National Center for Toxicological Research

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NCTR Quarter Page

NCTR Director Retires

On December 13, 2005, NCTR recognized Dr. Daniel Casciano, NCTR's Director for 6½ years, at his retirement celebration. Dr. Casciano joined the NCTR as a research scientist in 1973. During his 32 years at the NCTR, Dr. Casciano transitioned from bench research scientist to become Director of Genetic and Reproductive Toxicology; NCTR Deputy Director for Research; Acting Director of NCTR; and then NCTR Director.

As NCTR's Director, Dr. Casciano demonstrated exemplary leadership, scientific contributions, and vision to foster the FDA Critical Path Initiative by enhancing the NCTR's unique systems toxicology capabilities. Dr. Casciano developed and implemented an integrated plan to apply genomic, proteomic, and metabolomic technologies to toxicological and biological problems. By validating these emerging technologies to assess the safety of regulated products, these measures can aid FDA reviewers in risk assessment and position NCTR/FDA to transition to and to promote a personalized medicine paradigm.

Dr. von Eschenbach, acting FDA Commissioner, recently announced that Dr. William Slikker, the Deputy Center Director for Research, will be the Acting Director, NCTR.

"You have distinguished yourself as an accomplished leader, innovator, and visionary during the tenure of your government career. Your record of accomplishments as a scientist and leader is truly noteworthy. You can be proud of your career." Dr. Andrew C. von Eschenbach, Acting Commissioner of the FDA, in a citation to Dr. Casciano.

FDA and Industry to Collaborate on Better Ways to Predict Liver Toxicity in Human Drug Trials

From a November 2, 2005, FDA Press Release

The FDA and BG Medicine, a Massachusetts-based biotechnology research company, have agreed to collaborate on a project designed to overcome one of the obstacles to efficient development of safe drugs. The Liver Toxicology Biomarker Study (LTBS), to be conducted under a Cooperative Research and Development Agreement between the NCTR and the pharmaceutical industry, aims to discover signs of human liver toxicity in a standard test used in the initial stages of drug development.

"Liver toxicity is a common reason for drug development failure. By identifying biomarkers for liver toxicity at the start of the development process, this research should yield important benefits for industry, the FDA, and the public." Dr. Janet Woodcock, FDA's Deputy Commissioner for Operations.

Early detection of potential safety problems is one of the main objectives of the FDA's Critical Path Initiative, which seeks to modernize drug development by making the process more predictable and successful, and less costly. The LTBS has been designed by FDA and BG Medicine with input from other pharmaceutical companies and will be conducted, with their collaboration, at the NCTR laboratory in Jefferson, AR and BG Medicine in Waltham, MA.

MicroArray Quality Control (MAQC) Project Holds Workshop

The third MAQC workshop was held in Palo Alto, CA, December 1-2, 2005. The MAQC, an FDA-initiated effort spearheaded by NCTR and CDER scientists, seeks to develop consensus standards for the performance and presentation of microarray data. Representatives from more than 50 organizations representing industry, academia, government agencies, and other stakeholders reviewed MAQC datasets derived from two large human RNA pools developed in the project by industry partners and analyzed on ten commercial microarray platforms.

It is widely accepted that microarray data are crucial to pharmacogenomic and toxicogenomic efforts for advancing medical product development and safety, and personalized medicine. Plans were set to publish twelve manuscripts to make the MAQC data available to the scientific community.

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.

Allred, C.D., Twaddle, N.C., Allred, K.F., Churchwell, M.I., Ju, Y.H., Helferich, W.G. and Doerge, D.R., Soy processing affects metabolism and disposition of dietary isoflavones in ovariectomized Balb/c mice, *Journal of Agricultural & Food Chemistry*

Anderson, K., Kadlubar, F.F., Kuldorff, M., Harnack, L., Gross, M., Lang, N.P., Rothman, N., Sinha, R. and Barber, C., Dietary intake of heterocyclic amines and benzo(a)pyrene: associations with pancreatic cancer, *CEBP*

Brezna, B., Kweon, O., Stingley, R.L., Freeman, J.P., Khan, A.A., Polk, A.R., Jones, R.C. and Cerniglia, C.E., Molecular Characterization of Cytochrome P450 Genes in the Polycyclic Aromatic Hydrocarbon Degrading Mycobacterium vanbaalenii PYR-1, *Applied Microbiology and Biotechnology*

Cerniglia, C.E. and Sutherland, J.B., Relative roles of bacteria and fungi in polycyclic aromatic hydrocarbon biodegradation and bioremediation of contaminated soils, *Fungi Biogeochemical Cycles*

Elkins, C., and Beenken, K., Modeling the tripartite drug efflux pump archetype: structural and functinal studies of the macromolecular constituents reveal more than their names imply, *Journal of Chemotherapy*

Ferguson, S.A., Berry, K.J., Cisneros, F.J. and Gough, B.J., Chronic oral treatment of rats with 13-cis-retinoic acid (isotretinoin) or all-trans-retonic acid does not alter depression-like behavior in rats, *Toxicological Science*

Ferguson, S.A. and Gray, E.P., Aging effects on elevated plus maze behavior in Spontaneously Hypertensive, Wistar-Kyoto and Sprague-Dawley male and female rats, *Physiology & Behavior*

Kadlubar, F.F., The Path to Personalized Medicine, *Foundation of Sapporo Cancer Seminar 25th Anniversary*

Kim, S., Kweon, O., Freeman, J.P., Jones, R.C., Adjei, M.D., Joo, J., Edmondson, R.D. and Cerniglia, C.E., Molecular cloning and expression of genes encoding a novel dioxygenase involved in low- and high-molecular-weight polycyclic aromatic hydrocarbon degradation in Mycobacterium vanbaalenii PYR-1, *Applied Environmental Microbiology*

Lyn-Cook, B.A., Yan, Y., Moore, S.A., Word, B.R., Hammons, G.J. and Taylor, S.D., Increased Levels of NAD(P)H: Quinone Oxidoreductase 1 (NQ)1) in Pancreatic Tissues from Smokers and Pancreatic Adenocarcinomas: A Potential Biomarker of Early Damage in the Pancreas, *Cell Biology and Toxicology*

Mei, N., Xia, Q., Chen, L., Moore, M., Fu, P.P. and Chen, T., Photomutagenicity of Retinyl Palmitate by Ultraviolet A Irradiation in Mouse Lymphoma Cells, *Toxicology Scientific 2005*

Nayak, R.R., Stewart, T.M., Cerniglia, C.E. and Nawaz, M.S., *In vitro* antimicrobial susceptibility, genetic diversity and prevalence of UDP-glucose 4-epimerase (galE) gene in *Campylobacter* coli and Campylobacter jejuni from turkey production facilities, *Food Microbiology*

Paule, M.G., Animal models and the cognitive effects of ethanol, *Animal Models of Cognitive Impairment*

Sawyer, J.R., Binz, R.L., Wang, J. and Moore, M., Multicolor Spectral Karyotyping of the L5178Y Tk+/- -3.72C Mouse Lymphoma Cell Line, *Environmental and Molecular Mutagenesis*

Scallet, A.C., Schmued, L.C. and Johannessen, J., Neurohistochemical biomarkers of the marine neurotoxicant, domoic acid, *Neurotoxicology and Teratology Special Issue on Marine Toxins*

Slikker, W., Young, J.F., Corley, R.A., Dorman, D.C., Conolly, R.B., Knudsen, T.B., Erstad, B.L., Luecke, R., Faustman, E., Timchalk, C. and Mattison, D., Improving predictive modeling in pediatric drug development: pharmacokinetics, pharmacodynamics and mechanisitic modeling, *Annals of New York Academy of Sciences*

Tolleson, W.H., Human melanocyte biology, toxicology, and pathology, *Journal of Environmental Science and Health*

Virmani, A., Gaetani, F. and Binienda, Z.K., Effects of metabolic modifiers such as carnitines, coenzyme Q10, and PUFAs against different forms of neurotoxic insults: Metabolic inhibitors, MPTP and methamphetamine, *Annals of the New York Academy of Sciences*

Young, J.F., Tsai, C., Chen, J.J., Latendresse, J.R. and Kodell, R.L., Database Composition Can Affect the Structure-Activity Relationship Prediction, *Journal of Toxicology and Environmental Health*

Zhang, X., Tan, W., Maio, X., Ning, B., Liu, Z., Song, W., Kadlubar, F.F., Lin, D., Hong, Y., Guo, T., Zhang, X. and Qiang, B., Identification and Functional Analysis of Genetic Variants of Cyclooxygenase-2 and Their Association with Risk of Esophageal Cancer, *Gastroenterology*

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