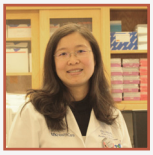


ISSUE 4 | 2015

MARKEY *quarterly*

SEASONAL NEWS FOR MARKEY CANCER CENTER FACULTY AND STAFF

ADVANCING SCIENCE ONE PATIENT AT A TIME

CLINICAL TRIALS PROVIDE A SAFE WAY TO LOOK AT NEW TREATMENT OPTIONS

"Every drug used right now as standard of care started in a clinical trial," says Susanne Arnold, MD, Associate Director for Clinical Translation. "Clinical trials are how we make progress in cancer treatment, and they are the way we will cure cancer."

Markey's NCI-designation comes with the expectation that 10% of patients should be enrolled in clinical trials. To help meet that expectation, a staff of over 20 in the Clinical Research Office (CRO) coordinates and facilitates Markey's clinical cancer trials. This task is accomplished by supporting the clinical trial process, including implementing and regulating trials; providing a centralized clinical trial database; and integrating with investigational pharmacy support, financial accounting, data safety monitoring and quality assurance. The CRO assists physician investigators in the design and subsequent conduct of clinical trials through its support of the Investigator Initiated Trial Protocol Development Unit. It performs all regulatory reporting and quality assurance needed to comply with good clinical practice in the performance of clinical trials.

"The CRO supports Markey's mission by bringing our science, as well as NCI and industry partner science, to Kentucky," says Dr. Arnold. "This effort brings the wealth of the nation's brain trust to Markey patients."

LEARN MORE ABOUT MARKEY CLINICAL TRIALS
Visit the CRO website or download the Markey Cancer Center Clinical Trials iPhone app.

Every patient in a clinical trial helps advance science. As the Medical Director of the CRO, Frederick Ueland, MD, oversees Clinical Care and Research Teams (CCARTs) and leads efforts to increase both the number of clinical trials offered and the number of patients enrolled on those trials. "My primary goal is to increase the clinical trial opportunities for our patients at Markey so they don't need to travel elsewhere to receive innovative care," says Dr. Ueland. "Clinical trials are a safe way to offer new treatments for patients who may have failed standard therapy. We are motivated by the hope of improving patient outcomes while advancing the science of medicine."

Focus is key to advancing science for better treatments. "We need to be thoughtful about the trials we have available; they need to

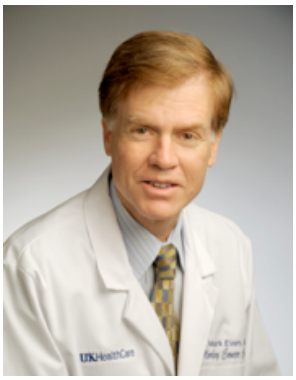
MARKEY BY THE NUMBERS

Votes cast for Jennifer Bradley in the 2016 Rare Life Award Contest 20,723

Number of wreaths submitted to the Expressions of Courage online auction 59

FROM THE DIRECTOR

B. MARK EVERS, MD, DIRECTOR, MARKEY CANCER CENTER



As 2015 came to an end, we had the opportunity to look back on our successes at Markey, both for the patients we treat and in celebration of those we have treated. Whether implementing a research focus to identify clinical trials that best meet the needs of our patient population and advance the science of cancer care, or bringing together the Markey community at an end of the year event to raise funds for our Expressions of Courage Survivor Art Celebration, our faculty and staff proved time and time again that we remain dedicated to the prevention, detection, diagnosis and treatment of cancer.

Because Kentucky ranks among the highest in cancer mortality in the United States, it is critical for us to offer clinical trials that provide patients with additional treatment options when standard therapy is not enough. Our Clinical Care and Research Teams meet regularly to determine what clinical trials are needed to help as many Kentuckians as possible. These meetings cover a range of topics, from current and potential studies, to the patient population, to safety regulations. Thankfully, we have an incredible team in the Clinical Research Office devoted to supporting all clinical trial efforts with the ultimate goal of improving patient outcomes.

Improved patient outcomes lead to a growing number of cancer survivors. Our faculty and staff continue to expand awareness of the Expressions of Courage Survivor Art Celebration. We closed 2015 with an online wreath auction that included support from Markey employees and local businesses, raising about $3,000. This money will be used for the Expressions of Courage Survivor Art Celebration, a popular event held in June in honor of National Cancer Survivorship Month.

These are just a few of the many successes at Markey. Our task for 2016 is to build on these accomplishments as we move forward with our mission of reducing the morbidity and mortality of cancer. If 2015 is any indication, we are in for an exciting year.

CLINICAL TRIALS, continued

match our patient population," says Dr. Ueland. Kentucky has some of the highest cancer mortality in the Unites States, and the highest incidence rate of lung and colorectal cancer. Although Markey seeks to have as many trials open as possible, Dr. Ueland says the goal is to open the trials that have the best chance of helping the largest number of Kentuckians. "With that in mind, one of our new CRO initiatives is to request that the CCART teams renew their focus on research," says Dr. Ueland.

There are two types of recurring meetings centered on patient care. Tumor boards allow all disciplines to discuss modalities of therapy for a particular patient. "Depending on the patient's diagnosis, a clinical trial may be brought up; and if appropriate, the patient could potentiall be enrolled into a clinical trial specific to that disease group," says Bryan Courtney, Director of Clinical Research Operations for the CRO. "The monthly Research CCARTs look more broadly at the overall research aims for a disease group. What clinical trials do we need to open for our patient population? What clinical trials do we have open to accrual and what are the barries for patient recruitment? What issues are our clinical trial patients having?"

Current and developing Research CCART meetings include: breast, early therapeutics, gastrointestinal, genitourinary, head and neck, hematology, gynecologic oncology, lung, melanoma sarcoma, neuro oncology and radiation oncology. These meetings review the status of active protocols and discuss obstacles to participation as well as adverse events. The Research CCARTs also debate new protocol feasibility, assign a merit score for each and rank the importance of all protocols in the pipeline.

"We encourage our investigators to think beyond patient care, to actively translate the science to clinical medicine," says Dr. Ueland. "At the University of Kentucky, we are more than teaching physicians; we are novel thinkers who push ideas forward from concepts to treatment realities. We accomplish this each day with teams that are engaged in the process. Having the CRO at the table in Research CCART meetings is one way to enhance communication and stimulate high quality, safe clinical research."

"Cancer research is patient and physician-driven," says Mr. Courtney. However, the role of the CRO is essential for the success of that research. "All cancer-related therapeutic clinical trials are conducted through the CRO," says Mr. Courtney. The CRO's clinical, regulatory and finance personnel help physicians with trial development, enroll and follow participants, monitor safety and effectiveness, protect subjects from injury and ensure Markey follows federal guidelines for research.

Together as a team, physicians and the CRO are advancing science one patient at a time.

FIND A RESEARCHER ONLINE

You can now access a directory of Markey researchers, complete with updated profiles and links to key publications. Email the Research Communications Office at mccrco@uky.edu for instructions on how to be included in the directory.

MEET A MARKEY MOVER

FREDERICK UELAND, MD, CLINICAL RESEARCH OFFICE MEDICAL DIRECTOR.

This quarter, Markey Quarterly introduces you to Dr. Frederick Ueland, Clinical Research Office Medical Director.

Good afternoon Dr. Ueland, Thank you for talking with us today. Would you care to start by telling us how long you've been at UK and about your new leadership role with the Clinical Research Office (CRO)?

I joined the faculty in 1998 after completing my residence and fellowship here at UK. My clinical interests include advanced pelvic surgery, the evaluation of ovarian tumors with ultrasound and biomarkers, chemotherapy and clinical trials. Clinical research has always been an important culture in the Division of Gynecologic Oncology, and we have had success in matching our open clinical trials with our patient population. Dr. Evers recently asked if I would help reinvigorate the CRO, believing that our methods might help the Clinical Care and Research Teams (CCARTs) succeed. Markey has several areas of research excellence, but there is opportunity for an enhanced focus on clinical trial research. I hope to apply the lessons we've learned in gynecologic oncology to help Markey provide the right mix of science and treatment opportunities.

I see myself as more of an organizer, a facilitator. I want to make research easier for investigators and safer for patients. I want to streamline the process for patients and staff while maintaining a high level of quality. And I hope to increase patient and physician participation.

What are your goals for the clinical research office, what changes would you like to see?

Streamlining and growth. As Markey grows, so does the number and complexity of our clinical trials. If the CRO is to succeed, we need to mirror the expansion of the research mission. The last few months we have hired to a number of key positions and reorganized some of the internal structure. We will also be expanding our Phase I group this year which will be critical to our mission of clinical cancer research.

One of our primary challenges is to modernize the regulatory aspect of clinical research. We are looking at possible ways to transition to electronic communications, but we must comply with all the regulatory challenges of the FDA, NCI, IRB, and others. There is an imposing amount of paperwork embedded in the current process. Moving to an electronic system, like UK HealthCare has done with patient records, would greatly improve efficiencies. This is not just our challenge here at UK, but a vision for all NCI cancer institutions. It's not something Markey can do alone, but we can be part of the change.

We are also establishing new Research CCART meetings that help organize each disease team, connect the investigators with the CRO and encourage each CCART to consider the merits of each trial before it is opened. Now, when a group considers new protocols, the discussion centers on scientific merit and which ones have the most potential for impacting our patient population. The Research CCARTs prioritize their pipeline and rank in order the most promising protocols. Then the CRO can more rapidly open the trials that are important to the cancer center. In the end, we'd like to open the trials that impact the most people.


Dr. Frederick Ueland.

Another critical element for our success in clinical research is to better integrate our physician scientists with the clinical research team. I believe the Research CCARTs are helping with this integration. The clinical research associates and research nurses attend the monthly research meetings, and become more familiar with the investigators, the progress of the trials and other important research issues. To be successful, clinical research must be done by a well-organized team, and the CRO is an important part of that team. Markey has great leadership, high quality investigators and a devoted and high performing CRO. That is the foundation for a great team.

Why are clinical trials important for an NCI-designated cancer center like Markey?

For NCI designation, it is important to contribute to the science of medicine, and offer novel opportunities for treatment to our patients. That includes exceptional basic science, but also translational science. We try to have the right mix of national collaborative group trials, industry trials and investigator-initiated trials designed by our own investigators. Clinical trials are translating new ideas for treatment into reality, creating new standards of care. Our success with clinical trials is one way to measure of how much translational science we are doing.

What inspires you to participate in clinical trials?

It's very important for our patients to have access to treatment when standard care fails. Translational research is an ethical way to give patients access to new opportunities, to help advance the science of medicine and to help those who follow in our footsteps. It is very rewarding to see a patient have a favorable response to a new therapeutic breakthrough, and to know that they didn't have to leave our state to get it. We think these things make the Markey unique in the region, and important for Kentuckians.

WHO SHOULD BE OUR NEXT MARKEY MOVER?

Email Markey's Research Communications Office at mccrco@uky.edu with your idea.

NOTEWORTHY

WELCOME

Kory Brinker, BCBR SRF
Sarah Buzo, Director's Office
Caressa Colburn, CRO
Megan Eder, CRO
Mandy Hensley, CRO
Joan Kahl, BCBR SRF
Lili Liu, Min Chen, MD, PhD /Susanne Arnold, MD, laboratory
Elizabeth Rush, CRO
Huan Song, CESB
Danielle Story, Research Communications Office
Chunyan Wang, CESB
Wei Wang, Toxicology
Justin Werker, CRO

PRESENTATIONS & PUBLICATIONS

Markey authors were responsible for 176 manuscripts and publications in journals from October through December 2015. Notable publications include the following.

Braun KL, Stewart S, Baquet C, Berry-Bobovski L, Blumenthal D, Brandt HM, Buchwald DS, Campbell JE, Coe K, Cooper LC, Espinoza P, Henry-Tillman R, Hargreaves M, James A, Kaur JS, Viswanath K, Ma GX, Mandelblatt J, Meade C, Ramirez A, Scarinci I, Tanjasiri SP, Thompson B, Vines AI, Dignan M. The national cancer institute's community networks program initiative to reduce cancer health disparities: Outcomes and lessons learned. Prog Community Health Partnersh 2015; 9:21-32.

Carpenter BL, Chen M, Knifley T, Davis KA, Harrison SMW, Stewart RL, O'Connor KL. Integrin alpha 6 beta 4 promotes autocrine epidermal growth factor receptor (egfr) signaling to stimulate migration and invasion toward hepatocyte growth factor (hgf). J Biol Chem 2015; 290:27228-27238.

Edwards DN, Machwe A, Chen L, Bohr VA, Orren DK. The DNA structure and sequence preferences of wrn underlie its function in telomeric recombination events. Nat Commun 2015; 6.

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Jyoti A, Fugit KD, Sethi P, McGarry RC, Anderson BD, Upreti M. An in vitro assessment of liposomal topotecan simulating metronomic chemotherapy in combination with radiation in tumor-endothelial spheroids. Sci Rep 2015; 5.
Keeney JTR, Miriyala S, Noel T, Moscow JA, St Clair DK, Butterfield DA. Superoxide induces protein oxidation in plasma and tnf-alpha elevation in macrophage culture: Insights into mechanisms of neurotoxicity following doxorubicin chemotherapy. Cancer Lett 2015; 367:157-161.

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Sethi P, Jyoti A, Swindell EP, Chan R, Langner UW, Feddock JM, Nagarajan R, O'Halloran TV, Upreti M. 3d tumor tissue analogs and their orthotopic implants for understanding tumor-targeting of microenvironment-responsive nanosized chemotherapy and radiation. Nanomedicine 2015; 11:2013-2023.

Son YO, Pratheeshkumar P, Roy RV, Hitron JA, Wang L, Divya SP, Xu M, Luo J, Chen G, Zhang Z, Shi XL. Antioncogenic and oncogenic properties of nrf2 in arsenic-induced carcinogenesis. J Biol Chem 2015; 290:27090-27100.

Stamatkin C, Ratermann KL, Overley CW, Black EP. Inhibition of class ia pi3k enzymes in non-small cell lung cancer cells uncovers functional compensation among isoforms. Cancer Biol Ther 2015; 16:1341-1352.

Xiong G, Flynn TJ, Chen J, Trinkle C, Xu R. Development of an ex vivo breast cancer lung colonization model utilizing a decellularized lung matrix. Integr Biol (Camb) 2015; 7:1518-1525.

Ye Q, Cai WJ, Evers BM, Solit D, Rosen N, She QB. Role of cap-dependent translation in response to upstream kinase-targeted therapy in colorectal cancer. Clin Cancer Res 2015; 21.

Zhang JJ, Ponomareva LV, Nandurkar NS, Yuan YX, Fang L, Zhan CG, Thorson JS. Influence of sugar amine regiochemistry on digitoxigenin neoglycoside anticancer activity. Acs Med Chem Lett 2015; 6:1053-1058.

NOTEWORTHY, continued

GRANTS

Kristin Ashford, PhD, WHNP-BC, FAAN, was awarded National Institute on Drug Abuse funding for "The impact of electronic cigarettes (e-cigs) on perinatal immune responsiveness and birth outcomes in Appalachia."

John D'Orazio, MD, PhD, was awarded Melanoma Research Alliance funding for "Beta defensin 3: UV induction and effects on melaocyte genome stability."

Eric Durbin, DrPH, was awarded National Cancer Institute funding for "SEER 2015-04; Expanding SEER to Include Molecular Profiling in Non-Small Cell Lung Cancer (NSCLC)."

B. Mark Evers, MD, was awarded National Cancer Institute funding for "Novel pRNA Nanoparticle Delivery as Directed Therapy for Colorectal Cancer Metastasis."

Bin Huang, DrPH, was awarded National Cancer Institute funding for "SEER 2015-06: Feasibility and Biases - Linking Kentucky Cancer Registry Data with External Claims Based Data to Argument Comorbidity and Treatment."

Robin Vanderpool, DrPH, was awarded Center for Chronic Disease Prevention & Health funding for "SIP 14-011: Appalachian Center for Cancer Education, Screening, and Support (ACCESS)."

AWARDS, RECOGNITIONS & SELECTIONS

Nina Barnes, MSN, RN, CNML, has been named Nursing Director for the Oncology Service Line.

Roberto Cardarelli, DO, MPH, was the recipient of the Advancing Implementation Science in Community/ Academic Partnered Research funding opportunity from the Association of American Medical Colleges and The Patrick and Catherine Weldon Donaghue Medical Research Foundation for his proposal, "Reducing the lung cancer burden in Northeast Kentucky through an academic/ community partnership: A Terminate Lung Cancer (TLC) Study". Dr. Caradelli's proposal was noted as one of the top two poised for the greatest near-term impact to improve population health outcomes.

Roger Fleischman, MD, PhD, has been awarded Distinguished Emeritus status by the American Society of Hematology. This distinction was established in 2001 to recognize individuals whose exemplary service and efforts in the advancement to the field of hematology have forwarded the interests of the Society, and the field as a whole.

Hardin Memorial Health Joins Markey Cancer Center Research Network

Hardin Memorial Health (HMH) has joined the Markey Cancer Center Research Network, allowing patients across Central Kentucky to participate in Markey-led and some major NCI-led clinical trials closer to home, in Elizabethtown.

HMH is an integrated system of health care providers serving Hardin, Meade, Nelson, LaRue, Breckinridge, Grayson, Hart, Bullitt, Green and Taylor counties.

HMH now is one of four research sites of the Markey Research Network. The HMH cancer care team was invited to join the network based on previous performance in research, including a study to identify the best approaches to help cancer patients quit smoking, which will help improve their response to cancer treatments.

Inclusion in the research network is an extension of an existing partnership. In 2014, HMH joined Markey's Affiliate Network, which focuses on sharing new evidence-based findings and access to refer patients to clinical trials. Since 2013, the Hardin Memorial Cancer Care team has participated in the Kentucky Clinical Trials Network, housed at Markey, which focuses on lung cancer research.

MARKEY DIFFERENCE MAKERS

Congratulations to the following Markey Difference Makers for the fourth quarter of 2015.

Robert Adams
Cathy Anthony
Susanne Arnold
Marcia Ballard
Jenny Delap
Robin Fisher
Donna Gilbreath
Terry Keys
Geri McDowell
Wilma Maloney
Rachel Miller
Michele Ratcliffe
Heather Russell-Simmons
Joseph Scandrani
Sandra Thompson
Catherine Wade
Barry Warner

Do you know a Markey Difference Maker?
Nominations are now accepted online.

Online Auction Raises Money for Expressions of Courage Celebration

The Markey Cancer Center hosted an online wreath auction to raise money for the annual Expressions of Courage Celebration, a creative exhibit celebrating those who have been affected by cancer. Expressions of Courage began in 2014 and is held in June to coincide with National Cancer Survivorship Month.

Wreaths were displayed in the lobby of the Combs Center Research Building Dec. 7-10 during a live online auction. The highest bid for a wreath was $145, with about $3,000 raised overall.

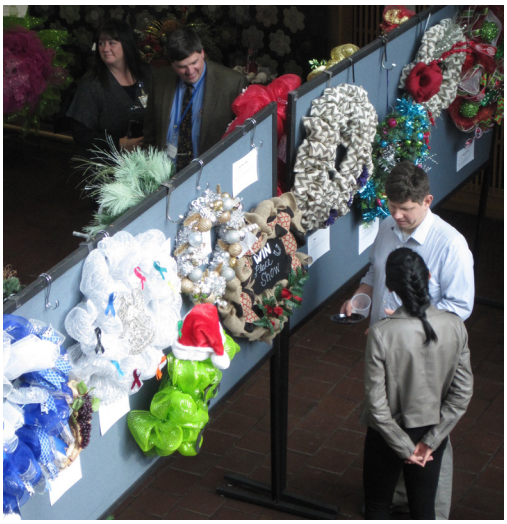
“The wreath auction really seemed to bring out the holiday spirit in all of those involved from the planning committee to those who donated and purchased wreaths,” said Amber Silberman, a Markey nurse and member of the Expressions of Courage committee.

Renee Rainey brought the idea of a wreath auction to the Expressions of Courage committee and Joel Wheeler created the auction website. Wreathes were donated by Markey patients, UK employees and local businesses.

Due to the success of the auction, plans are underway to repeat the event. Details will be available later this year.

Judges named winners in the following categories:

- Highest Bid
  #2, Snowman, contributed by Tina Cox
- Most Creative
  #21, Merry Glitzmas, contributed by by Kristi Jenkins and Kelli Desimone
- Most Elegant
  #20, A Traditional Southern Christmas, contributed by House by JSD Designs
- Most Heartwarming
  #37, Little Red Wagon, contributed by Mark Gibson

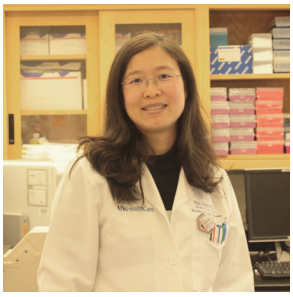


Expressions of Courage wreaths on display.

Research Results in Funding to Study Prevention of Stem Cell Damage During Cancer Treatment, Scores at Second Percentile

Ying Liang, MD, PhD, assistant professor of toxicology and cancer biology, recently received a prestigious R01 grant from the National Institutes of Health, totaling $1.88 million over five years. It was her first such award and she scored at the second percentile.

Liang has dedicated her career to studying Latexin, a gene that affects stem cell damage from chemotherapy and radiation. This gene, which Liang helped discover while she was a PhD candidate at UK and member of Dr. Gary van Zant’s laboratory, could hold a key to protecting healthy blood and stem cells during cancer treatments, the ultimate aim of Liang’s work.



Dr. Ying Liang.

Liang hopes that understanding the molecular mechanisms of the gene that affects stem cell vulnerability to cancer therapies could eventually lead to methods to protect these cells during treatment.

In 2012, she received a KL2 Career Development Award from the UK Center for Clinical and Translational Science. She has also received substantial support from the Markey Cancer Center, the departments of internal medicine and toxicology and cancer biology, and the Office of Grant Development.

This support allowed her to focus on identifying the function of the Latexin gene in bone marrow stem cells in normal and diseased conditions. Specifically, the impact of the gene on human leukemia stem cells that were transferred to mice. She found that 80 percent of mice exposed to radiation after the gene was down-regulated survived without stem cell problems and did not die from secondary illnesses, compared with only 20 percent that received radiation without inhibiting the gene.

Over the next five years, her R01 grant will build on this research to determine if deleting the Latexin gene makes stem cells more resistant to damage during cancer treatments and to understand the mechanism of the effect. She will also employ human models as well as state-of-the-art molecular and genomic techniques. Vital to the research project are interdisciplinary collaborations with Gerhard Hildebrant, MD, PhD, chief of the Division of Hematology and Blood and Marrow Transplantation, and Chi Wang, PhD, assistant professor of cancer biostastics.

Liang hopes that understanding the mechanism of the gene could allow the development of a treatment, before or after radiation, to protect against radiation-induced damage to bone marrow.