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MARKEY *quarterly*

SEASONAL NEWS FOR MARKEY CANCER CENTER FACULTY AND STAFF

TRANSLATIONAL RESEARCH IS A CORNERSTONE AT MARKEY

GROUP WORKS TO APPLY BASIC SCIENCE TO THE CLINICAL SETTING FOR BREAST CANCER

Breast cancer awareness is a popular topic in October, especially when you see pink ribbons tied around the trees outside the Markey buildings. Despite this awareness, breast cancer is the second leading cause of cancer death in women, according to the American Cancer Society. Researchers across campus are working everyday to address this serious disease, and at Markey, that work begins with the translation of basic and clinical research to clinical practice.

“We work hard each day at Markey to understand what makes cancer deadly,” says Kathleen O’Connor, PhD, Professor, Molecular & Cellular Biochemistry; Associate Director of Cancer Education, Markey Cancer Center. Behavioral and outreach researchers work to make our current standard of care practices available to our population while basic, translational and clinical research strive to not only understand the biology of cancer, but to develop new therapies or repurpose current therapies for other uses. “How we model things physiologically is an important component to translational research,” says Dr. O’Connor.

In her laboratory, Dr. O’Connor’s team models breast cancer invasion. Taking cell lines, patient tumors and special culturing conditions, they manipulate genes and block protein function through inhibitors which allows her team to identify signaling pathways involved in spread of breast cancer. Her research also has a focus in how epigenetics play into breast cancer. Using next-generation gene sequencing and large databases, Dr. O’Connor’s laboratory is interested in determining major players in breast cancer. Of particular novel interest is the integrin $\alpha6\beta4$ and its association with the most aggressive types of cancer. “We know integrin can control aggressive behavior of cancer. We also find it can drive expression of metastatic genes by changing cancer epigenetics. The integrin does this in part by changing DNA repair,” says Dr. O’Connor. “We want to learn how its signaling relates to cancers and see if we can use this information improve how we treat breast cancer.”

MARKEY BY THE NUMBERS

Monthly transvaginal sonography (TVS) screens offered by the Ovarian Cancer Screening Research Program	1,000
@UKMarkey followers on Twitter	250

FROM THE DIRECTOR

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

Everyday, teams of researchers in laboratories across the University of Kentucky focus on a variety of interests with the goal of applying their findings to improving patient care. Here at Markey, our translational research efforts to apply basic research to the clinical setting are often driven by collaboration. Whether it's clinicians who treat patients from across this region working with researchers who are developing novel approaches to patient care, or healthcare providers and scientists from different institutions all over the world joining forces for a broader understanding of the disease, one goal unites us: to reduce cancer incidence and mortality as well as improve survival and the quality of life.



As the only academic cancer center serving central Appalachia, a “distressed” region with significant health problems including the highest cancer incidence in the United States, our work at Markey is critical to advance science for our patient population. Every therapy today used to treat and cure our patients started as a hypothesis. Those ideas were planned, designed and implemented in research programs that have impacted the prevention, detection, diagnosis and treatment of cancer.

I am proud of the many individuals we have at Markey who are world-recognized as leaders in translational development for identifying novel therapeutics and delivery systems. Their expertise, along with the support of so many others here, make it possible for Markey, Kentucky’s only NCI-designated cancer center, to lead the way in providing state-of-the-art care to our patient population.

YOUR VOTE SUPPORTS MARKEY’S JIN SHIN JYUTSU PROGRAM

For her devotion to the Markey Cancer Center Jin Shin Jyutsu program, Jennifer Bradley has been nominated for a Buffalo Trace Distillery Eagle Rare Life Honor. The Rare Life Honor recognizes six categories: Courage, Leadership, Survival, Devotion, Character and Heroism. Decided by online votes, the overall winner receives \$50,000 for the charity of his or her choice. Voting is open through December, and individuals can vote more than once by clicking here.



TRANSLATIONAL RESEARCH continued

As part of the Breast Translational Group, made up of basic scientists, biostatisticians, informaticists and clinicians, Dr. O'Connor and her colleagues meet monthly to discuss how to translate basic science into the clinic and to generate resources for the entire research community.

One of those resources is the Breast Translational Group tissue microarrays (TMA). Although possible to buy commercial TMAs, these TMAs have few representative triple-negative breast cancers. To address this issue, the group created a unique resource where half of the TMA samples are triple-negative. Made possible by collaborations within the group, this resource is available to all MCC researchers through the Biospecimen and Tissue Procurement Shared Resource Facility (BSTP SRF).

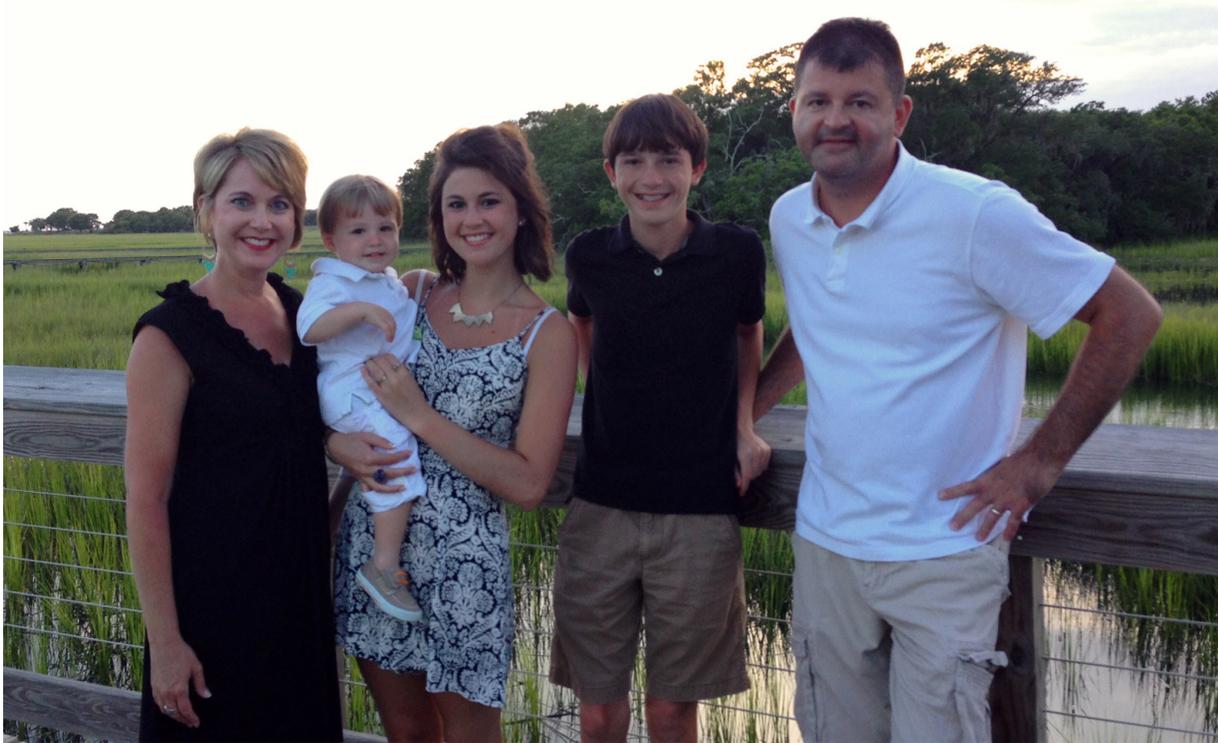
The Breast Translational Group’s current project is a triple-negative breast cancer clinical trial. With the use of an avatar model, individual patients will have their tumor tissue grown in mice and 3D cultures. As each patient receives neoadjuvant therapy, researchers test alternative, FDA-approved therapies on the mice and 3D cultures to see what might work better for that patient. Patient treatment can then be adjusted based on those results. The key to this trial is intervention early in the course of cancer treatment, before the cancers evolve into something untreatable. “There are no markers to say which population will respond best to which treatment,” says Dr. O'Connor. “Long-term, we hope to find markers and then develop a simple test that will tell us which treatment will work best for patients.”

It is this focus on the physiological needs of patient care that drives Markey’s research. “Translation of basic and clinical science is instrumental to why we are here,” says Dr. O'Connor.

MEET A MARKEY MOVER

MELISSA HOUNSHELL

This quarter, Markey Quarterly introduces you to Melissa Hounshell, Community Outreach Director.



Melissa Hounshell, Markey’s Community Outreach Director, (left) with her family CJ, Haley, Nick and Jeff.

Good afternoon, Melissa. Thank you for talking with us. Where are you from originally and what brought you to Markey?

I’m from Salyersville, KY, originally, but I have lived in Winchester for more than 20 years. I came to UK in 2007 after working many years in TV news. Both of my parents were treated at Markey. After working in UK Public Relations, I became Markey’s marketing manager. In 2014, I changed positions to Community Outreach Director

What is your role at Markey?

As Community Outreach Director, I travel frequently. In fact, I’m rarely on campus. In one week’s time, I may be in Pikeville, Hazard, McKee, Frankfort, Lexington and Georgetown. I spend much of my time talking with people of all ages about the importance of cancer screenings and health and wellness. In many cases, I explain that valuable resources and screening opportunities are just around the corner.

Do any past experiences contribute to your success in your current role?

I always say it is easy for me to share the good stories of research, clinical care and education because I’ve lived through those aspects of Markey with my parents. Markey has some of the best people on the planet working here. We should all be proud of the work we do.

What do you like best about your job?

Well, I’m a talker and a “people person” so this job is perfect for me. I travel the state and talk about something I’m very passionate about. In the process, I meet all kinds of wonderful people who are so thankful for Markey. It’s truly a blessing to hear their stories.

What should other employees know about your role?

Much of my job is simply taking the time to talk with people about screenings that are needed throughout life. We can all do that every day... just encourage and empower people to get those important check-ups and know your family history.

How do you spend your time outside of work?

I’m a mother of three great children. Haley is 17, Nick is 14 and CJ is 19 months. My husband, Jeff, and I love to travel with the family. We enjoy college football, home renovations, weekend getaways and eating. Jeff loves to cook and I love to sample it. I also enjoy decorating during the holidays. I usually have a tree for every holiday and several for Christmas. Please don’t judge me

WHO SHOULD BE OUR NEXT MARKEY MOVER?

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

NOTEWORTHY

WELCOME

Lindsey Baker, KCR
Ranjani Balasuriya, CRO
Quan Chen, Bin Huang Laboratory
Sara Emery, Administration
Rushi Goswami, Mark Stevens Laboratory
Tine Johnson, CRO
Liqing Li, Cai Huang Laboratory
Elisha Maxson, Administration
Vicki Rice, Administration
Courtney Shacklette, CCSRF
Danielle Story, Research Communications Office

PRESENTATIONS & PUBLICATIONS

Markey authors were responsible for 131 manuscripts and publications in journals from July through September 2015. Notable publications include the following.

McKenna MK, Gachuki BW, Alhakeem SS, Oben KN, Rangnekar VM, Gupta RC, Bondada S. Anti-cancer activity of withaferin a in b-cell lymphoma. *Cancer Biology & Therapy* 2015;16:1088-1098.

Shrestha-Bhattarai T, Burikhanov R, Hebbar N, Qiu S, Zhao YM, Zambetti GP, Rangnekar VM. Paracrine apoptotic effect of the tumor suppressor p53 is mediated by secreted par-4. *Cancer Res* 2015;75.

Zaytseva YY, Harris JW, Mitov MI, Kim JT, Butterfield DA, Lee EY, Weiss HL, Gao T, Evers BM. Increased expression of fatty acid synthase provides a survival advantage to colorectal cancer cells via upregulation of cellular respiration. *Oncotarget* 2015;6:18891-18904.

Nalabothula N, Al-Jumaily T, Eteleeb AM, Flight RM, Shao XR, Moseley H, Rouchka EC, Fondufe-Mittendorf YN. Genome-wide profiling of parp1 reveals an interplay with gene regulatory regions and DNA methylation. *Plos One* 2015;10.

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 Sep 30;6:8331.

Dolecek TA, Dressler EV, Thakkar JP, Liu M, Al-Qaisi A, Villano JL. Epidemiology of meningiomas post-public law 107-206: The benign brain tumor cancer registries amendment act. *Cancer* 2015;121:2400-2410.

GRANTS

Kristen Ashford, PhD, 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”.

B. Mark Evers, MD and Robin Vanderpool, DrPH were awarded National Cancer Institute funding for “Supplement: University of Kentucky Markey Cancer Center Support Grant - NON CHE”.

B. Mark Evers, MD and Mark Dignan, PhD, MPH, were awarded National Cancer Institute funding for “Supplement: University of Kentucky Markey Cancer Center - Cancer Center Support Grant - Reducing Cancer Health Disparities in GMaP Region 1”.

Emilia Galperin, PhD, was awarded National Institute of General Medical Sciences funding for “Deciphering the Molecular Mechanisms Underlying Active Scaffoldin”.

Yvonne Fondufe-Mittendorf, PhD, was awarded National Science Foundation funding for “Investigating the novel role of PARP-1 in contrancriptional splicing”.

Fredrick Onono, PhD, was awarded National Cancer Institute funding for “Intestinal Phosphatidylcholine exposure and breast cancer risk”.

AWARDS, RECOGNITIONS & SELECTIONS

D. Allan Butterfield, PhD, Alumni Association Endowed Professor of Biological Chemistry and Director of the Redox Metabolism Shared Resource Facility in the Markey Cancer Center at the University of Kentucky, has been named an Associate Vice President for Research at UK.



B. Mark Evers, MD, Director of the University of Kentucky Markey Cancer Center, Professor and Vice-Chair for Research in the Department of Surgery and Markey Cancer Foundation, Endowed Chair, was selected as the 2015 recipient of the Outstanding Alumnus Award, the University of Tennessee College of Medicine Alumni Association’s highest honor.

NOTEWORTHY, continued

Stuart Jarrett, PhD, was selected by the Society for Investigative Dermatology as October’s featured “Meet the Investigator,” a new monthly series aimed at introducing the investigative dermatology community to up-and-coming investigators in the dermatology community.

Frederick R. Ueland, MD, has accepted the role of Director of the Clinical Research Organization. Dr. Ueland will oversee Clinical Care and Research Teams and lead efforts to increase both the number of clinical trials offered and the number of patients enrolled on those trials.

David Williams, BSN, RN, has accepted the role of Markey Hematology Program Practice Manager.

The Comprehensive Breast Care Center received accreditation from the American College of Radiology for the Affirm Stereotactic Biopsy Guidance System.

Plant Extract From Traditional Indian Medicine May Fight Blood Cancer

A University of Kentucky study shows that withaferin A, a component of *Withania somnifera* (winter cherry) plant extract, may hold promise as a new treatment for non-Hodgkin’s lymphoma.

Winter cherry extract was used in traditional Ayurvedic Indian medicine for thousands of years before it caught the interest of Subbarao Bondada, a University of Kentucky College of Medicine professor and researcher for the UK Markey Cancer Center. Because withaferin A shows promise in treating other cancers without the side effects associated with current treatments, Bondada’s laboratory tested it against lymphoma. Non-Hodgkin’s lymphoma is one of the most common cancers in the U.S. and is known for being particularly aggressive.

Unlike other studies using withaferin A to treat cancer, Bondada’s study, published in the journal *Cancer Biology and Therapy*, is the first to test the chemical against a blood cancer. Previous studies using withaferin A focused on cancers producing tumors that grow as a mass in tissue, more commonly known as solid tumors.

Katie McKenna, a graduate student in Bondada’s laboratory, found that withaferin A prevented the lymphoma cells from dividing and ultimately killed them. Specifically, they found withaferin A directly targeted a signaling pathway in the cancer it needs to survive.

Because withaferin A shows promise in treating non-Hodgkin lymphoma, Bondada’s team is now testing the chemical on chronic lymphocytic leukemia cells.

Bondada’s group collaborated with University of Louisville Professor Ramesh Gupta, who aided in the isolation of withaferin A. This work was funded by the National Cancer Institute to the UK Markey Cancer Center, the National Institutes of Health, Office of Vice President for Research for Core Research facilities and the Sabinsa Corporation.

MARKEY DIFFERENCE MAKERS

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

- | | |
|------------------|-------------------|
| Donna Areaux | Lisa Minke |
| Eugenia Caldwell | Stephenie Mullins |
| Farrah Cates | Angela Pennington |
| Sheila Cummins | Michele Ratcliffe |
| Jenny Delap | Princeton Reese |
| Philip Desimone | Joseph Scandrani |
| Connie Donatucci | Barbara Simon |
| Mark Filburn | Evelyn Smith |
| Lori Fritz | Melanie Spicer |
| Kimberly Haire | Donica Sweat |
| Miranda Hatfield | Joseph Valentino |
| Lura Henry | Edna Ware |
| Melanie Hunter | Melanie Wilson |
| Jill Lee | Jo Wright |
| Peggy Meece | Kathryn Zeller |
| Rachel Miller | |

Do you know a Markey Difference Maker?

The Markey Difference Maker award recognizes the above-and-beyond dedication and talent of those who go about the business of treating cancer patients, finding efficiencies in business procedures, improving working conditions, and, generally, making life easier for everyone associated with Markey: patients, caregivers, families, providers, administrators and staff. Nominations are now accepted online.

RCO HAS MOVED BACK TO COMBS

The Research Communications Office has moved back to the Combs Research Building. You can find us in rooms 100C, 100D and 203.