

IET Update

Michigan State University

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Strategic planning Vision for MSU Toxicology

The MSU Institute for Environmental Toxicology recently completed a five year strategic plan for building upon the success of the toxicology effort at MSU. The plan represents the culmination of a two year planning and visioning process involving affiliated faculty, University administrators, an outside consultant, and three external reviewers.

IET Director Lawrence Fischer reports that the plan provides direction for strengthening MSU's toxicology efforts in graduate education, extramural funding, and community outreach and will enhance MSU's reputation as a nationally recognized academic center for toxicological sciences.

"Toxicology is a discipline that defies categorization as it crosses

many disciplinary boundaries," Fischer said. "The challenge is to continue to bring together faculty with disparate expertise from a variety of departments."

In a final report from two of the

"Toxicologists at MSU enjoy a good reputation among peers and continue to be leaders in the field."

--External Reviewer

external reviewers, an observation was made that "Currently, there remains an impressive cadre of

See Plan, page 2

Evidence of Toxicology Research Excellence:

IET-administered grants:

- NIH/NIEHS Superfund Basic Research Program
-nearly 2.5 million each year, now in 15th year of funding
- NIH/NIEHS Training Grant
-about \$275,000 each year, now in 15th year of funding

Annual Competitive Extramural Funding by IET-affiliated faculty*:

- NIH – over \$7 million
- EPA – over \$500,000
- LSC – over \$1 million
- NSF – over \$350,000
- Other sources – nearly \$5 million

In relationship to MSU overall, IET-affiliated faculty netted 33 percent of NIH funding granted to MSU in 2001 and received the only NIH training grant given to the University.*

**Based on 2001 funding.*



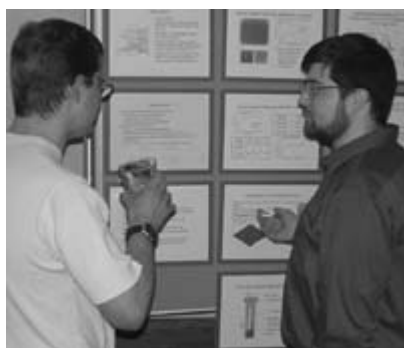
Trainee enthusiasm marks IET research night

The IET recently hosted a research evening at the Coral Gables Restaurant in East Lansing for trainees in the Multidisciplinary Doctoral Program in Environmental Toxicology.

Lively discussions characterized the event, as trainees from various departments and in various stages of their graduate careers exchanged experiences and shared their research results over dinner and in more formal poster presentations and talks.

Nearly all the doctoral students and several postdoctoral fellows in the Program attended. The event also attracted several first-year students considering application to the Multidisciplinary Doctoral Program.

Two talks were given by students about to defend their doctoral theses. Michael Lang, student in Resource Development, described his work identifying and monitoring potential hazards from runoff and other sources in the Red Cedar River, and Katie Coady, student in Zoology, summarized her studies of developmental effects in frogs exposed to atrazine at environmental concentrations.



Jason Stotter, right, Chemistry, discusses his research poster with Steve Bezdecny, Pharmacology and Toxicology.

IET Director Lawrence Fischer gave a short summary of the recently completed strategic planning process for MSU toxicology (see page 1).

Two dozen posters were presented in a poster session, representing the broad range of research being conducted at MSU in various areas of environmental toxicology. The posters included:

- development of new chemical and “nanochip” methods to detect environmental toxicants
- laboratory studies designed to understand effects of

chemicals on the central nervous system, immune system, liver and reproductive organs

- studies of fate of chemicals in the environment
- field studies on environmental chemical effects on birds, mink and other wildlife.

Robert Roth, professor of Pharmacology and Toxicology and IET-affiliated professor, noted that “kudos should go to our students and postdocs for making this gathering an enjoyable success.”



From left: Perna Sonthalia, Chemistry; Martha Perez, Crop and Soil Science; Dina Gersten, Pharmacology and Toxicology; Kirpal Sidhu, IET; Grace Mutaaga, Chemistry.

Plan, from page 1

productive scientists at MSU working in the field of toxicology, and there is every reason to expect that MSU will continue its substantial contributions to toxicology research and education into the future.”

The two reviewers also noted that, “MSU has one of the strongest and most productive graduate education programs in toxicology in the nation.” The third reviewer pointed out that “Toxicologists at MSU enjoy a good reputation among peers and continue to be leaders in the field.”

The faculty involved in preparing the strategic plan included Steve Bursian, Karen Chou, Patricia Ganey, John Giesy, Jay Goodman, Jack Harkema, Norbert Kaminski, John La Pres, John Linz, James Pestka, Robert Roth, James Trosko and Tim Zacharewski. In addition, consultant Brad Lawton of Strategic Partners played a significant role in researching and advising throughout the process and in writing the final report.

The plan is currently being reviewed by MSU’s administration for final decisions before implementation.

Alumni profile

Translating science into service

IET alumnus Stephanie Miles-Richardson has coupled her scientific expertise with a personal commitment to make an impact.

In her position as the Minority Health Program Manager, in the Office of Urban Affairs, Agency for Toxic Substances and Disease Registry (ATSDR), located in Atlanta, Georgia, Miles-Richardson is charged with providing leadership and policy over-site for programs in minority health and environmental justice. In her own words, it is an opportunity to “translate science into service.”

When Miles-Richardson came to MSU with a veterinary degree from the Tuskegee School of Veterinary Medicine already in hand, she envisioned a future related to public health, but most likely in veterinary pathology, perhaps in her research area of endocrine disruption in fish.

“Once I really got into environmental toxicology, I got excited,” she notes. And, a risk assessment

course she elected to take had an indelible impact. Taught by Mike Kamrin, IET-professor emeritus, and Karen Chou, professor of animal science, this course helped her identify public policy as an area she would find both personally gratifying as well as a good fit for her expertise and interests.

Miles-Richardson became a commissioned officer in the United States Public Health Service after completing her Ph.D. degree in Pathology and Environmental Toxicology and postdoctoral training at MSU six years ago. Initially, she served as a scientific and technical advisor for academic research with the Minority Health Professions Foundation but was promoted to her current position nearly two years ago.

Her responsibilities range from implementing research programs to developing educational models and working directly with communities affected by environmental hazards. She credits her multidisciplinary toxicology training at MSU as



Stephanie Miles-Richardson, DVM, PH.D., 1992 IET alumna.

essential for putting her technical skill to use in developing minimal risk levels and setting standards, as well as for effectively interacting with communities.

Miles-Richardson's genuine passion for her work shines through in her advice to current IET students: “Do something you love, and you'll never have to work.”

Giesy receives SETAC award

“The environmental toxicology program at Michigan State University is among the best in the world, due in no small part to your efforts of the past 22 years,” was part of the award citation Professor John Giesy recently received in recognition for a career of significant contributions to environmental education.

Giesy was one of nine top environmental scientists honored with an award at the 23rd Annual Meeting of the Society of Environmental Toxicology and Chemistry late last year, receiving the prestigious Environmental Education Award for 2002.

SETAC cited his training of over 100 graduate students, post docs or visiting scientists, noting that his

list of former students “is a veritable Who's Who of excellence in environmental science.”

Giesy was also cited for short courses he has taught world wide and his many endeavors in educating leaders of business, industry and government on ecological risk assessments and manufacturing safety. In addition, his efforts to educate the public through numerous media appearances was noted, as was his education of peers through the publication of some 500 scientific papers.

In accepting the award, Giesy credited his “attentive, diligent, receptive” students and commented that as an educator “first and foremost”, being recognized for

education is the greatest honor he could receive.

Giesy was previously honored by with a SETAC founders Award for his career as a research scientist and is a charter member and former president of SETAC.



John Giesy.

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Student profile: Kirsten Fertuck

Awards and honors highlight doctoral training

For future doctoral students, Kirsten Fertuck will be a tough act to follow.

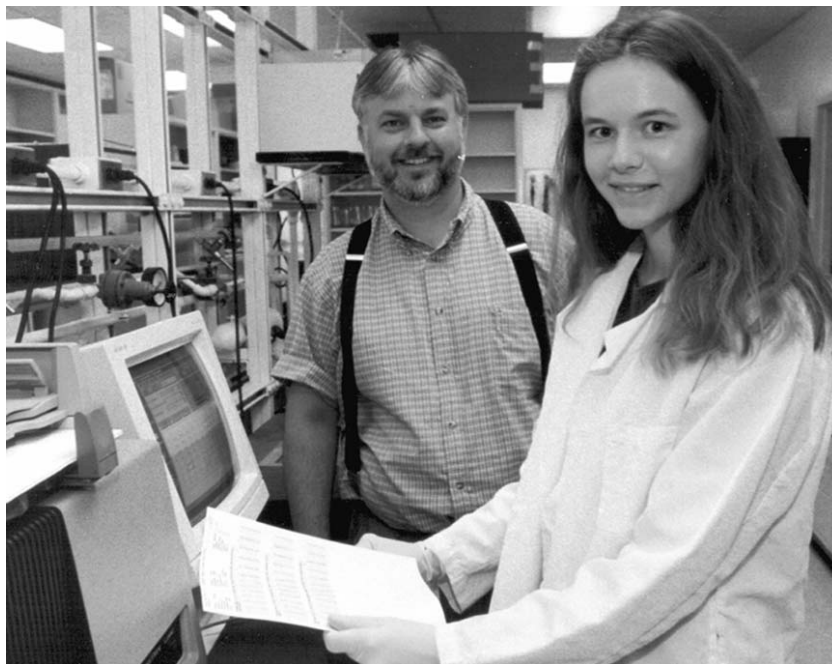
The IET multidisciplinary doctoral student has received an impressive five full years of non-departmental funding including this year's Barnett Rosenberg Fellowship awarded by the College of Natural Science, last year's highly competitive Covance Fellowship from the Society of Toxicology, and three years of previous funding through MSU fellowships.

Fertuck has also been the recipient of ten prestigious honors including the 2002 Outstanding Graduate Student Award from the MSU Chapter of Sigma Xi. She is particularly proud of her 1999 honorable mention in the Howard Hughes Predoctoral Fellowship in Biological Sciences. Meanwhile, she has over two dozen publications, presentations and posters to her credit.

As an undergraduate Fertuck was no less impressive, raking in four different competitive scholarships related to academic achievement and graduating with high distinction.

She chose MSU for her doctoral training in order to work with IET-affiliated professor Tim Zacharewski.

Fertuck had heard Zacharewski in a guest lecture at the University of Toronto. Zacharewski was then at the nearby University of Western Ontario. When nearing graduation, Fertuck contacted him about joining his lab and learned he had moved to MSU's Biochemistry and Molecular Biology Department. Undaunted, she packed her bags and left Canada, though she was thankful to still be close enough to visit family



Kirsten Fertuck and her advisor Tim Zacharewski.

in Toronto regularly.

Fertuck majored in environmental toxicology in her undergraduate program. Adding biochemistry to her doctoral training was a departure but she noted that the multidisciplinary option made it easy to meld her interests.

"If I had switched to biochemistry completely, I would be trying to incorporate environmental toxicology on my own," she said. "The dual degree has allowed me to maintain a broad focus."

Fertuck's research involves the mechanisms of polycyclic aromatic hydrocarbon (PAH) interference with estrogen action. PAHs are common byproducts from the burning of carbon compounds, including from car exhaust or

manufacturing processes. She relishes the controversy and scientific challenge of refining tests used to detect estrogenic activity.

"Some researchers have reported certain PAH's to be estrogenic while other researchers have found these same compounds to act as anti-estrogens," she said. "So finding which *in vitro* tests can be reconciled with findings from tests in animals is an important question." Their latest work has involved using microarrays to identify new gene transcripts that are affected by estrogens, and then examining the effects of PAHs on these markers.

Fertuck expects to complete her degree in the spring and then plans on post doctoral training. She is currently deciding between several training options.

Student profile: Belinda Hawkins

EPA beckons recent graduate

Belinda Hawkins will soon be one block from the White House, working as a post doc at the U.S. Environmental Protection Agency in Washington, D.C.

Hawkins recently completed her Ph.D. dissertation work, earning the IET-administered multidisciplinary degree in Pharmacology and Toxicology and Environmental Toxicology.

Before coming to MSU, she did a stint as a Public Health Sanitarian for the Oakland County Health Division in Southfield, Michigan. She holds a B.S. degree from Indiana State University in Environmental Health Science and Industrial Hygiene.

Hawkins noted that MSU's multidisciplinary degree allowed her to add biological science to her

training in physical sciences as well as providing a way to blend in a strong interest in ecology. The multidisciplinary approach also kept her options open regarding career direction. Originally, she thought she would go into research, but found she was drawn to regulatory toxicology.

Her research has focused on the effects of the drug cyproheptadine on insulin synthesis in the endocrine pancreas. She recently was honored with the Scientific Achievement Award for the best poster presentation by a graduate student at the Michigan Chapter of the Society of Toxicology's Fall Meeting. Her advisor has been IET Director, Lawrence Fischer.

She advises current and future toxicology graduate students to "make sure to pick a research project you love". She can attest that her enthusiasm for her research sustained her when the work was difficult and the hours were long.

She believes her research training and understanding will be essential to becoming an effective regulator.

Hawkins was funded by the National Institutes of Environmental Health Sciences training grant, awarded through IET.



Belinda Hawkins, recent IET Ph.D. graduate.

Notable affiliates of IET:

W. Emmett Braselton, professor and section chief of the Veterinary Diagnostic Center's Toxicology Section, retired after 25 years at MSU. A retirement reception was held in his honor in February. The College of Veterinary Medicine newsletter noted "Under his leadership, the Toxicology Section became nationally recognized for its excellence in veterinary diagnostic medicine."

James Pestka, professor of Food Science and Human Nutrition; and Microbiology and Molecular Genetics, recently authored [Mycotoxins: Risks in Plant, Animal, and Human](#)

[Systems](#) for The Council for Agricultural Science and Technology. The report, available at <http://www.cast-science.org>, provides policymakers and others with the most complete current information on mycotoxins, along with recommendations for minimizing their risk to plants, animals, and humans. This comprehensive report, a collaborative effort by 38 international scientists, covers mycotoxin-producing fungi; mycotoxin control in crops, foods, and feeds; mycotoxin-caused disease in humans and animals; mycotoxin testing, control, and international regulation; economics; and research

and policy recommendations.

James Luyendyk, IET multidisciplinary doctoral candidate, recently published "Augmentation of Aflatoxin B1 Hepatotoxicity by Endotoxin: Involvement of Endothelium and the Coagulation System" in [Toxicology Science](#). He also received the Best Poster Presentation award in the resident/intern/graduate student category at the 2002 Phi Zeta Research Day. He serves as co-chair of the Society of Toxicology Student Advisory Committee and as a committee chair for the Michigan Regional Chapter of SOT.

MSU strong at 2003 SOT Meeting

The 42nd Annual Society of Toxicology meeting was held March 9-13, 2003 in Salt Lake City, Utah. Representation from Michigan State University scientists included over 40 abstracts as well as two awards.

Awards:

William D. Atchison, IET-affiliated professor of Pharmacology and Toxicology, is the recipient of the 2003 SOT AstraZeneca Traveling Lectureship Award. The award, given in recognition of excellence in research and service in toxicology, will provide funding for Atchison to undertake a lecture tour of Europe. The awards are intended to familiarize recipients with research and regulatory issues in Europe while also bringing a North American perspective to those issues. A proposed itinerary combines Atchison's interests in the toxicology of industrial-type chemicals with his interests in several areas of pharmaceuticals. Lecture sites include University and pharmaceutical labs in The Netherlands, Germany, Spain and The United Kingdom. He will have the opportunity to discuss GABA_A receptors, methylmercury neurotoxicology, calcium-dependent pharmacology and other cellular actions with scientists investigating in similar areas.

Rebecca Watson, a graduate student working with Jay Goodman, IET-affiliated professor of Pharmacology and Toxicology, received a travel award from the Regulatory and Safety Evaluation Specialty Section and the second place award for the best student presentation from the Carcinogenesis Specialty Section.

Abstracts:

Carcinogenesis

Altered Methylation as a Possible Biomarker of Toxicity. *J. McKin; R. Watson; G. Cockerell; J. Goodman.*

Epigenetics Of Cancer.

R. Roberts; J. Moggs; J. Goodman; J. Trosko.

Aberrant DNA Methylation is a Mechanism Involved in Tumor Promotion. *R. Watson; G. Curtin; D. Doolittle; J. Goodman.*

Induction of Differentiation by Kaempherol in GJIC-Sufficient but not in GJIC-Deficient Colon Cancer Cells. *Y. Nakamura; C. Chang; T. Mori; K. Sato; K. Ohtsuki; B. Upham; J. Trosko.*

Polycyclic Aromatic Hydrocarbons with Bay-like Structures Inhibited Gap Junctional Intercellular Communication in Immortalized Human Pancreatic Ductal Epithelial Cells. *M. Tai; B. Upham; J. Trosko.*

The Role of Phosphatidylcholine PLC in the Inhibition of Gap Junction Communication, Activation of MAPK, and the Release of Arachidonic Acid by Specific Isomers of Methylated Anthracenes. *B. Upham; P. Tithof; J. Trosko.*

Endocrine System

Interaction Analysis of Synthetic Xenoestrogens and Phytoestrogens In Vivo. *G. Charles; C. Gennings; T. Zacharewski; B. Gollapudi; E. Carney.*

Cyproheptadine Alters Translation Initiation in RINm5F Cells. *B. Hawkins; L. Fischer.*

Food Safety/Nutrition

Kinetics of Deoxynivalenol (Vomitoxin) Distribution and Clearance Following Oral Exposure in the Mouse. *P. Yordanova; Z. Islam; J. Pestka.*

Human Cytokine mRNA Response to Deoxynivalenol (vomitoxin) Using Whole Blood Cultures. *K. Penner; J. Gray; J. Pestka.*

Gene Expression

A Diorthochlorinated PCB Congener 2,2',4,4'-tetrachlorobiphenyl (TCB) Activates Extracellular Signal Regulated Kinases (ERKs) Independent of Protein Kinase C (PKC) in JB6 Mouse Epidermal Cells. *B. Madhukar, O. Hernandez-Maldonado.*

Use of an Empirical Bayes Screening Approach and Gene Ontology Annotations to Filter and Interpret Microarray Data from the Uteri of Estrogen-Treated Mice. *K. Fertuck; J. Eckel; C. Gennings; T. Zacharewski.*

Temporal Gene Expression Profiles of Human Fetal Astrocyte Cells Treated with a Neurotoxicant, 6-Aminonicotinamide. *T. Yamada; L. Burgoon; K. Kwain; M. Fielden; J. Trosko; T. Zacharewski.*

Airway Cytokine Gene Expression as a Biomarker of Chemical-Induced Airway Allergenicity. *N. Kaminski; A. Farraj; J. Harkema.*

Genomics, Proteomics and Bioinformatics

In Silico Identification of Estrogen Response Elements in Human and Mouse Sequences. *Y. Sun; K. Fertuck; T. Zacharewski.*

DBZACH: An Integrative Toxicogenomic Supportive Relational Database System. *L. Burgoon; P. Boutros; E. Dere; Y. Sun; R. Aiyar; J. Vakhari; T. Zacharewski.*

Hypersensitivity

Pathologic and Immunologic Responses in the Respiratory Tract of A/J Mice After Intranasal Sensitization and Challenge with Trimellitic Anhydride. *A. Farraj; J. Harkema; N. Kaminski.*

Immunotoxicity

Temporal Effects of Ah Receptor Ligands on Ch12Lx Murine B-Cell Lymphoma Cell Gene Expression: CDNA Microarray Analysis, Real-Time PCR Verification and Bioinformatic Assessment. *M. Fielden; D. Boverhof; T. Zacharewski.*

Tetrahydrocannabinol (THC) Increases Intracellular Calcium in a Cannabinoid Receptor-Dependent Manner In T Cells. *G. Rao; N. Kaminski.*

Inhibition of Interleukin-2 (IL-2) by the Endogenous Cannabinoid, 2-arachidonyl Glycerol, is Partly Mediated Through Peroxisome Proliferator-Activated Receptor-(PPAR-). *C. Rockwell; N. Kaminski.*

Transcriptional Regulation of the HS4 Domain through a DRE and B Motif. *C. Sulentic; Y. Na; S. Fintushel; N. Kaminski.*

Deoxynivalenol-Induced Apoptosis Mediated by p38 MAPK-Dependent p53 gene Induction in RAW 264.7 Macrophages. *H. Zhou; J. Pestka.*

Role of IL-1beta in LPS Potentiation of Deoxynivalenol-Induced Leukocyte Apoptosis in Mice. *Z. Islam; J. Pestka.*

Omega-3 Fatty Acids from Fish Oil Suppress IGA Nephropathy Induced by the Mycotoxin Deoxynivalenol. *Q. Jia; H. Zhou; Z. Islam; J. Pestka.*

Suppression of Deoxynivalenol-Induced IL-6 by Fish Oil and Relationship to Mitogen-Activated Protein Kinase Activation. *Y. Moon; J. Pestka.*

Effects of Dietary Omega-3 Fatty Acids on Deoxynivalenol-Induced Global Gene Expression *In Vivo*. *S. Kinser; Q. Jia; A. Laughter; P. Cornwell; C. Corton; J. Pestka.*

Dose Response Effects of Eicosapentaenoic Acid on Experimental IGA Nephropathy Induced by the Trichothecene Deoxynivalenol. *Y. Shi; J. Pestka; Q. Jia.*

Hck- and PKR-Dependent Mitogen-Activated Protein Kinase Phosphorylation and AP-1, C/EBP and NF-kappaB Activation Precede Deoxynivalenol-Induced TNF-alpha and MIP-2 Expression. *J. Pestka; H. Zhou.*

Expression of Cyclooxygenase-2 in HL-60 Cells Exposed to Polychlorinated Biphenyls. *S. Bezdecny; R. Roth; P. Ganey.*

Inhalants, Particles & Gases

Comparative Dose-Related Effects of Inhaled Carbon Black Particles in the Lungs of Rats, Mice, and Hamsters. *A. Elder; N. Corson; R. Gelein; P. Mercer; J. Finkelstein; P. Keng; J. Harkema; K. Driscoll; G. Oberdorster.*

Rats, But Not Hamsters, have Persistent Alveolitis and Type II Cell Proliferation After Chronic Inhalation of Carbon Black Particles. *J. Harkema; J. Wagner; J. Simon; S. McBride; A. Elder; K. Driscoll; G. Oberdorster.*

Mucous Cell Metaplasia in Rat Nasal Epithelium After a 13-Week Exposure to Carbon Black Particles. *J. Harkema; J. Wagner; L. Bramble; A. Elder; G. Oberdorster.*

Effects of Co-exposures of Concentrated Ambient Particles and Allergen on the Lungs of Brown Norway Rats. *J. Wagner; J. Harkema; C. Siotis; E. Timm; N. Kaminski; M. Kleinman; J. Froines.*

Liver/Gastrointestinal System

Activation of Signal Transduction Pathways in Hepatic Parenchymal Cells are Required for Neutrophil-dependent Killing. *B. Copple; B. Woolley; C. Rondelli; P. Ganey; R. Roth.*

15-Deoxy-Prostaglandin J2 Enhances Allyl Alcohol-Induced Toxicity in Rat Hepatocytes. *J. Maddox; R. Roth; P. Ganey.*

Modest Inflammation Renders Ranitidine Hepatotoxic: Is there a Relationship to Drug Idiosyncrasy? *J. Luyendyk; J. Maddox; G. Cosma; P. Ganey; G. Cockerell; R. Roth.*

The Role of the Coagulation System in Synergistic Liver Injury Caused by Monocrotaline and Bacterial Endotoxin Coexposure. *S. Yee; P. Ganey; R. Roth.*

Matrix Metalloproteinases in Monocrotaline-Induced Liver Injury. *U. Hanumegowda; B. Copple; M. Shibuya; P. Ganey; R. Roth.*

Neurotoxicity

Camp and Retinoic Acid Induced Differentiation of Human SVG Cells: Morphologic and Transcriptional Effects. *L. Burgoon; K. Kwan; J. Trosko; T. Zacharewski.*

Expression of Calbindin D-28k Correlates with Decreased Methylmercury (Mehg) Cytotoxicity in Myenteric Plexus Neurons. *J. Edwards; W. Atchison.*

Stem Cells

Use and Application of Stem Cells in Toxicology. *G. Cosma; M. Thiede; S. Strom; J. Johnson; J. Trosko.*

Use of Human Adult Pluripotent Stem Cells to Screen for Genotoxic/Epigenetic Toxicants. *J. Trosko.*

For more information on MSU-IET, visit our web site at www.iet.msu.edu





Tiedje lab discovery

River microbe gobbles up pollution

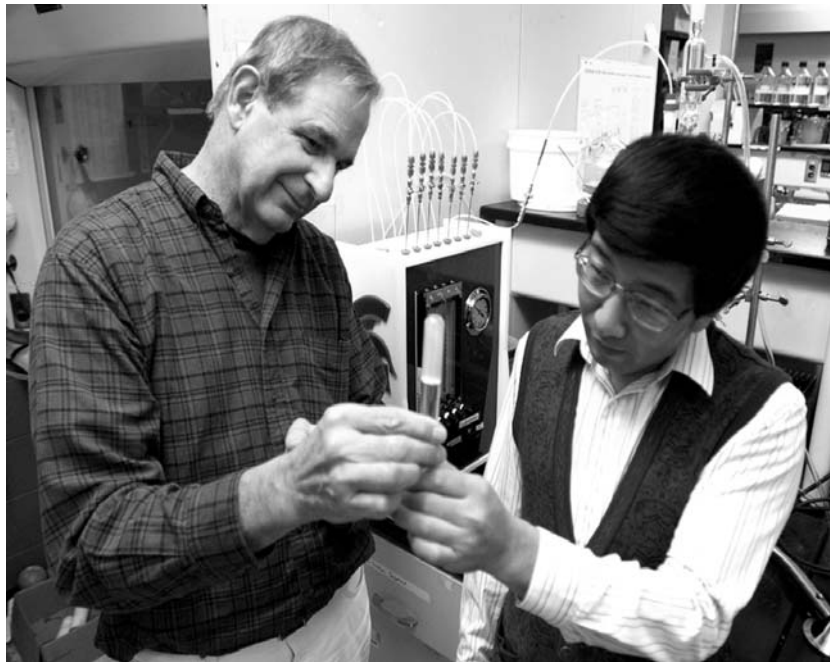
Scientists in IET-affiliated professor James Tiedje's lab discovered a river-bottom microbe that loves nothing more than to eat TCA, a common pollutant found in half of the U.S. superfund sites.

Previously no one knew how to biodegrade TCA in groundwater, Tiedje said.

The beneficial bacterium, called TCA1, grows only if it is fed TCA (trichloroethane), a ubiquitous environmental pollutant that has had widespread use as an industrial solvent and has often been disposed of improperly, according to the MSU team's report published in the November 2002 issue of Science. TCA contaminates groundwater and erodes the ozone layer when released into the atmosphere.

TCA1 breathes in TCA and breathes out chloroethane a less toxic chemical, which can be eaten by aerobic (oxygen-requiring) microbes in soil.

The scientists found TCA1 living in the bottom of the Hudson River in New York and also occurring naturally in Michigan's Kalamazoo River.



Jim Tiedje and postdoctoral student Baolin Sun.

In related work, the Tiedje lab is also studying other anaerobic (non-oxygen-requiring) dechlorinating populations, including those that dechlorinate PCBs, in

the IET-administered Superfund Basic Research Program grant from the National Institutes of Environmental Health Sciences.

