

DEPT. OF TOXICOLOGY AND CANCER BIOLOGY NEWSLETTER

VOLUME 1, ISSUE 3

Recent Grants (June-August)

| Name | Title | Sponsor |
|------------|---|-----------------|
| Li, Zhiguo | Career Development Award: Center for Appalachian Research in Environmental Sciences | NIEHS (UKY P30) |
| Liu, Xia | Circulating Tumor Cell-Neutrophil Clusters in Breast Cancer Metastasis | NIGMS (UKY P20) |

Recent Publications (June-August)

| |
|--|
| Drury J , Rychahou RG, He D, Jafari N, Wang C, Lee EY, Weiss HL, Evers BM, Zaytseva YY . Inhibition of fatty acid synthase upregulates expression of CD36 to sustain proliferation of colorectal cancer cells, <i>Frontiers in Oncology</i> , July 31, 2020, https://doi.org/10.3389/fonc.2020.01185 |
| R. Panarsky, D.R. Crooks, A.N. Lane , Y. Yang, T.A. Cassel, T. Fan , W. M. Linehan, J. A. Moscow (2020) Fumarate hydratase-deficient renal cell carcinoma cells respond to asparagine by activation of the unfolded protein response and stimulation of the hexosamine biosynthetic pathway. <i>Cancer & Metabolism</i> . 8 , 7 |
| Wang, T., Gnanaprakasam, J., Hong, B., Sun, H., Liu, L., Miller, E., Song, X., Cassel, T.A., Sun, Q., Vicente-Munoz, S., Warmoes, M.O., Lane, A.N. , Song, X., Fan, T W-M.* , & Wang, R* (2020). Inosine is an alternative carbon supply that supports effector T cell proliferation and antitumor function under glucose restriction. <i>Nature Metabolism</i> 2 , 635-347 |
| H. Wu, T. Reizel, Y. J. Wang J. L. Lapiro, B. T. Kren, J. Schug, S. Rao, A, Morgan, A. Herman, L. L. Shekels, M. Rasette, A. N. Lane , T. A. Cassel, T. W. M. Fan , J. C. Manivel, S. Gunewardena, U. Apte, P. Sicinski, K. H. Kaestner, J. H. Albrecht* (2020). A negative reciprocal regulatory axis between cyclin D1 and HNF4α modulates cell cycle progression and metabolism in the liver. <i>PNAS</i> 117 , 17177-17186 |
| Fan, T. W-M.* , Higashi, R.M. , Chernavskaya, Y. & Lane, AN.* Resolving metabolic heterogeneity in experimental models of the tumor microenvironment from a Stable Isotope Resolved Metabolomics perspective <i>Metabolites</i> 10 , 249 |
| Y. Zhong, K. Mohan, J. Liu, A. Al-Attar, R. M. Flight, P. Lin, Q. Sun, M. O. Warmoes, R.R. Deshpande, H. Liu, K. Sik Jung, M. I. Mitov, N. Lin, D. A. Butterfield, S. Lu, J. Liu, H. N. B. Moseley, T. W. M. Fan , M. E. Kleinman, Q. J. Wang (2020) Loss of <i>CLN3</i> , the gene mutated in Juvenile Neuronal Ceroid Lipofuscinosis, leads to metabolic impairment and autophagy induction in retina pigment epithelium. <i>Biochim Biophys</i> |
| Lane, A.N. (2020) Bacterial Repression: the Lac and Trp systems. <i>Encyclopedia of Biophysics</i> , Springer. In press |

Study Sections

| |
|---|
| Dr. Jian Fu: Innate Immunity and Inflammation Study Section, Center for Scientific Review, for the term beginning July 01, 2020 and ending June 30, 2024. |
| Dr. Daret St Clair: Study section meeting is MOSS Q02 |
| Dr. Jin-Ming Yang: NIH, Fellowship: Oncological Sciences ZRG1 F09B-M (2) |
| Dr. R.M. Higashi: NIH Imaging Probes and Contrast Agents – IPCA. Special Study Section. June 11-12 ,2020 |
| Dr. Nathan Vanderford: NIH, Special Emphasis Panel/Scientific Review Group 2021/01 ZRG1 F16-L (20) L |

Recent Graduation



Dr. Alexandra Arenas.
Mentored by Dr. Haining Zhu.
Defended July 2020.

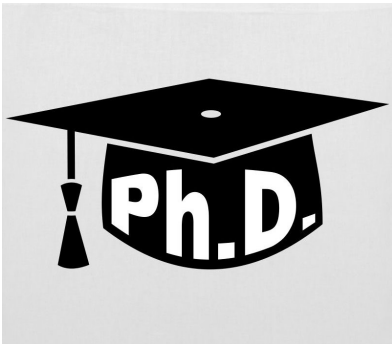


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NEWSLETTER ITEMS

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Congratulations Are in Order!



Dr. Nathan Vanderford (Faculty): It was announced by the Awards Committee of the Society of Research Administrators International, that Dr. Vanderford was selected as a **recipient of the Hartford-Nicholson Award for 2020**. This award was presented to him in recognition of his contributions to the knowledge of research administrators, as well as his dedication to the continuous study and development of the field. The award results from his strong advocacy for SRAI as Editor-in-Chief of the Journal and devoted encouragement to others in the profession.

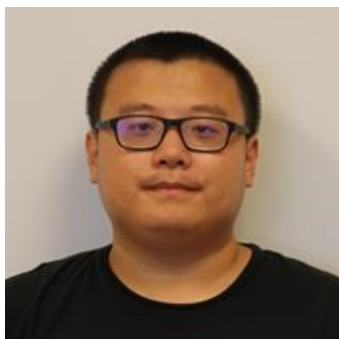
Congratulations, Dr. Vanderford!



Dr. Mojtaba Bakhtiari (Post-Doc): Dr. Bakhtiari has been selected to **become a post-doctoral fellow on the T32 Cancer Biology Training Grant**. Below is a brief explanation of his research and how he feels about getting the grant:

“In 2018 I joined to Dr. Brainson's lab. In her lab, our research focuses on using novel murine models of lung cancer to understand how to increase efficiency of common therapies including radiation and chemotherapy. In this research, I will be exploring the hypothesis that low methionine leads to stabilization of Polycomb Repressive Complex 2 and more well-differentiated lung cancer cells that are more targetable with chemotherapy and radiation. I am so happy that I have been selected as a post-doctoral fellow for this grant. I believe that our research will impact thousands of people in the future.”

Congratulations, Dr. Bakhtiari!



Chaohao Li (Ph.D. Student): Every year there's the opportunity for department graduate students to compete for Graduate Student Award, including categories of Yulan Sun's Memorial Early Publication Award and Outstanding Graduate Student Award. This award was established in the honor of Dr. Yulan Sun, a former outstanding graduate student in Dr. St. Clair's lab. All current graduate students in the department are eligible to apply.

In the current year, **Mr. Chaohao Li, a third-year graduate student in Dr. Xiaoqi Liu's lab, is the awardee of the Early Publication Award**. Chaohao's application was reviewed in detail by all members of the Awards Committee, and a unanimous agreement concluded that Chaohao qualifies and exemplifies in all aspects of this particular award. For more details of Chaohao's published research [click here](#).

Below is a brief background on Chaohao and his research:

“I was enrolled in UK in 2018 and have been working with Dr. Liu for three years. During the period of my Ph.D. program, I focused on how to deal with the issue of drug resistance in prostate cancer. Prostate cancer is driven by AR signaling, and enzalutamide is one of the important drug to inhibit AR. Enzalutamide was approved by FDA to treat late stage prostate cancer, which is effective to elongate patients' survival for about 6 months. However, cancer cells eventually develop resistance to this drug, and this is a big challenge to treat patients in clinic. Based on the large sequencing results in our lab, we've identified several candidates that can be targeted to overcome enzalutamide resistance, of which the EphB4 is a good one. We performed a series of experiments, both *in vitro* and *in vivo*, to demonstrate that inhibition of EphB4 was able to offset cancer cells' resistance to enzalutamide, which provides a new revenue to medicate prostate cancer patients that show less or no response to enzalutamide. Our results were published in the Journal of Biological Chemistry in March this year. I'm glad that my research achievement was admitted and helped me to win the Yulan Sun early publication award. I want to say thank you to Dr. Liu, my committee members and all the people that helped me. I am dedicated to my research and will continue to work hard!”

Congratulations, Chaohao!

Alumni Spotlight



Matt Devalaraja, DVM, Ph.D. is the Founder, Chief Scientific Officer and Head of R&D of Corvidia Therapeutics. Matt got his training in Veterinary Medicine in India and came to US for further education. He earned a Masters in Food Microbiology from Penn State University prior to joining the Ph.D. program at University of Kentucky in 1992. He worked with Dr. Daret St. Clair, initially on the sequencing of human MnSOD gene and subsequently on understanding of “transcriptional regulation of the gene by proinflammatory cytokines such as TNF- α ”. Due to his diverse interests, he worked on several side projects while in Ph.D. As part of that, he worked closely with Drs. McClain, Vore and Rangnekar. He graduated in 1997. Subsequently he did a brief, 18 months, postdoctoral fellowship at Vanderbilt University with Dr. Ann Richmond working on multiple projects, such as the “role of Interleukin-1 α in melanoma” and “orchestration of wound healing by neutrophils thru CXCR2”.

He got a lucky break from postdoc in 1999 to join the Department of Inflammation Research at Parke-Davis Pharmaceuticals in Ann Arbor, MI which was acquired by Pfizer one year later. At Parke-Davis/Pfizer, he discovered and patented unique synergistic interactions between colony stimulating factors and chemokines that recruit/activate monocytes/neutrophils; and proposed that most inflammatory and autoimmune diseases are exacerbated by these pathogenic mechanisms. He developed the first biologic program for Pfizer Immunology and the first biologic program for the site of Ann Arbor Pfizer, in anti-M-CSF antibody. With that growth came naturally and Matt became the Head of Biologics Discovery for the Ann Arbor, Pfizer in which capacity he initiated, oversaw and progressed numerous drug discovery and clinical development programs across Immunology, Infectious Diseases, Dermatology, Cardiovascular and Neuroscience therapeutic areas. In 2007, as Pfizer was closing the site of Ann Arbor, Matt decided to take up the job at Human Genome Sciences as Head of Immunology Research, Pharmacokinetics and Toxicology. At HGS he not only built the pipeline of discovery programs but also shepherded three Phase 3 programs and help successfully file BLAs for all of them. At HGS, he was instrumental in obtaining the FDA approval of first ever lupus drug in Benlysta and the first biodefense drug approval based on the “Animal Rule” in raxibacumab. As GSK acquired HGS in 2012, Matt took up a job at AstraZeneca in a newly created group, Emerging Innovations/New Opportunities group. In this group which was science centric and disease agnostic, Matt helped create a portfolio of 22 phase 2 programs for various AstraZeneca compounds in 3 years thru orthogonal thinking and nontraditional means of creating ideas. While at AZ, he created a new Intellectual Property for precise patient selection based on a SNP in TMPRSS6 gene that uniquely sensitizes IL-6 mediated cardiomyocyte death, only in the context of ischemia reperfusion. This scientific finding formed the basis for the spinout of Corvidia Therapeutics out of AstraZeneca. He spun the company out in 2016 with 3 other founders and raised over \$100M thru Series A, B and additional raises. He was the Chief Scientific Officer and Head of R&D for Corvidia Therapeutics. Recently, in June 2020, Corvidia was acquired by Novo Nordisk for a total of \$2.1B with \$725M upfront. Matt will continue to work for Novo Nordisk as the CSO of its US Development Inc. Matt is a member of American Heart Association, American Society of Nephrology and life member of International Cytokine Society. Matt serves on the boards of AUM Biosciences and P2D Biosciences.

Matt’s wife Radhika also graduated from Graduate Center for Toxicology with Ph.D. She worked at Pfizer in the Drug Safety group but sacrificed her career as she moved with Matt as he took on various roles. She currently works at a local toxicology CRO. They have two kids, Samir who is finishing up his MD, Ph.D. at University of Pennsylvania and Sindhura, who just finished her undergrad and looking to go to Law School.

Student Spotlight



Jonathan Gallup is a second year Masters of Forensic Toxicology and Analytical Genetics student. Below is a little about Jonathan and why he chose our program:

“My name is Jonathan Gallup and I’ve always had a passion for chemistry; however, my interest in toxicology wasn’t really present until my senior year of college at Clemson University. I took my first toxicology class as an elective that year and it opened a world of

possibilities for me, which led me to come to the University of Kentucky for my masters in forensic toxicology. I chose this program because it will allow me to further pursue knowledge in toxicology while also helping others by working to find the truth and the cold, hard, scientific facts of crime cases. With excellent professors like Mike Ward, Dr. Isabel Mellon, and Dr. Nathan Vanderford, I’ll be trained in not only the scientific theory of forensic science, but also as an expert witness. A large part of our program also covers the ethical dilemmas that come with the responsibility of presenting the unbiased truth. As forensic scientists, it is not our job to bring justice, but to uphold scientific integrity and share the knowledge we find with others so that they can carry out a verdict. After I graduate, I plan to work for a forensic lab for a few years then eventually pursue my Ph.D. in Forensic Toxicology.”

SEEKING ALUMNI

We love hearing from our alumni!

We are looking for alumni to spotlight in our upcoming newsletters. If you would like to be spotlighted, please contact Morgan Rothermel at Morgan.Rothermel@uky.edu

“It is my sincerest prayer that this contribution help UKY to continue to foster talented medical minds and hearts.”

- Chemi D., a donor to the Toxicology and Cancer Biology Dept.