Interdepartmental Toxicology Annual Newsletter 2007

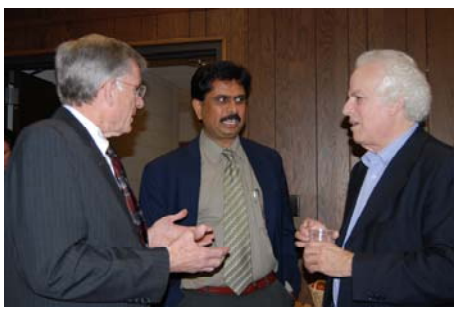
Five members of the Iowa State University faculty have been awarded the distinction of being named fellows by the American Association for the Advancement of Science (AAAS). Newly named fellows from ISU include **Marit Nilsen-Hamilton**, professor in the department of biochemistry, biophysics and molecular biology - for distinguished contributions to the fields of biochemistry, cell biology and mathematical biology.

When **Joel Coats** is named a fellow of the Entomological Society of America at its annual meeting this December, he won't be alone. Several of his former students will be there to help him enjoy the honor. More: http://www.iastate.edu/~nscentral/news/2007/oct/coats.shtml. Award acknowledges outstanding contributions in research, teaching, extension or administration (Dec 9-12 in San Diego, CA). He has been on the faculty of the Department of Entomology for 29 years and is currently Interim Chair of that Department.

Governor Chet Culver (Iowa) has appointed **Ruth MacDonald** to the Iowa Department of Economic Development Board. MacDonald will represent the life sciences industry on the board. She is chair of the Department of Food Science and Human Nutrition. Her term on the board begins immediately and expires in 2010.

In her research, Dr. MacDonald is conducting tests with mice to study the relationship between cancer and diets that contain isoflavones, products found in soybeans that mimic the action of estrogen. Dr. MacDonald and her colleagues provide hope that diet can make a difference in preventing cancer. For example, her research found a delayed onset of mammary tumors in mice fed diets containing soy isoflavones. Tests conducted on colon and prostate tumors in mice also found reductions in their size or number, providing hope that the inclusion of isoflavones and soy proteins in the diet may reduce the occurrence of some types of cancer.

Polish television journalist Barbara Czarnecka visited campus to work on a report about genetically modified crops. She interviewed Rick Helmich, USDA collaborator, entomology; Jon Tollefson, entomology; **Jeff Wolt**, Biosafety Institute for Genetically Modified Agrciultural Products; and **Gary Munkvold**, plant pathology/Seed Science Center. Global Agriculture Programs arranged the tour for the USDA, which sponsored the trip. Other stops included area farms, West Central Cooperative and an organic seed producer. The report will be broadcast on Polish national television.



At the College of Veterinary Medicine Fall Convocation held on Wed August 29, Dr. **Anumantha Kanthasamy** was presented with a medallion to recognize his promotion to an endowed CHAIR in Neurotoxicology: The W. Eugene & Linda Lloyd Chair in Neurotoxicology. Dr. Kanthasamy, middle, speaks with Nobel Prize winner Stanley Pruisner (right), during a workshop at Iowa State. College of Veterinary Medicine Dean John Thomson (left) is a strong supporter of the Toxicology Graduate program and the Iowa Center for Advanced Neurotoxicology (ICAN).

Dr. Richard Martin, Biomedical Sciences, was awarded the Bueding-von Brand Lectureship for 2007 by the American Society of Parasitology June 25. The award took place in Merida, Mexico, at the annual meeting of the American Society of Parasitologists. The Bueding-von Brand Lectureship was established to recognize international and national scientist who have made major research contributions to the field of biochemistry, molecular biology and pharmacology of parasitic helminthics. The Tribune, Wednesday, July 25, 2007, page 2.

George Kraus will be the new director of the Institute for Physical Research and Technology (IPRT) at Iowa State University. He begins his new position July 1, 2007, and will work three-fourths time as director. He will also continue his faculty position in the department of chemistry.

Kraus has been at ISU since 1976 when he joined the department of chemistry as an assistant professor. In 1981 he was promoted to associate professor, in 1986 to full professor, and in 2004 he was named university professor. He has held several administrative positions, including department chair of chemistry from 1993 to 1999 and more recently as director of the Center for Catalysis (an IPRT center) and assistant director of the Bio-related Initiatives of the Ames Laboratory.

John Brighton, Iowa State's vice president for research and economic development, said he and the search committee were very impressed with Kraus' academic credentials and his leadership experience over a long period of time. Kraus received his bachelor's degree from the University of Rochester and his doctorate from Columbia University. He has had a strong research record with interests in new synthetic reactions and their application to the synthesis of biologically active natural products, forensic chemistry, green chemistry and biobased products.

Kraus said he is honored to become the director of this unique enterprise and looks forward to building upon the solid foundation laid by Tom Barton. Barton recently returned to the Iowa State chemistry faculty after serving as director of the U.S. Department of Energy's Ames Laboratory since 1988 and IPRT since 1998. IPRT was established in 1987 as a network of scientific research centers. In addition to performing world-class scientific research, IPRT provides a wide variety of technical assistance to Iowa companies. Its broad mission is to promote interdisciplinary research in the physical sciences and engineering and specifically to foster development of new technologies. Staffed by world-class faculty and scientists and backed by unique facilities and equipment, IPRT helps develop Iowa's economy through research, company assistance and educational programs. Mike Krapfl, ISU News Service, June 15, 2007

Recent Funding for toxicology faculty. **Richard Martin**, Biomedical Sciences, "Modulation and Resistance of Lavamisole Receptor Channels" from the National Institutes of Health. **Jo Anne Powell-Coffman**, Genetics Development and Cell Biology, "Regulatory circuits that control transcriptional responses to hypoxia."

Dr. Diane Birt, a Mary B. Welch Distinguished Professor in the College of Human Sciences and director of the Center for Research on Botanical Supplements, has advanced the understanding of the relationship between diet and cancer prevention, and what impact factors such as overeating, obesity and even food portions might have on the disease. Her research has ranged from looking at how plant flavonoids and genetically modified alfalfa can inhibit colon cancer, to how resveratrol (a component of red wine) can be utilized as a cancer preventative, and to how control of adrenaline can reduce cancer-producing substances in the body. Iowa State University. Where Breakthroughs Happen. November 2006. A letter from the President

The Iowa Center for Research on Botanical Dietary Supplements at Iowa State University was created in 2002 by the NIH Office of Dietary Supplements. In addition to Iowa State, the center includes researchers at the University of Iowa, Yale University and the U.S. Department of Agriculture's North Central Regional Plant Introduction Station in Ames. A total of 27 researchers are involved (including 13 graduate students).

The five-year-old research center, dedicated to understanding and improving *Echinacea* and *Hypericum perforatum* (St. John's wort), has received $4.4 million in continuation funding from the National Institutes of Health. The renewal is for three years.

During the past five years, center researchers have gained insight into the antiviral, anti-inflammatory and immune-boosting mechanisms of specific species of *Echinacea*, and the antiviral and anti-inflammatory activity of different populations of *Hypericum*.

In the renewal, researchers will continue to conduct the anti-viral, anti inflammatory and pain receptor studies to see how components can block inflammation by stimulating the receptor to down regulate it.

"In the next three years, we'll include emphasis on bioavailability," Birt said. "We don't know if the chemicals we've identified are absorbed. We'll also be looking at the mechanism, focusing on cellular, signaling, pathways and receptors."

And they will add a third plant, *Prunella*. Also known as self heal, *Prunella* has been used to treat ailments such as inflammatory bowel disease, fever, headache and diarrhea.

"*Prunella* grows well in Iowa. We have made some extracts and saw very good activity-both antiviral and anti-inflammatory, so it fits well with what we're doing," Birt said.

Jacek Koziel, agricultural and biosystems engineering, is helping learn more about the problem of "ladybug taint," an abnormal aroma and flavor that may affect wine when the insects are picked and processed with the grapes. Koziel studied the Asian ladybird beetle's characteristic odor using a highly-sensitive multidimensional gas chromatograph and a panel of human 'sniffers' to characterize and identify the odors. Four chemicals were found to cause 28 different odors. All of the chemicals belong to a class of compounds called methoxypyrazines, which are potent odor-producing compounds also found in other animals and plants. The compounds are not considered harmful to humans, but are easily detected by the human nose. Although he and his associates did not conduct any actual wine studies, recent studies by others have shown that an increase in ladybug toxins can significantly decrease the natural fruit and floral intensities in wine. (American Chemical Society, March 25)

VEISHA 2007

An internationally recognized seed pathologist, **Gary Munkvold**, has been named Seed Science Endowed Chair at Iowa State University for a three-year term. The position was made possible by an anonymous donor and gives Munkvold the opportunity to lead a research, outreach and teaching program in seed health in the department of plant pathology and the Seed Science Center.

"I'm extremely grateful and honored," says Seed Science Endowed Chair Gary Munkvold. "Without the seed science endowment, it wouldn't be possible for the ISU College of Agriculture to fill the seed pathology position at this time and therefore, I wouldn't have had this opportunity to return to the ISU faculty."

Munkvold came to Iowa State from Pioneer Hi-Bred International, Inc., where he served as research coordinator for the Pathology, Entomology and Seed Science Group. Munkvold was a plant pathology faculty member at Iowa State from 1993 through 2002, with research and extension responsibilities for agronomic crops. His research focused on the transmission of important seedborne pathogens and the reduction of mycotoxins (toxin produced by a fungus) in foods and feeds.

"I'm living proof of the significant of private donations to our public university. I'm thankful to the donors for making this possible. This is an especially meaningful moment in my career," says Munkvold. "I have a distinct responsibility to set a precedent of excellence in research, teaching, service and outreach that will serve as a worthy model for my successors. I take that very seriously."

Ravindra Singh received the 2006 Presidential Early Career Award for Scientists and Engineers. Singh was appointed associate professor of biomedical sciences at the ISU's College of Veterinary Medicine on July 1, 2007. His award-winning research focused on correcting the spinal muscular atrophy (SMA) gene while he was at the University of Massachusetts Medical School. Singh will continue his research on SMA at Iowa State University.

Graduate Student Recruitment. Toxicology is always looking for good graduate students so if you interact with undergrads or students completing MS degrees who are interested in graduate degrees in Toxicology, ask them to take a look at us: www.toxicology.iastate.edu We presently have 33 faculty doing research in a variety of different areas. Our major areas of strength are: neurotoxicology, agrichemical, veterinary, molecular and food toxicology. Three new faculty joined the toxicology program this year including Dr. Singh, above, Dr. Rowe and Dr. Palic. Dr. Eric Rowe, Biomedical Sciences, centers his research around glial/neuron interactions in both the healthy brain and in neurodegenerative disorders. Dr. Dusan Palic, Veterinary Microbiology and Preventive Medicine (VMPM), is a veterinary specialist in aquatic animal medicine. You can read about some of the research and awards of the faculty throughout this newsletter.

Since last fall (2006), Toxicology has had several graduates. **Nasser Syed** (MS/Hsu/Biomedical Sciences "Arginine vasopressin and somatostatin receptors in rat astrocytes. **Lindsey Gereszek** (MS/Coats/Entomology) "Effects of dietary conjugated linoleic acid on European corn borer survival, growth, fatty acid composition, and fecundity", **Kelsey Prihoda** (MS/Coats/Entomology) "Development of methods to assess the fate and effects of *Bacillus thuringiensis* (Bt) Cry1F and Cry3Bb1 proteins." **Zhong Ye** (MS/Hendrich/FSHN) "Identification of urinary isoflavone excretion phenotypes related to the cholesterol lowering ability of soy protein in Golden Syrian hamsters". **Dingfei Hu** (Ph.D./Coats/Entomology) "Environmental fate and chemistry of a veterinary antibiotictylosin and monoterpenoid pesticidesthymol and phenethyl propionate", **Hirofumi Kosaki** (MS/Coats/Entomology) "Environmental studies on the fate and effects of pharma proteins produced in transgenic maize", **Terry Webster** (MS/Hyde/VDPAM) "A new robust technique for testing of glucocorticosteroids in dogs and horses". Fall 2007 graduates include **Netra Agarkar** (MS/Bobik/DiSpirto, BBMB), and **Christopher Choi** (Ph.D./tox minor/Kanthasamy/Biomedical Sciences).

The Plant Sciences Institute has united insect physiologist **Bryony Bonning** (Entomology) and molecular Virologist Allen Miller (Plant Pathology) in a quest to control crop damage brought about by aphid infestations. Bonning and Miller are on their way to genetically engineer plants for aphid resistance in an effort to cut billion dollar losses to U.S. farmers due to aphid damage. Their approach could offer an alternative to pricy and environmentally unfriendly chemical pesticides.

Be it backyard asparagus, acres of cotton, the prize rose bush or this year's soybean crop, all are on an aphid's preferred menu. They do not eat roots, leaves or seeds but rather feed on the phloem or plant sap, slowly robbing the plant of its hard-earned nutrition.

Ladybugs, a natural predator of aphids simply cannot eat them fast enough, explains Miller, director of the Center for Plant Responses to Environmental Stresses and professor of plant pathology. Aphids reproduce asexually. "They are born pregnant, essentially carrying their own grandchildren," says Miller. To sum up, they reproduce a lot in a very short period of time.

Aphids are also responsible for the transmission of more than 200 viruses from plant to plant, many of which bring about additional crop loss. In the case of luteoviruses, aphids are the sole mode of transmission.

Captializing on this uniqueness, Bonning and Miller are working to combine a gene encoding an insect-specific toxin with that of a luteovirus coat protein.

One such insect-specific toxin is found in the venom of the North African scorpion. Bonning and Miller have attached the toxin to a viral coat protein molecule—one of 1800 copies of this molecule that can form a wrapper around the luteovirus.

The researchers anticipate that when the toxin-coat protein complex is ingested by the aphid, the coat protein will deliver the toxin into the body cavity where it will break down cells inside the aphid gut, reducing it to a gelatinous mass, killing the aphid.

Preliminary data with the coat protein fused to a fluorescent marker protein confirms that the coat protein does usher the toxin into the aphid body cavity.

"It is a novel idea and it works," says Bonning, an expert in insect physiology. The next step is to generate transgenic plants that can express the coat protein-toxin-fusion product. Then, when an aphid taps into the phloem, it will eat up the toxin.

"Viruses are not always bad," points out Miller. "They are extremely useful tools for problems such as insect control."

The insect families Lepidoptera (caterpillars, moths) and Coleoptera (beetles) feed on the external structures of the plant and have been successfully controlled in an environmentally friendly manner with insect-specific Bt toxins. Because Bt toxin is typically applied as a topical insecticide or expressed on external structures in genetically engineered plants, aphids tape the sap and feast unscathed.

"Transgenic plant approaches haven't worked as well in controlling pests from the Hemiptera (the insect order that includes plant bugs and aphids) that feed on the xylem and phloem, and in some cases these insects now compromise the success of Bt technology," says Bonning.

Because aphid crop damage is not immediate, anything that slows the aphid population until harvest, even if it does not eradicate them is enough to offer significant relief to farmers.

"Our approach started as fundamental high-risk research with a clear applied goal," says Miller. "Someone has to do it and companies generally want universities to do this basic research. Plant Sciences Institute seed money for our basic research allowed us to make enough progress to secure USDA funding."

2006 Annual Report Plant Sciences Institute.

Around Ames News

On Sept. 17: Ames' Elwood Drive was no more. That is, we just won't be calling it that. In an effort to make the campus more accessible and easier to navigate for visitors, the road will become known as University Boulevard. The name change, which was approved by the city council in April, will apply to the stretch of road currently known as Elwood Drive, as well as to part of Pammel Road. The new University Boulevard will run from the Ames city limits south of Highway 30 to the intersection with Stange Road. Crews will change signs on Highway 30, in the city of Ames, and on campus beginning Sept. 17 -- a date that was intentionally chosen to avoid confusion among new students as they begin the fall semester.

In a special election, Ames' bond referendum to construct a city aquatic center on 13th Street near Squaw Creek got the thumbs up (76 percent of the vote). Ames residents will pay for the $9.5 million project through a combination of a property tax increase and a $2 million donation from Don and Ruth Furman. The passage of the bond means the demolition of Carr Pool, the city's main outdoor public swimming facility that has been open since 1928. Ames parks and recreation director Nancy Carroll and Ames mayor Ann Campbell said they were thrilled with the outcome of the vote. The new aquatic center is expected to open in summer 2009.

New entry way on University Boulevard (formerly Ellwood Drive) coming in from Highway 30 towards Campus. (Photo: ISU Alumni News Flash)

Ames has a new Super Walmart due to open this spring.

The new mall at the intersection of 13th and I-35 is still in the discussion stage. The old mall at North Grande is doing some redevelopment.

The Interdepartmental Toxicology Graduate program wishes to you and your family the best for the holiday season and upcoming new year.

The 150 Anniversary Party for Iowa State

VEISHA 2007

Toxicology Graduate Students will number 26 for spring 2008 including two new admits; one from India (joins Dr. Singh's lab) and one from Serbia (joins Dr. Palic's lab). For Fall 2007 we recruited five new students, 3 domestic and 2 international. The domestic students are from Tuskegee University (AL), Virginia Commonwealth and Saint Cloud State (MN). The international students are from China (China Agricultural University) and from Ghana, Africa (University of Ghana).

Last spring the Toxicology Graduate Students invited Dr. Curtis D. Klaassen, Department of Pharmacology, University of Kansas Medical Center, to present the 2007 Daniel J. Zaffarano Lecture,

"Nuclear receptors and other transcription factors in hepatobiliary disposition of xenobiotics". Dr. Klaassen is the editor for our favorite textbook, Casarett and Doull's Toxicology, The Basic Science of Poisons. The spring faculty and graduate student retreat was held at Reiman Gardens in Ames.

Selected Recent Publications

(bold = present tox students; underline = tox alumni; italics = tox faculty)

Wu, X., *Murphy, P*., Cunnick. J., *Hendrich S*. (2007) Synthesis and characterization of deoxynivalenol glucuronide: its comparative immunotoxicity with deoxynivalenol. Fd Chem Toxicol, in press.

Landgren CA, Kohut ML, *Hendrich S* (2006) Low-level dietary deoxynivalenol and acute exercise stress result in immunotoxicity in BALB/c mice. J Immunotoxicol 3: 173-8.

Zhong Y, Renouf M, Lee S-O, Hauck CC, *Murphy PA, Hendrich S* (2006) High urinary isoflavone excretion phenotype decreases plasma cholesterol in Golden Syrian hamsters fed soy protein. J Nutr 136: 2773-2778.

Renouf M, Lee S-O, *Hendrich S* (2006) Isoflavone excretion phenotypes influence plasma cholesterol in Golden Syrian hamsters. Nutr. Res. 26: 77-83.

Cai, L., *J.A. Koziel*, A.T. Nguyen, Y. Liang, and H. Xin. Evaluation of zeolite for control of odorants emissions from simulated poultry manure storage. 2007. Journal of Environmental Quality, 36(1), 184-193.

Cai L., *J.A. Koziel*, J. Davis, Y.C. Lo and H. Xin. 2006. Characterization of VOCs and odors by in vivo sampling of beef cattle rumen gas using SPME and GC-MS-olfactometry. Analytical and Bioanalytical Chemistry, 386(6):1791-1802.

Schroeder, S.E., *Reddy, M.B. & Schalinske, K.L.* (2007) Retinoic acid modulates hepatic iron homeostasis in rats by attenuating the RNA-binding activity of iron regulatory proteins. J. Nutr., 137: 2686-2690, 2007

Hanson, L.N., Engelman, H.M., Alekel, D.L., *Schalinske, K.L*., Kohut, M.L. & *Reddy, M.B.* (2006) Effects of soy isoflavones and phytate on homocysteine, C-reactive protein, and iron status in postmenopausal women. Am. J. Clin. Nutr. 84: 774-780.

Hailin Tang , HuarongLi, *Bonning, B.* (2007) Tissue specificity of a baculovirus-expressed, basement membrane-degrading protease in larvae of Heliothis virescens. Tissue Cell. 39(6):431-43.

Martin, R.J. and Robertson, A.P. (2007) Mode of action of levamisole and pyrantel, anthelmintic resistance, E153 and Q57. Parasitology. 134, 1093-1104.

(The Tox 2007 retreat with **Dingfei Hu**, **Chris Choi** and **Hirofumi Kosaki** in the foreground.)

The Kanthasamy Lab has two publications listed as top 25 hottest articles published in Qtr 1 results, NeuroToxicology 2007.

#2. Interaction of metals with prion protein: Possible role of divalent cations in the pathogenesis of prion diseases Article *Neurotoxicology, Volume 27, Issue 5, 1 September 2006, Pages 777-787* **Choi, C.J**.; *Kanthasamy, A.*; *Anantharam, V.; Kanthasamy, A.G.*

#4. Proteasome inhibitor MG-132 induces dopaminergic degeneration in cell culture and animal models **Article** *Neurotoxicology, Volume 27, Issue 5, 1 September 2006, Pages 807-815* Sun, F.; *Anantharam, V.*; Zhang, D.; Latchoumycandane, C.; *Kanthasamy, A.; Kanthasamy, A.G.*

Shen, C., Shao, Z., and *J.A. Powell-Coffman*, (2006). The *Caenorhabditis elegans rhy-1* gene inhibits HIF-1 hypoxia-inducible factor activity in a negative feedback loop that does not include *vhl-1*. *Genetics* Vol 174 (3):1205-14

Qin, H., Zhai, Z., and *Powell-Coffman, J.A.* (2006) The *Caenorhabditis elegans* AHR-1 transcription complex controls expression of soluble guanylate cyclase genes in the URX neurons and regulates aggregation behavior. *Developmental Biology*, 298: 20580

Verma, S., Robertson, A.P. and *Martin, R.J.* (2007). The neuropeptide, KHEYLRF-NH2 (AF2), increases voltage-activated calcium currents in Ascaris suum muscle. British Journal of Pharmacology. 151, 888-899.

Robertson, A. P. and *Martin, R. J.* (2007). Ion-channels on parasite muscle: pharmacology and physiology. Invertebrate Neuroscience. 7, 209-212.