DEPT. OF TOXICOLOGY AND CANCER BIOLOGY NEWSLETTER

Volume 6, Issue 1

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Recently Accepted or Published Manuscripts:

Dr. Luksana Chaiswing:

Ho J, Sukati S, Taylor T, Carter S, Fuller B, Marmo A, Sorge C, D'Orazio J, Butterfield DA, Bondada S, Weiss H, St Clair DK, **Chaiswing L**. Extracellular vesicles released by all patients contain HNE-adducted proteins: Implications of collateral damage. Free Radic Biol Med. 2024 Dec 4; 227:312-321. doi: 10.1016/j.freeradbiomed.2024. PMID: 39643137

Clair, D. S., Kasarskis, E., Clair, W. S., & Chaiswing, L. (2024). Superoxide Dismutase and Catalase. Reference Module in Biomedical Sciences. https://doi.org/10.1016/B978-0-323-95488-4.00063-2

Dr. Xia Liu:

Ngule C, Shi R, **Ren X**, Jia H, Oyelami F, Li D, Park Y, Kim J, Hemati H, Zhang Y, Xiong X, Shinkle A, Vanderford NL, Bachert S, Zhou B, Wang J, Song J, **Liu X**, **Yang JM**. NAC1 promotes stemness and regulates myeloid-derived cell status in triple-negative breast cancer. *Mol Cancer* 23, 188 (2024). https://doi.org/10.1186/s12943-024-02102-y

Dr. Xiaoqi Liu:

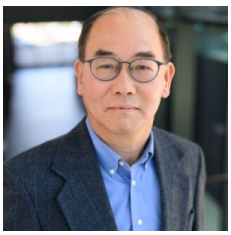
Peng, J., Nouri, M., Maasoumyhaghighi, H., Liu, J., and **Liu, X.** (2025) Plk1, a promising therapeutic target for prostate cancer treatment. *Serican Journal of Medicine*. Vol. 1, No 1, 23189. http://doi.org/10.17161/serican.vol1.23189.

Simpson, K., Allison, D.B., He, D., Liu, J., Wang, C., and **Liu, X.** (2025) Metformin in overcoming enzalutamide resistance in castration-resistant prostate cancer. *J. of Pharmacology and Experimental Therapeutics.* 392, 100034. doi: 10.1124/jpet.124.002424. PMID: 39379144.

Maasoumyhaghighi, H., Nouri, M., Liu, J., and **Liu, X.** (2025) Molecular mechanisms driving lineage plasticity in prostate cancer: Nanog and beyond. *Cancer Heterogeneity and Plasticity*. 2(1):0001. https://doi.org/10.47248/chp2502010001.

Wang, L., He, D., Li, Q., Orren, D., Wang, C., Liu, J., Li, Z., and **Liu., X.** (2025) PLK1 phosphorylates WRN at Replication Forks. *J. of Pharmacology and Experimental Therapeutics.* 392, 100051.

Featured Publications:

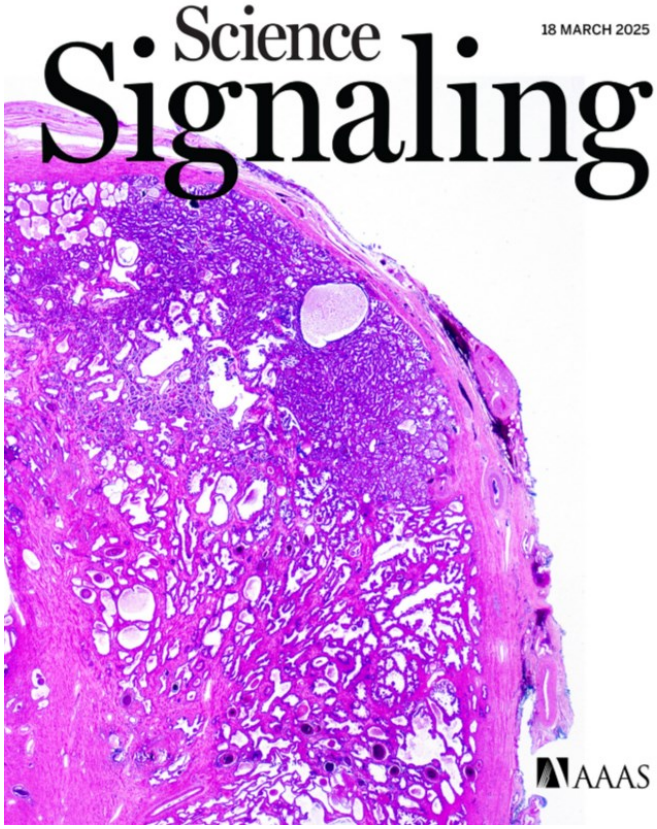


Nugle C, Shi R, **Ren X**, Jia H, Oyelami F, Li D, Park Y, Kim J, Hemati H, Zhang Y, Xiong X, Shinkle A, Vanderford NL, Bachert S, Zhou B, Wang J, Song J, **Liu X**, **Yang JM**. NAC1 promotes stemness and regulates myeloid-derived cell status in triple-negative breast cancer. *Mol Cancer* 23, 188 (2024). https://doi.org/10.1186/s12943-024-02102-y

The nucleus accumbens-associated protein 1 (NAC1), a member of the BTB/POZ family of transcriptional co-regulators, has increasingly emerged as a key molecular player in oncogenesis. Our study revealed that NAC1 plays an extraordinary role in sustaining cancer stemness and reshaping the tumor microenvironment (TME) to facilitate immune suppression in triple-negative breast cancer (TNBC), a particularly aggressive and treatment-resistant subtype. Mechanistically, NAC1 exerts its influence through the CD44-JAK1-STAT3 axis, a well-established pathway regulating tumor initiation and progression. We also showed that NAC1 plays a crucial role by promoting the secretion of immunosuppressive cytokines, including IL-6, G-CSF, and TGF-β1. These cytokines not only sustain CSC stemness but also condition myeloid-derived suppressor cells (MDSCs), a population of immune cells known for suppressing T-cell and NK-cell activity. Importantly, we found that the impact of NAC1 on tumor progression is strikingly dependent on the integrity of the host immune system. This phenomenon was elucidated through contrasting outcomes in NK cell-competent nude mice and NK cell-deficient NSG mice. The duality of NAC1 in promoting tumor survival and evading host immunity underscores NAC1 as a compelling therapeutic target in TNBC by simultaneously eliminating CSCs, disrupting the CD44-JAK1-STAT3 axis, and reverse MDSC-mediated immune suppression.

Featured Publications:

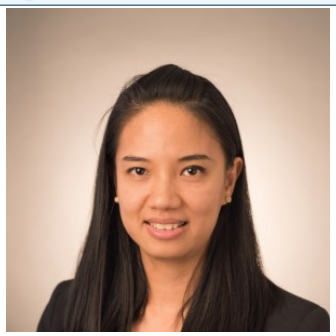
Drs. Xiaoqi Liu, Hsin-Sheng Yang:



Zhang, Q., Peng, J., Zhang, Y., Liu, J., He, D., Zhao, Y., Wang, X., Li, C., Kong, Y., Wang, R., Mao, F., Wang, C., Wang, Q., Zhang, M., Wang, J., **Yang, H.S**., and **Liu, X.** (2025) The kinase PLK1 promotes Hedgehog signaling-dependent resistance to the anti-androgen enzalutamide in metastatic prostate cancer. *Science Signaling*, 18, eadi5174.

Enzalutamide, an androgen receptor inhibitor, is utilized for treating patients with metastatic castration-resistant prostate cancer (mCRPC). However, acquired resistance to enzalutamide presents a significant clinical challenge, necessitating novel strategies for overcoming this resistance. In this study, DTCB graduate student Qiongsi Zhang and postdoc fellow Dr. Jia Peng demonstrated that PLK1 phosphorylates PDCD4 at serine 239 (S239), leading to PDCD4 degradation by enhancing its binding to βTRCP2, thereby promoting enzalutamide resistance. Mechanistically, phosphorylation of PDCD4 at S239 upregulates the expression of UDP -glucuronosyltransferase 2B15 (UGT2B15) through activation of the c-MYC-Hedgehog axis. This pathway circumvents the androgen receptor, thereby reducing cellular sensitivity to enzalutamide treatment. Inhibition of UGT2B15 enhances enzalutamide-induced cell apoptosis and growth arrest in a manner dependent on PDCD4-S239 phosphorylation. These findings provide a novel insight into the role of PLK1-mediated PDCD4 phosphorylation in enzalutamide resistance and suggest a potential therapeutic strategy to overcome resistance in prostate cancer. This work, a result of collaboration between the labs of Drs. Xiaoqi Liu and Hsin-Sheng Yang, was supported by NIH R01 CA272483 (MPI: Liu and Yang). The story was chosen as the cover image of the same issue of Science Signaling (March 18, 2025).

Faculty Activity:



Dr. Luksana Chaiswing:

Jan 2025. "Imaging of 4HNE-adducted protein in extracellular vesicles (RedoxEVs) of GBM patients." Annual Research Conference (ARC25) KY INBRE. Louisville, KY, USA.

Dr. Changhai Tian:

Tian, CH. Cardiac extracellular vesicles bridge heart and brain crosstalk after cardiac injury. The Bugher Foundation Collaborative Symposium 2025, Los Angles, California, February 3-4, 2025 (Invited oral presentation).

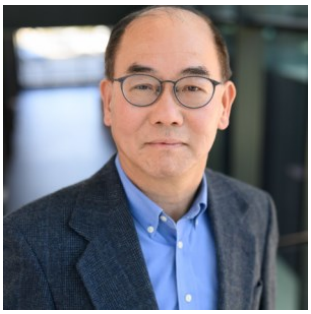
Qingxuan Li, Ramzi. Hamdalla, Neha Dhyani, Lie Gao, Tara L. Rudebush, Irving H. Zucker, and **Changhai Tian**. Cardiac Injury Potentially Contributes to Neuroinflammation via Extracellular Vesicles. (Poster presentation, International Stroke Conference, February 5-7, 2025, Los Angeles, California, USA).

2025 Served as an Ad hoc interviewer for IBS Graduate Program, University of Kentucky, January 17, 2025.
2025 Bugher Foundation Collaborative Symposium (AHA Awardee invited), Los Angeles, California, USA, February 3-4, 2025.
2025 International Stroke Conference, Los Angeles, California, USA, February 5-7, 2025.

Dr. Nathan Vanderford:

Member/Co-chair, National Institutes of Health, National Cancer Institute R25 Youth Enjoy Science Research Education Program Special Emphasis Study Section (2025/05 ZCA1 RTRB-R (M2))

Dr. Jinming Yang



Participation in the NIH Study Section of ZRG1 BTC-M 02M on December 5, 2024.

Faculty Awards and Recognition:

Associate Professor Nathan Vanderford named as AACE Fellow!

Department of Toxicology & Cancer Biology Associate Professor Nathan Vanderford, Ph.D., has been named a fellow of the American Association for Cancer Education (AACE), joining an elite group of cancer education leaders.

Nominees must be an outstanding member of the cancer education community who is nominated by a peer and selected based on the following criteria:

- Established record as a cancer educator
- Current member of the American Association for Cancer Education
- Current contributor to the field of cancer education
- Established leader of national or international organizations or committees
- Demonstrated impact in multidisciplinary, interprofessional, or trans professional educational endeavors
- Sustained record of scholarship
- Recipient of recognition, awards, and/or invitation to service as a visiting professor or invited speaker
- Effective mentor

Vanderford was selected through a rigorous peer-review process that recognizes individuals who have demonstrated exemplary commitment to cancer education and training.

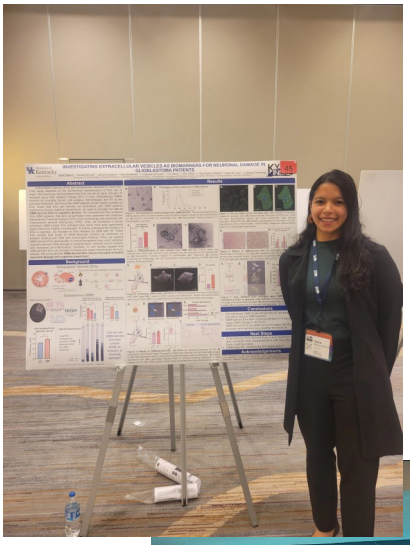
Vanderford, who serves as assistant director of pathway programs and student success at UK Markey Cancer Center, leads several initiatives including the Appalachian Career Training in Oncology (ACTION) Program, a National Cancer Institute (NCI)-funded program that provides cancer-focused career training to Appalachian Kentucky students. Vanderford is also site director of Markey Cancer Center's Summer Healthcare Experience (SHE) in Oncology Program, which introduces students to cancer careers through hands-on learning.

The AACE, founded in 1947, has evolved into an international organization dedicated to promoting equity in cancer care and reducing the global cancer burden. Fellows of the organization work to identify trends in cancer education, steer advances in the field, and mentor the next generation of cancer educators. Fellows must demonstrate sustained scholarship, leadership in national or international organizations, and effectiveness as mentors.

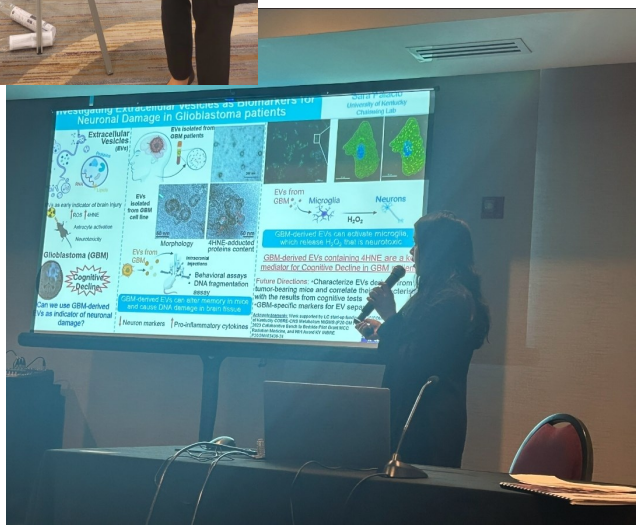
Lab Activity:

Dr. Luksana Chaiswing:

The KY INBRE Annual Research Conference, Louisville, KY January 31—February 24, 2025



Assistant Professor Luksana Chaiswing, PhD, delivers an oral presentation at KY INBRE Annual Research Conference.



Sara Macias Palacio selected for **Oral Presentation and Poster Presentation** at KY INBRE Annual Research Conference!

New Faces:

The Forensics Program welcomed three (3) new students for the Spring 2025 semester, joining our current cohort!

Left to right: Terrisha Buckley, Wintana Demoz, Ananya Maria Paul

DTCB Visiting Scholar, Alireza Tavakolpournegari, earns Ph.D.!

Alireza Tavakolpournegari has successfully defended his thesis and was awarded his Ph.D. on February 7th, 2025! Alireza's thesis was entitled, "Toxicological assessment of nanoplastics using immune cells: a study on polystyrene and polyethylene terephthalate nanoplastics."

The environmental presence of micro/nanoplastics (MNPLs) is a growing concern due to their potential implications for human health and ecosystems. MNPLs can originate from two primary sources: the physicochemical and biological degradation of larger plastic items (secondary MNPLs) or through industrial processes that manufacture these materials at the nanoscale for various commercial applications (primary MNPLs). The toxicological profile of MNPLs is influenced by their size and the capacity of cells and organisms to internalize them, raising questions about their health risks and biological effects. In my dissertation I aimed to explore the multifaceted aspects of nanotoxicology concerning MNPLs, emphasizing their interactions with biological systems and potential health hazards. I examined the biological effects of polystyrene MNPLs of varying sizes on three different human hematopoietic cell lines. In addition, I focused on the health risks posed by secondary MNPLs, particularly polyethylene terephthalate (PET) NPLs resulting from the degradation of plastic water bottles. Utilizing mouse alveolar macrophages (MH-S) as the target cells, this investigation concentrated on the cells that internalized the PETNPLs, providing a realistic assessment of their potential adverse effects. Together, the findings emphasize that size, exposure duration, and the specific biological context play critical roles in determining the toxicological effects of MNPLs, paving the way for future research into the mechanisms underlying their interactions with biological systems.

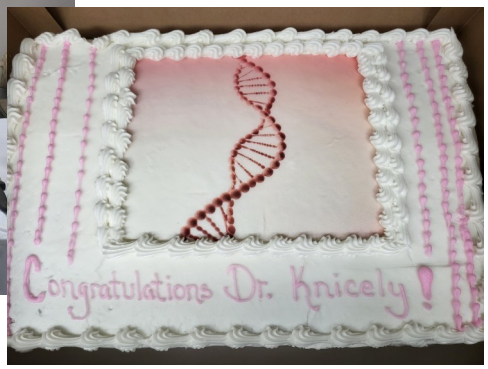
Alireza plans to continue his research focus on the Environmental Toxicity and mutagenesis, furthering his hypothesis on inflammatory mechanisms and carcinogenic potential of Environmental pollutants including nanoplastics based on the observations during his PhD research and his research at the University of Kentucky as a visiting scholar.

Breanna Knicely Earns Ph.D.!

Dr. Breanna Knicely successfully defended her thesis, “Regulation of Human DNA Mismatch Repair” on March 7th, 2025, gaining her PhD.

Breanna completed her work within Dr. Eva Goellner’s lab and will be departing at the end of March to her next adventure!

A party was hosted to celebrate Breanna on March 7th, immediately following her defense and was attended by family, students, and faculty.



Student Forum Activity:

Student Forum Serves as Guest Judges for FCPS Science Fair!

On February 1st , students served as guest judges for the Fayette County Public School System at Frederick Douglass High School.

This is the second year the student forum has participated!

Left to Right: Kevin Fulp, Niyi Obaleye, Christian Gosser, Jerika Durham

Not Pictured: Mariah Geisen

Student Forum on Ice!

Graduate students skated on thin ice on February 22nd, enjoying an outing to the Lexington Ice Center.

No reports have been received of falls, however, it is believed they have a nondisclosure agreement.

Left to Right: Xiangzhen Wei, Cheng Zhang, Yinping Jiang, Kevin Fulp, Mariah Geisen, Sara Macias Palacio, Andrew Shinkle, Niyi Obaleye

Spring 2025 Semester: DTCB Monday Seminars
12:00-1:00 PM
MN 463

Mar 03 — Dr. Junran Zhang, Ohio State University (Dr. T. Izumi)

Mar 10 — Dr. Wenliang Li, UT Health Houston (Dr. Q. Wei)

Mar 24 — Dr. Luksana Chaiswing, University of Kentucky (Dr. X. Liu)

Mar 31 — Student Seminar: Jerika Durham (Dr. K. Zaytseva)

Apr 07 — Dr. Maria S. Sosa, Albert Einstein College (Dr. J-M Yang)

Apr 14 — Dr. Antino Allen, UAMS College of Pharmacy (Dr. L. Chaiswing)

Apr 21 — Dr. Xiaojing Ma, Weill Cornell University (Dr. Xia Liu)

May 05 — Dr. Changhai Tian, University of Kentucky (Dr. X. Liu)

Department of Toxicology & Cancer Biology

FORENSICS POSTER SESSION

Held by the 2025 graduating class of the Forensics program.

Date: Thursday, May 8, 2025
Time: 1:00 PM - 3:00 PM
Location: Atrium of BBSRB

The posters describe the students' internship experiences.

College of Medicine
Department of Toxicology and Cancer Biology

Spring 2025 Semester: DTCB Faculty Grant Talk Series

12:00-1:00 PM

HKRB 410

Mar 07 — Dr. Changhai Tian

Apr 04 — Dr. Will Fong

Apr 18 — Dr. Guan-Yu Xiao

Spring 2025 Semester: DTCB Trainee Talk Series
12:00-1:00 PM
MN 463

Mar 14 — Amos Akinyemi (Li) & Md Rakibul Alam (Li)

Mar 28 — Christian Gosser (Brainson) & Avery Childress (Brainson)

Apr 25 — Sai Wu (Liu) & Min Zhang (Liu)

May 2 — Han Cong (Fong) & Dave-Preston Esoe (Brainson)

NEWSLETTER ITEMS

Want to include something in the next newsletter? Send your stuff to Cherish Oliver at ToxAndCancerBio@uky.edu

College of Medicine
Department of Toxicology and Cancer Biology