Partnerships

Innovative partnerships for innovative research solutions

Solving today's public health issues requires innovative, multidisciplinary, integrative approaches. The National Center for Toxicological Research (NCTR), with its internationally recognized research staff, unique facilities, and scientific capabilities, provides the opportunity to conduct collaborative research that addresses a wide variety of specific public health questions. NCTR is actively seeking new opportunities for collaborative partnerships.

Opportunities for Leveraging Resources with NCTR

Interagency Agreement (IAG): Formal financial partnerships with other government agencies

Collaborative Research and Development Agreement (CRADA): Formal financial partnerships with non-governmental organizations, nonprofit organizations, and private companies

Material Transfer Agreement (MTA): Formal agreements providing a mechanism for NCTR to receive material items from nongovernmental organizations

Intra-Agency Agreement: Cost-reimbursement partnerships with other FDA Centers

Memorandum of Understanding (MOU): Formal agreements for collaborative research or other partnership activities

Informal Collaboration: Informal agreements to work collaboratively on projects of mutual interest

Visiting Scientists: Opportunities for scientists to conduct research on the NCTR campus

NCTR: Your outstanding partner in collaborative research projects

Throughout its history, NCTR has actively sought and participated in collaborative, cooperative partnerships with other scientific and regulatory organizations. These opportunities to leverage resources, both public and private, have led to substantial research advances that have resulted in significant improvements in long-term public health. An overview of selected examples of on-going or completed collaborations for each type are included.

Interagency Agreement (IAG)

FDA/NIH: In 1992, the Food and Drug Administration (FDA) entered into an IAG with the National Institutes of Health (NIH). This agreement concentrated on FDA's priority National Toxicology Program (NTP) nominations of chemicals/agents and utilized the unique resources and facilities at the NCTR. The research conducted under the IAG provides FDA, and the public health community, the ability to better assess safety of a number of FDA-regulated products. The 1992 agreement provided support for research with five FDA priority chemicals. Since then, the agreement has expanded to include collaborative research on five putative endocrine disrupter compounds, including three multigenerational studies for developmental effects and two chronic cancer studies. In 1998, NCTR opened a FDA/NIEHS Phototoxicology Research and Testing Laboratory. The facility is state-of-the-art and provides the opportunity to study the effects of compounds in combination with simulated solar light. Currently the IAG includes the evaluation of AIDS therapeutic drugs, dietary supplements, mycotoxins, such as fumonisin, and acrylamide, a chemical produced when some food products, such as potatoes, are cooked at high temperatures. All research under this IAG is designed with input from FDA regulatory scientists, NCTR and NIEHS scientists, experts from universities, and often experts from the regulated industry. The IAG utilizes resources from public funds and exceptional scientific expertise to provide the best possible assessment of product safety resulting in accomplishment of the missions of the FDA and NIH.

NCTR/EPA: The Environmental Protection Agency (EPA) has entered into several IAGs with NCTR. These partnerships have provided important information that has been used in neurotoxicity risk assessment, risk assessment associated with waterborne and foodborne pathogens, and the development of an endocrine disruptor knowledge base. Currently research is being conducted for an infectivity model for *crytosporidium*.

NCTR/FAA: The Federal Aviation Administration (FAA) has entered into an IAG with NCTR scientists to develop a rapid sensor detection method to screen for explosives. This work supports the national security effort.

NCTR/NIH: The National Institutes of Health (NIH) is supporting studies with NCTR evaluating the effects of exposure to Agent Orange.

NCTR/DOD: Collaborative IAG epidemiology studies between NCTR and the Department of Defense (DOD) are currently being conducted to understand how genetic differences can impact susceptibility to the recurrence of breast cancer. Women are being evaluated for metabolic status and associations developed, between the various metabolic phenotypes and genotypes, and the recurrence of breast cancer following high-dose radiation and chemotherapy. The FDA Office of Women's Health (OWH) has also provided funding for this important research endeavour.

FDA/NIEHS Phototoxicology Research and Testing Laboratory

Created in 1998 to meet the basic science research and testing needs of the NTP, NIEHS, and FDA

Cooperative Research and Development Agreement (CRADA)

NCTR/AstraZeneca: NCTR's Division of Neurotoxicology recently concluded a CRADA with AstraZeneca to study the effects of long-term blockage of glutamate receptors and/or sodium channel blockage on neurobehavioral endpoints. AstraZeneca is currently supporting a study to determine whether ketamine-like agents, a known NMDA receptor antagonist frequently used as an anesthetic in children, and remacemide, an anti-epileptic agent with both NMDA receptor antagonist and sodium channel blocking properties, cause adverse effects similar to those noted in previous studies. Researchers have confirmed that administration of these agents during the brain growth spurt results in widespread neuronal apoptosis in the rat. Further evidence in a nonhuman primate model is in progress.

NCTR/Litmus: The NCTR Division of Chemistry developed small disks called Food Quality Indicators (FQIs) as rapid chemical sensors to assess food for freshness. These FQIs were evaluated by the Canadian Centre for Fisheries Innovation, St. John's, Newfoundland, Canada. This independent evaluation confirmed that the FQI is rapid, sensitive, rugged, and simple enough that multiple analysts can obtain results of equal and high quality. A CRADA has been developed with Litmus to develop a commercial outlet for this FQI and also to support the further development of FQI technologies.

NCTR/Argus Research Laboratories: A CRADA with Argus Research Laboratories provides for the sharing of historical data from the Argus Research Laboratories. Tumor incidence in SKH-1 mice exposed to simulated solar light (SSL) is obtained from Argus and entered into the NCTR MultiGen database. These data are being summarized and analyzed for tumor incidence. In turn, NCTR will share its tumor incidence data for SKH-1 mice exposed to SSL at the NCTR. The combined database and the statistical methods developed for analyzing that data will be shared between the two organizations.

NCTR/UALR: A CRADA has been developed between NCTR and the University of Arkansas at Little Rock (UALR). Under this partnership arrangement, scientists from NCTR's Division of Neurotoxicology and the UALR explore their initial observations that animals exposed to cocaine during gestation fail to adapt to important changes in their environment. The studies will examine additional aspects of behavioral adaptability by changing "the rules of the game" for a variety of behavioral tasks.

NCTR/Sigma Tau Research, Inc.: NCTR's Division of Neurotoxicology is collaborating with Sigma Tau Research, Inc. to characterize the early genomic biomarkers of mitochondrial dysfunction, a frequently observed effect of neurotoxicants. This research may provide information on a standardized microarray system that will allow for the screening of agents with the potential to predict brain injury.

NCTR/RxGen: A CRADA between the NCTR Metabolomics research team and RxGen will develop a method for predicting human hepatotoxicity through the identification of characteristic high-resolution proton nuclear magnetic resonance (NMR) spectroscopic profiles in biofluids and liver tissue.

NCTR/ACC and NCTR/EPA: A CRADA between NCTR and the American Chemistry Council (ACC) successfully developed a statistically robust 3D-QSAR model to predict *in vitro* rat uterine estrogen receptor binding activity. This model is a part of the estrogen knowledge base and, in conjunction with the IAG with the Environmental Protection Agency (EPA), was a key component for the Endocrine Disruptor Knowledge Base (EDKB) used by EPA and other organizations.

NCTR/EPRI: In 1990 the NCTR and Electric Power Research Institute (EPRI), an association representing all sectors of the electric utility industry, entered into a CRADA. The purpose of the CRADA was to assess the potential hazard to human health from the by-products of gasification, which contain polycyclic hydrocarbons. A two-year tumor bioassay was among the studies conducted, and the NCTR used the data to generate a risk assessment. In addition, the data have been made available to aid in toxicological assessments by other agencies, including the U.S. Environmental Protection Agency, U.S. Department of Energy, the Department of Human Services in Australia, and the National Institute of Public Health in the Netherlands.

Material Transfer Agreement

Material Transfer Agreements (MTAs) provide a mechanism whereby materials can be exchanged between government and nongovernmental organizations. While most MTAs are established so that NCTR can receive materials, there are situations where NCTR provides materials to other organizations under a MTA. Materials transferred under these MTA agreements are key resources for the conduct of important health studies. Exchanged materials include test chemicals, unique cell cultures, bacterial samples, tissues, software, microarrays, DNA, and other types of research materials. Organizations with which NCTR has utilized the MTA mechanism include: DuPont, Lilly, Pfizer, the University of Texas, the Ludwig Institute for Cancer Research, the Imperial Cancer Research Fund, ILEX Oncology, MAYO, the Massachusetts Institute of Technology, The Microarray Center in Toronto, Canada, Waters Corporation, and McGill University.

Intra-Agency Agreement

Consistent with its role within the FDA, NCTR actively participates in collaborative research with the other FDA Centers. For some high priority research projects, NCTR receives financial resources from the other Centers to facilitate the timely conduct and completion of important studies. For example, ketamine studies (supported in part by the Center for Drug Evaluation and Research (CDER)) may provide pivotal information for assessing the potential public health risk associated with ketamine's use as an anesthetic agent in children. The Center for Food Safety and Applied Nutrition's (CFSAN's) collaboration on identifying methods for the safety testing of pigments used for tattooing could determine if tattoo inks have toxic or phototoxic potential.

NCTR/FDA Office of Women's Health: The FDA Office of Women's Health (OWH) has provided funding for a number of important research projects that provide insight into issues important for women's health. Projects in which NCTR has participated include studies to: 1) develop the methodologies to assay hydroxylation of endogenous estrogens as that process relates to the development of breast cancer; 2) identify the effects of dietary supplements that apply specifically to women; 3) develop *in vitro* model systems for the study of mechanisms of gender-specific and ethnicity-specific toxicity; 4) determine in a variety of models, including humans, if tamoxifen is acting through a genotoxic mechanism by characterizing DNA adducts from suspected tamoxifen metabolites; 5) investigate whether the thymidine kinase-deficient genotype in mice is lupus prone and perhaps, therefore, an appropriate model for the development of lupus; and 6) develop a human hepatocyte cell line to analyze gender differences in the metabolism of pharmaceutical drugs.

NCTR/Office of the Commissioner: The FDA Commissioner's office provides special funding for a small number of high priority research projects. NCTR has actively competed for this funding and has participated in a number of studies including several projects involving the quality control issues related to the use of the new microarray technology and the development of a new rapid flow cytometric technique for measuring genetic damage (micronuclei) induced by chemical or pharmaceutical drug exposure.

The Center for Drug Evaluation and Research (CDER) and the NCTR are cooperating in searching for an understanding of why some drugs injure only certain people. They are developing an innovative, clinical trial design using available biofluids, such as serum and urine, to develop biomarkers from metabolomic, proteomic, and genomic integrated analyses for the detection of individuals with a risk for liver toxicity, and for the early detection of toxicity.

Memorandum of Understanding

NCTR/Arkansas Department of Health: NCTR has a work sharing agreement with the State of Arkansas Department of Health to share expertise and laboratory infrastructure in support of the state's public health preparedness and response to bioterrorism.

Informal Collaboration

NCTR scientists are active collaborators with investigators at numerous national and international organizations in a wide variety of research projects. Organizations with which NCTR scientists collaborate include:

Agricultural Research Service Biosciences Research Laboratory in Fargo, ND
Arkansas Cancer Research Center
Arkansas Children's Hospital
Central Arkansas Veterans Health Care Systems
Environ
Environmental Protection Agency
Harvard University
Health Canada
Institute of Statistical Science in Taiwan
Litron Laboratories
Lovelace Inhalation Toxicology Research Institute
Massachusetts Institute of Technology
MD Anderson
NASA Johnson Space Center
National Cancer Institute
National Institute of Health Sciences, Tokyo, Japan
National Institute of Standard Technology (NIST)
National Institutes of Health
New York Department of Health
North Carolina State University
State University of New York–Stony Brook
U.S. Department of Agriculture
University of Arkansas at Little Rock
University of Arkansas for Medical Sciences
University of Mississippi
University of Montreal
Wake Forest University
Washington School of Medicine

Visiting Scientists

NCTR is a mecca for visiting scientists from all over the world. The NCTR campus includes a dormitory facility in which visiting scientists can live, free of charge, close to campus for short periods of time. The facilities and resources of NCTR and the multidisciplinary NCTR scientific staff provide a unique opportunity for visiting scientists to learn new technologies, share their specific skills and knowledge, and actively participate in important public health research. The relaxed NCTR atmosphere and the internationally diverse NCTR staff provide a comfortable environment for visitors.

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