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National Center for Toxicological Research  
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870-543-7000  
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# NCTR Quarter Page

## Systems Toxicology: New Research Division

An important function of the FDA is to use risk management to provide the most health promotion and protection at the least cost to the public. Presently, this is accomplished by safety assessment of FDA-regulated products in surrogate organisms and to a lesser extent in humans. NCTR has developed a unique and sophisticated analytical infrastructure to assess the safety of FDA-regulated products using genomics, proteomics, metabolomics, in conjunction with traditional biomarkers of safety, and toxicoinformatics. This system approach is directed towards the creation of a more relevant and quantitative risk assessment paradigm. Presently, risk assessment depends greatly on statistical models that may or may not have biological relevance. The systems biology approach to toxicity testing can provide the FDA with data that are more easily extrapolated to the human, making data interpretation more facile and relevant. Under the guidance of Dr. Yvonne Dragan, the Systems Toxicology Research Division at NCTR will use proof of concept protocols to identify new disease markers and drug targets that will aid in the design of products to prevent, diagnose and treat disease.

## Jefferson Labs of the FDA Enhance & Update Security

Security of government employees, contractors, visitors, facilities, equipment and personal property is of utmost importance to the management of the Jefferson Labs of the FDA (NCTR & ARL). In response to America's environment of heightened security, the FDA Security Office provided funding to upgrade and enhance the security posture of the FDA Jefferson Labs. Thursday July 29, 2004 marked the *grand opening* of the renovated Security Building-21 and the implementation of numerous enhanced safety and security operational procedures. Capital improvements include the installation of a mail sorter with downdraft protection, metal detectors, x-ray scanners, safety lights, video cameras, fencing, signs, and electronic gates.

## 2004 Summer Science Research Program: Student Contributions

The Summer Science Research Program (SSRP), administered by the Oak Ridge Institute for Science and Education in Oak Ridge, TN, provides undergraduate and graduate students appointments and sponsor-provided stipends based on academic classification in biological sciences, chemistry, computer science, mathematics, medicine, pharmacology, toxicology, and other related scientific disciplines. The NCTR 2004 SSRP, chaired by Dr. Tucker Patterson, sponsored five SSRP students: Kimberly Berry, a senior at UALR, (mentor, Dr. Sherry Ferguson); Patrick Lang, a junior UAF (mentor, Dr. Brian Coles); Mason Pearce, a senior at ASU (mentor by Dr. Carrie Valentine); Stella Yeung, a sophomore at Trinity University, mentored by Dr. William Witt; and Jonathan Young, a graduate student at UALR, mentored by Dr. John Chelonis. The students participated in research studies involving the biological effects of potentially toxic chemicals that have a major impact on public health and the environment and presented their scientific findings in a formal seminar setting to research scientists and support staff at NCTR. The NCTR SSRP mentors presented each student with a *Certificate of Appreciation* for their contributions to FDA/NCTR research following their presentations.



Dr. William Witt, Director, Division of  
Veterinary Services and Stella Yeung  
Photo by Tucker Patterson

## Recent Publications

NCTR conducts research designed to protect the public's health. Results from some of these research projects have recently been accepted for publication in nationally recognized scientific journals.

- Choi, Y., Poisson Regression Trees for Analysis of Count Data with Extra Variation, *Computational Statistics and Data Analysis*.
- Cisneros, F.J., *Uncaria tomentosa* (Cat's Claw - UNA DE GATO) extract protects mice against ozone induced lung inflammation, *Journal of Ethnopharmacology*.
- Cui, Y., Photodecomposition of pigment yellow 74, a pigment used in tattoo inks, *Photochemistry and Photobiology*.
- Delongchamp, R.R., Median-of-subsets Normalization of Intensities for cDNA Array Data, *DNA and Cell Biology*.
- Elkins, C., Bile-mediated aminoglycoside sensitivity in *Lactobacillus* likely res125 mutants from increased membrane permeability by cholic acid, *Applied and Environmental Microbiology*.
- Fang, H., Classification of cDNA array genes that have a highly significant discriminative power due to their unique distribution in four brain regions, *DNA and Cell Biology*.
- Hu, L., Determination of Kavalactones in Dietary Supplements and Selected Functional Foods Containing *Piper methysticum* by Liquid Chromatography with PDA-UV Detection, *Journal of AOAC International*.
- Joo, J., A mixture-of-genotypes model for the distribution of thermostable phenol sulfotransferase activity, *Biometrical Journal*.
- Lang, Q., Sample Preparation and Determination of Ginkgo Terpene Trilactones in Selected Beverage, Snack, and dietary Supplement Products by Liquid Chromatography with Evaporative Light Scattering Detection, *Journal of AOAC International*.
- Lyn-Cook, B.A., Cyclooxygenase-2 (Cox-2) and NAD(P):quinine Oxidoreductase (NQO1) are Potential Chemopreventive Targets of Isothiocyanates in Pancreatic Cancer, *CEBP*.
- Mei, N., Differential mutagenicity of riddelliine in liver endothelial and parenchymal cells of transgenic Big Blue rats, *Cancer Letters*.
- Moon, H., An Age-Adjusted Bootstrap-based Poly-k Test, *Statistics in Medicine*.
- Moon, H., A Comparison of Microbial Dose-Response Models Fitted to Human Data, *Regulatory Toxicology and Pharmacology*.
- Pogribny, I.P., Genomic hypomethylation is specific for preneoplastic liver in folate/methyl deficient rats and does not occur in non-target tissue, *Mutation Research*.
- Ratnasinghe, L., Aspirin Use and Mortality from Cancer in a Prospective Cohort Study, *Anticancer Research*.
- Roberts, D.W., Inhibition of extrahepatic human cytochromes P450 1A1 and 1B1 by metabolism of isoflavones found in *Trifolium pratense* (Red Clover), *J. Agricul. Food Chem.*
- Scallet, A.C., Developmental neurotoxicity of ketamine: morphometric confirmation, exposure parameters, and multiple fluorescent labeling of apoptotic neurons, *Toxicological Sciences*.
- Slikker, W., Dose-dependent transitions in mechanisms of toxicity, *Toxicology and Applied Pharmacology*.
- Slikker, W., Dose-dependent transitions in mechanisms of toxicity: CASE STUDIES, *Toxicology and Applied Pharmacology*.
- Stingley, R.L., Novel organization of genes in a phthalate degradation operon of *Mycobacterium vanbaalenii* PYR-1, *Microbiology*.
- Stingley, R.L., Molecular characterization of a phenanthrene degradation pathway in *Mycobacterium vanbaalenii* PYR-1, *Biochemical and Biophysical Research Communications*.
- Tong, W., Assessment of prediction confidence and domain extrapolation of two structure-activity relationship models for predicting estrogen receptor binding activity, *Environmental Health Perspectives*.
- Tsai, C., Gene Selection for Sample Classifications in Microarray Experiments, *DNA and Cell Biology*.
- Wang, J., Time course of cII gene mutant manifestation in the liver, spleen and bone marrow of N-ethyl-N-nitrosourea-treated Big Blue transgenic mice, *Toxicological Sciences*.
- West, R.W., Change-point alternatives to the NOAEL, *Journal of Agricultural, Biological and Environmental Statistics*.
- Wilson, W., Characterization of a common deletion polymorphism of the UGT2B17 gene linked to UGT2B15, *Genomics*.
- Young, J.F., Building an Organ-Specific Carcinogenic Database for SAR Analyses, *Journal of Toxicology and Environmental Health, Part A*.

**CONTACT INFORMATION:** The NCTR Quarter Page is published four times a year by the Division of Planning & Resource Management at the National Center for Toxicological Research.

FOR MORE INFORMATION ABOUT NCTR CONTACT DR. DAN CASCIANO, NCTR DIRECTOR AT DCASCIANO@NCTR.FDA.GOV OR [870] 543-7517.



DHHS/FDA/NCTR  
3900 NCTR Road  
Jefferson, AR 72079

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