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INSTITUTE FOR INTEGRATIVE TOXICOLOGY

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Above: Current and past MSU SOT Presidents gathered at the annual IIT Alumni and Friends Reception at the 56th Annual Society of Toxicology Meeting. Pictured from left: Dr. James Bus, Dr. Norbert Kaminski, Dr. Patricia Ganey, Dr. Michael Holsapple, Dr. Jerry Hook, Dr. Jay Goodman, and Dr. Ken Wallace.

IIT AFFILIATES SUCCESSFUL AT 56TH SOT MEETING IN BALTIMORE

Students and faculty of the MSU Institute for Integrative Toxicology were well represented at this year's 56th annual Society of Toxicology (SOT) meeting in Baltimore, Maryland with numerous abstracts presented and many special honors awarded.

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 March 12-16, 2017.

The following IIT-affiliates received awards or honors at this year's meeting (numbers before paragraphs correspond to pictures on page 3):

1. A paper by Dr. **Rance Nault** (EITS graduate), **Kelly Fader** (EITS trainee with Dr. Zacharewski), and **Dr. Timothy Zacharewski** titled, "Pyruvate Kinase Isoform Switching and Hepatic Metabolic Reprogramming

IIT AFFILIATES SUCCESSFUL AT SOT cont.

...continued from page 1

by the Environmental Contaminant 2,3,7,8-Tetrachlorodibenzo-p-dioxin," was awarded Honorable Mention in the SOT Toxicological Sciences Paper of the Year category.

2. Jiajun (Brian) Zhou, training with Dr. Norbert Kaminski, received third place for his student presentation, "Suppression of the IgM Response by 2,3,7,8-Tetrachlorodiobenzo-p-Dioxin (TCDD) Involves Impairment of Immunoglobulin Secretion by Human Primary B," by the Immunotoxicology Specialty Section of the SOT. He also was awarded the Ronald and Sharon Rogowski Fellowship for Food Safety and Toxicology for the summer of 2017.

3. Kelly Fader, training with Dr. Timothy Zacharewski, was the recipient of two awards from the Mechanisms Specialty Section of the SOT, the Carl C. Smith Graduate Student Award - Second Place and the Sheldon D. Murphy Student Travel Award for her abstract, "Hepcidin Deficiency, Systemic Iron Overloading, and

Heme Accumulation in 2,3,7,8-Tetrachlorodibenzo-p-Dioxin-Elicited Hepatotoxicity."

4. Joseph Henriquez, training with Dr. Norbert Kaminski, received 3rd place in the best student presentation category from the SOT Immunotoxicology Specialty Section for his abstract, "Tetrahydrocannabinol (THC) Suppresses Type I Interferon-Mediated Activation of Healthy and HIV-Infected T Cells."

5. Kevin Baker, (pictured center) training with Dr. James Luyendyk, was a finalist for the Carl C. Smith Award from the Mechanisms Specialty Section for his abstract, "Bile Acid Stimulation of Tissue Factor Procoagulant Activity in Hepatocytes Requires Non-Apoptotic Phosphatidylserine Externalization."

6. Melissa Bates, EITS trainee, and her mentor, Dr. James Pestka, were awarded Paper of the Year by two SOT specialty sections, the Immunotoxicology Specialty Section and the Occupational and Public Health Specialty Section for their publication, "Silica-Triggered Autoimmunity in Lupus-Prone Mice Blocked by Docosahexaenoic Acid."

7. Isabella M. Reichardt, undergraduate student from the University of Wisconsin, received a Pfizer Undergraduate Travel Award for her research in the lab of Dr. Bill Atchison during summer 2016. Her abstract was titled, "mRNA Expression Profile of Nrf2-ARE Pathway and Excitatory Amino Acid Transporter 3 During Methylmercury Exposure in NSC34 Motor Neurons."

Rosa Jaiman, training with Dr. William Atchison, was one of four recipients of the "3-Minute Shark Tank Impact Travel Award," from the AUB Neuroscience Roadmap Scholar Program. She traveled to the University of Alabama at Birmingham to the NEURAL conference to give her presentation where she had 3 minutes to convince the judges of the importance of her research. As a winner, she received a travel award of \$1,000 to attend SOT.

IIT AFFILIATES RECEIVE PRESITIGOUS AWARDS

 $T_{\rm gate-Palmolive} \ {\rm Awards} \ {\rm at\ this\ year's\ SOT\ Annual\ Meeting} \ {\rm in\ Baltimore,\ Maryland}.$

IIT faculty member, Almudena Veiga-Lopez, received the Colgate-Palmolive Grant for Alternative Research which identifies and supports efforts that promote, develop, refine or validate scientifically acceptable animal alternative methods to facilitate the safety assessment of new chemicals and formulations. She was awarded for her project, "Novel 3D Microfluidic Chip for Placental Toxscreening." 2011 EITS graduate, Peer Karmaus, now with St. Jude Children's Research Hospital in Memphis, Tennessee, received the Colgate-Palmolive Postdoctoral Fellowship Award in *In Vitro* Toxicology which is given to advance the development of alternatives to animal testing in toxicological research. Karmaus was awarded for his project titled, "Assessing Xenobiotic Perturbation of Immunity at the Single Cell Level Using Human CD4+ Naïve T Cells."

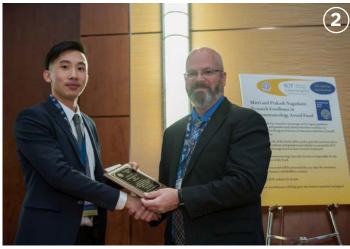




Far Left: Almudena Veiga-Lopez, Ph.D., receives her Colgate-Palmolive Grant for Alternative Research for her abstract, "Novel 3D Microfluidic Chip for Placental Toxscreening."

At Left: Peer Karmaus, Ph.D. receives his Colgate-Palmolive Postdoctoral Fellowship Award in *In Vitro* Toxicology from Dr. Patricia Ganey, incoming SOT President.



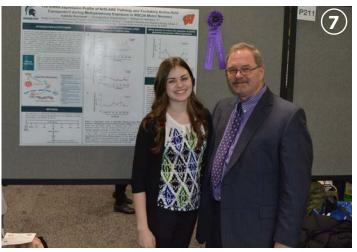












GANEY BEGINS SOT PRESIDENTIAL TERM



IIT-affiliated faculty member, Dr. Patricia Ganey is now President of the SOT. In 2017-18 she will lead SOT Council in focusing on a strategy to coordinate the mentoring activities within the Society, strengthening the global partnership with colleagues in Asia, and launching interactions with other biomedical societies to foster a greater appreciation of the value of the discipline of toxicology.

PROTEIN INVOLVED IN BLOOD CLOTTING STIMULATES LIVER REPAIR

TIT affiliated faculty Lmember, Dr. James Luyendyk and a team of researchers including EITS alumni, Dr. Anna Kopec and Dr. Nikita Joshi, have uncovered a new pathway in the body that stimulates liver repair. Using an experimental model of high-dosage acetaminophen, the team found that liver injury activated blood clotting. which then stimulated liver repair.

The study, "Fibrin(ogen) drives repair after

acetaminophen-induced liver injury via leukocyte α M β 2 integrin-dependent upregulation of Mmp12," was published in the Journal of Hepatology in April.

Fibrinogen is a large, complex, soluble blood plasma protein. During coagulation, this protein is converted to insoluble fibrin deposits, a factor in blood clotting. These fibrin deposits are what the team discovered is critical to



trigger liver repair after an acetaminophen overdose. The fibrin molecule plays a key role in activating a type of immune cell, known as a macrophage, which helps remove cellular debris and repair the liver.

Initially hypothesizing that the fibrin deposits were damaging, the team was surprised to find their results showed otherwise.

"This pathway of repair has never

been described before and could lead to new strategies to promote liver repair," said Luyendyk. "Tissue injury is tightly connected to the activation of blood clotting, meaning this new pathway could be very important in treating liver damage not just by acetaminophen overdose, but other causes as well."

While the liver's ability to repair is well documented, in some cases, the process can be insufficient or break down, and

can lead to failure of the organ and requirement of a liver transplant. "Discovery of drugs that can promote repair of the already injured liver would address an important unmet need," Luyendyk said.

EITS STUDENT ACHIEVEMENTS



Brandon Armstrong, training with Dr. Cheryl Murphy, received a travel award to attend the Society of Environtmental Toxicology and Chemistry (SETAC) North America meeting in Orlando, Florida.



Sophia Kaska, training with Dr. Michelle Mazei-Robinson, was selected to participate in the 2017 American Society for Pharmacology and Experimental Therapeutics (ASPET) Washington Fellows Program. Kaska traveled to Washington DC this spring where she met with members of Congress and advocated for increased funding of biomedical research on Capitol Hill.



Jenna Strickland, training with Dr. Bryan Copple, attended the International Neurotoxicology Association Meeting in Florianopolis, Brazil on May 20-24, 2017. She was invited to give a talk on high throughput screening methods in neurotox-

icology based on her work at the US EPA prior to starting graduate school at MSU. At the EPA, Strickland worked in the EPA's Phase II ToxCast Libraries using multi-well microelectrode array (MEA) plates to look for changes in neural network function in response to treatment with ToxCast compounds. While at the meeting, Strickland was the recipient of the Young Investigator Award and the David Ray Award. The EITS program was pleased to provide funds in partial support of Strickland's travel to this meeting.

THREE MSU SRP LABORATORIES COLLABORATE

Three laboratories affiliated with the MSU Superfund Program are collaborating to investigate the bioavailability of dioxins when bound to activated carbon - the laboratories of Dr. Norbert Kaminski (Project 1), Dr. Stephen Boyd (Project 6), and Dr. Syed Hashsham (Project 4).

The focus of this ongoing collaboration is on characterizing the properties of activated carbon for the purpose of environmental remediation. Specifically,

activated carbon is a material that is becoming more widely used to remediate chemically contaminated soils and sediments due largely to its cost effectiveness versus more traditional cleanup methods such as dredging or excavating. Activated carbon particles are very porous allowing lipophilic persistent environmental contaminants like dioxins to articulate into the activated carbon and adhere to it. The idea is that the activated carbon will sequester the contaminant in a form that is no longer bioavailable to fish, mammals, and humans.

The collaborative laboratory experiments utilize a mammalian mouse

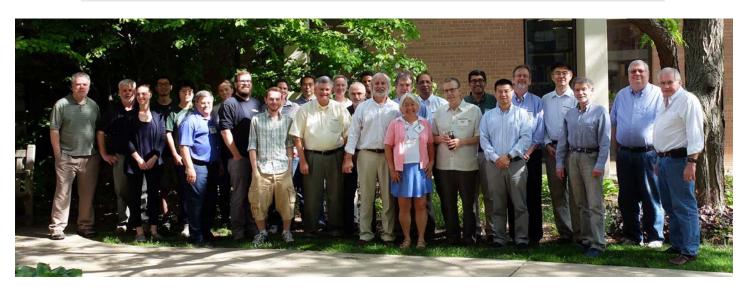


Photos: The laboratories of Dr. Norbert Kaminski, Dr. Stephen Boyd, and Dr. Syed Hashsham joined together for an experiment focusing on characterizing the properties of activated carbon for the purpose of environmental remediation for the MSU Superfund Project.

model. Boyd's group prepared and then orally administered microporous activated carbon adsorbed with dioxins (TCDD). To test the bioavailability of the TCDD, Kaminski's laboratory assessed modulation of the immune system, a hallmark of TCDD toxicity. Hashsham's laboratory analyzed the changes in the composition of the microorganisms (i.e., gut microbiome) within the GI tract.

The results from these collaborative experiments show that microporous activated carbon does successfully sequesters TCDD to minimize bioavailability as evidence by a loss of TCDD biological activity in the mouse model.





Above: The MSU Superfund Program held a meeting on May 17-18, 2017 on the campus of MSU to meet with its External Advisory Committee. Each project and core presented recent progress over the two day meeting. The meeting culminated with a closed session of the External Advisory Committee evaluating research progress and providing recommendations on future direction.

NEW FACULTY JOIN IIT

Over the past several months the MSU IIT was pleased to add three new affiliated faculty members: Dr. Alison Bernstein, Dr. Kin Sing Lee, and Dr. Masako Morishita.

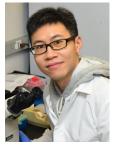


Alison Bernstein Assistant Professor, Translational Science and Molecular Medicine

Dr. Bernstein received her B.A. in Biological Basis of Behavior from the University of Penn-

sylvania in 2000, her Ph.D. in Molecular Genetics and Genomics from Washington University in St. Louis in 2009, and was a postdoctoral fellow studying Neuroscience, Neuroepigenetics and Neurotoxicology at Emory University from 2009 to 2016.

Dr. Bernstein's current research focuses on how epigenetic modifications mediate neurotoxicological effects and gene-environment interactions underlying sporadic neurodegenerative diseases. Although these diseases are generally diseases of the aged, the neurodegenerative process begins long before clinical diagnosis. Thus, exposures that occur early in life may contribute to sporadic forms of disease by directly affecting the vulnerability of neurological systems. Epigenetic modifications are thought to imprint environmental experiences on the genome, resulting in stable alterations in phenotype. Thus, linking epigenetic changes with functional outcomes will help to elucidate the mechanisms underlying sporadic neurodegenerative diseases and further our understanding of the complex relationship between toxicity, epigenetics and neuronal vulnerability.



Kin Sing Lee Assistant Professor, Pharmacology and Toxicology

Dr. Lee received his B.S. in Chemistry from Hong Kong University of Science and Technol-

ogy in 2003, his Ph.D. in Chemistry from Michigan State University in 2010, and was a postdoctoral fellow studying Medicinal Chemistry and Chemistry Biology at the University of California at Davis from 2010 to 2016.

Dr. Lee is broadly interested in 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. He is particularly interested in studying the molecular mechanisms by which the dietary omega-3 (DHA or EPA) to omega-6 (e.g. soybean oil) ratio affects human health and human responses to environmental toxicants. It has been shown that these fatty acids affect human health partly through their metabolites and one of the major metabolites derived from the dietary lipids are the corresponding epoxides. Both omega-3 and omega-6 fatty acid epoxides are potent signaling molecules and play an important role in inflammation, blood pressure regulation, pain perception and angiogenesis. However, how they initiate their biological effects remain unknown. The tools and the methods developed not only will help us better understand how these dietary lipids modulate human health but also could potentially be new therapeutics for different diseases.



Masako Morishita Associate Professor, Family Medicine

Dr. Morishita received her B.S.E. in Chemical Engineering in 1994, her M.S. in Environmental

Health Sciences in 1998, and her Ph.D. in Environmental Health Sciences in 2003, all from the University of Michigan.

Dr. Morishita's research focuses on exposure science including improving physicochemical characterization of indoor and outdoor airborne particulate matter, quantification of biological burden and biomarkers of trace elements and metals, and emission source identification using receptor modeling—all of which are essential for human/animal exposure assessment and toxicological/ epidemiological studies in multidisciplinary research projects. She incorporates measurement and analytical tools to understand the sources and fates of nanoparticles and ambient air pollutants, and their potential impacts to the environment and human health. She is currently leveraging her exposure science expertise to conduct intervention studies focusing on the reduction of personal exposure to fine particulate matter and adverse cardiovascular responses in urban communities, protecting the health and quality of life of the elderly and other vulnerable populations. She seeks to continue extending her future efforts in community-based environmental health research, focusing on interventions that mitigate exposure and improve health outcomes.

FACULTY ACHIEVEMENTS

Dr. Thomas Pinnavai, Professor Emeritus of Chemistry, was named 2016-2017 AAAS Fellow by the American Association for the Advancement of Science. Pinnavaia was recognized for distinguished contributions to the field of inorganic materials chemistry, particularly for innovative synthesis of mesophases via supramolecular assembly and the intercalation of lamellar solids. **Dr. Gina Leinninger**, Assistant Professor, Physiology and the Neuroscience Program, received the Teacher-Scholar Award from The College of Natural Science.

Dr. Jay Goodman, Professor, Pharmacology and Toxicology, was elected to serve on the Society of Toxicology's Nominating Committee in 2017-2018.

EITS GRADUATES SPRING 2017



Brandon Armstrong Fisheries and Wildlife Mentor, Cheryl Murphy

Dr. Brandon Armstrong received his Ph.D. in December of 2016 after completing the dual major program in Fisheries and Wildlife and Environmental Toxicology. His dissertation was, "Using computational models to scale sublethal effects of stressors to adverse population outcomes in fish." Armstrong continues on at MSU this semester, teaching two courses, Conservation Biology and Introduction to Organismal Biology. He is actively applying for postdoctoral positions and is in the process of submitting manuscripts from his dissertation research. In the next five years, Armstrong hopes to be transitioning from a postdoctoral researcher to an assistant professor at a university and continuing his research focused on scaling sublethal effects of anthopogenic stressors on individuals to population level responses in fish.



Alexandra Colón-Rodriguez Comparative Medicine and Integrative Biology

Mentor, Bill Atchison

Dr. Alexandra Colón-Rodriguez received her Ph.D. in December of 2016 after completing the dual major program in Comparative Medicine and Integrative Biology and Environmental Toxicology. Her dissertation was, "Role of α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor

on methylmercury-induced calcium dysregulation on motor neurons."

In January, Colón-Rodriguez started her postdoctoral training with Dr. Megan Dennis at the University of California Davis Genome Center/M.I.N.D. Institute. The Dennis lab is a genetics/neurogenomics lab. One of the main projects of the lab to which I will be contributing is focused on functional and genetic dissection of interconnected genes mutated in children with autism and epilepsy using zebrafish. Her main goal as a postdoctoral student is to learn a new model (Zebrafish) and novel techniques such as RNAseq, electroencephalogram (EEG), and the use of CRISPR Cas 9 as a tool for creating mutants to understand neurological disease. Colón-Rodriguez will also be continuing her mentoring and outreach efforts and she plans to pursue opportunities in academia or government once she has completed her postdoctoral training.

UPCOMING EVENTS SUMMER/FALL 2017

IIT Seminar Series

The IIT is excited to continue its seminar series that features experts and faculty in the field of toxicology this coming fall with plans to host 9 different speakers throughout the 2017/2018 academic year. As of this publication, the following speakers have been confirmed:

September 8, 2017 - Dr. Jon Cook, Pfizer

November 10, 2017 - Dr. Jason Richardson, Northeast Ohio Medical University

December 8, 2017 - Dr. Stacey Missmer, MSU Obstetrics, Gynecology and Reproductiive Biology

More information on seminar speakers, dates, and times will be available in the bi-weekly Toxicology Track newsletters this fall. Email lstjohn@msu.edu to join our mailing list!

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