AWARDS ANNOUNCEMENTS AND REMINDERS

Pilot Project Program Videos
CIEHS has now released two Pilot Project Awardee Spotlight videos. Mayukh Banerjee, Ph.D., received the CIEHS Career Development Pilot Project Award in 2020. Click HERE to learn more about Dr. Banerjee's award entitled "APC11 is a novel target for arsenic-mediated zinc displacement leading to cell cycle disruption". Venkatakrishna Rao Jala, Ph.D., received the CIEHS Interdisciplinary Pilot Project Award in 2020. Click HERE to learn more about Dr. Jala's award entitled "Microbial metabolites protect against arsenic induced gut barrier dysfunction".

Save the Date for Research!Louisville
CIEHS is sponsoring two symposia in Research!Louisville in which CIEHS voucher and pilot project awardees will present on their projects. ITEMFC/IHSFC Research Voucher presentations will occur on Tuesday, October 26th, from 1-3 pm in the CTRB room 124. View more information about ITEMFC/IHSFC presentations HERE. Pilot Project Program presentations will occur on Thursday, October 28th, from 1-4 pm in the CTRB room 124. View more information on Pilot Project Program presentations HERE.

Anti-Racism Seminar
CIEHS held the center's first Anti-Racism seminar on August 12th (virtual and in person) with a total of 25 attendees. We are also planning an Anti-Racism discussion as part of the annual retreat on November 10th (2-5PM) as well as holding three training sessions in December, January, and February.
CIEHS Environmental Health Series Seminar with Special Guest Dr. Miroslav (Mirek) Styblo
In case you missed Dr. Mirek Styblo's seminar entitled "Humanized mouse models for arsenic toxicology" you can view the presentation HERE. Dr. Styblo is a Professor of Nutrition at the Gillings School of Global Public Health University of North Carolina - Chapel Hill. This EHS series seminar occurred on Thursday, September 2nd.

CIEHS Environmental Health Series Seminar with Dr. John Wise, Jr
CIEHS welcomes Dr. John Wise, Jr, as the next EHS seminar speaker on Thursday, October 7th, at 11 AM. Dr. Wise, Jr's presentation is entitled "A Toxic Aging Coin: Cr(VI) Neurotoxicity and Brain Aging". This will be a hybrid event. Click HERE to access the MS Teams link or attend in person at the Clinical and Translational Research Building (CTRB) room 124. View the CIEHS EHS seminar schedule HERE.

ITEMFC Research Voucher Awards Cycle 3
Congratulations to CIEHS members who received a Cycle 3 ITEMFC Research Voucher Award!

**Principal Investigator:** Banrida Wahlang, Ph.D.
**Collaborator:** Matthew Cave, M.D
**Title:** Sex-dependent effects on gut microbiome associated with PCB exposures
**Description:** Polychlorinated biphenyls (PCBs) are environmental chemicals or toxicants that have been associated with numerous health effects in people who are exposed to them. These health effects include liver disease, reproductive defects, and cardiovascular diseases. While extensive research has been performed on how PCBs induce organ damage and toxicity using experimental models, little is known about how PCBs behave with regards to their toxic actions, in the context of sex and gender. The proposed project seeks to understand how exposures to chemicals such as PCBs can cause changes in the composition of gut bacteria in the body, how these changes can impact liver health, and if these changes are different in males vs. females. Such studies will help to better understand the relationship between these environmental contaminants with sex and gender, and if men or women are more at risk to such PCB-associated health effects.

**Principal Investigator:** Madhavi Rane, Ph.D.
**Collaborator:** Lu Cai, M.D., Ph.D., Michael Merchant, Ph.D., Shesh Rai, Ph.D.
**Title:** Effects of whole life exposure to low-dose cadmium on post weaning high fat diet-induced pathogenesis in the kidney
**Description:** Obesity and cadmium (Cd) exposure are both independent risk factors for chronic kidney disease (CKD) and end stage renal disease (ESRD) necessitating dialysis or kidney transplantation. Since no current effective therapies exist to prevent progression to CKD, understanding how environmental exposure to Cd and diet-induced obesity simultaneously contribute to the pathogenesis of CKD is urgently needed. The current study, examining the dual effects of obesity (high-fat-diet) and cadmium exposure on kidney damage, is novel and will lead to generation of molecular target-based therapies to slow down progression to ESRD.
Throughout the summer, Dr. Huntington-Moskos facilitated in two programs aimed at working with youth interested in becoming healthcare providers. First, the 2nd Youth Exchange Session, which serves to introduce students to environmental health and its importance in communities across the nation, took place in May. Dr. Huntington-Moskos used virtual tools such as Padlet to gather additional feedback regarding the talk on youth, the climate crisis and air pollution given by Dr. Natasha DeJarnett of the Envirome Institute. The second initiative, the 2021 Summer Environmental Health Program, was conducted in seven sessions over the month of June and was developed in partnership with the South Central Kentucky AHEC. Dr. Huntington-Moskos engaged students interested in healthcare careers about environmental health concerns through distributing radon kits, taking inventory of possible chemical exposures in the home, identifying how personal care products can also adversely affect one’s health, and explaining how bees, water, and microplastics impact the environment that we inhabit.

Additionally, the Community Engagement Core in collaboration with the Administrative Core have made substantial progress on updating the CEC website throughout the past month. Current progress includes a series of interviews with Pilot Project Program awardees and community-led research projects. A list of resources and a request form for communities and community partners are also important additions to the website. The CEC section of the CIEHS webpage will continue to expand over the coming months. The CEC’s first Stakeholder Advisory Board meeting was held on Thursday, September 30th. During the month of October, the CEC will be launching its social media campaign and interviewing community members from one of the Pilot Project Program awards. Please be sure to follow the CEC on social media! We are on Instagram as UL_CEC and on Facebook as the Community Engagement Core of CIEHS.

Special thank you to Dr. Neal, Dr. Sanyang, Dr. Dunn, Dr. Wise, Jr. and Ms. Beth Adams for their time and willingness to be interviewed. Additionally, we thank our new stakeholder advisory board members: Dr. Ritchie Taylor, Ms. Beth Adams, Dr. Lauren Heberle, and Ms. June Ezell. If you have any questions regarding CEC efforts please feel free to reach out to the CEC Community Resources Coordinator, Josie Willis @ Josephine.willis@louisville.edu.

Awards Announcements and Reminders Continued

Trainee Travel Fund
CIEHS has initiated a fund to support student and Post-Doc travel to present an abstract (oral or poster) reporting Environmental Health Research at National and International meetings. We are currently accepting applications for travel awards HERE. In order to make a donation to support this travel fund, click HERE to contribute now.
Notes from the Director:

September 30, 2021

CIEHS is well into its second year and our efforts promoting environmental health research are bearing fruit. Our members are succeeding in earning new grants from NIEHS and other agencies and the grant portfolio is growing. Collaborations, often supported by research vouchers or pilot project funds, are forming resulting in high quality publications. These accomplishments are recognized in the newsletters, on social media and on the CIEHS website. Speaking of the website, Sarah Jump is doing a spectacular job updating and expanding the website. It is now a great resource for information on CIEHS activities and research interests of its members. The website will continue to be improved with your help in providing information to Sarah. We encourage you to visit and poke around!

Applications for the next round of research vouchers will be due soon. The vouchers provide funds to gather needed data to respond to reviews of manuscripts and grants, or to subsidize ‘omics experiments in the cores. Examples of recent awards are in this newsletter and all awards are posted on the CIEHS website.

The RFA for new pilot project grants will be issued soon. There will be some modifications to the program that will be discussed at the CIEHS annual retreat on Nov 10. We think you will appreciate the changes. We are videotaping interviews with pilot awardees and posting these short videos on the website and social media. Links to two pilot project videos are above in this newsletter. The videos provide a quick way to learn about innovative research being conducted by CIEHS members.

The NIH and in particular, the NIEHS is emphasizing diversification in research and anti-racism. CIEHS fully supports these efforts and, as mentioned elsewhere in this newsletter, held a workshop recently that was attended by about half the CIEHS membership. We learned important things to be developed in order to be of greater assistance to all our members. Dr. Antle will be presenting another anti-racism session at the retreat. This session will be a prelude to a three-part workshop series CIEHS is offering in subsequent months.

We strongly encourage all members to participate in the retreat. In addition to the anti-racism session and discussions of changes in the pilot project program, we will have discussion of opportunities presented by new industrial operations in the region. We also will be seeking member input regarding what we are doing well and new ways that CIEHS might support member research.

Unfortunately, COVID-19 is still with us and the delta variant is fueling a high infection rate. We will continue to offer hybrid seminars and encourage those who are comfortable to attend in person. Masks are required! The Co-Immunity project led by Dr. Aruni Bhatnagar is generating data on the spread and the infection rate. They found that an incidence in their sample of 3,000 people that is twice as high as official reported. Additionally, the >7-fold difference in infection rate between vaccinated and unvaccinated individuals demonstrates that vaccines are working. See the article on WFPL.org for details.

A final note on upcoming NIH requirements for data sharing and data management plans. UofL assembled a task force to develop data management policy for UofL researchers. The task force made a presentation on the new requirements and the work being done toward developing the UofL policy at the September 30 UofL Research Forum. (Contact Will Metcalf to get link to the meeting recording.) An appropriate data management and sharing plan will be required in all federal grant applications. The NIH published the Final NIH Policy for Data Management and Sharing (NOT-OD-21-013). We encourage everyone to take note of these new requirements.
MEMBER GRANT AWARDS FOR JUNE/JULY

Congratulations to CIEHS members who received new grants in the months of June and July 2021! We are so proud of all the hard work of our CIEHS members. You truly are making UofL a nationally recognized premier metropolitan research University and promoting interdisciplinary collaborative research in our Center! You can also view these grants by following this [LINK](#).

<table>
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<tr>
<th>PI Name</th>
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<tr>
<td>Bhatnagar, Aruni</td>
<td>Dejarnett, Natasha Krystal</td>
<td>Diversity Supplement to Urban Greenness and Cardiovascular Health</td>
<td>National Institutes of Health</td>
<td>$150,924.00</td>
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<tr>
<td>Antle, Becky</td>
<td></td>
<td>Coalition for Supporting Young Adults in Louisville: Special Projects for Connecting Vulnerable Youth</td>
<td>Youth Build Louisville</td>
<td>$12,500.00</td>
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<tr>
<td>Wise, John Pierce</td>
<td>Kouokam, Calvin J.</td>
<td>Supplement- Particulate Cr (VI) Toxicity in Human Lung Epithelial Cells and Fibroblasts</td>
<td>National Institutes of Health</td>
<td>$105,054.00</td>
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<td>Klinge, Carolyn Muriel</td>
<td>Cave, Matthew C.</td>
<td>Supplement- M6A Epitranscriptomics in Toxicant Associated Steatohepatitis</td>
<td>National Institutes of Health</td>
<td>$54,600.00</td>
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<tr>
<td>Hein, David W.</td>
<td>Bhatnagar, Aruni; Srivastava, Sanjay; Wise, John Pierce</td>
<td>UofL Environmental Health Sciences Training Program</td>
<td>National Institutes of Health</td>
<td>$400,713.00</td>
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This administrative supplement is to support Dr. Natasha Dejarnett's involvement in the community engagement and exposure assessment activities of the ongoing NIEHS supported project - "Urban Greenness and Cardiovascular Health" (ES 029846-03). Work supported by the supplement will test the role of discrimination in modifying the relationship between the urban greenspaces and cardiovascular disease risk and will examine whether the health effects of increasing greenness are mediated by changes in area temperature and temperature gradients.

Through our Cross System Assessment Project with CSYA, we are equipping programs who serve system involved youth with evidence-based tools to assess and discuss the wide variety of mental health challenges youth face. Earlier accurate assessments can lead to more effective interventions and better outcomes. Our trauma-informed approach recognizes that providers are also experiencing elevated mental health challenges and we provide space for them to name these challenges and support one another.

Hexavalent chromium (Cr(VI)) is a human lung carcinogen with widespread occupational and environmental exposure. How Cr(VI) causes human cancer is unknown. Our study aims to define the cellular mechanism for inflammation and translating it to animals, providing broad context to address the question of how Cr(VI)-induced chromosomal instability is interrelated with the inflammatory response. In addition, we will determine the ability of the food dye E162 (betanin) from the Red Beetroot (Beta Vulgaris Rubra) to modulate Cr(VI)-induced RAD51 Loss, inflammation and neoplastic transformation.

Environmental pollutants (polychlorinated biphenyls (PCB)) increase toxicant-associated steatohepatitis (TASH) in the context of a high fat diet. Whether PCB-induced modification of the epitranscriptome is involved in TASH is unknown. The major goal of this exploratory project is to determine if PCBs alter the liver N(6)methyladenosine epitranscriptome in TASH resulting in sex-specific gene changes and disease pathology.

The environmental health problems faced by the nation are multi-factorial in nature, and therefore require multi-disciplinary approaches for effective intervention. Our training program emphasizes the importance of multidisciplinary training and translation of basic science findings to obtain rigorous, reproducible and transparent results that benefit the patient and/or community. This multi-disciplinary translational program interfaces with the NIH Roadmap and the NIEHS strategic plan. This grant also supports stipends, tuition, and travel for six predoctoral and three postdoctoral fellows.

Total New Awards June/July 2021: $723,791.00
Congratulations to the CIEHS members with articles published in the month of July! 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.


**Impact Statement:** Exposure to acrolein is linked with cardiopulmonary toxicity and cardiovascular disease (CVD) risk in humans, yet the mechanisms by which acrolein exposure confers CVD risk is unclear. This study showed that acrolein in isolated blood vessels is vasorelaxant at low levels (physiological) yet vaso toxic at high levels (toxicological), while the major metabolite of acrolein, 3-hydroxypropyl mercapturic acid (3HPMA), was weakly vasoactive and non-toxic indicating it likely does not directly account for vascular injury. These findings support the continued use of 3HPMA as a biomarker of acrolein exposure and warrant further research on mechanisms of acrolein-induced vascular injury to develop interventions that can protect human health.


**Impact Statement:** This is a commentary for a recent study that has brought us many hopes for the potential gene therapy for diabetic cardiomyopathy (DCM). The authors first noticed the significant increase in O-GlcNAc modified proteins in the heart tissues of patients with diabetes, which was positively and inversely correlated with their HbA1c or blood glucose levels and with cardiac ejection fraction, respectively. Then the authors transferred O-GlcNAcase gene with adeno-associated viral vector to diabetic mice with diastolic dysfunction, a typical early feature of DCM. The gene therapy significantly reduced diabetes-increased expression of O-GlcNAc proteins and expressions of pro-fibrotic genes coding the proteins involved in fibrosis, and interstitial and perivascular type I and type III collagen deposition and improved diastolic dysfunction. Therefore, this is a milestone to confirm the potential therapeutic reversion of DCM by correcting the balance of O-GlcNAcylation in the diabetic heart, even though there remain some unanswered issues.


**Impact Statement:** Tian et al. demonstrated that T2D decreased cardiac function and KLF15 expression, while increasing cardiac fibrosis. SDF-1 increased KLF-15 expression, decreased cardiac fibrosis, and increased cardiac function in T2D mice, providing a novel therapeutic option for treatment of cardiac fibrosis in T2D patients.


**Impact Statement:** During the height of the COVID-19 pandemic in 2020 when vaccines were not largely available, we observed mask usage in Louisville's public areas. Differences in mask usage were observed by geographic areas, size and type of public area, and by perceived age and sex, which can aid public health practitioners in their efforts to promote COVID-19 prevention practices.


**Impact Statement:** This systematic review showed that patients and other stakeholders perceive high-quality cancer care to be adequate control of physical and psychosocial symptoms. Results were used to inform feasibility testing of patient reported outcome measures (PROMs) as performance measures in six U.S. cancer centers.


**Impact Statement:** Exposure to fine air borne particulate matter is associated with cardiovascular, immunological, and cognitive disorders, but the mechanism for this is unclear. This study provides evidence that such exposures alters the expression of protein at the genetic level and that this can occur in a group of bone marrow stem cells. This mechanism may underlie adverse outcomes associated with other inhalation exposures, such as that to cigarette smoke.

Impact Statement: Although breast cancer patients whose initial breast tumor expressed estrogen receptor alpha (ERα) are successfully treated with drugs targeting ERα, many patients develop resistance to these endocrine therapies and disease progression to metastasis remains a major clinical problem. This paper summarizes the role of long non-coding RNAs (lncRNA) regulated by miR-29 in endocrine-resistant breast cancer cells and clinical samples.


Impact Statement: Porphyromonas gingivalis is a major pathogen in periodontal diseases and possesses an array of colonization and virulence factors contributing to retention, survival, and proliferation in the dynamic and diverse ecosystems of the oral cavity. The P. gingivalis genome contains one system, the orphan response regulator (RR) RprY, that controls heterotypic community development. This study employed multiple approaches including in vitro kinase assays and phosphoproteomics to delineate the system by which RprY is activated.


Impact Statement: The myeloid inhibitory C-type lectin receptor CLEC12A limits neutrophil activation and pro-inflammatory pathways in experimental models of inflammatory arthritis. Phosphoproteomic analysis identified candidate signaling molecules regulated by CLEC12A. Further studies defined early molecular events underpinning CLEC12A signaling in human neutrophils modulating cytokine synthesis. Targeting this pathway could be useful therapeutically to dampen inflammation.


Impact Statement: Clinical trials with survival endpoints are typically designed to enroll patients for a specified number of years, (usually 2-3 years) with another specified duration of follow-up (usually 2-3 years). With random accrual time and follow-up time lead to complex censoring patterns. Conflicting findings were observed for comparing cardiovascular events in patients who took Rofecoxib (Vioxx). Here, using extensive simulation studies, we assess the impact of such censorings on statistical procedures for comparing two treatment groups. Clinical studies with survival outcome should be properly designed to maintain power by considering the censoring patterns.


Impact Statement: This study used geospatial mapping to determine if child behavior problems were associated with proximity to coal-burning power plants with cool ash storage sites containing known neurotoxins. Results indicated that children living closer to these coal-burning plants had increased risk of anxiety, ADHD and social problems suggesting a need for further consideration of environmental exposures in improving child neurobehavioral health.


Impact Statement: The aim of this study was to develop a pharmacokinetic model to evaluate ceftazidime pharmacokinetics in a cohort that included a predominant number of children and adolescents with obesity and assess the efficacy of two different dosing strategies. The results show that dosing 40 mg/kg every six hours intravenously (maximum dose 8 grams/day) met the target minimum inhibitory concentration for efficacy. This research is critical because obese patients tend to have poorer outcomes with infections therefore dosing antibiotics appropriately may improve their outcome.


Impact Statement: We found that cancer patients living in areas with high levels of vegetation had a higher likelihood of cancer survival. We also found that this association was not impacted by air pollution, as some have suspected.


Impact Statement: This paper enables samples sites to be selected to ensure objective and equitable estimates for COVID-19 infection prevalence throughout Louisville, Kentucky. With such sampling, wastewater testing data is utilized to inform public health response and variant tracking.
Congratulations to the CIEHS members with articles published in the month of August! 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.


**Impact Statement:** Several factors hinder the diagnosis of Alzheimer’s disease at an early stage, in particular, the divergence of 10-15 years between the onset of the underlying neuropathological changes and patients becoming symptomatic. This study surveyed patients with mild cognitive impairment (MCI), who were at risk of conversion to AD, with a local/regional-based computer-aided diagnosis system. The experimental results showed an encouraging performance of the proposed system when compared with related work.


**Impact Statement:** The purpose of this study was to examine the relationship between views of greenness and Patient Health Questionnaire-9 (PHQ-9) score. The findings suggest urban greening interventions that focus on greenness satisfaction may be a strategy to reduce depression.


**Impact Statement:** Levels of fine particulate matter (PM2.5) air pollution are associated with chronic cardiovascular disease in humans; however, understanding of the early changes that foster chronic vascular disease is incomplete. Because perivascular adipose tissue (PVAT) inflammation is implicated in chronic vascular diseases, we investigated early changes in aortic PVAT following short-term air pollution exposure in mice. We found that PM2.5-exposed mice had changes consistent with oxidative stress, vascular dysfunction and insulin resistance in aortic PVAT. The PM2.5-induced changes were absent in mice with overexpression of extracellular superoxide dismutase in the lungs implicating pulmonary oxidative stress as necessary in detrimental vascular changes in PM2.5-exposed mice. As our study connects inhaled PM2.5 and pulmonary oxidative stress with vascular derangement, we expect future research will test potential interventions that may protect public health from the deleterious cardiovascular effects of air pollution exposure.


**Impact Statement:** Amniotic fluid embolism (AFE) is a rare leading cause of unpredictable maternal death in industrialized countries. We present the management and sudden hemodynamic collapse of a patient due to a suspected AFE complicated by an undiagnosed patent foramen ovale.


**Impact Statement:** This work discusses the intentional use of data visualizations in the report back of research findings to community members. Open-source tools can be effectively used to create data visualizations, discuss environmental exposure findings, and promote science literacy.


**Impact Statement:** Phosphoserine aminotransferase 1 (PSAT1) expression has been observed in multiple tumor types and is associated with poorer clinical outcomes. PSAT1’s role in cancer progression has not been fully characterized. Biochemical studies identified an interaction of PSAT1 with pyruvate kinase M2 (PKM2). Further studies demonstrated in response to epidermal growth factor receptor activation, PSAT1 contributed to lung cancer cell migration, in part, by promoting nuclear PKM2 translocation.


**Impact Statement:** Most of the human diseases and plants traits are complex quantitative in nature and controlled by polygenes. Hence, the developed method, and the software tool will help the researchers to establish the link between the genotypes (e.g., gene sets) with the phenotypes (e.g., complex traits). This may have substantial application in molecular crop breeding and establishing the biological basis of diseases.


**Impact Statement:** Manganese is an essential trace element however overexposure can lead to neurotoxicity. This study looked at children living near coal ash storage sites who may be at risk for manganese overexposure. Neuropsychological testing found that children with the highest Mn levels had poorer eye hand coordination and reduced ability to sustain attention compared to those with low Mn levels. Findings are in agreement with previous studies supporting the need to monitor child environmental exposures due to the potential for increased neurobehavioral problems.