DEPT. OF TOXICOLOGY AND CANCER BIOLOGY NEWSLETTER

Volume 3, Issue 4

Table of Contents

Pg 1:
- New Post-Award Grant Support
- New Grants
- Featured Publications

Pg 2:
- Featured Publications cont.
- Recently Accepted or Published Manuscripts

Pg 3:
- Recently Accepted or Published Manuscripts cont.
- Faculty Activity

Pg 4:
- Faculty Activity cont.

Pg 5:
- Faculty Activity cont.
- Welcome New Lab Members

Pg 6:
- Welcome New Lab Members cont.
- Lab Activity

Pg 7:
- Student Forum Activities
- Recent Graduations
- Student Awards
- Forensic Internships

SUPPORT THE DEPARTMENT

Gifts to the department will be directed toward emerging needs and opportunities for our students, faculty research support, and unrestricted support for the department.

Click here to learn more and donate.

Thank you for your support!

New Post-Award Grant Support for Department:

Sponsored Research Administrative Services (SRAS) is now providing our department Post-Award Grant Support.

Post-Award Grant Support: **Scott Lutin** will be your contact for any items related to a grant after it has been awarded. Examples include: he will provide monthly budget updates, assist with RPPRs, no-cost extensions, effort changes, etc. Scott's email: scott.lutin@uky.edu

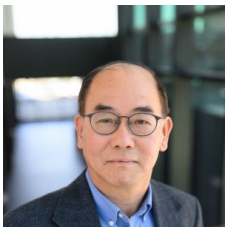
Pre-Award Grant Support: **Whittney Sherman** will continue to be your contact for any items related to a grant before it is awarded. You will continue to work with her to submit grants, Just-in-Time requests, Internal Approval Forms routed, etc.

New Grants (New grants are shared once the department receives PADR 1 stating the account has been created):

Dr. Will Fong, Assistant Professor, was awarded an American Cancer Society Institutional Research Grant. The grant, entitled "Determining the Role of AR-repressed Gene, CCDC83 in Conferring Anti-Androgen Resistance in Prostate Cancer" will last one year with a total budget of $30,000.

Dr. Jinghui Liu, a Research Assistant Professor at Dr. Xiaoqi Liu's lab, was awarded an American Cancer Society Institutional Research Grant. The grant, entitled "Inhibiting CK1a increases the efficacy of enzalutamide in castration-resistant prostate cancer" will last one year with a total budget of $30,000.

Featured Publications:



This year, **Dr. Jin-Ming Yang**'s group of our department published two papers in ***Science Advances***. The paper published on February 2 entitled, "Elongation Factor-2 Kinase is a Critical Determinant of the Fate and Antitumor Immunity of CD8+ T Cells", reports their findings that eukaryotic elongation factor-2 kinase, a key regulator of protein synthesis and stress response, has a critical role in regulating the fate and cytocidal activity of CD8+ T cells. Their findings indicate that eEF-2K is essential for sustaining the viability and function of cytotoxic CD8+ T cells, and suggest that therapeutic augmentation of this kinase in CD8+ T cells may be exploited as a novel approach to reinforcing CAR-T therapy against cancer.

The second report published on June 29 entitled, "NAC1 Modulates Autoimmunity by Suppressing Regulatory T Cell-Mediated Tolerance", tells the story on how they discovered NAC1, a nuclear factor, acts as a key determinant of immune tolerance. They found that depletion of NAC1 can significantly reinvigorate the FoxP3+ regulatory T cells and enhance tolerance to autoimmunity. Based in this finding, targeting of NAC1 warrants further exploration as a potential tolerogenic strategy for treatment of autoimmune disorders such as autoimmune arthritis, colitis, and diabetes. Both discoveries would have important implications in immunotherapy for cancer and autoimmune diseases, respectively.

Featured Publications cont.:



As the first author and co-corresponding author, **Dr. Changhai Tian** recently published his research work on ***Circulation Research*** (2022 Sep 30), a leading journal in the cardiovascular field. His work discovered a unique communication pathway between the injured heart and a specific autonomic regulatory area in the central nervous system. Learn how myocardial extracellular vesicles regulate pre-sympathetic neuronal discharge in heart failure, especially emphasize the contribution of cardiac non-coding RNAs to the sympathetic excitation of brain via extracellular vesicles. The findings may help to develop the therapeutic intervention for mental health problems among people with heart failure.



Dr. Ka-wing (Will) Fong, Assistant Professor of College of Medicine at University of Kentucky was the first author of the below study published in ***Molecular Cell*** (2022 Dec. 06) and Dr. Jindan Yu, Professor of Feinberg school of Medicine at Northwestern University was the corresponding author.

PALI1 is a newly identified accessory protein of the Polycomb repressive complex 2 (PRC2) that catalyzes H3K27 methylation. However, the roles of PALI1 in cancer are yet to be defined. Here, we report that PALI1 is upregulated in advanced prostate cancer (PCa) and competes with JARID2 for binding to the PRC2 core subunit SUZ12. PALI1 further interacts with the H3K9 methyltransferase G9A, bridging the formation of a unique G9A-PALI1-PRC2 super-complex that occupies a subset of G9A-target genes to mediate dual H3K9/K27 methylation and gene repression. Many of these genes are developmental regulators required for cell differentiation, and their loss in PCa predicts poor prognosis. Accordingly, PALI1 and G9A drive PCa cell proliferation and invasion in vitro and xenograft tumor growth in vivo. Collectively, our study shows that PALI1 harnesses two central epigenetic mechanisms to suppress cellular differentiation and promote tumorigenesis, which can be targeted by dual EZH2 and G9A inhibition.



Dr. Evan Kong, a Postdoc Scholar with Dr. Xiaoqi Liu, recently published an article to describe a non-mitotic mechanism through which PLK1 accelerates lung cancer development (Kong et al., ***Science Signaling***, 2022, 15, eabj4009). In the classical Kras/Tp53-mutant lung adenocarcinoma mouse model, PLK1 elevation resulted in activation of a receptor tyrosine kinase RET, consequently activation of the MAPK pathway. Dr. Kong went on to show that co-targeting RET and MAPK pathway induced tumor regression and prolonged survival. The finding was highlighted on ***Science***, 2022, 378, 37.

Recently Accepted or Published Manuscripts:

Dr. Xiaoqi Liu:

1. Kong, Y., Allison, D.B., Zhang, Q., He, D., Li, Y., Mao, F., Li, C., Li, Z., Zhang, Y., Wang, J., Wang, C., Brainson, C.F., and **Liu, X**. (2022) The kinase PLK1 promotes the development of Kras/Tp53-mutant lung adenocarcinoma through transcriptional activation of the receptor RET. Science Signaling, 15 (754), eabj4009. DOI: 10.1126/scisignal.abj4009. PMID: 36194647 (Cover story of the issue).

Dr. Min Chen:

1. **Chen M***, Marrs B, Qi L, Knifley T, Weiss HL, D'Orazio JA and O'Connor KL. Integrin α6β4 signals through DNA damage response pathway to sensitize breast cancer cells to cisplatin. Frontiers in Oncology, 2022 (*Co-corresponding author)

Recently Accepted or Published Manuscripts cont.:

Drs. Lane, Fan and Higashi:

1. A. Ali, S. Davidson, Fraenkel, I. Gilmore, T. Hankemeier, J. Kirwan, **A. N. Lane***, I. Lanekoff, M. Larion, L-I McCall, M. Murphy, J. Sweedler, C. Zhu. (2022). Single cell metabolism-current and future trends. Metabolomics 18:77 Front Cover

2. S. Kang, L. Liu, T Wang, M. Cannon, P. Lin, **T. W.-M. Fan**, D. A. Scott, H-S. Joyce Wu, **A. N. Lane**, and R. Wang* (2022) GAB functions as a bioenergetic and signaling gatekeeper to control T cell inflammation. Nat. Metabolism 4, 1322–1335

3. **T. W-M. Fan***, Q. Sun, **R. M. Higashi** (2022) Ultrahigh resolution MS1/MS2-based Reconstruction of Metabolic Networks in Mammalian Cells Reveals Changes for Selenite and Arsenic Action J. Biol. Chem. 298: 102586

Dr. Luksana Chaiswing:

1. **Miller, C.E.;** Xu, F.; Zhao, Y.; Luo, W.; Zhong, W.; Meyer, K.; Jayswal, R.; Weiss, H.L.; St. Clair, W.H.; St. Clair, D.K.; **Chaiswing, L.** Hydrogen Peroxide Promotes the Production of Radiation-Derived EVs Containing Mitochondrial Proteins. Antioxidants 2022, 11, 2119. https://pubmed.ncbi.nlm.nih.gov/36358489/

Dr. Eva Goellner:

1. **Daniels, H.G.,** Knicely, B.K., Miller, A.K., Thompson, A., Plattner, R., and **Goellner, E.M.** (October 2022) "Inhibition of ABL1 by tyrosine kinase inhibitors leads to a downregulation of MLH1 by Hsp70-mediated lysosomal protein degradation" Frontiers in Genetics 13:940073.

Faculty Activity:

Dr. Xiaoqi Liu:

1. Dr. Xiaoqi Liu organized the MCC Prostate Cancer Action group meetings for Fall 2022. The monthly meetings include presentations from the labs of Drs. Derek Allison, Luksana Chaiswing, Zhiguo Li, Xiaoqi Liu, Vivek Rangnekar, and Qiou Wei. Two lab members presented on each meeting.

2. Dr. Xiaoqi Liu presented a talk entitled "Plk1 in Cr(VI)-associated lung cancer progression" on the 11th Metal Toxicity and Carcinogenesis Conference, October 16-19, 2022 in Montreal, Quebec, Canada.

3. Drs. Xiaoqi Liu, Jinghui Liu, Yanquan Zhang, Will Fong, and Zhiguo Li attended the annual meeting of Society of Basic Urologic Research, Nov 10-13.

4. Dr. Xiaoqi Liu was invited to give an oral presentation entitled "The kinase PLK1 promotes the development of Kras/Tp53-mutant lung adenocarcinoma through transcriptional activation of the receptor RET" on the CBIS 13th Biennial meeting in Las Vegas, Nevada from December 19 to 22.

Dr. Changhai Tian:

1. American Heart Association (AHA) Regenerative Cell Biology - 2023 Fellowship Basic Science 5 Committee, November 15, 2022.

2. Serve as a judge for 2022 annual SfRBM's Young Investigator Award Committee, November 16-19, 2022, Orlando, Florida, USA.

3. Poster presentation, the Society for Redox Biology and Medicine's 29th Annual Conference, November 18, 2022, Orlando, Florida, USA.

Faculty Activity cont.:

Dr. Luksana Chaiswing:

1. 68th Annual Meeting, Radiation Research Society (RRS), Waikoloa HI, Oct 18th 2022, Title "Targeting mitochondrial redox capacity coupled with mitochondrial protein translation to improve radiation efficacy"
2. Society for Redox Biology and Medicine (SfRBM) 29th Annual Conference, NOV 19th 2022, Orlando FL, Title "Mitochondrial ROS Heterogeneity: Adaptive Vulnerability That Can be Targeted to Sensitize Resistant Prostate Cancer to Radiation"

Drs. Fan, Lane and Higashi:

Study Sections:

T. Fan: U01-Integrating Biospecimen Science Approaches into Clinical Assay Development. November 10, 2022

Presentations:

T. Fan:

1. "NMR for elucidating metabolic networks in stable isotope-resolved metabolomic studies" 7th Gateway Symposium October 20-21, 2022
2. Innate immune activation by checkpoint inhibition in human patient-derived lung cancer tissues Roswell Park Institute CCC October 26 2022
3. Innate immune activation by checkpoint inhibition in cultured human lung cancer tissues Metabolomics Society EMN Webinar December 1, 2022

R.M. Higashi:

1. Direct nanoelectrospray ultra-high resolution mass spectrometry in stable-isotope labeled metabolomics SciX 2022, Covington 10/7/22

A.N. Lane:

1. NMR-based Isotope Editing, Chemoselection and Isotopomer Distribution Analysis in Stable Isotope Resolved Metabolomics SciX 2022, Covington 10/7/22
2. NMR-based Stable Isotope Resolved Metabolomics from Cells to Organisms OMSMS, Columbus OH 10/13/22
3. NMR-based Isotope Editing, Chemoselection and Isotopomer Distribution Analysis in Stable Isotope Resolved Metabolomics, 7th Gateway Symposium October 20-21, 2022
4. NMR-based Stable Isotope Resolved Metabolomics from Cells to Organisms, 7th Gateway Symposium October 20-21, 2022

Conferences Organized.

7th Gateway Symposium: NMR in Metabolism: New methods & applications. October 20-21, 2022. Organizers: **A.N. Lane & T. W-M. Fan**

Dr. Eva Goellner:

1. Served on NIH Cancer Etiology Study Section. October 2022.

Dr. Jin-Ming Yang:

1. Served on NIH Study Section F09C. November 2022.

Faculty Activity cont.:

Dr. Christine Brainson:

1. Served on NIH TIO (Translational Immuno-Oncology) Study Section, three times.
2. DoD LCRP Panel.

Dr. Jian Fu:

1. Served on NIH III (Innate Immunity and Inflammation) Study Section, three times.

Dr. Nathan Vanderford:

1. Chaired NIH Risk, Prevention and Health Behavior Fellowship Special Emphasis Study Section. October 2022.
2. Elected Chair-Elect of the University of Kentucky College of Medicine Faculty Council.
3. Presented at the Cancer Biology Training Consortium Annual Retreat. The Appalachian Career Training in Oncology (ACTION) Program: A YES Program at the University of Kentucky Markey Cancer Center. Cancer Biology Training Consortium 2022 Cancer Biology Annual Retreat. Hyatt Regency Hill Country Resort and Spa. San Antonio, TX.
4. Presented at the University of California, Berkeley. Capturing the Interactions of Appalachian Kentucky Youth with Cancer through Photovoice. University of California, Berkeley, School of Education. Berkeley, CA.

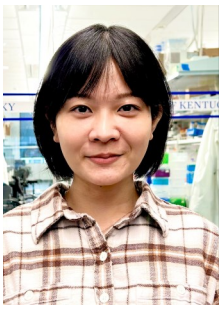
New Lab Members:



Dr. Qian Cheng: Dr. Qian Cheng is a new Postdoctoral Scholar in Dr. Tian's lab. He earned his Doctor of Medicine Degree at Medical College of Dalian University in 2012 and obtained his Anesthesiology Master's Degree at Fudan University in 2015. He then became a trainee of Standardized Resident Training in Fudan University Affiliated Huadong Hospital and thereafter has been an anesthesiologist for 5 years in Fudan University Shanghai Cancer Center (FUSCC). His research experience involved the mechanistic studies of chemokine receptor CXCR7 in lung cancer and the protective effects of Ropivacaine and Dexmedetomidine on oxidative stress-induced brain injury. His clinical research was mainly focused on Maneuver Techniques of Nonventilated Lung Collapse in Thoracic Surgery. Currently, his research directions will focus on the heart-brain communications during acute and chronic heart failure. His hobbies include music and outdoor sports, among them soccer is his favorite.



Dr. Lei Wang is a new Postdoctoral Scholar in Dr. Xiaoqi Liu's lab. He earned his Master's degree at Chinese Academy of Science in 2013 and obtained his PhD of Biochemistry and Molecular Biology at University of Bern in 2018. He continued postdoc research at University of Bern and University of Cincinnati. His research was mainly focused on lipid transportation across membrane and autophagy. Currently, his research directions will focus on the DNA damage repair in the development of cancer. His hobbies include outdoor sports, such as hiking and swimming.



Dr. Jia Peng is a new Postdoctoral Scholar in Dr. Xiaoqi Liu's lab. She got her Master of Medicine degree at Anhui Medical University in 2017 and then obtained her PhD in Surgery degree at The Chinese University of Hong Kong in 2022. Her research area included molecular targeted therapies and oncogenes in NSCLC. At present, her research work will focus on Plk1 in cancer treatment. She's a cat lover and also likes other furry animals. Swimming and jogging can always keep her relaxed and energetic.

New Lab Members:



Dr. Meng Wu joined the lab of Dr. Xiaoqi Liu as a Scientist II recently. Dr. Wu received his PhD from East China Normal University in 2012. After postdoc training at University of Georgia, Dr. Wu joined the faculty of Soochow University and was promoted to Associate Professor in 2019. Dr. Wu has extensive research experience in prostate cancer research. In particular, Dr. Wu is an expert in prostate reconstitution in nude mice.

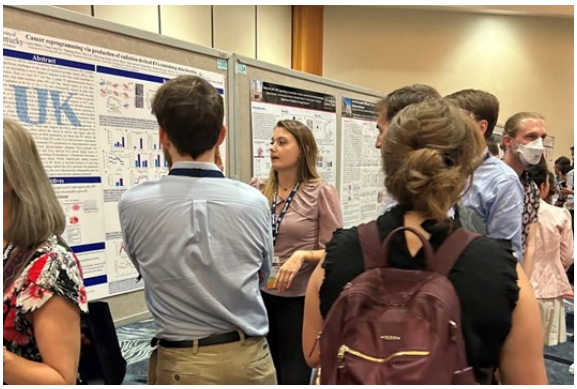


Dr. Josi Tessmann is a new Postdoctoral Scholar in Dr. Kate Zaytseva's laboratory. She received her Master's degree in Science at Federal University of Pelotas in 2017 and her PhD in Oncology at Brazilian National Cancer Institute (INCA) in 2022. Dr. Tessmann's interests are to better understand the mechanisms of metastasis in colorectal cancer and develop new therapeutic approaches for this disease. In Dr. Zaytseva's laboratory, she will also be working on understanding the impact of environmental pollutants such as PFAS and PFOS on colorectal cancer initiation and progression.

Lab Activity: Dr. Luksana Chaiswing's Lab

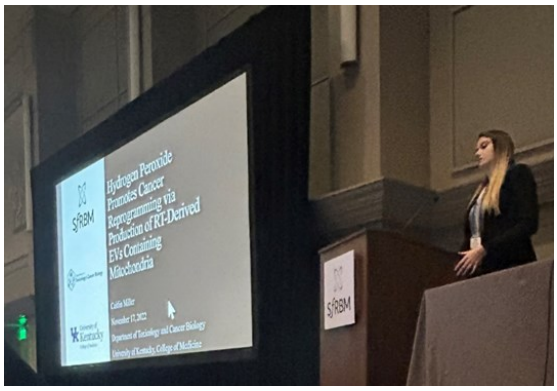


DTCB members at Society for Redox Biology and Medicine (SfRBM) 29th Annual Conference, Orlando FL, Nov 16 to Nov 22, 2022

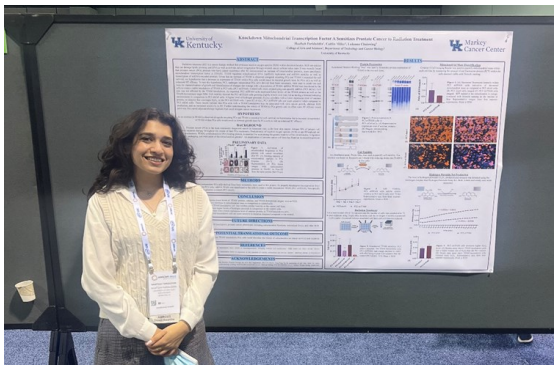


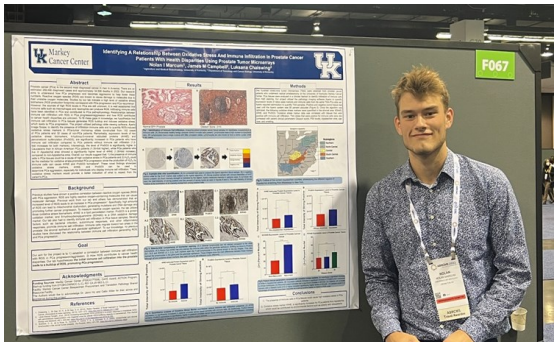
Caitlin Miller received travel awards from Dr. Matt Devalajara and Markey Cancer Center to present her work at 68th Radiation Research Society (RRS) Annual Meeting, Waikoloa HI, Oct 16th 2022.

(Right): Caitlin Miller's abstract was selected for oral presentation at SfRBM 29th Annual Conference, Orlando FL, Nov 17, 2022



(Right): Haafsah Fariduddin (Markey Cancer Strong Scholar) and Nolan Marcum (ACTION scholar), undergrad students, present their posters at 2022 ABRCMS, Nov 9-12, Anaheim, CA. They both received travel awards from ABRCMS and Markey Cancer Center.





The Student Forum continues to coordinate activities for all students to participate in!
Keep an eye on your email for future activities and meetings.

Recent Activities: Pumpkin Patch, attended the Diwali Event put on in conjunction with the DEI Committee, Trivia at Pivot Brewery and there are several dates in December they will volunteer with the Hope Center to serve meals to underserved populations in Lexington.



December 3: First date of serving with the Hope Center.



Some of our students dressed up as fluorescent conjugated antibodies for Halloween!

Recent PhD Graduation:

Dr. Jenni Ho (Daret St. Clair)
Dr. Ho is now a Clinical Research Coord. III at Cincinnati Children's Hospital for their Phase I Leukemia studies.



Congratulations!

Hannah Daniels (Eva Goellner) was selected as the UK COM Applicant for the NIH F99/K00 Predoctoral to Postdoctoral Fellow Transition Award! Way to go, Hannah!



Kristin Miller (Eva Goellner) won the 2022 WIMS Rising Star award. This award is given to outstanding students or postgrad trainees. Awesome accomplishment, Kristin!



Recent PhD Graduation:

Dr. Xiaojing Cui (Ying Liang)
Dr. Cui is now a Postdoctoral Scholar in Dr. Liang's lab.



Our MS in Forensic Toxicology and Analytical Genetics second year students start their required internships next semester - check out where they are all going!

Holly Bendel:
TN Bureau of Investigation
UKY Genomics Lab

Ravyn Borrum:
Lexar Labs - Lexington
Integrated Dx

Robyn Borrum:
Integrated Dx
UKY Vet. Diagnostic Lab

Tiffany Burton:
KY State Police Forensic Lab
KY Newborn Screening Lab

Trudy Colaco:
UKY Vet. Diagnostic Lab
UKY Pathology & Lab Medicine - Toxicology Section

Brittany Ferguson:
KY Division of Water
UKY Superfund Research Center - Project 2

Kendyll Freeman:
Wisconsin DOJ Forensic Lab
UKY Gluck Equine Research Center - Dr. Graves (Genetics)

Amanda Haw:
UKY Vet. Diagnostic Lab
KY Division of Labs - Microbiology

Corinne Hill:
KY Newborn Screening Lab
KY Division of Labs - Microbiology

Mohammad Jaloudi:
Dr. Xiaoqi Liu's Lab
Drs. Fan, Lane and Higashi's Lab

Kathleen Reed:
UKY Gluck Research Center - Dr. Stanley (Tox)
UKY Pathology & Lab Medicine - Toxicology Section

Trinity Rudd:
LabTox - Lexington
Univ. of Rochester Medical Center Clinical Lab - Dr. Victoria Zhang

Samantha Stanley:
KY Division of Labs - Environmental Chemical
LGC - Lexington

Cassandra Whitlatch:
UKY Gluck Equine Research Center - Dr. Graves (Genetics)
KY State Police Forensic Lab

Anumitha Senthil Rajan:
Dr. Tadahide Izumi's Lab
Will do second internship Summer 2023

Good luck to each of you! We can't wait to hear about your experiences at the poster presentation at the end of the next semester (May 2023)!

Thank you Students, Faculty and Staff for all of your hard work and dedication this semester! We hope everyone enjoys their Winter Break! See you in January!