

INSTITUTE FOR INTEGRATIVE TOXICOLOGY

Kaplan Returns to MSU as Kenneth E. Moore Distinguished Alumnus Award Winner

Dr. Barbara Kaplan, former IIT-affiliated faculty member and current Associate Professor at Mississippi State University, recently returned to MSU as the Department of Pharmacology and Toxicology's Kenneth E. Moore Distinguished Alumnus. Kaplan gave her award lecture, *"From Michigan State University* to Mississippi State University: Science and So Much Moore," on November 6, 2024.

Kaplan received her Ph.D. in Pharmacology and Toxicology from MSU in 2001. After a postdoctoral experience at the University of Chicago, she returned to MSU as an Assistant Professor from 2004 to 2013 to work with Dr. Norbert Kaminski. During this time, she joined the affiliated faculty of the Institute for



Integrative Toxicology and was a vital researcher and teacher in the field of immunotoxicology. She joined the faculty of Mississippi State University in August of 2013.

Dr. Kaplan's research broadly focuses on elucidation of the mechanisms by which drugs and chemicals alter immunity. Specifically, her laboratory has been investigating AHR ligand effects on immune respons-

es initiated in a mouse model of multiple sclerosis, experimental autoimmune encephalomyelitis (EAE).

Congratulations to Dr. Kaplan on this prestigous honor! 🛇

in this issue....

Kaplan Moore Alumnus Award1
Research Evening2
New EITS Students2
IT Seminar Series Fall 20243
Recent EITS Graduate
Two Faculty Promotions4
_einninger Promotion & Award4
MSU SRC News5
CRIS News6
Trosko Marquis Who's Who7

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Celebrating Student Research at the 2024 EITS Research Evening

The Institute for Integrative Toxicology's Annual Research Evening showcased trainees in the Environmental and Integrative Toxicological Sciences Graduate Training program and their accomplishments. This year's event took place on Thursday, December 5, 2024 in the Lincoln Room at the MSU Kellogg Center. The event included dinner, student posters and platform presentations.

Three EITS graduate students gave platform presentations:



Saamera Awali, training in the lab of Dr. Cheryl Rockwell, spoke on, "The effect of tBHQ and Nrf2 activation on dendritic cell function during influenza A infection." Awali is a doctoral student

in the Department of Pharmacology and Toxicology and has focused her graduate research on the effects of a commonly used food additive, tBHQ, on dendritic cell function in the context of an influenza A infection. Awali hypothesizes that the transcript factor Nrf2, which is activated by tBHQ, plays a major role in reducing dendritic cell maturation and activation, overall inhibiting the ability of dendritic cells to properly present antigen to T cells, which is their primary function.



Rachel Bauer, training in the lab of Dr. Courtney Carignan, spoke on, "Investigating immunotoxicity of per- and poly-fluoroalkyl substances using functional measures in a highly exposed population." Bauer

is a doctoral student in the Department of Pharmacology and Toxicology and has focused her research on PFAS exposure and its impact on the immune system. In a Michigan community affected by PFAS-contaminated drinking water, Bauer assessed whether serum PFAS levels were associated with reduced SARS-CoV-2 IgG spike antibody levels in vaccinated adults, and alterations in immune cell populations. Overall, she found serum PFAS to be negatively associated with anti-SARS-CoV-2 IgG spike antibodies and associated with changes in leukocyte subpopulations.



Jacob Reynolds,

training in the lab of Dr. Brian Johnson, spoke on, "Refinement of a Microphysiological Model of Orofacial Development for Chemical Testing." Reynolds is a doctoral student

in the Department of Biomedical Engineering. Orofacial clefts are one of the most common structural birth defects that arise from a complex, multi-factorial etiology. Reynolds work focuses on engineering ways to study the complex cell-cell interactions of development and identify potential harmful exposures with a primary focus on the Sonic Hedgehog (SHH) pathway. To accomplish this, he utilizes computer numerical control (CNC) machining to create plate based microfluidic devices that create a 3D microtissue of the epithelial-mesenchyme interaction that is essential to proper orofacial development.

To those who attended, thank you for joining us for this special evening of celebration, camaraderie, and learning!

IIT Welcomes New EITS Students

The IIT is pleased to welcome several new students to the Environmental and Integrative Toxicological Sciences (EITS) multi-disciplinary graduate program. New students include:

» Jesmin Ara Biochemistry and Molecular Biology Mentor: John LaPres



» Kameron Kennicott Molecular, Cellular and Integrative Physiology *Mentor:* Yun Liang

» Jacob Reynolds Biomedical Engineering Mentor: Brian Johnson



» Alexandra Swartz Fisheries and Wildlife Mentor: Cheryl Murphy



To learn more about the research interests of our current EITS students, please visit: <u>https://iit.msu.edu/training/eits/current-students.html</u>.

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IIT Seminar Series Fall 2024

The IIT was excited to host a wonderful lineup of speakers for the Fall 2024 IIT Seminar Series.



The semester-long series began in September with **Dr. Imran Shah**, U.S. Environmental Protection Agency, who spoke on, "Integrating Artificial Intelligence, Systems Modeling and Sin-

gle-Cell Analysis for Advancing Chemical Safety."

Dr. Shah has over 25 years of experience leading computational biology and cheminformatics research in academia, biotechnology, and the US EPA. His work uses artificial intelligence (AI) / machine learning (ML) and systems biology approaches to analyze large-scale heterogeneous biological and chemical datasets to model the health effects of drugs and chemicals. Dr. Shah has pioneered methods for identifying toxicological tipping points by modeling cellular resilience to chemicals using systems biology and single-cell approaches.

On October 14, the IIT hosted **Dr. John Clarke**, to speak on, "*Microcystin-LR Hepatotoxicity in Healthy*



Pharmaceutical Sciences at Washington State University Health Sciences Spokane.

Microcystin-LR (MCLR) is a potent hepatotoxin that may play a role in the progression of metabolic dysfunction- associated steatotic liver disease (MASLD) to more advanced stages, such as metabolic dysfunctionassociated steatohepatitis (MASH) and hepatocellular carcinoma (HCC). The Clarke laboratory investigates whether there is differential susceptibility to MCLR exposure and toxicity between healthy rodents and those with MASLD.

The final seminar of the series was given by IIT-affiliated faculty member **Dr. Joseph Zagorski** on November 19. He spoke on, "Development of a Human Hepatocyte: Endothelial Cell Coculture Model to Determine Differential Potencies of Pyrroligidine Alkaloids."

Versus Metabolic Dysfunction-Associated Steatotic Liver Disease Rodents." Dr. Clarke is an Associate Professor and Vice-Chair in the Department of Pharmaceutical Sciences, College of Pharmacy and



The broad interest of Dr. Zagorski's research centers on ingredient safety and molecular toxicology. Currently, Zagorski is working on developing models of developmental immunotox-

icology, co-culture models systems with human hepatocytes, and the utilization of 3D culture systems to predict toxicity. At the Center for Research on Ingredient Safety, his goal is to develop alternative model systems, utilizing primary human cells and tissues. This includes the implementation of a developmental immunotoxicology model system, using primary human CD34+ stem cells from cord blood, to determine effects of toxicants on the developing immune system. The overarching goal of his research is to utilize these models to promote public health and support research for ingredient safety.

The IIT was excited to be able to offer such a diverse array of learning opportunities through the wide variety of seminars this fall.

Recent EITS Graduate



Bradley Ryva

Pharmacology and Toxicology Mentor, Rita Strakovsky

Dr. Bradley Ryva received his Ph.D. after completing the dual major program in Pharmacology and Toxicology and Environmental Toxicology. His dissertation was, "Endocrine Disrupting Chemicals and Nausea and Vomiting During Pregnancy."

Ryva is continuing in the MSU DO/Ph.D.

program and is currently in the clinical portion of his medical school training at Trinity Health Ann Arbor, with anticipated graduation in 2026. Ryva continues to work with Dr. Strakovsky on work related to his dissertation topic that investigated persistent nausea during pregnancy, as well as potential new projects and avenues of research. After medical school, Ryva plans to complete a medical residency in Obstetrics and Gynecology.

Two IIT-Affiliated Faculty Receive Promotions

The IIT would like to congratulate affiliated faculty members, Dr. Kin Sing Lee and Dr. Ilce Medina Meza, who recently received faculty promotions to Associate Professor.



Dr. Kin Sing Stephen Lee is an Associate Professor in the Department of Pharmacology and Toxicology. Lee's laboratory focuses on using chemical biology methods to study the interactions between dietary lipids (what we eat), environmental chemicals (what we are exposed to) and human health (our body) at the molecular level. His laboratory is particularly interested in studying the

molecular mechanisms on how the dietary omega-3 (DHA or EPA) to omega-6 (e.g. soybean oil) ratio affects human health and human responses to environmental toxicants. The overall goal of Lee's research is to develop new chemical tools to elucidate the mechanism by which dietary lipids affect human health. The tools and the methods developed

not only will help us better understand how these dietary lipids affect human health but also could potentially be new therapeutics for different diseases.



Dr. Ilce Medina Meza is an Associate Professor in the Department of Biosystems and Agricultural Engineering. The goals of her laboratory are to elucidate molecular mechanisms governing oxidative stress, and to translate the findings to develop biomarkers for prevention and treatment of chronic diseases (e.g. cardiovascular and neurodegenerative diseases). Current projects are

focused on 1) developing drug modulators of cholesterol oxidation to damp inflammation on cardiovascular disease; 2) metabolomic mapping of oxysterols and other lipid peroxides for risk assessment in highly susceptible populations; and 3) Fingerprinting of plant secondary metabolites and understanding their role in life processes.

Leinninger Receives Promotion & Red Cedar Distinguished Professorship



IIT-affiliated faculty member **Gina Leinninger** was recently promoted to full professor and was also awarded the title of Red Cedar Distinguished Professor for her leadership and

research achievements. This distinction is awarded to Spartans with "exemplary scholarly accomplishments" and who demonstrate "teaching innovation and excellence" by the Office of Research and Innovation, the Office of the Provost and in the case of Lenninger, the College of Natural Science. Faculty awardees retain the title of "Red Cedar Distinguished Professor" for the duration of their service at MSU. Each also receives scholarly support for the first three years after their award. The funds are provided equally by the nominating college(s), the Vice President for Research and

Innovation, and the Provost.

The Leinninger Laboratory studies how neurons in the lateral hypothalamic area (LHA) contribute to energy balance and obesity. The LHA is crucial area of the brain for regulating feeding, drinking, sleep and locomotor behaviors that can directly affect weight. Indeed, LHA neurons regulate some of the same brain circuits that mediate reward sensing and addiction (i.e. dopamine neurons.) There are several populations of LHA neurons that differ in their expression of neuropeptides and where they project within the brain (including populations containing neurotensin, orexin, leptin receptor and others) suggesting that these neuronal populations control different aspects of metabolic sensing and physiological output behavior. The goal of the Leinninger lab is to understand how discrete neuronal populations in the LHA contribute to energy balance and physiology as a whole. They utilize novel mouse models, state-of-the art neuronal tract tracing and neuronal regulation techniques to interrogate LHA

neurons and their role in physiology.

"We have to eat to survive," Leinninger said. "Yet, eating too much promotes the development of obesity, a disease that increases risk for type 2 diabetes, stroke, cancer, chronic pain, and shortens life span. I'm motivated to understand how the brain normally controls feeding we need to live, what goes awry, and how this knowledge can guide treatments to help individuals lose weight and reverse metabolic disease."

Leinninger also said she will use the award to help support and train the next generation of talented researchers, including those from groups that are historically underrepresented in science.

Congratulations to Dr. Leinninger on her promotion and the distinctive recognition of Red Cedar Distinguished Professor!

For more information on Dr. Leinninger and her award, please visit: https://physiology.natsci.msu. edu/physiology-news/gina-leinninger-honored-with-red-cedar-distinguished-professor-award.aspx

MSU Superfund Research Center News



Above: The MSU Community Engagement Core recently hosted a community meeting during which the Michigan Department of Health and Human Services (MDHHS), Department of Environment, Great Lakes, and Energy (EGLE), Allegan County Health Department (ACHD), and Michigan State University (MSU) Toxic Action Lab provided updates regarding efforts to support community health in the Otsego area. Information and questions regarding the health inquiry form, the annual community health survey and cancer rates was discussed by the state and local agencies in attendance. The community was invited to attend.

MSU SRC Annual Community Health Survey Results

The Community Engagement Core (CEC) of the MSU Superfund Research Center is a collaboration between faculty and students at MSU and staff of the Michigan Department of Health and Human Services (MDHHS). Together, they selected three Michigan communities affected by environmental contamination. The goal of the CEC is to listen to major concerns through an annual community health survey and a local advisory group made up of people living and working in the target communities.

The CEC strives to empower residents by working together to ensure MDHHS' ongoing efforts to educate communities about the best ways to keep themselves healthy are directly responsive to the major concerns of the residents. The CEC then works to evaluate the extent to which these targeted health education efforts help to foster a trusting relationship between the MDHHS and the selected communities. Overall, the team also works with partners and investigators in the larger Superfund Research Center and across the entire program to better position them to build trust with the various individuals and groups impacted by their work.

Each spring, the CEC fields the Annual Community Health Survey. The survey—designed in collaboration with the MDHHS and the Allegan, Macomb, and Saginaw County Health Departments—collects the major concerns that people living in these communities experience regarding their collective health. The findings are then used to guide MDHHS' health education efforts which, with the help of a Local Advisory Group, are redesigned to ensure they directly address salient community vulnerabilities.

The Community Engagement Core recently shared their findings for year two of the annual survey. View the PDF links below or at <u>https://iit. msu.edu/centers/superfund/core3.</u> <u>html</u> to learn more about the year one and year two results for each community:

Year 2

Otsego Year 2 Findings (PDF) Saginaw Year 2 Findings (PDF) St. Clair Shores Year 2 Findings (PDF)

Year 1

Otsego Year 1 Findings (PDF) Saginaw Year 1 Findings (PDF) St. Clair Shores Year 1 Findings (PDF)

Center for Research on Ingredient Safety News



Exciting Changes: Revitalized Brand, New Website & More

The Center for Research on Ingredient Safety is excited to unveil the revitalization of their brand, along with a new website, and upgraded newsletter—all designed to better serve the CRIS community and enhance user experience. The exciting changes include:

New website & URL

Visit CRIS at <u>cris.msu.edu</u>. They've worked to make finding information and resources on ingredient safety easier. Additionally, they have enhanced the readability of CRIS's content so it's easier for everyone to engage.

Reimagined newsletter

A redesigned newsletter with a new

format and enhanced brand consistency will encourage sharing and collaboration across the CRIS community and beyond.

More robust digital interface

The new digital interface on the CRIS website allows the Center to expand the type of content they share, from long-form articles and interactive features to multimedia resources like videos and podcasts. This upgrade will give them more options for sharing science.

Enhanced analytical capacity

Behind the scenes, CRIS has strengthened their analytical tools to better understand and meet the needs of the global community, ensuring they remain at the forefront of ingredient safety communication.

What to expect going forward?

As CRIS learns more and expands their reach, they will continue to tweak and update their content and interfaces. While they don't anticipate more changes in the coming weeks, please feel free to reach out to CRIS with any questions, concerns, or suggestions at cris@msu.edu.

These updates mark a significant step forward in the CRIS mission to share science-based knowledge and foster a well-informed community.

2024 CRIS Annual Science Symposium: Plastic Recycling & Chemical Contaminants in Recycled Plastic

The 2024 Center for Research on Ingredient Safety Science Day held on October 2, 2024 at the MSU Union, focused on plastic recycling and chemical contaminants in recycled plastic.

Sessions inlcuded:

» Anne Germain, M.S., Chief Operating Officer & Senior Vice President of Regulatory Affairs for the National Waste & Recycling Association Talk Title: Recycling and contamina

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» Greg Curtzwiler, Ph.D., Assistant Professor, Iowa State University Talk title: Composition of Extractable Chemicals in Recycled Polyolefins

- » Sean Fischer, Ph.D., Regulatory Review Scientist, U.S. Food and Drug Administration Talk Title: Regulatory Considerations for the Use of Recycled Plastics in Food Packaging
- » Reid Van Lehn, Ph.D., Hunt-Hougen Associate Professor, University of Wisconsin-Madison Talk Title: Polymer Recycling and Contaminant Removal from Multilayer Plastic Packaging by Solvent-Targeted Recovery and Precipitation
- » Jennifer L. Port, Chief Process Sustainability, ExxonMobil

Technology and Engineering Company Talk Title: Advanced Recycling – Innovating to Support Plastics Circularity

The symposium day concluded with a panel discussion with the 2024 speakers answering community questions.

If you were unable to attend, you can still catch up on all the insightful sessions. Most are now available for you to watch on <u>YouTube</u>!

Please share them with any friends and colleagues who might benefit from the sessions. \diamond

Trosko Included in Marquis Who's Who



IIT-affiliated faculty member, Dr. James Trosko, has recently been included in Marquis Who's Who which chronicles the lives of the most accomplished individuals and inno-

vators from every significant field of endeavor, including politics, business, medicine, law, education, art, religion and entertainment. Individuals profiled are selected on the basis of current reference value. Factors such as position, noteworthy accomplishments, visibility and prominence in a field are all taken into account during the selection process.

Dr. Trosko was a founding member of the Institute for Integrative Toxicology in 1978 and retired from MSU in 2014 and is now a Distinguished Professor Emeritus. During his 48 years here at MSU, Trosko taught thousands of students and helped many more people worldwide through his scientific discoveries. His research has taken him from Michigan to Japan to Sicily to Korea. He has been recognized as a model teacher and an internationally-recognized basic science cancer researcher. Over the course of his career. Trosko has used his extensive research in radiation and chemical-induced human health effects to publish close to 500 peer-reviewed articles in professional journals including Nature, Science, Cancer Research, Toxicological Science and the Journal of Stem Cell Research and Therapy.

Trosko was a freshman in college when Sputnik went overhead and the great science race began. This event not only enabled Trosko to get a college education but also stimulated him to become a scientist. During his time as a graduate student at MSU, Trosko interacted with the late Barnett Rosenberg, during the period when he discovered the anti-cancer drug, cisplatin. Trosko was included on Rosenberg's historic paper in *Nature* because he demonstrated that the drug was not mutagenic. Trosko was then awarded an American Cancer Society fellowship to do postdoctoral research at Oak Ridge National Laboratory. His time there led to the discovery of the role of radiation-induced DNA damage, and its repair and mutation formation in human cells.

After accepting an assistant professor position at MSU in 1966, Trosko was also able to study with Dr. Van R. Potter at the McArdle Laboratory of Cancer Research at the University of Wisconsin. It was during this time that Trosko changed his research direction to "chemical carcinogenesis" and his whole philosophy and world view of how he should direct his research efforts in the years to come. Under Dr. Potter's mentorship, Trosko made a major discovery that chemicals which promote growth of cancer are not mutagenic, but worked by "epigenetic" mechanisms. It was at this time that Trosko coined the term, "epigenetic toxicants." During the next few years, he started to detect chemicals that promoted the growth of tumors, caused birth defects, were reproductive - and neuro-toxicants. In addition, he also could detect cancer preventive and chemotherapeutic chemicals. All this was done based on assuming the "stem cell theory of cancer."

In the early 1990's, through several opportunities and awards to study abroad, Trosko gained a more scientifically sound picture of how the Japanese, Sicilian-Mediterranean & Korean diets could affect childhood diseases. Together with his discovery that normal human adult stem cells are target cells for cancer, he then developed a 3-D assay to screen for drugs, nutrients, toxins, toxicants that could affect these stem cells.

During the later part of his career, Trosko was a pioneer in developing a new concept to provide a mechanistic explanation of the "Barker Hypothesis," namely that events early in embryonic/fetal/neonatal development can alter the risk to chronic diseases, such as cancer, to the individual later in life, simply by altering the quantity of adult stem cells in utero.

While Trosko is unaware of who nominated him for this award he believes, "The award should have been given to the thousands of undergraduate, graduate, medical, postdoctoral students, colleagues, visiting scholars and collaborators who contributed to the success of my laboratory over the past fiifty plus years. Without their creativity, skills and passion for science, none of the many achievements associated with our lab would have been noted internationally. My teaching, my mentoring, which was not to make "mini-me" copies, but to unlock their own potentials in basic research, and my outreach were all meant to highlight what Michigan State University has afforded all of us."



Institute for INTEGRATIVE TOXICOLOGY

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