

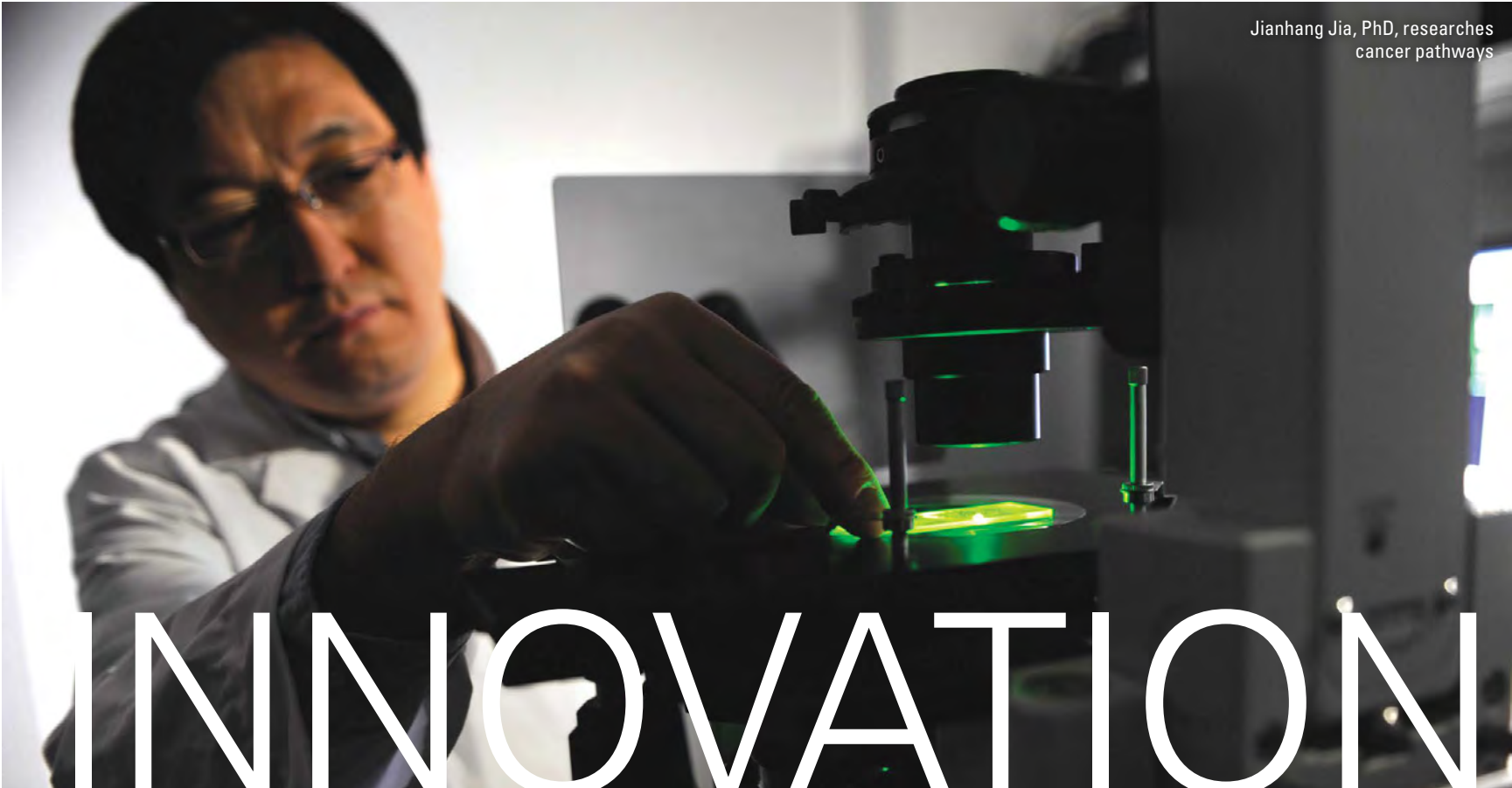
OUR FUTURE IS BRIGHT

MARKEY CANCER CENTER | 2013-14 ANNUAL REPORT

UKHealthCare®
Markey Cancer Center

Kentucky's Only NCI-Designated Center





Jianhang Jia, PhD, researches cancer pathways

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MARKEY CANCER CENTER GROWING BY LEAPS AND BOUNDS

I am pleased to share this report with you on another exciting year for the Markey Cancer Center. We continue to serve more patients than ever as our team grows, as does our reputation for world-class care.

Markey saw 150 more new patients over the past year, and our total annual patient visits increased to 85,000. That marks an increase of almost 30 percent over the past five years.

After securing designation from the National Cancer Institute last year, we have continued our efforts to expand our programs and welcome new providers and researchers. One of the highlights of the past year was bringing oncofertility specialist Leslie A. Appiah, MD, to the Markey Cancer Center. Dr. Appiah is a board-certified gynecologist who specializes in preserving the fertility and reproductive health of pediatric, adolescent and adult cancer patients.

In addition to this new oncofertility program at Markey, we have recruited many other specialists to join us. They include four medical oncologists; three hematology and blood and marrow transplant specialists; three surgical oncologists; two genitourinary cancer surgeons; and two oral and maxillofacial surgeons.

Along with outstanding clinical care, we continue to make sure our patients have everything they need for their overall well-being as they undergo treatment with us. Markey's Psych-Oncology Services team, which

includes a financial counselor, dietitian, patient navigator and social workers, assesses our patients' needs on a personal and emotional level. We believe these services are vital to helping our patients achieve some of the highest cancer survival rates in the state.

Through our ever-expanding Markey Cancer Center Affiliate Network, we are broadening our reach across Kentucky and the region. Our affiliate network has grown to include 13 affiliates, and Methodist Hospital in Henderson, Ky., recently became our first affiliate in Western Kentucky. We support our affiliates so they can provide high-quality cancer care closer to where patients live. Kentucky continues to face some of the highest rates of cancer incidence in the nation, but as our affiliate network grows, so does our ability to step up our fight against cancer.

Research remains a bright spot for Markey as well. Since the end of calendar year 2012, Markey's total research funding from both peer-reviewed and non-peer-reviewed sources has increased by \$7.3 million. And Markey researchers continue to share their findings with their peers. In 2014, Markey authors published 528 scientific articles, 49 more than the previous year.

Our future is bright, but we must continue the hard work that has led us here. Now that we have achieved NCI designation, our next goal is to be designated a Comprehensive Cancer Center. Only 41 of the 68 NCI-designated centers in the country hold this status. It will be the next step in ensuring all our patients receive the best possible cancer care right here in Kentucky.



I want to thank our dedicated physicians, researchers and staff members for all they do every day. We are also grateful for our volunteers, community supporters and, of course, the Markey Cancer Foundation. Their hard work is the reason our success continues.

Sincerely,

B. Mark Evers, MD
Director, Lucille P. Markey Cancer Center

ONCOFERTILITY SPECIALIST JOINS MARKEY TEAM



UK has added an oncofertility specialist to its team. Leslie A. Appiah, MD, joins UK HealthCare as a board-certified gynecologist with expertise in oncofertility and fellowship training in pediatric and adolescent gynecology.

Dr. Appiah brings five years of experience from Cincinnati Children's Hospital Medical Center, where she served as director of oncofertility and fellowship director of pediatric and adolescent gynecology.

She will serve as director of oncofertility at UK. She works closely with subspecialists in reproductive endocrinology and infertility, the Markey Cancer Center and Kentucky Children's Hospital. Appiah and her team collaborate to preserve the fertility and reproductive health of pediatric, adolescent and adult cancer and blood disorder patients of all genders.

Dr. Appiah attended medical school at the University of Texas Southwestern Medical Center at Dallas. She completed her residency in OB-GYN at Sinai Hospital of Baltimore and a clinical fellowship in pediatric and adolescent gynecology at Texas Children's Hospital. She has received several teaching awards including the Johns Hopkins Excellence in Teaching Award.

Her interests include fertility preservation, minimally invasive surgery, congenital anomalies of the reproductive tract, hormone replacement therapy and endometriosis.

MARKEY RESEARCHERS DEVELOP WEB-BASED APP TO PREDICT GLIOMA MUTATIONS

A new web-based program developed by UK Markey Cancer Center researchers will provide a simple, free way for health care providers to determine which brain tumor cases require testing for a genetic mutation.

Gliomas – a type of tumor that begins in the brain or spine – are the most common and deadly form of brain cancer in adults, making up about 80 percent of malignant brain cancer cases. In some of these cases, patients have a mutation in a specific gene, known as an IDH1 mutation, and patients who have this tend to survive years longer than those who do not carry the mutation.

Developed by UK researchers Li Chen, PhD, Eric Durbin, DrPH, and Craig Horbinski, MD, PhD, in collaboration with software architect Isaac Hands of the UK Markey Cancer Center Cancer Research Informatics Shared Research Facility, the program uses a statistical model to accurately predict the likelihood that a patient carries the IDH1 mutation and requires screening.

Gliomas are often tested for IDH1 mutation following surgery to remove the tumor, but undergoing this type of testing often requires stringent insurance pre-approvals due to rising health care costs, Horbinski said.

"Currently, there are no universally accepted guidelines for when gliomas should be tested for this mutation," Horbinski said. "Obtaining insurance pre-approval for additional molecular testing is becoming more commonplace, and this program will assist health care providers with an evidence-based rationale for when IDH1 screening is necessary."



MARKEY PATIENTS, SURVIVORS SHOWCASE THEIR EXPRESSIONS OF COURAGE

Facing a cancer diagnosis is no easy feat. Patients at the UK Markey Cancer Center have always inspired the community with their strength and courage, and this year was no exception, as Markey honored the experiences of those who have battled cancer with a day of recognition and celebration.

To celebrate National Cancer Survivorship Month last June, Markey held its inaugural Expressions of Courage event, an art exhibit showcasing original, artistic expressions connected in some way to an experience with a cancer diagnosis, or crafted by or in memory of a Markey patient whose battle has ended.

"We sent out over 6,000 letters," said Cindy Robinson, a nurse practitioner at Markey and one of the organizers behind the event. "And we asked people for any type of creative modality that they wanted to share with us to share their cancer journey, whether it be positive or negative."

More than 30 artists responded. Entries of visual arts included paintings, drawings, photography, sculpture and quilting. The performing arts involved vocal music, instrumental music and dancing, and poetry and short stories encompassed the literary arts.

The creations were on display all day in the Combs Research Building at Markey, with readings and performances starting in the afternoon and continuing into the early evening.

"The artwork is very moving and inspiring and actually will bring tears to your eyes if you read some of the pieces," Robinson said. "We have some pieces here from patients who are no longer with us, and we personally know those people."

Expressions of Courage was made possible by gifts from the Markey Cancer Foundation and Biological Systems Consulting, Inc. With the help of Carla Repass, assistant director for administration at Markey, and fellow Markey staff members Christie Daniels, Valeria Moore and Mincha Parker, Robinson said she felt they planned and pulled off the cancer center's first-of-its-kind celebration with flair.

Shawna Cassidy Quan of Richmond, Ky., was one of the survivors in attendance, having been diagnosed with four different primary cancers over the course of 15 years. Her expression of courage was an essay about her struggles with her multiple diagnoses.

"You figure out the answers to a lot of your problems even while you're sitting down writing," Quan said. "It's just been a wonderful, therapeutic thing for me."



Markey celebrates the inaugural Expressions of Courage Survivor event.

STRENGTH

ONE YEAR AFTER NCI DESIGNATION, MARKEY CONTINUES TO GROW

A year ago, a crowd of hundreds gathered in Pavilion A of UK Albert B. Chandler Hospital to celebrate a long-awaited special announcement – the unveiling of the UK Markey Cancer Center as the state’s first and only National Cancer Institute-designated cancer center.

The designation was the culmination of years of tireless work by the faculty and staff of Markey and its supporting service lines and colleges – all guided by Director Mark Evers, MD, who came to UK in 2009 with the vision of propelling Markey to NCI designation.

“Even before earning the NCI designation, we’d already taken extraordinary steps in the past few years in terms of combating cancer incidence and mortality through preventive measures, treatments and research,” Dr. Evers said. “But having the support and approval of the NCI has already made a huge impact in terms of both research and our clinical care.”

PATIENT CARE AT MARKEY

As the word spread about Markey’s NCI designation, clinicians and staff experienced an increase in the patient population in almost every clinical area. In 2014, Markey saw nearly 150 more new patients over the previous year, with total patient visits increasing from roughly 82,000 last year to more than 85,000 this year – which also marks a 29 percent increase in patient visits compared to just five years ago.

In particular, Markey’s outpatient clinics are growing – the Comprehensive Breast Care Center, the Multi-Disciplinary Clinic and the Gynecology-Oncology Clinic saw patient growth of 29 percent, 10 percent and 5 percent, respectively, over the past year.

With such an increase in patient volume – and variety – Dr. Evers and his team has also stepped up recruitment, seeking out the best cancer specialists in their fields to join the Markey Cancer Center.

Markey’s already vast team of specialists now includes a bevy of new team members added in the past year, including four medical oncologists; three hematology and blood and marrow transplantation specialists; three surgical oncologists; two genitourinary cancer surgeons; two oral and maxillofacial surgeons; and a specialist in oncofertility, a new program starting up at the cancer center.

CANCER RESEARCH

Over the past two years, Markey has increased its funding from the NCI by 27 percent and from other National Institutes of Health divisions by 16 percent. Overall, since the end of calendar year 2012, Markey’s total research funding from both peer-reviewed and non-peer-reviewed sources has increased by \$7.3 million.

Additionally, Markey researchers continue to push major findings out to their peers in academia – in 2014, Markey authors published 528 scientific articles, 49 more than the previous year.

THE FUTURE OF CANCER CARE IN KENTUCKY

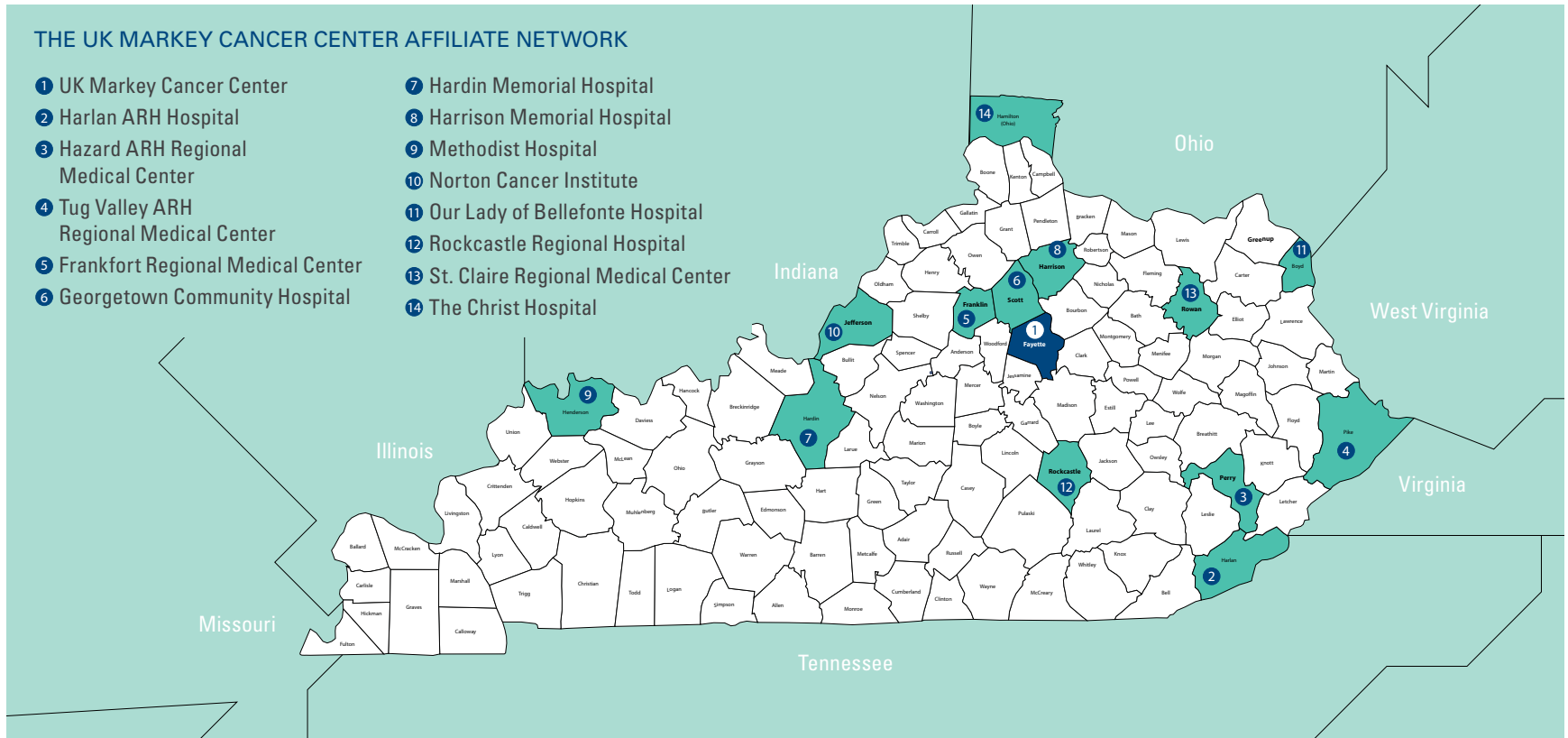
Following last year’s announcement of Markey’s NCI designation, Dr. Evers joked with his staff that they had one day to celebrate – and the next day, they’d be back in full swing, ready to propel Markey to the next level of designation: an NCI-designated Comprehensive Cancer Center. Currently, 41 of the 68 total NCI-designated cancer centers in the country hold a comprehensive cancer center status.

To earn this top level of designation, cancer centers must show a depth and breadth of research in each of three major areas: laboratory, clinical and population-based research, as well as substantial transdisciplinary research that bridges these scientific areas. Additionally, outreach is especially important, and comprehensive cancer centers must demonstrate professional and public education and outreach capabilities, including the dissemination of clinical and public health advances in the communities they serve.

“Our progress in the past year has been spectacular, but we can – and should – do more,” Dr. Evers said. “As the only NCI-designated cancer center in Kentucky, it’s our responsibility to be the leader in cancer care and to always seek out new ways to reduce rates of cancer incidence and death in the state, and to make sure that we can also offer the best possible care for our patients right here in Kentucky. Earning a comprehensive cancer center designation from the NCI will be another big step in that direction.”

THE UK MARKEY CANCER CENTER AFFILIATE NETWORK

- ① UK Markey Cancer Center
- ② Harlan ARH Hospital
- ③ Hazard ARH Regional Medical Center
- ④ Tug Valley ARH Regional Medical Center
- ⑤ Frankfort Regional Medical Center
- ⑥ Georgetown Community Hospital
- ⑦ Hardin Memorial Hospital
- ⑧ Harrison Memorial Hospital
- ⑨ Methodist Hospital
- ⑩ Norton Cancer Institute
- ⑪ Our Lady of Bellefonte Hospital
- ⑫ Rockcastle Regional Hospital
- ⑬ St. Claire Regional Medical Center
- ⑭ The Christ Hospital



MARKEY'S REACH ACROSS THE STATE

Though based in Lexington, Markey strives to provide access to top-notch cancer care across the state and beyond through the Markey Cancer Center Affiliate Network.

The Affiliate Network is a group of health care facilities that provide high-quality cancer services and programs in their communities with the support and guidance of the UK Markey Cancer Center, allowing patients to receive their care closer to home.

Evaluations are under way for several other hospitals, including out-of-state facilities, extending Markey's reach further and establishing it as the destination cancer center for the region.

UKHealthCare
Affiliate Network

Markey Cancer Center

DEALING WITH THE UNFORESEEN SIDE EFFECTS OF CANCER

HOW WOULD YOU REACT IF YOU'D JUST BEEN TOLD YOU HAVE CANCER?

"You freak out," said 57-year-old Tony Stone, a current patient at the UK Markey Cancer Center. "You don't know what to do."

Stone, who hails from Liberty, Ky., came to Markey last fall after getting diagnosed with stage IV throat cancer at a local hospital. The diagnosis came just six months after he retired from a long career – 36 years – as an iron worker.

The timing wasn't just poor because it put an end to Stone's well-deserved break – it also meant a serious blow to his finances. Stone had elected to forego health insurance upon retirement because he couldn't continue to afford the \$900/month payments without his job.

Faced with what seemed like insurmountable expenses and a terminal disease, Stone made the initial trip to Markey on a friend's recommendation. Though he knew to expect top-of-the-line medicine and treatment from the cancer center, he hadn't expected the other aspect of cancer care he would receive at Markey – the emotional and personal support from Markey's Psych-Oncology Services team.

Located on the third floor of Markey's Whitney-Hendrickson building, the Psych-Oncology team is devoted to providing much-needed assistance to Markey's patients. Every day, financial counselor Michele Ratcliffe, clinical dietitian Rachel Miller, American Cancer Society patient navigator Melanie Hunter, oncology social workers Jenny Delap, Miranda Hatfield, Lelia Gillespie and Angie Pennington, and licensed clinical social worker Joan Scales meet

with new and ongoing patients to assess their needs on a more personal and emotional level.

In general, research shows that hospital patients who receive counseling and support for psychosocial distress have reduced hospitalizations, length of stays, physician visits, emergency department visits and prescriptions.

Markey's Psych-Oncology team was assembled specifically to deal with the non-medical "side effects" of cancer – while oncologists, radiation medicine specialists and surgeons can recommend and perform specific medical treatments, this team focuses on fixing the everyday stressors that may impede a patient's ability to get the full benefits of their medical care.

"The question we focus on is 'What are the tangible, basic needs that we can get for the patient?'" Scales said.

For many patients, those needs include assistance with paying for medication, getting insurance, creating a living will or an advanced directive, help with transportation or lodging costs, or referrals to national programs that may offer further assistance.

In Stone's case, it first meant help with his finances – Delap helped him apply for disability and insurance coverage to help pay for the 35 radiation sessions and three rounds of chemotherapy he endured.

Because of the location of his cancer and subsequent radiation – the head and neck area – Stone was unable to physically eat his food during and following treatment, and a feeding tube was placed in his stomach. And that's where Miller came in. As Markey's dietitian, her job is to

ensure that patients are getting the nutrition they need to stay strong through their treatments.

"Staying nourished can become a chore during cancer treatment, especially for patients who have lost their appetites or don't feel well enough to eat," Miller said. "It's a catch-22, because you need to be fully nourished at the same time that you feel the least like eating."

Sometimes, a patient's needs are even more basic. Hunter, who is Kentucky's only American Cancer Society patient navigator, said the first thing she was able to do for Stone was get him a bandanna to cover his head as his hair began to fall out.

She often fulfills similar cosmetic requests by procuring wigs and other head coverings, or by referring patients to the ACS's Look Good... Feel Better program, which is facilitated on site by a licensed cosmetologist and helps patients combat the appearance-related side effects of cancer treatment. Additionally, she makes patient referrals to a variety of services that can assist with funding transportation or lodging during treatment.

Hunter has fulfilled some unique requests in her time at Markey – including making sure that an out-of-town patient's dog was taken care of during a long stay at the cancer center – but she says that any little thing she can do to help ease the patient's mind during their time at Markey is worth it.

"It may not seem like much, but it's one less thing for them to worry about," she said.



Markey's Psych-Oncology Team helps patients navigate emotional side of cancer treatment.

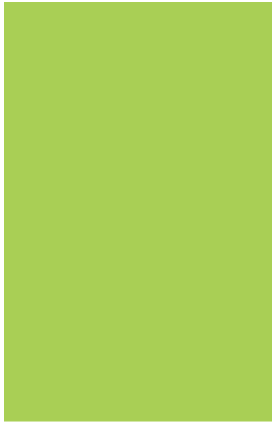
Michele Ratcliffe, Angie Pennington, Rachel C. Miller, Joan Scales, Jenny Delap, Melanie Hunter and Lelia Gillespie (Mandy Hatfield not pictured).

SUPPORT





Eugenia Caldwell and Farrah Cates participate in Markey's first Mamm's Day Out.



OUTREACH



Melissa Hounshell and Carla Repass established a cancer outreach program in 2014.

MARKEY RESEARCHERS SHOW POTENTIAL FOR TARGETING AGGRESSIVE BREAST CANCERS



A new study led by UK Markey Cancer Center researcher Peter Zhou, MD, PhD, professor of molecular and cellular biochemistry, shows that targeting Twist, a nuclear protein that is an accelerant of the epithelial-mesenchymal transition (EMT) program in human cells, may provide an effective approach for treating triple-negative breast cancer.

Triple-negative breast cancer has an activated EMT program, which is a process that provides cells with the increased plasticity (or flexibility) to adapt to stressed environments during embryonic development, wound healing, tissue fibrosis and metastasis. EMT provides tumor cells with stem cell-like characteristics, making them resistant to therapeutics and increasing their chances for early metastasis.

Triple-negative breast cancer in particular is associated with an aggressive clinical history, development of recurrence, distant metastasis and shorter patient survival, especially in younger women. It lacks effective targeted therapies and often displays early metastatic spread to brain and lung, sites known to be associated with an estimated five-year survival of less than 20 percent.

Published in *Cancer Cell*, the study found that the nuclear protein Twist acts similarly to a virus protein. Using protein purification, Zhou's team identified that Twist interacted with a key nuclear transcription regulator BRD4. When many DNA viruses (such as papillomaviruses) enter into human "host" cells during infection, they hijack host cell machinery to replicate and synthesize their viral DNA and proteins. BRD4 is the virus's favored molecule and is often seized by DNA papillomaviruses for gene transcription during replication and growth.

Twist uses a similar strategy to recruit BRD4 to the genomic regions that are regulated by Twist. Many of these genomic regions contain oncogenes, such as those of survival proteins, growth factors and molecules that enhance cell migration and invasion. By recruiting BRD4 to these genomic regions, Twist accelerates cell growth and invasion by "waking up" the expression of these oncogenes.

Additionally, the study showed that two BRD4 inhibitors can specifically disrupt the interaction of Twist with BRD4, resulting in the suppression of invasion, stem cell-like characteristic and tumorigenicity of triple-negative breast cancer cells.

"This finding has significant clinical ramification, because drugs that can target the Twist-BRD4 interaction provide a new hope for treating life-threatening triple-negative breast cancer," Zhou said.

Jian Shi, PhD, a post-doctoral fellow at UK Markey Cancer Center, was the first author of this study, and other collaborators include UK Markey Cancer Center Director Mark Evers, MD, and researchers Chi Wang, PhD, and Haining Zhu, PhD. Previously, Zhou and his team have studied the role of the Snail complex – also known as the cellular "brake" in contrast to Twist's accelerant – in the EMT program.

HOPE

BUTTERFIELD'S RESEARCH GARNERS INTERNATIONAL RECOGNITION

After 39 years of working in the UK Department of Chemistry, you might suspect one would get bored with the work. But professor Allan Butterfield, MD, describes his current project as "one of the most intellectually stimulating projects I've ever worked on."

Butterfield, whose many titles include director of the UK Markey Cancer Center's Free Radical Biology in Cancer Shared Resource Facility, studies oxidative stress in the brain. This includes the effect of oxidative stress on the development of Alzheimer's disease (AD), and, in collaboration with Daret St. Clair, PhD, Markey's associate director for basic research, the study of chemotherapy-induced cognitive impairment (CICI), known colloquially as "chemo brain" by the cancer patients who experience it.

This research is not only stimulating, but groundbreaking as well. Butterfield was recently awarded the 2014 Alkmeon International Prize for his work, an accolade that puts him in the same company as many Nobel Laureates and members of the National Academy of Sciences.

"I am truly honored to receive this award," Butterfield said. "The Alkmeon International Prize represents worldwide peer recognition of the decades of brain research by our highly talented graduate and undergraduate students, postdoctoral scholars, and visiting scientists in our laboratory that has led to numerous discoveries illuminating molecular mechanisms of brain disorders like AD and CICI."

Among the 14 million cancer survivors in the U.S., many suffer from symptoms of CICI, which include negative impacts on reasoning and multitasking, confusion, and fatigue – all major quality-of-life issues. These side effects can be long lasting – decades, in extreme cases – and can have a significant negative impact on a patient's ability to function and even work post-treatment.

Since Markey earned its status as a National Cancer Institute-designed cancer center, this problem has become even more of a focus for Butterfield, St. Clair, and many other researchers and physicians at UK. The term "bench to bedside" is often used when describing research at an academic medical center like UK, but St. Clair describes CICI research as "bedside to bench and back," noting that to try and find solutions to the problems patients were reporting, the team had to go back to the lab and recreate the problem in animal models so that they could begin their basic science testing.

Facilitating these types of back-and-forth investigations means a great deal of collaboration between basic science and physician researchers. Jeffrey Moscow, MD, and John Hayslip, MD, are heavily involved in the CICI research from the clinical side.

"We are very fortunate that at Markey we have physicians who not only focus on the cure of cancer with the best available methods, but are also interested in finding ways to improve the quality of life for patient during and after cancer therapy," St. Clair said. "Our physicians work as a team with basic scientists to research ways to improve cancer treatment with reduce side effects."



RECOGNITION

NEW UK STUDY HELPS SCIENTISTS UNDERSTAND MELANOMA DEVELOPMENT

A new study by John D’Orazio, MD, PhD, associate professor and Drury Pediatric Research Endowed Chair, shows how a genetic defect in a specific hormonal pathway may make people more susceptible to developing melanoma, the deadliest type of skin cancer.

Fair-skinned people who tend to burn (rather than tan) from sun exposure have a much higher risk for melanoma than darker-skinned people. On the surface, it appears that the amount of melanin, the natural substance in the skin that determines pigment and acts as the skin’s “natural sunscreen,” would be the only determinant of melanoma risk. However, the truth is more complicated.

Published in *Molecular Cell*, the study looked at the role of the melanocortin1 receptor (MC1R), the receptor on melanocytes in the skin that gets called into action following ultraviolet exposure to help the skin lay down more UV-blocking melanin to protect itself. Fair-skinned people are more likely to inherit a defect in this receptor, and as a result, cannot make enough melanin to fully protect themselves from UV damage.

Since UV from sunlight or tanning beds is a major cause of melanoma, inherited problems in the MC1R means that the skin lacks natural protection by melanin, which acts as a biologic sunblock. This leads to more UV light chronically getting through to the sensitive layers of the epidermis, where it can contribute to cancer.

However, the UK study showed that MC1R defects contribute to melanoma development in ways other than melanin production. Besides regulating the amount of melanin that gets made in the skin, MC1R also controls how well melanocytes can repair their DNA from UV damage. Having defects in MC1R signaling delays the body’s ability to clear out existing DNA damage in the skin – leading to an increased potential for cancerous mutations.

“Knowing whether people have a specific genetic predisposition for melanoma could potentially save many lives,” D’Orazio said. “If you happen to be born with a problem in this MC1R hormonal pathway, then you need to be extra careful with respect to UV safety.”

D’Orazio and his research team found an important molecular link between MC1R signaling and DNA repair in their study. The team hopes to use this information to develop new melanoma-preventive treatments, like additives that can be included in sunblocks to ramp up the skin’s ability to deal with UV damage.

PREVENTION

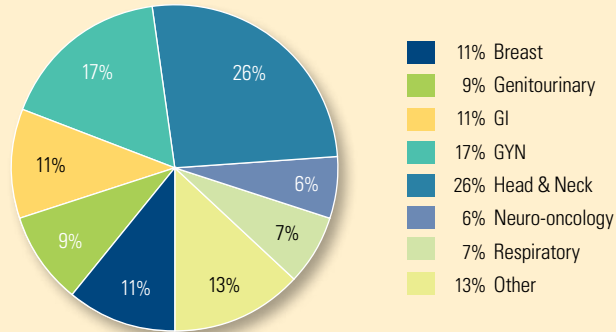


FY14 MARKEY CANCER CENTER YEAR AT A GLANCE

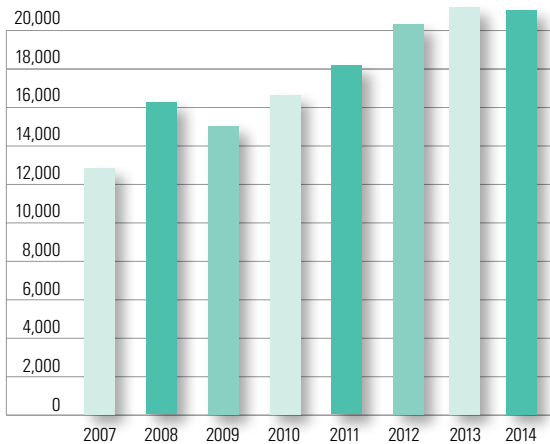


COMPASSION

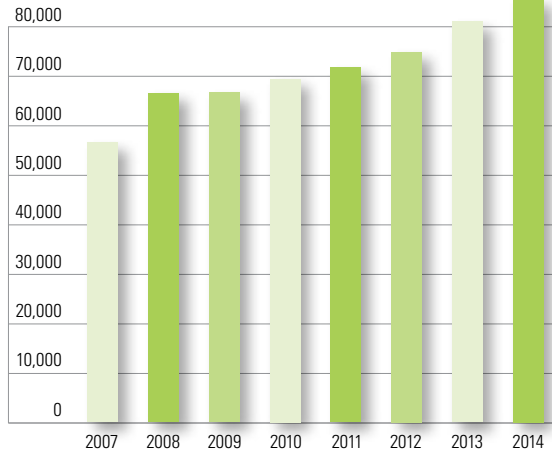
2014 SURGERY DISCHARGES



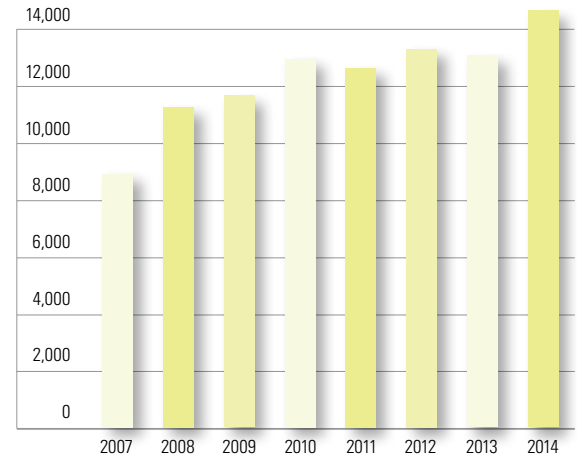
OUTPATIENT RADIATION VISITS



TOTAL OUTPATIENT CANCER VISITS



OUTPATIENT CHEMOTHERAPY VISITS



MARKEY
MAKES A DIFFERENCE

U.K. HealthCare.
Markey Cancer Center

DEDICATION

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Markey makes a difference.

For more information on the UK Markey Cancer Center,
call toll free **866-340-4488** or visit **Markey.uky.edu**



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