DEPT. OF TOXICOLOGY AND CANCER BIOLOGY NEWSLETTER

Volume 2, Issue 4

Table of Contents

Pg 1:
- New Grants

Pg 2:
- New Grants (cont.)
- Recent Publications
- Faculty Activity

Pg 3:
- Faculty Activity (cont.)

Pg 4:
- Faculty Activity (cont.)
- Faculty Awards and Recognitions
- CESB/RM SRF. RPPA
- Faculty Grant Talks
- Staff and Student Seminars

Pg 5:
- Student Activity

Pg 6:
- Student Activity (cont.)
- DTCB 2021 Holiday Party
- Staff Announcements

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.

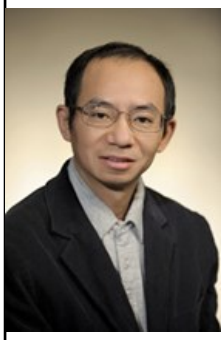
Thank you for your support!

THANK YOU!

Dr. and Mrs. Michael Graziano gave a donation of $2,000 to the department. Many thanks for their thoughtful gift and support!



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



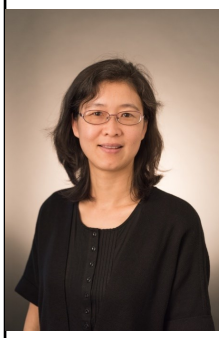
Jian Fu (PI in grant below):

NIH R01 AI167297 , "HDAC6 Regulation of Myeloid Cell Responses in Sepsis" Total funding: $1,912,500 for 5 years. Sepsis is a life-threatening disease caused by dysregulated host responses to infection. Sepsis remains a major health problem worldwide with high mortality. Myeloid cell responses such as endotoxin tolerance, epigenetic modification, metabolic failure, and apoptosis are profoundly affected in sepsis, which leads to systemic dysfunction of immune cells and progenitor cells. The regulation of myeloid cell responses in sepsis remains largely unknown. The histone deacetylase HDAC6 regulates a variety of cellular responses. However, HDAC6 regulation of myeloid cell responses in sepsis has not been investigated. Our preliminary studies indicate that HDAC6 is a key mediator of cell signaling in myeloid cells. Myeloid-specific HDAC6 deletion reduces the mortality in septic mice. Furthermore, selective HDAC6 inhibition can modulate myeloid cell responses in the mouse models of sepsis. In the proposed studies, we will test the hypothesis that HDAC6 activation mediates myeloid cell dysfunction in sepsis, and HDAC6 inhibition could improve myeloid cell function and survival rate in sepsis.



Teresa Fan (PI in grant below):

Research Institute at Nationwide Children's Hospital, "Modulation of Asparagine Bioavailability and Stress Response Signaling to Enhance T Cell Robustness and Maximize Immunotherapy" Total funding: $60,435. The *objective* of this proposal is to enhance T_{eff} cell metabolic fitness to maximize anti-tumor response in the metabolically restricted tumor microenvironment. Subcontract with Dr. Ruoning Wang at Nationwide Children's Hospital.



Ying Liang (PI in grant below):

NIH R01 DK130478-01, "COVID 19: Mechanism of the Short- and Long-Term Effects of COVID-19-Induced Alarmins on Hematopoietic Stem and Progenitor Cells" Total funding: $1,178,750 for 3 years. This grant is to investigate the long-term consequence of COVID-19 infection in hematopoietic stem/progenitor cell and immune function. Co-investigator is Dr. Gang Huang at UT Health San Antonio.



Eva Goellner (PI in grant below):

Phi Beta Psi Sorority, "Novel DNA Mismatch Repair Interacting Proteins in Colon and Endometrial Cancers" Total funding: $30,296. New competitive renewal for "Phi Beta Psi Sorority Research Grant" for 1 year.

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



Changhai Tian (PI in grant below):

NIH R01 HL153176 , "Nrf2 Regulation of Oxidative Stress in Heart Failure and Extra Vesicular Communication" Total funding: $229,830. This project is focused on the extracellular vesicle-mediated intra- and inter-organ communication during the heart failure and explores the underlying mechanism by which extracellular vesicles contribute to the progression of cardiac-cerebral symptoms in heart failure. Co-investigator is Dr. Irving H. Zucker, University of Nebraska Medical Center.

Recently Accepted or Published Manuscripts:

Xiaoqi Liu:

1. Farah E, Zhang Z, Utturkar SM, Ratliff TL, **Liu X**. Targeting DNMTs to overcome enzalutamide resistance in prostate cancer. Mol Cancer Ther. 2021 Nov 2:molcanther.0581.2021. doi: 10.1158/1535-7163.MCT-21-0581. Online ahead of print. PMID: 34728570.

Rick Higashi and Teresa Fan:

1. Farah Daneshmandi S, Cassel TA, **Higashi RM**, **Fan TW-M**, Seth P. (2021) 6-Phosphogluconate dehydrogenase (6PGD) a key checkpoint in reprogramming of regulatory T-cells metabolism and function. eLife 10:e67476

Dr. Jin-Ming Yang Publication in Science Advances

Ref: Ms. No. abl9783

Title: Elongation Factor-2 Kinase is a Critical Determinant of the Fate and Antitumor Immunity of $CD8^+$ T Cells

Summary: Eukaryotic elongation factor-2 kinase (eEF-2K) is a key regulator of protein synthesis and has important roles in modulating stress responses and cellular metabolism. In this study, we uncovered a previously unappreciated but critical role of eEF -2K in regulating the fate and cytocidal activity of $CD8^+$ T cells. The following is a summary of our main findings:

*eEF-2K supports the survival and promotes cytocidal activity of $CD8^+$ T cells.

*Loss of eEF-2K leads to hyper-activation of the Akt-mTOR-S6K signaling and metabolic reprograming in CD8+ T cells.

*Loss of eEF-2K results in premature senescence and exhaustion of $CD8^+$ T cells.

*eEF-2K is crucial for the antitumor efficacy of CAR-T therapy.

*$CD8^+$ T cells lacking eEF-2K show reduced ability to infiltrate tumor microenvironment.

These findings indicate that eEF-2K is critically required 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.

Faculty Activity:

Xiaoqi Liu:

1. NIH study section: NCI Clinical and Translational Exploratory/Development Studies. Oct 21-22, 2021 via Webex.
2. NIH study section: NCI, ZRG1 OTC1-T. Small: Business: The Cancer Drug Development and Therapeutics. Nov 18-19, 2021 via Webex.
3. Lab activity: Dr. Xiaoqi Liu and his lab (12 lab members) attended the Society of Basic Urologic Research (SBUR) annual meeting. Nov 4-7, 2021 via virtual format.

Faculty Activity (continued):

Jin-Ming Yang:

NIH study section: Molecular Oncogenesis (MONC). Oct 27-28, 2021.

Jian Fu:

NIH study section: Innate Immunity and Inflammation (III) Study Section. Oct 2021.

Rick Higashi:

NIH study section: Served on NIGMS K99/R00 Study Section. Dec 3, 2021.

Andrew Lane:

1. Workshop organizing: Biomedical Research Session organizers Elixir International Fluxomics Workshop (virtual). Oct 5-8, 2021.
2. Presentation: *Experimental Models and Methods for Stable Isotope Tracing*. Elixir Fluxomics Workshop. Oct 5-8, 2021.

Teresa Fan:

1. Workshop organizing: Biomedical Research Session organizers Elixir International Fluxomics Workshop (virtual). Oct 5-8, 2021.
2. Presentation: *Exploring human tumor metabolism in situ & in preclinical models using Stable Isotope –Resolved Metabolomics (SIRM).* Elixir Fluxomics Workshop. Oct 5-8, 2021.
3. Presentation: *Innate immune activation by checkpoint inhibition in human patient-derived lung cancer tissues*. Wake Forest Cancer Center, NC. Dec 3, 2021.

Nathan Vanderford:

1. Member/ Co-chair: NIH study section: Prevention and Health Behavior F16 Fellowship Special Emphasis Study Section (2022/01 ZRG1 F16-L (20) L). Oct 25-26, 2021.
2. Member: NIH study section: National Institute of Allergy and Infectious Diseases R25 Research Education Program Special Emphasis Study Section (2022/01 ZAI1 RCU-D (J1) 1). Dec 10, 2021.

Ying Liang:

NIH study section: Basic Biology of Blood, Heart, and Vasculature (BBHV). Ad hoc reviewer. Oct 7-8, 2021.

Hsin-Sheng Yang:

OTC-M(80) Cancer Therapeutics & Drug Development Special Panel. Nov 4-5, 2021.

Qiou Wei:

Accepted appointment to serve as committee member of the UKY Wednesday Medical IRB for a 3 year term. Nov 15, 2021– June 30, 2024.

Tadahide Izumi:

NIH study section: ZCA1 RPRB-H (J1) NCI Program Project III (P01). Oct 20-21, 2021.

Christine Brainson:

1. Served on DOD Cell and Experimental Therapeutics. Sept 28-29, 2021.
2. NIH study section: Cancer Diagnostics and Treatments (CDT) SBIR/STTR. Nov 8-9, 2021.

Faculty Activity (continued):

Luksana Chaiswing:

Serving as reviewer for the Mike Slive Foundation's 2021-2022 grant cycle.

Kate Zaytseva:

Lab activity: AACR Special Conference: Colorectal Cancer. Attendees: Dr. Zaytseva, Mariah Geisen, Courtney Kelson. Oct. 21-22, 2021 via virtual format.

Faculty Awards and Recognitions:



Nathan Vanderford:

Academy of Medical Educators awarded Dr. Vanderford with the Academy of Medical Educator Excellence in Medical Education Award in the areas of Leadership, Innovation and Evaluation. Oct 2021.

Xiaoqi Liu, Eva Goellner, and Joe Kim:

Office of Biomedical Education and Biomedical Graduate Student Organization "Exceptional Mentor" recognition. Dr. Liu, Dr. Goellner, and Dr. Kim were recognized in the same list. Oct 2021.

CESB/RM SRF. Reverse Phase Protein Arrays (RPPA)

Tired of doing hundreds of Western blots? RPPA enables analysis of thousands of samples simultaneously using a small amount of sample (10 μL), and up to 16 targets per slide.

CESB/RM SRF has SOPs.
The ArrayJet Marathon spotter can deliver 250x 10 nL of sample to each of 16 pads per slide. Each pad is developed with a different specific antibody. Typically multiple replicates are spotted on each slide to give good statistics.
CESB provides advice and SOPs, as well as performing the spotting and slide scanning. Slides are provided at cost. CESB has an inventory of more than 300 Elisa-grade Antibodies, which can be provided at cost (typically 1-2 μL). A development cassette and Mapix software dongle can also be borrowed.

Contacts: Teresa Cassel: tacassel@uky.edu [spotting and SOPs]
Teresa Fan: twmfan@gmail.com [general advice and experimental design]
Andrew Lane: Andrew.lane@uky.edu [keeper of the cassette and Mapix dongle]

DTCB Faculty Grant Talk Series, Fall 2021 Semester

Sept 3, 2021: Study section experience:
Qing-Bai She (DT), Ren Xu (TME), Kate Zaytseva (TCB)
Sept 17, 2021: Hsin-Sheng Yang
Oct 1, 2021: Tadahide Izumi
Oct 15, 2021: David Orren
Oct 29, 2021: Qiou Wei
Nov 12, 2021: Study section experience:
Ying Liang/ Hsin-Sheng Yang/ Xiaoqi Liu

DTCB Staff and Student Seminars, Fall 2021 Semester

Sept 10, 2021: Kendall Simpson (Dr. Goellner) and Jenni Ho (Dr. St. Clair)
Sept 24, 2021: Xiaojing Cui (Dr. Liang) and Pratik Thapa (Dr. Wei)
Oct 8, 2021: Qiongsi Zhang (Dr. Xiaoqi Liu) and Aziza Alshahrani (Dr. Wei)
Oct 22 2021: Dr. Hami Hemati Chahardeh (Dr. Xia Liu) and Dr. Mohammad Burhan Uddin (Dr. Lane)
Nov 5, 2021: Kristin Miller (Dr. Goellner) and Hannah Daniels (Dr. Goellner)
Nov 19, 2021: Katelyn Jones (Dr. Xiaoqi Liu) and Xinyi Wang (Dr. Xiaoqi Liu)







Student Activity:

The Student forum has had several events in the months of October and November:

Aug 27, 2021: First Year Meet and Greet
Sept 20, 2021: Trivia Night at Pivot Brewery (They came in 1st place!)
Oct 10, 2021: Hiking at Berea Pinnacles
Oct 28, 2021: Post-Graduate Discussion Panel "Job Search After Graduate School"
Oct 29, 2021: Halloween Night with Pumpkin painting and snacks
Nov 5, 2021: Volunteering at the Ronald McDonald House
Nov 19, 2021: Volunteering at the Ronald McDonald House

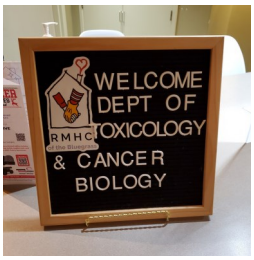
***The Student Forum had asked the faculty for donations so the students could buy and prepare meals at the Ronald McDonald House on 2 different occasions. Not only did the faculty raise enough to provide a generous meal for the 40 guests staying at the RMDH on both occasions, but we had enough funds to continue more charity in sponsoring a child for the holidays this year! UK's Office of Student Organizations and Activities as well as the Office for Student Success had sponsored their annual Circle of Love program where participants are given wish lists for children within Fayette County's public schools and asked to provide what they could from the lists. With the extra funds from the faculty we were able to sponsor 10 children with clothing and gifts this year!

*Link to the Circle of Love article for more info: http://uknow.uky.edu/professional-news/give-gifts-kids community-through-circle-love

















ACTION Students Document Cancer Crisis in Appalachia in New Photography Exhibit

Link to article: https://uknow.uky.edu/arts-culture/action-students-document-cancer-crisis-appalachia-new-photography-exhibit

Annual DTCB Holiday Party



The 2021 Department of Toxicology and Cancer Biology Holiday Party took place December 10, 2021 in the Harris Ballroom at the Bill Gatton Student Center in Lexington, KY. It was an festive evening filled with socializing, food, and drink, while following UK COVID Protocols. Thank you to students Katelyn Jones and Kendall Simpson for helping to organize it! We look forward to next year's!



Baby Watch 2021



David Kirk, Department Administrator for Toxicology & Cancer Biology, and his wife, Shena, welcomed their second child on October 10, 2021. A healthy baby boy – Shepherd Hayes Kirk. Shepherd joins a big sister, Harper. Congratulations Kirk family!

Morgan Rothermel, Education and Research Coordinator for Toxicology & Cancer Biology, and her husband, Eric, welcomed their second child on November 2, 2021. A healthy baby boy – Ayden Daniel Rothermel. Ayden joins a big brother, Gabe. Congratulations Rothermel family!



Thank you all for a great semester and have a nice Winter Break!

Forensic Students 1st Internships for 2022 Spring Semester

KY Energy & Environment Cabinet:
Sean Donaldson

UKY Pathology Lab—Genomics:
Alexis Enriquez-Jones

North Louisiana Crime Lab:
Olivia Fowler

Dr. Xiaoqi Liu's Lab (UKY):
Christian Gosser

SteelFusion Clinical Tox Lab:
Genell Jasper

Kentucky State Police:
Marshall Heath

Dr. Lorri Morford's Lab (UKY):
Thu Nguyen

St. Louis University Forensic Toxicology Lab:
Kennedy Plude

KY Newborn Screening Lab:
Kelly Rademacher
Jordan Brown

UKY Veterinary Diagnostic Lab—Toxicology:
Jordyn Rose

UKY Genetic Testing at Gluck Research Center:
Elena Shelepak

Dr. Eunsook Lee's Lab (FL A&M):
Kaleigh Wingate

Dr. Will Fong's Lab (UKY):
Dave-Preston Esoe

NEWSLETTER ITEMS

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

