



IIT UPDATE

INSTITUTE FOR INTEGRATIVE TOXICOLOGY



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Goodman Completes 48-Year Career at MSU with Symposium

Jay Goodman, professor of pharmacology and toxicology and IIT affiliated faculty member, became “emeritus” on January 1, 2019, after a storied 48-year career at MSU. Dr. Goodman will continue to contribute to both the Department of Pharmacology and Toxicology and IIT as a part-time, fixed term faculty member - continuing to teach and lead the MSU Superfund Training Core.

The IIT and Department of Pharmacology and Toxicology celebrated Dr. Goodman with a symposium in honor of his research, “*Advancing Science-Based Safety Assessment of Chemicals*,” held Monday, April 1. Colleagues, former students and friends gathered for the event. Speakers included: Dr. James Bus, Dr. Samuel Cohen, Dr. Elaine Faustman, Dr. James Klaunig, Dr. Ruth Roberts, and Dr. William Slikker, Jr. The symposium was moderated by Dr. David Doolittle. The day concluded with a celebration dinner at the MSU Kellogg Center.

Goodman earned a Ph.D. in pharmacology at the University of Michigan, proceeded to postdoctoral training at the University of Wisconsin’s McArdle Laboratory for Cancer Research and then joined the then-Department of Pharmacology at MSU as an assistant professor in 1971.

At MSU, Goodman’s research focused on epigenetic factors that might be involved in rodent liver carcinogenesis. He employed phenobarbital (PB), a non-geno-

toxic compound and 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 epidemiologic 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 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 one of these is being explored as a potential biomarker for non-genotoxic compound-induced rodent liver tumors. “Indeed, Dr. Goodman has been one of the pioneers and leaders in the area of epigenetic mechanisms of chemical-induced tumorigenesis. It is important to emphasize that early in Dr. Goodman’s career, when he first began investigating epigenetic mechanisms of tumorigenesis,

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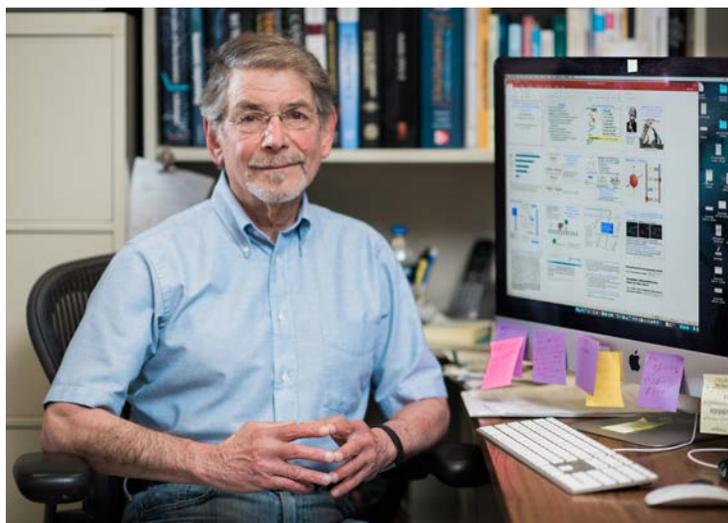
Goodman Retires After 48 Years cont.

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that was a period in time when the primary emphasis in the field was on genotoxicity,” said Dr. Norbert Kaminski, professor of pharmacology and toxicology and director of the IIT.

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 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 commented, “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 science-based safety assessment.”

A prolific author, lecturer and leader who has leant his expertise on numerous academic and regulatory committees, Goodman is also a former president of the Society of Toxicology and served as the MSU Department of Pharmacology and Toxicology’s interim chair from 2001-2002.

Among the many honors he’s received throughout his career include the Society of Toxicology’s Merit Award, the International Society of Regulatory Toxicology and Pharmacology’s International Achievement Award, and the John Barnes Prize Lecture from the British Toxicology Society. Most recently,

this spring, Goodman was selected to receive the 2019 Pharmaceutical Research and Manufacturers of America Foundation Award in Excellence in Pharmacology/Toxicology from the PhRMA Foundation. The Award in Excellence Program honors former Foundation grant recipients for outstanding career achievements. Awards are given to scientists who received a foundation grant at the outset of their careers in a discipline important to the research-based pharmaceutical industry and went on to distinguish themselves

through their scientific and/or academic achievements. Goodman was presented with this award in April during the American Society for Pharmacology and Experimental Therapeutics annual meeting in Orlando, Florida.

“Dr. Jay Goodman has been a major contributor to the field of mechanistic toxicology. He always went beyond just identifying which chemical substances cause harm to really understanding why. This greatly advanced the field and improved overall risk assessment in regulatory toxicology,” said Richard Neubig, chair of the MSU Department of Pharmacology and Toxicology. “He has been a highly sought-after advisor and consultant both nationally and internationally and trained a number of outstanding toxicologists during his career at Michigan State University.”

IIT Faculty Achievements Spring 2019

Cheryl Rockwell

Associate Professor, Department of Pharmacology and Toxicology

Dr. Cheryl Rockwell received the 2019 Toxicology Early Career Award from the American Society for Pharmacology and Experimental Therapeutics (ASPET) Division for Toxicology. The award was established to recognize excellent original research by early career investigators in the area of toxicology.

Dr. Rockwell is being recognized for her excellent history of funding and publications in high quality journals, as well as her active role in multiple toxicologically-based societies, and her demonstrated success in mentoring the next generation of toxicologists.

Dr. Rockwell received her PhD from Michigan State University in 2005. As a postdoc, she trained at the University of Missouri Kansas City and the University of Kansas Medical Center. She became an assistant professor at Michigan State University in 2011, where she received tenure in 2017. She has published over 30 peer-reviewed papers as well as a book on immunotoxicology protocols. In 2016, she received an Outstanding New Environmental Scientist award from the NIEHS. She has been a member of ASPET since 2009 and recently served on the editorial board of *Molecular Pharmacology*.



Sudin Bhattacharya

Assistant Professor, Department of Biomedical Engineering, Department of Pharmacology and Toxicology, Center for Research on Ingredient Safety, Institute for Quantitative Health Science and Engineering

Dr. Sudin Bhattacharya won the Edward Carney Award for Predictive Toxicology at the 2018 Annual Meeting of the American Society for Cellular and Computational Toxicology (ASCCT) held in Bethesda, Maryland. The annual award is given to recognize excellence in predictive toxicology and 2018 marks the fourth year the award has

been bestowed. Bhattacharya received the award for his presentation, “*Integrating Genomics and Epigenomics into Predictive Toxicology of the Aryl Hydrocarbon Receptor.*”



Norbert Kaminski

Professor, Department of Pharmacology and Toxicology; Director, Institute for Integrative Toxicology; Interim Director, Center for Research on Ingredient Safety

Dr. Norbert Kaminski will serve as the new Scientific Advisor for ILSI North America’s Food and Chemical Safety committee. In this role, Dr. Kaminski will help ensure the saliency of the scientific output from work produced by the many sub-committees.

Established in 2007, ILSI North America brings scientists from the U.S. and Canadian governments, academia, and industry to work cooperatively and with shared responsibility to advance the understanding and application of science to improve public health.

Dr. Kaminski’s research is in the general areas of immunopharmacology and immunotoxicology and encompasses a number of extramurally funded projects. A major emphasis of all of the projects is the elucidation of molecular mechanisms for impairment of signal transduction cascades and gene expression during lymphocyte activation by drugs and chemicals.



Matthew Zwiernik

Assistant Professor, Department of Animal Science; Director, Wildlife Toxicology Laboratory

Dr. Matthew Zwiernik was appointed to the Environmental Protection Agency Science Advisory Board (SAB) for a 3 year term beginning in January 2019.

Having expert scientists on the SAB who bring wide-ranging scientific perspectives and come from all across the country has been a point of emphasis for this Administration. In FY 2019, 30 states and the District of Columbia will be repre-

sented on the SAB and its standing committees.

Dr. Zwiernik’s research focuses on assessing the impacts of environmental chemical exposure to wildlife ranging from oil spills to superfund sites. His work combines direct measures of wildlife exposure and population health with controlled laboratory studies identifying mechanism of action and toxicity.



Michelle Mazei-Robison

Assistant Professor, Department of Physiology, Neuroscience Program

Dr. Michelle Mazei-Robison received the 2019 Division for Neuropharmacology Early Career Award from the American Society for Pharmacology and Experimental Therapeutics (ASPET) Division for Neuropharmacology. The award was established to honor a young independent investigator working in neuropharmacology.

Dr. Mazei-Robison is being recognized for her excellence in understanding the molecular mechanisms that underlie changes in VTA dopamine neuron signaling, morphology, and activity induced in neuropsychiatric disorders such as addiction and depression.

Her lab studies the molecular mechanisms that underlie changes in ventral tegmental area (VTA) dopamine (DA) neuron signaling, morphology, and activity in neuropsychiatric disorders.

She uses an array of cutting-edge techniques such as translating ribosome affinity purification and viral-mediated gene transfer to identify cell type-specific transcriptional and structural changes induced by chronic stress and opiate drugs. The functional consequences of candidate genes are interrogated in a wide array of behavioral assays to evaluate addictive- and depressive-like behaviors. Her lab has identified similar changes induced by both stress and opiates in the VTA, suggesting shared mechanisms for comorbid depression and opiate abuse. Given the current opiate epidemic, her work to define neuroadaptations responsible for altered opiate reward and intake are particularly exciting and may be critical for improved treatment. 🌟



IIT Affiliates Succeed at 58th SOT Meeting in MD

Students and faculty of the MSU Institute for Integrative Toxicology were excited to attend and present at this year's 58th annual Society of Toxicology (SOT) meeting held in Baltimore, Maryland.

The SOT annual meeting is the largest toxicology meeting and exhibition in the world, with more than 80 scientific sessions and 2,100 abstract presentations. This year's meeting was held at the Baltimore Convention Center from

March 10-14, 2019.

The following students and faculty affiliated with IIT received recognition:

- » **Robert Freeborn**, EITS trainee with Dr. Cheryl Rockwell, received 3 prestigious awards: the Mechanisms Specialty Section Carl C. Smith Graduate Student Award, the Risk Assessment Specialty Section Robert J. Rubin Student Award, and the Immunotoxicology Specialty Section Best Presentation by a Stu-

dent Award. Freeborn was awarded for his abstract, "*The Synthetic Food Additive tBHQ Impairs Host-Defense to Influenza Infection.*"

- » **Jeremy Gingrich**, EITS trainee with Dr. Almudena Veiga-Lopez, received the Food Safety Specialty Section Frank C. Lu Graduate Student of the Year Award for his abstract, "*Comparative Toxicokinetic Study of Three Bisphenols (BPA, BPS, and BPF) in a Sheep Pregnancy Model.*"



Top left: Dr. Rance Nault accepts his John Doull Risk Assessment Award from the Risk Assessment Specialty Section.

Top right: Dr. Almudena Veiga-Lopez (center) with her lab.

Center: Dr. Lauren Hardy (far right) accepts her Postdoctoral Student Travel Award from the Mechanisms Specialty Section.

Bottom left: EITS alumnus, Jinpeng Li (right), accepts the MB Research Award from the In Vitro and Alternative Toxicology Methods Specialty Section.

Bottom right: Cheryl Rockwell (center) with her lab.



- » **Jiajun “Brian” Zhou**, EITS trainee with Dr. Norbert Kaminski, received the Mitzi and Prakash Nagarkatti Research Excellence in Immunotoxicology Travel Award from the Immunotoxicology Specialty Section for his abstract, “*Lymphocyte-specific Protein Tyrosine Kinase (LCK) Plays a Significant Role in Suppression of the Immunoglobulin M (IgM) Response in Human CD5+ Innate-like B Cells (ILBs).*”
- » **Lance Blevins**, postdoctoral researcher with Dr. Norbert Kaminski, received the Best Postdoctoral Presentation from the Immunotoxicology Specialty Section of the SOT for his paper titled, “*Identification and Characterization of a Sensitive Immunologic Target of TCDD: CD5+ Innate-like B Cells*”. Using human primary peripheral blood B cells, Dr. Blevins demonstrates the preferential sensitivity of CD5+ innate-like B cells to aryl hydrocarbon receptor (AHR) activation and provides insight into mechanisms associated with AHR activation in human B cells. Others who contributed to this work include Jiajun Zhou, Nick Wawee, Robert Crawford, Sudin Bhattacharya and Norbert Kaminski.
- » **Yining Jin**, postdoctoral researcher with Dr. Cheryl Rockwell, received the Immunotoxicology Specialty Section HESI Young Investigator Award and the American Association of Chinese in Toxicology SIG AACT/InnoStar Best Abstract award. The awards were for Yining’s abstract and presentation, “*Effects of the Food Additive tBHQ on OVA-Elicited Food Allergy in Mice.*”
- » **Rance Nault**, postdoctoral researcher with Dr. Timothy Zacharewski, received the Carcinogenesis Specialty Section Postdoctoral Fellowship & Young Investigator Award and the Risk Assessment Specialty Section John Doull Risk Assessment Endowment Award for his abstract, “*Application of Toxicogenomics for the Risk Assessment of the Food Contaminant Acetamide.*”
- » **Asmita Pant**, postdoctoral researcher with Dr. James Luyendyk, received the 3rd place for the Gabriel L. Plaa Education Award from the Mechanisms Specialty Section.
- » **Lauren Hardy**, postdoctoral researcher on the MSU IIT Training Grant working with Dr. James Luyendyk, received the Mechanisms Specialty Section Postdoctoral Student Travel Award for her abstract, “*Tissue transglutaminase cross-linking activity alters fibrin(ogen)-mediated pro-inflammatory responses in macrophages.*”
- » **María Poidomani**, an undergraduate in the laboratory of Dr. Cheryl Rockwell, was awarded a Pfizer SOT Undergraduate Travel Award for her abstract, “*The Role of Nrf2 in Regulation of Th17 Differentiation in Primary Murine CD4 T Cells.*”
- » **Dr. Sudin Bhattacharya**, along with MSU IIT Superfund Researchers, Dr. Qiang Zhang and Rory Connolly, received the 2019 Best Paper Award

in Applying Risk Assessment from the SOT Risk Assessment Specialty Section for their paper, “*Bridging the Data Gap From in vitro Toxicity Testing to Chemical Safety Assessment Through Computational Modeling.*” which was published in *Frontiers in Public Health* in September of 2018.

- » **Dr. William Atchison**, received the 2019 Distinguished Neurotoxicologist Award from the SOT Neurotoxicology Specialty Section. Dr. Atchison has demonstrated a life-long commitment to neurotoxicology with significant research contributions to neurotoxicology, neuropharmacology, and neurobiology. His work has significantly advanced the understanding of metal neurotoxicity, particularly the cellular mechanisms of methyl mercury toxicity.
- » **Dr. Jinpeng Li**, EITS alumnus, received the MB Research Award for distinction in practical in vitro and alternative toxicology methods from the In Vitro and Alternative Methods Specialty Section.

The highlight of the week was the IIT Alumni and Friends Reception held on Tuesday, March 12, for all current and former students, postdocs, faculty and friends of Michigan State University. The evening reception was a welcome opportunity to catch up with old acquaintances and meet with new friends. The IIT looks forward to the next SOT Meeting in Anaheim, California, in March 2020. 🌟

Student Accomplishments and Awards



EITS alumnus, **Sophia Kaska**, chaired the session, “*Addressing the Opioid Epidemic Through Science and Policy,*” at the 2019 ASPET Annual Meeting at Experimental Biology, held in Orlando, Florida, April 6-9. Kaska is currently a postdoctoral researcher in the Department of Medicinal Chemistry at the University of Kansas.

The IIT awarded travel funds to several EITS trainees for this spring and upcoming summer: **Geoff Rhodes, Jenna Strickland, Kelly Fader, Monica Rios, Kathryn Wierenga, Mike Rizzo, Russell Fling, Robert Freeborn, Brian Zhou, Dawn Henderlong, Wenjie Qi, Tyler Firkus, Laura Mark, Isha Khan, Nikita Saha Turna, Vanessa Benham, Janice Albers, Jeremy Gingrich, Omara Kana, Diana Pa-cyga, Sean Nguyen, Yike Shen, and Jianzhou He.** These students will be traveling to meetings across the country

in the coming months to present their research and learn more in their fields.



Rance Nault, postdoctoral researcher with Dr. Timothy Zacharewski, attended the Bio-Trac Single Cell RNA-Seq Workshop in Germantown, Maryland, December 10-13, 2018. Single-cell sequencing is an emerging technique which allows the evaluation of gene expression with unprecedented resolution. Through hands-on training during the workshop, Nault developed the critical skills to perform both wet lab and computational analysis. “Developing these skills is essential for the use of these tools in my own research applying toxicogenomics in the evaluation of AhR-mediated fatty liver disease pathogenesis and enabling the dissection of mechanisms at the cellular level,” said Nault.

Tewari-Singh and Bruner Join IIT Faculty

The IIT is pleased to introduce Dr. Neera Tewari-Singh as an affiliated faculty member and Dr. Leon Bruner as an adjunct faculty member.



Neera Tewari-Singh

Assistant Professor, Biosystems and Agricultural Engineering

Dr. Neera Tewari-Singh received her B.S. in Botany, Chemistry, and Zoology from Lucknow University in 1991, her M.S. in Life Sciences from Jawaharlal Nehru University in 1993, and her Ph.D. in Molecular Biology from Jawaharlal Nehru University in 2001, with her Ph.D. research conducted at the Leibniz University Hannover, Germany.

Technological advances and increasing industrialization pose an enhanced risk of occupational and/or accidental exposure to chemical agents in addition to their potential use in warfare and terrorism. The major long-term goal of Dr. Tewari-Singh's research is to pursue both basic and translational studies to develop approved and more effective targeted countermeasures/therapies against mainly the dermal and ocular injuries from chemical threat agent exposures. The chemical agents of interest include vesicating and nettle agents (sulfur mustard, nitrogen mustard, lewisite and phosgene oxime), industrial agents/pollutants and pesticides (chloropicrin, polycyclic aromatic hydrocarbons etc.) that can cause harmful effects/mass casualties as well as long-term ailments to the human population. Developing effective and targeted medical interventions is a critical component of the modern global strategy to overcome the challenges of chemical emergencies in both civilian and military populations, making her research highly significant.

Current funded grants in her lab focus on investigating the role of mast cells and related inflammatory responses to elucidate skin, systemic and/or lung injury mechanisms that contribute to severe toxicity/long-term illnesses from vesicating agents' exposure in civilian population as well as war veterans. Outcomes from these studies are anticipated to identify novel molecular targets for therapeutic intervention and further drug development to effectively treat injuries from these chemical threat agents. Under other collaborative projects, she is studying mechanisms and testing as well as optimizing therapies to treat ocular injuries from chemical threat agents and ocular inflammatory diseases (diabetic and non-diabetic corneal inflammation and dry eye). Additionally,

she is also elucidating the role of aryl hydrocarbon receptor in polycyclic aromatic hydrocarbons-induced exacerbation in skin inflammatory diseases (psoriasis and atopic dermatitis) for better targeted treatment strategies.

Her lab integrates clinical and biological responses, molecular toxicology, biochemistry, signal transduction, immunology, imaging, and cutting-edge systems toxicology 'omics' tools to elucidate toxic mechanisms (mainly related to inflammation, DNA damage and oxidative stress). For these studies, they employ in vivo (mice, rats, rabbits and minipigs), ex vivo (rabbit and human tissues) and in vitro (cell culture) model systems.



Leon Bruner

IIT Adjunct Faculty Member

Dr. Leon Bruner received his B.S. in Veterinary Science, his Doctor of Veterinary Medicine, and his Ph.D. in Pharmacology, from Michigan State University.

Dr. Leon Bruner is a thirty-year veteran of the consumer products industry. Most recently, Dr. Bruner served as Executive Vice President for Science & Regulatory Affairs and Chief Science Officer at the Grocery Manufacturer's Association (GMA) in Washington, DC. The Science and Regulatory Affairs organization carried out a broad range of member services in areas including science policy, product safety, education, training and applied consumer product safety research.

Before joining GMA, Dr. Bruner held a variety of positions at The Procter & Gamble Company and The Gillette Company. He served as Vice President and Director of the Corporate Environment, Health and Safety Organization in P&G's Gillette organization where he was responsible for product safety, regulatory compliance, workplace safety, environmental compliance, quality, sustainability and business continuity planning.

Prior to joining the Gillette Company, Dr. Bruner worked for P&G's Health and Beauty Care organization based in London, England. In this position he was internationally-recognized as an expert in the development, validation and regulatory acceptance of toxicity test methods. He has written numerous peer-reviewed scientific articles and several book chapters on these subjects. ●

Save the Date: Upcoming Events Fall 2019

» **Center for Research on Ingredient Safety Annual Meeting**
November 13 - 15, 2019:
MSU's Executive Henry Center

» **Superfund Research Program Annual Meeting**
November 18-20, 2019:
Seattle, Washington

» **IIT Research Evening**
December 4, 2019:
MSU Kellogg Center

IIT Seminar Series Spring 2019 Wraps Up

The IIT welcomed four fantastic speakers this spring semester as part of the IIT Seminar Series.



Matthew Campen
Professor, Department of Pharmaceutical Sciences, University of New Mexico

Dr. Campen spoke on January 11 on, “Circulating Molecular Shrapnel: Identifying links between inhaled toxicants and neurological outcomes.”



Rita Strakovsky
Assistant Professor, Human Nutrition, Michigan State University

Dr. Strakovsky, an IIT-affiliated faculty member, spoke on February 8 on, “Gestational Exposure to Parabens and Fetal Growth.”



Michael Honeycutt
Texas Commission on Environmental Quality

Dr. Honeycutt spoke on April 12 on, “Regulating Air Quality - Nothing Simple is Ever Easy: A

Case Study with Ozone.”



Patricia Hunt
Professor, School of Molecular Biosciences, Center for Reproductive Biology, Washington State University

Dr. Hunt spoke on May 6 on, “Making Errors

While Making Gametes.” This seminar was co-hosted with the Reproductive and Developmental Sciences Program at MSU.

The IIT is looking forward to hosting seven more prestigious speakers for the

2019/2020 academic year:

- » **Tracie Baker**, Assistant Professor, Institute of Environmental Health Sciences, Department of Pharmacology, Wayne State University will speak on **September 10**.
- » **Patrick Allard**, Assistant Professor, Institute for Society and Genetics, University of California Los Angeles, will speak on **October 8**.
- » **Gary Krishnan**, Senior Research Fellow, Eli Lilly and Company, will speak on **November 12**.
- » **Bernard Goldstein**, Professor Emeritus, Environmental and Occupational Health, University of Pittsburgh, will speak on **January 14**.
- » **Mark Harris**, Managing Principal Scientist and Cofounder, ToxStrategies, will speak on **February 11**.
- » **Teresa WM Fan**, Professor, Edith D. Gardner Chair in Cancer Research, Toxicology and Cancer Biology, University of Kentucky, will speak on **April 14**.
- » **Donna Zhang**, Professor, Department of Pharmacology and Toxicology, University of Arizona, will speak on **May 12**. 🍀

Amalfitano New Dean of College of Osteopathic Medicine

IIT-affiliated faculty member, Dr. Andrea Amalfitano, has been appointed to serve as dean of Michigan State University’s College of Osteopathic Medicine. He has served as the interim dean for the college since February 2016.

Previously, Amalfitano was director of MSU’s Clinical and Translational Sciences Institute, professor of microbiology and molecular genetics and pediatrics, and held the Osteopathic Heritage Foundation Endowed Professor of Pediatrics, Microbiology and Molecular Genetics.

Prior to joining MSU in 2005, he served as an associate professor at Duke University in the

Department of Pediatrics and the Department of Pathology, Molecular Genetics and Microbiology.

His research focuses on determining the feasibility of cutting-edge therapeutics, including gene transfer, to treat both acquired and genetic diseases and then translating that knowledge into the clinical realm. His scholarly efforts in both clinical medicine and applied genetics have led to the development of innovative treatments for infants, children and adults affected by a variety of diseases, including lethal muscular dystrophies, cancer, autoimmune disorders and autism.



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