

CIT Update

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CIT Administrative Offices Relocated

The CIT Administrative Offices have been moved to the Food Safety and Toxicology Building on the south side of the MSU campus, just east of Farm Lane. Constructed in 1998, the building also houses the National Food Safety and Toxicology Center.

Many of the CIT-affiliated faculty have laboratory and office space in the building which is also in closer proximity to numerous other CIT-affiliated faculty in nearby scientific facilities.

The CIT had previously been located in Holden Hall.

The new address is on the first floor of the building in suite 165C Food Safety and Toxicology Building, Michigan State University, East Lansing, MI, 48824. The phone and



Food Safety and Toxicology Bldg.

fax numbers as well as internet address remained the same.

Director's Message

2005 continues to be an exciting and successful year for the toxicology community at Michigan State University.

A number of MSU predoctoral and postdoctoral trainees were recognized this year for their outstanding achievements by the Society of Toxicology at the 2005 Annual Meetings in New Orleans. Dr. Frances Tukov was the recipient of the prestigious Colgate-Palmolive Postdoctoral Fellowship Award. Gautham Rao was awarded Best Submission by a Graduate Student from the Immunotoxicology Specialty Section, and five MSU trainees were recipients of Travel Awards to the Annual Meeting including Lyle Burgoon, Cora Fong, Josh Kwekel, Steve Bezdecny and Ajith Vengellur.

MSU toxicology faculty also received honors and awards in the first part of this year. Dr. Jay Goodman was the recipient of the 2005 John Barnes Prize Lecture from the British Toxicological Society and was also appointed to the International Scientific Program Planning Committee for the 11th International Congress of Toxicology to be held in Montreal, Canada, in July of 2007. Drs. John Kaneene and Stephen Boyd were named University Distinguished Professors. Likewise, this year our faculty have been highly successful in competing for extramural research support from a variety of sources including the National Institutes of Health and the U.S. Environmental Protection Agency.

A number of activities are presently ongoing within the CIT that are

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CIT Faculty Earn University Distinguished Professor Title

Two CIT-affiliated faculty have been named University Distinguished Professors in recognition of their achievements in the classroom, laboratory and community.

Stephen A. Boyd, crop and soil sciences, and John B. Kaneene, large animal clinical sciences, were among ten MSU professors to receive the honor for 2005.

MSU has given the title since



Stephen A. Boyd

1989 and the newly named individuals bring the total number of MSU University Distinguished Professors to just 94; seven of whom are currently affiliated with the CIT. Boyd and Kaneene join the following CIT-affiliates who have previously been elevated to the rank: Jack Harkema, Veronica Maher, Justin McCormick, Thomas Pinnavaia and James Tiedje.

Boyd is internationally recognized for his research and teaching of the fundamental chemical and biological processes associated with contaminated soil. Receiving worldwide attention, some recent work he published in the journal *Environmental Science and Technology* showed how dousing soils with solutions rich in everyday minerals and salts can enhance the sponge-like properties of soil clays to soak up pesticides.

Boyd's laboratory and associated collaborators have secured millions of dollars in research grant funds, have been co-authors of more than 150 peer-reviewed journal articles, and have conducted hundreds of presentations across the world. His research encompasses the movement of organics in soil; microbial and catalytic degradation; sorption and degradation of organic contaminants, pesticides and metals in soils and sediments; the remediation of contaminated soils, subsoils and sediments; and the effects of contaminant biodegradation on toxicity.

Boyd also has been a pace setting educator in graduate and undergraduate education in the environmental sciences and has served as a key investigator in the CIT's Superfund Basic Research Program project on the bioremediation of PCBs.

John B. Kaneene is renown for his application of epidemiological methods in understanding disease dynamics in populations, and the use of these methods in designing, implementing, and evaluating prevention and control strategies.

One of his areas of research is in the epidemiology of food-borne pathogens and their relationships to the development of antimicro-

bial drug resistance in animal and human populations, particularly *Campylobacter*, *Salmonella*, and *E. coli*. He is also actively involved in epidemiological studies and risk assessments of bovine tuberculosis in wildlife, livestock, and pets. As director and founder of the Population Medicine Center, Kaneene addresses issues involving epidemiology, preventive medicine, and public health on a variety of diseases.

Kaneene has trained dozens of pre- and post-doctoral students as well as veterinary medicine students; scientific publications bearing his name number over 200; and he is directly involved with the teaching of six courses.

The University Professor designation is among the highest honors that can be bestowed on a faculty member by the university. Those selected for the title have been recognized nationally and internationally for the importance of their teaching, research and public service achievements.

Individuals holding the professorship receive, in addition to their salary, a stipend of \$5,000 per year for five years to support professional activities.



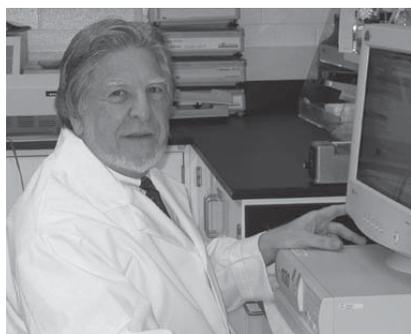
John Kaneene

Discovery Sheds Light on Cancer's Origin

James Trosko, professor of pediatrics and human development and CIT affiliate, and colleagues have found that a gene—known as Oct4—expressed in normal adult stem cells could hold the key to answering the question of how cancer originates.

The research, detailed in the February 2005 issue of *Carcinogenesis*, demonstrated that some normal adult stem cells express the Oct4 gene, a finding that supports the stem cell theory of carcinogenesis.

There was already scientific acceptance that the Oct4 gene was located in embryonic stem cells as well as tumor cells. The new observations show that adult stem cells



James Trosko

expressing Oct4 could be the target cells that initiate the carcinogenic process.

Using techniques pioneered in their lab, Trosko's team isolated adult

human stem cells to test for the expression of the Oct4 gene, whose job as a "regulatory" gene is to control the expression of other genes. They found that adult human stem cells express Oct4, but differentiated cells—those already on the way to becoming a specialized type of cell such as a kidney cell—do not.

In their paper, the researchers noted that the prevailing paradigm of carcinogenesis has a normal "mortal" cell becoming "immortalized". Their hypothesis holds that a stem cell or its early derivative daughter cell has not yet lost Oct4 expression and therefore would be naturally "immortal" until it was induced to become "mortalized", or to differentiate. This would mean that the carcinogenic process blocks the natural regulation of genes such as Oct4, which when shut off in normal cells would trigger a terminal differentiation process.

If Oct4 positive stem cells could serve as a screening marker for carcinogenesis initiation, Trosko explained, there are implications not only for the identification of pre-malignant and malignant cells, but also for identifying new cancer chemoprevention and chemotherapeutic treatments.

Trosko's co-authors included Mei-Hui Tai, a visiting research associate in physiology; Chia-Cheng

Chang, professor of pediatrics and human development; and L. Karl Olson, associate professor of physiology; Matti Kiupel, assistant professor of pathobiology and diagnostic investigation; and Joshua Webster, graduate student in veterinary medicine.

MSU Nets Two of Three EPA STAR Grants

The Environmental Protection Agency recently announced the establishment of an EPA National Center for Computational Toxicology and at the same time announced that MSU CIT-affiliated faculty would receive two of three Science to Achieve Results (STAR) grants to conduct computational toxicology research.

Timothy Zacharewski's lab received \$748,000. Zacharewski and his researchers will use a rat model to study changes in gene expression caused by estrogenic endocrine disrupting agents and develop a computational model to integrate the data.

John Giesy's research group received \$750,000 to use a small fish model to study chemically induced changes in gene expression patterns in cells, tissues, and organs that play a pivotal role in a particular endocrine pathway.

Zacharewski and Giesy's projects were chosen from nearly 250 applicants in this competitive program. The third grant was awarded to the University of Florida.

All the grants are related to developing innovative systems biology approaches to identify hazards and access risks from endocrine disrupting chemicals. Systems biology uses computational methods to create an integrated physiological and biochemical model of an organism's or cell's biology.

As EPA Science Advisor and Assistant Administrator for Research and Development, Paul Gillman, explains the new approaches will make it possible to study normal biological processes and discover how environmental chemicals can change these processes, disrupt pathways and lead to disease or other adverse health effects.

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focused primarily on enhancing our graduate training programs as well as increasing the visibility of our center within and outside of MSU. Currently, the curriculum for the graduate training program in Environmental and Integrative Toxicological Sciences is under review. Changes have been proposed that place a greater emphasis on "omics" technologies and their application to toxicologic investigations.

In addition, there is a proposal to modify several of our standing toxicology courses to more fully integrate lectures in pathology with basic principles of toxicology in a target organ format. The proposed changes are aimed at capitalizing on faculty strengths in order to better

prepare our trainees for a career in toxicological sciences in the twenty first century.

A second activity underway is to enhance the CIT web site. University web sites have become one of the primary resources for information being utilized by prospective trainees and are therefore a vital recruiting tool for today's graduate programs. It is anticipated that the new CIT web site will go live this fall.

Lastly, in light of the very strong attendance last year in New Orleans, we plan to hold a MSU Alumni Reception at the 2006 Annual Meeting of the Society of Toxicology in San Diego where we hope to see everyone.

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Trainee profile: Gautham Rao

Toxicology Expands Options

Gautham Rao's commitment to his work is clear in his advice for future CIT students to "pick a field that interests you—because you will spend four or five years thinking about it at night."

A recent doctoral graduate in pharmacology and toxicology, and environmental toxicology, Rao has been active in CIT Director Norb Kaminski's project on immune regulation by cannabinoids.

Cannabinoid compounds have been widely reported to alter immune function, particularly in T cells, but the mechanism has not been elucidated. Rao has been working on the involvement of intracellular calcium on the regulation of interleukin-2 by delta-9-tetrahydrocannabinol (THC), the primary psychoactive constituent in marijuana. Rao and his colleagues believe that THC may be working through a third but yet unidentified cannabinoid receptor to regulate intracellular calcium in resting T cells and that this mechanism contributes to the inhibition of

interleukin-2 production by THC in T cells.

"It is exciting to be working on a novel project which has not been previously done," Rao said.

Rao has submitted 17 abstracts and has five publications related to the project. He was honored with the best submission by a graduate student award from the immunotoxicology specialty section of the Society of Toxicology in 2005.

He has also received travel awards from the International Cannabinoid Research Society, the American Society of Pharmacology and Experimental Therapeutics, and the 2005 Experimental Biology meeting. He was a National Institutes of Health Ruth Kirschstein National Research Service predoctoral fellow and also a MSU Graduate Student Dissertation fellow.

Rao says he chose toxicology to have a lot of career options.

"It related to so many different fields, immunology for example, and

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Gautham Rao, doctoral candidate in pharmacology/toxicology and environmental toxicology.

Trainee profile: Grace Muna

Using Chemistry to Solve Environmental Problems

Grace Muna loved the idea of using chemistry to solve environmental problems. The opportunity to combine environmental toxicology



Grace Muna, recent doctoral graduate in Chemistry and environmental toxicology.

with chemistry was what made MSU rise to the top in her selection of a graduate school.

She has been working with Professor Greg Swain to develop electrochemical methods to detect pollutants and recently completed her doctoral degree in Chemistry and environmental toxicology.

In Swain's lab, Muna has helped to develop an extraction technique that is faster and less expensive than current protocols set by the Environmental Protection Agency. Her thesis project involved electro-oxidation and detection of chlorinated phenols using boron-doped thin-film diamond electrodes.

Historically, the fouling of the electrode has plagued electrochemical detection methods for chlorinated phenol analysis. Diamond is a new electrode material that shows little tendency to be deactivated and fouled by adsorbed reaction and

products and intermediates during the oxidation of chlorinated phenols. This new electrode reopens the door to electrochemical detection of these pollutants.

Muna has published two papers on the topic and submitted a third. She recently began postdoctoral training at Iowa State University.

Muna credits the dual degree program with "making her realize how chemistry can be applied." She noted that the toxicology courses and electives such as environmental economics stretched her and showed her how to apply knowledge to solve a problem.

Muna plans to return to her native Kenya where there are many issues with pollutants and the environment and hopes to specifically work on drinking water issues. She enjoys teaching and hopes to remain in academics.

Trainee profile: James Luyendyk

Honors, Service and Creativity Marks Training

Recent CIT doctoral graduate, James Luyendyk, has come a long way from the accounting major he started out with in his undergraduate days.

Surprisingly, it was Hollywood that gave him the needed boost in finding a career path better suited to his talents and interests. After seeing the 1996 movie "The Rock" in which actor Nicholas Cage plays a biochemist who deals with "one of the most deadly substances the earth has ever known," Luyendyk switched his major to biochemistry and has never looked back.

His graduate research at MSU focused on the methods of idiosyncratic drug reactions—those that occur in less than five percent of people taking a drug for which the liver is the primary target. These reactions have significant impact both on human health and the pharmaceutical industry, but their mechanisms are not understood.

Working with the hypothesis that an underlying inflammatory response in some patients might precipitate idiosyncratic liver injury, Luyendyk and colleagues in Professor Bob Roth's lab, have worked to develop an animal model. Luyendyk has used genomics technology for hypothesis generation and has investigated mechanisms of toxicity in the model including the hemostatic

system, neutrophils and hypoxia.

"It is great to see a relationship to human health," Luyendyk says. "I had the opportunity to look at genomics, in vivo, in vitro, statistics and basically to dabble in a lot of different things. Toxicology offers a chance to be very creative."

His work has resulted in seven presentations and nine publications, four of which received best paper awards: two from the Michigan Regional Chapter of the Society of Toxicology; one from the American Society for Pharmacology and Experimental Therapeutics, Toxicology Division; and one from the Phi Zeta Research day sponsored by the MSU College of Veterinary Medicine. He was a National Institute of Environmental Health Sciences training grant fellow and also received the SOT Novartis Graduate Student Fellowship in 2004.

He completed his doctorate in pharmacology and toxicology, and environmental toxicology, by late 2004 and has held a postdoctoral position in Roth's lab for the past nine months. He just began a second postdoctoral position at the Scripps Research Institute in LaJolla, California.

Luyendyk's enthusiasm for toxicology is evident in both his service to the Society of Toxicology, taking on the chairperson positions on the

Postdoctoral Task Force and the Student Advisory Committee; as well as his dynamic presentations to fellow colleagues at past CIT-sponsored research evenings.

He advises future students that while the dual degree may be more work "what you get in return is ten-fold."

After completing his postdoctoral training, Luyendyk plans to pursue a career in academics.



James Luyendyk, completed his doctoral degree in pharmacology/toxicology and environmental toxicology followed by postdoctoral training, both with the CIT.

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was more interesting," he said.

He noted that the dual degree course electives helped him a great deal with comprehensive exams. For example, a pathology course gave him an understanding he knows he could not have gained simply from lab training. Risk assessment, he feels, will be very useful in industrial applications later.

Rao is still keeping his options open. He plans to do postdoctoral training but is interested in government, industry and academic settings.

Three CIT Faculty Noted as Highly Cited Researchers

Three faculty affiliated with the MSU-CIT were recognized as being "highly cited researchers" over the past two decades. ISIHighlyCited.com lists the most highly cited scholars in 21 broad subjects related to life sciences, medicine, physical sciences, engineering and social sciences.

Microbiology Professor James M. Tiedje's work is frequently cited by researchers in microbiology and also in ecology and environment. Food Science Professor James J. Pestka was noted for being highly cited in

agricultural sciences; while Zoology Professor John P. Giesy is listed as the fourth most cited researcher in the ecology and environment category.

ISIHighlyCited.com is maintained by Thomson ISI, which has long tracked international journal citations in order to evaluate the impact on knowledge generation and dissemination of the journals and the scientists who publish in them.

The three CIT faculty join 16 other MSU scientists listed as highly cited.

MSU Prominent at SOT Meeting

MSU-CIT scientists were at the forefront at the 2005 Society of Toxicology annual meeting that took place in New Orleans.

Postdoctoral trainee Frances Tukov left the meeting assured of special support for his academic endeavors. Tukov was honored with the Colgate-Palmolive Postdoctoral Fellowship Award in In Vitro Toxicology. He will be developing an in vitro model for studying drug-induced idiosyncratic liver injury under the auspices of Professor Robert Roth.

Darrell Boverhoff, a trainee with Timothy Zacharewski was one of three finalists in the Novartis Graduate Fellowship. The Novartis and the Colgate-Palmolive fellowships are the SOT's top student awards.

In addition, Gautham Rao, a student of CIT director, Norb Kaminski, took first place for the best predoctoral presentation from the immunotoxicology specialty section.

Five MSU students received SOT travel awards to attend the meeting, including Lyle Burgoon, Cora Fong, and Josh Kwekel from the Zacharewski lab; Steven Bezdecny from Patricia Ganey's lab; and Ajith Vengellur from John LaPres' lab.

Overall attendance at the meeting set a record high of 6,125 attendees. Nearly 40 abstracts from MSU scientists were included in the meeting's poster presentations.

The following abstracts were presented:

Biomarkers/Biomonitoring:

Toxicologic and Pathologic Surveillance of Search & Rescue Dogs Deployed to the World Trade Center, The Pentagon and The Staten Island Fresh Kills Landfill Sites, W. Rumbelha; S. Fitzgerald; E. Braselton; C. Otto; A. Downend

Carcinogenesis:

Changes in the Methylation Status of GC-Rich Regions of DNA During the Promotion Stage of Skin Tumorigenesis, A. Carnell-Bachman; G. Curtin; D. Doolittle; J. Goodman

β -Sitossterol in Psyllium Seed Husk Restores Gap Junctional Intercellular Communication in Ha-ras Transfected Rat Liver Epithelial Cells, Y. Nakamura; I. Hiroki; N. Yoshikawa; K. Sato; K. Ohtsuki; C. Chang; B. Upham; J. Trosko

Epigenetic Effects of Oxidative Stress, B. Upham; J. Trosko

Diethanolamine (DEA) and Phenobarbital (PB) Produce an Altered Pattern of Methylation in GC-rich Regions of DNA in B6C3F1 Mouse Hepatocytes Similar to that Resulting from Choline Deficiency, J. Goodman; L. Kamendulis; A. Carnell-Bachman

Mode of Action and Human Relevance of Phenobarbital-Like Rodent Liver Carcinogenesis, A. Boobis; B. Lake; E. Harpur; J. Rice; J. Goodman



Gautham Rao (left) received a best presentation award and Frances Tukov took the coveted Colgate-Palmolive Postdoctoral Fellowship at the SOT meeting.

Gene Regulation:

Analysis of Gene Expression During Uterine Induction and Regression in Immature, Ovariectomized Rats Following Treatment with Ethynyl Estradiol, J. Kwekel, H. Dalgleish; L. Burgoon; J. Harkema; T. Zacharewski

Microarray Examination of TCDD Mediated Changes in Gene Expression in Hepa1C17 Murine Hepatoma Cells, E. Dere; D. Boverhoff; L. Burgoon; T. Zacharewski

DBZACH: A Comprehensive Toxicogenomic Information Management and Knowledge Discovery System, R. Aiyar; L. Burgoon; P. Boutos; E. Dere; S. Doran; S. Pai; J. Vakharia; R. Rotman; A. Adams; B. Lau; R. Patel; T. Zacharewski

Protocols for the Assurance of Microarray Data Quality and Process Control, L. Burgoon, J. Eckel_Passow; C. Gennings; D. Boverhoff; J. Burt; C. Fong; T. Zacharewski

Temporal Gene Expression Analysis of Mouse Hepa-1C17 Cells Treated with 17 β -Estradiol by cDNA Microarray, C. Fong; L. Burgoon; R. Gupta; D. Humes; T. Zacharewski

Computational and Empirical Investigation of Estrogen and Dioxin Elicited Effects: A Comparative Analysis, T. Zacharewski

Effects of Estrogen on Immature, Ovariectomized Mice: A Multi-approach, Tissue-by-Tissue Comparison, J. Burt; L. Burgoon; D. Humes; J. Kwekel; A. Harney; J. Harkema; T. Zacharewski

Role of Nutrigenomics in Safety Assessment of Functional Foods, M. Soni; T. Zacharewski

Non-Additive Dose Dependent Gene Expression Patterns Exhibited by a Mixture of 17-Alpha Ethynylestradiol and Genistein In Vivo, R. Gupta; L. Burgoon; A. Harney; D. Boverhoff; J. Kwekel; C. Gennings; T. Zacharewski

Activation of the Transcription Factor AP-1 by 2, 2', 4, 4'-Tetrachlorobiphenyl (TCB) Involves Extracellular Signal-Regulated Kinases (ERKs) Enhanced Expression of c-fos Protooncogene and Rat Liver Cells, G. Chen; B. Madhukar; B. Wood

Liver:

Augmentation of Lipopolysaccharide-Induced Gene Expression and Liver Injury by Rantidine but not Famotidine, J. Luyendyk; L. Lehman-McKeeman; D. Nelson; V. Bhaskaran; B. Car; G. Cantor; C. North; S. Newport; J. Maddox; P. Ganey; R. Roth

Libopolysaccharide Potentiates Acetaminophen Hepatotoxicity, S. Newport; C. Dugan; X. Deng; P. Ganey; R. Roth; J. Maddox

Inhalants and Cardiopulmonary:

Exposure to Concentrated Ambient Particles in Detroit Alters Heart Rate Variability in Spontaneously Hypertensive Rats, J. Wagner; L. Wichers; M. Morishita; A. Rohr; G. Keeler; J. Harkema

YM1/2 Chitinase Proteins in Murine Nasal Epithelium after a 13-week Inhalation Exposure to Ultrafine Carbon Black Particles, J. Harkema; P. Santhanam; J. Wagner; L. Bramble; A. Elder; G. Oberdorster

Exposure to Concentrated Ambient Particles in Detroit, Michigan Causes Heart Rate and Thermoregulatory Changes in Spontaneously Hypertensive and Wistar-Kyoto Rats, A. Rohr; J. Wagner; M. Morishita; G. Keeler; J. Harkema

Immunotoxicity:

Δ 9-Tetrahydrocannabinol Alters Host Resistance to Influenza A/PR/8 Infection in C57BL/6 Mice, J. Buchweitz; N. Kaminski; J. Harkema

SOT, continued from 6

Interferon-Gamma Reverses TCDD-Mediated Suppression of the IGM Antibody Response and Attenuates CYP1A1 Induction, N. Kaminski; B. Kim; R. Crawford; M. Holsapple

Δ 9-Tetrahydrocannabinol (Δ 9-THC) Elicits a Calcium

See SOT, page 7

Faculty Spotlight: Giesy Named Canada Research Chair

World renowned ecotoxicologist, John Giesy, will soon retire from his 25 year career as MSU professor. However, as professor emeritus he plans to not only remain actively engaged at MSU with graduate students and ongoing projects with the US EPA, State of Michigan and Dow Chemical; but also has accepted the Canada Research Chair of Environmental Toxicology and Chemistry, placed at the University of Saskatchewan (U of S).

The U of S successfully competed to obtain the chair and recently recruited Giesy to fill the position. He will be a professor of Biomedical Sciences in the Western Veterinary College and a member of the Toxicology Centre, a multidisciplinary program much like the CIT at MSU.

Giesy, who came to MSU in 1981 after eight years at the University of Georgia, will not have teaching or administrative responsibilities, freeing him to fully concentrate on research and training. Positions are being provided for any of his many associates and students who wish to go; although some will stay at MSU under his direction with grants such as the EPA Star Grant highlighted on page 3.

Giesy has set an enviable pace in productivity, resulting in the publication of over 500 peer-reviewed articles and over 800 lectures world-wide. He has secured more than \$41 million in grants and contracts to conduct studies across the globe. He has also trained dozens of students and is one of the most highly cited researchers in the world.

Not surprisingly, Giesy has received numerous National and International awards and honors for his work as a scientist, educator and public servant. An honor he holds as key, however, is the



John Giesy developed this unique underground “window” to unobtrusively observe kingfishers, one of the top predators on the Tittabawassee River.

recent recognition his research group received as the fourth most cited lab in all fields of ecology by Thomson ISI. (See article on page 5.)

“It shows that what we are doing at MSU is being paid attention to and valued,” Giesy said.

Giesy’s work in many other countries, including China, Japan, Korea and Vietnam, will continue to expand. He has been active in establishing numerous studies and monitoring programs aimed at preventing the environment from falling victim to economic development. He maintains a lab base in Hong Kong for these efforts.

Whether conducting ecological risk assessment around Michigan’s Tittabawassee River or in Beijing, China; Giesy

relishes the scientist’s role as the “quiet voice of reason” between land owners, corporate concerns, government, and affected citizens.

So far, he says two research accomplishments come to the forefront in importance to him. One was the discovery of perfluorinated compounds (PFAs) in the environment by his lab which led to them being banned and the development of replacement “green chemicals.” The other is an in vitro assay using molecular techniques that permit researchers to screen for endocrine disruptor effects. He estimates the new approach will save some 250 million rats.

Giesy will maintain an MSU office in years to come, allowing his MSU legacy to continue growing.

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Elevation in T Cells Through the TRPC Channels, G. Rao; N. Kaminski

The Endogenous Cannabinoid, 2-Arachidonyl-Glycerol, Suppresses NF-AT Nuclear Translocation and Interferon- γ Kaminski

Metals:

The Role of Hypoxia Inducible Factor 1 α in Cobalt Chloride Induced Cell Death in Mouse Embryonic Fibroblasts; A. Vengellur; J. LaPres

Persistent Organic Chemicals:

The Role of Superoxide Anion in 2, 2', 4, 4'-Tetrachlorobiphenyl-Induced Upregulation of COX-2 in HL-60 Cells, S. Bezdecny; R. Roth; P. Ganey

Temporal and Dose-Dependent Hepatic Gene Expression Patterns in Mice Provide New Insights into TCDD-Mediated Hepatotoxicity, D. Boverhof; L. Burgoon; C. Tashiro; B. Chittim; J. Harkema; T. Zacharewski

Pesticides:

Profiling Gene Expression in Human H295R Adrenocortical Carcinoma Cells and Rat Testes to Identify Pathways of Toxicity for Conazole Fungicides, H. Ren; J. Schid; J. Retier;

Y. Turpaz; X. Zhang; P. Jones; J. Newsted; J. Giesy; D. Wolf; C. Wood; W. Bao; D. Dix

Magnetic Resonance Imaging and Computational Fluid Dynamics Simulations of Rabbit Nasal Airflows for Hybrid CFD/PBPK Modeling of Methyl Iodine, H. Trease; K. Minard; L. Trease; R. Corley; J. Kimbell; J. Harkema; J. Kinzell; M. Gargas

Receptors:

Involvement of Kinase Signaling Pathways in Ah-Receptor Mediated Gene Expression in Rat Liver Cells, B. Madhukar; G. Chen; C. Sorrentino; M. Denison

Grants/Contracts Received by CIT faculty affiliates

Nearly 5 million accepted by MSU Board

MSU CIT-affiliated faculty netted over four million dollars in research contracts and grants that have been accepted by the MSU Board of Trustees at their meetings so far in 2005. Totalling \$4,301,953, these awards come from a wide variety of sources including the National Institutes of Health; the United States Departments of Agriculture and of Energy; the State of Michigan; other government agencies; corporations and other Universities. The following list includes the principle investigator (PI), the PI's primary department, co-PIs, amount (rounded to the nearest dollar), title, agency and date awarded.

Bourquin, Leslie D; Food Science & Human Nutrition; \$99,865; Improving the Safety of Fresh Fruits and Vegetables with Chlorine Dioxide Gas Using a Miniaturized Industrial-Size Tunne; Purdue University; Sept. 2004.

Ewart, Susan L; Large Animal Clinical Sciences; \$315,762; Positional Candidate Genes for Airway Responsiveness; NIH/PHS; Aug. 2004; \$123,549; Asthma Positional Candidate Genes in Mice and Humans; Children's Hospital of Cincinnati; April 2005.

Giesy, John P; Zoology; \$53,838; Development of an Assay Using the H295r Cell Line to Identify Chemical Modulators of Steroidogenesis and Aromatase Activity; Entrix Inc.; April 2005.

Goodman, Jay I; Pharmacology & Toxicology; \$50,000; Altered DNA Methylations in Carcinogenesis; R J Reynolds Tobacco Company; December 2004; \$1,000; Examination of Altered DNA Methylation as a Mechanism Underlying Diethanolamine Carcinogenesis; American Chemistry Council; April 2005.

Harkema, Jack R; Pathobiology & Diagnostic Investigation; Wagner, James G; \$45,610; Detroit Exposure and Cardiovascular Health Studies: Toxicological Component; Electric Power Research Institute; August 2004;

\$216,214; Fine Airborne Particles and Allergic Airway Disease; Health Effects Institute, May 2004; \$167,440; Nasal Injury in Infant Monkeys Exposed to Ozone; Uema, Jack R; Pathobiology & Diagnostic Investigation; \$27,609; UNC Knockout Studies; University of North Carolina; May 2005.

Hollingworth, Robert; Entomology CANR; Miyazaki, Satoru; \$4,000; IR-4 Fungicide/Herbicide/Insecticide and Field Efficacy Studies; Rutgers University; October 2004; Chen, Zhongxia; \$12,000; A National Agricultural Program: Clearance of Chemicals and Biologics for Minor or Special Uses/Pesticides; Rutgers University; August 2004.

Kaminski, Norbert E; Pharmacology & Toxicology; \$261,625; CB1/CB2 Dependent and Independent T Cell Modulation; NIH/PHS; February 2005.

Kaneene, John B; Diagnostic Center for Population & Animal Health; Mauer, Whitney Allyson; \$200,467; Michigan Stridesystem to Report Integrated Diseases Events: Phase IV; Michigan Community Health; October 2004; Daniel L; Wolf, Christopher A; \$123,819; Michigan Johnes Disease Control Program; USDA - Animal and Public Health Inspection Service; Sept. 2004.

Karmaus, Wilfried J; Epidemiology; \$20,814; Ambient Air Pollution and Adverse Birth Outcomes; Michigan Community Health; October 2004.

Linz, John E; Food Science and Human Nutrition; \$213,038; Iafatoxin B1 Biosynthesis in *Aspergillus Parasiticus*; NIH/PHS; April 2005.

McCormick, J Justin; COM Research and Advanced Study Programs; Maher, Veronica M; \$332,638; Tranformation of Infinite Life Span Human Fibroblasts; NIH/PHS; May 2005.

Paneth, Nigel; Epidemiology; \$162,470; Molecular Antecedents of Brain Damage in Preterm Infants; Children's Hospital of Boston; December 2004; Rahbar, Mohammad H; \$136,036; Phase 1 Study of Thyroid Hormone in Prematures; New York Medical College; December 2004.

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