



CIEHS Up to Date News and Accomplishments

Awards Announcements and Reminders

CIEHS Research Voucher Application

CIEHS Research Voucher applications are now being accepted to support integration of OMICS and exposure studies, and proposals which leverage pre-existing biorepositories and human subjects research facilities. Applications for this cycle are due by **Friday, August 5, 2022!** For the August 5th submission date, priority will be given to proposals focusing on exposome and/or climate change and or/ environmental justice. Research voucher applications are submitted online, find out more information [HERE](#).

Walter H. Watson, Ph.D. Awarded OEFC Voucher Award

Congratulations to Dr. Walter Watson who was recently awarded the CIEHS Medium OEFC Research Voucher Award. View on the CIEHS website [HERE](#).

Principal Investigator: [Walter H. Watson, Ph.D.](#)

Collaborators: [J. Christopher States, Ph.D.](#), [Ana Ferragut-Cardoso, Ph.D.](#)

Title: Comparative keratinocyte responses to environmental arsenic
Description: Environmental arsenic is a world-wide health problem, and the skin is one of the major target organs of arsenic toxicity. Our OEFC Research Voucher Award from the CIEHS will help us answer the question of why some skin cells are resistant to arsenic toxicity while others are not. We will use ICP-MS to assess rates of arsenic import and export by different keratinocyte cells. The results should shed light on how differences in formation and export of glutathione-arsenic complexes translate into differences in sensitivity to cell death and transformation into cancer cells.

Walter H. Watson, Ph.D.

Awarded a CIEHS Medium OEFC Research Voucher Award

Congratulations to Dr. Watson for his newly awarded OEFC Research Voucher Award from the CIEHS entitled "Comparative keratinocyte responses to environmental arsenic". 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!



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ENVIRONMENTAL HEALTH SCIENCES

Dr. Walter Watson Social Media Post

Dr. J. Christopher States received a diversity supplement on the CIEHS P30 grant. This supplement provides two years' support for Dr. Jamie L. Young in her new appointment as Assistant Professor of Pharmacology and Toxicology. Her research will focus on the role of chromium and PFAS exposure in liver disease etiology.

Have a CIEHS Core Question?

Do you have questions pertaining to a specific CIEHS Core? Several CIEHS Cores have their own service email accounts where you can reach out to the core directly.

CIEHS advises using these service accounts to ensure a timely response.

Center for Integrative Environmental Health Sciences (CIEHS) Administration Core
ciehs@louisville.edu

Integrated Health Science Facility Core (IHSFC)
ihsfc@louisville.edu

Pilot Project Program (PPP)
pilotprojects@louisville.edu

Biostatistics and Informatics Facility Core (BIFC)
bifc@louisville.edu

Omics & Exposure Facility Core (OEFC)
oefc@louisville.edu

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Awards Announcements and Reminders Continued

2022 Exposome Symposium & NIEHS EHSCC Meeting in NY

Colleen Quinter and Drs. J. Christopher States, Matthew Cave, Natasha DeJarnett and Luz Huntington-Moskos traveled to New York City, NY for the 2022 Exposome Symposium (July 12-13) and NIEHS EHSCC Directors Meeting July (13-15). Dr. Matthew Cave presented on Environmental Liver Disease at the 2022 NYC Exposome Symposium at Mount Sinai. Dr. States attended multiple Center Director meetings and plenary sessions. Dr. Natasha DeJarnett represented the CIEHS P30 Center as an Early Stage Investigator and presented her poster/gave a presentation on her work entitled "Climate Changed Health: Assessing Temperatures and Heart Health in an Urban Greening Intervention Study". Dr. Huntington-Moskos attended several breakout sessions for the Community Engagement Core. The NIH P30 Business Administrator's had multiple meetings/presentations surrounding topics of interest to Business Admins including a presentation by Dr. Claudia Thompson, NIEHS Branch chief; Jenny Greer, NIEHS Chief Grants Management Officer; Dr. Linda Bass, Scientific Review Officer and Deputy Branch Chief; and Martha Barnes, Program Analyst for Human Subjects Research. Read more about the NIEHS EHSCC Directors Meeting on page 4.



J. Christopher States, Luz Huntington-Moskos,
Colleen Quinter, Matthew Cave, Natasha DeJarnett (left to right)



Dr. Natasha DeJarnett

Banrida Wahlang, Ph.D, NIH K01 Awardee

Dr. Banrida Wahlang, MOT Subgroup Leader, received the NIH K01 Award for her work entitled "Evaluating mechanisms of sex differences in environmentally-induced metabolic diseases". Dr. Loretta Jophlin, MOT RIG member, is also a previous NIH K01 awardee for her work entitled "Interaction of the Microtubule Cytoskeleton and Perilipin-2 Regulates Hepatic Lipid Droplets- a Potential Therapeutic Target for Fatty Liver Disease".

Natasha K. DeJarnett, PhD, MPH, featured on Faulkner Focus

Dr. Natasha DeJarnett, MOT RIG member, was featured on Fox News 'The Faulkner Focus' as a member of the 'Voters Voices' panel on June 8, 2022, to speak about top concerns of the upcoming 2022 midterm election and opportunities for protection of health. View the segment HERE.

Alex P. Carll, PhD, MSPH, WLKY Interview

Dr. Alex Carll was interviewed by Louisville's WLKY news station for his recent \$3.6 million grant from the Food and Drug Administration and National Institutes of Health to research chemicals found in e-cigarettes. Dr. Carll emphasizes the toxicity of certain flavors, "It's not necessarily my place as a scientist to say what's right and what's wrong when it comes to flavors, but I can inform at least on the toxicity of individual flavorant chemicals." Watch the full interview HERE.

Gregory Barnes, MD, PhD, New Patent

Dr. Gregory Barnes, CIEHS Neuro RIG Leader, in collaboration with Dr. Ayman El-Baz and postdoctoral researchers Mohammed Elmogly and Fatmaelzahraa El-gamel are inventors on a newly issued patent, U.S. 11,151,717. This patent is for a non-invasive personalized computer-aided diagnosis system for early detection of Alzheimer's Disease (AD). This system can provide a comprehensive diagnosis of the different stages of AD.

Luz Huntington-Moskos, Ph.D., RN, CPN, promoted to Associate Professor

Congratulations Dr. Huntington-Moskos, Community Engagement Core Director, for being promoted to Associate Professor with tenure. Dr. Huntington-Moskos gives many thanks to people who have helped her along the way including CIEHS Director, Dr. J. Christopher States.

Awards Announcements and Reminders Continued

Natasha K. DeJarnett, PhD, MPH, quoted in the Courier Journal

Dr. [Natasha DeJarnett](#) was quoted in the July 19, 2022 Courier Journal e-Edition article entitled "LG&E says it's on track to cut carbon emissions". The article covers LG&E's commitment to achieving net zero by 2050 despite the U.S. Supreme Court's ruling 6-3 against the Environmental Protection Agency. Dr. DeJarnett comments on Louisville's "fenceline communities", communities that have only a chain link fence separating them from chemical plants. Dr. DeJarnett said, "A challenge is that often, decisions are not informed by health. We need to ensure that health voices are at the table, voices of the community are at the table, voices of those that will be affected by the decision." Read the full article [HERE](#).

CIEHS Environmental Health Series Seminar

CIEHS welcomes Dr. [Cynthia Corbitt](#), Neuro RIG member, as the next speaker for the monthly Environmental Health Series (EHS) seminar on Thursday, August 4th at 11 AM ET. This will be a hybrid event.

Click [HERE](#) in case you missed Dr. [Banrida Wahlang](#)'s seminar entitled "Mechanisms of Environmental Contributions to Fatty Liver Disease" on July 7th. You can find all of the past CIEHS EHS seminars on our [YouTube channel](#) and a full seminar schedule on the CIEHS [website](#).

Pilot Project Awardee Spotlight: Dr. Edrisa Sanyang

Edrisa Sanyang, Ph.D., received the CIEHS Community-Engaged Pilot Project Award in 2020. Learn more about Dr. Sanyang's award entitled "Firefighter Practices and Exposure in Response to Covid-19 in Northwestern Kentucky" by watching the recent Pilot project Awardee Spotlight video [HERE](#).

Natasha K. DeJarnett, PhD, MPH, Co-Lead Author

Dr. [Natasha DeJarnett](#) has been named co-lead author of the [2022 Lancet Countdown](#) on Health and Climate Change and companion U.S. policy brief, which will be published in October. The Lancet Countdown report is an international research collaboration that monitors and reports annually on the relationship between health and climate.

Congratulations to Jilian Winn, BA, research assistant in the Department of Psychological and Brain Sciences and student of Lonnie Sears, PhD, who received a Developmental Neurotoxicology 2022 Conference Award for her presentation entitled "Neurobehavioral Health of Children Living Near Coal Ash Storage Sites", which included research from her senior thesis.

Community Engagement Core Corner

During the months of June and July, the CEC participated in a number of activities. Over a two-week period at the end of June, Dr. Huntington-Moskos met with the Girls Incorporated organization in Owensboro, Kentucky where she taught a group of young women about environmental health topics including disaster preparedness, radon awareness, personal care products, bees as pollinators, and safe drinking water. In mid-July, Dr. Huntington-Moskos along with Ms. Quinter, Dr. DeJarnett, Dr. Cave, and Dr. States attended the annual NIEHS meeting in New York City. Our collaboration with Mr. Tony Arnold of the University of Louisville's Brandeis School of Law is growing. Watch our CEC webpage for a [bi-monthly blog posts authored by the Resilience Justice Fellows, discussing the intersection of environmental law and environmental health](#). The blogs will discuss an array of topics including green and blue infrastructure, air quality, PFAS, climate change, and health equity in relation to environmental justice.



CIEHS table at SPHIS Gray Street Farmer's Market



Screenshot of Dr. Tony Arnold's blog series 'Environmental Justice and Health: A Blog for Communities'

The Gray Street Farmer's Market has been an excellent venue for the CEC to reach out to the university community and surrounding neighbors. The market is held on the first Thursday of every month and we encourage our CIEHS investigators and staff to attend after the monthly CIEHS seminar. The remaining of the dates are August 4th, September 1st, and October 6th. Feel free to stop by and spin our prize wheel!

Finally, we are sad to note that Ms. Josie Willis is no longer part of the CIEHS CEC staff. We greatly value the time she invested in the CEC over the past year and wish her the best in her future endeavors.

Notes from the Director:

July, 2022

As noted above, several of us attended the NIEHS Core Center Directors meeting hosted by Mt. Sinai Medical Center P30 Center in NY City. The meeting was very informative and we learned about the new directions for the NIEHS. Despite not receiving the extra \$100 million to support climate change research in its budget, Dr. Woychik indicated that he intends to emphasize the topic. He pointed to the webpage on the NIH Climate Change and Health Initiative, three NOSI's (NOT-ES-22-006, NOT-ES-22-009, NOT-ES-22-010) and an RFA (RFA-ES-22-003) related to climate change and encouraged people to apply.

The Climate Change and Health topic was explored in a session featuring short talks by Early Stage Investigators. Our own Dr. Natasha DeJarnett presented her work on assessing extreme temperatures and heart health highlighting the effects of heat islands. Dr. Carina Gronlund from University of Michigan (M-LEEd) discussed the ramifications of flooding in Detroit noting that incidents were not simply related to proximity to rivers and low elevations. Dr. Rima Habre from University of Southern California (USEHSC) presented on health effects of wildfire smoke exposure highlighting the complexity of wildfire smoke plumes and the difficulty in modeling chemistry and dynamics. Dr. Jacob Simmering from University of Iowa (EHSRC) presented his study on increased incidence of kidney stones associated with warmer weather and the sex dependence of stone occurrence. Dr. Robbie Parks from Columbia University (CEHJNM) focused his presentation on the health impacts of tropical cyclones and that the impacts include long-term effects in addition to the acute effects.

Dr. Woychik also spent some time discussing the initiative in personalized environmental health. This concept is championed by Drs. Dana Dolinoy (U. Michigan Ann Arbor), Andrea Baccarelli (Columbia University) and Cheryl Walker (Baylor College of Medicine), all EHSCC Directors. The definition integrates Genes x Epigenetics x Data x Exposome. The goal is to understand how genetic susceptibility modified by epigenetics interacts with environmental exposures throughout the lifespan and to use 'big data' approaches. It is no coincidence that the CIEHS goals share much with this concept. Now if the study sections would only get on board! 😊

Looking toward the future NIEHS emphasis on these topics, we are looking to promoting research with the current voucher solicitation and a second RFA for pilot awards later this year. Bear in mind that pilot award applications must convince reviewers of their potential to generate data to support and NIEHS R01 application. Thus, preliminary data are needed. If you have a good idea but no preliminary data, a medium research voucher application would be appropriate.

MEMBER GRANT AWARDS MARCH & APRIL 2022

Congratulations to the CIEHS members who had new grants, supplements and competitive renewals activated/awarded in the months of March & April 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
Barve, Ashutosh Jayant	Jophlin, Loretta Lynn	LAM-2018-01- Prospective Clinical Trial to Detect Liver Cancer through Quantification of cfDNA Methylation in Blood Samples (CLiMB) Protocol LAM-2018-01	SC liver Research Consortium	\$218,414.00

This is a clinical trial designed to evaluate the performance of a multi-analyte blood test alone, ultrasound alone and the combination of both the multi-analyte blood test and ultrasound for the detection of HCC within a population that is at high risk for HCC due to liver cirrhosis.

Sandell, Lisa Leopold	LeBlanc, Amanda Jo	Therapeutic vascularization to support repair of damaged salivary glands	National Institutes of Health	\$371,391.00
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Loss of salivary gland function is a devastating condition. Millions of people lose salivary gland function from autoimmune disease or cancer radiation treatment, and therapies to promote gland repair are needed. Repair of salivary gland tissues requires re-growth of blood vessels that can support salivary gland tissue as it heals from damage.

Carll, Alex P		Systematic identification of cardiotoxic e-cigarette flavorants	National Institutes of Health	\$713,734.00
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Electronic cigarettes (e-cigs) aerosolize a mixture of chemical solvents, flavor additives and nicotine, and inhalation of the resultant aerosol by e-cigarette users has unknown effects on the heart. In this project, we will examine how specific flavoring chemicals that are inhaled during e-cigarette use impact the function of mouse and human heart cells and tissues. Ultimately, this study will advance knowledge of the toxicity of e-cigarettes, which will direct new regulation of e-liquid constituents based on their potential for adverse effects on the heart.

Total New Awards March & April 2022: \$1,303,539.00

MAY PUBLICATIONS HIGHLIGHTS

Congratulations to the CIEHS members with articles published in the month of May! 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. Nail AN, McCaffrey LM, **Banerjee M**, Ferragut Cardoso AP, **States JC**. Chronic arsenic exposure suppresses ATM pathway activation in human keratinocytes. *Toxicol Appl Pharmacol*. 2022 Jul 1;446:116042. doi: 10.1016/j.taap.2022.116042. Epub 2022 May 2. PMID: [35513056](#).
Impact Statement: *Our research sheds direct light on the most accepted explanation for the mode of action of arsenic carcinogenicity in arsenic's major target organ, skin. Arsenic is known to induce DNA breaks without directly interacting with DNA. We have discovered that a major signaling protein for DNA break repair, ataxia telangiectasia-mutated (ATM), has reduced activation in human keratinocytes chronically exposed to inorganic arsenic. ATM plays an important role in DNA repair by activating enzymes that can fix DNA strand breaks in cells, preventing the accumulation of mutations in cells and carcinogenesis. Thus, it could be hypothesized that arsenic-induced tumors may be more sensitive to certain cancer treatments that induce DNA damage or inhibit DNA repair, such as radiotherapy or PARP inhibitors, respectively. Based on these findings, additional studies are needed determine whether arsenic-induced tumors are sensitive to specific chemotherapeutic regimens. Results from these future studies could be used to design new strategies to treat arsenic-induced cancers.*
2. Berlowitz JB, Xie W, Harlow AF, Hamburg NM, Blaha MJ, **Bhatnagar A**, Benjamin EJ, Stokes AC. E-Cigarette Use and Risk of Cardiovascular Disease: A Longitudinal Analysis of the PATH Study (2013-2019). *Circulation*. 2022 May 17;145(20):1557-1559. doi: 10.1161/CIRCULATIONAHA.121.057369. Epub 2022 May 6. PMID: [35514292](#).
Impact Statement: *Despite increasing popularity of electronic cigarettes (e-cigarettes), the long-term health effects of habitual e-cigarette use remain unclear. Our results suggest that combining smoking with e-cigarette use does not reduce cardiovascular disease (CVD) events and that quitting both products is required to ensure a mitigation of risk.*
3. Gibson JM, Chu T, Zeng W, Wethall AC, Kong M, Mellen N, Devlin Phinney LA, **Cai J**. Perinatal methadone exposure attenuates myelination and induces oligodendrocyte apoptosis in neonatal rat brain. *Exp Biol Med (Maywood)*. 2022 Apr 27;15353702221090457. doi: 10.1177/15353702221090457. Epub ahead of print. PMID: [35475383](#).
Impact Statement: *Methadone (MTD) is a common medication treatment for opioid use disorder (OUD) during pregnancy. In this study, pregnant rats were administered a dosing approximately equivalent to the OUD treatment and the effects of passive in utero and postnatal MTD exposure on myelin development was investigated in neonatal rat brain. The findings reveal the potential mechanism(s) underlying the association between myelin impairment and antenatal opioid exposure. Our study alongside others concerns for fetal brain development when using MTD to manage the OUD during pregnancy. Improved understanding of the effects of opioid exposure will allow us to design treatments for OUD during pregnancy that minimize effects on the fetal brain or target postnatal treatment to mitigate the effects of antenatal opioid exposure.*
4. Halder S, Xie Z, Nantz MH, **Fu XA**. Integration of a micropreconcentrator with solid-phase microextraction for analysis of trace volatile organic compounds by gas chromatography-mass spectrometry. *J Chromatogr A*. 2022 Apr 22;1673:463083. doi: 10.1016/j.chroma.2022.463083. Epub ahead of print. PMID: [35508097](#).
Impact Statement: *This paper reports a simple method of integrating microfabricated preconcentrators with commercial SPME fibers in a two-stage concentration processes to achieve rapid and reliable measurement of trace VOCs in environmental air by GC-MS. This approach has been demonstrated for measurements of toxic VOCs including benzene, toluene, ethylbenzene, xylene (BTEX) and trichloroethene (TCE).*
5. Monreal G, Koenig SC, Slaughter MS, Morello GF, Prina SR, Tompkins LH, **Huang J**, Gellman BN, Dasse KA. Feasibility testing of the Inspired Therapeutics NeoMate mechanical circulatory support system for neonates and infants. *PLoS One*. 2022 May 11;17(5):e0266822. doi: 10.1371/journal.pone.0266822. PMID: 35544516; PMCID: [PMC9094552](#).
Impact Statement: *In this article, we present the development of the prototype Inspired Therapeutics NeoMate System for pediatric left ventricular assist device (LVAD) support, and feasibility testing in static mock flow loops (H-Q curves), dynamic mock flow loops (hemodynamics), and in an acute healthy ovine model (hemodynamics and clinical applicability).*

MAY PUBLICATIONS HIGHLIGHTS CONTINUED

6. Sagaram M, Parthasarathy R, Condon SL, Closson CF, Kong M, Schwandt ML, **Jophlin LL**, Feng W, Barve AJ, Vatsalya V. Theragnostic Efficacy of K18 Response in Alcohol Use Disorder with Clinically Significant Fibrosis Using Gut-Liver Axis. *Int J Mol Sci.* 2022 May 23;23(10):5852. doi: 10.3390/ijms23105852. PMID: 35628661; PMCID: [PMC9143806](#).
Impact Statement: *Fibrosis in early-stage alcohol-associated liver disease (ALD) is commonly under-diagnosed in routine clinical practice. This study characterized the liver-injury and cell death response in alcohol use disorder (AUD) patients with ALD who also exhibited fibrosis and assessed the efficacy of standard of care (SOC) treatment in the improvement in liver injury..*
7. Teng Y, Mu J, Xu F, Zhang X, Sriwastva MK, Liu QM, Li X, Lei C, Sundaram K, Hu X, Zhang L, **Park JW**, Hwang JY, Rouchka EC, Zhang X, Yan J, **Merchant ML**, Zhang HG. Gut bacterial isoamylamine promotes age-related cognitive dysfunction by promoting microglial cell death. *Cell Host Microbe.* 2022 May 25:S1931-3128(22)00265-7. doi: 10.1016/j.chom.2022.05.005. Epub ahead of print. PMID: [35654045](#).
Impact Statement: *The gut microbiome has recently revealed itself to be a major player in human health and disease. Here, Drs. Huang-Ge Zhang and collaborators including CIEHS members Michael Merchant and Jun Won Park, show that a small metabolite, isoamylamine (IAA) produce by the bacteria Ruminococcaceae is enriched in aged mice and elderly people. Interestingly a bacteriophage belonging to the Myoviridae family that infects Ruminococcaceae are reduced in these settings. IAA induced cognitive declines in young mice is reversed by Myoviridae phage administration. IAA promoted apoptosis of microglial cells through a p53 dependent mechanism. Our results linked microbiome metabolites to direct transcriptional co-regulation of genomic DNA. These findings suggest a molecular mechanism connecting gut metabolism to gene expression in the brain with implications for disease development.*
8. Bhattacharyya A, Pal S, Mitra R, **Rai S**. Applications of Bayesian shrinkage prior models in clinical research with categorical responses. *BMC Med Res Methodol.* 2022 Apr 28;22(1):126. doi: 10.1186/s12874-022-01560-6. PMID: 35484507; PMCID: [PMC9046716](#).
Impact Statement: *Developing accurate prediction method benefits personalized medicine, involving patient's demographic, history, and gene signatures. Bayesian shrinkage models have emerged as popular and flexible methods of variable selection in regression settings. This work discusses variable selection and illustrates its application to multiple clinical studies, such as Pima Indians Diabetes, Colon cancer, ADNI, and OASIS Alzheimer's data sets. Informative priors can be used for robust and efficient prediction with accuracy of 91.6% (95% CI: 88.5, 94.7). The proposed method is robust to conduct both variable selection and prediction.*
9. Miller HA, **Rai SN**, Yin X, Zhang X, Chesney JA, van Berkel VH, Frieboes HB. Lung cancer metabolomic data from tumor core biopsies enables risk-score calculation for progression-free and overall survival. *Metabolomics.* 2022 May 14;18(5):31. doi: 10.1007/s11306-022-01891-x. PMID: [35567637](#).
Impact Statement: *Metabolomics has emerged as a powerful method to provide insight into cancer progression, including separating patients into low- and high-risk groups for overall (OS) and progression-free survival (PFS). This proof-of-concept study evaluates metabolites as biomarkers obtained directly from tumor core biopsies along with covariates age, sex, pathological stage at diagnosis (I/II vs. III/IV), histological subtype, and treatment vs. no treatment. A prediction model is developed to stratify patients into low- and high-risk groups based on log-transformed intensities of key metabolites. Risk scores based on 10 metabolites for OS and 5 metabolites for PFS were significant predictors of survival. Risk scores were validated with SPLS-DA classification model (AUROC 0.868 for OS and AUROC 0.755 for PFS, when combined with covariates. Thus, metabolomic analysis of lung tumor core biopsies has the potential to differentiate patients into low- and high-risk groups based on OS and PFS events and probability.*
10. King KM, McKay T, Thrasher BJ, **Wintergerst KA**. Maximal Oxygen Uptake, VO2 Max, Testing Effect on Blood Glucose Level in Adolescents with Type 1 Diabetes Mellitus. *Int J Environ Res Public Health.* 2022 May 3;19(9):5543. doi: 10.3390/ijerph19095543. PMID: 35564936; PMCID: [PMC9102981](#).
Impact Statement: *Individuals with type 1 diabetes face many challenges when participating in sporting activities and general exercise. This publication offers some glucose control guidance for athletes participating in maximal aerobic exercise. In addition to benefiting individuals with T1D, this article may also be beneficial to coaches, physical educators, and parents of children participating in sporting activities.*
11. Yuan J, Wang T, Wang L, Li P, Shen H, Mo Y, **Zhang Q**, Ni C. Transcriptome-wide association study identifies PSMB9 as a susceptibility gene for coal workers' pneumoconiosis. *Environ Toxicol.* 2022 May 4. doi: 10.1002/tox.23554. Epub ahead of print. PMID: [35506645](#).
Impact Statement: *Coal workers' pneumoconiosis (CWP) is a type of typical occupational lung disease caused by prolonged inhalation of coal mine dust. The individuals' different genetic background may underlie their different susceptibility to develop pneumoconiosis, even under the same exposure level. This study aimed to identify susceptibility genes associated with CWP. We have identified PSMB9 as a novel susceptibility gene for CWP and provided important insights into the further exploration of the CWP pathogenesis.*

JUNE PUBLICATIONS HIGHLIGHTS

Congratulations to the CIEHS members with articles published in the month of June! 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. Bastick JC, **Banerjee M**, **States JC**. Zinc supplementation prevents arsenic-induced dysregulation of ZRANB2 splice function. *Environ Toxicol Pharmacol*. 2022 Jun 25;94:103921. doi: 10.1016/j.etap.2022.103921. Epub ahead of print. PMID: [35764259](#).

***Impact Statement:** This publication adds support to the hypothesis that zinc supplementation could mitigate the toxic effects of chronic low level arsenic exposure.*

2. Jiang M, Li F, Liu Y, Gu Z, Zhang L, Lee J, He L, Vatsalya V, Zhang HG, Deng Z, Zhang X, **Chen SY**, Guo GL, Barve S, **McClain CJ**, Feng W. Probiotic-derived nanoparticles inhibit ALD through intestinal miR194 suppression and subsequent FXR activation. *Hepatology*. 2022 Jun 11. doi: 10.1002/hep.32608. Epub ahead of print. PMID: [35689610](#).

***Impact Statement:** Intestinal farnesoid X receptor (FXR) plays a critical role in alcohol-associated liver disease (ALD). We aimed to investigate whether alcohol-induced dysbiosis increased intestinal microRNA194 (miR194) that suppressed Fxr transcription and whether Lactobacillus rhamnosus GG-derived exosome-like nanoparticles (LDNPs) protected against ALD through regulation of intestinal miR194-FXR signaling in mice.*

3. Sutaria SR, Gori SS, Morris JD, Xie Z, **Fu XA**, Nantz MH. Lipid Peroxidation Produces a Diverse Mixture of Saturated and Unsaturated Aldehydes in Exhaled Breath That Can Serve as Biomarkers of Lung Cancer-A Review. *Metabolites*. 2022 Jun 18;12(6):561. doi: 10.3390/metabo12060561. PMID: 35736492; PMCID: [PMC9229171](#).

***Impact Statement:** The paper provides a comprehensive review of saturated and unsaturated aldehydes in exhaled breath and their sources from lipid peroxidation. Some of these aldehydes in exhaled breath have been reported as biomarkers of lung cancer.*

4. Wise JTF, Salazar-González RA, Walls KM, Doll MA, Habil MR, **Hein DW**. Hexavalent chromium increases the metabolism and genotoxicity of aromatic amine carcinogens 4-aminobiphenyl and β -naphthylamine in immortalized human lung epithelial cells. *Toxicol Appl Pharmacol*. 2022 Jun 2;449:116095. doi: 10.1016/j.taap.2022.116095. Epub ahead of print. PMID: [35662664](#).

***Impact Statement:** Human carcinogens to which humans are exposed by inhalation include 4-aminobiphenyl, β -naphthylamine and hexavalent chromium. Whereas the effects of the individual carcinogens have been investigated, this study investigated the effects of co-exposure of these carcinogens in human lung cells. The study documented that hexavalent chromium increased N-acetyltransferase 1 activity contributing to increased genotoxicity from 4-aminobiphenyl or β -naphthylamine.*

5. Yan K, Mei Z, Zhao J, Prodhan MAI, Obal D, Katragadda K, Doelling B, Hoetker D, Posa DK, He L, Yin X, Shah J, Pan J, **Rai S**, Lorkiewicz PK, Zhang X, Liu S, **Bhatnagar A**, Baba SP. Integrated Multilayer Omics Reveals the Genomic, Proteomic, and Metabolic Influences of Histidyl Dipeptides on the Heart. *J Am Heart Assoc*. 2022 Jun 22:e023868. doi: 10.1161/JAHA.121.023868. Epub ahead of print. PMID: [35730646](#).

***Impact Statement:** To identify histidyl dipeptide-mediated responses in the heart, we used an integrated triomics approach, which involved genome-wide RNA sequencing, global proteomics, and unbiased metabolomics to identify the effects of cardiospecific transgenic overexpression of the carnosine synthesizing enzyme, carnosine synthase (Carns), in mice. Our result showed that higher myocardial levels of histidyl dipeptides were associated with extensive changes in the levels of several microRNAs, which target the expression of contractile proteins, β -fatty acid oxidation, and citric acid cycle (TCA) enzymes. Global proteomic analysis showed enrichment in the expression of contractile proteins, enzymes of β -fatty acid oxidation, and the TCA in the Carns transgenic heart. Integration of multiple data sets suggested that β -fatty acid oxidation and TCA pathways exhibit correlative changes in the Carns transgenic hearts at all 3 levels. Conclusions Taken together, these findings reveal a central role of histidyl dipeptides in coordinated regulation of myocardial structure, function, and energetics.*

6. Kumar R, Adhikari S, Driver EM, Smith T, **Bhatnagar A**, Lorkiewicz PK, Xie Z, Hoetker JD, Halden RU. Towards a novel application of wastewater-based epidemiology in population-wide assessment of exposure to volatile organic compounds. *Sci Total Environ*. 2022 Jun 27:157008. doi: 10.1016/j.scitotenv.2022.157008. Epub ahead of print. PMID: [35772546](#).

***Impact Statement:** This is the first study to utilize wastewater to detect urinary biomarkers of volatile organic compounds (VOCs) exposure. These preliminary results suggest the wastewater-based epidemiology approach as a potentially powerful tool to assess community health exposures to indoor and outdoor air pollutants.*

JUNE PUBLICATIONS HIGHLIGHTS CONTINUED

7. Polivka BJ, **Huntington-Moskos L**, Antimisiaris DE, Cavallazzi RS, Folz RJ. Phenotyping older adults with asthma by means of cluster analysis. *Ann Allergy Asthma Immunol.* 2022 Jun 10;S1081-1206(22)00501-4. doi: 10.1016/j.anai.2022.06.003. Epub ahead of print. PMID: [35697194](#).
Impact Statement: Whereas a number of publications have identified asthma phenotypes in adults, few have focused only on older adults. As a component of a randomized controlled trial of older adults (≥ 50 years old) with persistent asthma, Baptist et al identified 4 phenotypic clusters. The purpose of this study was to compare findings from the Baptist et al study with cluster analysis findings from a cohort of older adults with asthma participating in a longitudinal observational study.
8. McLeish KR, Shrestha R, Vashishta A, **Rane MJ**, Barati MT, Brier ME, Lau MG, Hu X, Chen O, Wessel CR, Spalding T, Bush SE, Ijemere K, Hopkins CD, Cooke EA, Tandon S, Manning T, Uriarte SM, **Huang J**, Yan J. Differential Functional Responses of Neutrophil Subsets in Severe COVID-19 Patients. *Front Immunol.* 2022 May 31;13:879686. doi: 10.3389/fimmu.2022.879686. PMID: 35711435; PMCID: [PMC9197482](#).
Impact Statement: Normal Density Neutrophils and Low Density Neutrophils from COVID-19 patients possess complementary functional capabilities that may act cooperatively to determine disease severity. We predict that global neutrophil responses that induce COVID-19 ARDS will vary depending on the proportion of neutrophil subsets.
9. Brady MP, Chava S, Tandon S, **Rane MJ**, Barati MT, Caster DJ, Powell DW. Serum and Urine Interferon Gamma-Induced Protein 10 (IP-10) Levels in Lupus Nephritis. *J Clin Med.* 2022 Jun 3;11(11):3199. doi: 10.3390/jcm11113199. PMID: 35683585; PMCID: [PMC9181282](#).
Impact Statement: Lupus nephritis (LN) is a severe complication of systemic lupus erythematosus and current diagnostics and treatments are inadequate. Our report identifies a potential diagnostic marker for LN and will therefore provide impactful insight for improved LN patient care.
10. **Watson WH**, Ritzenthaler JD, Torres-Gonzalez E, Arteel GE, Roman J. Mice lacking $\alpha 4$ nicotinic acetylcholine receptors are protected against alcohol-associated liver injury. *Alcohol Clin Exp Res.* 2022 Jun 20. doi: 10.1111/acer.14893. Epub ahead of print. PMID: [35723023](#).
Impact statement: Liver disease associated with long-term heavy drinking of alcoholic beverages is a major health problem with no FDA-approved therapies. In this paper, we describe a previously unknown mediator of alcohol's adverse effects on the liver: the alpha4 subunit of nicotinic acetylcholine receptors. These neurotransmitter receptors are known to be important in the brain, where they are involved in the reward pathways activated by both nicotine and alcohol. The discovery that they are also expressed in the liver and contribute to some of the earliest manifestations of alcohol-associated liver disease points to a new target for potential therapeutic interventions.
11. Rajesh M, Xin Y, **Young JL**, **Cai L**. Editorial: Cardiovascular Diseases Related to Diabetes and Obesity. *Front Endocrinol (Lausanne).* 2022 May 23;13:916142. doi: 10.3389/fendo.2022.916142. PMID: 35677720; PMCID: [PMC9169566](#).
Impact Statement: Worldwide, the prevalence of obesity continues rising unabated due to the rapid urbanization in the developed and developing countries and poor lifestyle habits. Obesity is also attributed to the development of major cardiovascular diseases (CVD), diabetes, arthritis, behavioral changes, depression, cancers, and hepatic diseases. Therefore, a special issue focus on the CVDs related to diabetes and obesity has been released, for which this editorial was and also briefly introduced the contents of the twelve publications, with a hope to set the stage for delving further in deciphering the crucial link between obesity and diabetes.

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