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

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

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

**Walter H. Watson, Ph.D.**
**Awarded a CIEHS Medium OEFC Research Voucher Award**
Congratulations to Dr. Watson for his newly awarded OEFC Research Voucher Award from the CIEHS entitled “Comparative keratinocyte responses to environmental arsenic”. We are so proud of all the hard work of our CIEHS members. You truly are making UofL, a nationally recognized premier metropolitan research University and promoting interdisciplinary collaborative research in our Center.

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

**Have a CIEHS Core Question?**
Do you have questions pertaining to a specific CIEHS Core? Several CIEHS Cores have their own service email accounts where you can reach out to the core directly. CIEHS advises using these service accounts to ensure a timely response.

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

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

**Pilot Project Program (PPP)**
pilotprojects@louisville.edu

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

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

**CONNECT WITH US ON SOCIAL MEDIA:**

---

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

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

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

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

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

Luz Huntington-Moskos, Ph.D., RN, CPN, promoted to Associate Professor
Congratulations Dr. Huntington-Moskos, Community Engagement Core Director, for being promoted to Associate Professor with tenure. Dr. Huntington-Moskos gives many thanks to people who have helped her along the way including CIEHS Director, Dr. J. Christopher States.
During the months of June and July, the CEC participated in a number of activities. Over a two-week period at the end of June, Dr. Huntington-Moskos met with the Girls Incorporated organization in Owensboro, Kentucky where she taught a group of young women about environmental health topics including disaster preparedness, radon awareness, personal care products, bees as pollinators, and safe drinking water. In mid-July, Dr. Huntington-Moskos along with Ms. Quinter, Dr. DeJarnett, Dr. Cave, and Dr. States attended the annual NIEHS meeting in New York City. Our collaboration with Mr. Tony Arnold of the University of Louisville’s Brandeis School of Law is growing. Watch our CEC webpage for a bi-monthly blog posts authored by the Resilience Justice Fellows, discussing the intersection of environmental law and environmental health. The blogs will discuss an array of topics including green and blue infrastructure, air quality, PFAS, climate change, and health equity in relation to environmental justice.

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

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

July, 2022

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

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

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

Looking toward the future NIEHS emphasis on these topics, we are looking to promoting research with the current voucher solicitation and a second RFA for pilot awards later this year. Bear in mind that pilot award applications must convince reviewers of their potential to generate data to support and NIEHS R01 application. Thus, preliminary data are needed. If you have a good idea but no preliminary data, a medium research voucher application would be appropriate.
MEMBER GRANT AWARDS MARCH & APRIL 2022

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

<table>
<thead>
<tr>
<th>PI Name</th>
<th>Other Investigator</th>
<th>Long Title</th>
<th>Sponsor</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barve, Ashutosh Jayant</td>
<td>Jophlin, Loretta Lynn</td>
<td>LAM-2018-01 - Prospective Clinical Trial to Detect Liver Cancer through Quantification of cfDNA Methylation in Blood Samples (CLIMB) Protocol LAM-2018-01</td>
<td>SC liver Research Consortium</td>
<td>$218,414.00</td>
</tr>
</tbody>
</table>

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

| Sandell, Lisa Leopold | LeBlanc, Amanda Jo | Therapeutic vascularization to support repair of damaged salivary glands | National Institutes of Health | $371,391.00 |

Loss of salivary gland function is a devastating condition. Millions of people lose salivary gland function from autoimmune disease or cancer radiation treatment, and therapies to promote gland repair are needed. Repair of salivary gland tissues requires re-growth of blood vessels that can support salivary gland tissue as it heals from damage.

| Carli, Alex P | | Systematic identification of cardiotoxic e-cigarette flavorants | National Institutes of Health | $713,734.00 |

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

Total New Awards March & April 2022: $1,303,539.00
Congratulations to the CIEHS members with articles published in the month of May! Member names will be bolded and impact statements for the publications are italicized. You may also read the publication by clicking on the PMID underlined.


**Impact Statement:** Our research sheds direct light on the most accepted explanation for the mode of action of arsenic carcinogenicity in arsenic's major target organ, skin. Arsenic is known to induce DNA breaks without directly interacting with DNA. We have discovered that a major signaling protein for DNA break repair, ataxia telangiectasia-mutated (ATM), has reduced activation in human keratinocytes chronically exposed to inorganic arsenic. ATM plays an important role in DNA repair by activating enzymes that can fix DNA strand breaks in cells, preventing the accumulation of mutations in cells and carcinogenesis. Thus, it could be hypothesized that arsenic-induced tumors may be more sensitive to certain cancer treatments that induce DNA damage or inhibit DNA repair, such as radiotherapy or PARP inhibitors, respectively. Based on these findings, additional studies are needed determine whether arsenic-induced tumors are sensitive to specific chemotherapeutic regimens. Results from these future studies could be used to design new strategies to treat arsenic-induced cancers.


**Impact Statement:** Despite increasing popularity of electronic cigarettes (e-cigarettes), the long-term health effects of habitual e-cigarette use remain unclear. Our results suggest that combining smoking with e-cigarette use does not reduce cardiovascular disease (CVD) events and that quitting both products is required to ensure a mitigation of risk.


**Impact Statement:** Methadone (MTD) is a common medication treatment for opioid use disorder (OUD) during pregnancy. In this study, pregnant rats were administrated a dosing approximately equivalent to the OUD treatment and the effects of passive in utero and postnatal MTD exposure on myelin development was investigated in neonatal rat brain. The findings reveal the potential mechanism(s) underlying the association between myelin impairment and antenatal opioid exposure. Our study alongside others concerns for fetal brain development when using MTD to manage the OUD during pregnancy. Improved understanding of the effects of opioid exposure will allow us to design treatments for OUD during pregnancy that minimize effects on the fetal brain or target postnatal treatment to mitigate the effects of antenatal opioid exposure.


**Impact Statement:** This paper reports a simple method of integrating microfabricated preconcentrators with commercial SPME fibers in a two-stage concentration processes to achieve rapid and reliable measurement of trace VOCs in environmental air by GC–MS. This approach has been demonstrated for measurements of toxic VOCs including benzene, toluene, ethylbenzene, xylene (BTEX) and trichloroethene (TCE).


**Impact Statement:** In this article, we present the development of the prototype Inspired Therapeutics NeoMate System for pediatric left ventricular assist device (LVAD) support, and feasibility testing in static mock flow loops (H-Q curves), dynamic mock flow loops (hemodynamics), and in an acute healthy ovine model (hemodynamics and clinical applicability).

**Impact Statement:** Fibrosis in early-stage alcohol-associated liver disease (ALD) is commonly under-diagnosed in routine clinical practice. This study characterized the liver-injury and cell death response in alcohol use disorder (AUD) patients with ALD who also exhibited fibrosis and assessed the efficacy of standard of care (SOC) treatment in the improvement in liver injury.


**Impact Statement:** The gut microbiome has recently revealed itself to be a major player in human health and disease. Here, Drs. Huang-Ge Zhang and collaborators including CIEHS members Michael Merchant and Jun Won Park, show that a small metabolite, isoamylamine (IAA) produce by the bacteria Ruminococccaceae is enriched in aged mice and elderly people. Interestingly a bacteriophage belonging to the Myoviridae family that infects Ruminococccaceae are reduced in these settings. IAA induced cognitive declines in young mice is reversed by Myoviridae phage administration. IAA promoted apoptosis of microglial cells through a p53 dependent mechanism. Our results linked microbiome metabolites to direct transcriptional co-regulation of genomic DNA. These findings suggest a molecular mechanism connecting gut metabolism to gene expression in the brain with implications for disease development.


**Impact Statement:** Developing accurate prediction method benefits personalized medicine, involving patient's demographic, history, and gene signatures. Bayesian shrinkage models have emerged as popular and flexible methods of variable selection in regression settings. This work discusses variable selection and illustrates its application to multiple clinical studies, such as Pima Indians Diabetes, Colon cancer, ADNI, and OASIS Alzheimer's data sets. Informative priors can be used for robust and efficient prediction with accuracy of 91.6% (95% CI: 88.5, 94.7). The proposed method is robust to conduct both variable selection and prediction.


**Impact Statement:** Metabolomics has emerged as a powerful method to provide insight into cancer progression, including separating patients into low- and high-risk groups for overall (OS) and progression-free survival (PFS). This proof-of-concept study evaluates metabolites as biomarkers obtained directly from tumor core biopsies along with covariates age, sex, pathological stage at diagnosis (II/III vs. III/VI), histological subtype, and treatment vs. no treatment. A prediction model is developed to stratify patients into low- and high-risk groups based on log-transformed intensities of key metabolites. Risk scores based on 10 metabolites for OS and 5 metabolites for PFS were significant predictors of survival. Risk scores were validated with SPLS-DA classification model (AUROC 0.868 for OS and AUROC 0.755 for PFS, when combined with covariates. Thus, metabolomic analysis of lung tumor core biopsies has the potential to differentiate patients into low- and high-risk groups based on OS and PFS events and probability.


**Impact Statement:** Individuals with type 1 diabetes face many challenges when participating in sporting activities and general exercise. This publication offers some glucose control guidance for athletes participating in maximal aerobic exercise. In addition to benefiting individuals with T1D, this article may also be beneficial to coaches, physical educators, and parents of children participating in sporting activities.


**Impact Statement:** Coal workers' pneumoconiosis (CWP) is a type of typical occupational lung disease caused by prolonged inhalation of coal mine dust. The individuals' different genetic background may underlie their different susceptibility to develop pneumoconiosis, even under the same exposure level. This study aimed to identify susceptibility genes associated with CWP. We have identified PSMB9 as a novel susceptibility gene for CWP and provided important insights into the further exploration of the CWP pathogenesis.
JUNE PUBLICATIONS HIGHLIGHTS

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

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

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

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

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

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

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

**Impact Statement:** Whereas a number of publications have identified asthma phenotypes in adults, few have focused only on older adults. As a component of a randomized controlled trial of older adults (≥50 years old) with persistent asthma, Baptist et al identified 4 phenotypic clusters. The purpose of this study was to compare findings from the Baptist et al study with cluster analysis findings from a cohort of older adults with asthma participating in a longitudinal observational study.


**Impact Statement:** Normal Density Neutrophils and Low Density Neutrophils from COVID-19 patients possess complementary functional capabilities that may act cooperatively to determine disease severity. We predict that global neutrophil responses that induce COVID-19 ARDS will vary depending on the proportion of neutrophil subsets.


**Impact Statement:** Lupus nephritis (LN) is a severe complication of systemic lupus erythematosus and current diagnostics and treatments are inadequate. Our report identifies a potential diagnostic marker for LN and will therefore provide impactful insight for improved LN patient care.


**Impact statement:** Liver disease associated with long-term heavy drinking of alcoholic beverages is a major health problem with no FDA-approved therapies. In this paper, we describe a previously unknown mediator of alcohol’s adverse effects on the liver: the alpha4 subunit of nicotinic acetylcholine receptors. These neurotransmitter receptors are known to be important in the brain, where they are involved in the reward pathways activated by both nicotine and alcohol. The discovery that they are also expressed in the liver and contribute to some of the earliest manifestations of alcohol-associated liver disease points to a new target for potential therapeutic interventions.


**Impact Statement:** Worldwide, the prevalence of obesity continues rising unabated due to the rapid urbanization in the developed and developing countries and poor lifestyle habits. Obesity is also attributed to the development of major cardiovascular diseases (CVD), diabetes, arthritis, behavioral changes, depression, cancers, and hepatic diseases. Therefore, a special issue focus on the CVDs related to diabetes and obesity has been released, for which this editorial was and also briefly introduced the contents of the twelve publications, with a hope to set the stage for delving further in deciphering the crucial link between obesity and diabetes.

**CONNECT WITH US ON SOCIAL MEDIA:**