

NEWSLETTER

CIEHS Up to Date News and Accomplishments

Awards Announcements and Reminders

February 2022 Student & Post-Doc Travel Awardees

Congratulations to students and post-docs who received a CIEHS Travel Award in the month of February 2022! Awardees underlined and mentor names are in bold. For more information [CLICK HERE](#). Contribute to helping other students and post-docs travel to a national or international conference to report Environmental Health Research [HERE](#).

Jonathan Bastick
Christopher States, Ph.D.

Jamie Young
Matt Cave, Ph.D.

Belinda Petri
Carolyn Klinge, Ph.D.

Idoia Meaza Isusi
John P. Wise, Sr., Ph.D.

James Wise
David Hein, Ph.D.

Sweta Ghosh
Venkatakrishna Jala, Ph.D.

Aggie Williams
John P. Wise, Sr., Ph.D.

Jingjing Zhao
Timothy O'Toole, Ph.D.

Jennifer Toyoda
John P. Wise, Ph.D.

Haiyan Lu
John P. Wise, Sr., Ph.D.

Ana Ferragut Cardoso
Christopher States, Ph.D.

WELCOME OUR NEW MEMBERS:

MOT RIG:

Barbara J. Clark, Ph.D.

**Anna M. Gumpert, Ph.D.,
SMBA**

**Craig J McClain, M.D., AGAF,
FACG, FAASLD, FACN**

**Kupper A. Wintergerst, MD,
FAAP**

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Student and post-doc awardee SM post

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 [THIS LINK](#) for the NIH Assisted Referral Tool (ART) tool.

Awards Announcements and Reminders Continued

Aruni Bhatnagar, Ph.D., FAHA accepted faculty of the Yale School of Public Health

Aruni Bhatnagar, CIEHS Career Development Director, Smith and Lucille Gibson Professor of Medicine, Chief of the Division of Environmental Medicine and Director of the Christina Lee Brown Envirome Institute of the School of Medicine, has accepted an adjunct appointment to the faculty of the [Yale School of Public Health](#). This appointment highlights the critical importance of understanding the role of the environment in health and his pioneering scholarship.

Jiapeng Huang, M.D. Patent

Congratulations to Dr. Jiapeng Huang on his newest US Patent NO. 11,257,35 entitled "System and method for opportunity-based reminding or compliance with one or more health protocols". Learn more about Dr. Huang's patent [HERE](#).

John P. Wise, Sr., Ph.D. Special Guest on SOT Adverse Reactions Podcast

Dr. John Wise, Sr., CIEHS Deputy Director, was featured on the [Society of Toxicology](#) (SOT) podcast, *Adverse Reactions*. Dr. Wise discusses his research on the effects of metals in whales/alligators and chromosome instability. He also discusses how you can help others relate to the importance of environmental health. Listen to Dr. Wise's featured segment entitled "Toxicology Is a Wise Choice: One Health, Many Ecosystems" [HERE](#).

2022 Inaugural UofL Research and Scholarship Awards

Congratulations to the CIEHS members below who were recognized at the Inaugural UofL Research and Scholarship Awards! Special congrats to Dr. Becky Antle, CIEHS Tracking and Evaluation Leader, who received the Collaborator of the Year award!

- Becky Antle, Ph.D., MSSW, LMFT
- Natasha DeJarnett, Ph.D., MPH
- Xiao-An Fu, Ph.D.
- Luz Huntington-Moskos, ph.D., R.N., C.P.N.
- J. Christopher States, Ph.D.
- John P. Wise, Sr., Ph.D.

Vicki Hines-Martin, PhD, PMHCNS, RN, FAAN top cited publication by Wiley, Inc.

Congratulations to Dr. Vicki Hines-Martin, CEC Associate Director, for her 2020 publication entitled "Achieving Health Equity Through Eradicating Structural Racism in the United States: A Call to Action for Nursing Leadership" in the Journal of Nursing Scholarship which was recognized by Wiley, Inc. as a top cited publication.

CIEHS Environmental Health Series Seminar

CIEHS welcomed external speaker, Dr. Michael Aschner, for the March 2022 EHS seminar. If you were unable to attend this presentation entitled "Manganese Neurotoxicity: what can we learn from worms?" you can view the recording on the CIEHS YouTube channel [HERE](#). The upcoming EHS seminar features Dr. Petra Haberzettl, MOT RIG member, on April 7th. Dr. Haberzettl's presentation is entitled "Pulmonary Oxidative Stress, a potential mechanistic pathway to air pollution-induced cardiovascular and metabolic toxicity." You can find all of the past CIEHS seminars on our [YouTube channel](#) and a full seminar schedule on the CIEHS [website](#).

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

Michael Aschner, PhD



*Presentation Entitled:
"Manganese Neurotoxicity:
what can we learn from worms?"*

Dr. Michael Aschner serves as the Harold and Muriel Block Chair in Molecular Pharmacology at Albert Einstein College of Medicine in Bronx, New York.

**Seminar occurred on:
Thursday, March 3**

UNIVERSITY OF
LOUISVILLE
CENTER FOR INTEGRATIVE
ENVIRONMENTAL HEALTH
SCIENCES

2022 SOT Awards and Announcements

Congratulations to CIEHS members who served as chairs and won awards at the Society of Toxicology (SOT) annual meeting that occurred March 27-31 (Members names in bold).

Awards

Toxicologist Mentoring Award

John P. Wise Sr., Ph.D.

Bristol Myers Squibb Graduate Student Research Training Award to Promote Diversity in Toxicology.

Aggie Williams (**Wise** lab)

Best Postdoctoral Publication Awards

Qian Lin, Ph.D.

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.

First Place Stratacor Postdoctoral Research Award from the Dermal Toxicology Specialty Section

Alexandra Nail, Ph.D. (**States** lab)

First Place Metals Specialty Section Postdoctoral Research Award

Ana Ferragut Cardoso, Ph.D. (**States** lab)

Title: "Overexpression of miR-186 accelerates chromosomal instability in arsenic-exposed human keratinocytes".

Bruce A. Fowler Metals Young Investigator Endowment Fund Award from the Metals Specialty Section

John Wise, Jr., Ph.D.

Celebrating Women in Toxicology Award from the Women in Toxicology Special Interest Group

Jamie Young, Ph.D. (Cave lab)

Graduate Student Leadership Committee Three Minute Thesis competition

Idoia Meaza (**Wise** lab)- First place Graduate Student Category

Title: "MISSING protein. Have you seen it? REWARD is to cure cancer!"

Alexandra Nail, Ph.D. (**States** lab)- First place Postdoctoral category

Title: "Assessing the Impact of Chronic Arsenic Exposure on DNA Repair Choice"

Environmental Carcinogenesis Merit Award for Graduate Students from the Carcinogenesis Specialty Section

Jennifer Toyoda (**Wise** lab)

Third Place Darm V. Singh Graduate Student Award from the Carcinogenesis Specialty Section

Idoia Meaza (**Wise** lab)

Fourth Place Darm V. Singh Graduate Student Award from the Carcinogenesis Specialty Section

Haiyan Lu (**Wise** lab)

Third Place Graduate Student Research Award from the Metals Specialty Section

Idoia Meaza (**Wise** lab)

Second Place Graduate Student Research Award from the Metals Specialty Section

Aggie Williams (**Wise** lab)

Honorable Mention for Best Abstract from the Risk Assessment Specialty Section

Anand Ramalingam, Ph.D. (**Carll** lab)

Serving as Chair or Co-Chair

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

Chair: **Lu Cai, M.D., Ph.D.**, Cardiovascular Effects of Environmental Metals: New Preclinical and Clinical Insights

Chair: Idoia Meaza (**Wise** lab), Metals I

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

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

Co-Chair: **Jamie Young, Ph.D.**, Cadmium and the Developmental Origins of Disease: The Implication of Early-Life Exposures on Health Later in Life

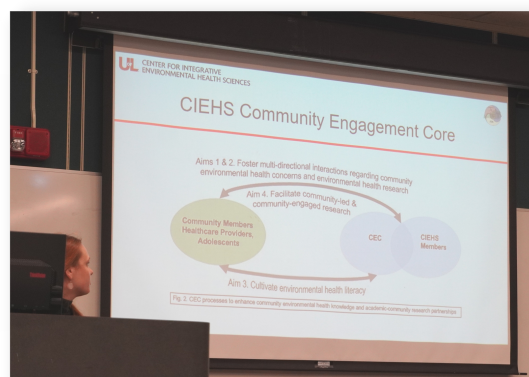
Community Engagement Core Corner

During the months of February and March, our CEC team has been busy. Our current efforts have centered on hosting our Stakeholder Advisory Board, supporting Dr. Kouokam as he prepared for the Kentucky Science Center's Youth Science Summit, ongoing outreach/partnership efforts, supporting Dr. Young and the PFAS project in Henderson, a continued partnership with the UK CARES, and preparation for presentations at the University of Louisville's 7th Annual UofL Engaged Scholarship Symposium.

Let us share just a few more details with you.... Our community stakeholders provided valuable feedback on our disaster preparedness project led by a CIEHS CEC and UK-CARES CEC partnership. Stakeholders also provided substantial insight into improving our Pilot Project review process. In addition to the vital work with our stakeholders, CIEHS investigator Dr. J. Calvin Kouokam provided excellent community outreach with his presentation on heavy metals in concrete dust at the Kentucky Science Center's virtual Youth Science Summit. The video of his presentation is now available on the CIEHS CEC Youth tab [HERE](#). The CEC continues to work side-by-side with Dr. Jamie Young by pulling together relevant educational materials for PFAS educational modules. Finally, on March 25th, Dr. Huntington-Moskos and Ms. Willis both shared presentations at the 7th Annual UofL Engaged Scholarship Symposium. Dr. Huntington-Moskos presented on engaging with youth to cultivate environmental health literacy while Ms. Willis presented on how the CEC has strived to traverse the digital divide between the CEC and Trigg County community members.



CIEHS CEC t-shirt design



Ms. Josie Willis presenting at the UofL Engaged Scholarship Symposium

We are excited to share that the CIEHS CEC now has t-shirts with our new "Environmental Health for All" logo on them---- thanks to Ms. Sarah Jump! The CEC also gives a special thanks to our newest SAB member, Ms. Catherine Malin of the South Central AHEC for serving on our board. Additionally, thank you to the Kentucky Science Center, Dr. Anna Hoover, and Rachael Hamilton of the Air Pollution Control District for their expertise and collaboration. The CEC staff certainly appreciates our colleagues who help keep this work moving forward including our CIEHS Admin Core colleagues: Ms. Colleen Quinter, Ms. Sarah Jump, and Mx. Luis Salazar Guzman. Their continued support of our efforts and assistance with digital expertise and creativity is invaluable.

Notes from the Director:

March 31, 2022

As I write this, we are about to enter our third year. We have accomplished much in the 21 months since we first received the notice of grant award for the P30. Our pilot project and research voucher programs are robust. Thus far, we have funded 10 pilot projects and 23 research vouchers totaling over a half million dollars. The next round of pilot projects is about to be awarded. There will be some improvements and clarifications in the programs forthcoming, so keep an eye out for the notices.

The Neurodevelopmental Toxicology Research Interest Group hosted Dr. Michael (Miki) Aschner from the Albert Einstein College of Medicine as our invited speaker in March. He made a great presentation and met with several of the members to discuss research.

We are planning a Center-wide meeting for early May. Notices will be sent out by email as soon as we can get the date set. CIEHS is entering a critical stage in preparation for the renewal application. Thank you to those who responded to the surveys that Dr. Becky Antle's team distributed. This information is important to tell us what we are doing well and where we need to focus more effort. Topics for discussion at the upcoming meeting were developed from the responses.

We had a great showing at SOT2022. Key participation and contributions to the meeting have been announced on the website. Our members organized symposia and workshops, and many members received awards. See elsewhere in this newsletter for a complete listing.

Our members are publishing impactful papers, getting patents and grants awarded. Recently published manuscripts, and awarded patents and grants are listed in this newsletter. As always, CIEHS announces each of these on social media to help publicize your accomplishments. Please assist Sarah Jump by providing the impact statements.

I have the honor of being a host for the Society of Toxicology Global Senior Scholar Exchange Program. My guest is Dr. John Placheril from the University of Rajasthan in Jaipur, India. He will be visiting UofL for the month of April. I hope that many of you will be able to spend some time with him so that he can gain a full appreciation of the toxicology research at UofL.

MEMBER GRANT AWARDS FOR DEC 2021 & JAN 2022

Congratulations to CIEHS members who received new grants in the months of December 2021 & January 2022! We are so proud of all the hard work of our CIEHS members. You can also view these grants on the CIEHS website [HERE](#).

PI Name	Other Investigator	Long Title	Sponsor	Amount
Park, Juw Won		Identifying and characterizing translation of circular RNAs using high-throughput sequencing data	National Institutes of Health	\$460,156.00
<p>Over the past two decades, studies have discovered a special form of mechanism that produces a circular form of RNA (circRNA). The purpose of this research is to identify and characterize translated circRNAs using next generation sequencing technology. This research will provide researchers with critical information regarding the translated circRNAs in existing sequencing datasets, in addition to enhancing research experiences in multi-disciplinary bioinformatics research among college undergraduates in University of Louisville.</p>				
Karimi, Seyed Mohammad	Dupre, Natalie Cecilia.	Analyzing COVID-19 and Projecting COVID-19 Hospitalizations for City of Louisville/Jefferson County, Kentucky	Louisville/Jefferson Co Metro Government	\$41,144.25
<p>We worked with Louisville's COVID-19 data and estimated the number of hospitalizations that would occur under different scenarios of vaccination in children ages 5-11. If only 10% of 5-11-year-olds got fully vaccinated in Fall 2021, then we estimated that Jefferson County would have 4 times as many active COVID-19 hospitalizations by the end of Jan 2022, compared to if 40% of 5 to 11 age group got vaccinated in Fall 2021.</p>				
Karia, Samir	Sullivan, Janice	A Multi-site Collaborative for Pediatric Epilepsy Surgery Outcomes Beyond Seizure Freedom	Children's National Health System	\$7,500.00
<p>The Pediatric Epilepsy Research Consortium (PERC) is a network of US Pediatric Epilepsy Centers dedicated to collaborative research into the diagnosis, evaluation, and treatment of pediatric patients with epilepsy. This collaboration provides an opportunity to standardize common data elements captured for all patients evaluated for epilepsy surgery. From this data, there is potential to characterize the evaluation for epilepsy surgery in the US and utilize this data to further explore treatment needs for patients and ultimately patient outcome. Dr. Samir Karia, Pediatric Neurology, is leading this effort at the University of Louisville.</p>				
Brothers, Kyle B	Barnes, Gregory Neal	Utility of Genomic Sequencing in Community Care Contexts	National Institutes of Health	\$818,720.00
<p>Families with children who have identified deficits in speech and/or sensory or musculoskeletal impairments without a known cause may be referred for genetic testing to find out whether there is a genetic cause. However, there is little research into how parents and caregivers use this diagnosis to inform decisions about therapeutic services, access to school services, or how a genomic diagnosis informs the practice of the community professionals who provide these services. This project will examine how a genomic diagnosis shapes the care that children receive from community professionals, including physical and occupational therapists, speech-language pathologists, special education teachers, behavior analysts, and mental health providers.</p>				
Tan, Yi	Cai, Lu	Fibroblast Growth Factor 1 Prevents Hyperlipidemia and Atherosclerosis	National Institutes of Health	\$553,582.00
<p>The objective of this study is to define how FGF1 protects against atherosclerosis and whether there is a clinical translational potential of the novel non-mitogenic variant FGF1ΔHBS for preventing atherosclerosis by inhibiting hepatic cholesterol biosynthesis and suppressing intestinal cholesterol absorption without risk of hyperproliferation. We will first optimize the doses of FGF1 protection against atherosclerosis in two distinct atherogenic animal models and determine the roles of endogenous FGF1 in the development of atherosclerosis. Next, we will determine the effects and mechanism of FGF1 on hepatic cholesterol biosynthesis and intestinal cholesterol absorption. This project will reveal new insight into the underlying mechanism behind FGF1 protection against atherosclerosis as well as provide fundamental evidence supporting the non-mitogenic variant FGF1ΔHBS as a novel therapeutic approach for prevention of atherosclerosis in future clinical practice.</p>				
Thrasher, Bradly Jackson	Wintergerst, Kupper Anthony	Type 1 Diabetes Exercise Initiative Pediatric Study (T1DexiP): The Effect of Exercise on Glycemic Control in Youth with Type 1 Diabetes	Jaeb Center for Health Research	\$11,000.00
<p>The Type 1 Diabetes Exercise Initiative Pediatric Study (T1DEXIP Study) will help researchers learn more about the effects of exercise in youth living with type 1 diabetes mellitus. This is a 10 day at home study which requires participants to maintain their daily activity/exercise, log food and exercise, wear a continuous glucose monitor, and share data with the research team. Please visit www.jaeb.org/t1dexip/ to learn more.</p>				

Total New Awards December 2021 & January 2022: \$1,892,102.25

JANUARY PUBLICATIONS HIGHLIGHTS

Congratulations to the CIEHS members with articles published in the month of January! 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. Ferragut Cardoso AP, **Banerjee M**, Al-Eryani L, Sayed M, Wilkey DW, **Merchant ML**, **Park JW**, **States JC**. Temporal Modulation of Differential Alternative Splicing in HaCaT Human Keratinocyte Cell Line Chronically Exposed to Arsenic for up to 28 Wk. *Environ Health Perspect*. 2022 Jan;130(1):17011. doi: 10.1289/EHP9676. Epub 2022 Jan 24. PMID: 35072517; PMCID: [PMC8785870](#).
Impact Statement: *The majority of human genes encode multiple protein isoforms. The isoforms are produced from mRNA isoforms edited from the primary transcripts by alternative splicing. This manuscript uses a model cell culture system to show that exposure to an inorganic arsenic compound that naturally contaminates drinking water in many parts of the world markedly disrupts the alternative splicing producing many errant mRNAs, and that the mRNA isoforms produced change over time with chronic exposure. One of the targets of the arsenic appears to be the splicing factor network itself.*
2. Ghosh S, **Banerjee M**, Haribabu B, **Jala VR**. Urolithin A attenuates arsenic-induced gut barrier dysfunction. *Arch Toxicol*. 2022 Feb 5. doi: 10.1007/s00204-022-03232-2. Epub ahead of print. PMID: [35122514](#).
Impact Statement: *Chronic exposure to inorganic arsenic leads to an increase in both the onset and progression of several human diseases targeting multiple organs (liver, kidney, bladder, skin, intestines, and central nervous system), which is referred to as 'arsenicosis'. Gut microbial Urolithin A is derived from ellagic acid and ellagitannins (major poly phenolic components in berries and pomegranate) by gut commensal bacteria. The current study reports the beneficial effects of Urolithin A against adverse effects of trivalent arsenic on human gut epithelia, where treatment with Urolithin A protected against arsenic-induced gut epithelial damage. These studies will pave a pathway for preventive and therapeutic applications to mitigate arsenic-elicited adverse health effects, which are currently unavailable.*
3. Lorkiewicz P, Keith R, Lynch J, Jin L, Theis W, Krivokhizhina T, Riggs D, **Bhatnagar A**, **Srivastava S**, **Conklin DJ**. Electronic Cigarette Solvents, JUUL E-Liquids, and Biomarkers of Exposure: In Vivo Evidence for Acrolein and Glycidol in E-Cig-Derived Aerosols. *Chem Res Toxicol*. 2022 Jan 19. doi: 10.1021/acs.chemrestox.1c00328. Epub ahead of print. PMID: [35044764](#).
Impact Statement: *In this study, we identify the formation of 2 toxicants, acrolein and glycidol, from the e-cigarette solvent vegetable glycerin. This finding may improve public health via use of a potential biomarker of e-cigarette use such that e-cigarette use can be quantified. Subsequently, the amount of e-cigarette use can be associated with biomarkers of harm including those that reflect cardiorespiratory injury. Overall, this finding may allow us to better predict health risks of chronic use of e-cigarettes.*
4. **Cave MC**, Pinkston CM, **Rai SN**, **Wahlang B**, Pavuk M, Head KZ, Carswell GK, Nelson GM, **Klinge CM**, Bell DA, Birnbaum LS, Chorley BN. Circulating MicroRNAs, Polychlorinated Biphenyls, and Environmental Liver Disease in the Anniston Community Health Survey. *Environ Health Perspect*. 2022 Jan;130(1):17003. doi: 10.1289/EHP9467. Epub 2022 Jan 6. PMID: 34989596; PMCID: [PMC8734566](#).
Impact Statement: *This environmental epidemiology study determined associations between PCB pollutant exposures and liver disease in residents living near a chemical plant.*
5. Fan H, Li Y, Yuan F, Lu L, Liu J, Feng W, Zhang HG, **Chen SY**. Up-regulation of microRNA-34a mediates ethanol-induced impairment of neural crest cell migration in vitro and in zebrafish embryos through modulating epithelial-mesenchymal transition by targeting Snail1. *Toxicol Lett*. 2022 Jan 14;358:17-26. doi: 10.1016/j.toxlet.2022.01.004. Epub ahead of print. PMID: [35038560](#).
Impact Statement: *Fetal alcohol spectrum disorder (FASD) is among the most devastating consequences of the widespread use and abuse of alcohol in pregnant women. The prevalence of FASD in the United States and Western European countries is estimated to be as high as 1–5 per 100 children. The findings from this study elucidate a novel mechanism by which alcohol impairs neural crest cell migration through modulating microRNAs and epithelial-mesenchymal transition and suggests that miR- 34a may represent a novel therapeutic target for the development of approaches to ameliorate or prevent FASD.*
6. Abouleisa RRE, Salama ABM, Ou Q, Tang XL, Solanki M, Guo Y, Nong Y, McNally L, Lorkiewicz PK, Kassem KM, Ahern BM, Choudhary K, Thomas R, Huang Y, Juhardeen HR, Siddique A, Ifthikar Z, Hammad SK, El-Baz AS, Ivey KN, **Conklin DJ**, Satin J, Hill BG, Srivastava D, Bolli R, Mohamed TMA. Transient Cell Cycle Induction in Cardiomyocytes to Treat Subacute Ischemic Heart Failure. *Circulation*. 2022 Jan 21. doi: 10.1161/CIRCULATIONAHA.121.057641. Epub ahead of print. PMID: [35061545](#).
Impact Statement: *In this study, we gained mechanistic insights into the process of forced cardiomyocyte proliferation and advanced the clinical feasibility of this approach by minimizing the oncogenic potential of the cell cycle factors via use of a novel transient and cardiomyocyte-specific viral construct. These findings may lead to clinical interventions to repair the heart after acute heart attack and to delay or prevent progression to heart failure.*
7. Zhao J, Gomes D, Jin L, Mathis SP, Li X, Rouchka EC, Bodduluri H, **Conklin DJ**, **O'Toole TE**. Polystyrene bead ingestion promotes adiposity and cardiometabolic disease in mice. *Ecotoxicol Environ Saf*. 2022 Jan 27;232:113239. doi: 10.1016/j.ecoenv.2022.113239. Epub ahead of print. PMID: [35093814](#).
Impact Statement: *Modern society produces and uses huge amounts of plastics and a large percentage of these ultimately accumulate in water systems and landfills, where they eventually degrade into particles of smaller size. While emerging evidence has documented that these microplastics are abundant in water supplies and the food chain where their human consumption is inevitable, the health consequences of such consumption are not completely known. In this study, we supplied mice with drinking water containing different sizes and doses of polystyrene beads and found that they developed obesity and showed early signs of insulin resistance/diabetes. Thus, the consumption of microplastics may promote early cardiovascular disease.*

JANUARY PUBLICATIONS HIGHLIGHTS CONTINUED

8. Carlisle SM, Trainor PJ, Doll MA, **Hein DW**. Human Arylamine N-Acetyltransferase 1 (NAT1) Knockout in MDA-MB-231 Breast Cancer Cell Lines Leads to Transcription of NAT2. *Front Pharmacol*. 2022 Jan 3;12:803254. doi: 10.3389/fphar.2021.803254. PMID: 35046826; PMCID: [PMC8762260](#).
Impact Statement: RNAseq was utilized to interrogate differential gene expression across three biological replicates of previously constructed and characterized MDA-MB-231 breast cancer cell lines expressing parental, increased, decreased, or knockout levels of N-acetyltransferase 1 (NAT1). 3,889 genes were significantly associated with NAT1 N-acetylation activity; 1,756 were positively associated and 2,133 were negatively associated with enrichment of genes involved in cell adhesion.
9. Rayens MK, McGeeney T, Wiggins A, Bucher A, Ickes M, **Huntington-Moskos L**, Clark P, Hahn E. Smoke-free Ordinances and Youth Tobacco Use in Kentucky. *Am J Health Promot*. 2022 Jan 27:8901171211066913. doi: 10.1177/08901171211066913. Epub ahead of print. PMID: [35081759](#).
Impact Statement: Nearly half of U.S. youth are not protected by smoke-free laws. This study underscores the association between comprehensive laws and decreased likelihood for both cigarette and smokeless tobacco use among high school students in a state with high use rates overall.
10. Kotla NG, Singh R, Baby BV, Rasala S, Rasool J, Hynes SO, Martin D, Egan LJ, Vemula PK, **Jala VR**, Rochev Y, Pandit A. Inflammation-specific targeted carriers for local drug delivery to inflammatory bowel disease. *Biomaterials*. 2022 Feb;281:121364. doi: 10.1016/j.biomaterials.2022.121364. Epub 2022 Jan 5. PMID: [35066288](#).
Impact Statement: Delivering drugs directly to the inflamed intestinal sites to treat inflammatory bowel disease (IBD), particularly Crohn's and ulcerative colitis, is highly challenging. In collaboration with Drs. Kotla, Yury Rochev and Abhay Pandit from CÚRAM, SFI Research Centre for Medical Devices, National University of Ireland Galway, Ireland, we report the development of a strong anionic charged inflammation targeted nanocarriers (IT-NCs) loaded with an immunosuppressant model drug. The results suggest that IT-NCs have promising therapeutic potential as delivery carriers' in colitis management.
11. Speer RM, Meaza I, Toyoda JH, Lu Y, Xu Q, Walter RB, Kong M, Lu H, **Kouokam JC**, **Wise JP Sr**. Particulate hexavalent chromium alters microRNAs in human lung cells that target key carcinogenic pathways. *Toxicol Appl Pharmacol*. 2022 Jan 28:115890. doi: 10.1016/j.taap.2022.115890. Epub ahead of print. PMID: [35101437](#).
Impact Statement: microRNAs play a role in virtually all biological processes, and thus, it is essential to understand their role in human disease, in particular cancer. Our recent publication is at the forefront of understanding how hexavalent chromium-altered microRNAs contribute to environmental carcinogenesis and advances the fields of environmental toxicology, human health, and cancer research. This work provides cancer researchers valuable data to better understand pathways to target cancer treatments and risk assessors information to update safety standards to better protect public health.
12. Faulkner CS, White CM, Manatsathit W, Lamb B, Vatsalya V, **McClain CJ**, **Jophlin LL**. Blood phosphatidylethanol (PEth) positivity associates with unfavorable waitlist-related outcomes for patients medically appropriate for liver transplant. *Alcohol Clin Exp Res*. 2022 Jan 31. doi: 10.1111/acer.14786. Epub ahead of print. PMID: [35102553](#).
Impact Statement: Excessive alcohol use is a leading etiology of liver disease and indication for liver transplantation. This study explores the association of phosphatidylethanol (PEth) results with liver transplant waitlist-focused patient outcomes. This study reporting a comprehensive account of PEth utilization at a liver transplant center demonstrates that liver transplant waitlist-related outcomes associate with PEth test results.
13. Oh YJ, Dent MW, Freels AR, Zhou Q, Lebrilla CB, **Merchant ML**, Matoba N. Antitumor activity of a lectin targeting cancer-associated high-mannose glycans. *Mol Ther*. 2022 Jan 22:S1525-0016(22)00030-2. doi: 10.1016/j.ymthe.2022.01.030. Epub ahead of print. PMID: [35077861](#).
Impact Statement: Aberrant protein glycosylation is a hallmark of cancer, but few drugs targeting cancer glyco-biomarkers are currently available. CIEHS members assisting the lab of Nobuyuki Matoba, Ph.D. (UL Department of Pharmacology & Toxicology and Brown Cancer Center) showed that a fusion protein termed a 'lectin body' comprised of the high-mannose glycan-binding lectin Avaren and human immunoglobulin G1 (IgG1) Fc (AvFc) selectively recognizes a range of cell lines derived from lung, breast, colon, and blood cancers at nanomolar concentrations. Proteomics studies identified specific AvFc interaction with epidermal growth factor receptor (EGFR) and insulin-like growth factor 1 receptor (IGF1R). AvFc blocked EGFR and IGF1R signaling in cell culture models of cancer and induced potent Fc-mediated cytotoxic effects and significantly restricted A549 and H460 tumor growth in severe combined immunodeficiency (SCID) mice. These findings provided evidence that increased abundance of high-mannose glycans in the glycocalyx of cancer cells can be a druggable target, and AvFc may provide a new tool to probe and target this tumor-associated glyco-biomarker.
14. Sriwastva MK, Deng ZB, Wang B, Teng Y, Kumar A, Sundaram K, Mu J, Lei C, Dryden GW, Xu F, Zhang L, Yan J, Zhang X, **Park JW**, **Merchant ML**, Egilmez NK, Zhang HG. Exosome-like nanoparticles from Mulberry bark prevent DSS-induced colitis via the AhR/COPS8 pathway. *EMBO Rep*. 2022 Jan 7:e53365. doi: 10.15252/embr.202153365. Epub ahead of print. PMID: [34994476](#).
Impact Statement: Proof of concept research demonstrated that exosome-like nanoparticles (MBELNs) derived from edible mulberry bark conferred protection against colitis in a mouse model through promoting heat shock protein family A (Hsp70) member 8 (HSPA8)-mediated activation of the AhR signaling pathway and induction of COP9 Constitutive Photomorphogenic Homolog Subunit 8 (COPS8). The results suggest that MBELNs represent an undescribed mode of inter-kingdom communication in the mammalian intestine and edible plant-derived ELNs may hold the potential as new agents for the prevention and treatment of gut-related inflammatory disease.

JANUARY PUBLICATIONS HIGHLIGHTS CONTINUED

15. Das S, **Rai SN**. Statistical methods for analysis of single-cell RNA-sequencing data. *MethodsX*. 2021 Nov 17;8:101580. doi: 10.1016/j.mex.2021.101580. PMID: 35004214; PMCID: [PMC8720898](#).
- Impact Statement:** *Analyzing the Single-cell RNA-sequencing (scRNA-seq) data in presence of biological confounding factors including dropout events is a challenging task. In this article, we present a novel statistical approach for various analyses of the scRNA-seq Unique Molecular Identifier (UMI) counts data, including model-based fitting of observed UMI data, cell type detection, estimation of cell capture rates, estimation of gene specific model parameters, estimation of the sample mean, and sample variance of the genes.*
16. Bhattacharyya A, Chakraborty T, **Rai SN**. Stochastic forecasting of COVID-19 daily new cases across countries with a novel hybrid time series model. *Nonlinear Dyn*. 2022 Jan 13:1-16. doi: 10.1007/s11071-021-07099-3. Epub ahead of print. PMID: 35039713; PMCID: [PMC8754528](#).
- Impact Statement:** *In this paper, we develop a hybrid forecasting model that can generate real-time out-of-sample forecasts of COVID-19 outbreaks for five profoundly affected countries, namely the USA, Brazil, India, the UK, and Canada. A novel hybrid approach based on the Theta method and autoregressive neural network (ARNN) model, named Theta-ARNN (TARNN) model. Daily new cases of COVID-19 are nonlinear, non-stationary, and volatile; thus, a single specific model cannot be ideal for future prediction of the pandemic. The proposed method outperforms traditional univariate and hybrid forecasting models for the test datasets on an average.*
17. Riggs DW, Malovichko MV, Gao H, McGraw KE, Taylor BS, Krivokhizhina T, **Rai SN**, Keith RJ, **Bhatnagar A**, **Srivastava S**. Environmental exposure to volatile organic compounds is associated with endothelial injury. *Toxicol Appl Pharmacol*. 2022 Jan 16;437:115877. doi: 10.1016/j.taap.2022.115877. Epub ahead of print. PMID: [35045333](#).
- Impact Statement:** *In this study, we hypothesized that ambient exposure to VOCs amplifies cardiovascular disease (CVD) risk by depleting circulating angiogenic cells (CACs). We found that Low-level ambient exposure to VOCs is associated with CAC depletion, which could compromise endothelial repair and angiogenesis, and exacerbate CVD risk.*
18. Jin J, **Wahlang B**, Thapa M, Head KZ, Hardesty JE, Srivastava S, **Merchant ML**, **Rai SN**, **Prough RA**, **Cave MC**. Proteomics and metabolic phenotyping define principal roles for the aryl hydrocarbon receptor in mouse liver. *Acta Pharm Sin B*. 2021 Dec;11(12):3806-3819. doi: 10.1016/j.apsb.2021.10.014. Epub 2021 Oct 21. PMID: 35024308; PMCID: [PMC8727924](#).
- Impact Statement:** *PCB pollutant exposures activate the aryl hydrocarbon receptor and are associated with liver disease. This study used genetic mouse models to determine the role of this receptor and PCBs acting through this receptor in liver disease.*
19. Ritzenthaler JD, Torres-Gonzalez E, Zheng Y, Zelko IN, Van Berkel V, Nunley DR, Kidane B, Halayko AJ, Summer R, **Watson WH**, Roman J. The pro-fibrotic and senescence phenotype of old lung fibroblasts is reversed or ameliorated by genetic and pharmacological manipulation of Slc7a11 expression. *Am J Physiol Lung Cell Mol Physiol*. 2022 Jan 5. doi: 10.1152/ajplung.00593.2020. Epub ahead of print. PMID: [34984918](#).
- Impact Statement:** *Fibroblasts from the lungs of old mice have low expression of the transporter for the amino acid cystine and high expression of markers of senescence and genes associated with fibrosis. Restoration of the cystine transporter made the old cells look more like young cells. These findings point the way toward new therapies designed to counteract the disrepair responses typically seen in the aging lung.*
20. Xiong L, Zhou B, **Young JL**, Xu J, **Wintergerst K**, **Cai L**. Effects of whole-life exposure to low-dose cadmium with post-weaning high-fat diet on offspring testes in a male mouse model. *Chem Biol Interact*. 2022 Feb 1;353:109797. doi: 10.1016/j.cbi.2022.109797. Epub 2022 Jan 5. PMID: [34998821](#).
- Impact Statement:** *Several studies have reported testicular impairments caused by cadmium (Cd) or obesity alone, therefore, this study examined the combined effect of Cd and obesity on the testes and its underlying mechanism remains unclear. demonstrated that exposure to Cd or HFD alone significantly disrupted testicular structure and increased germ cell apoptosis at both 10 and 24 weeks. However, co-exposure to Cd and HFD did not induce the toxic effects that were induced by either alone, which was associated with the activation of the JAK/STAT pathway. These unexpected results need to be further investigated in the future study.*
21. **Young JL**, **Cave MC**, Xu Q, Kong M, Xu J, Lin Q, Tan Y, **Cai L**. Whole life exposure to low dose cadmium alters diet-induced NAFLD. *Toxicol Appl Pharmacol*. 2022 Feb 1;436:115855. doi: 10.1016/j.taap.2021.115855. Epub 2022 Jan 3. PMID: 34990729; PMCID: [PMC8796138](#).
- Impact Statement:** *This study is one of the first to investigate the impact of whole life cadmium exposure (in utero throughout adulthood) on the development high fat diet-induced Nonalcoholic fatty liver disease NAFLD, taking into consideration that environmental exposures can be life-long, spanning multiple windows of susceptibility. Results confirm the multi-hit nature of NAFLD and highlight the urgent need to better understand the interaction of diet and environmental exposures, such as heavy metals, in driving disease severity and progression.*
22. Mo Y, Zhang Y, Zhang Y, Yuan J, Mo L, **Zhang Q**. Nickel nanoparticle-induced cell transformation: involvement of DNA damage and DNA repair defect through HIF-1 α /miR-210/Rad52 pathway. *J Nanobiotechnology*. 2021 Nov 17;19(1):370. doi: 10.1186/s12951-021-01117-7. PMID: 34789290; PMCID: [PMC8600818](#).
- Impact Statement:** *Nickel nanoparticles (Nano-Ni) are increasingly used in industry and biomedicine with the development of nanotechnology. However, the genotoxic and carcinogenic effects of Nano-Ni and the underlying mechanisms are still unclear. This study unraveled the mechanisms underlying Nano-Ni-induced cell malignant transformation. The combined effects of Nano-Ni-induced DNA damage and DNA repair defects through HIF-1 α /miR-210/Rad52 pathway probably contribute to Nano-Ni-induced genomic instability and ultimately cell transformation. Our findings will provide information to further elucidate the molecular mechanisms of Nano-Ni-induced genotoxicity and carcinogenicity.*

FEBRUARY PUBLICATIONS HIGHLIGHTS

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

- Xie W, Tackett AP, Berlowitz JB, Harlow AF, Kathuria H, Galiatsatos P, Fetterman JL, Cho J, Blaha MJ, Hamburg NM, Robertson RM, DeFilippis AP, Hall ME, **Bhatnagar A**, Benjamin EJ, Stokes AC. Association of Electronic Cigarette Use with Respiratory Symptom Development among US Young Adults. *Am J Respir Crit Care Med*. 2022 Jan 28. doi: 10.1164/rccm.202107-1718OC. Epub ahead of print. PMID: [35089853](#).
Impact Statement: *This study aimed to determine whether e-cigarette use is associated with the development of respiratory symptoms in young adults. The research found that former and current e-cigarette use was associated with higher odds of developing wheezing-related respiratory symptoms, after accounting for cigarette smoking and other combustible tobacco product use.*
- Cohen JE, Krishnan-Sarin S, Eissenberg T, Gould TJ, Berman ML, **Bhatnagar A**, Barnett TE, Soule E, Popova L, Tan ASL, Blank MD, Ling PM, O'Connor R. Balancing Risks and Benefits of E-Cigarettes in the Real World. *Am J Public Health*. 2022 Feb;112(2):e1-e2. doi: 10.2105/AJPH.2021.306607. PMID: 35080942; PMCID: [PMC8802586](#).
Impact Statement: *This publication is a review of Balfour's article entitled "Balancing Consideration of the Risks and Benefits of E-Cigarettes". We challenge the public health and scientific community to move away from characterizing scientists as "opponents" or "supporters" of e-cigarettes.*
- Zhang H, Wang Y, Men H, Zhou W, Zhou S, Liu Q, **Cai L**. CARD9 Regulation and its Role in Cardiovascular Diseases. *Int J Biol Sci*. 2022 Jan 1;18(3):970-982. doi: 10.7150/ijbs.65979. PMID: 35173530; PMCID: [PMC8771857](#).
Impact Statement: *CARD9 is an adaptor protein expressed on myeloid cells and located downstream of pattern recognition receptors (PRRs), which transduces signals involved in innate immunity, has been extensively investigated in various fungal diseases. However, this review summarized the information for its regulating role in activating p38 MAPK, NF- κ B, and NLRP3 inflammasome in various CVDs via promoting the production of proinflammatory cytokines and chemokines, leading to cardiac remodeling and dysfunction.*
- Sundaram K, Mu J, Kumar A, Behera J, Lei C, Sriwastva MK, Xu F, Dryden GW, Zhang L, **Chen S**, Yan J, Zhang X, **Park JW**, **Merchant ML**, Tyagi N, Teng Y, Zhang HG. Garlic exosome-like nanoparticles reverse high-fat diet induced obesity via the gut/brain axis. *Theranostics*. 2022 Jan 1;12(3):1220-1246. doi: 10.7150/thno.65427. PMID: 35154484; PMCID: [PMC8771565](#).
Impact Statement: *Obesity is a global epidemic and reversing obesity induced chronic inflammation including brain inflammation is a hallmark of obesity via the gut-brain axis. This study demonstrated that garlic exosome-like nanoparticles (GaELNs) that inhibit systemic as well as brain inflammatory activity and reverse a HFD induced obesity in mice. These results demonstrate how nanoparticles from a healthy diet can inhibit unhealthy high-fat diet induced brain inflammation and reveal a link between brain microglia/diet to brain inflammatory disease outcomes via diet-derived exosome-like nanoparticles.*
- Salazar-González RA, Doll MA, **Hein DW**. Arylamine N-Acetyltransferase 1 Activity is Regulated by the Protein Acetylation Status. *Front Pharmacol*. 2022 Jan 27;13:797469. doi: 10.3389/fphar.2022.797469. PMID: 35153780; PMCID: [PMC8828969](#).
Impact Statement: *Histone deacetylases (HDACs) and Sirtuins (SIRT) may have an important role on the N-acetyltransferase 1 (NAT1) acetylation status, affecting its catalytic capacity and having an impact on the downstream functions of this protein. We investigated the contribution of Lysine deacetylases (KDAC) in the catalytic activity of NAT1 using two different breast cancer cell lines: MDA-MB-231 (ER-, PR-, HER2-) and ZR-75-1 (ER+, PR+, HER2+) and tested the ability of Sirtuin and HDAC inhibitors to impact the transcription, translation and function of NAT1. We transiently knocked down (KD) Sirtuin 1/2 and evaluated the role of these specific proteins in the same experimental outcomes. The results show that the acetylation status of NAT1 is an important factor that might have a relevant role in the progression of cancer.*
- Doll MA, Ray AR, Salazar-González RA, Shah PP, Vega AA, Sears SM, Krueger AM, Hong KU, Beverly LJ, **Hein DW**. Deletion of arylamine N-acetyltransferase 1 in MDA-MB-231 human breast cancer cells reduces primary and secondary tumor growth in vivo with no significant effects on metastasis. *Mol Carcinog*. 2022 Feb 8. doi: 10.1002/mc.23392. Epub ahead of print. PMID: [35133049](#).
Impact Statement: *Previous studies showed that inhibition or depletion of N-acetyltransferase (NAT1) in human breast cancer cells diminishes anchorage-independent growth in culture, suggesting that NAT1 contributes to breast cancer growth and metastasis. Metastasis of parental and NAT1 knockout (KO) cells was investigated in vivo in a mouse xenograft model. NAT1 KO MDA-MB-231 cells produced primary tumors smaller than those formed by parental cells, which was contributed by an increased rate of apoptosis in KO cells. The frequency of lung metastasis, however, was not altered in NAT1 KO cells suggesting that NAT1 contributes to primary and secondary tumor growth in vivo in MDA-MB-231 breast cancer cells but does not appear to affect its metastatic potential.*
- Nathala P, Salunkhe V, Samanapally H, Xu Q, Furmanek S, Fahmy OH, Deepti F, Glynn A, McGuffin T, Goldsmith DC, Petrey J, Ali T, Titus D, Carrico R, Ramirez J, Antimisiaris D, Clifford SP, Pahwa S, Roser L, Kong M, **Huang J**; Center of Excellence for Research in Infectious Diseases (CERID) Coronavirus Study Group on behalf of the COVID-19 Cardiovascular Research Group (COVID-CVRG). Electrocardiographic Features and Outcome: Correlations in 124 Hospitalized Patients With COVID-19 and Cardiovascular Events. *J Cardiothorac Vasc Anesth*. 2022 Jan 13;S1053-0770(22)00042-8. doi: 10.1053/j.jvca.2022.01.011. Epub ahead of print. PMID: 35165040; PMCID: [PMC8757653](#).
Impact Statement: *In hospitalized patients with COVID-19 and cardiovascular events, electrocardiogram at various stages of COVID-19 hospitalization showed significantly different features with dissimilar clinical outcome correlations.*

FEBRUARY PUBLICATIONS HIGHLIGHTS CONTINUED

8. Xu Q, Liu Y, Cepulis D, Jerde A, Sheppard RA, Reichle W, Scott L, Oppy L, Stevenson G, Bishop S, Clifford SP, Liu P, Kong M, **Huang J**. Hand Hygiene Behaviours Monitored by an Electronic System in the Intensive Care Unit-A Prospective Observational Study. *J Hosp Infect*. 2022 Feb 2;S0195-6701(22)00032-9. doi: 10.1016/j.jhin.2022.01.017. Epub ahead of print. PMID: [35122887](#).
Impact Statement: *Patterns of healthcare workers' hand hygiene behaviors are complex and variable, which could facilitate targeted and personalized interventions to improve hand hygiene compliance.*
9. Zhang G, Kang Y, Cathey D, **LeBlanc AJ, Cai J, Cai L, Wang S, Huang J**, Keller BB. Sulforaphane Does Not Protect Right Ventricular Systolic and Diastolic Functions in Nrf2 Knockout Pulmonary Artery Hypertension Mice. *Cardiovasc Drugs Ther*. 2022 Feb 14. doi: 10.1007/s10557-022-07323-1. Epub ahead of print. PMID: [35157168](#).
Impact Statement: *Nrf2 is essential in sulforaphane-mediated prevention of right ventricular dysfunction and pulmonary hypertension. Increasing Nrf2 activity in patients by supplements or intakes of vegetables may have therapeutic potential for pulmonary hypertension.*
10. Tracy EP, Steilberg V, Rowe G, Benson D, Nunes SS, Hoying J, Murfee WL, **LeBlanc AJ**. State of the Field: Cellular Therapy Approaches in Microvascular Regeneration. *Am J Physiol Heart Circ Physiol*. 2022 Feb 18. doi: 10.1152/ajpheart.00674.2021. Epub ahead of print. PMID: [35179976](#).
Impact Statement: *This is a comprehensive review that gives the most recent update on cellular and exosomal therapeutic approaches in treating vascular and microvascular dysfunction. Relevant and recent clinical and animal studies utilizing cellular therapies to restore vascular function are highlighted throughout the text, and the figures and tables provided in the review are particularly helpful visual representations and also an excellent reference guide.*
11. Cummins TD, Korte EA, Bhayana S, **Merchant ML**, Barati MT, Smoyer WE, Klein JB. Advances in proteomic profiling of pediatric kidney diseases. *Pediatr Nephrol*. 2022 Feb 26. doi: 10.1007/s00467-022-05497-2. Epub ahead of print. PMID: [35220505](#).
Impact Statement: *Early detection of adult and pediatric CKD and detailed mechanistic understandings of the kidney damage may be helpful in delaying or curtailing disease progression. Clinically, serum creatinine and albumin levels can be indicative of CKD, but often are a lagging indicator only significantly affected once kidney function has severely diminished. The evolution of proteomics and mass spectrometry technologies has begun to provide a powerful research tool in defining these mechanisms and identifying novel biomarkers of CKD. This review addresses the potential for improving the clinical toolkit toward better treatment of pediatric kidney diseases aided by current and future development of proteomic applications.*
12. Kumar A, Sundaram K, Teng Y, Mu J, Sriwastva MK, Zhang L, Hood JL, Yan J, Zhang X, **Park JW, Merchant ML**, Zhang HG. Ginger nanoparticles mediated induction of Foxa2 prevents high-fat diet-induced insulin resistance. *Theranostics*. 2022 Jan 1;12(3):1388-1403. doi: 10.7150/thno.62514. PMID: 35154496; PMCID: [PMC8771553](#).
Impact Statement: *High-fat diets (HFD) are known to increase the risk of obesity and type 2 diabetes. While diet manipulation is a foundation of prevention and treatment of obesity and diabetes, the molecular mechanisms mediating diet-based prevention of insulin resistance remain open. Here, we report that treatment with orally administered ginger-derived nanoparticles (GDNP) prevents insulin resistance by restoring homeostasis in gut epithelial Foxa2 mediated signaling in mice fed a high-fat diet (HFD).*
13. Smith HAB, Besunder JB, Betters KA, Johnson PN, Srinivasan V, Stormorken A, Farrington E, Golianu B, Godshall AJ, Acinelli L, Almgren C, Bailey CH, Boyd JM, Cisco MJ, Damian M, deAlmeida ML, Fehr J, Fenton KE, Gilliland F, Grant MJC, Howell J, Ruggles CA, Simone S, Su F, **Sullivan JE**, Tegtmeier K, Traube C, Williams S, Berkenbosch JW. 2022 Society of Critical Care Medicine Clinical Practice Guidelines on Prevention and Management of Pain, Agitation, Neuromuscular Blockade, and Delirium in Critically Ill Pediatric Patients With Consideration of the ICU Environment and Early Mobility. *Pediatr Crit Care Med*. 2022 Feb 1;23(2):e74-e110. doi: 10.1097/PCC.0000000000002873. PMID: [35119438](#).
Impact Statement: *The Society of Critical Care Medicine Practice guidelines for managing pediatric patients who require pain relief, sedation and other medications provides guidance to keep the patients comfortable and safe. These guidelines provide comprehensive clinical practice guidance for those caring for critically ill infants and children with one of the goals being to prevent adverse and long term effects from these medications.*
14. Coleman CJ, **Yeager RA**, Pond ZA, Riggs DW, **Bhatnagar A**, Arden Pope C 3rd. Mortality risk associated with greenness, air pollution, and physical activity in a representative U.S. cohort. *Sci Total Environ*. 2022 Feb 14;824:153848. doi: 10.1016/j.scitotenv.2022.153848. Epub ahead of print. PMID: [35176374](#).
Impact Statement: *This study found that physical inactivity and exposure to air pollution were highly associated with mortality risk and that risk was especially lower among highly active individuals in areas with higher greenness. This study contributes evidence that greener environments are associated with lower risk of mortality and may help ameliorate the effects of exposure to air pollution, especially among highly active individuals.*

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