UPDATE



INSTITUTE FOR INTEGRATIVE TOXICOLOGY

in this issue....

3 rd Track Added to EITS1
New CRIS Website4
PBPK Short Course5
EITS Student Achievements 5
New Journal Club Launched 6
Alumni Highlight6
Recent EITS Graduates 7
Upcoming Events7

Institute for INTEGRATIVE TOXICOLOGY

Food Safety & Toxicology Bldg. 1129 Farm Lane, Rm 165 East Lansing, MI 48824

Phone: 517.353.6469 Fax: 517.355.4603 E-mail: tox@msu.edu

Norbert Kaminski, Director Lauren St.John, Editor





THIRD TRACK ADDED TO EITS DOCTORAL PROGAM

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 this fall, 2016.

The new FTIS track has been brought about it in partnership with the recent established Center for Research on Ingredient Safety (CRIS). CRIS is an independent, academic, science-based center within the IIT that serves 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. With MSU's longstanding focus on food and health and with the commitment of the MSU administration and the

...continued on page 3

HOW DOES THE EITS PROGRAM WORK?



Biomedical Toxicology Track

- » PHM 830: Experimental Design and Data Analysis
- » PHM 980, Sec. 302: Pharmacokinetics
- » PHM 816: Integrative Tox
- » BMB 961: Selected Topics in Biochemistry II - Genomics
- TBD, Special Topics in Toxicology
- » Plus one course chosen from a list of approved electives

Food Toxicology & Ingredient Safety Track

- » PHM 980, Sec. 302: Pharmacokinetics
- » PHM 816: Integrative Tox
- » PHM 830: Experimental Design and Data Analysis
- » FSC 807: Advanced Food Toxicology
- » FSC 981: Food and Environmental Risk Assessment
- » FSC ???: Current Issues in Ingredient Safety

Environmental Toxicology Track

- » CSS 865: Environmental Fate of Organic Contaminants in Soils
- » BE 891, Sec. 003: Advanced Topics in Biosystems Engineering, Human & Envir. Risk Analysis
- » PHM 450: Introduction to Chemical Toxicology (*or*) PHM 816: Integrative Toxicology
- » CSUS 846: Law of Environmental Regulation
- » Plus two courses chosen from a list of approved electives

Ph.D. in Environmental Toxicology & Chosen Discipline

THIRD TRACK ADDED TO EITS PROGRAM cont.

Students entering the Ph.D. Program in Environmental and Integrative Toxicological Sciences are first accepted into one of the 17 disciplinary doctoral programs that partner with EITS and then enter the EITS Graduate Program near the end of their first year. Students then choose one of three tracks to complete. Completion of the requirements of both EITS and their home doctoral program results in granting of the Ph.D. Degree in the chosen discipline and Environmental Toxicology.

...continued from page 1

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 EITS doctoral program is a multidisciplinary training program that provides students with extensive research training in a specific basic science discipline as well as toxicology. Students accepted into a disciplinary Doctor of Philosophy degree program (e.g. pharmacology, biochemistry and molecular biology, etc.) may apply subsequently for admission to the EITS program. Trainees acquire a broad base of knowledge through an interactive program of courses, seminars, workshops and scientific meetings as well as by becoming an active member of a research laboratory and the general scientific community campus-wide. Until recently, trainees have chosen from one of two curricular tracks: the "Biomedical Toxicology Track" serves students entering with a strong background in mammalian biology and the "Environmental Toxicology Track" is a choice for students in the fields of chemistry, engineering and other fields and who enter with less mammalian biology background. Each track has its own set of course requirements, yet each student who completes the multidisciplinary course of study earns a Ph.D. degree in their chosen basic science discipline with a dual major in environmental toxicology. 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 tracks.

The EITS graduate program continues to be one of the premier toxicology training programs in the U.S. and is now in its 28th consecutive year of training grant support from the National Institute of Environmental Health Sciences (NIEHS), the longest held NIH training grant at MSU. This grant provides stipend support for 7 predoctoral and 2 postdoctoral fellows each year.

With the development of the third track, the EITS program continues to grow. The program now partners with 17 graduate programs across campus and has 30 doctoral students currently enrolled. For more information on the new Food Toxicology and Ingredient Safety track in the EITS program, please contact Kasey Baldwin, kbaldwin@msu. edu.

THOUGHTS FROM THE DIRECTORS:



"CRIS was established on the MSU campus as a program for food and consumer product safety that will broadly build capability in chemical ingredient safety with targeted focus in three specific areas: scientific research, risk communication, and education & training. I am very excited that the new track in the EITS program, Food Toxicology and Ingredient Safety (FTIS), is designed to touch on all three areas. From an education & training perspective, FTIS will prepare students to become

the next generation of specially trained toxicologists to serve the food and consumer products industries, or to participate as government scientists in the development and implementation of regulatory and public health policy on ingredient safety, or to become the next generation of educators to address ingredient safety."

~Michael Holsapple

Director, Center for Research on Ingredient Safety



"We're excited to launch the new EITS track. This track will provide training that will enhance career opportunities for our students in academia and industry as well as in government regulatory agencies such as the FDA. The curriculum that emphasizes coursework in basic science and toxicology with exposure to risk assessment and regulation practices will leave our students well prepared for a future in food and ingredient safety."

> **~Robert Roth** Director, EITS Graduate Program

CRIS WEBSITE GETS NEW DOMAIN AND LOOK

The Center for Research on Ingredient Safety (CRIS) is excited to debut their new stand-alone, searchable website that draws upon all the elements of CRIS, from research to training to communication. The CRIS website began as a sub-category of the IIT website, but it now has its own web address, http:// cris.msu.edu, with more robust content. The need for change, and to expand and develop the CRIS website was suggested at a special meeting of the CRIS advisory committees that took place in June. They recommended a stand-alone website for greater visibility and branding, searchable content, additional content directly relating the elements of the organization to the CRIS strategic plan, and additional links to CRIS's other

communication portals.

The new website now has seven main tabs: About, Members, Governance, Research, Training, Communication and Contact. Under "About" visitors can read about the Center's Mission, Vision and Core Values, and it's Strategic Plan. The "Members" tab not only lists current members, but has links to details on how to become a member of CRIS, and to the bylaws of CRIS for current members. Under "Governance" is information and links on the CRIS Director, Internal Advisory Committee, External Advisory Committee, Emerging Issues Committee and Committee Charters. The next three tabs, "Research," "Training," and "Communication", represent the three elements on which CRIS was founded. New information on the current research at CRIS, as well as information on upcoming research proposals and areas of study can be found under "Research." Details on the third track of the Environmental and Integrative Toxicological Sciences program at MSU, the Food Toxicology and Ingredient Safety Track, can be found under "Training." And lastly, the "Communication" tab features information on the ASU Communications Team, as well as links to the CRIS Connects Newsletter, CRIS Bits Blog, Risk Bites, and Upcoming Events.

If you have feedback or suggestions about the new CRIS website, please let us know by contacting, Heather Dover, doverhea@msu.edu. 🕿



product ingredient safety that will broadly build capability





FACULTY ACHIEVEMENT

Dr. Brian Gulbransen, IIT affiliated faculty member, was the recipient of the 2016 Beverly Petterson Bishop Award for Excellence in Neuroscience from the American Physiological Society. The award is presented annually at the Experimental Biology meeting and is awarded to an investigator who demonstrates outstanding neuroscience/neurophysiology research. Dr. Gulbransen will receive a \$20,000 award for use in his research program studying the role of glia in neuroinflammation in the intestine.

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 prin-

ciples of physiologically based pharmacokinetic (PBPK) modeling and introduced the application of this technique in chemical health risk assessment and drug development.

Upon completion of this course, participants were able to:

 Understand the fundamental concepts underlying PBPK modeling

- » Describe the absorption, distribution, metabolism, and elimination of chemicals using mass balance differential equations
- » Build PBPK models to simulate tissue dosimetry using Berkeley Madonna®



» Appreciate the application of PBPK models in human health risk/safety assessment and drug development

The course comprised lectures and hands-on computer simulation exer-

cises. 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. ►

EITS STUDENT ACHIEVEMENTS



Isola Brown, training with Dr. Brian Gulbransen, was awarded a Ruth L. Kirschstein National Research Service Award Individual PreDoctoral Fellowship (F31 NRSA) from the National

Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) at the Nation Institute for Health for her project, "Enteric Glial Cell Dysregulation of Oxidative Balance Contributes to Enteric Neuron Loss in Inflammation."



Sophia Kaska, training with Dr. A.J. Robison, was awarded 2nd place in the Division of Neuropharmacology's graduate student best poster presentation competition at the an-

nual American Society for Pharmacology and Experimental Therapeutics (ASPET) meeting in San Diego, California for her poster, "The Effects of Ventral Tegmental Area Rictor Knockout on Susceptibility to Chronic Social Defeat Stress and Stress-Induced Changes in Morphine Reward."



with Dr. Norbert Kaminski, received a travel award to attend the 2016 AHR Conference: "The Aryl Hydrocarbon Receptor as a Central Mediator of Health and Disease,"

Jinpeng Li, training

in Rochester, New York, August 3-6, 2016. Li was awarded for his project, "Aryl Hydrocarbon Receptor (AHR) Activation by 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) Impairs Early Stages of Human B Lymphopoiesis."



Mike Rizzo, training with Dr. Norbert Kaminski, received the Arthur Falek Early Career Investigator Award for the most outstanding Pre-Doctoral Poster Presentation from the Society of

NeuroImmune Pharmacology (SNIP) Conference in Krakow, Poland. The primary objective of the SNIP conference each year is to bring together scientists from the fields of neuroscience, immunology and pharmacology, to share their research and discuss key issues regarding neuroimmune pharmacology.

The title of Rizzo's project was, "Δ9-Tetrahydrocannabinol (THC)-mediated Suppression of Human Plasmacytoid Dendritic Cell and CD14+ Monocyte Maturation."



Alexandra Turley, training with Dr. Cheryl Rockwell, was awarded a fellowship with ILSI North America in Washington, D.C. for summer 2016. Turley will be in D.C. for 12 weeks conducting a case

study for a food-related chemical using the RISK21 approach. The RISK21 approach involves using both the exposure data and the tox data for a compound to determine the risk of a compound. Turley will apply this method using both traditional tox data and Toxcast data and comparing the two to see if they give similar or different results.

MSU COMPUTATIONAL AND SYSMEMS BIOLOGY JOURNAL CLUB LAUNCHED

The MSU Superfund Program's Training Core is pleased to announce the launch of a Computational and Systems Biology (CSB) Journal Club for the MSU community and external members of the MSU Superfund Program. This Journal Club will be coordinated by Dr. Sudin Bhattacharya, Institute for Integrative Toxicology, MSU.

Mathematical modeling and computational approaches integrating large-omic data sets are playing vital roles in 21st century biology, and have the potential to transform nearly every branch of the biosciences. In this journal club, which will meet once a month, they will study examples of the application of CSB tools to a variety of biological problems. The Journal Club was launched in April 2016 and a review article titled "Next-Generation Genomics: an Integrative Approach" (Hawkins et al, Nat. Rev. Genet. 2010) was discussed.

The Journal Club has continued through the summer each month with the following presentations:

- Tuesday, April 26, Rance Nault, EITS doctoral student training with Dr. Timothy Zacharewski (Project 3), presented the article, "A Genome-wide CRISPR Screen in Primary Immune Cells to Dissect Regulatory Networks" (Parnas et al, Cell, 2015)
- » Thursday, June 2, Dr. Jay Goodman, MSU, presented a session titled, "Some People are Rats, but are any of Them Large Mice?" Three articles were discussed: "Genomic responses in mouse models poorly mimic human inflammatory diseases" (Seok et al, PNAS, 2013), "Normalizing the environ-

ment recapitulates adult human immune traits in laboratory mice" (Beaura et al, Nature, 2016), "Mice in the ENCODE spotlight" (Carninci, Nature, 2014).

- Tuesday, July 5, Dr. Sudin Bhattacharya, MSU, presented a session titled, "Chromatin States: Causal or Merely Predictive?" Three articles were discussed: "Histone modification levels are predictive for gene expression" (Karlic et al, PNAS, 2010), "Histone modification: cause or cog?" (Henikoff and Shilatifard, Trends in Genet., 2011), "On the use of the word 'epigenetic" (Ptashne, Curr. Biol., 2007)
- Tuesday, August 2, Dr. Rory Connolly, Senior Research Biologist, US EPA, presented a session titled, "Everything You Always Wanted to Know About Non-monotonic Dose Response." Three articles were discussed: "The learning curve" (Fagin, Nature, 2012), "Population variability in biological adaptive responses to DNA damage and the shapes of carcinogen dose-response curves" (Conolly et al, TAP, 2005), "Non-monotonic dose-response relationships: Mechanistic basis, kinetic modeling, and implications for risk assessment" (Conolly et al, Tox. Sci., 2004)

Journal club sessions will continue throughout the fall with the next meeting taking place on September 6, 2016. For more information, please contact Sudin Bhattacharya, sbhattac@msu.edu. ♠

ALUMNI HIGHLIGHT: KYLE POULSEN



Kyle Poulsen Postdoctoral Research Fellow Learner Research Institute, The Cleveland Clinic Dr. Kyle Poulsen received his Ph.D. in December of 2013 after completing the dual

degree program in Pharmacology and Toxicology and Environmental Toxicology. His dissertation was, "Trovafloxacin Potentiates Lipopolysaccharide-Induced Tumor Necrosis Factor-Alpha in a Macrophage Cell Line: Mechanistic Insights to Idiosyncratic Liability."

After graduation, Poulsen began a postdoctoral position in the laboratory of Dr. Laura Nagy. She is located in the Lerner Research Institute within the Cleveland Clinic, a thriving research community with a high level of collaboration between basic scientists and clinicians. The Nagy lab focuses on studying chronic liver diseases such as alcoholic hepatitis, fibrosis and non-alcoholic fatty liver disease (NAFLD).

In addition to helping the lab generate data and publish their work, Poulsen also mentors undergraduate and graduate students and regularly presents his work at interdisciplinary lab meetings. He also collaborates with international colleagues, which has given him access to decades of research expertise towards understanding and treating liver disease. Poulsen attends and presents his research findings at many national and international meetings throughout the year. He will attend his second international conference in September 2016.

Poulsen expressed that his education as an EITS student remains an invaluable part of his foundation in science as he progresses through his career. He said, "The additional coursework provided me a fundamental grasp of so many disciplines and techniques prior to beginning my postdoc, and it only hastens my ability to adopt new techniques and perspectives to my skill set. Outside of the classroom, attending the numerous EITS-sponsored seminars given by scientists from industry, government and academia gave me pivotal insights into what it takes to develop a sustained, successful research career. I have also recognized that being amongst a group of students from diverse laboratories during my EITS training contributed to my development as a scientist; through the continuous exchange of ideas and collaborating to tackle difficult subject matter whilst balancing a novel research project." 🔊

EITS GRADUATES SUMMER 2016



Phillip Brooks

Comparative Medicine and Integrative Biology

Mentor, Linda Mansfield

Dr. Phillip Brooks received his Ph.D. in August of 2016 after completing the dual degree program in Comparative Medicine and Integrative Biology and Environmental Toxicology. His dissertation was, "Composition of Gut Microbiota Affects C. jejuni-Mediated Inflammation and Autoimmunity in Murine Models."

Brooks will be starting a post-doctoral appointment with Dr. C. Titus Brown in the lab for Data Intensive Biology at the University of California-Davis this fall.



Natasha Kovalova Pharmacology and Toxicology Mentor, Norbert Kaminski

Dr. Natasha Kovalova received her Ph.D. in July of 2016 after completing the dual degree program in Pharmacology and Toxicology and Environmental Toxicology. Her dissertation was, "Role of Aryl Hydrocarbon Receptor Polymorphisms on TCDD-mediated CYPIBI Induction and IgM Suppression by Human B Cells."

After graduation, Kovalova will

be working as a post-doctoral scientist at the Eli Lilly Company, conducting research, writing papers and presenting her research at national meetings. Her work will be focused on optimizing therapeautic antibodies to reduce immunogenicity.



Nikita Joshi

Pharmacology and Toxicology Mentor, James Luyendyk

Dr. Nikita Joshi received her Ph.D. in July of 2016 after completing the dual degree program in Pharmacology and Toxicology and Environmental Toxicology. Her dissertation was, "Hepatoprotective Functions of the Hemostatic System in Experimental Xenobiotic-Induced Biliary Injury."

Joshi continues to work in the lab of Dr. James Luyendyk this summer as she applies for research opportunities in industry and academia.



Rance Nault Biochemistry and Molecular Biology Mentor, Timothy Zacharewski

Dr. Rance Nault received his Ph.D. in July of 2016 after completing the dual degree program in Biochemistry and Molecular Biology and Environmental Toxicology. His dissertation was, "TCDD-Elicited Metabolic Reprogramming in the Progression of Non-Alcoholic Fatty Liver Disease."

Nault continues to work in the

UPCOMING EVENTS FALL 2016

IIT Seminar Series

The Institute for Integrative Toxicology is excited to once again host a seminar series this year that will feature experts and students in the field of toxicology.

Be on the lookout for speakers, dates and times coming soon!

CRIS Annual Meeting

The CRIS Annual Meeting will be held on MSU's campus October 5-6, 2016. Please contact Heather Dover at doverhea@ msu.edu for more details.

EITS Research Evening

The Institute for Integrative Toxicology will host our annual Research Evening to showcase trainees in the Environmental and Integrative Toxicological Sciences Training Program and their accomplishments on Wednesday, November 30, 2016, 5:15 to 8:00 p.m., in the Lincoln Room of the MSU Kellogg Center. The event will include dinner, student presentations and a poster session. Please RSVP by November 18 to Kasey Baldwin, kbaldwin@msu.edu or call 353-6469.



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