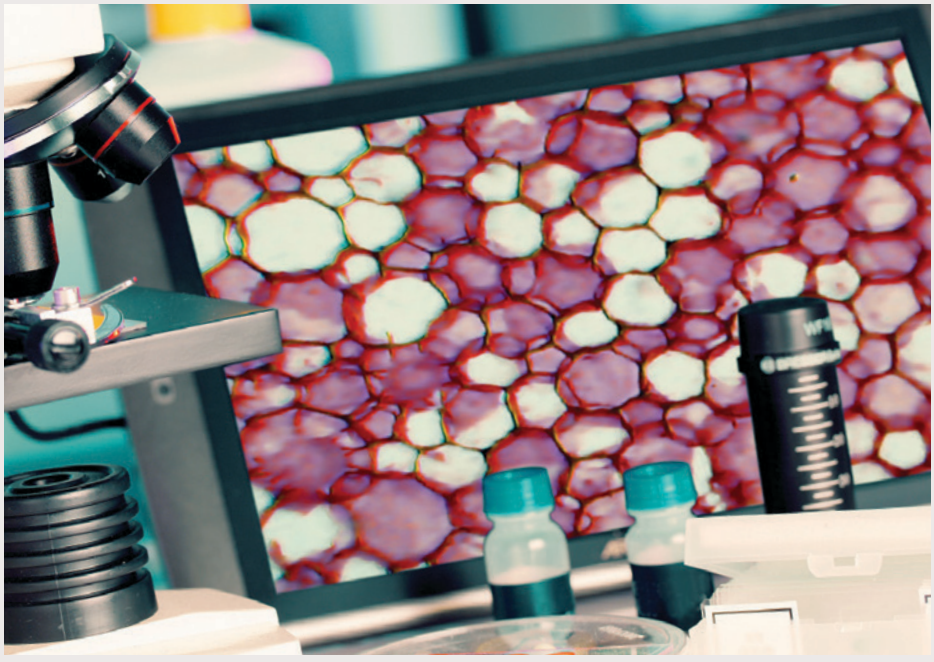
Stanley M. Marks, MD
Chairman, UPMC Hillman Cancer Center
Chief, Division of Hematology/Oncology, UPMC Shadyside

Circulating Cell-Free DNA and Breast Cancer Biopsies: The Liquid Approach

The advent of the so-called liquid biopsy in recent years has garnered significant attention and research within the field of oncology. And rightly so. The benefits of this approach to research and clinical practice are numerous, and the literature has seen a considerable increase in published findings where the measurement of circulating tumor cell-free DNA (cfDNA) within studies has played significant roles in understanding aspects of basic cancer biology, disease progression, and response to treatment modalities.

Less invasive by way of blood draws, analyzing a patient's circulating cfDNA affords the ability to readily biopsy metastatic disease that has infiltrated difficult-to-reach areas, such as the brain, bones, liver, and other delicate structures. The technique allows for a much easier way to longitudinally biopsy these patients in a way that is simply not practical, desirable, or safe using traditional methods. "The approach allows us to obtain a snapshot in time of the patient's complete tumor picture. For example, in the case of metastatic disease, with one blood draw we can see aspects of different tumors in different locations within the body through the unique signatures and markers of their cfDNA," says **Adrian Lee, PhD**, Pittsburgh Foundation Endowed Chair in Precision Medicine, professor of Pharmacology and Chemical Biology, and co-leader of the Hillman Breast and Ovarian Cancer Program at UPMC Hillman Cancer Center.

Dr. Lee's translational research is focused on several primary areas related to understanding and targeting the insulin-like growth factor pathways in breast cancer, including the role of ESR1 mutations seen primarily in relapsed and metastatic disease. In recent years, Dr. Lee and colleagues have become interested in using the detection of circulating cfDNA in their studies of ESR1 mutations in primary, relapsed, and metastatic breast cancer. The first of their studies on this topic, the findings of which were published in 2016 in the journal *Clinical Cancer Research,* showed several unexpected results and subsequently led to further studies and a phase II clinical trial currently in progress.



Analyzing ESR1 Mutations in Breast Cancer

Estrogen receptor alpha and the ESR1 gene are implicated in most instances of breast cancer, and ESR1 mutations have been shown to be significant with respect to metastatic and relapsed cases of breast cancer, and indicative of, or possibly driving, treatment-resistant disease conditions. Three years ago, as research was coming out showing mutations of ESR1 to be important indicators of advanced disease and disease refractory to endocrine therapy, Dr. Lee's group began to take interest in the findings and designed a study[1] to see what they could find in a small cohort of active patients from the breast cancer clinic at UPMC Hillman Cancer Center using newly acquired ddPCR (droplet digital polymerase chain reaction) technology that allows for incredibly sensitive and specific quantitative data regarding cfDNA findings within a sample.

"We enrolled 40 randomly selected women with advanced breast disease into the study, taking serial blood draws over time to see what we might find in terms of ESR1 mutations," says Dr. Lee. The study also examined samples from primary tumors and brain metastases derived from the large, onsite tissue bank at the University of Pittsburgh. The results were a bit surprising to Dr. Lee and his collaborators, and also indicative of just how fast the science is progressing in the field.

Primary tumors showed the smallest frequency of ESR1, mutation at 7 percent. Bone and brain metastases samples showed mutation rates of 9.1 percent and 12.5 percent, respectively. In the cfDNA samples, mutations of ESR1 were found in 24.1 percent of the population. "With our research and that of others, it's clear that these ESR1 mutations are important. But, we still don't know exactly what having any of the mutations means relative to their specific influences over disease state, and what a corresponding clinical indication would be in terms of therapy. This is where our current clinical trial picks up on these findings — beginning to look at the clinical implications," says Dr. Lee.

This trial[2] is a phase II examination of cases of metastatic breast cancer being treated with either fulvestrant or tamoxifen after having had a previous treatment with an aromatase inhibitor. Patients will be randomized into one of two treatment arms and administered either the fulvestrant or tamoxifen, and both will be tested via cfDNA examinations for ESR1 mutations prior to and after treatment.

"Our goal is to do basic science that gets into the clinic. This research is a great example of starting from scratch and rapidly progressing to the clinic in just a few short years. It's rare for us that our research progresses at such a pace, but it is indicative of just how fast the science is moving and what kind of promise it holds for bettering our understanding of this disease in its many forms."

Future Applications for cfDNA

The use of the liquid biopsy for measuring and detecting circulating cfDNA from tumors may, in the future, also extend to surveillance of individuals who are at high risk for developing breast cancer, or monitoring for signs of recurrent disease in individuals who have had a first line therapy or surgical resection of a primary tumor. There is some data in the literature now showing that women with detectable levels of cfDNA six months or a year after surgery have a higher risk for relapse than if they did not. "As a surveillance mechanism, I think a lot of people feel this approach holds great promise. It is a very personalized approach, because we would know in advance the mutations in the tumor the patient had and can look for it after the fact. We do this at the moment with cancer antigens, but they are very nonspecific and generally don't work well," says Dr. Lee.

The ability to detect changes at the molecular or DNA level within a patient's blood, before even the most sensitive imaging tests could detect the presence of a primary tumor or likely formation of one, or before the manifestation of symptoms occur signaling disease, could allow for greater precision of treatment at a time when the malignancy is in its earliest state of formation. "Because of the sensitivity and specificity of this kind of test, we may be able to use the approach for early detection of cancer in individuals with known genetic predispositions or other high-risk scenarios, such as women with dense breast tissue. This kind of routine clinical application of the testing platform is in the future, but the potential is there if we know what biomarkers or DNA mutations to look for in these individuals. It all depends on what the individual's cancer looks like," says Dr. Lee.

Much more research is needed before such an ability is possible, but it's the possibility of these sorts of advances that continues to drive Dr. Lee and his research colleagues to pursue and unlock the complex mysteries of cancer development and progression.

"None of these advances are or would be possible without the work of so many researchers and clinicians, and of course our patients who literally devote parts of themselves to help further our research. Our work is for them but would not be possible without them."

References and Further Reading

1 Wang P, Bahreini A, Gyanchandani R, Lee AV, Oesterreich S, et al. Sensitive Detection of Mono- and Polyclonal ESR1 Mutations in Primary Tumors, Metastatic Lesions, and Cell Free DNA of Breast Cancer Patients. *Clin Cancer Res.* 2016; 22(5): 1130-1137.

2 Phase II Treatment of Metastatic Breast Cancer With Fulvestrant or Tamoxifen. ClinicalTrials.gov Identifier: NCT02913430.

3 Gyanchandani G, Kota KJ, Jonnalagadda AR, Minteer T, Knapick BA, Oesterreich S, Brufsky AM, Lee AV, Puhalla SL. Detection of ESR1 Mutations in Circulating Cell-Free DNA From Patients With Metastatic Breast Cancer Treated With Palbociclib and Letrozole. *Oncotarget.* 2017; 8(40): 66901-66911.

Adrian Lee, PhD
Pittsburgh Foundation Endowed Chair in Precision Medicine
Professor of Pharmacology and Chemical Biology
Director, Institute for Precision Medicine
Co-Leader, Hillman Breast and Ovarian Cancer Program

Melanoma Immunotherapy and the Microbiome

The ongoing evolution of our understanding of the importance of the human microbiome to a myriad of physiological and disease processes may very well reshape much of medical science. Indeed, its influence and manipulation has already taken root and produced promising results in many disciplines — for example, gastroenterology in the treatment of clostridium difficile infections and inflammatory bowel disease.

The microbiome's role in cancer development and therapy modulation is in its infancy, but already there are signs and preliminary research that the flora and fauna — the vast multitudes of microbes that inhabit the human body — may play a role in not only the development of certain malignancies but also how an individual reacts to various therapeutic regimens. The makeup of one's microbiome may factor quite significantly in whether a person responds, or fails to respond, to treatment. Modulating or changing the microbiome of an individual may one day allow previously failed therapies to be successful in more patients.

The successes over the last three to five years with immune checkpoint inhibitors (e.g., anti CTLA-4 and anti-PD-1 and PD-L1 agents) in metastatic melanoma have produced curative efficacy in the range of 30 to 40 percent. However, this still leaves a full 60 percent of patients in the nonresponder category. With the yearly incidence of new melanoma cases in the United States approaching 76,000, approximately 9,000 of which are advanced or metastatic cases, converting even a small percentage of advanced case nonresponders to these immunotherapies would benefit a significant number of patients. A patient's microbiome composition may be the key to unlocking the efficacy of immunotherapy agents for some of the patients who currently do not respond to the therapy.

A New Clinical Trial

The role of the microbiome in advanced melanoma treatment with immunotherapy agents is being pursued by **Diwakar Davar, MD**, medical oncologist, and **Hassane Zarour, MD**, cancer immunologist and co-leader of the Melanoma Program at UPMC Hillman Cancer Center, in a new clinical trial set to begin recruiting patients in 2018. Drs. Davar and Zarour are both part of the Melanoma Program at UPMC, and are co-investigators on the new investigator-initiated trial seeking to understand whether a change to an individual's microbiome may trigger a response to immunotherapy in a percentage of cases of metastatic melanoma who do not initially respond to the treatment.

Drs. Davar and Zarour will enroll 20 patients with advanced metastatic melanoma who have undergone treatment with pembrolizumab (Keytruda) and have failed or become nonresponsive to the therapy during their treatment regimen. These individuals will receive a fecal microbiota transplant (FMT) obtained from patients who have proven to be long-term responders to pembrolizumab. The FMT will be administered via colonoscopy with an initial single dose, after which this group of patients will again receive pembrolizumab therapy with their responsiveness to treatment monitored. Responding patients who subsequently progress may be offered a second FMT.

"Our first goal is to understand exactly what proportion of the 60 percent of immunotherapy nonresponders are not responding to treatment with pembrolizumab, because of an altered intestinal microflora," says Dr. Davar.

"FMT is safe, and such a strategy truly has the potential to significantly improve the clinical outcome of advanced melanoma patients who have failed PD1 therapy and who have no other good therapeutic option," says Dr. Zarour.

This research conducted by Drs. Zarour and Davar will identify whether responses to therapy (if seen) are dependent on a single microbe or a group of networked microbes. It will also investigate the mechanisms used by the gut microbiome to stimulate potent antitumor immune responses in melanoma patients.

References

1 Fecal Microbiota Transplant (FMT) in Melanoma Patients. ClinicalTrials.gov Identifier: NCT03341143.

Diwakar Davar, MD
Assistant Professor of Medicine

Hassane Zarour, MD
Professor of Medicine, Immunology, and Dermatology
Co-Leader, Hillman Melanoma Program

Naïve T Cell Depletion and Chronic Graft-versus-Host Disease: New Research and Clinical Trials

Graft-versus-Host disease (GVHD), in both its acute and chronic forms, continues to be a major source of morbidity and mortality in allogeneic peripheral blood stem cell transplantation (alloSCT). Donor T cells, which recognize host tissues as nonself ("alloreactive T cells"), attack recipient tissues, mediating GVHD. However, alloreactive T cells also attack patient leukemia and lymphoma cells, mediating the so-called "graft-versus-leukemia" (GVL) effect.

Warren D. Shlomchik, MD, professor of Medicine and Immunology, director of Hematopoietic Stem Cell Transplantation and Cell Therapies, and scientific director of the Hematopoietic Malignancy Program at UPMC Hillman Cancer Center, has made major contributions in understanding the biology of both GVHD and GVL, and one of his discoveries is now being tested in the clinic with very promising results.

Dr. Shlomchik's lab was the first to publish that naïve T cells (T cells that have never responded to a pathogen or allergen) are more potent than memory T cells at inducing GVHD in mouse models. In close collaboration with colleagues at the Fred Hutchinson Cancer Research Center (supported by the National Institutes of Health [NIH]), Dr. Shlomchik and the FHCRC group developed and published a successful methodology for depleting stem cell grafts of these naïve T cells.[4] This work, along with numerous other studies beginning in the early 2000s, culminated in Dr. Shlomchik's first in human clinical trial using allografts depleted of naïve T cells. In this initial phase I/II trial, which ultimately enrolled 41 patients with acute leukemia or advanced myelodysplastic syndrome (MDS), there was only a 9 percent incidence of chronic GVHD. This compares very favorably to an approximate incidence of nearly 50 percent in patients receiving grafts, which include a full complement of T cells. While the incidence of acute GVHD was not reduced, all acute GVHD responded to first line therapies. Dr. Shlomchik and colleagues also showed that T cell memory was effectively transferred from the donor to the recipients as intended. Importantly, overall survival has been at least comparable to transplant studies with similar patients, and because of the low chronic GVHD rate, patients have been more rapidly tapered from their immunosuppression.

Current and Future Naïve T Cell Depletion Trials

Dr. Shlomchik and his collaborators at the Fred Hutchinson Cancer Research Center (Marie Bleakley, MD, principal investigator) are currently conducting a four-arm phase II clinical trial[2] of naïve T cell depletion, built upon the phase I trial results. The first trial only enrolled patients with HLA-matched related donors and employed a single high-intensity myeloablative conditioning regimen, which, due to its intensity, excluded patients older than 55. In contrast, the current trial enrolls patients with both HLA-matched related and unrelated donors, and includes both a high-intensity and a lower-intensity conditioning regimen.

Patients aged 18 to 49 will be enrolled into the higher-intensity arms, whereas subjects between 50 and 60, and younger patients ineligible for the higher-intensity regimen, will be enrolled in the lower-intensity conditioning arms. Key objectives will be estimating the rates of chronic and acute GVHD and relapse. Specific immunosuppressive treatments and their duration used to treat GVHD will also be tracked.

Planning the Next Studies

This next investigation of naïve T cell depleted grafts will be a phase III randomized clinical trial comparing naïve T cell depletion to standard transplant in pediatric patients with acute leukemia. Children's Hospital of Pittsburgh of UPMC will be one of the sites. The anticipation is that the first subject in this trial will be enrolled between May and September 2018. There also are plans for a randomized phase II study to evaluate naïve T cell depletion versus other transplant approaches in adults with leukemia and MDS.

References and Further Reading

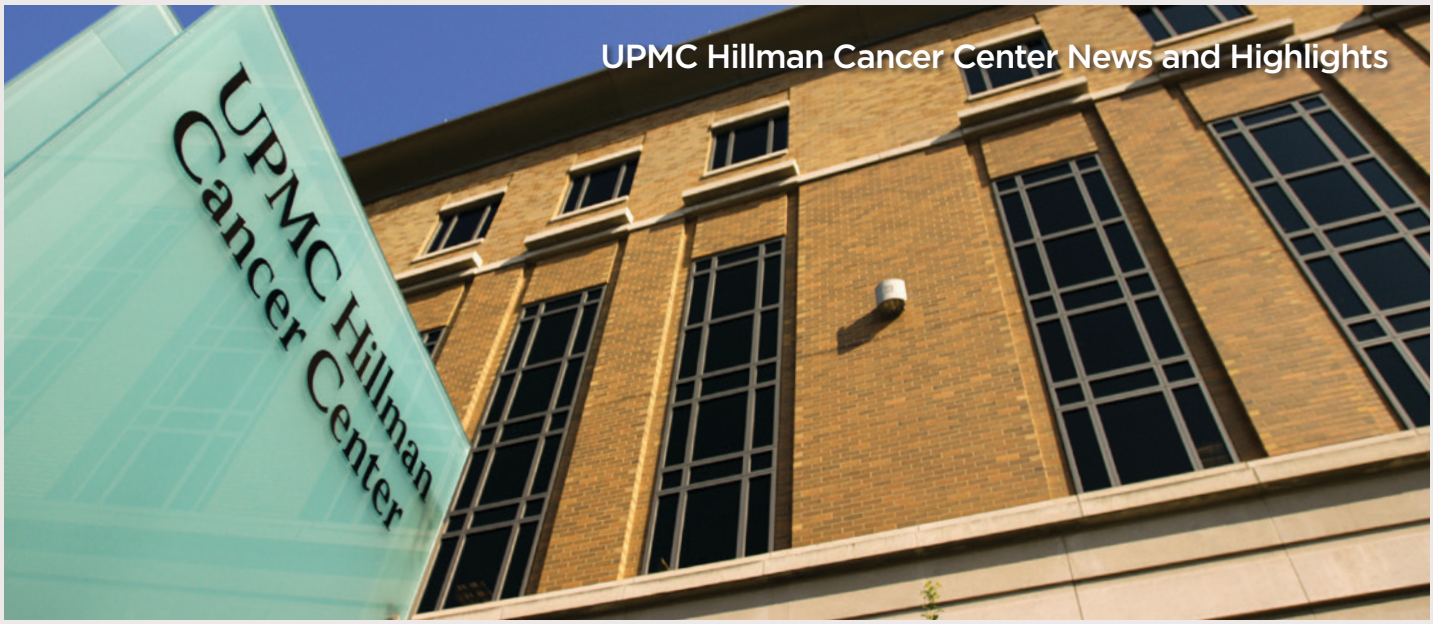
1 Selective Depletion of CD45RA+ T Cells From Allogeneic Peripheral Blood Stem Cell Grafts for the Prevention of GVHD. ClinicalTrials.gov Identifier: NCT00914940.

2 Selective Depletion of CD45RA+ T Cells From Allogeneic Peripheral Blood Stem Cell Grafts From HLA-Matched Related and Unrelated Donors in Preventing GVHD. ClinicalTrials.gov Identifier: NCT02220985.

3 Bleakley M, Heimfeld S, Loeb KR, Jones LA, Chaney C, Seropian S, Gooley TA, Sommermeyer F, Riddell SR, Shlomchik WD. Outcomes of Acute Leukemia Patients Transplanted With Naïve T Cell-depleted Stem Cell Grafts. *J Clin Invest.* 2015; 125(7): 2677-2689.

4 Bleakley M, Heimfeld S, Jones LA, Turtle C, Riddell SR, Shlomchik W. Engineering Human Peripheral Blood Stem Cell Grafts That Are Depleted of Naïve T Cells and Retain Functional Pathogen-Specific Memory T Cells. *Biol Blood Marrow Transplant.* 2014; 20(5): 705-716.

Warren D. Shlomchik, MD
Professor of Medicine and Immunology
Director, Hematopoietic Stem Cell Transplant and Cell Therapy
Scientific Director, Hematopoietic Malignancy Program



The Next Generation of Patient Care

New Cancer Hospital Will Transform Clinical and Translational Research Efforts

In November 2017, UPMC announced a bold plan to revolutionize patient care with the creation of three leading-edge, specialty hospitals that will offer next-generation treatments in patient-focused, technology-enhanced settings unique to health care. Backed by a $2 billion investment from UPMC, the all-new UPMC Hillman Cancer Center Hospital, UPMC Heart and Transplant Hospital, and UPMC Vision and Rehabilitation Hospital will add to UPMC's complement of advanced specialty care hospitals.

Beginning in 2022, patients of UPMC Hillman Cancer Center, a name that is synonymous with unmatched excellence in cancer care, will receive specialized treatment in the new UPMC Hillman Cancer Hospital, located on the UPMC Shadyside campus. The new hospital will continue to provide advanced care and an expertise in rare cancers, including access to clinical trials and the latest technology. This new home will make it even easier for our researchers and clinicians to work side by side to bring leading-edge cancer treatment to patients.

Henry L. Hillman Foundation Donates $30 Million to the Hillman Fellows for Innovative Cancer Research Program

UPMC and the University of Pittsburgh received a $30 million commitment from the Henry L. Hillman Foundation for the continued support of the Hillman Fellows for Innovative Research Program. The new contribution — $3 million per year for 10 years — will advance the mission of researchers at Pitt and UPMC Hillman Cancer Center to cultivate novel cancer discoveries that improve care for patients around the world.

The Hillman Fellows program started in 2004 with a $20 million contribution from the late philanthropists Henry and Elsie Hillman. The program provides seed funding to scientists and encourages partnerships with young researchers to cultivate innovative anticancer methods that improve cancer treatment, detection, and prevention worldwide. Since its inception, the Hillman Fellows program has directly supported the research of more than 100 scientists. The new funds also will be used to accelerate high-priority scientific research, such as linking novel cancer genomics and immunology to personalized patient care.

"The Fellows program has accelerated the move of cancer research from the bench to the bedside and helped to establish UPMC Hillman Cancer Center as a model for others around the world," said **Stanley M. Marks, MD**, chairman of UPMC Hillman Cancer Center, which is one of the largest treatment networks in the country with more than 60 locations. "We have been able to recruit world-class cancer researchers and financially support their groundbreaking efforts, all because of the vision of Henry and Elsie Hillman."

David Roger, president of the Hillman Family Foundations, said, "Having top quality research at UPMC Hillman Cancer Center was very important to Mr. and Mrs. Hillman. They were both extraordinarily proud to be associated with the work of so many brilliant doctors and scientists who have been a part of the program."

Robert L. Ferris, MD, PhD, a past fellow who recently was named director of UPMC Hillman Cancer Center, said, "The Fellows program has been responsible for funding research at UPMC in stem cell biology, cancer vaccines, and cellular therapies over the past 10 years. We are working toward groundbreaking immunotherapy and other discoveries that can cure some cancers and developing more effective treatments for this disease. Without this critical support from the Henry L. Hillman Foundation, this life-changing work would simply not be possible."

2017 Awards and Accolades

Yuan Chang, MD, and **Patrick Moore, MD**, were awarded the 2017 Paul Ehrlich and Ludwig Darmstaedter Prize. The duo, whose Chang-Moore Laboratory, located at UPMC Hillman Cancer Center, is credited with discovering two of the seven known human viruses that directly cause cancer. One of the most prestigious awards in the field of medicine, the prize is awarded annually to medical researchers who have made significant contributions in the fields of immunology, cancer research, microbiology, and chemotherapy.

Greg Delgoffe, PhD, received the 2017 National Institutes of Health (NIH) Director's New Innovator Award to continue his groundbreaking research on immunotherapy in the tumor microenvironment. Studies from the Delgoffe lab in the UPMC Hillman Cancer Center Tumor Microenvironment Center suggest that the metabolic makeup of the tumor microenvironment has a critical influence on the immune response to cancer and could provide the basis for why immunotherapy works for some but not all cancer patients. Dr. Delgoffe's work aims to find ways to rebalance these metabolic interactions by providing energy to the T cells that can destroy the cancer cells and depleting the suppressive cells that may inhibit immunotherapy responses.

John Kirkwood, MD, was inducted into the OncLive® 2017 Giants of Cancer Care®. Dr. Kirkwood is an internationally renowned expert in melanoma research at UPMC Hillman Cancer Center and was among 12 health care professionals nationwide to be recognized for advancing the field of oncology through contributions in research and clinical practice.

UPMC Establishes Immune Transplant and Therapy Center

In February, UPMC and the University of Pittsburgh announced the establishment of the UPMC Immune Transplant and Therapy Center, a bold and ambitious effort to revolutionize the way the world thinks about — and treats — a variety of diseases and conditions.

With the establishment of the UPMC Immune Transplant and Therapy Center, we've brought our brightest minds in immunotherapy research together in the areas of cancer, organ transplantation, and aging to collaborate, share ideas, and drive further development in this promising new frontier of medicine.

- **Cancer**
  We have deployed immunotherapy to develop protocols for the treatment of melanoma, head and neck cancer, hematologic malignancies, and lung cancer that can not only extend the patient's life, but also improve its quality. We are also exploring immunotherapy for what are traditionally considered to be immune non-responsive cancers, such as sarcoma, breast cancer, and pancreatic cancer.
- **Organ Transplantation**
  Driven by our pioneering efforts and expertise in transplant medicine, UPMC is setting its sights on a new frontier: immune transplantation in conjunction with organ transplantation, including living-donor liver transplants and combined lung and bone marrow transplants.
- **Aging**
  By exploring the basic biology of aging, we can better understand the molecular basis of why some individuals remain healthy well into old age while others do not. Through this research, we can develop improved treatment options and prevention strategies for age-related conditions like frailty, Alzheimer's disease, and atherosclerosis.

For more information visit **ITTC.UPMC.com** or call the UPMC Immune Transplant and Therapy Center at **1-888-4UPMC-ITTC (1-888-487-6248)**.

Upcoming Events: Save the Date

11th Annual Symposium on Technical and Clinical Advances in Radiation Oncology: Recent Technological Advances in Treatment Planning and Treatment

Saturday, March 3

8 a.m. to 4:30 p.m.
Herberman Conference Center, 2nd Floor
UPMC Cancer Pavilion — Pittsburgh, Pa.

Contact: Mary Kate Egan, eganmk@upmc.edu, 412-623-3651

2nd Annual Nursing Hematologic Cellular Therapy Conference: The Application and Implications for Nursing Care of the Patient Undergoing Cellular Therapy and Immunotherapy

Thursday, March 15

8 a.m. to 5 p.m.
Herberman Conference Center, 2nd Floor
UPMC Cancer Pavilion — Pittsburgh, Pa.

Contact: Mary Kate Egan, eganmk@upmc.edu, 412-623-3651

6th Annual Survivorship Conference: Maintaining Health During Survivorship

Friday, March 23

8 a.m. to 5 p.m.
Herberman Conference Center, 2nd Floor
UPMC Cancer Pavilion — Pittsburgh, Pa.

Contact: Mary Kate Egan, eganmk@upmc.edu, 412-623-3651

UPMC 2018 Multidisciplinary Thyroid Cancer Symposium

Saturday, May 12

7:30 a.m. to 4:30 p.m.
Herberman Conference Center, 2nd Floor
UPMC Cancer Pavilion — Pittsburgh, Pa.

Contact: Melissa Martin, martinml4@upmc.edu, 412-623-6437

UPMC
LIFE CHANGING MEDICINE
200 Lothrop St.
Pittsburgh, PA 15213-2582

UPMC HILLMAN CANCER CENTER

UPMC Hillman Cancer Center gives patients access to comprehensive care through an entire network of medical, radiation, and surgical oncologists, evidence-based treatment options, and the latest advances in cancer clinical care. We are proud to be one of the nation's top centers for cancer care and research, where our nationally and internationally recognized specialists are changing the landscape of oncology.

A Network of Physicians and Locations

UPMC Hillman Cancer Center offers convenient access to cancer care and innovative treatments close to home for cancer patients throughout western Pennsylvania and beyond. This model of patient care provides easy access to care for an aging western Pennsylvania population and accommodates referrals between specialists in Pittsburgh and our more than 60 locations.

With more than 180 affiliated oncologists, this network represents a collection of some of the nation's most highly qualified and respected physicians and researchers in cancer medicine.

A Resource for You: UPMC Physician Resources brings world-class physicians and free educational opportunities to your computer. Learn new information while watching CME-accredited videos in the convenience of your home or office. Find out more at UPMCPhysicianResources.com/Cancer.

To learn more about UPMC Hillman Cancer Center, please visit **UPMCPhysicianResources.com/Cancer.**

UPMC PHYSICIAN RESOURCES

ADDRESS CORRESPONDENCE TO:

UPMC Hillman Cancer Center

5150 Centre Ave.
Pittsburgh, PA 15232

Robert L. Ferris, MD, PhD
Director, UPMC Hillman Cancer Center

Stanley M. Marks, MD
Chairman, UPMC Hillman Cancer Center

For more information about UPMC Hillman Cancer Center clinical services, call **412-647-2811** or visit **UPMCHillman.com**.

A $17 billion world-renowned health care provider and insurer, Pittsburgh-based UPMC is inventing new models of patient-centered, cost-effective, accountable care. UPMC provides more than $900 million a year in benefits to its communities, including more care to the region's most vulnerable citizens than any other health care institution. The largest nongovernmental employer in Pennsylvania, UPMC integrates 80,000 employees, more than 30 hospitals, 600 doctors' offices and outpatient sites, and a more than 3.2 million-member Insurance Services Division, the largest medical insurer in western Pennsylvania. As UPMC works in close collaboration with the University of Pittsburgh Schools of the Health Sciences, *U.S. News & World Report* consistently ranks UPMC Presbyterian Shadyside on its annual Honor Roll of America's Best Hospitals. UPMC Enterprises functions as the innovation and commercialization arm of UPMC, and UPMC International provides hands-on health care and management services with partners on four continents. For more information, go to UPMC.com.

USNW506775 AS/MP 2/18