OMSU INSTITUTE FOR INTEGRATIVE TOXICOLOGY



2015-2016 ANNUAL REPORT

MICHIGAN STATE

IIT ANNUAL REPORT 2015-2016

IIT HISTORY AND MESSAGE

- 4 A Tradition of Excellence
- 5 Message from Director Norbert Kaminski

HIGHLIGHTS

6 2015-2016 Highlights

EITS TRAINING PROGRAM

- 8 EITS Training Program Review
- 9 Graduate Spotlights
- 11 EITS Student Melissa Bates Forms Research Partnerships
- 12 EITS Graduates

IIT CENTERS

- 13 MSU Superfund Research Program
- 14 Center for Research on Ingredient Safety
- 15 Great Lakes Air Center for Integrated Environmental Research

FACULTY FEATURES

- 16 Dr. Stephen Boyd
- 17 Dr. Jay Goodman
- 18 Dr. James Tiedje

FACULTY PUBLICATIONS

20 Publications of IIT Faculty

PROFESSIONAL SERVICE

36 Professional Service of IIT Faculty

AFFILIATES

- 41 IIT Affiliated Faculty
- 42 Departments / Ph.D. Programs
- 42 Deans

Managing Editor: Writing and Design Lauren St.John

> Photos MSU University Relations, SOT, IIT Staff

IIT Staff

Norbert E. Kaminski, Ph.D., Director Robert A. Roth, Ph.D., Graduate Program Director Amy Swagart, IIT Fiscal Officer Kasey Baldwin, IIT Administrative Assistant Adelle Simmons, EITS Graduate Secretary Lauren St.John, Communications/Webmaster

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A TRADITION of EXCELLENCE

The Michigan State University Institute The Michigan State Constraint of Integrative Toxicology (IIT) is a multidisciplinary academic unit that supports and coordinates research and graduate education activities for faculty interested in various aspects of toxicology. The Institute is a successor to the Institute for Environmental Toxicology and the Center for Environmental Toxicology, the latter founded in 1978. While the name of the unit has changed over the years to denote changes in the leadership and academic position, the mission has been the same. For over 30 years, toxicology at Michigan State has provided excellence in training graduate students, facilitating research, and providing service to the State of Michigan when needed. The successes generated in these endeavors have resulted in recognition of Michigan State as a leader in academic toxicology.

The Center for Environmental Toxicology was initiated primarily to assist the State of Michigan with environmental contamination issues such as those arising from the PBB (polybrominated biphenyls) incident in the early 1970s. That unfortunate event was initiated by the accidental contamination of feed for dairy cattle with PBBs. These dioxin-like chemicals and dioxin itself remain a major topic of research at Michigan State University.

Several years after the founding of the Center for Environmental Toxicology, a dual-degree Ph.D. program in environmental toxicology was offered in conjunction with several cooperating departments. The characteristics of the program were unique at that time as students were required to complete the Ph.D. requirements of a department of their choice in addition to the didactic requirements and toxicology research specified by the Center. The quality of this multi-departmental effort was recognized by the National Institutes of Health in 1989 with the award of a Training Grant from the National Institute for Environmental Health Sciences. This grant has been competitively renewed ever since, providing over 28 years of continuous funding. Graduates of MSU's toxicology program number over 200 and can be found in academia, industry, and governmental positions.

MESSAGE from the DIRECTOR



In reflecting over this past year's accomplishments, I decided to devote this year's Director's message to an area that often does not garner the level of visibility it ought to but ultimately is the life-blood of any successful academic unit, its graduate program.

Graduate training in toxicology at MSU was launched in 1982, offering a dual doctoral degree in cooperation with a number of basic discipline programs. The graduate program in Environmental and Integrative Toxicological Sciences (EITS), today, partners with seventeen graduate programs at MSU offering its unique style of collaborative education in toxicology. Trainees receive strong training in one of seventeen disciplinary programs and also complete course work and research in toxicology for the dual degree. The program currently has 34 doctoral trainees. Since its inception, graduate training in toxicology has been a source of tremendous pride for IIT faculty, trainees and its alum. Graduate training in toxicology at MSU is nationally and internationally recognized for excellence and our graduates are highly sought by government, academia and the private sector. Adding significant visibility to our program has been the long-term support the EITS has received from the National Institutes of Health by way of funding for a training grant from the National Institute for Environmental Health Sciences, currently in year twenty-eight of continuous funding.

This year the EITS graduate program established a third educational track which is aligned with our new Center on Research in Ingredient Safety. The track maintains its strong commitment to training in both toxicology and the basic sciences with an emphasis on risk assessment and regulatory policy. There is much enthusiasm around this new EITS track, which reflects, at least in part, the concept behind CRIS; specifically, a partnership between academia and the private sector. Toward this end courses are being developed, some of which will capitalize on the expertise of scientists in the private sector and government and their participation as invited speakers. By doing so, we believe that our trainees will be better prepared to assume permanent position, especially in government and the private sector as our next generation of toxicologists.

Ultimately for every academic unit, its graduate program is its foundation as it underpins all activities. The quality of the graduate program determines the quality of the student recruited each year, the quality of its faculty and the quality of the scholarship that is conducted. The IIT looks forward to 2017 and the continued success of the EITS graduate program.

Morb faminali"

Norbert E. Kaminski, Ph.D., IIT Director

2015-2016 HIGHLIGHTS

This year's highlights showcase the accomplishments of not only the IIT, but also of the faculty and trainees involved in continuing to expand the quality and leadership of Michigan State University in academic toxicology.

IIT Affiliates Successful at 55th SOT Meeting in Louisiana

Students and faculty of the MSU Institute for Integrative Toxicology were highly honored at this year's 55th annual Society of Toxicology (SOT) meeting in New Orleans, Louisiana 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 7,000 scientists from industry, academia and government from various countries around the globe. This year's meeting was held March 13 -17, 2016.

The following students in the MSU-IIT's Environmental and Integrative Toxicological Science (EITS) training program received awards or honors: Nikita Joshi, Natalia Kovalova, Jinpeng Li, Ashley Maiuri, Rance Nault, and Alexandra Turley.

Postdoctoral student, Dr. Anna Kopec, and undergraduate students, Jessica Ray and Lizbeth Perez-Castro, also received awards.

Affiliated faculty members, Dr. Timothy Zacharewski, Dr. James Luyendyk, Dr. Ning Li, Dr. James Wagner and Dr. Jack Harkema received special awards as well.

Li Awarded USDA Grant to Study Fresh Produce, Food Safety



Hui Li, Associate Professor in Plant, Soil and Microbial Sciences and IIT-affiliated faculty member, has been awarded a \$475,000 grant from the U.S. Department of Agriculture to study human exposure to the harmful chemicals present in fresh produce.

Addressing a primary aspect of food safety, Li's research

will focus on produce absorption of pharmaceutical and personal care products, commonly known as chemicals of emerging concern, or CECs. Consumption of these chemicals may lead to increased antibiotic resistance and other health issues.

The three-year project is made possible by the USDA's Agriculture and Food Research Initiative. It will extend through October 2018 in collaboration with fellow IIT-affiliated faculty **Stephen Boyd** and **Wei Zhang**, as well as Ray Hammerschmidt, all from the Department of Plant, Soil and Microbial Sciences at MSU. ゑ

IIT Welcomes Three New Affiliated Faculty Members

This past year the MSU-IIT added three new affiliated faculty members Dr. Sudin Bhattacharya, Dr. Ned Jackson, and Dr. Wei Zhang. These faculty join the IIT as research collaborators as well as contributors to the Environmental and Integrative Toxicological Sciences Graduate Training Program.



Sudin Bhattacharya

Assistant Professor, Institute for Integrative Toxicology

Dr. Bhattacharya is broadly interested in several areas of computational toxicology. A major focus of his work is the application of computational methods to study the signaling and transcriptional regulatory networks that underlie the determination of cell fate, and the perturbation of these networks by environmental pollutants

like dioxin. Specifically, he is interested in integrating diverse genomic data sets to map and model transcriptional regulatory networks and their environmental perturbation in the immune system and the liver.



Wei Zhang

Assistant Professor, Department of Plant, Soil and Microbial Sciences, Environmental Science and Policy Program

Dr. Zhang is interested in the quality and sustainability of soil and water resources, with emphasis on the movement of water, solutes (e.g., nutrients, agrochemicals, and environmental toxins), and fine particles such as microorganisms, abiotic colloids, and engineered nanoparticles in natural and engineered systems, particularly in unsaturated soils. His current research focuses on the fate and transport of emerging contaminants in the soilwater-biota continuum within the framework of "one health". The overarching goal of his research is to promote human and environmental health by understanding fundamental transport processes and developing sustainable agricultural practices.



James E. "Ned" Jackson Professor, Chemistry

Dr. Jackson is excited to join the illustrious ranks of IIT members. Jackson group efforts bring mechanistic organic chemistry to problems of "greening" energy and chemicals production and pharmaceutical synthesis. Based on fossil-free (solar, wind, nuclear) electric power, electrocatalytic conversions of organic compounds are under study to bypass reagent-based chemistry and

the resulting byproduct/waste streams. For instance, a recent finding is an electroactivated method that replaces classical halocarbon alkylating agents with simple alcohols to alkylate amines, a step widely practiced in drug manufacture. The large-scale goal is to open the door to replacement of fossil fuel (petroleum) with bio-derived feedstocks in our energy and chemical technologies and industries. This work has grown out of long term collaborations with chemical engineers Dennis Miller and Chris Saffron, and analytical chemist Greg Swain at MSU.

Third Track Added to EITS Doctoral Program

The Institute for Integrative Toxicology (IIT) is excited to announce the addition of a third track to the Environmental and Integrative Toxicological Sciences (EITS) doctoral program. The Food Toxicology and Ingredient Safety (FTIS) track will be available to students fall 2016.

The new FTIS track has been brought about in partnership with the recent established Center for Research on Ingredient Safety (CRIS). With MSU's longstanding focus on food and health and with the commitment of the MSU administration and the food industry in support of CRIS and its mission, considerable demand for doctoral training in the toxicology of ingredients in foods and other products is anticipated. The FTIS track will meet this demand with graduate training that will prepare students to be leaders in the area of food toxicology and ingredient safety in industry, government, and academia. This training will involve thesis research as well as formal coursework in basic biomedical and toxicological sciences and in risk assessment/regulation of foodborne chemicals and other ingredients.

The new "Food Toxicology and Ingredient Safety Track" is designed for students interested in the safety of food-borne and consumer product ingredients and has somewhat greater emphasis on risk evaluation and regulation of ingredients than the other two EITS doctoral tracks.

For more information on the new Food Toxicology and Ingredient Safety track in the EITS program, please contact Adelle Simmons, asimmons@msu.edu.

PBPK Modeling Short Course a Success



The Institute for Integrative Toxicology hosted an intensive 3 day short course, May 18-20, 2016, on "Introduction to Physiologically Based Pharmacokinetic (PBPK) Modeling".

The short course covered the principles of physiologically based pharmacokinetic (PBPK) modeling and introduced the application of this technique in chemical health risk assessment and drug development.

The course comprised lectures and hands-on computer simulation exercises. The IIT offered this course through the Training Core and the Research Translation Core within the MSU-SRP. The course instructors were Qiang Zhang, Emory University, Sudin Bhattacharya, MSU, and Rory B. Conolly from the US EPA.

Rockwell Receives NIEHS ONES Award



Cheryl Rockwell, Assistant Professor in Pharmacology and Toxicology and IIT-affiliated faculty member, has been selected as one of five exceptional early-career scientists to receive a grant as part of the Outstanding New Environmental Scientist (ONES) Program. The National Institute of Environmental Health Sciences (NIEHS) created the ONES award to support researchers, in the formative stages of their

careers, who conduct cutting-edge research to study how the environment influences human health.

As a junior investigator, this award is vital for expanding and maintaining Rockwell's research program. Specifically, this award will allow her to pursue her investigation into how the food additive, tBHQ, modulates T cell differentiation as well as the downstream effects on allergy and the role of the transcription factor Nrf2 in this process. Her lab's preliminary data suggests that activation of Nrf2 by tBHQ promotes the differentiation of CD4 T cells into Th2 cells, a phenotype involved in allergic responses. The main purpose of this research project is to determine the mechanism for these effects.

"It is a tremendous honor to have been selected for this prestigious award," said Rockwell. "I am personally acquainted with a number of previous ONES awardees and am thus well aware of the notable accomplishments of the alumni of this program. I cannot describe how thrilled and grateful I am to be considered among the ranks of the ONES investigators."

ptin Receptor Neurons

EITS BRAINING PROGRAM

A dministered through the Institute for Integrative Toxicology, the doctoral program in Environmental and Integrative Toxicological Sciences (EITS) trains future leaders in the discipline of toxicology. It continues to be one of the premier toxicology training programs in the U.S. The EITS is a "dual major" program that emphasizes excellent basic science training from one of our 17 partnering graduate programs coupled with didactic and research training in toxicology by MSU faculty. Currently, 34 doctoral students are enrolled in the EITS program, distributed among several of our partnering PhD programs. I am happy to report that we have recently added the graduate program in Physiology as an EITS partnering program.

The EITS program has featured two curricular tracks. The Biomedical Track provides training to students entering with a strong background in mammalian biological sciences and an interest in mechanisms of toxicity. The Environmental Track serves students with backgrounds in the biomedical sciences such as chemistry, engineering, invertebrate biology, and ecology, and has had a greater emphasis on training in risk assessment and regulation of environmental chemicals. In 2016, we developed a third track in Food Toxicology and Ingredient Safety; beginning in 2017, this track will attract students with an interest in safety of foodborne and consumer product ingredients. It was instituted in part to align with the mission of the developing Center for Research on Ingredient Safety at MSU.

As in years past, our current trainees have received awards at the 2016 Annual Meeting of the Society of Toxicology (SOT) or from other organizations. Our students continue to demonstrate good citizenship with service on Society committees at the regional and national levels as well as within MSU. Students who graduated in the past year are typically in postdoctoral positions at various academic institutions in the U.S. and other countries.

The IIT seminar program has been modified and is now largely organized by our capable students with guidance from Dr. Kaminski and myself. Our annual Research Evening was again a success, with poster presentations and after dinner talks by three of our senior trainees. The year ahead will feature a succession plan for the program directorship as well as a review of the Environmental Track headed by Dr. Cheryl Murphy.

The 2015-2016 academic year marked the 28th consecutive year that the EITS program has enjoyed training grant support from the National Institute for Environmental Health Sciences (NIEHS). This grant provides stipend support for 7 predoctoral and 2 postdoctoral fellows each year. Generous supplemental funding from Interim Dean Judith Stoddart of the Graduate School provides additional support for stipends and for fellowships that enable students to travel to scientific meetings to present the results of their research. With excellent trainees and a strong, research-intensive IIT faculty that values graduate education, the EITS training program continues to thrive.

Robert Roth, EITS Program Director

GRADUATE SPOTLIGHTS

EITS graduates are sought for careers in industry, government and academia. They leave the program with extensive research training in a specific basic science discipline as well as in toxicology, preparing them to interact with multidisciplinary teams focused on the goal of solving current and preventing future threats to human, animal and environmental health.

Below we feature three recent graduates and their paths after graduation from the EITS program.



Phillip Brooks

Postdoctoral Research Scientist Lab for Data Intensive Biology, University of California Davis

During his g r a d u ate training at MSU, Brooks realized he had a strong interest in bioinfor-

matics and sought out as many training opportunities in that area as he could. As his interest in bioinformatics increased with his experiences, he decided to pursue the field as a postdoctoral scientist. He chose the Lab for Data Intensive Biology at University of California Davis led by Dr. C. Titus Brown to further develop his bioinformatics analysis skillset. Brooks had met Dr. Brown while he was a faculty member at MSU, taking a few of his bioinformatics workshops and even assisting in teaching one. Dr. Brown left MSU for UC Davis in 2015 and started the Lab for Data Intensive Biology in the Department of Population Health and Reproduction in the School of Veterinary Medicine. Brooks joined Dr. Brown there in September 2016.

As a Postdoctoral Research Scientist in the Lab for Data Intensive Biology, Brooks is focused on method development for metagenomics - the study of all of the genomic content in a sample, using soil as a model for his research. As sequencing technology advances so does the amount of sequencing data that scientists produce. To keep up with data analysis needs, an abundance of tools for metagenomics analysis have been developed. Unfortunately, in practice, many tools produce different results on the same dataset. Currently, Brooks is benchmarking metagenomics analysis tools on in silico data sets and implementing these tools to characterize some of the largest metagenomics data sets currently available. The results of his project will significantly increase knowledge of the strengths and weaknesses of tools for metagenomics analysis and provide methods for further analysis.

So far, Brooks experience at UC Davis has exceeded his expectations, "The lab is a great place to learn, and I find new challenges every day." Brooks has been able to participate in many of the bioinformatics workshops the lab holds frequently, both as a student and as a facilitator, and has benefited from both greatly.

Brooks was thankful for his time as an EITS student, as it helped to cement his interest in bioinformatics and gave him the skills needed to secure a postdoctoral position. "The EITS program broadened my knowledge, enhanced my ability to think critically, and provided many opportunities for professional development."

As for the future, Brooks remains undecided on his long-term career goals but knows that the demand for biologists with training in bioinformatics is steadily growing and looks forward to continuing his work in this area.

At a glance:

Department: Comparative Medicine & Integrative Biology

Mentor: Linda Mansfield

Dissertation: "Composition of Gut Microbiota Affects C. Jejuni-Mediated Inflammation and Autoimmunity in Murine Models"

Defended: August 2016

Significant Achievements During Graduate School:

- Best Oral Presentation by a Ph.D. Candidate - Phi Zeta Research Day - 2014
- » Alliance for Graduate Education Fellowship - 2015
- » NIEHS Training Grant Recipient 2012-2015
- » Graduate Student Facilitator, MSU Summer Research Opportunities Program (SROP) - 2014-2015



away from lab work in an academic setting. She was specifically interested in working for the FDA because it provided an opportunity to directly impact consumers and improve what they are exposed to. Today, Clark is excited to have a career in regulatory science as a Toxicologist at the US FDA within the Center for Tobacco Products (CTP). She works daily with a team of toxicologists that have been tasked with aiding the protection of public health as related to tobacco use.

Her daily activities include: serving as a technical specialist for risk assessment activities in reviewing tobacco product applications, supporting the

Erica Clark

Toxicologist, US FDA, Center for Tobacco Products

Even before pursuing her Ph.D., Clark knew that she wanted to eventually transition development of research, and providing support for regulatory documents on a broad range of tobacco products; developing new evaluation and assessment procedures to be used by the industry to determine the relative toxicity of tobacco products; and planning and performing investigations to develop new methods and means of extrapolating findings.

A large portion of Clark's work at the FDA requires the critical review of published and proprietary literature. "The course work and research program of EITS prepared me with the necessary skills to evaluate the research and ideas presented to me," said Clark of her time in the program.

Clark looks forward to her future at the FDA, "Being a Toxicologist at the FDA is challenging and there is something new every day. I feel very fortunate to have such a rewarding career at this time in my life."

At a glance:

Department: Food Science & Human Nutrition

Mentor: James Pestka

Dissertation: "Impact of Sex and Age on Deoxynivalenol (DON)-Induced Anorexia Using a Murine Model"

Defended: August 2015

Significant Achievements During Graduate School:

- » Ronald and Sharon Rogowski Fellowship for Food Safety and Toxicology - 2015
- » Gerber Endowment Fund in Pediatric Nutrition and Food Science - 2014
- » ConAgra Foods Holly Fryer Endowed Scholarship - 2014
- » Food Safety Specialty Section Burdock Group Travel Award - 2014
- » Pre-doctoral Fellowship, NIEHS Training Grant in Environmental Toxicology - 2013-2015



Natasha Kovalova

Postdoctoral Scientist, Eli Lilly Company

Kovalova er quite sure whether she wanted to remain in academia for the

rest of her career, but she did know that seeing her research applied in real life to improve the lives of people around the world was paramount. With her goal in mind to become an expert in the field of immunotoxicology, Kovalova chose a postdoctoral scientist position at the Eli Lily Company in Indianapolis, Indiana.

At Eli Lilly Co, Kovalova will be focused on optimizing therapeutic antibodies to reduce immunogenicity. Biotherapeutics are a comparatively new group of drugs that have already shown to be essential for some groups of patients and to greatly improve the quality of life and provide a treatment where there was previously none. Unfortunately, biologics are frequently immunogenic in human patients, an issue that can affect the efficacy and potency of biologic drugs in humans. Identification of immunogenic regions in biologic products and their subsequent removal is a heavily researched area. However, no comprehensive assay or system currently exists that demonstrates whether de-immunization strategies currently being utilized ultimately reduce or eliminate immunogenicity. The overall goal of Kovalova's post-doctoral project is to evaluate different de-immunization approaches using a combination of in silico, in vitro, and in vivo analysis.

Kovalova believes that to be successful in the industry environment, a scientist must have the ability to work well independently and as part of a team. She was grateful for her training with the EITS program that prepared her for the next step of her career, "Aside from the additional coursework that was extremely helpful, EITS taught me how to effectively communicate and collaborate with scientists in my field providing me with essential tools for success."

So far, working at the Eli Lilly Co. has been a great experience for

At a glance:

Department: Pharmacology & Toxicology

Mentor: Norbert Kaminski

Dissertation: "Role of Aryl Hydrocarbon Receptor Polymorphisms on TCDD-mediated CYPIBI Induction and IgM Suppression by Human B Cells"

Defended: July 2016

Significant Achievements During Graduate School:

- » IITS Best Poster Presentation Award 2016
- » Society of Toxicology Travel Award 2014
- » Research Enhancement Award 2012
- » Graduate School Travel Award 2011

Kovalova, "I enjoy a fast-paced, goaloriented framework that we have here. There are plenty of opportunities to grow, learn and collaborate, and I am looking forward to continuing my work here."

EITS Student Melissa Bates Forms Research Partnerships

The decision to become an EITS student holds many benefits, one of which, a wide network of over seventy affiliated faculty members who conduct toxicology-related research spanning investigations of environmental (air, water, soil), occupational, food-borne and pharmaceutical agents. The research partnerships that MSU toxicologists have forged over the decades in conducting interdisciplinary research have been highly beneficial in the context of research

productivity, education and service. For

EITS students, this network of expert faculty has proved invaluable in expanding and strengthening their research and career opportunities. For EITS graduate student, Melissa Bates, the research partnership already formed between her mentor and advisor, Dr. James Pestka, and Dr. Jack Harkema, proved essential to her research findings.

Melissa Bates began her career at MSU as an undergraduate in the Food Science program. Her first steps into research began when her undergrad course instructor, Dr. Steve Bursian put out a call for undergraduate volunteers to work on research in his lab. Taking the job with Dr. Bursian, he then suggested she meet with Dr. James Pestka, who was also looking for an undergraduate research assistant. Learning to love research and already intrigued by food, Bates believes you should, "study what you love," and so decided to stay on for graduate school in Food Science, continuing her work with Dr. Pestka and at his urging, enrolling in the Environmental and Integrative Toxicological Sciences Training Program for a dual degree in Food Science and Environmental Toxicology.

Her current research project began from the foundation of a Lupus Foundation of America grant that Drs. Pestka, Harkema, and J. Fenton had received, "Prevention of Silica-Triggered Lupus by Lipidome Modulation." Continuing and expanding upon the research, Bates, with the guidance of EITS affiliated faculty, Pestka and Harkema, has found that consuming an omega-3 fatty acid called DHA, or docosahexaenoic acid, can stop

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a known trigger of lupus and potentially other autoimmune disorders.

"What we discovered was that when lupus was triggered by crystalline silica, a toxic mineral also known as quartz which is linked to human autoimmunity, DHA blocked the activation of the disease," said Bates. The preclinical study looked at the effect of DHA on lupus lesions in the lungs and kidneys of female mice that were already genetically predisposed to the disease. Their results were overwhelming positive.

A University Distinguished Professor in the Department of Pathobiology and Diagnostic Investigation, Dr. Harkema's extensive knowledge of inhalation toxicology and lung pathology played a vital role in conducting and reviewing the findings of the study. "Ninety-six percent of the lung lesions were stopped with DHA after being triggered by the silica," said Harkema, "I've never seen such a dramatic protective response in the lung before."

Lupus is considered a genetic disease and is triggered not only by inhaling crystalline silica toxicants, but also by other environmental factors such as sun exposure. Quartz is the most common, and most dangerous, form of crystalline silica and is often found in agriculture, construction and mining industries where workers can breathe in the mineral dust.

Although it's still unknown exactly why DHA is able to prevent the onset of lupus, Bates research provides scientists with a better model for looking at just how much DHA is needed to ward off the environmental trigger of the disease.

"What we do know is this study is a clear indication that eating DHA can prevent this one type of environmental triggering of lupus," Pestka said. "It can suppress many of the disease's signaling pathways, which current drugs on the market now try to target and treat."

Bates findings, "Silica-triggered autoimmunity in lupus-prone mice blocked by docosahexaenoic acid consumption," was recently published in PLOS ONE and was featured on MSU Today. She looks forward to graduating in spring 2017 and hopes to continue this research as sa postdoctoral student in the lab of Dr. Pestka.

You can tell all of the faculty in EITS genuinely care about their students and give their most to support them. Everyone genuinely cares about the research they're doing and wants to see others succeed. EITS faculty have served as great role models for me; I love the enthusiasm they have for science."

- Melissa Bates







Heidi Hannon Pharmacology and Toxicology Mentor, William Atchison

"Assessing the Role of the Transient Receptor Potential Ankyrin 1 Channel in Methylmercury-Induced Neurotoxicity"

Erica Clark Food Science and Human Nutrition Mentor, James Pestka

"Impact of Sex and Age on Deoxynivalenol (DON)-Induced Anorexia Using a Murine Model"

Phillip Brooks Comparative Medicine and Integrative Biology Mentor, Linda Mansfield

"Composition of Gut Microbiota Affects C. jejuni-Mediated Inflammation and Autoimmunity in Murine Models"

Nikita Joshi Pharmacology and Toxicology Mentor, James Luyendyk

"Hepatoprotective Functions of the Hemostatic System in Experimental Xenobiotic-Induced Biliary Injury"

Natasha Kovalova Pharmacology and Toxicology Mentor, Norbert Kaminski

"Role of Aryl Hydrocarbon Receptor Polymorphisms on TCDD-mediated CYP1B1 Induction and IgM Suppression by Human B Cells"

Rance Nault Biochemistry and Molecular Biology Mentor, Timothy Zacharewski

"TCDD-Elicited Metabolic Reprogramming in the Progression of Non-Alcoholic Fatty Liver Disease"

IT CENTERS REVIEW



MSU-SRP MSU Superfund Research Program

The MSU Superfund Research Program (MSU SRP) has had continuous funding from the National Institute of Environmental Health Sciences Superfund Research Program since 1988. The program is now in its 3rd year of a 6-year cycle of funding. The overall goal of the MSU SRP is to conduct 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.

The pollutants under investigation are a subclass of chemicals belonging to the halogenated aromatic hydrocarbon family that bind and activate the aryl hydrocarbon receptor (AhR). These chemicals, which include chlorinated dibenzo-p-dioxins, dibenzofurans, biphenyls and polyaromatic hydrocarbons, are environmentally persistent, lipid soluble and accumulate in the food chain leading to human and wildlife exposure.

The MSU SRP is a highly integrated, multidisciplinary research effort consisting of six research projects and six supporting core units. The research team of 22 investigators includes faculty at Michigan State University (16), Rutgers University (2), Emory University (1), Purdue University (1), Texas A&M University (1) and the United States Environmental Protection Agency (1). A dozen graduate and postdoctoral students also contribute to research.

Legacy industrial processes resulted in the contamination of the Tittabaswassee River by dioxin-like compounds, which was first identified in the 1980's and more recently is being remediated. One of the major activities of the MSU Superfund Program has been to work with the community to provide information to help minimize exposure to these contaminants. In the summer of 2016, the Community Engagement Core of the MSU SRP conducted a survey of anglers on the Saginaw and Tittabaswassee Rivers. Although human exposure can occur through a number of pathways, fish consumption is a major concern. To better understand this community's informational and engagement needs, the current survey evaluated the anglers' fishing habits, knowledge, and risk perceptions. Participants were also asked about their perceptions of and contact with the Michigan Department of Health and Human Service's River Walker program whose staff walk along the Saginaw and Tittabawassee Rivers and speak with anglers regarding the risk posed by fish and strategies for avoiding exposure.

Along with this effort, the Research Translation Core of the MSU SRP has worked with the Michigan Department of Health and Human Services (MDHHS) to create a Michigan Safe Fish App, which will allow the user to connect with the State Fish Advisory Program as well as the MSU SRP. The purpose of this mobile fish application is to connect the community to information about the risk of toxic chemicals in fish caught in local waters as well as fish consumed from the market. Information on safe portion sizes and allowable frequency of consumption will be available in app; as well as methods of reducing exposure risks when consuming fish, including information on choosing fish low in chemicals, how to clean catches properly, and preparing fish. The app also includes a point system (called Eat 8!) where users can track the amount of fish portions consumed each month. Other features of the app include a "Fish ID" section where users can scroll through pictures of local fish to properly identify their catch. Catch and location can be stored in the database of the app. The app will also provide access to the "Eat Safe Fish Guidelines" provided by the MDHHS. The MI Safe Fish App is currently in the final stages of revision and will be released to the public soon.



CRIS Center for Research on Ingredient Safety

The Center for Research on Ingredient Safety at Michigan State University is an independent, academic, sciencebased center that will serve as a reliable and unbiased source for information on the safe use of chemical ingredients in consumer packaged goods including foods, beverages, cosmetics and household consumer products. It was established in April 2014 in collaboration with the Department of Food Science and Human Nutrition and the Institute for Integrative Toxicology at MSU as well as the Grocery Manufacturers Association (GMA). Financial support from the GMA and many of its members, allied companies and organizations was contributed to MSU as gifts and, to date, has gone exclusively to support the "Food and Consumer Product Ingredient Safety Endowed Chair," a position now filled by Dr. Michael Holsapple, CRIS Founding Director.

CRIS comprises three major components: Research, Risk Communication, and Training. The research focus at MSU is on expanding the opportunity to conduct basic and applied research on the safety and toxicology of ingredients in food, packaging, cosmetics and household care products. CRIS communicates these findings to consumers, policymakers, and industry in a timely fashion to support evidence-informed decision making. The communication strategy for CRIS has been developed through a partnership between MSU and Arizona State University (ASU). The Environmental and Integrative Toxicological Sciences (EITS) doctoral program at MSU contributed to CRIS this year by adding new toxicology training with emphasis on food and ingredient safety. Through the addition of a third track in the EITS program, the Food Toxicology and Ingredient Safety Track, CRIS will provide customized education in mechanisms of toxicity, ingredient safety, policy and risk assessment to prepare students to serve multiple sectors, including industry, government, and academics.

This past year, Dr. Holsapple co-organized the 2015 CRIS Annual Meeting (November 11-12, 2015) and the 2016 CRIS Annual Meeting (October 4-6, 2016). The CRIS Strategic Map was created through a facilitated meeting of the CRIS stakeholders in January 20-21, 2016, who developed the following Mission and Vision for the Center through consensus:

- » Mission: Conduct research and provide insight on the safety of ingredients in food and consumer products to support evidence-informed decisions by consumers, industry and policy makers.
- » Vision: Credible, relevant information on ingredient safety is accessible to a wide range of decision makers.

Besides the implementation of the CRIS strategic map, Dr. Holsapple has emphasized the importance of other documents to facilitate the management of expectations by the CRIS stakeholders: bylaws, and charters for each of the advisory committees. Dr. Holsapple developed and implemented a strategy to take full advantage of the two tenure track positions that were awarded to CRIS by the MSU leadership. Specifically candidates have been identified for both the computational biologist / toxicologist position, and the exposure science / modeling position, and it is anticipated that these positions will be filled by the end of 2016 or early in 2017.

In the communication arm of CRIS, many important strides were made this year. A refreshed, stand-alone, searchable website was debuted that draws upon all the elements of CRIS, from research to training to communication. In addition, a monthly e-newsletter, CRIS Connects, was launched that goes out to all CRIS partners and stakeholders. Lastly, at ASU, the CRIS Research Fellow was successfully recruited (Dr. Keri Szjeda), and CRIS Bits, a blog devoted to ingredient safety, was launched.



GLACIER Great Lakes Air Center for Integrated Environmental Research

The Great Lakes Air Center for Integrated Environmental Research (GLACIER) is one of four Clean Air Research Centers in the nation that are funded (32 million dollar budget for five years) by the U.S. Environmental Protection Agency (EPA). It is a multidisciplinary center with the objective to explore one of the most prevalent and important global healthenvironment interfaces: the inter-relationships between facets of the cardiometabolic syndrome (CMS) and air pollution. CMS is among the leading causes of death and threats to worldwide health. In tandem, exposure to outdoor air pollution, most notably ambient fine particle matter (PM2.5), remains highly prevalent and ranks among the leading causes of global mortality.

In conjunction with 3 core facilities (Administration, Exposure Characterization, and Biostatistics and Data Management) GLACIER consists of 3 controlled exposure projects that each address specific aspects of the CMS-air pollution interface. The projects are scientifically integrated and interactive which will foster synergistic insights and cohesive synthesis of conclusions.

On June 6 and 7, 2016, GLACIER hosted the Clean Air Research Centers (CLARC) Annual Meeting that took place at the University of Michigan in Ann Arbor, MI. On the first day of this meeting, Center Directors from Harvard, SCAPE, CCAR and GLACIER provided an update of their individual center's research activities in year 5 as well as highlighting the major accomplishments and challenges, including collaborative inter-center research, over the past five years. On day two, oral reports on EPA intramural and collaborative research was provided by Dr. Kathie Dionisio and Dr. Robert Devlin. Talks on future directions for air pollution and health research at the EPA were given by Dan Costa, Scott Jenkins and Rich Cook. A panel discussion/critique on the successes and challenges of the CLARC program was provided by invited discussants, Drs. Jeff Brook (Health Canada), Bert Brunekreef (Utrecht University), Dan Costa (US EPA, Moderator), and Robert Devlin (US EPA). Ms. Kasey Baldwin and Amy Swagart from our Administrative Core did an outstanding job in making all the logistical arrangements for this successful meeting. Other highlights from the year include:

- » The collaborative efforts of Drs. Robert Brook (UM) and Jack Harkema (MSU) were recently featured by MSU's AgBioResearch in their 2015 Annual Report, The Air We Breathe: Studying the Impact of Air Pollution in Rural Environments.
- The Society of Toxicology's Inhalation and Respiratory Specialty Section awarded Dr. Kazuyoshi Kumagai and his co-authors, Ryan Lewandowski, Daven Jackson-Humbles, Ning Li, Steven Van Dyken, James Wagner and Jack Harkema with the Paper of the Year Award at the 2016 SOT Annual Meeting for their publication, "Ozone-induced Nasal Type 2 Immunity in Mice is Dependent on Innate Lymphoid Cells." The paper was published in the American Journal of Respiratory Cell and Molecular Biology. Dr. Kumagai, a visiting toxicologic pathologist from Tokyo, Japan, worked in the laboratory of Dr. Harkema for two years (2014-2016).
- » Dr. Harkema was a co-author on, "National Institute of Environmental Health Sciences: 50 Years of Advancing Science and Improving Lung Health," an article celebrating the achievements of NIEHS in lung health that also called for more funding in this important area of biomedical, clinical and public health research.



University Distinguished Professor, Crop and Soil Sciences

Dr. Stephen Boyd's first step in becoming the University Distinguished Professor he is today began at Gratiot Community Hospital in Alma, Michigan where he worked as an orderly. His mother, an R.N. there, had helped him procure the job. With few career role models in his small hometown of St. Louis, MI, he began to look up to the doctors and decided to attend Central Michigan University as a pre-med student. Taking a variety of science courses as a pre-med major, he especially enjoyed and excelled in his chemistry courses. His career path was forever changed when, as a freshman, his chemistry professor Dr. Douglass West invited him to work as an undergraduate research assistant after he received the high score on a chemistry exam. Boyd, working under the tutelage of Dr. West, learned how to do research, how to write for publication and most importantly, found his interest in chemistry growing.

"Dr. West was the role model I had been looking for," said Boyd.

After graduating as a chemistry major, his next step was to start graduate school at Princeton in a traditional chemistry program. The further he advanced in chemistry though, the more abstract it became and he began thinking about applied areas of chemistry. A book from the Princeton library led him to his next interest, "agricultural chemistry". The book was outdated and the agricultural chemistry programs had morphed into biochemistry, but Boyd's application found its way to the Agronomy Department at Purdue University, where he was accepted and he took leave of Princeton after his first year.

When he arrived at the Purdue University Agronomy Department in the mid-1970s, a great deal of the landmark environmental legislation was in its infancy, including the Clean Water Act and the creation of the US EPA. His next career focus came at the hands of two Purdue faculty members (Dr. Sommers and Nelson), who had a grant from the EPA to research the fate and impacts of contaminants present in biosolids (sewer sludge) from wastewater treatment plants required under the Clean Water Act. Sewer sludges were beginning to be applied to cropland for their fertilizer value. This is where Boyd's interest in soil science sprouted and merged with chemistry, and he sought out faculty positions in the field of environmental soil chemistry upon graduation.

Having skipped a postdoctoral position, Boyd came directly to MSU as an Assistant Professor of soil chemistry in October 1980, two months prior to his formal graduation. Honored to have been offered such a position, he quickly accepted but failed to negotiate a startup package or details such as lab and office space. However, looking back he now realizes that, "The presence of experienced faculty to collaborate with was more important than a startup package of any kind." He found mentors and collaborators in Dr. Max Mortland and Dr. James Tiedje. He worked on the anerobic degradation of PCBs in sediments with Dr. Tiedje and binding of contaminants to soil components like clays with Dr. Mortland.

Having found his niche he began to build a research program focused on how chemicals interact with geosorbents (solid components of soil and sediments) and how that interaction affects the bioavailability of chemicals to bacteria and humans. Now in his 37th year at MSU, Boyd says, "I've spent my career working at the interface between environmental chemistry and biology on an issue called bioavailability - how the binding of a contaminant molecule to some geosorbent affected the bioavailability of that chemical to bacteria that could degrade it or to humans and wildlife whose health could be adversely affected."

A major portion of his research project is now focused on a newer technology that utilizes sorbent amendments to remediate chemically contaminated soils and sediments. Adding sorbents such as activated carbon to a contaminated site is far less expensive than traditional cleanups that typically involve dredging or excavating followed by disposal in a landfill. The idea is that the sorbent will sequester the contaminant in a form that is not bioavailable to fish, mammals, humans, etc. Boyd was surprised at how rapidly this went from a concept to actual utilization at major sites such as the Tittabawasee River contaminated with dioxins. Having searched and found no studies utilizing a mammalian model to determine the bioavailability of chemicals sequestered by activated ...continued on page 19

16 » IIT Annual Report



Professor, Pharmacology & Toxicology

Upon graduating high school in New York City, Goodman was not quite sure

of a career path. He liked science and wanted to pursue something practical so he decided to attend college to be a pharmacist. Admitted to the Long Island University's College of Pharmacy, he enjoyed the curriculum but after taking a part-time job at a local pharmacy at the end of his first year, he decided a career as retail pharmacist was not for him. He continued on though, seeing that there were other career opportunities for pharmacists and because he found the science courses interesting and challenging. The tipping point for his real career move came at the hands of Goodman's physiology professor, Dr. Shirley Krause. After taking an elective course involving research in her laboratory, she suggested that he apply to the Pharmacology Doctoral Program at the University of Michigan. In light of her history of steering students to this Program who went on to do well, her recommendation letter sealed his acceptance and Goodman journeyed to U of M as

one of "Shirley's Boys" - as the group of young men she sent to this Pharmacology Ph.D. Program were referred to.

Goodman views those four years at U of M as, "the best four years of my life in terms of intellectual development." His thesis research project involved species differences in the metabolism of methyl alcohol. This alcohol is uniquely poisonous to humans as compared to rodents and monkeys, and his research sought to test the hypothesis that aspects of methanol metabolism differs between sensitive and resistant species, and that discerning these differences might provide insight into why humans are uniquely susceptible. As he proceeded through his thesis project, some broad reading of the scientific literature caused his research interest to evolve into a focus on carcinogenesis. He decided to study postdoctorally at the University of Wisconsin's McArdle Laboratory for Cancer Research, in the laboratory of Dr. Van Potter where Goodman was the first non-biochemistry Ph.D. that he mentored. "It was a terrific introduction to the field," said Goodman.

When Goodman was ready to make his next move, he applied for several

faculty positions across the country. It wasn't until a recommendation from his Ph.D. mentor (based on a chance conversation that he had at a scientific meeting with Jerry Hook, a member of the faculty of MSU's Pharmacology Department who told him that a position was open), that he chose to apply to MSU's Department of Pharmacology (later renamed the Department of Pharmacology and Toxicology). Goodman accepted the position in September of 1971 and found himself back in Michigan. Ted Brody, the chair of the department when Goodman started, told him he needed to do three things to be successful: "One, you have to maintain an extramurally funded research project. Two, you need to be invited to scientific activities outside of MSU that shine a good light on MSU so publish papers, get yourself known, get yourself invited to present seminars and symposia lectures, and get involved in professional organizations. And three, you must do a good job teaching." Goodman found this succinct advice to be an exceptionally good guideline for what to focus on and he has strived to follow it throughout his career. "I am deeply, deeply appreciative to MSU in terms of the opportunities I have had for career development and advancement," said Goodman.

When he came to MSU, Goodman began to research the chemical causes of cancer, chemical carcinogenesis. In his postdoctoral studies, he had begun to look at chemical induced damage to DNA, i.e., adduct formation, and the ability of cells to repair this damage. Adducts which are not repaired might serve as substrates for mutations. At MSU, he pursued this further and moved from the general question of damage and repair to looking at specific regions of the genome where DNA could be damaged and repaired. The two regions he focused on were the regions that were expressed (DNA is being transcribed to RNA) versus those regions in the genome were genes are quiescent. There was selective persistence of DNA adducts in transcriptionally repressed regions of the genome. Cell replication prior to DNA repair could lead to mutations that facilitate carcinogenesis. However, these regions would have to become transcriptionally active in order for the mutations to have a chance to affect phenotype. This led Goodman into the field of epigenetics, e.g., factors controlling gene expression which "sit" above the base sequence of DNA ("epi" is a prefix from Greek which means "on" or "over"). He began to look ...continued on page 19



University Distinguished Professor, Crop & Soil Sciences, Microbiology & Molecular Genetics

From an early age, Dr. James Tiedje recognized that microbes were a part of life, specifically, his life growing up on an Iowa farm. His family raised pigs, dairy cattle and crops to feed the animals. One of his fond farm memories was inoculating legume seeds with Rhizobium bacteria with his father - he would dump the inoculum into a wagon of seed and mix it until every seed had a black spot on it. Even the manure aroma in the air reminded him that microbes were at work.

Fascinated by science and then microbiology, Tiedje attended Iowa State University to study Agronomy. The summer of his junior year, he worked on a microbiology project mapping serotypes of soybean Rhizobia across the state of Iowa and his deep interest in microbiology continued to grow. He went on to graduate school at Cornell University and studied soil microbiology and microbial ecology. His thesis examined the microbial metabolism of pesticides in soil - this work fueled by the Rachel Carson era after she wrote "Silent Spring," which brought attention to the problem of pesticides accumulating in the environmental food chain.

Tiedje came to MSU in 1968, "I chose MSU because, of the positions potentially open at the time, this state had the best history of funding higher education." The Pesticide Research Center at MSU had just formed and Tiedje joined them, helping to expand their research into biodegradation. His main focus in those early years was on new herbicides and pesticides and their fate in the environment. After recognizing that other industrially produced chemicals were entering the environment, his work shifted to research on chlorinated compounds - both products and byproducts of manufacturing. They, like pesticides raised the same questions of food chain accumulation and persistence in the environment. By the 1980s, several MSU professors, including Tiedje, had developed a nationally recognized strength in anaerobic microbiology. Tiedje's group made a breakthrough discovering that some anaerobic microbes could remove chlorine from the aromatic organic molecules. So they thought - if these

anaerobic bacteria can do this with a simple compound, what chlorinated pollutants might they dechlorinate? They then discovered that these previously unknown bacteria could dechlorinate PCBs, which ushered in a decade long period of work on what became known as microbial reductive dechlorination.

The dechlorination research of Tiedje and his peers has led to successful remediation of some of the chlorinated pollutants contaminating our environment - especially chlorinated solvents which were widely used and often not properly disposed. Heavier than water, these chlorinated solvents go to the bottom of the aquifer making other remediation technologies virtually impossible. These anaerobic microbes use the dechlorination process in place of oxygen to respire and hence produce energy for their growth. If these microbes have organic carbon as their food forgrowth and no oxygen, they will instead dechlorinate those solvents (or other chlorinated organics) for their respiration and hence growth. These microbes actually need the pollutant to get ahead of their microbe cousins. The research led to new remediation technologies, both engineered and naturally-occurring, that helped remove these solvents from the environment.

From PCBs and chlorinated solvents, Tiedje's work then shifted to dioxins, which were much more difficult to remediate. Part of MSU's Superfund Research Project, Tiedje's team works to discover why dioxins are so difficult for nature's microbes to degrade. Answers could lead one day to dioxin biodegradation. The research can also identify molecular markers to aid in site assessment for biodegradation potential or activity.

Antibiotic resistance is Tiedje's most recent area of research. He notes that antibiotic resistance genes are a new type of environmental pollutant. In a recent study, Tiedje found that in large swine farms where antibiotics are used continuously in feed for growth promotion and disease prevention, multidrug-resistant bacteria are likely the norm rather than the exception. "Our results clearly show a large diversity of resistance genes on swine farms together with genes that enable them to be shared among bacteria, some of which could be pathogens" Tiedje said. "The current research is aimed to guide practice to minimize risk from environmental sources of antibiotic resistance genes and help preserve effectiveness of current antibiotics."

As founder and director of MSU's ...continued on page 19

...BOYD continued from page 16

carbon, Boyd set out to determine if activated carbon actually reduced the bioavailability of contaminants such as dioxins to mammals as an indication of how effective the remedy would be for humans.

...GOODMAN continued from page 17

into epigenetic mechanisms that might underlie carcinogenesis – methylation of DNA was the first epigenetic parameter he evaluated.

Goodman began to focus on epigenetic factors that might be involved in rodent liver carcinogenesis. He employed phenobarbital (PB), a non-genotoxic compound, which is a drug used to treat epilepsy in people and animals which is very effective at causing hepatic cancer in susceptible strains of rodents. However, a very extensive body of epidemiology data indicates that PB is not a human carcinogen even when people take the drug for decades and achieve blood levels that are very similar to what rodents experience when they develop PB-induced liver tumors. Goodman began to study epigenetic factors, e.g., DNA methylation, in susceptible versus relatively resistant strains of rodents, hypothesizing that the resistant ones were more like humans. Goodman was able to demonstrate that the ability of PB to perturb epigenetic status was greater

His most recent studies have used microporous activated carbon to successfully eliminate the bioavailability of the most toxic form of dioxin, TCDD, in a mammalian (mouse) model by measuring suppression of the immune system, which is a hallmark of dioxin toxicity.

in the sensitive compared to resistant strains of rodents. Thus, furthering our understanding of the role epigenetic alterations play in the mechanisms underlying carcinogenesis. Subsequent research discerned a number of genes associated with PB-induced tumorigenesis and altered transcription of some of these is being explored in the search for potential biomarkers for non-genotoxic compound-induced liver tumors.

When the EPA issued new guidelines for Cancer Risk Assessment in 1985, for the first time it included a section on epigenetics and research from Goodman's laboratory was featured. His work has helped support the hypothesis that rodent liver tumors induced by PB-like non-genotoxic chemicals are not relevant for human risk assessment. This is typically referred to as the PB-like concept. The practical significance here is that there are many very helpful/useful chemicals, including but not limited to medicines, which cause rodent liver tumors and have PB-like characteristics. Consequently, a number of important Binding of TCDD to activated carbon reduced the bioeffective dose to zero, and no TCDD-induced suppression of immune function occurred. Further studies are planned to evaluate other black carbons with differing pore structures.

chemicals (including medicines) have been able to reach the market and remain on the market despite the fact that they can cause rodent liver cancer.

Interestingly, Goodman's basic interest in discerning mechanisms underlying species differences in susceptibility to chemical-induced toxicity is a common theme that spans his Ph.D. thesis project to his current research interests. Goodman says, "What excites me about research in toxicology is the combination of the theoretical and the practical. As we try to understand the mechanism of action of a particular chemical we learn more about basic biology and this new knowledge can provide insight regarding the enhancement of sciencebased safety assessment."

In addition to pursuing research in toxicology and teaching pharmacology and toxicology, Goodman has been a member of numerous boards and advisory committees, and he has a longstanding commitment to the Society of Toxicology, serving as President of the Organization, 1999-2000.

...TIEDJE continued from page 18

Center for Microbial Ecology (CME), Tiedje looks to continue this important work on microbial ecology through his own research and that of his colleague's. The CME was founded in 1989 with funding by the National Science Foundation as one of the first eleven Science and Technology Centers in the nation. Today, the CME is a center without walls, funded through individual research grants of its members, with a group focus on microbial ecology and bioremediation. **♦**

FACULTY PUBLICATIONS

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Ying Z, Braunstein Z, Kankanala SR, Xia C, Wang X, Bramble LA, Wagner JG, Lewandowski R, Sun Q, Harkema JR, Rajagopalan S. Repeated ozone exposure exacerbates insulin resistance and activates innate immune response in genetically susceptible mice. Inhal Toxicol. 2016 Aug;28(9):383-92. doi:10 .1080/08958378.2016.117 9373. Epub 2016 May 31. PubMed PMID: 27240593; PubMed Central PMCID: PMC4911226.

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Wu, Felicia

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Yang, Chengfeng

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Zacharewski, Timothy R.

Joshi N, Kopec AK, Ray JL, Cline-Fedewa H, Nawabi A, Schmitt T, Nault R, Zacharewski TR, Rockwell CE, Flick MJ, Luyendyk JP (2016). Fibrin deposition following bile duct injury limits fibrosis through an α M β 2dependent mechanism. Blood. 127(22):2751-62. PubMed PMID: 26921287.

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Zhang, Wei

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Zwiernik, Matthew J.

Folland WR, Newsted JL, Fitzgerald SD, Fuchsman PC, Bradley PW, Kern J, Kannan K, Remington RE, Zwiernik MJ (2016). Growth and reproductive effects from dietary exposure to Aroclor 1268 in mink (Neovison vison), a surrogate model for marine mammals. Environ Toxicol Chem. 35(3):604-18. PubMed PMID: 26313468.

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FACULTY PROFESSIONAL SERVICE

The affiliated faculty of the IIT participate in many external activities that promote the development of research and science in their chosen field. These activities include editorial boards, review groups or study sections, scientific advisory boards and committees, and officers in scientific societies.

Andrechek, Eran R.

- » NIH Study Section, NIH Oncological Sciences F09B (F30, F31, F32)
- » Study Section Member, DoD Study Section
- » Review Panelist, Canadian Breast Cancer Foundation
- » Grant Reviewer, FAMRI / University of Miami
- » Review Panelist, Cancer Research UK Review
- » Review Panelist, Wake Forest Comprehensive Cancer Center NCI Review

Bourquin, Leslie D.

- » Chair, NSF International Global Food Safety Advisory Council
- » Technical Committee Member, World Bank Global Food Safety Partnership
- » Consumer Goods Forum, Global Food Safety Iniative, GFSI Technical Committee Member
- » Advisory Council Member, International Food Protec-tion Training Institute (IFPTI)
- » Editorial Board, Foods Journal

Buchweitz, John P.

- » Representative, MISOT K-12 Education Committee
- » Councilor, SOT Comparative and Veterinary Specialty Section

Bursian, Steven J.

- » Editorial Board, Journal of Toxicology
- » Member, Health Advisory Board of NSF International

Copple, Bryan L.

» NIH Study Section, ZRG1 DKUS-N (10) B Small Busi-ness: Digestive Sciences

Ewart, Susan L.

 Reviewer and Standing Committee Member, National Institutes of Health; Allergy, Immunology, and Transplantation Research Committee (AITC)

Ganey, Patricia E.

- » Editorial Board, Journal of Pharmacology and Experimental Therapeutics
- » Editorial Board, Journal of Toxicology and Environmental Health
- » Editorial Board, Toxicology
- » Member, SOT Finance Committee
- » Chair, SOT Scientific Program Committee
- » Councilor, International Union of Toxicologists for the SOT
- » Vice President, Society of Toxicology

Goodman, Jay I.

- » Editorial Board, Toxicology
- » Associate Editor, Regulatory Pharmacology and Toxicology
- » Member, Board of Directors, Toxicology Forum

Goudreau, John L.

- » Board of Directors, National Board of Osteopathic Medical Examiners
- » Chair, Key Features-Clinical Decision Making Task Force, National Board of Osteopathic Medical Examiners
- » Level 3 Advisory Committee, National Board of Osteopathic Medical Examiners
- » NOMD Study Section, National Institutes for Neurological Disorders and Stroke
- » NSD-B Study Section, National Institutes for Neurological Disorders and Stroke
- » Professional Advisory Board, Michigan Parkinson Foundation
- » Credentialing Committee, Parkinson Study Group
- » Scientific Review Committee, Parkinson Study Group
- » Mentoring Committee, Parkinson Study Group
- » Recruitment Committee, NINDS, STEADY-PD III Study

Gulbransen, Brian D.

» Grant Review Panel, National Institutes of Health SPARC

- » Grant Review Panel, Crohn's & Colitis Foundation of Canada
- » Abstract Review Panel, FNM 2016 Joint International Meeting (Federation of Neurogastroenterology and Motility Meeting)
- » Digestive Disease Week (DDW) 2016 Abstract Reviewer; American Gastroenterological Association (AGA); Enteric Neurobiology Section: Cell and Molecular Biology (Including Neurons, Glia, ICC, Smooth Muscle and Stem Cells)
- » American Physiological Society GI & Liver Physiology Section Trainee Development Committee
- Membership Committee, American Society of Neurochemistry (ASN)
- » Digestive Disease Week (DDW) 2015 Abstract Reviewer; American Gastroenterological Association (AGA); Neurogastroenterology & Motility section
- » Member of the American Neurogastroenterology and Motility Society (ANMS), American Gastroenterological Society (AGA), Michigan Physiological Society (MPS) and American Physiological Society (APS).
- » Editor, Purinergic Signalling, Frontiers Autonomic Neuroscience, Frontiers in Cellular Neuroscience
- » Guest Associate Editor, Frontiers in Cellular Neuroscience Research Topic
- » Guest Editor, BioMed Research International
- » Ad-hoc Grant Reviewer, UK Biotechnology and Biological Science Research Council (BBSRC)
- » Ad-hoc Grant Reviewer, French National Research Agency ANR (Pathophysiology evaluation committee)
- » Ad-hoc Grant Reviewer, Wellcome Trust, UK

Harkema, Jack R.

- » Chair, Environmental, Occupational and Population Health Assembly, American Thoracic Society
- » Councilor, Executive Committee of the Society of Toxicologic Pathologists
- » Editorial Board, Journal of Experimental and Toxicologic Pathology
- » Editorial Board, Journal of Toxicologic Pathology
- » Director, EPA Great Lakes Air Center for Integrated Environmental Research
- » Member, Directors of EPA Clean Air Research Centers
- » Member, EPA Clean Air Science Advisory Committee
- Member, Board of Directors, American Thoracic Society (ATS)

Hayes, A. Wallace

» Editor-in-Chief: Food and Chemical Toxicology; Ocular and Cutaneous Toxicology

- » Editor, Americas, Human and Experimental Toxicology
- » Member, Globalization Committee, American Board of Toxicology
- » Member, US Food and Drug Administration, Food Ad-visory Committee
- » Invited Speaker, Workshop on GRAS Determinations, International Society of Regulatory Toxicology and Pharmacology, Washington, DC.
- » Subject Matter Expert, Member Panel on Update and Validate Risk Ranking Model to Inform High Risk Food List, Institute of Food Technologists (US FDA Project)
- » Chair, Systems Toxicology: Future of Risk Assessment.
 7th International Congress of Asian Society of Toxicology, Jeju Island, South Korea
- Member, FDA Pediatric Advisory Committee [Food Safety & Pediatric Population], September 14-15, 2015.
 Washington, DC.
- Member, Joint Committee on Generally Recognized as Safe Publicly Available Standards, NSF International, Michigan

Hegg, Colleen C.

- » Reviewer, NIH NIDCD Fellowship Application review
- » Co-Chair, Judging, College of Veterinary Medicine Phi Zeta Research Day
- » Advocate in Science, Susan G. Komen for the Cure
- » Officer, SOT Stem Cell Specialty Section

Hollingworth, Robert M.

- » Editorial Board, Insecticide Resistance Newsletter
- » Officer, Agrochemicals Division, American Chemical Society
- » Member, National Research Council Panel to Review California Department of Pesticide Regulation's Risk Assessment Procedures

Jackson, James E.

- » Review Panel Member, NSF proposal review and American Chemical Society award panels
- » Co-organizer, Symposium #334, "Green and Sustainable Chemistry Education for Tomorrow's Citizens of the World" as part of Pacifichem 2015
- » Member, American Chemical Society
- » Member, National Academy of Inventors
- » Member, Michigan Green Chemistry Round Table
- » Member (and past chair), Meridian Township Environmental Commission
- » Member of the steering committees organizing "GreenUp," the MI DEQ annual Green Chemistry conference

Jones, A. Daniel

- » External Advisory Committee, UC Davis NIEHS Superfund Basic Research Program
- » Review Editor, Frontiers in Plant Metabolism and Che-modiversity
- » Founding Advisory Board Member, North American Af-filiate Chapter of the Metabolomics Society

Kaminski, Norbert E.

- » Chair, External Review Committee for the Interdisciplinary Program in Toxicology at Texas A&M University
- » Past President, Society of Toxicology
- » NIEHS National Advisory Environmental Health Sciences Council
- » Member, Joint Committee for NSF/ANSI Standard 500 GRAS-PAS Ingredient Review
- » Member, National Academy of Sciences, Institute of Medicine Committee on the Health Effects of Marijuana
- » Editorial Board, Toxicology
- » Member, Endowment Fund Board, Society of Toxicology

LaPres, John J.

- » Director, BioMolecular Sciences Recruiting Program
- » Associate Editor, Toxicology Reports
- » National Toxicology Program: Special Emphasis Panel to review Draft Report on Carinogens Monograph on Cobalt and Certain Cobalt Compounds

Leinninger, Gina M.

- » Reviewer, Pharmacology, Biochemistry and Behavior, PLOS Genetics, Obesity, Diabetes, International Journal of Obesity, Endocrine, Endocrinology, Molecular Metabolism, Nature
- » The Endocrine Society Annual Meeting Steering Committee
- » Abstract Reviewer, The Obesity Society
- » Early Career Reviewer, NIH Neuroendocrinology, Neuroimmunology, Rhythms and Sleep (NNRS) Study Section
- » Ad Hoc Reviewer, Integrative Physiology of Obesity and Diabetes (IPOD), NSF
- » Ad Hoc Reviewer, Michigan Diabetes Research Center

Mazei-Robison, Michelle

- » Study Section Member, Harnessing genome editing technologies to functionally validate genetic variants in substance use disorders, ZDA1 JXR-G
- » Study Section Member, Molecular Neuropharmacology and Signaling study section

Murphy, Cheryl A.

- » Editorial Board, Ecotoxicology
- » Working Group, Principal Leader, "Dynamic models to link molecular perturbations to individual impacts for ecological risk assessment of chemicals", sponsored by the National Institute for Mathematical and Biological Synthesis (NIMBioS)
- » Technical Panel Member, Chesapeake Bay Endocrine Disrupting Chemical Science Plan (USGS), "Establishing a strategy for assessing risk of endocrine-disrupting compounds to aquatic and terrestrial organisms"
- » Expert Panel Member, Chesapeake Bay Endocrine Disrupting Chemical Science Plan (USGS), "Establishing a strategy for assessing risk of endocrine-disrupting compounds to aquatic and terrestrial organisms"
- » Organizer of session "Systems Biology Approaches for Advancing Adverse Outcome Pathways for Risk Assessment" as Society for Environmental Toxicology and Chemistry North America, 36th Annual Meeting, Salt Lake City, UT, November 2015

Olson, L. Karl

» Merit Review Panel for Endocrinology-A, Department of Veterans Affairs

Paneth, Nigel S.

- » National Scientific Advisory Committee, March of Dimes Foundation
- » External Advisory Committee, University of Pennsylvania MPH Program
- » Scientific and Editorial Board, Supercourse in Epidemiology, University of Pittsburgh
- » Scientific Advisory Group, Norwegian Mother and child Cohort (MoBa) and Danish National Birth Cohort (DNCB) combined cerebral palsy study (MOBAND)
- » Member, NIH panel to review the study section structure of the "Health of the Population" Integrated Review Group of NIH CSR

Pestka, James J.

- Member, Environmental Health Sciences Review Committee (EHSRC) for the National Institute of Environmental Health Sciences (NIEHS)
- » Member, Society of Toxicology/Food and Drug Administration Colloquia on Emerging Toxicological Science Challenges in Food and Ingredient Safety
- » Chairman, Member USDA-ARS, United States Wheat and Barley Scab Initiative, Food Safety, Toxicology, and Utilization Research Committee
- » Member, Western Regional Research Committee (W-3122 USDA Multistate project), Beneficial and Adverse Effects of Natural, Bioactive Dietary Chemicals on Human Health and Food Safety

Petroff, Brian K.

» Section Chief, Endocrinology, DCPAH

Rosenman, Kenneth D.

- » Co-Leader, Occupational Health Work Group, Conference of State and Territorial Epidemiologists
- » Secretary, Board of Directors of the Michigan Occupational and Environmental Medical Association
- » Member, Michigan State Medical Society Liason Committee with Public Health
- » Member, National Academies Institute of Medicine's Committee on Developing a Smarter National Surveillance System for Occupational Safety and Health in the 21st Century

Roth, Robert A.

- » Editorial Board, Toxicology and Applied Pharmacology
- » Editorial Board, Journal of Toxicology and Environmental Health
- » Associate Editor, Journal of Pharmacology and Experimental Therapeutics
- Member/Consultant, Technical Committee on the Application of Genomics to Mechanism-based Risk Assessment, ILSI, Health and Environmental Sciences Institute (HESI)
- » Member, NIH Study Section: Xenobiotic and Nutrient Disposition and Action
- » Member, Endowment Fund Board, Society of Toxicology
- » External Advisory Committee, Curriculum in Toxicology, University of North Carolina at Chapel Hill
- » External Advisory Committee, Graduate Program in Pharmacology, University of Kansas Medical Center

Tiedje, James M.

- » National Resource Council Committee on Incorporating 21st Century Science into Risk-Based Evaluations
- » Science Advisory Committee, Environmental Molecular Sciences Lab, Pacific Northwest National Laboratory
- » Science Advisory Committee, Joint Genome Institute
- » Bioscience External Science Advisory Committee, Berkeley National Laboratory
- » Treasurer and Executive Committee, American Society for Microbiology
- » Class Chair, National Academy of Sciences
- » Chair, Genome Canada's Large Scale Applied Research Program
- » Chair, the Biosciences Capability Review at Los Alamos Natl Lab
- » Science Advisory Committee, Denmark's CENPERM (Cntr for Permafrost change in Greenland) Project

Uhal, Bruce D.

- » Executive Guest Editor, Current Pharmaceutical Design
- » Member, Frontiers in Pediatrics
- » Member, GlaxoSmithKline's ACE2/MAS Experts Advisory Board

Veiga-Lopez, Almudena

- » Ad hoc Grant Reviewer, National Science Centre Grant Reviewer, Poland 2016
- » Ad hoc Abstract Reviewer, 98th Endocrine Society Annual Meeting 2016
- » Graduate Student Affairs & Curriculum Committee, Department of Animal Sciences, Michigan State University
- » Education Committee, NICHD T32 Reproductive and Developmental Sciences Training Program, Michigan State University

Wagner, James G.

- » Associate Editor, Inhalation Toxicology
- » Editorial Board, Particle and Fibre Toxicology
- » Vice President, Cardiovascular Toxicology Specialty Section, National Society of Toxicology
- Member, Continuing Education Committee, Society of Toxicology
- » Member, Regional Chapter Collaboration and Communication, Society of Toxicology
- » Member, Committee for Threshold Limit Values for Chemical Substances (TLV-CS); American Conference of Governmental Industrial Hygienists (ACGIH)
- » Section Author, EPA Integrated Science Assessment for PM2.5
- » Reviewer, World Trade Center Cooperative Research Agreements PAR-16-098, NIOSH/CDC

Wu, Felicia

- » Area Editor for Health Risk Assessment, Risk Analysis
- » Section Editor for Economics and Policy, World Mycotoxin Journal
- » Consulting Editor for Risk Communication, Archives of Environmental and Occupational Health
- » Member, Computational Task Force, World Health Organization (WHO) Foodborne Disease Burden Epidemiology Reference Group
- » Expert Panelist, Joint FAO/WHO Expert Committee on Food Additives (JECFA)
- » Chair, Communications Committee, Society for Risk Analysis

Yang, Chengfeng

- » Review panelist, NIEHS/NIH Revision Awards for Creating Virtual Consortium for Translational/Transdisciplinary Environmental Research
- » Review panelist, NIEHS/NIH Superfund Research Program (SRP) Special Emphasis Panel/Scientific Review Group
- » Scientific reviewer, United Kingdom Medical Research Council (MRC) cancer research proposal
- » Scientific reviewer, The Union for International Cancer Control (UICC) International Cancer Technology Transfer Fellowships (ICRETT) Program
- » Scientific reviewer, The Cancer ITMO of the French National Alliance for Life and Health Sciences (AVIESAN), in collaboration with the French National Cancer Institute
- » Academic editor: PLOS ONE; Scientific Reports (Nature Publishing Group)
- » Journal manuscript reviewer: The Journal of Biological Chemistry, Current Cancer Drug Target, Molecular Cancer, PLOS ONE, Molecular Carcinogenesis, Toxicology, In Vitro Toxicology, Applied Pharmacology

Zacharewski, Timothy R.

- » Editorial Board, Toxicological Sciences
- » Editorial Board, Toxicology & Applied Pharmacology
- » Ad-Hoc Committee Member, National Institutes of Health – Systemic Injury by Environmental Exposure (SIEE) Study Section, ZRG1 DKUS C Special Emphasis Panel
- Member, National Institutes of Health/NIEHS Outstanding New Environmental Scientist (ONES) Study Section
- » External Reviewer, Promotion & Tenure, New York University

Zhang, Wei

- » Panel member, USDA/NIFA Water for Agriculture Challenge Area
- » Panel member, USDA/NIFA Higher Education Challenge Grants Program
- » Associate Editor, Canadian Journal of Soil Science
- » Committee Member, SSSA Soil Physics and Hydrology Division Mentoring Committee
- » Member of Multistate Research Project W3188: Soil, Water, and Environmental Physics Across Scales
- » Member of Multistate Research Project NC1187: The Chemical and Physical Nature of Particulate Matter Affecting Air, Water and Soil Quality

» Member of Multistate Research Project W2082: Evaluating the Physical and Biological Availability of Pesticides and Contaminants in Agricultural Ecosystems

Zwiernik, Matthew J.

- » Society of Environmental Toxicology and Chemistry, Global Advisory Group, Wildlife Toxicology
- » Technical Advisor, Pine River Superfund Citizen Task Force

IT AFFILIATED FACULTY

Andrea Amalfitano, Professor, Microbiology & Molecular Genetics, and Pediatrics

Eran R. Andrechek, Assistant Professor, Department of Physiology

William D. Atchison, Professor, Pharmacology & Toxicology

Jamie J. Bernard, Assistant Professor, Pharmacology & Toxicology

Matthew P. Bernard, Assistant Professor, Pharmacology & Toxicology

Sudin Bhattacharya, Assistant Professor, Institute for Integrative Toxicology

Leslie D. Bourquin, Professor, Food Science & Human Nutrition

Stephen A. Boyd, University Distinguished Professor, Plant, Soil and Microbial Sciences

John P. Buchweitz, Assistant Professor and Toxicology Section Chief, Diagnostic Center for Population & Animal Health, Department of Pathobiology & Diagnostic Investigation

Steven J. Bursian, Professor, Animal Science

Stephan A. Carey, Assistant Professor, Small Animal Clincial Sciences

Karen Chou, Associate Professor, Animal Science

Bryan L. Copple, Associate Professor, Pharmacology & Toxicology

Susan L. Ewart, Professor, Large Animal Clinical Sciences

Patricia E. Ganey, Professor, Pharmacology & Toxicology

Jay I. Goodman, Professor, Pharmacology & Toxicology

John L. Goudreau, Associate Professor, Pharmacology & Toxicology, and Neurology

Brian D. Gulbransen, Assistant Professor, Neuroscience Program, Department of Physiology

Jack R. Harkema, University Distinguished Professor, Pathobiology & Diagnostic Investigation

Syed A. Hashsham, Edwin Willits Associate Professor, Civil & Environmental Engineering; Adjunct Associate Professor, Crop & Soil Sciences, and the Microbial Ecology Center

A. Wallace Hayes, IIT Adjunct Faculty, Senior Science Advisor, Spherix Consulting

Colleen C. Hegg, Associate Professor, Pharmacology & Toxicology

Robert M. Hollingworth, Professor Emeritus, Entomology

Michael P. Holsapple, Director, Center for Research on Ingredient Safety; Professor and Endowed Chair, Food Science and Human Nutrition

James E. Jackson, Professor, Chemistry

A. Daniel Jones, Professor, Biochemistry & Molecular Biology, and Chemistry

Norbert E. Kaminski, Director, Institute for Integrative Toxicology; Professor, Pharmacology & Toxicology

John B. Kaneene, University Distinguished Professor and Director, Large Animal Clinical Sciences

John J. LaPres, Associate Professor, Biochemistry & Molecular Biology

Gina M. Leinninger, Assistant Professor, Department of Physiology, Neuroscience Program

Hui Li, Associate Professor, Plant, Soil & Microbial Sciences

Ning Li, Assistant Professor, Pathobiology & Diagnostic Investigation

John E. Linz, Professor, Food Science & Human Nutrition, and Microbiology & Molecular Genetics

David T. Long, Professor, Geological Sciences

Keith J. Lookingland, Associate Professor, Pharmacology and Toxicology

James P. Luyendyk, Associate Professor, Pathobiology& Diagnostic Investigation

Jane F. Maddox, Assistant Professor, Pharmacology & Toxicology

Burra V. Madhukar, Associate Professor, Pediatrics & Human Development

Linda S. Mansfield, University Distinguished Professor, Large Animal Clinical Sciences, Microbiology & Molecular Genetics

Michelle Mazei-Robison, Assistant Professor, Department of Physiology, Neuroscience Program

Laura R. McCabe, Professor, Physiology

J. Justin McCormick, University Distinguished Professor, Microbiology & Molecular Genetics, Biochemistry & Molecular Biology

Thomas P. Mullaney, Professor, Pathobiology & Diagnostic Investigation

Cheryl A. Murphy, Assistant Professor, Fisheries & Wildlife

Lawrence Karl Olson, Associate Professor, Physiology

Nigel S. Paneth, University Distinguished Professor, Epidemiology, and Pediatrics

James J. Pestka, University Distinguished Professor, Microbiology & Molecular Genetics, Food Science & Human Nutrition

Brian K. Petroff, Associate Professor, Diagnostic Center for Population and Animal Health, Pathobiology and Diagnostic Investigation

Thomas J. Pinnavaia, University Distinguished Professor, Chemistry **A.J. Robison**, Assistant Professor, Department of Physiology, Neuroscience Program

Cheryl E. Rockwell, Assistant Professor, Pharmacology & Toxicology

Kenneth D. Rosenman, Professor, Medicine

Robert A. Roth, Professor, Pharmacology & Toxicology; Graduate Program Director, Center for Integrative Toxicology

Craig Rowlands, Adjunct Professor, Institute for Integrative Toxicology

James G. Sikarskie, Associate Professor, Small Animal Clinical Sciences

Greg M. Swain, Professor, Chemistry

Brian J. Teppen, Professor, Plant, Soil & Microbial Sciences

James M. Tiedje, University Distinguished Professor, Plant, Soil & Microbial Sciences, and Microbiology & Molecular Genetics

James E. Trosko, Professor, Pediatrics & Human Development

Bruce D. Uhal, Professor, Physiology

Brad L. Upham, Associate Professor, Pediatrics & Human Development Almudena Veiga-Lopez, Assistant Professor, Department of Animal Sciences

Thomas C. Voice, Professor, Civil & Environmental Engineering

James G. Wagner, Associate Professor, Pathobiology & Diagnostic Investigation

Michael R. Woolhiser, Adjunct Professor, Center for Integrative Toxicology

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

Chengfeng Yang, Associate Professor, Institute for Integrative Toxicology, and Physiology

Timothy R. Zacharewski, Professor, Biochemistry & Molecular Biology

Wei Zhang, Assistant Professor, Plant, Soil and Microbial Sciences

Matthew J. Zwiernik, Assistant Professor, Department of Animal Science, Director, Wildlife Toxicology Laboratory

Academic Dept. / Disciplinary Ph.D. Programs

(Participate in the IIT's EITS graduate program.)

Animal Science Biochemistry & Molecular Biology Cell & Molecular Biology Chemistry Comparative Medicine & Integrative Biology Earth & Environmental Sciences Fisheries & Wildlife Food Science & Human Nutrition Forestry Genetics Integrative Biology Microbiology & Molecular Genetics Neuroscience Pathobiology & Diagnostic Investigation Pharmacology & Toxicology Plant, Soil, & Microbial Sciences Physiology

Deans

John Baker, College of Veterinary Medicine Ronald Hendrick, College of Agriculture and Natural Resources

Leo Kempel, College of Engineering

Norman J. Beauchamp, College of Human Medicine William D. Strampel, College of Osteopathic Medicine

R. James Kirkpatrick, College of Natural Science **Doug Buhler**, Director, AgBioResearch



Institute for INTEGRATIVE TOXICOLOGY

Michigan State University 1129 Farm Lane Food Safety and Toxicology, Rm 165 East Lansing, MI 48824 Phone 517.353.6469 Fax 517.355.4603 E-mail: tox@msu.edu

www.iit.msu.edu