



IIT UPDATE

INSTITUTE FOR INTEGRATIVE TOXICOLOGY



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IIT Affiliates Successful at 57th SOT Meeting in San Antonio, Texas

Students and faculty of the MSU Institute for Integrative Toxicology were excited to attend and present at this year’s 57th annual Society of Toxicology (SOT) meeting held in San Antonio, Texas. The IIT’s own, Dr. Patricia Ganey, presided over the events as President of the SOT this year.

The SOT annual meeting is the largest toxicology meeting and exhibition in the world, attracting more than 6,500 scientists from industry, academia and government from various countries around the globe. This year’s meeting was held at the Henry B. Gonzalez Convention Center from March 11-15, 2018.

The following students and faculty affiliated with IIT received recognition:

- » **Michael Rizzo**, EITS trainee with Dr. Norbert Kaminski, received 2nd place for Best Presentation by a Graduate Student from the Immunotoxicology Specialty Section for his abstract, “HIV-infected Cannabis Users Display Lower Levels of Circulating CD16⁺ Monocytes and Plasma IP-10 Compared to Non-using HIV-infected Individuals.”
- » **Adrianna Suazo** received a Pfizer SOT Undergraduate Student Travel Award for her abstract, “Acute MeHg Exposure Alters Immunofluorescence of the Renshaw Cell Area in C57BL/6J Mice.” Suazo is a student at Northern New Mexico College and conducted her research in the lab of Dr. William Atchison in summer 2017.

- » **Kimberly A. Rivera-Caraballo** received the Perry J. Gehring Diversity Student Travel Award for her abstract, “Expression of Excitatory Amino Acid Transporter miRNA During Methylmercury Exposure in Mouse Spinal Cord Astrocytes and Neuroblastoma Spinal Cord NSC-34 Cells.” Rivera-Caraballo is a student at the University of Puerto Rico at Humacao and conducted her research in the lab of Dr. William Atchison in summer 2017.
- » **Lauren Poole**, postdoctoral student on the MSU IIT Training Grant, gave a platform presentation, “Thrombin-Mediated Fibrin Polymer Formation Does Not Exacerbate Experimental Hepatic Fibrosis.” The presentation was for the Platform Session: Animal Models, chaired by former EITS student, Dr. Anna Kopec.
- » **Dr. Debrup Chakraborty**, postdoctoral researcher in Dr. Jamie Bernard’s lab, received two awards for his abstract, “Visceral adiposity-stimulated genotoxicity and malignant transformation of epithelial cells.” He received the Postdoctoral Fellowship and Young Investigator Award from the Carcinogenesis Specialty Section and the Postdoctoral Travel Award sponsored by Charles River from the Dermal Toxicology Specialty Section.
- » **Dr. Sudin Bhattacharya** received the 2018 Young Investigator Award from the Association of Scientists of Indian Origin (ASIO).

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IIT at 57th SOT Meeting cont.

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- » **Dr. Jack Harkema**, received the 2018 Career Achievement Award from the Inhalation and Respiratory Toxicology Specialty Section of the SOT.
- » **Dr. Courtney Sulentic**, former MSU student, and **Dr. Barbara Kaplan**, former MSU student and faculty, were elected as Councilors for the SOT. Their terms will begin in May 2018.
- » **Dr. James Luyendyk** was selected

as the incoming Co-Chair of the Committee for Diversity Initiatives and was elected Jr. Councilor for the Mechanisms Specialty Section.

- » The following EITS trainees received travel support from the IIT: **Peter Dornbos**, **Kelly Fader**, **Jeremy Gingrich**, **Joseph Henriquez**, **Monica Rios-Cabanillas**, **Mike Rizzo**, **Vickie Ruggiero**, **Alexandra Turley**, **Kate Wierenga**, and **Brian Zhou**.

The highlight of the week was the IIT Alumni and Friends Reception held in the President's Suite for all current and former students, postdocs, faculty and friends of Michigan State University. The evening reception was a welcome opportunity to catch up with old acquaintances and meet with new friends. The IIT looks forward to the next SOT Meeting in Baltimore, Maryland in March 2019. 🍷



Top left: Dr. James Luyendyk and MSU IIT postdoctoral trainee, Lauren Poole.



Top right: A peek of the Alumni and friends reception.

Middle left: Five past SOT Presidents from Michigan State University: Dr. James Bus, Dr. Norbert Kaminski, current SOT President Dr. Patricia Ganey, Dr. Jay Goodman, and Dr. Ken Wallace.



Middle right: Dr. Norbert Kaminski with former students, Dr. Barbara Kaplan and Dr. Courtney Sulentic, who were both elected as SOT councilors this year.



Bottom left: Dr. Debrup Chakraborty, postdoctoral researcher, with mentor, Dr. Jamie Bernard.



Bottom right: Dr. Sudin Bhattacharya, recipient of the 2018 Young Investigator Award from the Association of Scientists of Indian Origin

Liby and Bernard Collaborate to Fight Cancer

IIT affiliated faculty members, **Dr. Karen Liby** and **Dr. Jamie Bernard**, were recently featured in the March issue of *Cancer Prevention Research* for their work on a promising drug that may stop a gene associated with obesity from triggering breast and lung cancer, as well as prevent these cancers from growing.

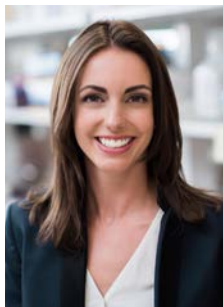
Dr. Karen Liby, associate professor in Department of Pharmacology and Toxicology, along with her laboratory, including EITS student, **Di Zhang**, led the first preclinical study, “*Chemoprevention of Preclinical Breast and Lung Cancer with the Bromodomain Inhibitor I-BET-762.*” Results showed that the drug, I-BET-762, exhibits signs of significantly delaying the development of existing breast and lung cancers by zeroing in on how a cancerous gene, called c-Myc, acts.

“I-BET-762 works by targeting DNA so that this gene can’t be expressed,” Liby said. “It does this by inhibiting a number of important proteins – both in cancer and immune cells – ultimately reducing the number of cancer cells in mice by 80 percent.”

These proteins are important because they play a critical role in what occurs between cells. For example, a particular protein, known as pSTAT3, can become activated in immune cells



Dr. Karen Liby



Dr. Jamie Bernard

and stop them from doing their job, such as fighting off an invading cancer. The offending protein also can become overproduced in cancer cells and act as a shield – ultimately protecting the tumor.

The second study, “*A BET Bromodomain Inhibitor Suppresses Adiposity-Associated Malignant Transformation,*” was led by Dr. Jamie Bernard, an assistant professor in the Department of Pharmacology and Toxicology. Along with her laboratory, including EITS student, **Vanessa Benham**, Bernard applied Liby’s findings to precancerous cells.

“We looked directly at the effect I-BET-762 had on human cells that could become tumorigenic, but weren’t quite yet,” Bernard said. “We found that the drug prevented more than 50 percent of these cells from becoming cancerous.”

The c-Myc gene is induced by visceral fat, which is found around the inner organs of the body as opposed to subcutaneous fat, which is located under the skin. This visceral fat is more dangerous to your health.

“Almost half a million of all new cancers have been linked to obesity,” Bernard said. “There is evidence that visceral fat and high-fat diets can increase cancer risk; and while current cancer treatments have helped to lower cancer mortality, the number of obesity-associated cancers continues to climb.”

Due to the limited success in reducing high mortality rates of breast and lung cancer, new approaches for prevention are desperately needed, Bernard said.

Drugs that act similarly to I-BET-762 also are being tested in clinical trials for the treatment of a variety of other cancers including leukemia, lymphoma, brain tumors and myeloma. Liby and Bernard hope I-BET-762 will increase breast and lung cancer patients’ chances of survival.

“The goal is our findings will clarify what needs to be targeted and therefore, can be used to prevent cancer in high-risk patient populations,” Bernard said.

Kaminski & Rizzo Find THC May Help HIV Patients

IIT Director, **Dr. Norbert Kaminski** and his EITS trainee, **Mike Rizzo**, recently discovered that a chemical found in marijuana, known as tetrahydrocannabinol, or THC, has been found to potentially slow the process in which mental decline can occur in up to 50 percent of HIV patients. Their findings were published in the journal *AIDS*.

“It’s believed that cognitive function decreases in many of those with HIV partly due to chronic inflammation that occurs in the brain,” said Dr. Kaminski. “This happens because the immune system is constantly being stimulated to fight off disease.”

Kaminski and Rizzo discovered that the compounds in marijuana were able to act as anti-inflammatory agents, reducing the number of inflammatory white blood cells, called monocytes, and decreasing the proteins they release in the body.

“This decrease of cells could slow down, or maybe even stop, the inflam-



Dr. Norbert Kaminski



Mike Rizzo

matory process, potentially helping patients maintain their cognitive function longer,” Rizzo said.

The study involved taking blood samples from 40 HIV patients who reported whether or not they used marijuana. Then, they isolated the white blood cells from each donor and studied inflammatory cell levels and the effect marijuana had on the cells.

HIV, which stands for human immunodeficiency virus, infects and can destroy or change the functions of im-

mune cells that defend the body. With antiretroviral therapy – a standard form of treatment that includes a cocktail of drugs to ward off the virus – these cells have a better chance of staying intact.

Yet, even with this therapy, certain white blood cells can still be overly stimulated and eventually become inflammatory.

“We’ll continue investigating these cells and how they interact and cause inflammation specifically in the brain,” Rizzo said. “What we learn from this could also have implications to other brain-related diseases like Alzheimer’s and Parkinson’s since the same inflammatory cells have been found to be involved.”

Knowing more about this interaction could ultimately lead to new therapeutic agents that could help HIV patients specifically maintain their mental function.

Doseff and Medina Meza Join IIT Faculty

The IIT is pleased to introduce Dr. Andrea Doseff and Dr. Ilce Medina Meza as new IIT-affiliated faculty members.



Ilce Medina Meza

Assistant Professor, Biosystems and Agricultural Engineering

Dr. Medina Meza received her B.S. and M.Sc. in Chemical Engineering from the Technological Institute of Orizaba in 1998 and 2002, and her Ph.D. in Food Science from the Technological Institute of Veracruz / University of Bologna in 2011.

Dr. Medina Meza's research focuses on the effects of oxidative stress on peroxidation of lipids and steroids. The goals of the laboratory are to elucidate molecular mechanisms governing oxidative stress, and to translate their 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 dampen inflammation on cardiovascular disease, and 2) metabolomic mapping of oxysterols and other lipid peroxides for risk assessment in highly susceptible populations, 3) Fingerprinting of plant secondary metabolites and understanding their role in life processes.

The laboratory focuses in the following omics areas:

- » *Lipidomics*: Mechanism of free radicals reactions on lipids, steroids and lipoproteins (e.g., LDL and HDL) using model, in vitro and in vivo systems. Critical for this research is to determine the products of lipid oxidation and the molecular mechanisms by which these compounds contribute to major chronic diseases.
- » *Metabolomics*: Plant secondary metabolite fingerprinting, developing new strategies for identifying metabolites by mass spectrometry methods GC-MS, LC/MS/MS, IF-TR, EPR and NMR, as well as modeling of metabolic pathways to understand their role on life processes.
- » *Processomics*: Understanding the impact of traditional and novel processing technologies on the bioavailability and functionality of phytochemicals on food systems. A novel

kinetic approach is used for mechanistic and predictive modelling through Chemical Reaction Networks. They rely in several mathematical and multivariate statistical approaches (parametric and non-parametric statistics, and chemical reaction networks, among others).



Andrea Doseff

Professor, Physiology, Pharmacology & Toxicology

Dr. Doseff received her B.Sc. in Biology and Faculty of Science from the University of Buenos Aires, Argentina, and her Ph.D. in Cell Cycle Regulation from Cold Spring Harbor Laboratory in New York.

Dr. Doseff's research focuses on understanding the mechanisms that regulate apoptosis and cell fate. These mechanisms are essential for normal cellular and immune function, contributing to normal development and controlling cancer and other inflammatory diseases. The laboratory uses genome-wide analyses, proteomics, molecular, biochemical, cellular and animal models to elucidate the gene and protein regulatory networks that regulate cell death. They are integrating these approaches to elucidate how cell death proteins and its regulators define cell fate, reduce cancer resistance and control immune-function. In addition, they study the role of plant compounds (phytochemicals) in the regulation of immune cell function. They have developed new approaches to identify targets of phytochemicals in humans, contributing to the discovery of new mechanisms by which dietary phytochemicals control cancer and immune-function. These findings are significant providing opportunities for immune-oncology and immune-regulatory therapies. The Doseff lab's research revealed the role of phytochemicals in halting cancer development and metastasis by modulating gene expression and RNA splicing. Towards the development of foods for health, they are working in functional foods that increase the efficacy of phytochemicals, facilitating the implementation of novel alternative approaches for the prevention and treatment of cancer and other inflammatory diseases. ♡

Student Travel Awards

Di Zhang, EITS trainee with Dr. Karen Liby, recently received two travel awards. The first, a travel award to attend the ASPET Annual Meeting at Experimental Biology in San Diego, CA for her abstract, "Nanoformulated Tazoparib enhances the efficacy and reduces the toxicity of this PARP inhibitor in a preclinical model of BRCA-deficient breast cancer." The second award was the 2018 Noa Noy Memorial Fund Travel Award for the Federation for American Societies of Experimental Biology 4th International Conference on Retinoids for her abstract, "Screening new retinoids for the prevention of lung cancer."

The IIT awarded travel funds to several EITS trainees for this spring and upcoming summer: **Vanessa Benham, Joseph Henriquez, Mike Rizzo, Katherine Roth, Jenna Strickland, Di Zhang, Loan Cao, Taylor Dunivin, Tyler Firkus, Jianzhou He, Sean Nguyen, Wenjie Qi, Yike Shen, and Kate Wierenga**. These students will be traveling to meetings across the country in the coming months to present their research and learn more in their fields.

IIT Faculty Achievements

Jack Harkema

University Distinguished Professor, Albert C. and Lois E. Dehn Endowed Chair in Veterinary Medicine, Department of Pathobiology and Diagnostic Investigation

Dr. Jack Harkema is one of only three veterinarians to be part of the first class of American Thoracic Society (ATS) Fellows. The ATS Fellow designation is a mark of distinction, conferring recognition on members for their accomplishments, dedication, and contributions to the Society, as well as to the fields of pulmonary, critical care, and sleep medicine.

From 2014–2017, Harkema served as the chair of the ATS Environmental, Occupational and Population Health Assembly and a member of the ATS Board of Directors. Harkema will also be presented with the Val Vallyathan Award from the ATS Assembly on Environmental, Occupational, and Population Health. This award recognizes an in-

dividual who has made outstanding contribution to basic and translation science in environmental or occupational respiratory diseases.

Harkema will be recognized in May at the ATS' 2018 International Conference in San Diego, CA for both honors. "It's a great honor to be recognized by colleagues in my field of study," says Harkema. "As a research veterinarian, I have advocated for linking human, animal, and environmental health. These societies have provided my laboratory the opportunity to share our discoveries with outstanding inhalation toxicologists, pulmonary physicians, environmental epidemiologists, and other respiratory researchers who embody the One Health concept."



A. Daniel Jones

Professor, Biochemistry and Molecular Biology, Chemistry; Director, RTSF Mass Spectrometry Facility

Dr. Dan Jones was recently appointed to the PFAS Scientific Advisory Committee. Dr. Jones joins five other scientists and toxicologists on the review panel that will recommend possible regulatory measures for per- and polyfluoroalkyl substances called PFAS or PFCs. The panelists were selected based on their expertise in the areas of epidemiology, toxicology, water quality, biochemistry and molecular biology. The panel will objectively assess the scientific information surrounding the issue of health advisory levels,

health outcomes, remediation and mitigation, and environmental pathways. Michigan hopes to be a leader in addressing PFAS contamination, which is being found in ever more areas around the state and country.

Dr. Jones' research focuses on the influence of genetics and environment on rates of biosynthesis and degradation of metabolites by using mass spectrometry. This information can be used to assess stress, toxicity, and disease.



John Kaneene

University Distinguished Professor, Department of Large Animal Clinical Sciences; Director, Center for Comparative Epidemiology

Dr. John Kaneene received the 2018 Ralph Smuckler Award for Advancing International Studies and Programs at MSU. This award recognizes a senior faculty member for their significant and lasting impact on the advancement of international scholarship, teaching and public service at MSU. Kaneene's research on infectious zoonotic diseases spans 20 countries and five continents over his 35-year career. While at MSU, he has

received continuous external funding from numerous sources such as NIH, USAID, USDA-FAS, USDA-Borlaug Fellowships, the Mastercard Foundation, Bill and Melinda Gates Foundation, and the Carneie Fellowship Foundation, totaling over 17 million dollars in support. Kaneene accepted this award on March 29 at the MSU International Awards Ceremony.

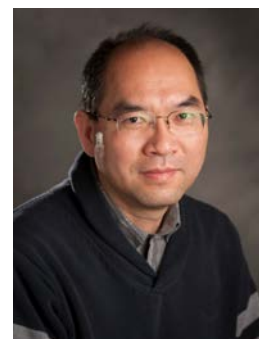


Hui Li

Associate Professor, Plant, Soil and Microbial Sciences

Dr. Hui Li was the recipient of the 2017 Jackson Soil Chemistry and Mineralogy Award. The honor, presented by the Soil Science Society of America, is given to a midcareer scientist who has made outstanding contributions to soil chemistry and mineralogy. Nominees are judged on four criteria: significance and originality of research, excellence in creative reasoning and skill in obtaining data, quality of teaching at the undergraduate or graduate level, and impact of the research on soil science and the larger society. Throughout

his nearly 20 years in the field, Li has established himself as an expert in the environmental fate and transformation of chemicals of emerging concern, as well as organic contaminants and pesticides in soils and their impacts on ecosystems and human health. He has also made significant contributions to advancing the understanding of the molecular-scale mechanisms involved in sorption and transformations of pharmaceuticals and organic contaminants on soil mineral surfaces. ♡



Recent EITS Graduates 2017/2018



Isola Brown
Pharmacology and Toxicology
Mentor, Brian Gulbransen

Dr. Isola Brown received her Ph.D. after completing the dual major program in Pharmacology and Toxicology and Environmental Toxicology. Her dissertation was, “*Enteric Glial Cell Regulation of Oxidative Stress and Immune Homeostasis During Gastrointestinal Inflammation.*”

Brown is now a Postdoctoral Research Fellow in the Robert M. Berne Cardiovascular Research

Center at the University of Virginia, working in the lab of Dr. Brant Isakson. She currently studies heterocellular signaling and communication in the vasculature. Specifically, she is studying the role of the endothelial cells that line our blood vessels in the pathology of viral infections, and how alterations in endothelial signaling mechanisms may be protective during infection.

Brown hopes to continue with a career in academia and in five years hopes to have an active research lab and teaching career.



Ya-Hui Chuang
Plant, Soil and Microbial Sciences
Mentor, Hui Li

Dr. Ya-Hui Chuang received her Ph.D. after completing the dual major program in Plant, Soil and Microbial Sciences and Environmental Toxicology. Her dissertation was, “*Uptake, Accumulation and Metabolism of Chemicals of Emerging Concern in Vegetables.*”

Chuang is now a Postdoctoral Researcher in the Department of Civil, Environmental and

Geodetic Engineering at Ohio State University. Her research is focused on the sorption of algal toxin (e.g., microcystin) in the soil after land application of water residuals.

Chuang’s goal is to continue her work in the academic field with research focused on the fate of emerging contaminants in the soil-water-plant continuum.



Sophia Kaska
Pharmacology and Toxicology
Mentor, Michelle Mazei-Robison

Dr. Sophia Kaska received her Ph.D. after completing the dual major program in Pharmacology and Toxicology and Environmental Toxicology. Her dissertation was, “*Investigating the Role of Ventral Tegmental Area TORC2 in Stress and Stress-Induced Changes in Opiate Reward.*”

Kaska is now a Postdoctoral Researcher in the Department of Medicinal Chemistry at the

University of Kansas. She is currently involved in drug discovery research for neuropsychiatric diseases such as opiate addiction and schizophrenia.

After completing her postdoctoral education, Kaska hopes to pursue a career in science policy and/or science education and outreach in the Washington, D.C. area.



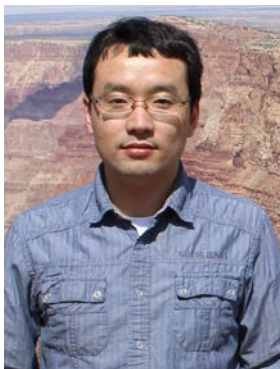
Theresa Lansdell
Pharmacology and Toxicology
Mentor, John Goudreau

Dr. Theresa Lansdell received her Ph.D. after completing the dual major program in Pharmacology and Toxicology and Environmental Toxicology. Her dissertation was, “*The Role of Parkin in Maintaining Proteasome Activity Following Acute Neurotoxic Insult.*”

Lansdell is currently working as a Postdoctoral Researcher in the lab of Dr. Stacie Demel at Michigan State University. A recent GWAS study indicates that there is an association be-

tween SNPs located nearby the HDAC-9 gene and intracranial aneurysm. She hopes to learn more about how these SNPs put patients at a higher risk for forming intracranial aneurysms. To this end, she will be studying the effects of these SNPs on HDAC-9 expression and on the vascular renin angiotensin system in vascular smooth muscle cells derived from patient samples.

In five years, she hopes to be early in her career as an independent investigator. She hopes to combine her predoctoral and postdoctoral skill sets to study the effects of cerebral vascular disease on neurodegeneration.



Jinpeng Li

Genetics

Mentor, Norbert Kaminski

Dr. Jinpeng Li received his Ph.D. after completing the dual major program in Genetics and Environmental Toxicology. His dissertation was, “Aryl hydrocarbon receptor activation by 2,3,7,8-tetrachlorodibenzo-p-dioxin impairs human B lymphopoiesis.”

Li is now a Postdoctoral Fellow in Toxicology and Environmental Research and Consulting (TERC) at the Dow Chemical Company. His

research is focused on developing alternative models to facilitate predictive toxicology.

Li believes the knowledge that he learned from the IIT curriculum and the training he received in the Kaminski laboratory provided him with a solid foundation for his current research and career development. He hopes to continue learning and conducting toxicological research and in the future, hopes to apply his research findings in the real world.



Brittany Winner

Pharmacology and Toxicology

Mentor, John Goudreau

Dr. Brittany Winner received her Ph.D. after completing the dual major program in Pharmacology and Toxicology and Environmental Toxicology. Her dissertation was, “UCH-L1 as a Susceptibility Factor for Nigrostriatal and Mesolimbic Dopamine Neurons after Neurotoxicant Exposure and Aging.”

Winner is now an ORISE Postdoctoral Fellow at the United States Army Medical Research

Institute of Chemical Defense (USAMRICD). Her projects include researching the neurotoxic effects of botulinum toxin and nerve agent.

In five years, Winner hopes to continue working in government research, perhaps as a Principal Investigator.



Joseph Zagorski

Cell and Molecular Biology

Mentor, Cheryl Rockwell

Dr. Joseph Zagorski received his Ph.D. after completing the dual major program in Cell and Molecular Biology and Environmental Toxicology. His dissertation was, “The Role of the NRF2/KEAP1 Signaling Pathway in the Early Events Following Jurkat T Cell Activation.”

Zagorski is now a Postdoctoral Researcher at Helen DeVos Children’s Hospital. He works

in the translational pediatric cancer lab of Dr. Giselle Sholler. They are currently running clinical trials and doing academic research on solid pediatric cancer tumors, with the most common diagnosis being neuroblastoma. Their work ranges from strictly academic, to high throughput drug screening, to personalized medicine and clinical trial development.

In the next five years, Zagorski hopes to transition into a PI role or a research assistant professor role. 🍷

IIT Seminar Series

The IIT was happy to host six fantastic speakers this past year as part of the IIT Seminar Series:

- » **Dr. Jon Cook**, Chief Toxicology Scientist, Pfizer, spoke on, “Why Toxicologists Should be Trained in Precision Medicine Principles,” on September 8, 2017.
- » **Dr. Rachel Murphy**, MSU NIEHS Training Grant postdoctoral fellow, spoke on, “In vitro examination of drug induced idiosyncratic renal and liver injury,” on October 13, 2017.
- » **Dr. Jason Richardson**, Northeast Ohio Medical University, spoke on, “Novel Targets for Reducing Neuroinflammation in Parkinson’s Disease,” on November 10, 2017.
- » **Dr. Jianrong Wang**, Michigan State University, spoke on, “Integrative Modeling of Regulatory Genomics and Epigenomics to Understand Human Disease Mechanisms,” on January 12, 2018.

» **Dr. Jon Wambaugh**, U.S. EPA, spoke on, “Establishing Real World Context for High Throughput Toxicity Testing,” on February 9, 2018.

» **Dr. Susan Hester**, U.S. EPA, spoke on, “Opening the Archives - Novel Methods to Advance Whole Transcriptomic Analyses of Archival Tissues,” on April 13, 2018.

The IIT looks forward to hosting another engaging set of speakers for the 2018/2019 academic year, beginning with:

- » **September 14** - **Dr. Tomás Guilarte**, Dean, Robert Stempel College of Public Health and Social Work, Florida International University
- » **October 12** - **Dr. Edward Calabrese**, Professor, University of Massachusetts Amherst



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