



IIT UPDATE

INSTITUTE FOR INTEGRATIVE TOXICOLOGY



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IIT-Affiliated Faculty Help Form New Center for PFAS Research

Six IIT-affiliated faculty members, Drs. Cheryl Murphy, Sudin Bhattacharya, Courtney Carignan, A. Daniel Jones, Hui Li, and Brian Teppen, have recently joined forces with nine other researchers across campus to form the Center for PFAS Research. This group, with knowledge spanning diverse fields across campus, are linking their expertise in an effort to understand more about PFAS and its effects on health and the environment. Per- and polyfluoroalkyl substances (PFAS) are a class that includes at least 4,000 chemicals. Many of these have been used in fire-fighting foams for fuel fires, water and stain-resistant coatings for furniture, carpeting, footwear, textiles, paper food packaging and more. Unlike the case for nearly all other organic pollutants, PFAS in soil and water are not degraded by biological or biogeochemical processes.

The Center for PFAS Research, in collaboration with MSU AgBioResearch, will serve as a hub for academic, public health, state, federal, and industry research endeavors surrounding PFAS and emerging contaminants. The main goals of the Center for PFAS Research are to quantify and communicate PFAS risks, and mitigate their impacts on human health, agriculture and natural resources. Researchers at the Center will aim to quantify exposure and risk for humans, livestock, crops, fish and wildlife as well as develop and test remediation strategies and technologies. A number of

researchers will also be exploring safer PFAS alternatives. Investment into PFAS research is timely and appropriate because there are no focused and coordinated efforts to explore PFAS impact on agricultural and natural resources in the U.S. There is also a significant investment by the state of Michigan (estimated at \$50 million so far) into PFAS-related issues, which is well above the current federal level, and more than any other state in the U.S.

The Center will use an organized framework to unite researchers across disciplines to tackle this complex ecological and agricultural problem. Tapping into MSU's vast knowledge base, research disciplines engaged with the Center will include biologists, toxicologists, risk assessors, computer scientists, modelers, mathematicians, chemists, physicists, ecologists and engineers as well as exposure, data and social researchers. Center for PFAS Research Director and IIT-affiliated faculty member, Dr. Cheryl Murphy, is looking forward to bringing even more expertise on board with the Center as their funding and research gets underway. "The PFAS problem is very complicated, but we are excited to tap into the vast array of expertise across campus that could help us tackle this problem. MSU is the perfect place to launch such a center"

On January 10, 2020, the U.S. House of Representatives passed the PFAS Action Act which designates certain PFAS as haz-

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PFAS Research Center cont.

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ardous substances. If this Act is enacted, and PFAS are declared hazardous substances, then under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA, aka Superfund), significant remediation funds become accessible for PFAS. The

Center for PFAS Research will facilitate MSU's readiness for when PFAS are declared hazardous substances, so that MSU can quickly respond to funding opportunities and provide sound science to support the risk assessment of particular PFAS compounds.

To learn more about the Center for PFAS Research at MSU, please visit:

<https://www.canr.msu.edu/news/msu-announces-new-center-for-pfas-research>

<https://www.canr.msu.edu/pfas-research/index> 📍

Bernard Awarded R01 Grant to Study How Obesity Impacts the Carcinogenicity of Chemical Exposure



IIT-affiliated faculty member, **Dr. Jamie Bernard**, was recently awarded a R01 grant from the National Institute for Environmental Health Sciences for her project, "Mechanistic Role of

Obesity in Benzo(a)pyrene-initiated Cancer." Bernard, in collaboration with Dr. Sophia Lunt, MSU, and Dr. Weston Porter, Texas A&M University, will receive \$1,537,350 to perform this research over the next four years.

"We currently have an unprecedented obesity epidemic with no signs of reversing course," explained Bernard on the basis of the project. "While the cancer biology field has a mechanistic understanding of how obesity can make existing cancers more aggressive, we still have a very limited understanding about how obesity increases the risk of developing cancer in the first place."

Bernard and her team have demonstrated that factors from adipose tissue, specifically those released from belly fat, influence the metabolism of chemicals by providing an environment that favors the bioactivation of carcinogens. They hypothesize that this influences cancer risk in obesity which helps shed light on a major unknown – how does obesity

cause cancer? By studying this question, Bernard and her team, hope to be one of the first to show that toxicological risk changes due to obesity. Understanding these mechanisms will provide insights into new targets for cancer prevention and determine how excess adipose tissue may increase one's vulnerability to specific carcinogenic exposures.

Bernard is an Assistant Professor in the Department of Pharmacology and Toxicology at MSU. The Bernard laboratory studies the mechanisms that underlie the onset of carcinogenesis, so they can find new targets for prevention. 📍

EITS Alumnus Burgoon Joins IIT Faculty



The IIT is pleased to welcome EITS alumnus, **Dr. Lyle Burgoon**, as a new adjunct faculty member.

Dr. Burgoon received his A.B. in Pre-Medicine and Biology from Augustana College in 1999.

In 2005, he received his Ph.D. in Pharmacology and Toxicology and Environmental Toxicology from Michigan State University. Burgoon was mentored by Dr. Timothy Zacharewski during his time as an EITS graduate student. Bur-

goon also completed his postdoctoral studies in Biochemistry and Molecular Biology at MSU. Today, Burgoon is the Director at the Center for Existential Threat Analysis and Leader of Bioinformatics and Computational Toxicology at the US Army Engineer Research and Development Center.

Dr. Burgoon's primary research interests focus on: 1) applied toxicology and risk assessment in the military environment (toxic industrial chemicals, CBRNE (chemical, biological, radiological, nuclear, and high yield explosive) weapons of mass destruction), 2) applied toxicology and risk assessment of civilian accidental releases and mass casualty events, 3) predictive computational toxicology, physiologically-based

pharmacokinetic modeling (PBPK) and artificial intelligence, and 4) applied biostatistics in toxicology and chemical/drug safety assessment (i.e., metascience applied to toxicology). Dr. Burgoon's research programs are funded by the US Defense Threat Reduction Agency, the Office of the Secretary of Defense, and the US Army Futures Command. Dr. Burgoon has recently started a research program focused on metascience applied to toxicology -- specifically, studying how defects in study designs, pseudoreplication and sample bias are contributing to the replication crisis in toxicology, and how these defects impact safety/risk assessments, policies, and drug/chemical regulations. 📍

Wu Receives Grant to Study Fungus that Causes Liver Cancer



Felicia Wu, John A. Hannah Distinguished Professor in the Department of Food Science and Human Nutrition and Department of Agricultural, Food and Resource Economics and

IIT-affiliated faculty member, along with David Hennessy, Elton R. Smith Chair in the Department of Agricultural, Food and Resource Economics, were recently awarded a \$478,000 USDA-National Institute of Food and Agriculture, or NIFA, grant for their project “Aflatoxin Reduced By Bt Corn? Examining Crop In-

surance Claims for Real World Impacts of Technologies for Food Safety.”

This grant will allow the team to examine whether transgenic, or genetically modified, Bt corn has lower levels of a certain fungal toxin, aflatoxin, that causes liver cancer. Aflatoxin is produced by fungi that infect corn when there is insect damage – you may have noticed that vegetables and fruits that were eaten by insects often have a ring of mold around the insect bites.

Bt corn is genetically modified to produce pesticides that target insects, but it is harmless to humans and other animals, and has less insect damage, and therefore less fungal infection. Does this mean that Bt corn can reduce the presence of aflatoxin? If so, then it could have huge economic and health benefits. Aflatoxin causes liver cancer,

and therefore the FDA controls it strictly, sometimes at a substantial cost to corn growers, Wu said.

“We will use crop insurance claims around the United States from corn growers in 2001-2016 to determine if aflatoxin-related insurance claims are decreased as a function of Bt corn planting,” Wu said.

Jina Yu, professor at Beijing Normal University-Hong Kong Baptist University United International College and former Wu Ph.D. student contributed to preliminary research on Bt corn and aflatoxin reduction for the grant. Another collaborator on this grant is Gary Munkvold, professor of plant pathology and microbiology at Iowa State University. 🌱

CRIS Symposium on Cannabidiol (CBD)



The Center for Research on Ingredient Safety is pleased to announce a scientific symposium to be held November 11-12, 2020 focused exclusively on cannabidiol (CBD). The free event is open to the public and will be held virtually from 12:00 - 3:30 p.m. each day. Registration is now open at: go.msu.edu/cris20. The symposium will feature lectures from researchers, lawyers and industry experts including:

» **Mitzi Nagarkatti, Ph.D.**

University of South Carolina School of Medicine
“Cannabinoid-induced changes in gut microbiome and suppression of inflammation”

» **Alan Boobis, Ph.D.**

Imperial College London
“UK safety assessment of CBD as a novel food”

» **Barbara Kaplan, Ph.D.**

Mississippi State University
“Inhibition of Peripheral Immune Function and Neuroinflammation by CBD in EAE”

» **Helen Turner, Ph.D.**

Chaminade University
“Cannabinoid and terpene regulation of ionotropic receptor pathways”

» **Brad Lampe, M.P.H.**

NSF International
“Derivation of an acceptable daily intake of orally-consumed cannabidiol (CBD) in adult consumers: challenges and limitations”

» **Sylvia Laman, M.S.**

NSF International
“Strategy for Evaluating Hemp-Based Products as Dietary Supplements”

» **Andrew Shen, Ph.D.**

U.S. Food & Drug Administration
“Effects of Perinatal Cannabidiol (CBD) Exposure on Developmental Outcomes: A Focus on Neurocognitive and Motor Functioning”

» **Patrick McCarthy, Esq.**

ValidCare, LLC
“Answering FDA’s Call for CBD Safety Data”

» **Asa Waldstein**

Boulder Hemp-CBD Group
“Consumer Demand and the CBD Market: Intersections & Insights”

» **Ricardo Carvajal, J.D., M.S.**

Hyman, Phelps & McNamara, P.C.
“Hemp-Derived CBD: A Primer on Key Regulatory Issues” 🌱

Recent EITS Graduates



Kevin Baker
Pharmacology and Toxicology
Mentor, James Luyendyk

Dr. Kevin Baker received his Ph.D. after completing the dual major program in Pharmacology and Toxicology and Environmental Toxicology. His dissertation was, “Mechanisms Regulating Tissue Factor: Factor Via-Dependent Coagulation in Liver Disease.”

Baker has accepted a toxicological Scientist

position at Takeda Pharmaceuticals in Cambridge, MA. At his new position, Baker will use molecular and cellular biology and next generation sequencing technologies to investigate mechanisms of drug-induced toxicity. He will be collaborating with other investigative toxicologists at Takeda Pharmaceuticals to make safer medicines.



Jianzhou He
Plant, Soil and Microbial Sciences
Mentor, Wei Zhang

Dr. Jianzhou He received his Ph.D. after completing the dual major program in Plant, Soil and Microbial Sciences and Environmental Toxicology. His dissertation was, “Environmental Application and Implication of Engineered Nanomaterials in Soil, Water and Plant Systems.”

Dr. He accepted a postdoctoral position at the University of Arizona in the Department of Chemical and Environmental Engineering. His research there will involve investigating sorptive remediation of per- and polyfluoroalkyl substances in contaminated groundwater using cationic hydrophobic polymers.

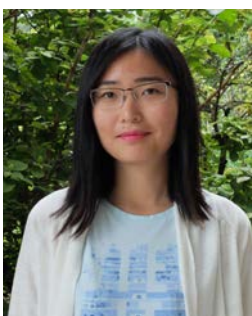


Sean Nguyen
Cell and Molecular Biology
Mentor, Margaret Petroff

Dr. Sean Nguyen received his Ph.D. after completing the dual major program in Cell and Molecular Biology and Environmental Toxicology. His dissertation was, “Placental Extracellular Vesicle Trafficking in Murine Pregnancy.”

Nguyen recently accepted a data science post-

doctoral fellow position with Insight Data Science. The seven week intensive fellowship training program bridges the gap between academia and a career in data science. Nguyen will learn industry-specific skills needed to work in the growing field of big data at leading companies.



Yike Shen
Plant, Soil and Microbial Sciences
Mentor, Wei Zhang

Dr. Yike Shen received her Ph.D. after completing the dual major program in Plant, Soil and Microbial Sciences and Environmental Toxicology. Her dissertation was, “Antibiotic Resistance and Bacterial Microbiome in Lettuce-Soil Systems.”

Shen is now a postdoctoral research scientist

at the Department of Environmental Health Sciences at Columbia University Mailman School of Public Health. Shen works in the laboratory of Precision Environmental Health, led by Dr. Andrea Baccarelli, working on the human gut microbiome aspect of a birth cohort.



Di Zhang
Pharmacology and Toxicology
Mentor, Karen Liby

Dr. Di Zhang received her Ph.D. after completing the dual major program in Pharmacology and Toxicology and Environmental Toxicology. Her dissertation was, “Applying Synthetic Chemistry and Nanoparticle Delivery to Enhance Drug Efficacy and Reduce Toxicity for Cancer Prevention and Treatment.”

Zhang is now a postdoctoral fellow at the Dana-Farber Cancer Institute in Boston. Cancer

immunotherapy has shown tremendous success; however, several major challenges such as the lack of ideal targetable tumor surface antigens, tumor-mediated immunosuppression and the potential for severe immune-mediated toxicity, still limit the application of cancer immunotherapy. Zhang’s vision is to develop transformative therapeutics that can overcome these challenges. She will leverage the power of synthetic biology, bioinformatics, and machine learning to develop effective cancer immunotherapies. ♡

Nault and MSU Superfund Team Publish Exciting Developments in Single-Cell RNA Sequencing



Postdoctoral researcher and EITS alumnus, **Rance Nault**, in collaboration with a team of MSU Superfund scientists including **Kelly Fader**, **Sudin Bhattacharya** and **Timothy Zacharewski**,

recently published exciting research on single-cell RNA sequencing. The paper, “Single nuclei RNA sequencing assessment of the hepatic effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin,” was published in August 2020 in the journal, Cellular and Molecular Gastroenterology and Hepatology.

The liver is composed of several different cell types working together to maintain normal function. Exposure to chemicals, drugs, and supplements can modulate these normal processes, and in some cases even lead to toxicity and disease. Traditionally, evaluation of how foreign compounds modify gene expression is achieved by averaging their levels in a tissue sample and as a

result some cell type specific responses can be lost. As innovative technologies are emerging to allow the measurement of gene expression levels in a single cell or nucleus, the objective of the study by Nault was to demonstrate its application for characterizing the cell-specific effects of the persistent environmental contaminant 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD, aka dioxin). Nault and his team showed that single-nuclei RNA sequencing can be used to demonstrate shifts in cell populations.

Single-cell RNA sequencing is most commonly performed on freshly collected tissues. In typical toxicology study designs multiple doses are used to establish safety of chemicals, drugs, and supplements. The number of samples, coupled with the severe effects observed at higher doses, present a significant hurdle in the use of this technology. The work by Nault shows that by using nuclei isolated from frozen livers, it is possible to identify known responses caused by dioxin exposure, as well as gain novel insight into how specific cell populations respond.

Demonstration of the feasibility and value of a single-nuclei RNA sequencing approach was a first critical step for in-

vestigating more complex study designs. Future efforts by Nault and the team of MSU Superfund researchers will explore the use of this technology to characterize the cell-specific sensitivity upon exposure to liver toxicants in order to better understand the development and progression of non-alcoholic fatty liver disease.

Nault’s research was generated under Project 3, “TCDD-Elicited Steatosis: The Role of Aryl Hydrocarbon Receptor Regulation in Lipid Uptake, Metabolism, and Transport,” and Core A, “Computational Modeling of Mammalian Biomolecular Responses,” of the MSU Superfund Project. Led by Dr. Zacharewski, Project 3 explores the adverse effects of dioxin and related compounds, commonly found Superfund contaminants, on liver metabolism and function. By using innovative technologies such as single-nuclei RNA sequencing, this MSU Superfund team is able to gain further insight on the role of aryl hydrocarbon receptor (AhR)-mediated changes in lipid metabolism which leads to the accumulation of fat, inflammation, and scarring of liver tissue. 🍀

EITS Student Jenna Strickland Awarded John A. Penner Fellowship in Hematology, Thrombosis and Inflammation



EITS graduate student, **Jenna Strickland**, was one of two students to receive the John A. Penner Fellowship in Hematology, Thrombosis and Inflammation for the academic year 2020-2021.

Strickland is a student working with Dr. Bryan Copple. The award includes a stipend of \$32,000, health insurance, and 100% of all tuition and fees.

Strickland is currently working on elucidating the mechanism(s) underlying macrophage dysfunction that occur in acute liver failure patients with the poorest prognosis. Elucidation of this mechanism could inform development of drugs to reverse macrophage dysfunction leading to liver repair and ultimately reversal of acute liver failure in patients. Additionally, the Copple laboratory has

developed a high-throughput assay that can detect differentiation of proinflammatory macrophages into pro-repair macrophages for use as a drug screening platform to identify chemicals/drugs that stimulate this process. Drugs identified from this screen could ultimately be used to restore macrophage function and liver repair in patients with acute liver failure and fibrosis.

Congratulations to Jenna on this prestigious honor! 🍀



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