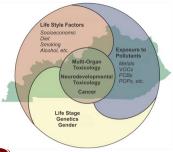


CENTER FOR INTEGRATIVE ENVIRONMENTAL HEALTH DECEMBER/JANUARY 2021-2022 | VOLUME 3, NO. 1 SCIENCES



NEWSLETTER

CIEHS Up to Date News and Accomplishments

Awards Announcements and Reminders

Community Engagement Video

The CIEHS Community Engagement Core has released the first community experience video. Janice and Sacha were enduring health problems related to the air quality impact of a local hemp processing facility in western Kentucky. The community members were able to get in touch with the Center for Integrative Environmental Health Sciences Community Engagement Core (CEC) through local connections. The CEC helped bring together this community to help stop this unexpected and unwelcome environmental exposure. View the community experience video on the CIEHS YouTube channel <u>HERE</u>. If you or someone you know is experiencing an environmental health concern in your community, please reach out to our center by filling out the CEC request form <u>HERE</u>.



CIEHS Environmental Health Series Seminar with Alexandra Nail, Ph.D. CIEHS welcomes Dr. Alexandra Nail as the next EHS seminar guest on Thursday, February 3rd, at 11 AM, presentation entitled "Arsenic Dysregulation of the DNA Damage Response in Human Keratinocytes". This will be a virtual event. View the January CIEHS EHS seminar with Lonnie L Sears, Ph.D. <u>HERE</u>, presentation entitled "Neurobehavioral Health in Children Living Near Coal Power Plants". You can find all of the past CIEHS seminars on our <u>YouTube channel</u> and a full seminar schedule on the <u>CIEHS website</u>.

Need assistance deciding which study section to choose? The NIH provides a tool to help investigators identify study sections that could potentially be appropriate to review your grant applications. Follow <u>THIS LINK</u> for the NIH Assisted Referral Tool (ART) tool.

WELCOME OUR NEW MEMBERS:

Administrative Core: Luis Salazar Guzman

Thank you!

A special thanks to all for a successful External Advisory Committee (EAC) meeting. We received great constructive feedback to help strengthen all segments of the center. We appreciate all of your hard work and support for this review that occurred on January 12, 2022!

CONNECT WITH US ON SOCIAL MEDIA:

Awards Announcements and Reminders Continued

Natasha K. DeJarnett, Ph.D., MPH Awarded BCES

Congratulations to Dr. Natasha DeJarnett, MOT RIG member, who was awarded the professional designation of <u>Board Certified Environmental</u> <u>Scientist</u> (BCES), concentrating in Environmental Toxicology, by the <u>American Academy of Environmental Engineers and Scientists (AAEES)</u>. This accord places DeJarnett among the top four percent of environmental engineering experts!

John P. Wise, Sr., Ph.D. RIVER Grant Press Release

Dr. John Wise, Sr. announced his newly awarded \$6.7 million RIVER grant during a press conference on Wednesday, January 26th. This grant funds a study to investigate why metals cause chromosome instability in humans but not in whales. The press conference was covered by local TV news WAVE3 and WHAS along with Louisville Business First. Find the full press release on the CIEHS website <u>HERE.</u> You can also review this event on the University of Louisville YouTube channel <u>HERE</u>.



Dr. John Wise, Sr. announcing RIVER Grant UofL OCM photo credit

Natasha K. DeJarnett, Ph.D., MPH featured in Citizens' Climate Radio Segment

Dr. Natasha DeJarnett, MOT RIG member, was featured in <u>Citizens' Climate Radio</u> episode 66: Hospitality in a time of climate change. DeJarnett spoke about how people are being displaced as a result of severe weather phenomena caused by climate change at an alarming rate compared to past weather phenomena. Listen to the full segment <u>HERE</u>.

Western Kentucky Tornado Relief

The CIEHS <u>Community Engagement Core</u> has been encouraged by a number of community partners in several western Kentucky counties to contribute to the <u>Team Western Kentucky Tornado Relief Fund</u>. The flexibility of financial donations will be essential and does not require the same sort of physical storage that item donations require. For other support resources, <u>WFPL</u> provides a list of ways to aid the tornado survivors <u>HERE</u>. Please continue to keep tornado survivors in western Kentucky in your thoughts.

Matthew Cave, MD quoted in NIEHS Environmental Factor Newsletter

Dr. Matthew Cave, IHSFC Core Director, has been quoted in the December issue of the <u>National Institute of Environmental Health (NIEHS)</u> <u>Environmental Factor</u> newsletter. Dr. Cave speaks on overnutrition, chemicals and the association with nonalcoholic fatty liver disease (NAFLD). Cave states "So, why should we be concerned about environmental health and the liver? As a liver physician, I can tell you there is an epidemic." Read more about the association of NAFLD and environment/nutrition <u>HERE</u>.

Anti-Racism Workshop

Thank you to everyone who attended the second Anti-Racism workshop facilitated by UofL's Center for Family & Community Well-Being. The third workshop will be on Wednesday, February 23rd from 2PM-4PM. It is not too late to sign up for the third workshop on February 23! Click <u>HERE</u> to register for workshop #3.

DEI Events

On February 2nd, 2022 at 4:30 PM the UofL Anne Braden Institute for Social Justice Research will feature guest speaker Jarvis R. Givens, PhD from the department of African & African American Studies at Harvard University for a virtual Black History Month presentation on the book "The Fugitive Life of Black Teaching: A History of Pedagogy & Power". You can attend this talk via MS Teams <u>HERE.</u>

In case you missed the virtual Martin Luther King celebration on January 17th, sponsored by UofL's African American Theatre Program, which includes a keynote address by Asst. Professor Sidney Monroe Williams, an interview with Elmer Lucille Allen, and artistic presentations, you can view the recording on YouTube <u>HERE</u>.



Tornado Relief Social Media post including #KentuckyStrong

The Anne Braden Institute's Black History Month Talk THE FUGITIVE LIFE OF BLACK TEACHING: A HISTORY OF PEDAGOGY AND POWER FEBRUARY 2, 2022 | 4:30 PM

Jarvis R. Givens, Ph.D is an assistant professor at the Harvard Graduate School of Education and a Faculty Affiliate in the department of African & African American Studies at Harvard University. He published his first book, Fugitive Pedacogy; Carter G. Woodson and the Art of Black Teaching in 2021.

Professor Givens offers the term "fugitive pedagogy" to characterize African Americans' subversive traditions of teaching and learning from the slavery era through Jim Crow. Using the life of famed educator and historian Carter G. Woodson as a lens, Givens reveals a expansive world of African American teachers who cultivated dreams and aspiration in generations of study



despite a world order built on black subjection. And as he will demonstrate, much of this work took place through discrete, quiet acts of resistance. Givens insists that black educators' pedagogical traditions were essential to the Long Black Freedom Struggle and formed the roots of anti-racis Leaching in the United States.

Join on Microsoft Teams: tinyurl.com/4b75kma9 EDUCATORS ARE HIGH 9 GOCOURAGED TO ATTIND



The Anne Braden Institute's Black History Month Talk Poster

Awards Announcements and Reminders

Continued

ITEMFC Research Voucher Awards

Congratulations to investigators who were awarded cycle 4 & Cycle 5 ITEMFC Research Voucher Awards! Learn more about the ITEMFC awards <u>HERE.</u>

Cycle 4 - October 2021 ITEMFC Voucher Awards

Principal Investigator: Barbara J. Clark, Ph.D. **Collaborator:** Carolyn M. Klinge, Ph.D. **Title:** STARD5 and lipid dysregulation with ER stress

Principal Investigator: Anna Gumpert, Ph.D.

Collaborator: Daniel Conklin, Ph.D. **Title**: Combined Effects of Air Pollution and Hypertension on Cardiovascular Remodeling

Cycle 5 - December 2021 Ready to Go ITEMFC Voucher Awards

Principal Investigator: Venkatakrishna Jala, Ph.D. Collaborator: Matthew Cave, M.D. **Title:** Combating environmental toxin, PCB-126 associated toxicities

Principal Investigator: Carolyn Klinge, Ph.D. **Collaborator:** Matthew C. Cave, M.D., Yan Li, M.D., Ph.D.,

Xiang Zhang, Ph.D.

Title: Epitranscriptome in a murine model of diet and PCB-induced HCC

Principal Investigator: J. Christopher States, Ph.D. **Collaborator:** Juw Won Park, Ph.D.

Title: Gene Fusions and In/del Mutations in Arsenic-induced Skin Cancer

Principal Investigator: Banrida Wahlang, Ph.D.

Collaborator: Carolyn Klinge, Ph.D., Matthew C. Cave, M.D. **Title:** Alterations in gut microbiome caused by long-term exposure to PCBs

Principal Investigator: Kupper Wintergerst, MD

Collaborator: Lu Cai, M.D., Ph.D., Yi Tan, Ph.D., Sara Watson, M.D. **Title:** Serum nonessential and essential metals in children

with type 1 & type 2 diabetes

Cycle 3 - December 2021 Ready to Go IHSFC Voucher Awards

Congratulations to investigators who were awarded cycle 3 Ready to Go IHSFC Research Voucher Awards! Learn more about the IHSFC Voucher Awards <u>HERE</u>.

Principal Investigator: Timothy O'Toole, Ph.D. **Collaborator:** NA

Title: Markers of physical strength and aging in the NEAT cohort

Principal Investigator: Lonnie Sears, Ph.D

Collaborator: Kristina Zierold, Ph.D. (UAB), Lu Cai, M.D., Ph.D., Clara Sears, Ph.D.

Title: Metal(loid) body burden in children living near coal power plants

Community Engagement Core

Corner

During the months of December and January, the Community Engagement Core has been busy supporting three communityengaged projects being conducted in: 1) Henderson, 2) Trigg County, and 3) Louisville, Kentucky, respectively. Outreach efforts with a focus on the PFAS exposure in Henderson, Kentucky have begun. Dr. Jamie Young is building community connections to provide support collaboration for water sample collection. With our Trigg County community partners, planning for a community gathering is underway and will be held later in the spring. Lastly, on December 11th, the CEC staff teamed up with members from the Wise Lab to study concrete dust in Louisville, Kentucky; this effort included isopod collection at/around the Waterfront Park. We at the CEC are excited to see these efforts grow to benefit communities across Western Kentucky and Greater Louisville.



Dr. Luz Huntington-Moskos (left) & Dr. Calvin Kouokam (right) searching for isopods

The impact of the December 10th tornadoes is of great concern to the CIEHS. We continue to reach out to our community partners to better understand how to support and aid communities in the months to come. Discussions with center investigators to develop disaster-focused, community-engaged research projects are present and ongoing. Additional environmental health outreach continues through presentations with our AHEC West and AHEC South Central partners and through an op-ed piece spearheaded by our Community Resource Coordinator, Ms. Josie Willis. This op-ed piece focused on radon awareness was submitted to the Messenger-Inquirer (Owensboro) and the Murray Ledger.

Feedback and evaluation regarding our website continues. The CEC staff would like to say how much we appreciate the time that several researchers and community members have taken to review our website and provide us with valuable feedback. Our Stakeholder Advisory Board has been very generous with their input to guide our CEC efforts and help us improve communication and outreach. A special thanks to Ms. Sarah Jump for recording and editing the first of several community member testimonials, which can be found on the <u>CIEHS YouTube channel</u> or on the <u>CEC portion of the CIEHS website</u>.

Notes from the Director:

We hope that you are coping well with the constant upheaval due to the ever changing COVID situation. The data are starting to look like the U.S. is rounding the corner on that Omicron variant surge. It is not quite clear yet whether Louisville has peaked but the sewage monitoring data suggest the peak in cases is near. CIEHS continues to adapt to the situation by switching to virtual meetings when advisable. We hope to be able to return to in-person meetings soon. Our next invited speaker is Dr. Michael (Miki) Ashner who will be presenting the seminar and visiting with CIEHS members March 3. His visit, be it in-person or virtual, will be hosted by the Neurodevelopmental Toxicology RIG. We are looking forward to his visit and the collaborations that may evolve.

The CIEHS research voucher and pilot project programs have been successful in recruiting investigators to environmental health science. Several new members have joined CIEHS during this fiscal year. We welcome them and look forward to their contributions to the research productivity of the membership.

CIEHS held the second review by its External Advisory Committee on January 12, 2022. The meeting was held on Zoom due to the Omicron surge and high positivity rate in Louisville. The Committee indicated that overall CIEHS is progressing well. They gave us good feedback on our programs with some suggestions for improvement. These improvements will be announced over the next few months as we implement changes in our voucher and pilot project programs. Stay tuned!

The second Research Performance Progress Report (RPPR) is being filed as this is being written. Thank you to all who contributed to the report itself, and to all who help make CIEHS a vibrant center with high impact on environmental health in Louisville and its regional community. Special thanks to Colleen Quinter for her skill in coordinating and keeping track of all the various components. An issue that arose in preparing the report was that only about a third of the publications with CIEHS members as authors have cited the P30 grant. This lack of citation will pose a problem when it comes time to prepare the competitive renewal. It is important that members recognize the contribution of the intellectual environment supported by CIEHS by citing P30ES030283 in their publications. We are looking forward to our third year of funding and supporting the outstanding environmental health science research and community outreach of the CIEHS membership.

The spring meetings are fast approaching. Many of our members and their laboratories participate in the Society of Toxicology. SOT plans for people to attend in person but they must show evidence of full vaccination for admission.

Students and post-docs presenting their environmental health science research at national meetings are eligible for a CIEHS travel award. Information and application form is available <u>here</u>. The CIEHS travel award fund was founded to fund these awards. Please consider contributing <u>here</u>.

CIEHS held two anti-racism workshops in addition to the workshop at the annual retreat. The third workshop is scheduled for February 23. There are still openings for those interested. Watch for a reminder email with registration information.

As you are aware, western Kentucky was struck by devastating tornadoes in December. CIEHS is developing a plan to provide our scientific expertise in responding to environmental disasters. The effort is being led by Dr. Luz Huntington-Moskos, our Community Engagement Core Director, and Dr. John Wise, Sr., our Deputy Director. They welcome all interested in contributing to this effort to contact them. Dr. Aruni Bhatnagar is arranging for interested CIEHS members to meet with local American Red Cross representatives to formulate a plan.

Upcoming Symposia and Meetings

John Wise, Jr., Ph.D. & Jamie Young Ph.D. at ISTERH Symposium in Germany

Congratulations to Drs. John Wise, Jr. and Jamie Young for serving as chair or co-chair for the upcoming International Society for Trace Element Research in Humans (ISTERH) symposium held in Aachen, Germany during the month of June 2022. Young will be serving as chair of a symposium entitled "Sexual Dimorphism in Metal-Associated Diseases" and will be presenting her accepted abstract entitled "Whole-life, low-dose cadmium exposure exacerbates diet-induced non-alcoholic fatty liver disease in male, but not female mice". Wise, Jr will be serving as co-chair for a symposium entitled "Metal Exposures throughout the Life Course: Epidemiological, Toxicological, and Exposure Challenges".

2022 SOT Meeting

Congratulations to CIEHS members who have accepted abstracts, are serving as chairs, and are awardees for the Society of Toxicology (SOT) annual meeting March 27-31, 2022 (Members names in bold). *Additional information can be received from the <u>SOT Online Planner</u>.

Awards

Toxicologist Mentoring Award John P. Wise Sr., Ph.D.

<u>Bristol Myers Squibb Graduate Student Research Training Award to Promote Diversity in Toxicology</u> Aggie Williams, BA (**Wise** GRA)

Project Title: "Particulate Hexavalent Chromium Exposure Suppresses BCDX2 Complex Response in Human Lung Cells"

Best Postdoctoral Publication Awards

Qian Lin, PhD

Title: "Activating Adenosine Monophosphate–Activated Protein Kinase Mediates Fibroblast Growth Factor 1 Protection from Nonalcoholic Fatty Liver Disease in Mice."

Authors: Lin, Qian, Zhifeng Huang, Genxiang Cai, Xia Fan, Xiaoqing Yan, Zhengshuai Liu, Zehua Zhao, Jingya Li, Jia Li, Hongxue Shi, Maiying Kong, Ming-Hua Zheng, **Daniel J. Conklin**, Paul N. Epstein, Kupper A. Wintergerst, Moosa Mohammadi, **Lu Cai**, Xiaokun Li, Yu Li, and Yi Tan. 2021.

<u>First Place Postdoctoral Research Award from the Dermal Toxicology Special Section</u> Alexandra Nail, PhD (**States** postdoctoral student)

Serving as Chair or Co-Chair

Chair: Mayukh Banerjee, Ph.D. Title: Metals II

Chair: Lu Cai, M.D., Ph.D.

Title: Cardiovascular Effects of Environmental Metals: New Preclinical and Clinical Insights

Chair: Idoia Meaza Title: Metals I (**Wise** GRA)

Chair: John P. Wise Sr., Ph.D. Title: All for One and One for All: One Environmental Health in Toxicology

Chair: **Jamie Young Ph.D.** Title: Let's Talk About Sex—Through the Lenses of a Toxicologist!

Co-Chair: Jamie Young, Ph.D.

Title: Cadmium and the Developmental Origins of Disease: The Implication of Early-Life Exposures on Health Later in Life

2022 SOT Meeting Continued

Accepted Abstracts (presenters underlined & abstract titles in italics)

Amraotkar A., Zhao J., Gomes D., Kumar M., Subheeswar M., **Bhatnagar A. B**, and <u>O'Toole T.</u> Does Carnosine Supplementation Protect from Air Pollution Exposure? The Nucleophilic Defense against PM Toxicity (NEAT) Trial

Banerjee M., Ferragut Cardoso A., Al-Eryani L., Kalbfleisch T., Srivastava S., Pan J., **Rai S. N.**, and **States J. C.** Longitudinal Dynamic Transcriptome Changes in a HaCaT Cell Line Model of Arsenic-Induced Squamous Cell Carcinogenesis

Bastick J. C., Banerjee M., and States J. C. Zinc Mitigates Arsenic-Induced Dysregulation of ZRANB2 Splice Function

Cai L., and James K. Chronic exposure to low-dose Cd induces or exacerbates obese-induced cardiac pathogenesis in mouse model

Cai L. Both Zn and Cd Induce Cardiac Metallothionein, but Zn Protects, while Cd Damages the Heart in Metabolic Syndrome or Diabetes

<u>Cave M.</u>, Pinkston C., Rai S., Wahlang B., Carswell G., Pavuk M., Birnbaum L., and Chorley B. *MicroRNA Liver Toxicity Biomarkers* Associated with Dioxin-Like Compounds Exposures in ACHS-II

Dai X., Wang K., Lin Q., Chen O., **Conklin D. J.**, Wintergerst K. A., **Cai L.**, Deng Z., and Tan Y. Nrf2 Transcriptional Upregulation of IDH2 to Tune Mitochondrial Dynamics and Rescue Angiogenic Function of Diabetic EPCs

<u>Ferragut Cardoso A. P.</u>, Nail A. N., **Banerjee M.**, **Wise S. S.**, and **States J. C**. Overexpression of miR-186 Accelerates Chromosomal Instability in Arsenic-Exposed Human Keratinocytes

Flores, M., and Wise, Sr., J.P. Space Toxicology: An Emerging Environmental Health Field

Gripshover T., **Wahlang B.**, Head K., **Young J,** Luo J., and <u>Cave M</u>. Investigating the Effects of PCB 126 in an Acute Rodent Alcohol Model

Habil M. R., Doll M. A., and **Hein D. W.** The impact of N-acetyltransferase 2 (NAT2) haplotype on beta-naphthylamine metabolism and its associated mutagenesis

Huang J. Metallomics profile in pulmonary hypertension patients.

Jin L., Xie Z., Lorkiewicz P., and Conklin D. J. Direct Effects of Biogenic Volatile Organic Compounds (BVOC) and BVOC Metabolites on Vascular Function

Kouokam, J.C., <u>Speer</u>, R.M., Meaza, I., Toyoda, J.H., Lu, H., Kong, M. and Wise, Sr., J.P. Analysis of the effects of particulate hexavalent chromium on global gene expression in human fibroblasts reveal the involvement of inflammation

Kucera C., Ramalingam A., Stephens D., Hodges A., **Conklin D. J.**, **Bhatnagar A.**, and **Carll A. P**. *E-cigarette Aerosols Induce* Arrhythmia in Mice Dependent on E-liquid and Device Characteristics

Li J., Wang W., Lin Q., Barati M. T., Zheng Z., Tan Y., **Cai L.**, and **Rane M**. Modulation of Renal Profibrotic Signaling in Diabetic Kidneys and TGF-β-Treated HK-11 Cells Is Associated with Altered Expression of KLF 5 Isoforms 1 and 3

Li Z., Li J., **Young J.**, Tan Y., **Rane M.**, and <u>Cai L.</u> Divergent Effects of Low and High Cadmium Exposures on High Fat Diet-Induced p38 MAPK Activation and Renal Damage

Lu, H., Wise, S.S., Hoyle, G., Toyoda, J.H., Speer, R.M, Croom-Perez, T.J., Meaza, I., Wise, Jr., J.P., Kouokam, J.C., Young J.L., Cai, L., Kondo, K., and Wise, Sr., J.P. Particulate hexavalent chromium inhibits homologous recombination repair in rat lung

Lu, H., Wise, S.S., Toyoda, J.H., Wise Jr. J.P., Speer, R.M, Bolt, A.M., Meaza, I., Wise, C.F., Wise, J.T.F., Young, J.L., and <u>Wise Sr. J.P.</u> Of Whales and Men, How Great Whales Evade Metal Induced Cancer.

Malovichko M. V., Taylor B. S., McFall S. A., Sithu S. D., Wickramasinghe N., **Conklin D. J.**, Hill B. G., Hellman J. L., and **Srivastava S**. *Trichloroethylene Exposure Triggers Adipose Tissue Inflammation in Mice*

2022 SOT Meeting Continued

Meaza I., Toyoda, J.H., Lu, H., Williams, A.R., and **Wise Sr. J.P.** Chromate-Induced Loss of RAD51 and Increased Chromosome Instability in Human Bronchial Epithelial Cells.

Meaza, I., Toyoda, J.H., Lu. H., Williams, A.R., Kouokam, J.C., and Wise, Sr., J.P. Missing Protein! Have You Seen it? Reward: to Cure Cancer

<u>Nail A.N.</u>, Assessing the Impact of Chronic Arsenic Exposure on DNA Repair Choice. Graduate Student Leadership Committee (GSLC) Three-Minute Thesis Competition

<u>Nail A. N.</u>, McCaffrey L., **Ferragut Cardoso A. P.**, **Banerjee M.**, and **States J. C.** *Chronic Arsenic Exposure Reduces DNA Damage Response Activation in Human Keratinocytes*

Nystoriak M., Luo L, **Bhatnagar A.**, and <u>Conklin D. J.</u> Altered Electrical Properties of hiPSC-Derived Cardiomyocytes in the Presence of E-cigarette Aerosol Constituent Aldehydes

Petri B. J., Piell K. M., Wahlang B., Andreeva K., Rouchka E. C., Jin J., Hardesty J. E., Merchant M. L., Pan J., Rai S. N., Cave M. C., and <u>Klinge C. M.</u>. Multi-'Omics Analysis Identifies PCB-Regulated Pathways in Nonalcoholic Fatty Liver Disease

<u>Richardson A.</u>, Krivokhizhina T., Lorkiewicz P., **D'Souza S.**, Srivastava S., **Bhatnagar A.**, and **Conklin D. J**. Effects of Electronic Cigarette Flavorant Additives on Human Platelet Aggregation Ex Vivo

<u>Salazar-Gonzalez R. A.</u>, Doll M. A., and **Hein D. W**. *Metabolism and genotoxicity of new psychoactive substances (NPS) and 4,4'*oxydianiline (ODA) is modified by N-acetyltransferase 2 genetic polymorphism

Toyoda, J.H., Speer, R.M., Meaza, I., Lu, H., **Kouokam, J.C.**, Williams, A.R., and **Wise, Sr., J.P.** *Hexavalent Chromium Induces Numerical Chromosome Instability Via Securin Disruption in Human Cells but Not in Whale Cells*

Watson W. H., and Burke T. J. Arsenic and Sulforaphane Increase TNF-Induced IL-8 Expression by Inhibiting HNF-4α

<u>Wahlang B.</u>, Singhal R., Andreeva K., Rouchka E. C., Beier J. I., **Cave M. C.**, and **Srivastava S.** Sex-Dependent Effects of Vinyl Chloride on the Hepatic Transcriptome: Implications on Toxicant-Associated Steatohepatitis

Walls K. M., **Hein D. W.**, and Hong K. U. *Heterocyclic amines induce changes in glucose production and insulin signaling in human hepatocytes*

<u>Williams, A.R</u>., Speer, R.M., Browning, C.L., Meaza, I., Toyoda, J., and **Wise, Sr., J.P**. *Particulate Hexavalent Chromium Exposure* Suppresses BCDX2 Complex Response in Human Lung Cells

<u>Wise, Jr.J.P.</u>, Young J. L., Lu H., Meaza I. I., Toyoda J., Wise S. S., Speer R., Croom-Perez T., Cai L., Wise, Sr J.P. A Toxic Aging Coin: Cr(VI) Neurotoxicity and Gerontogenicity

<u>Wise J. T.</u>, Salazar-González R. A., Doll M. A., and **Hein D. W.** *Incubation with hexavalent chromium increases the N-acetylation and genotoxicity of aromatic amine carcinogens 4-aminobiphenyl and* β *-naphthylamine in human lung cells*

<u>Wise S. S.</u>, Toyoda J. H., Lu H., Meaza I. I., and Wise Sr J. P. Chromosome Instability and Cellular Transformation of Human Lung Cells Chronically Treated with Particulate Hexavalent Chromium

Young J.L. Whole-Life Exposure to Cadmium Exacerbates Diet-Induced Liver Disease

Zhao J., Gomes D., Jin L., Mathis S., Li X., Rouchka E. C., Bodduluri H., **Conklin D. J.**, and **O'Toole T. E.** *Microplastics exposure promotes adiposity and cardiometabolic diseases in mice*

MEMBER GRANT AWARDS FOR SEP, OCT AND NOV 2021

Congratulations to CIEHS members who received new grants in the months of September, October and November 2021! We are so proud of all the hard work of our CIEHS members. You can also view these grants on the CIEHS website <u>HERE</u>.

PI Name	Other Investigator	Long Title	Sponsor	Amount
Wise, Jr., John	Cai, Jun; Cai, Lu	Cr(VI)-Induced DNA Damage Contributes to Brain Aging	National Institutes of Health	\$234,125.00
accomplished by assessing toxic of acts as a 'gerontogen'. This project young, middle-aged, and geriatric	effect across the age spectrum (ct aims to determine how chroni c rats. We propose the geriatric r ng. Subsequent studies will furt	d toxicology from two perspectives. First is how age young vs adult vs geriatric). Second is how chemica ic exposure to hexavalent chromium (Cr[VI]) will inc rats will be more susceptible to damaging effects of her evaluate this proposed mechanism, consider Cr puting to premature aging.	ls induce or accelerate aging, luce neurotoxicity and prema ʿ Cr(VI), and we propose a nov	or how a chemical iture brain aging in /el clastogenic
Powell, David W. Caster, Dawn J.	Rane, Madhavi	ABIN1 dysfunction in Lupus Nephritis	National Institutes of Health	\$596,388.00
This study will determine the cellular and molecular mechanisms by which genetic variants for the ABIN1 gene TNIP1 regulates monocyte, neutrophil and B cell activity in lupus nephritis. Successful completion of this study will define novel and precision diagnostics and targets for the treatment of high-risk African American systemic lupus erythematosus patients with lupus nephritis.				
Sar, Bibhuti K.	Antle, Becky F	Promoting Recovery and Resilience in Traumatized Children and Youth through Community Partnerships	SAMHSA	\$400,000.00
Smith, Theodore Russell	Bhatnagar, Aruni; Yeager, Ray	Precision Public Health Interventions Playbook: Wastewater and COVID Vaccinations	Rockefeller Foundation	\$500,000.00
		ness and action by developing partnerships betwee develop and implement hyperlocal marketing and c		
Duncan, Scott Davis	Sullivan, Janice	Evaluation of Preterm Infants Fed Post- Discharge Preterm Infant Formula with Added Human Milk Oligosaccharide 2-Fucosyllactose	Abbott Nutrition	\$67,295.00
0	accharide. The primary outcome	ealthy, preterm infants fed a milk-based preterm in of this study is to measure change in weight-for-ag		
McMasters, Kelly Marc	Rai, Shesh Nath	Targeting Wnt10b in Melanoma Immune Surveillance	U.S. Department of Defense	\$469,125.00
This project aims at understandin improve survival in melanoma pa		melanoma disease progression. Successful comple n our body known as Wnt10b.	tion of this project will reduc	e recurrence and
Smith,Theodore Russell	Yeager,Ray Anthony	Augmenting traditional clinical genomic surveilland of SARS-CoV-2 with wastewater data to provide valuable complementary insights for public health	ROCKETEIIer	\$500,000.00
		surveillance for COVID-19 variants by UofL by estal and developing novel interventions targeted at ado		
Barnes, Gregory Neal		LOI Leadership Education in Neuro- developmental and Other Related Disabilities (LEN training program as a part of a consortium amon University of Kentucky (UK), University of Louisvill (UL) and Eastern Kentucky University (EKU)	g Kentucky Res. Fdn	\$67,948.00
		lities (LEND) programs provide long-term, graduate ing program is to improve the health of infants, chi		

NOVEMBER PUBLICATIONS HIGHLIGHTS

Congratulations to the CIEHS members with articles published in the month of November! 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.

 Banerjee M, Al-Eryani L, Srivastava S, Rai SN, Pan J, Kalbfleisch TS, States JC. Delineating the Effects of Passaging and Exposure in a Longitudinal Study of Arsenic-Induced Squamous Cell Carcinoma in a HaCaT Cell Line Model. Toxicol Sci. 2021 Nov 3:kfab129. doi: 10.1093/toxsci/kfab129. Epub ahead of print. PMID: <u>34730829.</u>

Impact Statement: This work provides strong evidence of the requirement for passage matched controls in long term (chronic) exposure studies in cultured cells. Using passage matched controls identifies changes in gene expression that are related to the passage of time and not to the exposure, thus reducing artifacts that otherwise would be interpreted as due to the exposure.

2. Petriello MC, Mottaleb MA, Serio TC, Balyan B, **Cave MC**, Pavuk M, Birnbaum LS, Morris AJ. Serum concentrations of legacy and emerging per- and polyfluoroalkyl substances in the Anniston Community Health Surveys (ACHS I and ACHS II). Environ Int. 2021 Nov 8;158:106907. doi: 10.1016/j.envint.2021.106907. Epub ahead of print. PMID: <u>34763231</u>.

Impact Statement: We participate in a longstanding multicenter and interagency collaboration examining the metabolic health effect of PCB and dioxin exposures in residents living near a former PCB production facility in Anniston, Alabama. PFAS exposures have also been associated with metabolic diseases. Here we determined higher concentrations of PFAS in Anniston participants than the general US residential population. This finding will allow us to examine associations between PFAS exposures and previously collected disease biomarkers in this cohort.

3. Jin L, **Conklin DJ**. A novel evaluation of endothelial dysfunction ex vivo: "Teaching an Old Drug a New Trick". Physiol Rep. 2021 Nov;9(21):e15120. doi: 10.14814/phy2.15120. PMID: 34755498; PMCID: <u>PMC8579072.</u>

Impact Statement: Endothelial dysfunction (ED) is sine qua non of atherosclerosis and other cardiovascular diseases in humans, yet the mechanisms that contribute to ED are still being investigated. Our study demonstrates a novel methodological twist using an old drug (L-NAME) to screen for ED in murine aorta following acute exposure to toxicants including air pollution, aldehydes, and tobacco-derived aerosols. This approach complements currently existing tools providing greater insight into the mechanisms of vascular injury due to environmental toxicants.

4. Leggett CS, Doll MA, Salazar-González RA, Habil MR, Trent JO, **Hein DW**. Identification and characterization of potent, selective, and efficacious inhibitors of human arylamine N-acetyltransferase 1. Arch Toxicol. 2021 Nov 16. doi: 10.1007/s00204-021-03194-x. Epub ahead of print. PMID: <u>34783865.</u>

Impact Statement: The study identifies potent, selective, and efficacious inhibitors of human arylamine N-acetyltransferase 1 (NAT1) important in the activation of arylamine carcinogens. The ability to inhibit NAT1 could reduce breast cancer metastasis particularly to bone.

- Wang L, Cai H, Wang Y, Liu J, Chen T, Liu J, Huang J, Guo Q, Zou W. Enhanced recovery after elective craniotomy: A randomized controlled trial. J Clin Anesth. 2022 Feb;76:110575. doi: 10.1016/j.jclinane.2021.110575. Epub 2021 Nov 2. PMID: <u>34739947</u>.
 Impact Statement: Implementation of an enhanced recovery after elective craniotomy protocol had significant benefits over conventional perioperative management. It was associated with a significant reduction in postoperative length of stay, medical cost, and postoperative complications.
- 6. Polivka BJ, Eldeirawi K, Huntington-Moskos L, Nyenhuis SM. Mask Use Experiences, COVID-19, and Adults with Asthma: A Mixed-Methods Approach. J Allergy Clin Immunol Pract. 2021 Nov 14:S2213-2198(21)01262-9. doi: 10.1016/j.jaip.2021.10.071. Epub ahead of print. PMID: 34785392; PMCID: PMC8590602.

Impact Statement: This study reports that most adults with asthma reported wearing a mask in public places. Lower asthma control and longer daily mask wearing were associated with more self-reported problems with wearing masks. To increase wearability, study participants recommended using a comfortable mask that fits, staying calm, breathing slowly and deeply were recommended. Recommendations also included taking safe "mask breaks" when needed.

NOVEMBER PUBLICATIONS HIGHLIGHTS CONTINUED

7. Kotla NG, Isa ILM, Rasala S, Demir S, Singh R, Baby BV, Swamy SK, Dockery P, Jala VR, Rochev Y, Pandit A. Modulation of Gut Barrier Functions in Ulcerative Colitis by Hyaluronic Acid System. Adv Sci (Weinh). 2021 Nov 10:e2103189. doi: 10.1002/advs.202103189. Epub ahead of print. PMID: <u>34761543.</u>

Impact Statement: This study was accomplished in collaboration (lead the project) with Drs. Yury Rochev, Abhay Pandit, CÚRAM, SFI Research Centre for Medical Devices, National University of Ireland Galway, Galway, H91 W2TY, Ireland. The goal of this study is to discover the compounds and mechanisms that can enhance gut barrier function in ulcerative colitis conditions. Current study showed that treatment with biphasic hyaluronan (HA) enema suspension, naïve-HA systems protect against gut barrier dysfunction in ulcerative colitis by increasing tight junction proteins. These studies provide novel approaches to target ulcerative colitis.

8. Lindsey ML, LeBlanc AJ, Ripplinger CM, Carter JR, Kirk JA, Hansell Keehan K, Brunt KR, Kleinbongard P, Kassiri Z. Reinforcing rigor and reproducibility expectations for use of sex and gender in cardiovascular research. Am J Physiol Heart Circ Physiol. 2021 Nov 1;321(5):H819-H824. doi: 10.1152/ajpheart.00418.2021. Epub 2021 Sep 15. PMID: <u>34524922</u>.

Impact Statement: This is an editorial from the Editor-in-chief and the 7 Associate Editors of the American Journal of Physiology Heart and Circulatory Physiology that states our expectation that males and females be incorporated into all studies unless a very strong rationale prevents the authors from doing so, starting in 2023. Some examples of rationale include examining processes that occur only in one sex (i.e. cardiovascular complications of pregnancy), or testing the effects of oral contraceptives on cardiovascular health. By including studies utilizing both sexes/genders, this will result in a more complete, unbiased and reliable data set that more accurately mirrors the population.

 Schneider G, Kaliappan A, Nguyen TQ, Buscaglia R, Brock GN, Hall MB, DeSpirito C, Wilkey DW, Merchant ML, Klein JB, Wiese TA, Rivas-Perez HL, Kloecker GH, Garbett NC. The Utility of Differential Scanning Calorimetry Curves of Blood Plasma for Diagnosis, Subtype Differentiation and Predicted Survival in Lung Cancer. Cancers (Basel). 2021 Oct 23;13(21):5326. doi: 10.3390/cancers13215326. PMID: 34771491; PMCID: <u>PMC8582427</u>.

Impact Statement: The recent increase in the number of lung cancer cases unrelated to the well-known risk factors, and the high falsepositive rate of low-dose CT scans, indicate a need to develop new, non-invasive methods for lung cancer detection. Our results using differential scanning calorimetry (DSC) supported by targeted proteomic studies suggests the DSC curve features could be useful for differentiation of lung cancer patients from controls with some capable of distinction between subtypes and stages of lung cancer.

 Trace ME, Feygin YB, Williams PG, Winders Davis D, Brothers KB, Sullivan JE, Calhoun AW. Attention-Deficit/Hyperactivity Disorder Practice Patterns: A Survey of Kentucky Pediatric Providers. J Dev Behav Pediatr. 2021 Nov 17. doi: 10.1097/DBP.000000000001037. Epub ahead of print. PMID: <u>34799539</u>.

Impact Statement: Kentucky ranks among the highest in the nation for attention-deficit/hyperactivity disorder (ADHD) prevalence in children aged 4 to 17 years. In 2011, the American Academy of Pediatrics (AAP) released a clinical practice guideline based on the DSM-IV. A guideline revision based on the Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition (DSM-5) was released in October 2019. In this study, we assessed and described a sample of Kentucky pediatric providers' ADHD practices using the 2011 guideline and DSM-5 diagnostic criteria. Although pediatricians in the KY AAP that responded adhere to the DSM-5 criteria for diagnosing ADHD, pediatric providers' practices would benefit from education in improvements in pharmacotherapy titration, surveillance of coexisting conditions associated with ADHD, discussion of psychosocial interventions, and school support strategies.

DECEMBER PUBLICATIONS HIGHLIGHTS

Congratulations to the CIEHS members with articles published in the month of December! 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.

 ElNakieb Y, Ali MT, Elnakib A, Shalaby A, Soliman A, Mahmoud A, Ghazal M, Barnes GN, El-Baz A. The Role of Diffusion Tensor MR Imaging (DTI) of the Brain in Diagnosing Autism Spectrum Disorder: Promising Results. Sensors (Basel). 2021 Dec 7;21(24):8171. doi: 10.3390/s21248171. PMID: 34960265; PMCID: <u>PMC8703859</u>.

Impact Statement: Autism spectrum disorder (ASD) diagnosis is usually subjective, and scores can vary from one specialist to another. Previous literature suggests differences in brain development, environmental, and/or genetic factors play a role in developing autism, yet scientists still do not know exactly the pathology of this disorder. This paper provides a study of implementing feature engineering tools to find discriminant insights from brain imaging of white matter connectivity and using a machine learning framework for an accurate classification of autistic individuals.

2.Men H, Young JL, Zhou W, Zhang H, Wang X, Xu J, Lin Q, Tan Y, Zheng Y, Cai L. Early-Life Exposure to Low-Dose Cadmium Accelerates Diethylnitrosamine and Diet-Induced Liver Cancer. Oxid Med Cell Longev. 2021 Nov 28;2021:1427787. doi: 10.1155/2021/1427787. PMID: 34876963; PMCID: <u>PMC8645401</u>.

Impact Statement: Although maternal exposure to cadmium causes obesity and metabolic changes in the offspring, including nonalcoholic fatty liver disease-like pathology, whether maternal cadmium exposure accelerates liver cancer in the offspring is unknown. This study investigated the impact of early-life exposure to cadmium on the incidence and potential mechanisms of hepatocellular carcinoma (HCC) in offspring subjected to postweaning HCC induction, and confirmed that early-life exposure to low-dose cadmium accelerates liver cancer development induced by a DEN/HFCD in male mice, probably due to chronic lipotoxicity and inflammation.

3. Bao T, Liu J, Leng J, **Cai L.** The cGAS-STING pathway: more than fighting against viruses and cancer. Cell Biosci. 2021 Dec 14;11(1):209. doi: 10.1186/s13578-021-00724-z. PMID: 34906241; PMCID: <u>PMC8670263</u>.

Impact Statement: In the classic cGAS-stimulator of interferon genes (STING) pathway, downstream signals can control the production of type I interferon (IFN) and NF-κB to promote the activation of pro-inflammatory molecules, which are mainly induced during antiviral responses. However, this review mainly highlights the functions of the cGAS-STING pathway in chronic inflammatory diseases, with focus on the important role of cGAS-STING pathway in the chronic inflammatory status in diabetes and diabetes-related complications.

 Zhou W, Young JL, Men H, Zhang H, Yu H, Lin Q, Xu H, Xu J, Tan Y, Zheng Y, Cai L. Sex differences in the effects of whole-life, lowdose cadmium exposure on postweaning high-fat diet-induced cardiac pathogeneses. Sci Total Environ. 2021 Dec 5;809:152176. doi: 10.1016/j.scitotenv.2021.152176. Epub ahead of print. PMID: <u>34875320.</u>

Impact Statement: We previously showed the development of cardiac remodeling (hypertrophy or fibrosis) in mice with either postweaning high-fat diet (HFD, 60% kcal fat) feeding or exposure to chronic low-dose cadmium. Here, we determined whether whole-life exposure to environmentally relevant, low-dose cadmium affects the susceptibility of offspring to post-weaning HFD-induced cardiac pathologies and function, and confirmed that whole-life 5 ppm cadmium exposure significantly increases the susceptibility of female offspring to HFD-induced cardiac remodeling and dysfunction.

 Li F, Chen J, Liu Y, Gu Z, Jiang M, Zhang L, Chen SY, Deng Z, McClain CJ, Feng W. Deficiency of Cathelicidin Attenuates High-Fat Diet Plus Alcohol-Induced Liver Injury through FGF21/Adiponectin Regulation. Cells. 2021 Nov 27;10(12):3333. doi: 10.3390/cells10123333. PMID: 34943840; PMCID: PMC8699208.

Impact Statement: Alcohol consumption and obesity are known risk factors of steatohepatitis. In this paper, Dr. Wenke Feng, Professor of Medicine, and his collaborators, including some in the CIEHS, demonstrated that deficiency of CRAMP is against a high-fat diet plus acute alcohol-induced liver injury. These results suggest that targeting CRAMP could be an effective approach for the prevention/treatment of high-fat diet plus alcohol consumption-induced steatohepatitis.

DECEMBER PUBLICATIONS HIGHLIGHTS CONTINUED

 Zhao CB, Yu J, Kong M, Han J, Du H, Huang J. Ketamine for Monitored Anesthesia Care during Transcatheter Aortic Valve Replacement. J Perianesth Nurs. 2021 Dec 28:S1089-9472(21)00147-7. doi: 10.1016/j.jopan.2021.06.007. Epub ahead of print. PMID: 34972624.

Impact Statement: Employing Ketamine as an adjunct during monitored anesthesia care for transcatheter aortic valve replacement is a feasible option.

- 7. Majumder S, Pushpakumar S, Juin SK, Jala VR, Sen U. Toll-like receptor 4 mutation protects the kidney from Ang-II-induced hypertensive injury. Pharmacol Res. 2021 Dec 9;175:106030. doi: 10.1016/j.phrs.2021.106030. Epub ahead of print. PMID: <u>34896544</u>. *Impact Statement:* This article describes the mechanism of how TLR4 activation suppresses autophagy, induces apoptosis and kidney injury in Ang-II-induced hypertension, and TLR4 mutation protects the kidney.
- 8. Das S, Rai A, **Merchant ML**, **Cave MC**, **Rai SN**. A Comprehensive Survey of Statistical Approaches for Differential Expression Analysis in Single-Cell RNA Sequencing Studies. Genes (Basel). 2021 Dec 2;12(12):1947. doi: 10.3390/genes12121947. PMID: 34946896; PMCID: <u>PMC8701051.</u>

Impact Statement: Differential Expression (DE) analysis in presence of noises from different sources remains a key challenge in Single-cell RNA-sequencing (scRNA-seq) studies. Earlier practices for addressing this involved borrowing methods from bulk RNA-seq, which are based on non-zero differences in average expressions of genes across cell populations. We evaluate the performance of 19 widely used methods in terms of 13 performance metrics on 11 real scRNA-seq datasets. Our findings suggest that some bulk RNA-seq methods are quite competitive with the single-cell methods, but their performance depends on the underlying models. However, the multi-criteria and combined-data analysis indicates that DECENT and EBSeq are the best options for DE analysis. Our evaluation provides proper guidelines for selecting the proper tool which performs best under particular experimental settings in the context of the scRNA-seq.

9. Xu F, Mu J, Teng Y, Zhang X, Sundaram K, Sriwastva MK, Kumar A, Lei C, Zhang L, Liu QM, Yan J, McClain CJ, Merchant ML, Zhang HG. Restoring Oat Nanoparticles Mediated Brain Memory Function of Mice Fed Alcohol by Sorting Inflammatory Dectin-1 Complex Into Microglial Exosomes. Small. 2021 Dec 13:e2105385. doi: 10.1002/smll.202105385. Epub ahead of print. PMID: <u>34897972.</u> *Impact Statement:* This study focuses on the molecular mechanism(s) underlying how oat nanoparticles (oatN) contributes to the inhibition of microglial cell mediated inflammation. The findings from this study are significant in that it provides a basis for developing mechanism-driven novel approaches for prevention of microglial cell mediated chronic inflammation of the brain via non-invasive oral administration.

10. Wu B, **Pal S**, Kang J, Guo Y. Distributional independent component analysis for diverse neuroimaging modalities. Biometrics. 2021 Oct 25. doi: 10.1111/biom.13594. Epub ahead of print. PMID: <u>34694629.</u>

Impact Statement: Analysis of images derived from various neuroimaging modalities involves some common goals such as dimension reduction, denoising, and feature extraction. However, since these modalities have vastly different data characteristics, the current analysis is usually performed using distinct analytical tools that are only suitable for a specific imaging modality. In this paper, we present a Distributional Independent Component Analysis (DICA) that represents a new approach that performs decomposition on the distribution level, providing a unified framework for extracting features across imaging modalities with different scales and representations.

11. Wu B, **Pal S**, Kang J, Guo Y. Rejoinder to discussions of "distributional independent component analysis for diverse neuroimaging modalities". Biometrics. 2021 Nov 15. doi: 10.1111/biom.13588. Epub ahead of print. PMID: <u>34780668.</u>

Impact Statement: This paper provides results and comments to address the questions raised in the discussions of our recent publication entitled "Distributional independent component analysis for diverse neuroimaging modalities".

DECEMBER PUBLICATIONS HIGHLIGHTS CONTINUED

12. Aqil F, Munagala R, Agrawal AK, Jeyabalan J, Tyagi N, **Rai SN**, Gupta RC. Anthocyanidins Inhibit Growth and Chemosensitize Triple-Negative Breast Cancer via the NF-κB Signaling Pathway. Cancers (Basel). 2021 Dec 13;13(24):6248. doi: 10.3390/cancers13246248. PMID: 34944868; PMCID: <u>PMC8699375.</u>

Impact Statement: Breast cancer is the most common female cancer diagnosed in the U.S. and the second most common cause of cancer death in women. Chemotherapeutics used to treat breast cancer often have side effects, which are sometimes life-threatening. Moreover, the tumors can develop resistance over time, making breast cancer treatment challenging. In this paper, we show that the oral administration of colored pigments isolated from bilberry/blueberry, called anthocyanidins (Anthos), significantly decrease tumor volume, inhibit the growth and metastasis of breast cancer, sensitize drug-resistant tumor cells, and exhibit a lower rate of lymph node and lung metastasis, compared to control. These mechanistic insights are expected to be valuable for clinical translation of berry Anthos, either alone or as adjuvant to chemotherapy, for the treatment of breast cancer patients.

13. Yusuf M, **Pan J**, **Rai SN**, Eldredge-Hindy H. Financial Toxicity in Women With Breast Cancer Receiving Radiation Therapy: Final Results of a Prospective Observational Study. Pract Radiat Oncol. 2021 Dec 9:S1879-8500(21)00301-5. doi: 10.1016/j.prro.2021.11.003. Epub ahead of print. PMID: <u>34896597.</u>

Impact Statement: In this prospective study of women with BC receiving RT, distinct factors including surgery type were significantly associated with FT. FT was strongly correlated with health-related QoL. Increased characterization of the relationship between FT and health-related QoL for women with BC receiving RT and defining clinical predictors of FT may help guide future studies investigating optimal targeted interventions for patients with BC at high risk for FT.

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