FDA Commissioner's Fellowship Program

Class of 2010

FDA Commissioner's Fellowship Program
2010 Fellows

FDA Commissioner's Fellowship Program
2010 Preceptors

FDA Commissioner's Fellowship Program
2010 Preceptors and Fellows by Center

CBER

Preceptor	Fellow
Andrew P. Byrnes	Gina Conenello
Luisa Gregori	Julie Nemecek
Ellen F. Lazarus	Yun-shang Piao
Jakob Reiser	Seraphin Kuate

CDER

Preceptor	Fellow
Darrell R. Abernethy	Pavel Zhichkin
Joga Gobburu	Michael Bewernitz
Rajanikanth Madabushi	Tzu-Yun Chang-McDowell
Akhilesh K. Nagaich	Sudipan Karmakar
Jack A. Ragheb	Kristina Howard
Mate Tolnay	Bazarrgchaa Damdinsuren
Nancy Xu	Zenghui Mi

CDRH

Preceptor	Fellow
Seungil Cho	Yongsoo Choi
Peter L. Goering	Martha Betz
Thomas P. Gross and Danica Marinac-Dabic	Xueying Liang
Markham C. Luke	Maryam Mokhtarzadeh and Suzanne Schwartz
Srinidhi Nagaraja	Shika Gupta
Berkman Sahiner	Omer Demirkaya
Joy Samuels-Reid	Brenda Lawrence

CFSAN

Preceptor	Fellow
Lauren S. Jackson	Elizabeth Grasso
John W. Larkin	Hongliu Ding
Stefano Luccioli	Ernest Kwegyir-Afful
Mary Lou Tortorello	Annemarie Buchholz

FDA Commissioner's Fellowship Program
2010 Preceptors and Fellows by Center, cont…

CVM

Preceptor	Fellow
Jamie L. Boehmer	Zohra Olumee-Shabon
Pak-Sin Chu	Wei Song
Maureen K. Davidson	Maria Cruz-Fisher
Hiranthi Jayasuriya	Kande Amarasinghe
Haile Yancy	Marla Swain

NCTR

Preceptor	Fellow
Zbigniew Binienda	Syed Imam
Tao Chen	Xinrong Chen
Steven L. Foley	Kuppan Gokulan
James C. Fuscoe	Yun Ge
Mark Hart	Haijing Hu
William Salminen	Ali Akhtar
Frederick A. Beland and Igor P. Pogribny	Natalie Simpson

OC

Preceptor	Fellow
John W. Gardner	Xingfang Li
Robert M. Nelson	Jason Gerson and Patricia Bright

ORA

Preceptor	Fellow
William B. Martin	Sarah Pierce
Tiffany Harmon	Soo Kwang Lee
Donna Williams-Hill	Rosalee Hellberg

Regenerative Medicine Project

Preceptor	Fellow
Charles N. Durfor, Elias Mallis, and Mercedes A. Serabian	Alexander Bailey and Rebecca Robinson

FDA Commissioner's Fellowship Program

2010 Fellows

Akhtar Ali, Ph.D.

National Center for Toxicological Research

Preceptor: William Salminen, Ph.D.

Scientific and Professional Background

2007-2010	Visiting Assistant Professor, University of Arkansas: Little Rock
2007-2010	ORISE Fellow, National Center for Toxicological Research
2005-2006	Senior Scientist, NeoPharm, Inc.
2000-2005	Research Instructor, UAMS
1997-2000	Research Scientist, Medical College of Georgia
1995-1997	Postdoctoral Research Associate, Yale University School of Medicine
1993-1995	Postdoctoral Research Associate, University of North Carolina: Chapel Hill
1990-1991	Postdoctoral Fellow, Creighton University School of Medicine
1990	Ph.D. Chemistry, Lucknow University

Research Interests

My academic interests encompass major areas of biochemistry, cell and molecular biology, and toxicology. Research interests include pharmacokinetic and toxicological evaluations of xenobiotics, therapeutic efficacy and toxicity determinations for preclinical assessment of synthetic drugs for osteoporosis and cancer treatments. Lately, my efforts have been focused on health benefits, and side effects of herbal dietary supplements used as weight loss products and alternative products for arthritis. With the abundance of conflicting information available about dietary supplements, it is utmost important to evaluate their complete toxicity profiles and determine safety, efficacy and mechanism of action of these compounds.

Commissioner's Fellowship Project Overview

Assessment of Acetaminophen induced liver injury and influence of dietary supplements: potential synergistic interactions.

Acetaminophen (APAP), also called as Paracetamol (4'-hydroxyacetanilide, *N*-acetyl *p*- aminophenol), is a widely used over-the-counter (OTC) analgesic and antipyretic drug. It is a leading cause of drug-induced liver injury (DILI) in the US. A recent FDA Advisory Committee recommended lowering the daily therapeutic dose of APAP in order to reduce the high number of DILI. It has been hypothesized that exposure to dietary supplements (DS) contributes to the high number of APAP DILI cases since DS cause various pharmacological and toxicological effects that could act synergistically with APAP. The objective of this study is to screen *in vitro* and *in vivo* toxicological affects of APAP alone and in combination with five commonly used DS namely black cohosh, ginkgo biloba, green tea, kava and usnic acid. A number of parameters/pathways will be evaluated to identify the mechanisms of toxicity of APAP and DS alone and in combination of both.

Kand e Amarasinghe, Ph.D.

Center for Veterinary Medicine

Preceptor: Hiranthi Jayasuriya, Ph.D.

Scientific and Professional Background

2010	USPTO Registered Patent Agent
2006-2009	Lead Scientist, General Electric Global Research Center
2002-2006	Scientist, Procter & Gamble Pharmaceuticals
2002	Ph.D. Organic Chemistry, Wayne State University
1994	B.S. Chemistry, University of Peradeniya

Research Interests

I have over seven years of combined research experience experience in pharmaceutical and diagnostic imaging industries. My interests include cardiovascular and diabetes drug discovery and research; discovery & development of diagnostic imaging agents for early diagnosis of diabetes; synthesis of biologically active organic molecules; and medicinal Chemistry and CMC.

Commissioner's Fellowship Project Overview

Development of sensitive and rapid LC/ Q-TOF High resolution mass spectroscopic methods for the detection of veterinary residues of small and large molecular veterinary drugs.

My research project will focus on developing a direct, rapid, and sensitive liquid chromatography/Q-TOF high resolution mass Spectrometry based analytical method for the detection of steroids and large molecular veterinary dug residues in animal and human tissue. Methyltestosterone (MT) is not approved for aquaculture in the U.S.A. Since MT may be metabolized in fish to its glucuronide through Phase II conjugation, a glucuronide may serve as a better marker for monitoring purposes in fish farming. A method will be developed to detect Methyltestosterone glucuronide in fish tissue to monitor MT use.

Methods are also lacking to monitor the metabolism of large molecular veterinary drugs that are mostly peptide based. Modifications to the structures of the large molecular drugs and excipients in formulations could result in improved stability and potency of these drugs. This can result in renewed residue safety concerns we have for them. Lack of high-quality residue data from laboratory studies of large molecular drugs poses a challenge in regulatory decision making. Therefore methods will be developed to obtain proof-of - concept information to address oral bioavailability that will be critical for the development of a guidance for large molecular drugs.

Alexander Bailey, Ph.D.

Center for Devices and Radiological Health and
Center for Biologics Evaluation and Research

Preceptors: Charles Durfor, Ph.D., Elias Mallis, B.S., and
Mercedes A. Serabian, M.S., D.A.B.T

Scientific and Professional Background

2009-2010	Postdoctoral Research Fellow, Fred Hutchinson Cancer Research Center
2008-2009	Postdoctoral Research Fellow, University of Virginia
2004-2008	Ph.D. Biomedical Engineering, University of Virginia
2000-2004	B.S. Mechanical Engineering, Tufts University

Research Interests

My primary research interests are in the areas of adult stem cells and their use in regenerative medicine, as well as the development of multi-scale computational models to understand complex biological phenomena. Primarily, this has focused on identification of rate-limiting steps in the trafficking of therapeutically delivered stem cells to sites of ischemic injury. Other areas of interest include adipose-derived stem cells, micro-vascular remodeling, and prostate cancer metastasis.

Commissioner's Fellowship Project Overview
Evaluation of tumorigenicity risk in cell-based regenerative medicine products: Preclinical review practice, product risk stratification, and enhancement of FDA review

The field of regenerative medicine is rapidly progressing, and many innovative cell-based therapies are being developed for the treatment of serious conditions. However, for these investigational products many of the biological properties that provide for the regeneration of missing, injured, or diseased tissues – self-renewal, plasticity, and high rates of proliferation – also raise concerns of tumor formation following administration. Prior to initiation of a first-in-human clinical trial, these concerns must be addressed through a comprehensive safety assessment. For these products however, the development of a standard and prescribed preclinical program to evaluate tumorigenic potential is difficult. In part, this is due to the variety and complexity of cell-based products, as well as a lack of clear understanding of product characteristics that may be predictive of tumorigenicity. As a result, the design and review of these studies are currently conducted using a case-by-case approach. This multi-center project will evaluate current scientific and regulatory knowledge related to the tumorigenicity of cell-based products, including risk-factors and the preclinical models, endpoints, and study designs that are used in tumorigenicity studies to assess this risk. The project will review data from both scientific literature and regulatory submissions. The review and evaluation of this data will then help inform regulatory decisions related to tumorigenicity risk and the evaluation of tumorigenicity studies within the agency. Project deliverables will help to maximize the safety of new cell-based therapies, ensure regulatory review practices continue to reflect the best available science, and foster innovation by providing a more predictable and transparent regulatory pathway.

Martha Betz, Ph.D.

Center for Devices and Radiological Health

Preceptor: Peter Goering, Ph. D.

Scientific and Professional Background

2009 Ph.D. Bioengineering, University of Maryland
2004 B.S. Chemical Engineering, Tufts University

Research Interests

Previously my research has focused on tissue engineering strategies for the regeneration of craniofacial bone using novel hydrogel scaffolds. Injuries to craniofacial bone are of interest because the body lacks an appropriate response for regeneration typically forming scar tissue rather than load-bearing bone. Engineered degradable hydrogels can have a significant impact on cell populations, specifically having profound effects on expression and transport of endogenous signaling molecules, proliferation, migration, and differentiation. I investigated their use in promoting differentiation of mesenchymal stem cells through increased osteogenic signaling and demonstrated enhanced bone regeneration in orbital floor defects.

Commissioner's Fellowship Project Overview

In vitro and in vivo toxicity of nanomaterials associated with FDA-regulated products

While nanotechnology has made great progress in recent years demonstrating development of new products, there is a relative lack of information relating to the safety of nanomaterials. The purpose of my fellowship project is to investigate properties of nanomaterials to elucidate what role they may play in adverse health effects. Currently, the FDA does not follow the standard definition of nanotechnology as materials with at least one dimension of 1-100 nanometers, and instead recognizes that larger (> 100 nm) particles may possess unique properties similar to nano-sized materials. Therefore, my research project involves investigating the toxicological effects of nano to sub-micron particles with specific emphasis on neuronal cell toxicity, systemic distribution profiles, and ability to cross the placental barrier. The knowledge gained in this project will assist FDA review scientists in assessing the safety of medical products which incorporate engineered nanomaterials or generate particulate wear debris. The project will also contribute to the development of consensus standards and guidance documents by identifying the most critical physicochemical properties and relevant test methods for assessing the safety and efficacy of nanomaterials used in FDA-regulated products.

Michael Bewernitz, Ph.D.

Center for Drug Evaluation and Research

Preceptor: Joga Gobburu, Ph.D.

Scientific and Professional Background

2008-2010 Post-Doctoral Associate, University of Florida
2008 Ph.D. Engineering, University of Florida
2007 M.S. Engineering, University of Florida
2002 B.S. Chemical Engineering, Michigan State University

Research Interests

My current research interests are modeling of drug activity, disease progression, clinical trials or combinations thereof to help design better clinical trials and optimize dosing. My doctoral research focused on characterizing the electroencephalogram profile changes induced by vagus nerve stimulation therapy in patients with epilepsy. My post-doctoral research focused on analyzing the effects of a vigilance-promoting drug on electroencephalogram recordings in sleep-deprived healthy volunteers using pharmacokinetic/ pharmacodynamic modeling. I hope to build on my interests and gain experience while conducting pharmacometric analyses at the FDA.

Commissioner's Fellowship Project Overview

Pharmacometric Analysis of Clinical Data

My fellowship project focuses on the application of statistical modeling and simulation techniques to analyze clinical data in order to assess drug safety and efficacy profiles. Examples include population pharmacokinetic/pharmacodynamic modeling and simulation, thorough QT prolongation analysis, and exposure-response analysis of available clinical data. The specific aim is to utilize pharmacometric analysis methods on clinical data in order to further our understanding of this strategy for enhancing the regulatory decision making process.

Patricia Bright, Ph.D.

Office of the Commissioner

Preceptor: Robert "Skip" Nelson, M.D., Ph.D.

Scientific and Professional Background

2006 Faculty, Johns Hopkins University, School of Medicine
2003 Research Associate, Johns Hopkins University, School of Medicine
2003 Ph.D. Epidemiology, University of North Carolina, School of Public Health
2000 B.S.N. Nurse (RN), University of Maryland, School of Nursing
1993 M.S.P.H. Epidemiology, University of North Carolina, School of Public Health
1986 B.A. Biology, Mount Holyoke College

Research Interests

I am interested in ethical issues that arise during clinical trials, particularly those involving infants, children, and pregnant women, and especially in intercultural and international settings. My recent work involved collaborating in Africa with Ugandan and U.S. investigators to organize, train, supervise, and report adverse events in clinical trials assessing prevention strategies to reduce maternal-to-child HIV transmission. My work included oversight of the first pediatric HIV vaccine trial in Africa. For my prior doctoral work, I had carried out a longitudinal study in a culturally and economically diverse population of American women (including adolescents). This observational study investigated possible side effects of medications on women's health.

Commissioner's Fellowship Project Overview
Implementing Pediatric Research Ethics in Resource Limited Settings

Historically, research studies evaluating medication safety and efficacy did not enroll children. However, many experts now recognize the importance of the data that pediatric clinical research can generate concerning the safety and effectiveness of FDA-regulated products in children -- when tempered by a careful assessment of ethical considerations. There are a multitude of ethical challenges, however, when implementing such clinical trials. Often implementers have to make difficult judgments and weigh complex trade-offs. In resource limited settings, expertise to support such decision making may be constrained and the clinical trials may pose additional ethical complexities. We will explore risk to pediatric participants in foreign clinical studies. We will also examine the role of the research study clinician in the context of inadequate local capacity/health care infrastructure and will focus on the ethics of ancillary care obligations. Our analysis will be disseminated so as to serve as a resource for those designing, implementing and overseeing pediatric research in resource limited settings.

Annemarie Buchholz, Ph.D.

Center for Food Safety and Applied Nutrition
Summit-Argo, IL

Preceptor: Mary Lou Tortorello, Ph.D.

Scientific and Professional Background

2010 Ph.D. Food Science, Michigan State University
2007 Laboratory Technician, Eastern Regional Research Center
2006 B.S. Biotechnology and Microbiology, Rutgers: the State University of New Jersey

Research Interests

My current research interests are in the area of microbial food safety, specifically focusing on the detection, transfer and survival of foodborne pathogens. Past projects have included: comparing the efficacy of peroxy-acetic acid and chlorine treatment for the reduction of *Salmonella* on alfalfa seed, evaluating the effect of Simulated Gastric Fluid and Bile Salts on the growth of *Listeria monocytogenes* when grown on frankfurters and Ready-to-Eat turkey, improving the technique and typing strains of *Staphylococcus aureus* by pulsed-field gel electrophoresis (PFGE), studying the efficacy of commercial sanitizers during leafy green processing, typing *Listeria monocytogenes* by PFGE and serotyping, and isolating, identifying and determining the thermal resistance of gas-producing microorganisms in maraschino cherries. My doctoral work focused on the transfer of *Escherichia coli* O157:H7 to leafy greens during simulated commercial processing.

Commissioner's Fellowship Project Overview
Indicator Methods to Evaluate Process Controls for Fresh Produce

Fresh produce has been recognized as an important vehicle of foodborne illness in recent years, and new approaches are needed to ensure safety. Microbiological monitoring of the pre- or post-harvest waters may be a useful component of risk reduction strategies, but more data are needed to verify its effectiveness. The microbiological quality of water is currently evaluated for fecal contamination through the use of bacterial indicators (fecal coliforms, total coliforms, generic *Escherichia coli* etc.) and bacteriophage (somatic coliphage). Incorporating microbiological monitoring into food safety programs requires much time, labor, and expense. Methods for microbial indicators may be used, but can be lengthy and difficult to conduct, and their correlation to the presence of pathogens is not always upheld. New automated, quantitative methods for indicator testing, have the potential to decrease labor and time of analysis and improve process control. An evaluation of how these methods hold up under conditions that affect the quality and characteristics of irrigation and produce processing water, specifically high organic content, background microflora and sanitizers, is necessary. The objective of this study is to evaluate quantitative microbial water quality indicator methods, for example, the bioMerieux TEMPO automated MPN procedure and the standard EPA MPN procedure, for enumerating total aerobic bacteria, generic *E. coli*, *Enterobacteriaceae* and coliphage in produce irrigation and processing waters for assessing washing and sanitization process controls for fresh produce.

Xinrong Chen, Ph.D.

National Center for Toxicological Research

Preceptor: Tao Chen, Ph.D., D.A.B.T.

Scientific and Professional Background

2009-2010	Instructor, University of Arkansas for Medical Sciences
2006-2009	Associate Research Assistant, Oklahoma Medical Research Foundation
2006	Ph.D. Toxicology, Oklahoma State University

Research Interests

My doctoral research focused on the transcriptional regulation of a Phase II Drug metabolism enzyme associated with xenobiotic detoxification. During my postdoctoral work, I studied the hematopoietic stem cell differentiation and lineage instability under pathological conditions such as virus infection. For the past 1.5 years, I have been investigating the important function of B and T lymphocytes involved in estrogen deficiency and inflammation induced bone loss (osteoporosis) by using conditional knock-out and immune-deficient mouse models.

Commissioner's Fellowship Project Overview
MicroRNA-34a Mediate Mutagenesis in a P53 dependent way

MicroRNAs (miRNAs) are small non-coding regulatory RNA molecules that regulate gene expression at the post-transcriptional level. miR-34a is a tumor suppressor miRNA whose expression is regulated by the tumor suppressor gene *P*53. The *P*53 gene responds to DNA damage, mutation induction and tumor formation. TK6, WTK1, and NH32 are human lymphoblast cell lines derived from a same progenitor with different *P*53 status: TK6 with the wild-type *P*53 genes, NH32 with null *P*53 alleles, and WTK1 with mutant form of *P*53. Previous studies showed that the spontaneous and mutagen-induced mutant frequencies in TK6 and NH32 cells were similar while they were significantly lower than those in WTK1 cells. It is unclear why NH32 and WTK1 cell lines, both of which have lost the function of *P53*, have such a big difference in their response to mutation induction. To elucidate the possible mechanisms involved in the differential mutagenic responses among the three cell lines, we hypothesize that the *P*53-regulated miR-34a is responsible for the higher mutant frequency in WTK1 cells and will examine this hypothesis by conducting following studies. First, we will measure the expression levels of miR-34a in TK6, WTK1 and NH32 cells. If the expression of miR-34a in the three cell lines correlates well with the mutant frequency in the respective cell line, we will challenge the cells using genotoxins and check whether the genotoxic stress will result in any changes in miR-34a expression. Second, by transfecting either miR-34a inhibitors or miR-34a precursors into the different cells, we will manipulate expression of miR-34a in the cells to determine the role of miR-34a in suppressing mutation induction. Finally, to define the cellular pathway involved in the function of miR-34a, we will apply computational analysis to search possible target genes regulated by miR-34a and confirm these target genes experimentally. Once the functions of miR-34a is confirmed to be closely related to mutation induction, this molecular will have great potential to be used as a biomarker to assess genotoxicity of chemicals and other agents.

Yong Soo Choi, Ph.D.

Center for Radiological Health and Research

Preceptor: Seungil Cho, Ph.D.

Scientific and Professional Background

2006-2010 Postdoctoral Fellow, University of Illinois at Chicago
2006 Ph.D. Chemistry, University of Illinois at Chicago

Research Interests

My postdoctoral research have focused on the development of new chemoprevention agents present in natural products such as deep ocean bacteria extracts and botanical extracts. Specifically, a screening assay targeting to estrogen receptors, cyclooxygenases, Keap1-Nrf, and quinone reductase-2 was developed based on mass spectrometry to find active compounds in these natural products. After finding potent candidate compounds, bio-efficacy of the compounds in rat tissues, including liver, serum, fat and mammary gland was also investigated using a LC-MS-MS method. I enjoyed the drug discovery and development programs that I have been involved with and was able to acquire very diverse skills and experience including separation of natural products, biological sample preparation, protein immobilization, and LC-MS-MS.

Commissioner's Fellowship Project Overview

Analysis of BPA released from polycarbonate- and polysulfone- based medical devices using liquid chromatography-mass spectrometry

While Bisphenol A (BPA) is widely used to produce polycarbonate and polysulfone plastics, many studies have showed negative health effect of BPA at low dose exposure, including, breast and prostate cancer, obesity, neurobehavioral problems, and reproductive abnormalities. Especially, medical devices, such as hemodialyzers or oxygenators can influence critical health impacts to patients because BPA released from these devices has direct contact with the blood stream during extracorporeal circulation. In this research project, a high throughput LC-MS method will be developed to establish reliable database for the BPA leachable from various medical devices.

Gina Conenello, Ph.D.

Center for Biologics Evaluation and Research

Preceptor: Andrew Byrnes , Ph.D.

Scientific and Professional Background

2009-2010	Postdoctoral research fellow, Mount Sinai School of Medicine
2005-2009	Ph.D. Biomedical Science, Mount Sinai School of Medicine
2003-2005	Post-baccalaureate fellow, New York State Department of Health
1999-2003	B.S. Biochemistry and Cell Biology, Bucknell University

Research Interests

My research interests lie in the fields of virology and infectious diseases. I pursued this interest as a field of study directly out of college with the NYS Dept. of Health Emerging Infectious Disease Fellowship. There I got my first chance to work with the FDA by participating in the Retail Food Study, which sampled retail meat products for antibiotic-resistant bacterial pathogens. It was also at the NYS Dept. of Health that I developed and interest and expertise in RNA viruses, particularly influenza. During my fellowship I conducted research on avian influenza and the SARS virus. Enjoying the complexity of the relatively small RNA viruses I moved on to graduate school to study under Dr. Peter Palese. The Palese laboratory has a long history of excellence in the influenza research field, from which I benefitted greatly. My graduate and post-doctoral work focused on the PB1-F2 protein, a newly discovered virulence factor of influenza A virus. My interests continue to be in influenza virus, but I am eager to branch out into other viral respiratory pathogens. My current Commissioner's Fellowship research will focus on adenovirus, and its use as a gene therapy vector.

Commissioner's Fellowship Project Overview
Improving adenovirus gene therapy vectors for systemic use

There are currently over 80 clinical trials using adenovirus vectors for gene therapy. Most clinical trials administer virus locally, with only a handful delivering virus intravenously (i.v.) because of safety and effectiveness concerns. Adenovirus targets the liver when administered i.v. but much of the virus is eliminated by cells in the liver. Many more diseases could be treated if we could improve the safety and targetability of adenovirus vectors. This work will study how adenovirus liver targeting is accomplished and what factors can be used to retarget the virus. Adenovirus has a high-affinity binding site for coagulation factor X (FX), and this is thought to be important for virus targeting to the liver. This project aims to determine the domains of the FX protein that are essential for liver targeting. We will mutate FX and determine how FX interacts with adenovirus, the complement system, and the liver. We will also develop novel assays to evaluate the coat of plasma proteins (opsonins) that immediately attaches to adenovirus after i.v. injection. The results of these experiments will allow us to devise new strategies to de-target adenovirus vectors from the liver and retarget them to other tissues.

Maria Cruz-Fisher, Ph.D.

Center for Veterinary Medicine

Preceptor: Maureen K. Davidson, Ph.D.

Scientific and Professional Background

2007-2010	Postdoctoral Scholar, University of California
2006	Ph.D. Microbiology and Molecular Genetics, Rutgers University
2000	B.S. Industrial Microbiology, University of Puerto Rico

Research Interests

I have long been interested in both the theoretical and applied aspects of microbiology. The physical world we experience appears very different at the microbial level. This is especially true of parasitic and/or pathogenic organisms, who must continuously overcome host defenses for survival. Pharmacology provides compounds for microbial control. However, lateral and horizontal gene transfer endows these microbes an ever-evolving array of biochemical tools for inactivating these compounds. Although antibiotic resistance had been largely studied on zoonotic pathogens, my main goal as a FDA Commissioner's Fellow is to study the mechanisms of resistance, and understand their evolutionary gene transfer among veterinary pathogens.

Commissioner's Fellowship Project Overview
Antibiotic Resistance of Campylobacter spp. from animals

Contamination of food with *Campylobacter* spp. is one of the leading causes of food-borne infections in humans in the United States, with about 1.4 million clinical cases per year. In the last couple of decades, there has been an increase of reported antibiotic resistance (AR) among *Campylobacter* spp., especially to macrolides and fluoroquinolones, from human clinical cases and livestock. This has raised concerns because some of these antibiotics also are used to treat human infections. Most of the information about the dissemination of *Campylobacter* spp. and the mechanisms of AR comes from studies of *C. jejuni* and *C. coli*, but little is known about these parameters in animal hosts or in other *Campylobacter* spp. The Center for Veterinary Medicine/Office of Research/Division of Animal and Food Microbiology (CVM/OR/DAFM) has recently acquired a large collection of isolates of *Campylobacter* spp. which span the last 50 years. This collection includes isolates from the time period before antibiotics were commonly used for treatment or growth promotion in food production animals. In our study, we are interested in investigating the prevalence and temporal appearance of AR in *Campylobacte*r spp. to antibiotics commonly used in the food production animals and the related antimicrobial agents used in treatment of human infections. Our specific objectives are to identify the species and subspecies of each isolate and to perform *in vitro* antimicrobial susceptibility testing against a panel of antibiotics that are used in animals Once antibiotic resistant isolates are identified, we will use molecular techniques to identify the genes responsible for AR and to determine relatedness of the isolates with the goal of determining whether there is an evolutionary pattern of acquisition of antibiotic resistance that correlates with the introduction, or common use, of each antibiotic in animals.

Bazarragchaa Damdinsuren, M.D., Ph.D.

Center for Drug Evaluation and Research

Preceptor: Mate Tolnay, Ph.D.

Scientific and Professional Background

2006-2010	Postdoctoral fellow, National Institute on Aging
2005-2006	JSPS Postdoctoral fellow, Osaka University, Japan
2005	Ph.D. Osaka University, Japan
1999-2000	Residency of surgery, National Cancer Center, Mongolia
1999	M.D. National Medical University, Mongolia

Research Interests

I have a combination of training as a Medical doctor and of research in the fields of normal and cancer cell biology, immunology and experimental oncology. My recent research aimed to understand how antigen recognition changes B cell physiology; including aspects of signal transduction and gene regulation (including role of NF-κB transcription factors), which affected B cell survival, differentiation, and interaction with other immune cells. My graduate work focused on liver cancer biology and effectiveness of immune- and chemo-therapy for this type of cancer. In the future, I am interested in working in areas of immune cell biology, oncology or tumor immunology. Also in a broader range, I have a longstanding interest in improving the human health by addressing efficacy and safety of therapeutic agents.

Commissioner's Fellowship Project Overview

The signaling and function of Fc-receptor like 5 protein in B lymphocytes.

Many co-receptors on immune cells deliver competing activating and inhibitory signals that are integrated to balance cellular responses to antigens. The Fc receptor-like (FCRL) family of co-receptors has been proposed to modulate antigen receptor signaling of B lymphocytes. The aim of my project is to study the function of FCRL5 in relation with its signaling in human B lymphocytes. The project's specific topics are: (1) study the signaling properties of FCRL5 in interaction with the antigen receptor and other co-receptors, in particular CD22, (2) study the roles of FCRL5 in B cell activation and cell fate determination. It is hoped that these studies will expand our understanding of FCRL5 biology. In addition, our studies could contribute to establishing FCRL5 as a potential disease marker as well as a therapeutic target in B cell malignancies.

Omer Demirkaya, Ph.D.

Center for Devices and Radiological Health

Preceptor: Berkman Sahiner, Ph.D.

Scientific and Professional Background

2009	American Board of Science in Nuclear Medicine certified—Molecular Imaging Sciences
1997-1998	Research Fellow, Physiological Imaging Research Lab, Mayo Clinic Foundation
1992-1996	Research Assistant, The Ohio State University/Cleveland Clinic Foundation
1992-1997	PhD Biomedical Engineering, The Ohio State University
1990-1992	MS Biomedical Engineering, The Ohio State University
1982-1987	BS Electrical Engineering, Middle East Technical University

Research Interests

As an imaging scientist, I have developed novel, quantitative and robust image processing and analysis methods to improve image quality and to extract accurate quantitative information from images acquired by in vitro or in vivo molecular imaging techniques. My research interests in molecular imaging with Positron Emission Tomography (PET) focus on improving image quality and extracting quantitative information (i.e., segmentation and quantification of tumor lesions in the PET/CT whole body images). I believe quality control (QC) in diagnostic imaging is an essential part of a quality assurance (QA) program for the assurance of image quality and radiation safety. To this end, I have developed image-processing tools that calculate the performance parameters of scintillation cameras from the data acquired according to the NEMA standards. We have been working on an application for trending daily QC uniformity images that is vendor-independent and provides automated and centralized processing, and paperless record keeping. This application can be adapted to remotely trend gamma cameras.

Commissioner's Fellowship Project Overview

An observer performance study with two CAD systems having the same standalone performance: Can readers' aided performances with the two systems differ?

Computer-aided detection (CAD) systems have been finding wider application in radiology in aiding radiologists in detection or diagnosis tasks. Conventionally, the contribution of a CAD system to reader performance is assessed using reader studies. There has been an increasing interest in developing sequestered data sets for training and testing CAD systems. It has been suggested that the use of sequestered datasets may obviate the need for reader studies for new devices: If a new device is tested on the same sequestered dataset as a predicate device, then a comparison of standalone performances of the two systems may suffice to demonstrate substantial equivalence. It is currently unknown whether differences between the new and predicate devices in the detection of difficult lesions and problematic false-positives should also be taken into account. The primary aim of this study is to test the hypothesis that *two CAD systems with similar standalone performances may yield significantly different observer performances with CAD*. For this purpose, we will first simulate two CAD systems with similar sensitivities and false-positive rates but different characteristics, using observer data generated from a previous study that investigated the effect of a CAD system on radiologists' performances in detecting lung nodules in thoracic CT scans. Then, we will perform a multi-reader multi-case observer study to compare the performances of the readers using the two CAD systems as a second-reader. We envisage that the readers' performances with CAD may be different despite the similarity in the standalone performances. We also expect to draw some valuable inferences as to the use of a common database to compare the performances of similar CAD systems.

Hongliu Ding, M.D., Ph.D.

Center for Food Safety and Applied Nutrition
Summit-Argo, IL

Preceptor: John Larkin, Ph.D.

Scientific and Professional Background

2008	Ph.D. Clinical & Population Health Research, U. of Massachusetts Medical School
2002	M.P.H. Epidemiology, University of Massachusetts
1998-2005	Postdoctoral Research Associate, U. of Massachusetts Medical School
1991	M.S. Pharmacology, Shanghai Second Medical University
1985-1988	Resident, Tianchang City Hospital
1985	M.D. Medicine, Anhui Medical University

Research Interests

I am a physician and medical researcher with a systematic training in basic and clinical sciences as well as expertise in epidemiology and public health research. As an epidemiologist at Brigham and Women's Hospital, Harvard Medical School, I have been conducting clinical research in investigating genetic and environmental risk factors and identifying biomarkers/predictors of disease risk, progression, prognosis, and treatment efficacy for aging associated diseases in patients. I am interested in exploring food and drug safety related research and health policy issues at FDA. Using a biostatistical approach, I will conduct quantitative risk analyses and build assessment models for risk predication and reduction based on data from laboratory experiments and epidemiological studies and reports.

Commissioner's Fellowship Project Overview
Evaluation of risk management options to reduce microbial hazards in sprouts through quantitative risk assessment

Microbial hazards that occur in any step within the food supply chain can lead to propagation of the contamination and cause widespread foodborne illnesses. Sprouted seeds pose a particular concern as the same conditions that encourage germination and growth of seeds also encourage the growth of bacterial pathogens. To provide the sprout industry with a science-based approach for the selection of optimal risk management programs to ensure food safety, this research will develop quantitative risk assessment models that can be used to evaluate different risk management options and to devise optimized sprout supply chain food safety programs. A series of models will be developed for assessing the risk associated with microbial contamination in sprouts and the extent of risk reduction that can be achieved through applications of a combination of mitigation steps and microbial sampling and testing programs. These models will be used to prioritize risk intervention strategies that can be applied at each stage of sprout production.

Yun Ge, M.D., Ph.D.

National Center for Toxicological Research

Preceptor: James Fuscoe, Ph.D.

Scientific and Professional Background

2004 B.S. University of Arkansas at Little Rock
2003 Ph.D. University of Arkansas for Medical Science
1999 M.S. University of Arkansas for Medical Science
1991 M.D. Beijing Medical University

Research Interests

I earned a Ph.D. in pharmacology, a master degree in pharmaceutical science from University of Arkansas for Medical Science, and a bachelor degree in computer science from University of Arkansas. I also obtained medicine degree from Beijing Medical University, China. Offering an exceptional educational background, over 5 years of post-PhD pharmacology/toxicology, statistics, bioinformatics (including SAS programming), and gene transcriptional research experience, I have achieved a strong record of performance in research planning, goal/objective development, and bolstering research support through networking.

Commissioner's Fellowship Project Overview
Sex and age related transcriptional networks for genes coding for hepatic phase I and II metabolism enzymes in rats

Sex- and age-dependent drug toxicities have been recognized by regulatory agencies and, in some cases, have been shown to be related to sex- and age-dependent expression of drug metabolizing enzymes (DMEs). Although sex- and age-dependent transcription of genes encoding DMEs may underlie these toxicities, the mechanism(s) are not completely understood. Functional genomics approaches in toxicological research have provided new and innovative strategies to address sex- and age-linked drug safety concerns. In this study, we will use computational bioinformatics approaches to characterize hepatic transcriptional regulation networks for DME genes based on PCR validated gene expression signatures in male and female rats aged 2, 5, 6, 8, 15, 21, 52, 78, and 104 weeks. Computational analysis of the promoter composition of drug metabolism genes will be used to deduce the regulatory transcriptional networks that mediate sex- and age-related differences for these DMEs. A detailed characterization of transcriptional regulatory networks responsible for the expression of hepatic phase I and II metabolism enzymes will provide a foundation for supporting drug safety assessment, guiding the selection of sex- and age-appropriate pharmacotherapy, and improving FDA regulatory science.

Jason Gerson, Ph.D.

Office of the Commissioner

Preceptor: Robert "Skip" Nelson, M.D., Ph.D.

Scientific and Professional Background

2009 Ph.D. Johns Hopkins Bloomberg School of Public Health
1996 A.B. Brown University

Research Interests

Two interests have led me to the FDA Commissioner's Fellowship program. The first is an interest in evaluating the quality and strength of evidence for regulatory action and policy-making. I am particularly interested in questions concerning how to incorporate evidence of biological mechanism in the evaluation of emerging therapies, or established therapies for which the empirical evidence is weak. For example, in pediatric research, therapeutic efficacy may depend on a trial being conducted at an early age when patients can derive maximum benefit from the therapy, before disease progression reduces chances for preserving quality of life. How should our interpretations of risk–benefit analyses be affected by evidence of age-related mechanisms? My second interest is in the ethical issues arising from pediatric participation in clinical trials, particularly for treatment of pediatric obesity. Obesity interventions include a mix of lifestyle, pharmacological and surgical interventions with varying degrees of safety and evidentiary support, particularly in pediatric populations. I am especially interested in comparative regulatory approaches to obesity, in understanding how the FDA and its international partners regulate in the context of both scientific uncertainty and different prevailing cultural norms.

Commissioner's Fellowship Project Overview
Linking Regulatory Science and Ethics in Pediatric Product Development

The critical need for pediatric research on drugs, devices, and biological products underscores the responsibility to assure that children are enrolled in clinical research that is both scientifically necessary and ethically sound. The overall aim of this project is to produce a concept paper concerning ethical issues in pediatric product development. In developing this concept paper, we will review a wide range of ethical considerations concerning the participation of children in clinical research, including: the moral status of children as a vulnerable population; the appropriate balance of risk and potential benefit in pediatric research; and ethical considerations underlying study design, including the choice of control group and clinical equipoise. The concept paper will propose a basic ethical framework to guide pediatric research, and suggest how this framework might be operationalized in linking regulatory science and ethics, an effort critical to the FDA's mission.

Kuppan Gokulan, Ph.D.

National Center for Toxicological Research

Preceptor: Steven L Foley, Ph.D.

Scientific and Professional Background

2000-2010	Senior Research Scientist, Texas A&M University
1998-2000	Postdoctoral Research Associate, Texas A&M University
1996-1977	Postdoctoral Fellow, University of Saskatchewan
1990-1995	Ph.D. Immunology & Biochemistry, All India Institute of Medical Sciences

Research Interests

My long term career goal is to identify alternative drug targets for multi-drug resistant and persistent bacterial pathogens by employing a structural and computational biological approach. I have a unique combination of research experience in Immunology (development of synthetic vaccine against HIV), Molecular Biology (cloning and site directed mutagenesis of virulent genes), Protein Chemistry (purification of enzymes, refolding and thermal shift assay), and Structural and Computational Biology. My current research is focused on utilizing X-ray crystallography techniques to solve the crystal structures of enzymes that are involved in fatty acid and amino acid metabolisms, and to identify its role in the persistence of *Mycobacterium tuberculosis.* I am also interested in high throughput screening and identifying small molecules that could potentially act as antibacterial agents.

Commissioner's Fellowship Project Overview

Structural and Functional Characterization of (VirB4, VirB11 and VirD4) Putative ATPases of type-IV Secretion System of Salmonella enterica Serovar Heidelberg

Salmonella enterica is one of the most common causes of foodborne infections in the United States. Antimicrobial resistance among these bacterial pathogens continues to be a major public health concern. An increasing number of reports of infections with multi-drug resistant strains of *S. enterica* over the last few decades have limited our capability to treat infections. Specifically, *S. enterica* serovar Heidelberg isolates from humans and poultry are often resistant to cephalosporins and other antimicrobial agents, which are important for the treatment of severe cases of salmonellosis. Recent studies have shown that *S. enterica* serovar Heidelberg isolates contains transmissible plasmids that contain genes important for virulence, colonization, persistence and drug resistance. The DNA sequence analysis of one set of these plasmids from *S. enterica* serovar Heidelberg strains in our laboratory revealed the presence of genes that encode type-IV secretion system (T4SS). Other bacterial species employ T4SS to inject toxins into the host cells. My research will focus on characterization of T4SS-containing plasmids from multi-drug resistant *S. enterica* serovar Heidelberg isolates to determine the potential role of the T4SS in colonization, invasion and the transfer plasmids containing antimicrobial resistance and/or virulence genes. A further understanding of the involvement of plasmid-encoded genes in antimicrobial resistance, colonization, invasion, and formation of the secretary apparatus will provide an improved understanding of resistance and molecular mechanism of virulence-associated secretion by the T4SS. My projects goals are two-fold; 1) to understand the involvement of T4SS encoding plasmids on the virulence of *S. enterica* serovar Heidelberg strains, 2) to resolve the structure of the putative ATPases of type-IV secretary system, which are the proteins that likely turn on/off the ability of the T4SS to secrete molecules from the bacteria to host or other bacterial cells. The outcome of the study will address several unresolved questions of bacterial pathogenesis and the identification of the putative ATPase structure will help to identify potential novel structure based drug/inhibitor targets against pathogenic bacteria.

Elizabeth Grasso, Ph.D.

Center for Food Safety and Applied Nutrition
Summit-Argo, IL

Preceptor: Lauren Jackson, Ph.D.

Scientific and Professional Background

2007-2010	Ph.D. Food Science and Technology, The Ohio State University
2005-2007	M.S. Food Science and Nutrition, The Ohio State University
2001-2005	B.S. Food Science, Pennsylvania State University

Research Interests

My research background has focused on food safety and food microbiology. During my M.S. I worked with attenuated total reflectance infrared spectroscopy as a rapid detection technique for the differentiation of endospore-forming bacteria. For my doctoral training in emerging food safety issues I studied three nonthermal intervention strategies; high pressure processing, electron-beam irradiation, and the use of antimicrobial surface coatings to minimize pathogenic foodborne microorganisms.

Commissioner's Fellowship Project Overview
Sanitation and processing conditions to reduce the risk of Salmonella contamination and transfer in nut butter products

Contamination of peanut butter and nut butter products by pathogenic *Salmonella enterica* serovars have led to an increasing number of product recalls and foodborne outbreaks. Post processing contamination of peanut butter will remain a significant health risk to consumers due to inherent characteristics of peanut butter products which allow pathogenic microorganisms to remain viable throughout the shelf life of the product. Current procedures used to clean peanut processing equipment may not be effective for eradicating *Salmonella* present on equipment surfaces. In addition, information is lacking on the mechanisms by which peanut butter becomes contaminated in the food processing environment. This project intends to: 1.) Determine the thermal resistances of *Salmonella* cultures grown in planktonic and sessile environments as well as lyophilized cells inoculated into peanut butter samples; 2.) Determine the contamination transfer rates between uninoculated peanut butter and food-contact materials previously contaminated via *Salmonella* biofilms; 3.) Determine the efficacy of the peanut butter 'push-through' method for equipment sanitation currently used in the food industry following equipment contamination; 4.) Evaluate commonly used commercial cleaning methods on Salmonella survival using commercial pilot plant scale processing equipment.

Shikha Gupta, Ph.D.

Center for Devices and Radiological Health

Preceptor: Srinidhi Nagaraja , Ph.D.

Scientific and Professional Background

2008-2010 Postdoctoral Fellow, State University of New York at Stony Brook
2007-2008 Scientific Consultant, Sidley Austin, LLP
2002-2008 Ph.D. Applied Science and Technology, University of California at Berkeley
1997-2001 B.S. Materials Science and Engineering, Massachusetts Institute of Technology

Research Interests

As an interdisciplinary scientist, I have a wide-range of research interests at the intersection of materials, mechanics, and medical devices. My doctoral research focused on microscale biomaterials characterization of both natural and synthetic materials used in orthopaedic devices. I developed of experimental testing standards for biomaterials microindentation and numerical analysis methods that permit the quantification of the nonlinear, time-dependent behavior of soft, hydrated materials. My postdoctoral training has also focused on orthopaedic tissues - specifically, how different repetitive patterns of mechanical unloading (disuse) affect long-term bone and muscle quantity, quality, and strength, how periods of recovery between cycles of disuse may affect these indices, and whether non-pharmacologic interventions can be used effectively to mitigate disuse-induced musculoskeletal atrophy

Commissioner's Fellowship Project Overview
The Effects of Prestrain on the Fatigue Life of Electropolished Nitinol Wires

Over the last decade, Nitinol, the nearly equiatomic metal alloy of nickel and titanium, has become a ubiquitous biomedical device material due to its unique material properties. Nitinol has been used primarily in cardiovascular devices to date, including stents, endovascular grafts, and vena cava filters. These intravascular devices are load bearing, and may be subjected to millions of cycles of multi-axial loading *in-vivo*, making them susceptible to fatigue failure. Designing against fatigue failure not only demands an understanding of in-service loads, but also of the material-level fatigue behavior of Nitinol under different modes of deformation. Since Nitinol is present as thin wire in many of these devices, an understanding of the mechanical properties in the wire geometry is requisite. Many intravascular devices are now implanted using minimally invasive surgery in which the device must be crimped, or radially compressed, onto a delivery device such as a catheter before being be inserted or deployed. However, little is known about the effects of such crimp-induced strain on the fatigue performance of the Nitinol, and, consequently, the durability of the device *in-vivo*. Bending is the predominant mode of deformation experienced by the wires due to crimping and pulsatile blood flow. The present project aims to elucidate the effects of prestrain on the low and high-cycle bending fatigue life of Nitinol wires using rotary bend testing. Better knowledge of the mechanical behavior of Nitinol will inform the development of more robust testing standards, provide insight into the types of bench tests requisite for proving the safety and efficacy of different Nitinol devices, and aid in identifying the mechanisms of post-market failures.

Rosalee Hellberg, Ph.D.

Office of Regulatory Affairs
Irvine, CA

Preceptor: Donna Williams-Hill, Ph.D.

Scientific and Professional Background

2010	Post-doctoral scholar, Oregon State University
2006-2009	Ph.D. Food Science and Technology, Oregon State University
2004-2006	M.S. Food Science and Technology, Oregon State University
1998-2002	B.A. Biochemistry, Lewis & Clark College

Research Interests

My research interests encompass a variety of topics, including food safety, public health, and molecular biology. The focus of my Ph.D. work was to improve upon and develop novel methods for the DNA-based identification of commercially-important seafood species. I employed techniques such as polymerase chain reaction (PCR)-restriction fragment length polymorphism (RFLP), DNA barcoding, and real-time multiplex PCR to identify salmon and trout species in commercial food products. I have also conducted a number of studies examining the levels of nutrients and heavy metals in seafood. As a post-doctoral scholar, I participated in the development of communication materials designed to inform healthcare professionals and their patients about the benefits and risks of seafood. In my position as an FDA Commissioner's Fellow, I will be researching the detection of norovirus and Hepatitis A virus in a variety of food systems.

Commissioner's Fellowship Project Overview
Development of Novel Methods for the Detection and Characterization of Norovirus

Noroviruses are the leading cause of foodborne illness worldwide, with an estimated 5.5 million cases annually in the United States. The current method of using DNA sequencing for characterization of noroviruses in outbreak situations can be problematic and time-consuming due to the high diversity of the norovirus genome. This Commissioner's Fellowship project is focused on the development of a novel, rapid method to detect and characterize noroviruses at the genotype and strain level. This method combines multiplex PCR with electrospray ionization mass spectrometry to determine the unique base compositions of target organisms. The first phase of the project involves the design and development of an assay plate to allow for differentiation of norovirus genotypes and strains, as well as detection of Hepatitis A virus. Following development, the assay plate will undergo optimization and validation testing with isolated virus strains and food samples. The results of this project will enhance the ability of public health officials to respond in norovirus outbreak situations and contribute to routine surveillance of noroviruses in foods.

Kristina Howard, D.V.M., Ph.D.

Center for Drug Evaluation and Research

Preceptor: Jack A. Ragheb, M.D., Ph.D.

Scientific and Professional Background

2005-2010	Research Assistant Professors, North Carolina State University
2001-2005	Ph.D. Immunology, North Carolina State University
2000-2001	Associate Veterinarian, Lums Pond Animal Hospital
1996-2000	D.V.M. Virginia-Maryland Regional College of Veterinary Medicine

Research Interests

The focus of my research to date has been vaccine development and host immune response to viral infection, with emphasis on the mucosal immune system. My ongoing research interests are in understanding how the host immune system responds to therapeutic modalities in the context of infectious and autoimmune diseases. I am also interested in the development and testing of therapeutic biologic compounds to treat persistent viral infection and cancer.

Commissioner's Fellowship Project Overview

Testing Immunogenicity of Therapeutic Proteins in a Humanized Mouse Model

Therapeutic proteins represent an important and rapidly growing sector of the pharmaceutical industry. Many of these proteins act directly on components of the immune system and present new paradigms for safety and efficacy testing. In addition, the manufacturing processes used to create these drugs can result in particulates (protein aggregates) that can significantly increase the immunogenicity of the product. The immune systems of non-human primates and rodents are sufficiently different from humans that studies in these models may not accurately predict outcomes in humans. Thus, it is important to develop and utilize new animal models, such as immunologically humanized mice, to advance drug testing. This project will utilize immunologically humanized mice to test an approved therapeutic protein for which clinical data in humans is available. Results from the humanized mice will be compared with actual clinical experience to validate the utility of this animal model. The ability to test therapeutic proteins in an animal model that can accurately predict immunogenicity as well as adverse events in humans would aid in the development of safer and more efficacious drug products.

Haijing Hu, Ph.D.

National Center for Toxicological Research

Preceptor: Mark Hart, Ph.D.

Scientific and Professional Background

2009-2010	Research Scientist, Walter Reed Army Institute of Research
2006-2009	Research Fellow, National Institutes of Health
2003-2006	Postdoctoral training, Purdue University
2003	Ph.D. Cornell University

Research Interests

I am interested in studying bacterial diseases for the development of effective therapies and vaccines. I studied antimicrobial peptides during my Ph.D. study at Cornell University. After graduation, I went to Purdue University to study the pathogenesis of *Bacillus anthracis*. Using *in situ* fluorescent staining, we demonstrated that spores germinate in macrophages and are rapidly inactivated. Two germination systems are involved within macrophages. To further study the host responses to bacterial infections, I then worked at NIAID, NIH where I applied Fluorescence Resonance Energy Transfer (FRET) techniques to visualize the interaction between the host immune system and the anthrax toxin in a mouse model. Through collaboration, I researched new techniques for anthrax detection and potential anthrax vaccine. I worked at Walter Reed Army Institute of Research afterwards developing a subunit human vaccine for Brucellosis.

Commissioner's Fellowship Project Overview

Expression of hyaluronidase Staphylococcus aureus UAMS-1 and its derivatives

Hyaluronic acid, also called hyaluronan, is widely distributed throughout connective, epithelial and neural tissues. As a major component of extracellular matrix, this compound contributes significantly to cell proliferation and migration. *Staphylococcus aureus* secrets hyaluronidase which has been shown to contribute to subcutaneous infection in mouse model. It was noted that higher hyaluronidase activity was detected when *sarA*, which encodes a DNA binding protein, was deleted. Based on above results, we propose that SarA regulates hyaluronidase gene expression by binding to the promoter region. In this study, we plan to:

- Use qPCR to compare the expression of hyaluronidase in various *Staphylococcus aureus strains* including mutants with regulator deleted.
- Identify the SarA binding site on the promoter region of hyaluronidase genes.
- Identify the transcription start point and the binding region.

SarA is an important regulatory protein in *Staphylococcus* gene expression. Several SarA binding sequences have been identified. The result of this study will provide information of SarA binding sites and binding affinity, as well as provide an insight into the differential expression of two hyaluronidase genes (hysA1 and hysA2) in *Staphylococcus aureus* UAMS-1.

Syed Imam, Ph.D.

National Center for Toxicological Research

Preceptor: Zbigniew Binienda, D.V.M., Ph.D.

Scientific and Professional Background

2005-2010	Assistant Professor of Medicine & Pharmacology, UT Health Science Center
2002-2005	Postdoctoral Fellow, NIH/NIA
2002	Ph.D. Neurotoxicology, Hamdard University & US FDA/NCTR
1996	M.S. Toxicology, Hamdard University

Research Interests

The main research goal of my laboratory is to understand the molecular basis of neurodegeneration, which can be implicated to develop therapeutic trials for neurodegenerative diseases. The broad areas of investigation in my lab include the study of the molecular mechanisms of neuronal cell death, novel cell death and cell survival pathways and their correlation with the molecular basis of Parkinson's disease (PD), α-synucleinopathies and related neurodegenerative disorders. We strive to identify regulatable targets that can be manipulated by chemical or genetic means for pharmaceutical and therapeutic intervention. Presently, my laboratory is focused on role of signaling kinases in the regulation of various components of PD as a therapeutic target in animal models and in PD patients. Our novel finding that oxidative stress sensitive tyrosine kinase renders parkin, an E3 ubiquitin ligase, non-functional has opened up various new avenues to understand progression of nigro-striatal degeneration during the pathogenesis of PD. We are investigating the role of cell signaling regulation of α-synuclein and LRRK2 in the pathogenesis of PD. Furthermore, we have ongoing pre-clinical studies on the role of kinase inhibitors as a potential therapeutic approach in slowing down the progression of PD. Furthermore, my laboratory has a very strong background in the oxidative-stress mediated neurotoxicity induced by substituted amphetamines as well as in DNA damage and repair in aging brain. My laboratory has set-up extensive collaborations with various PD research and clinical centers in USA and Europe that include Morris Udall Center of Excellence for PD Research at Johns Hopkins School of Medicine, Department of Neurology at UCSD, Hertie Institute of Clinical Brain Research at University of Tubingen, Germany and Brain Mind Institute of Swiss Federal Institute of Technology, Switzerland.

Commissioner's Fellowship Project Overview
Assessment of iron oxide nanoparticles-induced neurotoxicity.

HYPOTHESIS: Iron-oxide will induce mitochondrial dysfunction and dopaminergic neurotoxicity via reactive oxygen (ROS) and reactive nitrogen species (RNS). **SPECIFIC AIMS: (1)** To determine if treatment with different sizes of iron oxide nanoparticles to SHSY-5Y Neuroblastoma cells would result in cytotoxicity via free radical generation. **(2)** To determine if acute/chronic exposure of varying sizes of iron oxide nanoparticles would alter neurochemical release as measured by *in vivo* microdialysis, mitochondrial function, induce changes in anti-oxidant systems and cause cell death via generation of ROS in different regions of rat brain.

Engineered nanomaterials are widely used in cosmetics, food packaging, drug delivery systems, therapeutics, biosensors, etc. Thus, the exposure of the population to nanomaterials continues to increase as their application expands. Dairy products, cereals, breads and beverages are fortified with vitamins and minerals such as iron, magnesium or zinc, and probiotics, bioactive peptides, antioxidants, etc. Some of these ingredients are being added to foods as nanoparticles (NP). Active ingredients are being nano-encapsulated and include vitamins and fatty acids which are sold commercially for use in processing and preservation of beverages, meats, cheese and other foods. NP are intentionally added to many foods to improve flow properties (e.g., how well they pour), color and stability during processing, or to increase shelf life. For example: Toddler Health's fortified chocolate and vanilla 'nutritional drinks' include 300 nm particles of SunActive® iron. Iron oxide is also added to cosmetic pigments (lipstick) and nano-iron oxide magnetic particles are used in agrochemicals to deliver and concentrate different substances on plants or maybe used as vectors for diagnostic and therapeutic interventions (Li et al., 2009). Therefore, the FDA regulatory interest in nanomaterials ranges from their use in agriculture and fortified foods and unintentional contamination from food processing machines and the migration of manufactured nanomaterials from packaging into foods. These studies are designed to provide neurotoxicity profile of iron oxide nanoparticles thereby producing scientific information regarding the exposure limit of these particles and neurochemical alterations induced by the exposure to these nanoparticles. The data obtained will be helpful in setting a regulatory guideline for risk-assessment of the use of iron oxide nanoparticles.

Sudipan Karmakar, Ph.D.

Center for Drug Evaluation and Research

Preceptor: Akhilesh K. Nagaich, Ph.D.

Scientific and Professional Background

2009-2010	Research Instructor, Baylor College of Medicine
2004-2009	Postdoctoral Associate, Baylor College of Medicine
1998-2003	Ph.D. Molecular Biology, Indian Institute of Chemical Biology
1995-1997	M.S. Biochemistry, Kolkata University
1992-1995	B.S. Chemistry, Kolkata University

Research Interests

My research interests are broadly focused on different aspects of cancer biology, starting from early cancer initiating signaling process to drug resistance. My post-doctoral research mainly involved studying the complex regulation of transcriptional activity of estrogen receptor (ERa) by nuclear receptor co-regulators (co-activator or co-repressor) in relation to endocrine resistance of breast cancer. I discovered that a well known co-repressor SMRT (Silencing Mediator of Retinoic acid and Thyroid hormone receptor) which is generally known to repress nuclear receptor mediated transcription, is involved in activation of ERa in a gene specific and context dependent manner and in so doing SMRT is actively involved in breast cancer cell proliferation and survival. I also found that SMRT expresses in primary breast cancer patients (n=587) that received no adjuvant treatment, which indicates that SMRT expression is correlated with tumor recurrence. During my research tenure, I also came to learn and characterize epigenetic re-programming of SMRT that may be crucial in promotion of breast carcinogenesis, tumor recurrence and poor overall survival. I wish to apply and extend my experience further to determine diverse epigenetic control mechanisms of gene expression in relation to drug resistance and thereby achieve my long term career goal to discover new bio-markers that would aid in diagnosis and treatment decisions.

Commissioner's Fellowship Project Overview

Role of a forkhead box protein FOXA1 in regulating glucocorticoid receptor activity and glucocorticoid mediated breast cancer cell proliferation and survival

Breast cancer is the most common type of cancer among women in the United States. Although various treatment options (e.g. endocrine, radio/chemo- or targeted therapy) are now available to combat this disease, breast cancer still remains the second leading cause of death in women in this country. Glucocorticoids are well known for their immunosuppressant activity and are generally used as an antiemetic agent to reduce nausea and vomiting associated with chemotherapy treatment. Glucocorticoids are also given to breast cancer patients for their antitumorigenic activity. However, recent studies indicate that glucocorticoids are not equally effective in all types of breast cancer and have antiapoptotic activity in certain types of breast cancer. Our preliminary data indicate that glucocorticoid receptor (GR) activity is dependent on a forkhead box transcription factor (FOXA1), the level of which varies among the various breast cancer subtypes (luminal type being the highest expresser, low in basal type and absent in triple negative). In this fellowship program, I seek to investigate the GR activity and its effect on breast cancer cell proliferation and survival in various breast cancer cell subtypes. The outcome of this study would determine the effectiveness of glucocorticoids against various subtypes of breast tumors and therefore, establish a foundation for, a) pursuing glucocorticoid treatment to enhance the efficacy of endocrine-therapy, radiotherapy and chemotherapy for breast cancer patients in a safer and effective manner, b) defining a subpopulation of breast cancer patients who are likely to benefit from or be adversely affected by glucocorticoid treatment, leading to a more personalized medication for the treatment of breast cancer.

Seraphin Kuate, Ph.D.

Center for Biologics Evaluation and Research

Preceptor: Jakob Reiser, Ph.D.

Scientific and Professional Background

2007-2010	CRTA Research Fellow, National Institutes of Health
2005-2008	M.S. Epidemiology, University of Bielefeld
2002-2007	Postdoctoral Research Fellow, Ruhr-University of Bochum
1999-2002	Ph.D. Molecular Virology/Immunology, Ruhr-University of Bochum
1994-1996	M.S. Biochemistry, University of Yaoundé I

Research Interests

My research interests include the development and characterization of lentiviral, and adenoviral vectors for gene transfer and genetic vaccinations; the design and characterization of different classic and genetic vaccination approaches against viral infections; and the epidemiology of infectious diseases.

Commissioner's Fellowship Project Overview
Design and testing of safety-improved lentiviral vectors

Gene therapy holds great potential for treating a variety of inherited and acquired diseases, some of which are as yet incurable. One strategy for delivering therapeutic genes into patient's cells is to use virus-based vectors. Over the past decade, a variety of investigators have developed gene therapy vectors based on human immunodeficiency virus (HIV). These are referred to as lentiviral vectors. Lentiviral vectors have been genetically modified so that their likelihood of reproducing in target cells as replication-competent lentiviruses (RCL) is diminished.

Our goal is to improve the safety of lentiviral vectors by further reducing the risk of RCL formation. The vector and packaging constructs that are used for the production of lentiviral vectors for clinical applications contain sequence overlaps that can potentially lead to RCL precursors through homologous recombination.

My research plans include the following: (1) Development of safety-improved lentivirus-based vectors through reduction of sequence overlaps in order to minimize potential recombination events between vector and packaging constructs; (2) Development of a sensitive cell-based assay for the detection of recombination intermediates, and (3) Establishment of an assay to test the mobilization of such recombination intermediates involving envelopes from endogenous retroviruses.

Ernest Kwegyir-Afful, Ph.D.

Center for Food Safety and Applied Nutrition

Preceptor: Stefano Luccioli, M.D.

Scientific and Professional Background

2005-2010	Postdoctoral Fellowship, University of Pittsburgh School of Medicine
2005	Ph.D. Neurology and Cognitive Sciences, University of Maryland
1999	M.Phil Part I, Biochemistry, University of Ghana
1997	B.S. Biochemistry and Psychology, University of Ghana

Research Interests

Trained as a neurophysiologist, my previous research involved investigating the function of neural circuits thought to participate in somatosensory perception, goal-directed motor movements, absence epilepsy and memory consolidation. While the immediate activity of neural circuits is regulated by neurotransmitters, long-term modulatory effects of environmental toxins, nutrition and socio-economic activities have been observed. My interests include understanding how nutrition and food additives may affect neural development and how considerations of such factors affect risk estimates during traditional food safety risk assessments. I am also interested in understanding how the results from such risk and benefit analysis are used to inform policy making decisions.

Commissioner's Fellowship Project Overview
Risk and Benefit Analysis of Food Allergen Thresholds

Food allergic reactions can be life-threatening and not only present a disease burden for society but also have a negative impact on quality of life of affected consumers and their families. Since no preventative treatments are currently available, the food label is the best risk management tool used to mitigate the risk for reactions and adverse health consequences. However, allergen avoidance is difficult and finding nutritious foods to eat may present a burden on consumers. Moreover, since labeling laws do not advise on allergen thresholds or potentially safe levels of allergen exposure, products containing potentially insignificant amounts of allergen carry a label, thus contributing to less availability of "safe" nutritious food choices for allergic consumers.

The purpose of this project is to use statistical models of available food challenge data to estimate population thresholds for peanut, milk and soy containing products. Using this data and current exposure estimates, we will quantitate the risks and benefits associated with implementing these thresholds as risk management tools. We will also employ an animal model of peanut allergy to understand dose-responses associated with increasing threshold concentrations. Knowledge of these thresholds and their associated risks/benefits can be used to set guidelines for labeling exemptions and thus to improve the label efficacy of allergenic ingredients by allowing availability of more nutritious food choices with low risk for allergic reaction.

Brenda Lawrence, M.D.

Center for Devices and Radiological Health

Preceptor: Joy Samuels-Reid, M.D

Scientific and Professional Background

2007-2008	Practicing internist and pediatrician
2003-2006	Internal medicine and pediatric resident – University of Rochester, Strong Memorial Hospital
2002-2003	Internal medicine and pediatric intern – Tufts University, Baystate Medical Center
1995-2002	Medical student, graduate student and student pathology fellow, University of Rochester School of Medicine and Dentistry
1993-1995	Research Biologist, National Institute of Allergy and Infectious Disease
1992-1993	Undergraduate Fellow, National Institute of Mental Health
1990-1993	Undergraduate student, Smith College

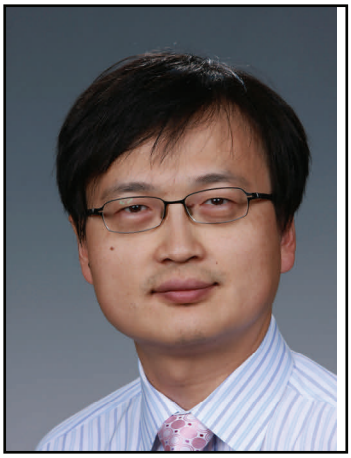
Research Interests

My previous research experiences have been in the areas of immunology, neuroscience and genetics. The appeal of each project was the possibility of a better understanding of human health and illness, as well as improved outcomes for patients. I am interested in the developing technologies that bridge research to clinical application, bringing safe and effective treatments to patients.

Commissioner's Fellowship Project Overview

Adverse Event Reporting for Pediatric Medical Devices: Rapid Signal Identification Development

The identification of harmful medical devices affecting the vulnerable population of children is a vexing, ongoing challenge. The objective of the project is to improve processes in the area of adverse event reporting of medical devices, particularly as it pertains to the pediatric population. Initial efforts involve studying the post-market issues related to current reporting systems and databases, as well as working with pre-market review of devices with pediatric implications. The goal is to develop an improved identification method of problematic devices, while also educating event reporters, device users and clinicians on how to report concerns as they occur.



Soo Kwang Lee, Ph.D.

Office of Regulatory Affairs
Atlanta, GA

Preceptor: Tiffany Harmon, Ph.D.

Scientific and Professional Background

2007-2010	Post-doctoral fellow, Pacific Northwest National Laboratory (PNNL)
2007	Ph.D. Toxicology, University of Georgia
	M.S. Organic Chemistry, University of Pittsburgh
	B.S. Chemistry, Seoul National University

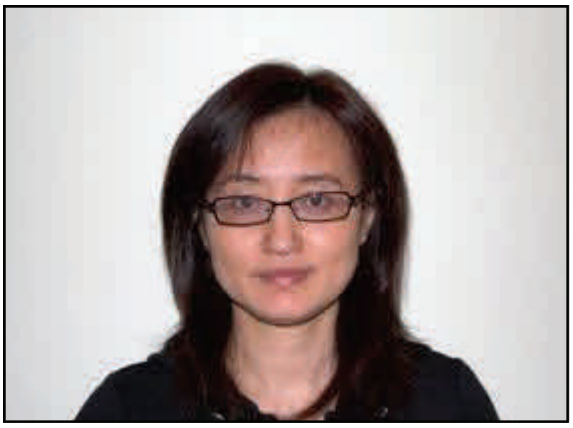
Research Interests

My research interests include the interdisciplinary toxicological evaluation of drugs/ chemicals and relevant biomarkers utilizing *in vitro/in vivo* studies and *in silico* toxicology, as well as the analysis of biologics (GCMS, LCMS), metabolisms, mixture interactions, PK/ PD, PBPK modeling.

Commissioner's Fellowship Project Overview

Develop and validate a LC-MS method for the analysis of vitamin K and related compounds in infant and adult nutritional products

The Atlanta Center for Nutrient Analysis (ACNA) in Southeast Regional Laboratory (SRL) is responsible for the analysis of nutrient profiles in all food products (domestic and imported) with nutritional labeling. ACNA ensures the accuracy of labeling of infant formula as well as other medical and nutritional foods, including multi-component dietary supplements. Nutritional formulas present significant extraction and chromatographic separation challenges to the current method, due to different chemical characteristics, disparate concentrations and complex sample matrices. Current AOAC Official Methods, adopted by ACNA, for the analysis of various vitamins mandate the single-analyte approach for each vitamin primarily by HPLC or microbiological methods. The purpose of the current project is to develop and validate a robust LC-MS method for the analysis of vitamin K and other fat soluble vitamins in infant and other nutritional products. The proposed LC-MS method is expected to provide enhanced sensitivity and accuracy over the existing methods.



Xingfang Li, M.D.

Office of the Commissioner

Preceptor: John W. Gardner, M.D., Ph.D.

Scientific and Professional Background

2009-2010	Psychogenics Inc.
2002-2009	Pfizer Inc.
2001	M.S., in Biomedical Informatics, UMDNJ and NJIT
1998-2002	Memory Pharmaceuticals
1992-1998	Postdoctoral Research Fellow, New York University
1992	M.S., in Neurophysiology, Peking Union Medical College
1985	M.D., Wannan Medical College

Research Interests

My research interests are focused mainly on an integrated data system with standardized data formats. Not only can a centralized data system manage data more efficiently to facilitate an FDA review process, but also it can benefit health care industry submitters for the submission processes and easily gathering very important information from the FDA. In addition to the data system, I am also interested in pharmacovigilance and post-marketing surveillance for medicinal products.

Commissioner's Fellowship Project Overview

Information Technology for Pharmacovigilance: Future Directions and Challenges from Regulatory Agency Perspectives

In pharmacovigilance, making the right decisions at the right time is critical. As in all risk assessment, a judgment has to be made based upon available information. Access to up-to-date and accurate information is crucial. Three key information management domains are needed to enhance and integrate: (1) *access* to information (data); (2) *interface*, or user-friendly tools supported by a robust architecture, to efficiently convert information into knowledge; and (3) *data standards*. These three domains interact to influence the way we receive, manage, and communicate information. My project work will focus on enhancing and integrating information management to ensure the data quality.

Xueying (Sharon) Liang, M.D., Ph.D.

Center for Devices and Radiological Health

Preceptors: Thomas P. Gross, M.D., M.P.H. and
Danica Marinac-Dabic, M.D., Ph.D.

Scientific and Professional Background

2007-2010	Postdoctoral Fellow, Genetic Epidemiology, National Institutes of Health
2007	Ph.D. Human Genetics, Vanderbilt University
2005	M.S. Applied Statistics, Vanderbilt University
1999	M.S. Biochemistry and Molecular Biology, Beijing Institute of Radiation Medicine
1996	M.D. Tianjin Medical University

Research Interests

Being trained as a Genetic Epidemiologist with the medical degree background, I have always been interested in health related issues. My diverse educational and professional experience enables me to bridge different fields. My research interests have focused on improving public health through integrated approaches by combining information from different data sources. Exploring and mining available epidemiology databases, extracting and analyzing data to evaluate the safety and effectiveness of public health related products is my primary interest. Comparative methodology study to evaluate epidemiology database establishment methods is also on my top ranked research interest list.

Commissioner's Fellowship Project Overview
Innovative methodologies for evidence synthesis for cardiovascular devices

Monitoring the safety and effectiveness of approved medical devices is important for public health. However, there are limitations in the data components needed for post-approval decision making, including but not limited to: randomized controlled trials are normally small, short-term and not generalizable to greater patient population; and passive reporting surveillance system is limited in obtaining complete adverse event reports due to the voluntary nature of the system.

My project is a part of broader CDRH initiative to develop systematic approach to synthesize evidence to improve regulatory decision making. Evidences from premarket studies and FDA mandated post-approval studies and registries containing postmarket data will be collected and analyzed. Variables will be identified and summarized from published studies by systematic literature review according to their importance for safety and effectiveness evaluation of cardiovascular devices. Post-market registries will be evaluated based on characteristics critical for post-market surveillance. The data from this project will be used to develop hierarchical modeling to earlier refine new therapies and earlier detect problems of postmarket devices. This systematic approach will not only advance regulatory science in FDA, but also benefit sponsors of medical devices and public.

Tzu-Yun Chang-McDowell, Ph.D.

Center of Drug Evaluation and Research

Preceptor: Rajanikanth Madabushi, Ph.D.

Scientific and Professional Background

2010	Ph.D. Epidemiology and Public Health, University of Maryland
2007-2010	Research Analyst/Programmer, University of Maryland
2003-2007	Study Coordinator/Research Analyst (Full-Time), University of Maryland
2004	M.A. Kinesiological Sciences, University of Maryland,
2000	B.S. School of Physical Therapy, National Taiwan University

Research Interests

My general research interests lie in the field of translational science using epidemiological and statistical techniques. My previous research involved the investigation of the prognostic factors and other health outcomes among Veterans with Multiple Sclerosis using active surveillance system and large administrative databases. My epidemiological training along with strong computational background in programming, data mining, and statistical analysis have driven my interest towards the area of applied research in public health. Specifically, I am very excited for the opportunity to work as a Commissioner's Fellow to conduct quantitative research and modeling using data from ongoing national studies, established clinical trials, and surveillance systems to guide regulatory decisions as well as promote public health.

Commissioner's Fellowship Project Overview
Improve Pre-Market Safety Assessment of Cardiovascular Risk due to Unintended Elevations of Blood Pressure for New Molecular Entities

Elevated blood pressure has long been recognized as a major risk factor for cardiovascular modality and mortality. There is evidence to illustrate that even small elevations in blood pressure are associated with a significant increase in risk of cardiovascular diseases (CVD). Drug induced elevation in blood pressure has been documented for a number of pharmaceutical agents. However, in the pre-market arena, there are currently no implemented regulatory standards or criteria to systemically review safety issues associated with drug induced blood pressure and its potential long term effects on CVD risk. As a consequence, risk-benefit evaluation for a new molecular entity cannot be appropriately assessed. This project seeks to improve pre-market safety assessments of the potential CVD risk due to unintended elevation of blood pressure for new molecular entities through a comprehensive quantitative assessment.

Zenghui Mi, M.D., Ph.D.

Center for Drug Evaluation and Research

Preceptor: Nancy Xu, M.D.

Scientific and Professional Background

2002-2005	CRTA Fellow, National Cancer Institute at Frederick
1999-2002	Postdoctoral Fellow, UT Health Science Center at San Antonio
1999	Ph.D. in Pharmacology, State University of New York at Buffalo
1989	M.D., Beijing Medical University

Research Interests

My current research focuses on clinical trial data management and database design and build. Besides my clinical research, I also have many years of experience in drug discovery and development. My drug research interests lie predominately in the areas of pharmacokinetics/pharmacodynamics (PK/PD), drug membrane transport, drug mechanism, preclinical drug evaluation, and drug screening studies, especially with bone density and cancer drugs.

Commissioner's Fellowship Project Overview

Renal function and drug dosing

In the US, over twenty-one million people have impaired kidney function and are at increased risks of drug related adverse events. Currently, several serum creatinine-based equations are being used for the estimation of renal function and drug dosing adjustments in patients with renal impairment. However, these equations cannot provide an optimal approach to estimate renal function across weight strata to enhance drug safety. Recently, our research group developed a new modified equation for renal function estimation. Facilitated by this progress, my research will focus on testing: 1) whether the new equation has better renal function estimation compared with other estimation equations being used, in terms of accuracy and bias; 2) whether the new equation has the best correlations with other pharmacokinetics parameters; 3) whether the new equation will give the best predictions on drugs' safety and efficacy outcomes and, therefore, be used for dose adjustment in the product label.

Maryam Mokhtarzadeh, M.D.

Center for Devices and Radiological Health

Preceptor: Markham Luke, M.D., Ph.D.

Scientific and Professional Background

2010 Post-doctoral Fellowship, Jules Stein Eye Institute, UCLA
2008 Residency, Kresge Eye Institute, Wayne State University
2005 Internship, Sinai Grace Hospital, Detroit Medical Center
2004 M.D. Johns Hopkins School of Medicine
2000 A.B. Chemistry, Princeton University

Research Interests

With experience in both clinical ophthalmology, and ophthalmology related research, I am interested in the interface between medicine, public policy, innovation, and regulation. My previous research projects have included work on genetic eye diseases, refractive surgery, ophthalmic surgical innovations, dry eye syndrome, and corneal transplant techniques. I hope to build on my interests and experience while working in the device approval and regulation section of the CDRH.

Commissioner's Fellowship Project Overview
Regulatory Classification of Five Unclassified Ophthalmic Devices

The Medical Device Amendments to the Food, Drug, and Cosmetic Act were enacted in 1976. These amendments categorized device types into one of three classes (Class I, II, or III) based on the risks posed by the device and the regulatory oversight needed to assure the safety and effectiveness of the device before it enters the US market. However, some well characterized, pre-Amendment ophthalmic devices are still unclassified and five of these device types were presented for classification recommendations at different Ophthalmic Devices Advisory Panel meetings that took place between 1996 and 2000. As of yet, these devices are unclassified because new regulations (and in some cases special controls guidance documents) have yet to be created in order to complete the classification process. The specific objective of this project is to write these classification documents proposing the promulgation of a rule for final classification and to present these documents to other centers within the FDA for final review and clearance. The devices to be classified include: scleral plugs, punctal plugs, lacrimal system repair devices, corneal storage and transport systems, and eyelid weights. Achieving progress towards the finalized regulations and special controls necessary to classify these five devices will contribute to the FDA's mission to protect the public health by facilitating availability and access to devices through the least burdensome path to approval, while maintaining assurance of safety and effectiveness.

Julie Nemecek, Ph.D.

Center for Biologics Evaluation and Research

Preceptor: Luisa Gregori, Ph.D.

Scientific and Professional Background

2006-2010	IRTA Postdoctoral Fellow, National Institutes of Health
2006	Ph.D., Microbiology, University of Wisconsin-Madison
2000	B.A. Biological Sciences, Cornell University

Research Interests

As a postdoctoral fellow at the National Institutes of Health, I worked with Reed Wickner in the study of yeast prions, which serve as an excellent model for understanding prion diseases in humans and animals. We designed a genetic screen for identifying and confirming new prions in yeast which can be used to identify infectious proteins in other organisms. Through this technique, I identified a prion form of the *S. cerevisiae* metacapase Mca1p—the only caspase of yeast. This protein is believed to play a crucial role in yeast apoptosis. The prion form of this caspase has a dramatic mutagenic effect on the mitochondrial DNA of yeast. Interestingly, the damage caused by [MCA] to the mitochondrial DNA has a protective effect under certain growth conditions. Additional work involvsing the use of solid-state NMR verified that the Mca1p amyloid form is a parallel in-register β-sheet, as is the case with other yeast prions.

Commissioner's Fellowship Project Overview
Detection of Prions in Infected Blood via Protein Misfolding Cyclic Amplification (PMCA)

Our work will investigate whether protein misfolding cyclic amplification (PMCA) is a viable technique for amplification of abnormal prion protein from variant Creutzfeldt-Jakob Disease (vCJD)-infected macaque blood. vCJD is a prion disease that affects humans and can be experimentally transmitted to macaques. Prions are altered forms of a host protein believed by many to be the infectious agents of transmissible spongiform encephalopathies (TSEs). PMCA is an in vitro protein amplification technique analogous to the polymerase chain reaction (PCR) used to amplify DNA. By taking advantage of prions' innate ability to self-propagate, the abnormal prion protein present in potentially infected samples will be amplified via cycles of sonication and incubation and detected via Western blotting. In this proposal, PMCA will be adapted and optimized for detection of prions in blood. Blood, however, is known to contain low levels of infectious material, compared to brain or other tissues from infected animals. Compounding this issue, transmission by blood is highly efficient and requires only very low levels of prion protein. A highly sensitive and efficient PMCA using blood as a substrate will be developed during the course of this work. This assay will be invaluable for further development of a blood screening test to identify vCJD-infected donors and thus prevent transmission of vCJD by blood transfusion.

Zohra Olumee-Shabon, Ph.D.

Center for Veterinary Medicine

Preceptor: Jamie Boehmer, Ph.D.

Scientific and Professional Background

Research Associate Children's National Medical Center 2004–2007
Post Doctoral Fellow National Institute of Health 2000-2004
Ph.D. Chemistry, George Washington University, Washington, D.C., 1999
B.Sc. Chemistry, George Mason University, VA 1992

Research Interests

In the last few years, I have acquired extensive experience in the detection, identification, and quantification of protein and peptide expression levels. My research has been focused on the development of novel methodologies to study proteins, defining the proteome profile of cellular and sub-cellular organelle under normal and disease states, and detailed investigation of specific proteins and peptides to determine their possible biological and clinical importance.

Commissioner's Fellowship Project Overview
Biomarkers of Inflammation and Effects of Non-Steroidal Anti-Inflammatory Drugs Following Experimental Induction of Mastitis with Lipopolysaccharide in Goats

Recent veterinary biomarker discovery initiatives have focused on the identification of sensitive and reliable indicators for use in evaluating the efficacy of adjunctive therapies faonrim thaels t.r eMatym reenste oarfc ihn filsa imnvmoaltvieodn aapsspolicciaattieodn w oift hm caossli fsopremct rmomasetittriisc -inb afsoeodd pprrootdeuocminigc methodologies to the discovery of biomarkers of inflammation in complex biological matrices including goat milk and plasma. I investigate differential protein expression in caprine milk during experimentally induced coliform mastitis using 2-dimensional gel electrophoresis (2D-GE) and liquid chromatography followed by tandem mass spectrometry (LC-MS/MS). The biomarkers identified in this research will be vital to the potential establishment of regulatory criteria aimed at assessing the efficacy of nonsteroidal anti-inflammatory drugs for treating inflammation in ruminant species.

Yun-shang Piao, Ph.D.

Center for Biologics Evaluation and Research

Preceptor: Ellen F. Lazarus, M.D.

Scientific and Professional Background

2009-2010 Research Scientist, National Institutes of Heath
2005-2008 Research Assistant Professor, Montana State University
2004-2005 Visiting Scientist, University of Texas M. D. Anderson Cancer Center
2002-2004 Visiting Scientist, Karolinska Institute
1997-2002 Team Leader, Chinese Academy of Sciences
1997 Ph.D. Biochemistry & Molecular Biology, University of Oulu

Research Interests

I am a physiologist with expertise in endocrinology, reproductive medicine, and oncology. My research interests include reproductive hormones, pregnancy, gynecological disorders, and hormone-related cancers.

Commissioner's Fellowship Project Overview
Assessment of risks to living donors of human cells, tissues, and cellular and tissue-based products (HCT/Ps)

HCT/Ps are increasingly used in medical and cosmetic procedures. While recovery of HCT/Ps from living donors is generally performed according to established procedures in a manner that assures their safety, there are potential risks from tissue donation. For example, oocyte donors are exposed to risks of ovarian hyperstimulation syndrome, surgical complications and theoretically, development of hormone-related cancers. Peripheral blood stem cell donors face known risks related to growth factor administration and apheresis, and theoretical long-term risks of leukemia and other blood dyscrasias. Infant cord blood donors may be exposed to risks resulting from deviations from standard perinatal care during cord blood recovery. All living donors are exposed to short-term risks of phlebotomy to obtain samples for eligibility determination. Further, the results of donor testing may disclose medical conditions or health predispositions. Federal and state oversight of HCT/Ps focus on recipient safety. Voluntary guidelines promulgated by professional organizations include some provisions for donor safety. However, the extent of donor protection afforded under these guidelines is difficult to measure because they are limited in scope and enforcement power. In this study, we will identify gaps in scientific knowledge about risks for living donors of HCT/Ps and evaluate current oversight of donor safety.

Sarah Pierce, Ph.D.

Office of Regulatory Affairs
Irvine, CA

Preceptor: William B. Martin, Ph.D.

Scientific and Professional Background

2010 Ph.D. Chemistry, University of Texas at Austin
2004 B.S. Chemistry, Duke University

Research Interests

My graduate research focused on developing mass spectrometric methods to investigate nucleic acid interactions with novel drugs. Specifically, my research focused on assessing the effectiveness of novel anti-cancer drugs designed to target specific nucleic acids sequences and structures. Through mass spectrometric techniques the relative binding affinity and specificity of a variety of anti-cancer drugs were screened. The successful analysis of these anti-cancer drugs aided in structural refinement and improved sequence targeting of future drug structure iterations.

Commissioner's Fellowship Project Overview

Project title: Rapid Detection and Identification of Foodborne Bacterial Pathogens via PCR/ ESI-MS

In order to contain and prevent outbreaks of foodborne bacteria, the source of the pathogen needs to be quickly identified. Current methods of detecting, isolating, and identifying bacteria to an actionable level can take weeks. Epidemiological studies can provide possible culprits, but the isolation of the bacterium involved in the outbreak is necessary to identify the affected products. In a collaborative effort with CFSAN and the North Carolina State Department of Health, this work evaluates a novel technology for the detection and identification of a variety of bacterial pathogens found in food. The method combines PCR amplification of DNA with mass spectrometric detection of the resulting amplicons. The use of mass spectrometry as a detection method allows for the identification of bacteria in mixed culture preventing the need for an isolation step. Due to the use of PCR primers covering a range of bacterial species, a variety of bacteria can be identified in one multiplexed assay. This project involves the evaluation of this method for the identification of relevant foodborne pathogenic bacteria. After initial work to expand the limits of the current database by analyzing a large collection of bacteria, the analytical characteristics of the method will be determined. This project is a fundamental step towards fast, accurate identification of pathogens and is a part of a larger movement towards improving the agency's response to food emergencies.

Rebecca Robinson, Ph.D.

Center for Biologics Evaluation and Research and
Center for Devices and Radiological Health

Preceptors: Charles Durfor, Ph.D., Elias Mallis, B.S., and Mercedes A. Serabian, M.S., D.A.B.T

Scientific and Professional Background

2010 Ph.D. Biomedical Engineering, Yale University
2007 M.S. Biomedical Engineering, Yale University
2003 B.S. Biomedical Engineering, Columbia University

Research Interests

My research interests are focused on investigating drug delivery and tissue engineering therapies for repair in the central nervous system using synthetic polymer scaffolds. My recent work has focused on fabricating and characterizing degradable polymer constructs to deliver small-molecule tyrosine kinase inhibitors to promote optic nerve regeneration following injury. Specifically, efforts were made to determine the utility of degradable microspheres and nanospheres for sustained ocular drug delivery and the advantages of one construct over the other using a rodent optic nerve injury model. Other areas of interest include, synthetic polymer, hyaluronic acid, and natural-synthetic hybrid scaffold development with the goal of creating a central nervous system extracellular matrix mimic for study of nervous system pathologies.

Commissioner's Fellowship Project Overview
Mesh Mash: Past, present, and future surgical mesh and scaffold design and impact on FDA regulatory practices

The primary purpose of absorbable/degradable synthetic and biologic surgical meshes is to reinforce weakened soft tissue through encouraging tissue remodeling, either by tissue ingrowth into the implant or encapsulation of the implant. In the past ten years there has been an increase in the complexity of mesh device design as well as the number of adverse events associated with these devices—in 2008 FDA issued a Public Health Notice alerting patients and healthcare providers to the serious adverse events associated with use of surgical mesh for urogynecologic repair. In addition, since the current CDRH surgical mesh guidance was issued our understanding of the methods for implanting surgical mesh devices and their subsequent clinical performance has improved. This issue also extends to CBER review practices as many tissue-engineered/ regenerative-medicine (TERM) products involve a scaffold-based approach where the degradable scaffold is intended to encourage or promote tissue regrowth and/or remodeling yet maintain its integrity during this process. Given the recent concerns regarding adverse events and the change in pace of the field (i.e., scaffold/ mesh design and implantation techniques), premarket review practices require updating to address new concerns regarding the safety and effectiveness of surgical mesh devices and other scaffold-based products. To achieve this goal, my project will focus on establishing a database to catalog premarket submissions for surgical mesh devices at CDRH and scaffold-based products at CBER. Data inputted into the database will be used to recommend preclinical testing procedures and studies for surgical mesh devices and scaffold-based products that are expected to remodel or replace tissue. These recommendations will be used to inform development of new draft guidance for review of premarket submissions for urogynecologic surgical mesh. Finally, the results of this project will be used to facilitate communication and increase the knowledge base of reviewers of TERM products.

Suzanne Schwartz, M.D., Ph.D.

Center for Devices and Radiological Health

Preceptor: Markham Luke, M.D., Ph.D.

Scientific and Professional Background

1999-2010	Assistant Professor of Surgery, Weill Cornell Medical College
2003-2005	Graduate Studies, Weill Cornell Graduate School of Medical Sciences
1996-1999	Medical Director, Ortec International, Inc
1992-1994	Trauma and Injury Biology Fellow, Cornell University Medical College
1991-1992	Samuel and May Rudin Clinical Burn Fellow, New York Hospital-Cornell Medical Center
1988-1991	General Surgery Resident, Montefiore Hospital and Medical Center
1988	M.D. Albert Einstein College of Medicine
1983	B.A. Biological Sciences, Stern College for Women of Yeshiva University

Research Interests

As a clinical & translational researcher, I engage in studying burn trauma & the healing response. My main interest is in dysregulation of repair post-injury to disease states that render them more predisposed to 'failure to heal'. Most specifically, I focus on examining outcomes of diabetics post-burn, seeking predictors of wound dysrepair as well as identifying potentially modifiable factors that can improve outcome, with the intent of defining a customized, data-driven decision analysis approach for the injured diabetic. Aligned with this outcomes-based, patient-oriented study, my preclinical work has involved development and testing of novel technologies for modulating healing of cutaneous injuries in both healthy & diabetic animal models. I believe a strategy that advances a synergistic "team science" paradigm (seamless integration of biomaterials science, injury & repair biology, health services research and regulatory science) is critical today in facing the challenges and the unmet needs in public health.

Commissioner's Fellowship Project Overview

Assessing Trends and Identifying Drivers in Product Entry, Utilization and Delivery of Burn Care – A Cross-Sectional Study of US Landscape and a 15-Year Retrospective Analysis of Therapeutic and Diagnostic Products Cleared, Approved or Licensed for Marketing

Each year more than a million people in the US sustain burn injuries, with approximately 450,000 receiving medical treatment. In spite of progress in burn surgical and critical care, numerous areas for improvement and innovation persist. Starting in 1996, several landmark products were introduced with the promise of re-defining the burn wound treatment algorithm and, in turn, improving clinical outcomes. This proposal aims to address the following questions: *(1) Have availability of new products/technologies altered the clinical paradigm for burn care? (2) How have clinical outcomes of burn patients tracked during the equivalent 15-year timeframe since landmark products received marketing approval? (3) Has the burn professional community's drive to advance burn care been adequately matched by ongoing development of innovative approaches and bedside availability of new therapeutics and/or diagnostics?* My project will therefore examine the current state of burn wound management, identify unmet needs and evaluate obstacles that potentially hinder product development and transfer to the bedside. Burn centers and burn care providers will be surveyed to accomplish this objective. The proposal strives to incorporate into the FDA regulatory environment the evolving thinking on practice of burn care to address changing needs, so as to better define the trajectory of needed innovation. This landscape analysis may enable the Agency to be better prepared to provide predictable regulatory pathways. By seeking to identify the hurdles and perceptions that hamper advancement of burn care, this project aligns closely with the newly announced CDRH Innovation Initiative (Feb 2011) as well as the Center's Strategic Priorities for 2011.

Natalie Simpson, Ph.D.

National Center for Toxicological Research

Preceptor: Frederick Beland, Ph.D. and
Igor Pogribny, M.D., Ph.D.

Scientific and Professional Background

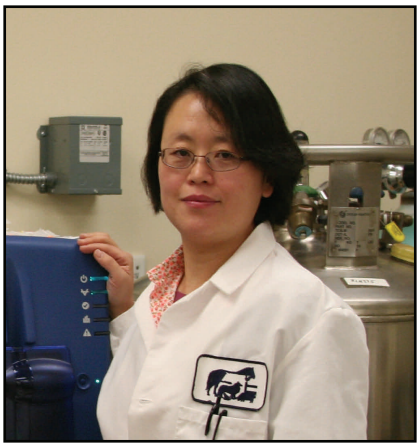
2002-2010 Ph.D. Basic Medical Sciences, New York University
1995-1999 B.S. Biology, Mary Washington College

Research Interests

During my graduate career I became interested in studying the gene expression and epigenetic changes that occur during breast cancer progression. In the laboratory of Dr. Michael Garabedian at NYU, I observed that human breast cancer patients, who express high levels of the Hsp90 co-chaperone p23 protein, are more likely to exhibit lymph node metastases and experience disease recurrence and mortality. Gene expression and epigenetic changes most likely underlie the negative effects associated with higher p23 expression in breast cancer patients, based on results from extensive *in vitro* studies obtained using a human breast adenocarcinoma MCF-7 cell line which, upon p23 overexpression, becomes invasive and drug resistant. For example, the histones at the promoters of many genes upregulated by p23 overexpression are hyperacetylated, including ABCC3, an ATP-dependent cassette transporter responsible for resistance to the chemotherapeutic drugs etoposide and doxorubicin. Additionally, upon p23 overexpression in MCF-7 cells, many metabolic pathways are altered the may affect histone modifications at genes regulating invasion and drug resistance in breast cancer. The focus of my research in the laboratory of Dr. Igor Pogribny at the NCTR will be to further explore the link between metabolism and histone modifications in cancer, as well as characterize the epigenetic changes, including changes in DNA and histone methylation, that occur during cancer progression. The ultimate goal of this work will be to identify biomarkers to improve early diagnosis and predict better therapies for cancer.

Commissioner's Fellowship Project Overview
An in vitro investigation of metabolically sensitive biomarkers in breast cancer progression.

My research centers on *in vitro* identification of protein, genetic, and metabolic biomarkers that can be expanded to the clinic to predict, for breast cancer patients, disease susceptibility and therapeutic response. Results from recent *in vivo* and in *vitro* studies have demonstrated substantial metabolic differences between breast cancers of non-invasive epithelial or invasive mesenchymal origin. We have discovered that the levels of metabolically sensitive epigenetic marks, including acetylated and methylated histones, are distinct between epithelial and mesenchymal cell lines. The significance of this observation is not only that histone modifications influence gene expression, chromatin assembly, and chromosome stability in cancer cells, but that these marks might serve as biomarkers to distinguish between less and more aggressive types of cancers. We have also established a correlation between particular epigenetic modifications and metabolite levels (i.e. glutamine and glutamate) in breast cancer cells. We are exploring, using a combination of metabolomic and molecular, chromatin, and cell biology techniques, the effects that metabolism-associated epigenetic changes have on drug resistance and gene expression, as well as their overall implications in breast cancer diagnosis, prognosis, and treatment.



Wei Song, Ph.D.

Center for Veterinary Medicine

Preceptor: Pak-Sin Chu, Ph.D.

Scientific and Professional Background

2004-2010	Scientist, Ricerca Bioscience, LLC
2008	Ph.D. Clinical-Bioanalytical Chemistry, Cleveland State University
2000-2004	Research Assistant, Cleveland Clinical Foundation
1996-1999	Instructor, Beijing Medical University
1996	B.S. Medicinal Chemistry, Beijing Medical University

Research Interests:

My previous research interests lay in development and application of analytical methodologies for the detection various biomarkers and pharmaceutical molecules in complex matrices by using GC-MS or LC-MS/MS. Coming from a contract research organization (CRO), I truly believe that this FDA commissioner's fellowship provide a great opportunity to receive intensive training in both regulatory science and basic research. This fellowship experience will further develop my expertise in analytical chemistry and allow me to solve the problems that may affect the food safety.

Commissioner's Fellowship Project Overview

A sensitive, high throughput analysis of multiple hormones in fish tissue by LC-MS/MS

Over the past several decades, growth hormones have been used in meat-producing animals to promote animal muscle development, improve meat quality, and increase feed efficiency. Low levels of hormone residues in edible animal tissue may have a significant impact on human puberty and may be associated with cancer development. In 2009, the U.S. imported about 5.2 billion pounds of seafood from Asia, Europe and Canada, which made up 84% of total seafood consumption. To ensure imported seafood safety, an analytical method for the detection of hormones in edible fish muscle at parts per billion levels is needed. This project will address the controversial question regarding the need of enzymatic hydrolysis for determining conjugated residues in muscle tissue. In addition, we will develop and make available a validated analytical method suitable for monitoring illegal use of hormones in fish. Such validated method is critical to understanding and monitoring the safety of food products from animals and will allow the Agency to respond to emerging drug residue problems, to prevent unsafe seafood importation, and to support FDA's fundamental mission of protecting and promoting public health.

Marla Swain, Ph.D.

Center for Veterinary Medicine

Preceptor: Haile F. Yancy, Ph.D.

Scientific and Professional Background

2007-2010	National Research Council Research Associate, Naval Research Lab
2007	Ph.D. Chemistry, Wayne State University
2001	B.S. Chemistry, Wayne State University
1995	B.S. Physiology, Michigan State University

Research Interests

My research experience has primarily involved the use of biomolecules as recognition elements in sensors for the detection of small proteins, neurotoxins and explosives. My graduate work focused on the development of a quantum dot-aptamer biosensor to detect the serine protease thrombin. Another unrelated project involved investigating how geometry (i.e. bond angles and positions of amino acids) plays a role in the formation of crosslinked amino acid cofactors that are formed post translation in metalloenzymes. My postdoctoral research efforts were aimed at using single domain antibodies derived from immunized llamas to detect botulinum neurotoxins A and B, ricin and the explosive compounds PETN and TNT. My laboratory experience ranges from molecular biology and protein chemistry to inorganic synthesis and it is my goal to use my technical experience to promote drug safety and effectiveness.

Commissioner's Fellowship Project Overview

The development of alternative in vitro screening methods for the screening of potentially toxic P-glycoprotein substrates

Certain breeds of dogs, such as Collies, have been observed to experience life-threatening toxicity after the administration of drugs such as avermectins, which are P-glycoprotein (P-gp) substrates. The altered pharmacokinetics of P-gp substrates in the effected dog breeds can be attributed to a mutation in the ABCB1 gene (ABCB1-1Δ) that leads to the expression of non-functional P-gp. As part of the Investigational New Animal Drug (INAD) process, newly introduced avermectins must undergo additional safety studies. These studies, which use Collies with the ABCB1-1Δ mutation, are becoming more difficult to conduct as the number of ivermectin sensitive colonies is decreasing. To address the need for other methods that evaluate P-gp substrate toxicity, we have developed a mouse model expressing the mutated form of the canine ABCB1 gene. This model will be used to assess parallels between the mouse model response to P-gp substrates and the adverse neurotoxic effects observed in ABCB1-1Δ homozygous recessive Collies. Results from this study will be used to investigate *in vitro* methods using cells derived from transgenic mice to assess the toxicity of newly introduced drugs that are P-gp substrates. These *in vitro* methods have the potential to provide the agency with the ability to predict the safety of new drugs without the use of Collie colonies. Furthermore, the objectives of this study are in line with FDA's Critical Path Initiative which involves improving and/or accelerating the approval process so that regulated products reach the market in a timelier manner.

Pavel Zhichkin, Ph.D.

Center for Drug Evaluation and Research

Preceptor: Darrell Abernethy, M.D., Ph.D.

Scientific and Professional Background

2001-2010	Project Leader/Associate Research Fellow, Albany Molecular Reasearch Inc.
1994-2001	Chemist/Senior Research Scientist
1994	Ph.D. Organic Chemistry. Moscow State University
1989	M.S. Chemistry. Moscow State University

Research Interests

My research interests include the prediction, recognition and reporting on adverse effects, including post-marketing surveillance, clinical and pre-clinical pharmacology and regulatory issues in small molecules drug development.

Commissioner's Fellowship Project Overview

Mechanism-based Prediction of Adverse Effects of Kinase Inhibitors

The current pharmacovigilance approach is to passively observe the postmarketing or trial signals of excess adverse drug reactions for the drug. A candidate signal is then studied from the point of statistical strength and mechanistic plausibility. The goal of my project is to develop a pro-active approach in which the mechanism of action of the drug is characterized using state-of-the-art cheminformatics, bioinformatics, network and mechanistic approaches helping inform the subsequent pharmacovigilance thus improving its sensitivity and specificity. We are planning to show the possibility of mechanism-based prediction of adverse effects of kinase inhibitor drugs based on their structure and available in vitro data (primarily kinase inhibition and other receptor screening profiles) and to try to quantify the advantages of the method as compared with random and best-guess (based on previous examples) approaches.

FDA Commissioner's Fellowship Program

2010 Preceptors

Darrell Abernethy, M.D., Ph.D.

Office of Clinical Pharmacology
Center for Drug Evaluation and Research

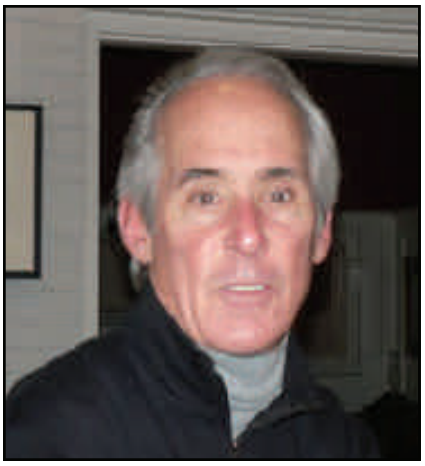
Fellow: Pavel Zhichkin, Ph.D.

Scientific and Professional Background

M.D., Ph.D. in Pharmacology
Academic Teaching and Research in Clinical Pharmacology
Clinical Training in Internal Medicine and Geriatrics

Research Interests

Use of pharmacological mechanisms to predict drug safety. Development of systems biology approaches to predict risk from drug exposure. Benefit/risk of drug use in older patients (>85 years).



Frederick Beland, Ph.D.

Division of Biochemical Toxicology
National Center for Toxicological Research
Jefferson, AR

Fellow: Natalie Simpson, Ph.D.

Scientific and Professional Background

B.A. Colorado College
M.S. Montana State University
Ph.D. Montana State University
FDA experience—33 years

Research Interests

The role of genetic and epigenetic changes in the etiology of cancer.

Zbigniew Binienda, Ph.D.

Head, Neurophysiology Laboratory
Division of Neurotoxicology
National Center for Toxicological Research
Jefferson, AR

Fellow: Syed Imam, Ph.D.

Scientific and Professional Background

D.V.M.
Ph.D.
FDA experience—19 years

Research Interests

Mitochondrial dysfunction, brain hypoxia, neurotransmitter systems, nanoparticles, neuroimaging, neurotoxicity

Jamie Boehmer, Ph.D.

Office of Research
Division of Animal Research
Center for Veterinary Medicine

Fellow: Zohra Olumee-Shabon, Ph.D.

Scientific and Professional Background

B.S. University of Maryland
M.S. Virginia Polytechnic Institute and State University
Ph.D. University of Maryland
FDA experience—6 years

Research Interests

Dr. Boehmer's primary research focus is the application of mass spectrometry-based proteomic approaches to the analysis and quantification of differential protein expression in complex biological matrices for the discovery of candidate biomarkers of disease in food animals. Dr. Boehmer's research supports efforts in the Office of New Animal Drug Evaluation (ONADE) to identify biomarkers that could be used to evaluate the efficacy of new veterinary drugs, especially drugs intended for use in food animals that have anti-inflammatory claims. Specific studies have involved the identification of biomarkers of coliform mastitis in bovine milk, as well as the evaluation of antimicrobial peptides present in bovine bronchial fluid during pneumonia. Analyses are currently being conducted to evaluate the response of candidate biomarkers to drug administration, which could facilitate the use of biomarkers to assess drug efficacy, and could lead to the approval of new veterinary drugs for use in food animals.

Andrew Byrnes, Ph.D.

Division of Cellular and Gene Therapies
Office of Cellular, Tissue and Gene Therapies
Center for Biologics Evaluation and Research

Fellow: Gina Conenello, Ph.D.

Scientific and Professional Background

B.S. , M.S. Yale University
Ph.D. University of Oxford
FDA experience—9 years

Research Interests

Adenoviruses are common DNA viruses that can be engineered to create non-replicating gene therapy vectors. There are close to 100 clinical trials in the US that use adenovirus vectors for gene delivery or anti-tumor therapy. Administering these vectors through the vascular system would be an ideal route in many situations, potentially allowing adenovirus vectors to target a variety of tissues or widely-disseminated metastatic tumors. One significant barrier is that adenovirus vectors are quickly cleared from the circulation by macrophages in the liver, which limits the amount of vector that can reach the intended target. We have recently identified the cellular receptors and processes that are responsible for this vector clearance, and further work is centered on how to design vectors that evade these receptors. Another difficult barrier to gene therapy with adenovirus vectors is the body's ability to detect virus-based vectors through the innate immune system, which can trigger a variety of potentially dangerous responses. We are studying macrophages, cytokines, complement and other types of mediators to learn why they have an innate ability to recognize and respond to adenovirus vectors. Our long term goal is to develop vectors that are safer and more effective.

Tao Chen, Ph.D., D.A.B.T.

Division of Genetic and Reproductive Toxicology
National Center for Toxicological Research
Jefferson, AR

Fellow: Xinrong Chen, Ph.D.

Scientific and Professional Background

B.S. Biology
M.S. Biology
Ph.D. Toxicology
American Board of Toxicology Diplomat
FDA experience—9 years

Research Interests

Mutagenesis and carcinogenesis, especially in early biomarkers for carcinogen exposure using mutation detection and analysis and gene expression analysis of mRNA and microRNA.

Seungil Cho, Ph.D.

Office of Science and Engineering Laboratories
Division of Chemistry and Material Science
Center for Devices and Radiological Health

Fellow: Yongsoo Choi, Ph.D.

Scientific and Professional Background

B.S. Chemistry, Seoul National University
M.S. Chemistry, Seoul National University
Ph.D. Chemistry, Seoul National University

Research Interests

Recently, the public has shown great concern over the release of xenoestrogens such as bisphenol A (BPA) from plastics. The xenoestrogenic activity of BPA is known to be critical in developing children. Its impact will be even more critical in pediatric patients who require BPA-based medical devices that have direct contact with the blood stream. Our current research project will develop analytical chemical methods to assess the level of BPA exposure from various pediatric medical devices. This project will help the FDA to establish appropriate regulation for BPA-based medical devices, to find alternative materials, and to understand release of hazardous chemicals from medical devices made of other polymers.

Pak-Sin Chu, Ph.D.

Division of Residue Chemistry
Center for Veterinary Medicine

Fellow: Wei Song, Ph.D.

Scientific and Professional Background

B.S. University of California, Davis
M.S. University of California, Davis
Ph.D. University of California, Davis

Research Interests

Dr. Chu's research focuses on analytical method development for drug residues in biological matrices and on their metabolism and disposition in animals. His current research efforts are aimed at developing analytical methodologies for hormones and for their metabolites. Conventional methods of determining hormone residues typically involve an initial hydrolysis of the phase II conjugates followed by derivatization and detection on gas chromatography–mass spectrometry. Information concerning the identity of the conjugates (glucuronides or sulfates), however, is lost after hydrolysis. For this reason, Dr. Chu is investigating new approaches of detecting and quantifying the intact phase II conjugates using liquid chromatography–tandem mass spectrometry.

Maureen Davidson, Ph.D.

Office of Research
Division of Animal and Food Microbiology
Center for Veterinary Medicine

Fellow: Maria Cruz-Fisher, Ph.D.

Scientific and Professional Background

M.S. MT (ASCP)
Ph.D. MT (ASCP)
FDA experience—3 years

Research Interests

Infectious diseases; Microbiology; Immunology; Host-parasite relationships in infectious diseases; virulence mechanisms of microorganisms; host defense mechanisms; development of diagnostic tests for infectious diseases of animals

Charles Durfor, Ph.D.

Division of General, Restorative and Neurological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Fellows: Alexander Bailey, Ph.D. and
Rebecca Robinson, Ph.D.

Scientific and Professional Background

B.S. College of William & Mary
Ph.D. University of Virginia

Research Interests

Since 1994, Dr. Durfor has served within the Center for Devices and Radiological Health's Office of Device Evaluation as Scientific Reviewer and IDE/PMA Team Leader in the Plastic and Reconstructive Surgery Branch. In this role he performed and supervised the review of the first cellular medical devices to receive FDA approval as well as other products composed of protein, polysaccharide and biomimetic components that are used to treat a diverse array of indications (e.g., wound repair, surgical adhesion prophylaxis, and cosmetic correction of soft tissue defects).

Steven Foley, Ph.D.

Division of Microbiology
National Center for Toxicological Research
Jefferson, AR

Fellow: Kuppan Gokulan, Ph.D.

Scientific and Professional Background

B.S. North Dakota State University
Ph.D. North Dakota State University
FDA experience—9 years

Research Interests

My research interests are largely been in the fields of bacterial pathogenesis, zoonoses, food safety, and molecular methods for pathogen characterization. Specific areas of interest include understanding the distribution of enteric pathogens, and their virulence and antimicrobial resistance factors in food production environments. By understanding the distribution mechanisms of pathogens, we may be able to develop interventions to reduce the spread of pathogenic microorganisms from food sources to humans. I am also interested in the development of methods to better understand the contribution of plasmid encoded genes to enhanced bacterial function. Plasmids are capable of horizontal gene transfer, which could facilitate the spread of antimicrobial resistance and increased virulence among bacteria leading to more difficult to treat infections. Thus a more comprehensive understanding of plasmid genetics and associated physiology should ultimately lead to improved public health.

James Fuscoe, Ph.D.

Director, Center for Functional Genomics
Division of Systems Toxicology
National Center for Toxicological Research
Jefferson, AR

Fellow: Yun Ge, Ph.D.

Scientific and Professional Background

Ph.D. University of Tennessee
FDA experience—8 years

Research Interests

The Center for Functional Genomics uses high-information content genomics technologies (e.g., expression microarrays, array CGH/SNP arrays) in the development of mechanistic and biomarker data to support improved safety assessments. Whole-genome commercial arrays, as well as in-house fabricated custom microarrays, show great promise in drug-safety evaluation, and FDA is actively encouraging this new technology. Major efforts include: (1) discovery and validation of preclinical predictive toxicology biomarkers, (2) development and application of new high-throughput tools, and (3) serving as an FDA resource for genomics issues. Of particular interest are (1) the translation of non-clinical predictive biomarkers to the clinic and (2) the global integration of genomic, proteomic, and metabolomic information for a systems toxicology approach to biomarker development.

John Gardner, M.D., Dr.P.H.

Office of Information Management
Office of the Commissioner

Fellow: Xingfang Li, M.D.

Scientific and Professional Background

M.S. Brigham Young University
M.P.H. Harvard University
M.D. University of Utah
Dr.P.H. Harvard University
FDA experience—5 years

Research Interests

Data systems for epidemiologic research and regulatory purposes to enhance public health and protection.

Joga Gobburu, Ph.D.

Division of Pharmacometrics
Office of Clinical Pharmacology
Office of Translational Sciences
Center for Drug Evaluation and Research

Fellow: Michael Bewernitz, Ph.D.

Scientific and Professional Background

FDA experience—10+ years

Research Interests

Learn-Apply' approach to drug development and regulatory decision making. Quantitative Clinical Pharmacology or Pharmacometrics. .Modeling and simulation of clinical trials. Clinical trial design. Dose optimization using Pharmacometrics. Quantifying the influence of policies and regulations

Peter Goering, Ph.D.

Laboratory of Toxicology
Division of Biology
Office of Science and Engineering Laboratories
Center for Devices and Radiological Health

Fellow: Martha Betz, Ph.D.

Scientific and Professional Background

Ph.D. Kansas University Medical center
Academy if Toxicological Sciences Fellow
FDA experience—23 years

Research Interests

The properties of nanomaterials - such as small size, large surface area, and high reactivity - that impart tremendous potential for technological advances are also the very properties that may be responsible for adverse clinical effects. There is a paucity of safety information and our lab is therefore focused on the physicochemical characterization of nanomaterials, identifying methods to assess potential hazards, understanding adverse biological effects, and characterizing absorption and tissue distribution in laboratory animal models and humans. This knowledge base is critical in order to develop a more consistent and predictable regulatory pathway for addressing issues of safety and efficacy of nano-based medical products.

Luisa Gregori, Ph.D.

Division of Emerging and Transfusion Transmitted Diseases
Officer of Blood Research and Review
Center for Biologics Research and Evaluation

Fellow: Julie Nemecek, Ph.D.

Scientific and Professional Background

Ph.D. University of Camerino, Italy
Post-Doctoral Fellowship, University of Florida, Gainesville, FL
FDA experience—1 year

Research Interests

Creutzfeldt-Jakob disease (CJD) and its variant (vCJD) are rare, fatal, neurodegenerative disorders known as transmissible spongiform encephalopathies (TSEs), or prion diseases. The nature of the agents causing TSEs and their mechanism of replication are still controversial issues. TSEs are transmissible by blood and blood and tissue products, but there is no ante-mortem test to screen donors. Our research focuses on TSE agents in blood with the final goal of reducing transfusion transmission risks and improving the safety of the blood supply. Specifically, we are interested in how infectivity is transmitted and replicates in blood, what blood components harbor infectivity, how to screen for infected blood donations and how to remove the infectious agent from blood. TSE assays are technically challenging, and traditional approaches have failed so far. We are testing a promising alternative technology called protein misfolding cyclic amplification (PMCA) that may have sufficient sensitivity to detect PrPTSE, the surrogate marker for infectivity, in plasma. We are also producing large panels of monkey plasma samples infected with vCJD agent as biological reference standards to validate blood screening tests. Our efforts to removal TSE infectivity from blood use affinity ligands immobilized on beads assembled into filter devices. In all our studies, we use experimental animal models to measure infectivity in blood, including examination of neuropathological changes in brains of the animals to confirm TSE.

Thomas Gross, M.D., M.P.H.

Director, Division of Postmarket Surveillance
Office of Surveillance and Biometrics
Center for Devices and Radiological Health

Fellow: Xueying Liang, Ph.D.

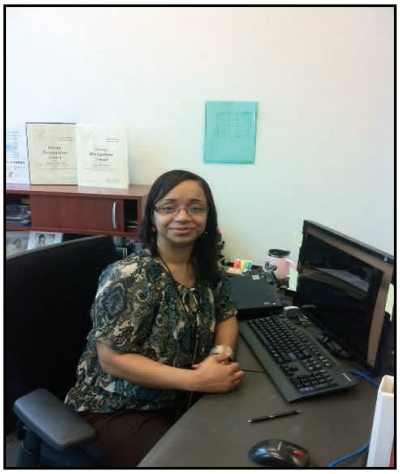
Scientific and Professional Background

M.D. University of Colorado Health Sciences Center
M.P.H. Johns Hopkins University School of Hygiene and Public Health

Research Interests

My interests have focused on building postmarket infrastructure and capabilities to provide general, and product-specific, surveillance and epidemiologic means to monitor and evaluate the performance of medical devices once approved for marketing. To that end, our Division has explored/implemented innovative surveillance methods, established a robust post-approval study program (largely based on observational studies), and is building a viable applied research program. We are leaders in medical device surveillance and epidemiology, and are the editors/authors of the first book on the subject (Medical Device Epidemiology and Surveillance).

In March 2008, the FDA announced its Sentinel Initiative. The initiative calls for establishing major public-private partnerships to provide the national infrastructure and capability to optimally monitor and evaluate the safety of FDA-regulated products, including medical devices. There is a need to develop a national infrastructure to effectively understand the postmarket performance of orthopedic implants (e.g., total hip or knee replacements). Complementary efforts have to be explored and developed to create a nationally-distributed network of implanting institutions to begin to provide both short- and long-term (through linked databases) national profiles of device-specific performance.



Tiffany Harmon

Branch Director, Atlanta Center for Nutrient Analysis
Southeast Regional Laboratory
Office of Regulatory Affairs
Atlanta, GA

Fellow: Soo Kwang Lee, Ph.D.

Scientific and Professional Background
B.A. State University of New York College at Buffalo
FDA experience — 19 years

Research Interests
As Branch Director of the Atlanta Center for Nutrient Analysis, I currently oversee method development projects related to vitamin and nutrient analysis of infant formulas and medical foods.

Mark Hart, Ph.D.

Division of Microbiology
National Center for Toxicological Research
Jefferson, AR

Fellow: Haijing Hu, Ph.D.

Scientific and Professional Background

B.S. Ouachito Baptist University
M.S. Oklahoma State University
Ph.D. Mississippi State University
FDA experience—7 years

Research Interests

Despite advancement of antimicrobial regimens and improved public health, Staphylococcus aureus, a gram-positive bacterium that resides on the skin and mucous membranes of approximately 30% of healthy individuals and as high as 90% of health care workers, remains an important bacterial pathogen responsible for numerous disease syndromes in humans and animals worldwide. Just as important is the continual rise in the number of methicillin (oxacillin)-resistant S. aureus (MRSA) not only in isolates acquired in hospitals, but also those encountered in the community. Because S. aureus is notorious for acquiring multiple antibiotic resistance determinants, it has become increasingly important that alternatives other than antibiotic therapy be developed for the prevention and treatment of diseases caused by S. aureus. In order to develop an alternative approaches, we believe a comprehensive analysis of all extracellular proteins produced by a number of representative S. aureus strains is required. Our recent efforts have utilized one-dimensional SDS-PAGE and nano liquid chromatography coupled with mass spectrometry in tandem to generate a comprehensive extracellular protein profile for S. aureus UAMS-1, a clinical osteomyelitis isolates, and its agr and sarA global regulator mutants. This approach has identified several differences with respect to the abundance of certain proteins which are now under investigation as to their role in virulence and whether or not these proteins could be used as potential targets for the development of therapies for the treatment of disease caused by S. aureus.

Lauren Jackson, Ph.D.

Office of Food Safety
Division of Food Processing Science and Technology
Food Chemistry and Nutrition Team
Center for Food Safety and Applied Nutrition
Bedrock Park , IL

Fellow: Elizabeth Grasso, Ph.D.

Scientific and Professional Background

B.S. Cornell University
M.S. University of Wisconsin-Madison
Ph.D. University of Wisconsin-Madison
FDA experience—18 years

Research Interests

Effects of processing on the formation, destruction and detection of natural toxins and chemical contaminants; Effects of processing on bioactive food components; Developing best practices for detecting and controlling food allergens and microbial pathogens in food manufacturing facilities.

Hiranthi Jayasuriya, Ph.D.

Division of Residue Chemistry
Center for Veterinary Medicine

Fellow: Kande Amarasinghe, Ph.D.

Scientific and Professional Background

Ph.D. University of Mississippi
2008 FDA Commissioner's Fellow

Research Interests

Structure elucidation of unknown metabolites, and metabolic profiling of steroids in animal tissue using the high resolution capabilities of the Q-TOF mass spectrometer. Validation of sensitive methods to analyze for steroid residues at lower ppb level in animal tissues by LC/MS/MS. Synthesis of analytical standards of steroidal analogs that is not commercially available.

John Larkin, Ph.D.

PEB/DFPST/OFS
Center for Food Safety and Applied Nutrition
Summit-Argo, IL

Fellow: Hongliu Ding, Ph.D.

Scientific and Professional Background

B.S. Food Science
M.S. Food Science
Ph.D. Food Engineering
FDA experience—22 years

Research Interests

Processing factors effecting extended shelf life of food,. New preservation technology. Software validation criteria for computerized process control systems. Validating low-acid canned food processing systems. Pasteurization processing for juice and tree nuts. Aseptically processed foods containing particulates.

Ellen Lazarus, M.D.

Captain, U.S. Public Health Service
Director, Division of Human Tissues
Office of Cellular, Tissue, and Gene Therapies
Center for Biologics Research and Evaluation

Fellow: Yun-Shang Piao, Ph.D.

Scientific and Professional Background

FDA experience—10 years

Research Interests

Blood and cell therapy product recovery technologies and effects on donors; in vitro assays for assessment of cell product characterization and potency.

Stefano Luccioli, M.D.

Office of Food Additive Safety
Center for Food Safety and Applied Nutrition

Fellow: Ernest Kwegyir-Afful, Ph.D.

Scientific and Professional Background

M.D, Georgetown University
FDA experience—7 years

Research Interests

Scientific policy-focused research on food allergies. Understanding health risks associated with low level food allergen exposures. Evaluating consumer databases to quantify allergenic hazards from food.

I am currently the program lead for CFSAN's Strategic Research Plan on food allergens. I also have clinical research affiliations at Georgetown University and have bench research experience with animal models of asthma

Markham Luke, M.D., Ph.D.

Clinical Deputy Office Director
Office of Device Evaluation
Center for Devices and Radiological Health

Fellow: Maryam Mokhtarzadeh, Ph.D., and
Suzanne Schwartz, Ph.D.

Scientific and Professional Background

M.D., Ph.D. Johns Hopkins University
Council for Excellence in Government Fellow
FDA experience—11 years

Research Interests

The Office of Device Evaluation, Center for Devices and Radiological Health (CDRH) conducts premarket review of cutting edge therapeutic and diagnostic device technologies. This component of the FDA evaluates the safety and effectiveness of new medical devices prior to their introduction into the marketplace. Dr. Luke has research interests in clinical study design, clinical endpoints assessment, and scale development (including patient-reported outcomes) for both efficacy and safety determination of medical products. Specific attributes of medical devices and their impact on blinding and variability when used in the hands of clinicians and impact on clinical trial validity and outcome are currently being assessed.

Rajanikanth Madabushi, Ph.D.

Office of Clinical Pharmacology
Center for Drug Evaluation and Research

Fellow: Tzu-Yun Chang-McDowell, Ph.D.

Scientific and Professional Background

FDA experience—4 years

Research Interests

1. Use of quantitative approaches to characterize the benefit-risk of prescription drugs to patients receiving new prescriptions.
2. To develop a model of the public health implications of different patterns for using antihypertensive drugs.
3. To optimize trial design for studying anti-hypertensives in pediatrics using modeling and simulation techniques.

Elias Mallis, B.S.

Chief, Cardiac Electrophysiology and Monitoring Devices
Division of Cardiovascular Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Fellows: Alexander Bailey, Ph.D.
and Rebecca Robinson, Ph.D.

Scientific and Professional Background

B.S. University of Maryland
FDA experience—15 years

Research Interests

As Branch Chief of the Cardiac Electrophysiology and Monitoring Branch of the Division of Cardiovascular Devices (DCD) in the Center for Devices and Radiological Health, Mr. Mallis has primary oversight for the regulatory review science evaluation of cardiovascular medical devices, including those which feature combinations of biologics and medical devices.

Danica Marinac-Dabic, M.D., Ph.D.

Director, Division of Epidemiology
Office of Surveillance and Biometrics
Center for Devices and Radiological Health

Fellow: Xueying Liang, Ph.D.

Research Interests

Three postmarket programs at CDRH: (1) Post-Approval Studies Program, that encompasses the design, review, monitoring and oversight of the post-approval studies mandated as a condition of approval; (2) Postmarket Surveillance Studies Program, in charge of postmarket studies mandated under Section 522 of the Act; and (3) Epidemiologic Research Program, designed to augment medical device regulatory research infrastructure and conduct independent epidemiologic research studies to ensure CDRH science-based regulatory decision making.

William Martin, Ph.D.

Pacific Regional Laboratory Southwest
Office of Regulatory Affairs
Irvine, CA

Fellow: Sarah Pierce, Ph.D.

Scientific and Professional Background

B.S. University of South Florida
Ph.D. University of South Florida
FDA experience—12 years

Research Interests

Strategic Improvement in Technology, Methodology and Capabilities involving Regulatory Biological/Microbiological Mass Spectrometry

Akhilesh Nagaich, Ph.D.

Division of Therapeutic Proteins
Office of Biotechnology Products
Office of Pharmaceutical Sciences
Center for Drug Evaluation and Research

Fellow: Sudipan Karmakar, Ph.D.

Scientific and Professional Background

Ph.D. Chemistry
FDA experience—4 years

Research Interests

The development of epigenetic therapies for cancer is one of the most actively emerging areas in clinical oncology. Epigenetic processes such as chromatin remodeling, DNA methylation, histone acetylation and RNAi-mediated gene silencing play a central role in the genesis of most cancers. Many cancer therapies targeting these processes are under development to optimize the treatment outcome of both hematopoietic malignancies and solid tumors. Despite major advances in pre-clinical findings, the majority of cancer therapies fail in clinical trials due to severe toxicity and off-target effects. Our long-term goal is to identify biomarkers to maximize the predictive value of preclinical data supporting clinical trials in cancer epigenetic therapies. The acquired information will aid in making more informed review decisions with respect to safety, efficacy and dosing of these drugs.

Srinidhi Nagaraja, Ph.D.

Office of Science and Engineering Laboratories
Division of Solid and Fluid Mechanics
Center for Devices and Radiological Health

Fellow: Shikha Gupta, Ph.D.

Scientific and Professional Background

Ph.D. Georgia Institute of Technology
M.S. Georgia Institute of Technology
B.S. University of Michigan

Research Interests

The Division of Solid and Fluid Mechanics (DSFM) within the Office of Science and Engineering Laboratories (OSEL) have three main research groups: solid mechanics, fluid mechanics, and ultrasonics. Within the solid mechanics group, our research projects are focused on investigating the root causes of failure in traditional and emerging medical products to help prevent future major adverse events. Current interests in this group are (1) Development of test methods to evaluate the effect of mechanical loading on bioabsorbable medical implants and (2) The effects of vertebroplasty devices on adjacent level fracture in women and (3) Investigation of factors resulting in mechanical failure of overlapped stents in swine.

Robert "Skip" Nelson, M.D., Ph.D.

Pediatric Ethicist
Office of Pediatric Therapeutics
Office of the Commissioner

Fellows: Jason Gerson, Ph.D. and Patricia Bright, Ph.D.

Scientific and Professional Background

B.A. Wesleyan University
M.D. Yale University School of Medicine
M.Div. Yale Divinity School
Ph.D. Harvard University
FDA experience—3 years

Research Interests

My research has focused on two broad areas of pediatric research ethics: the ethical aspects of pediatric clinical investigations involving FDA regulated products, and empirical investigations into different aspects of parent and child decision-making concerning research participation. At FDA, specific areas of interest include ethical aspects of different trial designs, the choice of control groups (including placebo controls), the use of animal models, the assessment of research risks and the possibility of direct benefit, and ethical aspects of international pediatric research. My academic research has focused on risk perception, voluntary choice, and the balancing of risks and potential benefits in making a decision about the design of clinical trials. My academic research has been funded by the Greenwall Foundation, the National Science Foundation, and the National Institutes of Health.

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

Division of Biochemical Toxicology
National Center for Toxicology Research
Jefferson, AR

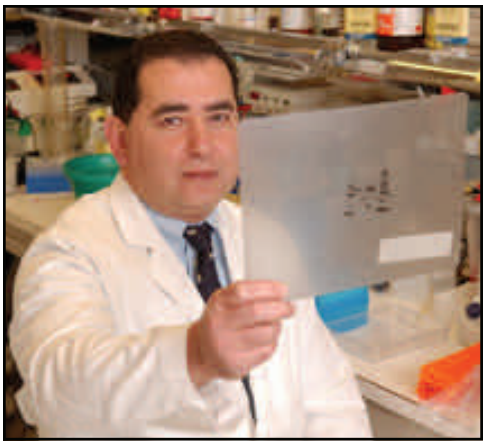
Fellow: Natalie Simpson, Ph.D.

Scientific and Professional Background

M.D. Ivano-Frankivsk Medical University
Ph.D. Kyiv National Medical University
FDA experience—18 years

Research Interests

The role of genetic and epigenetic changes in the etiology of cancer.



Jack Ragheb, M.D., Ph.D.

Laboratory of Immunology
Division of Therapeutic Proteins
Office of Biotechnology Products
Center for Drug Evaluation and Research

Fellow: Kristina Howard, D.V.M., Ph.D.

Scientific and Professional Background

M.D. John Hopkins University
Ph.D. John Hopkins University

Research Interests

Human Immunology, Immune Tolerance, and the Immunogenicity of Biologic Therapeutics. My labs research program represents a union of my long-standing interest in immune activation and immune tolerance with the regulatory mission of the Agency to understand the immunogenicity of biologic therapeutics and to develop means of circumventing it, including the induction of immune tolerance. Our studies encompass 3 of 5 research disciplines identified by the Agency as centrally important to our regulatory mission; manufacturing science, safety (immunogenicity), and biological characterization (cellular targets).

Jakob Reiser, Ph.D.

Division of Cell and Gene Therapies
Center for Biologics Evaluation and Research

Fellow: Seraphin Kuate, Ph.D.

Scientific and Professional Background

B.S. University of Zurich, Switzerland
Ph.D. University of Basel, Switzerland
FDA experience—2 years

Research Interests

Lentiviruses are complex retroviruses that include human immunodeficiency viruses such as HIV-1. We are working on the design of safer lentiviral vectors for transgene delivery in vitro, ex vivo and in vivo. A special emphasis is on targetable vectors for cell-specific transduction and on vectors capable of site-specific integration.

Berkman Sahiner, Ph.D.

Office of Science and Engineering Laboratories
Division of Imaging and Applied Mathematics
Center for Devices and Radiological Health

Fellow: Omer Demirkaya, Ph.D.

Scientific and Professional Background

B.S. Middle East Technical University
Ph.D. University of Michigan

Research Interests

The FDA evaluates computer aided diagnosis (CAD) devices that are intended for clinical use for their safety and effectiveness. Dr. Sahiner has been performing research on the design and evaluation of CAD devices for the past 16 years. He is an author or co-author of over 80 peer-reviewed journal articles on related areas. He has recently been active in the design of observer performance studies with radiologists to evaluate CAD systems for the detection of lung nodules on computerized tomography (CT) images and the characterization of breast masses as malignant or benign on ultrasound images. He has also been active in the design of CAD algorithms, development of methodologies to evaluate the outcomes of observer performance studies and computer classifiers. His research goals include the improvement of methodologies for the performance assessment of CAD devices and the performance assessment of radiologists assisted in the clinic with CAD.

William Salminen, Ph.D., D.A.B.T.

Director of the Center for Hepatotoxicity
Division of Systems Toxicology
National Center for Toxicological Research
Jefferson, AR

Fellow: Akhtar Ali, Ph.D.

Scientific and Professional Background

B.A. University of Rochester
Ph.D. University of Florida

Research Interests

The Center for Hepatotoxicology addresses critical liver-injury issues by applying a systems-toxicology approach. The goal is to improve the identification of hepatotoxic compounds prior to human exposure and to augment the detection of early signs of injury in humans induced by drugs, chemicals, and disease processes. Biomarkers will be identified using integrated genomics, metabolomics, proteomics, and bioinformatics approaches. In order to ensure that the integrated approach addresses real-world FDA needs, a broad working group was formed consisting of experts in preclinical and clinical liver toxicity.

Joy Samuels-Reid, M.D.

Chief Medical Officer
Office of Device Evaluation
Division of Anesthesiology, General Hospital, Infection Control and Dental Devices
Center for Devices and Radiological Health

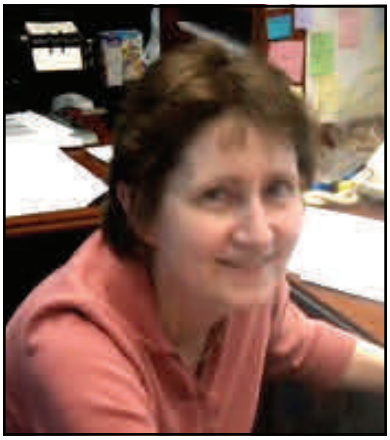
Fellow: Brenda Lawrence, M.D.

Scientific and Professional Background

M.D. College of Medicine, Howard University
Residency—Pediatrics; Fellowship—Sickle hemoglobinopathies
Fellow of the American Academy of Pediatrics

Research Interests

The Office of Device Evaluation in CDRH conducts premarket review of cutting edge therapeutic and diagnostic device technologies. This component of the FDA evaluates the safety and effectiveness of new medical devices prior to their introduction into the marketplace. In ODE's Division of Anesthesiology, General Hospital, Infection Control and Dental Devices, Dr. Samuels-Reid focuses on medical devices for the pediatric population.



Mercedes Serabian, M.S., D.A.B.T.

Chief, Pharmacology/Toxicology Branch
Division of Clinical Evaluation and Pharmacology/Toxicology
Office of Cellular, Tissue and Gene Therapies
Center for Biologics Evaluation Research

Fellows: Alexander Bailey, Ph.D.
and Rebecca Robinson, Ph.D.

Scientific and Professional Background

B.S. Virginia Polytechnic Institute and State University
M.S. American University
American Board of Toxicology Diplomat

Research Interests

The numerous products regulated by the Office of Cellular, Tissue, and Gene Therapies (OCTGT) include gene therapy (ex vivo transduction of cells and direct injection of product), tumor vaccines, xenotransplantation, human stem cells (embryonic, fetal, and adult), various human tissue preparations (fetal and adult), combination products (biologic-drug, biologic-device, etc…), and tissue engineered tissues. By law, each investigational product must be shown to be adequately safe, usually via the conduct of in vitro studies and/or in vivo studies in animals (termed 'preclinical'), for administration into humans with targeted diseases/injuries; however, this pathway for many of these products have few/no precedents to guide in the comprehensive assessment of safety. Ms. Serabian is responsible for overseeing the preclinical review, regulation, and policy development for all cell and gene therapy products that are under the regulatory purview of OCTGT/CBER. She leads an expert group of scientists that are responsible for the scientific review of all preclinical studies submitted to OCTGT in support of their safe use in human trials. This group interacts with individuals in Center for Devices and Radiological Health (CDRH) in the preclinical review of certain product that include tissue engineered products and regenerative medicine products, and biologic-device combinations. Areas of interactions with CDRH have included cardiac/vascular, orthopedic, and neurological. She is also the representative for CBER/FDA in the expert working groups for the International Conference on Harmonisation (ICH), providing expert input on the preclinical (Safety) guidelines that are published. She has also initiated a series of discussion between CBER pharmacology/toxicology staff and members of the Biotechnology Industry Organization (BIO), who are responsible for the preclinical testing of investigational biologics. She actively participates and oversees the participation of reviewers in her groups as representatives of OCTGT at intracenter, intercenter, interagency, national, and international meetings, workshops, and symposiums in the area of cellular and gene therapy.

Mate Tolnay, Ph.D.

Division of Monoclonal Antibodies
Office of Biotechnology Products
Center for Drug Evaluation and Research

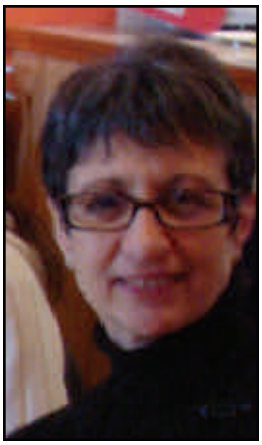
Fellow: Bazarragchaa Damdinsuren, Ph.D.

Scientific and Professional Background

M.S., Ph.D., Eotvos Lorand University, Budapest, Hungary
Uniformed Services University, Bethesda, Maryland
Research Assistant Professor, 1997-2004
FDA experience—5 years

Research Interests

B cells produce antibodies that mark pathogens for elimination. B cell activation is controlled at multiple steps through dynamic engagement of an array of receptors, ensuring adequate responses to clear pathogens yet avoiding excessive or autoimmune responses. The recent discovery of six Fc-receptor like (FCRL) proteins with signaling potential and preferential B lineage expression has considerably broadened the network of possible lymphocyte co-receptors. Importantly, FCRL are implicated in tumor development and autoimmunity. Due to their restricted expression on specific subsets of B cells, FCRL are also potential new tumor markers and candidate targets of tumor immunotherapy. Our laboratory has been investigating the regulation of FCRL gene expression and the functional roles of FCRL proteins. One current focus is to identify onco-viruses and oncogenes that perturb FCRL gene expression. Better understanding of the functions and transcriptional regulation of FCRL will help define the role of FCRL in tumor formation and progression. In addition, we aim to identify proteins that interact with FCRL5 either as ligands or as cellular proteins, in order to illuminate FCRL5 function. Better understanding of the functions and transcriptional regulation of FCRL will help define the role of FCRL in disease initiation and progression. Results of this work can: (1) Facilitate review of products targeting FCRL and related targets on B-lymphocytes, (2) Provide insight into mechanisms that lead to deregulated FCRL protein expression in diseased cells, (3) Elucidate the specific contributions of viral proteins and host oncogenes to cancer, and (4) Help with predicting potential adverse effects that may result if normal B cells are affected by therapies that target FCRL molecules.



Mary Lou Tortorello, Ph.D.

Office of Food Safety
Division of Food Processing Science and Technology
Center for Food Safety and Applied Nutrition
Summit-Argo, IL

Fellow: Annemarie Buchholz, Ph.D.

Scientific and Professional Background

B.S. Northern Illinois University
M.S. Loyola University of Chicago
Ph.D. Cornell University
FDA experience—18 years

Research Interests

Behavior of microorganisms in foods and food processing environments; mechanisms of control for ensuring microbiological safety of foods; development of improved methods for sampling, sample preparation, detection, and identification of microorganisms in foods and food processing environments.

Donna Williams-Hill, Ph.D.

Pacific Regional Laboratory Southwest
Office of Regulatory Affairs
Irvine, CA

Fellow: Rosalee Hellberg, Ph.D.

Scientific and Professional Background

B.S. Northern Illinois University
M.S. Illinois Institute of Technology
Ph.D. University of Southern California
FDA experience—9 years

Research Interests

Projects centering on the development of molecular methods to detect pathogens in foods:

1. Detection of high risk pathogens (select agents) including Bacillus anthracis, Yersinia pestis and Francisella tularensis using BSL-3 safety procedures;

2. Detection of low levels of E. coli O157:H7 internalized in leafy greens using qPCR;

3. Use of magnetic bead technology to detect Hepatitis A in food matrices.

Nancy Xu, M.D.

Division of Cardiovascular and Renal Products
Office of New Drugs I
Center for Drug Evaluation and Research

Fellow: Zenghui Mi, M.D., Ph.D.

Scientific and Professional Background

FDA experience—2 years

Research Interests

1. To improve tools to quantify and predict dose-related adverse event risk in patients with impaired renal function.

2. To develop novel predictive models of drug safety and efficacy in patients with impaired kidney function.

3. To streamline clinical trials in drug development from better quantification and prediction of dose-related safety and efficacy outcomes in the chronic kidney disease population.

Haile Yancy, Ph.D.

Division of Animal Research
Office of Research
Center for Veterinary Medicine

Fellow: Marla Swain, Ph.D.

Scientific and Professional Background

B.S. Jarvis Christian College
Ph.D. Howard University
FDA experience—10 years

Research Interests

Molecular biomarker discover and molecular assay development.

Food and Drug Administration
COMMISSIONER'S
Fellowship Program
Protecting Public Health
Through Science and Regulation

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