



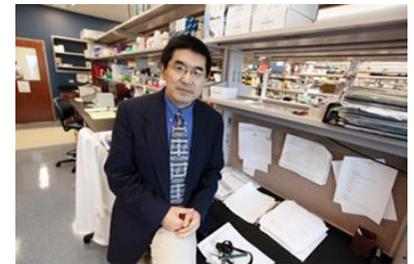
# Director's Update

July 25, 2017

## *Message from Ming You, MD, PhD, Director of the MCW Cancer Center*

Welcome to the latest edition of the Director's Update newsletter.

As you may recall, the National Cancer Institute (NCI) and our External Scientific Advisory Board (ESAB) told us that before submitting for designation we must increase our annual direct funding from the NCI. Because of this, we've created new support systems to assist investigators as they apply for NCI funding. We've already made some great progress, which is detailed in the summaries on the next three pages. In particular, I want to congratulate our Cancer Center members who received their first NCI R01 in the last year, including Dr. Kirsten Beyer, Dr. Peter LaViolette, Dr. Joan Neuner and Dr. Stuart Wong.



To continue this growth, we're launched an ongoing RFA for new and highly promising resubmissions of NCI R01s. This award provides funds for investigators to address reviewers' feedback and/or gather preliminary data and research for successful submissions. This RFA is available through the end of 2017 and LOIs will be accepted any time before November 1, 2017.

Additionally, the Cancer Center is pleased to provide intensive support and resources to help with all aspects of the pre-award process for any NCI grant submission. This includes grant development, editing, graphic design, scientific review and administrative coordination. Please let us know how we can help you in your grant process. To get started, please make a formal request by completing this [web form](#). Someone from the Cancer Center will respond within 48 business hours. For more information, contact Kitty Marquardt, Research Program Manager, at [kmarquardt@mcw.edu](mailto:kmarquardt@mcw.edu).

We are making great progress, but are not there yet. I encourage everyone to think about NCI P01s, SPOREs, NCI multi-PI R01s or U01s and NCI R01s, and let us know how we can help make you successful. Dean Kerschner has requested and receives monthly updates on our NCI funding situation, as well as an overall update. We're both excited to see what else we'll achieve by the time we submit our application for designation.

Thank you for all your hard work, and keep it up!

## Cancer Center Researchers Receive NIH & Other Peer Review Funding

By Rachel Italiano

Recent months have brought an influx of NCI, other NIH and Department of Defense peer-reviewed cancer funding to the Medical College of Wisconsin Cancer Center. These new grants include several projects that address specific cancer disparities in our region. Congratulations to all our researchers!



**Michele Battle, PhD**, received an R01 grant from the National Institute of Diabetes and Digestive and Kidney Diseases for her project titled "GATA4 in Development of a Normal Squamocolumnar Junction and Barrett's Esophagus." It explores the idea that abnormal re-

activation of the developmentally important transcription factor GATA4 in the esophagus contributes to the pathology of Barrett's esophagus (BE), a premalignant condition. Individuals with BE have an elevated lifetime risk of developing esophageal adenocarcinoma (EAC), a deadly cancer with a five-year survival rate of ~18%. If the study's hypothesis is correct, Dr. Battle and her team will identify GATA4 and its downstream targets to explore for future therapies and/or as biomarkers for BE and other pre-cancerous conditions.



**Kirsten Beyer, PhD, MPH**, was recently awarded an NCI R01 grant in May built upon her previous work regarding breast cancer disparities, which found that racial bias in housing is associated with breast cancer

survival among Black women in the Milwaukee area. Her current study will undertake a national study of segregation and breast cancer survival among Black, Hispanic and non-Hispanic women by constructing and comparing segregation measures, determining whether segregation is associated with survival via which pathways, and exploring the ways in which Black and Hispanic breast cancer survivors in a highly segregated metropolitan area navigate cancer survivorship in the context of segregation. The project is entitled "Racism, Residential Racial Segregation and Breast Cancer Survival Disparities among

Black, Hispanic and Non-Hispanic White Women."



**Peter LaViolette, PhD**, was awarded an NCI R01 for his work to individualize diagnoses and treatments for deadly brain glioblastomas. His project will provide a detailed understanding of how brain tumors, at the cellular level, appear on macroscopic imaging

by examining whole brain human samples and clinical MRI scans. Eventually, the need for tissue will be eliminated by the development of computational algorithms created using knowledge of microscopic cell structure to recognize patterns in MRI scans (radio-pathomics). By providing a complete picture of the microcellular features underlying brain tumor imaging, patient care and clinical decision-making will improve dramatically. His study is entitled "Brain Cancer Radio-Pathomics for Predicting Heterogeneous Cytology."



**Joan Neuner, MD, MPH**, was recently awarded a \$2.23 million R01 grant from the National Institute on Minority Health and Health Disparities (NIMHD) to study "Socioeconomic Disparities in Adherence to Oral Hormonal Therapy for Breast Cancer." The

research is based on her 2015 Journal of the National Cancer Institute (JNCI) paper which showed trends toward high rates of nonadherence in using Aromatase inhibitors were reversed with either copayment elimination or low-cost generics.



**Bin Ren, MD, PhD**, was recently awarded an R01 grant for his work in providing a comprehensive evaluation of arteriolar differentiation and capillary arterialization. Titled "Epigenetic and Transcriptional Regulation of Angiogenic Regulator CD36 and

Transformation of Capillaries into Small Arteries," the project will illuminate poorly explored and poorly understood aspects of vascular biology.



**Ling Wang, MD, PhD**, was awarded a Department of Defense Breast Cancer Research Program Breakthrough Award in April for her project "Regulation of Tumor Cell ANGPTL4 by Astrocyte-Secreted TGF-Beta2 in Triple-Negative Breast Cancer Brain

Metastases." Patients with triple-negative breast cancer (TNBC) have the worst outcomes among patients with breast cancer due to their high propensity for brain metastases and lack of response to hormone or HER2-targeted therapies. Therefore, identifying specific targets in TNBC cells that could be blocked to prevent brain lesions is critical to provide TNBC patients with better outcomes and quality of life.



**Adriano Marchese, PhD**, was awarded an R01 from the National Institute of General Medical Sciences for his project "GPCR Regulation of AKT Signaling." This project seeks to study the mechanisms governing G protein-coupled receptor (GPCR)

signaling, which play a critical role in many human diseases including cancers. The goal of the project is to characterize and explain the molecular mechanisms specific to chemokine receptor CXCR4, a specific GPCR that is over-expressed in many metastatic cancers. Understanding CXCR4 mechanisms may lead to the identification of new and innovative therapeutic targets to treat and prevent metastatic disease.



**Melinda Stolley, PhD**, MCWCC Associate Director of Prevention and Control was recently awarded an R21 grant for her project, "Every Day Counts: A Lifestyle Program for Women with Metastatic Breast Cancer

(MBC)." Trials using lifestyle interventions in early stage breast cancer survivors largely exclude women with MBC, although Stolley's formative work supports that women with MBC are interested in and capable of participating in a lifestyle intervention trial. "Every Day Counts" is a 12-week cognitive-behavior lifestyle intervention aimed specifically at women with MBC. It reflects a "first step" in a research trajectory to help discern how lifestyle behaviors influence quality

of life, prognosis and help make every day count for women with MBC.



**Vera Tarakanova, PhD**, received an R01 grant from the National Cancer Institute for her work involving gammaherpesviruses and their relation to the development of cancer.

Gammaherpesviruses infect a majority of adults and can lead to virus-driven B cell lymphomas. Preliminary studies identified a host transcription factor that is likely to oppose the formation of virus-driven lymphomas, and her current work revolves around determining how this host transcription factor opposes viral processes to restrict virus infection and, possibly, virus-driven cancer. The project is entitled "IRF-1: A Brake to Limit Gammaherpesvirus Infection and Pathogenesis."



**Robert Miao, PhD**, received a five-year, \$2.1 million R01 grant from the NIH's National Institute of Diabetes and Digestive Kidney Diseases to investigate the accumulation of lipids in liver cells leading to hepatic steatosis, a serious liver disease

that is increasingly common in the United States and a common risk factor for liver cancer. If successful, this research project will be the first to show how NgBR signaling regulates the molecular mechanisms driving hepatic steatosis.



**Jong-In Park, PhD**, successfully renewed his NCI R01 entitled "Mechanisms of MEK/ERK Growth Arrest Signaling." This \$2M grant continues Dr. Park's research into the MEK/ERK pathway which is frequently deregulated in cancer. This

makes the pathway a key target for new cancer therapies, including a promising strategy to use this pathway to exploit natural weaknesses of cancer cells associated with aberrant MEK/ERK activity.



**Liang Wang, MD, PhD**, received an NCI R01 for his project titled "Cell Free Nucleic Acid-Based Biomarkers in Advanced Prostate Cancer." Currently there is no clinical feature or molecular test that can reliably predict

treatment responses or clinical outcomes from androgen deprivation therapy in patients with advanced prostate cancer. Developing a predictive feature or biomarker as a factor to determine which patients will do well with a specific type of treatment will give clinicians an important tool to help determine treatment for late-stage prostate cancer patients with limited options. Identifying circulating cell free nucleic acid-based biomarkers -- often referred to as "liquid biopsy" -- that predict response to treatments will not only help clinicians in selecting the most effective treatment options, but will also provide important clues regarding mechanisms that underlie prostate cancer progression and recurrence.



**Ming You, MD, PhD**, director of the MCW Cancer Center and the Joseph F. Heil Jr. Professor of Oncogenesis, and **Balaraman Kalyanaraman, PhD**,

chair and professor in the Department of Biophysics and the Harry R. & Angeline E. Quadracci Professor in Parkinson's Research, have received a \$3.16M multi-investigator R01 grant from the National Cancer Institute to evaluate the potential of Mito-Honokiol to

prevent lung cancer and its metastasis. Co-investigators include Micael Hardy, PhD, Aix-Marseille University; Charles Myers, PhD, professor in the Department of Pharmacology and Toxicology; and Jacek Zielonka, PhD, research director at the Free Radical Research Center and Department of Biophysics. The project is entitled "Chemoprevention of Lung Cancer with Mitochondria-Targeted Honokiol."



**Stuart Wong, MD**, a nationally renowned physician scientist who specializes in head and neck cancers at the Froedtert and Medical College of

Wisconsin Cancer Center, received a \$2.6M NCI R01 multi-investigator grant with co-PI **Dr. Ming You**. This research evaluates a widely used Chinese herbal formula called Antitumor B as potent cancer preventive agents for squamous cell carcinomas, the most common malignancies of the oral cavity. The project is entitled "Inhibition of Oral Tumorigenesis by Antitumor B." [Click here to read more](#) about this exciting project, including the use of an innovative Window of Opportunity (WOO) clinical trial where participants receive Antitumor B in the window of time between their diagnostic biopsy and surgery to remove the tumor.

**Did we miss you?** If you received NCI, other NIH or other peer-reviewed cancer research funding in the past year and we didn't feature you here, please contact Communications Manager Anne Mathias at [amathias@mcw.edu](mailto:amathias@mcw.edu) and we'll be sure to highlight your work in the next issue.

## Congratulations, Dr. Myers!

Please join us in congratulating Dr. Charles Myers who was recently appointed Assistant Director of Research of the [MCW Cancer Center](#) by Ming You, MD, PhD.

As Assistant Director of Research Dr. Myers will play a significant role in helping the center prepare for NCI designation and work closely with Dr. You to review, improve, and finalize preparation of the center's formal application materials.

"Charley's input and guidance were invaluable for our recent chemoprevention large center grant submission and I am very happy that he's agreed to formally serve the Center in this important way," said Dr. You. "I look forward to a close collaboration in these final busy months leading up to our designation submission."

# Center Creates RFA and Support Services to Promote New R01 Pilot Grant Proposals



In an effort to advance cancer research with the goal of improving the health of Wisconsin citizens, we are

seeking pilot grant proposals to support new NCI R01 submissions or resubmissions on any type of cancer research. This is an ongoing RFA available through the end of 2017, with LOIs accepted any time before November 1, 2017. Pilot funds are available for those who submitted an NCI R01 that was scored but not funded and who plan to resubmit by March 2018. Funding is also available for investigators who plan to submit an NCI R01 by that same date, to fund preliminary research and data.

In addition to funding, the MCW Cancer Center is also offering intensive pre-award grant support for those submitting to the NCI. The following services are provided:

- Grant coordination and other administrative support services
- Editing and proofing
- Graphic design and development of scientific figures
- Internal and external scientific review services
- Literature searches, information gathering
- Coordination with needed cores, labs, equipment, services and expertise
- Biostatistics design
- Development of other attachments such as facilities sections
- Support with protocol development and IRB submissions
- Any other services the Center can provide to help you submit, or resubmit, a successful NCI grant.

To access these support services, please make a formal request by completing this [web form](#). Someone from the Cancer Center will respond within 48 business hours. For more information, contact Kitty Marquardt, Research Program Manager, at [kmarquardt@mcw.edu](mailto:kmarquardt@mcw.edu).

## MCW Cancer Center Announces Awardees of Pilot Grants

By *Rachel Italiano*

The MCW Cancer Center is pleased to announce the newly awarded winners of pilot grants. One of the most important functions of the MCW Cancer Center is to provide and identify cancer research funding opportunities, particularly for those investigators who do not yet have significant NIH or other extra-mural funding.

"These projects are just a sampling of the innovative and promising research that takes place at the Medical College of Wisconsin Cancer Center," said Ming You, MD, PhD, Cancer Center Director. "These researchers represent the talent and commitment that exists here and highlight the work we're doing to develop all of our active researchers into NCI funded investigators."

For this cycle, we awarded more than \$1 million in pilot funding to support new ideas and emerging investigators in cancer research. We are pleased to announce the following awards and congratulate these members on their creativity and scientific excellence.

MCW Cancer Center  
Pilot Funding Program



**Joseph Besharse, PhD**, was awarded a \$50,000 basic science pilot grant for his project, called "Circadian Clocks, Cancer and the Regulation of Aerobic Glycolysis." He highlights the confounding impact of circadian clock regulation on cancer, which is not typically taken into account in most cancer studies. Dr. Besharse hypothesizes that glycolytic metabolism is normally controlled through cell autonomous circadian clock regulation and that high aerobic glycolysis in cancer cells reflects mis-regulated clock function. An advanced tool kit is proposed for proper analysis of circadian components in lung cancer.

For his work titled "Preclinical Efficacy of Xanthohumol in Pancreatic Cancer," **Dr. Muthusamy Kunnimalaiyaan, PhD**, received a Basic Science pilot grant for \$50,000. Building on the foundation of a previous study, Dr. Kunnimalaiyaan proposes to further expand the research surrounding Notch1 and effect of XN treatment. This is novel and innovative because it uses a natural compound against highly aggressive pancreatic cancer and results could lead not only to the development of a clinical trial at MCW using XN alone or in combination with gemcitabine or other chemotherapeutic agents but also for the preparation of a potential R01 application.

**Silvia Munoz-Price, MD, PhD**, received a Clinical/Translational pilot grant award for \$100,000. Her work is entitled "Randomized Double-Blind Controlled Trial for the Treatment of NAAT(+)/toxin EIA(-) Clostridium Difficile in the Hematology Oncology Population." Although treatment options exist against clostridium difficile infection, yearly attributable deaths are estimated at 29,300. Since 2015, a colonization rate of 15% has been found at MCW, with 2/3 of these patients testing positive

for CDI upon admission. The study examines the use of oral vancomycin against a placebo.

**Demin Wang, PhD**, received a \$50,000 Highly Promising R01 award for his project, titled "Signaling Regulation of Early B Lymphopoiesis." The study has potential to lead to a paradigm shift in the understanding of the molecular mechanism underlying the regulation of B-cell lymphopoiesis, provide new clues to the pathogenesis of B-cell deficiencies and malignancies and help identify potential new targets for interventional therapies.

**Guan Chen, MD, PhD**, received a two-year, \$100,000 award from the Wisconsin Breast Cancer Showhouse (WBCS) and the MCW Cancer Center for his work on breast cancer. The WBCS is an organization that supports early stage breast cancer and prostate cancer research at MCW. His project is entitled "Disrupt a Signaling Circuit for the Treatment of Breast Cancer" and focuses on a gene known to contribute to triple negative breast cancer metastasis. Triple negative breast cancer (TNBC) has the worst prognosis among all types of breast cancers. His goal is to identify a novel target to disrupt the gene to establish a new treatment approach.

**Sarah White, MD, MS, FSIR**, was awarded a \$20,000 ACS supplemental grant to continue her work, "Develop a new magnetically triggered oxaliplatin nanoparticle to treat colorectal liver metastases."

Three individuals received a sub award of MCW's American Cancer Society Institutional Research Grant (ACS-IRG). The ACS-IRG is a training grant awarded to institutions in order to help new investigators establish cancer-focused research projects by providing pilot funding on a competitive basis. Each grant is for \$30,000.

**Dr. Pradeep Chaluvally-Raghavan's** project "RNA Activation Driven Ovarian Cancer," expects that the mechanistic studies on the role of miR551b in ovarian cancer are designed to increase understanding on the role of microRNA amplifications in ovarian



## CTO Representatives Attend AACI, Present Posters

By Rachel Italiano

Several representatives from the MCW Cancer Center Clinical Trials Office, Betty Oleson (BSN, RN, CCRP), Brenda Brito (BSBA), May Gan (MS, MBA, PMP, CCRP), Katy Schroeder (RN, OCN, CCRP), Rebecca Selle (BS, CCRP), Jim Thomas (MD, PhD), and Stacey Zindars (MS, CCRP), recently presented posters at the Association of American Cancer Institutes-Clinical Research Initiative ([AACI-CRI](#)) annual conference on July 12-13. The goal of the conference is to identify common challenges in clinical research and share solutions to help solve these challenges or improve them. It's a collaborative community of Cancer Center leadership teams from across the country who come together to share their experiences and learn from one another.

A poster session is always held on the first day of the meeting. This year, three MCW posters were submitted and accepted to the conference. They were "hopping with visitors all evening!" said Selle. She also noted that the session emphasizes inventive ideas applicable to everyday tasks. "One of the things I love most about my job is coming up with innovative and streamlined solutions to everyday tasks that were previously tedious

or cumbersome. The poster session is always filled with these types of ideas," she said.

Below is a list of the posters and authors:

### **Not All Tumors Are Created Equal: Evaluating the Impact of an Interdisciplinary Molecular Tumor Board**

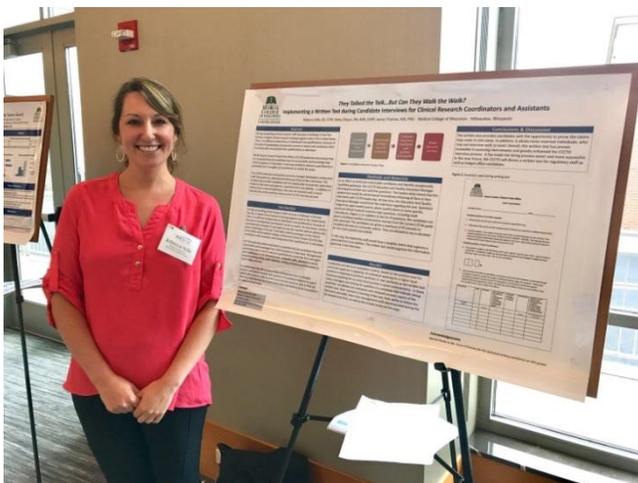
Allison Martin, PharmD; Ben George, MD; Elizabeth Weil, PharmD, BCOP; Angela Urmanski, PharmD, BCOP; Katrina Schroeder, RN, OCN, CCRP; Kayla Mendenhall, CPhT; Mindy Waggoner, PharmD, BCOP; Carolyn Oxencis, PharmD, BCPS, BCOP

### **They Told the Talk...But Can They Walk the Walk? Implementing a Written Test during Candidate Interviews for Clinical Research Coordinators and Assistants**

Rebecca Selle, BS CCRP; Betty Oleson, BSN, RN, CCRP; James Thomas, MD, PhD;

### **Improving Research Lab Sample Tracking and Cost Recovery by Implementing a Web-based System**

Wes Rood, BS; Megan Kocejda, BS; Brenda Brito, BSBA; Betty Oleson, BSN, RN, CCRP; Rebecca Selle, CCRP; James Thomas, MD, PhD



Rebecca Selle BS, CCRP (above left) and Katy Schroeder RN, OCN, CCRP (above right) present their posters at the AACI-CRI conference held in Chicago in July.

## In Brief

An at-a-glance look at new developments and events happening at the MCW Cancer Center



### **First Solid Tumor Retreat a Resounding Success**

Congratulations to Dr. Stuart Wong for leading the first annual Solid Tumor Retreat held Friday, July 21<sup>st</sup>. "It was a really a successful day and I want to congratulate Stu. I was impressed with the impact of the event and the depth of solid tumor research happening at MCW," said Ming You, Director of the MCW Cancer Center, who attended and presented at the retreat. Retreat organizer Dr. Stuart Wong shared, "I was very proud to spotlight the amazing work in solid tumor research and clinical care and encourage collaboration amongst my colleagues." The retreat included presentations by Drs. Stuart Wong, Ben George, Bryon Johnson, Weiguo Cui, Matthew Riese, Michael Dwinell, Nirav Shah and Parameswaran Hari.



### **Stolley Publishes Results in JCO**

Dr. Melinda Stolley and her team recently published the results of their community-based weight loss intervention for African American breast cancer survivors called "Moving Forward," in the *Journal of Clinical Oncology*. Because these results indicated that "Moving Forward" would be effective in Milwaukee, they are expanding the study. They have also received NCI R21 funding to examine a healthy eating and exercise program, "Every Day Counts," for women in southeastern Wisconsin with metastatic breast cancer. [Read more here.](#)



### **MCWCC Member Dr. Amanda Kong Appointed New Section Chief of Breast Surgery**

Dr. Amanda Kong, MCWCC member, has been appointed Section chief of Breast Surgery, a new section currently in development within the Division of Surgical Oncology. She was appointed assistant professor of surgery at MCW in 2008 and received a Master's degree in epidemiology from here in 2010. She was promoted to associate professor of surgery in 2014. Dr. Kong has received many honors, including being named Best Doctor by M Magazine and the Excellence in Professionalism Award from the faculty practice. Congratulations!



### **First Annual AHW Research Symposium Held**

*Changemakers in Science*, the first annual Advancing a Healthier Wisconsin Endowment (AHW) research symposium was held Wednesday, July 19 in the Alumni Center. Raul A. Urrutia, MD, incoming Director of the Human and Molecular Genetics Center, and newly appointed co-leader of the MCWCC Discovery & Developmental Therapeutics program presented the keynote. The innovative work of MCW investigators was highlighted throughout the symposium.



### **Dr. Beth Erickson Named to Inaugural Class of New National Fellowship**

Beth A. Erickson, MD, professor of radiation oncology, has become a member of the inaugural class of the American Brachytherapy Society Fellows (FABS). Fellows are recognized for their significant impact, contributions and accomplishments in the field of brachytherapy. Brachytherapy is the treatment of cancer by the insertion of radioactive implants directly into the tissue.



### **Study Indicated that Men with Returning Prostate Cancer Can Prolong Life with Anti-Male Hormone Therapy**

An NCI-funded study co-authored by Colleen Lawton, MD, was published in the *New England Journal of Medicine* and found that men whose prostate cancer returns after surgery are more likely to survive when they take drugs to block male hormones in addition to receiving radiation therapy. Specifically, the study showed that among men who received radiation and hormonal treatment, 76.3 percent were still alive after 12 years, compared to 71.3 percent who had radiation alone.



### **Dr. Janet S. Rader co-chairs Cervical Cancer Study published in Nature**

Corresponding author and co-chair Janet S. Rader, MD, and contributors Denise Uyar, MD, William Bradly, MD and Behnaz Behmaram, MD, published the article *Integrated Genomic and Molecular Characterization of Cervical Cancer* in the March 16, 2017, issue of the journal *Nature*. Their work describes molecular analyses of and reveals new potential therapeutic targets for cervical cancers.