IIT UPDATE

INSTITUTE FOR INTEGRATIVE TOXICOLOGY

June 2021

in this issue....

MICHIGAN STATE UNIVERSITY

IIT Welcomes Four New Faculty Members this Spring

The IIT is pleased to welcome four new faculty members this spring - Dr. Lance Blevins, Dr. Brian Johnson, Dr. Rance Nault, and Dr. David Tonucci.

Dr. Lance Blevins received his B.A. in Biology from the University of North Carolina at Chapel Hill in 2007. In 2016, he received his Ph.D. in Molecular and Cellular Biosciences (Immunology) from Wake Forest University. Blevins completed his postdoctoral work at MSU with Dr. Norbert Kaminski. Today, Blevins is an Assistant Professor here at the Institute for Integrative Toxicology.

Dr. Blevins research is generally focused on the field of adaptive immunology; specifically, he is interested in the regulation of lymphocyte effector functions during infection and by exposure to intoxicants and chemicals. A major emphasis of his research has been to identify human B cell subsets which exhibit selective sensitivity to Aryl hydrocarbon (AHR)-mediated immunotoxicity elicited by the xenobiotic, 2,3,7,8 tetrachlorodibenzo-p-dioxin (TCDD), a potent ligand of AHR, and other dioxin-like compounds. This research has identified human CD5-positive innate-like B cells (ILB) as being preferentially sensitive to AHR activation as evidenced by robust reductions in the ability to secrete immunoglobulin M (IgM) following exposure to TCDD, which is due in part to higher expression of AHR in CD5+ B cells compared to CD5- B cells. As there is a dearth of studies focused on human CD5+ ILB and the role of AHR, Blevins is currently focused on further characterization of this understudied immune cell population, while elucidating the molecular mechanism of TCDD-mediated immunotoxicity in CD5+ ILB.

Dr. Brian Johnson received his B.S. in Biology from Michigan Technological University in 2004. In 2013, he received his Ph.D. in Molecular and Environmental Toxicology from the University of Wisconsin. He continued on at the University of Wisconsin to complete his postdoctoral work from 2014 to 2019 in Biomedical Engineering. Today, Johnson is an Assistant Professor in the Department of Pharmacology and Toxi-

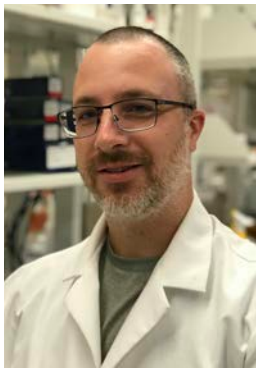
...continued on page 2

IIT Four New Faculty cont.

...continued from page 1

cology and the Department of Biomedical Engineering at MSU.

Johnson's interdisciplinary research laboratory specializes in the design, manufacturing, automation and testing of human derived models of development and disease to study intercellular signaling. They employ digital manufacturing (CNC machining and 3D printing) to construct biomimetic microenvironments that recapitulate intercellular signaling in development and disease. Current research directions include 1) identifying the potential for chemical mixtures to disrupt epithelial: mesenchymal signaling in orofacial development leading to cleft lip/palate 2) developing high-throughput multicellular models of breast and prostate cancers to identify mechanisms of treatment resistance and uncover therapeutic targets in the cancer microenvironment 3) using multicellular models of the hypothalamic: pituitary: thyroid axis to inform computational modeling of thyroid homeostasis and perturbation by chemical insults. Johnson's translational research goals are to develop strategies and enable technologies that increase precision in the treatment of disease and to identify chemical exposures that lead to birth defects in vulnerable populations.



Dr. Rance Nault received his B.Sc. in Biology from the University of Ottawa in 2009. In 2011, he received his M.Sc. in Physiology with a specialization in Chemical and Environmental Toxicology. Nault earned his Ph.D. from MSU in Biochemistry and Molecular Biology and Environmental Toxicology in 2016. During this time Nault was part of the IIT's EITS program, mentored by Dr. Timothy Zacharewski. Today, Nault is an Assistant Professor in the Department of Biochemistry and Molecular Biology at MSU.

Nault's research is focused on using high throughput 'omic' and targeted phenotypic endpoints to examine the health consequences of exposure to environmental and food contaminants. Technological innovations have enabled researchers to evaluate hundreds to thousands of molecules in a single sample, and along with these new platforms comes the challenges of analyzing, interpreting, and integrating the large datasets. Through a combination of wet lab and computational approaches, Nault leverages these technologies to investigate mechanisms and dose-responses of liver toxicants. Two current major areas of emphasis are (1) the use of single-cell sequencing technology to refine understanding of liver toxicity and (2) developing the framework to support the robust collection and sharing of high-quality data to promote reuse. The overarching long-term goal of Nault's research is to accelerate the mechanistic understanding of toxicant induced liver injury and improve the translation to human risk.

Dr. David Tonucci received his B.A. in Medical Anthropology at Case Western Reserve University in 1984. In 1994, he received his Ph.D. in Pharmacology and Therapeutics from SUNY Buffalo School of Medicine and Biomedical Sciences.

Dr. Tonucci's research interests focus on the safety evaluation of emerging technologies related to food ingredients and food technologies. A primary interest is identifying appropriate preclinical and clinical safety program design relevant to food ingredients made from biotechnology and synthetic biology.

Dr. Tonucci has spent much of his career developing programs to support the registration and approval of new food ingredients on a global scale. Dr. Tonucci is currently the Vice President for Regulatory & Toxicology at Artemys Foods and joins the IIT as an adjunct faculty member. Artemys is a biotechnology company focused on reducing the world's dependence on farm raised livestock. Their focus is developing 'cultured meat' to be used in combination with plant-based components to produce a more authentic meat substitute. As this is an emerging technology in the food industry, the development of a robust safety assessment process will be critical to successful commercialization.

As part of the safety assessment process, Dr Tonucci is also interested in developing more accurate intake assessments for novel food ingredients.

IIT Faculty Achievement

Dr. Jack Harkema was recently elected to serve as Chair of the American Thoracic Society's (ATS) Environmental Health Policy Committee (EHPC). Harkema will serve in this position for a three-year term starting in May 2021. The ATS is an international society, founded in 1905, with more than 16,000 members. It is the world's leading medical association dedicated to advancing clinical and scientific understanding of pulmonary diseases, critical illnesses and sleep-related breathing disorders.

The EHPC is responsible for helping develop the ATS's policy on outdoor air pollution, indoor air pollution, occupational respiratory health and climate change. It monitors, evaluates the scientific rationale for, and proposes policies that seek to control ambient air pollutants, occupational exposures to respiratory toxicants, and indoor air pollution, as well as to mitigate the health impacts of climate change.

Dr. Harkema has been a longtime member of ATS and was one of only three veterinarians in the inaugural class of ATS Fellows (2018). He has also served as the Chair of the Environmental, Occupational and Public Health Assembly.

Bernstein Receives Outstanding New Environmental Scientist Award

IIT-affiliated faculty member **Alison Bernstein** has received an Outstanding New Environmental Scientist (ONES) Award from the National Institute of Environmental Health Sciences for her project, "Dieldrin-induced differential gene methylation and parkinsonian toxicity." The award is in recognition of her research into the interaction of genetics and environmental exposure, specifically how some pesticides alter neurons in the brain that produce dopamine, a chemical that is lost in Parkinson's disease patients.

This grant will build on Bernstein's previous research exploring how toxic exposures contribute to increased risk of Parkinson's. The new research funded by this grant will enhance understanding of the epigenetic mechanisms underlying the well-documented epidemiological link between exposure to environmental toxicants and risk of Parkinson's disease. Specifically, Bernstein and her laboratory team will use a two-hit rodent model they recently developed that combines developmental pesticide exposure and the alpha-synuclein pre-formed fibril model and a 3D neuronal cell model. "These experiments will help to identify how developmental exposure to the pesticide dieldrin leads to increased susceptibility to Parkinson's disease using the alpha-synuclein pre-formed fibril model," said Bernstein. Dieldrin was commonly used on crops as an insecticide in the 1950s through 1970s and to kill termites into the 1980s. It eventually was banned by the U.S. Environmental Protection Agency.

Bernstein is an Assistant Professor in the Department of Translational Neuroscience in the College of Human Medicine. Research in the Bernstein lab focuses on how epigenetic modifications mediate neurotoxicological effects and gene-environment interactions underlying sporadic neurodegenerative diseases.

To read more about Bernstein and her ONES award, please visit: **https://msutoday.msu.edu/news/2021/alison-bernstein-recieves-outstanding-new-environmental-scientist-award**.

IIT Faculty & Students Honored Virtually by Society of Toxicology

This year's 60th Annual SOT meeting was held virtually over two weeks in March. Many IIT-affiliated faculty and students participated this year and several were recognized for their achievements.

» **Jenna Strickland**, EITS student training with Dr. Bryan Copple, received the Carl C. Smith Award, 2nd place, from the Mechanisms Specialty Section for her abstract, "*Exaggerated interleukin-10 expression inhibits macrophage-dependent liver repair in acetaminophen-induced acute liver failure.*"

» **Kathryn Wierenga**, EITS student training with Dr. James Pestka, received the Molecular & Systems Biology Specialty Section Graduate Student Research Award, 1st place, and the Immunotoxicology Specialty Section Best Presentation by a Student Award for her presentation, "*Phenotypic stability and application of a self-replicating murine alveolar macrophage model derived form fetal liver.*"

» **Dafna Groeneveld**, postdoctoral fellow in the laboratory of Dr. James Luyendyk, received the Professor Heimburger Award from CSL Behring for her research on, "*Novel hemostatic supplementation to prevent postoperative liver dysfunction after partial hepatectomy*."

» **Dan Rajasinghe**, postdoctoral fellow in the laboratory of Dr. James Pestka, received the Occupational and Public Health Specialty Section Best Manuscript - Postdoctoral Award, Food Safety Specialty Section Frank C. Lu Early Career Scientist Award, Immunotoxicology Specialty Section Best Presentation by a Postdoctoral Trainee Award, and the Mechanisms Specialty Section Sheldon D. Murphy Postdoctoral Endowment.

» **Dr. Jamie Bernard** received the James A. Swenberg Carcinogenesis Merit Award from the Carcinogenesis Specialty Section. The award recognizes outstanding individuals for their cumulative contributions to advancements in understanding the mechanisms of environmental agent-associated carcinogenesis.

» **Dr. Sudin Bhattacharya** was selected to serve as Co-Chair for the SOT 2021 Continuing Education Course on Advances in Single Cell Genomics for Toxicological Testing.

» **Dr. Rita Strakovsky** was invited to speak during the symposium, "From Conception to Cane: Unique Life-Stage Considerations for Reproductive Toxicity." Strakovsky spoke on, "*Endocrine-Disrupting Chemicals in Pregnant Women and Potential Modifying Factors*."

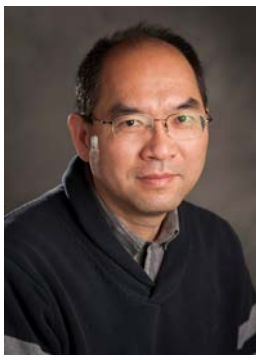
» **Dr. Norbert Kaminski** gave his 2020 Merit Award Lecture this year and spoke on, "*Unraveling the Molecular Mechanisms of Cannabinoid-Mediated Immune Modulation and Cannabinoid Receptor 2 as a Putative Therapeutic Target*."

» **Dr. Bill Atchison** was the recipient of supplemental funding from the Faculty United for Toxicology Undergraduate Recruitment and Education (FUTURE) Committee. The funds will be used to add capacity to Dr. Atchison's undergraduate summer research program, whose goal is to increase the number of underrepresented minority students trained in the neurosciences.

Congratulations to all the IIT-affiliated SOT award winners this year!

IIT Faculty Help Lead the Way in Environmental Antimicrobial Resistance Research at MSU

IIT-affiliated faculty members **Jim Tiedje** and **Hui Li** are part of a team of Michigan State University researchers that have helped MSU rank ninth globally in the quantity of research published related to environmental antimicrobial resistance.



Michigan State University ranks ninth in the world and is the only U.S. university in the top ten in terms of advancements in environmental antimicrobial resistance research, according to a recent announcement by the Global Health Research and Policy.

"This recognition that reflects on accomplishments dating back to 2000 further establishes and reinforces MSU as a long-time leader of environmental antimicrobial resistance research," said Jim Tiedje, University Distinguished Professor and founding director of the MSU Center for Microbial Ecology.

For decades, the university has positioned itself globally as one of the preeminent institutions in research related to environmental science. In 1989, MSU was awarded one of the first National Science Foundation Science and Technology Centers dubbed the MSU Center for Microbial Ecology.

"Our microbial resistance work is an extension of that center," Tiedje said. "The strength MSU has in this field is that of multidisciplinary expertise. We have researchers from a broad range of disciplines that have the expertise to come together to work on these problems."

Dr. Tiedje's research focuses on microbial ecology, physiology and diversity, especially regarding the nitrogen cycle, biodegradation of environmental pollutants and use of molecular methods to understand microbial community structure and function. His group has discovered several microbes that live by halorespiration on chlorinated solvents and is using genomics to better understand ecological functions, endemism and niche adaptation. He is particularly interested in the genomes of closely related populations where the organism's ecology is known so that a link can be made between genetic compositions to ecological outcomes.

MSU Department of Plant, Soil and Microbial Sciences Professor Hui Li is an environmental soil chemist who studies emerging contaminants. After starting work at MSU in 2005, he partnered with Tiedje and the MSU Center for Microbial Ecology to work toward methods to quantify the amount and diversity of antibiotics in the environment. He also looks at how bacteria respond to antibiotics in various environmental situations that demonstrate varying bioavailability to bacteria and selection pressure for resistance. As antibiotics are introduced into the environment, they are dissolved in water and absorbed by the soil. Li examines how these antibiotics become available to bacteria. "Different soil components create different bioavailability for the bacteria to access these antibiotics," Li said.

Tiedje and Li both have participated in the IIT's longstanding Superfund Research Program which conducts human health-oriented research on risks from exposure to chemicals commonly found in Superfund sites and on remediation technologies to eliminate the potential for exposure to chemicals from those sites.

Read more of this story by Justin Whitmore on MSUToday at: **https://msutoday.msu.edu/news/2021/leading-the-way-in-environmental-antimicrobial-resistance-research**
or at CANR at: **https://www.canr.msu.edu/news/msu-recognized-as-global-leader-in-environmental-antimicrobial-resistance-research.**

IIT Student Achievements

Nikita Saha Turna, EITS graduate student training with Dr. Felicia Wu, recently received two departmental scholarships from Food Science and Human Nutrition for her academic performance and research progress in the previous academic year – the P. Vincent Hegarty Food Science and Human Nutrition Quality in Education Fund Scholarship and the Dr. Rachel A. Schemmel Graduate Student Endowed Research Scholarship. Saha Turna also is the recipient of the Hiram E. Fitzgerald Engaged Scholar Fellowship from the MSU Graduate School which honors graduate students whose research focuses on the study or prevention of adverse childhood experiences.

Lauren Heine, EITS graduate student training with Dr. Jack Harkema, was recently awarded the Minority Trainee Development Scholarship Award from the American Thoracic Society. The scholarship provides the opportunity for trainees from underrepresented racial/ethnic groups in U.S.-based programs to present their research at the ATS International Conference. Heine's current research is focused on evaluating the efficacy of omega-3 fatty acids as a steroid-sparing therapy for lupus. More specifically, she is interested in how omega-3 fatty acids, when used in conjunction with glucocorticoids (GCs), can provide protection and inhibit inflammation following pulmonary exposure to inhaled toxicants such as crystalline silica or bacterial endotoxin while also reducing GC-induced toxicity.

In Memoriam: Jerry B. Hook (1938 –2021)

Jerry was a very well-known and highly respected Pharmacologist and Toxicologist whose research spanned the areas of mechanisms of drug action on the kidney, to the ontogeny of renal transport systems, to mechanisms of renal toxicity. He was critical in advancing the field of toxicology by helping to drive it from observational to a mechanism-based science. Jerry published more than 250 papers, review articles, and book chapters. He was the Editor of Toxicology of the Kidney (Target Organ Toxicology Series), 1981, and in collaboration with Robin Goldstein (who performed her doctoral thesis research in Jerry's laboratory), co-edited the second edition of the book, 1992.

Jerry received his PhD in Pharmacology from the University of Iowa in 1966 and later that year was recruited to join the faculty at Michigan State University (MSU) as an Assistant Professor in the new Department of Pharmacology. He contributed substantially to the department's toxicology expertise that led to its evolving to the Department of Pharmacology and Toxicology in 1978. He was an extensive collaborator and worked effectively across disciplines and departments. Jerry was named Founding Director of MSU's Center for Environmental Toxicology (CET) in 1981 and successfully developed multidisciplinary approaches aimed at resolving human and environmental toxicology issues. Jerry's achievements were the foundation for the CET to develop into today's Institute for Integrative Toxicology. Jerry served on the Editorial Boards of numerous journals and was a member of a number of advisory committees, notably the National Toxicology Program's Board of Scientific Counselors where he Chaired its Peer Review Panel. He was very active in a variety of scientific societies, including the American Society for Pharmacology and Experimental Therapeutics, the International Union of Pharmacology, the International Union of Toxicology, and the Society of Toxicology, where he was President from 1987 to 1988.

Jerry was regarded highly as a mentor and had a profound influence on graduate education in toxicology at MSU. Over the course of his 17 years as a faculty member, 5 post-doctoral fellows, 10 PhD students, and 4 MS students received their training in his laboratory. The Department's faculty considered him a caring and supportive colleague, always eager to engage in scientific discussion and share his knowledge/insight, with a particular passion for encouraging trainees. We were always proud to say, "Jerry Hook is my friend." Indeed, Jerry is regarded as an icon of MSU's Department of Pharmacology & Toxicology and of the field of toxicology.

In 1983, Jerry was recruited to join Smith Kline & French Laboratories (later becoming Smith Kline Beecham) as Vice President for Preclinical Research and Development, where he directed laboratories in the United States and United Kingdom, and rose to Senior Vice President and Director of Development. In 1993, he founded Lexin Pharmaceutical Company (LPC), a biotechnology company, and served as its CEO. Three years later, LPC merged into Sparta Pharmaceuticals, Inc. which Jerry headed until his retirement in 1999.

While we mourn the loss of Jerry, it is important to remember that the discipline of Toxicology has been enhanced by his pioneering contributions to our understanding of mechanisms underlying chemical-induced renal toxicity. We who worked with, or knew, Jerry are richer for having known the man, and it is our hope that he knew how much he was appreciated.

In Memoriam: Jerry B. Hook (1938–2021).

Dr. Jerry B. Hook passed on January 9, 2021. We express our heartfelt condolences to his wife, Dr. Jacqueline H. Smith, and all of the Hook family.

Written by former colleagues, Dr. Jay Goodman and Dr. Norbert Kaminski

IIT Welcomes New EITS Students

The IIT is pleased to welcome the following students who have joined the EITS program in the last year:

- **Husnain Ahmed**, training with Dr. Linda Mansfield
- **Rachel Bauer**, training with Dr. Courtney Carignan
- **Sierra Boyd**, training with Dr. Alison Bernstein
- **Morgen Clark**, training with Dr. Gemma Reguera
- **Devon Dattmore**, training with Dr. King Sing Stephen Lee
- **Joel Marty**, training with Dr. Norbert Kaminski
- **Sera Sermet**, training with Dr. Norbert Kaminski
- **Azam Ali Sher**, training with Dr. Linda Mansfield
- **Erin Zaluzec**, training with Dr. Lorenzo Sempere

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