DEPT. OF TOXICOLOGY AND CANCER BIOLOGY NEWSLETTER

VOLUME 2, ISSUE 1

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NEWSLETTER ITEMS

Want to include something in the next newsletter? Send your stuff to Morgan Rothermel at Morgan.Rothermel@uky.edu

THANK YOU!

Mrs. Leslie Lenz donated $500 to the department.

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

Christine Brainson:
American Institute for Cancer Research, "How Dietary Methionine Influences Lung Cancer Initiation and Chemosensitivity". Total funding: $165,000

Hsin-Sheng Yang:
Army Medical Research and Material Command, "A Novel Peptide Suppresses Invasion and Metastasis in Rictor-amplified Lung Cancer". Total funding: $153,000
"*This is a DoD Lung Cancer Concept Award with a total direct cost of $100,000 for one year. Recently, my lab discovered the RBD peptide derived from the tumor suppressor Pdcd4 specifically inhibits mTORC2 but not mTORC1 activity. Thus, this award is to test whether mTORC2-specific inhibition is an appropriate approach for the suppression of lung cancer with Rictor elevation*." - Dr. Hsin-Sheng Yang

Teresa Fan:
Subcontract PI, NCI R01 (PI: R. Wang, OSU), "Modulation of Asparagine Bioavailability and Stress Response Signaling to Enhance T Cell Robustness and Maximize Immunotherapy".

Luksana Chaiswing:
National Cancer Institute, "Targeting Mitochondrial Redox Capacity to Overcome Cancer Subtype that Regrowth After Radiation". Total funding: $1,749,940 over 5 years.

Recent Publications:

Xiaoqi Liu:
1. Liu, J., He, D., Cheng, L., Huang, C., Zhang, Y., Rao, X., Kong, Y., Li, C., Zhang, Z., Liu, J., Jones, K., Napier, D., Lee, E.Y., Wang, C., and Liu, X. (2020) p300 inhibition enhances the efficacy of programmed death-ligand 1 blockade treatment in prostate cancer. Oncogene, 39, 3939-3951.
2. Liu, E., Zhang, Z., Cheng, X., Liu X., and Cheng, L. (2020) SCNrank: spectral clustering for network-based ranking to reveal potential drug targets and its application in pancreatic ductal adenocarcinoma. BMC Medical Genomics, 13(Suppl 5):50.
3. Kong, Y., Zhang, Y., Mao, F., Zhang, Z., Li, Z., Wang, R., Liu, J., and Liu, X. (2020) Inhibition of EZH2 enhances the antitumor efficacy of metformin in prostate cancer. Mol. Cancer Ther., 19, 2490-2501.
4. Wang, R., and Liu, X. (2020) Epigenetic regulation of prostate cancer. Genes & Diseases, 7, 606-613.

Nathan Vanderford:
1. Hudson L, Sharp K, Alameh S, Prichard C, Ickes MJ and Vanderford NL. Cancer Curriculum for Appalachian Kentucky Middle and High Schools. Journal of Appalachian Health. 3(1): 43-55, 2021.

Teresa Fan, Andrew Lane, Richard Higashi:
1. D. R. Crooks*, N. Maio*, M. Lang, C. J. Ricketts, A. Ferguson, S. Turan, Y-Y Kim, G. M. Cawthon, C. D. Vocke, F. Sohelian, N. De Van Alda, P. Jailwala, M. Tandon, B. Tran, T. W.-M. Fan, A. N. Lane, Y. Yang, T. A. Rouault, W. M. Linehan (2021).The oncometabolite fumarate promotes mutations and loss of mitochondrial DNA in fumarate hydratase-deficient tumors. *Science Signaling* 14, eabc4436
2. Sun, Q., Fan, T. W-M.*, Lane, A.N. & Higashi, R.M.* (2021) Ion Chromatography-Ultra High-resolution MS^1/MS^2 Method for Stable Isotope-Resolved Metabolomics (SIRM) Reconstruction of Metabolic Networks. *Anal. Chem.* 93:2749-2757
3. M. J Merino, C. J. Ricketts, C. D. Vocke, Y. Yang, D. R. Crooks, T. W.-M. Fan, A. N. Lane, J. K. Killian, P. Meltzer, W. M. Linehan (2021). Multifocal renal cell carcinomas with somatic IDH2 mutation: report of a previously undescribed neoplasm. *Am. J. Surg. Path* 45:137–142
4. Y-H Chang, J. D. Hoffman, L. M. Yanckello, P. Lin, G. Nehra, G. Chlipala, S. D. McCulloch, M. Flythe, A. N. Lane, S. J. Green, A. M.S. Hartz, A-L Lin (2021) Apolipoprotein E genotype-dependent nutrigenetic effects to prebiotic inulin for reducing risk for Alzheimer's disease via gut-brain axis. *Nutritional Neurosciences* https://doi.org/10.1080/1028415X.2021.1889452
5. Daneshmandi, S., Cassel, T.A., Lin, P., Higashi, R.M., Wulf, G.B., Boussiotis, V., Fan, T. WM*, Seth, P.* (2021) Targeting 6-Phosphogluconate Dehydrogenase generates T effector cells with enhanced effector phenotype and anti-tumor function. *Cell reports* 34:108831

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Faculty Activity:

Xiaoqi Liu:
- Virtual seminar, "Polo-like kinase 1, from cell biology to cancer therapeutics" for Tianjin University, China
- Special Emphasis Panel, NCI Program Project Review III. February 17-18.

Nathan Vanderford:
- Special Emphasis Panel, Fellowships: Risks, Prevention and Health Behavior. March 4-5.
- Special Emphasis Panel, NIAID Research Education Program. April.

Jian Fu:
- Innate, Immunity and Inflammation Study Section. March 3-5.

Faculty Activity:

Andrew Lane:
- AHA Basic Study Section. March
- Workshop on Single Cell Metabolomics, February 26., Co-organizer

Teresa Fan:
- NCI U01 Study Section. March

Ying Liang:
- Special Emphasis Panel, NIH, NIDDK Hematology Central Coordinating Center
- Special Emphasis Panel, NIH, NHLBI

Dr. Vanderford was selected for the Appalachian Studies Association's annual Helen M. Lewis Community Service Award. Congratulations!

Undergrad, **Lauren Hudson**, who works with Dr. Vanderford, won first place in the Science Edu. category at the KY Academy of Science Annual Meeting. Awesome work!

Click here for the full story.

Undergrad, **Courtney Martin**, who works with Dr. Vanderford, won second place in UK's 5-minute fast track competition. Way to go!

Click here for the full story.

Undergrad, **Tyra Gilbert**, who works with Drs. Vanderford and Brainson, won first place in the Oswald Competition. Amazing job!

Click here for the full story.

DTCB Internal Fellowship Awardees:

Congratulations to our students who received DTCB Internal Fellowships!

PhD Thesis:

Fan Chen, Dr. Brainson's Lab.

"My awarded research focuses on the epigenetics in lung cancer and its relevant targeted therapies. My major project is studying the role of EZH2 inhibition in lung adenocarcinoma. I found that haplo- and full-insufficiency of EZH2 led to distinct phenotypes in the Kras/p53 mouse model. The tumors with low-Polycomb activity were more sensitive to demethylase inhibitor and BET inhibitor. I am also studying the cell-of-origins of EGFR mutant lung cancers and their differential sensitivities to tyrosine kinase inhibitors, and the combinatorial therapies of PI3K inhibitor and EZH2 inhibitor in PIK3CA mutant lung cancer."

Excellent Research:

Xiaojing Cui, Dr. Liang's Lab.

"I am a third-year graduate student. I have been working with Dr. Liang for two and a half years. After I joined her Lab, my research focuses on understanding the differences between male and female hematopoietic stem cells under normal and stress conditions. In this research, I am exploring how the special genes, such as latexin and Kdm5c, induce the gender difference. Our research is a new sight in hematopoietic stem cells. The project is very interesting, promising, but also challenging. I will continue to work hard and smart to figure it out in the near future."

Na Ding, Dr. Wei's Lab.

"Peroxiredoxin 4 (Prx4) is a member of the Prx family and is frequently upregulated in various cancers including prostate cancer. My study is mainly focus on identifying the secretory mechanism of Prx4 and the functional significance of both intracellular and extracellular Prx4 in prostate cancer."

Chaohao Li, Dr. Xiaoqi Liu's Lab.

"The emergence of resistance to androgen deprivation therapy is a major hindrance at the late stage of prostate cancer. I found that targeting EphB4, which was a receptor tyrosine kinase, and other vulnerabilities was very effective to solve this issue, thus enhancing the efficacy of drugs such as enzalutamide. Our collaborative work led to three co-authored publications and my first-author paper in JBC (PMID: 32184358). "

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Research:

Yanning Hao, Dr. Wei's Lab.
"Serotonin signaling plays a critical role in various physiological and pathological processes. The goal of this study is to investigate the role of serotonin signaling in human small cell lung cancer development and to test the hypothesis that disrupting the serotonin-TPH1-HTR axis inhibits cancer growth in vitro and in vivo."

Caitlin Miller, Dr. Chaiswing's Lab.
"The research goal in our lab is to identify the underlying mechanism that causes therapy induced resistance in cancer cells. Recently, we have identified that mitochondria are released during radiation. The main goal of my project is to determine if these mitochondria contribute to cancer survival after radiation. In addition, I have characterized the phenotypes of radiation resistant prostate cancer cells and found an increase in mitochondrial number, respiration, and ROS production. These findings were presented at the SfRBM annual meeting. I am grateful to have been given this award as it will assist me in furthering this exciting research."

Alston Zhang, Dr. Xiaoqi Liu's Lab.
"Enough evidence suggests that Cr(VI)-associated lung epithelial cell transformation often accompanies with alterations on cell cycle and cellular energy metabolism. Polo-like kinase 1 (PLK1), a key cell cycle regulator, might also regulate several metabolic pathways. In my study, I found that PLK1 is closely involved in pyruvate dehydrogenase E1 subunit alpha 1 (PDHA1)-related mitochondrial homeostasis during cell transformation and lung cancer progression. Articles related to this project are in preparation and will be published soon.".

Post-Doc:

Dr. Cuiping Zhang, Dr. Liang's Lab.
Dr. Cuiping Zhang is currently a Postdoctoral Scholar in Dr. Ying Liang lab. She has been handling several projects with different focuses on normal, stress and malignant hematopoiesis. Her first project is about the role of latexin protein in normal and stress hematopoiesis. She has published 5 papers and 3 of them are with the first authorship. She is also developing several new projects including leukemia niche, aging and sex/gender difference in leukemia, and the long-term effect of COVID-19 on hematopoietic stem and progenitor cells. All these accomplishments she has received strongly approve her hard working and super high research productivity.

Dr. Jinghui Liu, Dr. Xiaoqi Liu's Lab.
"With an epigenetics targeting screen, we identified histone acetyltransferase p300/CBP as a novel regulator of PD-L1 expression in cancer cells. We showed that p300/CBP was recruited to the promoter of CD274 (encoding PD-L1) by transcription factor IRF-1, resulting in acetylation of histone H3 at the CD274 promoter and subsequent CD274 transcription. Further, the p300/CBP inhibitor blocked the transcription of CD274 and repressed exosomal PD-L1 secretion, thus increasing the efficacy of PD-L1 blockade treatment in prostate cancer. This work, recently published in Oncogene (Liu et al., 2020, 39, 3939–3951), was reported in the weekly newsletter of ACIR (Accelerating Cancer Immunotherapy Research) and Nature Reviews Urology (2020, 17, 256) as highlight findings in Cancer Immunotherapy."

Our second year Master's of Forensic Toxicology and Analytical Genetics students are onto their final internships to complete their degree!

Cara Allen - UKY's Dept. of Pathology, Genomics Division
Taylor Childers - Americanna Laboratories
Moumita Dam - Dr. Christine Brainson's Lab
Jonathan Gallup - Spartanburg County Sheriff Forensic Lab
Isabel Snyder - KY's Dept. of Public Health Newborn Screening Lab

Student Spotlight: **Tanner DuCote**

Tanner is a native of Lafayette, Louisiana and earned a Bachelor of Science degree in Biology with a concentration in Microbiology. He entered the department after completing his first year in the Integrated Biomedical Sciences (IBS) program. Tanner chose this program after noticing the collaborative and supportive environment during his visit to campus. Additionally, he was impressed by the breadth and caliber of research being conducted at the university, as well as the outstanding reputation of the Markey Cancer Center. Tanner is a fourth-year doctoral candidate and a member of the Brainson Lab. He studies the epigenetic modifying enzyme EZH2 in the context of the squamous lung cancer tumor microenvironment. Moreover, he is determining how this enzyme can be targeted in treating the disease in combination with immune checkpoint inhibitors such as anti-PD1 therapy. Upon graduating, Tanner intends on pursuing a career in the biopharmaceutical industry working within medical affairs of cancer therapy.

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Alumni Spotlight: Dr. Beth Oesterling Owens

Dr. Beth Oesterling Owens sharpened her interest in characterizing the health effects of exposure to environmental contaminants while attending the University of Kentucky's Graduate Center for Toxicology (GCT) from 2003-2008. She is currently the Principal Associate National Program Director for the Health and Environmental Risk Assessment (HERA) National Research Program and Assistant Center Director for HERA for the Center for Public Health and Environmental Assessment (CPHEA) in the Office of Research and Development at the U.S. Environmental Protection Agency (EPA) in Cincinnati, Ohio. Beth came to UK's GCT with a budding interest in environmental health toxicology after participating in research on the effects of exposure to tire particles to respiratory cells during her undergraduate time at Bucknell University.

After rotating through GCT labs, Beth met Dr. Bernhard Hennig and his lab team that worked on understanding and minimizing the negative health and environmental impacts of chlorinated organic compounds found at Superfund sites across the U.S. The work going on in the Hennig lab reinforced Beth's interest in environmental health toxicology. While doing her graduate work, she was able to travel to conferences across the U.S. and Europe and expand on her understanding of environmental health science and policy in the U.S. With an EPA Headquarters in Cincinnati, UK's GCT was able to benefit from local collaborations and opportunities to better understand chemical risk assessment and toxicology in the federal government. It was these connections that led Beth to pursuing a post-doc at the EPA in Research Triangle Park, North Carolina and transitioning to a career in chemical risk assessment.

During Beth's post-doc at the National Center for Environmental Assessment at the EPA in NC, she evaluated the potential hazards associated with exposure to air pollutants to support the periodic review of the National Ambient Air Quality Standards (NAAQS) mandated under the Clean Air Act (CAA). Beth joined a group of scientists responsible for developing the Integrated Science Assessments (ISA) that comprehensively review, synthesize, and evaluate the most policy-relevant science related to the public health and welfare effects of the six criteria air pollutants, including ozone, particulate matter, and lead. During her time as a post-doc, Beth was fortunate to be chosen for a permanent federal position with the EPA, continuing the work to evaluate the health effects of exposure to ambient air pollutants.

Beth's husband, Phillip Owens, also graduated from UK's GCT and, at the same time, was completing a postdoc at University of North Carolina. After his post-doc, they moved up to Cincinnati, OH, where Phil started a lab at the University of Cincinnati that examines the effects of coagulation proteins, proteases, and receptors in the pathogenesis of cardiovascular disease. Beth continued working with EPA and began the exciting transition to identifying and characterizing the health hazards of, and providing an important source of toxicity information and toxicity values for, chemicals of concern to the Superfund Program, through development of Provisional Peer-Reviewed Toxicity Values (PPRTVs). These assessments help the boots-on-the-ground scientists and managers in the communities determine to what extent a chemical should be removed to avoid effects to human health. In addition to developing these important toxicity assessments, Beth served as the Director of the Superfund Health Risk Technical Support Center, which provides scientific technical support in the area of human health risk assessment to risk assessors within EPA's Superfund Program. Beth was promoted to the Branch Chief in Cincinnati and loved leading a powerhouse team of chemical assessors and gaining a better appreciation for supervisors and managers. Shortly after, the Office of Research and Development in EPA reorganized and Beth started her current roles as a leader in scientific planning to support and improve EPA's risk assessment decisions. Beth now plays a major role in formulating and implementing the research to fill gaps in scientific knowledge and understanding in chemical risk assessment, as well as communicating the important research being conducted within EPA's HERA research program. Throughout her time at EPA, Beth has continued to find her job at the nexus of application of science to environmental policy exciting and learns more about the field every day.

Beth currently lives in Cincinnati and keeps busy outside of work with her three kids. They love exploring outside, gardening, and finding new places to play.