

NEWSLETTER

CIEHS Up to Date News and Accomplishments

Awards Announcements and Reminders

2022 Pilot Project Program Awardees

Congratulations to the 2022 Pilot Project Program awardees. Learn more about the CIEHS Pilot Project Program [HERE](#).

Interdisciplinary Pilot Project Award:

Principal Investigator: Banrida Wahlang, Ph.D.
Collaborator: Shesh Rai, Ph.D. and Michael Merchant, Ph.D.
Title: "Sex-dependent Effects of Organochlorine Pesticides on Metabolic Diseases: Role of the Gut-Liver Axis"

Principal Investigator: Barbara Clark, Ph.D. and Carolyn Kling, Ph.D.
Consultant: Nichola Garbett, Ph.D.
Title: "STARD5 and lipid dysregulation in toxicant-associated steatohepatitis (TASH)"

Principal Investigator: Anna Gumpert, Ph.D.
Collaborator: Daniel Conklin, Ph.D.
Title: "Combines Effects of Air Pollution and Hypertension on Cardiovascular Remodeling"

2022 Center Meeting

Thank you to everyone who attended the center-wide meeting on May 17th. Below is a list of the presentations, if you missed the meeting but would like to view the recording, please contact sejump01@louisville.edu.

- Dr. Christoph States- State of the Center
- Sarah Jump- Expertise Finder demonstration
- Luis Salzar Guzman- Pilot Project Ordering Process
- Drs. Matthew Cave and Michael Merchant and Colleen Quinter- New consolidated OEFK/IHSFC research voucher process
- Dr. Aruni Bhatnagar- GreenHeart Project and other potential areas where collaborations are available.
- Drs. Becky Antle and Matthew Cave- Translational Research Stories



(Left to right) Drs. Mayukh Banerjee, Krishna Jala, Loretta Jophlin and Matthew Cave sharing their Translation of Research stories

Expertise Finder

CIEHS has now released an Expertise Finder tool to facilitate collaboration and consultation among researchers, trainees and community members.

The Expertise Finder is located on the CIEHS website [HERE](#).

Type a keyword in the input field to filter the list for research topics. Click on a topic to show CIEHS members who specialize in the subject.

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Awards Announcements and Reminders Continued

Leadership and Committee Update

Congratulations to Dr. Petra Haberzettl, who has been appointed as Associate Director for CIEHS. Dr. Haberzettl will also serve as a member of the Executive Committee and the Internal Advisory Committee. Congratulations to Dr. Calvin Kouokam and Banrida Wahlang who were elected by the Career Development Program mentees to serve on CIEHS leadership committees for a one-year term. Dr. Kouokam will serve on the Executive Committee (EC) and Dr. Banrida Wahlang will serve on the Internal Advisory Committee (IAC). Congratulations to Dr. Cynthia Corbitt will serve as member at large on the Internal Advisory Committee this year. We thank Dr. Timothy O'Toole for his service as member at large last year.

John Wise, Sr., Ph.D. & Dwayne Compton, Ed.D., M.Ed. 2022 Presidential Excellence Awardees

Congratulations to Dr. John Wise, Sr., CIEHS Deputy Director, and Dr. Dwayne Compton, CEC Advisor, for being honored with a 2022 Presidential Excellence award. Dr. Wise received the Distinguished Teaching Professor award and Dr. Compton received the Cardinal Principles Champion in Leadership award. Learn more about UofL's Presidential Excellence Awards [HERE](#).

Jiapeng Huang, M.D. 2022 Society of Cardiovascular Anesthesiologist Meeting

Dr. Jiapeng Huang moderated several sessions and workshops at the 2022 Society of Cardiovascular Anesthesiologist (SCA) Meeting in Palm Springs, CA. Sessions entitled "Artificial Intelligence and Machine Learning for Cardiac Anesthesiologists" & "Manage Right Heart Failure-Challenges and Opportunities" workshop entitled "3D TEE". Learn more about the SCA [HERE](#).

Matthew C. Cave, M.D. to speak at 2022 NYC Exposome Symposium-Mount Sinai

Dr. Matthew Cave, IHSFC Core Director, will be presenting during the Health Equity and the Exposome: Understanding the Hidden Ways Environment Drives Health Symposium at Mount Sinai's Icahn School of Medicine in New York City. The symposium takes place July 12-13, 2022. Learn more [HERE](#).

Student and Postdoc Accomplishments

Congratulations to students and postdocs of CIEHS members who have recently or will be defending their dissertations/ thesis.

Lyndsey Blair (**Natalie C. Dupré, ScD**)
Elizabeth Greenwell (**Charlie Zhang, Ph.D.**)
Gabrielle Rowe (**Amanda Jo LeBlanc, Ph.D.**)
Evan Tracy (**Amanda Jo LeBlanc, Ph.D.**)
Lindsey Wood (**Natalie C. Dupré, ScD**)

SfN Award

Congratulations to Dr. Tianci Chu (**Jun Cai lab**) who received the Postdoc/Resident Trainee Award by the Society for Neuroscience (SfN) Louisville Chapter at the [UofL 30th Annual Neuroscience Day](#).

CIEHS Environmental Health Series Seminar

CIEHS welcomes Dr. Fei Chen, from the Department of Pathology and a member of the Stony Brook Cancer Center, Renaissance School of Medicine, Stony Brook University, NY., as the next external speaker for the monthly environmental health series seminar on Thursday, June 2nd at 11 AM ET. This will be a hybrid event located in CTR room 124, to attend virtually register [HERE](#).

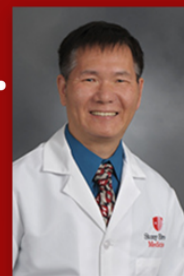
Click [HERE](#) in case you missed Dr. Alexandra Nail's seminar entitled "Chronic Arsenic Exposure Reduces DNA Damage Response Activation in Human Keratinocytes" on May 5th. You can find all of the past CIEHS seminars on our [YouTube channel](#) and a full seminar schedule on the CIEHS [website](#).

OEFC Inquiry Form

Omics & Exposure Facility Core (formerly ITEMFC) has released a new inquiry form that can be found and submitted electronically on the CIEHS website [HERE](#).

The Center for Integrative Environmental Health Sciences Presents EHS Seminar with Special Guest

Fei Chen, Ph.D.



Presentation Entitled:
"Mineral dust-induced gene and H3K36me3 in breast cancer metastasis"

Dr. Fei Chen is a Professor in the Department of Pathology and a member of the Stony Brook Cancer Center, Renaissance School of Medicine, Stony Brook University, NY. He is also the Co-leader of the Oncogenic Drivers and Mechanisms of Carcinogenesis program at Stony Brook Cancer Center. Dr. Chen's research focuses on environmental risk factors and epigenetic regulation in human cancer. Dr. Chen's contributions to science include identification of the mineral dust-induced gene (mdig) as a new oncogene, metabolomics and epigenetics of arsenic-induced cancer stem cells (CSCs), and arsenic activation of intracellular kinase cascade.

Thursday, June 2 | 11 AM ET
Attendance In-person: CTRB 124
Register for attendance via MS Teams

UNIVERSITY OF LOUISVILLE
CENTER FOR INTEGRATIVE ENVIRONMENTAL HEALTH SCIENCES

Awards Announcements and Reminders Continued

Colleen F. Quinter 2021 Staff Excellence Awards Nominee

Congratulations to Colleen F. Quinter, CIEHS Program Manager, for being nominated for the 2021 UofL Dean's Staff Excellence Awards-Performance Excellence in an Administrative Office!



Colleen Quinter and SOM Dean Toni Ganzel

Sharing Our Community Experience: Western Kentucky

The Community Engagement Core (CEC) has released a compilation video regarding a community in western Kentucky that was experiencing health problems related to the air quality impact of a local hemp processing facility. A community member was able to get in touch with the CEC through local connections. The CEC helped bring together this community to help stop this unexpected and unwelcome environmental exposure. Watch the full video [HERE](#).

Need Assistance?

If you are in need of assistance with a CIEHS related issue please email us at CIEHS@louisville.edu or visit us on the 13th floor of the Research Tower at 500 s Preston st. Louisville, KY and meet our new friend Veronika the Vulture.



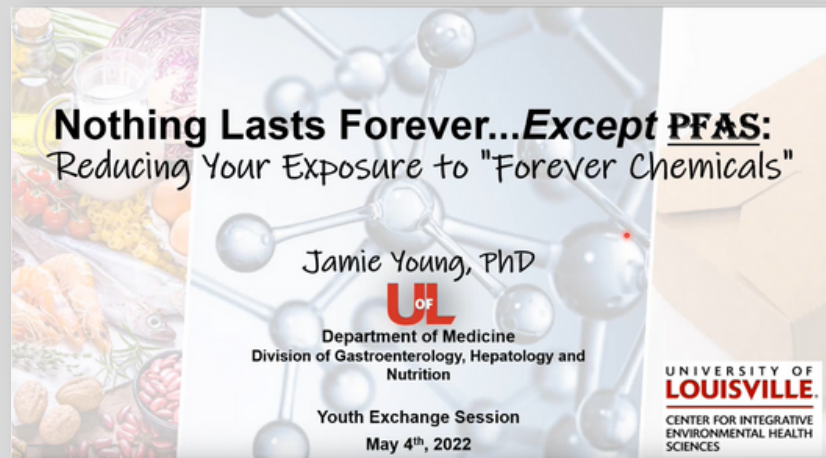
Veronika the Vulture

Community Engagement Core Corner

Throughout April and May, the CEC team has been working to advance a number of endeavors. Our team has been securing partnerships with the School of Music at the University of Louisville, the Girls Incorporated organization in Owensboro, and Dr. Tony Arnold of the Brandeis School of Law, preparing for the fourth Youth Exchange Session hosted by Dr. Jamie Young on reducing PFAS exposure, supporting the Concrete Dust team in the next steps of their research, creating posters for the John P. Wyatt Symposium, and welcoming our newest Stakeholder Advisory Board member, Ms. Velvet Dowdy!

Towards the end of April, Ms. Josie Willis attended the John P. Wyatt Environment & Health Symposium at the University of Kentucky to present a poster related to the disaster preparedness survey that has been developed through the UK/UL CEC collaboration. On May 4th, Dr. Jamie Young hosted our fourth Youth Exchange Session on PFAS, which is now available on the CIEHS YouTube channel. Dr. Young has also been interviewed about this community-engaged research project for a highlight on the CEC portion of the CIEHS website. The CEC would like to welcome Ms. Lidia Moore who will be interning with us for the summer and fall months. Ms. Sarah Jump has been instrumental in the creation of CEC pamphlets that can be distributed at future tabling events. The CEC also continues to work with Ms. Jump and Mx. Salazar Guzman to create content for our upcoming CEC podcast endeavor. If you are interested in being interviewed, please reach out to Ms. Willis at Josephine.willis@louisville.edu. We would love to promote our scientists!

Finally, we would love to highlight our newest collaborators-Dr. Tony Arnold of the University of Louisville's Brandeis School of Law and Ms. Velvet Dowdy of Henderson, Kentucky. Dr. Arnold is currently working on a resilience justice project with his law fellows in the Mill Creek watershed in southwestern Jefferson County. Ms. Velvet Dowdy is a retired high school Chemistry teacher from Henderson, Kentucky who serves on the PFAS Community Taskforce and has recently accepted a position on our Stakeholder Advisory Board!



Screen shot from Dr. Young's Youth Exchange Session

The CEC thanks Dr. States for treating Ms. Willis, Ms. Jump, Ms. Quinter, and Mx. Salazar Guzman to lunch on Administrative Professional's Day. Additionally, we thank Dr. Lorna Segal and Chris Millett of the University of Louisville's School of Music, Ms. Velvet Dowdy, Dr. Tony Arnold, Dr. Anna Hoover, the UK CARES CEC team, Catherine Malin of the AHCC South Central, Ms. Mojisola Lawson of the Environmental Health Sciences Club at the School of Medicine, and Dr. Ritchie Taylor of WKU.

Notes from the Director:

Unfortunately, COVID is still with us and the case loads, hospital admissions and transmission rate are all increasing both nationwide and in Kentucky. The community spread index in Jefferson County is currently 'medium'. Of concern is that people testing positive with a home test are often not reporting the result. Thus, the positivity rates are artifactually low. Please help keep the data accurate by either reporting the result or following up with a PCR test that will be reported. Stay vigilant, exercise discretion and stay healthy!

We had good attendance at the recent Center-wide meeting. We discussed the current state of the Center which is good. Our members are publishing at a good rate, although citation of the P30 is not as frequent as it should be. We announced recent additions to the CIEHS website.

Special thanks to Sarah Jump and Luis Salazar Guzman for their work implementing the expertise search and pilot project ordering functions. We also held a mini-workshop on using the NIEHS Translational Research Framework. Thank you to Drs. Cave and Antle for putting that together, and to Drs. Banerjee, Jala and Jophlin for presenting their translational research path. We also discussed the focus on obtaining new NIEHS grants. In one year, we will be writing the application for renewal of the P30 grant. To be eligible to apply, we must have a minimum of six separate NIEHS funded research project/program grants with a minimum of four separate principal investigators. The grants must have at least 12 calendar months of support beyond the P30 application deadline. We are emphasizing that people apply for R01 grants rather than R21 grants, not only because there is little difference in how much work and preliminary data are needed to be successful, but also because R21 grants applied for this year will expire too soon to count toward eligibility. Other criteria that the reviewers will be evaluating include how many publications cited the P30 and how successful we have been at fostering new NIEHS grants with the pilot projects and research vouchers. Reviewers also will evaluate the success of our early stage investigators at getting their research programs funded.

As recommended by our External Advisory Committee, we expanded the leadership. Dr. Petra Haberzettl as Associate Director, and Drs. Calvin Kouokam and Banrida Wahlang were elected by the Career Development Program mentees to serve one year terms on the Executive Committee and the Internal Advisory Committee respectively. Dr. Cynthia Corbitt will serve as member at large on the Internal Advisory Committee this year. We thank Dr. Timothy O'Toole for his service as member at large last year.

The NIEHS Center Directors Meeting is being hosted by the Icahn School of Medicine at Mt. Sinai P30 in July. They also are hosting an Exposome Symposium as a satellite meeting. Dr. Matt Cave will be one of the invited speakers at the Exposome Symposium. There is an option for virtual attendance at each of these meetings. See the website for further information.

Dr. Fei Chen will be visiting us June 1 -2 and will present a seminar on his research. We are looking forward to his seminar that will be presented in person. There is an option for virtual attendance if you cannot be present. Please see the notice elsewhere in this newsletter for the details.

There are lots of fun outdoor activities to enjoy this summer. I hope you get to partake of many of them.

MEMBER GRANT AWARDS FEBRUARY 2022

Congratulations to the CIEHS members who had new grants, supplements and competitive renewals activated/awarded in the month of February 2022! Below is a list of the new awards. We are so proud of all the hard work of our CIEHS members. You truly are making UofL a nationally recognized premier metropolitan research University and promoting interdisciplinary collaborative research in our Center! You can also view these grants on the CIEHS website [HERE](#).

PI Name	Other Investigator	Long Title	Sponsor	Amount
States, J.Christopher	Cave, Matthew C.; Conklin, Daniel	Summer Environmental Health Sciences Training Program	National Institutes of Health	\$49,738.00

This NIEHS Short-Term Institutional Training Grant supports 6 medical student trainees for a 10 week training experience for the next 5 years. The overarching scientific theme of research that links our faculty to this T35 Training Grant is the common interest of the faculty in research training of medical students in our laboratories in elucidating the health outcomes of exposure of normal and obese individuals to various environmental chemicals. In addition, we will use the T35 Training Grant to entice our medical students into our Distinction in Research Track, designed to allow students to pursue research interests throughout the years 2-4 of medical school curriculum with an eye toward building a pipeline of diverse translational clinician-researchers in the future.

Wise, John Pierce	Kouokam, Joseph	Supplement- Chromosome Instability Drives Metal-Induced Lung Cancer	National Institutes of Health	\$83,973.00
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Lung cancer is the number one cause of cancer death in the United States and metals are a major cause of the disease. Our study focuses on how hexavalent chromium, a metal with widespread exposure known to cause lung cancer, causes chromosome instability, a hallmark event in lung cancer. Our findings will transform our understanding of how metals cause chromosome instability and lung cancer, which may spur new potential treatment targets, new approaches to reduce and prevent metal-induced lung cancer, and new insights to better determine and manage safer exposure levels for this major public health concern. Important Co-investigators on the grant include Drs. Sandra Wise (University of Louisville), Ke Jian Liu (University of New Mexico), Tongzhang Zheng (Brown University), Stefan Mundlos (Max Planck Institute for Molecular Genetics in Germany) and Lynne Haber (University of Cincinnati) along with collaborators Drs. Matthew Cave (University of Louisville), Deborah Kelly (Penn State University), Kazuya Kondo (University of Tokushima), Michael Merchant (University of Louisville), Alvaro Puga (University of Cincinnati) Erik Tokar (National Institutes of Environmental Health Sciences), Ronald Walter (Texas State University), and Wesley Warren (University of Missouri).

Lawrenz, Matthew Bryan	Merchant, Michael L	Extracellular vesicles released in response to Yersinia pestis	National Institutes of Health	\$234,375.00
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Extracellular vesicles (EVs) are released by cells to mediate cell-to-cell communication and contribute to establishing the proper immune response during infection. Our goal is to define how Yersinia pestis, the causative agent of plague, alters EV production by immune cells to disrupt cell communication and inhibit the recruitment of immune cells to the site of infection (referred to as inflammation). Because inducing inflammation during early stages of plague can improve the therapeutic window for a patient, defining mechanisms used by Y. pestis to inhibit inflammation is not only important for our understanding the pathogenesis of this bacterium, but will help us to identify new approaches to improve current plague therapy.

Sterrett, Emma Maria	Harris, Lesley Beth	AICH Peer Health & Wellness Storefront	Crane House, the Asia Institute, Inc.	\$16,924.00
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The AICH Peer-to-Peer Support Storefront is dedicated to helping older, first and other generation Asian immigrants be heard, valued, and supported and to recognize health needs, seek appropriate care, manage chronic conditions, and maintain a satisfying quality of life.

Total New Awards February 2022: \$385,010.00

MARCH PUBLICATIONS HIGHLIGHTS

Congratulations to the CIEHS members with articles published in the month of March! Member names will be bolded and impact statements for the publications are italicized. You may also read the publication by clicking on the PMID underlined.

1. Wang X, Chen X, Zhou W, Men H, Bao T, Sun Y, Wang Q, Tan Y, Keller BB, Tong Q, Zheng Y, **Cai L**. Ferroptosis is essential for diabetic cardiomyopathy and is prevented by sulforaphane via AMPK/NRF2 pathways. *Acta Pharm Sin B*. 2022 Feb;12(2):708-722. doi: [10.1016/j.apsb.2021.10.005](https://doi.org/10.1016/j.apsb.2021.10.005). Epub 2021 Oct 15. PMID: [35256941](https://pubmed.ncbi.nlm.nih.gov/35256941/); PMCID: [PMC8897044](https://pubmed.ncbi.nlm.nih.gov/PMC8897044/).

Impact Statement: *The role of ferroptosis in the pathogenesis of diabetic cardiomyopathy (DCM) was comprehensively examined by examining the expression of key regulators of ferroptosis in type 2 diabetic mice with cardiomyopathy and a new ex vivo DCM model. Diabetes or AGEs was found to induce ferroptosis, reflected through increased levels of Ptg2 and lipid peroxides and decreased ferritin and SLC7A11 levels and typically morphological changes in cardiomyocytes, and inhibition of ferroptosis with ferrostatin-1 and deferoxamine, as well as Nrf2 activator, sulforaphane, prevented cardiac remodeling and dysfunction. These findings suggest that ferroptosis plays an essential role in the pathogenesis of DCM; sulforaphane prevents ferroptosis and associated pathogenesis via AMPK-mediated NRF2 activation.*

2. Wise JTF, Salazar-González RA, Habil MR, Doll MA, **Hein DW**. Expression of arylamine N-acetyltransferase 2 activity in immortalized human bronchial epithelial cells. *Toxicol Appl Pharmacol*. 2022 Mar 27;442:115993. doi: [10.1016/j.taap.2022.115993](https://doi.org/10.1016/j.taap.2022.115993). Epub ahead of print. PMID: [35353990](https://pubmed.ncbi.nlm.nih.gov/35353990/).

Impact Statement: *A recent meta-analysis reported N-acetyltransferase 2 (NAT2) slow and intermediate phenotypes had a significantly increased risk of lung cancer. NAT2 activity in humans is thought to be restricted to liver and gastrointestinal tract, and no studies to our knowledge have reported the expression of NAT2 activity in immortalized human lung epithelial cells. Given the importance of NAT2 in cancer and inhalation of various carcinogens directly into the lungs, we investigated NAT2 activity and documented that it is expressed and functional in human lung epithelial cells.*

3. **Hein DW**, Doll MA, Habil MR. Human N-Acetyltransferase 1 and 2 Differ in Affinity Towards Acetyl-Coenzyme A Cofactor and N-Hydroxy-Arylamine Carcinogens. *Front Pharmacol*. 2022 Feb 25;13:821133. doi: [10.3389/fphar.2022.821133](https://doi.org/10.3389/fphar.2022.821133). PMID: [35281898](https://pubmed.ncbi.nlm.nih.gov/35281898/); PMCID: [PMC8914035](https://pubmed.ncbi.nlm.nih.gov/PMC8914035/).

Impact Statement: *Following recombinant expression in bacteria, yeast, and mammalian cells, we report significant differences in affinity between human N-acetyltransferase 1 (NAT1) and N-acetyltransferase 2 (NAT2) for its required co-factor acetyl coenzyme A, as well as for N-hydroxy-arylamines activated via O-acetylation. The findings provide important information to understand the relative contribution of human NAT1 vs NAT2 towards N-acetylation and O-acetylation reactions in human hepatic and extrahepatic tissues.*

4. Doll MA, **Hein DW**. 560G>A (rs4986782) (R187Q) Single Nucleotide Polymorphism in Arylamine N-Acetyltransferase 1 Increases Affinity for the Aromatic Amine Carcinogens 4-Aminobiphenyl and N-Hydroxy-4-Aminobiphenyl: Implications for Cancer Risk Assessment. *Front Pharmacol*. 2022 Feb 22;13:820082. doi: [10.3389/fphar.2022.820082](https://doi.org/10.3389/fphar.2022.820082). PMID: [35273499](https://pubmed.ncbi.nlm.nih.gov/35273499/); PMCID: [PMC8902414](https://pubmed.ncbi.nlm.nih.gov/PMC8902414/).

Impact Statement: *Human arylamine N-acetyltransferase 1 (NAT1) catalyzes the N-acetylation of arylamine carcinogens such as 4-aminobiphenyl (ABP), and following N-hydroxylation, the O-acetylation of N-hydroxy-arylamine carcinogens such as N-hydroxy-ABP (N-OH-ABP). The effects of individual single nucleotide polymorphisms (SNPs) in the NAT1 coding exon on Michaelis-Menten kinetic constants was assessed for ABP N-acetyltransferase and N-OH-ABP O-acetyltransferase activity following transfection of human NAT1 into COS-1 cells. 560G>A (rs4986782) (R187Q) significantly reduced the apparent Km for ABP and N-OH-ABP a finding that was not observed with any of the other NAT1 SNPs tested. These findings suggest that the role of the 560G>A (rs4986782) (R187Q) SNP cancer risk assessment may be modified by exposure level to aromatic amine carcinogens such as ABP.*

5. Latif RK, Clifford SP, Ghafghazi S, Phipps Z, Chen JJ, Sangroula D, Khan AZ, Saleem J, Farah I, **Huang J**, Businger JR. Echocardiography and Management for Cardiac Trauma. *J Cardiothorac Vasc Anesth*. 2022 Feb 12;S1053-0770(22)00120-3. doi: [10.1053/j.jvca.2022.02.010](https://doi.org/10.1053/j.jvca.2022.02.010). Epub ahead of print. PMID: [35305892](https://pubmed.ncbi.nlm.nih.gov/35305892/).

Impact Statement: *This review article aims to analyze the pathophysiology of cardiac injuries in patients with trauma and the role of echocardiography for the accurate diagnosis of cardiac injury in trauma. This review, additionally, will offer a patient-centered, team-based, early management plan with a treatment algorithm to help improve the quality of care among these patients with cardiac trauma.*

MARCH PUBLICATIONS HIGHLIGHTS CONTINUED

6. Lu L, Che J, Cheng W, Dong R, **Huang J**, Yang Z, Lu J. A Retrospective Study of the Relationship Between Blood Transfusion and 30-Day Postoperative Outcomes in Patients Undergoing Isolated Off-Pump Coronary Artery Bypass Grafting. *Braz J Cardiovasc Surg.* 2022 Mar 3. doi: [10.21470/1678-9741-2021-0031](https://doi.org/10.21470/1678-9741-2021-0031). Epub ahead of print. PMID: [35244374](https://pubmed.ncbi.nlm.nih.gov/35244374/).
Impact Statement: *Perioperative blood transfusion increases the risks of postoperative pulmonary infection and short-term mortality in off-pump coronary artery bypass grafting patients.*
7. Fulghum KL, Audam TN, Lorkiewicz PK, Zheng Y, **Merchant M**, Cummins TD, Dean WL, Cassel TA, Fan TWM, Hill BG. In vivo deep network tracing reveals phosphofructokinase-mediated coordination of biosynthetic pathway activity in the myocardium. *J Mol Cell Cardiol.* 2022 Jan;162:32-42. doi: [10.1016/j.yjmcc.2021.08.013](https://doi.org/10.1016/j.yjmcc.2021.08.013). Epub 2021 Sep 3. PMID: [34487754](https://pubmed.ncbi.nlm.nih.gov/34487754/); PMCID: [PMC8766935](https://pubmed.ncbi.nlm.nih.gov/PMC8766935/).
Impact Statement: *This study tested how phosphofructokinase-1 (PFK1) activity controls the fate of glucose-derived carbon in murine hearts in vivo. PFK1 activity was regulated by cardiac-specific overexpression of kinase- or phosphatase-deficient 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase transgenes in mice (termed GlycoLo or GlycoHi mice, respectively). Stable isotope (C13) labeled glucose and deep network metabolic tracing revealed that low rates of PFK1 activity, potentially regulated by physical channeling, promoted selective routing of glucose-derived carbon to the purine synthesis pathway to form 5-aminoimidazole-4-carboxamide ribonucleotide. Additionally, PFK1 influenced glucose-derived carbon deposition in glycogen, but did not affect hexosamine biosynthetic pathway activity. These studies demonstrate the utility of deep network tracing to identify metabolic channeling and changes in biosynthetic pathway activity in the heart in vivo and present new potential mechanisms by which metabolic branch point reactions modulate biosynthetic pathways.*
8. Dongfeng Wu, **Shesh N. Rai** and Albert Seow. Estimation of preclinical state onset age and sojourn time for heavy smokers in lung cancer. *Statistics and Its Interface.* 15 (3), 2022. [Published Feb 14, 2022](https://doi.org/10.1016/j.sui.2022.02.002).
Impact Statement: *Using the pre-existing large data, we have devolved model to predict onset of early-stage of lung cancer in heavy smokers. The mean age (in years) to make the transition into the preclinical state was 70.94 or 71.15 for male and female heavy smokers respectively. About 90% of heavy smokers who are at risk for lung cancer would enter the preclinical state in age interval (55.7, 85.8) for males and (54.2, 87.7) for females, and the transition peaked around age 69 for both genders. Based on the result, low-dose CT should be started at age 55 and ended before 85 for heavy smokers. This provided important information to policy makers.*
9. Jessica Sparks, Xiaoyong Wu, Mika Kessans Knable, **Shesh N. Rai**, Vivek Sharma. Predictors of thrombosis in patients treated with bevacizumab. *Thrombosis Update.* 6, 2022 (DOI: <https://doi.org/10.1016/j.tru.2021.100095>). [Published March, 2022](https://doi.org/10.1016/j.tru.2021.100095).
Impact Statement: *We study the predictors of thrombosis in cancer patients treated with bevacizumab using a single center comprehensive retrospective cohort. The thrombotic events occurred in 24/116 (20.7%) of the hypertension cohort compared to 8/87 (9.2%) of the normotensive patients ($p = 0.026$) and in 15/52 (28.8%) of hyperlipidemic patients vs 17/151 (11.3%) of those with normal lipids ($p = 0.003$). The Khorana score was not a significant predictor in this population. In further analyzing our data, we found increasing thrombotic events with each addition of the most telling predictors of thromboses in our population: hypertension, hyperlipidemia, and greater than trace proteinuria, such that patients with all three risk factors present vs none had an odds ratio of 6.786 ($p = 0.004$). Incorporating these three risk factors into a clinical risk score may help stratify patients into lower and higher risk categories which may assist clinicians in making decisions about the use of prophylactic anticoagulation in this population.*
10. **States JC**, Peters JM. 2020-2021 Toxicological Sciences Paper of the Year. *Toxicol Sci.* 2022 Mar 28;186(2):177-178. doi: [10.1093/toxsci/kfac020](https://doi.org/10.1093/toxsci/kfac020). PMID: [35348797](https://pubmed.ncbi.nlm.nih.gov/35348797/).
This editorial announced the SOT Paper of the Year.
11. Xiong L, Bin Zhou, **Young JL**, Wintergerst K, **Cai L**. Exposure to low-dose cadmium induces testicular ferroptosis. *Ecotoxicol Environ Saf.* 2022 Mar 7;234:113373. doi: [10.1016/j.ecoenv.2022.113373](https://doi.org/10.1016/j.ecoenv.2022.113373). Epub ahead of print. PMID: [35272187](https://pubmed.ncbi.nlm.nih.gov/35272187/).
Impact Statement: *As an environmental pollutant, cadmium (Cd) has been widely reported to induce male infertility due to its gonadotoxicity. This study found for the first time that exposure to 5 ppm Cd significantly decreased the expression of SLC7A11, a marker of ferroptosis in mice, along with the expression of SLC40A1 mRNA and ferritin heavy chain (FTH) protein, whereas there was no obvious change in the mRNA expression of Tfrc, ZIP8, ZIP14, and NCOA4, suggesting that 5 ppm Cd exposure increased testicular ferroptosis, probably due to the reduction of stored iron export potency.*

APRIL PUBLICATIONS HIGHLIGHTS

Congratulations to the CIEHS members with articles published in the month of April! Member names will be bolded and impact statements for the publications are italicized. You may also read the publication by clicking on the PMID underlined.

1. Dwenger MM, Raph SM, Reyzer ML, Lisa Manier M, Riggs DW, Wohl ZB, Ohanyan V, Mack G, Pucci T, Moore JB 4th, Hill BG, Chilian WM, Caprioli RM, **Bhatnagar A**, Nystoriak MA. Pyridine nucleotide redox potential in coronary smooth muscle couples myocardial blood flow to cardiac metabolism. *Nat Commun.* 2022 Apr 19;13(1):2051. doi: 10.1038/s41467-022-29745-z. PMID: 35440632; PMCID: [PMC9018695](#).
Impact Statement: *This study shows that coronary dilation to increase myocardial blood flow during increased contractile demand is controlled by voltage-gated potassium channel. This metabolic sensitivity of the potassium channel is due to the ancillary subunits that bind to pyridine nucleotides to alter the gating characteristics of the channel.*
2. Wang K, Sun S, Zhang G, Lu Z, Chen H, Fan X, Gu C, Pan X, Lin Q, Chen O, **Cai L**, Dai X, Wang X, Lu C, Yan X, Tan Y. CXCR7 Agonist TC14012 Improves Angiogenic Function of Endothelial Progenitor Cells via Activating Akt/eNOS Pathway and Promotes Ischemic Angiogenesis in Diabetic Limb Ischemia. *Cardiovasc Drugs Ther.* 2022 Apr 26. doi: 10.1007/s10557-022-07337-9. Epub ahead of print. PMID: [35471717](#).
Impact Statement: *Endothelial progenitor cells (EPCs) play a critical role in repairing damaged vessels and triggering ischemic angiogenesis, but their number is reduced, and function is impaired under diabetic conditions. Improving EPC function has been considered a promising strategy to ameliorate diabetic vascular complications. In the present study, we showed that CXCR7 agonist TC14012 can prevent EPCs from high level of glucose-induced dysfunction and apoptosis, improve eNOS activity and NO production via CXCR7/Akt signal pathway, and promote EPC mobilization and diabetic ischemia angiogenesis.*
3. Lustig RH, Collier D, Kassotis C, Roepke TA, Ji Kim M, Blanc E, Barouki R, Bansal A, **Cave MC**, Chatterjee S, Choudhury M, Gilbertson M, Lagadic-Gossmann D, Howard S, Lind L, Tomlinson CR, Vondracek J, Heindel JJ. Obesity I: Overview and molecular and biochemical mechanisms. *Biochem Pharmacol.* 2022 May;199:115012. doi: 10.1016/j.bcp.2022.115012. Epub 2022 Apr 5. PMID: 35393120; PMCID: [PMC9050949](#).
Impact Statement: *The review article examines the molecular mechanisms contributing to obesity that may be impacted by environmental chemicals.*
4. Heindel JJ, Howard S, Agay-Shay K, Arrebola JP, Audouze K, Babin PJ, Barouki R, Bansal A, Blanc E, **Cave MC**, Chatterjee S, Chevalier N, Choudhury M, Collier D, Connolly L, Coumoul X, Garruti G, Gilbertson M, Hoepner LA, Holloway AC, Howell G 3rd, Kassotis CD, Kay MK, Ji Kim M, Lagadic-Gossmann D, Langouet S, Legrand A, Li Z, Le Mentec H, Lind L, Monica Lind P, Lustig RH, Martin-Chouly C, Munic Kos V, Podechard N, Roepke TA, Sargis RM, Starling A, Tomlinson CR, Touma C, Vondracek J, Vom Saal F, Blumberg B. Obesity II: Establishing causal links between chemical exposures and obesity. *Biochem Pharmacol.* 2022 May;199:115015. doi: 10.1016/j.bcp.2022.115015. Epub 2022 Apr 5. PMID: [35395240](#).
Impact Statement: *This review article examines the evidence that environmental chemicals have contributed to obesity.*
5. Polivka BJ, **Huntington-Moskos L**, Folz R, Barnett R. CE: Environments & Health: Chemicals in the Home That Can Exacerbate Asthma. *Am J Nurs.* 2022 May 1;122(5):34-39. doi: 10.1097/01.NAJ.0000829776.73698.e0. PMID: [35394947](#).
Impact Statement: *The authors describe how the use of cleaning and disinfectant products may affect asthma and asthma-related symptoms and report the findings of a recent study they conducted that identified how these products could reduce asthma control in older adults.*
6. Eldeirawi KM, Nyenhuis SM, **Huntington-Moskos L**, Polivka BJ. COVID-19 Related Anxiety Is Associated with Uncontrolled Asthma in Adults. *Ann Allergy Asthma Immunol.* 2022 Apr 22;S1081-1206(22)00308-8. doi: 10.1016/j.anai.2022.04.011. Epub ahead of print. PMID: 35470038; PMCID: [PMC9033292](#).
Impact Statement: *The COVID-19 pandemic has disproportionately affected people with chronic diseases, including asthma; these impacts were both physically and psychologically. Our findings underscore the need for health care providers to assess for the ongoing psychological impact of the pandemic and refer to mental health specialists.*

APRIL PUBLICATIONS HIGHLIGHTS CONTINUED

7. Hodges NA, Lampejo AO, Shang H, Rowe G, **LeBlanc AJ**, Katz AJ, Murfee WL. Viewing Stromal Vascular Fraction de novo Vessel Formation and Association with Host Microvasculature Using the Rat Mesentery Culture Model. *Microcirculation*. 2022 Apr 25:e12758. doi: 10.1111/micc.12758. Epub ahead of print. PMID: [35466504](#).

Impact Statement: *This study describes the use of the rat mesentery culture model as a novel tool to investigate cell therapy transplantation. Additionally, this model allows us to visualize many different cell types that are involved in microvascular growth over time using time-lapse microscopy.*

8. Shiri F, Feng H, Petersen KE, Sant H, Bardi GT, Schroeder LA, **Merchant ML**, Gale BK, Hood JL. Separation of U87 glioblastoma cell-derived small and medium extracellular vesicles using elasto-inertial flow focusing (a spiral channel). *Sci Rep*. 2022 Apr 12;12(1):6146. doi: 10.1038/s41598-022-10129-8. PMID: 35414673; PMCID: [PMC9005724](#).

Impact Statement: *Developing advanced methods to isolate nanoscale and microscale cell-derived extracellular vesicle (EV) types and subtypes are of significant interest to the EV research community in general given their functional, diagnostic and therapeutic potential. The elasto-inertial focusing system developed in the manuscript is a novel compact microfluidic device that mechanistically works like gold standard differential ultracentrifugation for EV isolation. Because of its compact size, it can potentially be integrated with other microfluidic lab-on-a-chip and similar technologies to enable scalable, continuous separation of small microliter to milliliter volume limited samples upstream or downstream on EV chip-based detection and capture devices.*

9. Lin Q, Chen O, **Wise JP Jr**, Shi H, **Wintergerst KA**, Cai L, Tan Y. FGF1 Δ HBS delays the progression of diabetic nephropathy in late-stage type 2 diabetes mouse model by alleviating renal inflammation, fibrosis, and apoptosis. *Biochim Biophys Acta Mol Basis Dis*. 2022 Apr 18;1868(8):166414. doi: 10.1016/j.bbadis.2022.166414. Epub ahead of print. PMID: [35447340](#).

Impact Statement: *Elderly adults are at higher risk for developing diabetic complications including diabetic nephropathy (DN), contributing to excess morbidity and mortality in elderly individuals. A non-mitogenic variant of fibroblast growth factor 1 (FGF1 Δ HBS) was found to prevent DN in an early-stage (2-month-old) type 2 diabetes (T2D) mouse model. The present study demonstrated that FGF1 Δ HBS was also able to delay the progression of renal dysfunction likely through activating PPAR α to prevent renal tubule cell death in late-stage T2D, exhibiting a promising translational potential in treating DN in elderly T2D individuals by ameliorating renal inflammation, fibrosis, and apoptosis.*

10. Faley TOC, Driver EM, Bowes DA, Holm RH, Talley D, **Yeager R**, **Bhatnagar A**, Smith T, Varsani A, Halden RU, Scotch M. Detection of Human, Porcine and Canine Picornaviruses in Municipal Sewage Sludge Using Pan-Enterovirus Amplicon-based Long-read Illumina Sequencing. *Emerg Microbes Infect*. 2022 Apr 27:1-25. doi: 10.1080/22221751.2022.2071173. Epub ahead of print. PMID: [35475464](#).

Impact statement: *The findings of this paper show that sludge from different stages wastewater treatment can be used for surveillance of viruses from humans and other animals. These results could be applied to improve population coverage and cost-effectiveness of largescale wastewater surveillance for viral disease outbreaks.*

11. Zhang Y, Mo Y, Yuan J, Zhang Y, Mo L, **Zhang Q**. MMP-3 activation is involved in copper oxide nanoparticle-induced epithelial-mesenchymal transition in human lung epithelial cells. *Nanotoxicology*. 2021 Dec;15(10):1380-1402. doi: 10.1080/17435390.2022.2030822. Epub 2022 Feb 2. PMID: [35108494](#).

Impact Statement: *Copper oxide nanoparticles (Nano-CuO) are widely used in medical and industrial fields and our daily necessities. However, the biosafety assessment of Nano-CuO is far behind their rapid development. Our study demonstrated that Nano-CuO exposure caused mitochondrial ROS generation, MAPKs activation, and MMP-3 upregulation. Nano-CuO exposure also caused cells to undergo EMT, which was through Nano-CuO-induced dysregulation of ROS/MAPKs/MMP-3 pathway. Our findings will provide further understanding of the potential mechanisms involved in metal nanoparticle-induced various toxic effects including EMT and pulmonary fibrosis.*

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