#### **CURRICULUM VITAE**

# Patricia Elaine Ganey, Ph.D.

#### **CURRENT ADDRESS:**

Patricia Elaine Ganey, Ph.D.

Professor

Department of Pharmacology and Toxicology

Center for Integrative Toxicology

1129 Farm Lane

214 Food Safety and Toxicology Building

Michigan State University

East Lansing, MI 48824

T: 517-432-1761 F: 517-432-2310 ganey@msu.edu

#### **EDUCATION:**

1981-1986 Doctor of Philosophy

Pharmacology and Toxicology-Environmental Toxicology

Michigan State University East Lansing, MI 48824

Thesis title: The Role of the Platelet and Platelet Mediators in the

Pulmonary Hypertensive Response to Monocrotaline Pyrrole

1976-1979 Bachelor of Science (graduated summa cum laude)

**Biological Sciences** 

The University of Maryland College Park, MD 20742

1974-1976 Mount Saint Mary's College

Emmitsburg, MD 21727

#### POSTDOCTORAL TRAINING:

1986-1989 Department of Pharmacology and Curriculum in Toxicology

University of North Carolina at Chapel Hill

Chapel Hill, NC 27514

NIH Postdoctoral Fellow; American Liver Foundation Fellow

#### PROFESSIONAL EMPLOYMENT:

2006 - Present Professor

Department of Pharmacology and Toxicology

Michigan State University

1998-2006 Associate Professor

Department of Pharmacology and Toxicology

Michigan State University

1996-1998 Assistant Professor

Department of Pharmacology and Toxicology

Michigan State University

1990-1996 Assistant Professor

Departments of Medicine and of Pharmacology and

Toxicology

Michigan State University

## HONORS, FELLOWSHIPS, AND SPECIAL AWARDS:

2014	Colgate-Palmolive Grant for Alternative Research from the Society of
	Toxicology
2010	Kenneth E. Moore Distinguished Alumna Award
	Department of Pharmacology and Toxicology
	Michigan State University
2002	Pfizer Research Excellence Award
1987-1989	National Research Service Award, NIEHS
1987	American Liver Foundation Postdoctoral Fellowship

1986-1987	NIH Postdoctoral Fellow, Curriculum in Toxicology, The University of
	North Carolina
1985	American Society of Pharmacology and Experimental Therapeutics
	Student Travel Award
1984	Hazelton Laboratories Corporation Predoctoral Fellowship (sponsored
	by the Society of Toxicology)
1981-1986	NIH Predoctoral Trainee, Michigan State University
1979-	Member of Phi Beta Kappa
1979	Graduated Summa Cum Laude, The University of Maryland
1974-1978	Maryland State Senatorial Scholarship
1974-1976	Mount Saint Mary's College Academic Scholarship

# SERVICE ACTIVITIES (SINCE 1994)

# **Service Off-campus**

# Elected Offices

2017-2018	President, Society of Toxicology
2016-2017	Vice President, Society of Toxicology
2015-2016	Vice President, Society of Toxicology  Vice President-Elect, Society of Toxicology
2012-2013	Past-Chair, Division of Toxicology, American Society of Pharmacology and
2012-2013	Experimental Therapeutics
2011-2012	Chair, Division of Toxicology, American Society of Pharmacology and
	Experimental Therapeutics
2010-2012	Secretary-Treasurer, Mechanisms Specialty Section, Society of Toxicology
2010-2011	Chair-Elect, Division of Toxicology, American Society of Pharmacology and
	Experimental Therapeutics
2008-2010	Councilor, Society of Toxicology
2006-2008	Member, Society of Toxicology Awards Committee
2002-2004	Secretary-Treasurer, Toxicology Division, American Society of Pharmacology
	and Experimental Therapeutics
2001-2004	Membership Committee, Society of Toxicology
2003-2004	Chair, Society of Toxicology Membership Committee
2000-2001	Past-President, Michigan Regional Chapter of the Society of Toxicology
1999-2000	President, Michigan Regional Chapter of the Society of Toxicology
1998-1999	President-Elect, Michigan Regional Chapter of the Society of Toxicology
1999-2001	Councilor, Mechanisms Specialty Section, Society of Toxicology

# Appointment to Committees

2017-Present	Member, Society of Toxicology Endowment Fund Board
2016-2018	Member, Society of Toxicology Board of Publications
2015-2018	Society of Toxicology Representative to Council of the International
	Union of Toxicologists (IUTOX)
2013-2015	Member, Society of Toxicology Board of Publications
2007-2008	Chair, Member Services Strategy Committee, Society of Toxicology
2003-2004	Member, Nominating Committee, American Society of Pharmacology
	and Experimental Therapeutics
1998-2001	Member, Continuing Education Committee, Society of Toxicology

## **Appointment to Editorial Boards**:

2004-Present	Toxicology
1999-2017	Journal of Pharmacology and Experimental Therapeutics
1998-Present	Journal of Toxicology and Environmental Health
1999-2005	Toxicological Sciences
1994-1999	Fundamental and Applied Toxicology

# **Volume Editor**

2010 Volume 9: Hepatic Toxicology in <u>Comprehensive Toxicology</u>, Academic Press, Elsevier, London

# Ad hoc reviewer for the following scientific journals

Biochemical Pharmacology

Biochemistry and Cell Biology

Biochimica et Biophysica Acta

Chemical Research in Toxicology

Chemico-Biological Interactions

Clinical Biochemistry

Clinical Chimistra Acta

Clinical and Experimental Pharmacology and Physiology

Clinical Immunology

**Environmental Health Perspectives** 

**Environmental International** 

**Environmental Toxicology and Pharmacology** 

Hormone and Metabolic Research

Hypertension

Journal of American Physiology

Journal of Leukocyte Biology

Life Sciences

Molecular Pharmacology

Neurotoxicology

Pesticide and Biochemical Physiology

Proceedings of the Society of Experimental Biology

**Toxicological Sciences** 

**Toxicology Letters** 

Toxicology and Applied Pharmacology

Toxicology In Vitro

### External reviewer for the following

Subcommittee for the Medical Research Council Centre for Drug Safety Science review 2018-2019

NIEHS Grant Review, periodically

Centennial Center for Environmental Toxicology at the University of Texas Medical Branch, Galveston

NIEHS Environmental Health Center at the University of California, Davis

Seagrant Program, University of Wisconsin-Green Bay

Sarah B. Morris Foundation, University of Missouri, Kansas City

Ireland's Health Research Board

NIH Rapid Access to Interventional Development (RAID) grant program 2006-2007

# Consultant for the following

NIEHS Center for Rural Health, Texas A&M University 2000

NTP, Office of the Report on Carcinogens; Aristolochic Acid-related Compounds Expert Panel, 2008

NTP, Office of the Report on Carcinogens; Riddelliine Expert Panel, 2008

**Dow Chemical Company** 

US Food and Drug Administration and Entelos Physiolab, 2006

Consulting Research Evaluation Association (review of results of a toxicity study before federal submission) 2005

Chemical Research in Toxicology: Editor Search 2012

Dainippon Sumitomo Pharma Co., Ltd. 2013

Kiyatec, Inc. 2014

NTP, Office of the Report on Carcinogens, Information Group; Trichloroethylene 2014

### Conference organization

Health Consequences from Xenobiotic - Gut Microbiome- Host Interactions, November 2010, Research Triangle Park, NC

Dioxin Toxicity: Mechanisms, Models, & Potential Health Risks, 2008, East Lansing, MI.

Superfund Basic Research Program 20<sup>th</sup> Anniversary Meeting, 2007, Research Triangle Park, NC.

Bioremediation & Biodegradation: Current advances in reducing toxicity, exposure and environmental consequences, 2002, Asilomar, CA. NIEHS-sponsored conference designed to bring together investigators in a variety of disciplines that are involved in remediation of hazardous chemicals and the evaluation of the effects of remediation processes.

Scientific Basis of Risk Assessment, a meeting of the Michigan Regional Society of Toxicology, 1999, East Lansing, MI. This meeting had three purposes. The first was to bring together nationally recognized scientists to discuss the scientific basis of risk assessment. The second purpose was to showcase graduate education in toxicology in Michigan by having one student from each of the major universities present a research seminar. The third purpose was to educate local high school teachers and their students about the use of science in risk assessment.

#### Service at MSU

#### Committee assignments

2014-2015 Search Committee for the founding director of the Center for Research

in Ingredient Safety (CRIS)

2014 Search Committee for faculty in the Department of Pharmacology and

Toxicology

2013-2014	Chair, Department of Pharmacology and Toxicology Faculty Advisory Committee
2013-Present	Department of Pharmacology and Toxicology Awards Committee
2013-Present	College of Veterinary Medicine Sexual Harassment Liaison
2013	Chair, Department of Pharmacology and Toxicology Grievance
	Hearing Board Committee
2012-2013	Chair, College of Veterinary Medicine Committee on Promotion and Tenure
2011-2014	Department of Pharmacology and Toxicology Faculty Advisory Committee
2011-2013	Biomolecular Sciences Gateway Admissions Committee
2011	Search Committee for faculty in the Department of Pathobiology and
	Diagnostic Investigation
2011-2015	College of Veterinary Medicine Committee on Promotion and Tenure
2010-2011	Department of Pharmacology and Toxicology Diversity Committee
2008-2010	Chair, College of Veterinary Medicine College Advisory Council
2008-2010	National Food Safety and Toxicology Center Faculty Advisory Council
2006-2008	College of Veterinary Medicine College Advisory Council
2007-Present	Department of Pharmacology and Toxicology Graduate Committee
2005-2015	Comparative Medicine and Integrative Biology Program Admissions
	and Advisory Committee
2004-2007	College of Veterinary Medicine Curriculum Committee
2006-2007	Chair, College of Veterinary Medicine Curriculum Committee
2007	Search Committee for CVM Associate Dean for Academic Affairs
2006	Pharmacology and Toxicology Seminar Coordinator
2006	Search Committee for Dean of College of Veterinary Medicine
2005-2006	Search Committee for Center for Integrative Toxicology faculty
2005	Center for Integrative Toxicology Curricular Review Committee
2004-2006	College of Veterinary Medicine Diversity Committee
2003-2004	Pharmacology and Toxicology Curriculum Committee
2003-2004	College of Veterinary Medicine Ad hoc Committee to Review Preclinical Curriculum
2003-2004	Member, National Food Safey and Toxicology Center Research Task Force
2002-2003	College of Veterinary Medicine Curriculum Review Task Force
2002-2003	Search Committee for Pharmacology and Toxicology faculty
2002-2004	Vice-Chair, College of Veterinary Medicine Graduate Studies and
2002 2007	Research Committee
2001-2004	College of Veterinary Medicine Graduate Studies and Research
	Committee

2001-2003	Pharmacology and Toxicology Safety Committee
2001-2002	Chair, Search Committee for Pharmacology and Toxicology faculty
2000-2001	Search Committee for National Food Safety and Toxicology Center
	faculty
2001	Search Committee for Interim Chair of Pharmacology and Toxicology
1999-2000	Chair, College of Veterinary Medicine Diversity Committee
1998	Search Committee, Pharmacology and Toxicology faculty
1996-1998	CVM Graduate Grievance Hearing Committee
1999-2000	Chair, Pharmacology and Toxicology Affirmative Action Committee
1996-1999	Pharmacology and Toxicology Affirmative Action Committee

# Intramural grant reviews

Michigan Agricultural Experiment Station Biomedical Science Research Grants Research Excellence Funding Applications

# **SOCIETY MEMBERSHIPS:**

2008-Present	International Endotoxin and Innate Immunity Society
1998-2001	International Endotoxin Society
1996-Present	American Society of Pharmacology and Experimental
	Therapeutics
1996-Present	Society for Leukocyte Biology
1993-Present	Michigan Regional Chapter of the Society of Toxicology
1987-1989	North Carolina Chapter of the Society of Toxicology
1987-Present	Society of Toxicology

# TEACHING ACTIVITIES (since 2000):

Year	Course	Lecture title	Type of	Audience
			lecture	
2000-2002	PHM 819 Principles	Moderator	Didactic	Graduate
	of Drug Action			Students
2000-2009	PHM 819 Principles	Drug absorption and	Didactic	Graduate
	of Drug Action	distribution		Students

Students Graduate Students
Students
Graduate
Students
Graduate
Students
Professional
Students
Professional
Students
Professional
Students
Dunta na la mal
Professional
Students
Professional
Students
Professional
Students
Professional
Students
Graduate
students

2002-2012	PHM 820 Cellular and Molecular Pharmacology and	Pathways to Cell Death	Didactic	Graduate Students
2002-2012	Toxicology PHM 820 Cellular and Molecular Pharmacology and Toxicology	Arachidonic acid metabolism and nonsteroidal anti- inflammatory drugs	Didactic	Graduate Students
2003-2005	PHM 556 Veterinary Pharmacology	Therapy for protozoal infections	Didactic	Professional Students
2003-2005	PHM 556 Veterinary Pharmacology	Therapy for fungal infections	Didactic	Professional Students
2004	VM 532 Veterinary Integrated Problem Solving	Case report: Ibuprofen toxicity in a dog 2 hours	Problem- based learning	Professional Students
2004-Present	PHM 450 Introduction to Chemical Toxicology	Passage of chemicals across membranes	Didactic	Undergraduate and Graduate Students
2004-Present	PHM 450 Introduction to Chemical Toxicology	Chemical absorption and distribution	Didactic	Undergraduate and Graduate Students
2004-Present	PHM 450 Introduction to Chemical Toxicology	Elimination of chemicals	Didactic	Undergraduate and Graduate Students
2004-Present	PDI 851 Advanced	Chemical-induced	Didactic	Graduate
Even years	General Pathology	Cell Injury		Students
2006-Present	Integrated Organ System Pharmacology – Week-long Short Course	Acetaminophen hepatotoxicity	Lecture and Laboratory	Continuing Education and Graduate Students
2007-Present Odd years	PHM 816 Integrative Toxicology: Mechanisms, Pathology and Regulation	Moderator	Didactic	Graduate Students
2007-Present Odd years	PHM 816 Integrative Toxicology:	General Concepts	Didactic	Graduate Students

	Mechanisms, Pathology and			
2007-Present Odd years	Regulation PHM 816 Integrative Toxicology: Mechanisms,	Pathways to Cell Death	Didactic	Graduate Students
	Pathology and Regulation			
2017-Present Odd years	PHM 816 Integrative Toxicology: Mechanisms,	Adverse Outcome Pathways	Flipped Learning	Graduate Students
2007	Pathology and Regulation VM 980 Topics in	Co-moderator	Lecture/	Graduate
2001	Toxicology: Pathways to Cell Death	- CO-MOGRACOI	Seminar	Students
2007	VM 980 Topics in Toxicology: Pathways to Cell Death	Introduction to Cell Death	Didactic	Graduate Students
2008	PDI 891 Topics in Particle Toxicology: Micro- to Nano- particles	Co-moderator	Didactic	Graduate Students
2010-2016	PHM 563 Medical Pharmacology	Nonsteroidal anti- inflammatory drugs	On-line	Professional Students
2010-2016	PHM 563 Medical Pharmacology	Other anti- inflammatory drugs – 2 hours	On-line	Professional Students
2010-2016	PHM 563 Medical Pharmacology	Case reports	In class interactive	Professional Students
2010-2014	PHM 980 Principles of Drug Action	Drug absorption and distribution	On-line	Graduate Students
2010-2014	PHM 980 Principles of Drug Action	Drug excretion	On-line	Graduate Students
2010-2014	PHM 980 Principles of Drug Action	Case reports and research articles – 2 hours	In class interactive	Graduate Students
2010-Present	PHM 557 Veterinary Toxicology	General Concepts in Toxicology	Didactic	Professional Students

2012-Present	PHM 553	Pharmacology of hemostasis and hematopoesis – 3 hours	Didactic	Professional Students
2012-Present	PHM 553	Gastrointestinal pharmacology – 3 hours	Didactic	Professional Students
2014-Present	PHM 802 Cellular, Molecular and Integrated Systems Pharmacology and Toxicology	Arachidonic acid metabolism and nonsteroidal anti- inflammatory drugs – 2 hours	Didactic	Graduate Students
2013-Present	PHM 801 Fundamental Principles of Pharmacology and Toxicology	Drug absorption, drug distribution, drug excretion, special topic – 3 hours	Didactic	Graduate Students

#### **GRANT SUPPORT AND CONTRACTS:**

## **Current:**

An assay to predict the potential of drug candidates to cause idiosyncratic, drug-induced liver injury

NIDDK R01-DK112695 02/01/2017-01/31/2020 PI (R. Roth, Co-PI), 11% effort \$225,000/yr direct costs

# **Environmental metals, excitotoxicity and ALS**

NIEHS R01-ES024064 03/01/2015-02/28/2020 Co-Investigator (W. Atchison, PI), 5% effort \$372,000/yr direct costs

# Michigan State University PREP: Increasing underrepresented minority representation in biomedical sciences

NIGMS R25-GM116761 2017-2020 Co-Investigator (W. Atchison, PI), 5% effort \$373,000/yr direct costs

# **Completed:**

# Prediction of idiosyncratic drug-induced liver injury from drug-cytokine interaction in vitro

Colgate-Palmolive Grant for Alternative Research 05/2014 – 04/2015 PI \$40,000

## Dichotomous roles of thrombin in acetaminophen hepatotoxicity

NIDDK R01-087886 2010-2014 Co-Investigator (R. Roth, PI), 5% effort \$225,000/yr direct costs

# Environmental, Microbial and Mammalian Biomolecular Responses to AhR Ligands

NIEHS P01 ES04911 04/01/2006-03/31/2012

PI of the program project: N. Kaminski

My role: PI of Project 4, 17% effort: "Influence of Ah Receptor Ligands on Inflammatory Responses: Consequences for Tissue Injury and Gene Expression" \$200,000/yr direct costs

# **Neutrophils and Hepatotoxicity**

NIEHS R01 004139 04/03/06-03/31/12 Co-Investigator (PI, R.Roth), 15% effort \$267,000/yr direct costs

# **Inflammation and Drug Idiosyncrasy**

NIDDK R01 061315 2008-2012 Co-Investigator (R. Roth, PI), 5% effort

# Gene Expression in Drug-inflammation Models as Predictive of Idiosyncratic ADRs

NIGMS R21 075865 09/19/2005-09/18/2009 Principal Investigator, 15% effort \$250,000/yr direct costs

# Inflammation/Drug Interaction: Towards Validation of an Animal Model for Idiosyncratic Drug-induced Liver Injury: A Collaborative Research Proposal

Pfizer. Inc.

01/2006-12/2007

Principal Investigator, 10% effort

\$130,000/year direct costs

#### **Health Hazards from Groundwater Contamination**

NIEHS P01 ES04911

04/01/2000-03/31/2006

PI of the program project: L.J. Fischer

My role: PI of Project 6 (20% effort): Activation of AhR-Dependent and AhR-

Independent Signaling Cascades in PCB-Induced Immune Dysfunction

\$100,000/yr direct costs

#### **Health Hazards from Groundwater Contamination**

NIEHS P01 ES04911

04/01/2000-03/31/2006

PI of the program project: L.J. Fischer

My role: Co-Director (5% effort) of Remediation Product Evaluation Core

\$100,000/yr direct costs

# SAMe Inhibits Inflammatory-mediated Enhanced Toxicity

NIH/NIAAAA014134

2002-2004

Co-Investigator (J. Maddox, PI), 10% effort

\$50,000/yr direct costs

#### **Modeling Inflammation-drug Interactions in Vitro**

Pfizer Corp.

01/01/2004-12/31/2004

Co-Investigator (R. Roth, PI), 5% effort \$120,000/yr direct costs

# Inflammation as a Determinant of Susceptibility to Drug Toxicity: Toward an Animal Model of Idiosyncratic Hepatotoxicity

Abbott Laboratories 01/01/2004-12/31/2004 Co-Investigator (R. Roth, PI), 5% effort \$94,000 direct costs

# **Endotoxin Enhancement of Hepatotoxicity: Role of PGD2**

NIH/NIEHS R01 ES08789 1998-2003 Principal Investigator, 20% effort \$192,000/yr direct costs

# **Neutrophils and Hepatotoxicity**

NIEHS R01 04139 1998-2003 Co-Investigator (R. Roth, PI), 10% effort \$200,000/year direct costs

# **Distal Events in the Hepatotoxicity of Endotoxin**

NIH/NIDDK R01 50728 1996-2001 Co-Investigator (R. Roth, PI), 30% effort \$128,000/yr direct costs

# Effect of O<sub>3</sub>/Endotoxin Coexposure on Airway Epithelium

NHLBI R01 1997-2001 Co-Investigator (J. Harkema, PI), 5% effort \$170,000/yr direct costs

# Inflammation as a Determinant of Susceptibility to Drug Toxicity: Toward an Animal Model of Drug Idiosyncrasy

Pharmacy & Upjohn Collaborative Agreement 2001-2003

Co-Investigator (R. Roth, PI), 5% effort \$113,000 direct costs

#### **Health Hazards from Groundwater Contamination**

NIEHS P01 ES04911

1988-2000

PI of the program project: L.J. Fischer

My role: PI of Project 5A (20%): Mechanisms and Consequences of Neutrophil

Activation by Hazardous Chemicals

\$100,000/yr direct costs

#### **Health Hazards from Groundwater Contamination**

NIEHS P01 ES04911

1995-2000

PI of the program project: L.J. Fischer

My role: Co-Director of Remediation Product Evaluation Core, 5% effort

\$100,000/yr direct costs

#### PATENTS:

2017: Provisional Application for Patent; Docket No. MSS-014.60; In Vitro Methods for Classifying Drugs According to Their Potential to Cause Liver Cell Injury

#### PARTICIPATION IN TRAINING GRANTS:

Research Education Program to Increase the Number and Diversity of Researchers in Health-related Research

Environmental and Integrative Toxicological Sciences

Research Training Program for Veterinary Students

Short-term Research Training Program for Veterinary Students

#### STUDENTS AND POSTDOCTORAL TRAINEES:

#### **Graduate Students:**

Primary advisor to:

Name: Ashley Maiuri

Degree/Year of Graduation: Ph.D. 2015, Pharmacology and Toxicology/Environmental

Toxicology

Thesis Title: In vitro Mechanisms of Cytotoxic Interaction of Cytokines

and Drugs Associated with Idiosyncratic, Drug-induced Liver

Injury

Current Position: Toxicology Consultant, Integrated Nonclinical Development

Solutions Inc, Ann Arbor, MI

Name: Aaron Fullerton

Degree/Year of Graduation: PhD, 2013, Pharmacology and Toxicology/Environmental

Toxicology

**Thesis Title:** Influence of Dioxin on T-cell Mediated Liver Injury Injury **Current Position:** Associate Scientist, Investigative Toxicology, Genentech,

San Francisco, CA

Name: Kevin Beggs (co-advisor)

Degree/Year of Graduation: PhD, 2013, Pharmacology and Toxicology/Environmental

Toxicology

Thesis Title: Molecular Mechanisms of Hepatocellular Apoptosis Induced

by Trovafloxacin-Tumor Necrosis Factor-Alpha Interaction

**Current Position:** Postdoctoral Fellow, University of Kansas Medical Center

Name: Kyle Poulsen (co-advisor)

Degree/Year of Graduation: PhD, 2013, Pharmacology and Toxicology/Environmental

Toxicology

Thesis Title: Molecular Mechanisms of Trovafloxacin Potentiation of

Lipopolysaccharide-induced Tumor Necrosis Factor

Release from RAW 264.7 Cells

**Current Position:** Postdoctoral Fellow, Cleveland Clinic Lerner Research

Institute

Name: Jingtao Lu

Degree/Year of Graduation: PhD, 2012, Biochemistry and Molecular

Biology/Environmental Toxicology

Thesis Title: Mechanisms of Amiodarone/Lipopolysaccharide-induced

Liver Injury: A Model of Idiosyncratic, Drug-induced

Hepatotoxicity

**Current Position:** Postdoctoral Fellow, ORISE, US Environmental Protection

Agency, Research Triangle Park, NC

Name: Erica Sparkenbaugh (coadvisor)

Degree/Year of Graduation: PhD, 2011, Pharmacology and Toxicology/Environmental

Toxicology

**Thesis Title:** The Role of Hypoxia, Neutrophil Elastase and HIF-1alpha in

Hepatocellular Injury

Current Position: Postdoctoral Fellow, University of North Carolina

Name: Christine Dugan

Degree/Year of Graduation: PhD, 2010, Cell and Molecular Biology/Environmental

Toxicology

**Thesis Title:** A Mouse Model of Halothane Hepatitis Based on Human

Risk Factors: A Sexaually Dimorphic Immune-mediated

Mechanism

Current Position: Internal Medicine Resident, MSU Kalamazoo Center for

Medical Studies Borgess/Bronson Hospitals

Name: Wei Zou (coadvisor)

Degree/Year of Graduation: PhD, 2010, Microbiology and Molecular

Genetics/Environmental Toxicology

**Thesis Title:** Mechanisms of Sulindac/LPS-induced Liver Injury in Rats:

An Animal Model of Idiosyncratic Hepatotoxicity

Current Position: Scientist, ProMetic, Washington, DC

Name: Steven Bezdecny

Degree/Year of Graduation: PhD, 2006, Pharmacology and Toxicology/Environmental

Toxicology

**Thesis Title:** Signal Transduction Pathways Involved in the Upregulation

of Cyclooxygenase-2 by 2,2',4,4'-Tetrachlorobiphenyl

Current Position: High School Teacher, Essex County, NJ

Name: Shawn Kinser

Degree/Year of Graduation: PhD, 2001, Pharmacology and Toxicology

Thesis Title: Mechanisms of Enhanced Allyl Alcohol Hepatotoxicity by

Endotoxin

Current Position: Dentist, Flat River Family Dentistry, Greenville, MI

Name: Jesus Olivero-Verbel

Degree/Year of Graduation: PhD, 1999, Pharmacology and Toxicology

**Thesis Title:** Activation of Phospholipase A<sub>2</sub> by Polychlorinated Biphenyls

(PCBs) and Other Chlorinated Compounds

Current Position: Vice Chancellor of Research, Universidad de Cartagena,

Cartagena, Colombia, South America

Name: Rosie Sneed, DVM

Degree/Year of Graduation: PhD, 2000, Pharmacology and Toxicology

Thesis Title: The Role of the Innate Immune System in the LPS-Induced

Potentiation of Allyl Alcohol Hepatotoxicity

**Current Position:** Associate Professor, University of the District of Columbia,

Washington, DC

#### Thesis committee member for:

Name	Program	Years
Omar Kana	Pharmacology and Toxicology	2019-Present
Jeremy Gingrich	Pharmacology and Toxicology	2018-Present
Katherine Roth	Pharmacology and Toxicology	2015 - Present
Mónica Rios-Cabanillas	Comparative Medicine and Integrative Biology	2015 - Present
Duanghathai Wiwatratana	Comparative Medicine and Integrative Biology	2015 - Present
Phillip Brooks	Comparative Medicine and Integrative Biology	2014 - 2017

Alexandra Colón-	Comparative Medicine and	2013 - 2017
Rodriguez	Integrative Biology	2013 - 2017
Alexandra Turley	Pharmacology and Toxicology	2013 - 2018
Bronlyn Wassink	Statistics and Probability	2013 - 2016
Erica Clarke	Food Science	2013 - 2016
Lauren Azevedo	Pharmacology and Toxicology; dual	2012 - 2013
Ladieli Azevedo	degree student in Osteopathic	2012 - 2013
	Medicine	
Heidi Hannon	Comparative Medicine and	2012 – 2017
Tiolar raimen	Integrative Biology	2012 2017
Shawna D'Ingillo	Pharmacology and Toxicology	2011 – 2013
Kazuhisa Miyakawa, BvSc	Pathobiology and Diagnostic	2010 – 2015
	Investigation	
Brenna Flannery	Food Science	2009 – 2012
Peer Karmaus	Biochemisty and Molecular Biology	2007 – 2012
Aaron McBride	Cell and Molecular Biology	2008 – 2009
Daher Ibrahim Aibo, BvSc	Comparative Medicine and	2007 – 2009
	Integrative Biology	
Chidozie Amuzie, BvSc	Comparative Medicine and	2005 – 2008
	Integrative Biology	
Dina Shnaider	Pharmacology and Toxicology	2004 – 2008
Nasr Aref	Large Animal Clinical Sciences	2004 – 2008
Hoon Yoo	Fisheries and Wildlife	2004 – 2008
Patrick Shaw	Pharmacology and Toxicology	2004 – 2008
Cora Fong	Biochemistry and Molecular Biology	2003 – 2007
Gautham Rao	Pharmacology and Toxicology	2002 – 2005
Stacey Wilder	Environmental Engineering	2001 – 2003
Andrea Satoh	Environmental Engineering	2000 – 2002 (MS)
		2003 – 2008 (PhD)
John Buchweitz	Pharmacology and Toxicology	1999 – 2001
James Luyendyk	Pharmacology and Toxicology	1999 – 2004
Aimen Farraj	Pharmacology and Toxicology	1999 – 2003
Steven Yee	Pharmacology and Toxicology	1998 – 2003
Min Kim	Human Nutrition	1998 – 2002
Robert Molner	Surgery	1998 – 2000
Rebecca Marcus	Pharmacology and Toxicology	1998 – 2000
Xinguang Li	Pharmacology and Toxicology	1996 – 2000
Frederic Moulin, DVM	Pharmacology and Toxicology	1994 – 1999
Marc Bailie, DVM	Pharmacology and Toxicology	1990 - 1994

### **Postdoctoral Trainees:**

Rachel Murphy, PhD 2017 - 2018

Jordan Bailey, PhD 2016 - 2018

Rohit Singhal, PhD 2009 - 2012

Jesus Olivero, PhD 2006 - 2008

Present position: Vice President for Research, Universidad de Cartagena,

Colombia, South America

Sachin Devi, PhD 2005-2007

Present position: Professor, LECOM School of Pharmacy, Sarasota, FL

Alan Brown, PhD 1993-1996; Supported by NRSA from NIH

Present position: Preclinical Safety CVM, Novartis Institutes for BioMedical

Research Inc., Cambridge, MA

Patricia Tithof, PhD, DVM 1993-1996

Present position: Senior Lecturer, Berry College, Mount Berry, GA

# **Undergraduate, Professional and High School Students:**

Anna Breier 2014-2015

Gurpreet Kaur 2014 Robert Parkins, III 2013

Ryan Albee 2010-2013

Mitchell Nothem 2010; ASPET SURF Melanie Seymour 2009; DVM student Sarah Thomas 2009; ASPET SURF

Allen MacDonald 2008-2010 Emilie Evenson 2007-2008

Peer Karmaus 2006

Nicole Chalmers 2005; ASPET SURF

Theresa Eagle 2004-2006; ASPET SURF

Alison Domzalski 2002-2003

Brook Woollev 2002

Natasha Tasheva 2001-2002

Ali Mahajerin 1996-1998; Professorial Assistant

Melinda Baker 1998-2000; Professorial Assistant

Kirsten Reuhle 1998 Wendy Holdan 1998

Sarah Kessel 1995-1997

Liz Schiamburg 1995; High School Honors Summer Program

Simi VanCise 1994-1995

Maria Colligan 1994

#### AWARDS AND HONORS WON BY TRAINEES:

#### **Graduate Students:**

Shawn Kinser, 2000: SOT Graduate Student Advisory Council, member

Shawn Kinser, 2000: SOT Graduate Student Travel Award Steve Bezdecny, 2005: SOT Graduate Student Travel Award

Christine Dugan, 2007: Council of Graduate Students Travel Award

Christine Dugan, 2008: Graduate Student Award from the SOT Toxicology and Exploratory Pathology Specialty Section

Aaron Fullerton, 2008: Young Investigator Award from the International Endotoxin and Innate Immune Society

Wei Zou, 2008: SOT Graduate Student Travel Award

Christine Dugan, 2009: Trainee Travel Award to attend "Pattern Receptors ad Innate Immune Signaling Pathways in Liver Diseases"

Christine Dugan, 2009: Graduate Student Poster Award, 1st place, Michigan SOT

Wei Zou, 2009; Graduate Student Best Abstract Award, 2<sup>nd</sup> place, Division of Toxicology, ASPET

Aaron Fullerton, 2009: Best Poster Award, 2<sup>nd</sup> place, Environmental Health Sciences Regional Showcase of Fellows

Christine Dugan, 2010: SOT Graduate Student Travel Award funded by Millennium Pharmaceuticals

Christine Dugan, 2010: Suzan Jean Snyder Award, MSU College of Osteopathic Medicine

Christine Dugan, 2010: Travel Award to attend the combined annual meeting of the Central Society for Clinical Research and the Midwestern Section of the American Federation for Medical Research

Christine Dugan, 2010: Dissertation Completion Fellowship

Jingtao Lu, 2010: SOT Graduate Student Travel Award

Kyle Poulsen, 2012: First Runner Up, Poster Competition, Michigan Regional Chapter of the SOT

Aaron Fullerton, 2010: Regional Chapter Graduate Student Representative

Aaron Fullerton, 2010: Regional Chapter Graduate Student Representative Travel Award

- Aaron Fullerton, 2011: SOT Graduate Student Travel Award
- Aaron Fullerton, 2011: Selected as one of three graduate students to give an oral platform presentation at the Michigan SOT 2011 Spring meeting at MPI Research, "Immunotoxicology and Safety Assessment—21st Century Advances and Challenges"
- Jingtao Lu, 2011: Graduate Student Travel Award from the Center for Integrative Toxicology
- Jingtao Lu, 2011: Graduate Student Travel Award from the SOT Comparative and Veterinary Specialty Section of SOT
- Jingtao Lu, 2011: Dissertation Completion Fellowship
- Aaron Fullerton, 2012: Dissertation Completion Fellowship
- Aaron Fullerton, 2012: Graduate Student Poster Award, 1st place, Michigan SOT
- Kyle Poulsen, 2013: Graduate Student Travel Award from the SOT
- Kyle Poulsen, 2013: Carl C. Smith Award for Meritorious Research Finalist and Honorable Mention, Mechanisms Specialty Section, SOT
- Ashley Maiuri, 2013: Center for Integrative Toxicology Graduate Student Travel Award (to travel to the SOT annual meeting)
- Ashley Maiuri, 2013: SOT Graduate Student Travel Award
- Ashley Maiuri, 2014: Center for Integrative Toxicology Research Travel Award (to spend time at the Hamner Institute in NC)
- Ashley Maiuri, 2014: Graduate Student Travel Award from the In Vitro and Alternative Methods Specialty Section, SOT
- Ashley Maiuri, 2014: Center for Integrative Toxicology Graduate Student Travel Award (to travel to the SOT annual meeting)
- Ashley Maiuri, 2016: Graduate Student Travel Award from the In Vitro and Alternative Methods Specialty Section, SOT

#### **Postdoctoral Trainees:**

- Francis Tukov, D.V.M., Ph.D.: 2005 Colgate-Palmolive Postdooctoral Fellowship Award in In Vitro Toxicology (SOT)
- Rohit Singhal, Ph.D., 2010: Postdoctoral Trainee Travel award, SOT Mechanisms Specialty Section

## **Undergraduate Students:**

Alison Domzalski, 2001: Award for poster presentation at the MSU Undergraduate

#### Research Forum

Theresa Eagle, 2005: SOT Pfizer Undergraduate Student Travel Award

## **Employee**:

Sandra Newport, research assistant, 2005: Staff Poster Award, 1st place, Michigan SOT

#### **INVITED TALKS:**

- 2018 The role of cytokines in drug-induced liver injury. University of Georgia Integrated Toxicology Program, Athens, GA
- 2017 Drug-cytokine interaction in idiosyncratic hepatotoxicity, World Preclinical Congress, Predicting Drug Toxicity, Boston, MA
- 2017 The role of cytokines in drug-induced liver injury, American College of Toxicology 38<sup>th</sup> Annual Meeting, Palm Springs, CA
- 2017 Career choices in Toxicology...and the future...., Toxicology Inaugural Weekend Workshop, Ames Iowa
- 2017 Mechanisms of cell death from interaction of cytokines with drugs that cause idiosyncratic liver injury, 44<sup>th</sup> Annual Meeting of the Japanese Society of Toxicology
- 2015 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin augments hepatotoxicity in a mouse model of immune-mediated liver injury, International Seminar on Cell Death and Inflammation, University de Cartagena, Cartagena, Colombia, South America
- 2015 Cell Death, International Seminar on Cell Death and Inflammation, University de Cartagena, Cartagena, Colombia, South America
- 2015 General Concepts in Toxicology, International Seminar on Cell Death and Inflammation, University de Cartagena, Cartagena, Colombia, South America
- 2014 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin augments hepatotoxicity in a mouse model of immune-mediated liver injury, Andrews University, Berrien Springs, MI

- 2013 Inflammatory stress and drug-induced liver injury, Environmental Mutagenesis and Genomics Society Annual Meeting, Monterey, CA
- 2012 Sex and inflammation in idiosyncratic, drug-induced liver injury, 11<sup>th</sup> Annual World Pharma Congress, Philadelphia, PA
- 2011 Sex and inflammation in idiosyncratic, drug-induced liver injury, The Hamner UNC Institute for Drug Safety Sciences, Research Triangle Park, NC
- 2010 Idiosyncratic liver injury from halothane: New thoughts on an old drug, 2010 Kenneth E. Moore Distinguished Alumna Lecture, Michigan State University, East Lansing, MI
- 2010 Microbial products enhance xenobiotic-induced liver injury, Health Consequences from Xenobiotic-Gut Microbiome-Host Interactions, Research Triangle Park, NC
- 2010 Acetaminophen toxicity, Environmental Studies 28: Global Environmental Health, Dartmouth Medical School, Hanover, NH
- 2010 Idiosyncratic Drug-induced Liver Injury: The Inflammatory Stress Hypothesis and Animal Models, Dartmouth Medical School, Hanover, NH
- 2009 Multiple modes of action an inflammatory stress-drug interaction model of idiosyncratic liver injury, Drug Metabolism Gordon Conference, Holderness, NH
- 2009 Inflammation as a susceptibility factor for hepatotoxicity: developing models of druginduced idiosyncratic reactions, University of North Carolina Curriculum in Toxicology, First Annual Postdoctoral Retreat, Guest Speaker, Chapel Hill, NC
- 2008 Idiosyncratic drug-induced liver injury and inflammatory stress, Experimental Biology Annual Meeting, San Diego, CA
- 2008 Hepatocyte systems for understanding mechanisms of drug-inflammation interactions that lead to liver injury, Annual Meeting of the Society of Toxicologic Pathologists, San Francisco, CA
- 2007 Progression and sensitivity factors in "intrinsic" and "idiosyncratic" drug-induced liver injury, Drug Metabolism Gordon Conference, Holderness, NH
- 2006 The contribution of Kupffer cell-derived mediators to acute hepatotoxicity, Astra

- Zeneca, Alderly Park, England
- 2006 The contribution of Kupffer cell-derived mediators to acute hepatotoxicity, Society of Toxicology Annual Meeting, San Diego, CA
- 2006 Inflammatory stress and susceptibility to drug-induced liver injury: Exploration of hepatic gene expression as predictive markers, Predictive Models of Drug Safety Assessment, NIH, Bethesda, MD
- 2004 Upregulation of Cyclooxygenase-2 in Neutrophils by Polychlorinated Biphenyls, Conference on Applying Molecular Technology Methods to Characterize and Reduce Risks to Humans and the Ecosystem, Seattle, WA
- 2004 Inflammation and Susceptibility to Chemical-induced Hepatotoxicity: Potential Implications for Drug-induced Idiosyncratic Responses, Department of Pharmacology, University of Toledo, Toledo, OH
- 2004 Inflammation and Susceptibility to Chemical-induced Hepatotoxicity, School of Public Health, University of Michigan, Ann Arbor, MI
- 2002 Does bioremediation reduce the biological activity of PCBs? Conference on Bioremediation and Biodegradation: Current Advances in Reducing Toxicity, Exposure and Environmental Consequences", Pacific Grove, CA
- 2001 Inflammation-mediated Potentiation of Hepatotoxicity and the Potential Implications for Drug-induced Idiosyncratic Responses, Pfizer Global Research, Ann Arbor, MI
- 2001 Inflammation Augments Acute Hepatotoxicity Caused by Mycotoxins, Gordon Research Conference on Mycotoxins and Phycotoxins, Williams College, MA
- 2000 Neutrophil Phospholipase A<sub>2</sub> as a Target for the Action of Polychlorinated Biphenyls, Environmental Toxicology Program, University of Illinois at Urbana-Champagne
- 2000 The Role of Phospholipase A<sub>2</sub> in Activation of Neutrophils by Polychlorinated Biphenyls, Chemical Industries Institute of Toxicology, Research Triangle Park, NC
- 2000 Cyclooxygenase-2 in Inflammation-mediated Modulation of Allyl Alcohol-induced, Biomedical Sciences Program, Marshall University
- 1999 Inflammation-mediated Modulation of Chemically Induced Hepatotoxicity,

- Environmental Toxicology Program, University of Texas Medical Branch at Galveston
- 1999 Inflammation-mediated Modulation of Chemically Induced Hepatotoxicity, Medical Technology Program, Michigan State University
- 1999 Inflammation During Chemically Induced Tissue Injury: Friend or Foe?, University of Cayey, Cayey, Puerto Rico
- 1998 Inflammation-mediated Modulation of Chemically Induced Hepatotoxicity, Department of Pharmaceutical Sciences, Wayne State University
- 1997 Inflammation-mediated Modulation of Chemically Induced Hepatotoxicity, Toxicology Program, University of Michigan
- 1997 Mechanisms of Activation of Neutrophils by Polychlorinated Biphenyls, Biological Actions of Non-Coplanar Polychlorinated Biphenyls, Symposium, Annual Meeting of the Society of Toxicology, Cincinnati, OH
- 1996 Signalling Mechanisms in Activation of Neutrophils by Xenobiotics, Symposium, World Congress on In Vitro Biology, San Francisco, CA
- 1995 Mechanisms of Inflammatory Liver Injury: Adhesion Molecules and Cytotoxicity of Neutrophils, Symposium, Annual Meeting of the Society of Toxicology, Baltimore, MD
- 1994 Department of Biology, Western Michigan University
- 1994 The Role of Cell Mediators in the Toxic Response, Session-in-Depth, Tissue Culture Association Meeting, Research Triangle Park, NC
- 1994 Studies on Drug Metabolism and Toxicity at Various Levels of Organization in the Liver, Short Course, International Society for the Study of Xenobiotics, Raleigh, NC
- 1989 North Carolina Chapter of the Society of Toxicology
- 1985 New Investigators' Colloquium, Annual Meeting of the Society of Toxicology, San Diego, CA

#### **PUBLICATIONS**

#### **Articles in Refereed Journals:**

- 1) Maiuri AR, Wassink B, Turkus JD, Breier AB, Lansdell T, Kaur G, Hession SL, Ganey PE, Roth RA. Synergistic cytotoxicity from drugs and cytokines in vitro as an approach to classify drugs according to their potential to cause idiosyncratic hepatotoxicity: A proof-of-concept study. J Pharmacol Exp Ther, 2017 362(3): 459-473. doi: 10.1124/jpet.117.242354. Epub 2017 Jul 7. PMID: 28687704
- 2) Roth RA, Maiuri AR, Ganey PE. Idiosyncratic drug-inducedd liver injury: Is drug-cytokine interaction the linchpin? J Pharmacol Exp Ther, 2017 360(2): 461-470. doi: 10.1124/jpet.116.237578. Epub 2016 Nov 15. PMID 28104833
- 3) Maiuri AR, Breier AB, Turkus JD, Ganey PE, Roth RA. Calcium contributes to the cytotoxic interaction between diclofenac and cytokines. Tox Sci 149(2): 372-384, 2016. doi: 10.1093/toxsci/kfv249. Epub 2015 Nov 24.PMID: 26609140
- 4) Miyakawa K, Joshi N, Sullivan BP, Albee R, Brandenberger C, Jaeschke H, McGill MR, Scott MA, Ganey PE, Luyendyk JP, Roth RA. Platelets and protease-activated receptor-4 contribute to acetaminophen-induced liver injury in mice. Blood, 2015, Oct 8;126(15):1835-43. doi: 10.1182/blood-2014-09-598656. Epub 2015 Jul 15. PMID: 26179083.
- Maiuri AR, Breier AB, Gora LF, Parkins RV, Ganey PE, Roth RA. Cytotoxic synergy between cytokines and NSAIDs associated with idiosyncratic hepatotoxicity is driven by mitogen-activated protein kinases. Tox Sci 146(2): 265-280, 2015; PMID: 25953702
- 6) Miyakawa K, Albee R, Letzig LG, Lehner AF, Scott M, Buchweitz JP, James LP, Ganey PE, Roth RA. A cytochrome P450-independent mechanism of acetaminophen-induced hepatocellular injury in cultured mouse hepatocytes. J Pharmacol Exp Ther, 354(2): 230-237, 2015; PMID: 26065700. *Highlighted paper*.
- 7) Beggs KM, Maiuri AR, Fullerton AM, Poulsen KL, Breier AB, Ganey PE, Roth RA. Trovafloxacin-induced replication stress sensitizes HepG2 cells to tumor necrosis factor-alpha-induced cytotoxicity mediated by extracellular signal-regulated kinase and ataxia telangiectasia and Rad3-related. Toxicology 331: 35-46, 2015, PMID:25748550.

- 8) Poulsen KL, Olivero-Verbel J, Beggs KM, Ganey PE, Roth RA. Trovafloxacin enhances LPS-stimulated production of TNF by macrophages: role of the DNA damage response. J Pharmacol Exp Ther 350(1): 164-170, 2014, PMID 24817034
- Poulsen KL, Albee RP, Ganey PE, Roth RA. Trovafloxacin potentiation of lipopolysaccharide-induced tumor necrosis factor release from RAW 264.7 cells requires ERK and JNK. J Pharmacol Exp Ther 349(2): 185-191, 2014, PMID 24525298
- 10) Beggs KM, Fullerton AM, Miyakawa K, Ganey PE, Roth RA. Molecular mechanisms of hepatocellular apoptosis induced by trovafloxacin-tumor necrosis factor-alpha interaction. Toxicol Sci 137(1): 91-101, 2014, PMID 24097668.
- 11) Fullerton AM, Roth RA, Ganey PE. Pretreatment with TCDD exacerbates liver injury from concanavalin A: critical role for NK cells. Toxicol Sci 136(1): 72-85, 2013; doi: 10.1093/toxsci/kft174; PMID: 23164664
- 12) Lu J, Roth RA, Malle E, Ganey PE. Roles of the hemostatic system and neutrophils in liver injury from coexposure to amiodarone and lipopolysaccharide. Toxicol Sci 136(1): 51-62, 2013; doi: 10.1093/toxsci/kft170; PMID: 23912913
- 13) Fullerton AM, Roth RA, Ganey PE. 2,3,7,8-TCDD enhances the sensitivity of mice to concanavalin A immune-mediated liver injury. Toxicol Appl Pharmacol 266: 317-327, 2013. PMID 23164664
- 14) Lu J, Miyakawa K, Roth RA, Ganey PE. Tumor necrosis factor-alpha potentiates the cytotoxicity of amiodarone in Hepa1c1c7 cells: roles of caspase activation and oxidative stress. Toxicol Sci 131(1):164-178, 2013. PMID 23042730
- 15) Coen MP, Rademacher PM, Zou W, Scott M, Ganey P, Roth R, Nelson SD. Comparative NMR-based metabonomic investigation of the metabolic phenotype associated with tienilic acid and tienilic acid isomer. Chem Res Toxicol 25(11): 2412-2422, 2012. PMID: 23013248
- 16) Singhal R, Ganey PE, Roth RA. Complement activation in acetaminophen-induced liver injury in mice. J Pharmacol Exp Ther 341(2): 377-385, 2012. PMID: 22319198
- 17) Sparkenbaugh EM, Ganey PE, Roth RA. Hypoxia sensitization of hepatocytes to neutrophil elastase-mediated cell death depends on MAPKs and HIF-1α. Am J Physiol Gastrointest Liver Physiol 302(7): G748-57, 2012. PMID: 22223132

- Zou W, Roth RA, Younis HS, Malle E, Ganey PE. Neutrophil-cytokine interactions in a rat model of sulindac-induced idiosyncratic liver injury. Toxicology 290(2-3):279-286, 2011.
- 19) Lu J, Jones AD, Harkema JR, Roth RA, Ganey PE. Amiodarone exposure during modest inflammation induces idiosyncrasy-like liver injury in rats: role of tumor necrosis factor-alpha. Toxicol Sci Jan 125(1): 126-133, 2012 doi: 10.1093/toxsci/kfr266
- 20) Sparkenbaugh EM, Saini Y, Greenwood KK, Lapres JJ, Luyendyk JP, Copple BL, Maddox JF, Ganey PE, Roth RA. The role of hypoxia inducible factor-1 alpha (HIF-1{alpha}) in acetaminophen hepatotoxicity. J Pharmacol Exp Ther. 338(2):492-502, 2011. PMID: 21576378
- 21) Olivero-Verbel J, Roth RA, Ganey PE. Dioxin alters inflammatory responses to lipopolysaccharide. Toxicol Environ Chem. 93(6): 1180-1194, 2011. http://www.tandfonline.com/doi/abs/10.1080/02772248.2011.577554
- 22) Dugan CM, Fullerton AM, Roth RA, Ganey PE. Natural killer cells mediate severe liver injury in a murine model of halothane hepatitis. Toxicol Sci 120(2):507-518, 2011.
- 23) Liguori MJ, Ditewig AC, Maddox JF, Luyendyk JP, Lehman-McKeeman LD, Nelson DM, Bhaskaran VM, Waring JF, Ganey PE, Roth RA, Blomme EA. Comparison of TNFα to lipopolysaccharide as an inflammagen to characterize the idiosyncratic hepatotoxicity potential of drugs: trovafloxacin as an example. Int J Mol Sci 11(11): 4697-4714, 2010.
- 24) Shaw PJ, Ganey PE, Roth RA. Idiosyncratic, drug-induced liver injury and the role of inflammatory stress with an emphasis on an animal model of trovafloxacin hepatotoxicity. Toxicol Sci, 118(1): 7-18, 2010.
- 25) Zou W, Roth RA, Younis HS, Burgoon LD, Ganey PE. Oxidative stress is important in the pathogenesis of liver injury induced by sulindac and lipopolysaccharide cotreatment. Toxicology, 272(1-3):32-8, 2010.
- 26) Dugan CM, MacDonald AE, Roth RA, Ganey PE. A mouse model of severe halothane hepatitis based on human risk factors. J Pharmacol Exp Ther, May:333(2):364-72, 2010.

- 27) Aibo DI, Birmingham NP, Lewandowski R, Maddox JF, Roth RA, Ganey PE, Wagner JG, Harkema JR. Acute exposure to ozone exacerbates acetaminophen-induced liver injury in mice. Toxicol Sci, May;115(1):267-85, 2010.
- 28) Roth RA, Ganey PE. Intrinsic vs idiosyncratic drug-induced hepatotoxicity -- Two villains or one? J Pharmacol Exp Ther, Mar;332(3):692-697, 2010.
- 29) Maddox JF, Amuzie CJ, Li M, Newport SW, Sparkenbaugh E, Cuff CF, Pestka JJ, Cantor GH, Roth RA, Ganey PE. Bacterial- and viral-induced inflammation increases sensitivity to acetaminophen hepatotoxicity. J Toxicol and Environ Health, Part A. 73 (1), 58-73, 2009. PMID: 19953420
- 30) Zou W, Beggs KM, Sparkenbaugh EM, Jones AD, Younis HS, Roth RA, Ganey PE. Sulindac metabolism and synergy with tumor necrosis factor-α in a drug-inflammation interaction model of idiosyncratic liver injury. J Pharmacol Exp Ther. 331(1), 114–121, 2009. PMID: 19638570
- 31) Zou W, Devi SS, Sparkenbaugh E, Younis HS, Roth RA, Ganey PE. Hepatotoxic interaction of sulindac with lipopolysaccharide: Role of the hemostatic system. Toxicol Sci. 108, 184-193, 2009. PMID: 19074762
- 32) Shaw PJ, Beggs KM, Sparkenbaugh EM, Dugan CM, Ganey PE, Roth RA. Trovafloxacin enhances TNF-induced inflammatory stress and cell death signaling and reduces TNF clearance in a murine model of idiosyncratic hepatotoxicity. Toxicol Sci. Oct;111(2):288-301, 2009. PMID: 19638433
- 33) Shaw PJ, Fullerton AM, Scott MA, Ganey PE, Roth RA. The role of the hemostatic system in murine liver injury induced by coexposure to lipopolysaccharide and trovafloxacin, a drug with idiosyncratic liability. Toxicol Appl Pharmacol. 236(3), 293-300, 2009.
- 34) Shaw P, Ganey PE, Roth RA. Trovafloxacin enhances the inflammatory response to a Gram-negative or a Gram-positive bacterial stimulus, resulting in neutrophil-dependent liver injury in mice. J Pharmacol Exp Ther. 330(1):72-78, 2009.
- 35) Shaw PJ, Ditewig AC, Waring JF, Liguori MJ, Blomme EA, Ganey PE, Roth RA. Coexposure of mice to trovafloxacin and lipopolysaccharide, a model of idiosyncratic hepatotoxicity, results in a unique gene expression profile and interferon gammadependent liver injury. Toxicol Sci. 107(1), 270-280, 2009.

- 36) Shaw PJ, Ganey PE, Roth RA. Tumor necrosis factor alpha is a proximal mediator of synergistic hepatotoxicity from trovafloxacin/lipopolysaccharide coexposure. J Pharmacol Exp Ther. 328(1), 62-68, 2009.
- 37) Deng X, Liguori MJ, Sparkenbaugh EM, Waring JF, Blomme EA, Ganey PE, Roth RA. Gene expression profiles in livers from diclofenac-treated rats reveal intestinal bacteria-dependent and -independent pathways associated with liver injury. J Pharmacol Exp Ther. 327(3), 634-644, 2008. PMID: 18801949
- 38) Deng X, Lu J, Lehman-McKeeman LD, Malle E, Crandall DL, Ganey, PE, Roth RA. p38 mitogen-activated protein kinase-dependent tumor necrosis factor-alphaconverting enzyme is important for liver injury in hepatotoxic interaction between lipopolysaccharide and ranitidine. J Pharmacol Exp Ther. 326(1), 144-152, 2008.
- 39) Ganey PE\*, Luyendyk JP\*, Newport SW, Eagle TM, Maddox JF, Mackman N, Roth RA. Role of the coagulation system in acetaminophen-induced hepatotoxicity in mice. Hepatology 46(4), 1177-1186, 2007. \*shared co-first author responsibility
- 40) Tukov FF, Luyendyk JP, Ganey PE, Roth RA. The role of tumor necrosis factor alpha in lipopolysaccharide/ranitidine-induced inflammatory liver injury. Toxicol Sci 100(1), 267-280, 2007.
- 41) Shaw PJ, Hopfensperger MJ, Ganey PE, Roth RA. Lipopolysaccharide and trovafloxacin coexposure in mice causes idiosyncrasy-like liver injury dependent on tumor necrosis factor-alpha. Toxicol Sci. 100(1), 259-266, 2007.
- 42) Bezdecny SA, Karmaus P, Roth RA, Ganey PE. 2,2',4,4'-Tetrachlorobiphenyl upregulates cyclooxygenase-2 in HL-60 cells via p38 mitogen-activated protein kinase and NF-kappaB. Toxicol Appl Pharmacol 221(3), 285-294, 2007.
- 43) Deng X, Luyendyk JP, Zou W, Lu J, Malle E, Ganey PE, Roth RA. Neutrophil interaction with the hemostatic system contributes to liver injury in rats cotreated with lipopolysaccharide and ranitidine. J Pharmacol Exp Ther 322(2), 852-861, 2007.
- 44) Roberts RA, Ganey PE, Ju C, Kamendulis LM, Rusyn I, Klaunig JE. Role of the Kupffer cell in mediating hepatic toxicity and carcinogenesis. Toxicol Sci 96, 2-15, 2007.

- 45) Deng X, Stachlewitz RF, Liguori MJ, Blomme EA, Waring JF, Luyendyk JP, Maddox JF, Ganey PE, Roth RA. Modest inflammation enhances diclofenac hepatotoxicity in rats: role of neutrophils and bacterial translocation. J Pharmacol Exp Ther 319(3), 1191-1199, 2006.
- 46) Copple BL, Roth RA, Ganey PE. Anticoagulation and inhibition of nitric oxide synthase influence hepatic hypoxia after monocrotaline exposure. Toxicology 225(2-3), 128-137, 2006.
- 47) Tukov FF, Maddox JF, Amacher DE, Bobrowski WF, Roth RA, Ganey PE. Modeling inflammation-drug interactions in vitro: a rat Kupffer cell-hepatocyte coculture system. Toxicol In Vitro 20(8), 1488-99, 2006.
- 48) Luyendyk JP, Lehman-McKeeman LD, Nelson DM, Bhaskaran VM, Reilly TP, Car BD, Cantor GH, Maddox JF, Ganey PE, Roth RA. Unique gene expression and hepatocellular injury in the lipopolysaccharide-ranitidine drug idiosyncrasy rat model: Comparison with famotidine. Toxicol Sci 90(2), 569-585, 2006.
- 49) Waring JF, Liguori MJ, Luyendyk JP, Maddox JF, Ganey PE, Stachlewitz RF, North C, Blomme EA, Roth RA. Microarray analysis of LPS potentiation of trovafloxacin-induced liver injury in rats suggests a role for proinflammatory chemokines and neutrophils. J Pharmacol Exp Ther 316, 1080-1087, 2006.
- 50) Luyendyk JP, Lehman-McKeeman LD, Nelson DM, Bhaskaran VM, Reilly TP, Car BD, Cantor GH, Deng X, Maddox JF, Ganey PE, Roth RA. Coagulation-dependent gene expression and liver injury in rats given lipopolysaccharide with ranitidine but not with famotidine. J Pharmacol Exp Ther 317, 635-643, 2006.
- 51) Maddox JF, Luyendyk JP, Cosma GN, Breau AP, Bible RH Jr, Harrigan GG, Goodacre R, Ganey PE, Cantor GH, Cockerell GL, Roth RA. Metabonomic evaluation of idiosyncrasy-like liver injury in rats cotreated with ranitidine and lipopolysaccharide. Toxicol Appl Pharmacol 212, 35-44, 2006.
- 52) Bezdecny SA, Roth RA, Ganey PE. Effects of 2,2',4,4'-tetrachlorobiphenyl on granulocytic HL-60 cell function and expression of cyclooxygenase-2. Toxicol Sci 84, 328-334, 2005.
- 53) Luyendyk JP, Shaw PJ, Green CD, Maddox JF, Ganey PE, Roth RA. Coagulation-mediated hypoxia and neutrophil-dependent hepatic injury in rats given lipopolysaccharide and ranitidine. J Pharmacol Exp Ther 314, 1023-1031, 2005.

- 54) Luster-Teasley SL, Ganey PE, DiOrio M, Ward III JS, Maleczka Jr RE, Trosko JE, Masten SJ. Effect of byproducts from the ozonation of pyrene: biphenyl-2,2',6,6'-tetracarbaldehyde and biphenyl-2,2',6,6'-tetracarboxylic acid on gap junction intercellular communication and neutrophil function. Environ Toxicol Chem 24, 733-740, 2005.
- 55) Luyendyk JP, Maddox JF, Green, CD, Ganey PE, Roth RA. Role of hepatic fibrin in idiosyncrasy-like liver injury from lipopolysaccharide-ranitidine coexposure in rats. Hepatology 40,1342-1351, 2004.
- 56) Kinser S, Sneed RA, Roth RA, Ganey PE. Neutrophils contribute to endotoxin enhancement of allyl alcohol hepatotoxicity. J Toxicol Environ Health 67, 911-928, 2004.
- 57) Luyendyk JP, Mattes WB, Burgoon LD, Zacharewski TR, Maddox JF, Cosma GN, Ganey PE, Roth RA. Gene expression analysis points to hemostasis in livers of rats cotreated with lipopolysaccharide and ranitidine. Toxicol Sci 80, 203-213, 2004.
- 58) Harrigan GG, Laplante RH, Cosma GN, Cockerell G, Goodacre R, Maddox JF, Luyendyk JP, Ganey PE, Roth RA. Application of high-throughput Fourier-transform infrared spectroscopy in toxicology studies: contribution to a study on the development of an animal model for idiosyncratic toxicity. Toxicol Letters 146,197-205, 2004.
- 59) Maddox JF, Domzalski AC, Roth RA, Ganey PE. 15-Deoxy Prostaglandin J<sub>2</sub> enhances allyl alcohol-induced toxicity in rat hepatocytes. Toxicol Sci 77, 290-298, 2004.
- 60) Copple BL, Rondelli CM, Maddox JF, Hoglen NC, Ganey PE, Roth RA. Modes of cell death in rat liver after monocrotaline exposure. Toxicol Sci 77, 172-182, 2004.
- 61) Hanumegowda UM, Copple BL, Shibuya M, Malle E, Ganey PE, Roth RA. Basement membrane and matrix metalloproteinases in monocrotaline-induced liver injury. Toxicol Sci 76, 237-246, 2003.
- 62) Roth RA, Luyendyk JL, Maddox JF, Ganey PE. Inflammation and drug idiosyncrasyis there a connection? J Pharmacol Exp Ther 307, 1-8, 2003.
- 63) Yee SB, Ganey PE, Roth RA. The role of Kupffer cells and TNF-alpha in monocrotaline and bacterial lipopolysaccharide-induced liver injury. Toxicol Sci 71, 124-132, 2003.

- 64) Copple BL, Ganey PE, Roth RA. Liver inflammation during monocrotaline hepatotoxicity. Toxicology 190, 155-169, 2003.
- 65) Yee SB, Hanumegowda UM, Hotchkiss JA, Ganey PE, Roth RA. Role of neutrophils in the synergistic liver injury from monocrotaline and bacterial lipopolysaccharide exposure. Toxicol Sci 72, 43-56, 2003.
- 66) Luyendyk JP, Maddox JF, Cosma GN, Ganey PE, Cockerell GL, Roth RA. Ranitidine treatment during a modest inflammatory response precipitates idiosyncrasy-like liver injury in rats. J Pharmacol Exp Ther 307, 9-16, 2003.
- 67) Yee SB, Harkema JR, Ganey PE, Roth RA. The coagulation system contributes to synergistic liver injury from exposure to monocrotaline and bacterial lipopolysaccharide. Toxicol Sci 74, 457-69, 2003.
- 68) Yee SG, Hanumegowda UM, Copple BL, Shibuya M, Ganey PE, Roth RA. Endothelial cell injury and coagulation system activation during synergistic hepatotoxicity from monocrotaline and bacterial lipopolysaccharide coexposure. Toxicol Sci 74, 203-214, 2003.
- 69) Luyendyk JP, Barton CC, Copple BL, Ganey PE, Roth RA. Augmentation of aflatoxin B<sub>1</sub> hepatotoxicity by endotoxin: involvement of endothelium and the coagulation system. Toxicol Sci 72, 171-181, 2003.
- 70) Copple BL, Hanumegowda U, Moulin FM, Ganey PE, Roth RA. Thrombin and protease-activated receptor-1 agonists promote lipopolysaccharide-induced hepatocellular injury in perfused livers. J Pharmacol Exper Ther 305, 417-425, 2003.
- 71) Maddox JF, Roth RA, Ganey PE. Allyl alcohol activation of protein kinase C δ leads to cytotoxicity of rat hepatocytes. Chem Res Toxicol 16, 609-615, 2003.
- 72) Kinser S, Copple BL, Roth RA, Ganey PE. Enhancement of allyl alcohol hepatotoxicity by endotoxin requires extrahepatic factors. Toxicol Sci 69, 470-481, 2002.
- 73) Yee SB, Copple BL, Ganey PE, Roth RA. The temporal relationship between bacterial lipopolysaccharide and monocrotaline exposures influences toxicity: Shift in response from hepatotoxicity to nitric oxide-dependent lethality. J Toxicol Environ Hlth, Part A 65, 961-976, 2002.
- 74) Luyendyk J, Shores K, Ganey PE, Roth RA. Bacterial lipopolysaccharide exposure

- alters aflatoxin B₁ hepatotoxicity: Benchmark dose analysis for markers of liver injury. Toxicol Sci 68, 220-225, 2002.
- 75) Copple BC, Woolley B, Banes A, Ganey PE, Roth RA. Anticoagulants prevent monocrotaline-induced hepatic parenchymal cell injury but not endothelial cell injury in the rat. Toxicol Appl Pharmacol 180, 186-196, 2002.
- 76) Copple BL, Banes A, Ganey PE, Roth RA. Endothelial cell injury and fibrin deposition in rat liver after monocrotaline exposure. Toxicol Sci 65, 309-318, 2002.
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