Blue and white FDA logo

# Bio-Sketches of

# National Center for Toxicological Research (NCTR)

# Principal Investigators

**LINK DIRECTLY TO NCTR RESEARCH DIVISIONS/OFFICES:**

* [**Office of the Center Director**](#OD)
* [**Office of Research**](#OR)
* [**Office of Scientific Coordination**](#OSC)
* [**Division of Biochemical Toxicology**](#DBT)
* [**Division of Bioinformatics and Biostatistics**](#DBB)
* [**Division of Genetic and Molecular Toxicology**](#DGMT)
* [**Division of Microbiology**](#DM)
* [**Division of Neurotoxicology**](#DNT)
* [**Division of Systems Biology**](#DSB)

## Office of the Center Director, NCTR

# Tucker A Patterson, Ph.D.

### **Director — National Center for Toxicological Research**

Tucker A. Patterson, Ph.D. was selected as Center Director at the FDA’s National Center for Toxicological Research (NCTR) in March 2023 after serving as the Acting Director since March 2022. Dr. Patterson continues to serve as the Deputy Director for Research in the Office of the Center Director/Office of Research, a position held since December 2020.

Prior to this appointment, he served two years as the Associate Director for Science & Policy and over seven years as the Associate Director and Health Science Program Manager in Regulatory Compliance & Risk Management at NCTR.

Dr. Patterson received a Bachelor of Science degree in chemistry from the University of Arkansas at Fayetteville and a doctorate in pharmacology from the University of South Carolina. He completed a two-year postdoctoral fellowship with the Center for the Neurobiology of Aging at the University of Florida and continued his postdoctoral training at NCTR through a postgraduate research appointment with the Oak Ridge Institute for Science and Education and as a staff fellow. Dr. Patterson worked for three years as a toxicologist for the State of Arkansas at the Livestock and Poultry Commission prior to returning to NCTR in 2001 where he worked in the Division of Neurotoxicology as a senior scientist until 2010.

Dr. Patterson has been involved in neuroscience and neurotoxicology research for more than thirty years and has authored or co-authored over 100 peer-reviewed scientific articles and book chapters. [VIEW FULL BIO – Dr. Tucker A Patterson](https://www.fda.gov/about-fda/fda-organization/tucker-patterson)

**Titles and links to selected publications**

[**Three-Dimensional Structural Insights Have Revealed the Distinct Binding Interactions of Agonists, Partial Agonists, and Antagonists with µ Opioid Receptor (Review)**](https://www.mdpi.com/1422-0067/24/8/7042)**.**

[**Mold2 Descriptors Facilitate Development of Machine Learning and Deep Learning Models for Predicting Toxicity of Chemicals (Book Chapter)**](https://link.springer.com/chapter/10.1007/978-3-031-20730-3_12)**.**

[**Machine Learning for Predicting Organ Toxicity (Book Chapter)**](https://link.springer.com/chapter/10.1007/978-3-031-20730-3_22)**.**

[**Machine Learning for Predicting Gas Adsorption Capacities of Metal Organic Framework (Book Chapter)**](https://link.springer.com/chapter/10.1007/978-3-031-20730-3_28)**.**

[**Machine Learning Models for Rat Multigeneration Reproductive Toxicity Prediction**](https://www.frontiersin.org/articles/10.3389/fphar.2022.1018226/full)**.**

[**Machine Learning Models for Predicting Liver Toxicity (Book Chapter)**](https://link.springer.com/protocol/10.1007/978-1-0716-1960-5_15)**.**

[**Machine Learning Models for Predicting Cytotoxicity of Nanomaterials**](https://pubs.acs.org/doi/10.1021/acs.chemrestox.1c00310)**.**

[**Application of Nonhuman Primate Models in the Studies of Pediatric Anesthesia Neurotoxicity**](https://journals.lww.com/anesthesia-analgesia/Fulltext/9900/Application_of_Nonhuman_Primate_Models_in_the.313.aspx)**.**

[**Elucidation of Agonist and Antagonist Binding Mechanisms of ER-α by Integration of Molecular Docking, Molecular Dynamics Simulations and Quantum Mechanical Calculations**](https://pubmed.ncbi.nlm.nih.gov/34502280/)**.**

[**AI-Powered Drug Repurposing for Developing COVID-19 Treatments (Book Chapter)**](https://www.sciencedirect.com/science/article/pii/B9780128240106000058?via%3Dihub)**.**

[**The NMDA Receptor System and Developmental Neurotoxicity (Book Chapter)**](https://link.springer.com/referenceworkentry/10.1007%2F978-3-030-71519-9_194-1)**.**

[VIEW FULL BIO – Tucker A Patterson, Ph.D.](https://www.fda.gov/about-fda/fda-organization/tucker-patterson)

# Gonçalo Gamboa da Costa, Ph.D.

### **Senior Science Advisor — Office of the Center Director**

Dr. Gamboa da Costa’s research interests are focused on the in-depth toxicological evaluation of food adulterants and food additives. He was the principal investigator of key toxicological studies sponsored by NTP aiming to clarify the combined toxicity of melamine and cyanuric acid. These food adulterants were implicated in the kidney illness and death of large numbers of cats and dogs in the U.S. in 2007, as well as the deaths of at least six infants and the hospitalization of an estimated 300,000 infants in China in 2008. Dr. Gamboa da Costa is also responsible for ongoing studies that aim to clarify certain toxicological aspects of brominated vegetable oil, a food additive.  
  
The studies conducted by Dr. Gamboa da Costa typically encompass not only guideline endpoints such as histopathology and clinical chemistry, but also the toxicokinetic evaluation of the parent toxicant and its metabolites or the quantification of covalent DNA adducts stemming from genotoxicants, enabling a more comprehensive evaluation of the mechanisms of toxicity.  
  
Given Dr. Gamboa da Costa’s expertise in synthetic organic chemistry and mass spectral-based analytical methodologies, he is regularly invited to collaborate with national and international research teams on a range of topics in toxicology. [VIEW FULL BIO – Dr. Gonçalo Gamboa da Costa](https://www.fda.gov/about-fda/science-research-nctr/goncalo-gamboa-da-costa)

**Titles and links to selected publications**

[**A Rapid and Highly Sensitive UPLC-ESI-MS/MS Method for the Analysis of the Fatty Acid Profile of Edible Vegetable Oils**](https://pubmed.ncbi.nlm.nih.gov/33246283/)**.**

[**Pharmacokinetics of Oseltamivir Phosphate and Oseltamivir Carboxylate in Non-Pregnant and Pregnant Rhesus Monkeys**](https://europepmc.org/article/med/31927005)**.**

[**A Two-Year Toxicology Study of Bisphenol A (BPA) in Sprague-Dawley Rats: CLARITY-BPA Core Study Results**](https://pubmed.ncbi.nlm.nih.gov/31365888/)**.**

[**Effects of Human Sulfotransferases on the Cytotoxicity of 12-Hydroxynevirapine**](https://pubmed.ncbi.nlm.nih.gov/30028994/)**.**

[**Simple and Rapid Quantification of Brominated Vegetable Oil in Commercial Soft Drinks by LC-MS**](http://www.ncbi.nlm.nih.gov/pubmed/27451219)**.**

[**Toxicity Evaluation of Bisphenol A Administered by Gavage to Sprague Dawley Rats From Gestation Day 6 Through Postnatal Day 90**](http://www.ncbi.nlm.nih.gov/pubmed/27506224)**.**

[**Metabolic Activation of 2-Amino-1-Methyl-6-Phenylimidazo [4,5-b]Pyridine and DNA Adduct Formation Depends on p53: Studies in Trp53(+/+),Trp53(+/-) and Trp53(-/-) Mice**](http://www.ncbi.nlm.nih.gov/pubmed/26335255)**.**

[**Evaluation of Serum and Liver Toxicokinetics for Furan and Liver DNA Adduct Formation in Male Fischer 344 Rats**](http://www.ncbi.nlm.nih.gov/pubmed/26364877)**.**

[**Exceptionally Long-Term Persistence of DNA Adducts Formed by Carcinogenic Aristolochic Acid I in Renal Tissue from Patients with Aristolochic Acid Nephropathy**](http://www.ncbi.nlm.nih.gov/pubmed/24921086)**.**

[**Performance of Urinary and Gene Expression Biomarkers in Detecting the Nephrotoxic Effects of Melamine and Cyanuric Acid Following Diverse Scenarios of Co-Exposure**](http://www.ncbi.nlm.nih.gov/pubmed/23022069)**.**

[**Timing and Route of Exposure Affects Crystal Formation in Melamine and Cyanuric Exposed Male and Female Rats: Gavage vs. Feeding**](http://www.ncbi.nlm.nih.gov/pubmed/22963836)**.**

[**Urinary Biomarker Detection of Melamine and Cyanuric Acid-Induced Kidney Injury in Rats**](http://www.ncbi.nlm.nih.gov/pubmed/22610612)**.**

[**Dose-Response Assessment of Nephrotoxicity from a Twenty-Eight-Day Combined-Exposure to Melamine and Cyanuric Acid in F344 Rats**](http://www.ncbi.nlm.nih.gov/pubmed/22579976)**.**

[**Pharmacokinetics of Melamine and Cyanuric Acid and their Combinations in F344 Rats**](http://www.ncbi.nlm.nih.gov/pubmed/22228804)**.**

[**Gene Expression of Biomarkers of Nephrotoxicity in F344 Rats Co-Exposed to Melamine and Cyanuric Acid for Seven Days**](http://www.ncbi.nlm.nih.gov/pubmed/21784140)**.**

[**Low-Level Quantification of Melamine and Cyanuric Acid in Limited Samples of Rat Serum by UPLC-Electrospray Tandem Mass Spectrometry**](http://www.ncbi.nlm.nih.gov/pubmed/21345750)**.**

[**Dose-Response Assessment of Nephrotoxicity from a 7-Day Combined Exposure to Melamine and Cyanuric Acid in F344 Rats**](http://www.ncbi.nlm.nih.gov/pubmed/21030430)**.**

[**Detection and Quantitation of N-(Deoxyguanosin-8-yl)-2-Amino-1-Methyl-6-Phenylimidazo[4,5-b]Pyridine Adducts in DNA Using Online Column-Switching Liquid Chromatography Tandem Mass Spectrometry**](http://www.ncbi.nlm.nih.gov/pubmed/20598652)**.**

[**Quantification of 3-Nitrobenzanthrone-DNA Adducts Using Online Column-Switching HPLC-Electrospray Tandem Mass Spectrometry**](http://www.ncbi.nlm.nih.gov/pubmed/19916526)**.**

[**DNA Adduct Formation from Acrylamide via Conversion to Glycidamide in Adult and Neonatal Mice**](http://www.ncbi.nlm.nih.gov/pubmed/14565774)**.**

[VIEW FULL BIO – Gonçalo Gamboa da Costa, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/goncalo-gamboa-da-costa)

# Donna L. Mendrick, Ph.D.

### **Associate Director of Regulatory Activities — Office of the Center Director**

Dr. Mendrick has over 25 years of experience in the fields of in vitro biology, computational modeling, pathology, pharmacogenomics, pharmacology, toxicology—in vitro and in vivo assays using small molecules, toxicogenomics, immunology, in vivo efficacy, and safety assessment of recombinant therapeutic proteins and disease modeling. She is now focused on examining the usefulness of new alternate methodologies in research and regulatory settings and artificial intelligence. [VIEW FULL BIO – Dr. Donna L. Mendrick](https://www.fda.gov/about-fda/science-research-nctr/donna-mendrick)

**Titles and links to selected publications**

[**Perspectives on the Evaluation and Adoption of Complex In Vitro Models in Drug Development: Workshop with the FDA and the Pharmaceutical Industry (IQ MPS Affiliate)**](https://pubmed.ncbi.nlm.nih.gov/35064273/)**.**

[**FutureTox IV Workshop Summary: Predictive Toxicology for Healthy Children**](https://pubmed.ncbi.nlm.nih.gov/33555348/)**.**

[**An FDA/CDER Perspective on Nonclinical Testing Strategies: Classical Toxicology Approaches and New Approach Methodologies (NAMs)**](https://pubmed.ncbi.nlm.nih.gov/32325112/)**.**

[**"Natural" is Not Synonymous With "Safe": Toxicity of Natural Products Alone and in Combination with Pharmaceutical Agents**](https://pubmed.ncbi.nlm.nih.gov/32197968/)**.**

[**Biology-Inspired Microphysiological Systems to Advance Patient Benefit and Animal Welfare in Drug Development**](https://pubmed.ncbi.nlm.nih.gov/32113184/)**.**

[**The US Federal Tox21 Program: A Strategic and Operational Plan for Continued Leadership**](https://pubmed.ncbi.nlm.nih.gov/29529324/)**.**

[**A Hybrid Gene Selection Approach to Create the S1500+ Targeted Gene Sets for Use in High-Throughput Transcriptomics**](https://pubmed.ncbi.nlm.nih.gov/29462216/)**.**

[**Metabolic Syndrome and Associated Diseases: From the Bench to the Clinic**](https://pubmed.ncbi.nlm.nih.gov/29106690/)**.**

[**FutureTox III: Bridges for Translation**](https://pubmed.ncbi.nlm.nih.gov/27780885/)**.**

[**Molecular Docking for Identification of Potential Targets for Drug Repurposing**](https://pubmed.ncbi.nlm.nih.gov/27334201/)**.**

[**Adverse Outcome Pathways: From Research to Regulation Scientific Workshop Report**](https://pubmed.ncbi.nlm.nih.gov/26774756/)**.**

[**Machine Learning Methods for Predicting HLA-Peptide Binding Activity**](https://pubmed.ncbi.nlm.nih.gov/26512199/)**.**

[**Translating Extracellular microRNA into Clinical Biomarkers for Drug-Induced Toxicity: From High-Throughput Profiling to Validation**](https://pubmed.ncbi.nlm.nih.gov/26501984/)**.**

[**HLADR: a Database System for Enhancing the Discovery of Biomarkers for Predicting Human Leukocyte Antigen-Mediated Idiosyncratic Adverse Drug Reactions**](https://pubmed.ncbi.nlm.nih.gov/26501190/)**.**

[**Molecular Docking to Identify Associations Between Drugs and Class I Human Leukocyte Antigens for Predicting Idiosyncratic Drug Reactions**](https://pubmed.ncbi.nlm.nih.gov/25747444/)**.**

[**FutureTox II: In Vitro Data and In Silico Models for Predictive Toxicology**](https://pubmed.ncbi.nlm.nih.gov/25628403/)**.**

[**Biomarkers of Tobacco Smoke Exposure**](https://pubmed.ncbi.nlm.nih.gov/25735858/)**.**

[**Correlating In Vitro Data to In Vivo Findings for Risk Assessment**](https://pubmed.ncbi.nlm.nih.gov/24248035/)**.**

[**Transcriptional Profiling to Identify Biomarkers of Disease and Drug Response**](https://pubmed.ncbi.nlm.nih.gov/21332316/)**.**

[**Translational Medicine and the Value of Biomarker Qualification**](https://pubmed.ncbi.nlm.nih.gov/20811041/)**.**

[VIEW FULL BIO – Donna L. Mendrick, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/donna-mendrick)

# Rajesh Nayak, Ph.D.

### **Associate Director, Regulatory Compliance & Risk Management — Office of the Center Director**

Dr. Rajesh Nayak is the Associate Director of Regulatory Compliance & Risk Management (RCRM) at FDA’s National Center for Toxicological Research (NCTR). He received a Bachelor of Science degree in chemistry, a Bachelor of Science (Technology) degree in chemical engineering and technology, and a Master of Science (Technology) degree in food and fermentation technology from the University of Mumbai. He earned a Master of Science and a Ph.D. in animal and veterinary sciences from West Virginia University. He joined NCTR’s Division of Microbiology as an Oak Ridge Institute for Science and Education postdoctoral fellow in 2001. Dr. Nayak's overall goal during this time was to conduct scientific research that supplemented FDA's regulatory decisions to ensure the safety of foods and antibiotics in the “farm-to-the-fork” continuum. As a principal investigator, Dr. Nayak’s research focused on four broad categories:

* Epidemiology, surveillance, and microbial source tracking of food-animal infectious pathogens through the food production environment using genotyping methods
* Threat assessment of emerging pathogens and their genetic characteristics using microarray, sequencing and bioinformatics platforms
* Investigating the mechanisms of drug resistance and pathogenesis in bacterial pathogens isolated from food, feed, environment, humans and veterinary sources
* Molecular tools for detecting of bacterial pathogens and their genetic traits

Dr. Nayak has authored or co-authored more than 70 peer-reviewed scientific publications and book chapters and has given over 145 presentations at national and international conferences. In 2015, Dr. Nayak joined RCRM as a Senior Health Scientist where he led NCTR and FDA biosafety programs and provided guidance to research scientists and support staff on the regulatory compliance of hazardous biological agent and toxins.

In 2018, Dr. Nayak was named Associate Director of RCRM. The mission of RCRM is to ensure the safety and security of employees at the Jefferson Laboratories campus in Arkansas and to ensure research conducted at NCTR is compliant with state and federal regulations. RCRM is responsible for the following programs: chemical safety, biological safety, radiological safety, controlled substances, quality assurance, occupational health and medical surveillance, laboratory safety, hazardous waste management, industrial hygiene, physical security, records management, and archives. Dr. Nayak serves as a senior advisor and subject matter expert to NCTR and FDA leadership on food safety, antimicrobial resistance, laboratory safety, environmental safety, and occupational safety and health. He serves as an NCTR representative on several FDA committees and working groups. [VIEW FULL BIO – Dr. Rajesh Nayak](https://www.fda.gov/about-fda/science-research-nctr/rajesh-nayak)

**Titles and links to selected publications**

[**Microbial Genetics and Clonal Dissemination of Salmonella enterica Serotype Javiana Isolated from Human Populations in Arkansas, USA**](https://pubmed.ncbi.nlm.nih.gov/36297250/)**.**

[**Pragmatic Strategy for Fecal Specimen Storage and the Corresponding Test Methods for Clostridioides difficile Diagnosis**](https://pubmed.ncbi.nlm.nih.gov/34451512/)**.**

[**Genotypic and Phenotypic Characterization of Incompatibility Group FIB Positive Salmonella enterica Serovar Typhimurium Isolates from Food Animal Sources**](https://pubmed.ncbi.nlm.nih.gov/33158112/)**.**

[**Whole Genome Sequences of 66 Incompatibility Group FIB Plasmid-Carrying Salmonella enterica Serovar Typhimurium Isolates from Food Animal Sources**](https://pubmed.ncbi.nlm.nih.gov/33158112/)**.**

[**Immunomagnetic Capture of Big Six Shiga Toxin-Producing Escherichia coli Strains in Apple Juice with Detection by Multiplex Real-Time PCR Eliminates Interference from the Food Matrix**](https://pubmed.ncbi.nlm.nih.gov/31414899/)**.**

[**Impact of Co-carriage of IncA/C Plasmids with Additional Plasmids on the Transfer of Antimicrobial Resistance in Salmonella enterica Isolates**](https://pubmed.ncbi.nlm.nih.gov/29549790/)**.**

[VIEW FULL BIO – Rajesh Nayak, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/rajesh-nayak)

# Bradley Schnackenberg, Ph.D.

### **Associate Director, Office of Scientific Coordination — Office of the Center Director**

Dr. Bradley J. Schnackenberg is the Associate Director of the Office of Scientific Coordination (OSC) at FDA’s National Center for Toxicological Research (NCTR). He received a B.S. in cell biology and a Ph.D. in physiology and cell biology from the University of Kansas. He was a Lineberger Comprehensive Cancer Center postdoctoral fellow in the Program in Molecular Biology and Biotechnology at the University of North Carolina at Chapel Hill before joining the faculty in the Department of Pediatrics at the University of Arkansas for Medical Sciences and conducting research within the Lung Cell Biology Laboratory at the Arkansas Children’s Hospital Research Institute. In 2008, he was selected into the inaugural class of the FDA commissioner’s fellowship program and subsequently joined NCTR’s Office of Research in 2010. During his tenure in the Office of Research, Dr. Schnackenberg was responsible for coordinating the scientific review and approval of research protocols to ensure alignment with FDA and NCTR programmatic objectives and advising research investigators on scientific policy including human subject research, animal care and use, and technology transfer. He served as an alternate member to the FDA Research Involving Human Subjects Committee. In 2017, Dr. Schnackenberg was named Associate Director of OSC and currently serves as the liaison between NCTR and the Center for Tobacco Products (CTP).

The mission of OSC is to enable the research mission of NCTR/FDA by providing the professional support necessary to conduct toxicological studies. The support functions of OSC include Veterinary Services and Microbiology Surveillance, Toxicology Program Support, Experimental Liaison Support, the Analytical Chemistry Group, the Statistical Support Group, the NCTR-ORA Nanotechnology Core Facility, and Contract Officer Representatives for three onsite contracts that provide support in the areas of animal care, pathology, and laboratory equipment maintenance and repair. The OSC also provides program management for the Performance Agreement between NCTR and CTP. [VIEW FULL BIO – Dr. Bradley Schnackenberg](https://www.fda.gov/about-fda/science-research-nctr/bradley-schnackenberg)

[VIEW FULL BIO – Bradley Schnackenberg, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/bradley-schnackenberg)

## Office of Research, NCTR

### Research Division Directors within Office of Research

* [**Frederick A. Beland, Ph.D.**](#FBeland)  
  Division of Biochemical Toxicology, Director
* [**Weida Tong, Ph.D.**](#WTong)  
  Division of Bioinformatics and Biostatistics, Director
* [**Robert H. Heflich, Ph.D.**](#RHeflich)  
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* [**Laura Schnackenberg, Ph.D.**](#LSchnackenberg)  
  Division of Systems Biology, Director

## Office of Scientific Research, NCTR

# [Bradley Schnackenberg, Ph.D.](#BSchnackenberg)

### **Associate Director — Office of Scientific Coordination**

[VIEW FULL BIO – Bradley Schnackenberg, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/bradley-schnackenberg)

# Matthew Bryant, Ph.D.

### **Supervisory Toxicologist — Office of Scientific Coordination**

Dr. Bryant collaborates with researchers on key aspects of toxicology studies, including verifying the identity and purity of test articles using analytical chemistry techniques. Concentration verification of test substances has been a key concern, especially when natural products or mixtures are being studied and the characterization of more complex mixtures, such as tobacco smoke, is of particular interest. Dr. Bryant’s group makes use of a variety of analytical methods to analyze a diverse range of drugs and toxic compounds in dose vehicles, such as drinking water, diet pellets or powder, and oral or intravenous solutions. The characterization of test articles in complex mixtures is a focus of collaborations with the inhalation toxicology facility that utilizes tobacco smoking machines or other specialized test article delivery apparatus. Evaluating the stability or homogeneity of test articles in dose vehicles or formulations is important, not just for simple solutions, but for complex vehicles such as creams or diet admixtures. Sensitive analytical methods are used to test for trace amounts of the test article or potential contaminants in background materials, including bedding, diet, drinking water, and cages. Animal studies often require that proper amounts of certain nutrients – vitamins, protein, fat – are in the food, or that certain known or suspected contaminants – pesticides, trace metals – are below a target level.

Dr. Bryant is interested in:

* Bioanalytical methodology, especially the use of hyphenated mass spectrometry (e.g. HPLC/mass spectrometry (MS), gas chromatography (GC)/MS and MS/MS technology) for trace level analysis of compounds and/or their metabolites in plasma, urine, and tissues. Applications of such analytical methods to toxicology, biochemical epidemiology, and drug discovery and development have been a key area for study.
* The use of electrophilic metabolites of carcinogens with nucleophilic target molecules, such as DNA, surrogate blood proteins hemoglobin, and albumin, as tools for studying the mechanism of their toxic effects in vivo. In particular, he has studied the use of sensitive GC/MS techniques to quantify hemoglobin adducts of carcinogenic aromatic amines and applications to exposure assessment and biochemical epidemiology.
* Research that seeks to enhance the success rate of drugs by optimizing their absorption, distribution, metabolism, and excretion (ADME) or pharmacokinetic properties. Research can often be done to select the best compounds based on their biophysical properties, such as solubility or permeability, or through screening assays that seek to optimize absorption or biological half-life. Once the limiting ADME or toxicology (ADMET) issue is identified, screening assays are used to select the best compounds that not only are efficacious but have optimized ADMET properties. Such assays include solubility, absorption, P450 inhibition, protein binding, permeability, or in vitro (microsomal) stability. Fast pharmacokinetic studies are conducted in animal models to help select compounds for more costly efficacy studies in key animal models for the specific disease category. Such pharmacokinetic screening assays require the use of modern bioanalytical techniques, such as HPLC tandem MS analysis to screen many compounds in various chemical series. Feedback is often provided to synthetic chemistry groups that utilize this structure-activity relationship data to improve the molecules. Only compounds with the best in vitro ADMET properties or in vivo pharmacokinetics are advanced for efficacy or more detailed pharmacokinetic studies in animal models before they are recommended for development as full clinical candidates. The role of drug metabolism and pharmacokinetics, combined with modern bioanalytical assays, has improved the success rate for drug candidates in clinical studies.

[VIEW FULL BIO – Dr. Matthew Bryant](https://www.fda.gov/about-fda/science-research-nctr/matthew-bryant)

**Titles and links to selected publications**

[**The Role of CYP 3A4 and 1A1 in Amiodarone-Induced Hepatocellular Toxicity**](https://www.ncbi.nlm.nih.gov/pubmed/27113703)**.**

[**Differential Effects of Silver Nanoparticles and Silver Ions on Tissue Accumulation, Distribution, and Toxicity in the Sprague Dawley Rat Following Daily Oral Gavage Administration for 13 Weeks**](https://www.ncbi.nlm.nih.gov/pubmed/26732888)**.**

[**Effects of Maternal and Lactational Exposure to 2-Hydroxy-4-Methoxybenzone on Development and Reproductive Organs in Male and Female Rat Offspring**](https://www.ncbi.nlm.nih.gov/pubmed/25707689)**.**

[**Toxicity Evaluation of Bisphenol A Administered by Gavage to Sprague Dawley Rats From Gestation Day 6 Through Postnatal Day 90**](https://www.ncbi.nlm.nih.gov/pubmed/24496637)**.**

[**Supported Liquid Extraction in Combination with LC-MS/MS for High-Throughput Quantitative Analysis of Hydrocortisone in Mouse Serum**](https://www.ncbi.nlm.nih.gov/pubmed/19847778)**.**

[**A Sensitive and High-Throughput LC-MS/MS Method for the Quantification of Pegylated-Interferon-α2a in Human Serum Using  Monolithic C18 Solid Phase Extraction for Enrichment**](https://www.ncbi.nlm.nih.gov/pubmed/19447689)**.**

[**Metabolism-Based Identification of a Potent Thrombin Receptor Antagonist**](https://www.ncbi.nlm.nih.gov/pubmed/17201416)**.**

[**A Novel Approach to Perform Metabolite Screening During the Quantitative LC-MS/MS Analyses of In Vitro Metabolic Stability Samples Using a Hybrid Triple-Quadrupole Linear Ion Trap Mass Spectrometer**](https://pubmed.ncbi.nlm.nih.gov/16206149/)**.**

[**Identification of a Novel, Orally Bioavailable Histamine H(3) Receptor Antagonist Based on the 4-Benzyl-(1H-Imidazol-4-yl) Template**](https://www.ncbi.nlm.nih.gov/pubmed/11958998)**.**

[**Direct Cocktail Analysis of Drug Discovery Compounds in Pooled Plasma Samples Using Liquid Chromatography-Tandem Mass Spectrometry**](https://www.ncbi.nlm.nih.gov/pubmed/11885864)**.**

[**Antitumor Activity of SCH 66336, An Orally Bioavailable Tricyclic Inhibitor of Farnesyl Protein Transferase, In Human Tumor Xenograft Models and Wap-ras Transgenic Mice**](https://www.ncbi.nlm.nih.gov/pubmed/9810004)**.**

[**Epoxybutene-Hemoglobin Adducts In Rats And Mice: Dose Response For Formation And Persistence During And Following Long-Term Low-Level Exposure To Butadiene**](https://www.ncbi.nlm.nih.gov/pubmed/9630466)**.**

[**Pharmacokinetic Screening for Selection of New Drug Discovery Candidates is Greatly Enhanced through the Use of LC-API/MS/MS**](https://www.ncbi.nlm.nih.gov/pubmed/9297838)**.**

[**2,6-Dimethylaniline-Hemoglobin Adducts From Lidocaine in Humans**](https://www.ncbi.nlm.nih.gov/pubmed/7955068)**.**

[**Detection and Characterization of DNA Adducts at the Femtomole Level by Desorptive Ionization Mass Spectrometry**](https://www.ncbi.nlm.nih.gov/pubmed/8319622)**.**

[**Development of Fast Atom Bombardment Mass Spectral Methods for the Identification of Carcinogen Nucleoside Adducts**](https://www.ncbi.nlm.nih.gov/pubmed/24243047)**.**

[**Decline of the Hemoglobin Adduct of 4 Aminobiphenyl During Withdrawal from Smoking**](https://www.ncbi.nlm.nih.gov/pubmed/2293553)**.**

[**Elevated Blood Levels of Carcinogens in Passive Smokers**](https://www.ncbi.nlm.nih.gov/pubmed/2782507)**.**

[**Hemoglobin Adducts of Aromatic Amines: Associations with Smoking Status and Type of Tobacco**](https://www.ncbi.nlm.nih.gov/pubmed/3200858)**.**

[**Hemoglobin Adducts of 4 Aminobiphenyl in Smokers and Nonsmokers**](https://www.ncbi.nlm.nih.gov/pubmed/3791245)**.**

[VIEW FULL BIO – Matthew Bryant, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/matthew-bryant)

# Mani Chidambaram, M.Sc., Ph.D.

### **Staff Fellow — Office of Scientific Coordination**

Dr. Chidambaram is interested in:

* Quantitative analytical chemistry techniques including solid phase extraction, high performance liquid chromatography (HPLC/UPLC), gas chromatography (GC), HPLC-mass spectrometry, GC-mass spectrometry. Trace level analysis of toxic or suspect compounds in various matrices, including food, drug formulations and biological samples, such as plasma, urine and tissues.
* Synthesis and characterization of organic molecules of medicinal interests.
* Synthesis and characterization of metal complexes of biological interest and their characterization by physical chemistry techniques such as spectroscopy, magnetic susceptibility measurements, electron spin resonance spectroscopy, circular dichroism, and atomic absorption spectrophotometry.
* Metal-protein interactions, including exchange reactions involving stopped-flow techniques, radioactivity, gel-filtration, electrophoresis, oxygen concentration measurements, isolation of proteins from serum and plant materials. Special interest in trace elements, especially iron and copper.

[VIEW FULL BIO – Dr. Mani Chidambaram](https://www.fda.gov/about-fda/science-research-nctr/mani-chidambaram)

**Titles and links to selected publications**

[**Toxicity Evaluation of Bisphenol A Administered by Gavage to Sprague Dawley Rats from Gestation Day 6 Through Postnatal Day 90**](https://pubmed.ncbi.nlm.nih.gov/24496637/)**.**

[**Pharmacokinetic Distribution of 67Cu(II)2[3,5-Diisopropyl(Carboxy- 14C)Salicylate]4 Among Murine Tissues**](https://pubmed.ncbi.nlm.nih.gov/15544486/)**.**

[**In Vitro Studies on Iron Bioavailability: Probing the Concentration and Oxidation-reduction of Pinto Bean Iron with Ferrous Chromogens**](https://pubmed.ncbi.nlm.nih.gov/2484376/)**.**

[VIEW FULL BIO – Mani Chidambaram, M.Sc., Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/mani-chidambaram)

# Hong Fang, Ph.D.

### **Health Information Scientist — Office of Scientific Coordination**

Dr. Fang’s main research interest is to apply bioinformatics, chemoinformatics, knowledge base and big data methodologies, and predictive toxicology approaches to address issues in the areas of:

* Data science
* Bioinformatics
* Drug labeling
* Medical informatics
* Health informatics
* Databases
* Toxicology
* Clinical applications
* Data-oriented research (data mining)
* Adverse drug reactions (ADR)
* Pharmacogenomics and precision medicine
* Biomarker development and application

Dr. Fang has over 15 years of experience applying data mining, pattern recognition, machine learning, classification, molecular modeling, bioinformatics, and chemoinformatics approaches in these areas. Her research experience is broad, ranging from applying bioinformatics methods to studying specific diseases and toxicity to managing and coordinating large software development programs. For example, Dr. Fang developed integrated bioinformatics approaches for biomarker discovery for lupus, chronic fatigue syndrome, drug-induced liver injury, cancer, brain function, and more. Currently, she is leading an effort to develop the FDALabel database — a web-based application — to query and mine FDA drug labeling data. One goal of this project is to integrate FDA labeling data with various medical ontologies, such as the Medical Dictionary for Regulatory Application (MedDRA) and the Unified Medical Language System (UMLS) to enhance the use of drug labeling data and its readiness for integration with other FDA databases such as the FDA Adverse Event Reporting System.

As a senior health information scientist and project manager within NCTR’s Office of Scientific Coordination Dr. Fang leads several large bioinformatics projects. She has led and coordinated efforts that resulted in widely used software to support FDA‘s drug safety, genomic research, review, study of adverse drug reaction (ADR), and precision medicine. Some of the [bioinformatics tools](https://www.fda.gov/science-research/bioinformatics-tools/fdalabel-full-text-search-drug-product-labeling) that she helped develop include:

* [FDALabel](https://nctr-crs.fda.gov/fdalabel/ui/search): a full-text search web-based database of the FDA drug labeling system which is a resource in study of drug safety, pharmacovigilance, and precision medicine
* [ArrayTrack](https://www.fda.gov/science-research/bioinformatics-tools/arraytracktm-hca-pca-standalone-package-powerful-data-exploring-tools): an integrated genomics tool to support FDA review and research on genomics and pharmacogenomics
* [LTKB](https://www.fda.gov/science-research/bioinformatics-tools/liver-toxicity-knowledge-base-ltkb) (Liver Toxicity Knowledge Base): a collection of diverse drug-induced liver injury data to assess risk of drug-induced liver injury
* [EDKB](https://www.fda.gov/science-research/bioinformatics-tools/endocrine-disruptor-knowledge-base) (Endocrine Disruptor Knowledge Base): an integrated database to prioritize chemicals for potential endocrine disruption

Dr. Fang has mentored and supervised many young scientists, postdoctoral fellows, and summer interns – one student each year for six consecutive years. She also has many publications that are widely recognized with high citations – a total of 14,765 citations from 152 manuscripts and an H-Index of 57, as of July 2021, from Google Scholar Citations. [VIEW FULL BIO – Dr. Hong Fang](https://www.fda.gov/about-fda/science-research-nctr/hong-fang)

**Titles and links to selected publications**

[**FDALabel for Drug Repurposing Studies and Beyond**](https://pubmed.ncbi.nlm.nih.gov/33235392/)**.**

[**Study of Pharmacogenomic Information in FDA-approved Drug Labeling to Facilitate Application of Precision Medicine**](https://pubmed.ncbi.nlm.nih.gov/32032705/)**.**

[**Potential Reuse of Oncology Drugs in the Treatment of Rare Diseases**](https://www.ncbi.nlm.nih.gov/pubmed/27461952)**.**

[**FDA Drug Labeling: Rich Resources to Facilitate Precision Medicine, Drug Safety, and Regulatory Science**](https://www.ncbi.nlm.nih.gov/pubmed/27319291)**.**

[**Exploring the FDA Adverse Event Reporting System to Generate Hypotheses for Monitoring of Disease Characteristics**](https://www.ncbi.nlm.nih.gov/pubmed/24448476)**.**

[**A Comprehensive Assessment of RNA-Seq Accuracy, Reproducibility and Information Content by the Sequence Quality Control Consortium**](https://www.ncbi.nlm.nih.gov/pubmed/25150838)**.**

[**An Investigation of Biomarkers Derived from Legacy Microarray Data for their Utility in the RNA-Seq Era**](https://www.ncbi.nlm.nih.gov/pubmed/25633159)**.**

[**Towards Interoperable Bioscience Data**](https://www.ncbi.nlm.nih.gov/pubmed/22281772)**.**

[**Next-Generation Sequencing and its Applications in Molecular Diagnostics**](https://www.ncbi.nlm.nih.gov/pubmed/21463242)**.**

[**Meta-Analysis of Microarray Data Using a Pathway-Based Approach Identifies a 37-Gene Expression Signature for Systemic Lupus Erythematosus in Human Peripheral Blood Mononuclear Cells**](https://bmcmedicine.biomedcentral.com/articles/10.1186/1741-7015-9-65)**.**

[**An FDA Bioinformatics Tool for Microbial Genomics Research on Molecular Characterization of Bacterial Foodborne Pathogens Using Microarrays**](https://www.ncbi.nlm.nih.gov/pubmed/20946615)**.**

[**The MicroArray Quality Control (MAQC)-II Study of Common Practices for the Development and Validation of Microarray-Based Predictive Models**](https://pubmed.ncbi.nlm.nih.gov/20676074/)**.**

[**GOFFA: Gene Ontology for Functional Analysis- Software for Gene Ontology-Based Functional Analysis of Genomic and Proteomic Data**](https://www.ncbi.nlm.nih.gov/pubmed/17118145)**.**

[**The MicroArray Quality Control (MAQC) Project Shows Inter- and Intraplatform Reproducibility of Gene Expression Measurements**](https://www.ncbi.nlm.nih.gov/pubmed/16964229)**.**

[**Performance Comparison of One-Color and Two-Color Platforms Within the Microarray Quality Control (MAQC) Project**](https://www.ncbi.nlm.nih.gov/pubmed/16964228)**.**

[**Gene Expression Profile Exploration of a Large Dataset on Chronic Fatigue Syndrome**](https://www.ncbi.nlm.nih.gov/pubmed/16610953)**.**

[**Bioinformatics Approaches for Cross-Species Liver Cancer Analysis Based on Microarray Gene Expression Profiling**](https://www.ncbi.nlm.nih.gov/pubmed/16026603)**.**

[**ArrayTrack-Supporting Toxicogenomic Research at the FDA’s National Center for Toxicological Research (NCTR)**](https://www.ncbi.nlm.nih.gov/pubmed/14630514)**.**

[**Study of 202 Natural, Synthetic, and Environmental Chemicals for Binding to the Androgen Receptor**](https://pubmed.ncbi.nlm.nih.gov/14565775/)**.**

[**Decision Forest: Combining the Predictions of Multiple Independent Decision Tree Models**](https://www.ncbi.nlm.nih.gov/pubmed/12653517)**.**

[**Structure-Activity Relationship for a Large Diverse Set of Natural, Synthetic and Environmental Chemicals**](https://www.ncbi.nlm.nih.gov/pubmed/11258977)**.**

[VIEW FULL BIO – Hong Fang, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/hong-fang)

# Xiaobo He, Ph.D.

### **Visiting Scientist — Office of Scientific Coordination**

Dr. He collaborates with other NCTR scientists on projects funded by the Center for Tobacco Products, the National Toxicology Program, and FDA. His primary duty is to conduct mass spectral analyses of complex mixtures of interest to the FDA, such as natural products, trace metals, drugs, colors, and tobacco-related products. Dr. He’s main research interests include: 1) establishment and application of bioanalytical methodology for trace analysis of compounds and their metabolites in bio-samples using mass spectral approaches; 2) pharmacokinetic / pharmacodynamic modelling by in vivo and in vitro assays; and 3) application of metabolomic / proteomic / lipidomic techniques to toxicological studies. [VIEW FULL BIO – Dr. Xiaobo He](https://www.fda.gov/about-fda/science-research-nctr/xiaobo-he)

**Titles and links to selected publications**

[**Effects of Glutathione and Cysteine on Pyrrolizidine Alkaloid-induced Hepatotoxicity and DNA Adduct Formation in Rat Primary Hepatocytes**](https://pubmed.ncbi.nlm.nih.gov/32500832/)**.**

[**Quantitation of DNA Reactive Pyrrolic Metabolites of Senecionine – A Carcinogenic Pyrrolizidine Alkaloid by LC/MS/MS Analysis**](https://pubmed.ncbi.nlm.nih.gov/31883605/)**.**

[**Comprehensive Identification of Amadori Compound-modified Phosphatidylethanolamines in Human Plasma**](https://pubmed.ncbi.nlm.nih.gov/31188577/)**.**

[**1-Formyl-7-hydroxy-6,7-dihydro-5H-pyrrolizine (1-CHO-DHP): A Potential Proximate Carcinogenic Metabolite of Pyrrolizidine Alkaloids**](https://pubmed.ncbi.nlm.nih.gov/31120748/)**.**

[**Primary and Secondary Pyrrolic Metabolites of Pyrrolizidine Alkaloids Form DNA Adducts in Human A549 Cells**](https://pubmed.ncbi.nlm.nih.gov/30366057/)**.**

[**Synthesis, Purification and Mass Spectrometric Characterization of Stable Isotope-labeled Amadori-glycated Phospholipids**](https://pubmed.ncbi.nlm.nih.gov/30533579/)**.**

[**Pyrrolizidine Alkaloid Secondary Pyrrolic Metabolites Construct Multiple Activation Pathways Leading to DNA Adduct Formation and Potential Liver Tumor Initiation**](https://pubmed.ncbi.nlm.nih.gov/29855181/)**.**

[**Pyrrolizidine Alkaloid-derived DNA Adducts are Common Toxicological Biomarkers of Pyrrolizidine Alkaloid N-oxides**](https://pubmed.ncbi.nlm.nih.gov/28987376/)**.**

[**7-Glutathione-pyrrole and 7-cysteine-pyrrole are Potential Carcinogenic Metabolites of Pyrrolizidine Alkaloids**](https://pubmed.ncbi.nlm.nih.gov/28418776/)**.**

[**Detection of Pyrrolizidine Alkaloid DNA Adducts in Livers of Cattle Poisoned with Heliotropium europaeum**](https://pubmed.ncbi.nlm.nih.gov/28125883/)**.**

[**7-Cysteine-pyrrole Conjugate: A New Potential DNA Reactive Metabolite of Pyrrolizidine Alkaloids**](https://pubmed.ncbi.nlm.nih.gov/26761716/)**.**

[**7-N-Acetylcysteine-pyrrole Conjugate—A Potent DNA Reactive Metabolite of Pyrrolizidine Alkaloids**](https://pubmed.ncbi.nlm.nih.gov/28911605/)**.**

[**7-Glutathione Pyrrole Adduct: A Potential DNA Reactive Metabolite of Pyrrolizidine Alkaloids**](https://pubmed.ncbi.nlm.nih.gov/25768656/)**.**

[VIEW FULL BIO – Xiaobo He, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/xiaobo-he)

# Nathan Koonce, Ph.D.

### **Staff Fellow — Office of Scientific Coordination**

Dr. Koonce’s main research interest is in regulatory science with a focus on physico-chemical characteristics of nanomaterials and the structure-activity relationship on safety and efficacy. His background in cancer therapeutics and tumor models has led to an interest in FDA-approved and next-generation nano-based therapeutics for cancer therapy. Dr. Koonce also has an interest in non-pharmaceutical based nanomaterials as they relate to public safety/toxicity. He has expertise in nanomaterial characterization, toxicity and immunotoxicity assays, rodent models, and in vivo imaging techniques. Dr. Koonce’s current research investigates:

* Physico-chemical characteristics of nanomaterials and effects on toxicity and biodistribution
* Toxicity of nanomaterial in feminine-hygiene products
* Characterization and efficacy of nano-based therapeutics

[VIEW FULL BIO – Dr. Nathan Koonce](https://www.fda.gov/about-fda/science-research-nctr/nathan-koonce)

**Titles and links to selected publications**

[**Galectin-1 Inhibitor OTX008 Induces Tumor Vessel Normalization and Tumor Growth Inhibition in Human Head and Neck Squamous Cell Carcinoma Models**](https://www.ncbi.nlm.nih.gov/pubmed/29232825)**.**

[**Real-Time Monitoring of Circulating Tumor Cell (CTC) Release After Nanodrug or Tumor Radiotherapy Using In Vivo Flow Cytometry**](https://www.ncbi.nlm.nih.gov/pubmed/28822765)**.**

[**Combination of Gold Nanoparticle-Conjugated Tumor Necrosis Factor-α and Radiation Therapy Results in a Synergistic Antitumor Response in Murine Carcinoma Models**](https://www.ncbi.nlm.nih.gov/pubmed/26461001)**.**

[**Targeting Artificial Tumor Stromal Targets for Molecular Imaging of Tumor Vascular Hypoxia**](https://www.ncbi.nlm.nih.gov/pubmed/26308944)**.**

[**Indirect Tumor Cell Death After High-Dose Hypofractionated Irradiation: Implications for Stereotactic Body Radiation Therapy and Stereotactic Radiation Surgery**](https://www.ncbi.nlm.nih.gov/pubmed/26279032)**.**

[**Nanoparticle Delivered Vascular Disrupting Agents (VDAs): Use of TNF-Alpha Conjugated Gold Nanoparticles for Multimodal Cancer Therapy**](https://www.ncbi.nlm.nih.gov/pubmed/23544801)**.**

[**Photothermal Nanodrugs: Potential of TNF-Gold Nanospheres for Cancer Theranostics**](https://www.ncbi.nlm.nih.gov/pubmed/23443065)**.**

[**Microbeam Radiation Therapy Alters Vascular Architecture and Tumor Oxygenation and is Enhanced by a Galectin-1 Targeted Anti-Angiogenic Peptide**](https://www.ncbi.nlm.nih.gov/pubmed/22607585)**.**

[**Conductive Thermal Ablation of 4T1 Murine Breast Carcinoma Reduces Severe Hypoxia in Surviving Tumour**](https://www.ncbi.nlm.nih.gov/pubmed/22335229)**.**

[**Vascular Disrupting Agent Arsenic Trioxide Enhances Thermoradiotherapy of Solid Tumors**](https://www.ncbi.nlm.nih.gov/pubmed/22272199)**.**

[**Repression of Multiple Myeloma Growth and Preservation of Bone with Combined Radiotherapy and Anti-Angiogenic Agent**](https://www.ncbi.nlm.nih.gov/pubmed/20518660)**.**

[**Prevention and Mitigation of Acute Death of Mice After Abdominal Irradiation by the Antioxidant N-Acetyl-Cysteine (NAC)**](https://www.ncbi.nlm.nih.gov/pubmed/20426657)**.**

[VIEW FULL BIO – Nathan Koonce, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/nathan-koonce)

# Sanghamitra Majumdar, Ph.D.

### **Visiting Scientist — Office of Scientific Coordination**

Dr. Majumdar’s primary research interest lies in exploring the scope and challenges towards the safe and sustainable use of ENMs in medicine, food and agriculture industries. Although a wide range of nanomaterials have demonstrated their benefits in various applications, there is a lack of comprehensive understanding of their environmental/biological fate, mode of action and biological response. In the past, Dr. Majumdar has contributed significantly to the understanding of interactions of ENMs with crops at physiological, cellular and molecular levels. Her research on nano-plant interaction traversed a “farm to fork approach” providing a holistic understanding of ENMs’ influence on food safety. Her research findings provided insights on the route of uptake of ENMs by plants and its subsequent impact on biochemical machinery and protein-protein interaction in legumes and accumulation in the food chain. She also investigated the properties of various surface ligands that can influence the stability of nanomaterials in natural media, mode of their entry into the plant via specific channel proteins, subcellular sequestration, micronutrient acquisition by roots, and impact on the plant metabolic machinery and oxidative response. In order to comprehend the underlying mechanism of interactions between potential nano-based agrochemicals and agricultural crops. Dr. Majumdar utilized untargeted and targeted omic technologies, including proteomic and metabolomics using LC-MS and matrix assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF) techniques. By integrating proteomics and metabolomics, she has successfully elucidated the mode of action of copper-based ENMs, which increases crop yield by leveraging the photosynthetic activities in the chloroplast, energy transfer in the mitochondria and carbohydrate assimilation. These mechanistic approaches and key findings will enable sustainable agricultural applications of nanomaterials, which are good candidates for crop growth, yield, increased nutrient bioavailability and would help in amending toxicity concerns from overuse of conventional agrochemicals.

Dr. Majumdar has expertise in ENM characterization, toxicity and biochemical assays, proteomics, metabolomics, and detection and quantitation of inorganic (metal ions) and organic (small and large molecules) species in environmental and biological samples using mass-spectrometry-based analytical techniques. Given her expertise in mass-spectroscopy-based analytical tools, Dr. Majumdar has contributed towards the development of analytical methods for detection of pesticides, antibiotics, phytochemicals, and mycotoxin in food and animal feed using high resolution LC-MS platforms under the FDA-FERN program.

At NCTR, she extended her expertise in LC-MS techniques towards the development of collaborative consensus ASTM standards on chemical characterization of nanomaterial-enabled drugs and consumer products, which will provide guidance to the regulatory agencies and industry. She is also exploring novel analytical techniques to identify and quantify sub-micron to micron-sized plastic particles in simple and complex matrices, including food, biological and environmental samples. Dr. Majumdar also retains strong interest in elucidation of biomarkers of response and toxicokinetic evaluation of next-generation nanomaterial-based therapeutics and their interference with general metabolic machinery with additional influence due to age, sex and physiological conditions in animals and/or humans. [VIEW FULL BIO – Dr. Sanghamitra Majumdar](https://www.fda.gov/about-fda/science-research-nctr/sanghamitra-majumdar)

**Titles and links to selected publications**

[**Omics to Address the Opportunities and Challenges of Nanotechnology in Agriculture**](https://www.tandfonline.com/doi/full/10.1080/10643389.2020.1785264)**.**

[**Proteomic, Gene and Metabolite Characterization Reveal the Uptake and Toxicity Mechanisms of Cadmium Sulfide Quantum Dots in Soybean Plants**](https://pubs.rsc.org/en/content/articlelanding/2019/en/c9en00599d)**.**

[**Surface Coating Determines the Response of Soybean Plants to Cadmium Sulfide Quantum Dots**](https://www.sciencedirect.com/science/article/pii/S2452074818301848)**.**

[**Effect of Metalloid and Metal Oxide Nanoparticles on Fusarium Wilt of Watermelon**](https://pubmed.ncbi.nlm.nih.gov/30673561/)**.**

[**Co-exposure of Imidacloprid and Nanoparticle Ag or CeO2 to Cucurbita pepo (zucchini): Contaminant Bioaccumulation and Translocation**](https://www.sciencedirect.com/science/article/pii/S2452074818300624)**.**

[**A Collaborative Study: Determination of Mycotoxins in Corn, Peanut Butter, and Wheat Flour Using Stable Isotope Dilution Assay (SIDA) and Liquid Chromatography–Tandem Mass Spectrometry (LC-MS/MS)**](https://pubmed.ncbi.nlm.nih.gov/27983809/)**.**

[**Weathering in Soil Increases Nanoparticle CuO Bioaccumulation Within a Terrestrial Food Chain**](https://pubmed.ncbi.nlm.nih.gov/28024451/)**.**

[**Exposure of Cucurbita pepo to Binary Combinations of Engineered Nanomaterials: Physiological and Molecular Response**](https://pubs.rsc.org/en/content/articlelanding/2017/EN/C7EN00219J)**.**

[**Soil Organic Matter Influences Cerium Translocation and Physiological Processes in Kidney Bean Plants Exposed to Cerium Oxide Nanoparticles**](https://pubmed.ncbi.nlm.nih.gov/27343939/)**.**

[**Cerium Biomagnification in a Terrestrial Food Chain: Influence of Particle Size and Growth Stage**](https://pubmed.ncbi.nlm.nih.gov/27343939/)**.**

[**Molecular Response of Crop Plants to Engineered Nanomaterials**](https://pubmed.ncbi.nlm.nih.gov/27301997/)**.**

[**Carbon Nanomaterials in Agriculture: A Critical Review**](https://pubmed.ncbi.nlm.nih.gov/26941751/)**.**

[**Environmental Effects of Nanoceria on Seed Production of Common Bean (Phaseolus vulgaris): A Proteomic Analysis**](https://pubmed.ncbi.nlm.nih.gov/26488752/)**.**

[**Monitoring the Environmental Effects of CeO2 and ZnO Nanoparticles Through the Life Cycle of Corn (Zea mays) Plants and In Situ μ-XRF Mapping of Nutrients in Kernels**](https://pubmed.ncbi.nlm.nih.gov/25648544/)**.**

[**Particle-Size Dependent Accumulation and Trophic Transfer of Cerium Oxide through a Terrestrial Food Chain**](https://pubmed.ncbi.nlm.nih.gov/25340623/)**.**

[**Exposure of Cerium Oxide Nanoparticles to Kidney Bean Shows Disturbance in the Plant Defense Mechanisms**](https://pubmed.ncbi.nlm.nih.gov/24981679/)**.**

[**Exposure Studies of Core–shell Fe/Fe3O4 and Cu/CuO NPs to Lettuce (Lactuca sativa) Plants: Are They a Potential Physiological and Nutritional Hazard**](https://pubmed.ncbi.nlm.nih.gov/24462971/)**?**

[**Citric Acid Modifies Surface Properties of Commercial CeO2 Nanoparticles Reducing Their Toxicity and Cerium Uptake in Radish (Raphanus sativus) Seedlings**](https://pubmed.ncbi.nlm.nih.gov/24462971/)**.**

[**Applications of Synchrotron μ-XRF to Study the Distribution of Biologically Important Elements in Different Environmental Matrices: A Review**](https://pubmed.ncbi.nlm.nih.gov/23146389/)**.**

[**Interaction of Nanoparticles with Edible Plants and Their Possible Implications in the Food Chain**](https://pubmed.ncbi.nlm.nih.gov/21405020/)**.**

[VIEW FULL BIO – Sanghamitra Majumdar, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/sanghamitra-majumdar)

# Goutam Palui, Ph.D.

### **Staff Fellow — Office of Scientific Coordination**

Dr. Palui designed and synthesized functional “polymer and block copolymer” systems with the goal of creating new materials that address key issues in society. Macromolecules can autonomously self-assemble into a hierarchy of secondary, tertiary, and even quaternary structures which can be utilized as synthetic proteins. Dr. Palui’s research activities aim to judiciously incorporate chirality (a chiral molecule/ion is non-superposable on its mirror image) into synthetic homopolymers and block polymers to create materials that mirror these advanced functions but have improved “anti-biofouling” properties for marine vessels, medical implants, or algae-resistant glass. Another aspect of his research includes the synthesis of precision polymer with improved thermal and mechanical properties.

Dr. Palui improved understanding of the biological (as well as non-biological) systems by interfacing the “inorganic nanocrystals” (such as semiconductor, metallic, and magnetic nanoparticles) coated with various synthetic polymer ligands. Engineering the surface of nanoparticles with different reactive end-functionality to attach biomolecules and finally apply them for biotechnology including live-cell imaging, brain imaging, protein tracking, etc. His primary areas of experience include:

* The design and synthesis of poly (ethylene glycol)-based new biocompatible polymers to coat the hydrophobic nanoparticles, introducing various bio-conjugation techniques—attaching proteins, peptides, and drugs.
* The design, synthesis, and characterization of various peptide and pseudopeptide molecules which self-assemble in aqueous, as well as organic media, to provide nano-structured gel materials.

[VIEW FULL BIO – Dr. Goutam Palui](https://www.fda.gov/about-fda/science-research-nctr/goutam-palui)

**Titles and links to selected publications**

[**Non-Invasive Characterization of the Organic Coating of Biocompatible Quantum Dots Using Nuclear Magnetic Resonance Spectroscopy**](https://pubs.acs.org/doi/10.1021/acs.chemmater.8b01033)**.**

[**Bio-Orthogonal Coupling as a Means of Quantifying the Ligand Density on Hydrophilic Quantum Dots**](https://www.ncbi.nlm.nih.gov/pubmed/26854900)**.**

[**Controlling the Architecture, Coordination, and Reactivity of Nanoparticle Coating Utilizing an Amino Acid Central Scaffold**](https://www.ncbi.nlm.nih.gov/pubmed/26621185)**.**

[**Preparation of Compact Biocompatible Quantum Dots Using Multicoordinating Molecular-Scale Ligands Based on a Zwitterionic Hydrophilic Motif and Lipoic Acid Anchors**](https://www.ncbi.nlm.nih.gov/pubmed/25974095)**.**

[**Photoligation of an Amphiphilic Polymer with Mixed Coordination Provides Compact and Reactive Quantum Dots**](https://www.ncbi.nlm.nih.gov/pubmed/25797052)**.**

[**UV and Sunlight Driven Photoligation of Quantum Dots: Understanding the Photochemical Transformation of the Ligands**](https://www.ncbi.nlm.nih.gov/pubmed/25612193)**.**

[**Understanding the Self-Assembly of Proteins onto Gold Nanoparticles and Quantum Dots Driven by Metal-Histidine Coordination**](https://www.ncbi.nlm.nih.gov/pubmed/24134196)**.**

[**Multidentate Zwitterionic Ligands Provide Compact and Highly Biocompatible Quantum Dots**](https://www.ncbi.nlm.nih.gov/pubmed/24003892)**.**

[**Photoinduced Phase Transfer of Luminescent Quantum Dots to Polar and Aqueous Media**](https://www.ncbi.nlm.nih.gov/pubmed/22938162)**.**

[**Growth of In Situ Functionalized Luminescent Silver Nanoclusters by Direct Reduction and Size Focusing**](https://www.ncbi.nlm.nih.gov/pubmed/22957671)**.**

[**On the pH-Dependent Quenching of Quantum Dot Photoluminescence by Redox Active Dopamine**](https://www.ncbi.nlm.nih.gov/pubmed/22394283)**.**

[**Poly(ethylene glycol)-based Multidentate Oligomers for Biocompatible Semiconductor and Gold Nanocrystals**](https://www.ncbi.nlm.nih.gov/pubmed/22201293)**.**

[**Multidentate Catechol-based Polyethylene Glycol Oligomers Provide Enhanced Stability and Biocompatibility to Iron Oxide Nanoparticles**](https://www.ncbi.nlm.nih.gov/pubmed/22176202)**.**

[**Organogels from Different Self-Assembling New Dendritic Peptides: Morphology, Reheology, and Structural Investigations**](https://www.ncbi.nlm.nih.gov/pubmed/20041726)**.**

[**Fabrication of Luminescent CdS Nanoparticles on Short Peptide based Hydrogel Nanofibers: Tuning of Optoelectronic Properties**](https://www.ncbi.nlm.nih.gov/pubmed/19544511)**.**

[VIEW FULL BIO – Goutam Palui, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/goutam-palui)

# Angel Paredes, Ph.D.

### **Research Biologist — Office of Scientific Coordination**

Dr. Paredes is interested in conducting FDA-relevant research that explores the structural impact of drug treatment and drug-host interactions. In any biological or biochemical process that occurs in the body, whether natural or induced by a manmade pharmacological reaction, there is always a structural impact. This is a consequence of the structure-function relationship that drives all biology. Whether that structural effect is beneficial or deleterious is the basis for the therapeutic effect any drug is designed to elicit. Specifically, Dr. Paredes is interested in identifying the global structural changes that accompany the treatment of humans and veterinary animals to FDA-regulated products including food, drugs, makeup, and nanotechnology. He can use his expertise in electron microscopy to investigate these changes in tissues and organs at the sub-microscopic level. He would like to continue to develop one technology in particular — Serial Block Face Scanning Electron Microscopy (SBFSEM). This instrument, which he presently uses to conduct research, allows his laboratory to slice through tissues from treated animals, gathering images after each slice. The result is digital reconstructions of affected tissues that can be analyzed by very powerful image analysis software. Using this technology he plans to highlight the toxicological effects of FDA-regulated drugs. The data from his research will help FDA ensure product safety in the future. [VIEW FULL BIO – Dr. Angel Paredes](https://www.fda.gov/about-fda/science-research-nctr/angel-paredes)

**Titles and links to selected publications**

[**Virulence Characteristics of mecA-Positive Multidrug-Resistant Clinical Coagulase-Negative Staphylococci**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7284987/)**.**

[**Characterization of Nanomaterials: Tools and Challenges**](https://www.sciencedirect.com/science/article/pii/B9780128141304000117)**.**

[**A Randomized Controlled Laboratory Study on the Long-term Effects of Methylphenidate on Cardiovascular Function and Structure in Rhesus Monkeys**](https://www.accessdata.fda.gov/scripts/publications/search_result_record.cfm?id=61975&highlight=1)**.**

[**Electron Microscopy Techniques Employed to Explore Mitochondrial Defects in the Developing Rat Brain Following Ketamine Treatment**](https://www.accessdata.fda.gov/scripts/publications/search_result_record.cfm?id=61557&highlight=1)**.**

[**Investigating the Susceptibility of Mice to a Bacterial Challenge After Intravenous Exposure to Durable Nanoparticles**](https://www.accessdata.fda.gov/scripts/publications/search_result_record.cfm?id=57954&highlight=1)**.**

[**Size- and Coating-Dependent Cytotoxicity and Genotoxicity of Silver Nanoparticles Evaluated Using In Vitro Standard Assays**](https://www.accessdata.fda.gov/scripts/publications/search_result_record.cfm?id=55520&highlight=1)**.**

[**Differential Effects of Silver Nanoparticles and Silver Ions on Tissue Distribution and Toxicity in the Sprague Dawley Rat Following Daily Oral Gavage Administration for 13-Weeks**](http://www.ncbi.nlm.nih.gov/pubmed/26732888)**.**

[**Microscopy: Transmission Electron Microscopy**](https://www.sciencedirect.com/science/article/pii/B9780123847300002160)**.**

[**Fatty Aldehydes in Cyanobacteria are a Metabolically Flexible Precursor for Adversity of Biofuel Products**](https://www.researchgate.net/publication/236057979_Fatty_Aldehydes_in_Cyanobacteria_Are_a_Metabolically_Flexible_Precursor_for_a_Diversity_of_Biofuel_Products)**.**

[**Espiritio Santo Virus: A New Birnavirus that Replicates in Insect Cells**](https://www.ncbi.nlm.nih.gov/pubmed/22171264)**.**

[**DNA Ejection by Cryo-Electron Tomography of Spore-Binding Phage**](https://www.ncbi.nlm.nih.gov/pubmed/?term=DNA%20Ejection%20by%20Cryo-Electron%20Tomography%20of%20Spore-Binding%20Phage)**.**

[**Reconstitution of the Platelet Glycoprotein Ib-IX Complex in Phospholipid Bilayer Nanodiscs**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Reconstitution%20of%20the%20Platelet%20Glycoprotein%20Ib-IX%20Complex%20in%20Phospholipid%20Bilayer%20Nanodiscs.)**.**

[**Plasma Restoration of Endothelial Glycocalyx in a Rodent Model of Hemorrhagic Shock**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Plasma%20Restoration%20of%20Endothelial%20Glycocalyx%20in%20a%20Rodent%20Model%20of%20Hemorrhagic%20Shock.)**.**

[**Sindbis Virus as a Model for Studies of Conformational Changes in a Metastable Virus and the Role of Conformational Changes in In Vitro Antibody Neutralization**](https://www.ncbi.nlm.nih.gov/pubmed/19475572)**.**

[**Intra- and Intermembrane Pairwise Molecular Recognition between Synthetic Hydrogen-Bonding Phospolipids**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Intra-%20and%20Intermembrane%20Pairwise%20Molecular%20Recognition%20between%20Synthetic%20Hydrogen-Bonding%20Phospolipids.)**.**

[**Sindbis Virus Conformational Changes Induced by a Neutralizing Anti-E1 Monoclonal Antibody**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Sindbis%20Virus%20Conformational%20Changes%20Induced%20by%20a%20Neutralizing%20Anti-E1%20Monoclonal%20Antibody.)**.**

[**Structure of Halothiobacillus Neapolitanus Carboxysomes by Cryo-Electron Tomography**](https://www.ncbi.nlm.nih.gov/pubmed/17028023)**.**

[**Structural Biology of Old World and New World Alphaviruses**](https://www.ncbi.nlm.nih.gov/pubmed/16358426)**.**

[**Conformational Changes in Sindbis Virions Resulting from Exposure to Low pH and Interactions with Cells Suggest that Cell Penetration may Occur at the Cell Surface in the Absence of Membrane Fusion**](https://www.ncbi.nlm.nih.gov/pubmed/15207623)**.**

Co-led the development of ASTM Standard E3143-18b, "[**Standard Practice for Performing Cryo-Transmission Electron Microscopy of Liposomes**](http://www.astm.org/cgi-bin/resolver.cgi?E3143)[**External Link Disclaimer**](http://www.fda.gov/about-fda/website-policies/website-disclaimer),"ASTM International, West Conshohocken, PA, 2018, DOI: 10.1520/E3143-18B, [www.astm.org](https://www.astm.org/).

[VIEW FULL BIO – Angel Paredes, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/angel-paredes)

# Anil Patri, Ph.D.

### **Director, Nanotechnology Core Facility — Office of Scientific Coordination**

Dr. Patri’s group conducts regulatory-science research with a focus on nanomaterial characterization, structure activity, and stability studies that help to determine the nanomaterial’s impact on safety and efficacy. Dr. Patri and his laboratory members are pursuing collaborative consensus standards development that can help regulatory agencies and industry, supported by the National Toxicology Program.  
  
The Nanocore was established as an FDA collaborative resource between NCTR, the Office of Regulatory Affairs (ORA), and the National Toxicology Program. Nanocore staff members from both NCTR and ORA along with FDA’s Center for Drug Evaluation and Research and Center for Devices and Radiological Health scientists provide hands-on training for reviewers from FDA product centers sponsored by the Nanotechnology Task Force. The labs are well-equipped with extensive state-of-the-art instrumentation for nanomaterial physico-chemical, in vitro, and in vivo assessment, including:

* Scanning and Transmission Electron Microscopes equipped with Energy-Dispersive X-ray Spectroscopy detectors
* Specialized Field-Emission Scanning Electron Microscope with 3-View capability
* Low Voltage Electron Microscope
* Atomic Force Microscopes
* Optical, Confocal Raman, and Hyperspectral Imaging instruments
* UV-Visible Spectrophotometry (UV-Vis), Fourier Transform Infrared (FTIR), Fluorescence, Raman spectroscopy
* Nanoparticle Tracking Analysis
* Dynamic, Static and X-ray Scattering instruments
* High Performance Liquid Chromatography with UV-Vis, Fluorescence, Charged Aerosol Detector, and Evaporative Light Scattering Detector
* Ultra-High Performance Liquid Chromatography with Mass Spectrometry
* Asymmetric, Centrifugal Field Flow Fractionation instruments with multi-angle laser light scattering, dynamic light scattering and refractive index
* Inductively Coupled Plasma Mass Spectrometry
* Thermogravimetric Analyzer with Differential Scanning Calorimetry
* Hyphenated Thermogravimetric Analyzer with FTIR-Gas Chromatography-Mass Spectrometry
* Quartz Crystal Microbalance
* 96-well plate readers
* Ultrasound imaging for animal studies

Current Major Collaborative Projects include:

* Standards development for nanomaterial characterization and in vitro assessment
* Liposomal drug products characterization, in vitro and in vivo assessment
* Physico-chemical attributes of nanomaterial and their influence on radiation enhancement
* Physiologically based pharmacokinetic analysis of liposomal drug formulations
* Assessment of nanomaterial in feminine-hygiene products
* Detection, identification, characterization, and quantitation of various attributes of nanomaterial in pristine state and in complex matrices
* Investigation of nanomaterial in sunscreens
* Biodistribution of gadolinium imaging agents
* Genotoxicity of nanomaterial
* Nanomaterial in dental composites and their effects on microbiota
* Nanoparticle permeability through the gastrointestinal surface
* Epigenetic effects of nanomaterial

[VIEW FULL BIO – Dr. Anil Patri](https://www.fda.gov/about-fda/science-research-nctr/anil-patri)

**Titles and links to selected publications**

[**Optimization of Detection of Gadodiamide Brain Retention in Rats Using Quantitative T 2 Mapping and Intraperitoneal Administration**](https://pubmed.ncbi.nlm.nih.gov/35278003/)**.**

[**Regulatory Landscape of Nanotechnology and Nanoplastics From a Global Perspective**](https://www-webofscience-com.fda.idm.oclc.org/wos/woscc/full-record/WOS:000647701300001)**.**

[**Effect of Titanium Dioxide Nanoparticles on DNA Methylation in Multiple Human Cell Lines**](https://www-webofscience-com.fda.idm.oclc.org/wos/woscc/full-record/WOS:000513200700001)**.**

[**Comparative Evaluation of US Brand and Generic Intravenous Sodium Ferric Gluconate Complex in Sucrose Injection: Physicochemical Characterization**](https://www-webofscience-com.fda.idm.oclc.org/wos/woscc/full-record/WOS:000424131600025)**.**

[**Investigating the Susceptibility of Mice to a Bacterial Challenge After Intravenous Exposure to Durable Nanoparticles**](https://www-webofscience-com.fda.idm.oclc.org/wos/woscc/full-record/WOS:000407832500005)**.**

[**Repetitive Application of Sunscreen Containing Titanium Dioxide Nanoparticles on Human Skin**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Repetitive+Application+of+Sunscreen+Containing+Titanium+Dioxide+Nanoparticles+on+Human+Skin)**.**

[**Protein Corona Composition Does Not Accurately Predict Hematocompatibility of Colloidal Gold Nanoparticles**](https://www.ncbi.nlm.nih.gov/pubmed/24512761)**.**

[**Commensal Bacteria Control Cancer Response to Therapy by Modulating the Tumor Microenvironment**](https://www.ncbi.nlm.nih.gov/pubmed/24264989)**.**

[**Common Pitfalls in Nanotechnology: Lessons Learned from NCI's Nanotechnology Characterization Laboratory**](https://www.ncbi.nlm.nih.gov/pubmed/22772974)**.**

[**Challenges and Opportunities in the Advancement of Nanomedicines**](https://pubmed.ncbi.nlm.nih.gov/23064314/)**.**

[**Best Practices in Cancer Nanotechnology: Perspective from NCI Nanotechnology Alliance**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Best+Practices+In+Cancer+Nanotechnology%3A+Perspective+From+NCI+Nanotechnology+Alliance)**.**

[**Nanoparticle Size and Surface Charge Determine Effects of PAMAM Dendrimers on Human Platelets In Vitro**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Nanoparticle+Size+And+Surface+Charge+Determine+Effects+Of+PAMAM+Dendrimers+On+Human+Platelets+In+Vitro)**.**

[**Dendrimer-Induced Leukocyte Procoagulant Activity Depends on Particle Size and Surface Charge**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Dendrimer-Induced+Leukocyte+Procoagulant+Activity+Depends+On+Particle+Size+And+Surface+Charge.)**.**

[**Dendronized Bi-2-Quinoline Ligands and Their Metal Complexes: Dendron Synthesis and Metalloassembly**](https://www.researchgate.net/publication/272726795_Dendronized_Bi-2-quinoline_Ligands_and_Their_Metal_Complexes_Dendron_Synthesis_and_Metalloassembly)**.**

[**Lipid Component Quantitation by Thin Layer Chromatography**](https://www.ncbi.nlm.nih.gov/pubmed/21116959)**.**

[**Detecting and Measuring Free Gadolinium in Nanoparticles for MRI Imaging**](https://pubmed.ncbi.nlm.nih.gov/21116958/)**.**

[**SEM X-Ray Microanalysis of Nanoparticles Present in Tissue or Cultured Cell Thin Sections**](https://www.ncbi.nlm.nih.gov/pubmed/21116957)**.**

[**Biological Tissue and Cell Culture Specimen Preparation for TEM Nanoparticle Characterization**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Biological+Tissue+And+Cell+Culture+Specimen+Preparation+For+TEM+Nanoparticle+Characterization.)**.**

[**Chromatographic Methods for the Quantification of Free and Chelated Gadolinium Species in MRI Contrast Agent Formulations**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Chromatographic+Methods+For+The+Quantification+Of+Free+And+Chelated+Gadolinium+Species+In+MRI+Contrast+Agent+Formulations.)**.**

[**Energy Dispersive X-Ray Analysis of Titanium Dioxide Nanoparticle Distribution after Intravenous and Subcutaneous Injection in Mice**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Energy+Dispersive+X-Ray+Analysis+Of+Titanium+Dioxide+Nanoparticle+Distribution+After+Intravenous+And+Subcutaneous+Injection+In+Mice.)**.**

[VIEW FULL BIO – Anil Patri, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/anil-patri)

# Sandra Pena-Luengas, Ph.D.

### **Chemist — Office of Scientific Coordination**

Throughout her career, Dr. Pena-Luengas has focused on developing and validating novel methods to be applied in different fields of science, such as organic chemistry, nanotechnology, materials science, materials chemistry, photochemistry and medicinal chemistry and has experience with the following analytical instrumentation:

* Solid Phase Micro Extraction Gas Chromatography with Mass Selective Detection (SPME/GC/MS) and GC/MS/MS.
* Headspace Gas Chromatography with Mass Selective Detection (HS/GC/MS).
* Solid Phase Extraction Gas Chromatography with Mass Selective Detection (SPE/GC/MS).
* Solid Phase Extraction Liquid Chromatography with Tandem Mass Selective Detection (SPE/LC/MS/MS).
* Solid Phase Extraction Ultra High Performance Liquid Chromatography (UHPLC) QSight 225 Triple Quadrupole (3QMS).
* Inductively Coupled Plasma-Mass Spectrometry (ICP/MS)
* UV-vis spectrophotometry
* Photoluminescence (PL) spectroscopy
* Fourier Transform Infrared (FTIR)
* X-Ray Diffraction (XRD)
* Confocal Microscopy
* Fluorescence Microscopy
* Scanning Electron Microscopy (SEM)
* Transmission Electron Microscopy (TEM)

Dr. Pena-Luengas is very interested in the use of analytical methodology for the selective detection and analysis of natural and synthetic compounds and/or their derivatives, not only in plasma, urine, and tissues, but also in natural matrices such as water, plants, and animals. Applications of such analytical methods, especially for cancer, toxicological studies and nanomedicine, have been key areas of study. [VIEW FULL BIO – Dr. Sandra Pena-Luengas](https://www.fda.gov/about-fda/science-research-nctr/sandra-pena-luengas)

**Titles and links to selected publications**

[**Zinc Oxide Nanoparticles and Photodynamic Therapy for the Treatment of B-Chronic Lymphocytic Leukemia**](http://sedici.unlp.edu.ar/handle/10915/80008)**.**

[**Enhanced Singlet Oxygen Production by Photodynamic Therapy and a Novel Method for its Intracellular Measurement**](https://www.researchgate.net/publication/269415017_Enhanced_Singlet_Oxygen_Production_by_Photodynamic_Therapy_and_a_Novel_Method_for_Its_Intracellular_Measurement)**.**

[**B-Chronic Lymphocytic Leukemia Autophagyc Cell Death by the Use of Manganese-Doped Zinc Oxide Nanoparticles and Photodynamic Therapy**](https://www.researchgate.net/publication/278029474_B-chronic_lymphocytic_leukemia_autophagyc_cell_death_by_the_use_of_manganese_doped_zinc_oxide_nanoparticles_and_photo-dynamic_therapy)**.**

[**Synthesis of Fe3O4/ZnO Core-Shell Nanoparticles and Their Applications in Photodynamic Therapy**](https://www.researchgate.net/publication/231745181_Synthesis_of_Fe3O4ZnO_Core-shell_Nanoparticles_for_Photodynamic_Therapy_Applications)**.**

[**Multifunctional Fe3O4/ZnO Core-Shell Nanoparticles for Photodynamic Therapy**](https://www.researchgate.net/publication/235710295_Multifunctional_Fe3O4ZnO_core-shell_nanoparticles_for_photodynamic_therapy)**.**

[**Development of SPME-HPLC Methodology for Detection of Nitro-Explosives**](https://www.spiedigitallibrary.org/conference-proceedings-of-spie/6553/65531W/Development-of-SPME-HPLC-methodology-for-detection-of-nitroexplosives/10.1117/12.720362.short?SSO=1)**.**

[**Enhanced Raman Scattering of TNT on Nanoparticle Susbstrates: Ag Colloides Prepared by Reduction with Hydroxylamine Hydrochloride and Sodium Citrate**](https://www.spiedigitallibrary.org/conference-proceedings-of-spie/6538/653824/%20Enhanced-Raman-scattering-of-TNT-on-nanoparticle-substrates--Ag/10.1117/12.720342.short)**.**

[VIEW FULL BIO – Sandra Pena-Luengas, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/sandra-pena-luengas)

# Arjun Sharmah, Ph.D.

### **Visiting Scientist — Office of Scientific Coordination**

Dr. Sharmah's research interests include:

* Study of interactions between nanomaterials and biological moieties
* Analytical method development
* Study of nanomaterials and ionizing radiation for targeted cancer therapy and drug payload delivery
* Synthesis of higher-order nanostructures and their advanced characterization
* Toxicity of nanomaterials and their environmental impact
* Protein chemistry and molecular conjugation for spectroscopic and imaging applications
* Theoretical study of interaction of radiation with nanomaterials and reaction kinetics

[VIEW FULL BIO – Dr. Arjun Sharmah](https://www.fda.gov/about-fda/science-research-nctr/arjun-sharmah)

**Titles and links to selected publications**

[**Towards Development of Fluorescence Quenching-Based Biosensors for Drought Stress in Plants**](https://pubmed.ncbi.nlm.nih.gov/31698903/)**.**

[**Sealable Spherical Mesoporous Silica Shell Nanoreactors as Fiducial Nanoscale Probes for X-rays**](https://pubmed.ncbi.nlm.nih.gov/30293419/)**.**

[**Theoretical Study of X-ray Induced Energy Transfer (XIET) from Nanomaterial Donors to Nanomaterial Acceptors**](https://pubs.acs.org/doi/10.1021/acs.jpcc.8b01696)**.**

[**Concentration-Dependent Association Between Weakly Attractive Nanoparticles in Aqueous Solutions**](https://pubs.acs.org/doi/10.1021/acs.jpcc.6b06062)**.**

[**X-ray-Induced Energy Transfer between Nanomaterials Under X-ray Irradiation**](https://pubs.acs.org/doi/abs/10.1021/acs.jpcc.5b11859)**.**

[**Electron Paramagnetic Resonance Spectroscopy Investigation of Radical Production by Gold Nanoparticles in Aqueous Solutions Under X-ray Irradiation**](https://pubmed.ncbi.nlm.nih.gov/27124587/)**.**

[**Influence of Particle Size on Persistence and Clearance of Aerosolized Silver Nanoparticles in the Rat Lung**](https://pubmed.ncbi.nlm.nih.gov/25577195/)**.**

[**Persistence of Silver Nanoparticles in the Rat Lung: Influence of Dose, Size, and Chemical Composition**](https://pubmed.ncbi.nlm.nih.gov/25231189/)**.**

[**Chemical Enhancement by Nanomaterials Under X-ray Irradiation**](https://pubmed.ncbi.nlm.nih.gov/22260210/)**.**

[VIEW FULL BIO – Arjun Sharmah, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/arjun-sharmah)

# Raul Trbojevich, Ph.D.

### **Chemist — Office of Scientific Coordination**

Dr. Trbojevich is skilled in developing new analytical chemistry methods for identification and quantitation of chemical compounds in inorganic, organic, and complex biological samples. His research supports ICP-MS, HPLC, UPLC, GC-MS-MS, UV-Vis, and fluorescence spectroscopy. Dr. Trbojevich is experienced with other spectroscopy techniques, including FT-IR, Raman spectroscopy, and NMR spectroscopy.

In the area of nanotechnology, Dr. Trbojevich has expertise in the wet chemical synthesis of metals and semiconductor nanoparticles, and their characterization for new material science applications. [VIEW FULL BIO – Dr. Raul Trbojevich](https://www.fda.gov/about-fda/science-research-nctr/raul-trbojevich)

**Titles and links to selected publications**

[**Assessment of Silver Release and Biocidal Capacity from Silver Nanocomposite Food Packaging Materials**](https://pubmed.ncbi.nlm.nih.gov/32898598/)**.**

[**Assessment of Antimicrobial Effect of Food Contact Materials Containing Silver on Growth of *Salmonella* Typhimurium**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Assessment%20of%20antimicrobial%20effect%20of%20food%20contact%20materials%20containing%20silver%20on%20growth%20of%20salmonella%20typhimurium.)**.**

[**Toxicity Evaluation of Bisphenol A Administered by Gavage to Sprague-Dawley Rats from Gestation Day 6 Through Postnatal Day 90**](https://www.ncbi.nlm.nih.gov/pubmed/27506224)**.**

[**Relevance of Nanocomposite Packaging on the Stability of Vacuum-Packed Dry Cured Ham**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Relevance%20of%20nanocomposite%20packaging%20on%20the%20stability%20of%20vacuum-packed%20dry%20cured%20ham.)**.**

[**Comparative Study of Silver Nanoparticles Permeation Using Side-Bi-Side and Franz Diffusion Cells**](https://www.researchgate.net/publication/295247631_Comparative_study_of_silver_nanoparticle_permeation_using_Side-Bi-Side_and_Franz_diffusion_cells)**.**

[**Colour Stability of Cooked Ham Packed Under Modified Atmospheres in Polyamide Nanocomposite Blends**](https://www.researchgate.net/publication/284124077_Colour_stability_of_cooked_ham_packed_under_modified_atmospheres_in_polyamide_nanocomposite_blends)**.**

[**Effects of Maternal and Lactational Exposure to 2-Hydroxy-4-Methoxybenzone on Development and Reproductive Organs in Male and Female Rat Offspring**](https://pubmed.ncbi.nlm.nih.gov/25707689/)**.**

[**Metallic-Based Micro and Nano-Structured Materials in Food Contact Materials and Active Food Packaging**](https://www.researchgate.net/publication/232701461_Metallic-based_micro_and_nanocomposites_in_food_contact_materials_and_active_food_packaging)**.**

[**Preparation and Isolation of Gold Nanoparticles Coated with A Stabilizer and Sol-Gel Compatible Agent**](https://www.researchgate.net/publication/231997247_Preparation_and_isolation_of_gold_nanoparticles_coated_with_a_stabilizer_and_sol-gel_compatible_agent)**.**

[**Chemical Solution Technique to Prepare Perovskite PZT and PLZT Thin Films and Powders**](https://www.researchgate.net/publication/233222815_Chemical_solution_technique_to_prepare_perovskite_PZT_and_PLZT_thin_films_and_powders)**.**

[**Fabrication of PbS Nanoparticles Embedded in Silica Gel by Reverse Micelles and Sol-Gel Routes**](https://www.researchgate.net/publication/248054527_Fabrication_of_PbS_Nanoparticles_Embedded_in_Silica_Gel_by_Reverse_Micelles_and_Sol-Gel_Routes)**.**

[VIEW FULL BIO – Raul Trbojevich, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/raul-trbojevich)

## Division of Biochemical Toxicology, NCTR

# Frederick Beland, Ph.D.

### **Director — Division of Biochemical Toxicology**

The focus of Dr. Beland's research has been to assess the carcinogenic potential of chemicals of interest to FDA and to understand the mechanisms responsible for the carcinogenic response. These investigations involve conducting chronic bioassays in experimental animals and conducting in vitro and in vivo mechanistic studies to determine if the responses observed in experimental animals are relevant to humans. An important component of these studies is the elucidation of dose-response relationships that can be used to guide risk assessments. Recent studies have focused on acrylamide, furan, anti-retroviral drugs (e.g., zidovudine and nevirapine), and inorganic arsenic. [VIEW FULL BIO – Dr. Frederick Beland](https://www.fda.gov/about-fda/science-research-nctr/frederick-beland)

**Titles and links to selected publications**

[**Covalent Histone Modification by an Electrophilic Derivative of the Anti-HIV Drug Nevirapine**](https://pubmed.ncbi.nlm.nih.gov/33802579/)**.**

[**Flow Cytometry Analysis of Anti-Polyethylene Glycol Antibodies in Human Plasma**](https://pubmed.ncbi.nlm.nih.gov/33437656/)**.**

[**Butyrate-Containing Structured Lipids Inhibit RAC1 and Epithelial-to-Mesenchymal Transition Markers: A Chemopreventive Mechanism Against Hepatocarcinogenesis**](https://pubmed.ncbi.nlm.nih.gov/32920087/)**.**

[**Reduction By, Ligand Exchange Among, and Covalent Binding to Glutathione and Cellular Thiols Link Metabolism and Disposition of Dietary Arsenic Species with Toxicity**](https://pubmed.ncbi.nlm.nih.gov/32889486/)**.**

[**Epigenetic Effects of Low-Level Sodium Arsenite Exposure on Human Liver HepaRG Cells**](https://link.springer.com/article/10.1007/s00204-020-02872-6)**.**

[**Characterization of the Variability in the Extent of Nonalcoholic Fatty Liver Induced by a High-Fat Diet in the Genetically Diverse Collaborative Cross Mouse Model**](https://pubmed.ncbi.nlm.nih.gov/32304142/)**.**

[**Pharmacokinetics of Oseltamivir Phosphate and Oseltamivir Carboxylate in Non-Pregnant and Pregnant Rhesus Monkeys**](https://pubmed.ncbi.nlm.nih.gov/31927005/)**.**

[**Apoptosis Contributes to the Cytotoxicity Induced by Amodiaquine and its Major Metabolite N-desethylamodiaquine in Hepatic Cells**](https://pubmed.ncbi.nlm.nih.gov/31629065/)**.**

[**In Vivo Localization and Postmortem Stability of Benzo[a]pyrene-DNA Adducts**](https://onlinelibrary.wiley.com/doi/abs/10.1002/em.22337)**.**

[**Gene Expression and Cytosine DNA Methylation Alterations in Induced Pluripotent Stem-Cell-Derived Human Hepatocytes Treated with Low Doses of Chemical Carcinogens**](https://pubmed.ncbi.nlm.nih.gov/31555880/)**.**

[**Metabolism and Disposition of Arsenic Species from Controlled Dosing with Sodium Arsenite in Adult and Neonatal Rhesus Monkeys. VI. Toxicokinetic Studies Following Oral Administration**](https://pubmed.ncbi.nlm.nih.gov/31421213/)**.**

[**Comparative Pharmacokinetic and Biodistribution Study of Two Distinct Squalene-Containing Oil-in-Water Emulsion Adjuvants in H5N1 Influenza Vaccines**](https://www.sciencedirect.com/science/article/pii/S0273230019302004)**.**

[**Gene Expression and DNA Methylation Alterations During Non-alcoholic Steatohepatitis-Associated Liver Carcinogenesis**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6549534/)**.**

[**Metabolism and Disposition of Arsenic Species from Controlled Dosing with Dimethylarsinic Acid (DMAV) in Adult Female CD-1 Mice. V. Toxicokinetic Studies Following Oral and Intravenous Administration**](https://pubmed.ncbi.nlm.nih.gov/31091427/)**.**

[**Gene Expression and DNA Methylation Alterations in the Glycine N-Methyltransferase Gene in Diet-Induced Nonalcoholic Fatty Liver Disease-Associated Carcinogenesis**](https://pubmed.ncbi.nlm.nih.gov/31086990/)**.**

[**Experimental and Pan-Cancer Genome Analyses Reveal Widespread Contribution of Acrylamide Exposure to Carcinogenesis in Humans**](https://pubmed.ncbi.nlm.nih.gov/30846532/)**.**

[**Genotoxic and Epigenotoxic Alterations in the Lung and Liver of Mice Induced by Acrylamide: A 28 Day Drinking Water Study**](https://pubmed.ncbi.nlm.nih.gov/30807115/)**.**

[VIEW FULL BIO – Frederick Beland, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/frederick-beland)

# Luísa Camacho, Ph.D.

### **Deputy Director — Division of Biochemical Toxicology**

Dr. Camacho’s research focuses on the conduct of animal studies to assess the pharmacokinetics and toxicity of products of interest to the FDA. A particular emphasis of her research has been on toxicological studies that include exposures during the perinatal period of life. She complements toxicity assessments with molecular endpoints to characterize molecular mechanisms for compounds of interest and to identify potential novel biomarkers of toxicity. These studies are conducted in close collaboration with colleagues from FDA product centers, the National Institutes of Health, and NCTR. Dr. Camacho served as a scientific coordinator of the Consortium Linking Academic and Regulatory Insights on Bisphenol A Toxicity (CLARITY-BPA), a collaborative research program between the FDA, the National Institute of Environmental Health Sciences, and university-based researchers that provided data for the safety assessment of bisphenol A, an indirect food additive. Other studies included the comparison of the dose-response and temporal dynamics of traditional (blood urea nitrogen and serum creatinine) and novel (serum micro ribonucleic acids) biomarkers of nephrotoxicity upon a combined exposure to melamine and cyanuric acid, and the evaluation of the toxicity of the plasticizer di(2-ethylhexyl)phthalate (DEHP) and of the dietary supplements nattokinase and lumbrokinase. Current research efforts include the characterization of the pharmacokinetics of cannabidiol in a rat model upon oral and dermal exposures, and the evaluation of the performance of a 3D bioprinted human skin equivalent model for in vitro permeation testing. [VIEW FULL BIO – Dr. Luísa Camacho](https://www.fda.gov/about-fda/science-research-nctr/luisa-camacho)

**Titles and links to selected publications**

[**A Robust Biostatistical Method Leverages Informative but Uncertainly Determined qPCR Data for Biomarker Detection, Early Diagnosis, and Treatment**](https://pubmed.ncbi.nlm.nih.gov/35100319/)**.**

[**Effects of Intravenous and Oral Di(2-ethylhexyl) Phthalate (DEHP) and 20% Intralipid Vehicle on Neonatal Rat Testis, Lung, Liver, and Kidney**](https://pubmed.ncbi.nlm.nih.gov/32540476/)**.**

[**A Two-Year Toxicology Study of Bisphenol A (BPA) in Sprague-Dawley Rats:  CLARITY-BPA Core Study Results**](https://pubmed.ncbi.nlm.nih.gov/31365888/)**.**

[**Data on the Effect of Heat and Other Technical Variables on the Detection of microRNAs in Human Serum**](https://pubmed.ncbi.nlm.nih.gov/30976632/)**.**

[**Identification of Whole Blood mRNA and microRNA Biomarkers of Tissue Damage and Immune Function resulting from Amphetamine Exposure or Heat Stroke in Adult Male Rats**](https://pubmed.ncbi.nlm.nih.gov/30779732/)**.**

[**Effects of a 28-Day Dietary Co-Exposure to Melamine and Cyanuric Acid on the Levels of Serum microRNAs in Male and Female Fisher 344 Rats**](https://www.ncbi.nlm.nih.gov/pubmed/27621052)**.**

[**Comparison of Endpoints Relevant to Toxicity Assessments in 3 Generations of CD-1 Mice Fed Irradiated Natural and Purified Ingredient Diets with Varying Soy Protein, Isoflavone, and Thiamine Contents**](https://www.ncbi.nlm.nih.gov/pubmed/27234134)**.**

[**NIEHS/FDA CLARITY-BPA Research Program Update**](https://www.ncbi.nlm.nih.gov/pubmed/26232693)**.**

[**Effects of Oral Exposure to Bisphenol A on Gene Expression and Global Genomic DNA Methylation in the Prostate, Female Mammary Gland, and Uterus of NCTR Sprague-Dawley Rats**](https://www.ncbi.nlm.nih.gov/pubmed/25862956)**.**

[**Comparison of Lifestage-Dependent Internal Dosimetry for Bisphenol A, Ethinyl Estradiol, a Reference Estrogen, and Endogenous Estradiol to Test an Estrogenic Mode of Action in Sprague-Dawley Rats**](https://www.ncbi.nlm.nih.gov/pubmed/24496641)**.**

[**Toxicity Evaluation of Bisphenol A Administered by Gavage to Sprague-Dawley Rats from Gestation Day 6 Through Postnatal Day 90**](https://www.ncbi.nlm.nih.gov/pubmed/24496637)**.**

[**A New Approach to Synergize Academic and Regulatory-Compliant Research: the CLARITY-BPA Research Program**](https://www.ncbi.nlm.nih.gov/pubmed/23747832)**.**

[**The Estrogenic Content of Rodent Diets, Bedding, Cages and Water Bottles and Its Impact on Bisphenol A Studies**](https://www.ncbi.nlm.nih.gov/pubmed/23562095)**.**

[**Performance of Urinary and Gene Expression Biomarkers in Detecting the Nephrotoxic Effects of Melamine and Cyanuric Acid Following Diverse Scenarios of Co-Exposure**](https://www.ncbi.nlm.nih.gov/pubmed/23022069)**.**

[**Effects of Acrylamide Exposure on Serum Hormones, Gene Expression, Cell Proliferation, and Histopathology in the Testes of Fischer 344 Rats**](https://www.ncbi.nlm.nih.gov/pubmed/22459607)**.**

[**Gene Expression of Biomarkers of Nephrotoxicity in F344 Rats Co-Exposed to Melamine and Cyanuric Acid for Seven Days**](https://www.ncbi.nlm.nih.gov/pubmed/21784140)**.**

[VIEW FULL BIO – Luísa Camacho, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/luisa-camacho)

# Si Chen, Ph.D.

### **Staff Fellow — Division of Biochemical Toxicology**

A major focus of Dr. Chen’s research is elucidating the molecular mechanisms of drug and herbal dietary supplement-associated liver toxicity. Dr. Chen has conducted several mechanistic studies on the hepatotoxic effects of FDA-regulated products, including goldenseal, Ginkgo biloba, usnic acid, sertraline, dronedarone, and nitroxides. Another major focus of Dr. Chen’s research is screening and identifying the micro ribonucleic acids (miRNA) that are responsible for drug resistance in ovarian cancer and investigating the underlying molecular mechanisms of candidate miRNAs using both bioinformatics and biochemical approaches. [VIEW FULL BIO – Dr. Si Chen](https://www.fda.gov/about-fda/science-research-nctr/si-chen)

**Titles and links to selected publications**

[**Characterization of Cytochrome P450s (CYP)-Overexpressing HepG2 Cells for Assessing Drug and Chemical-Induced Liver Toxicity**](https://pubmed.ncbi.nlm.nih.gov/33576714/)**.**

[**The Role of Hepatic Cytochrome P450s in the Cytotoxicity of Sertraline**](https://pubmed.ncbi.nlm.nih.gov/32372212/)**.**

[**MicroRNAs hsa-miR-495-3p and hsa-miR-486-5p Suppress Basal and Rifampicin-induced Expression of Human Sulfotransferase 2A1 (SULT2A1) by Facilitating mRNA Degradation**](https://www.ncbi.nlm.nih.gov/pubmed/?term=31445882)**.**

[**The Role of Hepatic Cytochrome P450s in the Cytotoxicity of Dronedarone**](https://www.ncbi.nlm.nih.gov/pubmed/?term=29616291)**.**

[**DNA Damage-induced Apoptosis and Mitogen-activated Protein Kinase Pathway Contribute to the Toxicity of Dronedarone in Hepatic Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=29399883)**.**

[**ROS Generation and JNK Activation Contribute to 4-methoxy-TEMPO-induced Cytotoxicity, Autophagy, and DNA Damage in HepG2 Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=28993908)**.**

[**Endoplasmic Reticulum Stress and MAPK Signaling Pathway Activation Underlie Leflunomide-induced Toxicity in HepG2 Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=28988120)**.**

[**Activation of the Nrf2 Signaling Pathway in Usnic Acid-induced Toxicity in HepG2 Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=27369375)**.**

[**Endoplasmic Reticulum Stress Induction and ERK1/2 Activation Contribute to Nefazodone-induced Toxicity in Hepatic Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=27613715)**.**

[**Development of HepG2-derived Cells Expressing Cytochrome P450s for Assessing Metabolism-associated Drug-induced Liver Toxicity**](https://www.ncbi.nlm.nih.gov/pubmed/?term=26477383)**.**

[**MicroRNAs as Pharmacogenomic Biomarkers for Drug Efficacy and Drug Safety Assessment**](https://www.ncbi.nlm.nih.gov/pubmed/?term=26501795)**.**

[**Ginkgo biloba Leaf Extract Induces DNA Damage by Inhibiting Topoisomerase II Activity in Human Hepatic Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=26419945)**.**

[**Endoplasmic Reticulum Stress and Store-operated Calcium Entry Contribute to Usnic Acid-induced Toxicity in Hepatic Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=25870318)**.**

[**Reactive Oxygen Species and c-Jun N-terminal Kinases Contribute to TEMPO-induced Apoptosis in L5178Y Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=25882087)**.**

[**Mechanisms of Tolvaptan-induced Toxicity in HepG2 Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=25858412)**.**

[**The Role of Autophagy in Usnic Acid-induced Toxicity in Hepatic Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=25078063)**.**

[**Sertraline Induces Endoplasmic Reticulum Stress in Hepatic Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=24194395)**.**

[**Autophagy in Drug-induced Liver Toxicity**](https://www.ncbi.nlm.nih.gov/pubmed/?term=29249890)**.**

[**Sertraline, an Antidepressant, Induces Apoptosis in Hepatic Cells Through the Mitogen-activated Protein Kinase Pathway**](https://www.ncbi.nlm.nih.gov/pubmed/?term=24194395)**.**

[**Endoplasmic Reticulum Stress in Drug- and Environmental Toxicant-induced Liver Toxicity**](https://www.ncbi.nlm.nih.gov/pubmed/?term=24598041)**.**

[VIEW FULL BIO – Si Chen, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/si-chen)

# Kenneth Barry Delclos, Ph.D.

### **Research Pharmacologist — Division of Biochemical Toxicology**

There has been much interest and controversy in recent years concerning the potential health effects of chemical agents that affect hormone signaling, so-called “endocrine disrupters.” Dr. Delclos’s laboratory has been involved in studies with several hormonally active compounds to assess their reproductive toxicity and carcinogenic activity across generations and to assess the impact of developmental exposure. An example is a major effort to address regulatory issues on the toxicity of Bisphenol A (BPA), a compound the FDA regulates primarily in food-contact materials. Studies were designed to address data gaps and deficiencies in study designs in many of the existing studies and a two-year study included participation from a large group of academic investigators, many of whom are critical of the current FDA safety assessment of BPA. Results from these studies continue to inform safety assessments of BPA in the U.S. and internationally. Results of the studies of endocrine disrupters have also indicated the ability of dietary components to modulate or induce toxic responses.  For example, a daily oral bolus of lipid administered to neonatal rats disrupted spermatogenesis, apparently through a gut hormone-mediated mechanism. Since analogues of a major gut hormone involved in glucose regulation — glucagon-like peptide 1 — are currently approved for use in the treatment of pediatric Type 2 diabetes and obesity, this observation may warrant further investigation as to its relevance in humans.  Currently, the laboratory is investigating the reproductive toxicity of oral antidiabetic agents that are increasingly used off-label to treat gestational diabetes mellitus despite unknown long-term effects on offspring. [VIEW FULL BIO – Dr. Kenneth Barry Delclos](https://www.fda.gov/about-fda/science-research-nctr/kenneth-delclos)

**Titles and links to selected publications**

[**Effects of Intravenous and Oral Di(2-Ethylhexyl) Phthalate (DEHP) and 20% Intralipid Vehicle on Neonatal Rat Testis, Lung, Liver, and Kidney**](https://pubmed.ncbi.nlm.nih.gov/32540476/)**.**

[**A Two-Year Toxicology Study of Bisphenol A (BPA) in Sprague-Dawley Rats: CLARITY-BPA Core Study Results**](https://pubmed.ncbi.nlm.nih.gov/31365888/)**.**

[**NTP Research Report on the CLARITY-BPA Core Study: A Perinatal and Chronic Extended-Dose-Range Study of Bisphenol A in Rats**](https://pubmed.ncbi.nlm.nih.gov/31305969/)**.**

[**Advancing Human Health Risk Assessment**](https://pubmed.ncbi.nlm.nih.gov/32626449/)**.**

[**Comparison of Endpoints Relevant to Toxicity Assessments in 3 Generations of CD-1 Mice Fed Irradiated and Natural and Purified Ingredient Diets with Varying Soy Protein and Isoflavone Contents**](https://www.ncbi.nlm.nih.gov/pubmed/27234134)**.**

[**NIEHS/FDA CLARITY-BPA Update**](https://www.ncbi.nlm.nih.gov/pubmed/26232693)**.**

[**Effects of Oral Exposure to Bisphenol A on Gene Expression and Global Genomic DNA Methylation in Prostate, Female Mammary Gland, and Uterus of NCTR Sprague-Dawley Rats**](https://www.ncbi.nlm.nih.gov/pubmed/25862956)**.**

[**Investigation of the Effects of Subchronic Low Dose Oral Exposure to Bisphenol A (BPA) and Ethinyl Estradiol (EE) on Estrogen Receptor Expression in the Juvenile and Adult Female Rat Hypothalamus**](https://www.ncbi.nlm.nih.gov/pubmed/24752507)**.**

[**Toxicity Evaluation of Bisphenol A Administered by Gavage to Sprague-Dawley Rats from Gestation Day 6 Through Postnatal Day 90**](https://www.ncbi.nlm.nih.gov/pubmed/24496637)**.**

[**Comparison of Life-Stage-Dependent Internal Dosimetry for Bisphenol A, Ethinyl Estradiol, a Reference Estrogen, and Endogenous Estradiol to Test an Estrogenic Mode of Action in Sprague Dawley Rats**](https://www.ncbi.nlm.nih.gov/pubmed/24496641)**.**

[**A New Approach to Synergize Academic and Regulatory-Compliant Research: The CLARITY-BPA Research Program**](https://www.ncbi.nlm.nih.gov/pubmed/23747832)**.**

[**Lactational Transfer of Bisphenol A in Sprague-Dawley Rats**](https://www.ncbi.nlm.nih.gov/pubmed/20933065)**.**

[**Genistein and Ethinyl Estradiol Dietary Exposure in Multigenerational and Chronic Studies Induce Similar Proliferative Lesions in Mammary Gland of Male Sprague-Dawley Rats**](https://www.ncbi.nlm.nih.gov/pubmed/19383540)**.**

[**Overlapping but Distinct Effects of Genistein and Ethinyl Estradiol (EE2) in Female Sprague-Dawley Rats in Multigenerational Reproductive and Chronic Toxicity Studies**](https://www.ncbi.nlm.nih.gov/pubmed/19159674)**.**

[**Few Effects of Multi-Generational Dietary Exposure to Genistein or Nonylphenol on Sodium Solution in Male and Female Sprague-Dawley Rats**](https://www.ncbi.nlm.nih.gov/pubmed/19452615)**.**

[**Multigenerational Exposure to Ethinyl Estradiol Affects Bone Geometry, but Not Bone Mineral Density in Rats**](https://www.ncbi.nlm.nih.gov/pubmed/18467201)**.**

[**Dietary Modulation of P-Nonylphenol-Induced Polycystic Kidneys in Male Sprague-Dawley Rats**](https://www.ncbi.nlm.nih.gov/pubmed/16554316)**.**

[**Lactational Transfer of the Soy Isoflavone, Genistein, in Sprague-Dawley Rats Consuming Dietary Genistein**](https://www.ncbi.nlm.nih.gov/pubmed/16257506)**.**

[VIEW FULL BIO – Kenneth Barry Delclos, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/kenneth-delclos)

# Tariq Fahmi, M.D., Ph.D.

### **Research Biologist — Division of Biochemical Toxicology**

Dr. Fahmi's research interests include:

* Immunology, especially sex-based differences in immune responses
* Nanotoxicology, especially immunotoxicity of nanomaterials
* Immunopathology
* Oncology, especially tumor biology and immunology

Dr. Fahmi’s current research projects and other research efforts at NCTR:

* Sex-based differences in immune responses to nanoparticles
* Immunotoxicity of cobalt chromium particles generated from prosthetic implants
* Effects of physico-chemical properties of nanoparticles on radioenhancement and DNA damage in cancer cells
* Effects of physico-chemical properties of graphitic materials on cytotoxicity
* Development of immunotoxicological collaborative consensus-standards for nanomaterial assessment with other stakeholders, through standards development organizations, such as the American Society for Testing and Materials (ASTM International)
* Development lead of two immunotoxicological test methods:
  + ASTM E3238-20—"Standard Test Method for Quantitative Measurement of the Chemoattractant Capacity of a Nanoparticulate Material In Vitro" (2020)
  + ASTM E3351-22—"Standard Method for Detection of Nitric Oxide Production In Vitro” (2022)

Dr. Fahmi's previous research efforts:

* Investigated the possible mechanisms of cell death following exposure to nanomaterials. Conducted several research projects that involved 1) the delivery and measurement of the toxicity of different nanomaterials and 2) the development of methods to evaluate nanoparticle toxicity. Investigated the role of endonucleases in the mechanism of graphene and carbon nanotubes cytotoxicity. Helped develop 1) a photoacoustic in vitro flow cytometry method to evaluate nanomaterial toxicity and 2) multi-functional nanomaterials for targeting circulating cancer cells.
* Investigated the role of serotonin transporters in protecting placental cells against cell death.
* Worked with cancer models by investigating the effects of altered expression of human UDP-glucurosyltransferase (UGT) genes in breast and pancreatic cancers. Demonstrated the role of UGTs as lipid controllers in cellular homeostasis and helped identify them as possible targets for future clinical therapeutic development.
* Worked on determining the role of endonuclease and apoptotic proteins and the mechanisms of acute and chronic tissue injury related to cancer and other toxic injuries.
* Investigated the differential distribution of T cell subsets in mammary tumor-bearing animals and potential contribution of T cell localization to tumor-associated immunosuppression.

[VIEW FULL BIO – Dr. Tariq Fahmi](https://www.fda.gov/about-fda/science-research-nctr/tariq-fahmi)

**Titles and links to selected publications**

[**DNase I Induces Other Endonucleases in Kidney Tubular Epithelial Cells by Its DNA-Degrading Activity**](https://pubmed.ncbi.nlm.nih.gov/33212932/)**.**

[**Serotonin Transporter Protects the Placental Cells Against Apoptosis in Caspase 3-Independent Pathway**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Serotonin+Transporter+Protects+the+Placental+Cells+Against+Apoptosis+in+Caspase+3-Independent+Pathway.)**.**

[**Mechanism of Graphene-Induced Cytotoxicity: Role of Endonucleases**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Mechanism+of+Graphene-Induced+Cytotoxicity%3A+Role+of+Endonucleases.)**.**

[**Photoacoustic In Vitro Flow Cytometry for Nanomaterial Research**](https://www.ncbi.nlm.nih.gov/pubmed/28417068)**.**

[**Mutant Profilin1 Transgenic Mice Recapitulate Cardinal Features of Motor Neuron Disease**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Mutant+Profilin1+Transgenic+Mice+Recapitulate+Cardinal+Features+of+Motor+Neuron+Disease.)**.**

[**Human UDP-Glucuronosyltransferases: Effects of Altered Expression in Breast and Pancreatic Cancer Cell Lines**](https://pubmed.ncbi.nlm.nih.gov/25996841/)**.**

[**Impact of Hydroxychloroquine on Atherosclerosis and Vascular Stiffness in the Presence of Chronic Kidney Disease**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Impact+of+Hydroxychloroquine+on+Atherosclerosis+and+Vascular+Stiffness+in+the+Presence+of+Chronic+Kidney+Disease.)**.**

[**Regulation of Apoptotic Endonucleases by EndoG**](https://pubmed.ncbi.nlm.nih.gov/25849439/)**.**

[**Novel High-Throughput Deoxyribonuclease 1 Assay**](https://www.ncbi.nlm.nih.gov/pubmed/25326282)**.**

[**Single-Walled Carbon Nanotube and Graphene Nanodelivery of Gambogic Acid Increases its Cytotoxicity in Breast and Pancreatic Cancer Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Single-Walled+Carbon+Nanotube+and+Graphene+Nanodelivery+of+Gambogic+Acid+Increases+its+Cytotoxicity+in+Breast+and+Pancreatic+Cancer+Cells.)**.**

[**Circulating Tumor Cell Identification by Functionalized Silver-Gold Nanorods with Multicolor, Super-Enhanced SERS and Photothermal Resonances**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Circulating+Tumor+Cell+Identification+by+Functionalized+Silver-Gold+Nanorods+with+Multicolor%2C+Super-Enhanced+SERS+and+Photothermal+Resonances.)**.**

[**Immune Compartmentalization of T Cell Subsets in Chemically-Induced Breast Cancer**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Immune+Compartmentalization+of+T+Cell+Subsets+in+Chemically-Induced+Breast+Cancer.)**.**

[VIEW FULL BIO – Tariq Fahmi, M.D., Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/tariq-fahmi)

# Kiara Fairman, M.S., Pharm.D.

### **Research Biologist — Division of Biochemical Toxicology**

Dr. Fairman’s research interests are broad and include making physiologically based pharmacokinetic (PBPK) modeling widely available in clinical practice for individualized bedside medicine and using PBPK modeling for unique and underrepresented patient populations such as pregnancy, ethnicity, and disease state modeling. Dr. Fairman also desires to incorporate new advancements such as artificial intelligence (AI) and machine learning into PBPK modeling. Her current research goals are to learn AI and collaborate with AI experts to incorporate AI into a PBPK model for automation and model confidence building as a tool for regulatory use. Her expertise is in PBPK modeling, pharmacy, and chemistry and she is further interested in medicinal chemistry, natural products, and clinical pharmacology research. [VIEW FULL BIO – Dr. Kiara Fairman](https://www.fda.gov/about-fda/science-research-nctr/kiara-fairman)

**Titles and links to selected publications**

[**Physiologically Based Pharmacokinetic (PBPK) Modeling of RNAi Therapeutics: Opportunities and Challenges**](https://pubmed.ncbi.nlm.nih.gov/33577889/)**.**

[**Physiologically Based Pharmacokinetic Modeling: A Promising Tool for Translational Research and Regulatory Toxicology**](https://www.sciencedirect.com/science/article/abs/pii/S2468202020300176?via%3Dihub)**.**

[VIEW FULL BIO – Kiara Fairman, M.S., Pharm.D.](https://www.fda.gov/about-fda/science-research-nctr/kiara-fairman)

# Jia-Long Fang, Ph.D.

### **Research Biologist — Division of Biochemical Toxicology**

Dr. Fang has over twenty years of research experience in biochemical carcinogenesis and toxicology. He has designed, developed, and executed in vitroand in vivo research studies that address the biological mechanisms underlying the toxicities of drugs and chemicals. Throughout his career at NCTR, Dr. Fang’s research has been focused on the biological mechanisms of action underlying the toxicity of chemicals regulated by ─ or of interest to ─ FDA. Some of these chemicals are ethanol, urethane, tolvaptan, and antiretroviral drugs, including zidovudine, lamivudine, and nevirapine. More recently, Dr. Fang has been leading a research team to investigate the toxicities of topically applied triclosan. [VIEW FULL BIO – Dr. Jia-Long Fang](https://www.fda.gov/about-fda/science-research-nctr/jia-long-fang)

**Titles and links to selected publications**

[**Absorption and Metabolism of Triclosan After Application to the Skin of B6C3F1 Mice**](https://www.ncbi.nlm.nih.gov/pubmed/25410937)**.**

[**Human Sulfotransferases Enhance the Cytotoxicity of Tolvaptan**](https://www.ncbi.nlm.nih.gov/pubmed/26660633)**.**

[**Effect of Triclosan,Triclocarban, 2,2',4,4'-Tetrabromodiphenyl Ether, and Bisphenol A on the Iodide Uptake, Thyroid Peroxidase Activity, and Expression of Genes Involved in Thyroid Hormone Synthesis**](https://www.ncbi.nlm.nih.gov/pubmed/26827900)**.**

[**Mechanisms of Tolvaptan-Induced Toxicity in HepG2 Cells**](https://www.ncbi.nlm.nih.gov/pubmed/25858412)**.**

[**Dose-Response Assessment of the Dermal Toxicity of Triclosan in B6C3F1 Mice**](http://dx.doi.org/10.1039/c4tx00152d)**.**

[**Differential Effects of Triclosan on the Activation of Mouse and Human Peroxisome Proliferator-Activated Receptor Alpha**](https://www.ncbi.nlm.nih.gov/pubmed/25193434)**.**

[**Extracellular Signal-Regulated Kinases 1/2 and Akt Contribute to Triclosan-Stimulated Proliferation of JB6 Cl 41-5a Cells**](https://www.ncbi.nlm.nih.gov/pubmed/25033989)**.**

[**Differential Gene Expression in Human Hepatocyte Cell Lines Exposed to the Antiretroviral Agent Zidovudine**](https://www.ncbi.nlm.nih.gov/pubmed/24292225)**.**

[**Differential Responses of Human Hepatocytes to the Non-Nucleoside HIV-1 Reverse Transcriptase Inhibitor Nevirapine**](https://www.ncbi.nlm.nih.gov/pubmed/24067722)**.**

[**XPC is Essential for Nucleotide Excision Repair of Zidovudine-Induced DNA Damage in Human Hepatoma Cells**](https://www.ncbi.nlm.nih.gov/pubmed/21192964)**.**

[**Occurrence, Efficacy, Metabolism, and Toxicity of Triclosan**](https://www.ncbi.nlm.nih.gov/pubmed/20859822)**.**

[**Long-term Exposure to Zidovudine Delays Cell Cycle Progression, Induces Apoptosis, and Decreases Telomerase Activity in Human Hepatocytes**](https://www.ncbi.nlm.nih.gov/pubmed/19541796)**.**

[**Interference of Cell Cycle Progression by Zidovudine and Lamivudine in NIH 3T3 Cells**](https://www.ncbi.nlm.nih.gov/pubmed/18936108)**.**

[**Correlation Between the UDP-Glucuronosyltransferase (UGT1A1) TATAA Box Polymorphism and Carcinogen Detoxification Phenotype: Significantly Decreased Glucuronidating Activity Against Benzo(a)pyrene-7,8-Dihydrodiol(-) in Liver Microsomes From Subjects with the UGT1A1\*28 Variant**](https://www.ncbi.nlm.nih.gov/pubmed/14744740)**.**

[**Characterization of Benzo(a)pyrene-Trans-7,8-Dihydrodiol Glucuronidation by Human Tissue Microsomes and Overexpressed UDP-Glucuronosyltransferase Enzymes**](https://www.ncbi.nlm.nih.gov/pubmed/11929814)**.**

[**Detection of DNA Adducts of Acetaldehyde in Peripheral White Blood Cells of Alcohol Abusers**](https://www.ncbi.nlm.nih.gov/pubmed/9111191)**.**

[VIEW FULL BIO – Jia-Long Fang, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/jia-long-fang)

# Peter Fu, Ph.D.

### **Senior Research Chemist — Division of Biochemical Toxicology**

Dr. Fu’s research interests include chemical carcinogenesis of pyrrolizidine alkaloids, polycyclic aromatic hydrocarbons (PAHs), and nitro-PAHs as well as structure activity relationships, DNA adducts as biomarkers, herbal dietary supplements, and nanotoxicology. Pyrrolizidine alkaloid-containing plants are widespread in the world and are probably the most common type of poisonous plants affecting livestock, wildlife, and humans. Many pyrrolizidine alkaloids are hepatotoxic and tumorigenic and represent a threat to human health and safety. Regulatory agencies worldwide have issued bans and alerts on products containing pyrrolizidine alkaloids. To date, however, there are no practical analytical methods to quantify the total toxic pyrrolizidine alkaloid content present in herbal plants and products, or in foods, such as herbal dietary supplements, honey, and milk. Therefore, mechanism-based analytical methods must be developed to assess the risk posed by pyrrolizidine alkaloids in herbal plants and herbal products. Dr. Fu’s current research focuses on the quantitation of pyrrolizidine alkaloid-DNA adducts and pyrrolizidine alkaloid-protein adducts as mechanism-based methods for this need. Dr. Fu’s mechanistic studies determined that different types of tumorigenic-pyrrolizidine alkaloids exert tumorigenicity through a common metabolic-activation pathway. These findings are highly significant and strongly imply that a common metabolic mechanism is involved. Furthermore, the consistent type of DNA damage produced correlated with the biological effects of pyrrolizidine alkaloids. Dr. Fu proposes that, upon metabolism of the herbal products in vivo, in vitro, or in the cultured cells, quantitation of the level of the DHP-DNA adducts should be an assessable, reliable, and mechanism-based bioassay. Dr. Fu has also developed an LC/MS analytical method to quantify blood DHP-protein adducts as a noninvasive biomarker of pyrrolizidine alkaloid tumorigenicity and exposure. The levels of DHP-protein adducts in the blood correlated well with the levels of DHP-DNA adducts in the liver. This LC/MS/MS analytical method has the potential to be used for assessing human exposures to pyrrolizidine alkaloids. [VIEW FULL BIO – Dr. Peter Fu](https://www.fda.gov/about-fda/science-research-nctr/peter-fu)

**Titles and links to selected publications**

[**Pyrrolizidine Alkaloids Derived DHP-DNA Adducts are a Common Biological Biomarker of Pyrrolizidine Alkaloid-Initiated Tumorigenicity**](http://www.ncbi.nlm.nih.gov/pubmed/23937665)**.**

[**Mechanism of Nanotoxicity - Generation of Reactive Oxygen Species**](http://dx.doi.org/10.1016/j.jfda.2014.01.005)**.**

[**Enzyme-Like Activity of Nanomaterials**](http://dx.doi.org/10.1080/10590501.2014.907462)**.**

[**Metabolic Activation of Pyrrolizidine Alkaloids: Insights into the Structural and Enzymatic Basis**](http://pubs.acs.org/doi/abs/10.1021/tx500071q)**.**

[**Reaction of Dehydropyrrolizidine Alkaloids with Valine and Hemoglobin**](http://pubs.acs.org/doi/abs/10.1021/tx5002139)**.**

[**Metabolic Activation of Pyrrolizidine Alkaloids Leading to Phototoxicity and Photogenotoxicity in Human HaCaT Keratonicytes**](http://dx.doi.org/10.1080/10590501.2014.969980)**.**

[**UVA Photoirradiation of Benzo[a]pyrene Metabolites – Induction of Cytotoxicity, Rective Oxygen Species, and Lipid Peroxidation**](https://www.ncbi.nlm.nih.gov/pubmed/23552265)**.**

[**7-Glutathione Pyrrole Adduct - A Potential DNA Reactive Metabolite of Pyrrolizidine Alkaloids**](http://pubs.acs.org/doi/abs/10.1021/tx500417q)**.**

[**Pyrrolizidine Alkaloids: Toxic Phytochemicals Found in Food**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Pyrrolizidine%20Alkaloids%3A%20Toxic%20Phytochemicals%20Found%20in%20Food.%20Peter%20Fu)**.**

[**Absolute Configuration, Stability, and Interconversion of 6,7-Dihydro-7-Hydroxy-1-Hydroxymethyl-5H- Pyrrolizine Valine Adducts and Their Phenylthiohydantoin Derivatives**](http://dx.doi.org/10.1016/j.jfda.2015.01.004)**.**

[**Toxicity of Engineered Metal Oxide Nanomaterials by Nano-Bio-Eco Interactions: A Review and Perspective**](http://pubs.rsc.org/en/content/articlelanding/2015/en/c5en00094g#!divAbstract)**.**

[**Platinum Nanoparticles: Efficient and Stable Catechol Oxidase Mimetics**](http://pubs.acs.org/doi/full/10.1021/acsami.5b05180)**.**

[**Synthesis and Phototoxicity of Isomeric 7,9-Diglutathione Pyrrole Adducts: Formation of Reactive Oxygen Species and Induction of Lipid Peroxidation**](http://www.sciencedirect.com/science/article/pii/S1021949815000745)**.**

[**Blood Pyrrole-Protein Adducts – A Biomarker of Pyrrolizidine Alkaloid-Induced Liver Injury in Humans**](http://www.tandfonline.com/doi/full/10.1080/10590501.2015.1096882)**.**

[**A Novel Ultra-Performance Liquid Chromatography Hyphenated with Quadrupole Time of Flight Mass Spectrometry Method for Rapid Estimation of Total Toxic Retronecine-Type of Pyrrolizidine Alkaloids in Herbs Without Requiring Corresponding Standards**](http://dx.doi.org/10.1016/j.foodchem.2014.11.093)**.**

[**Cytotoxicity of Pyrrolizidine Alkaloid in Human Hepatic Parenchymal and Sinusoidal Endothelial Cells: Firm Evidence for the Reactive Metabolites of Pyrrolizidine Alkaloid-Induced Hepatotoxicity**](http://dx.doi.org/10.1016/j.cbi.2015.09.011)**.**

[**7-Cysteine-Pyrrole Conjugate - A New Potential DNA Reactive Metabolite of Pyrrolizidine Alkaloids**](http://dx.doi.org/10.1080/10590501.2015.1135593)**.**

[**Food Chemical Carcinogens: Sources and Mechanisms of Exogenous DNA Adduct Formation**](https://www.researchgate.net/publication/310842158_Food_Chemical_Carcinogens_Sources_and_Mechanism_of_Exogenous_DNA_Adduct_Formation)**.**

[**The Long Persistence of Pyrrolizidine Alkaloid-Derived DNA Adducts In Vivo: Kinetic Study Following Single and Multiple Exposures in Male ICR Mice**](http://www.ncbi.nlm.nih.gov/pubmed/27125825)**.**

[**Pyrrolizidine Alkaloid-Protein Adducts - Potential Non-Invasive Biomarkers of Pyrrolizidine Alkaloid-Initiated Liver Toxicity and Exposure**](http://pubs.acs.org/doi/full/10.1021/acs.chemrestox.6b00120)**.**

[VIEW FULL BIO – Peter Fu, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/peter-fu)

# Lei Guo, Ph.D.

### **Research Biologist — Division of Biochemical Toxicology**

Dr. Guo's research focuses on mechanistic studies of drug- and herbal dietary supplement-associated toxicities. She uses multiple in vitro models and approaches, including, but not restricted to, molecular and biochemical methods, genomic analyses, and in silico molecular docking for evaluation and prediction of toxicity and elucidation of toxic mechanisms. Her research results demonstrate that this combined approach is useful for hazard identification and that in-depth molecular mechanistic studies can provide toxicological information for FDA-relevant products. [VIEW FULL BIO – Dr. Lei Guo](https://www.fda.gov/about-fda/science-research-nctr/lei-guo)

**Titles and links to selected publications**

[**A Mechanism of Perhexiline's Cytotoxicity in Hepatic Cells Involves Endoplasmic Reticulum Stress and P38 Signaling Pathway**](https://pubmed.ncbi.nlm.nih.gov/33309543/)**.**

[**Characterization of Cytochrome P450s (CYP)-overexpressing HepG2 Cells for Assessing Drug and Chemical-Induced Liver Toxicity**](https://pubmed.ncbi.nlm.nih.gov/33576714/)**.**

[**Roles of CYP3A4, CYP3A5 and CYP2C8 Drug-Metabolizing Enzymes in Cellular Cytostatic Resistance**](https://pubmed.ncbi.nlm.nih.gov/33775687/)**.**

[**Mitochondrial Dysfunction and Apoptosis Underlie the Hepatotoxicity of Perhexiline**](https://pubmed.ncbi.nlm.nih.gov/32861758/)**.**

[**The Role of Hepatic Cytochrome P450s in the Cytotoxicity of Sertraline**](https://pubmed.ncbi.nlm.nih.gov/32372212/)**.**

[**The Role of Hepatic Cytochrome P450s in the Cytotoxicity of Dronedarone**](https://link.springer.com/article/10.1007/s00204-018-2196-x)**.**

[**Mitochondrial Dysfunction Induced by Leflunomide and its Active Metabolite**](https://pubmed.ncbi.nlm.nih.gov/29427785/)**.**

[**DNA Damage-Induced Apoptosis and Mitogen-Activated Protein Kinase Pathway Contribute to the Toxicity of Dronedarone in Hepatic Cells**](https://onlinelibrary.wiley.com/doi/full/10.1002/em.22173)**.**

[**Endoplasmic Reticulum Stress and MAPK Signaling Pathway Activation Underlie Leflunomide-Induced Toxicity in HepG2 Cells**](https://pubmed.ncbi.nlm.nih.gov/24598041/)**.**

[**Activation of the Nrf2 Signaling Pathway in Usnic Acid-Induced Toxicity in HepG2 Cells**](http://www.ncbi.nlm.nih.gov/pubmed/27369375)**.**

[**The Role of CYP 3A4 and 1A1 in Amiodarone-Induced Hepatocellular Toxicity**](http://www.ncbi.nlm.nih.gov/pubmed/27113703)**.**

[**Development of HepG2-Derived Cells Expressing Cytochrome P450s for Assessing Metabolism-Associated Drug-Induced Liver Toxicity**](http://www.ncbi.nlm.nih.gov/pubmed/26477383)**.**

[**Endoplasmic Reticulum Stress and Store-Operated Calcium Entry Contribute to Usnic Acid-Induced Toxicity in Hepatic Cells**](http://www.ncbi.nlm.nih.gov/pubmed/25870318)**.**

[**The Role of Autophagy in Usnic Acid-Induced Toxicity in Hepatic Cells**](http://www.ncbi.nlm.nih.gov/pubmed/25078063)**.**

[**Sertraline Induces Endoplasmic Reticulum Stress in Hepatic Cells**](http://www.ncbi.nlm.nih.gov/pubmed/24865413)**.**

[**Sertraline, an Antidepressant, Induces Apoptosis in Hepatic Cells through the Mitogen-Activated Protein Kinase Pathway**](http://www.ncbi.nlm.nih.gov/pubmed/24194395)**.**

[**Mechanism Study of Goldenseal-Associated DNA Damage**](http://www.ncbi.nlm.nih.gov/pubmed/23747414)**.**

[**Mitochondrial Dysfunction Induced by Sertraline, an Antidepressant Agent**](http://www.ncbi.nlm.nih.gov/pubmed/22387747)**.**

[**Similarities and Differences in the Expression of Drug-Metabolizing Enzymes between Human Hepatic Cell Lines and Primary Human Hepatocytes**](http://www.ncbi.nlm.nih.gov/pubmed/21149542)**.**

[**Methysticin and 7,8-Dihydromethysticin Are Two Major Kavalactonesin Kava Extract to Induce CYP1A1**](http://www.ncbi.nlm.nih.gov/pubmed/21908763)**.**

[VIEW FULL BIO – Lei Guo, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/lei-guo)

# George Hammons, Ph.D.

### **Senior Research Scientist — Division of Biochemical Toxicology**

George Hammons works as a senior investigator focused on understanding the role of cytochromes P-450 in the metabolic activation of carcinogens. Additionally, he looks to develop approaches for characterizing these enzymes and elucidating their catalytic mechanisms. He is also interested in the application of these understandings and developments to human-risk assessment. His area of focus similarly includes developing potential chemopreventive strategies with dietary agents and identifying potential early biomarkers for pancreatic cancer. He has now established a research agenda in epigenetics. This includes the role of epigenetics in disease and toxicology, particularly in the harm from tobacco smoke, as he is considered an expert in tobacco toxicology. Included in this focus, is the role of epigenetics in the regulation of enzymes involved in the activation of pro-toxicants, and most recently the role of epigenetics in the toxicity of nanoparticles. [VIEW FULL BIO – Dr. George Hammons](https://www.fda.gov/about-fda/science-research-nctr/george-hammons)

**Titles and links to selected publications**

[**Cigarette Smoke Condensate and Individual Constituents Modulate DNAMethyltransferase (DNMT) Expression in Human Liver Cells**](https://pubmed.ncbi.nlm.nih.gov/26770776/)**.**

[**Cytotoxicity of Chronic Exposure to Four Cigarette Smoke Condensates (CSCs) in Two Cell Lines**](https://www.researchgate.net/publication/274085970_Cytotoxicity_of_Chronic_Exposure_to_4_Cigarette_Smoke_Condensates_in_2_Cell_Lines)**.**

[**Expression of Drug Transporters in Human Kidney:  Impact of Sex, Age, and Ethnicity**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4352278/)**.**

[**Prolactin (PRL) and Dehydroepiandrosterone (DHEA) Levels in Women with Sytemic Lupus Eryghematous:  The Role of Extrapituitary Prolactin Promoter Polymorphism at -1149G/T**](https://pubmed.ncbi.nlm.nih.gov/26583155/)**.**

[**Effect of Cigarette Smoke Condensate on Gene Promoter Methylation in Human Lung Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Effect%20of%20cigarette%20smoke%20condensate%20on%20gene%20promoter%20methylation%20in%20human%20lung%20cells.)**.**

[**Increased Expression of Toll-Like Receptors (TRLs) 7 and 9 and Other Cytokines in Systemic Lupus Erythematosus (SLE) Patients:  Ethnic Differences and Potential New Targets for Therapeutic Drugs**](https://www.researchgate.net/publication/262683540_Increased_expression_of_Toll-like_receptors_TLRs_7_and_9_and_other_cytokines_in_systemic_lupus_erythematosus_SLE_patients_Ethnic_differences_and_pote)**.**

[**Cigarette Smoke Condensate Induces Differential Expression and Promoter Methylation Profiles of Critical Genes Involved in Lung Cancer in NL-20 Lung Cells In Vitro:  Short-Term and Chronic Exposure**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Cigarette%20smoke%20condensate%20induces%20differential%20expression%20and%20promoter%20methylation%20profiles%20of%20critical%20genes%20involved%20in%20lung%20cancer%20in%20NL-20%20lung%20cells%20In)**.**

[**Epigenetics in Tobacco Smoke Toxicology**](https://www.researchgate.net/publication/286156872_Epigenetics_in_tobacco_smoke_toxicology?_sg=bFnesO9Ryc83opJ48Z3ThDhcm0sgMfS4wTkadOnmFNERkqGt0NRFDGlzQssh-QcJvwWI57BPxyRYKA8Bg8xWTg)**.**

[**Age and Gender Affect DNMT3a and DNMT3b Expression in Human Liver**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Age%20and%20gender%20affect%20DNMT3a%20and%20DNMT3b%20expression%20in%20human%20liver.)**.**

[**Indole-3-Carbinol (I3C) Modulates Expression of DNA Methyltransferases 1, 3a, and 3b in Pancreatic Cancer Cells:  Effects of Gender and a Novel (C→T) Polymorphism in the Promoter Region of DNMT 3b**](http://www.sciencedirect.com/science/article/pii/S0006291X11013593)**.**

[**Search for an Association Between the Human CYP1A2 Genotype and CYP1A2 Metabolic Phenotype**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Search%20for%20an%20association%20between%20the%20human%20CYP1A2%20genotype%20and%20CYP1A2%20metabolic%20phenotype.)**.**

[**Increased Levels of NAD(P)H: Quinone Oxidoreductase 1 (NQO1) in Pancreatic Tissues from Smokers and Pancreatic Adenocarcinomas:  A Potential Biomarker of Early Damage in the Pancreas**](https://pubmed.ncbi.nlm.nih.gov/16532285/)**.**

[**Modulation of the Constitutive Activated STAT3 Transcription Factor in Pancreatic Cancer Prevention:  Effects of Indole-3-Carbinol (I3C) and Genistein**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Modulation%20of%20the%20constitutive%20activated%20STAT3%20transcription%20factor%20in%20pancreatic%20cancer%20prevention%3A%20%20Effects%20of%20indole-3-carbinol%20(I3C)%20and%20genistein.)**.**

[**Increased Expression of Heterogeneous Nuclear Ribonucleoprotein A2/B1 (hnRNP) in Pancreatic Tissue from Smokers and Pancreatic Tumor Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Increased%20expression%20of%20%09heterogeneous%20nuclear%20ribonucleoprotein%20A2%2FB1%20(hnRNP)%20in%20pancreatic%20tissue%20from%20smokers%20and%20pancreatic%20tumor%20cells.)**.**

[**Specific Site Methylation in the 5’-Flanking Region of CYP1A2: Interindividual Differences in Human Livers**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Specific%20site%20methylation%20in%20the%205%E2%80%99-flanking%20region%20of%20CYP1A2%3A%20%20%09Interindividual%20differences%20in%20human%20livers.)**.**

[**Increased Expression of Hepatic DNA Methyltransferase in Smokers**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Increased%20expression%20of%20hepatic%20DNA%20methyltransferase%20in%20smokers.)**.**

[**Chemopreventive Effects of Tea Extracts and Various Components on Human Pancreatic and Prostate Tumor Cells In Vitro**](https://www.ncbi.nlm.nih.gov/pubmed/10624710)**.**

[**Effects of Chemoprotective Agents on the Metabolic Activition of the Carcinogenic Arylamines PhIP and 4-Aminobiphenyl in Human and Rat Liver Microsomes**](https://www.ncbi.nlm.nih.gov/pubmed/10227043)**.**

[**Metabolism of Carcinogenic Heterocyclic and Aromatic Amines  by Recombinant Human Cytochrome P450 Enzymes**](https://www.ncbi.nlm.nih.gov/pubmed/9111224)**.**

[**Increased DT-Diaphorase Activity in Transformed and Tumorigenic Pancreatic Acinar Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Increased%20DT-diaphorase%20activity%20in%20transformed%20and%20tumorigenic%20pancreatic%20acinar%20cells.)**.**

[**Modification of Cytochrome P450 1A2 Enzymes by the Mechanism Based Inactivator 2 Ethynylnaphthalene and the Photoaffinity Label 4 Azido-Biphenyl**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Modification%20of%20cytochrome%20P450%201A2%20enzymes%20by%20the%20mechanism%20based%20inactivator%202%20ethynylnaphthalene%20and%20the%20photoaffinity%20label%204%20azido-biphenyl.)**.**

[**4 Aminobiphenyl Hemoglobin Adduct Formation as an Index of In Vivo N Oxidation by Hepatic Cytochrome**](https://www.ncbi.nlm.nih.gov/pubmed/?term=4%20Aminobiphenyl%20hemoglobin%20adduct%20formation%20as%20an%20index%20of%20in%20vivo%20N%20oxidation%20by%20hepatic%20cytochrome)**.**

[**2 Ethynyl- Naphthalene as a Mechanism Based Inactivator of the Cytochrome P 450-Catalyzed N Oxidation of 2 Naphthylamine**](https://www.ncbi.nlm.nih.gov/pubmed/?term=2%20Ethynyl-%20naphthalene%20as%20a%20mechanism%20based%20inactivator%20of%20the%20cytochrome%20P%20450-catalyzed%20N%20oxidation%20of%202%20naphthylamine.)**.**

[**Metabolic Oxidation of Carcinogenic Arylamines by Rat, Dog, and Human Hepatic Microsomes and by Purified Flavin Containing and Cytochrome P 450 Monooxygenases**](https://pubmed.ncbi.nlm.nih.gov/4016738/)**.**

[**Proton Exchange Reactions of Acetone and Butanone: Resolution of Catalysis by Acetoacetate Decarboxylase**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Proton%20exchange%20reactions%20of%20acetone%20and%20butanone%3A%20%20Resolution%20of%20catalysis%20by%20acetoacetate%20decarboxylase.)**.**

[VIEW FULL BIO – George Hammons, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/george-hammons)

# Miao Li, Ph.D., Master of Medicine, DABT

### **Visiting Scientist — Division of Biochemical Toxicology**

Dr. Li’s research mainly focuses on the development and application of PBPK modeling to support therapeutic dose adjustment and chemical risk assessment. His research interests include life-stage modeling, in vitro to in vivo extrapolation, population modeling, model parameter analysis, and model extrapolation across species. Dr. Li uses life-stage PBPK models to ensure drug safety and efficacy, applies in vitro to in vivo extrapolation to determine model parameter values, and uses population modeling to simulate variabilities in patients. Currently, he is working on developing perinatal life-stage PBPK models for COVID-19 therapeutics to support dosage adjustment. Dr. Li is skilled in pharmacokinetic data analysis and developing PBPK models with commercial software or programming languages. [VIEW FULL BIO – Dr. Miao Li](https://www.fda.gov/about-fda/science-research-nctr/miao-li)

**Titles and links to selected publications**

[**Physiologically Based Pharmacokinetic (PBPK) Modeling of RNAi Therapeutics: Opportunities and Challenges**](https://pubmed.ncbi.nlm.nih.gov/33577889/)**.**

[**Physiological Parameter Values for Physiologically Based Pharmacokinetic Models in Food-Producing Animals. Part III: Sheep and Goat**](https://pubmed.ncbi.nlm.nih.gov/33350478/)**.**

[**Physiologically Based Pharmacokinetic Modeling: A Promising Tool for Translational Research and Regulatory Toxicology**](https://www.sciencedirect.com/science/article/abs/pii/S2468202020300176)**.**

[**Physiologically Based Pharmacokinetic Model Calibration, Evaluation, and Performance Assessment**](https://www.sciencedirect.com/science/article/pii/B9780128185964000102?via%3Dihub)**.**

[**Physiological Parameter Values for Physiologically Based Pharmacokinetic Models in Food-Producing Animals. Part I: Cattle and Swine**](https://pubmed.ncbi.nlm.nih.gov/32270548/)**.**

[**Development and Application of a Population Physiologically Based Pharmacokinetic Model for Penicillin G in Swine and Cattle for Food Safety**](https://pubmed.ncbi.nlm.nih.gov/28627373/)**.**

[**Cytochrome c Adducts with PCB Quinoid Metabolites**](https://pubmed.ncbi.nlm.nih.gov/26062463/)**.**

[**Does Dietary Copper Supplementation Enhance or Diminish PCB126 Toxicity in the Rodent Liver**](https://pubmed.ncbi.nlm.nih.gov/23527585/)**?**

[**Glia Activation Induced by Peripheral Administration of Aluminum Oxide Nanoparticles in Rat Brains**](https://pubmed.ncbi.nlm.nih.gov/19523415/)**.**

[VIEW FULL BIO – Miao Li, Ph.D., Master of Medicine, DABT](https://www.fda.gov/about-fda/science-research-nctr/miao-li)

# Beverly Lyn-Cook, Ph.D.

### **Interdisciplinary Research Biologist — Division of Biochemical Toxicology**

Dr. Lyn-Cook is a research biologist with vast research experience in the areas of cell and molecular biology, cancer research, pharmacogenomics, epigenetics, lupus, and sex differences in drug efficacy. Her major research expertise is in the cancer field ─ with emphasis on endometrial, pancreatic, and breast cancer ─ where she has developed in vitro assays using human cells to discover biomarkers of cancer etiology and progression, as well as to examine differences in cancer drug treatments. She has further developed a research program on sex differences in response to various drugs. Dr. Lyn-Cook focuses on drug transporters and genetic variations in genes involved in metabolism, biotransformation, and drug excretion to better understand mechanistic and toxic actions of drugs alone or in combination with dietary agents. In a collaborative project with university scientists, Dr. Lyn-Cook has initiated a research program on systemic lupus erythematosus (SLE). In this program she is investigating genetic and epigenetic mechanisms involved in SLE etiology and differences in efficacy of FDA drugs or biologics in African Americans and European American women with lupus. She has shown the importance of epigenetics in SLE by examining peripheral blood mononuclear cells and serum from lupus and age-matched control patients. She has identified potential new therapeutic targets for treating lupus patients. Currently, Dr. Lyn-Cook is examining the use of FDA-approved epigenetic drugs to treat triple-negative breast cancer, an aggressive form of cancer with many subtypes that respond to very few current drug regimens. [VIEW FULL BIO – Dr. Beverly Lyn-Cook](https://www.fda.gov/about-fda/science-research-nctr/beverly-lyn-cook)

**Titles and links to selected publications**

[**The Food and Drug Administration Office of Women’s Health: Impact of Science on Regulatory Policy: An Update**](https://www.ncbi.nlm.nih.gov/pubmed/?term=The%20Food%20and%20Drug%20Administration%20Office%20of%20Women%E2%80%99s%20Health%3A%20Impact%20of%20Science%20on%20Regulatory%20Policy%3A%20An%20Update.)**.**

[**MicroRNAs: Potential Diagnostic and Therapeutic Targets for Breast Cancer**](http://www.eurekaselect.com/128675)**.**

[**Prolactin and Dehydroepiandrosterone Levels in Women with Systemic Lupus Erythematosus: The Role of the Extrapituitary Prolactin Promoter Polymorphism at −1149G/T**](https://www.hindawi.com/journals/jir/2015/435658/)**.**

[**Expression of Drug Transporters in Human Kidney: Impact of Sex, Age, and Ethnicity**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Expression%20of%20Drug%20Transporters%20in%20Human%20Kidney%3A%20Impact%20of%20Sex%2C%20Age%2C%20and%20Ethnicity.)**.**

[**Cytotoxicity of Chronic Exposure to 4 Cigarette Smoke Condensates in 2 Cell Lines**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Cytotoxicity%20of%20Chronic%20Exposure%20to%204%20Cigarette%20Smoke%20%20Condensates%20in%202%20Cell%20Lines.)**.**

[**Increased Expression of Toll-like Receptors (TLRs) 7 and 9 and Other Cytokines in Systemic Lupus Erythematosus (SLE) Patients: Ethnic Differences and Potential New Targets for Therapeutic Drugs**](https://pubmed.ncbi.nlm.nih.gov/24865418/)**.**

[**ATP-Binding Cassette Genes Genotype and Expression: A Potential Association with Pancreatic Cancer Development and Chemoresistance**](https://www.ncbi.nlm.nih.gov/pubmed/?term=ATP-Binding%20Cassette%20Genes%20Genotype%20and%20Expression%3A%20A%20Potential%20Association%20with%20Pancreatic%20Cancer%20Development%20and%20Chemoresistance%3F)**?**

[**Ethnic Differences in DNA Methyltransferases Expression in Patients with Systemic Lupus Erythematosus**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Ethnic%20Differences%20in%20DNA%20Methyltransferases%20Expression%20in%20Patients%20with%20Systemic%20Lupus%20Erythematosus.)**.**

[**Restoration of the Methylation Status of Hypermethylated Gene Promoters by MicroRNA-29b in Human Breast Cancer: A Novel Epigenetic Therapeutic Approach**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Restoration%20of%20the%20Methylation%20Status%20of%20Hypermethylated%20Gene%20Promoters%20by%20MicroRNA-29b%20in%20Human%20Breast%20cancer%3A%20A%20Novel%20Epigenetic%20Therapeutic%20Approach.)**.**

[**Characterization of UDP-Glucuronosyl-Transferase (UGT1A1) Promoter Polymorphisms and Gene Expression on Ethnicity, Stage of Disease, and Menopausal Status in Breast Cancer**](https://pubmed.ncbi.nlm.nih.gov/30349745/)**.**

[**Epigenetics in Tobacco Smoke Toxicology**](https://www.researchgate.net/publication/286156872_Epigenetics_in_tobacco_smoke_toxicology)**.**

[**Enhanced Efficacy of Gemcitabine by Indole-3-Carbinol in Pancreatic Cell Lines: The role of Human Equilibrative Nucleotide Transporter 1 (hENT1)**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Enhanced%20Efficacy%20of%20Gemcitabine%20by%20Indole-3-Carbinol%20in%20Pancreatic%20Cell%20Lines%3A%20The%20role%20of%20Human%20Equilibrative%20Nucleotide%20Transporter%201%20(hENT1).)**.**

[**Transcriptional Activity of DNMT3B in Pancreatic Cancer Cells: Effects of -149 (C→T) Promoter Polymorphism**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Transcriptional%20Activity%20of%20DNMT3B%20in%20Pancreatic%20Cancer%20Cells%3A%20Effects%20of%20-149%20(C%E2%86%92T)%20Promoter%20Polymorphism.)**.**

[**Gender Differences in Gemcitabine (Gemzar) Efficacy in Cancer Cells: Effect of Indole-3-Carbinol**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Gender%20Gifferences%20in%20Gemcitabine%20(Gemzar)%20Efficacy%20in%20Cancer%20Cells%3A%20Effect%20of%20Indole-3-Carbinol.)**.**

[**The Role of UDP-Glucuronosyltransferases and Drug Transporters in Breast Cancer Drug Resistance**](https://www.ncbi.nlm.nih.gov/pubmed/21403613)**.**

[**Novel Identification of UDP-Glucuronosyltransferase 1A10 as an Estrogen-Regulated Target Gene**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Novel%20Identification%20of%20UDP-Glucuronosyltransferase%201A10%20as%20an%20Estrogen-Regulated%20Target%20Gene.)**.**

[**Identification of UDP-Glucuronosyltransferase 1A10 in Non-Malignant and Malignant Human Breast Tissues**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Identification%20of%20UDP-Glucuronosyltransferase%201A10%20in%20Non-Malignant%20and%20Malignant%20Human%20Breast%20Tissues.)**.**

[**Indole-3-Carbinol (I3C) Modulates Expression of DNA Methyltransferases 1, 3a, and 3b in Pancreatic Cancer Cells: Effects of Gender and a Novel (C→T) Polymorphism in the Promoter Region of DNMT 3b**](https://www.researchgate.net/publication/285700521_Indole-3-carbinol_I3C_modulates_expression_of_DNA_methyltransferases_1_3a_and_3b_in_pancreatic_cancer_cells_Effects_of_gender_and_a_novel_C_T_polymor)**.**

[**Increased Levels of NAD(P)H: Quinone Oxidoreductase 1(NQO1) in Pancreatic Tissues from Smokers and Pancreatic Adenocarcinomas:  A Potential Biomarker of Early Damage in the Pancreas**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Increased%20Levels%20of%20NAD(P)H%3A%20Quinone%20Oxidoreductase%201(NQO1)%20in%20Pancreatic%20%20%20Tissues%20from%20Smokers%20and%20Pancreatic%20Adenocarcinomas%3A%20%20A%20Potential%20Biomarker%20of)**.**

[**Modulation of the Constitutive Activated STAT3 Transcription Factor in Pancreatic Cancer Prevention: Effects of Indole-3-Carbinol (I3C) and Genistein**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Modulation%20of%20the%20Constitutive%20Activated%20STAT3%20Transcription%20Factor%20in%20Pancreatic%20Cancer%20%20%20Prevention%3A%20Effects%20of%20Indole-3-Carbinol%20(I3C)%20and%20Genistein.)**.**

[VIEW FULL BIO – Beverly Lyn-Cook, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/beverly-lyn-cook)

# Darshan Mehta, Ph.D.

### **Visiting Scientist — Division of Biochemical Toxicology**

Dr. Mehta’s research interests lie in modeling chemical effects in biological systems using computational and statistical modeling methods. He specializes in the development and utilization of PBPK models for predicting the disposition of chemicals in animals and humans. These PBPK models are useful in determining the internal tissue dosimetry for a given exposure scenario as well as in understanding the ADME (absorption, distribution, metabolism, and excretion) profile of chemicals in intact biological organisms. Dr. Mehta is skilled in multiple computer programming languages and in various data analysis, cheminformatics, and PBPK modeling software platforms. He looks forward to collaborating with other FDA product centers to help advance the mission of protecting and promoting public health. [VIEW FULL BIO – Dr. Darshan Mehta](https://www.fda.gov/about-fda/science-research-nctr/darshan-mehta)

**Titles and links to selected publications**

[**Challenges in Predicting the Pharmacokinetics of Drugs in Premature and Mature Newborns: Example with Piperacillin and Tazobactam**](https://www.sciencedirect.com/science/article/pii/B9780128189023000191)**.**

[**Toxicokinetic and Genotoxicity Study of NNK in Male Sprague-Dawley Rats Following Nose-Only Inhalation Exposure, Intraperitoneal Injection, and Oral Gavage**](https://pubmed.ncbi.nlm.nih.gov/33944952/)**.**

[**Study of Pharmacogenomic Information in FDA-approved Drug Labeling to Facilitate Application of Precision Medicine**](https://pubmed.ncbi.nlm.nih.gov/32032705/)**.**

[**Characterizing Biopersistence Potential of the Metabolite 5:3 Fluorotelomer Carboxylic Acid After Repeated Oral Exposure to the 6:2 Fluorotelomer Alcohol**](https://pubmed.ncbi.nlm.nih.gov/31923437/)**.**

[**Fundamentals of Physiologically Based Pharmacokinetic Modeling**](https://www.sciencedirect.com/science/article/pii/B9780128185964000035)**.**

[**Chemical Absorption and Writing Code for Portals of Entry**](https://www.sciencedirect.com/science/article/pii/B9780128185964000059)**.**

[**Ontogeny Equations with Probability Distributions for Anthropomorphic Measurements in Preterm and Term Neonates and Infants for Use in a PBPK Model**](https://www.sciencedirect.com/science/article/pii/S2468111318301403?via%3Dihub)**.**

[**Study of Serious Adverse Drug Reactions Using FDA-approved Drug Labeling and MedDRA**](https://pubmed.ncbi.nlm.nih.gov/30871458/)**.**

[**Cheminformatics in Modern Regulatory Science**](https://onlinelibrary.wiley.com/doi/abs/10.1002/9783527806539.ch8)**.**

[VIEW FULL BIO – Darshan Mehta, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/darshan-mehta)

# Igor Pogribny, M.D., Ph.D.

### **Research Biologist — Division of Biochemical Toxicology**

Dr. Pogribny’s research interests and experience are centered in three major areas: 1) to elucidate the role and significance of genetic and epigenetic alterations in the development and progression of cancer, 2) to investigate and establish the role of epigenetic alterations as indicators of exposure to genotoxic and non-genotoxic carcinogens ─ critical for the primary prevention of neoplasia in humans, and 3) to conduct research on nonalcoholic fatty liver disease (NAFLD).

NAFLD is strongly associated with metabolic syndrome and obesity. It includes a range of liver injury from simple steatosis to nonalcoholic steatohepatitis (NASH), fibrosis, and cirrhosis, and is a major health problem and leading cause of chronic liver disease in the United States and Western countries. Dr. Pogribny’s laboratory aims to better understand the role of individual genetic and genomic ─ including epigenomic ─ susceptibility factors in the development of NAFLD.  Identification of these susceptibility factors may facilitate the development of diagnostic tools that can be used to identify high-risk individuals to help prevent NAFLD-related liver cancer. [VIEW FULL BIO – Dr. Igor Pogribny](https://www.fda.gov/about-fda/science-research-nctr/igor-pogribny)

**Titles and links to selected publications**

[**Furan-Induced Transcriptomic and Gene-Specific DNA Methylation Changes in the Livers of Fischer 344 Rats in a 2-Year Carcinogenicity Study**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Furan-induced%20transcriptomic%20and%20gene-specific%20DNA%20methylation%20changes%20in%20the%20livers%20of%20Fischer%20344%20rats%20in%20a%202-year%20carcinogenicity%20study)**.**

[**Irreversible Down-Regulation of mir-375 in the Livers of Fischer 344 Rats after Chronic Furan Exposure**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Irreversible%20down-regulation%20of%20miR-375%20in%20the%20livers%20of%20Fischer%20344%20rats%20after%20chronic%20furan%20exposure.)**.**

[**Differentially Expressed MicroRNAs Provide Mechanistic Insight into Fibrosis-Associated Liver Carcinogenesis in Mice**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Differentially%20expressed%20microRNAs%20provide%20mechanistic%20insight%20into%20fibrosis-associated%20liver%20carcinogenesis%20in%20mice.)**.**

[**Epigenetic Alterations Induced by Genotoxic Occupational and Environmental Human Chemical Carcinogens: A Systematic Literature Review**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Epigenetic%20alterations%20induced%20by%20genotoxic%20occupational%20and%20environmental%20human%20chemical%20carcinogens%3A%20A%20systematic%20literature%20review.)**.**

[**Status of Hepatic DNA Methylome Predetermines and Modulates the Severity of Non-Alcoholic Fatty Liver Injury in Mice**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Status%20of%20hepatic%20DNA%20methylome%20predetermines%20and%20modulates%20the%20severity%20of%20non-alcoholic%20fatty%20liver%20injury%20in%20mice.)**.**

[**MicroRNA Changes, Activation of Progenitor Cells, and Severity of Liver Injury in Mice Induced by Choline and Folate Deficiency.**](https://www.ncbi.nlm.nih.gov/pubmed/?term=MicroRNA%20changes%2C%20activation%20of%20progenitor%20cells%2C%20and%20severity%20of%20liver%20injury%20in%20mice%20induced%20by%20choline%20and%20folate%20deficiency.)

[**MicroRNA Responses to the Genotoxic Carcinogens Aflatoxin B1 and Benzo[A]Pyrene in Human HepaRG Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=MicroRNA%20responses%20to%20the%20genotoxic%20carcinogens%20aflatoxin%20B1%20and%20benzo%5Ba%5Dpyrene%20in%20human%20HepaRG%20cells.)**.**

[**The Role of MicroRNAs in the Development and Progression of Chemical-Associated Cancers**](https://www.ncbi.nlm.nih.gov/pubmed/?term=The%20role%20of%20microRNAs%20in%20the%20development%20and%20progression%20of%20chemical-associated%20cancers.)**.**

[**Persistence of Furan-Induced Epigenetic Aberrations in the Livers of F344 Rats**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Persistence%20of%20furan-induced%20epigenetic%20aberrations%20in%20the%20livers%20of%20F344%20rats.)**.**

[**Genetic and Epigenetic Changes in Fibrosis-Associated Hepatocarcinogenesis in Mice**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Genetic%20And%20Epigenetic%20Changes%20In%20Fibrosis-Associated%20Hepatocarcinogenesis%20In%20Mice.)**.**

[VIEW FULL BIO – Igor Pogribny, M.D., Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/igor-pogribny)

# Camila S. Silva, Ph.D.

### **Research Biologist — Division of Biochemical Toxicology**

Dr. Silva has participated in studies using animal models to assess the toxicity of products of interest to the FDA, including the food adulterants melamine and cyanuric acid and the dietary supplements nattokinase and lumbrokinase. As a response to the COVID-19 pandemic, Dr. Silva used her background in virology and molecular biology to develop a method to monitor wastewater samples for the presence of the new coronavirus SARS-CoV-2. This method is being applied for routine detection of the virus and to help surveil the extent of the COVID-19 epidemic in local communities in Arkansas. Dr. Silva plays an important role in the optimization of methods, sample preparation and processing, and data analysis to support ongoing studies in the Division of Biochemical Toxicology. She is investigating the use of miRNA and gene expression as molecular endpoints to assist in toxicity assessments and the molecular mechanisms by which compounds of interest to the FDA induce toxicity. [VIEW FULL BIO – Dr. Camila S. Silva](https://www.fda.gov/about-fda/science-research-nctr/camila-silva)

**Titles and links to selected publications**

[**A Robust Biostatistical Method Leverages Informative but Uncertainly Determined qPCR Data for Biomarker Detection, Early Diagnosis, and Treatment**](https://pubmed.ncbi.nlm.nih.gov/35100319/)**.**

[**Reproducibility Challenges for Biomarker Detection with Uncertain but Informative Experimental Data**](https://pubmed.ncbi.nlm.nih.gov/33021389/)**.**

[**Data on the Effect of Heat and Other Technical Variables on the Detection of MicroRNAs in Human Serum**](https://pubmed.ncbi.nlm.nih.gov/30976632/)**.**

[**Identification of Whole Blood mRNA and microRNA Biomarkers of Tissue Damage and Immune Function Resulting from Amphetamine Exposure or Heat Stroke in Adult Male Rats**](https://pubmed.ncbi.nlm.nih.gov/30779732/)**.**

[**Effects of a 28-day Dietary Co-Exposure to Melamine and Cyanuric Acid on the Levels of Serum microRNAs in Male and Female Fisher 344 Rats**](https://pubmed.ncbi.nlm.nih.gov/27621052/)**.**

[**Human Respiratory Coronaviruses Detected In Patients with Influenza-Like Illness in Arkansas, USA**](https://pubmed.ncbi.nlm.nih.gov/27588218/)**.**

[**Effects of α-tocopherol Supplementation on Liver of Rats Chronically Exposed to Ethanol**](https://pubmed.ncbi.nlm.nih.gov/23942415/)**.**

[**Investigation on the 19S ATPase Proteasome Subunits (Rpt1-6) Conservation and Their Differential Gene Expression in Schistosoma Mansoni**](https://pubmed.ncbi.nlm.nih.gov/23052763/)**.**

[**Vitamin E Alters Inflammatory Gene Expression in Alcoholic Chronic Pancreatitis**](https://pubmed.ncbi.nlm.nih.gov/22890014/)**.**

[**Schistosoma Mansoni Encodes SMT3B and SMT3C Molecules Responsible for Post-Translational Modification of Cellular Proteins**](https://pubmed.ncbi.nlm.nih.gov/18243776/)**.**

[**Schistosoma Mansoni: Gene Expression of the Nucleotide Excision Repair Factor 2 (NEF2) During the Parasite Life Cycle, and in Adult Worms After Exposure to Different DNA-Damaging Agents**](https://pubmed.ncbi.nlm.nih.gov/17850756/)**.**

[**Characterization of the Gene Expression Related to the Process of DNA Damage Tolerance in Schistosoma Mansoni**](https://pubmed.ncbi.nlm.nih.gov/17308764/)**.**

[**The Influence of Iron, Vitamin B(12), and Folate Levels on Soluble Transferrin Receptor Concentration in Pregnant Women**](https://pubmed.ncbi.nlm.nih.gov/12867292/)**.**

[VIEW FULL BIO – Camila S. Silva, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/camila-silva)

# Yunan Tang, Ph.D., DABT

### **Toxicologist — Division of Biochemical Toxicology**

Dr. Tang conducts inhalation studies in collaboration with FDA’s Center for Tobacco Products (CTP) to characterize and quantify the health risk associated with selected chemicals found in cigarette smoke. Tobacco smoke contains more than 7,000 chemical compounds, including over 70 that are known to cause cancer. According to the Center for Disease Control and Prevention and CTP, it is currently estimated that 19.3% of adults in the United States smoke cigarettes and that 480,000 people die prematurely each year from tobacco-related diseases in the United States. CTP was formed following the mandates of the 2009 Family Smoking Prevention Tobacco Control Act. This act provides a broad authority to regulate the manufacturing, distribution, and marketing of tobacco products. [VIEW FULL BIO – Dr. Yunan Tang](https://www.fda.gov/about-fda/science-research-nctr/yunan-tang)

**Titles and links to selected publications**

[**90-Day Nose-Only Inhalation Toxicity Study of 4-(methylnitrosamino)-1-(3-pyridyl)-1- butanone (NNK) in Sprague-Dawley Rats**](https://www.sciencedirect.com/science/article/pii/S0278691521008139?via%3Dihub)**.**

[**14-Day Nose-Only Inhalation Toxicity and Haber's Rule Study of NNK in Sprague-Dawley Rats**](https://pubmed.ncbi.nlm.nih.gov/34329464/)**.**

[**Toxicokinetic and Genotoxicity Study of NNK in Male Sprague Dawley Rats Following Nose-Only Inhalation Exposure, Intraperitoneal Injection, and Oral Gavage**](https://pubmed.ncbi.nlm.nih.gov/33944952/)**.**

[**Evaluation of 4-(Methylnitrosamino)-1-(3-Pyridyl)-1-Butanone (NNK) Mutagenicity Using In Vitro and In Vivo Pig-a Assays**](https://pubmed.ncbi.nlm.nih.gov/30595212/)**.**

[**CCR7 Maintains Non-Resolving Lymph Node and Adipose Inflammation in Obesity**](http://www.ncbi.nlm.nih.gov/pubmed/27207557)**.**

[**Atf3 Negatively Regulates Ptgs2/Cox2 Expression During Acute Inflammation**](http://www.ncbi.nlm.nih.gov/pubmed/25619459)**.**

[**Increased Saturated Fatty Acids in Obesity Alter Resolution of Inflammation in Part by Stimulating Prostaglandin Production**](http://www.ncbi.nlm.nih.gov/pubmed/23785121)**.**

[**Proresolution Therapy for the Treatment of Delayed Healing of Diabetic Wounds**](http://www.ncbi.nlm.nih.gov/pubmed/23043160)**.**

[**Chronic Alcohol Exposure Disturbs Lipid Homeostasis at the Adipose Tissue-Liver Axis in Mice: Analysis of Triacylglycerols Using High-Resolution Mass Spectrometry in Combination With In Vivo Metabolite Deuterium Labeling**](http://www.ncbi.nlm.nih.gov/pubmed/23405143)**.**

[**Overexpression of Endothelial Nitric Oxide Synthase Prevents Diet-Induced Obesity and Regulates Adipocyte Phenotype**](http://www.ncbi.nlm.nih.gov/pubmed/22896587)**.**

[**Proresolving Lipid Mediators and Diabetic Wound Healing**](http://www.ncbi.nlm.nih.gov/pubmed/22374140)**.**

[**Chronic Alcohol Exposure Stimulates Adipose Tissue Lipolysis in Mice: Role of Reverse Triglyceride Transport in the Pathogenesis of Alcoholic Steatosis**](http://www.ncbi.nlm.nih.gov/pubmed/22234172)**.**

[**Activation of Peroxisome Proliferator-Activated Receptor-Gamma by Rosiglitazone Improves Lipid Homeostasis at the Adipose Tissue-Liver Axis in Ethanol-Fed Mice**](http://www.ncbi.nlm.nih.gov/pubmed/22173916)**.**

[**Deficiency of the Leukotriene B4 Receptor, BLT-1, Protects Against Systemic Insulin Resistance in Diet-Induced Obesity**](http://www.ncbi.nlm.nih.gov/pubmed/21742977)**.**

[**Resolvin D1 Decreases Adipose Tissue Macrophage Accumulation and Improves Insulin Sensitivity in Obese-Diabetic Mice**](http://www.ncbi.nlm.nih.gov/pubmed/21478260)**.**

[**Zinc Supplementation Partially Prevents Renal Pathological Changes in Diabetic Rats**](http://www.ncbi.nlm.nih.gov/pubmed/19369054)**.**

[**IFN-Beta1a Inhibits the Secretion of Th17-Polarizing Cytokines in Human Dendritic Cells Via TLR7 Up-Regulation**](http://www.ncbi.nlm.nih.gov/pubmed/19265172)**.**

[**Degenerate TCR Recognition and Dual DR2 Restriction of Autoreactive T-Cells: Implications for the Initiation of the Autoimmune Response in Multiple Sclerosis**](http://www.ncbi.nlm.nih.gov/pubmed/18412170)**.**

[**Effect of Folic Acid on Prenatal Alcohol-Induced Modification of Brain Proteome in Mice**](http://www.ncbi.nlm.nih.gov/pubmed/17697403)**.**

[**The Maternal Combined Supplementation of Folic Acid and Vitamin B12 Suppresses Ethanol-Induced Developmental Toxicity in Mouse Fetuses**](http://www.ncbi.nlm.nih.gov/pubmed/16439097)**.**

[VIEW FULL BIO – Yunan Tang, Ph.D., DABT](https://www.fda.gov/about-fda/science-research-nctr/yunan-tang)

# Volodymyr Tryndyak, Ph.D.

### **Research Biologist — Division of Biochemical Toxicology**

Dr. Tryndyak conducts studies with emphasis on developing epigenetic biomarkers that can be used in epidemiological and clinical studies to identify individuals in the population who may be susceptible to specific diseases. His research focuses on the mechanisms applicable for the identification of agents with carcinogenic potential using in vivo and in vitro models to facilitate the assessment of risk to human health. Using high-throughput approaches, Dr. Tryndyak has investigated genetic and epigenetic alterations after carcinogen exposure to understand mechanisms of cancer development and to identify biomarkers, especially non-invasive biomarkers, of cancer progression. Considering the genetic and epigenetic diversity in the human population, individualized and targeted approaches are key aspects of his research. Using a multiparental Collaborative Cross mouse population model, Dr. Tryndyak investigated interindividual- and sex-specific variations in the development of nonalcoholic fatty liver disease (NAFLD) to better understand the molecular mechanisms and drivers of the disease development and molecular determinants of interindividual susceptibility to NAFLD. Progression of NAFLD may lead to liver cancer development and early identification of these factors may help to prevent liver cancer.

The biopersistence of environmental toxicants in humans and animals, such as short-chain perfluorinated alkyl substances (PFAS), is of great concern for the FDA. Dr. Tryndyak, in collaboration with NCTR and Center for Food Safety and Applied Nutrition researchers, is investigating the role of renal organic anion transporters in toxicokinetics of C6-fluorotelomer alcohol, a major impurity in PFAS, and its metabolites. The results of these studies will be used to construct a biologically based dose-response model for C6-fluorotelomer alcohol and its metabolites in humans and rodents.

Coronavirus disease 2019 (COVID-19) is a worldwide pandemic respiratory disease associated with high transmission rates and mortality. COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The shedding of detectable viral RNA in the feces of infected individuals enables its detection in community wastewater. Dr. Tryndyak is conducting next-generation sequencing analysis of RNA extracted from wastewater collected in selected metropolitan areas of Arkansas to detect presence of SARS-CoV-2 virus, determine SARS-CoV-2 viral load, and identify any coronavirus variants of the local community. This will be a valuable public health tool worldwide as it allows the monitoring of the disease on a populational scale. [VIEW FULL BIO – Dr. Volodymyr Tryndyak](https://www.fda.gov/about-fda/science-research-nctr/volodymyr-tryndyak)

**Titles and links to selected publications**

[**Epigenetic Effects of Low-level Sodium Arsenite Exposure on Human Liver HepaRG Cells**](https://pubmed.ncbi.nlm.nih.gov/32844245/)**.**

[**Characterization of the Variability in the Extent of Nonalcoholic Fatty Liver Induced by a High-Fat Diet in the Genetically Diverse Collaborative Cross Mouse Model**](https://pubmed.ncbi.nlm.nih.gov/32304142/)**.**

[**Gene Expression and Cytosine DNA Methylation Alterations in Induced Pluripotent Stem-Cell-Derived Human Hepatocytes Treated with Low Doses of Chemical Carcinogens**](https://pubmed.ncbi.nlm.nih.gov/31555880/)**.**

[**Gene Expression and DNA Methylation Alterations During Non-alcoholic Steatohepatitis-Associated Liver Carcinogenesis**](https://pubmed.ncbi.nlm.nih.gov/31191608/)**.**

[**Effect of Aflatoxin B1, Benzo[a]pyrene, and Methapyrilene on Transcriptomic and Epigenetic Alterations in Human Liver HepaRG Cells**](https://pubmed.ncbi.nlm.nih.gov/30157460/)**.**

[**Identification of Chromatin-Accessible Domains in Non-Alcoholic Steatohepatitis-Derived Hepatocellular Carcinoma**](https://pubmed.ncbi.nlm.nih.gov/29603380/)**.**

[**Cellular and Molecular Effects of Prolonged Low-Level Sodium Arsenite Exposure on Human Hepatic HepaRG Cells**](https://pubmed.ncbi.nlm.nih.gov/29301061/)**.**

[**Furan-Induced Transcriptomic and Gene-Specific DNA Methylation Changes in the Livers of Fischer 344 Rats in a 2-year Carcinogenicity Study**](https://pubmed.ncbi.nlm.nih.gov/27387713/)**.**

[**MicroRNA Changes, Activation of Progenitor Cells and Severity of Liver Injury in Mice Induced by Choline and Folate Deficiency**](https://pubmed.ncbi.nlm.nih.gov/26878785/)**.**

[**Genotoxic, Epigenetic, and Transcriptomic Effects of Tamoxifen in Mouse Liver**](https://pubmed.ncbi.nlm.nih.gov/25123088/)**.**

[**Interstrain Differences in the Severity of Liver Injury Induced by a Choline- and Folate-Deficient Diet in Mice are Associated with Dysregulation of Genes Involved in Lipid Metabolism**](https://pubmed.ncbi.nlm.nih.gov/22872676/)**.**

[**Plasma MicroRNAs are Sensitive Indicators of Inter-Strain Differences in the Severity of Liver Injury Induced in Mice by a Choline- and Folate-Deficient Diet**](https://pubmed.ncbi.nlm.nih.gov/22561871/)**.**

[**Coupling Global Methylation and Gene Expression Profiles Reveal Key Pathophysiological Events in Liver Injury Induced by a Methyl-Deficient Diet**](https://pubmed.ncbi.nlm.nih.gov/20938992/)**.**

[**The Role of Epigenetic Events in Genotoxic Hepatocarcinogenesis Induced by 2-Acetylaminofluorene**](https://pubmed.ncbi.nlm.nih.gov/20188851/)**.**

[**E-cadherin Transcriptional Down-Regulation by Epigenetic and microRNA-200 Family Alterations is Related to Mesenchymal and Drug-Resistant Phenotypes in Human Breast Cancer Cells**](https://pubmed.ncbi.nlm.nih.gov/19839049/)**.**

[**Down-Regulation of the microRNAs miR-34a, miR-127, and miR-200b in Rat Liver During Hepatocarcinogenesis Induced by a Methyl-Deficient Diet**](https://pubmed.ncbi.nlm.nih.gov/18942116/)**.**

[**Hepatic Epigenetic Phenotype Predetermines Individual Susceptibility to Hepatic Steatosis in Mice Fed a Lipogenic Methyl-Deficient Diet**](https://pubmed.ncbi.nlm.nih.gov/19450891/)**.**

[**Epigenetic Reprogramming of Liver Cells in Tamoxifen-Induced Rat Hepatocarcinogenesis**](https://pubmed.ncbi.nlm.nih.gov/17219426/)**.**

[**Effect of Long-Term Tamoxifen Exposure on Genotoxic and Epigenetic Changes in Rat Liver: Implications for Tamoxifen-Induced Hepatocarcinogenesis**](https://pubmed.ncbi.nlm.nih.gov/16632870/)**.**

[**Histone H3 Lysine 9 and H4 Lysine 20 Trimethylation and the Expression of Suv4-20h2 and Suv-39h1 Histone Methyltransferases in Hepatocarcinogenesis Induced by Methyl Deficiency in Rats**](https://pubmed.ncbi.nlm.nih.gov/16497704/)**.**

[**Identification of Differentially Methylated Sites Within Unmethylated DNA Domains in Normal and Cancer Cells**](https://pubmed.ncbi.nlm.nih.gov/16824473/)**.**

[VIEW FULL BIO – Volodymyr Tryndyak, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/volodymyr-tryndyak)

# Qiangen Wu, Ph.D.

### **Visiting Scientist/Staff Fellow — Division of Biochemical Toxicology**

Dr. Wu’s research mainly focuses on the metabolic activity pathways leading to the toxicity and tumorgenicity of FDA-regulated products—especially tobacco products. He investigates the metabolism of toxic chemicals that lead to cytotoxicity, genotoxicity, and carcinogenicity. Using tandem mass spectrometry and high-resolution mass spectrometry, Dr. Wu investigates the formation of the exogenous and endogenous DNA adducts and elucidates the mechanism of tumorgenicity mediated by free radical or nucleophilic metabolites after exposure to carcinogens. Currently, Dr. Wu is working on the effects of vehicles on the pharmacokinetics profile of nicotine in rats following nose-only inhalation exposure.

Using mass spectrometry, Dr. Wu is also evaluating the pharmacokinetics of cannabidiol and its major metabolites in rats upon dermal exposure and in pregnant rats and their pups after oral cannabidiol administration. [VIEW FULL BIO – Dr. Qiangen Wu](https://www.fda.gov/about-fda/science-research-nctr/qiangen-wu)

**Titles and links to selected publications**

[**Toxicity of Ortho-phthalaldehyde Aerosols in a Human In Vitro Airway Tissue Model**](https://pubmed.ncbi.nlm.nih.gov/33556243/)**.**

[**In Vitro Dosimetry Analyses for Acrolein Exposure in Normal Human Lung Epithelial Cells and Human Lung Cancer Cells**](https://pubmed.ncbi.nlm.nih.gov/33385576/)**.**

[**Performance of High-Throughput CometChip Assay Using Primary Human Hepatocytes: A Comparison of DNA Damage Responses with In Vitro Human Hepatoma Cell Lines and In Vivo Rodent Liver Tissues**](https://pubmed.ncbi.nlm.nih.gov/32318794/)**.**

[**The Role of Hepatic Cytochrome P450s in the Cytotoxicity of Sertraline**](https://pubmed.ncbi.nlm.nih.gov/32372212/)**.**

[**Apoptosis Contributes to the Cytotoxicity Induced by Amodiaquine and its Major Metabolite N-Desethylamodiaquine in Hepatic Cells**](https://pubmed.ncbi.nlm.nih.gov/31629065/)**.**

[**Effects of Cellular Differentiation in Human Primary Bronchial Epithelial Cells: Metabolism of 4-(methylnitrosamine)-1-(3-pyridyl)-1-butanone**](https://pubmed.ncbi.nlm.nih.gov/30552994/)**.**

[**Primary and Secondary Pyrrolic Metabolites of Pyrrolizidine Alkaloids Form DNA Adducts in Human A549 Cells**](https://pubmed.ncbi.nlm.nih.gov/30366057/)**.**

[**Quantitative Comparison of In Vitro Genotoxicity Between Metabolically Competent HepaRG Cells and HepG2 Cells Using the High-Throughput High-Content CometChip Assay**](https://pubmed.ncbi.nlm.nih.gov/30788552/)**.**

[**Evaluating Mode of Action of Acrolein Toxicity in an in vitro Human Airway Tissue Model**](https://pubmed.ncbi.nlm.nih.gov/30204913/)**.**

[**The Role of Hepatic Cytochrome P450s in the Cytotoxicity of Dronedarone**](https://pubmed.ncbi.nlm.nih.gov/29616291/)**.**

[**Toxaphene-Induced Mouse Liver Tumorigenesis is Mediated by the Constitutive Androstane Receptor**](https://pubmed.ncbi.nlm.nih.gov/28218408/)**.**

[**The Role of CYP 3A4 and 1A1 in Amiodarone-Induced Hepatocellular Toxicity**](https://pubmed.ncbi.nlm.nih.gov/27113703/)**.**

[**Perfluorooctanoic Acid Exposure Triggers Oxidative Stress in the Mouse Pancreas**](https://pubmed.ncbi.nlm.nih.gov/28962265/)**.**

[**Differential Gene Expression in Human Hepatocyte Cell Lines Exposed to the Antiretroviral Agent Zidovudine**](https://pubmed.ncbi.nlm.nih.gov/24292225/)**.**

[**Role of DNA Repair Pathways in Response to Zidovudine-Induced DNA Damage in Immortalized Human Liver THLE2 Cells**](https://pubmed.ncbi.nlm.nih.gov/23675285/)**.**

[**Cytotoxicity and Inhibitory Effects of Low-Concentration Triclosan on Adipogenic Differentiation of Human Mesenchymal Stem Cells**](https://pubmed.ncbi.nlm.nih.gov/22726953/)**.**

[**XPC is Essential for Nucleotide Excision Repair of Zidovudine-Induced DNA Damage in Human Hepatoma Cells**](https://pubmed.ncbi.nlm.nih.gov/21192964/)**.**

[VIEW FULL BIO – Qiangen Wu, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/qiangen-wu)

# Jinghai Yi, Ph.D.

### **Staff Fellow — Division of Biochemical Toxicology**

Dr. Yi’s research interests include 1) inhalation toxicology, 2) aerosol generation and characterization, and 3) design, fabrication, setup, validation, and operation of whole-body and nose-only inhalation exposure systems. He conducts inhalation studies in collaboration with CTP to characterize and quantify the health risk associated with selected chemicals found in tobacco products.

Dr. Yi’s awards and research projects are listed below.

* Lila Albin Paper Award for 2017 (co-author)
* Principle Investigator (PI), “Support and Infrastructure for Center for Tobacco Products/NCTR Inhalation Facility,” FDA Center for Tobacco Products, 10/2017- 09/30/2023
* PI, “A 5-Day Nose-Only Nicotine Inhalation Toxicity Pilot Study in Sprague-Dawley Rats,” FDA Center for Tobacco Products, 11/2021-2022
* PI, “Pharmacokinetic Analysis of Nicotine in Sprague-Dawley Rats,” FDA Center for Tobacco Products, 11/2017-ongoing
* Consultant of a NIH SBIR grant, “Aerosol Delivery of Surfactant for ARDS,” Grant Number: 1R43HL127834-01, 09/2015-05/2016 (PI: Yeates)
* PI of a NIOSH contract, “Inhalation Facility of Desktop 3D Printer Emissions,” Contract Number: 212-2015-M-63382, 08/2015-08/2016
* Co-investigator of a NIOSH contract, “Cardiovascular Effect of Desktop 3D Printer Emissions,” 08/2015-08/2016
* PI of a NIH SBIR grant, “Ultra-High Dose Rate Aerosol Drug Delivery,” Grant Number: R43HL078281-01, 12/2004-12/2005
* Co-investigator of a NIH SBIR grant, “Concentrated Aerosol Delivery and Quantization System,” 09/2001-07/2004. (PI: Yeates).
* Co-investigator of a NIH SBIR grant, “Water and Ion Measurement System,” Grant Number: 5R44HL067008, (PI: Wong)
* Co-investigator of a NIH SBIR grant, Grant Number: 2R44RR015150-02A1 (PI: Mao)

[VIEW FULL BIO – Dr. Jinghai Yi](https://www.fda.gov/about-fda/science-research-nctr/jinghai-yi)

**Titles and links to selected publications**

[**Particle and Organic Vapor Emissions from Children’s 3-D Pen and 3-D Printer Toys**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6995422/)**.**

[**Fluidic and Thermal Properties of Heliox Enable the Efficient Generation and Delivery of High Concentrations of Solid-Phase Fine Particle Aerosols from Viscous Liquids**](https://www.tandfonline.com/doi/full/10.1080/02786826.2019.1584388)**.**

[**Estrous Cycle-Dependent Modulation of In Vivo Microvascular Dysfunction After Nanomaterial Inhalation**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Estrous+Cycle-Dependent+Modulation+of+In+Vivo+Microvascular+Dysfunction+After+Nanomaterial+Inhalation.)**.**

[**Maternal Engineered Nanomaterial Inhalation During Gestation Alters the Fetal Transcriptome**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Maternal+Engineered+Nanomaterial+Inhalation+During+Gestation+Alters+the+Fetal+Transcriptome.)**.**

[**Reactive Oxygen Species Damage Drives Cardiac and Mitochondrial Dysfunction Following Acute Nano-Titanium Dioxide Inhalation Exposure**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Reactive+Oxygen+Species+Damage+Drives+Cardiac+and+Mitochondrial+Dysfunction+Following+Acute+Nano-Titanium+Dioxide+Inhalation+Exposure.)**.**

[**Maternal Engineered Nanomaterial Exposure in Growing Progeny**](https://www.physiology.org/doi/full/10.1152/ajpheart.00634.2016)**.**

[**Heterogeneous Vascular Bed Responses to Pulmonary Titanium Dioxide Nanoparticle Exposure**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Heterogeneous+Vascular+Bed+Responses+to+Pulmonary+Titanium+Dioxide+Nanoparticle+Exposure.)**.**

[**Characterization of Chemical Contaminants Generated by a Desktop Fused Deposition Modeling 3-Dimensional Printer**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Characterization+of+Chemical+Contaminants+Generated+by+a+Desktop+Fused+Deposition+Modeling+3-Dimensional+Printer.)**.**

[**Maternal Engineered Nanomaterial Exposure Disrupts Progeny Cardiac Function and Bioenergetics**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Maternal+Engineered+Nanomaterial+Exposure+Disrupts+Progeny+Cardiac+Function+and+Bioenergetics.)**.**

[**Emission of Particulate Matter from a Desktop Three-Dimensional (3D) Printer**](https://www.ncbi.nlm.nih.gov/pubmed/27196745)**.**

[**Impacts of Prenatal Nanomaterial Exposure on Male Adult Sprague-Dawley Rat Behavior and Cognition**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Adult+Behavioral+Consequences+of+Prenatal+Engineered+Nanomaterial+Exposure+in+Rodents.)**.**

[**Comparative Plasma Proteomic Studies of Pulmonary TiO2 Nanoparticle Exposure in Rats Using Liquid Chromatography Tandem Mass Spectrometry**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Comparative+Plasma+Proteomic+Studies+of+Pulmonary+TiO2+Nanoparticle+Exposure+in+Rats+Using+Liquid+Chromatography+Tandem+Mass+Spectrometry.)**.**

[**Uterine Microvascular Sensitivity to Nanomaterial Inhalation: An In VivoAssessment**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Uterine+Microvascular+Sensitivity+to+Nanomaterial+Inhalation%3A+an+In+Vivo+Assessment.)**.**

[**Microvascular and Mitochondrial Dysfunction in the Female F1 Generation After Gestational TiO2 Nanoparticle Exposure**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Microvascular+and+Mitochondrial+Dysfunction+in+the+Female+F1+Generation+After+Gestational+TiO2+Nanoparticle+Exposure.)**.**

[**A New Ion Mobility – Linear Ion Trap Instrument for Complex Mixture Analysis**](https://www.ncbi.nlm.nih.gov/pubmed/?term=A+New+Ion+Mobility+%E2%80%93+Linear+Ion+Trap+Instrument+for+Complex+Mixture+Analysis.)**.**

[**Whole-Body Nanoparticle Aerosol Inhalation Exposures**](https://www.ncbi.nlm.nih.gov/pubmed/23685643)**.**

[**Does the Barker Hypothesis Apply to Maternal Engineered Nanomaterial Exposure and Fetal Microvascular Function**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Does+the+Barker+Hypothesis+Apply+to+Maternal+Engineered+Nanomaterial+Exposure+and+Fetal+Microvascular+Function%3F)**?**

[**Nanoparticle Inhalation Alters Arteriolar Vasoreactivity through Sympathetic and Cyclooxygenase-Mediated Pathways**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Nanoparticle+Inhalation+Alters+Arteriolar+Vasoreactivity+through+Sympathetic+and+Cyclooxygenase-Mediated+Pathways.)**.**

[**Dispersion of a Particle-laden Air Jet in a Confined Rectangular Crossflow**](https://www.sciencedirect.com/science/article/pii/S0032591001005034)**.**

[VIEW FULL BIO – Jinghai Yi, Ph.D.](https://pubmed.ncbi.nlm.nih.gov/30349745/)

## Division of Bioinformatics and Biostatistics, NCTR

# Weida Tong, Ph.D.

### **Director — Division of Bioinformatics and Biostatistics**

Dr. Weida Tong is Director of the Division of Bioinformatics and Biostatistics at FDA’s National Center for Toxicological Research (NCTR). He has been an FDA Senior Biomedical Research and Biomedical Product Assessment Service expert since 2011, an Arkansas Research Alliance fellow since 2016, and a member of the Arkansas Academy of Computing since 2021. He has served on science advisory boards for several multi-institutional projects in Europe and the U.S. and also holds adjunct appointments at several universities. His primary research interests are in the fields of bioinformatics, artificial intelligence (AI), molecular modeling and data analytics for biomarker discovery, drug safety and repurposing, pharmacogenomics/toxicogenomics, and precision medicine. Currently, he directs several FDA mission-critical projects in his division:

* Supervising the FDA-led community-wide MicroArray and SEquencing Quality Control (MAQC/SEQC) consortium to analyze technical performance and practical utility of emerging genomics technologies with an emphasis on regulatory application and precision medicine.
* Developing the Liver Toxicity Knowledge Base to address drug safety concerns related to drug-induced liver injury (DILI).
* Designing and developing computer-based technology to support FDA’s effort on bioinformatics and scientific computing (e.g., development of the FDA genomic tool, ArrayTrack, to support pharmacogenomics data review in FDA).
* Developing machine learning and AI for digital health and drug repositioning.
* Conducting molecular modeling and quantitative structure activity relationship models on various toxicological endpoints such as endocrine disruption and carcinogenicity.

Dr. Tong has published over 300 peer-reviewed papers and book chapters. [VIEW FULL BIO – Dr. Weida Tong](https://www.fda.gov/about-fda/science-research-nctr/weida-tong)

**Titles and links to selected publications**

[**Unraveling Gene Fusions for Drug Repositioning in High-Risk Neuroblastoma**](https://pubmed.ncbi.nlm.nih.gov/33967751/)**.**

[**Trade-off Predictivity and Explainability for Machine-Learning Powered Predictive Toxicology: An In-Depth Investigation with Tox21 Data Sets**](https://pubs.acs.org/doi/10.1021/acs.chemrestox.0c00373)**.**

[**Introduction to Special Issue: Computational Toxicology**](https://pubmed.ncbi.nlm.nih.gov/33583184/)**.**

[**Impact of Sequencing Depth and Library Preparation on Toxicological Interpretation of RNA-Seq Data in a “Three-Sample” Scenario**](https://pubmed.ncbi.nlm.nih.gov/33354967/)**.**

[**DeepDILI: Deep Learning-Powered Drug-Induced Liver Injury Prediction Using Model-Level Representation**](https://pubmed.ncbi.nlm.nih.gov/33356151/)**.**

[**FDALabel for Drug Repurposing Studies and Beyond**](https://pubmed.ncbi.nlm.nih.gov/33235392/)**.**

[**Advancing Genomics for Rare Disease Diagnosis and Therapy Development**](https://pubmed.ncbi.nlm.nih.gov/33101045/)**.**

[**Regulatory Landscape of Dietary Supplements and Herbal Medicines from a Global Perspective**](https://pubmed.ncbi.nlm.nih.gov/32305367/)**.**

[**Landscape of circRNAs Across 11 Organs and 4 Ages in Fischer 344 Rats**](https://pubmed.ncbi.nlm.nih.gov/32692164/)**.**

[**A Comprehensive Rat Transcriptome Built from Large Scale RNA-seq-Based Annotation**](https://academic.oup.com/nar/article/48/15/8320/5880465)**.**

[**Can Transcriptomic Profiles from Cancer Cell Lines be Used for Toxicity Assessment**](https://pubs.acs.org/doi/10.1021/acs.chemrestox.9b00288#:~:text=Moreover%2C%20if%20PRank%20analysis%20was,assessment%2C%20particularly%20in%20predicting%20DILI.)**?**

[**The Landscape of Hepatobiliary Adverse Reactions Across 53 Herbal and Dietary Supplements Reveals Immune-Mediated Injury as a Common Cause of Hepatitis**](https://pubmed.ncbi.nlm.nih.gov/31720699/)**.**

[**Drug-Induced Liver Injury Severity and Toxicity (DILIst): Binary Classification of 1278 Drugs by Human Hepatotoxicity**](https://pubmed.ncbi.nlm.nih.gov/31669330/)**.**

[VIEW FULL BIO – Weida Tong, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/weida-tong)

# Minjun Chen, Ph.D.

### **Staff Fellow — Division of Bioinformatics and Biostatistics**

Dr. Chen's primary research interests encompass bioinformatics, drug safety, biomarker discovery, and toxicogenomics. His current research focus is in two areas:

* Development of the Liver Toxicity Knowledge Base to address the concerns from public health and regulatory agencies related to liver toxicity caused by drugs and herbal dietary supplements.
* Identification of biomarkers for predicting the outcome of chemotherapy of breast-cancer patients in support of precision medicine.

[VIEW FULL BIO – Dr. Minjun Chen](https://www.fda.gov/about-fda/science-research-nctr/minjun-chen)

**Titles and links to selected publications**

[**Whole Exome Sequencing Reveals Genetic Variants in HLA Class II Genes Associated with Transplant-free Survival of Indeterminate Acute Liver Failure**](https://pubmed.ncbi.nlm.nih.gov/35905417/)**.**

[**BERT-Based Natural Language Processing of Drug Labeling Documents: A Case Study for Classifying Drug-Induced Liver Injury Risk**](https://pubmed.ncbi.nlm.nih.gov/34939028/)**.**

[**Elevated Bilirubin, Alkaline Phosphatase at Onset, and Drug Metabolism are Associated with Prolonged Recovery from DILI**](https://pubmed.ncbi.nlm.nih.gov/33845060/)**.**

[**The Landscape of Hepatobiliary Adverse Reactions Across 53 Herbal and Dietary Supplements Reveals Immune-Mediated Injury as a Common Cause of Hepatitis**](https://pubmed.ncbi.nlm.nih.gov/31720699/)**.**

[**Cancer Genomics Predicts Disease Relapse and Therapeutic Response to Neoadjuvant Chemotherapy of Hormone Sensitive Breast Cancers**](https://pubmed.ncbi.nlm.nih.gov/32424219/)**.**

[**The Development of a Database for Herbal and Dietary Supplement Induced Liver Toxicity**](https://pubmed.ncbi.nlm.nih.gov/30274144/)**.**

[**Drug-Induced Liver Toxicity**](https://link.springer.com/book/10.1007%2F978-1-4939-7677-5)**.**

[**Therapeutic Bile Acids and the Risks for Hepatotoxicity**](https://doi.org/10.1111/apt.14678)**.**

[**Direct-Acting Antivirals for Chronic Hepatitis C: Can Drug Properties Signal Potential for Liver Injury**](https://www.ncbi.nlm.nih.gov/pubmed/28327365)**?**

[**A Model to Predict Severity of Drug-Induced Liver Injury in Humans**](https://www.ncbi.nlm.nih.gov/pubmed/27302180)**.**

[**Drug-Induced Liver Injury: Interactions Between Drug Properties and Host Factors**](https://www.ncbi.nlm.nih.gov/pubmed/25912521)**.**

[**A Testing Strategy to Predict Risk for Drug-Induced Liver Injury in Humans Using High-Content Screen Assays and the 'Rule-of-Two' Model**](http://www.ncbi.nlm.nih.gov/pubmed/24958025)**.**

[**Quantitative Structure-Activity Relationship Models for Predicting Drug-Induced Liver Injury Based on FDA-Approved Drug Labeling Annotation and Using a Large Collection of Drugs**](http://www.ncbi.nlm.nih.gov/pubmed/23997115)**.**

[**High Lipophilicity and High Daily Dose of Oral Medications Are Associated with Significant Risk for Drug-Induced Liver Injury**](http://www.ncbi.nlm.nih.gov/pubmed/23258593)**.**

[**The Liver Toxicity Knowledge Base: A Systems Approach to a Complex End Point**](http://www.ncbi.nlm.nih.gov/pubmed/23486446)**.**

[**A Decade of Toxicogenomic Research and Its Contribution to Toxicological Science**](http://www.ncbi.nlm.nih.gov/pubmed/22790972)**.**

[**FDA-Approved Drug Labeling for the Study of Drug-Induced Liver Injury**](http://www.ncbi.nlm.nih.gov/pubmed/21624500)**.**

[VIEW FULL BIO – Minjun Chen, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/minjun-chen)

# Xi Chen, Ph.D.

### **Staff Fellow — Division of Bioinformatics and Biostatistics**

Dr. Chen is an accomplished researcher with over a decade of experience in bioinformatics, molecular biology, and developmental biology. With her cross-disciplinary training, she possesses in-depth knowledge of bioinformatics and biostatistics tools, databases, medicine, and biology. Her research interests focus on developing statistical and computational methods to integrate multi-omics data, identify functional variants, and discover biomarkers, with the aim of interpreting medical big data and obtaining a novel and insightful understanding of their biological and clinical significance at the molecular level. She is also interested in using data mining methods and systems-biology strategies for both basic biological research and translational medicine investigations.

Recently, Dr. Chen has been exploring the use of artificial intelligence (AI) as an alternative method to animal studies. She is developing generative AI frameworks to advance safety assessment in the field of pharmacovigilance and toxicology without using animal testing. With the wealth of animal data available, generative AI offers a promising approach to simulating virtual animal experiments, generating multi-dimensional profiles similar to traditional animal studies, and approximating populations of diverse individual animals. This can help to improve the accuracy of toxicity prediction, enhance the translation of animal data to human outcomes, as well as reduce the need for animal testing in drug development. Dr. Chen's expertise and research interests are aimed at advancing the use of big data and artificial intelligence in biomedical research, with the ultimate goal of improving human health. [VIEW FULL BIO – Dr. Xi Chen](https://www.fda.gov/about-fda/science-research-nctr/xi-chen)

**Titles and links to selected publications**

[**Tox-GAN: An Artificial Intelligence Approach Alternative to Animal Studies—A Case Study with Toxicogenomics**](https://pubmed.ncbi.nlm.nih.gov/34971401/)**.**

[**AI-Powered Drug Repurposing for Developing COVID-19 Treatments**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8865759/)**.**

[**Unraveling Gene Fusions for Drug Repositioning in High-Risk Neuroblastoma**](https://pubmed.ncbi.nlm.nih.gov/33967751/)**.**

[**DICE: A Drug Indication Classification and Encyclopedia for AI-Based Indication Extraction**](https://pubmed.ncbi.nlm.nih.gov/34409286/)**.**

[**AI-Based Language Models Powering Drug Discovery and Development**](https://pubmed.ncbi.nlm.nih.gov/34216835/)**.**

[VIEW FULL BIO – Xi Chen, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/xi-chen)

# Binsheng Gong, Ph.D.

### **Visiting Scientist — Division of Bioinformatics and Biostatistics**

Dr. Gong has more than 15 years of distinguished research and education experiences and a record of exceptional scientific accomplishments in the field of bioinformatics, with emphasis on investigating the next-generation sequencing (NGS) and microarray technologies and biological/medical “big data” mining and data interpretation. The biological/medical “big data” incorporates personal genomic/transcriptomic data, clinical data, and many other data generated from high-throughput technologies. Data mining and interpretation develops and performs methods, software, workflows to manage and analyze the “big data” and interpret the biological/clinical meanings by integrating data and knowledge bases. This research supports basic biological study and translational medicine as well as drug development and drug-safety investigation. His current research interests include:

* Examining the emerging technologies, particularly on NGS, to understand the impact of technical issues and bioinformatics methods
* Evaluating the utility of these emerging technologies and methods in clinical and safety assessments with quality-control matrix and procedures
* Biomarker identification for DILI and predictive toxicity, using data-mining methodology and systems-biology strategies
* Developing standard operating procedures for NGS applications, such as ultralow-frequency mutations detection by duplex sequencing, biomarker identification by RNA sequencing, and small RNA sequencing
* Genome-wide identification and characterization of circular RNAs and novel microRNAs for human, monkey, mouse, and rat

[VIEW FULL BIO – Dr. Binsheng Gong](https://www.fda.gov/about-fda/science-research-nctr/binsheng-gong)

**Titles and links to selected publications**

[**The Concordance Between RNA-Seq and Microarray Data Depends on Chemical Treatment and Transcript Abundance**](https://www.ncbi.nlm.nih.gov/pubmed/25150839)**.**

[**A Comprehensive Assessment of RNA-Seq Accuracy, Reproducibility and Information Content by the Sequencing Quality Control Consortium**](https://www.ncbi.nlm.nih.gov/pubmed/25150838)**.**

[**An Investigation of Biomarkers Derived from Legacy Microarray Data for Their Utility in the RNA-Seq Era**](https://www.ncbi.nlm.nih.gov/pubmed/25633159)**.**

[**Mechanistic Roles of MicroRNAs in Hepatocarcinogenesis: A Study of Thioacetamide with Multiple Doses and Time-Points of Rats**](https://www.ncbi.nlm.nih.gov/pubmed/28596526)**.**

[**The FDA's Experience with Emerging Genomics Technologies-Past, Present, and Future**](https://www.ncbi.nlm.nih.gov/pubmed/27116022)**.**

[**Comprehensive Assessments of RNA-Seq by the SEQC Consortium: FDA-Led Efforts Advance Precision Medicine**](https://www.ncbi.nlm.nih.gov/pubmed/26999190)**.**

[**Discovering Functional Modules by Topic Modeling RNA-Seq Based Toxicogenomic Data**](https://www.ncbi.nlm.nih.gov/pubmed/25083553)**.**

[VIEW FULL BIO – Binsheng Gong, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/binsheng-gong)

# Wenjing Guo, Ph.D.

### **Visiting Scientist — Division of Bioinformatics and Biostatistics**

Dr. Guo’s primary research interest is to apply machine learning and artificial intelligence in various areas including nanomaterials, food and drug safety, and predictive toxicology. Her research includes: 1) designing machine learning algorithms to increase the efficiency of identifying persistent organic pollutant contamination in food and 2) developing deep learning models to enhance the prediction performance of gas adsorption capacities in nanomaterials. Dr. Guo is also interested in using big data analytics to evaluate the safety of drugs. She is working on a project using big data analytics to quantitatively measure the safety concerns for the drugs that have been used to treat COVID-19 patients. [VIEW FULL BIO – Dr. Wenjing Guo](https://www.fda.gov/about-fda/science-research-nctr/wenjing-guo)

**Titles and links to selected publications**

[**Informing Selection of Drugs for COVID-19 Treatment Through Adverse Events Analysis**](https://pubmed.ncbi.nlm.nih.gov/34234253/)**.**

[**Software-Assisted Pattern Recognition of Persistent Organic Pollutants in Contaminated Human and Animal Food**](https://pubmed.ncbi.nlm.nih.gov/33525602/)**.**

[**Nanomaterial Databases: Data Sources for Promoting Design and Risk Assessment of Nanomaterials**](https://pubmed.ncbi.nlm.nih.gov/34207026/)**.**

[**Elucidating Interactions Between SARS-CoV-2 Trimeric Spike Protein and ACE2 Using Homology Modeling and Molecular Dynamics Simulations**](https://pubmed.ncbi.nlm.nih.gov/33469527/)**.**

[**Identification of Epidemiological Traits by Analysis of SARS-CoV-2 Sequences**](https://pubmed.ncbi.nlm.nih.gov/33925388/)**.**

[**Development of a Nicotinic Acetylcholine Receptor nAChR α7 Binding Activity Prediction Model**](https://pubmed.ncbi.nlm.nih.gov/32159345/)**.**

[**Persistent Organic Pollutants in Food: Contamination Sources, Health Effects and Detection Methods**](https://pubmed.ncbi.nlm.nih.gov/31717330/)**.**

[**QUICK: Quality and Usability Investigation and Control Kit for Mass Spectrometric Data from Detection of Persistent Organic Pollutants**](https://pubmed.ncbi.nlm.nih.gov/31671576/)**.**

[**Similarities and Differences Between Variants Called with Human Reference Genome HG19 or HG38**](https://pubmed.ncbi.nlm.nih.gov/30871461/)**.**

[**Computational Prediction Models for Assessing Endocrine Disrupting Potential of Chemicals**](https://pubmed.ncbi.nlm.nih.gov/30633647/)**.**

[**Structural Changes Due to Antagonist Binding in Ligand Binding Pocket of Androgen Receptor Elucidated Through Molecular Dynamics Simulations**](https://pubmed.ncbi.nlm.nih.gov/29867496/)**.**

[VIEW FULL BIO – Wenjing Guo, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/wenjing-guo)

# Stephen Harris

### **Computer Scientist — Division of Bioinformatics and Biostatistics**

Mr. Harris’s primary interests are large-scale application architecture, system security, and knowledge representation in database systems. He also has interest in machine-learning algorithms, and feature selection in trained models resulting from machine-learning algorithms. [VIEW FULL BIO – Stephen Harris](https://www.fda.gov/about-fda/science-research-nctr/stephen-harris)

**Titles and links to selected publications**

[**FDA Drug Labeling: Rich Resources to Facilitate Precision Medicine, Drug Safety, and Regulatory Science**](https://www.ncbi.nlm.nih.gov/pubmed/27319291)**.**

[**Superconvergence of Weak Galerkin Finite Element Approximation for Second Order Elliptic Problems by L2-Projection Methods**](https://doi.org/10.1016/j.amc.2013.11.065)**.**

[**EADB: An Estrogenic Activity Database for Assessing Potential Endocrine Activity**](https://www.ncbi.nlm.nih.gov/pubmed/23897986)**.**

[**A Unifying Ontology to Integrate Histological and Clinical Observations for Drug-Induced Liver Injury**](https://www.ncbi.nlm.nih.gov/pubmed/23395088)**.**

[**SNPTrackTM – An Integrated Bioinformatics System for Genetic Association Studies**](https://www.ncbi.nlm.nih.gov/pubmed/23245293)**.**

[**atBioNet – An Integrated Network Analysis Tool for Genomics and Biomarker Discovery**](https://bmcgenomics.biomedcentral.com/articles/10.1186/1471-2164-13-325)**.**

[**An FDA Bioinformatics Tool for Microbial Genomics Research on Molecular Characterization of Bacterial Foodborne Pathogens Using Microarrays**](https://www.ncbi.nlm.nih.gov/pubmed/20946615)**.**

[**ISA Software Suite: Supporting Standards-Compliant Experimental Annotation and Enabling Curation at the Community Level**](https://www.ncbi.nlm.nih.gov/pubmed/20679334)**.**

[**The EDKB: an Established Knowledge Base for Endocrine Disrupting Chemicals**](https://www.ncbi.nlm.nih.gov/pubmed/20946616)**.**

[**The MAQC-II Project: A Comprehensive Study of Common Practices for the Development and Validation of Microarray-Based Predictive Models**](https://www.ncbi.nlm.nih.gov/pubmed/20676074)**.**

[**ArrayTrack – An FDA and Public Genomic Tool**](https://link.springer.com/content/pdf/10.1007%2F978-1-60761-175-2.pdf)**.**

[**Investigation of Reproducibility of Differentially Expressed Genes in DNA Microarrays through Statistical Simulation**](https://www.ncbi.nlm.nih.gov/pubmed/19278560)**.**

[**The Balance of Reproducibility, Sensitivity, and Specificity of Lists of Differentially Expressed Genes in Microarray Studies**](https://www.ncbi.nlm.nih.gov/pubmed/18793455)**.**

[**An Integrated Bioinformatics Infrastructure Essential for Advancing Pharmacogenomics and Personalized Medicine in the Context of the FDA's Critical Path Initiative**](https://www.ncbi.nlm.nih.gov/m/pubmed/24980713/)**.**

[**The MicroArray Quality Control (MAQC) Project Shows Inter- and Intraplatform Reproducibility of Gene Expression Measurements**](https://www.ncbi.nlm.nih.gov/pubmed/16964229)**.**

[**Rat Toxicogenomic Study Reveals Analytical Consistency Across Microarray Platforms**](https://www.ncbi.nlm.nih.gov/pubmed/17061323)**.**

[**Microarray Scanner Calibration Curves: Characteristics and Implications**](https://www.ncbi.nlm.nih.gov/pubmed/16026596)**.**

[**Models of Steroid Binding Based on the Minimum Deviation of Structurally Assigned C-13 NMR Spectra Analysis (MiDSASA)**](https://www.ncbi.nlm.nih.gov/pubmed/15272857)**.**

[**Development of Public Toxicoinformatics Software for Microarray Data Management and Analysis**](https://www.ncbi.nlm.nih.gov/pubmed/15120974)**.**

[**ArrayTrack--Supporting Toxicogenomic Research at the U.S. Food and Drug Administration National Center for Toxicological Research**](https://www.ncbi.nlm.nih.gov/pubmed/14630514)**.**

[VIEW FULL BIO – Stephen Harris](https://www.fda.gov/about-fda/science-research-nctr/stephen-harris)

# Huixiao Hong, Ph.D.

### **Senior Biomedical Research and Biomedical Product Assessment Service Expert — Division of Bioinformatics and Biostatistics**

Dr. Hong has a wide spectrum of research interests, including chemoinformatics, computational chemistry, next-generation sequencing data analysis, genome-wide association studies, proteomics, and systems biology. His current research goals are to generate safety signatures of drugs for the treatment of COVID-19 patients via big data analytics and artificial intelligence, and to identify candidate polypharmacy drugs for repurposing for COVID-19 treatment through computational chemistry approaches. Additionally, he is looking to construct an androgenic-activity database to enhance the endocrine disruptor knowledge base and to develop a knowledge base for management of opioid agonist and antagonist activities of chemicals. Dr. Hong is also working to develop predictive models using a variety of machine learning and deep learning algorithms to assist in the safety evaluation of FDA-regulated products. [VIEW FULL BIO – Dr. Huixiao Hong](https://www.fda.gov/about-fda/science-research-nctr/huixiao-hong)

**Titles and links to selected publications**

[**Assessing Reproducibility of Inherited Variants Detected with Short-Read Whole Genome Sequencing**](https://pubmed.ncbi.nlm.nih.gov/34980216/)**.**

[**Achieving Robust Somatic Mutation Detection with Deep Learning Models Derived from Reference Data Sets of a Cancer Sample**](https://genomebiology.biomedcentral.com/articles/10.1186/s13059-021-02592-9)**.**

[**Machine Learning Models for Predicting Cytotoxicity of Nanomaterials**](https://pubs.acs.org/doi/10.1021/acs.chemrestox.1c00310)**.**

[**Machine Learning Models for Predicting Liver Toxicity**](https://pubmed.ncbi.nlm.nih.gov/35188640/)**.**

[**Machine Learning Models on Chemical Inhibitors of Mitochondrial Electron Transport Chain**](https://pubmed.ncbi.nlm.nih.gov/34920224/)**.**

[**Integrative Approaches for Studying the Role of Noncoding RNAs in Influencing Drug Efficacy and Toxicity**](https://pubmed.ncbi.nlm.nih.gov/35296201/)**.**

[**Establishing Community Reference Samples, Data and Call Sets for Benchmarking Cancer Mutation Detection Using Whole-Genome Sequencing**](https://pubmed.ncbi.nlm.nih.gov/34504347/)**.**

[**Toward Best Practice in Cancer Mutation Detection with Whole-Genome and Whole-Exome Sequencing**](https://pubmed.ncbi.nlm.nih.gov/34504346/)**.**

[**Identification of Epidemiological Traits by Analysis of SARS-CoV-2 Sequences**](https://pubmed.ncbi.nlm.nih.gov/33925388/)**.**

[**Nanomaterial Databases: Data Sources for Promoting Design and Risk Assessment of Nanomaterials**](https://pubmed.ncbi.nlm.nih.gov/34207026/)**.**

[**Elucidating Interactions Between SARS-CoV-2 Trimeric Spike Protein and ACE2 Using Homology Modeling and Molecular Dynamics Simulations**](https://pubmed.ncbi.nlm.nih.gov/33469527/)**.**

[**Informing Selection of Drugs for COVID-19 Treatment Through Adverse Events Analysis**](https://www.nature.com/articles/s41598-021-93500-5)**.**

[**Software-Assisted Pattern Recognition of Persistent Organic Pollutants in Contaminated Human and Animal Food**](https://pubmed.ncbi.nlm.nih.gov/33525602/)**.**

[**Elucidation of Agonist and Antagonist Dynamic Binding Patterns in ER-α by Integration of Molecular Docking, Molecular Dynamics Simulations and Quantum Mechanical Calculations**](https://pubmed.ncbi.nlm.nih.gov/34502280/)**.**

[**Developing QSAR Models with Defined Applicability Domains on PPARγ Binding Affinity Using Large Data Sets and Machine Learning Algorithms**](https://pubs.acs.org/doi/abs/10.1021/acs.est.0c07040)**.**

[**Predictive Models to Identify Small Molecule Activators and Inhibitors of Opioid Receptors**](https://pubmed.ncbi.nlm.nih.gov/34047186/)**.**

[**Cross-Oncopanel Study Reveals High Sensitivity and Accuracy with Overall Analytical Performance Depending on Genomic Regions**](https://pubmed.ncbi.nlm.nih.gov/33863344/)**.**

[**Human Transthyretin Binding Affinity of Halogenated Thiophenols and Halogenated Phenols: An In Vitro and In Silico Study**](https://pubmed.ncbi.nlm.nih.gov/33964751/)**.**

[**Development of a Nicotinic Acetylcholine Receptor nAChR α7 Binding Activity Prediction Model**](https://pubmed.ncbi.nlm.nih.gov/32159345/)**.**

[**Applicability Domains Enhance Application of PPARγ Agonist Classifiers Trained by Drug-like Compounds to Environmental Chemicals**](https://pubs.acs.org/doi/full/10.1021/acs.chemrestox.9b00498)**.**

[VIEW FULL BIO – Huixiao Hong, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/huixiao-hong)

# Hyeonju Kim, Ph.D.

### **Visiting Scientist — Division of Bioinformatics and Biostatistics**

Dr. Kim’s research interests and expertise are in stochastic processes, extreme value theory, and high-dimensional data analysis in a wide range of applications, such as survival and event history analysis and quantitative genetics. She is currently working on covariate shift or transfer learning in machine learning. [VIEW FULL BIO – Dr. Hyeonju Kim](https://www.fda.gov/about-fda/science-research-nctr/hyeonju-kim)

**Titles and links to selected publications**

[**Flexible Multivariate Linear Mixed Models for Structured Multiple Traits**](https://www.biorxiv.org/content/10.1101/2020.03.27.012690v7.abstract)**.**

[**A Pragmatic Intervention Utilizing Financial Incentives for Pregnancy Weight Management: A Feasibility Randomized Controlled Trial**](https://formative.jmir.org/2021/12/e30578)**.**

[**Speeding Up eQTL Scans in the BXD Population Using GPUs**](https://academic.oup.com/g3journal/article/11/12/jkab254/6353031)**.**

[**Importance of Multiple Reinforcing Comments and Areas for Change in Optimizing Dietary and Exercise Self-Monitoring Feedback in Behavioral Weight Loss Programs: Factorial Design**](https://www.jmir.org/2020/11/e18104/)**.**

[**Sustainability in the Stochastic Ramsey Model**](https://link.springer.com/article/10.1007/s40953-015-0020-5)**.**

[VIEW FULL BIO – Hyeonju Kim, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/hyeonju-kim)

# Jae Hyun Kim, Ph.D.

### **Staff Fellow — Division of Bioinformatics and Biostatistics**

Dr. Kim’s research background is in software system design and full-stack development. His primary research interest lies in natural language processing (NLP) and its application in the field of regulatory science. He is exploring how NLP and machine learning can be used to make the work of regulatory scientists more effective. By automating the process of extracting information from regulatory documents, Dr. Kim aims to reduce the time and effort required by regulatory scientists to obtain and analyze information. [VIEW FULL BIO – Dr. Jae Hyun Kim](https://www.fda.gov/about-fda/science-research-nctr/jae-hyun-kim)

**Titles and links to selected publications**

[**CYPminer: An Automated Cytochrome P450 Identification, Classification, and Data Analysis Tool for Genome Data Sets Across Kingdoms**](https://pubmed.ncbi.nlm.nih.gov/32349673/)**.**

[**Characterization and Protective Efficacy of Type Three Secretion Proteins as a Broadly Protective Subunit Vaccine Against Salmonella enterica Serovars**](https://pubmed.ncbi.nlm.nih.gov/29311233/)**.**

[**Comparative Characterization of Crofelemer Samples Using Data Mining and Machine Learning Approaches with Analytical Stability Data Sets**](https://pubmed.ncbi.nlm.nih.gov/28743607/)**.**

[**Improved Comparative Signature Diagrams (CSDs) to Evaluate Similarity of Storage Stability Profiles of Different IgG1 mAbs**](https://pubmed.ncbi.nlm.nih.gov/26886311/)**.**

[**Biosimilarity Assessments of Model IgG1-Fc Glycoforms Using a Machine Learning Approach**](https://pubmed.ncbi.nlm.nih.gov/26869422/)**.**

[**Correlating the Impact of Well-Defined Oligosaccharide Structures on Physical Stability Profiles of IgG1-Fc Glycoforms**](https://pubmed.ncbi.nlm.nih.gov/26869421/)**.**

[VIEW FULL BIO – Jae Hyun Kim, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/jae-hyun-kim)

# Dan Li, Ph.D.

### **Visiting Scientist — Division of Bioinformatics and Biostatistics (Research-to-Review and Return Branch)**

Dr. Li's primary interests include the development of computational algorithms and tools to analyze various types of data—such as genomic and textual data—to provide evidence for quality control, clinical applications, and regulatory activities. His current research focuses on uncovering signals from advanced genomic data—such as deep targeted sequencing—and providing reproducible, high-quality results for regulatory science and precision medicine. Additionally, Dr. Li is interested in Artificial Intelligence (AI) and Machine Learning (ML) algorithms and applications. He is working on developing predictive AI/ML models using various types of datasets to discover safety and efficacy signals and assist with the pharmacovigilance of FDA-regulated products. [VIEW FULL BIO – Dr. Dan Li](https://www.fda.gov/about-fda/science-research-nctr/dan-li)

**Titles and links to selected publications**

[**Deep Oncopanel Sequencing Reveals within Block Position-Dependent Quality Degradation in FFPE Processed Samples**](https://pubmed.ncbi.nlm.nih.gov/35768876/)**.**

[**FDA-Led Consortium Studies Advance Quality Control of Targeted Next Generation Sequencing Assays for Precision Oncology**](https://pubmed.ncbi.nlm.nih.gov/35282311/)**.**

[**Cross-Oncopanel Study Reveals High Sensitivity and Accuracy with Overall Analytical Performance Depending on Genomic Regions**](https://pubmed.ncbi.nlm.nih.gov/33863344/)**.**

[**Evaluating the Analytical Validity of Circulating Tumor DNA Sequencing Assays for Precision Oncology**](https://pubmed.ncbi.nlm.nih.gov/33846644/)**.**

[**Gene Regulation Analysis Reveals Perturbations of Autism Spectrum Disorder during Neural System Development**](https://pubmed.ncbi.nlm.nih.gov/34946850/)**.**

[**Linking Pharmacogenomic Information on Drug Safety and Efficacy with Ethnic Minority Populations**](https://pubmed.ncbi.nlm.nih.gov/33113799/)**.**

[VIEW FULL BIO – Dan Li, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/dan-li)

# Dongying Li, Ph.D.

### **Staff Fellow — Division of Bioinformatics and Biostatistics**

Dr. Li’s research focuses on investigating epigenetic mechanisms that contribute to drug-induced liver injury and inter-individual differences in drug response. Specifically, she is interested in understanding the role of noncoding ribonucleic acids (RNAs), such as microRNAs and long noncoding RNAs, in regulating the expression of drug metabolizing enzymes, which are essential to drug efficacy and toxicity. Dr. Li is invested in leveraging big data and integrating computational, in vitro, and in vivo analyses to identify novel, actional biomarker candidates for early and accurate prediction of liver toxicity. Her research activities are highly in line with FDA’s priority in predictive toxicology and using alternative methods for toxicological studies. [VIEW FULL BIO – Dr. Dongying Li](https://www.fda.gov/about-fda/science-research-nctr/dongying-li)

**Titles and links to selected publications**

[**Characterization of Cytochrome P450s (CYP)-Overexpressing HepG2 Cells for Assessing Drug and Chemical-Induced Liver Toxicity**](https://pubmed.ncbi.nlm.nih.gov/33576714/)**.**

[**Biochemical Features and Mutations of Key Proteins in SARS-CoV-2 and Their Impacts on RNA Therapeutics**](https://pubmed.ncbi.nlm.nih.gov/33482149/)**.**

[**Impact of Sequencing Depth and Library Preparation on Toxicological Interpretation of RNA-seq Data in a “Three-Sample” Scenario**](https://pubmed.ncbi.nlm.nih.gov/33354967/)**.**

[**Identification of Translational MicroRNA Biomarker Candidates for Ketoconazole-Induced Liver Injury Using Next-Generation Sequencing**](https://pubmed.ncbi.nlm.nih.gov/33078836/)**.**

[**Linking Pharmacogenomic Information on Drug Safety and Efficacy with Ethnic Minority Populations**](https://pubmed.ncbi.nlm.nih.gov/33113799/)**.**

[**Mitochondrial Dysfunction and Apoptosis Underlie the Hepatotoxicity of Perhexiline**](https://pubmed.ncbi.nlm.nih.gov/32861758/)**.**

[**The Role of Hepatic Cytochrome P450s in the Cytotoxicity of Sertraline**](https://pubmed.ncbi.nlm.nih.gov/32372212/)**.**

[**Long Noncoding RNA LINC00844-Mediated Molecular Network Regulates Expression of Drug Metabolizing Enzymes and Nuclear Receptors in Human Liver Cells**](https://pubmed.ncbi.nlm.nih.gov/32222775/)**.**

[**Coordinated Regulation of UGT2B15 Expression by Long Noncoding RNA LINC00574 and hsa-miR-129-5p in HepaRG Cells**](https://pubmed.ncbi.nlm.nih.gov/32086297/)**.**

[**Using a Lentivirus-Based Inducible RNAi Vector to Silence a Gene**](https://pubmed.ncbi.nlm.nih.gov/31989556/)**.**

[**FREMSA: A Method That Provides Direct Evidence of the Interaction between microRNA and mRNA**](https://pubmed.ncbi.nlm.nih.gov/31989576/)**.**

[**MicroRNAs hsa-miR-495-3p and hsa-miR-486-5p Suppress Basal and Rifampicin-Induced Expression of Human Sulfotransferase 2A1 (SULT2A1) by Facilitating mRNA Degradation**](https://pubmed.ncbi.nlm.nih.gov/31445882/)**.**

[**Regulation of Cytochrome P450 Expression by microRNAs and Long Noncoding RNAs: Epigenetic Mechanisms in Environmental Toxicology and Carcinogenesis**](https://pubmed.ncbi.nlm.nih.gov/31305208/)**.**

[**Membrane-Associated Androgen Receptor (AR) Potentiates its Transcriptional Activities by Activating Heat Shock Protein 27 (HSP27)**](https://pubmed.ncbi.nlm.nih.gov/29934310/)**.**

[**Interplay between Cytoplasmic and Nuclear Androgen Receptor Splice Variants Mediates Castration Resistance**](https://pubmed.ncbi.nlm.nih.gov/27671337/)**.**

[**A Whole Blood Assay for AR-V7 and ARv567es in Patients with Prostate Cancer**](https://pubmed.ncbi.nlm.nih.gov/27449259/)**.**

[**Cingulin and Actin Mediate Midbody-Dependent Apical Lumen Formation During Polarization of Epithelial Cells**](https://pubmed.ncbi.nlm.nih.gov/27484926/)**.**

[**Identification of Rare DNA Sequence Variants in High-Risk Autism Families and their Prevalence in a Large Case/Control Population**](https://pubmed.ncbi.nlm.nih.gov/24467814/)**.**

[**Kinesin-2 Mediates Apical Endosome Transport During Epithelial Lumen Formation**](https://pubmed.ncbi.nlm.nih.gov/24843830/)**.**

[**FIP5 Phosphorylation During Mitosis Regulates Apical Trafficking and Lumenogenesis**](https://pubmed.ncbi.nlm.nih.gov/24591568/)**.**

[VIEW FULL BIO – Dongying Li, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/dongying-li)

# Ting Li, Ph.D.

### **Visiting Scientist — Division of Bioinformatics and Biostatistics**

Dr. Li’s research interests focus on developing and applying advanced artificial intelligence (AI) methodologies for drug safety research and the extension of their potential application in the FDA review process. This research includes:

* Developing quantitative structure-activity relationships models using advanced AI methodologies for various safety endpoints important to the FDA, such as drug-induced liver injury (DILI), carcinogenicity, and mutagenicity.
* Developing AI and machine learning models using genomic data to predict toxicological endpoints.
* Developing generative adversarial networks methods to translate genomic profiles from one organ to another.

[VIEW FULL BIO – Dr. Ting Li](https://www.fda.gov/about-fda/science-research-nctr/ting-li)

**Titles and links to selected publications**

[**Best Practice and Reproducible Science are Required to Advance Artificial Intelligence in Real-World Applications**](https://pubmed.ncbi.nlm.nih.gov/35848999/)**.**

[**Adaptability of AI for Safety Evaluation in Regulatory Science: A Case Study of Drug-Induced Liver Injury**](https://pubmed.ncbi.nlm.nih.gov/36425225/)**.**

[**DeepCarc: Deep Learning-Powered Carcinogenicity Prediction Using Model-Level Representation**](https://pubmed.ncbi.nlm.nih.gov/34870186/)**.**

[**DICE: A Drug Indication Classification and Encyclopedia for AI-Based Indication Extraction**](https://pubmed.ncbi.nlm.nih.gov/34409286/)**.**

[**Correlations Between Sleep Disturbance and Brain Cortical Morphometry in Healthy Children**](https://link.springer.com/article/10.1186/s41606-021-00068-0)**.**

[**Drug-Induced Liver Injury Severity and Toxicity (DILIst): Binary Classification of 1279 Drugs by Human Hepatotoxicity**](https://pubmed.ncbi.nlm.nih.gov/31669330/)**.**

[**DeepDILI: Deep Learning-Powered Drug-Induced Liver Injury Prediction Using Model-Level Representation**](https://pubmed.ncbi.nlm.nih.gov/33356151/)**.**

[**Deep Learning on High-Throughput Transcriptomics to Predict Drug-Induced Liver Injury**](https://pubmed.ncbi.nlm.nih.gov/33330410/)**.**

[**Cortical Morphometry is Associated with Neuropsychological Function in Healthy 8‐Year‐Old Children**](https://pubmed.ncbi.nlm.nih.gov/32639653/)**.**

[**Brain Cortical Structure and Executive Function in Children May Be Influenced by Parental Choices of Infant Diets**](https://pubmed.ncbi.nlm.nih.gov/32527846/)**.**

[**Scoring Matrix Combined with Machine Learning for Heterogeneously Structured Entity Resolution**](https://dl.acm.org/doi/10.5555/3344081.3344085)**.**

[**Scoring Matrix for Unstandardized Data in Entity Resolution**](https://ieeexplore.ieee.org/abstract/document/8947848)**.**

[VIEW FULL BIO – Ting Li, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/ting-li)

# Jie Liu, Ph.D.

### **Staff Fellow — Division of Bioinformatics and Biostatistics**

Dr. Liu’s specialized research focuses on the computational toxicology for risk evaluation and safety assessment. She has developed toxicity databases and computational models for liver and other organ toxicity prediction by integrating data from multiple sources. Currently, Dr. Liu is working on the development of computational models and toxicity databases for endocrine toxicity prediction. [VIEW FULL BIO – Dr. Jie Liu](https://www.fda.gov/about-fda/science-research-nctr/jie-liu)

**Titles and links to selected publications**

[**Nanomaterial Databases: Data Sources for Promoting Design and Risk Assessment of Nanomaterials**](https://pubmed.ncbi.nlm.nih.gov/34207026/)**.**

[**BPA Replacement Compounds: Current Status and Perspectives**](https://pubs.acs.org/doi/10.1021/acssuschemeng.0c09276)**.**

[**Identification of Epidemiological Traits by Analysis of SARS-CoV-2 Sequences**](https://pubmed.ncbi.nlm.nih.gov/33925388/)**.**

[**Elucidation of Agonist and Antagonist Dynamic Binding Patterns in ER-α by Integration of Molecular Docking, Molecular Dynamics Simulations and Quantum Mechanical Calculations**](https://pubmed.ncbi.nlm.nih.gov/34502280/)**.**

[**Utility of Generational Developmental and Reproductive Toxicity and Juvenile Animal Study Protocols for the Infant Safety Assessment of Food Contact Materials**](https://www.researchgate.net/publication/328459728_Utility_of_generational_developmental_and_reproductive_toxicity_and_juvenile_animal_study_protocols_for_the_infant_safety_assessment_of_food_contact_materials)**.**

[**Predicting Organ Toxicity Using In Vitro Bioactivity Data and Chemical Structure**](https://pubmed.ncbi.nlm.nih.gov/28768096/)**.**

[**Systematically Evaluating Read-Across Prediction and Performance Using a Local Validity Approach Characterized by Chemical Structure and Bioactivity Information**](https://pubmed.ncbi.nlm.nih.gov/27174420/)**.**

[**Using ToxCast™ Data to Reconstruct Dynamic Cell State Trajectories and Estimate Toxicological Points of Departure**](https://pubmed.ncbi.nlm.nih.gov/26473631/)**.**

[**Predicting Hepatotoxicity Using ToxCast In Vitro Bioactivity and Chemical Structure**](https://pubmed.ncbi.nlm.nih.gov/25697799/)**.**

[VIEW FULL BIO – Jie Liu, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/jie-liu)

# Zhiyuan (Julian) Lu, Ph.D.

### **Staff Fellow — Division of Bioinformatics and Biostatistics**

Dr. Lu’s research at NCTR involves statistical analysis of retrospective healthcare data using various methods. His work has included developing inference methods to the FDA Adverse Event Reporting System (FAERS), classifying medical text using natural language processing methods, and analyzing the electronic health record MIMIC-III dataset for causal effects. The general goal of past and present research is developing methods to more completely utilize the large amount of existing medical data to better monitor and understand the state of healthcare. [VIEW FULL BIO – Dr. Zhiyuan (Julian) Lu](https://www.fda.gov/about-fda/science-research-nctr/zhiyuan-lu)

**Titles and links to selected publications**

[**Medical Information Mart for Intensive Care: A Foundation for the Fusion of Artificial Intelligence and Real-World Data**](https://www.frontiersin.org/article/10.3389/frai.2021.691626)**.**

[**Intelligent Sampling and Inference for Multiple Change Points in Extremely Long Data Sequences**](https://arxiv.org/pdf/1710.07420.pdf)**.**

[VIEW FULL BIO – Zhiyuan (Julian) Lu, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/zhiyuan-lu)

# Joseph Meehan

### **Computer Scientist — Division of Bioinformatics and Biostatistics**

Mr. Meehan serves as a team leader for bioinformatics software development, where he is responsible for the development of new software for diverse research applications, including regulatory informatics, toxicogenomics, and machine learning.

He is the NCTR principal investigator on a collaborative project to develop and enhance regulatory review and research tools at FDA’s Center for Drug Evaluation and Research, including efforts to port a critical regulatory database to Oracle, capture pharmacology and toxicology review data from review documents, and retrospectively extract review information from FDA approval letters using pattern matching and natural language processing. [VIEW FULL BIO – Joseph Meehan](https://www.fda.gov/about-fda/science-research-nctr/joseph-meehan)

**Titles and links to selected publications**

[**Applying Network Analysis and Nebula (Neighbor-Edges Based and Unbiased Leverage Algorithm) to Toxcast Data**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Applying+Network+Analysis+and+Nebula+(Neighbor-Edges+Based+and+Unbiased+Leverage+Algorithm)+to+Toxcast+Data.)**.**

[**Alignment of Short Reads: A Crucial Step for Application of Next-Generation Sequencing Data in Precision Medicine**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Alignment+of+Short+Reads%3A+A+Crucial+Step+for+Application+of+Next-Generation+Sequencing+Data+in+Precision+Medicine.)**.**

[**An Investigation of Biomarkers Derived from Legacy Microarray Data for Their Utility in the RNA-Seq Era**](https://www.ncbi.nlm.nih.gov/pubmed/?term=An+Investigation+of+Biomarkers+Derived+from+Legacy+Microarray+Data+for+their+Utility+in+the+RNA-Seq+Era.)**.**

[**Assessing Technical Performance in Differential Gene Expression Experiments with External Spike-in RNA Control Ratio Mixtures**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Assessing+Technical+Performance+in+Differential+Gene+Expression+Experiments+with+External+Spike-In+RNA+Control+Ratio+Mixtures.)**.**

[**The Concordance Between RNA-Seq and Microarray Data Depends on Chemical Treatment and Transcript Abundance**](https://www.ncbi.nlm.nih.gov/pubmed/?term=The+Concordance+between+RNA-Seq+and+Microarray+Data+depends+on+Chemical+Treatment+and+Transcript+Abundance.)**.**

[**Whole Genome Sequencing of 35 Individuals Provides Insights into the Genetic Architecture of Korean Population**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Whole+Genome+Sequencing+of+35+Individuals+Provides+Insights+into+the+Genetic+Architecture+of+Korean+Population.)**.**

[**Meta-Analysis of Pulsed-Field Gel Electrophoresis Fingerprints Based on a Constructed Salmonella Database**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Meta-Analysis+of+Pulsed-Field+Gel+Electrophoresis+Fingerprints+based+on+a+Constructed+Salmonella+Database.)**.**

[**Data Mining Tools for Salmonella Characterization: Application to Gel-Based Fingerprinting Analysis**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Data+Mining+Tools+for+Salmonella+Characterization%3A+Application+to+Gel-Based+Fingerprinting+Analysis.)**.**

[**The Microarray Quality Control (MAQC)-II study of Common Practices for the Development and Validation of Microarray-Based Predictive Models**](https://www.ncbi.nlm.nih.gov/pubmed/?term=The+Microarray+Quality+Control+(MAQC)-II+Study+of+Common+Practices+for+the+Development+and+Validation+of+Microarray-Based+Predictive+Models.)**.**

[VIEW FULL BIO – Joseph Meehan](https://www.fda.gov/about-fda/science-research-nctr/joseph-meehan)

# Baitang Ning, Ph.D.

### **Research Biologist — Division of Bioinformatics and Biostatistics**

Dr. Ning leads a research team focusing on studies of molecular pharmacogenomics and pharmacoepigenomics in the application of personalized medicine. He has designed, developed, and established in silico, in vivo, in vitro, and molecular pharmacological approaches to identify and evaluate genetic variations and epigenetic mechanisms for inter-individual differences in drug metabolizing enzymes and drug targeting enzymes, which could help FDA reviewers better understand the inter-individual variability of drug efficacy and safety. His research activities align with FDA’s mission and the Critical Path Initiative for personalized medicine. [VIEW FULL BIO – Dr. Baitang Ning](https://www.fda.gov/about-fda/science-research-nctr/baitang-ning)

**Titles and links to selected publications**

[**Biochemical Features and Mutations of Key Proteins in SARS-CoV-2 and Their Impacts on RNA Therapeutics**](https://pubmed.ncbi.nlm.nih.gov/33482149/)**.**

[**Long Noncoding RNA Linc00844-Mediated Molecular Network Regulates Expression of Drug Metabolizing Enzymes and Nuclear Receptors in Human Liver Cells**](https://pubmed.ncbi.nlm.nih.gov/32222775/)**.**

[**Advances and Challenges in Studying Noncoding RNA Regulation of Drug Metabolism and Development of RNA Therapeutics**](https://pubmed.ncbi.nlm.nih.gov/31518552/)**.**

[**Multiple MicroRNA Function as Self-Protective Modules in Acetaminophen-Induced Hepatotoxicity in Humans**](https://www.ncbi.nlm.nih.gov/pubmed/29067470)**.**

[**A Systematic Evaluation of MicroRNAs in Regulating Human Hepatic CYP2E1**](https://www.ncbi.nlm.nih.gov/pubmed/28438567)**.**

[**MicroRNA hsa-miR-25-3p Suppresses the Expression and Drug Induction of CYP2B6 in Human Hepatocytes**](http://www.ncbi.nlm.nih.gov/pubmed/27311985)**.**

[**Re-Annotation of Presumed Noncoding Disease/Trait-Associated Genetic Variants by Integrative Analyses**](http://www.ncbi.nlm.nih.gov/pubmed/25819875)**.**

[**Suppression of CYP2C9 by MicroRNA hsa-mir-128-3p in Human Liver and Association with Hepatocellular Carcinoma**](http://www.ncbi.nlm.nih.gov/pubmed/25704921)**.**

[**A Comprehensive Assessment of RNA-Seq Accuracy, Reproducibility and Information Content by the Sequencing Quality Control Consortium**](http://www.ncbi.nlm.nih.gov/pubmed/25150838)**.**

[**Toxicogenomics and Cancer Susceptibility: Detection by Next-Generation Sequencing**](http://www.ncbi.nlm.nih.gov/pubmed/24875441)**.**

[**Gene Expression Variability in Human Hepatic Drug Metabolizing Enzymes and Transporters**](http://www.ncbi.nlm.nih.gov/pubmed/23637747)**.**

[**Similarities and Differences in the Expression of Drug Metabolizing Enzymes Between Human Hepatic Cell Lines and Primary Hepatocytes**](http://www.ncbi.nlm.nih.gov/pubmed/21149542)**.**

[**The MicroArray Quality Control (MAQC)-II Study of Common Practices for the Development and Validation of Microarray-Base Predictive Models**](http://www.ncbi.nlm.nih.gov/pubmed/20676074)**.**

[**Systematic and Simultaneous Gene Profiling of 84 Drug-Metabolizing Genes in Primary Human Hepatocytes**](http://www.ncbi.nlm.nih.gov/pubmed/18270363)**.**

[**A Variant of the Cockayne Syndrome B Gene ERCC6 Confers Risk of Lung Cancer**](http://www.ncbi.nlm.nih.gov/pubmed/17854076)**.**

[**Synergic Effect of Polymorphisms in ERCC6 5' Flanking Region and Complement Factor H on Age-Related Macular Degeneration Predisposition**](http://www.ncbi.nlm.nih.gov/pubmed/16754848)**.**

[**Common Genetic Polymorphisms in the 5’-Flanking Region of the SULT1A1 Gene: Association of Haplotypes and Platelet Enzymatic Activity**](http://www.ncbi.nlm.nih.gov/pubmed/15970794)**.**

[**Human Glutathione S-transferase A2 Polymorphisms: Variant Expression, Distribution in Prostate Cancer Cases/Controls and a Novel Form**](http://www.ncbi.nlm.nih.gov/pubmed/15128049)**.**

[**Increased Transcriptional Activity of the CYP3A4\*1B Promoter Variant**](http://www.ncbi.nlm.nih.gov/pubmed/14673875)**.**

[VIEW FULL BIO – Baitang Ning, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/baitang-ning)

# Paul Rogers, Ph.D.

### **Biostatistician — Division of Bioinformatics and Biostatistics**

Dr. Rogers's expertise and experience are in computational epidemiology, high-performance computing, generalized estimating equations, scientific information systems, geographic information systems (GIS), research database applications, and statistical software. In addition, his interests include population-based research, pharmacoepidemiology, rare-event modeling, and applications of GIS to epidemiology. Currently, he is conducting research with the National Health and Nutrition Examination Survey on nonsteroidal anti-inflammatory drugs, associated risk factors, and prevalence within the US population. [VIEW FULL BIO – Dr. Paul Rogers](https://www.fda.gov/about-fda/science-research-nctr/paul-rogers)

**Titles and links to selected publications**

[**Assessment of a Modified Sandwich Estimator for Generalized Estimating Equations with Application to Opioid Poisoning in MIMIC-IV ICU Patients**](https://www.mdpi.com/2571-905X/4/3/39)**.**

[**Medical Information Mart for Intensive Care: A Foundation for the Fusion of Artificial Intelligence and Real-World Data**](https://www.frontiersin.org/articles/10.3389/frai.2021.691626/full)**.**

[**The Use of a Poisson Regression to Evaluate Antihistamines and Fatal Aircraft Mishaps in IMC**](https://pubmed.ncbi.nlm.nih.gov/29562970/)**.**

[**Pilots Using Selective Serotonin Reuptake Inhibitors Compared to Other Fatally Injured Pilots**](https://pubmed.ncbi.nlm.nih.gov/28806612/)**.**

[**Development of a Geographic Information System for Risk-Informed Decision Making in Aerospace Medicine**](https://pubmed.ncbi.nlm.nih.gov/27779959/)**.**

[**Ethanol and Drugs Found in Civil Aviation Accident Pilot Fatalities, 1989-2013**](https://pubmed.ncbi.nlm.nih.gov/27099086/)**.**

[**Modification of the Sandwich Estimator in Generalized Estimating Equations with Correlated Binary Outcomes in Rare Event and Small Sample Settings**](https://pubmed.ncbi.nlm.nih.gov/26998504/)**.**

[**The +Gz Recovery of Consciousness Curve**](https://pubmed.ncbi.nlm.nih.gov/24843787/)**.**

[**Toxicological Findings in Fatally Injured Pilots of 979 Amateur-Built Aircraft Accidents**](https://pubmed.ncbi.nlm.nih.gov/23447851/)**.**

[**Increased Cannabinoids Concentrations Found in Specimens from Fatal Aviation Accidents Between 1997 and 2006**](https://pubmed.ncbi.nlm.nih.gov/20074884/)**.**

[**Evaluating Probabilistic Risk Assessment Methodology for use in the Medical Certification of Airmen**](https://pubmed.ncbi.nlm.nih.gov/19817246/)**.**

[**The FAA’s Postmortem Forensic Toxicology Proficiency-Testing Program; the Second Seven Years**](https://pubmed.ncbi.nlm.nih.gov/19470227/)**.**

[**Comprehensive Healthcare Inspection Summary Report Fiscal Year 2018**](https://www.va.gov/oig/pubs/VAOIG-19-07040-243.pdf)**.**

[**Descriptive Characteristics of Atrial Fibrillation in Civil Aviation 1993-2005**](https://www.faa.gov/data_research/research/med_humanfacs/oamtechreports/2010s/media/201710.pdf)**.**

[**Fatal Aviation Accidents: Fiscal Years 2009-2013**](https://www.faa.gov/data_research/research/med_humanfacs/oamtechreports/2010s/media/201519.pdf)**.**

[**Prevalence of Ethanol and Drugs in Civil Aviation Accident Pilot Fatalities, 2009-2013**](https://www.faa.gov/data_research/research/med_humanfacs/oamtechreports/2010s/media/201513.pdf)**.**

[**Risk in the US Pilot Population from 1983-2005; Diabetes Prevalence and Flight Safety**](https://www.faa.gov/data_research/research/med_humanfacs/oamtechreports/2010s/media/201505.pdf)**.**

[**An Analysis of the U.S. Pilot Population From 1983-2005: Evaluating the Effects of Regulatory Change**](https://www.faa.gov/data_research/research/med_humanfacs/oamtechreports/2000s/media/200909.pdf)**.**

[**The Second Seven Years of the FAA’s Postmortem Forensic Toxicology Proficiency-Testing Program**](https://www.faa.gov/data_research/research/med_humanfacs/oamtechreports/2000s/media/200824.pdf)**.**

[**Development of an Aeromedical Scientific Information System for Aviation Safety**](https://www.faa.gov/data_research/research/med_humanfacs/oamtechreports/2000s/media/200801.pdf)**.**

[VIEW FULL BIO – Paul Rogers, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/paul-rogers)

# Dong Wang, Ph.D.

### **Senior Staff Fellow — Division of Bioinformatics and Biostatistics**

Dr. Dong Wang has interest and experience in various aspects of statistics and bioinformatics:  risk assessment, statistical genomics, reproducibility, high-dimensional modeling, Bayesian methods, and post-market surveillance. Currently, he is conducting research on 1) measurement error models regarding biomarkers based on deep-sequencing technology, 2) constructing Bayesian networks for drug-induced liver toxicity by integrating in vitro and in vivo data in addition to expert knowledge, and 3) developing functional analysis models for cardiotoxicity. [VIEW FULL BIO – Dr. Dong Wang](https://www.fda.gov/about-fda/science-research-nctr/dong-wang)

**Titles and links to selected publications**

[**Integrating Adverse Outcome Pathways (AOPs) and High Throughput In Vitro Assays for Better Risk Evaluations, a Study With Drug-Induced Liver Injury (DILI)**](https://pubmed.ncbi.nlm.nih.gov/31707421/)**.**

[**In Silico Prediction of the Point of Departure (POD) with High-Throughput Data**](https://link.springer.com/chapter/10.1007/978-3-030-16443-0_15)**.**

[**Infer the In Vivo Point of Departure With ToxCast In Vitro Assay Data Using a Robust Learning Approach**](https://pubmed.ncbi.nlm.nih.gov/29995190/)**.**

[**A Strategy for Evaluating Biomarkers Based on Emerging Technologies Using a Measurement Error Framework**](https://www.lexjansen.com/phuse-us/2018/ab/AB05.pdf)**.**

[**Characterization of Founder Viruses in Very Early SIV Rectal Transmission**](https://www.ncbi.nlm.nih.gov/pubmed/28027479)**.**

[**Arabidopsis MSH1 Mutation Alters the Epigenome and Produces Heritable Changes in Plant Growth**](https://www.ncbi.nlm.nih.gov/pubmed/25722057)**.**

[**The Effects of Nonnormality on the Analysis of Supersaturated Designs: A Comparison of Stepwise, SCAD and Permutation Test Methods**](https://www.tandfonline.com/doi/abs/10.1080/00949655.2011.621953)**.**

[**Prediction of Genetic Values of Quantitative Traits with Epistatic Effects in Plant Breeding Populations**](https://www.ncbi.nlm.nih.gov/pubmed/22892636)**.**

[**Anticancer Peptidylarginine Deiminase (PAD) Inhibitors Regulate the Autophagy Flux and the Mammalian Target of Rapamycin Complex 1 Activity**](https://www.ncbi.nlm.nih.gov/pubmed/22605338)**.**

[**Identifying QTLs and Epistasis in Structured Plant Populations Using Adaptive Mixed LASSO**](https://link.springer.com/article/10.1007/s13253-010-0046-2)**.**

[**Development of an Internet Based System for Modeling Biotin Metabolism Using Bayesian Networks**](https://www.ncbi.nlm.nih.gov/pubmed/21356565)**.**

[**Bayesian Mixture Structural Equation Modeling in Multiple-Trait QTL Mapping**](https://www.ncbi.nlm.nih.gov/pubmed/20667167)**.**

[**Structural Equation Modeling of Gene-Environment Interactions in CHD**](https://www.ncbi.nlm.nih.gov/pubmed/21241273)**.**

[**Modeling Epigenetic Modifications Under Multiple Treatment Conditions**](https://www.sciencedirect.com/science/article/pii/S016794730900365X)**.**

[VIEW FULL BIO – Dong Wang, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/dong-wang)

# Leihong Wu, Ph.D.

### **Bioinformatician — Division of Bioinformatics and Biostatistics**

Dr. Wu’s research interest is to apply bioinformatics — particularly, Artificial Intelligence (AI) and Machine Learning (ML) — to biomedical research and informatics. Specifically, Dr. Wu’s work has focused on the development of algorithms for biological and pharmaceutical research tasks such as drug safety, QSAR modeling, and genomics. Dr. Wu’s research addresses some of the most pressing issues in understanding and applying novel bioinformatics database tools and frameworks that enhance the accuracy, safety, and efficiency of drug discovery, repositioning, and efficacy studies.

His current interests focus on developing AI/machine learning algorithms in various drug- and food-associated research areas including hepatotoxicity, genomics, and text mining. Dr. Wu’s current research interests include:

* Developing innovative AI algorithms for big data analysis, including multi-platform biological data such as gene expression, sequencing, and bioassays
* Designing and developing AI/machine learning framework to facilitate regulatory science
* Developing advanced predictive models using deep learning for biomarker identification of DILI and predictive toxicology research
* Developing innovative machine learning algorithms for text-mining in massive FDA regulatory documents
* Developing convolutional neural network architectures for advanced imaging analysis in drug and food safety assessment
* Designing and developing databases and visualization tools that promoting AI for regulatory use, including FDALabel

[VIEW FULL BIO – Dr. Leihong Wu](https://www.fda.gov/about-fda/science-research-nctr/leihong-wu)

**Titles and links to selected publications**

[**DLI-IT: A Deep Learning Approach to Drug Label Identification Through Image and Text Embedding**](https://pubmed.ncbi.nlm.nih.gov/32293428/)**.**

[**Technical Advance in Targeted NGS Analysis Enables Identification of Lung Cancer Risk-associated Low Frequency TP53, PIK3CA, and BRAF Mutations in Airway Epithelial Cells**](https://pubmed.ncbi.nlm.nih.gov/31711466/)**.**

[**A Deep Learning Model to Recognize Food Contaminating Beetle Species Based on Elytra Fragments**](https://www.sciencedirect.com/science/article/pii/S0168169918312821)**.**

[**HetEnc: A Deep Learning Predictive Model for Multi-Type Biological Dataset**](https://www.ncbi.nlm.nih.gov/pubmed/?term=HetEnc%3A+a+deep+learning+predictive+model+for+multi-type+biological+dataset)**.**

[**Study of Serious Adverse Drug Reactions Using FDA-Approved Drug Labeling and MedDRA**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Study+of+serious+adverse+drug+reactions+using+FDA-approved+drug+labeling+and+MedDRA)**.**

[**Integrating Drug’s Mode of Action into Quantitative Structure–Activity Relationships for Improved Prediction of Drug-Induced Liver Injury**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Integrating+Drug%E2%80%99s+Mode+of+Action+into+Quantitative+Structure%E2%80%93Activity+Relationships+for+Improved+Prediction+of+Drug-Induced+Liver+Injury)**.**

[**Direct Comparison of Performance of Single Nucleotide Variant Calling in Human Genome with Alignment-Based and Assembly-Based Approaches**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Direct+comparison+of+performance+of+single+nucleotide+variant+calling+in+human+genome+with+alignment-based+and+assembly-based+approaches)**.**

[**NETBAGs: A Network-Based Clustering Approach with Gene Signatures for Cancer Subtyping Analysis**](https://www.ncbi.nlm.nih.gov/pubmed/?term=NETBAGs%3A+a+network-based+clustering+approach+with+gene+signatures+for+cancer+subtyping+analysis)**.**

[VIEW FULL BIO – Leihong Wu, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/leihong-wu)

# Joshua Xu, Ph.D.

### **Supervisory Computer Scientist — Division of Bioinformatics and Biostatistics**

Dr. Xu’s experience includes about 20 years developing bioinformatics software and systems and conducting bioinformatics research. He has worked closely with the FDA’s Voluntary eXploratory Data Submission program to review and analyze the submissions involving pharmacogenomics, genetic data, and personalized medicine. Dr. Xu has in-depth expertise and experience in software design and development, data mining, genomics data analysis, image analysis, high-performance computing, and artificial intelligence. He has led several systems-development projects at NCTR including SNPTrack—an integrated solution for managing, analyzing, and interpreting genetic association study data. His recent endeavor has been with the Sequencing Quality Control (SEQC2) project, a large and international collaborative consortium led by FDA to evaluate the technical reliabilities and scientific applications of the next generation sequencing (NGS) technologies.

Dr. Xu’s research interests lie in onco-panel sequencing, liquid biopsy, genomics, bioimaging data analysis, text mining, and artificial intelligence. As the principle investigator, he is leading a large working group as part of the SEQC2 consortium to assess the reproducibility and detection sensitivity of oncopanel sequencing, including liquid biopsy. Oncopanel sequencing targets some small regions of the genome and can detect rare, but clinically relevant, sub-clonal mutations. Accurate diagnosis and subsequent tailoring of therapy depends on thorough characterization of tumor mutational spectra. A cross-lab evaluation of eight pan-cancer comprehensive panels and five circulating-tumor DNA liquid-biopsy assays is currently underway. The working group has over 200 participants from academia, government agencies, and industry (including eight companies providing oncopanels and 30 testing laboratories). The scope and complexity of this comprehensive study is unprecedented and aims to provide recommendation in support for FDA’s mission in regulatory oversight of NGS diagnostic tests. [VIEW FULL BIO – Dr. Joshua Xu](https://www.fda.gov/about-fda/science-research-nctr/joshua-xu)

**Titles and links to selected publications**

[**Study of Pharmacogenomic Information in FDA-approved Drug Labeling to Facilitate Application of Precision Medicine**](https://pubmed.ncbi.nlm.nih.gov/32032705/)**.**

[**DLI-IT: A Deep Learning Approach to Drug Label Identification Through Image and Text Embedding**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7158001/)**.**

[**A Deep Learning Model to Recognize Food Contaminating Beetle Species Based on Elytra Fragments**](https://www.sciencedirect.com/science/article/pii/S0168169918312821)**.**

[**Liquid Biopsy and its Role in an Advanced Clinical Trial for Lung Cancer**](https://www.ncbi.nlm.nih.gov/pubmed/29405770)**.**

[**Comparing SVM and ANN Based Machine Learning Methods for Species Identification of Food Contaminating Beetles**](https://www.nature.com/articles/s41598-018-24926-7)**.**

[**Species Identification of Food Contaminating Beetles by Recognizing Patterns in Microscopic Images of Elytra Fragments**](https://www.ncbi.nlm.nih.gov/pubmed/27341524)**.**

[**An Image Analysis Environment for Species Identification of Food Contaminating Beetles**](http://www.aaai.org/ocs/index.php/AAAI/AAAI16/paper/view/12393)**.**

[**The FDA’s Experience with Emerging Genomics Technologies—Past, Present, and Future**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4973466/)**.**

[**Comparison Of RNA-Seq And Microarray-Based Models For Clinical Endpoint Prediction**](https://www.ncbi.nlm.nih.gov/pubmed/26109056)**.**

[**An Investigation Of Biomarkers Derived From Legacy Microarray Data For Their Utility In The RNA-Seq Era**](https://www.ncbi.nlm.nih.gov/pubmed/25633159)**.**

[**The Concordance Between RNA-Seq And Microarray Data Depends On Chemical Treatment And Transcript Abundance**](https://www.ncbi.nlm.nih.gov/pubmed/25150839)**.**

[**A Comprehensive Assessment Of RNA-Seq Accuracy, Reproducibility And Information Content By The Sequencing Quality Control Consortium**](https://www.ncbi.nlm.nih.gov/pubmed/25150838)**.**

[**Assessing Technical Performance in Differential Gene Expression Experiments with External Spike-in RNA Control Ratio Mixtures**](https://www.ncbi.nlm.nih.gov/pubmed/25254650)**.**

[**SNPTrackTM - An Integrated Bioinformatics System for Genetic Association Studies**](https://www.ncbi.nlm.nih.gov/pubmed/23245293)**.**

[VIEW FULL BIO – Joshua Xu, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/joshua-xu)

# Liang Xu, Ph.D.

### **Staff Fellow — Division of Bioinformatics and Biostatistics**

Dr. Xu’s research focuses on the application of computational chemistry methods in the structure-function relationship of disease-related proteins. He has applied computational modeling and simulations to characterize the conformational dynamics of intrinsically disordered proteins associated with many neurodegenerative diseases. Dr. Xu is currently working on SARS-Cov-2-related proteins with computational biophysical approaches. [VIEW FULL BIO – Dr. Liang Xu](https://www.fda.gov/about-fda/science-research-nctr/liang-xu)

**Titles and links to selected publications**

[**Structural Insights into the Human Mitochondrial Pyruvate Carrier Complexes**](https://pubmed.ncbi.nlm.nih.gov/34664967/)**.**

[**Identification of a New Allosteric Binding Site for Cocaine in Dopamine Transporter**](https://pubmed.ncbi.nlm.nih.gov/32649824/)**.**

[**Molecular Simulations Reveal Terminal Group Mediated Stabilization of Helical Conformers in Both Amyloid-β42 and α-Synuclein**](https://pubmed.ncbi.nlm.nih.gov/30917651/)**.**

[**Re-Designing the α-Synuclein Tetramer**](https://pubmed.ncbi.nlm.nih.gov/29971274/)**.**

[**Familial Mutations May Switch Conformational Preferences in α-Synuclein Fibrils**](https://pubmed.ncbi.nlm.nih.gov/28075555/)**.**

[**Allosteric Stabilization of the Amyloid-β Peptide Hairpin by the Fluctuating N-Terminal**](https://pubmed.ncbi.nlm.nih.gov/26666686/)**.**

[**Coupling of the Non-Amyloid-Component (NAC) Domain and the KTK(E/Q)GV Repeats Stabilize the α-Synuclein Fibrils**](https://pubmed.ncbi.nlm.nih.gov/26873872/)**.**

[VIEW FULL BIO – Liang Xu, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/liang-xu)

# Wei Zhuang, Ph.D.

### **Staff Fellow — Division of Bioinformatics and Biostatistics**

Dr. Zhuang’s research interests are to develop advanced statistical methods and innovatively apply existing approaches for the advancement of regulatory science, biomedical research, and public health. She has performed research on statistical genetics, epidemiological studies, missing data, pathway analysis, brain imaging, data mining, and microarray/quantitative polymerase chain reaction (qPCR)/sequencing data analysis. This research experience has allowed her to connect statistical methods with specific research problems in genetics, cardiotoxicity, the human aging process, Parkinson’s disease, and HIV-associated neuronal toxicity. Dr. Zhuang’s current primary research projects include:

* Development of a reproducible workflow to analyze real-world incomplete or uncertain qPCR data
* Statistical methods for whole-transcriptome sequencing data analysis

[VIEW FULL BIO – Dr. Wei Zhuang](https://www.fda.gov/about-fda/science-research-nctr/wei-zhuang)

**Titles and links to selected publications**

[**A Robust Biostatistical Method Leverages Informative but Uncertainly Determined qPCR Data for Biomarker Detection, Early Diagnosis, and Treatment**](https://pubmed.ncbi.nlm.nih.gov/35100319/)**.**

[**Elevated Bilirubin, Alkaline Phosphatase at Onset, and Drug Metabolism Are Associated with Prolonged Recovery from DILI**](https://pubmed.ncbi.nlm.nih.gov/33845060/)**.**

[**Reproducibility Challenges for Biomarker Detection with Uncertain but Informative Experimental Data**](https://pubmed.ncbi.nlm.nih.gov/33021389/)**.**

[**Phenotypically Enriched Genotypic Imputation in Genetic Association Tests**](https://www.ncbi.nlm.nih.gov/pubmed/27576319)**.**

[**The Heritability of Circulating Testosterone, Oestradiol, Oestrone and Sex Hormone Binding Globulin Concentrations in Men: The Framingham Heart Study**](https://www.ncbi.nlm.nih.gov/pubmed/23746309)**.**

[**Meta-Analyses Identify 13 Loci Associated with Age at Menopause and Highlight DNA Repair and Immune Pathways**](https://www.ncbi.nlm.nih.gov/pubmed/22267201)**.**

[**Pathway Analysis Following Association Study**](https://www.ncbi.nlm.nih.gov/pubmed/22373100)**.**

[**Circulating Testosterone and SHBG Concentrations are Heritable in Women: The Framingham Heart Study**](https://www.ncbi.nlm.nih.gov/pubmed/21752884)**.**

[**Meta-Analysis of Genome-Wide Association Data Identifies Two Loci Influencing Age at Menarche**](https://www.ncbi.nlm.nih.gov/pubmed/19448620)**.**

[**Striatal [11C]dihydrotetrabenazine and [11C]methylphenidate Binding in Tourette Syndrome**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2677509/)**.**

[**Classification of HIV-1-Mediated Neuronal Dendritic and Synaptic Damage Using Multiple Criteria Linear Programming**](https://www.ncbi.nlm.nih.gov/pubmed/15365193)**.**

[VIEW FULL BIO – Wei Zhuang, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/wei-zhuang)

# Wen Zou, Ph.D.

### **Visiting Scientist — Division of Bioinformatics and Biostatistics**

Dr. Zou's research expertise in broad scientific areas include microbiology, molecular biology, food safety, bioinformatics, statistics, text mining, and data mining. Her primary research is in the areas of:

* Microbial next-generation sequencing data analysis and data mining
* Safety-signal detection from FDA Spontaneous Reporting Systems (SRSs) and Electronic Health Records
* Big-data analysis and visualization on knowledge discovering and safety-signal detection

Dr. Zou has been a Principal Investigator (PI), Co-PI, or participating scientist in more than ten research projects at NCTR and with other FDA Centers. Currently, she is the PI for two projects:

* Developing a novel data-mining and data-visualization method for safety surveillance of the FDA adverse event reporting systems
* Bioinformatics methodology development for microbial next-generation sequencing data analysis and data mining

[VIEW FULL BIO – Dr. Wen Zou](https://www.fda.gov/about-fda/science-research-nctr/wen-zou)

**Titles and links to selected publications**

[**Mechanistic roles of MicroRNAs in Hepatocarcinogenesis : A Study of Thioacetamide with Multiple Doses and Time-Points of Rats**](https://www.ncbi.nlm.nih.gov/pubmed/?term=scientific+reports+2017%2C3054)**.**

[**Best Setting of Model Parameters in Applying Topic Modeling on Textual Documents**](https://dl.acm.org/citation.cfm?doid=3107411.3108195)**.**

[**Endocrine Disrupting Chemicals Mediated Through Binding Androgen Receptor are Associated with Diabetes mellitus**](https://www.ncbi.nlm.nih.gov/pubmed/29295509)**.**

[**A Novel Procedure on Next Generation Sequencing Data Analysis Using Text Mining Algorithm**](https://www.ncbi.nlm.nih.gov/pubmed/27177941)**.**

[**Text Mining for Identifying Topics in the Literatures About Adolescent Substance Use and Depression**](https://www.ncbi.nlm.nih.gov/pubmed/26993983)**.**

[**Biomarker Identification from Next-Generation Sequencing Data for Pathogen Bacteria Characterization and Surveillance**](https://www.ncbi.nlm.nih.gov/pubmed/26501894)**.**

[**Molecular Regulation of MiRNAs and Potential Biomarkers in the Progression of Hepatic Steatosis to NASH**](https://www.ncbi.nlm.nih.gov/pubmed/26506944)**.**

[**A Heuristic Approach to Determine an Appropriate Number of Topics in Topic Modeling**](https://www.ncbi.nlm.nih.gov/pubmed/26424364)**.**

**Statistics in Big Data.**

[**Asymmetric Author-Topic Model for Knowledge Discovering of Big Data in Toxicogenomics**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Front+Pharmacol.+2015%2C+zou)**.**

[**Differential Gene Expression in Staphylococcus sureus Exposed to Orange II and Sudan III Azo Dyes**](https://www.ncbi.nlm.nih.gov/pubmed/25720844)**.**

[**A Composite Prediction Model for Subgroup Identification via Bicluster Analysis**](https://www.ncbi.nlm.nih.gov/pubmed/25347824)**.**

[**Topic Modeling for Cluster Analysis of Large Biological and Medical Datasets**](https://www.ncbi.nlm.nih.gov/pubmed/25350106)**.**

[**Data Mining Tools for Salmonella Characterization: Application to Gel-Based Fingerprinting Analysis**](https://www.ncbi.nlm.nih.gov/pubmed/24267777)**.**

[**Identification of Bicluster Regions in a Binary Matrix and its Application**](https://www.ncbi.nlm.nih.gov/pubmed/23940779)**.**

[**Meta-Analysis of Pulse-Field Gel Electrophoresis Fingerprints Based on a Constructed Salmonella Database**](https://www.ncbi.nlm.nih.gov/pubmed/23516614)**.**

[**A Prediction System for Rapid Identification of Salmonella Serotypes Based on the Pulse-Field Gel Electrophoresis Fingerprints**](https://www.ncbi.nlm.nih.gov/pubmed/22378901)**.**

[**Microarray Analysis of Virulence Gene Profiles in Salmonella Serovars from Food/Food Animal Environment**](https://www.ncbi.nlm.nih.gov/pubmed/21389588)**.**

[**Evaluation of Pulsed-Field Gel Electrophoresis Profiles for Identification of Salmonella Serotypes**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Journal+of+Clinical+Microbiology+2010%2C+zou)**.**

[**An FDA Bioinformatics Tool for Microbial Genomics Research on Molecular Characterization of Bacterial Foodborne Pathogens using Microarrays**](https://www.ncbi.nlm.nih.gov/pubmed/20946615)**.**

[**Metabolism of Azo Dyes by Human Skin Microbiota**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Journal+of+Medical+Microbiology+2010%2C+zou)**.**

[**Microarray Analysis of Antimicrobial Resistance Genes in Salmonella from Preharvest Poutry Environment**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Journal+of+Applied+Microbiology+2009%2C+zou)**.**

[**Azoreductase from Staphylococcus aureus**](https://www.ncbi.nlm.nih.gov/pubmed/23045013)**.**

[VIEW FULL BIO – Wen Zou, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/wen-zou)

## Division of Genetic and Molecular Toxicology, NCTR

# Robert Heflich, Ph.D.

### **Director — Division of Genetic and Molecular Toxicology**

Over the years, Dr. Heflich has pursued various research interests to modernize the practice of regulatory genetic toxicology, including developing more relevant, human-based in vitro models, and using advanced genetic analysis techniques designed to evaluate sequence changes in genes responsible for human diseases. A particular long-term interest involves the development of approaches to measure and analyze mutations in laboratory animals.  Studies have been conducted to evaluate the transgenic *gpt, lacI, cII,* and *φX174 am3* reporter genes and the endogenous *Hprt, Tk,*and *Pig-a* genes in mice and rats. The overall goal of these efforts is the application of sensitive and predictive in vivo mutation assays for regulatory purposes. Some of his other research interests include the development and characterization of relevant in vitro assays for evaluating the risks associated with tobacco product exposure. Descriptions of two recent research activities follow:

One of the more exciting developments over the last 10 years has been the move to evaluate genetic toxicity dose-response data quantitatively to better estimate human risk. Although it has been known for some time that not all genotoxic carcinogens have linear dose responses, dose response data are rarely used to evaluate the safety of regulated products. This changed when European regulators accepted in vivo mutation data to support a threshold for the carcinogenicity of ethylmethane sulfonate, which was found as a contaminant in a batch of the AIDS drug nelfinivir (Viracept) in 2007. Dr. Heflich and colleagues from HESI/ILSI (now HESI) have explored ways of quantitatively evaluating genetic toxicology data and developing Points of Departure (PoDs) that can be used to establish virtually safe doses for human exposure. Dr. Heflich also has used these methods to distinguish between the genotoxicity produced by related tobacco products that claim to have equivalent or reduced toxicity. These efforts have the potential of making better use of genetic toxicology data for making regulatory decisions.

The in vivo *Pig-a* gene mutation assay is currently being developed as a regulatory test. Dr. Heflich and his colleagues co-invented the test in 2008, and subsequently have made important discoveries as to its sensitivity to various types of genotoxins, the manifestation and persistence of the response, its ability to integrate into general toxicology studies, and in identifying the mutations that are responsible for inducing the mutant phenotype. Dr. Heflich has led International Workshop on Genotoxicity Testing and Health and Environmental Sciences Institute workgroups seeking to gain regulatory acceptance of the assay. Although the test already meets international regulatory guidelines (e.g., International Conference on Harmonization M7), he currently is working on an Organization for Economic Cooperation and Development (OECD)-approved plan to develop a Test Guideline (TG) for the assay. In April 2020, OECD approved a Detailed Review paper and validation document on the assay (see OECD publications listed below), which clears the way for development of a TG. Approval of an OECD TG will ensure that data from the test is widely accepted by regulatory agencies. [VIEW FULL BIO – Dr. Robert Heflich](https://www.fda.gov/about-fda/science-research-nctr/robert-heflich)

**Titles and links to selected publications**

[**The In Vivo Erythrocyte Pig-a Gene Mutation Assay — Part 1 —Detailed Review Paper and Performance Analysis**](http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm)**.**

[**The In Vivo Erythrocyte Pig-a Gene Mutation Assay — Part 2 — Validation Report**](http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm)**.**

[**Use of In Vitro 3D Tissue Models in Genotoxicity Testing: Strategic Fit, Validation Status and Way Forward. Report of the Working Group from the 7th International Workshop on Genotoxicity Testing (IWGT)**](https://pubmed.ncbi.nlm.nih.gov/32247552/)**.**

[**In Vitro Mammalian Cell Assays Based on the Pig-a Gene: A Report of the 7th International Workshop on Genetic Toxicology (IWGT) Workgroup**](https://pubmed.ncbi.nlm.nih.gov/31699348/)**.**

[**Celebrating 50 Years of EMGS: A Visionary Idea Continues**](https://pubmed.ncbi.nlm.nih.gov/31793064/)**.**

[**Mutation as a Toxicological Endpoint for Regulatory Decision-Making**](https://pubmed.ncbi.nlm.nih.gov/31600846/)**.**

[**Dr. Daniel Acosta and In Vitro Toxicology at the U.S. Food and Drug Administration’s National Center for Toxicological Research**](https://pubmed.ncbi.nlm.nih.gov/31628011/)**.**

[**Pig-a Gene Mutation Database**](https://pubmed.ncbi.nlm.nih.gov/31090953/)**.**

[**Evaluation of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) Mutagenicity Using In Vitro and In Vivo Pig-a Assays**](https://pubmed.ncbi.nlm.nih.gov/30595212/)**.**

[**Cigarette Whole Smoke Solutions Disturb Mucin Homeostasis in a Human In Vitro Airway Tissue Model**](https://pubmed.ncbi.nlm.nih.gov/30053496/)**.**

[**Analysis of Mutation in the Rat Pig-a Assay:  II) Studies with Bone Marrow Granulocytes**](https://pubmed.ncbi.nlm.nih.gov/30091248/)**.**

[**Quantitative Differentiation of Whole Smoke Solution-Induced Mutagenicity in the Mouse Lymphoma Assay**](https://pubmed.ncbi.nlm.nih.gov/29119619/)**.**

[VIEW FULL BIO – Robert Heflich, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/robert-heflich)

# Tao Chen, Ph.D., DABT

### **Research Toxicologist — Division of Genetic and Molecular Toxicology**

Dr. Chen led a team to conduct research for development and validation of genotoxic methods and evolution of genotoxicity of FDA-related products. Dr. Chen’s early research mainly addressed the validation of rodent transgenic mutation systems and development of different methods for molecular characterization of chemical-induced mutations. He has investigated mutagenicity and fundamental mechanisms of mutagens associated with FDA regulations such as tamoxifen, retinyl palmitate, aristolochic acid, acrylamide, and drug impurities using different genotoxicity endpoints. Recent research has focused on the evaluation of genotoxicity assays for assessing nanomaterials, the development of new microRNA assays to supplement current genotoxicity battery, and the assessment of chemical-induced somatic and germline mutations using next generation sequencing methods. [VIEW FULL BIO – Dr. Tao Chen](https://www.fda.gov/about-fda/science-research-nctr/tao-chen)

**Titles and links to selected publications**

[**Mutagenicity of Silver Nanoparticles Evaluated Using Whole Genome Sequencing in Mouse Lymphoma Cells**](https://pubmed.ncbi.nlm.nih.gov/33710943/)**.**

[**Expression of miR-34a is a Sensitive Biomarker for Exposure to Genotoxic Agents in Human Lymphoblastoid TK6 Cells**](https://pubmed.ncbi.nlm.nih.gov/32928372/)**.**

[**Cytotoxicity and Genotoxicity of Cadmium Oxide Nanoparticles Evaluated Using In Vitro Assays**](https://pubmed.ncbi.nlm.nih.gov/32247558/)**.**

[**Genotoxicity Assessment of Nanomaterials: Recommendations on Best Practices, Assays and Methods**](https://pubmed.ncbi.nlm.nih.gov/29701824/)**.**

[**Differential Genotoxicity Mechanisms of Silver Nanoparticles and Silver Ions**](https://pubmed.ncbi.nlm.nih.gov/27180073/)**.**

[**Size- and Coating-Dependent Cytotoxicity and Genotoxicity of Silver Nanoparticles Evaluated Using In Vitro Standard Assays**](https://pubmed.ncbi.nlm.nih.gov/27441588/)**.**

[**Decrease of 5-hydroxymethylcytosine in Rat Liver with Subchronic Exposure to Genotoxic Carcinogens Riddelliine and Aristolochic Acid**](https://pubmed.ncbi.nlm.nih.gov/25154389/)**.**

[**Integrated microRNA, mRNA, and Protein Expression Profiling Reveals microRNA Regulatory Networks in Rat Kidney Treated with a Carcinogenic Dose of Aristolochic Acid**](https://pubmed.ncbi.nlm.nih.gov/25952319/)**.**

[**A Comprehensive Assessment of RNA-seq Accuracy, Reproducibility and Information Content by the Sequencing Quality Control Consortium**](https://pubmed.ncbi.nlm.nih.gov/25150838/)**.**

[**Genotoxicity of 2-bromo-3'-chloropropiophenone**](https://pubmed.ncbi.nlm.nih.gov/23628427/)**.**

[VIEW FULL BIO – Tao Chen, Ph.D., DABT](https://www.fda.gov/about-fda/science-research-nctr/tao-chen)

# Azra Dad, Ph.D.

### **Staff Fellow — Division of Genetic and Molecular Toxicology**

Dr. Azra has worked on various projects as a Principal Investigator at NCTR. As an ORISE Fellow, she developed the *Pig-a* mutation assay in granulocytes, which provided very important information that contributed to the approval of a regulatory Test Guideline (TG470) for the in vivo *Pig-a* assay by the Organization for Economic Cooperation and Development. Her research analyzed the hypothesis that the *Pig-a* mutation assay measures mutations occurring in bone marrow precursor cells of exposed animals. She characterized and isolated the granulocyte population from rat bone marrow, identified and sorted *Pig-a* mutant cells through flow cytometry, and identified mutations in the sorted cells using next-generation sequencing.

As a staff fellow, Dr. Azra currently runs the DGMT in vitro inhalation toxicology lab and studies the impact of conventional combustible tobacco cigarettes and E-cigarettes on human lung tissue using organotypic primary human airway cultures exposed in vitro at the ALI. This study compares the toxicity and genotoxicity of smoke from conventional cigarettes with aerosols generated by puffing E-cigarettes. The aerosols are generated using robots that produce smoke and aerosols in a controlled, reproducible manner so that the effects on different cytological, respiratory, and genetic endpoints can be quantitatively and reproducibly evaluated. The work will develop tests that can be used by FDA’s Center for Tobacco Products in evaluating the products that they regulate. [VIEW FULL BIO – Dr. Azra Dad](https://www.fda.gov/about-fda/science-research-nctr/azra-dad)

**Titles and links to selected publications**

[***Pig‐a* Gene Mutations in Bone Marrow Granulocytes of Procarbazine‐Treated F344 Rats**](https://onlinelibrary.wiley.com/doi/abs/10.1002/em.22430)**.**

[**Molecular Analysis of GPI-Anchor Biosynthesis Pathway Genes in Rat Strains Used for the *Pig-a* Gene Mutation Assay**](https://www.sciencedirect.com/science/article/pii/S1383571820301261)**.**

[**Haloacetic Acid Water Disinfection Byproducts Affect Pyruvate Dehydrogenase Activity and Disrupt Cellular Metabolism**](https://pubs.acs.org/doi/full/10.1021/acs.est.7b04290)**.**

[VIEW FULL BIO – Azra Dad, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/azra-dad)

# Vasily Dobrovolsky, Ph.D.

### **Research Microbiologist — Division of Genetic and Molecular Toxicology**

Dr. Dobrovolsky is at the forefront of DGMT efforts in finding solutions to the complex problems faced by regulatory science in our modern technological society. Over the years he earned recognition for development and evaluation of tools for the assessment of safety and identification of potential hazards (i.e., carcinogens) among the products regulated by the U.S. Food and Drug Administration. His research interests involve the use of genetic engineering and various high throughput methodologies for designing in vitroand in vivo models capable of detecting and analyzing mutation. Dr. Dobrovolsky has used transgenic technology extensively for detecting hazards to the human genome. He designed a knockout mouse model for detecting mutation in the endogenous Tk locus. The model has been used to evaluate the mutagenicity of antiretroviral drugs. Anther model using a transgenic reporter, green fluorescent protein, has bridged the biology of mutation identification and high throughput scoring methodology using flow cytometry. The future use of targeted genome editing for therapeutic purposes (e.g., activating or deactivating endogenous genes or inserting transgenes using the Crispr/Cas9 system) warrants understanding potential negative side effects of the new therapy using various in vitro and in vivo models. Dr. Dobrovolsky was a co-inventor of the model for detecting mutation in the endogenous Pig-a gene and an enthusiastic promoter of its use in regulatory non-clinical research. The Pig-a model uses flow cytometry for detecting cells having a mutant phenotype. The essential contributions of Dr. Dobrovolsky include extending the in vivo Pig-a model to species other than rodents and to in vitro cell cultures, as well as proving that the mutant phenotype measured by flow cytometry truly reflects mutation in the Pig-a gene. The rodent Pig-a model is at an advanced stage of acceptance for regulatory use. Yet, certain aspects of the Pig-a based model of mutation detection remain to be fully characterized. The model has translation potential as it is compatible with the detection of mutation in humans. Understanding the limitations and applicability of detecting Pig-a mutation in human patients for diagnostic and monitoring purposes will require further refinement in instrumental approaches and multiple testing the methodology in clinical trials. Recently, massive parallel sequencing, known as next generation sequencing or NGS, became an affordable and powerful tool in biomedical research. A group of scientists led by Dr. Dobrovolsky is exploring approaches for using NGS in regulatory genetic toxicology safety assessments. NGS complements the in vivo Pig-a gene model by making a quantitative leap in the ability to characterize mutations and build mutational spectra. Looking forward, NGS is poised to revolutionize the field of genetic toxicology by detecting mutation in any gene of any tissue of any species. In order to fully realize this potential, novel approaches in NGS sequencing chemistry and computational analyses of massive data arrays are developed by the group. [VIEW FULL BIO – Dr. Vasily Dobrovolsky](https://www.fda.gov/about-fda/science-research-nctr/vasily-dobrovolsky)

**Titles and links to selected publications**

[**Mutation Analysis with Random DNA Identifiers (MARDI) Catalogs Pig-A Mutations in Heterogeneous Pools Of CD48-Deficient T Cells Derived From DMBA-Treated Rats**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Mutation%20Analysis%20With%20Random%20DNA%20Identifiers%20(MARDI)%20Catalogs%20Pig-A%20Mutations%20In%20Heterogeneous%20Pools%20Of%20CD48-Deficient%20T%20Cells%20Derived%20From%20DMBA-Treated%20Rats)**.**

[**The In Vivo Pig-A Assay: A Report of the International Workshop On Genotoxicity Testing (IWGT) Workgroup**](https://www.ncbi.nlm.nih.gov/pubmed/?term=The%20in%20vivo%20Pig-a%20assay%3A%20A%20report%20of%20the%20International%20Workshop%20on%20Genotoxicity%20Testing%20(IWGT)%20Workgroup.)**.**

[**CD48-Deficient T-Lymphocytes from DMBA-Treated Rats Have De Novo Mutations in The Endogenous Pig-A Gene**](https://www.ncbi.nlm.nih.gov/pubmed/?term=CD48-Deficient%20T-Lymphocytes%20From%20DMBA-Treated%20Rats%20Have%20De%20Novo%20Mutations%20In%20The%20Endogenous%20Pig-A%20Gene.)**.**

[**Confirmation Of Pig-A Mutation in Flow Cytometry-Identified CD48-Deficient T-Lymphocytes From F344 Rats**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Confirmation%20Of%20Pig-A%20Mutation%20In%20Flow%20Cytometry-Identified%20CD48-Deficient%20T-Lymphocytes%20From%20F344%20Rats.)**.**

[**Monitoring Humans for Somatic Mutation in the Endogenous Pig-A Gene Using Red Blood Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Monitoring%20humans%20for%20somatic%20mutation%20in%20the%20endogenous%20PIG-A%20gene%20using%20red%20blood%20cells.)**.**

[**Evaluation of Macaca mulatta As a Model for Genotoxicity Studies**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Evaluation%20Of%20Macaca%20Mulatta%20As%20A%20Model%20For%20Genotoxicity%20Studies.)**.**

[**Development of an In Vivo Gene Mutation Assay Using the Endogenous Pig-A Gene: I. Flow Cytometric Detection of CD59-Negative Peripheral Red Blood Cells and CD48-Negative Spleen T-Cells from the Rat**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Development%20Of%20An%20In%20Vivo%20Gene%20Mutation%20Assay%20Using%20The%20Endogenous%20Pig-A%20Gene%3A%20I.%20Flow%20Cytometric%20Detection%20Of%20CD59-Negative%20Peripheral%20Red%20Blood%20Cells%20And)**.**

[**On the Use of the T-Rex Tetracycline-Inducible Gene Expression System In Vivo**](https://www.ncbi.nlm.nih.gov/pubmed/17421042)**.**

[**Effect Of Arylformamidase (Kynurenine Formamidase) Gene Inactivation in Mice on Enzymatic Activity, Kynurenine Pathway Metabolites and Phenotype**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Effect%20Of%20Arylformamidase%20(Kynurenine%20Formamidase)%20Gene%20Inactivation%20In%20Mice%20On%20Enzymatic%20Activity%2C%20Kynurenine%20Pathway%20Metabolites%20And%20Phenotype.)**.**

[**Detection Of Mutation in Transgenic CHO Cells Using Green Fluorescent Protein as A Reporter**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Detection%20Of%20Mutation%20In%20Transgenic%20CHO%20Cells%20Using%20Green%20Fluorescent%20Protein%20As%20A%20Reporter.)**.**

[**7,12-Dimethylbenz[A]Anthracene-Induced Mutation in the Tk Gene Of Tk(+/-) Mice: Automated Scoring Of Lymphocyte Clones Using A Fluorescent Viability Indicator**](https://www.ncbi.nlm.nih.gov/pubmed/?term=7%2C12-Dimethylbenz%5BA%5DAnthracene-Induced%20Mutation%20In%20The%20Tk%20Gene%20Of%20Tk(%2B%2F-)%20Mice%3A%20Automated%20Scoring%20Of%20Lymphocyte%20Clones%20Using%20A%20Fluorescent%20Viabili)**.**

[**Tk+/- Mouse Model for Detecting In Vivo Mutation in An Endogenous, Autosomal Gene**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Tk%2B%2F-%20Mouse%20Model%20For%20Detecting%20In%20Vivo%20Mutation%20In%20An%20Endogenous%2C%20Autosomal%20Gene.)**.**

[VIEW FULL BIO – Vasily Dobrovolsky, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/vasily-dobrovolsky)

# Xiaoqing Guo, Ph.D.

### **Staff Fellow — Division of Genetic and Molecular Toxicology**

Since joining NCTR in 2008, Dr. Guo has worked intently to evaluate the mutagenicity and molecular-mechanistic analysis of chemicals of FDA regulatory interest using the in vitro genetic-toxicity assays included in the standard test battery. Dr. Guo is also an expert in conducting in vitro mouse lymphoma assay, the micronucleus assay, the Comet assay, in vivo mutation assays, and pathway-based mechanistic studies. She has used these assays to evaluate the mutagenicity of a variety of preparations of cigarette smoke (smoke condensates, whole-smoke solutions, whole smoke, and individual agents representing different chemical classes contained in cigarette smoke), nanomaterials, botanicals and mixtures, industrial compounds, and retail products.

Dr. Guo’s current research interest is developing pathway-based, medium- or high-throughput, and high-content (HTHC) approaches for genotoxicity testing. She also is interested in employing quantitative dose-response modeling approaches to evaluate the genotoxic dose-response relationships. Dr. Guo has successfully analyzed dose-response mouse-lymphoma assay data using several point-of-departure metrics, including benchmark dose and mutagenic potency. The conjunction of HTHC genetic-toxicity data and quantitative approaches provides a more efficient and streamlined process that may result in better regulatory decisions.

A major shortcoming of many previous studies is that assays were conducted in rodent- or human-cell lines without metabolic competence. Dr. Guo is interested in establishing appropriate in vitro cell models with metabolic competence, with the aim of generating data more relevant to human in vivo exposures. The resulting data may potentially be used to predict in vivo genotoxicity and for setting margin-of-exposure values to establish safe exposures levels for humans. Using the HTHC quantitative genotoxicity assays, Dr. Guo is collaborating with the Genetic Toxicology Group at the National Institute of Environmental Health Sciences/National Toxicology Program to test a number of chemicals in the Tox 21 library that have unusual responses observed in quantitative high-throughput screening assays. [VIEW FULL BIO – Dr. Xiaoqing Guo](https://www.fda.gov/about-fda/science-research-nctr/xiaoqing-guo)

**Titles and links to selected publications**

[**Comparative Genotoxicity of TEMPO and Three of its Derivatives in Mouse Lymphoma Cells**](https://www.ncbi.nlm.nih.gov/pubmed/29385624)**.**

[**Quantitative Differentiation of Whole Smoke Solution-Induced Mutagenicity in the Mouse Lymphoma Assay**](https://www.ncbi.nlm.nih.gov/pubmed/29119619)**.**

[**ROS Generation and JNK Activation Contribute to 4-Methoxy-TEMPO-Induced Cytotoxicity, Autophagy, and DNA Damage in HepG2 Cells**](https://www.ncbi.nlm.nih.gov/pubmed/28993908)**.**

[**Size- and Coating-Dependent Cytotoxicity and Genotoxicity of Silver Nanoparticles Evaluated Using In VitroStandard Assays**](https://www.ncbi.nlm.nih.gov/pubmed/27441588)**.**

[**Aloe vera: A Review of Toxicity and Adverse Clinical Effects**](http://www.ncbi.nlm.nih.gov/pubmed/26986231)**.**

[**Quantitative Analysis of In Vitro Mutagenicity Induced by Five Chemical Constituents of Tobacco Smoke**](http://www.ncbi.nlm.nih.gov/pubmed/26001754)**.**

[**Acetyl L-Carnitine Targets Adenosine Triphosphate Synthase in Protecting Zebrafish Embryos from Toxicities Induced by Verapamil and Ketamine: An In Vivo Assessment**](http://www.ncbi.nlm.nih.gov/pubmed/27191126)**.**

[**Developmental Toxicity Assay Using High Content Screening of Zebrafish Embryos**](http://www.ncbi.nlm.nih.gov/pubmed/24871937)**.**

[**Reactive Oxygen Species and C-Jun N-Terminal Kinases Contribute to TEMPO-Induced Apoptosis in L5178Y Cells**](http://www.ncbi.nlm.nih.gov/pubmed/25882087)**.**

[**Ginkgo biloba Leaf Extract Induces DNA Damage by Inhibiting Topoisomerase II Activity in Human Hepatic Cells**](https://pubmed.ncbi.nlm.nih.gov/26419945/)**.**

[**Mutant Frequency in Comparison to Oxidative DNA Damage Induced by Ochratoxin A in L5178Y Tk+/- (3.7.2C) Mouse Lymphoma Cells**](http://www.ncbi.nlm.nih.gov/pubmed/24164384)**.**

[**Assessment of the Toxic Potential of Grapheme Family Nanomaterials**](http://www.ncbi.nlm.nih.gov/pubmed/24673908)**.**

[**Mechanistic Evaluation of Ginkgo biloba Leaf Extract-Induced Genotoxicity in L5178Y Cells**](http://www.ncbi.nlm.nih.gov/pubmed/24595819)**.**

[**Nitroxide TEMPO: A Genotoxic and Oxidative Stress Inducer in Cultured Cells**](http://www.ncbi.nlm.nih.gov/pubmed/23517621)**.**

[**Acetyl L-Carnitine Protects Motor Neurons and Rohon-Beard Sensory Neurons Against Ketamine-Induced Neurotoxicity in Zebrafish Embryos**](http://www.ncbi.nlm.nih.gov/pubmed/23896048)**.**

[**Ketamine Attenuates Cytochrome P450 Aromatase Gene Expression and Estradiol-17 Levels in Zebrafish Early Life Stages**](http://www.ncbi.nlm.nih.gov/pubmed/23696345)**.**

[**Mutagenicity and DNA Adduct Formation by Aristolochic Acid in the Spleen of Big Blue Rats**](http://www.ncbi.nlm.nih.gov/pubmed/22508110)**.**

[**Nicotine Alters the Expression of Molecular Markers of Endocrine Disruption in Zebrafish**](http://www.ncbi.nlm.nih.gov/pubmed/22922325)**.**

[**Silver Nanoparticles Induced Genotoxicity and Oxidative Stress in Mouse Lymphoma Cells**](http://www.ncbi.nlm.nih.gov/pubmed/22576574)**.**

[**Mutagenicity of 11 Cigarette Smoke Condensates in Two Versions of the Mouse Lymphoma Assay**](http://www.ncbi.nlm.nih.gov/pubmed/20980367)**.**

[**The Genotoxicity of Acrylamide and Glycidamide in Big Blue Rats**](http://www.ncbi.nlm.nih.gov/pubmed/20200216)**.**

[VIEW FULL BIO – Xiaoqing Guo, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/xiaoqing-guo)

# Mugimane Manjanatha, Ph.D.

### **Supervisory Research Microbiologist — Division of Genetic and Molecular Toxicology**

Dr. Manjanatha has expanded his research to include development of a new transgenic rodent (TGR) mutational model, modification of the Comet assay for the detection of changes in DNA global methylation, and, most recently, the development of a human in vitro three-dimensional (3D) liver co-culture model.

His work on chemicals of interest to FDA using TGR mutational models has demonstrated that the types of transgene mutations induced by many carcinogenic chemicals in the target tissues are remarkably like the types of cancer-gene mutations induced by these chemicals in tumor tissues. Thus, the transgenic mutation assays serve as a highly reliable tool for predicting cancer-gene mutations and are extremely useful for safety assessment of FDA-relevant chemicals and drugs. In addition, his work on TGR assays in collaboration with researchers from industry, academia, and NCTR to evaluate the mutagenic mode-of-action of carcinogenic chemicals, such as ethylene oxide, vanadium pentoxide and vinyl acetate showed that transgenic, neutral reporter genes are valuable tools that are amenable for quantitative risk analysis by hazard identification and characterization. He was recently selected to serve as an FDA expert on Organization for Economic Co-Operation and Development (OECD) TGR assay Test Guideline (TG) 488 revision for including germ cell mutagenesis.

Dr. Manjanatha led a team of researchers from NCTR and FDA’s Center for Food Safety and Nutrition in successfully establishing the Single Cell Gel Electrophoresis assay (Comet assay) at NCTR. Using enzyme-modified Comet assays, the team evaluated the genotoxic mode-of-action of several FDA-relevant food mutagens – such as methyleugenol, furan, safrole, and estragole – and pharmaceuticals – such as doxorubicin and cyproterone acetate. Dr. Manjanatha was invited as a U.S. national expert on the Comet assay to write comments on the draft Organisation for Economic Co-Operation and Development (OECD) Comet assay test guideline in July 2013. The assay guideline was adopted by OECD (489-TG) in September 2014 and the assay has become a regulatory genetox assay used world-wide. Dr. Manjanatha has continued his work on the Comet assay and recently began working with an FDA commissioner’s fellow to develop a modified Comet assay that can detect DNA damage and epigenetic modifications such as global DNA methylation alteration on a single platform. He has applied this assay to test the safety of black cohosh extract used as a supplement by pre- and post-menopausal women for relief from menopausal symptoms.

Dr. Manjanatha has successfully developed a new transgenic, hairless-albino (THA) mouse model at NCTR to test in vivo mutagenesis as a short-term end point that could replace the requirement of a long-term photocarcinogenesis bioassay. Current validation studies show that THA mice are extremely sensitive to UV radiation and low UVB doses (20-40 mJ/cm2) induced 10-12-fold and 3-5-fold increases in the mutant frequency compared to the respective controls in the guanine phosphoribosyl transferase (GPT) and sensitive to P2 interference (Spi-) selection systems. Further, molecular analysis of the GPT mutants in skin showed UV-specific, C→T signature mutations exclusively at dipyrimidine sites. Further studies with this model are underway to evaluate the carcinogenic predictivity of short-term mutagenicity assays, the UVB circadian clock in skin, and the safety of cosmetics containing nanoparticles.

Dr. Manjanatha is interested in the development of a human in vitro 3D liver co-culture model (or kidney systems containing primary parenchymal and non-parenchymal cells on a 3D scaffold). The 3D liver model containing hepatocytes, stellate, Kupffer, and endothelial cells should be able to maintain liver function for at least up to 3 months and produce albumin, fibrinogen, transferrin and urea. Additionally, 3D liver co-cultures should maintain cytochrome P450 inducibility, form bile canaliculi-like structures and respond to inflammatory stimuli. Upon incubation with selected hepatotoxicants, including drugs which have been shown to induce idiosyncratic toxicity, this model should be able to detect in vivo drug-induced toxicity, including species-specific drug effects, when compared to monolayer hepatocyte cultures. In conclusion, in vitro cell-culture models that contain all liver-cell types and allow repeated drug-treatments for detection of in vivo-relevant adverse drug effects will be ideal. [VIEW FULL BIO – Dr. Mugimane Manjanatha](https://www.fda.gov/about-fda/science-research-nctr/mugimane-manjanatha)

**Titles and links to selected publications**

[**Appropriate In Vivo Follow-Up Assays to an In Vitro Bacterial Reverse Mutation (Ames) Test Positive Investigational Drug Candidate (Active Pharmaceutical Ingredient), Drug-Related Metabolite, and Frug-Related Impurities**](https://pubmed.ncbi.nlm.nih.gov/34454692/)**.**

[**Night Shift Schedule Causes Circadian Dysregulation of DNA Repair Genes and Elevated DNA Damage in Humans**](https://onlinelibrary.wiley.com/doi/10.1111/jpi.12726)**.**

[**Mechanistic Evaluation of Black Cohosh Extract-Induced Genotoxicity in Human Cells**](https://academic.oup.com/toxsci/article/182/1/96/6226518)**.**

[**Performance of High-Throughput CometChip Assay Using Primary Human Hepatocytes: A Comparison of DNA Damage Responses with In Vitro Human Hepatoma Cell Lines**](https://pubmed.ncbi.nlm.nih.gov/32318794/)**.**

[**Evaluation of Pyrrolizidine Alkaloid-Induced Genotoxicity Using Metabolically Competent TK6 Cell Lines**](https://www.sciencedirect.com/science/article/pii/S0278691520305524)**.**

[**Development and Application of TK6-Derived Cells Expressing Human Cytochrome P450s for Genotoxicity Testing**](https://pubmed.ncbi.nlm.nih.gov/32159784/)**.**

[**In Vivo Genotoxicity Testing Strategies: Report from the 7th International Workshop on Genotoxicity Testing (IWGT)**](https://pubmed.ncbi.nlm.nih.gov/31699340/)**.**

[**Genotoxicity Assessment of Nanomaterials: Recommendations on Best Practices, Assays and Methods**](https://pubmed.ncbi.nlm.nih.gov/29701824/)**.**

[**The Development and Validation of EpiComet-Chip, a Modified High-Throughput Comet Assay for the Assessment of DNA Methylation Status**](https://www.ncbi.nlm.nih.gov/pubmed/?term=The+Development+and+Validation+of+EpiComet-Chip%2C+a+Modified+High-Throughput+Comet+Assay+for+the+Assessment+of+DNA+Methylation+Status.)**.**

[**Dose and Temporal Evaluation of Ethylene Oxide-Induced Mutagenicity in the Lungs of Male Big Blue Mice Following Inhalation Exposure to Carcinogenic Concentrations**](https://pubmed.ncbi.nlm.nih.gov/28326610/)**.**

[**Evaluation of cII Gene Mutation in the Brains of Big Blue Mice Exposed to Acrylamide and Glycidamide in Drinking Water**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Evaluation+of+cII+Gene+Mutation+in+the+Brains+of+Big+Blue+Mice+Exposed+to+Acrylamide+and+Glycidamide+in+Drinking+Water.)**.**

[**In Vivo Alkaline Comet Assay and Enzyme-Modified Alkaline Comet Assay for Measuring DNA Strand Breaks and Oxidative DNA Damage in Rat Liver**](https://pubmed.ncbi.nlm.nih.gov/27166647/)**.**

[**Genetic Toxicology: Opportunities to Integrate New Approaches in Genetic Toxicology: An ILSI-HESI Workshop Report**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Genetic%20Toxicology%3A%20Opportunities%20to%20Integrate%20New%20Approaches%20in%20Genetic%20Toxicology%3A%20An%20ILSI-HESI%20Workshop%20Report.)**.**

[**In Vivo Genotoxicity of Estragole in Male F344 Rats**](https://www.ncbi.nlm.nih.gov/pubmed/25361439)**.**

[**Neonatal Exposure of 17β-Estradiol has No Effects on Mutagenicity of 7,12-Dimethylbenz[A]Anthracene in Reproductive Tissues of Adult Mice**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Neonatal%20Exposure%20of%2017%CE%B2-Estradiol%20has%20No%20Effects%20on%20Mutagenicity%20of%207%2C12-Dimethylbenz%5BA%5DAnthracene%20in%20Reproductive%20Tissues%20of%20Adult%20Mice.)**.**

[**Acrylamide-Induced Carcinogenicity in Mouse Lung Involves Mutagenicity: Acrylamide and Glycidamide-Induced cII Gene Mutations in the Lung of Big Blue Mice**](https://www.researchgate.net/publication/271590329_Acrylamide-induced_carcinogenicity_in_mouse_lung_involves_mutagenicity_CII_gene_mutations_in_the_lung_of_big_blue_mice_exposed_to_acrylamide_and_glyc)**.**

[**Evaluation of cII Mutations in Lung of Male Big Blue Mice Exposed by Inhalation to Vanadium Pentoxide for up to 8 Weeks**](https://pubmed.ncbi.nlm.nih.gov/26232257/)**.**

[**Development and Validation of a New Transgenic Hairless Albino Mouse Model for Photocarcinogenicity Studies**](https://pubmed.ncbi.nlm.nih.gov/26338542/)**.**

[**Evaluation of Genotoxicity of Doxorubicin in F344 Rats by Combing the Comet Assay, Flow Cytometric Peripheral Blood Micronucleus Test and Pathway-Focused Gene Expression Profiling**](https://www.researchgate.net/publication/258041037_Genotoxicity_of_Doxorubicin_in_F344_Rats_by_Combining_the_Comet_Assay_Flow-Cytometric_Peripheral_Blood_Micronucleus_Test_and_Pathway-Focused_Gene_Exp)**.**

[**Sex-Specific Dose-Response Analysis of Genotoxicity in Cyproterone Acetate-Treated F344 Rats**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Sex-Specific%20Dose-Response%20Analysis%20of%20Genotoxicity%20in%20Cyproterone%20Acetate-Treated%20F344%20Rats.)**.**

[VIEW FULL BIO – Mugimane Manjanatha, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/mugimane-manjanatha)

# Page McKinzie, Ph.D.

### **Research Microbiologist — Division of Genetic and Molecular Toxicology**

Gene mutations that are involved in cancer development occur in a small number of cells before they are numerous enough to be observed as a tumor. The early detection in human health care and the ability to use rodent models for human-cancer risk assessment both rely on the ability to quantify these few mutant cells from otherwise normal appearing samples. Additionally, sensitive quantification is also needed for accurately determining the composition of tumors, which are inherently heterogeneic. Tumors contain cooperating groups of cells, each with different mutations that are important for the growth, persistence, and metastasis of the cancer. The heterogeneity of tumors can also lead to a relapse after targeted therapy for single mutations, which makes the development of a high-throughput high-sensitivity mutation assay a priority for human health.

Dr. McKinzie is developing new methods for quantifying gene mutations that are involved in cancer formation by leveraging massively parallel sequencing to provide quantitative data for many gene mutations from each of many samples simultaneously. These methods require implementation of error-corrected sequencing methods that begin with proper handling of the sample, library preparation, and proper processing of the data that is produced from the sequencing run. Dr. McKinzie’s laboratory is focused on developing molecular biology and bioinformatics methods to produce highly accurate quantitation of cancer-causing mutations to greatly improve human-cancer risk assessment from various preclinical models. [VIEW FULL BIO – Dr. Page McKinzie](https://www.fda.gov/about-fda/science-research-nctr/page-mckinzie)

**Titles and links to selected publications**

[**Whole Genome Sequencing of Mouse Lymphoma L5178Y-3.7.2C (TK+/-) Reveals Millions of Mutations and Genetic Markers**](https://doi.org/10.1016/j.mrgentox.2016.12.001)**.**

[**Whole Genome and Normalized Mrna Sequencing Reveal Genetic Status of TK6, WTK1, and NH32 Human B-Lymphoblastoid Cell Lines**](https://www.ncbi.nlm.nih.gov/pubmed/26774668)**.**

[**Accumulation of K-ras Codon 12 Mutations in the F344 Rat Distal Colon Following Azoxymethane Exposure**](https://www.ncbi.nlm.nih.gov/pubmed/21370285)**.**

[**Oncomutations as Biomarkers of Cancer Risk**](https://www.ncbi.nlm.nih.gov/pubmed/20740637)**.**

[**ACB-PCR Measurement of K-ras Codon 12 Mutant Fractions in Livers of Big Blue Rats Treated with N-Hydroxy-2-Acetylaminofluorene**](https://www.ncbi.nlm.nih.gov/pubmed/17012303)**.**

[**Allele-Specific Competitive Blocker-PCR Detection of Rare Base Substitution**](https://www.ncbi.nlm.nih.gov/pubmed/15502227)**.**

[**Detection of Rare K-ras Codon 12 Mutations Using Allele-Specific Competitive Blocker PCR**](https://www.ncbi.nlm.nih.gov/pubmed/12034322)**.**

[**Prospects for Applying Genotypic Selection of Somatic Oncomutation to Chemical Risk Assessment**](https://www.ncbi.nlm.nih.gov/pubmed/11673089)**.**

[VIEW FULL BIO – Page McKinzie, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/page-mckinzie)

# Nan Mei, Ph.D.

### **Research Biologist — Division of Genetic and Molecular Toxicology**

Dr. Mei’s research program is focused on utilizing appropriate in vivo and in vitro mutation assays and toxicogenomic techniques to provide key toxicological information for FDA-priority chemicals. He uses the in vivo cII transgenic mutation assay (mouse and rat), the in vitro standard test battery for genotoxicity, and gene expression and pathway analysis to evaluate FDA-relevant chemicals or model carcinogens for their mutagenicity and for determining the mechanisms involved in chemically-induced genetic toxicity. His completed and ongoing projects include the evaluation of the mutagenic effects of direct mutagens, herbal dietary supplements, industrial compounds, nanoparticles, ingredients in cosmetics and other retail products, and tobacco products. Dr. Mei has incorporated toxicogenomic approaches into his research to elucidate molecular mechanisms and create gene signatures for developing potential biomarkers. His research results demonstrate that both in vivo and in vitro mutation assays serve as reliable tools for detecting the types of mutations found in cancer genes and are useful for the hazard-identification portion of human risk assessment. [VIEW FULL BIO – Dr. Nan Mei](https://www.fda.gov/about-fda/science-research-nctr/nan-mei)

**Titles and links to selected publications**

[**The Genotoxicity Potential of Luteolin is Enhanced by CYP1A1 and CYP1A2 in Human Lymphoblastoid TK6 Cells**](https://pubmed.ncbi.nlm.nih.gov/33727136/)**.**

[**Performance of HepaRG and HepG2 Cells in the High-Throughput Micronucleus Assay for In Vitro Genotoxicity Assessment**](https://www.tandfonline.com/doi/abs/10.1080/15287394.2020.1822972)**.**

[**Evaluation of Pyrrolizidine Alkaloid-Induced Genotoxicity Using Metabolically Competent TK6 Cell Lines**](https://www.sciencedirect.com/science/article/pii/S0278691520305524)**.**

[**Development and Application of TK6-Derived Cells Expressing Human Cytochrome P450s for Genotoxicity Testing**](https://pubmed.ncbi.nlm.nih.gov/32159784/)**.**

[**Genetic Toxicity Assessment Using Liver Cell Models: Past, Present, and Future**](https://pubmed.ncbi.nlm.nih.gov/31746269/)**.**

[**Aristolochic Acid-Induced Genotoxicity and Toxicogenomic Changes in Rodents**](https://pubmed.ncbi.nlm.nih.gov/32258091/)**.**

[**In Vivo Genotoxicity Testing Strategies: Report From the 7th International Workshop on Genotoxicity Testing (IWGT)**](https://pubmed.ncbi.nlm.nih.gov/31699340/)**.**

[**Benchmark Dose Modeling of In Vitro Genotoxicity Data: A Reanalysis**](https://pubmed.ncbi.nlm.nih.gov/30370005/)**.**

[**Comparative Genotoxicity of TEMPO and 3 of its Derivatives in Mouse Lymphoma Cells**](https://www.ncbi.nlm.nih.gov/pubmed/29385624)**.**

[**Quantitative Differentiation of Whole Smoke Solution-Induced Mutagenicity in the Mouse Lymphoma Assay**](https://www.ncbi.nlm.nih.gov/pubmed/29119619)**.**

[**ROS Generation and JNK Activation Contribute to 4-Methoxy-TEMPO-Induced Cytotoxicity, Autophagy, and DNA Damage in HepG2 Cells**](https://www.ncbi.nlm.nih.gov/pubmed/28993908)**.**

[**Review of Ginkgo biloba-Induced Toxicity, from Experimental Studies to Human Case Reports**](https://www.ncbi.nlm.nih.gov/pubmed/28055331)**.**

[**Aloe vera: A Review of Toxicity and Adverse Clinical Effects**](https://www.ncbi.nlm.nih.gov/pubmed/26986231)**.**

[**Quantitative Analysis of In Vitro Mutagenicity Induced by Five Chemical Constituents of Tobacco Smoke**](https://www.ncbi.nlm.nih.gov/pubmed/26001754)**.**

[**Ginkgo biloba Leaf Extract Induces DNA Damage by Inhibiting Topoisomerase II Activity in Human Hepatic Cells**](https://www.ncbi.nlm.nih.gov/pubmed/26419945)**.**

[**Neonatal Exposure of 17β-Estradiol has No Effects on Mutagenicity of 7,12-Dimethylbenz[A]Anthracene in Reproductive Tissues of Adult Mice**](https://www.ncbi.nlm.nih.gov/pubmed/27350812)**.**

[**Reactive Oxygen Species and C-Jun N-Terminal Kinases Contribute to TEMPO-Induced Apoptosis in L5178Y Cells**](https://www.ncbi.nlm.nih.gov/pubmed/25882087)**.**

[**Assessment of the Toxic Potential of Grapheme Family Nanomaterials**](https://www.ncbi.nlm.nih.gov/pubmed/24673908)**.**

[**Mechanistic Evaluation of Ginkgo biloba Leaf Extract-Induced Genotoxicity in L5178Y Cells**](https://www.ncbi.nlm.nih.gov/pubmed/24595819)**.**

[**Nitroxide TEMPO: A Genotoxic and Oxidative Stress Inducer in Cultured Cells**](https://www.ncbi.nlm.nih.gov/pubmed/23517621)**.**

[VIEW FULL BIO – Nan Mei, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/nan-mei)

# Meagan Myers, Ph.D.

### **Staff Fellow — Division of Genetic and Molecular Toxicology**

Dr. Myers’ research focuses on developing somatic hotspot-point mutations as quantitative biomarkers of cancer risk. Utilizing the highly-sensitive, Allele-specific Competitive Blocker PCR method, she has quantified levels of hotspot cancer-driver mutations, such as those found in *KRAS*, in various human tissues and tumors. Her research interests include defining normal and pathological levels of cancer-relevant mutations, with the ultimate goal of understanding how low-frequency mutant subpopulations in tumors may contribute to acquired resistance to cancer therapies.

**Detection of cancer-driver mutant subpopulations and their potential impact on molecularly-targeted therapy**  
Tumor mutations are being used as predictive biomarkers of therapeutic response to select the most effective treatments for individual cancer patients. Currently, this is being done without sufficient characterization of relevant oncogene mutations as quantitative biomarkers. Sensitive and quantitative analyses of prevalent cancer-driver mutations is necessary to understand the role of mutant-tumor subpopulations in patient response and to develop effective strategies to ensure such mutations do not lead to acquired drug resistance and/or relapse. Dr. Myers work has led to several significant findings, including:

* low-frequency cancer-driver point mutations are prevalent in the DNA of normal tissues
* many tumors carry subpopulations of these cancer-driver mutations that would go undetected by standard mutation detection techniques (e.g. DNA sequencing)
* these mutations co-occur frequently in normal and tumor samples.

**Oncomutational profile of triple-negative breast cancer**  
It is recognized that breast cancer is a heterogeneous disease, with respect to clinical features, prognosis, and response to cancer therapies. Yet, relatively little is known regarding the frequency and potential role of subclonal cancer-driver mutations in the different subtypes of breast cancer, including triple-negative breast cancer. Dr. Myers is the principal investigator of an FDA Office of Women’s Health (OWH)-funded project that aims to quantify cancer-driver mutations in breast-cancer subtypes to help direct personalized-medicine approaches to treat breast cancer, including triple-negative breast cancer. This project has received additional OWH funding to expand the racial diversity of the study to include additional ductal carcinomas from African American women.

**Mutation Detection applications of Droplet Digital PCR**  
Genetic testing plays a major role in the diagnosis, treatment, and management of cancer. The value of cancer-driver mutations in precision medicine, as both prognostic and predictive biomarkers, is evident for multiple cancer types. Given the intratumor heterogeneity present in many tumor types, however, accurately detecting and quantifying these specific cancer-driver mutations is challenging. Droplet Digital PCR (ddPCR), which quantifies target nucleic acids in a water-in-oil emulsion using microfluidics, has been marketed as an ultra-sensitive platform to accurately quantify low-frequency cancer-driver mutations in human-tumor DNA and DNA from liquid biopsies. The purported sensitivity and ease of use could make ddPCR a viable candidate for application as an in vitro diagnostic in the clinical setting, however, pre-analytical and analytical questions regarding the use of ddPCR have been raised. To address some of these concerns, Dr. Myers received protocol approval to assess the utility and analytical performance of ddPCR for detecting somatic-cancer variants through concordance to other methods such as next-generation sequencing and ACB-PCR. [VIEW FULL BIO – Dr. Meagan Myers](https://www.fda.gov/about-fda/science-research-nctr/meagan-myers)

**Titles and links to selected publications**

[**Breast Cancer Heterogeneity Examined by High-Sensitivity Quantification of PIK3CA, KRAS, HRAS, and BRAF Mutations in Normal Breast and Ductal Carcinomas**](http://www.ncbi.nlm.nih.gov/pubmed/27108388)**.**

[**Targeted Therapies with Companion Diagnostics in the Management of Breast Cancer: Current Perspectives**](https://www.ncbi.nlm.nih.gov/pubmed/26858530)**.**

[**Low-Frequency KRAS Mutations are Prevalent in Lung Adenocarcinomas**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Low-Frequency+KRAS+Mutations+Are+Prevalent+In+Lung+Adenocarcinomas)**.**

[**A Subset of Papillary Thyroid Carcinomas Contain KRAS Mutant Subpopulations at Level Above Normal Thyroid**](http://onlinelibrary.wiley.com/doi/10.1002/mc.21953/abstract;jsessionid=EB9A24165EBF430FFD88CABC8D392C98.f01t01)**.**

[**ACB-PCR Quantification of Somatic Oncomutation**](https://www.ncbi.nlm.nih.gov/pubmed/?term=ACB-PCR+Quantification+Of+Somatic+Oncomutation)**.**

**Mutagenesis and Genetic Toxicology.**

[**Temporal Changes in K-ras Mutant Fraction in Lung Tissue of Big Blue B6C3F(1) Mice Exposed to Ethylene Oxide**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Temporal+Changes+In+K-Ras+Mutant+Fraction+In+Lung+Tissue+Of+Big+Blue+B6C3F(1)+Mice)**.**

[**Personalized Cancer Treatment and the Myth of KRAS Wild-Type Colon Tumors**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Personalized+Cancer+Treatment+And+The+Myth+Of+KRAS+Wild-Type+Colon+Tumors)**.**

[**Assessment of K-Ras Mutant Frequency and Micronucleus Incidence in the Mouse Duodenum Following 90-Days of Exposure to Cr(VI) in Drinking Water**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Assessment+Of+K-Ras+Mutant+Frequency+And+Micronucleus+Incidence+In+The+Mouse+Duodenum+Following+90-Days+Of+Exposure+To+Cr(VI)+In+Drinking+Water)**.**

[**KRAS Mutant Tumor Subpopulations Can Subvert Durable Responses to Personalized Cancer Treatments**](https://www.ncbi.nlm.nih.gov/pubmed/?term=KRAS+Mutant+Tumor+Subpopulations+Can+Subvert+Durable+Responses+To+Personalized+Cancer+Treatments)**.**

[**ACB-PCR Measurement of H-ras Codon 61 CAA-->CTA Mutation Provides an Early Indication of Aristolochic Acid I Carcinogenic Effect in Tumor Target Tissues**](https://www.ncbi.nlm.nih.gov/pubmed/?term=ACB-PCR+Measurement+Of+H-Ras+Codon+61+CAA--%3ECTA+Mutation+Provides+An+Early+Indication+Of+Aristolochic+Acid+I+Carcinogenic+Effect+In+Tumor+Target+Tissues)**.**

[**Hotspot Oncomutations: Implications for Personalized Cancer Treatment**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Hotspot+Oncomutations%3A+Implications+For+Personalized+Cancer+Treatment)**.**

[**P53 Codon 271 CGT to CAT Mutant Fraction Does Not Increase in Nasal Respiratory and Olfactory Epithelia of Rats Exposed to Inhaled Naphthalene**](https://www.ncbi.nlm.nih.gov/pubmed/?term=P53+Codon+271+CGT+To+CAT+Mutant+Fraction+Does+Not+Increase+In+Nasal+Respiratory+And+Olfactory+Epithelia+Of+Rats+Exposed+To+Inhaled+Naphthalene)**.**

[**Oncomutations as Biomarkers of Cancer Risk**](https://www.ncbi.nlm.nih.gov/pubmed/20740637)**.**

[**Using Phix174 DNA as an Exogenous Reference for Measuring Mitochondrial DNA Copy Number**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Using%20Phix174%20DNA%20As%20An%20Exogenous%20Reference%20For%20Measuring%20Mitochondrial%20DNA%20Copy%20Number)**.**

[**Accumulation of Point Mutations in Mitochondrial DNA of Aging Mice**](https://www.ncbi.nlm.nih.gov/pubmed/12714177)**.**

[VIEW FULL BIO – Meagan Myers, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/meagan-myers)

# Barbara Parsons, Ph.D.

### **Research Microbiologist — Division of Genetic and Molecular Toxicology**

Methods for assessing the carcinogenic potential of new drug entities, food and drug contaminants, or other chemical exposures are absolutely necessary. Unfortunately, current methods are costly, time-consuming, and the application of rodent testing data to human-health protection is imprecise. Therefore, Dr. Parsons is collaborating with a group of scientists at NCTR, who are working to develop new approaches and novel biomarkers to improve carcinogenicity safety assessment. At the core of this work is the idea that hotspot cancer-driver mutations (CDMs) will be relevant and sensitive biomarkers of chemical carcinogenic effect and can be monitored as part of carcinogenic risk assessment.

Dr. Parsons’s group has developed proof-of-principle that following short-term exposures to model mutagenic carcinogens, ACB-PCR detect the induction of hotspot-point mutations (e.g., mutations in *KRAS*, *HRAS*, and *TP53*) in DNA isolated from tissues of exposed rodents. In fact, this work suggests that CDMs are highly-sensitive biomarkers of carcinogenic effect. The possibility that such mutations can also serve as reporters of chemicals considered to be non-genotoxic, cancer “promoters” (rather than genotoxic “initiators”) remains an important question to be investigated in the future.

Advancing the field of Personalized Medicine is another goal being addressed by Dr. Parsons and her lab at NCTR. Specifically, they have been developing the knowledge necessary to utilize hotspot CDMs as biomarkers of cancer susceptibility and therapeutic response in the clinical setting. Dr. Parsons and colleagues used ACB-PCR to quantify levels of *KRAS* and *PIK3CA* hotspot-point mutations in normal human tissues (breast, colon, lung, and thyroid), as well as in cancers that develop from those organs.  This work demonstrated that these hotspot CDMs occur at remarkably high levels in some tissues (e.g., *PIK3CA* H1047R in breast tissue) and their organ-specific prevalence mirrors the reported prevalence of the same mutations detected in tumors by DNA sequencing.

ACB-PCR analyses of hotspot CDMs, in a limited number of genes (*KRAS, HRAS, PIK3CA*, and *BRAF*), showed that low-frequency mutant-tumor subpopulations are remarkably common. Based on their analyses of*KRAS* G12D and G12V in colon and lung adenocarcinomas, for example, Dr. Parsons and colleagues predicted that virtually all colon and lung tumors will carry a *KRAS* mutation at some level.  This observation is consistent with the acquired resistance that develops predictably in the majority of colon- and lung-cancer patients treated with inhibitors of Epidermal Growth Factor Receptor (EGFR) (due to the pre-treatment existence of tumor subpopulations carrying *KRAS* or other CDMs). Combination treatments with multiple molecularly targeted anti-cancer drugs may be necessary to circumvent acquired resistance. This means models are needed to identify the most promising combination therapies for subsequent clinical evaluation. Given this need, Dr. Parsons’s group recently developed a 3D lung-tumor organoid model and showed that, under conditions of treatment an EGFR inhibitor (erlotinib), it could detect the outgrowth of mutant-tumor subpopulations known to cause resistance to treatment in the clinical setting. Thus, this model may be useful for identifying efficacious combination therapies that prevent the outgrowth of resistant-causing mutant subpopulations.

Most recently, Dr. Parson’s lab has begun developing error-corrected Next Generation Sequencing (NGS) methods to: 1) enable the analysis of a larger battery of hotspot CDMs. 2) compare the sensitivities of NGS, ddPCR, and ACB-PCR, and 3) identify which rodent CDMs have tissue-specific properties that mirror human CDMs. The intent of this work is to improve the translatability of carcinogenicity testing in rodents to human cancer-risk assessment. [VIEW FULL BIO – Dr. Barbara Parsons](https://www.fda.gov/about-fda/science-research-nctr/barbara-parsons)

**Titles and links to selected publications**

[**Variation in Organ‐Specific *PIK3CA* and *KRAS* Mutant Levels in Normal Human Tissues Correlates with Mutation Prevalence in Corresponding Carcinomas**](https://www.ncbi.nlm.nih.gov/pubmed/28755461)**.**

[**Breast Cancer Heterogeneity Examined by High-Sensitivity Quantification of *PIK3CA*, *KRAS*, *HRAS*, and *BRAF* Mutations in Normal Breast and Ductal Carcinomas**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Breast+Cancer+Heterogeneity+Examined+by+High-Sensitivity+Quantification+of+PIK3CA%2C+KRAS%2C+HRAS%2C+and+BRAF+Mutations+in+Normal+Breast+and+Ductal+Carcinomas)**.**

[**Quantification of *Kras* Mutant Fraction in the Lung DNA of Mice Exposed to Aerosolized Particulate Vanadium Pentoxide by Inhalation**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Quantification+Of+Kras+Mutant+Fraction+In+The+Lung+DNA+Of+Mice+Exposed+To+Aerosolized+Particulate+Vanadium+Pentoxide+By+Inhalation)**.**

[**Low-Frequency *KRAS* Mutations are Prevalent in Lung Adenocarcinomas**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Low-Frequency+KRAS+Mutations+Are+Prevalent+In+Lung+Adenocarcinomas)**.**

[**A Subset of Papillary Thyroid Carcinomas Contain *KRAS* Mutant Subpopulations at Levels Above Normal Thyroid**](https://www.ncbi.nlm.nih.gov/pubmed/?term=A+Subset+Of+Papillary+Thyroid+Carcinomas+Contain+KRAS+Mutant+Subpopulations+At+Levels+Above+Normal+Thyroid)**.**

[**Temporal Changes in K-Ras Mutant Fraction in Lung Tissue of Big Blue B6C3F₁ Mice Exposed to Ethylene Oxide**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Temporal+Changes+In+K-Ras+Mutant+Fraction+In+Lung+Tissue+Of+Big+Blue+B6C3F%E2%82%81+Mice+Exposed+To+Ethylene+Oxide)**.**

[**Personalized Cancer Treatment and the Myth of *KRAS* Wild-Type Colon Tumors**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Personalized+Cancer+Treatment+And+The+Myth+Of+KRAS+Wild-Type+Colon+Tumors)**.**

[***KRAS* Mutant Tumor Subpopulations Can Subvert Durable Responses to Personalized Cancer Treatments**](https://www.ncbi.nlm.nih.gov/pubmed/?term=KRAS+Mutant+Tumor+Subpopulations+Can+Subvert+Durable+Responses+To+Personalized+Cancer+Treatments)**.**

[**ACB-PCR Measurement of H-Ras Codon 61 CAA→CTA Mutation Provides an Early Indication of Aristolochic Acid I Carcinogenic Effect in Tumor Target Tissues**](https://www.ncbi.nlm.nih.gov/pubmed/?term=ACB-PCR+Measurement+Of+H-Ras+Codon+61+CAA%E2%86%92CTA+Mutation+Provides+An+Early+Indication+Of+Aristolochic+Acid+I+Carcinogenic+Effect+In+Tumor+Target+Tissues)**.**

[**Hotspot Oncomutations: Implications for Personalized Cancer Treatment**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Hotspot+Oncomutations%3A+Implications+For+Personalized+Cancer+Treatment)**.**

[**Oncomutations as Biomarkers of Cancer Risk**](https://www.ncbi.nlm.nih.gov/pubmed/20740637)**.**

[**ACB-PCR Quantification of K-RAS Codon 12 GAT and GTT Mutant Fraction in Colon Tumor and Non-Tumor Tissue**](https://www.ncbi.nlm.nih.gov/pubmed/?term=ACB-PCR+Quantification+Of+K-RAS+Codon+12+GAT+And+GTT+Mutant+Fraction+In+Colon+Tumor+And+Non-Tumor+Tissue)**.**

[**K-Ras Mutant Fraction in A/J Mouse Lung Increases as a Function of Benzo[A]Pyrene Dose**](https://www.ncbi.nlm.nih.gov/pubmed/?term=K-Ras+Mutant+Fraction+In+A%2FJ+Mouse+Lung+Increases+As+A+Function+Of+Benzo%5BA%5DPyrene+Dose)**.**

[**K-RAS Mutation in the Screening, Prognosis and Treatment of Cancer**](https://www.ncbi.nlm.nih.gov/pubmed/20477713)**.**

[**Populations of P53 Codon 270 CGT to TGT Mutant Cells in SKH-1 Mouse Skin Tumors Induced by Simulated Solar Light**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Populations+Of+P53+Codon+270+CGT+To+TGT+Mutant+Cells+In+SKH-1+Mouse+Skin+Tumors+Induced+By+Simulated+Solar+Light)**.**

[**Many Different Tumor Types have Polyclonal Tumor Origin: Evidence and Implications**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Many+Different+Tumor+Types+Have+Polyclonal+Tumor+Origin%3A+Evidence+And+Implications)**.**

[**Simulated Solar Light-Induced P53 Mutagenesis in SKH-1 Mouse Skin: A Dose-Response Assessment**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Simulated+Solar+Light-Induced+P53+Mutagenesis+In+SKH-1+Mouse+Skin%3A+A+Dose-Response+Assessment)**.**

[**ACB-PCR Measurement of K-Ras Codon 12 Mutant Fractions in Livers of Big Blue Rats Treated with N-Hydroxy-2-Acetylaminofluorene**](https://www.ncbi.nlm.nih.gov/pubmed/?term=ACB-PCR+Measurement+Of+K-Ras+Codon+12+Mutant+Fractions+In+Livers+Of+Big+Blue+Rats+Treated+With+N-Hydroxy-2-Acetylaminofluorene)**.**

[**Levels of 4-Aminobiphenyl-Induced Somatic H-Ras Mutation in Mouse Liver DNA Correlate with Potential for Liver Tumor Development**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Levels+Of+4-Aminobiphenyl-Induced+Somatic+H-Ras+Mutation+In+Mouse+Liver+DNA+Correlate+With+Potential+For+Liver+Tumor+Development)**.**

[**Allele-Specific Competitive Blocker-PCR Detection of Rare Base Substitution**](https://www.ncbi.nlm.nih.gov/pubmed/15502227)**.**

[**Prospects for Applying Genotypic Selection of Somatic Oncomutation to Chemical Risk Assessment**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Prospects+For+Applying+Genotypic+Selection+Of+Somatic+Oncomutation+To+Chemical+Risk+Assessment)**.**

[VIEW FULL BIO – Barbara Parsons, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/barbara-parsons)

# Dayton Petibone, Ph.D.

### **Biologist — Division of Genetic and Molecular Toxicology**

Investigating the effect p53 functional status has in toxicity is an overarching subject in Dr. Petibone’s research. The p53 protein activates gene expression and cell-signaling pathways:

* in response to stress stimuli
* to correct DNA damage
* to suppress tumor formation.

Constant exposure to endogenous and exogenous stressors can inflict damage to cells within the human body. This damage includes DNA mutation that can result in disease or cancer. To maintain a healthy status, cells must have a way to identify and correct DNA damage, so as not to transmit corrupted genetic information to subsequent generations of daughter cells. Following DNA damage, activation of p53-mediated signaling pathways has three primary cellular outcomes to restore stability: 1) cell cycle arrest with DNA repair and cell cycle restart, 2) cell senescence, or 3) apoptosis. However, if not corrected through p53-regulated pathways, mutated and proliferating pre-neoplastic cells might result in tumors. The p53 gene is one of the most studied targets in cancer research, and it is known that over half of the tumors which arise in humans harbor a mutation in the p53 gene. Evaluating the role of p53 in cellular responses to potentially toxic agents can provide useful information as to the level of toxicity and the mode-of-action for an agent, especially as p53 functional status relates to DNA damage.

Structural chromosome damage is a hallmark of cancer and assessing chromosome damage is critical when evaluating the potential genotoxicity of a suspected test agent. Whole-chromosome fluorescence in situ hybridization (FISH) of metaphase cells provides a means for rapidly and accurately analyzing structural chromosome aberrations with single-cell level resolution. FISH-painted metaphase cells labeled as described below allows for higher-throughput analysis compared to classic cytogenetic methods and allows for identifying chromosome exchanges.

* chromosomes 1, 2, and 4 labeled red
* chromosomes 3, 5, and 6 labeled green
* all chromosomes counter-stained blue.

These genetic exchanges include identifying reciprocal/non-reciprocal chromosome translocations, insertion events, and dicentric chromosomes to evaluate genotoxicity and predict carcinogenesis. Dr. Petibone specializes in developing and applying molecular FISH techniques for assessing the ability of potential genotoxicants to induce structural chromosome damage.

Gene-mutation tests are vital tools used for detecting genotoxicity as a means to predict carcinogenic potential. Despite their importance in making regulatory decisions, there are inherent limitations to the current mammalianin vitro gene-mutation assays. A main shortcoming of many in vitro gene-mutation assays is the use of nucleotide-metabolism genes as the mutagenesis target — genes which are not involved in carcinogenesis but serve as a proxy for cancer-relevant tumor-suppressor gene mutagenesis. Additionally, gene-mutation analysis often depends on extended time periods of mutant-clonal expansion, making the gene-mutation assays laborious and with limited adaptability for high-throughput screening.  Recently, Dr. Petibone has undertaken research to advance the development, modernization, and validation of existing gene-mutation assays specifically for high-throughput analysis, and the innovation of new gene-mutation assays that are relevant to human cancer. [VIEW FULL BIO – Dr. Dayton Petibone](https://www.fda.gov/about-fda/science-research-nctr/dayton-petibone)

**Titles and links to selected publications**

[**p53-Competent Cells and p53-Deficient Cells Display Different Susceptibility to Oxygen Functionalized Graphene Cytotoxicity and Genotoxicity**](https://www.ncbi.nlm.nih.gov/pubmed/?term=p53-competent+cells+and+p53-deficient+cells+display+different+susceptibility+to+oxygen+functionalized+graphene+cytotoxicity+and+genotoxicity)**.**

[**In Vivo Rat T-Lymphocyte Pig-A Assay: Detection and Expansion of Cells Deficient in the GPI-Anchored CD48 Surface Marker for Analysis of Mutation in the Endogenous Pig-A Gene**](https://pubmed.ncbi.nlm.nih.gov/28748462/)**.**

[**The Role of Surface Chemistry in the Cytotoxicity Profile of Graphene**](http://onlinelibrary.wiley.com/doi/10.1002/jat.3379/abstract)**.**

[**Autophagy Function and its Relationship to Pathology, Clinical Applications, Drug Metabolism, and Toxicity**](http://onlinelibrary.wiley.com/doi/10.1002/jat.3393/abstract)**.**

[**Whole Genome and Normalized Mrna Sequencing Reveal Genetic Status of TK6, WTK1, and NH32 Human B-Lymphoblastoid Cell Lines**](http://www.sciencedirect.com/science/article/pii/S1383571815002740)**.**

[**Confirmation of *Pig-A* Mutation in Flow Cytometry-Identified CD48-Deficient T-Lymphocytes Derived from Spleens of ENU-Treated F344 Rats**](http://mutage.oxfordjournals.org/content/30/3/315.long)**.**

[**Chromosome Painting of Mouse Peripheral Blood and Spleen Tissues**](https://link.springer.com/protocol/10.1007/978-1-4939-1068-7_8)**.**

[**p53 Alters the Biologically Effective Dose, Cytotoxicity, and Genotoxicity for Oxidized Graphene in Human Lymphoblastoid Cells**](https://www.hindawi.com/journals/jt/2014/872195/)**.**

[**Toxicity and Efficacy of Carbon Nanotubes and Graphene: The Utility of Carbon-Based Nanoparticles in Nanomedicine**](http://www.tandfonline.com/doi/full/10.3109/03602532.2014.883406)**.**

[**In Vivo Genotoxicity of Furan in F344 Rats at Cancer Bioassay Doses**](http://www.sciencedirect.com/science/article/pii/S0041008X1200124X)**.**

[**The Genetic Toxicity of Methylphenidate: A Review of the Current Literature**](http://onlinelibrary.wiley.com/doi/10.1002/jat.2721/abstract)**.**

[**Evaluation of P53 Genotype on Gene Expression in the Testis, Liver and Heart from Male C57BL/6 Mice**](https://link.springer.com/article/10.1007%2Fs11248-011-9526-6)**.**

[**Pubertal Delay in Male Non-Human Primates (Macaca mulatta) Treated with Methylphenidate**](http://www.pnas.org/content/108/39/16301.long)**.**

[**Effect of P53 Genotype on Gene Expression and DNA Adducts in ENU-Exposed Mice**](http://onlinelibrary.wiley.com/doi/10.1002/9780470744307.gat203/abstract)**.**

[**Oligonucleotide Immobilization using 10-(carbomethoxy)Decyl-Dimethylchlorosilane for mRNA Isolation and cDNA Synthesis on a Microfluidic Chip**](http://www.sciencedirect.com/science/article/pii/S0925400510009731)**.**

[**Cytogenetic Assessment of Methylphenidate Treatment in Pediatric Patients Treated for Attention Deficit Hyperactivity Disorder**](http://www.sciencedirect.com/science/article/pii/S1383571809001685)**.**

[**The Genetic Toxicology of Methylphenidate Hydrochloride in Non-Human Primates**](http://www.sciencedirect.com/science/article/pii/S1383571808003859)**.**

[**Routine Diagnostic X-ray Examinations and Increased Frequency of Chromosome Translocations Among United States Radiologic Technologists**](http://cancerres.aacrjournals.org/content/68/21/8825.long)**.**

[**Technique for Culturing Macaca mulatta Peripheral Blood Lymphocytes for Fluorescence in Situ Hybridization of Whole Chromosome Paints**](http://www.sciencedirect.com/science/article/pii/S1383571808000983)**.**

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[VIEW FULL BIO – Dayton Petibone, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/dayton-petibone)

# Javier Revollo, Ph.D.

### **Staff Fellow — Division of Genetic and Molecular Toxicology**

The flow cytometry-based *Pig-a* assay detects cells deficient in Glycosylphosphatidylinositol (or GPI)-anchored surface markers and provides a rapid and cost-effective enumeration of cells that are presumed to contain mutations in the endogenous X-linked *Pig-a* gene. Dr. Revollo is currently working on the validation of the *Pig-a* assay by genetically characterizing presumed *Pig-a* mutants derived from the assay.

Another research area that interests Dr. Revollo is the direct detection of somatic mutations. Somatic mutations are genetic alterations in cells that increase cancer risk. They can occur spontaneously but also result from DNA damage induced by the environment (e.g., sunlight) or genotoxic compounds (e.g, carcinogens). Current genetic toxicology assays can only estimate somatic-mutation rates by assaying the function of certain gene markers (e.g., *Pig-a*) or transgenes. Dr. Revollo is developing NGS methods capable of directly and efficiently identifying somatic mutations in the whole genome — in any tissue, and in any species, or any established cell culture — without the need for selecting and expanding cells that have mutations in only a few specific reporter genes. [VIEW FULL BIO – Dr. Javier Revollo](https://www.fda.gov/about-fda/science-research-nctr/javier-revollo)

**Titles and links to selected publications**

[**Whole Genome Sequencing of Mouse Lymphoma L5178Y-3.7.2C (TK+/-) Reveals Millions of Mutations and Genetic Markers**](https://pubmed.ncbi.nlm.nih.gov/28137362/)**.**

[**Mutation Analysis with Random DNA Identifiers (MARDI) Catalogs Pig-A Mutations in Heterogeneous Pools of CD48-Deficient T Cells Derived from DMBA-Treated Rats**](https://pubmed.ncbi.nlm.nih.gov/26683280/)**.**

[**Whole Genome and Normalized mRNA Sequencing Reveal Genetic Status of TK6, WTK1, and NH32 Human B-Lymphoblastoid Cell Lines**](https://pubmed.ncbi.nlm.nih.gov/26774668/)**.**

[**CD48-Deficient T-Lymphocytes from DMBA-Treated Rats have De Novo Mutations in the Endogenous Pig-A Gene**](https://pubmed.ncbi.nlm.nih.gov/26033714/)**.**

[**Confirmation of Pig-A Mutation in Flow Cytometry-Identified CD48-Deficient T-Lymphocytes from F344 Rats**](https://pubmed.ncbi.nlm.nih.gov/25820172/)**.**

[**Draft Genome Sequence of a Methicillin-Resistant Staphylococcus aureus ST1413 Strain for Studying Genetic Mechanisms of Antibiotic Resistance**](https://pubmed.ncbi.nlm.nih.gov/24604656/)**.**

[**HES1 is a Master Regulator of Glucocorticoid Receptor-Dependent Gene Expression**](https://pubmed.ncbi.nlm.nih.gov/24300895/)**.**

[**The Ways and Means that Fine Tune Sirt1 Activity**](https://pubmed.ncbi.nlm.nih.gov/23394938/)**.**

[**Glucocorticoids Regulate Arrestin Gene Expression and Redirect the Signaling Profile of G Protein-Coupled Receptors**](https://pubmed.ncbi.nlm.nih.gov/23045642/)**.**

[**Mechanisms Generating Diversity In Glucocorticoid Receptor Signaling**](https://pubmed.ncbi.nlm.nih.gov/19906239/)**.**

[**Nampt/PBEF/Visfatin Regulates Insulin Secretion in Beta Cells as a Systemic NAD Biosynthetic Enzyme**](https://pubmed.ncbi.nlm.nih.gov/17983582/)**.**

[**The Regulation of Nicotinamide Adenine Dinucleotide Biosynthesis by Nampt/PBEF/Visfatin in Mammals**](https://pubmed.ncbi.nlm.nih.gov/17268245/)**.**

[**Structure of Nampt/PBEF/Visfatin, a Mammalian NAD+ Biosynthetic Enzyme**](https://pubmed.ncbi.nlm.nih.gov/16783373/)**.**

[**The NAD Biosynthesis Pathway Mediated by Nicotinamide Phosphoribosyltransferase Regulates Sir2 Activity in Mammalian Cells**](https://pubmed.ncbi.nlm.nih.gov/15381699/)**.**

[**Sphingolipids are Essential for Differentiation but not Growth in Leishmania**](https://pubmed.ncbi.nlm.nih.gov/14609948/)**.**

[VIEW FULL BIO – Javier Revollo, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/javier-revollo)

# Ji-Eun Seo, Ph.D.

### **Staff Fellow — Division of Genetic and Molecular Toxicology**

Dr. Seo’s research involves developing new approach methodologies for better evaluating the preclinical genotoxicity of products intended for human use. She has established appropriate human-based in vitro cell models with metabolic competence with the aim of generating data more relevant to human in vivo exposures. Dr. Seo optimized cell culture systems for conducting HT genotoxicity assays in different types of human liver cells (e.g., HepaRG, HepG2, and primary human hepatocytes). These systems have been used to evaluate the genotoxicity of FDA-relevant compounds having different genotoxicity and carcinogenicity modes of action using the HT CometChip assay and HT flow-cytometry-based micronucleus (MN) assay. The HT genotoxicity data have been evaluated using computational dose-response modeling to derive benchmark dose metrics, which have been used to compare the genotoxicity of compounds in the different cell models. Dr. Seo has expanded the application of HT in vitro genotoxicity in a 3D culture system for better predicting in vivo genotoxicity. Recently, she adapted 3D HepaRG spheroids to the HT CometChip and MN assays for detecting DNA strand breaks and MN formation. Another research interest of hers is exploring approaches for using error-corrected next generation sequencing (ecNGS) to evaluate in vitro mutagenicity in mammalian cells. The advanced ecNGS technology combined with 3D HepaRG spheroids can improve the accuracy of mutagenicity evaluation and provide additional evidence for the risk assessment of mutagenic compounds. [VIEW FULL BIO – Dr. Ji-Eun Seo](https://www.fda.gov/about-fda/science-research-nctr/ji-eun-seo)

**Titles and links to selected publications**

[**Evaluation of an In Vitro Three-Dimensional HepaRG Spheroid Model for Genotoxicity Testing Using the High-Throughput CometChip Platform**](https://pubmed.ncbi.nlm.nih.gov/35791290/)**.**

[**Genotoxicity Evaluation Using Primary Hepatocytes Isolated from Rhesus Macaque (Macaca mulatta)**](https://pubmed.ncbi.nlm.nih.gov/34509578/)**.**

[**Mechanistic Evaluation of Black Cohosh Extract-Induced Genotoxicity in Human Cells**](https://pubmed.ncbi.nlm.nih.gov/33856461/)**.**

[**Employing Metabolomic Approaches to Determine the Influence of Age on Experimental Autoimmune Encephalomyelitis (EAE)**](https://pubmed.ncbi.nlm.nih.gov/33873097/)**.**

[**Performance of HepaRG and HepG2 Cells in the High-Throughput Micronucleus Assay for In Vitro Genotoxicity Assessment**](https://pubmed.ncbi.nlm.nih.gov/32981483/)**.**

[**Mitochondrial Dysfunction and Apoptosis Underlie the Hepatotoxicity of Perhexiline**](https://pubmed.ncbi.nlm.nih.gov/32861758/)**.**

[**Performance of High-Throughput CometChip Assay Using Primary Human Hepatocytes: A Comparison of DNA Damage Responses with In Vitro Human Hepatoma Cell Lines**](https://pubmed.ncbi.nlm.nih.gov/32318794/)**.**

[**Development and Application of TK6-Derived Cells Expressing Human Cytochrome P450s for Genotoxicity Testing**](https://pubmed.ncbi.nlm.nih.gov/32159784/)**.**

[**Genetic Toxicity Assessment Using Liver Cell Models: Past, Present, and Future**](https://pubmed.ncbi.nlm.nih.gov/31746269/)**.**

[**Quantitative Comparison of In Vitro Genotoxicity Between Metabolically Competent HepaRG Cells and HepG2 Cells Using the High-Throughput High-Content CometChip Assay**](https://pubmed.ncbi.nlm.nih.gov/30788552/)**.**

[**Whole Genome Sequencing Analysis of Small and Large Colony Mutants from the Mouse Lymphoma Assay**](https://pubmed.ncbi.nlm.nih.gov/30328498/)**.**

[**The Development of a Database for Herbal and Dietary Supplement Induced Liver Toxicity**](https://pubmed.ncbi.nlm.nih.gov/30274144/)**.**

[**Comparative Genotoxicity of TEMPO and 3 of Its Derivatives in Mouse Lymphoma Cells**](https://pubmed.ncbi.nlm.nih.gov/29385624/)**.**

[**Novel Genes in Brain Tissues of EAE-Induced Normal and Obese Mice: Upregulation of Metal Ion-Binding Protein Genes in Obese-EAE Mice**](https://pubmed.ncbi.nlm.nih.gov/27956064/)**.**

[**A Leading Role for NADPH Oxidase in an In-Vitro Study of Experimental Autoimmune Encephalomyelitis**](https://pubmed.ncbi.nlm.nih.gov/26928315/)**.**

[**Increased Levels of Brain Serotonin Correlated with MMP-9 Activity and IL-4 Levels Resulted in Severe Experimental Autoimmune Encephalomyelitis (EAE) in Obese Mice**](https://pubmed.ncbi.nlm.nih.gov/26820599/)**.**

[**Dependency of Experimental Autoimmune Encephalomyelitis Induction on MOG35-55 Properties Modulating Matrix Metalloproteinase-9 and Interleukin-6**](https://pubmed.ncbi.nlm.nih.gov/26464215/)**.**

[**Experimental Autoimmune Encephalomyelitis and Age-Related Correlations of NADPH Oxidase, MMP-9, and Cell Adhesion Molecules: The Increased Disease Severity and Blood-Brain Barrier Permeability in Middle-Aged Mice**](https://pubmed.ncbi.nlm.nih.gov/26439961/)**.**

[**Acute Toxicity and Tissue Distribution of CdSe/CdS-MPA Quantum Dots after Repeated Intraperitoneal Injection to Mice**](https://pubmed.ncbi.nlm.nih.gov/22733552/)**.**

[**In Vitro Screening of NADPH Oxidase Inhibitors and In Vivo Effects of L-leucinethiol on Experimental Autoimmune Encephalomyelitis-Induced Mice**](https://pubmed.ncbi.nlm.nih.gov/22554692/)**.**

[VIEW FULL BIO – Ji-Eun Seo, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/ji-eun-seo)

# Yiying Wang, Ph.D.

### **Staff Fellow — Division of Genetic and Molecular Toxicology**

Dr. Wang's primary research focus is on the development and utilization of alternative in vitro testing approaches to provide scientific information and to aid regulatory decisions related to drugs and consumer products. Her current research goals are to develop genotoxicity assays and mutation assays in airway organotypic tissue models and microphysiological systems as a means for providing data for the realistic assessment of human cancer risk. She also is interested in using an in vitro human co-culture system consisting of a placental barrier, that serves as a mediator controlling the molecular transport between mother and fetus, and human embryonic stem cells (hESCs), representing an alternative in vitro model of the developing embryo. The model is being used to study human embryo-fetal developmental toxicity. A third ongoing project uses an advanced human three-dimensional (3D) airway epithelium tissue model and novel aerosol and vapor exposure systems to assess respiratory toxicity under conditions mimicking human inhalation exposure. [VIEW FULL BIO – Dr. Yiyang Wang](https://www.fda.gov/about-fda/science-research-nctr/yiying-wang)

**Titles and links to selected publications**

[**Dr. Daniel Acosta and In Vitro Toxicology at the U.S. Food and Drug Administration's National Center for Toxicological Research**](https://pubmed.ncbi.nlm.nih.gov/31628011/)**.**

[**ACB-PCR Quantification of Low-Frequency Hotspot Cancer-Driver Mutations**](https://pubmed.ncbi.nlm.nih.gov/31989569/)**.**

[**Assessing the Respiratory Toxicity of Dihydroxyacetone Using an In Vitro Human Airway Epithelial Tissue Model**](https://pubmed.ncbi.nlm.nih.gov/30959092/)**.**

[**Effects of Cellular Differentiation in Human Primary Bronchial Epithelial Cells: Metabolism of 4-(methylnitrosamine)-1-(3-pyridyl)-1-butanone**](https://pubmed.ncbi.nlm.nih.gov/30552994/)**.**

[**Evaluation of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) Mutagenicity Using In Vitro and In Vivo Pig-a Assays**](https://pubmed.ncbi.nlm.nih.gov/30595212/)**.**

[**Cigarette Whole Smoke Solutions Disturb Mucin Homeostasis in a Human In Vitro Airway Tissue Model**](https://pubmed.ncbi.nlm.nih.gov/30053496/)**.**

[**Establishing a Novel Pig-a Gene Mutation Assay in L5178YTk+/- Mouse Lymphoma Cells**](https://pubmed.ncbi.nlm.nih.gov/29098723/)**.**

[**Spectrum of Benzo[a]pyrene-Induced Mutations in the Pig-a Gene of L5178YTk+/- Cells Identified with Next Generation Sequencing**](https://pubmed.ncbi.nlm.nih.gov/29150045/)**.**

[**Breast Cancer Heterogeneity Examined by High-Sensitivity Quantification of PIK3CA, KRAS, HRAS, and BRAF Mutations in Normal Breast and Ductal Carcinomas**](https://pubmed.ncbi.nlm.nih.gov/27108388/)**.**

[**ACB-PCR Quantification of Somatic Oncomutation**](https://pubmed.ncbi.nlm.nih.gov/24623241/)**.**

[**Temporal Changes in K-ras Mutant Fraction in Lung Tissue of Big Blue B6C3F₁ Mice Exposed to Ethylene Oxide**](https://pubmed.ncbi.nlm.nih.gov/24029818/)**.**

[**ACB-PCR Measurement of H-ras Codon 61 CAA→CTA Mutation Provides an Early Indication of Aristolochic Acid I Carcinogenic Effect in Tumor Target Tissues**](https://pubmed.ncbi.nlm.nih.gov/22729866/)**.**

[**Hotspot Oncomutations: Implications for Personalized Cancer Treatment**](https://pubmed.ncbi.nlm.nih.gov/22845481/)**.**

[**Aristolochic Acid-Induced Carcinogenesis Examined by ACB-PCR Quantification of H-Ras and K-Ras Mutant Fraction**](https://pubmed.ncbi.nlm.nih.gov/21642617/)**.**

[**p53 Codon 271 CGT to CAT Mutant Fraction Does Not Increase in Nasal Respiratory and Olfactory Epithelia of Rats Exposed to Inhaled Naphthalene**](https://pubmed.ncbi.nlm.nih.gov/21324376/)**.**

[**Oncomutations as Biomarkers of Cancer Risk**](https://pubmed.ncbi.nlm.nih.gov/20740637/)**.**

[VIEW FULL BIO – Yiying Wang, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/yiying-wang)

## Division of Microbiology, NCTR

# Steven Foley, Ph.D.

### **Director, SBRBPAS Expert — Division of Microbiology**

Dr. Foley’s multifaceted research program addresses FDA research needs in the areas of antimicrobial resistance and virulence in foodborne pathogens and the microbial characterization of FDA-regulated products. Plasmids that are present in *Salmonella enterica* and other enteric pathogens often contain multiple genes that can encode for antimicrobial resistance, increased colonization, and/or overall virulence. A long-term goal of Dr. Foley’s research is to better understand the role of plasmids in increased virulence among *Salmonella enterica*. In his previous studies, DNA sequencing of plasmids identified factors that are likely important for increased virulence and antimicrobial resistance in *Salmonella*. For example, his team’s research has demonstrated the contribution of plasmid-encoded VirB/D4 Type 4 Secretion Systems to increased invasion and survival in model systems. Several other plasmid types also appear to encode potential virulence factors, often along with antimicrobial-resistance genes, which is why Dr. Foley’s team aims to further elucidate their roles in virulence and whether there is a co-selection of increased virulence and resistance. To these ends, Dr. Foley is leading an FDA Office of Chief Scientist’s Challenge Grant-funded project to develop genetic approaches and methodologies to more efficiently cure plasmids and inactivate plasmid-associated genes to facilitate a functional analysis of their roles in bacterial physiology. Additionally, the team is developing a *Salmonella* virulence gene database to efficiently identify and compare virulence genes identified in whole genome sequencing (WGS) efforts. WGS can be a tool to better understand *Salmonella* diversity and the evolution of virulence.

Dr. Foley also seeks to better understand the factors that impact plasmid-transfer efficiency. Preliminary studies have shown that differential exposure to certain antimicrobial agents can impact the efficiency of plasmid transfer and the team’s ongoing research builds upon these earlier studies to evaluate a larger diversity of plasmids associated with *Salmonella* to identify their impact on pathogenicity (both looking at the pathogen and host sides of the equation) and to refine the understanding of the role of antimicrobial exposure that may influence plasmid transfer among *Salmonella* and other enteric organisms. These efforts have also led to the development of a plasmid gene database focused on identifying key plasmid-associated virulence and transfer genes from WGS data. The team plans to combine the bioinformatics approaches and laboratory methods to better understand the dissemination and diversity of plasmids. [VIEW FULL BIO – Dr. Steven Foley](https://www.fda.gov/about-fda/science-research-nctr/steven-foley)

**Titles and links to selected publications**

[**Incompatibility Group I1 (IncI1) Plasmids: A Review of their Genetics, Biology, and Public Health Relevance**](https://pubmed.ncbi.nlm.nih.gov/33910982/)**.**

[**Current Knowledge and Perspectives of Potential Impacts of Salmonella enterica on the Profile of the Gut Microbiota**](https://pubmed.ncbi.nlm.nih.gov/33203384/)**.**

[**Genotypic and Phenotypic Characterization of Incompatibility Group FIB Positive Salmonella enterica serovar Typhimurium Isolates from Food Animal Sources**](https://pubmed.ncbi.nlm.nih.gov/33158112/)**.**

[**The Gut Microbiome and Xenobiotics: Identifying Knowledge Gaps**](https://pubmed.ncbi.nlm.nih.gov/32658296/)**.**

[**Evaluation of the Genetics and Functionality of Plasmids in Incompatibility Group I1-Positive Salmonella enterica**](https://pubmed.ncbi.nlm.nih.gov/29265877/)**.**

[**Impact of Co-Carriage of IncA/C Plasmids with Additional Plasmids on the Transfer of Antimicrobial Resistance in Salmonella enterica Isolates**](https://pubmed.ncbi.nlm.nih.gov/29549790/)**.**

[**Comparative Genomic Analysis and Characterization of Incompatibility Group FIB Plasmid Encoded Virulence Factors of Salmonella enterica Isolated from Food Sources**](https://pubmed.ncbi.nlm.nih.gov/28768482/)**.**

[**Bacterial Populations Associated with Smokeless Tobacco Products**](https://pubmed.ncbi.nlm.nih.gov/27565615/)**.**

[**Transmissible Plasmid Containing Salmonella enterica Heidelberg Isolates Modulate Cytokine Production in Intestinal Epithelial Cells**](https://www.ncbi.nlm.nih.gov/pubmed/27082282)**.**

[**The Commensal Infant Gut Mobilome as a Reservoir for Persistent Multidrug Resistance Integrons**](https://www.ncbi.nlm.nih.gov/pubmed/26507767)**.**

[**Evaluation of Virulence and Antimicrobial Resistance in Salmonella enterica Serovar Enteritidis Isolates from Humans and Chicken- and Egg-Associated Sources**](https://www.ncbi.nlm.nih.gov/pubmed/24102082)**.**

[**Salmonella Pathogenicity and Host Adaptation in Chicken-Associated Serovars**](https://www.ncbi.nlm.nih.gov/pubmed/24296573)**.**

[**Impact of Plasmids, Including Those Encoding VirB4/D4 Type IV Secretion Systems on Salmonella enterica Serovar Heidelberg Virulence in Macrophages and Epithelial Cells**](https://www.ncbi.nlm.nih.gov/pubmed/24098597)**.**

[**DNA Sequence Analysis of Multidrug Resistance Encoding Plasmids from Salmonella enterica Serotype Heidelberg Isolates**](https://www.ncbi.nlm.nih.gov/pubmed/23251446)**.**

[**Recombinant Iss as a Potential Vaccine for Avian Colibacillosis**](https://www.ncbi.nlm.nih.gov/pubmed/22545546)**.**

[**Population Dynamics of Salmonella enterica Serotypes in Commercial Egg and Poultry Production**](https://www.ncbi.nlm.nih.gov/pubmed/21571882)**.**

[**Comparison of Salmonella enterica Serovar Heidelberg Isolated from Human Patients with Those from Animal and Food Sources**](https://www.ncbi.nlm.nih.gov/pubmed/21177888)**.**

[**Horizontal Gene Transfer Has Resulted in a Dominant Avian Clonal Type of Salmonella enterica Serovar Kentucky**](https://www.ncbi.nlm.nih.gov/pubmed/21203520)**.**

[**Evaluation of a Virulence Factor Profiling in the Characterization of Veterinary Escherichia coli**](https://www.ncbi.nlm.nih.gov/pubmed/20889790)**.**

[**Food Animal-Associated Salmonella Challenges: Pathogenicity and Antimicrobial Resistance**](https://www.ncbi.nlm.nih.gov/pubmed/17878285)**.**

[VIEW FULL BIO – Steven Foley, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/steven-foley)

# Youngbeom Ahn, Ph.D.

### **Micribiologist — Division of Microbiology**

The laboratory of microbiome and host interactions within the division has been established to investigate the effects of food-contaminant residues on the gastrointestinal-tract microbiota. Dr. Ahn’s current studies are focused on the impact of antibiotics on the human gastrointestinal-tract microbiota. Most studies on drug binding to fecal contents have used therapeutic human doses, rather than levels below or slightly above the minimal risk level allowed in edible tissues. The research project answered one of the International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products’ most pivotal methodological questions of whether residues entering the human colon remain biologically active by comparing the fecal binding of selected antibiotics concentrations with various incubation conditions using physiochemical, analytical chemistry, microbiological, and molecular methods.

Dr. Ahn is also collaborating with CDER on a project to explore strategies for resuscitation and enrichment of BCC strains in pharmaceutical products. The Centers for Disease Control (CDC) has requested that FDA issue a rule or policy that establishes *B. cepacia* as an objectionable organism in pharmaceuticals, and the United States Pharmacopeia (USP) has revisited the concept of including *B. cepacia* in its chapters. For USP to include this species as an organism of interest, they must have a test that can be done by nearly any microbiology laboratory using conventional technology. However, existing USP methods use enrichment in Trypticase Soy Broth, which is inadequate for all strains. The objectives of Dr. Ahn’s research are to 1) develop a resuscitative step and enrichment technique for BCC recovery and 2) develop methodology to detect BCC and its 16 related genomovars. He also looks to evaluate the use of modern molecular technologies to identify BCC. [VIEW FULL BIO – Dr. Youngbeom Ahn](https://www.fda.gov/about-fda/science-research-nctr/youngbeom-ahn)

**Titles and links to selected publications**

[**Loop-Mediated Isothermal Amplification (LAMP) Assay for Detecting Burkholderia cepacia Complex in Non-Sterile Pharmaceutical Products**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8468478/)**.**

[**Impact of Chronic Tetracycline Exposure on Human Intestinal Microbiota in a Continuous Flow Bioreactor Model**](https://pubmed.ncbi.nlm.nih.gov/34438936/)**.**

[**Detection of Campylobacter jejuni from Fresh Produce: Comparison of Culture- and PCR-Based Techniques, and Metagenomic Approach for Analyses of the Microbiome Before and After Enrichment**](https://pubmed.ncbi.nlm.nih.gov/33878155/)**.**

[**Reductive Debromination by Sponge-Associated Anaerobic Bacteria Coupled to Carbon Isotope Fractionation**](https://www.sciencedirect.com/science/article/abs/pii/S0964830520310246)**.**

[**A Comparison of Culture-Based, Real-Time PCR, Droplet Digital PCR and Flow Cytometric Methods for the Detection of Burkholderia cepacia Complex in Nuclease-Free Water and Antiseptics**](https://pubmed.ncbi.nlm.nih.gov/32671501/)**.**

[**Oligotrophic Media Compared with a Tryptic Soy Agar or Broth for the Recovery of Burkholderia cepacia Complex from Different Storage Temperatures and Culture Conditions**](https://pubmed.ncbi.nlm.nih.gov/31434364/)**.**

[**In vitro Test Systems to Determine Tetracycline Residue Binding to Human Feces**](https://pubmed.ncbi.nlm.nih.gov/30227174/)**.**

[**An In Vitro Study to Assess the Impact of Tetracycline on the Human Intestinal Microbiome**](https://www.ncbi.nlm.nih.gov/pubmed/29294359)**.**

[**Effects of Extended Storage of Chlorhexidine Gluconate and Benzalkonium Chloride Solutions on the Viability of *Burkholderia cenocepacia***](https://www.ncbi.nlm.nih.gov/pubmed/29032643)**.**

[**Novel Reductive Dehalogenases from the Marine Sponge Associated Bacterium Desulfoluna spongiiphila**](https://www.ncbi.nlm.nih.gov/pubmed/28618195)**.**

[**Improved High-Quality Draft Genome Sequence and Annotation of Burkholderia contaminans LMG 23361T**](https://www.ncbi.nlm.nih.gov/pubmed/28428315)**.**

[**Intrinsic Resistance of Burkholderia cepacia Complex to Benzalkonium Chloride**](https://www.ncbi.nlm.nih.gov/pubmed/27879334)**.**

[**Survival and Susceptibility of Burkholderia cepacia Complex in Chlorhexidine Gluconate and Benzalkonium Chloride**](http://www.ncbi.nlm.nih.gov/pubmed/25794566)**.**

[**Pleiotropic and Epistatic Behavior of a Ring-Hydroxylating Oxygenase System in the Polycyclic Aromatic Hydrocarbon Metabolic Network from Mycobacterium vanbaalenii PYR-1**](http://www.ncbi.nlm.nih.gov/pubmed/25070740)**.**

[**Evaluation of Liquid and Solid Culture Media for the Recovery and Enrichment of Burkholderia cenocepacia from Distilled Water**](http://www.ncbi.nlm.nih.gov/pubmed/24756630)**.**

[**Influence of Sterilized Human Fecal Extract on the Sensitivity of Salmonella enterica ATCC 13076 and Listeria monocytogenes ATCC 15313 to Enrofloxacin**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Influence%20of%20Sterilized%20Human%20Fecal%20Extract%20on%20the%20Sensitivity%20of%20Salmonella%20enterica%20ATCC%2013076%20and%20Listeria%20monocytogenes%20ATCC%2015313%20to%20Enrofloxacin.)**.**

[**In Vitro Analysis of the Impact of Enrofloxacin Residues on the Human Intestinal Microbiota Using H-NMR Spectroscopy**](http://www.ncbi.nlm.nih.gov/pubmed/23221505)**.**

[**Effect of Sterilized Human Fecal Extract on the Sensitivity of Escherichia coli ATCC 25922 to Enrofloxacin**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Effect%20of%20Sterilized%20Human%20Fecal%20Extract%20on%20the%20Sensitivity%20of%20Escherichia%20Coli%20ATCC%2025922%20to%20Enrofloxacin.)**.**

[**In Vitro Enrofloxacin Binding in Human Fecal Slurries**](http://www.ncbi.nlm.nih.gov/pubmed/22178170)**.**

[VIEW FULL BIO – Youngbeom Ahn, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/youngbeom-ahn)

# Marli Azevedo, Ph.D.

### **Micribiologist — Division of Microbiology**

Before joining FDA, Dr. Azevedo dedicated 10 years studying rotavirus immunity. Using gnotobiotic pigs, because of their similarity to human babies, Dr. Azevedo demonstrated viremia and virus infection in the respiratory tract of gnotobiotic piglets after infection with rotavirus. In addition, Dr. Azevedo has studied immune responses to rotavirus and identified correlates of protective immunity after rotavirus vaccination. Furthermore, she has tested and evaluated the immunogenicity and protective efficacy of several candidate human rotavirus vaccines and demonstrated the potential to use these vaccines against rotavirus disease in children. Dr. Azevedo has used the Murine norovirus model to better understand norovirus replication, disease pathogenesis, and host responses.

Dr. Azevedo’s current studies are focused on respiratory and enteric viruses, among them coronaviruses and noroviruses. Coronaviruses are responsible for causing acute respiratory tract infections in humans and respiratory, gastrointestinal, neuropathies, and systemic diseases in animals. Noroviruses are responsible for 60% of the food and waterborne gastroenteritis outbreaks. Twenty-three million Americans are sickened with norovirus yearly, accounting for 50,000 hospitalizations and 300 deaths.

She has used qRT-PCR, RT-PCR, plaque assay, virus isolation, cloning, sequencing, confocal microscopy, immunofluorescence assay, and cell culture, among other techniques, to study the mechanism of transmission of coronavirus and to determine the current strains circulating in humans and animals in Arkansas. She has identified feline and canine norovirus strains circulating in Arkansas. She is currently investigating the role of spike protein of SARS-CoV-2 on immune-mediated pathogenesis and the role of non-structural proteins in COVID-19 morbidity. Dr. Azevedo’s laboratory has also constructed a norovirus-like particle to assess the exposure to canine or feline norovirus by humans, which may also be used to further understand immune responses to norovirus. Her laboratory has also explored models of co-infection of norovirus and Salmonella to study possible models of inference between them, as well as host interactions.

Dr. Azevedo’s laboratory has demonstrated that infection of RAW 264.7 cells with S. enterica reduces the replication of Murine Norovirus Virus (MNV), in part by blocking virus entry early in the virus life cycle and inducing antiviral cytokines later in the infection cycle. In particular, bacterial infection prior to, or during MNV infection affected virus entry, whereas MNV entry remained unaltered when the virus infection preceded bacterial invasion. This block in virus entry resulted in reduced virus replication, with the highest impact on replication observed during conditions of co-infection. In contrast, bacterial replication showed a three-fold increase in MNV-infected cells, despite the presence of antibiotic in the medium. Most importantly, Dr. Azevedo presented evidence that the infection of MNV-infected macrophages by S. enterica blocked MNV-induced apoptosis, despite allowing virus replication. Apoptosis blockade was evidenced by reduction in DNA fragmentation and absence of poly-ADP ribose polymerase, caspase 9, and caspase 3 cleavage events. Suggesting a novel mechanism of pathogenesis whereby initial co-infection with these pathogens could result in prolonged infection by either of these pathogens or both together, by delaying cell death. Her laboratory is currently using knockout cells and bacterial factors to better understand their effect on norovirus replication and on host responses.

Dr. Azevedo’s laboratory also has investigated the effect of silica nanoparticles on norovirus replication and host-cell response during virus infection. Silica nanoparticles did not affect virus load; however, silica nanoparticles reduced the ability of macrophages to up-regulate genes encoding bone morphogenic proteins (BMPs), chemokine ligands, and cytokines for which expression levels were otherwise found to be up-regulated in response to MNV-1 infection. Furthermore, silica nanoparticles present during norovirus infection produced a genotoxic insult to macrophages. Taken together, her study suggests that important safety considerations should be given to reduce exposure to silica nanoparticles in the gastrointestinal tract, especially for individuals infected with noroviruses and possibly other foodborne viruses.

Dr. Azevedo’s lab has cloned and expressed the spike proteins of SARS-CoV-2, HCoV-NL-63 and HCoV-HUK1 in a baculovirus expression system. These proteins have been used to generate polyclonal antibodies that will allow further studies of coronavirus-related disease. Her lab has also generated stable cell lines expressing the non-structural proteins of SARS-CoV-2 and generated cell lines expressing both the CD32A and ACE-2 receptor. [VIEW FULL BIO – Dr. Marli Azevedo](https://www.fda.gov/about-fda/science-research-nctr/marli-azevedo)

**Titles and links to selected publications**

[**Conformational Changes of the Receptor Binding Domain of SARS-CoV-2 Spike Protein and Prediction of a B-cell Antigenic Epitope Using Structural Data**](https://pubmed.ncbi.nlm.nih.gov/33842877/)**.**

[**Elucidating Interactions Between SARS-CoV-2 Trimeric Spike Protein and ACE2 Using Homology Modeling and Molecular Dynamics Simulations**](https://pubmed.ncbi.nlm.nih.gov/33469527/)**.**

[**Genomics Analyses of Novel Canine Norovirus Reveal Species-Specific Clustering of GIV and GVI Norovirus**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6466045/)**.**

[**Reduced Vancomycin Susceptibility and Increased Macrophage Survival in Staphylococcus aureus Strains Sequentially Isolated from a Bacteraemic Patient During a Short Course of Antibiotic Therapy**](https://pubmed.ncbi.nlm.nih.gov/31136294/)**.**

[**Viral and Bacterial Co-Infection and Its Implications**](https://www.ncbi.nlm.nih.gov/pubmed?term=Viral%5BTitle%5D%20AND%20Bacterial%5BTitle%5D%20AND%20Co-Infection%5BTitle%5D%20AND%20Implications%5BTitle%5D)**.**

[**Titanium Dioxide Nanoparticles Evoke Proinflammatory Response during Murine Norovirus Infection Despite Having Minimal Effects on Virus Replication**](https://pubmed.ncbi.nlm.nih.gov/29930994/)**.**

[**Silicon Dioxide Impedes Antiviral Response and Causes Genotoxic Insult During Calicivirus Replication**](http://www.ncbi.nlm.nih.gov/pubmed/27547159?report=abstract)**.**

[**Infection of Murine Macrophages by Salmonella enterica Serovar Heidelberg Blocks Murine Norovirus Infectivity and Virus-Induced Apoptosis**](http://www.ncbi.nlm.nih.gov/pubmed/26658916)**.**

[**Human Respiratory Coronaviruses Detected in Patients with Influenza-Like Illness in Arkansas, USA**](http://www.ncbi.nlm.nih.gov/pubmed/27588218)**.**

[**Effects of Dietary Vitamin A Content on Antibody Responses of Feedlot Calves Inoculated Intramuscularly with an Inactivated Bovine Coronavirus Vaccine**](http://www.ncbi.nlm.nih.gov/pubmed/24066921)**.**

[**Human Rotavirus Virus-Like Particle Vaccines Evaluated in a Neonatal Gnotobiotic Pig Model of Human Rotavirus Disease**](http://www.ncbi.nlm.nih.gov/pubmed/23414408)**.**

[**Stability of Bovine Coronavirus on Lettuce Surfaces under Household Refrigeration Conditions**](http://www.ncbi.nlm.nih.gov/pubmed/22265299)**.**

[***Lactobacillus Acidophilus* and L. Reuteri Modulate Cytokine Responses in Gnotobiotic Pigs Infected with Human Rotavirus**](http://www.ncbi.nlm.nih.gov/pubmed/22348907)**.**

[**Development of γδ-T Cell Subset Responses in Gnotobiotic Pigs Infected with Human Rotaviruses and Colonized with Probiotic Lactobacilli**](http://www.ncbi.nlm.nih.gov/pubmed/21489639)**.**

[**Inactivated Rotavirus Vaccine Induces Protective Immunity in Gnotobiotic Piglets**](http://www.ncbi.nlm.nih.gov/pubmed/20558244)**.**

[**Innate Immune Responses to Human Rotavirus in Neonatal Gnotobiotic Piglet Disease Model**](https://www.ncbi.nlm.nih.gov/pubmed/20497255)**.**

[**Oral Versus Intranasal Prime/Boost Regimen Using Attenuated HRV or 2/6VLP with ISCOM Influences Protection and Antibody Secreting Cell Responses to Rotavirus in a Neonatal Gnotobiotic Pig Model**](http://www.ncbi.nlm.nih.gov/pubmed/20107005)**.**

[**Toll-Like Receptor and Innate Cytokine Responses Induced by Lactobacilli Colonization and Human Rotavirus Infection in Gnotobiotic Pigs**](http://www.ncbi.nlm.nih.gov/pubmed/19054578)**.**

[**Probiotic Lactobacillus Acidophilus Enhances the Immunogenicity of an Oral Rotavirus Vaccine in Gnotobiotic Pigs**](http://www.ncbi.nlm.nih.gov/pubmed/18524434)**.**

[**Virus-Specific Intestinal IFNγ Producing T Cell Responses Induced by Human Rotavirus Infection and Vaccines are Correlated with Protection Against Rotavirus Diarrhea in Gnotobiotic Pigs**](http://www.ncbi.nlm.nih.gov/pubmed/18456375)**.**

[VIEW FULL BIO – Marli Azevedo, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/marli-azevedo)

# Huizhong Chen, Ph.D.

### **Micribiologist — Division of Microbiology**

Lacking sterility assurance and contamination are the major risks to public health caused by drug compounding. Serious health problems and huge medical costs can be the consequence of inappropriate application of sporicidal agents. Bacterial endospores cause significant challenges for the pharmaceutical facilities because they are prevalent in the environment and intrinsically resistant to heat, desiccation, radiation, and chemical assault. Sporicidal activities are affected by many factors, like spore strain, quality of spore, organic load, carrier material, and contact time. False-positive sporicidal results could be observed due to ineffective neutralization method, inaccurate contact time, sporistatic effect, or bactericidal effect. Dr. Chen and his collaborators from other FDA centers are using a combination of current and traditional microbiological, toxicological, cell biological, and chemical techniques to elucidate and evaluate the effectiveness of sporicidal products and are setting up a database to support FDA regulation on sporicidal disinfectants.

Many different molecules are coproduced from food, drug, cosmetics, and xenobiotics by the host and its commensal microbiota. The changes in co-metabolites might indicate the commensal microbiome functional status in the host and, in turn, this functional status may potentially affect health conditions of the host. Dr. Chen is collaborating with scientists from NCTR and other FDA centers 1) to develop a new project to use metabolomics, next general sequencing, and immunology tools for functional assessment of commensal microbiota; 2) to find patterns of host-commensal microbiota co-metabolites; and 3) to link antibiotic resistance and mechanisms of xenobiotic metabolism to functional commensal microbiome.

Interactions between the microbiota and human host have implications for nutrition, infection, metabolism, toxicity, and cancer. There are potential risks that externally applied cosmetics containing nanoscale materials could impact the microbial ecology of the skin, which may affect human health by breaking the skin-permeability barrier which could encourage pathogen colonization and lead to an increased susceptibility to infection. Dr. Chen is collaborating with scientists from other FDA centers to examine the effects of nanoscale materials used in cosmetics and sunscreens on model microorganisms that are representative of the human skin microbiota to evaluate the potential risk of dermal exposure of nanomaterials to women’s health. He is using a combination of the most current microbiological, nanotechnological, cell biological, and omic techniques to elucidate the skin microbiota and host interactions in the presence of nanoscale materials used in cosmetics. [VIEW FULL BIO – Dr. Huizhong Chen](https://www.fda.gov/about-fda/science-research-nctr/huizhong-chen)

**Titles and links to selected publications**

[**Bile Acid Profile and Its Changes in Response to Cefoperazone Treatment in MR1 Deficient Mice**](https://pubmed.ncbi.nlm.nih.gov/32225042)**.**

[**Smokeless Tobacco Impacts Oral Microbiota in a Syrian Golden Hamster Cheek Pouch Carcinogenesis Model**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Smokeless+tobacco+impacts+oral+microbiota+in+a+Syrian+Golden+hamster+cheek+pouch+carcinogenesis+model.)**.**

[**Mutation Network-Based Understanding of Pleiotropic and Epistatic Mutational Behavior of Enterococcus faecalis FMN-Dependent Azoreductase**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Mutation+network-based+understanding+of+pleiotropic+and+epistatic+mutational+behavior+of+Enterococcus+faecalis+FMN-dependent+azoreductase.)**.**

[**Evaluation of Metabolism of Azo Dyes and Their Effects on Staphylococcus aureus Metabolome**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Evaluation+of+Metabolism+of+Azo+Dyes+and+Their+Effects+on+Staphylococcus+Aureus+Metabolome.)**.**

[**Metabolomics Evaluation of the Impact of Smokeless Tobacco Exposure on the Oral Bacterium Capnocytophaga sputigena**](http://www.ncbi.nlm.nih.gov/pubmed/27480511)**.**

[**Differential Gene Expression in Staphylococcus aureus Exposed to Orange II and Sudan III Azo Dyes**](http://www.ncbi.nlm.nih.gov/pubmed/25720844)**.**

[**A Comparison of Conventional Methods for the Quantification of Bacterial Cells After Exposure to Metal Oxide Nanoparticles**](http://www.ncbi.nlm.nih.gov/pubmed/25138641)**.**

[**Detection of Benzalkonium Chloride Resistance in Community Environmental Isolates of Staphylococci**](http://www.ncbi.nlm.nih.gov/pubmed/24586033)**.**

[**Identification of the Enzyme Responsible for N-Acetylation of Norfloxacin by Microbacterium sp. Strain 4N2-2**](http://www.ncbi.nlm.nih.gov/pubmed/23104417)**.**

[**Evaluation of Impact of Exposure of Sudan Azo Dyes and their Metabolites on Human Intestinal Bacteria**](http://www.ncbi.nlm.nih.gov/pubmed/22634331)**.**

[**Probing the NADH- and Methyl Red-binding Site of a FMN-Dependent Azoreductase (AzoA) from Enterococcus faecalis**](http://www.ncbi.nlm.nih.gov/pubmed/22387379)**.**

[**Toxicological Significance of Azo Dye Metabolism by Human Intestinal Microbiota**](http://www.ncbi.nlm.nih.gov/pubmed/22201895)**.**

[**EmmdR, a New Member of the MATE Family of Multidrug Transporters, Extrudes Quinolones from Enterobacter cloacae**](http://www.ncbi.nlm.nih.gov/pubmed/21822795)**.**

[**SugE, a New Member of the SMR Family of Transporters, Contributes to Antimicrobial Resistance in Enterobacter cloacae**](http://www.ncbi.nlm.nih.gov/pubmed/21576447)**.**

[**Effects of Orange II and Sudan III Azo Dyes and Their Metabolites on Staphylococcus aureus**](http://www.ncbi.nlm.nih.gov/pubmed/21451978)**.**

[**Identification and Molecular Characterization of a Novel Flavin-Free NADPH Preferred Azoreductase Encoded by azoB in Pigmentiphaga Kullae K24**](http://www.ncbi.nlm.nih.gov/pubmed/20233432)**.**

[**Sudan Azo Dyes and Para Red Degradation by Prevalent Bacteria of the Human Gastrointestinal Tract**](http://www.ncbi.nlm.nih.gov/pubmed/19580882)**.**

[**Metabolism of Azo Dyes by Human Skin Microbiota**](http://www.ncbi.nlm.nih.gov/pubmed/19729456)**.**

[**Decolorization of Water and Oil-Soluble Azo Dyes by Lactobacillus Acidophilus and Lactobacillus Fermentum**](http://www.ncbi.nlm.nih.gov/pubmed/19727875)**.**

[**Functional Role of Trp-105 of Enterococcus Faecalis Azoreductase (AzoA) as Resolved by Structural and Mutational Analysis**](http://www.ncbi.nlm.nih.gov/pubmed/18757799)**.**

[VIEW FULL BIO – Huizhong Chen, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/huizhong-chen)

# Bruce Erickson, Ph.D.

### **Senior Staff Fellow — Division of Microbiology**

Researchers and clinicians have known for decades that the human body harbors a complex bacterial population, and that the composition and complexity of this population varies with the area of the body (skin, oral, vaginal, gut), but the largest and most diverse microbiome is found in the intestinal tract. These microorganisms perform multiple functions, from metabolizing food components, drugs, and other xenobiotic compounds to providing a barrier to colonization of the gut by multiple pathogenic bacteria. Recent research has demonstrated that the intestinal microbiota plays an even larger role in human health, affecting obesity, metabolic syndrome, chronic inflammation, immune system function, and an expanding list of other health conditions. Dr. Erickson’s current work is directed toward understanding the role that the intestinal microbiota plays in human health and how differences or changes in the microbiota may affect the safety and effectiveness of drugs or medical treatments regulated by FDA.

Most recently, Dr. Erickson initiated a research effort to assess safety concerns associated with fecal microbiota transplantation (FMT). The FDA currently exercises a policy of enforcement discretion allowing the use of FMT to treat recurrent *Clostridium difficile* infections, or those that are not responsive to standard therapies. As more medical conditions are being connected to the disruption of the intestinal microbiome, FMT from healthy donors is being proposed as a potential treatment method. However, risks associated with pathogen contamination of FMT samples are not fully understood. This research effort will help establish thresholds for pathogen contamination and detection to assist the agency in developing science-based guidelines for the standardization and safety of FMT procedures.

In response to the current COVID-19 pandemic, Dr. Erickson is developing protein reagents to study the receptor binding, cell interactions, and antibody-dependent enhancement of infection by the novel coronavirus SARS-CoV-2 and related human coronaviruses.

Dr. Erickson has expertise in a wide range of molecular biology methods, and extensive experience in both anaerobic and aerobic microbiology — including in vitro culture systems for maintaining complex bacterial populations, and both culture-based and Next Generation Sequencing (NGS)-based methods for characterizing microbial populations of the intestinal microbiome. [VIEW FULL BIO – Dr. Bruce Erickson](https://www.fda.gov/about-fda/science-research-nctr/bruce-erickson)

**Titles and links to selected publications**

[**Assessment of Gut Microbiota Populations in Lean and Obese Zucker Rats**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Assessment+of+Gut+Microbiota+Populations+in+Lean+and+Obese+Zucker+Rats.)**.**

[**Functional Studies of the Recombinant CdtB, PltA, and PltB Subunits from Salmonella Enterica Serovar Javiana**](http://www.journalijar.com/article/4456/functional-studies-of-the-recombinant-cdtb,-plta-and-pltb-subunits-from-salmonella-enterica-serovar-javiana/)**.**

[**A Metallo-β-Lactamase Is Responsible for the Degradation of Ceftiofur by the Bovine Intestinal Bacterium Bacillus cereus P41**](https://www.ncbi.nlm.nih.gov/pubmed/24972871)**.**

[**Bovine Intestinal Bacteria Inactivate and Degrade the Third Generation Cephalosporins Ceftiofur and Ceftriaxone with Multiple β-Lactamases**](https://www.ncbi.nlm.nih.gov/pubmed/21876048)**.**

[**Echinacea Purpurea Supplementation Stimulates Select Groups of Human Intestinal Tract Microbiota**](https://www.ncbi.nlm.nih.gov/pubmed/17176365)**.**

[**A Membrane Array Method to Detect Specific Human Intestinal Bacteria in Fecal Samples Using Reverse Transcriptase-PCR and Chemiluminescence**](https://www.researchgate.net/publication/289132139_A_membrane-array_method_to_detect_specific_human_intestinal_bacteria_in_fecal_samples_using_reverse_transcriptase-PCR_and_chemiluminescence)**.**

[**DNA Microarray Analysis of Predominant Human Intestinal Bacteria in Fecal Samples**](https://www.ncbi.nlm.nih.gov/pubmed/15271382)**.**

[**A Rapid Method for Determining the Tuberculocidal Activity of Liquid Chemical Germicides**](https://www.ncbi.nlm.nih.gov/pubmed/11391467)**.**

[**Identification and Modification of Biphenyl Dioxygenase Sequences that Determine the Specificity of Polychlorinated Biphenyl Degradation**](https://www.ncbi.nlm.nih.gov/pubmed/9251195)**.**

[**Enhanced Biodegradation of Polychlorinated Biphenyls after Site-Directed Mutagenesis of a Biphenyl Dioxygenase Gene**](https://www.ncbi.nlm.nih.gov/pubmed/8285689)**.**

[**Nucleotide Sequencing and Transcriptional Mapping of the Genes Encoding Biphenyl Dioxygenase, a Multicomponent Polychlorinated-Biphenyl-Degrading Enzyme in Pseudomonas Strain LB400**](https://www.ncbi.nlm.nih.gov/pubmed/1569021)**.**

[**Nucleotide Sequencing of the Transcriptional Control Region of the Osmotically Regulated proU Operon of Salmonella Typhimurium and Identification of the 5’ Endpoint of the proU mRNA**](https://www.ncbi.nlm.nih.gov/pubmed/2548994)**.**

[**Nucleotide Sequence of the rpsU-dnaG-rpoD Operon from Salmonella Typhimurium and a Comparison of this Sequence with the Homologous Operon in Escherichia coli**](https://www.ncbi.nlm.nih.gov/pubmed/3005129)**.**

[**Overproduction of Escherichia coli NusA Protein**](https://www.ncbi.nlm.nih.gov/pubmed/6323250)**.**

[VIEW FULL BIO – Bruce Erickson, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/bruce-erickson)

# Kristina M. Feye, Ph.D.

### **Research Biologist — Division of Microbiology**

Dr. Feye’s expertise lies at the nexus of physiology, molecular biology, and genomics. Her research program primarily focuses on using traditional benchtop and cutting-edge bioinformatics approaches to study the host-microbiome-pathogen axis across the OneHealth spectrum. Additional interests include investigating how different pharmaceuticals, supplements, foodborne pathogens, or diets influence that axis. Dr. Feye is continuously working to expand her already broad background of interests and apply it to mission critical research at the FDA. [VIEW FULL BIO – Dr. Kristina M. Feye](https://www.fda.gov/about-fda/science-research-nctr/kristina-feye)

**Titles and links to selected publications**

[**Incidence of Salmonella Serovars Isolated from Commercial Animal Feed Mills in the United States and Serovar Identification Using CRISPR Analysis**](https://pubmed.ncbi.nlm.nih.gov/33190398/)**.**

[**Influential Factors on the Composition of the Conventionally Raised Broiler Gastrointestinal Microbiomes**](https://pubmed.ncbi.nlm.nih.gov/32029151/)**.**

[**Poultry Processing and the Application of Microbiome Mapping**](https://pubmed.ncbi.nlm.nih.gov/32029154/)**.**

[**The Preliminary Development of an In Vitro Poultry Cecal Culture Model to Evaluate the Effects of Original XPCTM for the Reduction of Campylobacter jejuni and Its Potential Effects on the Microbiota**](https://pubmed.ncbi.nlm.nih.gov/32038534/)**.**

[**Application of Amplon in Combination with Peroxyacetic Acid for the Reduction of Nalidixic Acid-Resistant Salmonella Typhimurium and Salmonella Reading on Skin-on, Bone-in Tom Turkey Drumsticks**](https://pubmed.ncbi.nlm.nih.gov/33248616/)**.**

[**A Historical Review on Antibiotic Resistance of Foodborne Campylobacter**](https://pubmed.ncbi.nlm.nih.gov/31402900/)**.**

[**Developments in Rapid Detection Methods for the Detection of Foodborne Campylobacter in the United States**](https://pubmed.ncbi.nlm.nih.gov/30728816/)**.**

[**The Efficacy of Sodium Bisulfate Salt (SBS) Alone and Combined With Peracetic Acid (PAA) as an Antimicrobial on Whole Chicken Drumsticks Artificially Inoculated with Salmonella Enteritidis**](https://pubmed.ncbi.nlm.nih.gov/30761312/)**.**

[**The Addition of ViriditecTM Aqueous Ozone to Peracetic Acid as an Antimicrobial Spray Increases Air Quality While Maintaining Salmonella Typhimurium, Non-pathogenic Escherichia coli, and Campylobacter jejuni Reduction on Whole Carcasses**](https://pubmed.ncbi.nlm.nih.gov/30671030/)**.**

[**A Microbiomic Analysis of a Pasture-Raised Broiler Flock Elucidates Foodborne Pathogen Ecology Along the Farm-To-Fork Continuum**](https://pubmed.ncbi.nlm.nih.gov/31448296/)**.**

[**Comparison of 16S rDNA Next Sequencing of Microbiome Communities from Post-scalder and Post-picker Stages in Three Different Commercial Poultry Plants Processing Three Classes of Broilers**](https://pubmed.ncbi.nlm.nih.gov/31214127/)**.**

[**Comparison of Acid Sanitizers on Salmonella Typhimurium Inoculated Commercial Poultry Processing Reuse Water**](https://www.frontiersin.org/articles/10.3389/fsufs.2018.00090/full)**.**

[**Saccharomyces cerevisiae Fermentation Products That Mitigate Foodborne Salmonella in Cattle and Poultry**](https://pubmed.ncbi.nlm.nih.gov/31024942/)**.**

[**Acute Systemic Inflammatory Response to Lipopolysaccharide Stimulation in Pigs Divergently Selected for Residual Feed Intake**](https://pubmed.ncbi.nlm.nih.gov/31610780/)**.**

[**The Implementation and Food Safety Issues Associated with Poultry Processing Reuse Water for Conventional Poultry Production Systems in the United States**](https://www.frontiersin.org/articles/10.3389/fsufs.2018.00070/full)**.**

[**Abrogation of Salmonella and E. coli O157: H7 in Feedlot Cattle Fed a Proprietary Saccharomyces cerevisiae Fermentation Prototype**](https://www.researchgate.net/publication/305679989_Abrogation_of_Salmonella_and_E_coli_O157H7_in_Feedlot_Cattle_Fed_a_Proprietary_Saccharomyces_cerevisiae_Fermentation_Prototype)**.**

[**Inhibition of the Virulence, Antibiotic Resistance, and Fecal Shedding of Multiple Antibiotic-Resistant Salmonella Typhimurium in Broilers Fed Original XPC™**](https://pubmed.ncbi.nlm.nih.gov/27566726/)**.**

[**Off-Target Drug Effects Resulting in Altered Gene Expression Events with Epigenetic and "Quasi-Epigenetic" Origins**](https://pubmed.ncbi.nlm.nih.gov/27025785/)**.**

[VIEW FULL BIO – Kristina M. Feye, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/kristina-feye)

# Kuppan Gokulan, Ph.D.

### **Staff Fellow — Division of Microbiology**

Dr. Gokulan’s research falls under several priority research areas of NCTR and FDA and includes generating experimental data to support regulatory reviewers in the areas of:

1. The impact of transmissible plasmids on bacterial uptake, colonization, and host gene expression during the early stages of *S. enterica* Heidelberg infection
2. The molecular mechanism of drug and multi-drug bacteria
3. The effects of residual levels of antibiotics/xenobiotics on the barrier functions of human intestinal epithelial cells
4. The evaluation of the toxicity of nanocrystal drugs using nonclinical models and collaborating with CDER and the University of Connecticut to address critical problems

Dr. Gokulan’s lab also investigates knowledge-gaps associated with drug nanocrystals and their interaction with the gastrointestinal (GI) tract. Intestinal commensal bacteria play an essential role in maintaining healthy intestinal tissue, the shaping and development of immune response, and preventing the adverse effect of pathogenic bacteria. Currently, more than 750 clinical trials are in-progress involving potential nanomedicine products. Of these, 38 are approved products/currently in use and 128 are investigative new drug (IND) applications, of which 14% are drug nanocrystals. Approximately 82% of drug nanocrystal IND applications are for oral administration. For FDA regulatory/reviewer guidance, the agency needs experimental data to assess the effect of drug nanocrystals on the human GI tract.

Dr. Gokulan is seeking to understand how the bacterial cell-wall enzymes modify the peptidoglycan layers and cell-wall components in drug/multidrug-resistance bacteria by employing a protein homology modeling and drug-docking approach to address drug resistance. Expression of soluble protein is a prerequisite for functional characterization and drug screening for therapeutic proteins and antibodies, so he has established protein over-expression by using three different hosts’ expression systems. Recently he also developed a cell culture-based, high-throughput screening assay for drug discovery against antibiotic-resistant bacteria. Specifically, one of the bacterial cell-wall enzymes that is involved in peptidoglycan synthesis (L-D-Transpeptidase), which is responsible for antibiotic resistance in enzymes, over-expressed in *E. coli*. This over-expressed system mimics the drug-resistant bacteria.

Another major focus of research in Dr. Gokulan’s laboratory is to understand the early host immune response during bacterial invasion and how the bacterial pathogens alter the host immune-response genes via signaling pathways to establish bacterial colonization within the host. He is investigating the factors that lead to persistent bacterial infection, even when the host mounts an immune response against the bacterial insult, and how pathogenic microbes evade the immune response. He is addressing the antibacterial effects of the aloin, which has been used in dietary supplements, laxatives, weight loss supplements, beverages, beauty/cosmetics products, and vitamins, against intestinal commensal bacterial species. However, there is limited information available on the toxicity of these aloe products. The present study provides an evaluation of minimum inhibitory concentration (MIC) for the intestinal microbiota, which will help identify the acceptable dietary intake value for consumption of aloin/Aloe Vera in consumer products without altering the intestinal microbiome.

Dr. Gokulan has established a virulence and persistence assay to monitor *Salmonella enterica* Heidelberg-induced cell toxicity using macrophages and intestinal epithelial cells. He is also involved in identifying unique virulence genes and transmissible plasmids that contribute to antibiotic resistance in foodborne pathogens. Understanding the involvement of plasmid-encoded genes in antimicrobial resistance, colonization, invasion, and formation of the secretary apparatus will provide an improved knowledge of resistance and molecular mechanism of virulence-associated secretion by the bacterial type IV secretion system (T4SS). The outcome of the study will address several unresolved questions of bacterial pathogenesis and bacterial secretion systems. [VIEW FULL BIO – Dr. Kuppan Gokulan](https://www.fda.gov/about-fda/science-research-nctr/kuppan-gokulan)

**Titles and links to selected publications**

[**Impact of Chronic Tetracycline Exposure on Human Intestinal Microbiota in a Continuous Flow Bioreactor Model**](https://pubmed.ncbi.nlm.nih.gov/34438936/)**.**

[**Co-Exposure to Boscalid and TiO2 (E171) or SiO2 (E551) Downregulates Cell Junction Gene Expression in Small Intestinal Epithelium Cellular Model and Increases Pesticide Translocation**](https://pubmed.ncbi.nlm.nih.gov/33869896/)**.**

[**Conformational Changes of the Receptor Binding Domain of SARS-CoV-2 Spike Protein and Prediction of a B-cell Antigenic Epitope Using Structural Data**](https://pubmed.ncbi.nlm.nih.gov/33842877/)**.**

[**Differential Toxicological Outcome of Corn Oil Exposure in Rats and Mice as Assessed by Microbial Composition, Epithelial Permeability and Ileal Mucosa Associated Immune Status**](https://pubmed.ncbi.nlm.nih.gov/33263755/)**.**

[**Human Intestinal Tissue Explant Exposure to Silver Nanoparticles Reveals Sex Dependent Alterations in Inflammatory Responses and Epithelial Cell Permeability**](https://pubmed.ncbi.nlm.nih.gov/33374948/)**.**

[**Sex-Dependent Effects on Liver Inflammation and Gut Microbial Dysbiosis After Continuous Developmental Exposure to Trichloroethylene in Autoimmune Prone Mice**](https://pubmed.ncbi.nlm.nih.gov/33250767/)**.**

[**Effects of Acute and Chronic Exposure to Residual Level Erythromycin on Human Intestinal Epithelium Cell Permeability and Cytotoxicity**](https://pubmed.ncbi.nlm.nih.gov/31489925/)**.**

[**The Impact of Pristine Graphene on Intestinal Microbiota Assessed Using a Bioreactor-Rotary Cell Culture System**](https://pubmed.ncbi.nlm.nih.gov/31260263/)**.**

[**A Single or Short Time Repeated Arsenic Oral Exposure in Mice Impacts mRNA Expression for Signaling and Immunity Related Genes in the Gut**](https://pubmed.ncbi.nlm.nih.gov/31233874/)**.**

[**Alteration in the mRNA Expression of Genes Associated with Gastrointestinal Permeability and Ileal TNF-α Secretion Due to the Exposure of Silver Nanoparticles in Sprague-Dawley Rats**](https://pubmed.ncbi.nlm.nih.gov/31084603/)**.**

[**Aloin Alters the Intestinal Bacterial Community Structure and Short Chain Fatty Acids Metabolism**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Gokulan+K%2C+Kolluru+P%2C+Cerniglia+CE%2C+and+Khare+S.+Aloin+alters+the+intestinal+bacterial+community+structure+and+short+chain+fatty+acids+metabolism)**.**

[**Drug Resistance in Mycobacterium tuberculosis and Targeting the L,D-Transpeptidase Enzyme**](https://www.ncbi.nlm.nih.gov/pubmed/30312987)**.**

[**Irreversible Effects of Trichloroethylene on the Gut Microbial Community and Gut-Associated Immune Responses in Autoimmune-Prone Mice**](https://www.ncbi.nlm.nih.gov/pubmed/30187502)**.**

[**Structure and Inhibitor Specificity of L,D-Transpeptidase (LdtMt2) from Mycobacterium Tuberculosis and Antibiotic Resistance: Calcium Binding Promotes Dimer Formation**](https://www.ncbi.nlm.nih.gov/pubmed/29524047)**.**

[**Exposure to Arsenite in CD-1 Mice During Gestational to Adult Developmental Stages: Effects on Intestinal Microbiota and Gut-Associated Immune Response**](https://www.ncbi.nlm.nih.gov/pubmed/30108172)**.**

[**An In Vitro Study to Assess the Impact of Tetracycline on the Human Intestinal Microbiome**](https://www.ncbi.nlm.nih.gov/pubmed/?term=An+in+vitro+study+to+assess+the+impact+of+tetracycline+on+the+human+intestinal+microbiome)**.**

[**Effects of Residual Levels of Tetracycline on the Barrier Functions of Human Intestinal Epithelial Cells**](https://www.ncbi.nlm.nih.gov/pubmed/28882639)**.**

[**Graphene and Carbon Nanotubes Activate Different Cell Surface Receptors on Macrophages Before and After Deactivation of Endotoxins**](https://www.ncbi.nlm.nih.gov/pubmed/28485474)**.**

[**Assessment of Antimicrobial Effects of Food Contact Materials Containing Silver on Growth of Salmonella typhimurium**](https://www.ncbi.nlm.nih.gov/pubmed/28007453)**.**

[VIEW FULL BIO – Kuppan Gokulan, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/kuppan-gokulan)

# Jing Han, Ph.D.

### **Research Microbiologist (Staff Fellow) — Division of Microbiology**

Dr. Han’s main research interests are in the fields of antimicrobial resistance, pathogenesis of foodborne pathogens, and genetic characterization of enteric bacteria using molecular techniques. Her research projects at NCTR include:

* Genetic characterization of antimicrobial resistance and associated genetic factors in Salmonella serovars associated with food animals and invasive human infections
* Sequencing and functional analysis of plasmids isolated from multi-antimicrobial resistant bacteria
* Evaluation of the relative selective potential of antimicrobial agents to trigger the dissemination of antimicrobial resistance and virulence factors to susceptible Salmonella
* Investigation of microbial populations in different tobacco products

[VIEW FULL BIO – Dr. Jing Han](https://www.fda.gov/about-fda/science-research-nctr/jing-han)

**Titles and links to selected publications**

[**Incompatibility Group I1 (IncI1) Plasmids: Their Genetics, Biology, and Public Health Relevance**](https://pubmed.ncbi.nlm.nih.gov/33910982/)**.**

[**Genotypic and Phenotypic Characterization of Incompatibility Group FIB Positive Salmonella enterica Serovar Typhimurium Isolates from Food Animal Sources**](https://pubmed.ncbi.nlm.nih.gov/33158112/)**.**

[**Whole Genome Sequences of 66 Incompatibility Group FIB Plasmid-carrying Salmonella enterica serovar Typhimurium Isolates from Food Animal Sources**](https://pubmed.ncbi.nlm.nih.gov/32001566/)**.**

[**Evaluation of Incompatibility Group I1 (IncI1) Plasmid-Containing Salmonella enterica and Assessment of the Plasmids in Bacteriocin Production and Biofilm Development**](https://pubmed.ncbi.nlm.nih.gov/31552285/)**.**

[**Impact of Co-Carriage of IncA/C Plasmids with Additional Plasmids on the Transfer of Antimicrobial Resistance in Salmonella enterica Isolates**](https://pubmed.ncbi.nlm.nih.gov/29549790/)**.**

[**Evaluation of the Genetics and Functionality of Incompatibility 1 (IncI1) Plasmids from Salmonella enterica**](https://pubmed.ncbi.nlm.nih.gov/29265877/)**.**

[**Cj1199 Affect the Development of Erythromycin Resistance in Campylobacter jejuni Through Regulation of Leucine Biosynthesis**](https://pubmed.ncbi.nlm.nih.gov/28144238/)**.**

[**Bacterial Populations Associated with Smokeless Tobacco Products**](https://pubmed.ncbi.nlm.nih.gov/27565615/)**.**

[**Evaluation of Virulence and Antimicrobial Resistance in Salmonella enterica Serovar Enteritidis Isolates From Humans and Chicken- and Egg-associated Sources**](https://pubmed.ncbi.nlm.nih.gov/24102082/)**.**

[**The Contribution of ArsB to Arsenic Resistance in Campylobacter jejuni**](https://pubmed.ncbi.nlm.nih.gov/23554953/)**.**

[**Impact of Plasmids, Including Those Encoding VirB4/D4 type IV Secretion Systems on Salmonella enterica Serovar Heidelberg Virulence in Macrophages and Epithelial Cells**](https://pubmed.ncbi.nlm.nih.gov/24098597/)**.**

[**DNA Sequence Analysis of Multidrug Resistance Encoding Plasmids from Salmonella enterica Serotype Heidelberg Isolates**](https://pubmed.ncbi.nlm.nih.gov/23251446/)**.**

[**Genetic Characterization of Antimicrobial Resistance in Salmonella enterica Serovars Isolated from Dairy Cattle in Wisconsin**](https://www.sciencedirect.com/science/article/abs/pii/S0963996911002432)**.**

[**A Fluoroquinolone Resistance Associated Mutation in GyrA Affects DNA Supercoiling in Campylobacter jejuni**](https://pubmed.ncbi.nlm.nih.gov/22919613/)**.**

[**Sequencing of Plasmids from a Multi-antimicrobial Resistant Salmonella enterica Serovar Dublin Strain**](https://www.sciencedirect.com/science/article/abs/pii/S0963996911002468)**.**

[**Characterization of Antimicrobial Resistance in Salmonella enterica Serovar Typhimurium Isolates from Food Animals in the U.S.**](https://www.sciencedirect.com/science/article/abs/pii/S0963996911002146)

[**Comparison of Salmonella enterica Serovar Heidelberg Isolates From Human Patients With Those From Animal and Food Sources**](https://pubmed.ncbi.nlm.nih.gov/21177888/)**.**

[**Evaluation of a Virulence Factor Profiling In the Characterization of Veterinary Escherichia coli**](https://pubmed.ncbi.nlm.nih.gov/20889790/)**.**

[**Antibiotic Resistance in Campylobacter: Emergence, Transmission and Persistence**](https://pubmed.ncbi.nlm.nih.gov/19257846/)**.**

[**Key Role of Mfd in the Development of Fluoroquinolone Resistance in Campylobacter jejuni**](https://pubmed.ncbi.nlm.nih.gov/18535657/)**.**

[VIEW FULL BIO – Jing Han, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/jing-han)

# Mark Hart, Ph.D.

### **Microbiologist — Division of Microbiology**

To our knowledge, the protective effect of *Lactobacillus* against *Staphylococcus* aureus proliferation and subsequent exotoxin production in the vaginal environment has not been adequately addressed in literature. Studies are underway to examine the protective role of naturally occurring and bio-engineered strains of *Lactobacillus* against TSST-1-producing strains of *S. aureus* in both co-culture and simulated vaginal models. Given the propensity of *S. aureus* to acquire multiple antibiotic-resistance determinants and the continual rise in methicillin-resistant *S. aureus* both in the hospital and community environments, isolation and characterization of novel virulence factors expressed by *S. aureus* continues to be a major focus of our laboratory. In addition, other host-pathogen interactions such as *S. aureus* with the influenza virus in causing severe pneumonia are studied. We are also interested in elucidating the mechanisms that allow *S. aureus* to survive phagocytic attack by determining the role enzymes, such as catalase and superoxide dismutase, play in removing the toxic effects of oxygen radicals generated by the body's professional phagocytes. [VIEW FULL BIO – Dr. Mark Hart](https://www.fda.gov/about-fda/science-research-nctr/mark-hart)

**Titles and links to selected publications**

[**A Naturally Occurring Point Mutation in the Hyaluronidase Gene (hysA1) of Staphylococcus aureus UAMS-1 Results in Reduced Enzymatic Activity**](https://pubmed.ncbi.nlm.nih.gov/34520677/)**.**

[**Virulence Characteristics of mecA-Positive Multidrug-Resistant Clinical Coagulase-Negative Staphylococci**](https://pubmed.ncbi.nlm.nih.gov/32369929/)**.**

[**CYPminer: An Automated Cytochrome P450 Identification, Classification, and Data Analysis Tool for Genome Data Sets Across Kingdoms**](https://bmcbioinformatics.biomedcentral.com/articles/10.1186/s12859-020-3473-2)**.**

[**Reduced Vancomycin Susceptibility and Increased Macrophage Survival in Staphylococcus aureus Strains Sequentially Isolated from a Bacteremic Patient During a Short Course of Antibiotic Therapy**](https://pubmed.ncbi.nlm.nih.gov/31136294/)**.**

[**Draft Genome Sequences of Two Staphylococcus aureus Strains Isolated in Succession from a Case of Bacteremia**](https://www.ncbi.nlm.nih.gov/pubmed/28596388)**.**

[**Infection of Murine Macrophages by Salmonella enterica Serovar Heidelberg Blocks Murine Norovirus Infectivity and Virus-Induced Apoptosis**](http://www.ncbi.nlm.nih.gov/pubmed/26658916)**.**

[***Staphylococcus aureus* Toxic Shock Syndrome Toxin-1 (TSST-1) Production and Lactobacillus Species Growth in a Defined Medium Simulating Vaginal Secretions**](http://www.ncbi.nlm.nih.gov/pubmed/25135489)**.**

[**Staphylococcus aureus Hyaluronidase is a CodY-Regulated Virulence Factor**](http://www.ncbi.nlm.nih.gov/pubmed/25069977)**.**

[**Evaluation of Virulence and Antimicrobial Resistance in Salmonella enterica Serovar Enteritidis Isolates from Humans and Chicken- and Egg-Associated Sources**](http://www.ncbi.nlm.nih.gov/pubmed/24102082)**.**

[**Hyaluronidase Expression and Biofilm Involvement in Staphylococcus aureus UAMS-1 and its sarA, agr and sarA agr Regulatory Mutants**](http://www.ncbi.nlm.nih.gov/pubmed/23393148)**.**

[**Inhibition of Staphylococcus aureus by Lysostaphin-Expressing Lactobacillus plantarum WCFS1 in a Modified Genital Tract Secretion Medium**](http://www.ncbi.nlm.nih.gov/pubmed/21984245)**.**

[**Influenza Virus Primes Mice for Pneumonia from Staphylococcus aureus**](http://www.ncbi.nlm.nih.gov/pubmed/21278211)**.**

[**Genotypic and Phenotypic Assessment of Hyaluronidase among Type Strains of a Select Group of Staphylococcal Species**](http://www.ncbi.nlm.nih.gov/pubmed/20130817)**.**

[***Lactobacillus*-Mediated Inhibition of Clinical Toxic Shock Syndrome Staphylococcus aureus Strains and Its Relation to Acid and Peroxide Production**](http://www.ncbi.nlm.nih.gov/pubmed/18926917)**.**

[**Relative Quantitative Comparisons of the Extracellular Protein Profiles of Staphylococcus Aureus UAMS-1 and its sarA, agr, and sarA agr Regulatory Mutants Using One-Dimensional Polyacrylamide Gel Electrophoresis and Nanocapillary Liquid Chromatography Coupled with Tandem Mass Spectrometry**](http://www.ncbi.nlm.nih.gov/pubmed/18539737)**.**

[VIEW FULL BIO – Mark Hart, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/jing-han)

# Jinshan Jin, Ph.D.

### **Visiting Scientist — Division of Microbiology**

Dr. Jin’s research is primarily focused on using current microbiological and omics techniques to evaluate the toxicities of FDA-regulated products, including smokeless tobacco products, azo dyes, nanomaterials, and compounding medicines. She is interested in studying how the interaction between microbiota and FDA-regulated products could affect human health, and ultimately provide data to aid FDA’s risk assessment of products. Dr. Jin has investigated the interaction between smokeless tobacco products on oral microbiota with metagenomic sequencing and she is undertaking a study on the interaction between the skin microbiota and nanomaterials present in sunscreens. Another focus of Dr. Jin’s research is establishing standardized methods for sporicidal efficacy assessment. Her most recent work is characterization of the in vitro cytotoxicity profile of compounded triamcinolone-moxifloxacin drug products. Dr. Jin is also interested in developing standard microbiological methods to address FDA’s safety concerns. [VIEW FULL BIO – Dr. Jinshan Jin](https://www.fda.gov/about-fda/science-research-nctr/jinshan-jin)

**Titles and links to selected publications**

[**Phylogenetically Diverse Bacteria Isolated from Tattoo Inks, an Azo Dye-Rich Environment, Decolorize a Wide Range of Azo Dyes**](https://annalsmicrobiology.biomedcentral.com/articles/10.1186/s13213-021-01648-2)**.**

[**Thiouracil SecA Inhibitors: Bypassing the Effects of Efflux Pumps and Attenuating Virulence Factor Secretion in MRSA and Bacillus anthracis**](https://link.springer.com/article/10.1007/s00044-021-02750-5)**.**

[**Smokeless Tobacco Impacts Oral Microbiota in a Syrian Golden Hamster Cheek Pouch Carcinogenesis Model**](https://www.ncbi.nlm.nih.gov/pubmed/29852249)**.**

[**Mutation Network-Based Understanding of Pleiotropic and Epistatic Mutational Behavior of Enterococcus faecalis FMN-Dependent Azoreductase**](https://www.ncbi.nlm.nih.gov/pubmed/29214224)**.**

[**Evaluation of Metabolism of Azo Dyes and Their Effects on Staphylococcus aureus Metabolome**](https://www.ncbi.nlm.nih.gov/pubmed/28786013)**.**

[**Biphasic Actions of SecA Inhibitors on Prl/Sec Suppressors: Possible Physiological Roles of SecA-Only Channels**](https://www.ncbi.nlm.nih.gov/pubmed/27856243)**.**

[**Effect of Smokeless Tobacco Products on Human Oral Bacteria Growth and Viability**](https://www.ncbi.nlm.nih.gov/pubmed/27756619)**.**

[**Using Chemical Probes to Assess the Feasibility of Targeting SecA for Developing Antimicrobial Agents against Gram-Negative Bacteria**](https://www.ncbi.nlm.nih.gov/pubmed/27753464)**.**

[**Metabolomics Evaluation of the Impact of Smokeless Tobacco Exposure on the Oral Bacterium Capnocytophaga sputigena**](https://www.ncbi.nlm.nih.gov/pubmed/27480511)**.**

[**Design, Synthesis and Evaluation of Triazole-Pyrimidine Analogues as SecA Inhibitors**](https://www.ncbi.nlm.nih.gov/pubmed/26607404)**.**

[**Evaluation of Small Molecule SecA Inhibitors Against Methicillin-Resistant Staphylococcus aureus**](https://www.ncbi.nlm.nih.gov/pubmed/26432604)**.**

[**SecA: A Potential Antimicrobial Target**](https://www.ncbi.nlm.nih.gov/pubmed/26062397)**.**

[**Design, Syntheses and Evaluation of 4-Oxo-5-Cyano Thiouracils as SecA Inhibitors**](https://www.ncbi.nlm.nih.gov/pubmed/25498235)**.**

[**Design, Synthesis and Biological Evaluation of Rose Bengal Analogues as SecA Inhibitors**](https://www.ncbi.nlm.nih.gov/pubmed/23794293)**.**

[VIEW FULL BIO – Jinshan Jin, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/jinshan-jin)

# Ashraf Khan, Ph.D.

### **Microbiologist — Division of Microbiology**

Dr. Khan’s research interests are in the fields of antimicrobial resistance in foodborne pathogens from food and clinical sources, and the role of efflux pumps genetic characterization of enteric bacteria using molecular techniques. His research projects at NCTR include:

* Analyzing the function of efflux pump genes and their regulation in multidrug-resistant *Salmonella enterica* and *E. coli.*
* Characterizing structural and regulatory genes responsible for antibiotic resistance, their role for low-level resistance [low minimum inhibitory concentration (MICs)], and their synergy with other resistance mechanisms (increased MICs) by analyzing efflux pump inhibition using efflux pump inhibitors.
* Whole-genome sequencing of multidrug-resistant *Salmonella* spp. isolated from food and clinical sources.
* Characterizing enterotoxigenic *Bacillus cereus* from dietary supplements.
* Multi-lab validation of isolation and identification of non-tuberculous *Mycobacteria* associated with tattoo-related skin infections.
* Developing a cultural method for the detection.

[VIEW FULL BIO – Dr. Ashraf Khan](https://www.fda.gov/about-fda/science-research-nctr/ashraf-khan)

**Titles and links to selected publications**

[**Antimicrobial Resistance and Related Gene Analysis of Salmonella from Egg and Chicken Sources by Whole-Genome Sequencing**](https://pubmed.ncbi.nlm.nih.gov/33930890/)**.**

[**Identification of Novel Plasmid Replicons Harboring β-Lactamase Resistant Genes in Ampicillin-Resistant Uropathogenic Escherichia coli**](https://scholar.google.ca/citations?view_op=view_citation&hl=en&user=VFC3doUAAAAJ&cstart=20&pagesize=80&sortby=pubdate&citation_for_view=VFC3doUAAAAJ:mJbmKSuM8toC)**.**

[**Analysis of Enterotoxigenic Bacillus cereus Strains from Dried Foods Using Whole Genome Sequencing, Ulti-Locus Sequence Analysis and Toxin Gene Prevalence and Distribution Using Endpoint PCR Analysis**](https://pubmed.ncbi.nlm.nih.gov/29990637/)**.**

[**Draft Genome Sequences of Ciprofloxacin-Resistant Salmonella enterica Strains with Multiple-Antibiotic Resistance, Isolated from Imported Foods**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Draft+Genome+Sequences+of+Ciprofloxacin-Resistant+Salmonella+enterica+Strains+with+Multiple-Antibiotic+Resistance%2C+Isolated+from+Imported+Foods.)**.**

[**Isolation and Characterization of Antimicrobial-Resistant Nontyphoidal Salmonella enterica serovars from Imported Food Products**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Isolation+and+Characterization+of+Antimicrobial-Resistant+Nontyphoidal+Salmonella+enterica+Serovars+from+Imported+Food+Products)**.**

[**Characterization of Extended-Spectrum Beta-Lactamase (ESBL) Producing Non-Typhoidal Salmonella (NTS) from Imported Food Products**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Characterization+of+Extended-Spectrum+Beta-Lactamase+(ESBL)+Producing+Non-Typhoidal+Salmonella+(NTS)+from+Imported+Food+Products)**.**

[**Detection and Functionality of the CdtB, PltA, and PltB from Salmonella enterica serovar Javiana**](https://www.ncbi.nlm.nih.gov/pubmed/24891290)**.**

[**The Sub-Species Characterization and Antimicrobial Resistance of Listeria monocytogenes Isolated from Domestic and Imported Food Products from 2004 to 2011**](https://www.sciencedirect.com/science/article/pii/S0963996914005262)**.**

[**Isolation and Molecular Characterization of Salmonella enterica serovar Enteritidis from Poultry House and Clinical Samples During 2010**](https://www.ncbi.nlm.nih.gov/pubmed/24290628)**.**

[**The tetA Gene Decreases Tigecycline Sensitivity of Salmonella enterica Isolates**](https://www.ncbi.nlm.nih.gov/pubmed/23746717)**.**

[**Isolation and Molecular Characterization of Salmonella enterica serovar Javiana from Food, Environmental and Clinical Samples**](https://www.ncbi.nlm.nih.gov/pubmed/23628778)**.**

[**Identification and Molecular Characterization of Class 1 Integrons in Multiresistant Escherichia coli Isolates from Poultry Litter**](https://www.ncbi.nlm.nih.gov/pubmed/22635994)**.**

[**Isolation and Characterization of Small qnrS1-Carrying Plasmids from Imported Seafood Isolates of Salmonella enterica that are Highly Similar to Plasmids of Clinical Isolates**](https://www.ncbi.nlm.nih.gov/pubmed/22151215)**.**

[**Molecular Characterization of Strains of Fluoroquinolone-Resistant Salmonella enterica serovar Schwarzengrund Carrying Multidrug Resistance Isolated from Imported Foods**](https://www.ncbi.nlm.nih.gov/pubmed/22010209)**.**

[**Molecular Characterization of Salmonella enterica serovar Saintpaul Isolated from Imported Seafood, Pepper, Environmental and Clinical Samples**](https://www.ncbi.nlm.nih.gov/pubmed/21645810)**.**

[**Identification and Characterization of Class 1 Integron Resistance Gene Cassettes Among Salmonella Strains Isolated from Imported Seafood**](https://www.ncbi.nlm.nih.gov/pubmed/19074612)**.**

[**Prevalence and Characterization of Salmonella enterica serovar Weltevreden from Imported Seafood**](https://www.ncbi.nlm.nih.gov/pubmed/17993374)**.**

[**Identification and Molecular Characterization of Salmonella spp. from Unpasteurized Orange Juices and Identification of New Serotype Salmonella Strain S. enterica serovar Tempe**](https://www.ncbi.nlm.nih.gov/pubmed/17367687)**.**

[**Occurrence of Non-O157 Shiga Toxin-Producing Escherichia coli in Ready-To-Eat Food from Supermarkets in Argentina**](https://www.ncbi.nlm.nih.gov/pubmed/16943019)**.**

[**Novel Organization of Genes in a Phthalate Degradation Operon of Mycobacterium vanbaalenii PYR-1**](https://www.ncbi.nlm.nih.gov/pubmed/15528661)**.**

[**Classification of a Polycyclic Aromatic Hydrocarbon-Metabolizing Bacterium, Mycobacterium sp. Strain PYR-1, as Mycobacterium vanbaalenii sp. nov**](https://www.ncbi.nlm.nih.gov/pubmed/12508859)**.**

[**Characterization of United States Outbreak Isolates of Vibrio parahaemolyticus Using Enterobacterial Repetitive Intergenic Consensus (ERIC) PCR and Development of a Rapid PCR Method for Detection of O3:K6 Isolates**](https://www.ncbi.nlm.nih.gov/pubmed/11814665)**.**

[**Identification of Predominant Human and Animal Anaerobic Intestinal Bacterial Species by Terminal Restriction Fragment Patterns (TRFPs): a Rapid, PCR-Based Method**](https://www.ncbi.nlm.nih.gov/pubmed/11851378)**.**

[**Detection of Multidrug-Resistant Salmonella typhimurium DT104 by Multiplex Polymerase Chain Reaction**](https://www.ncbi.nlm.nih.gov/pubmed/10620692)**.**

[VIEW FULL BIO – Ashraf Khan, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/ashraf-khan)

# Saeed Khan, Ph.D.

### **Research Microbiologist — Division of Microbiology**

Dr. Khan’s research interests and expertise include microbial physiology phages, and molecular biology of host-pathogen interactions, gene-expression studies, antimicrobial resistance, and genome comparisons. Dr. Khan uses state-of-the-art molecular tools to study host-pathogen interactions, gene-expression analysis, and antimicrobial-resistance genes in foodborne, animal, and human clinical isolates. He uses biochemical, molecular, and whole genome sequencing techniques to characterize bacterial isolates from different ecological niches. He also uses the real-time PCR analysis to study the expression of efflux pump and antimicrobial resistance genes and developed quantitative multiplex PCR assays to detect multiple antimicrobial resistance markers. He uses sequencing tools to study the mutations in genes responsible for fluoroquinolone resistance in bacteria from a variety of sources and also uses the next generation sequencing for several multidrug-resistant human clinical staphylococcal and enterococcal isolates. Currently, Dr. Khan is studying the differences among MRSA isolates that produce biofilms and carry a multitude of virulence and antimicrobial resistance factors, persistence of infection, survivability, diversity, and virulence using the whole genome sequencing techniques, proteomic profiles, and adhesion assays. Other projects that he is working in collaboration with scientists in the Division of Microbiology involve the mechanism of biofilm formation by S. aureus and uropathogenic E. coli. The research goals include understanding the mechanism of antimicrobial resistance, virulence, pathogenicity, and genetic evolution with a scope of developing countermeasure and mitigation strategies to control the spread of multidrug-resistant bacteria and help the Agency in making science-based prudent decisions for regulatory needs. [VIEW FULL BIO – Dr. Saeed Khan](https://www.fda.gov/about-fda/science-research-nctr/saeed-khan)

**Titles and links to selected publications**

[**Genotypic Characterization of Clinical Isolates of Staphylococcus aureus from Pakistan**](https://doi.org/10.3390/pathogens10080918)**.**

[**Dynamic Adaptive Response of Pseudomonas aeruginosa to Clindamycin/Rifampicin-Impregnated Catheters**](https://doi.org/10.3390/antibiotics10070752)**.**

[**Molecular Typing of β-lactamase and Tetracycline Resistant Escherichia coli Strains Isolated from Imported Shrimp**](https://austinpublishinggroup.com/bacteriology/fulltext/bacteriology-v6-id1102.php)**.**

[**Prevalence, Toxin Gene Profile, Antibiotic Resistance, and Molecular Characterization of Clostridium perfringens from Diarrheic and Non-Diarrheic Dogs in Korea**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Prevalence%2C+Toxin+Gene+Profile%2C+Antibiotic+Resistance%2C+and+Molecular+Characterization+of+Clostridium+perfringens+from+Diarrheic+and+Non-Diarrheic+Dogs+i)**.**

[**Investigating the Susceptibility of Mice to A Bacterial Challenge after Intravenous Exposure to Durable Nanoparticles**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Investigating+the+susceptibility+of+mice+to+a+bacterial+challenge+after+intravenous+exposure+to+durable+nanoparticles.)**.**

[**Evaluating the Potential of Gold, Silver, and Silica Nanoparticles to Saturate Mononuclear Phagocytic System Tissues Under Repeat Dosing Conditions**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Evaluating+the+Potential+of+Gold%2C+Silver%2C+and+Silica+Nanoparticles+to+Saturate+Mononuclear+Phagocytic+System+Tissues+Under+Repeat+Dosing+Conditions.)**.**

[**Diversity of Clostridium Perfringens Isolates from Various Sources and Prevalence of Conjugative Plasmids**](https://www.ncbi.nlm.nih.gov/pubmed/26608548)**.**

[**Draft Genome Sequence of Multidrug-resistant Enterococcus faecium Clinical Isolate VRE3, ST16, with Novel Structural Arrangement of Tn1546**](https://www.ncbi.nlm.nih.gov/pubmed/26272564)**.**

[**Draft Genome Sequence of a Methicillin-Resistant Staphylococcus aureus ST1413 Strain for Studying Genetic Mechanisms of Antibiotic Resistance**](https://www.ncbi.nlm.nih.gov/pubmed/24604656)**.**

[**Molecular Characterization of Fluoroquinolone-Resistant Aeromonas spp. Isolated from Imported Shrimp**](https://www.ncbi.nlm.nih.gov/pubmed/22923408)**.**

[**A Transcriptomic Expression Array, PCR and Disk Diffusion Analysis of Antimicrobial Resistance Genes in Multidrug-Resistant Bacteria**](https://www.researchgate.net/publication/305399093_A_transcriptomic_expression_array_PCR_and_disk_diffusion_analysis_of_antimicrobial_resistance_genes_in_multidrug-resistant_bacteria)**.**

[**Lysozyme as a Barrier to Growth of Bacillus anthracis Strain Sterne in Liquid Egg White, Milk and Beef**](https://www.ncbi.nlm.nih.gov/pubmed/21645824)**.**

[**Detection of aacA-aphD, qacEδ1, marA, floR, and tetA Genes from Multidrug-Resistant Bacteria: Comparative Analysis of Real-Time Multiplex PCR Assays Using EvaGreen® and SYBR® Green I Dyes**](https://www.ncbi.nlm.nih.gov/pubmed/21256956)**.**

[**Detection and Characterization of Virulence Genes and Integrons in Aeromonas veronii Isolated from Catfish**](https://www.ncbi.nlm.nih.gov/pubmed/20227596)**.**

[**The Survivability of Bacillus anthracis in Processed Liquid Eggs**](https://www.ncbi.nlm.nih.gov/pubmed/19171252)**.**

[**Genetic Diversity of Tn1546-Like Elements in Clinical Isolates of Vancomycin-Resistant Enterococci**](https://www.ncbi.nlm.nih.gov/pubmed/18462926)**.**

[**Heteroresistance to Vancomycin and Novel Point Mutations in Tn1546 of Enterococcus faecium ATCC 51559**](https://www.ncbi.nlm.nih.gov/pubmed/17936593)**.**

[**Direct In-Gel Hybridization of DNA with Digoxigenin-Labeled Probes. In Protocols for Nucleic Acid Analysis by Nonradioactive Probes**](https://www.ncbi.nlm.nih.gov/pubmed/17332635)**.**

[**Characterization of Class 1 Integron Resistance Gene Cassettes in Salmonella enterica Serovars Oslo and Bareily from Imported Seafood**](https://www.ncbi.nlm.nih.gov/pubmed/17068008)**.**

[**Molecular Characterization of Multidrug-Resistant Enterococcus spp. from Poultry and Dairy Farms: Detection of Virulence and Vancomycin Resistance Gene Markers by PCR**](https://www.ncbi.nlm.nih.gov/pubmed/15652217)**.**

[VIEW FULL BIO – Saeed Khan, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/saeed-khan)

# Sangeeta Khare, M.S., Ph.D.

### **Research Microbiologist — Division of Microbiology**

Dr. Khare works on cutting-edge xenobiotic-microbiome-host communication, host-pathogen interaction, and nanoparticle research. She has successfully used in vivo, ex vivo, and in vitro models for microbiome assessment during the interaction of xenobiotics to disclose science-based evidence for regulatory sciences. She applies advanced technologies that could be used as endpoints to evaluate the safety of xenobiotics in the gastrointestinal tract. For example, under an interagency agreement with NTP/NIEHS and FDA, her research team is performing risk assessments of several xenobiotic compounds (Aloin, Arsenic, Silver nanoparticle, BisphenolAF, Triclosan) using non-animal and animal models to delineate the impact on the intestinal microbiome and gut-associated immune response during exposure to acute/chronic/repeated exposure of xenobiotics. Moreover, recent efforts focus on the development of models that reveal translation from animal to human. The outcome of this research is in line with the FDA Strategic Policy Roadmap to “empower consumers to make better and more informed decisions about their diets and health.”

Another aspect of Dr. Khare’s research is to assess the impact of emerging nanomaterial on the gastrointestinal tract. Under a Broad Agency Announcement between the Arkansas Research Consortium in Nanotoxicity and the FDA, Dr. Khare led a project to perform safety assessments of carbon-based nanomaterial (Graphene and Carbon Nano Tubes). Dr. Khare’s laboratory has provided data that can be used as additional endpoints in the safety evaluation of nanotechnology-derived products which supplements the traditional metabolism, toxicity, and tissue-residue disposition information used in toxicology risk assessments.

The use of veterinary antimicrobial drugs in food-producing animals may result in antimicrobial-drug residues in or on the edible products derived from treated animals. There are ongoing concerns that the residual amount of antibiotic may cause emergence of antimicrobial resistance in intestinal-microbial populations, as well as lead to the development of cross-resistance for other classes of antibiotics. In collaboration with FDA’s Center for Veterinary Medicine, studies are in progress to evaluate the effects of residual amounts of antibiotics on the development of antibiotic resistance and gastrointestinal permeability. Dr. Khare’s laboratory uses in vitro and ex vivo models to address this emerging FDA concern and highlights the importance of evaluating toxicity of residual concentrations of antimicrobial agents in food. Data from these studies may aid in establishing guidance for human food-safety assessments.

Scientists from academia and other government agencies have reached out to Dr. Khare for collaborations. For example, she is a collaborator on a study conducted at the University of Arkansas for Medical Sciences to address links between environment pollutant exposure, obesity, and the microbiome. She has also collaborated with investigators from Harvard University to analyze the impact of edible nanomaterial on the intestinal microbiota. In collaboration with other scientists at NCTR her research group is making efforts to identify the link of intestinal microbiome with extraintestinal diseases using transgenic animals and collaborative cross animals. The outcomes of collaborative projects within NCTR and with FDA Product Centers, the NTP, and academic institutions are in line with the FDA’s Strategic Plan on Regulatory Science to “Evaluate Innovative Emerging Technologies” and “Modernize Toxicology to Enhance Product Safety.” The long-term goal of Dr. Khare’s research is to advance regulatory science by understanding the complex relationship of the gastrointestinal tract with commensal bacteria, invading enteric pathogens and residues (antibiotics, drugs, pesticides, herbicides, and additives) in consumed food products. The outcome of this research will provide a comprehensive understanding of the mechanistic interaction of xenobiotics-host-microbiome. These findings will form a basis to draft a decision tree for gastrointestinal risk assessment. [VIEW FULL BIO – Dr. Sangeeta Khare](https://www.fda.gov/about-fda/science-research-nctr/sangeeta-khare)

**Titles and links to selected publications**

[**Genotypic Characterization of Clinical Isolates of Staphylococcus aureus from Pakistan**](https://doi.org/10.3390/pathogens10080918)**.**

[**Dynamic Adaptive Response of Pseudomonas aeruginosa to Clindamycin/Rifampicin-Impregnated Catheters**](https://doi.org/10.3390/antibiotics10070752)**.**

[**Molecular Typing of β-lactamase and Tetracycline Resistant Escherichia coli Strains Isolated from Imported Shrimp**](https://austinpublishinggroup.com/bacteriology/fulltext/bacteriology-v6-id1102.php)**.**

[**Prevalence, Toxin Gene Profile, Antibiotic Resistance, and Molecular Characterization of Clostridium perfringens from Diarrheic and Non-Diarrheic Dogs in Korea**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Prevalence%2C+Toxin+Gene+Profile%2C+Antibiotic+Resistance%2C+and+Molecular+Characterization+of+Clostridium+perfringens+from+Diarrheic+and+Non-Diarrheic+Dogs+i)**.**

[**Investigating the Susceptibility of Mice to A Bacterial Challenge after Intravenous Exposure to Durable Nanoparticles**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Investigating+the+susceptibility+of+mice+to+a+bacterial+challenge+after+intravenous+exposure+to+durable+nanoparticles.)**.**

[**Evaluating the Potential of Gold, Silver, and Silica Nanoparticles to Saturate Mononuclear Phagocytic System Tissues Under Repeat Dosing Conditions**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Evaluating+the+Potential+of+Gold%2C+Silver%2C+and+Silica+Nanoparticles+to+Saturate+Mononuclear+Phagocytic+System+Tissues+Under+Repeat+Dosing+Conditions.)**.**

[**Diversity of Clostridium Perfringens Isolates from Various Sources and Prevalence of Conjugative Plasmids**](https://www.ncbi.nlm.nih.gov/pubmed/26608548)**.**

[**Draft Genome Sequence of Multidrug-resistant Enterococcus faecium Clinical Isolate VRE3, ST16, with Novel Structural Arrangement of Tn1546**](https://www.ncbi.nlm.nih.gov/pubmed/26272564)**.**

[**Draft Genome Sequence of a Methicillin-Resistant Staphylococcus aureus ST1413 Strain for Studying Genetic Mechanisms of Antibiotic Resistance**](https://www.ncbi.nlm.nih.gov/pubmed/24604656)**.**

[**Molecular Characterization of Fluoroquinolone-Resistant Aeromonas spp. Isolated from Imported Shrimp**](https://www.ncbi.nlm.nih.gov/pubmed/22923408)**.**

[**A Transcriptomic Expression Array, PCR and Disk Diffusion Analysis of Antimicrobial Resistance Genes in Multidrug-Resistant Bacteria**](https://www.researchgate.net/publication/305399093_A_transcriptomic_expression_array_PCR_and_disk_diffusion_analysis_of_antimicrobial_resistance_genes_in_multidrug-resistant_bacteria)**.**

[**Lysozyme as a Barrier to Growth of Bacillus anthracis Strain Sterne in Liquid Egg White, Milk and Beef**](https://www.ncbi.nlm.nih.gov/pubmed/21645824)**.**

[**Detection of aacA-aphD, qacEδ1, marA, floR, and tetA Genes from Multidrug-Resistant Bacteria: Comparative Analysis of Real-Time Multiplex PCR Assays Using EvaGreen® and SYBR® Green I Dyes**](https://www.ncbi.nlm.nih.gov/pubmed/21256956)**.**

[**Detection and Characterization of Virulence Genes and Integrons in Aeromonas veronii Isolated from Catfish**](https://www.ncbi.nlm.nih.gov/pubmed/20227596)**.**

[**The Survivability of Bacillus anthracis in Processed Liquid Eggs**](https://www.ncbi.nlm.nih.gov/pubmed/19171252)**.**

[**Genetic Diversity of Tn1546-Like Elements in Clinical Isolates of Vancomycin-Resistant Enterococci**](https://www.ncbi.nlm.nih.gov/pubmed/18462926)**.**

[**Heteroresistance to Vancomycin and Novel Point Mutations in Tn1546 of Enterococcus faecium ATCC 51559**](https://www.ncbi.nlm.nih.gov/pubmed/17936593)**.**

[**Direct In-Gel Hybridization of DNA with Digoxigenin-Labeled Probes. In Protocols for Nucleic Acid Analysis by Nonradioactive Probes**](https://www.ncbi.nlm.nih.gov/pubmed/17332635)**.**

[**Characterization of Class 1 Integron Resistance Gene Cassettes in Salmonella enterica Serovars Oslo and Bareily from Imported Seafood**](https://www.ncbi.nlm.nih.gov/pubmed/17068008)**.**

[**Molecular Characterization of Multidrug-Resistant Enterococcus spp. from Poultry and Dairy Farms: Detection of Virulence and Vancomycin Resistance Gene Markers by PCR**](https://www.ncbi.nlm.nih.gov/pubmed/15652217)**.**

[VIEW FULL BIO – Sangeeta Khare, M.S., Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/sangeeta-khare)

# Seong-Jae Kim, Ph.D.

### **Staff Fellow — Division of Microbiology**

Dr. Kim’s research initially focused on the bacterial biodegradation of polycyclic aromatic hydrocarbons (PAHs) with special emphasis on high-molecular-weight PAHs with four or more fused aromatic benzene rings. PAHs are one of the largest classes of compounds that consist of more than 200 chemicals with two or more benzene rings. These compounds have been identified to have carcinogenic, genotoxic, and mutagenic effects on experimental animals and have been implicated in different types of human cancers — mainly breast, lung, and colon cancers. Human exposure to carcinogenic PAH can occur by food intake, cigarette smoke, smoke from the burning of fossil fuels, and by occupational exposure. While the PAH carcinogenicity has long been suspected, studies elucidating biodegradation pathway have been lacking. Dr. Kim’s research has shown some of the mechanisms in the metabolism of PAHs in microorganisms using metabolic, genomic, and proteomic approaches. In particular, he and his team for the first time elucidated complete degradation pathways of low-molecular-weight PAH, pyrene and fluoranthene. Understanding of PAH metabolism and its degradative pathway is important in that it provides the FDA with fundamental information on the fate of carcinogenic PAHs in the environment and humans.  
   
Dr. Kim is currently in collaboration with FDA’s Center for Food Safety and Applied Nutrition (CFSAN), investigating whether tattoo and permanent makeup (PMU) inks are safe in terms of microbial contamination. Since the initial CFSAN investigation identified nontuberculous mycobacteria in tattoo ink samples collected from tattoo parlors during several outbreaks of tattoo-associated skin infections in 2011-2012, the FDA has had continuous concerns about the microbiological safety of tattoo ink products from a public health standpoint. In the studies that began in 2017, Dr. Kim’s NCTR research team has shown that commercial tattoo and PMU inks sold in the United States are often contaminated with a wide range of microorganisms including pathogenic bacteria. The results demonstrated the importance of monitoring these products marketed in the U.S. in terms of microbial contamination. Based on these results, the collaborative research is being expanded with several different targets, such as whether tattoo inks are contaminated with anaerobic bacteria. In addition, Dr. Kim has interests in assessing microbial contamination of tattoo and PMU inks manufactured in foreign countries, examining the impacts/effectiveness of sterilization and preservatives on microbial contamination, as well as developing molecular-based methods for direct detection of microbial contamination. [VIEW FULL BIO – Dr. Seong-Jae Kim](https://www.fda.gov/about-fda/science-research-nctr/seong-jae-kim)

**Titles and links to selected publications**

[**Microbial Contamination of Tattoo and Permanent Makeup Inks Marketed in the US: A Follow-Up Study**](https://pubmed.ncbi.nlm.nih.gov/32654157/)**.**

[**Microbiological Survey of Commercial Tattoo and Permanent Makeup Inks Available in the United States**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Microbiological+survey+of+commercial+tattoo+and+permanent+makeup+inks+available+in+the+United+States.)**.**

[**Dynamic Response of Mycobacterium vanbaalenii PYR-1 to BP Deepwater Horizon Crude Oil**](https://www.ncbi.nlm.nih.gov/pubmed/25888169)**.**

[**Comparative Functional Pan-Genome Analyses to Build Connections Between Genomic Dynamics and Phenotypic Evolution in Polycyclic Aromatic Hydrocarbon Metabolism in the Genus Mycobacterium**](https://www.ncbi.nlm.nih.gov/pubmed/25880171)**.**

[**Pleiotropic and Epistatic Behavior of a Ring-Hydroxylating Oxygenase System in the Polycyclic Aromatic Hydrocarbon Metabolic Network from Mycobacterium vanbaalenii PYR-1**](https://www.ncbi.nlm.nih.gov/pubmed/25070740)**.**

[**Functional Robustness of a Polycyclic Aromatic Hydrocarbon Metabolic Network Examined in a nidA Aromatic Ring-Hydroxylating Oxygenase Mutant of Mycobacterium vanbaalenii PYR-1**](https://www.ncbi.nlm.nih.gov/pubmed/22407691)**.**

[**Polycyclic Aromatic Hydrocarbon Metabolic Network in Mycobacterium vanbaalenii  PYR-1**](https://www.ncbi.nlm.nih.gov/pubmed/21725022)**.**

[**Substrate Specificity and Structural Characteristics of the Novel Rieske Nonheme Iron Aromatic Ring-Hydroxylating Oxygenases NidAB and NidA3B3 from Mycobacterium vanbaalenii PYR-1**](https://www.ncbi.nlm.nih.gov/pubmed/20714442)**.**

[**Proteomic Applications to Elucidate Bacterial Aromatic Hydrocarbon Metabolic Pathways**](https://www.ncbi.nlm.nih.gov/pubmed/19414279)**.**

[**A Polyomic Approach to Elucidate the Fluoranthene-Degradative Pathway in Mycobacterium vanbaalenii PYR-1**](https://www.ncbi.nlm.nih.gov/pubmed/17449607)**.**

[**Complete and Integrated Pyrene Degradation Pathway in Mycobacterium vanbaalenii PYR-1 Based on Systems Biology**](https://www.ncbi.nlm.nih.gov/pubmed/17085566)**.**

[**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**](https://www.ncbi.nlm.nih.gov/pubmed/16461648)**.**

[VIEW FULL BIO – Seong-Jae Kim, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/seong-jae-kim)

# Ohgew Kweon, Ph.D.

### **Staff Fellow — Division of Microbiology**

Dr. Kweon’s primary research interest is bridging the gap between genome and phenome. Despite an excess of bacterial data including genome sequences and functional genomics data (e.g., ribonucleic acid sequencing and proteomic data), considerable knowledge gaps exist between genome and phenome that hinder efforts toward the treatment of diseases and practical biotechnological applications. Pleiotropy and epistasis of biological data are key factors for successful genome-phenome mapping, essential for a better understanding of the microbial world. Motivated by those concepts, Dr. Kweon’s research activities concern the development and application of systemic methods to address questions in the pleiotropic and epistatic complexity of biological data. Dr. Kweon and his colleagues have introduced a method called Network Based Functional Pan-Genomics which systematically integrates the three different types of concepts: network, pan-genomics, and functional genomics. This approach allowed for phenotype-related functional pan-genomic comparison in the mycobacterial phenotype network at the genus level, which discovered pleiotropy- and epistasis-dependent evolutionary trajectories of the “PAH-degrading” phenotype in the genus Mycobacterium (Kweon, et al., BMC Evol Biol. 2015). Dr. Kweon specializes in high-throughput data analysis, protein structural analysis, and bioinformatics methods, as well as wet laboratory methods which generate genetic and functional genomics data. Currently, Dr. Kweon is working with several collaborators to develop computational tools for comparative genome analysis and enzyme identification/classification. Recently, Dr. Kweon and colleagues introduced CYPminer (v1), an automated cytochrome P450 identification, classification, and data analysis tool for genome data sets across kingdoms (Kweon, et al., BMC Bioinformatics. 2020). Pleiotropy and epistasis are open concepts for all biology questions. [VIEW FULL BIO – Dr. Ohgew Kweon](https://www.fda.gov/about-fda/science-research-nctr/ohgew-kweon)

**Titles and links to selected publications**

[**Phylogenetically Diverse Bacteria Isolated from Tattoo Inks, an Azo Dye-Rich Environment, Decolorize a Wide Range of Azo Dyes**](https://link.springer.com/article/10.1186/s13213-021-01648-2)**.**

[**Pragmatic Strategy for Fecal Specimen Storage and the Corresponding Test Methods for Clostridioides difficile Diagnosis**](https://pubmed.ncbi.nlm.nih.gov/34451512/)**.**

[**Microbial Contamination of Tattoo and Permanent Makeup Inks Marketed in the US: A Follow-Up Study**](https://pubmed.ncbi.nlm.nih.gov/32654157/)**.**

[**CYPminer: An Automated Cytochrome P450 Identification, Classification, and Data Analysis Tool for Genome Data Sets Across Kingdoms**](https://pubmed.ncbi.nlm.nih.gov/32349673/)**.**

[**An Update on the Genomic View of Mycobacterial High-Molecular-Weight Polycyclic Aromatic Hydrocarbon Degradation**](https://link.springer.com/referenceworkentry/10.1007%2F978-3-319-50418-6_31)**.**

[**Microbiological Survey of Commercial Tattoo and Permanent Makeup Inks Available in the United States**](https://pubmed.ncbi.nlm.nih.gov/29388315/)**.**

[**Intrinsic Resistance of Burkholderia cepacia Complex to Benzalkonium Chloride**](https://pubmed.ncbi.nlm.nih.gov/27879334/)**.**

[**Novel Insights into Polycyclic Aromatic Hydrocarbon Biodegradation Pathways Using Systems Biology and Bioinformatics Approaches**](https://www.caister.com/hsp/abstracts/biodegradation/09.html)**.**

[**Dynamic Response of Mycobacterium vanbaalenii PYR-1 to BP Deepwater Horizon Crude Oil**](https://www.ncbi.nlm.nih.gov/pubmed/25888169)**.**

[**Comparative Functional Pan-Genome Analyses to Build Connections Between Genomic Dynamics and Phenotypic Evolution in Polycyclic Aromatic Hydrocarbon Metabolism in the Genus Mycobacterium**](https://www.ncbi.nlm.nih.gov/pubmed/25880171)**.**

[**Pleiotropic and Epistatic Behavior of a Ring-Hydroxylating Oxygenase System in the Polycyclic Aromatic Hydrocarbon Metabolic Network from Mycobacterium vanbaalenii PYR-1**](https://www.ncbi.nlm.nih.gov/pubmed/25070740)**.**

[**Functional Robustness of a Polycyclic Aromatic Hydrocarbon Metabolic Network Examined in a Nida Aromatic Ring-Hydroxylating Oxygenase Mutant of Mycobacterium vanbaalenii PYR 1**](https://www.ncbi.nlm.nih.gov/pubmed/22407691)**.**

[**Polycyclic Aromatic Hydrocarbon Metabolic Network in Mycobacterium vanbaalenii PYR-1**](https://www.ncbi.nlm.nih.gov/pubmed/21725022)**.**

[**Substrate Specificity and Structural Characteristics of the Novel Rieske Nonheme Iron Aromatic Ring-Hydroxylating Oxygenases Nidab and Nida3b3 from Mycobacterium vanbaalenii PYR-1**](https://www.ncbi.nlm.nih.gov/pubmed/20714442)**.**

[**Proteomic Applications to Elucidate Bacterial Aromatic Hydrocarbon Metabolic Pathways**](https://www.ncbi.nlm.nih.gov/pubmed/19414279)**.**

[**ClassRHO: A Platform for Classification of Bacterial Rieske Non-Heme Iron Ring-Hydroxylating Oxygenases**](https://www.ncbi.nlm.nih.gov/pubmed/19095015)**.**

[**A New Classification System for Bacterial Rieske Non-Heme Iron Aromatic Ring-Hydroxylating Oxygenases**](https://www.ncbi.nlm.nih.gov/pubmed/18387195)**.**

[**A Polyomic Approach to Elucidate the Fluoranthene-Degradative Pathway in Mycobacterium vanbaalenii PYR-1**](https://www.ncbi.nlm.nih.gov/pubmed/17449607)**.**

[**Complete and Integrated Pyrene Degradation Pathway in Mycobacterium vanbaalenii PYR-1 Based on Systems Biology**](https://pubmed.ncbi.nlm.nih.gov/17085566/)**.**

[**Molecular Characterization of Cytochrome P450 Genes in the Polycyclic Aromatic Hydrocarbon Degrading Mycobacterium vanbaalenii PYR-1**](https://pubmed.ncbi.nlm.nih.gov/16317545/)**.**

[**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**](https://www.ncbi.nlm.nih.gov/pubmed/16461648)**.**

[VIEW FULL BIO – Ohgew Kweon, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/ohgew-kweon)

# Mohamed Nawaz, Ph.D.

### **Microbiologist — Division of Microbiology**

Dr. Nawaz’s research interests and expertise include:

* microbial metabolism
* physiology
* biochemistry
* molecular biology
* food safety.

He has applied state-of-the-art technologies, such as Next-Generation DNA sequencing methodologies to unambiguously detect an assortment of point mutations in the quinolone-resistance determining regions of various enzymes involved in bacterial DNA synthesis that confer resistance to FQ antibiotics. Dr. Nawaz’s research team is also involved in the application of state-of-the-art bioinformatics to study antibiotic-DNA-protein complexes that contribute to the prevalence of drug resistance. Regularly, he uses biochemical, molecular, and pulsed-field gel electrophoresis techniques to characterize bacterial isolates from aquaculture, animal, and human clinical ecosystems. Currently, Dr. Nawaz’s laboratory is studying the crucial role of efflux pumps in biofilm-mediated antibiotic resistance, as well as the colonization of uropathogenic *E. coli* and the identification of suitable efflux pump inhibitors that could safely reduce or eliminate the prevalence of antibiotic resistance in the ecosystem. [VIEW FULL BIO – Dr. Mohamed Nawaz](https://www.fda.gov/about-fda/science-research-nctr/mohamed-nawaz)

**Titles and links to selected publications**

[**Draft Genome Sequences of Two Methicillin-Resistant Clinical Staphylococcus aureus Isolates**](https://www.ncbi.nlm.nih.gov/pubmed/26868381)**.**

[**Detection and Functionality of the CdtB, PltA, PltB from Salmonella enterica serovar Javiana**](https://academic.oup.com/femspd/article/72/2/95/629542)**.**

[**Draft Genome Sequence of Multidrug-Resistant Enterococcus faecium Clinical Isolate VRE3, with a Sequence Type 16 Pattern and Novel Structural Arrangement of Tn1546**](https://www.ncbi.nlm.nih.gov/pubmed/26272564)**.**

[**Characterization of Novel Mutations Involved in Quinolone Resistance in Escherichia coli Isolated from Imported Shrimp**](https://www.ncbi.nlm.nih.gov/pubmed/25631675)**.**

[**Isolation and Characterization of Multidrug-Resistant Klebsiella spp. Isolated from Shrimp Imported from Thailand**](https://www.ncbi.nlm.nih.gov/pubmed/22405354)**.**

[**Molecular Characterization of Fluoroquinolone Resistant Aeromonas spp. Isolated from Imported Shrimp**](https://www.ncbi.nlm.nih.gov/pubmed/22923408)**.**

[**Molecular Characterization of High-Level Ciprofloxacin-Resistant Salmonella enterica with Multiple Antibiotic Resistance and Class 1 Integrons Isolated from Imported Foods**](https://www.ncbi.nlm.nih.gov/pubmed/22100280)**.**

[**Lysozyme as a Barrier to Growth of Bacillus anthracis Strain Sterne in Liquid Egg White, Milk and Beef**](https://www.ncbi.nlm.nih.gov/pubmed/21645824)**.**

[**Detection of Type III Secretion System Virulence and Mutations in gyrA and parC Genes Among Quinolone-Resistant Strains of Pseudomonas aeruginosa Isolated from Imported Shrimp**](https://www.ncbi.nlm.nih.gov/pubmed/21117986)**.**

[**Plasmid-Mediated Quinolone Resistance in Pseudomonas putida Isolates from Imported Shrimp**](https://www.ncbi.nlm.nih.gov/pubmed/21193671)**.**

[**Detection and Characterization of Virulence Genes and Integrons in Aeromonas veronii Isolated from Catfish**](https://www.ncbi.nlm.nih.gov/pubmed/20227596)**.**

[**Molecular Characterization of Tetracycline-Resistant Genes and Integrons from Avirulent Strains of Escherichia coli Isolated from Catfish**](https://www.ncbi.nlm.nih.gov/pubmed/19388830)**.**

[**The Survivability of Bacillus anthracis in Processed Liquid Eggs**](https://www.ncbi.nlm.nih.gov/pubmed/19171252)**.**

[**Heteroresistance to Vancomycin and Novel Point Mutations in Tn1546 of Enterococcus faecium ATCC 51559**](https://www.ncbi.nlm.nih.gov/pubmed/17936593)**.**

[**Isolation and Characterization of Tetracycline-Resistant Citrobacter spp. from Catfish**](https://www.ncbi.nlm.nih.gov/pubmed/17993380)**.**

[**Characterization of Class 1 Integron Resistance Gene Cassettes in Salmonella enterica Serovar Oslo and Bareily from Imported Seafood**](https://www.ncbi.nlm.nih.gov/pubmed/17068008)**.**

[**Biochemical and Molecular Characterization of Tetracycline-Resistant Aeromonas veronii Isolates from Catfish**](https://www.ncbi.nlm.nih.gov/pubmed/17021193)**.**

[**Isolation and Characterization of Fluoroquinolone-Resistant Escherichia coli from Poultry Litter**](https://www.ncbi.nlm.nih.gov/pubmed/15685943)**.**

[**A Simple and Efficient Triton X-100 Boiling and Chloroform Extraction Method of RNA Isolation from Gram-Positive and Gram-Negative Bacteria**](https://www.ncbi.nlm.nih.gov/pubmed/14659548)**.**

[**Molecular Characterization of Fluoroquinolone-Resistant Campylobacter spp. Isolated from Poultry**](https://www.ncbi.nlm.nih.gov/pubmed/12619802)**.**

[**Human Health Impact and Regulatory Issues Involving Antimicrobial Resistance in the Food Animal Production Environment**](https://www.researchgate.net/publication/237283535_Human_Health_Impact_and_Regulatory_Issues_Involving_Antimicrobial_Resistance_in_the_Food_Animal_Production_Environment)**.**

[VIEW FULL BIO – Mohamed Nawaz, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/mohamed-nawaz)

# Seongwon Nho, Ph.D.

### **Staff Fellow — Division of Microbiology**

Dr. Nho is experienced in biology techniques such as next generation sequencing, polymerase chain reaction usage, gene cloning and expression, electron microscopes, mass spectrometry, plaque assay, immunofluorescence assay, cell culture, and bioinformatics analysis. Dr. Nho’s current studies are focused on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Dr. Nho and his colleague generated recombinant SARS-CoV-2 spike glycoprotein reagents to study cell interactions and antibody-dependent enhancement. He and his colleague also are investigating the interaction between virus and host cells by generated pseudovirus expressing S, N, E, M, NSPs of SARS-CoV-2. He also seeks to understand calcium signaling that impacts the SARS-CoV-2 mediated cardiotoxicity. [VIEW FULL BIO – Dr. Seongwon Nho](https://www.fda.gov/about-fda/science-research-nctr/seongwon-nho)

**Titles and links to selected publications**

[**Pragmatic Strategy for Fecal Specimen Storage and the Corresponding Test Methods for Clostridioides difficile Diagnosis**](https://pubmed.ncbi.nlm.nih.gov/34451512/)**.**

[**Microbial Contamination of Tattoo and Permanent Makeup Inks Marketed in the US: A Follow-Up Study**](https://pubmed.ncbi.nlm.nih.gov/32654157/)**.**

[**CYPminer: An Automated Cytochrome P450 Identification, Classification, and Data Analysis Tool for Genome Data Sets Across Kingdoms**](https://pubmed.ncbi.nlm.nih.gov/32349673/)**.**

[**Taxonomic and Functional Metagenomic Profile of Sediment From a Commercial Catfish Pond in Mississippi**](https://pubmed.ncbi.nlm.nih.gov/30524416/)**.**

[**Microbiological Survey of Commercial Tattoo and Permanent Makeup Inks Available in the United States**](https://pubmed.ncbi.nlm.nih.gov/29388315/)**.**

[**Improving Safety of a Live Attenuated Edwardsiella ictaluri Vaccine Against Enteric Septicemia of Catfish and Evaluation of Efficacy**](https://pubmed.ncbi.nlm.nih.gov/29103702/)**.**

[**Evaluation of Three Recombinant Outer Membrane Proteins, OmpA1, Tdr, and TbpA, as Potential Vaccine Antigens Against Virulent Aeromonas hydrophila Infection in Channel Catfish (Ictalurus punctatus)**](https://pubmed.ncbi.nlm.nih.gov/28532667/)**.**

[**Comparative Genomics and Transcriptional Analysis of Flavobacterium columnare Strain ATCC 49512**](https://pubmed.ncbi.nlm.nih.gov/28469601/)**.**

[**Characterization of a Specific Monoclonal Antibody Against Immunoglobulin Light Kappa/L1 Chain in Olive Flounder (Paralichthys olivaceus)**](https://pubmed.ncbi.nlm.nih.gov/27840171/)**.**

[**Development of an Immunochromatography Assay Kit for Rapid Detection of Ranavirus**](https://pubmed.ncbi.nlm.nih.gov/26210698/)**.**

[**Identification of High-Risk Listeria monocytogenes Serotypes in Lineage I (Serotype 1/2a, 1/2c, 3a and 3c) Using Multiplex PCR**](https://pubmed.ncbi.nlm.nih.gov/26095922/)**.**

[**Comparative Genomic Characterization of Three Streptococcus parauberis Strains in Fish Pathogen, as Assessed by Wide-Genome Analyses**](https://pubmed.ncbi.nlm.nih.gov/24260382/)**.**

[**Heat Shock Protein Profiles on the Protein and Gene Expression Levels in Olive Flounder Kidney Infected with Streptococcus parauberis**](https://pubmed.ncbi.nlm.nih.gov/23542604/)**.**

[**RNA-Seq-Based Metatranscriptomic and Microscopic Investigation Reveals Novel Metalloproteases of Neobodo sp. as Potential Virulence Factors for Soft Tunic Syndrome in Halocynthia roretzi**](https://pubmed.ncbi.nlm.nih.gov/23300657/)**.**

[**Complete Genome Sequence and Immunoproteomic Analyses of the Bacterial Fish Pathogen Streptococcus parauberis**](https://pubmed.ncbi.nlm.nih.gov/21531805/)**.**

[**Comparative Sequence Analysis of a Multidrug-Resistant Plasmid from Aeromonas hydrophila**](https://pubmed.ncbi.nlm.nih.gov/23070174/)**.**

[**Enhanced Reliability of Avian Influenza Virus (AIV) and Newcastle Disease Virus (NDV) Identification Using Matrix-Assisted Laser Desorption/Ionization-Mass Spectrometry (MALDI-MS)**](https://pubmed.ncbi.nlm.nih.gov/21294514/)**.**

[**Innate Immune Response in the Hemolymph of an Ascidian, Halocynthia roretzi, Showing Soft Tunic Syndrome, Using Label-Free Quantitative Proteomics**](https://pubmed.ncbi.nlm.nih.gov/21256860/)**.**

[VIEW FULL BIO – Seongwon Nho, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/seongwon-nho)

# Kidon Sung, Ph.D.

### **Staff Fellow — Division of Microbiology**

Biofilms are protected from host immune defenses, antibiotic therapies, and biocides, and can be up to 1,000 times more resistant to antibiotics than planktonic cells. Binding of antibiotics to the extracellular matrix and poor penetration of antibiotics into the biofilm are considered to be mechanisms of biofilm-associated antibiotic resistance. Formation of biofilms and the high frequency of multi-drug resistant strains render medical device-related infections caused by nosocomial pathogens a serious public health problem, especially if the removal and reinsertion of the infected medical devices is necessary. Current prophylactic strategies use a constant flow of a sub-inhibitory concentration of antibiotic or biomaterials coated with antimicrobials. Significant concerns associated with antimicrobial-coated medical devices were raised because of the development of antimicrobial resistance, a short duration of efficacy, and a narrow spectrum of activity for pathogenic bacteria.

Dr. Sung’s research interest is identifying biofilm formation or antimicrobial resistance markers by using integrated transcriptomic and proteomic profiles of biofilms following consistent bacterial exposure to the antimicrobial medical devices. This study aids the FDA in: 1) designing management practices for biofilm control in antimicrobial-coated medical devices, 2) developing risk assessment models of biofilm growth in antimicrobial-coated materials, 3) understanding the role of different genes and proteins responsible for survival of biofilms in antimicrobial-coated materials, and 4) gaining insight into molecular mechanisms associated with the development of antimicrobial resistance and virulence that would potentially lead to improvements in extending the efficacy of current antimicrobials to control biofilms.

Dr. Sung is also interested in biofilm control using nanomaterials, development of rapid methods for detecting antibiotic resistant genes, molecular characterization of antimicrobial resistant pathogens, development of selective media to isolate foodborne pathogens, and interaction between pathogenic bacteria and human cells. [VIEW FULL BIO – Dr. Kidon Sung](https://www.fda.gov/about-fda/science-research-nctr/kidon-sung)

**Titles and links to selected publications**

[**Dynamic Adaptive Response of Pseudomonas aeruginosa to Clindamycin/Rifampicin-Impregnated Catheters**](https://pubmed.ncbi.nlm.nih.gov/32369929/)**.**

[**Detection of Campylobacter jejuni from Fresh Produce: Comparison of Culture- and PCR-Based Techniques, and Metagenomic Approach for Analyses of the Microbiome Before and After Enrichment**](https://pubmed.ncbi.nlm.nih.gov/33878155/)**.**

[**Virulence Characteristics of mecA-Positive Multidrug-Resistant Clinical Coagulase-Negative Staphylococci**](https://pubmed.ncbi.nlm.nih.gov/32369929/)**.**

[**Genotypic Characterization of ESBL-Producing E. coli from Imported Meat in South Korea**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Genotypic+Characterization+of+ESBL-Producing+E.+coli+from+Imported+Meat+in+South+Korea.)**.**

[**Comprehensive In Vitro and In Vivo Risk Assessments of Chitosan Microparticles Using Human Epithelial Cells and Caenorhabditis Elegans**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Comprehensive+In+Vitro+and+In+Vivo+Risk+Assessments+of+Chitosan+Microparticles+Using+Human+Epithelial+Cells+and+Caenorhabditis+Elegans.)**.**

[**Prevalence, Toxin Gene Profile, Antibiotic Resistance, and Molecular Characterization of Clostridium Perfringens from Diarrheic and Non-Diarrheic Dogs in Korea**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Prevalence%2C+Toxin+Gene+Profile%2C+Antibiotic+Resistance%2C+and+Molecular+Characterization+of+Clostridium+perfringens+from+Diarrheic+and+Non-Diarrheic+Dogs+i)**.**

[**Investigating the Susceptibility of Mice to a Bacterial Challenge after Intravenous Exposure to Durable Nanoparticles**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Investigating+the+susceptibility+of+mice+to+a+bacterial+challenge+after+intravenous+exposure+to+durable+nanoparticles.)**.**

[**Evaluation of Cephamycins as Supplements to Selective Agar for Detecting Campylobacter spp. in Chicken Carcass Rinses**](http://www.ncbi.nlm.nih.gov/pubmed/26915052)**.**

[**Characterization of Novel Mutations Involved in Quinolone Resistance in Escherichia Coli Isolated from Imported Shrimp**](http://www.ncbi.nlm.nih.gov/pubmed/25631675)**.**

[**Molecular Characterization, Antibiotic Resistance, and Virulence Factors of Methicillin-Resistant Staphylococcus Aureus Strains Isolated from Imported Meat in Korea**](http://www.ncbi.nlm.nih.gov/pubmed/25789540)**.**

[**Molecular Characterization of Fluoroquinolone-Resistant Aeromonas spp. Isolated from Imported Shrimp**](http://www.ncbi.nlm.nih.gov/pubmed/22923408)**.**

[**Effect of Sterilized Human Fecal Extract on the Sensitivity of Escherichia Coli ATCC 25922 to Enrofloxacin**](http://www.ncbi.nlm.nih.gov/pubmed/22274703)**.**

[**Lysozyme as a Barrier to Growth of Bacillus Anthracis Strain Sterne in Liquid Egg White, Milk and Beef**](http://www.ncbi.nlm.nih.gov/pubmed/21645824)**.**

[**Detection of aacA-aphD, qacEδ1, marA, floR, and tetA Genes from Multidrug-Resistant Bacteria: Comparative Analysis of Real-Time Multiplex PCR Assays Using EvaGreen® and SYBR® Green I Dyes**](http://www.ncbi.nlm.nih.gov/pubmed/21256956)**.**

[**The Survivability of Bacillus Anthracis (Stern Strain) in Processed Liquid Eggs**](http://www.ncbi.nlm.nih.gov/pubmed/19171252)**.**

[**Genetic Diversity of Tn1546-Like Elements in Clinical Isolates of Vancomycin-Resistant Enteroccoci**](http://www.ncbi.nlm.nih.gov/pubmed/18462926)**.**

[**Heteroresistance to Vancomycin and Novel Point Mutations in Tn1546 of Enterococcus Faecium ATCC 51559**](http://www.ncbi.nlm.nih.gov/pubmed/17936593)**.**

[**Biochemical and Molecular Characterization of Tetracycline-Resistant Aeromonas Veronii Isolates from Catfish**](https://www.ncbi.nlm.nih.gov/pubmed/17021193)**.**

[**Heat-Treated Campylobacter spp. and mRNA Stability as Determined by Reverse-Transcriptase Polymerase Chain Reaction (RT-PCR)**](https://www.ncbi.nlm.nih.gov/pubmed/15992307)**.**

[**Relationship of Messenger RNA Reverse Transcriptase-Polymerase Chain Reaction Signal to Campylobacter spp. Viability**](http://www.ncbi.nlm.nih.gov/pubmed/15283412)**.**

[VIEW FULL BIO – Kidon Sung, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/kidon-sung)

## Division of Neurotoxicology, NCTR

# John Talpos, Ph.D.

### **Director — Division of Neurotoxicology**

Throughout Dr. Talpos’s career, his primary research interest has always been translational models of human cognition, with a special interest in working memory, executive function, visual perception, and the hippocampus. The goal of his research is to discover the mechanisms of cognitive disruption in order to correct these impairments. Before joining NCTR, Dr. Talpos focused on cognitive disruption in central nervous system (CNS) disorders, such as schizophrenia, Alzheimer’s disease, and autism. While he still retains a strong interest in CNS disorders, since joining NCTR his research focus has switched to studying cognitive dysfunctions triggered by neurotoxic insults. Currently, his research focuses on the developmental toxicity associated with exposures to anesthesia or analgesia. Dr. Talpos collaborates with many members of the division to incorporate diverse methods into his research, including molecular imaging approaches and MRI. Dr. Talpos also has several active collaborations with FDA’s Center for Drug Evaluation and Research designed to assess the potential neurotoxicity of anesthesia and analgesia. [VIEW FULL BIO – Dr. John Talpos](http://wcms-internet.fda.gov/about-fda/science-research-nctr/john-talpos)

**Titles and links to selected publications**

[**Genotoxicity Evaluation Using Primary Hepatocytes Isolated from Rhesus Macaque (Macaca mulatta)**](https://pubmed.ncbi.nlm.nih.gov/34509578/)**.**

[**MicroPET/CT Assessment of Neurochemical Effects in the Brain After Long-Term Methylphenidate Treatment in Nonhuman Primates**](https://pubmed.ncbi.nlm.nih.gov/34265415/)**.**

[**Can SARS-CoV-2 Infect the Central Nervous System Via the Olfactory Bulb or the Blood-Brain Barrier**](https://pubmed.ncbi.nlm.nih.gov/33412255/)**?**

[**This is Your Teen Brain on Drugs: In Search of Biological Factors Unique to Dependence Toxicity in Adolescence**](https://pubmed.ncbi.nlm.nih.gov/32698050/)**.**

[**Regions of the Basal Ganglia and Primary Olfactory System are Most Sensitive to Neurodegeneration After Extended Sevoflurane Anesthesia in the Perinatal Rat**](https://pubmed.ncbi.nlm.nih.gov/32413489/)**.**

[**Acetyl-l-carnitine Does Not Prevent Neurodegeneration in a Rodent Model of Prolonged Neonatal Anesthesia**](https://pubmed.ncbi.nlm.nih.gov/32376384/)**.**

[**Sevoflurane Exposure Has Minimal Effect on Cognitive Function and Does Not Alter Microglial Activation in Adult Monkeys**](https://pubmed.ncbi.nlm.nih.gov/30605762/)**.**

[**Early Life Exposure to Extended General Anesthesia with Isoflurane and Nitrous Oxide Reduces Responsivity on a Cognitive Test Battery in the Nonhuman Primate**](https://pubmed.ncbi.nlm.nih.gov/30445043/)**.**

[**Symptomatic Thinking: The Current State of Phase III and IV Clinical Trials for Cognition in Schizophrenia**](https://pubmed.ncbi.nlm.nih.gov/28461223/)**.**

[**Dissociable Effects of NR2A and NR2B NMDA Receptor Antagonism on Cognitive Flexibility but not Pattern Separation**](https://www.ncbi.nlm.nih.gov/pubmed/26184010)**.**

[**Opposing Effects of Glutamatergic and GABAergic Pharmacological Manipulations on a Visual Perception Task with Relevance to Schizophrenia**](https://www.ncbi.nlm.nih.gov/pubmed/26014109)**.**

[**Biased MGlu5-Positive Allosteric Modulators Provide In Vivo Efficacy Without Potentiating MGlu5 Modulation of NMDAR Currents**](https://www.ncbi.nlm.nih.gov/pubmed/25937172)**.**

[**A Touch-Screen Based Paired-Associates Learning (PAL) Task for The Rat May Provide a Translatable Pharmacological Model of Human Cognitive Impairment**](https://www.ncbi.nlm.nih.gov/pubmed/24662914)**.**

[**Assessing Behavioural and Cognitive Domains of Autism Spectrum Disorders in Rodents: Current Status and Future Perspectives**](https://www.ncbi.nlm.nih.gov/pubmed/24048469)**.**

[**Animal Models of Working Memory: A Review of Tasks That Might be Used in Screening Drug Treatments for the Memory Impairments Found in Schizophrenia**](https://www.ncbi.nlm.nih.gov/pubmed/22464948)**.**

[**NMDA Receptors, Cognition and Schizophrenia--Testing the Validity of the NMDA Receptor Hypofunction Hypothesis**](https://www.ncbi.nlm.nih.gov/pubmed/21420987)**.**

[**Trial-Unique, Delayed Nonmatching-To-Location (TUNL): A Novel, Highly Hippocampus-Dependent Automated Touchscreen Test of Location Memory and Pattern Separation**](https://www.ncbi.nlm.nih.gov/pubmed/20692356)**.**

[**A Novel Touchscreen-Automated Paired-Associate Learning (PAL) Task Sensitive to Pharmacological Manipulation of The Hippocampus: A Translational Rodent Model of Cognitive Impairments in Neurodegenerative Disease**](https://www.ncbi.nlm.nih.gov/pubmed/19357840)**.**

[**A Comparison of Multiple 5-HT Receptors in Two Tasks Measuring Impulsivity**](https://www.ncbi.nlm.nih.gov/pubmed/16204332)**.**

[VIEW FULL BIO – John Talpos, Ph.D.](http://wcms-internet.fda.gov/about-fda/science-research-nctr/john-talpos)

# Timothy Flanigan, Ph.D.

### **Research Psychologist — Division of Neurotoxicology**

Dr. Flanigan has a broad interest in behavioral neuroscience and neurotoxicology. He is particularly interested in cognitive and affective behaviors and modeling them in rodents. He is also interested in how genetics, development, and aging interact with drugs and toxicants to affect these behaviors. [VIEW FULL BIO – Dr. Timothy Flanigan](https://www.fda.gov/about-fda/science-research-nctr/timothy-flanigan)

**Titles and links to selected publications**

[**Effects of Cyclophosphamide and/or Doxorubicin in a Murine Model of Postchemotherapy Cognitive Impairment**](https://www.ncbi.nlm.nih.gov/pubmed/29228376)**.**

[**Abnormal Vibrissa-Related Behavior and Loss of Barrel Field Inhibitory Neurons in 5xFAD Transgenics**](https://www.ncbi.nlm.nih.gov/pubmed/24655396)**.**

[**Effects of an Early Handling-Like Procedure and Individual Housing on Anxiety-Like Behavior in Adult C57BL/6J and DBA/2J Mice**](https://www.ncbi.nlm.nih.gov/pubmed/21533042)**.**

[VIEW FULL BIO – Timothy Flanigan, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/timothy-flanigan)

# Qiang Gu, Ph.D.

### **Biologist — Division of Neurotoxicology**

Dr. Gu’s research focuses on molecular changes associated with neurotoxicity in animal and cell-culture models. This effort is aimed at identifying biomarkers for neurotoxicity assessments as well as understanding signal-transduction cascades following neurotoxic insults and ultimately, molecular mechanisms underlying neurotoxicity. [VIEW FULL BIO – Dr. Qiang Gu](https://www.fda.gov/about-fda/science-research-nctr/qiang-gu)

**Titles and links to selected publications**

[**Downregulation of 14-3-3 Proteins in a Kainic Acid-Induced Neurotoxicity Model**](https://www.ncbi.nlm.nih.gov/pubmed/28840498)**.**

[**Decreased Mcl-1 Protein Level in the Striatum of a Parkinson’s Disease Animal Model**](https://www.ncbi.nlm.nih.gov/pubmed/29158176)**.**

[**The NMDA Receptors: Physiology and Neurotoxicology in the Developing Brain**](https://www.sciencedirect.com/science/article/pii/B9780128094051000183)**.**

[**Neural Cell Lines (Lineage)**](https://www.researchgate.net/publication/317346202_9_Neural_Cell_Lines_Lineage)**.**

[**In Vitro Detection of Cytotoxicity Using FluoroJade-C**](http://www.ncbi.nlm.nih.gov/pubmed/24462471)**.**

[**Optimizing Scan Parameters for Antibody Microarray Experiments: Accelerating Robust Systems Diagnostics for Life Sciences**](http://www.ncbi.nlm.nih.gov/pubmed/24754828)**.**

[**Proteomics Quality and Standard: From a Regulatory Perspective**](http://www.ncbi.nlm.nih.gov/pubmed/24316359)**.**

[**One-Step Labeling of Degenerative Neurons in Unfixed Brain Tissue Samples Using Fluoro-Jade C**](http://www.ncbi.nlm.nih.gov/pubmed/22546475)**.**

[**High-Throughput Identification of Molecular Targets of Brain Disorders Using Antibody-Based Microarray Analyses**](http://www.ncbi.nlm.nih.gov/pubmed/18759538)**.**

[**Experimental Approach for Assessing the Outcome Accuracy of Antibody Microarray Experiments**](http://www.ncbi.nlm.nih.gov/pubmed/17910491)**.**

[**Signal Stability of Cy3 and Cy5 on Antibody Microarrays**](http://www.ncbi.nlm.nih.gov/pubmed/17034643)**.**

[**Contribution of Acetylcholine to Visual Cortex Plasticity**](http://www.ncbi.nlm.nih.gov/pubmed/14521871)**.**

[**Neuromodulatory Transmitter Systems in the Cortex and Their Role in Cortical Plasticity**](http://www.ncbi.nlm.nih.gov/pubmed/12031406)**.**

[VIEW FULL BIO – Qiang Gu, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/qiang-gu)

# Zhen He, M.D., Ph.D.

### **Research Biologist — Division of Neurotoxicology**

Dr. He’s research interests include stroke, post-traumatic stress disorder, Alzheimer’s disease, aging, and stem-cell research. He began his career investigating the neurotoxicology of sex-hormone disrupter exposure in laboratory animals in 2008. He has recently focused on stem-cell activities in the 3rd ventricle stem-cell niche and in the surrounding areas where sexually dimorphic nuclei are located. Dr. He is an expert in rodent neurosurgery. He is a pioneer in establishing the endovascular occlusion models of anterior choroidal artery occlusion and hypothalamic artery occlusion in rats. He is also pioneering research establishing a rat 8-vessel-occlusion model by which partial-to-total ischemic damage in the dentate gyrus of the hippocampus is elicited. Dr. He successfully applied this global ischemic model in aged rats and defined age-related changes in preconditioning, death-processing mechanisms and microvascular phosphodiesterase 4D expression compared to young adult animals. [VIEW FULL BIO – Dr. Zhen He](https://www.fda.gov/about-fda/science-research-nctr/zhen-he)

**Titles and links to selected publications**

[**Neuroendocrine Cells**](https://www.taylorfrancis.com/books/e/9781498726016/chapters/10.1201/9781315370491-5)**.**

[**Estrogen Selectively Mobilizes Neural Stem Cells in the Third Ventricle Stem Cell Niche of Postnatal Day 21 Rats**](https://www.ncbi.nlm.nih.gov/pubmed/26041664)**.**

[**Stem Cell Activity May Partially Account for Postweaning Development of the Sexually Dimorphic Nucleus of the Preoptic Area in Rats**](https://pubmed.ncbi.nlm.nih.gov/23383001/)**.**

[**Development of the Sexually Dimorphic Nucleus of the Preoptic Area and the Influence of Estrogen-Like Compounds**](https://www.ncbi.nlm.nih.gov/pubmed/25206587)**.**

[**Ischemia-Induced Increase in Microvascular Phosphodiesterase 4D Expression in Rat Hippocampus Associated with Blood Brain Barrier Permeability: Effect of Age**](https://www.ncbi.nlm.nih.gov/pubmed/22860212)**.**

[**Low Oral Doses of Bisphenol A Increase Volume of the Sexually Dimorphic Nucleus of the Preoptic Area in Male, but Not Female, Rats at Postnatal Day 21**](https://www.ncbi.nlm.nih.gov/pubmed/22507915)**.**

[**Defining the Phosphodiesterase Superfamily Members in Rat Brain Microvessels**](https://www.ncbi.nlm.nih.gov/pubmed/?term=22860158)**.**

[**Fluorogold Induces Persistent Neurological Deficits and Circling Behavior in Mice Over-Expressing Human Mutant Tau**](https://www.ncbi.nlm.nih.gov/pubmed/?term=19355926)**.**

[**Aging is Neuroprotective During Global Ischemia but Leads to Increased Caspase-3 and Apoptotic Activity in Hippocampal Neurons**](https://www.ncbi.nlm.nih.gov/pubmed/?term=16918382)**.**

[**Aging Blunts Ischemic-Preconditioning-Induced Neuroprotection Following Transient Global Ischemia in Rats**](https://www.ncbi.nlm.nih.gov/pubmed/?term=16375718)**.**

[**Hippocampal Progenitor Cells Express Nestin Following Cerebral Ischemia in Rats**](https://www.ncbi.nlm.nih.gov/pubmed/?term=16148741)**.**

[**Increased Severity of Acute Cerebral Ischemic Injury Correlates with Enhanced Stem Cell Induction as Well as With Predictive Behavioral Profiling**](https://www.ncbi.nlm.nih.gov/pubmed/?term=16181088)**.**

[**Proestrus Levels of Estradiol During Transient Global Cerebral Ischemia Improves the Histological Outcome of the Hippocampal CA1 Region: Perfusion-Dependent and-Independent Mechanisms**](https://www.ncbi.nlm.nih.gov/pubmed/?term=11790387)**.**

[**Definition of the Anterior Choroidal Artery Territory in Rats Using Intraluminal Occluding Technique**](https://www.ncbi.nlm.nih.gov/pubmed/?term=11102635)**.**

[**Experimental Model of Small Deep Infarcts Involving the Hypothalamus in Rats: Changes in Body Temperature and Postural Reflex**](https://pubmed.ncbi.nlm.nih.gov/10583006/)**.**

[**Age-Related Ischemia in the Brain Following Bilateral Carotid Artery Occlusion--Collateral Blood Flow and Brain Metabolism**](https://www.ncbi.nlm.nih.gov/pubmed/?term=9021760)**.**

[**L-Arginine Ameliorates Cerebral Blood Flow and Metabolism and Decreases Infarct Volume in Rats with Cerebral Ischemia**](https://www.ncbi.nlm.nih.gov/pubmed/?term=8616623)**.**

[VIEW FULL BIO – Zhen He, M.D., Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/zhen-he)

# Syed Imam, M.S., Ph.D.

### **Staff Fellow — Division of Neurotoxicology**

Dr. Imam’s major focus consists of regulation of global oxidative damage and mitochondrial functions in neurons to prevent the progression of neurological disorders. The idea of drug development at its various stages including clinical trials and regulatory aspects have become a focal point of his research and he has spent the last three years studying various therapeutic molecules to prevent the progression of neurological disorders. To that effect, he discovered the role of Abl tyrosine kinase in Parkinson’s disease (PD), a breakthrough that has led to drug repositioning of various Abl inhibitors as successful therapeutics for PD. He has also developed a nanoconjugate of nicotine and NanoCeria for therapeutic use in the prevention of disease progression in Parkinson’s disease. This invention has received full US and International Patents.

Very recently, his research has focused on development of fluidic biomarkers of central nervous system (CNS) damage. This research has led to an active discussion regarding the development of circulating biomarkers in serum, plasma, cerebrospinal fluid, and urine that may indicate the early detection and progression of damage and toxicity to the CNS.

Finally, he has begun to utilize high-throughput neurophysiological approaches via multi-electrode technology to evaluate safety and efficacy of regulated products as well as new therapeutic candidates in an in vitro model of human primary neurons. [VIEW FULL BIO – Dr. Syed Imam](https://www.fda.gov/about-fda/science-research-nctr/syed-imam)

**Titles and links to selected publications**

[**Drug Discovery and Development: Biomarkers of Neurotoxicity and Neurodegeneration**](https://pubmed.ncbi.nlm.nih.gov/30253665/)**.**

[**Changes in the Metabolome and MicroRNA Levels in Biological Fluids Might Represent Biomarkers of Neurotoxicity: A Trimethyltin Study**](https://pubmed.ncbi.nlm.nih.gov/29105512/)**.**

[**Protein Kinases and Parkinson's Disease**](https://www.ncbi.nlm.nih.gov/pubmed/27657053)**.**

[**Neuroprotective and Therapeutic Strategies Against Parkinson's Disease: Recent Perspectives**](https://www.ncbi.nlm.nih.gov/pubmed/27338353)**.**

[**Iron Oxide Nanoparticles Induce Dopaminergic Damage: In Vitro Pathways and In VivoImaging Reveals Mechanism of Neuronal Damage**](https://www.ncbi.nlm.nih.gov/pubmed/26099304)**.**

[**Neuroprotective Efficacy of a New Brain-penetrating C-Abl Inhibitor in a Murine Parkinson's Disease Model**](https://www.ncbi.nlm.nih.gov/pubmed/23741470)**.**

[**Bone Marrow-Derived Microglia-Based Neurturin Delivery Protects Against Dopaminergic Neurodegeneration in a Mouse Model of Parkinson's Disease**](https://www.ncbi.nlm.nih.gov/pubmed/23295906)**.**

[**Novel Regulation of Parkin Function Through C-Abl-Mediated Tyrosine Phosphorylation: Implications for Parkinson's Disease**](https://www.ncbi.nlm.nih.gov/pubmed/21209200)**.**

[VIEW FULL BIO – Syed Imam, M.S., Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/syed-imam)

# Jyotshna Kanungo, M.S., M. Phil., Ph.D.

### **Research Biologist — Division of Neurotoxicology**

Her research interests include cellular and molecular aspects of neuronal development/degeneration (e.g., Alzheimer’s disease), cell signaling, stem-cell differentiation, and developmental toxicology. [VIEW FULL BIO – Dr. Jyotshna Kanungo](https://www.fda.gov/about-fda/science-research-nctr/jyotshna-kanungo)

**Titles and links to selected publications**

[**N-acetylcysteine Prevents Verapamil-Induced Cardiotoxicity with No Effect on the Noradrenergic Arch-Associated Neurons in Zebrafish**](https://pubmed.ncbi.nlm.nih.gov/32640352/)**.**

[**Cyclosporine Exacerbates Ketamine Toxicity in Zebrafish: Mechanistic Studies on Drug-Drug Interaction**](https://www.ncbi.nlm.nih.gov/pubmed/28569378)**.**

[**Puromycin-Resistant Lentiviral Control ShRNA Vector, pLKO.1 Induces Unexpected Cellular Differentiation of P19 Embryonic Stem Cells**](https://www.ncbi.nlm.nih.gov/pubmed/28322785)**.**

[**DNA-PK Deficiency in Alzheimer's Disease**](https://www.ncbi.nlm.nih.gov/pubmed/27376156)**.**

[**Advancing Toxicology Research Using In Vivo High Throughput Toxicology with Small Fish Models**](https://www.ncbi.nlm.nih.gov/pubmed/27328013)**.**

[**Retinoic Acid Signaling in P19 Stem Cell Differentiation**](https://www.ncbi.nlm.nih.gov/pubmed/27306567)**.**

[**Acetyl L-Carnitine Targets Adenosine Triphosphate Synthase in Protecting Zebrafish Embryos From Toxicities Induced by Verapamil and Ketamine: An In Vivo Assessment**](https://www.ncbi.nlm.nih.gov/pubmed/27191126)**.**

[**Distinct Effects of Ketamine and Acetyl L-Carnitine on the Dopamine System in Zebrafish**](https://www.ncbi.nlm.nih.gov/pubmed/26898327)**.**

[**Tumor Suppressors and Endodermal Differentiation of P19 Embryonic Stem Cells**](https://www.ncbi.nlm.nih.gov/pubmed/27413642)**.**

[**Developmental Toxicity Assay Using High Content Screening of Zebrafish Embryos**](https://www.ncbi.nlm.nih.gov/pubmed/24871937)**.**

[**Zebrafish Model in Drug Safety Assessment**](https://www.ncbi.nlm.nih.gov/pubmed/24502596)**.**

[**Ketamine Attenuates Cytochrome P450 Aromatase Gene Expression and Estradiol-17β Levels in Zebrafish Early Life Stages**](https://www.ncbi.nlm.nih.gov/pubmed/23696345)**.**

[**Acetyl L-Carnitine Protects Motor Neurons and Rohon-Beard Sensory Neurons against Ketamine-Induced Neurotoxicity in Zebrafish Embryos**](https://www.ncbi.nlm.nih.gov/pubmed/23896048)**.**

[**Ketamine induces Motor Neuron Toxicity and Alters Neurogenic and Proneural Gene Expression in Zebrafish**](https://www.ncbi.nlm.nih.gov/pubmed/22045596)**.**

[**DNA-Dependent Protein Kinase and DNA Repair: Relevance to Alzheimer's Disease**](https://www.ncbi.nlm.nih.gov/pubmed/23566654)**.**

[**L-Carnitine Rescues Ketamine-Induced Attenuated Heart Rate and MAPK (ERK) Activity in Zebrafish Embryos**](https://www.ncbi.nlm.nih.gov/pubmed/22027688)**.**

[**In Vivo Imaging and Quantitative Analysis of Changes in Axon Length using Transgenic Zebrafish Embryos**](https://www.ncbi.nlm.nih.gov/pubmed/21903162)**.**

[**Specific Inhibition of Cyclin-Dependent Kinase 5 Activity induces Motor Neuron Development In Vivo**](https://www.ncbi.nlm.nih.gov/pubmed/19523926)**.**

[**The Notch Signaling Inhibitor DAPT Down-Regulates Cdk5 Activity and Modulates the Distribution of Neuronal Cytoskeletal Proteins**](https://www.ncbi.nlm.nih.gov/pubmed/18662245)**.**

[**Cyclin-Dependent Kinase 5 Influences Rohon-Beard Neuron Survival in Zebrafish**](https://www.ncbi.nlm.nih.gov/pubmed/16911583)**.**

[**Gelsolin is a Dorsalizing Factor in Zebrafish**](https://www.ncbi.nlm.nih.gov/pubmed/12629212)**.**

[VIEW FULL BIO – Jyotshna Kanungo, M.S., M. Phil., Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/jyotshna-kanungo)

# Serguei Liachenko, M.D., Ph.D.

### **Director, Bio-Imaging Lab — Division of Neurotoxicology**

Current research interests include:

* discovering and developing nonclinical imaging biomarkers of drug toxicity and efficacy using magnetic resonance imaging and spectroscopy.
* investigating glutamine cycle involvement in neurotoxicity, neurological disorders, and addictive substances abuse
* elucidating the mechanisms of toxicity using magnetic resonance.
* continuous improvement of imaging/spectroscopic methods in nonclinical applications.

Dr. Liachenko’s expertise includes:

* biology
* pharmacology
* animal research
* bio-imaging, magnetic resonance, imaging analysis
* algorithms development
* additive (3D printing) and subtractive (3D milling) rapid prototyping.

Dr. Liachenko’s research goals include the development of imaging/spectroscopy biomarkers of toxicity to the stage of formal qualification by FDA, development of MRI toolboxes for routine applications in drug safety research, and elucidation of biochemical pathways of drug addiction using minimally invasive imaging technologies.

[VIEW FULL BIO – Dr. Serguei Liachenko](https://www.fda.gov/about-fda/science-research-nctr/serguei-liachenko)

**Titles and links to selected publications**

[**Magnetic Resonance Spectroscopic Analysis of Neurometabolite Changes in the Developing Rat Brain at 7 Tesla**](https://www.ncbi.nlm.nih.gov/pubmed/27663970)**.**

[**Longitudinal Diffusion Tensor Imaging of the Rat Brain after Hexachlorophene Exposure**](https://www.ncbi.nlm.nih.gov/pubmed/27555423)**.**

[**Quantification and Reproducibility Assessment of the Regional Brain T2 Relaxation in Naïve Rats at 7T**](https://www.ncbi.nlm.nih.gov/pubmed/27384412)**.**

[**Translational Biomarkers of Neurotoxicity: A Health and Environmental Sciences Institute Perspective on the Way Forward**](https://www.ncbi.nlm.nih.gov/pubmed/26609132)**.**

[**Iron Oxide Nanoparticles Induce Dopaminergic Damage: In Vitro Pathways and In Vivo Imaging Reveals Mechanism of Neuronal Damage**](https://www.ncbi.nlm.nih.gov/pubmed/26099304)**.**

[**Quantitative Assessment of MRI T2 Response to Kainic Acid Neurotoxicity in Rats In Vivo**](https://www.ncbi.nlm.nih.gov/pubmed/25904105)**.**

[**The Use of MRI to Assist the Section Selections for Classical Pathology Assessment of Neurotoxicity**](https://www.ncbi.nlm.nih.gov/pubmed/25265367)**.**

[VIEW FULL BIO – Serguei Liachenko, M.D., Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/serguei-liachenko)

# Fang Liu, Ph.D.

### **Staff Fellow — Division of Neurotoxicology**

Dr. Liu has been working on understanding the adverse effects of chemical exposures on the central and peripheral nervous system. Currently, there is public concern as to whether general anesthetics can cause adverse effects on pediatric patients. To support FDA’s mission to properly regulate the use of general anesthetics in young children, Dr. Liu focuses her research on understanding the effects of general anesthetics on the developing central nervous system, using various models. In recent years, she has employed neural stem cells which can recapitulate many important developmental procedures of the brain in vitro to study the developmental neurotoxicity of general anesthetics. [VIEW FULL BIO – Dr. Fang Liu](https://www.fda.gov/about-fda/science-research-nctr/fang-liu)

**Titles and links to selected publications**

[**In Vivo Monitoring of Sevoflurane-Induced Adverse Effects in Neonatal Nonhuman Primates Using Small-Animal Positron Emission Tomography**](https://www.ncbi.nlm.nih.gov/pubmed/?term=27183169)**.**

[**Relationship between Ketamine-Induced Developmental Neurotoxicity and NMDA Receptor-Mediated Calcium Influx in Neural Stem Cell-Derived Neurons**](https://www.ncbi.nlm.nih.gov/pubmed/?term=27132109)**.**

[**Potential Adverse Effects of Prolonged Sevoflurane Exposure on Developing Monkey Brain: From Abnormal Lipid Metabolism to Neuronal Damage**](https://www.ncbi.nlm.nih.gov/pubmed/26206149)**.**

[**Ketamine-Induced Toxicity in Neurons Differentiated from Neural Stem Cells**](https://www.ncbi.nlm.nih.gov/pubmed/26055230)**.**

[**Mechanisms of Tolvaptan-Induced Toxicity in HepG2 Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=25858412)**.**

[**Effects of Silver Nanoparticles on Human and Rat Embryonic Neural Stem Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=25904840)**.**

[**The Role of Autophagy in Usnic Acid-Induced Toxicity in Hepatic Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=25078063)**.**

[**Protective Effect of Acetyl-L-Carnitine on Propofol-Induced Toxicity in Embryonic Neural Stem Cells**](https://www.ncbi.nlm.nih.gov/pubmed/?term=24704589)**.**

[**Utilization of Neural Stem Cell-Derived Models to Study Anesthesia-Related Toxicity and Preventative Approaches**](https://www.ncbi.nlm.nih.gov/pubmed/?term=23846129)**.**

[**Ketamine-Induced Neuronal Damage and Altered N-Methyl-D-Aspartate Receptor Function in Rat Primary Forebrain Culture**](https://www.ncbi.nlm.nih.gov/pubmed/?term=23065140)**.**

[**Phototoxicity of Kava - Formation of Reactive Oxygen Species Leading to Lipid Peroxidation and DNA Damage**](https://www.ncbi.nlm.nih.gov/pubmed/23227797)**.**

[**Inhalation Anesthetic-Induced Neuronal Damage in the Developing Rhesus Monkey**](https://www.ncbi.nlm.nih.gov/pubmed/21708249)**.**

[**Changes in Gene Expression after Phencyclidine Administration in Developing Rats: A Potential Animal Model for Schizophrenia**](https://www.ncbi.nlm.nih.gov/pubmed/?term=20691775)**.**

[**Ketamine Anesthesia during the First Week of Life can Cause Long-Lasting Cognitive Deficits in Rhesus Monkeys**](https://www.ncbi.nlm.nih.gov/pubmed/?term=21241795)**.**

[**Ketamine-Induced Neurotoxicity and Changes in Gene Expression in the Developing Rat Brain**](https://www.ncbi.nlm.nih.gov/pubmed/?term=21886601)**.**

[**Anesthetic-Induced Oxidative Stress and Potential Protection**](https://www.ncbi.nlm.nih.gov/pubmed/20661539)**.**

[VIEW FULL BIO – Fang Liu, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/fang-liu)

# Shuliang Liu, Ph.D.

### **Visiting Scientist — Division of Neurotoxicology**

Since beginning at NCTR, Dr. Shuliang Liu has been conducting research on the adverse effects of general anesthetic exposure on the developing central nervous system (CNS). He has employed both in vivo and in vitro models to study the neurotoxicity of commonly-used general anesthetics on the developing CNS. The principal aim of Dr. Liu’s research is to evaluate the reversal effects of selected chemicals on anesthetic-induced neural cell damage. [VIEW FULL BIO – Dr. Shuliang Liu](https://www.fda.gov/about-fda/science-research-nctr/shuliang-liu)

**Titles and links to selected publications**

[**Potential Mechanisms for Phencyclidine/Ketamine-Induced Brain Structural Alterations and Behavioral Consequences**](https://www.ncbi.nlm.nih.gov/pubmed/31812709)**.**

[**Effects of Xenon-Based Anesthetic Exposure on the Expression Levels of Polysialic Acid Neural Cell Adhesion Molecule (PSA-NCAM) on Human Neural Stem Cell-Derived Neurons**](https://www.ncbi.nlm.nih.gov/pubmed/31522383)**.**

[**Protective Effects of Xenon on Propofol-Induced Neurotoxicity in Human Neural Stem Cell-derived Models**](https://www.ncbi.nlm.nih.gov/pubmed/31578707)**.**

[**Disturbed Energy Metabolism Present in Neonatal Monkeys after Sevoflurane Exposure as Evidenced with Marked Serum Lipid Changes: A Potential Causal Factor Leading to and Biomarkers for Neurotoxicity**](https://www.ncbi.nlm.nih.gov/pubmed/30292318)**.**

[**MicroPET/CT Assessment of FDG Uptake in Brain after Long-term Methylphenidate Treatment in Nonhuman Primates**](https://www.ncbi.nlm.nih.gov/pubmed/27307090)**.**

[**In Vivo Monitoring of Sevoflurane-induced Neuronal Injury in Neonatal Nonhuman Primates Using Small-Animal Positron Emission Tomography**](https://www.ncbi.nlm.nih.gov/pubmed/27183169)**.**

[**Positron Emission Topography with [18F]-FLT Revealed Sevoflurane-Induced Inhibition of Neural Progenitor Cell Expansion In Vivo**](https://www.ncbi.nlm.nih.gov/pubmed/25452743)**.**

[**Ketamine-Induced Neuronal Damage and Altered N-methyl-D-aspartate (NMDA) Receptor Function in Rat Primary Forebrain Culture**](https://www.ncbi.nlm.nih.gov/pubmed/23065140)**.**

[**Inhalation Anesthetic-Induced Neuronal Damage in the Developing Rhesus Monkey**](https://www.ncbi.nlm.nih.gov/pubmed/21708249)**.**

[VIEW FULL BIO – Shuliang Liu, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/shuliang-liu)

# Hector Rosas-Hernandez, Ph.D.

### **Visiting Scientist — Division of Neurotoxicology**

Dr. Rosas-Hernandez’s research interests include experimental modeling focused on the development of neurodegenerative disorders after TBI. Dr. Rosas-Hernandez is also interested in investigating the vascular dysfunction in TBI and Alzheimer’s disease, specifically the contribution of the blood-brain barrier to these pathologies. He is also studying the role of exosomes in the propagation of Alzheimer’s and Parkinson’s disease and has a particular interest in the use of novel technologies (i.e. microphysiological systems) to model the blood-brain barrier in vitro. [VIEW FULL BIO – Dr. Hector Rosas-Hernandez](https://www.fda.gov/about-fda/science-research-nctr/hector-rosas-hernandez)

**Titles and links to selected publications**

[**Stretch-Induced Deformation as a Model to Study Dopaminergic Dysfunction in Traumatic Brain Injury**](https://www.ncbi.nlm.nih.gov/pubmed/31529335)**.**

[**Amyloid Beta 25-35 Induces Blood-Brain Barrier Disruption In Vitro**](https://www.ncbi.nlm.nih.gov/pubmed/31267346)**.**

[**Characterization of Serum Exosomes from a Transgenic Mouse Model of Alzheimer's Disease**](https://www.ncbi.nlm.nih.gov/pubmed/30907317)**.**

[**Identification of Altered MicroRNAs in Serum of a Mouse Model of Parkinson's Disease**](https://www.ncbi.nlm.nih.gov/pubmed/30025832)**.**

[**Characterization of Uniaxial High-Speed Stretch as an In Vitro Model of Mild Traumatic Brain Injury on the Blood-Brain Barrier**](https://www.ncbi.nlm.nih.gov/pubmed/29458086)**.**

[**Isolation and Culture of Brain Microvascular Endothelial Cells for In Vitro Blood-Brain Barrier Studies**](https://www.ncbi.nlm.nih.gov/pubmed/29222791)**.**

[**Characterization of Biaxial Stretch as an In Vitro Model of Traumatic Brain Injury to the Blood-Brain Barrier**](https://www.ncbi.nlm.nih.gov/pubmed/28842857)**.**

[**Inhibition of Prolactin with Bromocriptine for 28 Days Increases Blood-Brain Barrier Permeability in the Rat**](https://www.ncbi.nlm.nih.gov/pubmed/26047726)**.**

[VIEW FULL BIO – Hector Rosas-Hernandez, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/hector-rosas-hernandez)

# Sumit Sarkar, Ph.D.

### **Research Biologist — Division of Neurotoxicology**

Over the last twelve years, Dr. Sarkar’s research work has been focused on the effects of various neurotoxicants in the brain vasculature and other components of the neurovascular unit. The components of the neurovascular units (pericytes, microglia, astrocytes, and neurons, as well as basal lamina) act as an intricate network to maintain the neuronal homeostatic microenvironment. Thus, disruptions to this intricate cell network due to neurotoxicant exposure can lead to neuronal malfunction and symptoms characteristic of central nervous system diseases. As the Division of Neurotoxicology’s expert on Alzheimer’s disease (AD), Dr. Sarkar has established collaborative studies with others. More recently, Dr. Sarkar’s laboratory has focused on two important areas of Alzheimer’s disease:  1) investigating the role of microvasculature and diet in altering neuropathology in rodent models of AD and 2) comparative intestinal and neuronal pathology for biomarker identification and its correlation with the microbiome in Alzheimer’s disease using AD Tg rats and postmortem tissues. [VIEW FULL BIO – Dr. Sumit Sarkar](https://www.fda.gov/about-fda/science-research-nctr/sumit-sarkar)

**Titles and links to selected publications**

[**Impaired Aβ Clearance Leads to Vascular Dysfunction in a Transgenic Mice Model of Alzheimer’s Disease**](https://doi.org/10.1016/j.neuroscience.2020.05.024)**.**

[**Characterization of Serum Exosomes from a Transgenic Mouse Model of Alzheimer's Disease**](https://pubmed.ncbi.nlm.nih.gov/30907317/)**.**

[**Increased Inflammation in BA21 Brain Tissue from African Americans with Alzheimer’s Disease**](https://pubmed.ncbi.nlm.nih.gov/31823110/)**.**

[**Brain Endothelial Dysfunction Following Pyrithiamine Induced Thiamine Deficiency in the Rat**](https://www.ncbi.nlm.nih.gov/pubmed/27984051)**.**

[**Vascular-Directed Responses of Microglia Produced by Methamphetamine Exposure:  Indirect Evidence That Microglia are Involved in Vascular Repair**](https://www.ncbi.nlm.nih.gov/pubmed/26970737)**?**

[**Oral Administration of Thioflavin T Prevents Beta Amyloid Plaque Formation in Double Transgenic AD Mice**](https://www.ncbi.nlm.nih.gov/pubmed/26510980)**.**

[**Histopathological and Electrophysiological Indices of Rotenone-Evoked Dopaminergic Toxicity: Neuroprotective Effects of Acetyl-L-Carnitine**](https://www.ncbi.nlm.nih.gov/pubmed/26321151)**.**

[**Chronic MPTP Treatment Produces Hyperactivity in Male Mice Which is not Alleviated by Concurrent Trehalose Treatment**](https://www.ncbi.nlm.nih.gov/pubmed/26111725)**.**

[**Neuroprotective Effect of the Chemical Chaperone, Trehalose, in a Chronic MPTP-Induced Parkinson's Disease Mouse Model**](https://www.ncbi.nlm.nih.gov/pubmed/25064079)**.**

[**Neurovascular Changes in Acute, Sub-Acute and Chronic Mouse Models of Parkinson's Disease**](https://www.ncbi.nlm.nih.gov/pubmed/24274908)**.**

[**In Situ Demonstration of Fluoro-Turquoise Conjugated Gelatin for Visualizing Brain Vasculature and Endothelial Cells and Their Characterization in Normal and Kainic Acid Exposed Animals**](https://www.ncbi.nlm.nih.gov/pubmed/?term=In%20Situ%20Demonstration%20of%20Fluoro-Turquoise%20Conjugated%20Gelatin%20for%20Visualizing%20Brain%20Vasculature%20and%20Endothelial%20Cells%20and%20Their%20Characterization%20in%20Normal%20and)**.**

[**Characterization of Myelin Pathology in the Hippocampal Complex of a Transgenic Mouse Model of Alzheimer’s Disease**](https://www.ncbi.nlm.nih.gov/pubmed/23157338)**.**

[**In Vivo Administration of Fluorescent Dextrans for the Specific and Sensitive Localization of Brain Vascular Pericytes and Their Characterization in Normal and Neurotoxin Exposed Brains**](https://www.ncbi.nlm.nih.gov/pubmed/22525936)**.**

[**Temporal Progression of Kainic Acid Induced Changes in Vascular Laminin Expression in Rat Brain with Neuronal and Glial Correlates**](https://www.ncbi.nlm.nih.gov/pubmed/22475395)**.**

[**Kainic Acid and 3-Nitropropionic Acid Induced Expression of Laminin in Vascular Elements of the Rat Brain**](https://www.ncbi.nlm.nih.gov/pubmed/20624377)**.**

[**Stress- and Lipopolysaccharide-Induced C-Fos Expression and Nnos in Hypothalamic Neurons Projecting to Medullary Raphe: A Triple Immunofluorescent Labeling Study**](https://www.ncbi.nlm.nih.gov/pubmed/17927775)**.**

[**Central Administration of Cocaine- and Amphetamine-Regulated Transcript Increases Phosphorylation of CAMP Response Element Binding Protein (CREB) in Corticotropin-Releasing Hormone-Producing Neurons but not in Prothyrotropin-Releasing Hormone-Producing Neurons in the Hypothalamic Paraventricular Nucleus**](https://www.ncbi.nlm.nih.gov/pubmed/14759497)**.**

[**Glucagon like Peptide-1 (7-36) Amide (GLP-1) Nerve Terminals Densely Innervate Corticotropin-Releasing Hormone Neurons in the Hypothalamic Paraventricular Nucleus**](https://www.ncbi.nlm.nih.gov/pubmed/12967720)**.**

[**Central Administration of Neuropeptide Y Reduces Alpha-Melanocyte-Stimulating Hormone-Induced Cyclic Adenosine 5’-Monophosphate Response Element Binding Protein (CREB) Phosphorylation in Pro-Thyrotropin-Releasing Hormone Neurons and Increases CREB Phosphorylation in Corticotropin-Releasing Hormones Neurons in the Hypothalamic Paraventricular Nucleus**](https://www.ncbi.nlm.nih.gov/pubmed/12488356)**.**

[**Intracerebroventricular Administration of Alpha-Melanocyte Stimulating Hormone Increases Phosphorylation of CREB in TRH- and CRH-Producing Neurons of the Hypothalamic Paraventricular Nucleus**](https://www.ncbi.nlm.nih.gov/pubmed/12113951)**.**

[VIEW FULL BIO – Sumit Sarkar, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/sumit-sarkar)

# Andrew Shen, Ph.D.

### **Staff Fellow — Division of Neurotoxicology**

Dr. Shen’s research focuses on characterizing the neurobehavioral and neurovascular consequences of drugs, heavy metals, and other compounds with potential neurotoxicity. In particular, his work aims to elucidate the connection between neurovascular dysfunction and changes in cognitive processes. His laboratory utilizes diverse methods to answer regulatory toxicology questions, which range from live-cell confocal microscopy and protein assays to neurobehavioral assays and complex cognitive tasks. Currently, Dr. Shen is collaborating with colleagues to assess potential developmental neurotoxicity of cannabidiol (CBD) as well as potential neuroimmune effects of developmental CBD exposure. [VIEW FULL BIO – Dr. Andrew Shen](https://www.fda.gov/about-fda/science-research-nctr/andrew-shen)

**Titles and links to selected publications**

[**Neurobehavioral and Neurochemical Effects of Perinatal Arsenite Exposure in Sprague-Dawley Rats**](https://pubmed.ncbi.nlm.nih.gov/34979254/)**.**

[**Methylmercury Exposure and its Implications for Aging**](https://www.sciencedirect.com/science/article/pii/B9780128180006000202)**.**

[**Isolation of Cerebral Capillaries from Fresh Human Brain Tissue**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6235165/)**.**

[**Preventing P-gp Ubiquitination Lowers Aβ Brain Levels in an Alzheimer’s Disease Mouse Model**](https://pubmed.ncbi.nlm.nih.gov/29997495/)**.**

[**Aging, Motor Function, and Sensitivity to Calcium Channel Blockers: An Investigation Using Chronic Methylmercury Exposure**](https://pubmed.ncbi.nlm.nih.gov/27481695/)**.**

[**A Bout Analysis Reveals Age-Related Methylmercury Neurotoxicity and Nimodipine Neuroprotection**](https://pubmed.ncbi.nlm.nih.gov/27196441/)**.**

[**Examination of Clozapine and Haloperidol in Improving Ketamine-Induced Deficits in an Incremental Repeated Acquisition Procedure in BALB/c Mice**](https://pubmed.ncbi.nlm.nih.gov/26514554/)**.**

[VIEW FULL BIO – Andrew Shen, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/andrew-shen)

# Cheng Wang, M.D., Ph.D.

### **Research Neurobiologist — Division of Neurotoxicology**

Dr. Wang is currently responsible for leading a research team that provides unique and highly specialized skills in neurotoxicology, pharmacology, anesthesiology, systems biology, and stem-cell biology research. His specific research interests include neural stem cell biology the application of systems biology in developmental neurotoxicological studies. He is also interested in activity-induced synaptic plasticity and neural-cell adhesion molecule and potential pediatric anesthetic-induced neural cell death and the potential role of neurotransmission (mechanistic studies). Dr. Wang also retains an interest in mitochondrial DNA damage and expression levels of DNA repair enzymes. [VIEW FULL BIO – Dr. Cheng Wang](https://www.fda.gov/about-fda/science-research-nctr/cheng-wang)

**Titles and links to selected publications**

[**In Vivo Monitoring of Sevoflurane-Induced Adverse Effects in Neonatal Nonhuman Primates Using Small-Animal Positron Emission Tomography**](http://www.ncbi.nlm.nih.gov/pubmed/27183169)**.**

[**Potential Adverse Effects of Prolonged Sevoflurane Exposure on Developing Monkey Brain: From Abnormal Lipid Metabolism to Neuronal Damage**](http://www.ncbi.nlm.nih.gov/pubmed/26206149)**.**

[**Protective Effect of Acetyl-L-Carnitine on Propofol-Induced Toxicity in Embryonic Neural Stem Cells**](http://www.ncbi.nlm.nih.gov/pubmed/24704589)**.**

[**A Minimally Invasive, Translational Biomarker of Ketamine-Induced Neuronal Death in Rats: Micropet Imaging Using 18F-Annexin V**](http://www.ncbi.nlm.nih.gov/pubmed/19638431)**.**

[**Strategies and Experimental Models for Evaluating Anesthetics: Effects on the Developing Nervous System**](http://www.ncbi.nlm.nih.gov/pubmed/18499593)**.**

[**Ketamine-Induced Neuronal Cell Death in the Perinatal Rhesus Monkey**](http://www.ncbi.nlm.nih.gov/pubmed/17426105)**.**

[**Blockade of N-Methyl-D-Aspartate Receptors by Ketamine Produces Loss Of Postnatal Day 3 Monkey Frontal Cortical Neurons in Culture**](http://www.ncbi.nlm.nih.gov/pubmed/16500925)**.**

[**Blockade of N-Methyl-D-Aspartate Receptors by Phencyclidine Causes the Loss of Corticostriatal Neurons**](http://www.ncbi.nlm.nih.gov/pubmed/15062989)**.**

[**Functional N-Methyl-D-Aspartate Receptors in O-2A Glial Precursor Cells: A Critical Role in Regulating Polysialic Acid-Neural Cell Adhesion Molecule Expression and Cell Migration**](http://www.ncbi.nlm.nih.gov/pubmed/8978823)**.**

[**PSA-NCAM is Required for Activity-Induced Synaptic Plasticity**](http://www.ncbi.nlm.nih.gov/pubmed/8816705)**.**

[**Requirement of Polysialic Acid for the Migration of the O-2A Glial Progenitor Cell from Neurohypophyseal Explants**](http://www.ncbi.nlm.nih.gov/pubmed/8027787)**.**

[VIEW FULL BIO – Cheng Wang, M.D., Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/cheng-wang)

# Xuan Zhang, M.D., Ph.D.

### **Research Biologist — Division of Neurotoxicology**

Dr. Zhang currently provides unique and highly specialized skills in neurotoxicology research. One of her main research interests is potential pediatric anesthetic-induced neural cell death and the potential role of neurotransmission. In addition, she retains an interest in the application of noninvasive imaging in developmental neurotoxicological studies as well as the application of dynamic molecular imaging approaches in pediatric-anesthetic studies. Dr. Zhang is also interested in the use of a variety of neuroimaging techniques to investigate the brain structures and neural circuitry associated with Attention Deficit Hyperactivity Disorder, as well as the effects of substance abuse and addiction on the brain and its development. [VIEW FULL BIO – Dr. Xuan Zhang](https://www.fda.gov/about-fda/science-research-nctr/xuan-zhang)

**Titles and links to selected publications**

[**MicroPET/CT Assessment of FDG Uptake in Brain after Long-Term Methylphenidate Treatment in Nonhuman Primates**](https://www.ncbi.nlm.nih.gov/pubmed/27307090)**.**

[**In Vivo Monitoring of Sevoflurane-Induced Adverse Effects in Neonatal Nonhuman Primates using Small-Animal Positron Emission Tomography**](http://www.ncbi.nlm.nih.gov/pubmed/27183169)**.**

[**Plasmodium Infection is Associated with Impaired Hepatic Dimethylarginine Dimethylaminohydrolase Activity and Disruption of Nitric Oxide Synthase Inhibitor/Substrate Homeostasis**](http://www.ncbi.nlm.nih.gov/pubmed/26407009)**.**

[**Application of MicroPET Imaging Approaches in the Study of Pediatric Anesthetic-Induced Neuronal Toxicity**](https://www.ncbi.nlm.nih.gov/pubmed/23400798)**.**

[**Inhalation Anesthetic-Induced Neuronal Damage in the Developing Rhesus Monkey**](https://www.ncbi.nlm.nih.gov/pubmed/21708249)**.**

[**Changes in Gene Expression after Phencyclidine Administration in Developing Rats: A Potential Animal Model for Schizophrenia**](https://www.ncbi.nlm.nih.gov/pubmed/20691775)**.**

[**MicroPET Imaging of Ketamine-Induced Neuronal Apoptosis with Radiolabeled DFNSH**](https://www.ncbi.nlm.nih.gov/pubmed/20963452)**.**

[**Anesthetic-Induced Oxidative Stress and Potential Protection**](https://www.ncbi.nlm.nih.gov/pubmed/20661539)**.**

[**A Minimally Invasive, Translational Biomarker of Ketamine-Induced Neuronal Death in Rats: MicroPET Imaging using 18F-Annexin V**](http://www.ncbi.nlm.nih.gov/pubmed/19638431)**.**

[VIEW FULL BIO – Xuan Zhang, M.D., Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/xuan-zhang)

## Division of Systems Biology, NCTR

# Laura Schnackenberg, Ph.D.

### **Director — Division of Systems Biology**

The Innovative Safety and Technologies Branch within the Division of Systems Biology at NCTR employs novel methodologies to evaluate a wide range of problems. In vivo and in vitro methods are being used to evaluate mechanisms of hepatotoxicity and cardiotoxicity. Additionally, novel alternative models including the use of a tissue chip are being developed to determine the utility in predicting drug-induced hepatotoxicity. Ongoing efforts also include the evaluation of individual patient-derived cells to better represent the population heterogeneity and reflect the differential drug responses noted clinically. Other novel alternative models including an engineered heart tissue model are being developed within the Branch. Translational studies are also ongoing to validate biomarkers in a clinical pediatric population of doxorubicin-induced cardiotoxicity that were identified in a mouse model. The Branch is also exploring the use of mass spectrometry-based technologies to rapidly detect viruses and bacterial pathogens. The technology is also being investigated for its utility in rapidly assessing brand and generic drugs. [VIEW FULL BIO – Dr. Laura Schnackenberg](https://www.fda.gov/about-fda/science-research-nctr/laura-schnackenberg)

**Titles and links to selected publications**

[**MALDI Imaging Mass Spectrometry: An Emerging Tool in Neurology**](https://pubmed-ncbi-nlm-nih-gov.fda.idm.oclc.org/34347208/)**.**

[**Metabolomics Test Materials for Quality Control: A Study of a Urine Materials Suite**](https://pubmed-ncbi-nlm-nih-gov.fda.idm.oclc.org/31703392/)**.**

[**Stability of the Human Plasma Proteome to Pre-analytical Variability as Assessed by an Aptamer-Based Approach**](https://pubmed-ncbi-nlm-nih-gov.fda.idm.oclc.org/31442052/)**.**

[**An Integrated Analysis of Metabolites, Peptides, and Inflammation Biomarkers for Assessment of Preanalytical Variability of Human Plasma**](https://pubmed-ncbi-nlm-nih-gov.fda.idm.oclc.org/31074987/)**.**

[**Aptamer-Based Proteomics Identifies Mortality-Associated Serum Biomarkers in Dialysis-Dependent AKI Patients**](https://pubmed-ncbi-nlm-nih-gov.fda.idm.oclc.org/30197987/)**.**

[**Multiple microRNAs Function as Self-Protective Modules in Acetaminophen-Induced Hepatotoxicity in Humans**](https://pubmed-ncbi-nlm-nih-gov.fda.idm.oclc.org/29067470/)**.**

[**Metabolomics Analysis of Urine Samples from Children after Acetaminophen Overdose**](https://pubmed-ncbi-nlm-nih-gov.fda.idm.oclc.org/28878168/)**.**

[**Dose-response Analysis of Epigenetic, Metabolic, and Apical Endpoints after Short-term Exposure to Experimental Hepatotoxicants**](https://pubmed-ncbi-nlm-nih-gov.fda.idm.oclc.org/28495587/)**.**

[**Early Metabolomics Changes in Heart and Plasma During Chronic Doxorubicin Treatment in B6C3F1 Mice**](http://www.ncbi.nlm.nih.gov/pubmed/26934058)**.**

[**Translational Biomarkers of Acetaminophen-Induced Acute Liver Injury**](http://www.ncbi.nlm.nih.gov/pubmed/25983262)**.**

[**Identification of a Metabolic Biomarker Panel in Rats for Prediction of Acute and Idiosyncratic Hepatotoxicity**](http://www.ncbi.nlm.nih.gov/pubmed/25379137)**.**

[**Metabolomics Evaluation of the Effects of Green Tea Extract on Acetaminophen-Induced Hepatotoxicity in Mice**](http://www.ncbi.nlm.nih.gov/pubmed/24080264)**.**

[**Evaluating Effects of Penicillin Treatment on the Metabolome of Rats**](http://www.ncbi.nlm.nih.gov/pubmed/23831706)**.**

[**Metabolomics Evaluation of Hydroxyproline as a Potential Marker of Melamine and Cyanuric Acid Nephrotoxicity in Male and Female Fischer F344 Rats**](http://www.ncbi.nlm.nih.gov/pubmed/22902825)**.**

[**The Liver Toxicity Biomarker Study Phase I: Markers for the Effects of Tolcapone or Entacapone**](http://www.ncbi.nlm.nih.gov/pubmed/22573522)**.**

[**¹³C NMR-Distance Matrix Descriptors: Optimal Abstract 3D Space Granularity for Predicting Estrogen Binding**](http://www.ncbi.nlm.nih.gov/pubmed/22681591)**.**

[**Serum Metabolomic Profiles from Patients with Acute Kidney Injury: A Pilot Study**](http://www.ncbi.nlm.nih.gov/pubmed/22429878)**.**

[VIEW FULL BIO – Laura Schnackenberg, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/laura-schnackenberg)

# Richard Beger, Ph.D.

### **Chief, Omics, Models, Imaging and Chemistry Branch — Division of Systems Biology**

Dr. Beger’s current research uses cutting-edge systems biology, proteomics, and metabolomics analysis of biofluid and tissues samples from in vitro, nonclinical, and clinical studies to discover and evaluate translational biomarkers of:

* drug-induced liver, kidney, heart, or neural toxicity
* drug or chemical addiction
* disease status

Dr. Beger is participating in national and international quality assurance/quality control metabolomics committees that include the creation of Metabolomics Quality Assurance and Quality Control Consortium (mQACC) and MEtabolomics standaRds Initiative in Toxicology (MERIT) to provide guidance on best practice, quality standards, and the reporting of analytical and computational metabolomics methods. He initiated NCTR and FDA research in tissue imaging with the purchase of MALDI TOF mass spectrometry to image:

* drugs
* drug metabolites
* endogenous metabolites (i.e., neurotransmitters, cholesterol, lipids)
* chemicals

Tissue imaging can be directly compared to histopathology and other imaging techniques to identify biomarkers and mechanisms in tissue. Dr. Beger is also the primary inventor of spectroscopic data activity relationship (SDAR) as well as three-dimensional SDAR modeling that has been used to model estrogen receptor binding, opioid binding, human Ether-à-go-go-Related Gene (hERG) inhibition, and other toxicological endpoints.

[VIEW FULL BIO – Dr. Richard Beger](https://www.fda.gov/about-fda/science-research-nctr/richard-beger)

**Titles and links to selected publications**

[**Distinct Lipid Signatures are Identified in the Plasma of Rats with Chronic Inflammation Induced by Estradiol Benzoate and Sex Hormones**](https://pubmed.ncbi.nlm.nih.gov/32895772/)**.**

[**Dissemination and Analysis of the Quality Assurance (QA) and Quality Control (QC) Practices of LC-MS Based Untargeted Metabolomics Practitioners**](https://pubmed.ncbi.nlm.nih.gov/33044703/)**.**

[**Progress Towards an OECD Reporting Framework for Transcriptomics and Metabolomics in Regulatory Toxicology**](https://pubmed.ncbi.nlm.nih.gov/34333066/)**.**

[**Metabolomics as a Truly Translational Tool for Precision Medicine**](https://pubmed.ncbi.nlm.nih.gov/34514887/)**.**

[**Current Concepts in Pharmacometabolomics, Biomarker Discovery, and Precision Medicine**](https://pubmed.ncbi.nlm.nih.gov/32230776/)**.**

[**Bile Acid Profile and its Changes in Response to Cefoperazone Treatment in MR1 Deficient Mice**](https://pubmed.ncbi.nlm.nih.gov/32225042/)**.**

[**Hepatic Transcript Profiles of Cytochrome P450 Genes Predict Sex Differences in Drug Metabolism**](https://pubmed.ncbi.nlm.nih.gov/32193355/)**.**

[**Determination of Structural Factors Affecting Binding to Mu, Kappa and Delta Opioid Receptors**](https://pubmed.ncbi.nlm.nih.gov/32107589/)**.**

[**Metabolomics Test Materials for Quality Control: A Study of a Urine Materials Suite**](https://pubmed.ncbi.nlm.nih.gov/31703392/)**.**

[**Stability of the Human Plasma Proteome to Pre-analytical Variability as Assessed by an Aptamer-Based Approach**](https://pubmed.ncbi.nlm.nih.gov/31442052/)**.**

[**Metabolomics-Based Pathway Changes in Testis Fragments Treated with Ethinylestradiol In Vitro**](https://pubmed.ncbi.nlm.nih.gov/31347792/)**.**

[**Use Cases, Best Practice and Reporting Standards for Metabolomics in Regulatory Toxicology**](https://pubmed.ncbi.nlm.nih.gov/31292445/)**.**

[**An Integrated Analysis of Metabolites, Peptides, and Inflammation Biomarkers for Assessment of Preanalytical Variability of Human Plasma**](https://pubmed.ncbi.nlm.nih.gov/31074987/)**.**

[**Towards Quality Assurance and Quality Control in Untargeted Metabolomics Studies**](https://pubmed.ncbi.nlm.nih.gov/30830465/)**.**

[**Aptamer-Based Proteomics Identifies Mortality-Associated Serum Biomarkers in Dialysis-Dependent AKI Patients**](https://pubmed.ncbi.nlm.nih.gov/30197987/)**.**

[**Computational Identification of Structural Factors Affecting the Mutagenic Potential of Aromatic Amines: Study Design and Experimental Validation**](https://pubmed.ncbi.nlm.nih.gov/29779177/)**.**

[**Immune Response Proteins as Predictive Biomarkers of Doxorubicin-Induced Cardiotoxicity in Breast Cancer Patients**](https://pubmed.ncbi.nlm.nih.gov/29224368/)**.**

[**Multiple microRNAs Function as Self-Protective Modules in Acetaminophen-Induced Hepatotoxicity in Humans**](https://pubmed.ncbi.nlm.nih.gov/29067470/)**.**

[**Evaluation of Metabolism of Azo Dyes and Their Effects on Staphylococcus aureus Metabolome**](https://pubmed.ncbi.nlm.nih.gov/28786013/)**.**

[**3D-SDAR Modeling of hERG Potassium Channel Affinity: A Case Study in Model Design and Toxicophore Identification**](https://pubmed.ncbi.nlm.nih.gov/28129595/)**.**

[**Metabolomics Enables Precision Medicine: "A White Paper, Community Perspective"**](https://pubmed.ncbi.nlm.nih.gov/27642271/)**.**

[**Translational Biomarkers of Acetaminophen-Induced Acute Liver Injury**](https://pubmed.ncbi.nlm.nih.gov/25983262/)**.**

[VIEW FULL BIO – Richard Beger, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/richard-beger)

# Mallikarjun Bidarimath, DVM, Ph.D.

### **Visiting Scientist — Division of Systems Biology**

Dr. Bidarimath’s long-term goal is to understand how aberrations in molecular and cellular mechanisms governing pregnancy events may lead to pregnancy-associated disorders. Pregnancy is a delicate yet complex physiological process that requires fine-tuning of many factors to ensure the survival of the conceptus to term. A successful mammalian pregnancy depends upon the establishment and maintenance of an adequate maternal-fetal interface as well as maternal immune tolerance to the semi-allogenic fetus. After fertilization, a non-pregnant uterus must undergo transformation into a cellular and molecular environment suitable for development and growth of the fetus. These processes are likely facilitated by a coordinated interaction between two distinct yet opposed organ systems — the endometrium and the placenta. A precise interaction between these compartments must occur to facilitate most pregnancy specific mechanisms including, but not limited to, placental development, angiogenesis, immunomodulation, and organogenesis. Any disturbance in the maternal-fetal dialog can have detrimental effects on the developing fetus, the outcome of pregnancy, or even postnatal development. Many reproductive system diseases or dysfunctions have unknown etiologies, however, infectious, non-infectious, and environmental factors are likely contributors. To prevent or reduce the burden of diseases, Dr. Bidarimath’s research is directed at understanding the mechanisms and identifying key target molecules that impact development of reproductive diseases. The reproductive system is under constant exposure to environmental hazards and other infectious agents. To identify the agents and characterize their effects, Dr. Bidarimath uses a variety of pathological and toxicological techniques to test laboratory and clinical samples as well as use genetically engineered mice and other laboratory rodents, human cells, and transcriptomic analysis.

Pregnant women have higher risk for a variety of infections, like the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). There has been growing concern over the long-term effect of SARS-CoV-2 in pregnant women, their newborns, and children. Recent studies indicate that SARS-CoV-2 infection during pregnancy may directly cause or be associated with placental injury and malperfusion, miscarriage, preeclampsia, stillbirth, and/or preterm delivery with adverse perinatal outcomes. In addition, infants born with SARS-CoV-2 infections suggest that viral transmission can occur from infected mothers to the developing fetus, resulting in adverse events independent of maternal symptoms. Latent virus and post-COVID effects have been identified in vital organs such as lungs, brain, heart, and kidneys as well as reproductive organs. A distinct set of proteins required for virus entry into the host cells are highly expressed in maternal organs (uterus), maternal-fetal interface (e.g. placenta) and fetal tissues. Previous studies have suggested that SARS-CoV-2 infection before and/or after birth presents additional health risks to the mother as well as newborns. However, it remains to be investigated if the SARS-CoV-2 infection-related effects on newborns or on the fetus during pregnancy are because of illness in the mother or as a result of vertical transmission via maternal-fetal interface. The vertical transmission is of concern as there have been reports of multisystemic inflammatory syndrome in children after SARS-CoV-2 infection, which is characterized by inflammation of multiple organs including brain, heart, and kidneys. A variety of drugs, including the anti-viral drug Remdesivir, have been approved to treat COVID-19 patients. However, it is not clear if these drugs affect placental perfusion and related pregnancy specific functions. There are reports of COVID-related changes in the placenta that may perturb the normal perfusion, which in turn may affect the drug clearance as well as overall fetal growth. More detailed investigations are required to accurately characterize drug-related effects during pregnancy compromised by SARS-CoV-2 infection and post-natal development. Dr. Bidarimath’s research is focused on using a combination of pathological and toxicological approaches to evaluate potential effects of SARS-CoV-2 infection and therapeutic administration in COVID-19 animal models in adults, during pregnancy, and during development. [VIEW FULL BIO – Dr. Mallikarjun Bidarimath](https://www.fda.gov/about-fda/science-research-nctr/mallikarjun-bidarimath)

**Titles and links to selected publications**

[**Insights Into Extracellular Vesicle/Exosome and miRNA Mediated Bi-Directional Communication During Porcine Pregnancy**](https://pubmed.ncbi.nlm.nih.gov/33937376/)**.**

[**Cells Expressing PAX8 are the Main Source of Homeostatic Regeneration of Adult Mouse Endometrial Epithelium and Give Rise to Serous Endometrial Carcinoma**](https://pubmed.ncbi.nlm.nih.gov/32998907/)**.**

[**WNT and Inflammatory Signaling Distinguish Human Fallopian Tube Epithelial Cell Populations**](https://pubmed.ncbi.nlm.nih.gov/32555344/)**.**

[**A Balancing Act: RNA Binding Protein HuR/TTP Axis in Endometriosis Patients**](https://pubmed.ncbi.nlm.nih.gov/28724967/)**.**

[**Pregnancy and Spontaneous Fetal Loss: A Pig Perspective**](https://pubmed.ncbi.nlm.nih.gov/28661560/)**.**

[**Extracellular Vesicle Mediated Intercellular Communication at the Porcine Maternal-Fetal Interface: A New Paradigm for Conceptus-Endometrial Cross-Talk**](https://pubmed.ncbi.nlm.nih.gov/28079186/)**.**

[**Altered Expression of Chemokines and their Receptors at Porcine Maternal-Fetal Interface During Early and Mid-Gestational Fetal Loss**](https://pubmed.ncbi.nlm.nih.gov/27503377/)**.**

[**A Distinct Pre-Existing Inflammatory Tumour Microenvironment is Associated with Chemotherapy Resistance in High-Grade Serous Epithelial Ovarian Cancer**](https://pubmed.ncbi.nlm.nih.gov/25826225/)**.**

[**Placental Growth Factor Deficiency is Associated with Impaired Cerebral Vascular Development in Mice**](https://pubmed.ncbi.nlm.nih.gov/26646502/)**.**

[**Placentation, Maternal-Fetal Interface, and Conceptus Loss in Swine**](https://pubmed.ncbi.nlm.nih.gov/26324112/)**.**

[**Distinct microRNA Expression in Endometrial Lymphocytes, Endometrium, and Trophoblast During Spontaneous Porcine Fetal Loss**](https://pubmed.ncbi.nlm.nih.gov/25596873/)**.**

[**mRNA Destabilizing Factors: Tristetraprolin Expression at the Porcine Maternal-Fetal Interface**](https://pubmed.ncbi.nlm.nih.gov/25496016/)**.**

[**Laser Capture Microdissection for Gene Expression Analysis**](https://pubmed.ncbi.nlm.nih.gov/25308266/)**.**

[**MicroRNAs, Immune Cells and Pregnancy**](https://pubmed.ncbi.nlm.nih.gov/24954225/)**.**

[**Are Pharmacological Interventions Between Conception and Birth Effective in Improving Reproductive Outcomes in North American Swine**](https://pubmed.ncbi.nlm.nih.gov/24941906/)**?**

[**The microRNAome of Pregnancy: Deciphering miRNA Networks at the Maternal-Fetal Interface**](https://pubmed.ncbi.nlm.nih.gov/24278102/)**.**

[**Studies on Cisternal and Alveolar Fractions & its Composition and Mammary Health of Murrah Buffaloes Administered Oxytocin**](https://pubmed.ncbi.nlm.nih.gov/17966274/)**.**

[**“Laser Capture Microdissection”**](https://www.sciencedirect.com/science/article/pii/B9780123944450000485)**.**

[VIEW FULL BIO – Mallikarjun Bidarimath, DVM, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/mallikarjun-bidarimath)

# Dan Buzatu, Ph.D.

### **Associate Co-Director, Innovative Technology Staff — Division of Systems Biology**

Dr. Buzatu’s research interests include:

* pathogen detection for food safety and clinical applications using flow cytometry
* mass spectrometry characterization of pathogens and chemicals
* advanced methods for sample clean-up in food and other complex biological matrices
* nanomaterial synthesis and applications
* mass spectrometry, flow cytometry; computational methods
* novel intellectual property, patents
* SDAR, RAPID-B, SpecID, and MRS commercialization for non-invasive diagnostics

[VIEW FULL BIO – Dr. Dan Buzatu](https://www.fda.gov/about-fda/science-research-nctr/dan-buzatu)

**Titles and links to selected publications**

[**Alignment-Independent Technique for 3D QSAR Analysis**](http://www.ncbi.nlm.nih.gov/pubmed/27026022)**.**

[**Level 2 Validation of a Flow Cytometric Method for Detection of Escherichia coli O157:H7 in Raw Spinach**](http://www.ncbi.nlm.nih.gov/pubmed/26318407)**.**

[**Instrumental Improvements and Sample Preparations that Enable Reproducible, Reliable Acquisition of Mass Spectra from Whole Bacterial Cells**](http://www.ncbi.nlm.nih.gov/pubmed/26443394)**.**

[**Partial Least Squares and k-Nearest Neighbor Algorithms for Improved 3D Quantitative Spectral Data-Activity Relationship Consensus Modeling of Acute Toxicity**](http://www.ncbi.nlm.nih.gov/pubmed/24464801)**.**

[**An Integrated Flow Cytometry-Based System for Real-Time, High Sensitivity Bacterial Detection and Identification**](http://www.ncbi.nlm.nih.gov/pubmed/24718659)**.**

[**Photobleaching with Phloxine B Sensitizer to Reduce Food Matrix Interference for Detection of Escherichia coli Serotype O157:H7 in Fresh Spinach by Flow Cytometry**](http://www.ncbi.nlm.nih.gov/pubmed/24010624)**.**

[**Complementary PLS and KNN Algorithms for Improved 3D-QSDAR Consensus Modeling of AhR Binding**](http://www.ncbi.nlm.nih.gov/pubmed/24257141)**.**

[**Reduction of Food Matrix Interference by a Combination of Sample Preparation and Multi-Dimensional Gating Techniques to Facilitate Rapid, High Sensitivity Analysis for Escherichia Coli Serotype O157 by Flow Cytometry**](http://www.ncbi.nlm.nih.gov/pubmed/22265313)**.**

[**13C NMR-Distance Matrix Descriptors: Optimal Abstract 3D Space Granularity for Predicting Estrogen Binding**](http://www.ncbi.nlm.nih.gov/pubmed/22681591)**.**

[**Development of a Flow Cytometry-Based Method for Rapid Detection of Escherichia coli and Shigella Spp. Using an Oligonucleotide Probe**](http://www.ncbi.nlm.nih.gov/pubmed/26913737)**.**

[**Improving Proton MR Spectroscopy of Brain Tissue for Noninvasive Diagnostics**](https://www.ncbi.nlm.nih.gov/pubmed/20882612)**.**

[VIEW FULL BIO – Dan Buzatu, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/dan-buzatu)

# Chengzhong Cai, M.D., Ph.D.

### **Visiting Scientist — Division of Systems Biology**

New approach methodologies, which encompass human-based alternatives to animal-based research, have been gaining increasing recognition for many different applications. Dr. Cai's main research interest is in developing 2D and 3D iPSC-based in vitro models for detecting and predicting drug-induced cardiotoxicity and neurotoxicity using a variety of technologies to measure endpoints such as flow cytometry, fluorescence and laser scanning microscopy, Seahorse extracellular flux technology, the CardioECR system, microelectrode array, and others to evaluate cardiomyocyte’s mitochondrial function, beat rate, impedance, beat amplitude, etc. He has significant roles in several in vitro model-based projects, including:

* Investigating the role of sex differences in response to oncologic drugs using iPSC-based engineered human heart tissue (founded by the Office of Women’s Health).
* In vitro toxicity assessment of opioids on neural precursor cell specification, proliferation, and differentiation (collaboration with the Center for Drug Evaluation and Research [CDER]).
* Studying the metabolic maturation of hiPSC-cardiomyocytes (CMs) and applying hiPSC-CMs for drug-induced cardiotoxicity studies (collaboration with CDER).

[VIEW FULL BIO – Dr. Chengzhong Cai](https://www.fda.gov/about-fda/science-research-nctr/chengzhong-cai)

**Titles and links to selected publications**

[**The Importin Beta Superfamily Member RanBP17 Exhibits a Role in Cell Proliferation and is Associated with Improved Survival of Patients with HPV+ HNSCC**](https://pubmed.ncbi.nlm.nih.gov/35850701/)**.**

[**Improving Cardiotoxicity Prediction in Cancer Treatment: Integration of Conventional Circulating Biomarkers and Novel Exploratory Tools**](https://pubmed.ncbi.nlm.nih.gov/33219404/)**.**

[**Sex-Related Differences in Drug-Induced QT Prolongation and Torsades de Pointes: A New Model System with Human iPSC-CMs**](https://pubmed.ncbi.nlm.nih.gov/30247688/)**.**

[**Fatty Acid-Based Medium Promoted Metabolic Maturation of Human Induced Pluripotent Stem Cell-Derived Cardiomyocytes**](https://www.ahajournals.org/doi/10.1161/circ.138.suppl_1.16287)**. (Conference Abstract)**

[**Real-Time Monitoring of Circulating Tumor Cell (CTC) Release after Nanodrug or Tumor Radiotherapy Using In Vivo Flow Cytometry**](https://pubmed.ncbi.nlm.nih.gov/28822765/)**.**

[**In Vivo Noninvasive Analysis of Graphene Nanomaterial Pharmacokinetics Using Photoacoustic Flow Cytometry**](https://pubmed.ncbi.nlm.nih.gov/28524252/)**.**

[**Photoacoustic In Vitro Flow Cytometry for Nanomaterial Research**](https://pubmed.ncbi.nlm.nih.gov/28417068/)**.**

[**Photoacoustic Flow Cytometry for Single Sickle Cell Detection In Vitro and In Vivo**](https://pubmed.ncbi.nlm.nih.gov/27699143/)**.**

[**In Vivo Photoacoustic Flow Cytometry for Early Malaria Diagnosis**](https://pubmed.ncbi.nlm.nih.gov/27078044/)**.**

[**Distal Pancreatectomy With En Bloc Celiac Axis Resection for Locally Advanced Pancreatic Cancer: A Systematic Review and Meta-Analysis**](https://pubmed.ncbi.nlm.nih.gov/26962836/)**.**

[**MicroRNA-3666 Regulates Thyroid Carcinoma Cell Proliferation via MET**](https://pubmed.ncbi.nlm.nih.gov/26937629/)**.**

[**Anatomical Study of Surgical Approaches for Minimally Invasive Transoral Thyroidectomy: eMIT and TOPP**](https://pubmed.ncbi.nlm.nih.gov/25854280/)**.**

[**In Vivo Long-Term Monitoring of Circulating Tumor Cells Fluctuation during Medical Interventions**](https://pubmed.ncbi.nlm.nih.gov/26367280/)**.**

[**A Cisplatin-Resistant Head and Neck Cancer Cell Line with Cytoplasmic p53(mut) Exhibits ATP-Binding Cassette Transporter Upregulation and High Glutathione Levels**](https://pubmed.ncbi.nlm.nih.gov/24913304/)**.**

[**Epidermal Growth Factor-Induced Modulation of Cytokeratin Expression Levels Influences the Morphological Phenotype of Head and Neck Squamous Cell Carcinoma Cells**](https://pubmed.ncbi.nlm.nih.gov/23111772/)**.**

[**SIVmac₂₃₉-Nef Down-Regulates Cell Surface Expression of CXCR4 in Tumor Cells and Inhibits Proliferation, Migration and Angiogenesis**](https://pubmed.ncbi.nlm.nih.gov/22753736/)**.**

[**Runx3 Expression in Lymph Nodes with Metastasis is Associated with the Outcome of Gastric Cancer Patients**](https://pubmed.ncbi.nlm.nih.gov/22848301/)**.**

[**Differential Expression of VEGF121, VEGF165 and VEGF189 in Angiomas and Squamous Cell Carcinoma Cell Lines of the Head and Neck**](https://pubmed.ncbi.nlm.nih.gov/20393000/)**.**

[**Involvement of LYVE-1-Positive Endothelial Cells in the Formation of Non-Lymphatic Vascular Malformations**](https://pubmed.ncbi.nlm.nih.gov/21083607/)**.**

[VIEW FULL BIO – Chengzhong Cai, M.D., Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/chengzhong-cai)

# Tao Han, Ph.D.

### **Senior Staff Fellow — Division of Systems Biology**

Over the years, Dr. Han’s research has focused primarily on drug-related hepatotoxicity and cardiotoxicity. One of his research interests is to identify early biomarkers by using omics technologies. He has published 38 research papers (author and co-author) related to mechanisms of hepatoxicity and cardiotoxicity. In a recently approved NCTR protocol, “Systems biology approach to identify early biomarkers of sunitinib‐induced cardiac toxicity in a mouse model,” he plans to use omics technologies to study the mechanism of cardiotoxicity induced by sunitinib (a tyrosine kinase inhibitor) in a mouse model. [VIEW FULL BIO – Dr. Tao Han](https://www.fda.gov/about-fda/science-research-nctr/tao-han)

**Titles and links to selected publications**

[**Doxorubicin-Induced Delayed-Onset Subclinical Cardiotoxicity in Mice**](https://pubmed.ncbi.nlm.nih.gov/34668590/)**.**

[**Hepatic Transcript Profiles of Drug Metabolizing Genes Predict Sex Differences in Drug Metabolism**](https://pubmed.ncbi.nlm.nih.gov/32193355/)**.**

[**Candidate Early Predictive Plasma Protein Markers of Doxorubicin-Induced Chronic Cardiotoxicity in B6C3F1 Mice**](https://pubmed-ncbi-nlm-nih-gov.fda.idm.oclc.org/30517846/)**.**

[**Transcript Profiling in the Testes and Prostates of Postnatal Day 30 Sprague-Dawley Rats Exposed Prenatally and Lactationally to 2-hydroxy-4-methoxybenzophenone**](https://pubmed.ncbi.nlm.nih.gov/30316929/)**.**

[**Sex and Age Differences in the Expression of Liver microRNAs During the Life Span of F344 Rats**](https://pubmed.ncbi.nlm.nih.gov/28174625/)**.**

[**Transcriptomics Analysis of Early Embryonic Stem Cell Differentiation Under Osteoblast Culture Conditions: Applications for Detection of Developmental Toxicity**](https://pubmed.ncbi.nlm.nih.gov/28189605/)**.**

[**Early Transcriptional Changes in Cardiac Mitochondria During Chronic Doxorubicin Exposure and Mitigation by Dexrazoxane in Mice**](http://www.ncbi.nlm.nih.gov/pubmed/26873546)**.**

[**Status of Hepatic DNA Methylome Predetermines and Modulates the Severity of Non-Alcoholic Fatty Liver Injury in Mice**](http://www.ncbi.nlm.nih.gov/pubmed/27103143)**.**

[**Sexual Dimorphism in the Expression of Mitochondria-Related Genes in Rat Heart at Different Ages**](https://www.ncbi.nlm.nih.gov/pubmed/25615628)**.**

[**Persistence of Furan-Induced Epigenetic Aberrations in the Livers of F344 Rats**](https://www.ncbi.nlm.nih.gov/pubmed/25539665)**.**

[**Effects of Oral Exposure to Bisphenol A on Gene Expression and Global Genomic DNA Methylation in the Prostate, Female Mammary Gland, and Uterus of NCTR Sprague-Dawley Rats**](https://pubmed.ncbi.nlm.nih.gov/25862956/)**.**

[**MicroRNA-155 Deficient Mice Experience Heightened Kidney Toxicity when Dosed with Cisplatin**](https://www.ncbi.nlm.nih.gov/pubmed/25015656)**.**

[**Transcriptomic Responses Provide a New Mechanistic Basis for the Chemopreventive Effects of Folic Acid and Tributyrin in Rat Liver Carcinogenesis**](https://www.ncbi.nlm.nih.gov/pubmed/24302446)**.**

[**Differential Gene Expression in Human Hepatocyte Cell Lines Exposed to the Antiretroviral Agent Zidovudine**](https://www.ncbi.nlm.nih.gov/pubmed/24292225)**.**

[**Early Biomarkers of Doxorubicin-Induced Heart Injury in a Mouse Model**](https://www.ncbi.nlm.nih.gov/pubmed/25448438)**.**

[**The Liver Toxicity Biomarker Study Phase I: Markers for the Effects of Tolcapone or Entacapone**](https://www.ncbi.nlm.nih.gov/pubmed/22573522)**.**

[**Technical Reproducibility of Genotyping SNP Arrays Used in Genome-Wide Association Studies**](https://www.ncbi.nlm.nih.gov/pubmed/22970228)**.**

[**Characterization of Whole Genome Amplified (WGA) DNA for Use in Genotyping Assay Development**](https://www.ncbi.nlm.nih.gov/pubmed/22655855)**.**

[**Coupling Global Methylation and Gene Expression Profiles Reveal Key Pathophysiological Events in Liver Injury Induced by a Methyl-Deficient Diet**](https://www.ncbi.nlm.nih.gov/pubmed/20938992)**.**

[VIEW FULL BIO – Tao Han, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/tao-han)

# Jessica Hawes, Ph.D.

### **Deputy Director — Division of Systems Biology**

Dr. Hawes’s research interests cover the broad spectrum of scientific topics studied within the Division of Systems Biology, including identifying scientific needs and knowledge gaps pertaining to FDA-regulated products and Regulatory Science through research and collaboration. Current research areas of interest include elucidating risks for special populations exposed to viral pathogens and therapeutics, vaccines, cannabinoids, immune responses, and rare diseases. [VIEW FULL BIO – Dr. Jessica Hawes](https://www.fda.gov/about-fda/science-research-nctr/jessica-hawes)

**Titles and links to selected publications**

[**Tandem Mass Spectrometric Sequence Characterization of Synthetic Oligonucleotides**](http://doi.org/10.1002/jms.4819)**.**

[**Development and Regulatory Challenges for Peptide Therapeutics**](https://journals.sagepub.com/doi/10.1177/1091581820977846?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed)**.**

[**Elucidating Interactions Between SARS-CoV-2 Trimeric Spike Protein and ACE2 Using Homology Modeling and Molecular Dynamics Simulations**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7813797/)**.**

[**NDA 209803 Steglatro (Ertugliflozin) Pharmacology/Toxicology Review and Evaluation**](https://www.accessdata.fda.gov/drugsatfda_docs/nda/2017/209803,209805,209806Orig1s000TOC.cfm)**.**

[**NDA 209805 Steglujan (Ertugliflozin; Sitagliptin Phosphate) Pharmacology/Toxicology Review and Evaluation**](https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=209805)**.**

[**NDA 209806 Segluromet (Ertugliflozin; Metformin Hydrochloride) Pharmacology/Toxicology Review and Evaluation**](https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=209806)**.**

[**U.S. Food and Drug Administration Approval: Carfilzomib for the Treatment of Multiple Myeloma**](https://clincancerres.aacrjournals.org/content/19/17/4559.long)**.**

[**NDA 202714 Kyprolis (Carfilzomib) Pharmacology/Toxicology Review and Evaluation**](https://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/202714Orig1s000TOC.cfm)**.**

[**Control of Proliferation in Astrocytoma Cells by the Receptor Tyrosine Kinase/PI3K/AKT Signaling Axis and the Use of PI-103 and TCN as Potential Anti-Astrocytoma Therapies**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3107099/)**.**

[**Genetically Engineered Mouse Models in Cancer Research**](https://www.sciencedirect.com/science/article/pii/S0065230X10060045?via%3Dihub)**.**

[**Bioluminescent Approaches for Measuring Tumor Growth in a Mouse Model of Neurofibromatosis**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6348901/)**.**

[**Novel Dual-Reporter Preclinical Screen for Anti-Astrocytoma Agents Identifies Cytostatic and Cytotoxic Compounds**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2693415/)**.**

[**Galanin Protects Against Behavioral and Neurochemical Correlates of Opiate Reward**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2504505/)**.**

[**Nf1 Expression is Dependent on Strain Background: Implications for Tumor Suppressor Haploinsufficiency Studies**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6687394/)**.**

[**Galanin and Galanin-Like Peptide Modulate Neurite Outgrowth via Protein Kinase C-Mediated Activation of Extracellular Signal-Related Kinase**](https://onlinelibrary.wiley.com/doi/10.1111/j.1460-9568.2006.04828.x)**.**

[**Galanin Attenuates Cyclic AMP Regulatory Element-Binding Protein (CREB) Phosphorylation Induced by Chronic Morphine and Naloxone Challenge in Cath.a Cells and Primary Striatal Cultures**](https://onlinelibrary.wiley.com/doi/10.1111/j.1471-4159.2005.03613.x)**.**

[**Galanin Can Attenuate Opiate Reinforcement and Withdrawal**](https://www.sciencedirect.com/science/article/abs/pii/S0143417904001398?via%3Dihub)**.**

[**GalR1, but not GalR2 or GalR3, Levels are Regulated by Galanin Signaling in the Locus Coeruleus Through a Cyclic AMP-Dependent Mechanism**](https://onlinelibrary.wiley.com/doi/10.1111/j.1471-4159.2005.03105.x)**.**

[**Characterization of GalR1, GalR2, and GalR3 Immunoreactivity in Catecholaminergic Nuclei of the Mouse Brain**](https://onlinelibrary.wiley.com/doi/10.1002/cne.20329)**.**

[**The Neuropeptide Galanin Modulates Behavioral and Neurochemical Signs of Opiate Withdrawal**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC166432/)**.**

[**The Docking Protein FRS2alpha Controls a MAP Kinase-Mediated Negative Feedback Mechanism for Signaling by FGF Receptors**](https://www.sciencedirect.com/science/article/pii/S1097276502006895?via%3Dihub)**.**

[VIEW FULL BIO – Jessica Hawes, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/jessica-hawes)

# Amy Inselman, Ph.D.

### **Staff Fellow — Division of Systems Biology**

The Biomarkers and Alternative Models Branch within the Division of Systems Biology at NCTR develops and evaluates cell-culture models to examine various types of toxicity and investigates whether such models could reduce or replace animals in safety testing of FDA-regulated products. Dr. Inselman’s current research interests are focused on human induced pluripotent stem cell (hiPSC)  models that may serve as alternatives to whole-animal studies for predicting developmental toxicity, including developmental neurotoxicity. Dr. Inselman established the mouse embryonic stem cell test (mEST) within the FDA and investigated whether additional differentiation endpoints (e.g. osteoblasts) could improve the predictive nature of the assay. Her present work is focused on developmental neurotoxicity and she leads a group investigating the effects of early opioid exposure on neural development using both in vitro and in vivo models. [VIEW FULL BIO – Dr. Amy Inselman](https://www.fda.gov/about-fda/science-research-nctr/amy-inselman)

**Titles and links to selected publications**

[**Dr. Daniel Acosta and In Vitro Toxicology at the U.S. Food and Drug Administration’s National Center for Toxicological Research**](https://pubmed.ncbi.nlm.nih.gov/31628011/)**.**

[**Potential Mechanisms for Phencyclidine/Ketamine-Induced Brain Structural Alterations and Behavioral Consequences**](https://pubmed.ncbi.nlm.nih.gov/31812709/)**.**

[**Transcript Profiling in the Testes and Prostrates of Postnatal Day 30 Sprague-Dawley Rats Exposed Prenatally and Lactationally to 2-Hydroxy-4-Methoxybenzophenone**](https://pubmed.ncbi.nlm.nih.gov/30316929/)**.**

[**Transcriptomics Analysis of Early Embryonic Stem Cell Differentiation Under Osteoblast Culture Conditions: Applications for Detection of Developmental Toxicity**](https://pubmed.ncbi.nlm.nih.gov/28189605/)**.**

[**Evaluation of Culture Time and Media in an In Vitro Testis Organ Culture System**](https://pubmed.ncbi.nlm.nih.gov/28398669/)**.**

[**Disrupting Cyclin Dependent Kinase 1 in Spermatocytes Causes Late Meiotic Arrest and Infertility in Mice**](https://www.ncbi.nlm.nih.gov/pubmed/26490841)**.**

[**Developing Osteoblasts as an Endpoint for the Mouse Embryonic Stem Cell Test**](https://www.ncbi.nlm.nih.gov/pubmed/25929818)**.**

[**Effects of Silver Nanoparticles on Human and Rat Embryonic Neural Stem Cells**](https://www.ncbi.nlm.nih.gov/pubmed/25904840)**.**

[**Effects of Maternal and Lactational Exposure to 2-Hydroxy-4-Methoxybenzone on Development and Reproductive Organs in Male and Female Rat Offspring**](https://www.ncbi.nlm.nih.gov/pubmed/25707689)**.**

[**Reevaluation of the Embryonic Stem Cell Test**](https://journals.tdl.org/regsci/index.php/regsci/article/view/9)**.**

[**Alternative Models in Developmental Toxicology**](https://www.ncbi.nlm.nih.gov/pubmed/22239077)**.**

[**Assessment of Research Models for Testing Gene-Environment Interactions**](https://www.ncbi.nlm.nih.gov/pubmed/21816149)**.**

[**Heat Shock Protein 2 Promoter Drives Cre Expression in Spermatocytes of Transgenic Mice**](https://www.ncbi.nlm.nih.gov/pubmed/20027617)**.**

[**A Missense Mutation in the Capza3 Gene and Disruption of F-Actin Organization in Spermatids of Repro32 Infertile Male Mice**](https://www.ncbi.nlm.nih.gov/pubmed/19341723)**.**

[VIEW FULL BIO – Amy Inselman, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/amy-inselman)

# E. Ellen Jones, Ph.D.

### **Staff Fellow, Biomarkers and Alternative Models Branch — Division of Systems Biology**

The implementation of cutting-edge technologies such as high-resolution MALDI imaging within FDA is critical as it corresponds to technology use by pharmaceutical companies in preclinical and clinical studies to identify biomarkers of drug efficacy and toxicity. This data is beginning to be included within FDA drug filings. These studies are performed using a state-of-the-art high-resolution FTICR mass spectrometer (scimaX MRMS 7T FTICR MS) capable of the mass accuracy and resolution required for small molecule imaging. The MALDI IMS team at FDA’s National Center for Toxicological Research (NCTR) is one of only a handful of groups across the country which possess both the instrumentation and experience needed to conduct this research. [VIEW FULL BIO – Dr. Ellen Jones](https://www.fda.gov/about-fda/science-research-nctr/e-jones)

**Titles and links to selected publications**

[**MALDI Imaging Mass Spectrometry: An Emerging Tool in Neurology**](https://pubmed.ncbi.nlm.nih.gov/34347208/)**.**

[**MALDI Mass Spectrometry Imaging of N-linked Glycans in Cancer Tissues**](https://pubmed.ncbi.nlm.nih.gov/28110657/)**.**

[**Tissue Localization of Glycosphingolipid Accumulation in a Gaucher Disease Mouse Brain by LC-ESI-MS/MS and High Resolution MALDI Imaging Mass Spectrometry**](https://pubmed.ncbi.nlm.nih.gov/28714776/)**.**

[**Feasibility Assessment of a MALDI FTICR Imaging Approach for the 3D Reconstruction of a Mouse Lung**](https://pubs.acs.org/doi/10.1007/s13361-017-1658-3)**.**

[**Proteomic Profiling of Serial Pre-Diagnostic Serum Samples for Early Detection of Colon Cancer in the U.S. Military**](https://pubmed.ncbi.nlm.nih.gov/28003179/)**.**

[**“Detection and Distribution of Sphingolipids in Tissue by FTICR MALDI IMS”**](https://link.springer.com/chapter/10.1007/978-3-319-20750-6_15)**.**

[**Tissue Biomarkers of Drug Efficacy: Case Studies Using a MALDI MSI Workflow**](https://pubmed.ncbi.nlm.nih.gov/26505686/)**.**

[**On-Tissue Localization of Ceramides and Other Sphingolipids by MALDI Mass Spectrometry Imaging**](https://pubmed.ncbi.nlm.nih.gov/25072097/)**.**

[**In-Depth Proteomic Analyses of Exosomes Isolated from Expressed Prostatic Secretions in Urine**](https://pubmed.ncbi.nlm.nih.gov/23533145/)**.**

[**Matrix Assisted Laser Desorption Ionization Imaging Mass Spectrometry Workflow for Spatial Profiling Analysis of N-Linked Glycan Expression in Tissues**](https://pubmed.ncbi.nlm.nih.gov/24050758/)**.**

[**Lectin Capture Strategies Combined with Mass Spectrometry for the Discovery of Serum Glycoprotein Biomarkers**](https://pubmed.ncbi.nlm.nih.gov/16760258/)**.**

[**SELDI-TOF MS Profiling of Serum for Detection of the Progression of Chronic Hepatitis C to Hepatocellular Carcinoma**](https://aasldpubs.onlinelibrary.wiley.com/doi/10.1002/hep.20577)**.**

[VIEW FULL BIO – E. Ellen Jones, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/e-jones)

# Kelly E. Mercer, Ph.D.

### **Staff Fellow — Division of Systems Biology**

Dr. Mercer’s current research has focused on development of novel in vivo models to screen newly engineered immunotherapies, such as Chimeric Antigen T Cell products for adverse effects and toxicities associated with treatment, such as severe inflammatory toxicity. SARS-CoV-2 infections also present a similar inflammatory toxicity called a “cytokine storm” and part of her research has shifted to projects related to characterizing the histopathological patterns of COVID-19 disease progression in vital organs, combining traditional histopathology and immunohistochemistry methodology with newer imaging techniques. [VIEW FULL BIO – Dr. Kelly Mercer](https://www.fda.gov/about-fda/science-research-nctr/kelly-mercer)

**Titles and links to selected publications**

[**Exercise Training and Diet-Induced Weight Loss Increase Markers of Hepatic Bile Acid (BA) Synthesis and Reduce Serum Total BA Concentrations in Obese Women**](https://pubmed.ncbi.nlm.nih.gov/33645254/)**.**

[**Fibroblast Growth Factor-21 to Adiponectin Ratio: A Potential Biomarker to Monitor Liver Fat in Children with Obesity**](https://pubmed.ncbi.nlm.nih.gov/33071964/)**.**

[**Xenometabolite Signatures in the UC Davis Type 2 Diabetes Mellitus Rat Model Revealed Using a Metabolomics Platform Enriched with Microbe-Derived Metabolites**](https://pubmed.ncbi.nlm.nih.gov/32508155/)**.**

[**Circulating miRNA Signatures Associated with Insulin Resistance in Adolescents with Obesity**](https://pubmed.ncbi.nlm.nih.gov/33328751/)**.**

[**Divergence in Aerobic Capacity Impacts Bile Acid Metabolism in Young Women**](https://pubmed.ncbi.nlm.nih.gov/32853107/)**.**

[**Infant Formula Feeding Increases Hepatic Cholesterol 7alpha Hydroxylase (CYP7A1) Expression and Fecal Bile Acid Loss in Neonatal Piglets**](https://pubmed.ncbi.nlm.nih.gov/30053282/)**.**

[**Modulating Sterol Concentrations in Infant Formula Influences Cholesterol Absorption and Synthesis in the Neonatal Piglet**](https://pubmed.ncbi.nlm.nih.gov/30513717/)**.**

[**Diet Supplementation with Soy Protein Isolate, but Not the Isoflavone Genistein, Protects Against Alcohol-Induced Tumor Progression in DEN-Treated Male Mice**](https://pubmed.ncbi.nlm.nih.gov/30362095/)**.**

[**Soy Protein Isolate Inhibits Hepatic Tumor Promotion in Mice Fed a High-Fat Liquid Diet**](https://pubmed.ncbi.nlm.nih.gov/28056552/)**.**

[**Soy Protein Isolate Protects Against Ethanol-Mediated Tumor Progression in Diethylnitrosamine-Treated Male Mice**](https://pubmed.ncbi.nlm.nih.gov/27006377/)**.**

[**Reactive Oxygen Species Differentially Regulate Bone Turnover in an Age-Specific Manner in Catalase Transgenic Female Mice**](https://pubmed.ncbi.nlm.nih.gov/27189961/)**.**

[**Alcohol Consumption, Wnt/Beta-catenin Signaling, and Hepatocarcinogenesis**](https://pubmed.ncbi.nlm.nih.gov/25427908/)**.**

[**p47phox-Nox2-Dependent ROS Signaling Inhibits Early Bone Development in Mice but Protects Against Skeletal Aging**](https://pubmed.ncbi.nlm.nih.gov/25922068/)**.**

[**Alcohol Consumption Promotes Diethylnitrosamine-Induced Hepatocarcinogenesis in Male Mice Through Activation of the Wnt/Beta-catenin Signaling Pathway**](https://pubmed.ncbi.nlm.nih.gov/24778325/)**.**

[**Vitamin D Supplementation Protects Against Bone Loss Associated with Chronic Alcohol Administration in Female Mice**](https://pubmed.ncbi.nlm.nih.gov/22892342/)**.**

[**Expression of Sulfotransferase Isoform 1A1 (SULT1A1) in Breast Cancer Cells Significantly Increases 4-hydroxytamoxifen-Induced Apoptosis**](https://pubmed.ncbi.nlm.nih.gov/21537383/)**.**

[**Identification of a Mammalian Mitochondrial Porphyrin Transporter**](https://pubmed.ncbi.nlm.nih.gov/17006453/)**.**

[**The Stem Cell Marker Bcrp/ABCG2 Enhances Hypoxic Cell Survival Through Interactions with Heme**](https://pubmed.ncbi.nlm.nih.gov/15044468/)**.**

[VIEW FULL BIO – Kelly E. Mercer, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/kelly-mercer)

# Noriko Nakamura, Ph.D.

### **Staff Fellow — Division of Systems Biology**

While animals are currently used to assess male reproductive toxicology, in vitro models have recently been developed as possible alternatives. However, the spermatogenic process of stepwise differentiation from spermatogonia through spermatocytes and spermatids, to mature sperm occurring in seminiferous tubules in testes is complicated, and it has been difficult to find in vitro systems that recapitulate the entire process. Recently, a novel in vitro testis organ culture system has been reported which produced spermatids and fertility-proven sperm from neonatal mouse testes beginning with only primitive spermatogonia. Dr. Nakamura’s research focuses on developing in vitro models to assess drug/chemical toxicity. Her interest is in male reproductive toxicology (prostate and spermatogenesis), and she is currently investigating this novel in vitro testis organ culture system to study factors that affect spermatogenesis.  As there are no in vitro models for assessing the drug/chemical toxicity for the prostate, Dr. Nakamura is evaluating in vitro prostate models using a human prostate cell line and identifying specific biomarker(s) for human prostate diseases. Her experimental approaches employ molecular biology, cellular biology, physiology and histology.

Dr. Nakamura has been working to develop an in vitro testicular toxicity model using microfluidic device system by collaborating with CBER researchers. Her goal will be to develop in vitro models for male reproductive toxicity tests using microfluidic device system to enhance drug safety. [VIEW FULL BIO – Dr. Noriko Nakamura](https://www.fda.gov/about-fda/science-research-nctr/noriko-nakamura)

**Titles and links to selected publications**

[**Gene Expression Profiling of Cultured Mouse Testis Fragments Treated with Ethinylestradiol**](https://pubmed.ncbi.nlm.nih.gov/31588058/)**.**

[**Testicular Function in Cultured Postnatal Mouse Testis Fragments is Similar to that of Animals During the First Wave of Spermatogenesis**](https://pubmed.ncbi.nlm.nih.gov/30703285/)**.**

[**Evaluation of an In Vitro Testis Organ Culture System for Assessing Male Reproductive Toxicity**](https://www.ncbi.nlm.nih.gov/pubmed/30575315)**.**

[**Testicular Function in Cultured Postnatal Mouse Testis Fragments Is Similar to That of Animals During the First Wave of Spermatogenesis**](https://www.ncbi.nlm.nih.gov/pubmed/30703285)**.**

[**Transcript Profiling in the Testes and Prostates of Postnatal Day 30 Sprague-Dawley Rats Exposed Prenatally and Lactationally to 2-Hydroxy-4-Methoxybenzophenone**](https://www.ncbi.nlm.nih.gov/pubmed/30316929)**.**

[**Evaluation of Culture Time and Media in an In Vitro Testis Organ Culture System**](https://www.ncbi.nlm.nih.gov/pubmed/28398669)**.**

[**Effects of Maternal and Lactational Exposure to 2-Hydroxy-4-Methoxybenzone on Development and Reproductive Organs in Male and Female Rat Offspring**](https://www.ncbi.nlm.nih.gov/pubmed/25707689)**.**

[**Early Postnatal Exposure to a Low Dose of Decabromodiphenyl Ether Affects Expression of Androgen and Thyroid Hormone Receptor-Alpha and its Splicing Variants in Mouse Sertoli Cells**](https://www.ncbi.nlm.nih.gov/pubmed/25479311)**.**

[**Correlation Between Human Maternal-Fetal Placental Transfer and Molecular Weight of PCB and Dioxin Congeners/Isomers**](https://www.ncbi.nlm.nih.gov/pubmed/25113211)**.**

[**Disruption of a Spermatogenic Cell-Specific Mouse Enolase 4 (Eno4) Gene Causes Sperm Structural Defects and Male Infertility**](https://www.ncbi.nlm.nih.gov/pubmed/23446454)**.**

[**Postnatal Exposure to Low-Dose Decabromodiphenyl Ether Adversely Affects Mouse Testes by Increasing Thyrosine Phosphorylation Level of Cortactin**](https://www.ncbi.nlm.nih.gov/pubmed/23038006)**.**

[VIEW FULL BIO – Noriko Nakamura, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/noriko-nakamura)

# Li Pang, M.D., M.Sc.

### **Research Biologist — Division of Systems Biology**

Dr. Pang’s research interests have included ion channel remodeling in cardiovascular disease, pharmacogenomics, gene therapy, and biomarker identification.  Her current research goal is to use a wide range of techniques – including cellular and molecular biology, biochemistry, viral gene transduction, patch clamp, microelectrode array, impedance, and high-resolution imaging – to comprehensively characterize potential regulatory applications of human iPSC-CMs to detect cardiotoxicity, including molecular and genetic biomarkers for oncology drug-induced cardiac injury prediction and personalized cardioprotective drug selection. [VIEW FULL BIO – Dr. Li Pang](https://www.fda.gov/about-fda/science-research-nctr/li-pang)

**Titles and links to selected publications**

[**Improving Cardiotoxicity Prediction in Cancer Treatment: Integration of Conventional Circulating Biomarkers and Novel Exploratory Tools**](https://pubmed.ncbi.nlm.nih.gov/33219404/)**.**

[**Repolarization Studies Using Human Stem Cell-Derived Cardiomyocytes: Validation Studies and Best Practice Recommendations**](https://pubmed.ncbi.nlm.nih.gov/32822771/)**.**

[**Effects of Electrical Stimulation on hiPSC-CM Responses to Classic Ion Channel Blockers**](https://pubmed.ncbi.nlm.nih.gov/32040191/)**.**

[**Workshop Report: FDA Workshop on Improving Cardiotoxicity Assessment with Human-Relevant Platforms**](https://pubmed.ncbi.nlm.nih.gov/31600125/)**.**

[**International Multisite Study of Human-Induced Pluripotent Stem Cell-Derived Cardiomyocytes for Drug Proarrhythmic Potential Assessment**](https://pubmed.ncbi.nlm.nih.gov/30257217/)**.**

[**Sex-Related Differences in Drug-Induced QT Prolongation and Torsades de Pointes: A New Model System with Human iPSC-CMs**](https://pubmed.ncbi.nlm.nih.gov/30247688/)**.**

[**Evaluation of Batch Variations in Induced Pluripotent Stem Cell-Derived Human Cardiomyocytes from 2 Major Suppliers**](https://pubmed.ncbi.nlm.nih.gov/28031415/)**.**

[**Comprehensive Translational Assessment of Human Induced Pluripotent Stem Cell Derived Cardiomyocytes for Evaluating Drug-Induced Arrhythmias**](https://pubmed.ncbi.nlm.nih.gov/27701120/)**.**

[**MicroRNA-Mediated Maturation of Human Pluripotent Stem Cell-Derived Cardiomyocytes: Towards a Better Model for Cardiotoxicity**](https://pubmed.ncbi.nlm.nih.gov/27265266/)**?**

[**Reversal of MicroRNA Dysregulation in an Animal Model of Pulmonary Hypertension**](https://pubmed.ncbi.nlm.nih.gov/26815432/)**.**

[**ATP-Binding Cassette Genes Genotype and Expression: A Potential Association with Pancreatic Cancer Development and Chemoresistance**](https://pubmed.ncbi.nlm.nih.gov/24883056/)**?**

[**Angiotensin II Upregulates Ca(V)1.2 Protein Expression in Cultured Arteries via Endothelial H(2)O(2) Production**](https://pubmed.ncbi.nlm.nih.gov/20639649/)**.**

[**High-Conductance, Ca(2+) -Activated K+ Channels: Altered Expression Profiles in Aging and Cardiovascular Disease**](https://pubmed.ncbi.nlm.nih.gov/19828830/)**.**

[**Vascular Smooth Muscle-Specific Knockdown of the Noncardiac Form of the L-type Calcium Channel by MicroRNA-Based Short Hairpin RNA as a Potential Antihypertensive Therapy**](https://pubmed.ncbi.nlm.nih.gov/19244098/)**.**

[**Angiotensin II Causes Endothelial-Dependent Increase in Expression of Ca(V)1.2 Protein in Cultured Arteries**](https://pubmed.ncbi.nlm.nih.gov/18848828/)**.**

[**Characterization of the Cardiac KCNE1 Gene Promoter**](https://pubmed.ncbi.nlm.nih.gov/17141204/)**.**

[**Vascular-Specific Increase in Exon 1B-Encoded CAV1.2 Channels in Spontaneously Hypertensive Rats**](https://pubmed.ncbi.nlm.nih.gov/16876682/)**.**

[**Tissue-Specific Expression of Two Human Ca(v)1.2 Isoforms Under the Control of Distinct 5' Flanking Regulatory Elements**](https://pubmed.ncbi.nlm.nih.gov/12832067/)**.**

[**Effects of Angiotensin-Converting Enzyme Inhibition on the Development of the Atrial Fibrillation Substrate in Dogs with Ventricular Tachypacing-Induced Congestive Heart Failure**](https://pubmed.ncbi.nlm.nih.gov/11714658/)**.**

[**Characterization of a Putative Insulin-Responsive Element and Its Binding Protein(s) in Rat Angiotensinogen Gene Promoter: Regulation by Glucose and Insulin**](https://pubmed.ncbi.nlm.nih.gov/11356707/)**.**

[VIEW FULL BIO – Li Pang, M.D., M.Sc.](https://www.fda.gov/about-fda/science-research-nctr/li-pang)

# Qiang Shi, Ph.D.

### **Visiting Scientist — Division of Systems Biology**

Dr. Shi’s main research focus is mechanisms and biomarkers for DILI. He has more than 15 years of experience in the culture of primary hepatocytes from multiple species with a mechanistic focus on drug-induced mitochondrial damage and metabolism-mediated hepatocyte injury. For biomarker studies, he uses in vitro systems and human clinical samples to explore novel translational DILI biomarkers, focusing on circulating micro-ribonucleic acids (microRNAs) in urine and blood. He has published more than 30 peer reviewed manuscripts on DILI. Dr. Shi’s most recent work involves the study of DILI induced by FDA-approved small-molecule kinase inhibitors and the use of liver-on-a-chip for liver adaptation in response to DILI. Long-term research goals include:

* Developing non-invasive translational biomarkers to predict DILI susceptibility, regeneration, and severity.
* Exploring alternative models, particularly in vitro models, to aid in the prediction of a chemical’s DILI risk.
* Enhancing the understanding of DILI mechanisms.

[VIEW FULL BIO – Dr. Qiang Shi](https://www.fda.gov/about-fda/science-research-nctr/qiang-shi)

**Titles and links to selected publications**

[**Recent Advances in Understanding the Hepatotoxicity Associated with Protein Kinase Inhibitors**](https://pubmed.ncbi.nlm.nih.gov/32050817/)**.**

[**Cytotoxicity of 34 FDA Approved Small-Molecule Kinase Inhibitors in Primary Rat and Human Hepatocytes**](https://www.ncbi.nlm.nih.gov/pubmed/?term=29655783)**.**

[**Drug-Induced Liver Injury in Children: Clinical Observations, Animal Models, and Regulatory Status**](https://www.ncbi.nlm.nih.gov/pubmed/?term=28820004)**.**

[**Effects of 31 FDA Approved Small-Molecule Kinase Inhibitors on Isolated Rat Liver Mitochondria**](https://www.ncbi.nlm.nih.gov/pubmed/?term=28032146)**.**

[**Human Induced Pluripotent Stem Cell-Derived Hepatocyte-Like Cells as a Potential New Tool to Understand Small Molecule Kinase Inhibitors Induced Hepatotoxicity**](https://www.americanpharmaceuticalreview.com/Featured-Articles/337335-Human-Induced-Pluripotent-Stem-Cell-Derived-Hepatocyte-Like-Cells-as-a-Potential-New-Tool-to-Understand-Small-Molecule-Kinase-Inhibitors-Induced-Hepatotoxicity/)**.**

[**The Cytochrome P450 Inhibitor SKF-525A Disrupts Autophagy in Primary Rat Hepatocytes**](https://www.ncbi.nlm.nih.gov/pubmed/26964495)**.**

[**Circulating MicroRNA and Long Noncoding RNA as Biomarkers of Cardiovascular Diseases**](https://www.ncbi.nlm.nih.gov/pubmed/26308238)**.**

[**A Comprehensive Study of the Association Between Drug Hepatotoxicity and Daily Dose, Liver Metabolism, and Lipophilicity using 975 Oral Medications**](https://www.ncbi.nlm.nih.gov/pubmed/26220713)**.**

[**Regorafenib Impairs Mitochondrial Functions, Activates AMP-Activated Protein Kinase, Induces Autophagy, and Causes Rat Hepatocyte Necrosis**](https://www.ncbi.nlm.nih.gov/pubmed/25445804)**.**

[**Drugs and Diseases Interacting with Cigarette Smoking in US Prescription Drug Labelling**](https://www.ncbi.nlm.nih.gov/pubmed/25701380)**.**

[**Inhibition of Cytochrome P450s Enhances (+)-Usnic Acid Cytotoxicity in Primary Cultured Rat Hepatocytes**](https://www.ncbi.nlm.nih.gov/pubmed/23686521)**.**

[**Circulating Extracellular Vesicles as a Potential Source of New Biomarkers of Drug-Induced Liver Injury**](https://www.ncbi.nlm.nih.gov/pubmed/24462978)**.**

[**Green Tea Epigallocatechin Gallate Binds to and Inhibits Respiratory Complexes in Swelling but not Normal Rat Hepatic Mitochondria**](https://www.ncbi.nlm.nih.gov/pubmed/24384371)**.**

[**Hopes and Challenges in Using miRNAs as Translational Biomarkers for Drug-Induced Liver Injury**](https://www.ncbi.nlm.nih.gov/pubmed/23547824)**.**

[**Mechanisms for Epigallocatechin Gallate Induced Inhibition of Drug Metabolizing Enzymes in Rat Liver Microsomes**](https://www.ncbi.nlm.nih.gov/pubmed/23010222)**.**

[**Hepatic Cytochrome P450s Attenuate the Cytotoxicity Induced by Leflunomide and its Active Metabolite A77 1726 in Primary Cultured Rat Hepatocytes**](https://www.ncbi.nlm.nih.gov/pubmed/21546349)**.**

[**Biomarkers for Drug-Induced Liver Injury**](https://www.ncbi.nlm.nih.gov/pubmed/20350268)**.**

[**Gene Expression Profiling in the Developing Rat Brain Exposed to Ketamine**](https://www.ncbi.nlm.nih.gov/pubmed/20080153)**.**

[VIEW FULL BIO – Qiang Shi, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/qiang-shi)

# Svetoslav Slavov, Ph.D.

### **Research Chemist — Division of Systems Biology**

* Molecular Modeling
* QSAR/QSPR
* Drug Design
* Computational Toxicology
* Statistics
* Quantum Mechanics
* Quantum Field Theory

[VIEW FULL BIO – Dr. Svetoslav Slavov](https://www.fda.gov/about-fda/science-research-nctr/svetoslav-slavov)

**Titles and links to selected publications**

[**Quantitative Structure-Toxicity Relationships in Translational Toxicology**](https://www.sciencedirect.com/science/article/pii/S2468202020300322)**.**

[**Computational Identification of Structural Factors Affecting the Mutagenic Potential of Aromatic Amines. Study Design and Experimental Validation**](https://pubmed.ncbi.nlm.nih.gov/29779177/)**.**

[**Determination of Structural Factors Affecting Binding to Mu, Kappa and Delta Opioid Receptors**](https://pubmed.ncbi.nlm.nih.gov/32107589/)**.**

[**Why are Most Phospholipidosis Inducers also hERG Blockers**](https://www.ncbi.nlm.nih.gov/pubmed/28551711)**?**

[**3D-SDAR Modeling of hERG Potassium Channel Affinity: A Case Study in Model Design and Toxicophore Identification**](https://www.ncbi.nlm.nih.gov/pubmed/28129595)**.**

[**Feature Selection from Mass Spectra of Bacteria for Serotyping Salmonella**](https://www.sciencedirect.com/science/article/abs/pii/S0165237016303023)**.**

[**Rigorous 3‐Dimensional Spectral Data Activity Relationship Approach Modeling Strategy for ToxCast Estrogen Receptor Data Classification, Validation, and Feature Extraction**](https://www.ncbi.nlm.nih.gov/pubmed/27509091)**.**

[**Computational Identification of a Phospholipidosis Toxicophore Using 13C and 15N NMR-Distance Based Fingerprints**](https://www.ncbi.nlm.nih.gov/pubmed/25228124)**.**

[**Partial Least Square and K‐Nearest Neighbor Algorithms for Improved 3D Quantitative Spectral Data–Activity Relationship Consensus Modeling of Acute Toxicity**](https://www.ncbi.nlm.nih.gov/pubmed/24464801)**.**

[**Identification of a Metabolic Biomarker Panel in Rats for Prediction of Acute and Idiosyncratic Hepatotoxicity**](https://www.ncbi.nlm.nih.gov/pubmed/25379137)**.**

[**Complementary PLS and KNN Algorithms for Improved 3D-QSDAR Consensus Modeling of AhR Binding**](https://www.ncbi.nlm.nih.gov/pubmed/24257141)**.**

[**13C NMR-Distance Matrix Descriptors: Optimal Abstract 3D Space Granularity for Predicting Estrogen Binding**](https://www.ncbi.nlm.nih.gov/pubmed/22681591)**.**

[**A Computational Study of the Binding of 3-(Arylidene) Anabaseines to Two Major Brain Nicotinic Acetylcholine Receptors and to the Acetylcholine Binding Protein**](https://www.ncbi.nlm.nih.gov/pubmed/20236734)**.**

[**Novel Carboxamides as Potential Mosquito Repellents**](https://www.ncbi.nlm.nih.gov/pubmed/20939392)**.**

[**Quantitative Correlation of Physical and Chemical Properties with Chemical Structure: Utility for Prediction**](https://www.ncbi.nlm.nih.gov/pubmed/20731377)**.**

[VIEW FULL BIO – Svetoslav Slavov, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/svetoslav-slavov)

# Jinchun Sun, Ph.D.

### **Visiting Scientist — Division of Systems Biology**

Dr. Sun’s field of expertise is in mass spectrometry-based metabolomics and lipidomics. She looks to discover novel and more effective biomarkers of diseases at different stages as well as biomarkers of preclinical and clinical safety issues. She studies these topics as part of an FDA-wide biomarkers-development effort. Dr. Sun directs and coordinates highly sophisticated investigations into the development and implementation of new and improved hypotheses in the metabolomics field. She also works with academic and pharmaceutical-research groups to identify biomarkers of toxicity and disease, and to elucidate mechanisms of toxicity or disease progress. Dr. Sun plans, organizes, performs, oversees, and coordinates collaborations with other researchers from different scientific backgrounds.  
  
Dr. Sun applies her research experience in developing novel LC/MS methodologies to discover more effective metabolic and lipidomic biomarkers of diseases or toxicity, thus to improve and protect the public. These studies are diverse ranging from preclinical animal studies to clinical studies involving human subjects. The goals of these projects are: 1) investigating potential biomarkers and mechanism(s) of toxicity and disease (e.g., acute kidney injury and lung cancer) using the cutting-edge LC/MS-based metabolomics technologies to analyze biofluids including urine, serum, and tissue extracts; 2) pharmacokinetics investigation of drug metabolism through urine analysis using metabolomics global profiling approaches; 3) applying LC/MS-based metabolomics in the microbiome field to study the host-microbiome interaction; 4) conducting and harmonizing quality control/quality assurance practice in the metabolomics field fostering collaborative efforts with other federal agencies, academia and pharmaceutical companies; 5) conducting MALDI-MS imaging researches when needed in acquiring the spatial distribution of a drug, neurotransmitters or lipids in liver, lung or brain tissues. [VIEW FULL BIO – Dr. Jinchun Sun](https://www.fda.gov/about-fda/science-research-nctr/jinchun-sun)

**Titles and links to selected publications**

[**Bile Acid Profile and its Changes in Response to Cefoperazone Treatment in MR1 Deficient Mice**](https://www.mdpi.com/2218-1989/10/4/127)**.**

[**Metabolomics Test Materials for Quality Control: Urine Pilot Study**](https://pubmed.ncbi.nlm.nih.gov/31703392/)**.**

[**Evaluation of the Performance of Lipidyzer Platform and its Application in the Lipidomics Analysis in Mouse Heart and Liver**](https://doi.org/10.1021/acs.jproteome.9b00289)**.**

[**Metabolomics Evaluation of the Effects of Smokeless Tobacco on Oral Microorganisms**](http://www.sciencedirect.com/science/article/pii/S0887233316301497)**.**

[**Comprehensive Analysis of Alterations in Lipid and Bile Acid Metabolism by Carbon Tetrachloride Using Integrated Transcriptomics and Metabolomics**](https://www.researchgate.net/publication/271659792_Comprehensive_analysis_of_alterations_in_lipid_and_bile_acid_metabolism_by_carbon_tetrachloride_using_integrated_transcriptomics_and_metabolomics)**.**

[**LC/MS-based Metabolomics Applications in Biomarker Discovery**](http://www.futuremedicine.com/doi/abs/10.4155/fseb2013.14.24)**.**

[**Evaluating Effects of Penicillin Treatment on the Metabolome of Rats**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Evaluating%20Effects%20of%20Penicillin%20Treatment%20on%20the%20Metabolome%20of%20Rats.)**.**

[**Metabolomics as a Tool for Personalizing Medicine: 2012 Update**](http://www.futuremedicine.com/doi/abs/10.2217/pme.13.8)**.**

[VIEW FULL BIO – Jinchun Sun, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/jinchun-sun)

# David A. Thorn, Ph.D.

### **Staff Fellow — Division of Systems Biology**

Dr. Thorn’s research supports the public-health fight against the growing opioid epidemic and the increasingly critical need to understand the brain mechanisms of drug addiction to develop more effective treatments and to facilitate informed regulatory policy.  Prior to joining FDA, Dr. Thorn published extensively on the pre-clinical development of a novel class of pain relievers which lack apparent abuse-related effects. When combined with opioids, these drugs significantly enhanced the therapeutic effects (pain relief) of opioids, while also decreasing some adverse effects (tolerance and dependence), potentially creating a safer opioid pain-treatment option. In addition, his research has identified drugs that may be useful in the treatment of cocaine and methamphetamine addiction. Dr. Thorn is applying in vivo pharmacology methods to advance knowledge on drug addiction, particularly to opioids and psychostimulants.

Another area of Dr. Thorn’s research efforts aim to combine emerging imaging techniques with behavioral pharmacology models to further comprehend the brain mechanisms of opioid addiction. To accomplish this, he is using matrix-assisted laser-desorption ionization imaging mass spectrometry (MALDI IMS) to investigate drug and neurotransmitter distributions in the brains of opioid-treated rats. Once these methods are established, Dr. Thorn will use this procedure for comprehensive rat studies focused on delineating the brain mechanisms underlying the abuse-related effects of opioids and individual differences of subjects in response to repeated opioid administration. [VIEW FULL BIO – Dr. David Thorn](https://www.fda.gov/about-fda/science-research-nctr/david-thorn)

**Titles and links to selected publications**

[**Tolerance and Cross-Tolerance to the Antinociceptive Effects of Oxycodone and the Imidazoline I2 Receptor Agonist Phenyzoline in Adult Male Rats**](https://www.ncbi.nlm.nih.gov/pubmed/28314949)**.**

[**Effects of the Imidazoline I2 Receptor Agonist 2-BFI on the Development of Tolerance and Behavioral/Physical Dependence to Morphine in Rats**](https://www.ncbi.nlm.nih.gov/pubmed/26776953)**.**

[**Agmatine Attenuates the Discriminative Stimulus and Hyperthermic Effects of Methamphetamine in Male Rats**](https://www.ncbi.nlm.nih.gov/pubmed/27232669)**.**

[**Effects of Trace Amine-Associated Receptor 1 Agonists on the Expression, Reconsolidation, and Extinction of Cocaine Reward Memory**](https://www.ncbi.nlm.nih.gov/pubmed/26822713)**.**

[**Antinociceptive Effects of Imidazoline I2 Receptor Ligands in the Formalin Test in Rats**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4842102/)**.**

[**Trace Amine-Associated Receptor Type 1 as a Target for the Development of Treatments for Stimulant Abuse**](https://www.ncbi.nlm.nih.gov/pubmed/27390752)**.**

[**Anti-Hyperalgesic Effects of Imidazoline I2 Receptor Ligands and Their Interactions with Oxycodone in a Rat Model of Inflammatory Pain**](https://www.ncbi.nlm.nih.gov/pubmed/26037946)**.**

[**Anti-Muscarinic Adjunct Therapy Accelerates Functional Human Oligodendrocyte Repair**](https://www.ncbi.nlm.nih.gov/pubmed/25716865)**.**

[**Effect of 1-substitution on Tetrahydroisoquinolines as Selective Antagonists for the Orexin-1 Receptor**](https://www.ncbi.nlm.nih.gov/pubmed/25643283)**.**

[**Behavioral Effects of the Cannabinoid CB1 Receptor Allosteric Modulator ORG27569 in Rats**](https://www.ncbi.nlm.nih.gov/pubmed/25431655)**.**

[**Effects of the Trace Amine Associated Receptor 1 Agonist RO5263397 on Abuse-Related Effects of Cocaine in Rats**](https://www.ncbi.nlm.nih.gov/pubmed/24743376)**.**

[**The Trace Amine Associated Receptor 1 Agonist RO5263397 Attenuates the Induction of Cocaine Behavioral Sensitization in Rats**](https://www.ncbi.nlm.nih.gov/pubmed/24561093)**.**

[**Behavioral Effects of the Imidazoline I2 Receptor Ligand BU99006 in Rats**](https://www.ncbi.nlm.nih.gov/pubmed/24518265)**.**

[**Anti-Hyperalgesic Effects of Imidazoline I2 Receptor Ligands in Rat Models of Inflammatory and Neuropathic Pain**](https://www.ncbi.nlm.nih.gov/pubmed/24329196)**.**

[**The GPR88 Receptor Agonist 2-PCCA Does Not Alter the Behavioral Effects of Methamphetamine in Rats**](https://www.ncbi.nlm.nih.gov/pubmed/23123351)**.**

[**Characterization of the Hypothermic Effects of Imidazoline I2 Receptor Agonists in Rats**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3402816/)**.**

[**Agmatine Attenuates Methamphetamine-Induced Conditioned Place Preference in Rats**](https://www.ncbi.nlm.nih.gov/pubmed/22329899)**.**

[**Effects of Imidazoline I2 Receptor Ligands on Morphine- and Tramadol-Induced Antinociception in Rats**](https://www.ncbi.nlm.nih.gov/pubmed/21970802)**.**

[VIEW FULL BIO – David A. Thorn, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/david-thorn)

# Vikrant Vijay, Ph.D.

### **Staff Fellow — Division of Systems Biology**

The overall goal of Dr. Vijay’s research is to safeguard public health by reducing harm from unsafe agents and to promote personalized medicine by discovering new biomarkers and understanding their role in the causation of drug-induced toxicity. Dr. Vijay is an expert in developing and utilizing diverse computational approaches to integrate, analyze, and interpret toxicological and omics data. For more than a decade, his research has focused on advancing predictive-toxicology and precision-medicine efforts. He made significant contributions to these fields by developing QSAR (Quantitative Structure Activity Relationship) models to predict dermal toxicity of biocides in occupational workers during his doctoral research. He also built a liver toxicity knowledge base to help predict drug-induced liver injury during his postdoctoral research. Dr. Vijay’s ongoing research aims to identify omics biomarkers from in vivo tests that may predict occurrence of adverse effects in response to drugs such as doxorubicin in certain individuals or subpopulations and molecular biomarkers that may predict age- and sex-related susceptibilities to drug toxicities.

Drugs are developed with an aim to treat disorders and significant effort is invested to make them effective and safe. While most patients have favorable outcomes with mild side effects, a minority develop serious or severe drug-induced adverse events. The reason for developing these adverse events in certain individuals can be diverse, and may be attributed to differences in genetics (molecular makeup), the way body interacts with drugs, physiological conditions, nutrition, sex, age, body composition, polypharmacy, environmental conditions, lifestyle habits, etc.

Any one or more of these aforementioned factors can cause different molecular events leading to adverse effects. An investigation of these molecular events has resulted in many predictive and diagnostic biomarkers and has improved our understanding of the toxicity mechanisms for several drugs. Therefore, Dr. Vijay’s current projects focus on using omics data to understand target organ susceptibility and possible age and/or sex differences to doxorubicin and two other classes of drugs, namely, tyrosine kinase inhibitors and drugs that affect mitochondria.

These are important regulatory science projects with major applications in FDA’s efforts to assure safe and effective drugs. [VIEW FULL BIO – Dr. Vikrant Vijay](https://www.fda.gov/about-fda/science-research-nctr/vikrant-vijay)

**Titles and links to selected publications**

[**MicroRNA-34a-5p as a Promising Early Circulating Preclinical Biomarker of Doxorubicin-Induced Chronic Cardiotoxicity**](https://pubmed.ncbi.nlm.nih.gov/35199358/)**.**

[**Doxorubicin-Induced Delayed-Onset Subclinical Cardiotoxicity in Mice**](https://pubmed.ncbi.nlm.nih.gov/34668590/)**.**

[**Progress Towards an OECD Reporting Framework for Transcriptomics and Metabolomics in Regulatory Toxicology**](https://pubmed.ncbi.nlm.nih.gov/34333066/)**.**

[**Gene Expression Profiling in Dorsolateral Prostates of Prepubertal and Adult Sprague-Dawley Rats Dosed with Estradiol Benzoate, Estradiol, and Testosterone**](https://pubmed.ncbi.nlm.nih.gov/32741896/)**.**

[**Hepatic Transcript Profiles of Cytochrome P450 Genes Predict Sex Differences in Drug Metabolism**](https://pubmed.ncbi.nlm.nih.gov/32193355/)**.**

[**Candidate Early Predictive Plasma Protein Markers of Doxorubicin-Induced Chronic Cardiotoxicity in B6C3F1 Mice**](https://pubmed.ncbi.nlm.nih.gov/30517846/)**.**

[**Transcript Profiling in the Testes and Prostates of Postnatal Day 30 Sprague-Dawley Rats Exposed Prenatally and Lactationally to 2-hydroxy-4-Methoxybenzophenone**](https://pubmed.ncbi.nlm.nih.gov/30316929/)**.**

[**In Vitro Modulation of Redox and Metabolism Interplay at the Brain Vascular Endothelium: Genomic and Proteomic Profiles of Sulforaphane Activity**](https://pubmed.ncbi.nlm.nih.gov/30139948/)**.**

[**Sex and Age Differences in the Expression of Liver microRNAs During the Life Span of F344 Rats**](https://www.ncbi.nlm.nih.gov/pubmed/28174625)**.**

[**Stably Expressed Genes Involved in Basic Cellular Functions**](https://www.ncbi.nlm.nih.gov/pubmed/28125669)**.**

[**Sex-Related Differential Susceptibility to Doxorubicin-Induced Cardiotoxicity in B6C3F1 Mice**](https://www.ncbi.nlm.nih.gov/pubmed/27644598)**.**

[**Early Metabolomics Changes in Heart and Plasma During Chronic Doxorubicin Treatment in B6C3F1 Mice**](https://www.ncbi.nlm.nih.gov/pubmed/26934058)**.**

[**Early Transcriptional Changes in Cardiac Mitochondria During Chronic Doxorubicin Exposure and Mitigation by Dexrazoxane in Mice**](https://www.ncbi.nlm.nih.gov/pubmed/26873546)**.**

[**Reproductive Hormone Levels and Differential Mitochondria-Related Oxidative Gene Expression as Potential Mechanisms for Gender Differences in Cardiosensitivity to Doxorubicin in Tumor-Bearing Spontaneously Hypertensive Rats**](https://www.ncbi.nlm.nih.gov/pubmed/26108538)**.**

[**Age and Sex Differences in Kidney MicroRNA Expression During the Life Span of F344 Rats**](https://www.ncbi.nlm.nih.gov/pubmed/25653823)**.**

[**Sexual Dimorphism in the Expression of Mitochondria-Related Genes in Rat Heart at Different Ages**](https://www.ncbi.nlm.nih.gov/pubmed/25615628)**.**

[**Early Biomarkers of Doxorubicin-Induced Heart Injury in a Mouse Model**](https://www.ncbi.nlm.nih.gov/pubmed/25448438)**.**

[**Life Cycle Analysis of Kidney Gene Expression in Male F344 Rats**](https://www.ncbi.nlm.nih.gov/pubmed/24116033)**.**

[**Sex Differences in Kidney Gene Expression During the Life Cycle of F344 Rats**](https://www.ncbi.nlm.nih.gov/pubmed/23902594)**.**

[**FDA-Approved Drug Labeling for the Study of Drug-Induced Liver Injury**](https://www.ncbi.nlm.nih.gov/pubmed/21624500)**.**

[VIEW FULL BIO – Vikrant Vijay, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/vikrant-vijay)

# Li-Rong Yu, Ph.D.

### **Team Leader — Division of Systems Biology**

Dr. Yu’s current research focuses on biomarker development and mechanisms of drug-induced toxicity using cutting-edge proteomics technologies and assays in both nonclinical models and clinical settings. He has developed mass spectrometry-based quantitative proteomics and phosphoproteomics approaches for better understanding of drug-induced liver injury (DILI) and cardiotoxicity in rodent models. His investigation in these areas has resulted in identification of nonclinical proteomic biomarker candidates of DILI or cardiac injury, and discovery of hepatotoxicity and mitochondrial dysfunction promoted by c-Jun N-terminal protein kinase (JNK) mediated phosphorylation of mitochondrial proteins. Translation of preclinical/nonclinical biomarkers to clinical use is a critical step in translational biomarker development. Dr. Yu evaluates and uses high throughput multiplex proteomic assays, including SOMAscan and Olink assays, to identify and verify predictive biomarkers of chemotherapy-induced cardiotoxicity in cancer patients. He has also conducted clinical studies and identified mortality-associated serum biomarkers in dialysis-dependent acute kidney injury (AKI-D) patients. While clinical biomarker development relies on quality clinical samples, pre-analytical variables may affect sample quality, thus confounding biomarker discovery and validation. Using SOMAscan assays, multiplex immunoassays, and mass spectrometry, Dr. Yu has identified potential metabolomic and proteomic biomarkers for quality assessment of human plasma samples processed and stored under variable pre-analytical conditions. Dr. Yu is participating in the Metabolomics Quality Assurance and Quality Control Consortium (mQACC) to provide guidance on best practice and reporting standards of quality control in metabolomics. [VIEW FULL BIO – Dr. Li-Rong Yu](https://www.fda.gov/about-fda/science-research-nctr/li-rong-yu)

**Titles and links to selected publications**

[**Stability of the Human Plasma Proteome to Pre-analytical Variability as Assessed by an Aptamer-Based Approach**](https://pubmed.ncbi.nlm.nih.gov/31442052/)**.**

[**An Integrated Analysis of Metabolites, Peptides, and Inflammation Biomarkers for Assessment of Preanalytical Variability of Human Plasma**](https://pubmed.ncbi.nlm.nih.gov/31074987/)**.**

[**Aptamer-Based Proteomics Identifies Mortality-Associated Serum Biomarkers in Dialysis-Dependent AKI Patients**](https://pubmed.ncbi.nlm.nih.gov/30197987/)**.**

[**Apoptosis of Enterocytes and Nitration of Junctional Complex Proteins Promote Alcohol-Induced Gut Leakiness and Liver Injury**](https://pubmed.ncbi.nlm.nih.gov/29458168/)**.**

[**Immune Response Proteins as Predictive Biomarkers of Doxorubicin-Induced Cardiotoxicity in Breast Cancer Patients**](https://pubmed.ncbi.nlm.nih.gov/29224368/)**.**

[**CHD4 Has Oncogenic Functions in Initiating and Maintaining Epigenetic Suppression of Multiple Tumor Suppressor Genes**](https://pubmed.ncbi.nlm.nih.gov/26934058/)**.**

[**Proteomic Analysis of Acetaminophen-Induced Hepatotoxicity and Identification of Heme Oxygenase 1 as a Potential PPlasma Biomarker of Liver Injury**](https://pubmed.ncbi.nlm.nih.gov/26873546/)**.**

[**Early Metabolomics Changes in Heart and Plasma During Chronic Doxorubicin Treatment in B6C3F1 Mice**](https://www.ncbi.nlm.nih.gov/pubmed/26934058)**.**

[**Proteomic Analysis of Acetaminophen-Induced Hepatotoxicity and Identification of Heme Oxygenase 1 as a Potential Plasma Biomarker of Liver Injury**](https://www.ncbi.nlm.nih.gov/pubmed/27634590)**.**

[**Early Transcriptional Changes in Cardiac Mitochondria During Chronic Doxorubicin Exposure and Mitigation by Dexrazoxane in Mice**](https://www.ncbi.nlm.nih.gov/pubmed/26873546)**.**

[**Critical Role of C-Jun N-Terminal Protein Kinase in Promoting Mitochondrial Dysfunction and Acute Liver Injury**](https://www.ncbi.nlm.nih.gov/pubmed/26491845)**.**

[**Integrated MicroRNA, mRNA, and Protein Expression Profiling Reveals MicroRNA Regulatory Networks in Rat Kidney Treated with a Carcinogenic Dose of Aristolochic Acid**](https://www.ncbi.nlm.nih.gov/pubmed/25952319)**.**

[**Proteomics Quality and Standard: from a Regulatory Perspective**](https://www.ncbi.nlm.nih.gov/pubmed/24316359)**.**

[**Phosphopeptide Enrichment Using Offline Titanium Dioxide Columns for Phosphoproteomics**](https://www.ncbi.nlm.nih.gov/pubmed/23625397)**.**

[**Functional Robustness of a Polycyclic Aromatic Hydrocarbon Metabolic Network Examined in a nidA Aromatic Ring-Hydroxylating Oxygenase Mutant of Mycobacterium Vanbaalenii PYR-1**](https://www.ncbi.nlm.nih.gov/pubmed/22407691)**.**

[**Pharmacoproteomics and Toxicoproteomics: The Field of Dreams**](https://www.ncbi.nlm.nih.gov/pubmed/22015715)**.**

[**Proteomic Analysis of Early Response Lymph Node Proteins in Mice Treated with Titanium Dioxide Nanoparticles**](https://www.ncbi.nlm.nih.gov/pubmed/21884834)**.**

[**Regulation of Microtubule-Based Microtubule Nucleation by Mammalian Polo-Like Kinase 1**](https://www.ncbi.nlm.nih.gov/pubmed/21690413)**.**

[**Distinct Roles of GCN5/PCAF-Mediated H3K9ac and CBP/p300-Mediated H3K18/27ac in Nuclear Receptor Transactivation**](https://www.ncbi.nlm.nih.gov/pubmed/21131905)**.**

[**Oxidant-Induced Apoptosis is Mediated by Oxidation of the Actin-Regulatory Protein Cofilin**](https://www.ncbi.nlm.nih.gov/pubmed/19734890)**.**

[**Quantitative Proteomics for Drug Toxicity**](https://www.ncbi.nlm.nih.gov/pubmed/19351682)**.**

[**Improved Titanium Dioxide Enrichment of Phosphopeptides from HeLa Cells and High Confident Phosphopeptide Identification by Cross-Validation of MS/MS and MS/MS/MS Spectra**](https://www.ncbi.nlm.nih.gov/pubmed/17924679)**.**

[**Phosphoproteomics for the Discovery of Kinases as Cancer Biomarkers and Drug Targets**](https://www.ncbi.nlm.nih.gov/pubmed/21136756)**.**

[**Self-Regulated Plk1 Recruitment to Kinetochores by the Plk1-PBIP1 Interaction is Critical for Proper Chromosome Segregation**](https://www.ncbi.nlm.nih.gov/pubmed/17081991)**.**

[**Regulation of Androgen Receptor Activity by Tyrosine Phosphorylation**](https://www.ncbi.nlm.nih.gov/pubmed/17045208)**.**

[**Global Analysis of the Cortical Neuron Proteome**](https://www.ncbi.nlm.nih.gov/pubmed/15231876)**.**

[**Evaluation of the Acid-Cleavable Isotope-Coded Affinity Tag Reagents: Application to Camptothecin-Treated Cortical Neurons**](https://www.ncbi.nlm.nih.gov/pubmed/15253428)**.**

[VIEW FULL BIO – Li-Rong Yu, Ph.D.](https://www.fda.gov/about-fda/science-research-nctr/li-rong-yu)