

**SOT** | Society of  
Toxicology  
Creating a Safer and Healthier World  
by Advancing the Science of Toxicology

# PRELIMINARY PROGRAM

## 49<sup>th</sup> Annual Meeting and ToxExpo™

March 7–11, 2010



# SALT LAKE CITY, UTAH



## Important Deadlines

**Early Bird Registration**  
**January 22, 2010**

**Housing Reservation**  
**February 11, 2010**

**Standard Registration**  
**February 12, 2010**

**Registration Cancellation**  
**February 12, 2010**

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Dear Colleagues:

I am cordially inviting you to attend the Society of Toxicology's 49<sup>th</sup> Annual Meeting and ToxExpo™, March 7–11 in Salt Lake City, Utah. Among the many highlights, this year's program will feature sessions grouped around the scientific themes of Cell Signaling, Gene-Environment Interactions, Metabolic Disease, Mitochondrial Basis of Disease, Toxicity Testing in the 21<sup>st</sup> Century, and Translational Toxicology. The five-day event promises to provide scientists with countless opportunities to explore the depth and breadth of the field of toxicology. This year's Regional Interest session, *Signaling Mechanisms for Metabolic Dysfunction Following Low-Level Arsenic Exposures: From Mouse to Man* will address an issue of relevance to mining states such as Utah. Featured scientific programs include the symposia, workshops, roundtables, historical highlights, and platform and poster sessions. These will address an array of topics that clearly demonstrate how the science of toxicology contributes to a safer and healthier world.

In addition to the scientific program, the Annual Meeting affords every attendee the opportunity to come together to learn about the latest scientific achievements from experts in a myriad of fields, including the keynote speakers and other featured lecturers. This year's Plenary Lecture will be given by Dr. Ferid Murad. Dr. Murad was one of three recipients to receive the 1998 Nobel Prize in Physiology or Medicine for his work on nitric oxide and its role in cell signaling. Continuing Education courses, as always, will offer both introductory and advanced topics, and will be targeting biologicals and cytokine biology in the course material.

The Annual Meeting in Salt Lake City also provides an important networking opportunity for the exchange of ideas and solutions to many issues that toxicologists face in their professional careers. In addition to affording attendees the chance to renew and foster relationships with their colleagues, the Meeting also provides an opportunity to see the latest products, services and technologies at the ToxExpo™, the largest toxicology trade show of its kind anywhere.

We look forward to seeing you in Salt Lake City. Help us make this 49<sup>th</sup> Annual Meeting an event to remember.

Sincerely,

Cheryl Lyn Walker, Ph.D.  
2009–2010 SOT President





# SOT | Society of Toxicology

**Creating a Safer and Healthier World  
by Advancing the Science of Toxicology**

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Dear Colleagues,

On behalf of the Scientific Program Committee and the Society of Toxicology, I would like to invite you to join us at our 49<sup>th</sup> Annual Meeting to be held from March 7–11, 2010, at the Salt Palace Convention Center in Salt Lake City, Utah.

The Scientific Program Committee has assembled an exciting program that provides an outstanding venue for discussion of the latest scientific advances in the toxicological sciences. Your participation will allow you to be active in important deliberations of the latest discoveries in toxicological sciences, the newest technologies to advance the pace of biomedical research, and approaches to risk management decisions affecting our world today. The Annual Meeting will also facilitate gathering with your colleagues in a setting that readily lends itself to discussion of the science and practice of toxicology.

With significant input from our Specialty Sections, Special Interest Groups, and SOT Committees, the program has been structured into 26 Symposia, 21 Workshops, 10 Roundtables, and 6 Keynote and named lectures. Recent developments will be featured at the meeting and complemented by thematic developments in six selected areas that include **Cell Signaling, Gene-Environment Interactions, Metabolic Disease, Mitochondrial Basis of Disease, Toxicity Testing in the 21<sup>st</sup> Century,** and **Translational Toxicology.** Special platform and poster sessions will be organized around these and other topics to take advantage of outstanding abstract submissions from the general membership, as well as special invitations extended to prominent scientists in their respective fields.

In addition to the opportunity to be a part of cutting-edge scientific developments, you will have the opportunity to renew professional relationships, network with old and new colleagues, actively pursue job opportunities and interview on-site with potential employers, or simply catch up on recent events in the public, private, and government sectors.

Our host city, Salt Lake City, is nestled against the Wasatch Mountains; this Rocky Mountain town and Capital of Utah offers an urban oasis just minutes away from an alpine escape. Where city culture meets sublime outdoor beauty, Salt Lake City is known to feature one of the most scenic backdrops in the country. A beautiful, safe, and vibrant city, Salt Lake City combines outstanding access to natural recreation, a bustling economy, dynamic nightlife, remarkable history, warm hospitality, and Utah's Greatest Snow on Earth™. So, join your Society of Toxicology colleagues in this beautiful and extraordinary city! Consider bringing the family along and extending your stay by a few days to fully experience Salt Lake City and beyond. For more information about Salt Lake City, visit [www.visitsaltlake.com](http://www.visitsaltlake.com).

The success of the Annual Meeting depends on your active participation and contributions. Please register now on-line at [www.toxicology.org](http://www.toxicology.org) or by completing and returning the enclosed Registration Form along with payment to:

SOT Registration  
P.O. Box 91895  
Washington, DC 20090-1895, U.S.A.

Come be part of the action! We look forward to seeing you in Salt Lake City.

Warmest Regards,

**Michael Holsapple, Ph.D., ATS**  
SOT Vice President and  
Scientific Program Committee Chairperson

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# SCIENTIFIC PROGRAM OVERVIEW

## Sunday, March 7

7:00 AM–7:45 AM

### SUNRISE CONTINUING EDUCATION COURSE

1. Biological Pathway Analysis: An Introduction to the Pathway Knowledge Bases for Toxicological Research

8:15 AM–12:00 NOON

### MORNING CONTINUING EDUCATION COURSES

2. Biologicals: Introduction to Drug Development
3. Comparative Biology of the Lung
4. Cytokines: Balancing Therapeutic Utility and Immune System-Mediated Toxicities
5. Nuclear Receptors: Role in Chemical Mode of Action and Targets for Toxicity Testing
6. Predictive Power of Novel Technologies (Cells to 'Omics): Promises, Pitfalls, and Potential Applications
7. Reproduction and Regulatory Impact

1:15 PM–5:00 PM

### AFTERNOON CONTINUING EDUCATION COURSES

8. Assessment of Ocular Toxicity in Toxicology Studies Conducted for Regulatory Purposes
9. Gene-Environment Interactions Influence Cytokine Biology in Immunotoxicity and Disease: Genomic, Genetic, and Epigenetic Perspectives
10. Mitochondrial Toxicity: Animal Models and Screening Methods in Drug Development
11. ICH Initiatives for Conducting Pharmaceutical Preclinical Safety Studies: New and Revised Guidelines and Challenges
12. Segment-Specific Renal Pathology for the Non-Pathologist
13. Technologies and Tools for Toxicity Testing in the 21<sup>st</sup> Century

## Monday, March 8

8:00 AM–9:00 AM

### PLENARY OPENING LECTURE

Discovery of Nitric Oxide and Cyclic GMP Cell Signaling and Their Role in Drug Development  
Lecturer: Nobel Laureate Ferid Murad

9:15 AM–12:00 NOON

### SYMPOSIA SESSIONS

- Mechanistic Role of Reactive Intermediate Protein Covalent Binding in Target Organ Toxicity: Past, Present, and Future
- Neurological Responses After Exposure to Inhaled Metal Particles
- Ovarian Toxicity: Current Concepts in Toxicology, Pathology, and Mechanisms
- Silica and Asbestos Immunotoxicity: Mechanisms to Fibrosis, Autoimmunity, and Modified Tumor Resistance

### WORKSHOP SESSIONS

- Does Background Disease Lead to Low Dose Linearity?
- Heart Smart: Innovative Approaches for Improving Cardiovascular Safety Through Collaboration
- Toxicology in the 21<sup>st</sup> Century: Stem Cells in Drug Discovery and Development

### PLATFORM SESSIONS

- Biomarkers of Target-Organ Toxicity
- Chemical and Biological Weapons—Sulfur Mustard
- Immunopharmacogenomics and Immune Regulation
- Mitochondrial-Mediated Mechanisms of Toxicity of Xenobiotics

9:30 AM–12:30 PM

### POSTER SESSIONS

- Carcinogenesis I
- Epigenetics
- Hypersensitivity, Autoimmunity, and Idiosyncratic Drug Reactions
- Investigations of Chemical Mixtures
- Mechanistic Aspects of Persistent Organic Chemical Toxicity
- Nanotoxicology I
- Neurodevelopmental Toxicity: General
- Screening and Predicting Toxicity: Computational Approaches to Identify Targets
- Toxicity Testing—Alternative Models I

12:10 PM–1:30 PM

### ROUNDTABLE SESSIONS

- Combination Toxicology Studies for Pharmaceutical Agents: Design Considerations and Impact on Clinical Development
- Melamine Contamination of Infant Formulas: Lessons Learned

### HISTORICAL HIGHLIGHTS SESSION

- Translating Toxicology to Public Health Protection: Lessons Learned from Superfund

12:30 PM–1:20 PM

### LEADING EDGE IN BASIC SCIENCE AWARD LECTURE

Toxicogenomics at NIEHS: How Genomics Is Impacting the Science of Toxicology  
Lecturer: Richard S. Paules

1:00 PM–4:30 PM

### POSTER SESSIONS

- Advances in Dermal Toxicology
- Biotransformation I
- Carcinogenesis II
- Chemical and Biological Weapons
- Environmental Impact of Xenobiotics
- Genetic Diversity and Response to Xenobiotics
- Nanotoxicology II
- Reproductive Toxicology
- Toxicity Testing—Alternative Models II

1:40 PM–4:25 PM

### SYMPOSIA SESSIONS

- Alterations in Regulatory T Cells: Novel Pathways to Immunotoxicology
- Faster Science for Better Decisions: Characterizing Environmental Contaminant Risk from High-Throughput Data
- Genotoxic Impurities in Drugs and Drug Products: What is the Right Way to Deal with Impurities in R&D *Versus* Regulatory Guidance?
- Metabolic Syndrome and Increased Sensitivity to Drug-Induced Liver Injury (DILI): Nonclinical Models and Clinical Implications
- Phthalate Reproductive and Developmental Toxicity: Implications for Cumulative Risk Assessment

### WORKSHOP SESSION

- Determination of the Contribution of Individual Stressors in Cumulative Risk Assessments

### REGIONAL INTEREST SESSION

- Signaling Mechanisms for Metabolic Dysfunction Following Low-Level Arsenic Exposures: From Mouse to Man

### PLATFORM SESSIONS

- Animal Models in the 21<sup>st</sup> Century
- Advances in Biomarkers of Renal Injury
- Lipid Metabolism and Apoptosis
- Methods and Animal Models in Cardiovascular Safety Pharmacology

4:35 PM–5:55 PM

### SOT/EUROTOX DEBATE

Threshold of Toxicological Concern (TTC): Is Based on Science or Politics?

**4:35 PM–5:55 PM**

**ROUNDTABLE SESSIONS**

- Inhaled Particles: From the Nose to the Brain?
- Safety of Vitamins and Minerals: Controversies and Perspectives
- The Evolution of the Extended One-Generation Study Design for Agricultural and Industrial Chemical Hazard Identification

**Tuesday, March 9**

**7:30 AM–8:50 AM**

**ROUNDTABLE SESSIONS**

- Can Animal Neurotoxicity Predict Human Dysfunction?
- Weighing Complex Data in Risk Decisions: Concepts of Evidence-Based Toxicology

**INFORMATIONAL SESSIONS**

- Human Hepatocytes Derived from Embryonic Stem Cells: A New Tool for *In Vitro* Toxicity Testing
- Recent Advances in Pulmonary Surfactant Toxicological Assessment and Therapeutics

**8:00 AM–8:50 AM**

**TRANSLATIONAL IMPACT AWARD LECTURE**

Translating Mechanism-Based Research into Antidotes: Trials, Tribulations, and Triumphs  
Lecturer: Kenneth E. McMartin

**9:00 AM–11:45 AM**

**SYMPOSIA SESSIONS**

- Anti-Drug Antibody-Mediated Toxicity in Nonclinical Toxicity Studies: Impact and Relevance to Human Safety
- Bile Salt Transport and Liver Injury
- MAP Kinase Signaling: A Common Target Eliciting Unique Tissue Responses
- Molecular Determinants of Mitochondrial Disease
- POPs: What's New and Why Should We Care?

**WORKSHOP SESSIONS**

- Opportunities to Modify Current Regulatory Testing Guidelines and Advance the Assessment of Carcinogenicity Risk in the 21<sup>st</sup> Century
- Research Advances and Enduring Needs in Children's Environmental Health Protection

**EDUCATION-CAREER DEVELOPMENT SESSION**

- Where Do I Go Now? Rational Career Development Planning for Early-Career Scientists

**PLATFORM SESSIONS**

- Epidemiological Insights: Effects of Environmental and Occupational Exposures
- Gene Environmental Interactions in Carcinogenesis
- Reproductive and Developmental Effects Using Fish Models

**9:00 AM–12:30 PM**

**POSTER SESSIONS**

- Animal Models—Emerging Methods
- Arsenic I
- Biological Modeling: Multiple Scales of Parameters, Structures, and Applications
- Developmental Toxicology
- DNA Damage and Repair
- Education
- Inflammation and the Pathogenesis of Toxicity
- Kidney I
- Metal Neurotoxicity: General
- Mutagenicity
- Nanotoxicology—Carbon Nanostructures
- Oxidative Injury and Redox Biology
- Pharmaceutical Toxicology I

**12:00 NOON–1:20 PM**

**ROUNDTABLE SESSIONS**

- The Ying and Yang of Immunomodulatory Biopharmaceuticals: What Have We Learned since MABEL and How Close Are We to the Clinical Dose?
- Women's Health: Toxicology and Safety of Complementary and Alternative Medicine

**EDUCATION—CAREER DEVELOPMENT SESSION**

- Science Communication in 2010: A New Decade in Toxicology and Need for Better Communication

**12:30 PM–1:20 PM**

**DISTINGUISHED TOXICOLOGY SCHOLAR AWARD LECTURE**

Toxic Injury: Initiation, Expansion, and Repair  
Lecturer: Harihara M. Mehendale

**1:00 PM–4:30 PM**

**POSTER SESSIONS**

- Ah Receptor Biology and Toxicology
- Apoptosis/Cell Death
- Biomarkers
- Biotransformation II
- Genotoxicity
- Neurodegenerative Disease
- Neurotoxicity of Pesticides
- Risk Assessment I: New Data and Derivations Across Chemicals from A to V
- Safety Assessment: Commercial and Consumer Products
- Pharmaceutical Toxicology II
- Safety Concerns of Food and Natural Products

**1:30 PM–4:15 PM**

**SYMPOSIA SESSIONS**

- Genetics: The Link between Exposures, Gene x Environment Interaction, and Toxicity
- It's Not Your Father's Aryl Hydrocarbon Receptor: New Biological Roles for a Misunderstood Receptor
- Mechanisms of Chemical-Induced Liver Cancer: Putting the Pieces Together
- New Strategies for the Use of Genetic Toxicology Data in Human Risk Assessment
- Recent Knowledge on Critical Regulators of Lipid Homeostasis in Metabolic Disease
- Zinc, Copper, and Their Metabolic Effect: Myths and Musts

**WORKSHOP SESSIONS**

- Immunotoxicity and Other Safety Considerations in the Development of Therapeutic Vaccines
- Widely Varying Strategies Implemented in Discovery to Reduce the Failure Rate of Clinical Lead Candidates in Development

**PLATFORM SESSIONS**

- Emphasis on the Embryo: HTS, PBPK, and Virtual Tissue Technologies
- Model Systems in Neurodevelopmental Toxicity
- Nanotoxicology—Pulmonary Effects
- Toxicity Detection—Alternatives to Animal Models

**Wednesday, March 10**

**7:30 AM–8:50 AM**

**INFORMATIONAL SESSIONS**

- Impact of Tungsten and Tungsten Alloys on Health Risk
- The 2009 Tennessee Fly Ash Spill: An Environmental Emergency Case Study

**EDUCATION—CAREER DEVELOPMENT SESSION**

- Career Alternatives in Toxicology: Lessons Learned

**8:00 AM–9:00 AM**

**KEYNOTE MEDICAL RESEARCH COUNCIL (MRC) LECTURE**

The Interplay Between Phosphorylation and Ubiquitination in Regulating the Innate Immune System  
Lecturer: Sir Philip Cohen

**9:00 AM–11:45 AM**

**SYMPOSIA SESSIONS**

- Gender Divergent Xenobiotic Responses
- Mitochondrial Toxicity in Disease and Death
- The Fetal Basis of Adult Disease

**9:00 AM–11:45 AM****WORKSHOP SESSIONS**

- Current Thinking and Experiences Related to Developmental and Reproductive Safety Assessment of Biotherapeutics
- Novel Research Approaches and Animal Models in Translational Toxicology
- Toxicity Testing in the 21<sup>st</sup> Century for Ecotoxicology
- Understanding Nonlinearities at the Low-End of the Dose-Response Curve: Insights from Molecular Network Analysis

**PLATFORM SESSIONS**

- Advances in Mycotoxin Toxicity
- Impact of Receptors and Gene Regulation in Toxicological Response
- Inhalation Toxicology of Ultrafine or Nanoparticles
- Reproductive and Developmental Toxicity of Phthalates

**9:00 AM–12:30 PM****POSTER SESSIONS**

- Causes and Progression of Hepatic Metabolic Dysfunction
- Gene Regulation
- Hepatotoxicity: Role of Bile Acid Metabolism and Homeostasis
- Immunotoxicology: Mechanisms
- Inhalation Toxicology
- Nanotoxicology—Gold or Silver Nanoparticles
- Neurodevelopmental Toxicity of Metals
- Signal Transduction
- Stem Cell Toxicology
- Studies in Pharmacokinetics and Disposition
- Toxicogenomics—Continuing Advances in Molecular Toxicology

**12:00 NOON–1:00 PM****FEATURED SESSION**

- A Conversation with the NIEHS Director: Linda Birnbaum

**12:00 NOON–1:20 PM****INFORMATIONAL SESSIONS**

- Life-Stage Adjustment Five Years Later—Experiences from the Cancer Risk Assessment Field
- Measuring Immune Responses in Monkeys for Drug Development: Opportunities and Challenges for Predicting Human Efficacy and Immunotoxicity
- The Tox21<sup>st</sup> Community and the Future of Toxicology Testing

**12:30 PM–1:20 PM****MERIT AWARD LECTURE**

Living with Passion—Opening Doors in Research, Teaching, and Service  
Lecturer: Marion Ehrich

**1:00 PM–4:30 PM****POSTER SESSIONS**

- Fetal Basis of Adult Disease
- Beneficial Effects of Natural Products
- Carcinogenesis: Breast and Reproductive
- Cardiovascular Toxicology
- Exposure Assessment and Emerging Biomonitoring Applications
- Immunotoxicology: Methods and Models
- Metals I
- Models and Mechanisms of Hepatotoxicity
- Pesticides: General
- Regulations and Policy in Toxicology
- Risk Assessment II: Methodological Challenges and Metals

**1:15 PM–2:15 PM****FEATURED SESSION**

- A Conversation with Seymour Garte, the Director of the Division of Physiological and Pathological Sciences, Center for Scientific Review (CSR)

**1:30 PM–4:15 PM****SYMPOSIA SESSIONS**

- Aging as a Determinant of Xenobiotic Toxicity
- TRPing the Sensor: The Role of TRP Channel Signaling in Cardiopulmonary Toxicity
- Zebrafish Models for Developmental Neurobehavioral Toxicology

**WORKSHOP SESSIONS**

- High-Throughput Electrophysiology—21<sup>st</sup> Century Toxicity Testing Approaches with Functional Outcomes
- Minerals and Metals: Pros and Cons of Deliberate Exposure
- ‘Omics Profiling of Cell and Tissue Interactions of Nanomaterials: Insight into Mechanisms of Action
- The Process of Defining Risk for Environmental Chemicals Having Significant Skin Exposure and Absorption Potential
- Translation of Non-clinical Models to Clinical Risk Management Strategies of Severe Infectious Diseases with Immunomodulatory Drugs

**PLATFORM SESSIONS**

- Insights Into Polyaromatic Hydrocarbon-Induced Toxicities
- Nanotoxicology—Metals and Metal Oxide Particles
- Predicting Hepatotoxicity: Computational Approaches to a Critical Target

**4:30 PM–5:50 PM****ROUNDTABLE SESSION**

- Overview of Current Regulatory Expectations for Oligonucleotide-Based Therapeutics: Case Studies for Different Classes of ODNs

**INFORMATIONAL SESSIONS**

- Seeking Funding for Undergraduate Research

**Thursday, March 11****7:30 AM–8:15 AM****ISSUES SESSION**

NAS Vision for Toxicity Testing in the 21<sup>st</sup> Century

**8:30 AM–12:00 NOON****POSTER SESSIONS**

- Drug-Induced Liver Injury
- Endocrine Toxicology
- Immune System Safety Evaluation/Developmental Immunotoxicology
- Juvenile Toxicity
- Metals II
- Receptors

**9:00 AM–11:45 AM****WORKSHOP SESSIONS**

- Blood-Based Genomic Profiles as Biomarkers of Exposure and Effect
- Humanized Models in Toxicology and Their Application to Hazard Characterization and Risk Assessment
- Systems Biology Approaches to Understanding Cell Signaling in Dermal and Ocular Toxicology
- Toxicological Challenges in Green Product Development

**2010 FEATURED SESSIONS  
(To Be Scheduled)****SPECIAL SESSIONS**

- Meet the EPA Administrator
- Meet the FDA Commissioner

# PRELIMINARY PROGRAM CONTENT REFERENCE

Maximize the value of your Annual Meeting attendance by familiarizing yourself with the following reference guide for the *Preliminary Program*.

## Preliminary Program Overview

Section	Description
Scientific Program Overview (pages ii–iv)	This reference guide lists the Annual Meeting sessions, and their scheduled dates and times, including Symposia, Workshops, and Roundtables, special lectures, and Platform and Poster Presentations. Please note that detailed information related to many of these sessions will not be available until the final <i>Program</i> is completed.
Thematic Session Index (pages vi–vii)	Each of the Annual Meeting sessions highlighted within the 6 themes are listed. The list of sessions is preceded by a brief description of each theme. Throughout the <i>Preliminary Program</i> , each of the scientific sessions tracked within a theme is identifiable by a  symbol. This year, the Society will highlight 55 thematic sessions.
2010 SOT Award Winners (pages 28–29)	These pages list each of your fellow members who have been awarded a prestigious SOT award in recognition of their esteemed accomplishments in the field of toxicology.
Continuing Education Courses (page 30–38)	These pages list the 2010 CE course descriptions and presenter information. These courses have separate registration fees. Each participant in a CE course will receive a copy of the course syllabus. Course syllabi are available for sale to non course registrants on-site at the meeting while supplies last.
Featured Sessions (pages 40–42)	This section lists the Keynote and other special lectures and sessions for the 2010 Annual Meeting. Detailed information for these sessions will be available in the final <i>Program</i> .
Scientific Sessions (pages 44–86)	The <i>Preliminary Program</i> layout is similar to that of the final <i>Program</i> . Specifically, this section lists the scientific sessions in date, time, and alphabetical order beginning with Symposium, Workshop, Roundtable, Historical Highlight, Informational, and finally the Education/Career Development sessions.
Special Events (pages 88–90)	This section lists the student events including the Student Mixer, <i>In Vitro</i> Lecture, and committee meetings, etc. This section also highlights several scientific and career development sessions of particular interest to the SOT Student and Postdoctoral membership.  A special highlight in this section includes the Educational Outreach initiatives undertaken each year at SOT including the Undergraduate Education Program.
Exhibits (pages 94–106)	ToxExpo™ is the profession's largest trade show and best resource for the latest information in technology, equipment, and services. This section contains the current list of exhibiting companies and Exhibitor Hosted Sessions.

## Scientific Session Types

### Education-Career Development Sessions (80 minutes)—

Sessions that provide tools and resources to toxicologists that will enhance their professional and scientific development (page 85)

### Exhibitor Hosted Sessions (60 minutes)—

Informative sessions developed by an exhibiting company (page 96)

### Featured Sessions (50–60 minutes)—

Keynote and other special lectures (page 40)

### Historical Highlights (80 minutes)—

Review of a historical body of science that has impacted toxicology (page 79)

### Informational Sessions (80 minutes)—

Scientific planning or membership development (page 80)

### Platform Sessions (165 minutes)—

Oral presentations that cover new areas, concepts, or data (see details in the final *Program*)

### Poster Sessions (180–210 minutes)—

Topic specific presentations that cover new areas, concepts, or data (see details in the final *Program*)

### Regional Interest Session (165 minutes)—

Central topics of relevance that describe public health and/or ecological problems of that region (page 87)

### Roundtable (80 minutes)—

Controversial subjects (page 73)

### Symposia Sessions (80 or 165 minutes)—

Cutting-edge science; new areas, concepts, or data (page 44)

### Thematic Sessions (80–210 minutes)—

Timely topics of relevance to toxicology (check the specific session type)

### Workshop Sessions (165 minutes)—

State-of-the-art knowledge in toxicology (page 60)

*Use the Itinerary Planner to plan your schedule (available in January) to make the most of your time at the Annual Meeting. See page 15 for more detail.*



## 2010 SESSIONS: THEMATIC APPROACH

The Scientific Program Committee has developed a slate of timely and highly informative symposium, workshop, roundtable, and other special sessions that span the spectrum of topics of interest to toxicologists.

The 2010 scientific themes listed here illustrate the core contributions toxicology makes to these areas. The sessions that will be highlighted within these themes are provided below.

### Cell Signaling

Cell signaling encompasses the broad range of pathways involved in how cells detect and respond to external stimuli and communicate with other cells. Key cellular responses regulated by cell signaling include cell death, differentiation, and cell motility. Understanding the contribution of cell signaling pathways to toxicity is often key to determining mechanisms of toxicity or the pathogenesis of biological responses elicited by chemicals or pharmaceuticals. Sessions in this theme highlight mechanistic roles for cell signaling pathways in toxic responses and disease pathogenesis.

- Alterations in Regulatory T Cells: Novel Pathways to Immunotoxicology—*Symposium Session*
- Impact of Receptors and Gene Regulation in Toxicological Response—*Platform Session*
- It's Not Your Father's Aryl Hydrocarbon Receptor: New Biological Roles for a Misunderstood Receptor—*Symposium Session*
- MAP Kinase Signaling: A Common Target Eliciting Unique Tissue Responses—*Symposium Session*
- Nuclear Receptors: Role in Chemical Mode of Action and Targets for Toxicity Testing—*Continuing Education Course (AM05)*
- 'Omics Profiling of Cell and Tissue Interactions of Nanomaterials: Insight into Mechanisms of Action—*Workshop Session*
- Receptors—*Poster Session*
- Systems Biology Approaches to Understanding Cell Signaling in Dermal and Ocular Toxicology—*Workshop Session*
- Toxicogenomics—Continuing Advances in Molecular Toxicology—*Poster Session*
- TRPing the Sensor: The Role of TRP Channel Signaling in Cardiopulmonary Toxicity—*Symposium Session*

### Gene-Environment Interactions

It is clear that disease susceptibility cannot be attributed only to variations in the human genome. The environment is major among the additional variables that define individual susceptibility to disease. A more precise determination of the influence of environmental exposures within a given genetic background on disease processes will be required to significantly improve the ability to predict, detect, treat, and monitor disease progression and disease response. The gene-environment interactions theme has been selected to highlight recent advances in this field that are relevant to the toxicological sciences.

- Ah Receptor Biology and Toxicology—*Poster Session*
- Epigenetics—*Poster Session*
- Gene-Environment Interactions Influence Cytokine Biology in Immunotoxicity and Disease: Genomic, Genetic, and Epigenetic Perspectives—*Continuing Education Course (PM09)*
- Gene Environmental Interactions in Carcinogenesis—*Platform Session*
- Gene Regulation—*Poster Session*
- Genetics: The Link between Exposures, Gene x Environment Interaction, and Toxicity—*Symposium Session*
- Genotoxicity—*Poster Session*
- Signal Transduction—*Poster Session*

### Metabolic Disease

Metabolic dysfunction, either acquired or inherited, affects biochemical reactions resulting in metabolic diseases. The incidence of acquired metabolic diseases is rising at an alarming rate. Perturbation of lipid and glucose metabolic pathways increases the risk of developing a number of chronic conditions such as obesity, diabetes, fatty liver disease, and cardiovascular disease. While genetic variability plays a role in individual susceptibility, environmental agents, drugs, and other toxicants are contributing factors. This theme will focus on the mechanistic changes in glucose and lipid metabolism induced by toxicants and the relationship to disease progression.

- Causes and Progression of Hepatic Metabolic Dysfunction—*Poster Session*
- Hepatotoxicity: Role of Bile Acid Metabolism and Homeostasis—*Poster Session*
- Metabolic Syndrome and Increased Sensitivity to Drug-Induced Liver Injury (DILI): Nonclinical Models and Clinical Implications—*Symposium Session*
- Recent Knowledge of Critical Regulators of Lipid Homeostasis in Metabolic Disease—*Symposium Session*
- Signaling Mechanisms for Metabolic Dysfunction Following Low-Level Arsenic Exposures: From Mouse to Man—*Regional Interest Session*
- Zinc, Copper, and Their Metabolic Effect: Myths and Musts—*Symposium Session*

## Mitochondrial Basis of Disease

Mitochondrial dysfunction has been found to be an important component in the progression of numerous human disease states. In addition, the mitochondrial genome is susceptible to oxidative stress and mutation due to the high percentage of coding DNA and its small size. Therefore, the mitochondria are a suspected target organelle of xenobiotics in different model organisms. This thematic area will highlight studies that evaluate the effect of xenobiotic exposure on mitochondrial function and the connection to the progression of disease.

- Drug-Induced Liver Injury—*Poster Session*
- Mitochondrial-Mediated Mechanisms of Toxicity of Xenobiotics—*Platform Session*
- Mitochondrial Toxicity: Animal Models and Screening Methods in Drug Development—*Continuing Education Course (PM10)*
- Mitochondrial Toxicity in Disease and Death—*Symposium Session*
- Molecular Determinants of Mitochondrial Disease—*Symposium Session*

## Toxicity Testing in the 21<sup>st</sup> Century

The NRC's 2007 report "Toxicity Testing in the Twenty-first Century: A Vision and a Strategy" articulated the critical need for development and validation of predictive high-throughput assays to replace current expensive and time-consuming animal tests. This theme includes applications of genomics and *in vitro* tests to identify pathways of toxicity and methods for using advanced computer power that make it feasible to analyze large volumes of complex data and use common data platforms to link existing and new exposure and effects databases.

- Animal Models—Emerging Methods—*Poster Session*
- Animal Models in the 21<sup>st</sup> Century—*Platform Session*
- High-Throughput Electrophysiology—21<sup>st</sup> Century Toxicity Testing Approaches with Functional Outcomes—*Workshop Session*
- Human Hepatocytes Derived from Embryonic Stem Cells: A New Tool for *In Vitro* Toxicity Testing—*Informational Session*
- Opportunities to Modify Current Regulatory Testing Guidelines and Advance the Assessment of Carcinogenicity Risk in the 21<sup>st</sup> Century—*Workshop Session*
- Predicting Hepatotoxicity: Computational Approaches to a Critical Target—*Platform Session*
- Screening and Predicting Toxicity: Computational Approaches to Identify Targets—*Poster Session*
- Toxicity Detection—*Alternatives to Animal Models*—*Platform Session*

- Technologies and Tools for Toxicity Testing in the 21<sup>st</sup> Century—*Continuing Education Course (PM13)*
- The Tox21<sup>st</sup> Community and the Future of Toxicology Testing—*Informational Session*
- Toxicity Testing—Alternative Models I—*Poster Session*
- Toxicity Testing—Alternative Models II—*Poster Session*
- Toxicity Testing in the 21<sup>st</sup> Century for Ecotoxicology—*Workshop Session*
- Toxicology in the 21<sup>st</sup> Century: Stem Cells in Drug Discovery and Development—*Workshop Session*

## Translational Toxicology

In most settings, translational science is described by the term "Bench to Bedside." Translational toxicology can be described as the transition of basic toxicology related-research into strategies to improve the performance of the science of toxicology. Thus, translational toxicology may be best described by the term "discovery to application." Sessions involving the translation of fundamental mechanistic observations into bioassays, biological models and other novel approaches that can be applied to toxicology research, and studies that describe the supporting biologic or mechanistic qualification of endpoints and detailed assay validation are highlighted in this theme.

- Advances in Biomarkers of Renal Injury—*Platform Session*
- Anti-Drug Antibody-Mediated Toxicity in Nonclinical Toxicity Studies: Impact and Relevance to Human Safety—*Symposium Session*
- Biomarkers of Target-Organ Toxicity—*Platform Session*
- Can Animal Neurotoxicity Predict Human Dysfunction?—*Roundtable Session*
- Does Background Disease Lead to Low Dose Linearity?—*Workshop Session*
- Emphasis on the Embryo: HTS, PBPK, and Virtual Tissue Technologies—*Platform Session*
- Humanized Models in Toxicology and Their Application to Hazard Characterization and Risk Assessment—*Workshop Session*
- Measuring Immune Responses in Monkeys for Drug Development: Opportunities and Challenges for Predicting Human Efficacy and Immunotoxicity—*Informational Session*
- Novel Research Approaches and Animal Models in Translational Toxicology—*Workshop Session*
- The Ying and Yang of Immunomodulatory Biopharmaceuticals: What Have We Learned since MABEL and How Close Are We to the Clinical Dose?—*Roundtable Session*
- Translation of Nonclinical Models to Clinical Risk Management Strategies of Severe Infectious Diseases with Immunomodulatory Drugs—*Workshop Session*
- Translating Toxicology to Public Health Protection: Lessons Learned from Superfund—*Historical Highlights*

# SOT AFFILIATES

**Abbott Laboratories**

Abbott Park, Illinois

**Alcon Research Ltd.**

Fort Worth, Texas

**American Chemistry Council**

Arlington, Virginia

**American Petroleum Institute**

Washington, D.C.

**Ani Lytics, Inc.**

Gaithersburg, Maryland

**AstraZeneca R&D**

Södertälje, Sweden

**BASi Evansville**

Mount Vernon, Indiana

**Battelle**

Columbus, Ohio

**Bayer HealthCare Pharmaceuticals**

Montville, New Jersey

**Biogen Idec, Inc.**

Cambridge, Massachusetts

**Boehringer Ingelheim  
Pharmaceuticals, Inc.**

Ridgefield, Connecticut

**Bristol-Myers Squibb Company**

Princeton, New Jersey

**CANTOX**

Mississauga, Canada

**Celgene Corporation**

Summit, New Jersey

**Celsis In Vitro Technologies**

Baltimore, Maryland

**Charles River**

Wilmington, Massachusetts

**Chevron Corporation**

Richmond, California

**Colgate-Palmolive Company**

Piscataway, New Jersey

**Covance Laboratories Inc.**

Madison, Wisconsin

**Daiichi Sankyo Company Limited**

Shizuoka, Japan

**The Dial Corporation, A Henkel  
Company**

Scottsdale, Arizona

**Dow Chemical Company**

Midland, Michigan

**Dow Corning Corporation**

Midland, Michigan

**Eli Lilly and Company**

Indianapolis, Indiana

**ExxonMobil Biomedical  
Sciences, Inc.**

Annandale, New Jersey

**Genentech, Inc.**

South San Francisco, California

**GlaxoSmithKline**

King of Prussia, Pennsylvania

**The Hamner Institutes for Health  
Sciences**

Research Triangle Park, North Carolina

**Hoffmann-La Roche, Inc.**

Nutley, New Jersey

**Honeywell International, Inc.**

Morristown, New Jersey

**ISIS Services, LLC**

San Carlos, California

**J&J Pharma R&D Companies  
(Centocor, J&JPRD, Tibotec)**

Raritan, New Jersey

**Metabolon, Inc.**

Research Triangle Park, North Carolina

**Millennium: The Takeda Oncology  
Company**

Cambridge, Massachusetts

**MPI Research**

Mattawan, Michigan

**Novartis Pharmaceuticals Corporation**

East Hanover, New Jersey

**Pfizer, Inc.**

Groton, Connecticut

**Procter & Gamble Company**

Cincinnati, Ohio

**RTC Research Toxicology Centre S.P.A.**

Pomezia, Italy

**sanofi-aventis**

Bridgewater, New Jersey

**Schering-Plough Research Institute**

Summit, New Jersey

**Seguani, Ltd.**

Ledbury, Herefordshire, United Kingdom

**Suburban Surgical Company, Inc.**

Wheeling, Illinois

**Syngenta**

Greensboro, North Carolina

**WIL Research Laboratories, LLC.**

Ashland, Ohio

**Wyeth Research**

Collegeville, Pennsylvania

# PRELIMINARY PROGRAM

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**SOT** | Society of Toxicology

## 49<sup>th</sup> Annual Meeting & ToxExpo™

March 7–11, 2010

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### Registration Express

*Register by January 22, 2010, with full payment and you'll receive your name badge and tickets in the mail before the meeting.*

## GENERAL INFORMATION

### Your Invitation to Attend

The Society of Toxicology's Annual Meeting is the premier event of the year for toxicologists. The meeting is the forum to showcase toxicology's novel discoveries and achievements. The SOT 49<sup>th</sup> Annual Meeting and ToxExpo™ in Salt Lake City is the place to be for:

**Scientific Programming:** The SOT Scientific Program Committee has created a wide range of scientific sessions that include special in-depth thematic sessions on cell signaling, gene-environment interactions, metabolic disease, mitochondrial basis of disease, toxicity testing in the 21<sup>st</sup> century and translational toxicology, 26 symposia, 21 workshops, 10 roundtable, 1 historical highlight, and 8 informational

sessions. Continuing Education courses this year target special areas including biologicals and cytokine biology. The scientific programs include a myriad of experts in all the disciplines of toxicology and includes Nobel Laureates.

**Global Perspectives:** The SOT Annual Meeting attracts toxicologists from around world from places like Ankara, Turkey; Hsinchu, Taiwan; Horn, Switzerland; Reus, Spain; Ansan, South Korea; Tepic, Mexico; Vilnius, Lithuania; Kobe, Japan; Ancona, Italy; Pecs, Hungary, and Tutzing, Germany. International toxicologists have a unique opportunity to meet in one place to exchange information, share ideas, and explore lessons learned.

**Value:** The SOT Annual Meeting registration rates are reasonable and SOT has made special arrangements with the hotels in

Salt Lake City to keep housing costs down this year. The Annual Meeting is the most cost-effective meeting you will attend because of the value you can bring back home and use on a daily basis.

**Networking:** With more than 6,500 attendees expected, the SOT 49<sup>th</sup> Annual Meeting offers unparalleled opportunities to network with scientists from around the world. Your participation allows you to be an active voice in important deliberations of the latest discoveries in toxicological sciences.

**A Unique Destination:** Salt Lake City is a surprising place with unexpected attractions to visit—all in a beautiful location at the foot of Utah's Wasatch Mountains. Salt Lake City is a large metropolitan area, yet offers year-round outdoor activities within minutes of this breathtaking city. The city

## ToxExpo™—A Great Opportunity for Exhibitors

### We've Got the Numbers You Want

More than 6,500 scientists and researchers attend SOT's Annual Meeting and ToxExpo™. What better opportunity to:

- meet face-to-face,
- build relationships with new prospects, and
- network with other exhibiting companies.

### New Faces/New Leads

Research shows that 55% of the professional toxicologists who will attend the 2010 Annual Meeting and ToxExpo™ did not attend the 2009 Meeting in Baltimore.

### On-Line Marketplace at ToxExpo.com

ToxExpo™ exhibitors are listed on-line year around to increase your visibility and exposure to your target audience. It's a rich resource for all the services and products toxicologists need throughout the year.

For more information on exhibiting at the largest Toxicology trade show in the world, please visit [www.toxexpo.com](http://www.toxexpo.com), or contact Liz Kasabian at SOT Headquarters: (703) 438-3115 ext. 1454 or e-mail: [liz@toxicology.org](mailto:liz@toxicology.org).

### A Global Audience

Nearly 20% of SOT's Annual Meeting and ToxExpo™ attendees are scientists from countries outside the U.S. All registrants are engaged in one or more of the following areas of research:

- Biological Modeling
- Biotechnology
- Biomarkers
- Carcinogenesis
- Comparative and Veterinary
- Dermal Toxicology
- Drug Discovery Toxicology
- Epigenetics
- Ethical, Legal, and Social Issues
- Food Safety
- Immunotoxicology
- *In Vitro* and Alternative Methods
- Inflammation and Disease
- Inhalation and Respiratory
- Mechanisms
- Medical Devices
- Metals
- Mixtures
- Molecular Biology
- Nanotoxicology
- Neurodegenerative Disease
- Occupational and Public Health
- Ocular Toxicology
- Regulatory and Safety Evaluation
- Reproductive and Developmental
- Risk Assessment
- Toxicologic and Exploratory Pathology

# 49<sup>TH</sup> ANNUAL MEETING AND TOXEXPO™

## GENERAL INFORMATION

has a rich history and offers vast cultural opportunities including the Ballet West, Utah Opera Company, Ririe-Woodbury Dance Company, Repertory Dance Theatre, Mormon Tabernacle Choir, and the Greatest Snow on Earth™ venues, and the beautiful cathedrals and temples of several different religious faiths.

### Why Attend ToxExpo™

ToxExpo™ is the profession's largest trade-show of its kind anywhere. Attendees and exhibitors from around the globe gather to exchange ideas and debut cutting-edge products, services, and technologies. Toxicologists and industry professionals have the unparalleled opportunity to gain first-hand knowledge on the latest advances from more than 350 exhibitors.

The following are the exhibit hours for the 2010 ToxExpo™:

Monday .....	9:00 AM–4:30 PM
Tuesday .....	8:30 AM–4:30 PM
Wednesday .....	8:30 AM–4:30 PM

ToxExpo™ is available all year. Visit [www.toxexpo.com](http://www.toxexpo.com) for the latest in toxicology-related products and services. The site offers access 24/7, 365 days per year, to resources for toxicologists worldwide. ToxExpo™ is a valuable tool for the policymaker, scientist, student, or anyone who is looking for the best that toxicology has to offer.

### An Invitation to International Attendees

The Society of Toxicology cordially invites scientists from around the world to attend its 49th Annual Meeting, March 7–11, 2010. Please note that individual invitations are not required for attendance at meetings of the Society of Toxicology. Since the meetings are open scientific events, SOT invites all interested scientists to attend.

If your travels require a visa, the U.S. is advising visa applicants to apply at least three to four months in advance of their travel date. To increase security for citizens and visitors, the U.S. has updated its policies for visas. We request that you contact the United States Consulate/Embassy and Currency Exchange in your own country regarding documentation and necessary information for your visit to the United States.

If you need a formal invitation for your visa application, you may request an invitation by sending your name, address, and fax number to the SOT Registration Department. If you have been accepted to make a presentation at the meeting, please include the name and date of your presentation. You will need to make your own hotel reservations and register for the meeting. If you need assistance, please contact the SOT Registration Department at tel: (703) 438-3115, fax: (703) 438-3113, or e-mail: [sothq@toxicology.org](mailto:sothq@toxicology.org).

Here are some sources of information to help you obtain a visa:

- <http://travel.state.gov/visa>  
A Web site designed with you in mind about current visa policies and procedures.
- [www.nationalacademies.org/visas](http://www.nationalacademies.org/visas)  
For additional visa information, contact International Visitors Office (IVO) of the National Academies of the Sciences at the above Web site. This should serve as a visa resource for all visiting scientists and scholars traveling to the United States. Additionally, a questionnaire is available that can be used to assist future travelers with the visa process.
- **Make an Appointment**  
Visit the U.S. Embassy or Consulate. Make sure you ask if there are any fees required. Most fees must be paid before your appointment. Wait times for appointments may be longer than in the past. Schedule the appointment as soon

as possible. Information on Visa wait times can be found at [http://travel.his.com/visa/tempvisitors\\_wait.php](http://travel.his.com/visa/tempvisitors_wait.php).

- **Get Your Documents Ready**  
Organize passport, applications, and documents to support the application with employment details (reason for travel along with financial status), and proof of payment of fees.
- **Submit Your Application**  
Send your application and passport along with supporting documents to the U.S. Embassy or Consulate.
- **Start Early**  
Additional reviews may be required. This could add an additional 4–6 weeks to the processing time.

### Accessibility for Persons with Disabilities

The Salt Palace Convention Center (SPCC) and most of the SOT hotels are accessible to persons with disabilities. If you require special services, please mark the appropriate box on the Annual Meeting Registration Form. The Salt Palace Business Center rents scooters and wheelchairs on a daily or weekly basis. For pricing and availability, call (801) 534-6301 or e-mail [businesscenter@saltpalace.com](mailto:businesscenter@saltpalace.com).

Scooters can also be rented from Scoot Around. For more information, please go to [www.scootaround.com](http://www.scootaround.com) or call (888) 441-7575. They will deliver to your hotel. If you require a sign language interpreter, please contact the American Sign Language Communication at [www.aslcomm.com](http://www.aslcomm.com) or call (801) 403-6606.

If you require more information about accessibility, please contact Heidi Prange at SOT Headquarters: (703) 438-3115 ext. 1424.

## GENERAL INFORMATION

### QUESTIONS?

#### CONTACT

TEL: (703) 438-3115

#### Career Resource and Development

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#### Meetings and Housing

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#### Membership

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#### Regional Chapters

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#### Registration

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#### Scientific Program

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kim@toxicology.org

#### Specialty Sections

Kim Von Brook .....Extension 1437  
kim@toxicology.org

#### Sponsorship and Affiliates

Liz Kasabian .....Extension 1454  
liz@toxicology.org

### Attire

The official attire for the Annual Meeting is business casual. No coat or tie is required! We encourage you to bring comfortable clothing and shoes. Because meeting rooms may seem cold, please bring a sweater or jacket and/or dress in layers.

### Climate

Salt Lake City weather is widely variable. The city lies in a semi-arid region in the Salt Lake Valley, surrounded by mountains and the Great Salt Lake, and receives little precipitation. During spring, temperatures warm steadily and rapidly. Wintry weather is usually last experienced by early-to-mid March. The average temperature for March is 43.1 F/6.2 C. For an up-to-date, detailed weather forecast, visit the National Weather Service Forecast Office at [www.wrh.noaa.gov/slc](http://www.wrh.noaa.gov/slc).

### Convention Center First Aid and Security

If an emergency should occur while at the Salt Palace Convention Center, proceed directly to the nearest pay phone, located throughout the facilities, and press the security button on the bottom of the phone. You will be connected directly to the 24-hour manned security department at the Convention Center. From any phone that is not a Convention Center pay phone, dial (801) 534-6320, which will connect directly to security.

The First Aid room is located across from Meeting Room 150. The First Aid Administrator will be on duty 7:00 AM–8:00 PM Sunday through Wednesday, and 7:00 AM–12:00 NOON on Thursday. In accordance with the State of Utah and Salt Lake City regulations, the First Aid Administrator is not permitted to dispense any medication.

### Green in Salt Lake City

Salt Lake City is surrounded by incredible natural beauty. The Salt Lake Convention & Visitors Bureau is proud to be part of a destination that is actively engaged in the journey to make the community an environmentally sustainable host for conventions, meetings, and visitors. The Salt Palace Convention Center strives to reduce, reuse, and recycle and believes that by carefully considering the environmental impact of all business decisions before they make them, they have been able to shrink the ecological footprint and will continue to do so. The following lists some of the ways the Center is going green:

- The 2006 expansion of the SPCC was awarded the U.S. Green Building Council's Silver LEED Certification for being designed and constructed utilizing environmentally responsible methods and materials.
- Bike racks are available in the parking structure to promote the use of alternative transportation.
- Preferred parking stalls are offered for all carpooling attendees/employees at SPCC.
- Utah Foods (caterer for the Convention Center) recycles all aluminum and cardboard products. In addition to the single source recycling program at the SPCC, recycling programs for grease and fry oil are in place.
- The Center provides weekly food donations to The Road Home Homeless Shelter, the Salt Lake Mission, and Utah Food Bank.
- 100% renewable Greenware products are available in the Center.
- 100% recycled paper napkins and compostable paper plates are used.
- The Center uses local food sources when possible, and uses organic food sources upon request.

# 49<sup>TH</sup> ANNUAL MEETING AND TOXEXPO™

## GENERAL INFORMATION

Learn how you can offset your travel to Salt Lake through their carbon offset program [www.visitsaltlake.com/carbon\\_offset](http://www.visitsaltlake.com/carbon_offset).

### Guest/Spouse Hospitality Center and Program

The SOT Guest/Spouse Hospitality Center provides guest participants (non-scientists) with a place to meet and socialize with other guests. To visit the Hospitality Center, guests must register for the Annual Meeting with the person they are accompanying. Guests are welcome to attend the Welcoming Reception, but will not have access to the scientific sessions or the Exhibit Hall. Please remember to wear your badge to all SOT events. The Guest Hospitality Center will be located in the Marriott Downtown.

### Housing Information

You may make your housing reservations through the on-line reservation system, The Housing Connection, found on the SOT Annual Meeting Web site.

The Society of Toxicology has reserved and arranged for SOT Annual Meeting attendee discounted room rates at various Salt Lake City hotels—known as the SOT hotel block. This block includes discounted room rates at many premier hotel chains.

Did you know that your choice of hotel for the SOT Annual Meeting has direct impact on Society's Strategic Planning Initiatives? Although we understand that making your reservations outside of the SOT block can sometimes be more economical, it decreases the money available to the Society to carry out its long-term goals and may cause the Society to have to pay attrition fees for unutilized rooms. In addition, the Society is unable to assist you if you have any difficulties with your room reservation, such as the hotel over-booking or misplacing your reservation.

SOT depends on the Annual Meeting revenue to fund other programs throughout the year and to keep future registration fees low. Please assist the Society by making your hotel reservation through The Housing Connection.

### Reservations and Deposits

The deadline date for new housing reservations is February 11, 2010. Based on availability, continue to make any requests through The Housing Connection until February 25. Beginning February 26, you may call the hotels directly for any housing requests. For information regarding your hotel room reservation on-site, please visit the SOT Housing Desk located in the South Foyer of the Salt Palace Convention Center.

**You may also make a reservation by the following method(s):**

- Fax: (801) 355-0250 (International and Domestic)
- Mail: The Housing Connection  
175 S. West Temple, Suite 140  
Salt Lake City, UT 84101  
United States

### Confirmations

Confirmation will be e-mailed, faxed, or mailed to you from The Housing Connection once your reservation has been booked. You will not receive a confirmation from your hotel. If you do not receive confirmation within 2 weeks, please call The Housing Connection at (801) 214-7282.

### Changes and Cancellations

The deadline for new reservations is Thursday, February 11, 2010. Continue to make any requests through The Housing Connection through February 25. If you cancel your reservation after February 25, 2010, you will be charged a \$25 processing fee. Beginning February 25 and up to 72 hours prior to your arrival, changes and cancellations must be made with your assigned hotel. Note: Some hotels charge an early departure fee.

Any cancellations made within 72 hours of arrival date will result in forfeiture of your first night's deposit and tax. For any new changes after February 26, please ask the hotel to send you a new e-mail or fax confirmation showing the change.

For best availability and immediate confirmation, make your hotel reservation *via* Internet or by phone. Faxed and mailed housing requests will take longer to process and your hotel selections may not be available.

## GENERAL INFORMATION

### Hotel Accommodations

#### 1) Courtyard by Marriott Downtown



\$139 Single/Double  
130 West 400 South  
Salt Lake City, Utah 84101  
Tel: (801) 531-6000  
Fax: (801) 531-1273  
Web site: [www.marriott.com/slccy](http://www.marriott.com/slccy)



Club: Marriott Rewards  
Check in: 3:00 PM  
Check out: 12:00 NOON  
2 blocks from Convention Center  
Complimentary self parking  
Complimentary wireless Internet access in guest room and throughout hotel

#### 2) Crystal Inn Downtown



\$102 Government Rate or  
\$132 Single/Double  
230 West 500 South  
Salt Lake City, UT 84101  
Tel: (801) 328-4466  
Fax: (801) 328 5653  
Web site: [www.crystalinnsaltlake.com](http://www.crystalinnsaltlake.com)



Club: N/A  
Check in: 3:00 PM  
Check out: 11:00 AM  
4 blocks from Convention Center  
Complimentary self parking  
Complimentary wireless Internet access in guest room and throughout hotel  
Complimentary breakfast  
Complimentary airport shuttle

#### 3) Grand America



\$199 Single/Double  
555 South Main Street  
Salt Lake City, UT 84111  
Tel: (801) 258-6000  
Fax: (801) 258-6911  
Web site: [www.grandamerica.com](http://www.grandamerica.com)



Club: N/A  
Check in: 3:00 PM  
Check out: 12:00 NOON  
5 blocks from Convention Center  
\$10/day self and \$15/day valet parking  
Complimentary wireless Internet access in guest room and throughout hotel

#### 4) Hilton Salt Lake City Center

##### SOT Co-Headquarters Hotel



\$163 Single/\$178 Double  
255 South West Temple  
Salt Lake City, UT 84101  
Tel: (801) 328-2000  
Fax: (801) 238-4888  
Web site: [www.saltlakecitycenter.hilton.com](http://www.saltlakecitycenter.hilton.com)



Club: Hilton HHonors  
Check in: 3:00 PM  
Check out: 12:00 NOON  
½ block from Convention Center  
\$13/day self and \$16/day valet parking  
Complimentary wireless Internet access in guest room and throughout hotel

#### 5) Hotel Monaco



\$165 Single/Double  
15 West 200 South  
Salt Lake City, UT 84101  
Tel: (801) 595-0000  
Fax: (801) 532-8500  
Web site: [www.monaco-saltlakecity.com](http://www.monaco-saltlakecity.com)



Club: Kimpton InTouch Loyalty Members  
Check in: 3:00 PM  
Check out: 12:00 NOON  
1 block from Convention Center  
\$15.50/day valet parking  
Complimentary wireless Internet access in guest room and throughout hotel

#### 6) Hyatt Place Salt Lake City Downtown



\$149 Single/Double  
55 North 400 West  
Salt Lake City, UT 84101  
Tel: (801) 456-6300  
Fax: (801) 456-6301  
Web site: [www.hyattplacesaltlakecitydowntown.com](http://www.hyattplacesaltlakecitydowntown.com)



Club: Hyatt Gold Passport  
Check in: 3:00 PM  
Check out: 12:00 NOON  
5 blocks from Convention Center  
\$10/day self parking  
Complimentary wireless Internet access in guest room and throughout hotel  
Complimentary breakfast

#### 7) Little America Hotel



\$139 Garden/\$159 Tower  
500 South Main Street  
Salt Lake City, UT 84101  
Tel: (801) 596-5700  
Fax: (801) 596-5911  
Web site: [www.littleamerica.com](http://www.littleamerica.com)



Club: N/A  
Check in: 3:00 PM  
Check out: 12:00 NOON  
5 blocks from Convention Center  
Complimentary self parking and \$7/day valet parking  
Complimentary wireless Internet access in guest room and throughout hotel

#### 8) Marriott City Center



\$159 Single/Double  
220 South State Street  
Salt Lake City, UT 84111  
Tel: (801) 961-8700  
Fax: (801) 961-8704  
Web site: [www.marriott.com/slecc](http://www.marriott.com/slecc)



Club: Marriott Rewards  
Check in: 3:00 PM  
Check out: 12:00 NOON  
2 blocks from Convention Center  
\$12/day self and \$16/day valet parking  
Complimentary wired Internet access in guest room—complimentary wireless Internet access in lobby

#### 9) Marriott Downtown

##### SOT Headquarters Hotel



\$168 Single/Double  
75 South West Temple  
Salt Lake City, UT 84101  
Tel: (801) 531-0800  
Fax: (801) 532-4127  
Web site: [www.marriott.com/slcut](http://www.marriott.com/slcut)



Club: Marriott Rewards  
Check in: 3:00 PM  
Check out: 12:00 NOON  
Across the street from Convention Center  
\$12/day self and \$16/day valet parking  
Wired internet access in guest room at \$12.95/day—wireless Internet in lobby as part of \$12.95

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## GENERAL INFORMATION

### 10) Radisson Hotel Downtown



\$102 Government Rate or  
\$152 Single/Double  
215 West South Temple  
Salt Lake City, UT 84101  
Tel: (801) 531-7500  
Fax: (801) 328-1289  
Web site: [www.radisson.com](http://www.radisson.com)



Club: Goldpoints Plus  
Check in: 3:00 PM  
Check out: 12:00 NOON  
1 block from Convention Center  
\$10/day self and \$13/day valet parking  
Complimentary wireless Internet access in  
guest room and throughout hotel

### 11) Residence Inn by Marriott City Center



\$159 Single/\$184 Double  
285 West Broadway  
Salt Lake City, UT 84101  
Tel: (801) 355-3300  
Fax: (801) 355-0440  
Web site: [www.marriott.com/slcri](http://www.marriott.com/slcri)



Club: Marriott Rewards  
Check-in: 3:00 PM  
Check-out: 12:00 NOON  
3 blocks from Convention Center  
Complimentary wireless Internet access in  
guest room and throughout hotel  
Complimentary breakfast

### 12) Salt Lake Plaza at Temple Square



\$147 Single/\$157 Double  
122 West South Temple  
Salt Lake City, UT 84101  
Tel: (801) 521-0130  
Fax: (801) 322-5057  
Web site: [www.plaza-hotel.com](http://www.plaza-hotel.com)



Club: N/A  
Check in: 3:00 PM  
Check out: 11:00 AM  
½ block from Convention Center  
\$5/day self parking  
Complimentary wireless Internet access in  
guest room and throughout hotel  
Complimentary airport shuttle

### 13) Sheraton Salt Lake City Hotel



\$149 Single/Double  
150 West 500 South  
Salt Lake City, UT 84101  
Tel: (801) 401-2000  
Fax: (801) 534-3450  
Web site: [www.sheraton.com/saltlakecity](http://www.sheraton.com/saltlakecity)



Club: Starwood Preferred Guest  
Check in: 3:00 PM  
Check out: 12:00 NOON  
4 blocks from Convention Center  
Complimentary self parking and \$10/day valet  
Parking  
Complimentary wireless Internet access in  
guest room and throughout hotel  
Complimentary airport shuttle

### 14) Shilo Inn Hotel



\$136 Single/Double  
206 South West Temple  
Salt Lake City, UT 84101  
Tel: (801) 521-9500  
Fax: (801) 359-6527  
Web site: [www.shiloinns.com](http://www.shiloinns.com)



Club: Star Rewards  
Check in: 4:00 PM  
Check out: 12:00 NOON  
Across the street from Convention Center  
Complimentary self parking  
Complimentary wireless Internet access in  
guest room and throughout hotel  
Complimentary breakfast  
Complimentary airport shuttle

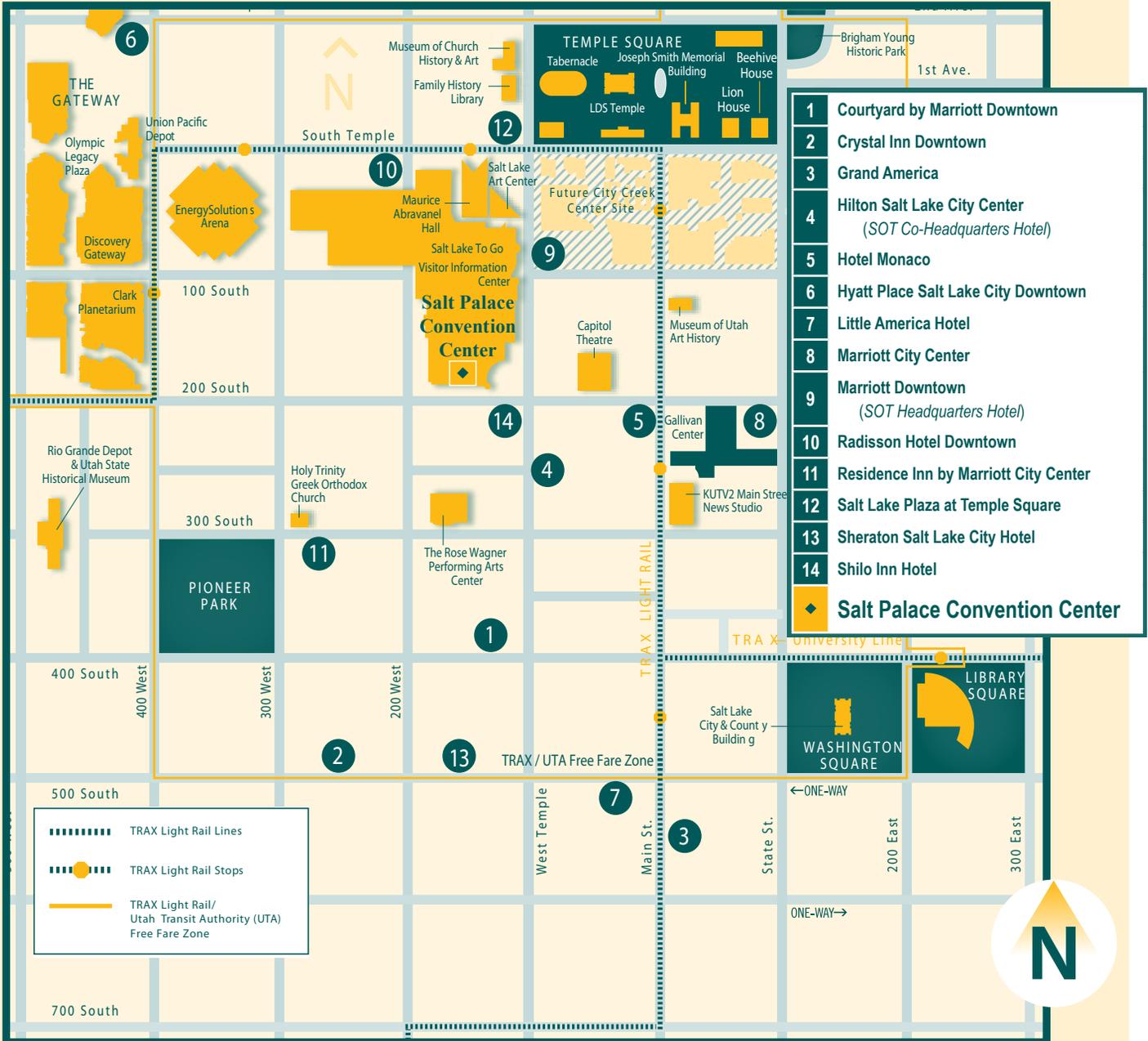
### Legend:

	<b>Valet Parking</b>
	<b>Self Parking</b>
	<b>Fitness Center</b>
	<b>Swimming Pool</b>
	<b>Business Center</b>
	<b>In-Room Wireless</b>
	<b>In-Room Safe</b>
	<b>Gift Shop</b>
	<b>Complimentary Breakfast</b>
	<b>Restaurant</b>

*All hotels have Internet access.  
Hotel sales tax is currently 12.71%*

## GENERAL INFORMATION

### Hotel Map



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## GENERAL INFORMATION

### Hotel Services

Hotel	Rewards Program	Blocks to Convention Center	Single/Double Rate	Restaurant	Comp Breakfast	In-Room Safe	Fitness Center	In-Door Pool	Business Center	In-Room Wireless Internet	Room Service	Gift Shop	Overnight Self Parking	AAA Rating
1) <b>Courtyard by Marriott Downtown</b>	Marriott Rewards	2 Blocks	\$139	✓		✓	✓	✓	✓	✓	✓		✓	3-Diamond
2) <b>Crystal Inn Downtown</b>	N/A	4 Blocks	\$132 \$102 govt	✓	✓		✓	✓	✓	✓			✓	3-Diamond
3) <b>Grand America</b>	N/A	5 Blocks	\$199	✓		✓	✓	✓	✓	✓	✓	✓	✓	5-Diamond
4) <b>Hilton Salt Lake City Center **</b>	Hilton H Honors	1/2 Block	\$163/178	✓		✓	✓	✓	✓	✓	✓	✓	✓	4-Diamond
5) <b>Hotel Monaco</b>	Kimpton In Touch Loyalty Members	1 Block	\$165	✓		✓	✓		✓	✓	✓			4-Diamond
6) <b>Hyatt Place Salt Lake City Downtown</b>	Hyatt Gold Passport	5 Blocks	\$149	✓	✓		✓		✓	✓			✓	3-Diamond
7) <b>Little America Hotel</b>	N/A	5 Blocks	\$139 Garden/ \$159 Tower	✓		✓	✓	✓	✓	✓	✓	✓	✓	4-Diamond
8) <b>Marriott City Center</b>	Marriott Rewards	2 Blocks	\$159	✓		✓	✓	✓	✓		✓	✓	✓	4-Diamond
9) <b>Marriott Downtown*</b>	Marriott Rewards	Across Street	\$168	✓		✓	✓	✓	✓		✓		✓	4-Diamond
10) <b>Radisson Hotel Downtown</b>	Goldpoints Plus	1 Blocks	\$152 \$102 govt	✓			✓	✓	✓	✓	✓	✓	✓	3-Diamond
11) <b>Residence Inn by Marriott City Center</b>	Marriott Rewards	3 Blocks	\$159/\$184		✓	✓	✓		✓	✓			✓	3-Diamond
12) <b>Salt Lake Plaza at Temple Square</b>	N/A	1/2 Block	\$147/\$157	✓		✓	✓		✓	✓	✓	✓	✓	3-Diamond
13) <b>Sheraton Salt Lake City Hotel</b>	Starwood Preferred Guest	4 Blocks	\$149	✓		✓	✓	✓	✓	✓		✓	✓	4-Diamond
14) <b>Shilo Inn Hotel</b>	Star Rewards	Across Street	\$136	✓	✓		✓	✓	✓	✓			✓	3-Diamond

\*SOT Headquarters Hotel

\*\*SOT Co-Headquarters Hotel

All hotel accommodations and rates may be subject to change.

Although we understand that making your reservations outside of the SOT hotel block can sometimes be more economical, it decreases the money available to the Society to carry out its strategic goals and may cause the Society to have to pay attrition fees for unutilized hotel rooms. In addition, the Society is unable to assist you if you have any difficulties with your room reservation, such as the hotel over-booking or misplacing your reservation.

SOT depends on the Annual Meeting revenue (hotel room commissions and rebates) to fund other programs throughout the year and to keep future registration fees low. Please assist the Society by making your hotel room reservation through The Housing Connection.

## GENERAL INFORMATION

### Internet Access

SOT knows the importance of staying connected to your daily activities while attending the Annual Meeting and provides you several ways to access the Internet.

SOT will provide computers you can use to access the Internet. These computers are available to attendees in the E-mail Center, located in the North Foyer of the Grand Ballroom on the lower concourse of the Salt Palace Convention Center.

### Wireless Internet Access in the Salt Palace Meeting Rooms

Salt Palace Wi-Fi is a self-service wireless network that is available to all event attendees. The cost is \$14.95 per day, based on a 24-hour time frame, and can be purchased directly from any wireless capable computer.

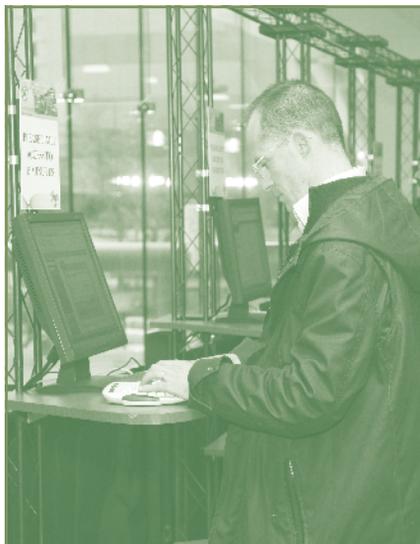
To access the Internet, connect to the “Salt Palace Wi-Fi” wireless network. Open the Internet browser, and you will be automatically directed to a screen where you can set up your user name, password, and pay for the service.

Please stop by the Business Center if you need assistance connecting to the Salt Palace Wi-Fi.

Free wireless Internet access is available through “Hot Zones,” which are designated areas in the Exhibit Hall that are clearly marked for laptop and handheld users.

### E-mail Center

The SOT Annual Meeting E-mail Center is provided to help you stay connected to your colleagues during the Annual Meeting. SOT members, 2010 Annual Meeting attendees including exhibitors, and CRAD Job Bank registrants can access the E-mail Center on the SOT Web site to send and receive e-mail messages during the 2010 Annual Meeting—just like a standard e-mail application. The difference? The 2010 SOT Annual Meeting E-mail Center gives you a unique mailbox without having to provide your personal e-mail address to correspondents.



The service will send an e-mail alert to you when you receive a message. Use the communication preference option to forward your incoming messages to your primary e-mail address or PDA.

Available 24/7, access to the E-mail Center is available any time of day and from any computer with an Internet connection, before, during, and after the 2010 Annual Meeting. Simply visit the SOT Web site and follow the E-mail Center link from the navigation.

To log into your mailbox, use your e-mail address and password or Annual Meeting badge number. If you do not know your login, you can use the SOT password retrieval request from the login on the SOT Web site or ask the Annual Meeting registration staff or E-mail Center attendant for assistance.

Job Bank users will have the option to send messages to the Annual Meeting E-mail Center mailboxes. E-mail Center users will have the option to send messages to Job Bank registrant mailboxes by name or Job Bank ID. Additionally, the E-mail Center provides extended communication permitting members and Job Bank registrants who do not attend the meeting to communicate with attendees. Even colleagues and family members can e-mail messages into the Center.

### Luggage/Coat Check

For your convenience, a luggage/coat check will be available in the Salt Palace Convention Center near the North Foyer of the Grand Ballroom (near Ballroom A) on the Lower Concourse. The luggage/coat check will be open Sunday, March 7 through Thursday, March 11. There will be a fee of \$2 per item checked and laptop computers will not be accepted.

#### Hours of operation:

Sunday.....	7:00 AM–8:30 PM
Monday .....	7:00 AM–8:30 PM
Tuesday .....	7:00 AM–8:00 PM
Wednesday.....	7:00 AM–8:00 PM
Thursday .....	7:00 AM–1:00 PM

*Luggage/coat check hours are subject to change.*

### Media Support Services

The Society of Toxicology welcomes accredited representatives of media organizations. Journalists receive complimentary registration for all meeting sessions as well as media kits. Interviews can be arranged with guest speakers and a press room will be available for reporters. For more information about the program, please contact

Martha Lindauer  
SOT Headquarters: (703) 438-3115  
E-mail: martha@toxicology.org

### Meeting Requests: Hospitality Suites and Ancillary Meetings

All requests for hospitality suites and ancillary meetings must be approved by SOT Headquarters. To reserve a meeting room or hospitality suite, go to [www.toxicology.org](http://www.toxicology.org) and complete the Ancillary Meeting Form on-line. Ancillary functions may only be hosted by SOT Affiliates, Exhibitors, or organizations affiliated with SOT.

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Hospitality suites and ancillary meeting space books fast. Submit your request now. Only meeting requests made by December 17, 2009, will be listed in the Annual Meeting Calendar and the *Program*.

### Meet Me at the Meeting Place

Looking for friends or new acquaintances? This centralized Meeting Place has been designated near the East Entrance of the Convention Center, which is across the street from the Marriott downtown. The Meeting Place makes it convenient to meet colleagues and is the ideal location for a photo op!

### Message Boards

Leave a quick note on the message boards. Note pads and push pins will be available to post messages on the message boards, which are near the E-mail Center located in the North Foyer of the Grand Ballroom of the Salt Palace Convention Center.

### Parking Information

The Salt Palace Convention Center has two covered parking areas, available seven days a week from 6:00 AM–9:00 PM. One garage is located at 200 South 185 West (south end has 600 stalls) and the other garage is located at 50 South 300 West (north west end has 400 stalls). The current parking rate per entrance is \$7 (subject to change) and does not include in/out privileges or overnight parking.

### Photography Policy and Session Etiquette for Attendees

Out of courtesy for the scientific presenters, we appreciate your compliance with the following policies:

- Cell phones and other electronic devices should be set on mute.

- Electronic capture of scientific sessions by any method is prohibited.
- Children under the age of 15 are not allowed in scientific sessions unless the session chair gives consent.

Session chairs are asked to enforce these policies and individuals who do not comply will be asked to leave the session.

- Photography of poster presentations is prohibited without the specific consent of the presenter(s)/author(s).
- Children under the age of 15 are prohibited from accessing the Exhibit Hall at any time.

If you have any questions regarding these policies, please contact the SOT Headquarter staff at the Registration Desk.

### Salt Lake City Activities

Salt Lake City's wide assortment of attractions includes concerts by the world-famous Mormon Tabernacle Choir, animal antics and winged wonders at the zoo or aviary, and a step back in time at the Family History Library. From the downtown hotels or the Salt Palace Convention Center, many historical sites, museums, artistic venues, and the beautiful cathedrals and temples of several different religious faiths are within walking distance. Here are just a few of the many popular attractions in Salt Lake City:

**Clark Planetarium**  
110 South 400 West  
(part of the Gateway Mall)  
(801) 456-STAR (7827)  
[www.clarkplanetarium.org](http://www.clarkplanetarium.org)

The Clark Planetarium includes a state-of-the-art Hansen Dome Theatre, ATK 3-D IMAX® Theatre, Planet Fun store, and free admission to exhibits. The IMAX® Theatre is five stories high and has 12,000 watts of surround sound, making it the Ultimate Film Experience and the next best thing to being there. Opens at 10:30 AM seven

days a week. A new stop on TRAX, the Planetarium stop, drops you at the front door.

**Family History Library**  
35 North West Temple  
(801) 240-2584  
[www.familysearch.org](http://www.familysearch.org)

Established in 1894, this library is the largest depository of genealogical records in the world and is open to the public at no charge. This collection includes millions of records from over 110 countries. Discover everything from a simple family tree, with branches reaching back through centuries, to original documents such as marriage records, ship manifests, court proceedings, probate records, and more. Open 8:00 AM–5:00 PM Monday, 8:00 AM–9:00 PM Tuesday–Saturday. For beginners, the nearby Family Search Center offers easy-to-use genealogy computers and friendly, supportive staff.

**Gallivan Center**  
239 South Main Street  
(801) 535-6110  
[www.slcgov.com](http://www.slcgov.com)

The Gallivan Center is Salt Lake's outdoor living room and is furnished with an array of unique art projects, an amphitheater, an ice rink and pond, a huge outdoor chessboard, and an aviary. During the 2002 Olympic Winter Games, the Gallivan Center was one of the busiest hotspots in downtown. See the Center's Web site for a calendar of events.

**Salt Lake Art Center**  
20 South West Temple  
(801) 328-4201  
[www.slartcenter.org](http://www.slartcenter.org)

Located right next to the Salt Palace Convention Center, the Salt Lake Art Center presents contemporary visual art exhibitions, which have aesthetic and social consciousness, and which are thought provoking to the community and to other artists. The center also offers a variety of education programs for all ages. Admission and all programs are free and open to the public.

## GENERAL INFORMATION

### Temple Square

50 West North Temple  
(801) 240-6615  
[www.visitemple-square.com](http://www.visitemple-square.com)

Occupying two full city blocks in the heart of downtown, Temple Square is Utah's most popular attraction, drawing in millions of visitors each year. Visitors can learn about The Church of Jesus Christ of Latter-day Saints or just enjoy the spotless, manicured series of gardens, buildings, and sculptures. Tour the Salt Lake Tabernacle, home to the world-famous Mormon Tabernacle Choir. On Thursday evenings, Choir rehearsals are open to the public at the Tabernacle. For more information about the Choir and their performances, visit their Web site at [www.mormontabernaclechoir.org](http://www.mormontabernaclechoir.org).

### The Utah State Capitol Building

350 North Main Street  
(801) 538-1800  
[www.utahstatecapitol.utah.gov](http://www.utahstatecapitol.utah.gov)

An architectural masterpiece built from Utah granite, the Utah State Capitol Building in Salt Lake City is one of the most popular tourist attractions for many reasons. Completed in 1915, the State Capitol is a lovely Renaissance-style building featuring depression-era murals in the rotunda, which depict events from Utah's past. The beauty of its architecture is available to see as well as the incredible views of the Wasatch and Oquirrh mountains, the Great Salt Lake, and the valley floor. Docent-guided tours available. Open Monday–Friday 8:00 AM–8:00 PM and Saturday–Sunday 8:00 AM–6:00 PM.

### Tracy Aviary

589 East 1300 South  
(801) 596-8500  
[www.tracyaviary.org](http://www.tracyaviary.org)

Tracy Aviary maintains a collection of approximately 400 birds representing about 135 different species in a tranquil wooded setting. Many of these birds are considered rare or endangered. Year-round exhibits, bird shows, and educational classes are offered. Open daily 9:00 AM–4:30 PM.

### Utah Museum of Natural History

1390 East 220 South, near the University of Utah  
(801) 581-6927  
[www.umnh.utah.edu](http://www.umnh.utah.edu)

You will enjoy your journey through the evolving world of natural and cultural sciences at the Utah Museum of Natural History. Visitors can enjoy Native American artifacts, dinosaur displays, and hands-on activities for the kids. See new discoveries in Utah's dinosaurs and Range Creek archeology. Learn about Utah's first humans. Enjoy special touring exhibitions. Open Mon–Sat 9:30 AM–5:30 PM, Sun 12:00 NOON–5:00 PM.

### Utah Opera and Utah Symphony

123 W South Temple  
(801) 533-5626/(801) 533-NOTE (ticket office)  
[www.utahopera.org](http://www.utahopera.org)  
[www.utahsymphony.org](http://www.utahsymphony.org)

Utah Opera produces four professionally staged, fully costumed operas with nationally and internationally known artists. Founded in 1940, the Utah Symphony has become a vital presence on the American music scene through its distinctive performances worldwide and its well-known recording legacy. The Symphony performs in the Abravanel Hall.

### Visit Salt Lake Connect Pass

The Visit Salt Lake Connect Pass is the best way to gain access to Salt Lake's most famous and fascinating attractions. With the pass, visitors can go to any of the 15 area attractions for one flat rate. The pass even includes one free meal at the Lion House Pantry and a free admission to an IMAX film and a planetarium film. Get these passes on-line at [www.visitsaltlake.com](http://www.visitsaltlake.com), or you may purchase them at the Visitor Information Center in the Salt Palace Convention Center.

### Ski Utah

Discover for yourself why Salt Lake's unforgettable skiing is renowned the world over. A fortunate combination of geologic features makes Utah's powder the fluffiest, most skiable snow in the world. The Ski Salt Lake resorts alone have over 6,950 skiable acres and over 335 trails. In addition to the 4 Ski Salt Lake resorts, 5 more resorts near Salt Lake share in The Greatest Snow on Earth™. Salt Lake area ski resorts include: Alta, Brighton, The Canyons, Deer Valley, Park City Mountain Resort, Snowbasin, Snowbird, Solitude, and Sundance. Bringing a non-skier along, or hoping to try something new? Many resorts offer plenty of other excellent winter activities, such as tubing, snowmobiling, sleigh rides, ice-skating, and more.

### Ski Salt Lake Super Pass

One great way to check out more than one world-class resort and save a few bucks is the Super Pass, which provides discounted access to the four ski areas closest to Salt Lake, each no more than 45 minutes away. The Super Pass includes one lift ticket per day at Alta, Brighton, Snowbird, or Solitude, plus free public transportation to each. Visit [www.saltlakesuperpass.com](http://www.saltlakesuperpass.com) for more information.

### Sports and Recreation

Utah is known for having the "Greatest Snow on Earth™," and while skiers and snowboarders are likely to vouch for this catchy phrase, snow sports are not the only ticket in town. Salt Lake boasts nine major sports venues and is home to five professional sports teams. The Utah Jazz (NBA Basketball), the Utah Blaze (AFL Arena Football), Real Salt Lake (Major League Soccer), the Utah Grizzlies (AHL Hockey), and the Salt Lake Stingers (AAA Baseball) offer fans a professional sports experience any time of year.

Salt Lake also puts you within a day's drive of 21 national parks, recreation areas, and monuments, including Yellowstone and

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Grand Teton to the north and Zion, Bryce, Arches, and Grand Canyon National Parks to the south.

### Shopping

Salt Lake is a western shopping oasis. Two major shopping malls sit in the heart of the city with hundreds of national brand stores like Nordstrom, Meier & Frank, and Eddie Bauer. Local specialty shops dot the Avenues neighborhood, as well as the “Ninth and Ninth” and Sugar House shopping districts. The Gateway is a multi-story, open-air upscale shopping arcade three blocks long and just moments from the convention district. Salt Lake also offers shopping with a historic twist. Trolley Square, a block of enclosed trolley barns dating back to the 19<sup>th</sup> century, is filled with high-end boutiques, specialty shops, and upscale national chains. The shops at Gardner Historic Village are housed in dozens of pioneer-era homes clustered around a 19<sup>th</sup> century flour mill. For a list of shops by location, visit [www.visitsaltlake.com/visit/activities/shopping](http://www.visitsaltlake.com/visit/activities/shopping).

### Dining and Nightlife

Salt Lake boasts a vibrant nightlife with more than 1,000 restaurants, brewpubs, dance halls, and bars. You are never far from your next great Salt Lake meal because a surprisingly diverse assortment of cafés and restaurants are waiting to cater to you, and over 140 of these restaurants and cafés are within walking distance of the Salt Palace Convention Center. In recent years, the city has become the culinary capital of Rocky Mountain Cuisine, home to 53 Zagat-rated restaurants and has one of the nation’s premier wine stores. Sample regional and Southwestern favorites at casual family restaurants or indulge in fresh pasta and seafood in more intimate surroundings. If you crave something exotic, you will find a delightful ethnic mix available, from Afghan to Vietnamese.

As the city lights come up each night, Salt Lake’s many clubs and night spots

keep things lively with a wide range of entertainment options. The city is home to a diverse mix of nightspots, including dance clubs, country/western saloons, jazz and blues clubs, sports bars, neighborhood hangouts, martini bars, techno-dance clubs, cigar bars and alternative lifestyle clubs. Taste the local flavor with award-winning microbrews and cosmopolitan cocktails. As partygoers during the Olympics discovered, it is easy to get a drink in Salt Lake! In addition, the state of Utah has just made it even easier by recently changing its liquor laws and ending the restrictions in which bars had to function as private clubs. For a listing of restaurants in each area, visit [www.visitsaltlake.com/visit/dining\\_and\\_nightlife](http://www.visitsaltlake.com/visit/dining_and_nightlife).

### Salt Lake City Fun Facts!

- The people of Salt Lake City consume more Jell-O per capital than any other city in the United States.
- Salt Lake City was the host of the Winter Olympic games in 2002—the first of the 21<sup>st</sup> century.
- Covering some 2,000 square miles, the Great Salt Lake is the second largest inland body of salt water in the world (behind the Dead Sea).
- The state symbol is the beehive for thrift and industry.
- The Mormon Temple in Salt Lake City, the world’s largest Mormon temple, took 40 years to construct and cost \$5 million when it officially opened in 1893.
- Salt Lake City has been named the “Fittest City in America” by Men’s Fitness magazine, as announced in the February 2009 issue.
- The most successful Disney Channel Original Movie, *High School Musical*, and its two sequels have been filmed at East and Murray High Schools in Salt Lake City.

- The average snowfall in the mountains near Salt Lake City is 500 inches (over 40 feet!)—that is nearly five times the average snowfall of Juneau, Alaska. However, do not let that scare you! The valley/downtown area receives about an eighth of that amount.
- Zions Mercantile Cooperative Institution was formed in Salt Lake City in 1868 as the first U.S. department store. It is now a Macy’s.
- The world’s first Kentucky Fried Chicken franchise was established in Salt Lake City in 1952.
- Temple Square lands on Forbes’ Top 25 Most Visited Tourist Attractions in America. Forbes Traveler has released a new ranking of the most popular tourist attractions in America, from #1 Times Square in New York (37.6 million visitors) to #25 Waikiki Beach in Hawaii (3.67 million visitors). Salt Lake’s Temple Square made the list at #16 with 5 million visitors per year.

### Satellite Meetings

Each year, SOT endorses several satellite meetings that are held in conjunction with the Annual Meeting. Satellite meetings are organized around scientific topics related to toxicology and are scheduled at the end of the Society’s program. The 2010 satellite meetings will be held in and around the Salt Lake area. Proposals for a Satellite Meeting should be sent by e-mail to [heidi@toxicology.org](mailto:heidi@toxicology.org) to the attention of Michael P. Holsapple, SOT Vice President and Scientific Program Committee Chair. Requests approved by December 17, 2009, will be published in the *Program*.

## GENERAL INFORMATION

### SOT Post Conference Weekend Get-Away to Park City, UT

SOT is pleased to offer Annual Meeting attendees a post conference package weekend get-away that includes heavily discounted rooms and ski packages at an award-winning hotel, the Hotel Park City. The Hotel Park City is a 30-minute drive from downtown Salt Lake City and is a member of the Leading Small Hotels of the World. The Hotel Park City offers luxurious suite accommodations, mountain base skiing with shuttle, a world-class spa and fine dining. For information on the Hotel Park City go to, [www.hotelparkcity.com](http://www.hotelparkcity.com). Watch the SOT Web site for more information or send an e-mail to Heidi Prange at [heidi@toxicology.org](mailto:heidi@toxicology.org) to receive more information.

### SOT Resource Pavilion

Do you know all the resources available through SOT and where to find them? Stop by the SOT Resource Pavilion to learn about SOT activities, membership benefits, strategic initiatives, and the endowment. Find materials to support the discipline of toxicology and educational materials for K-12 and public outreach. It is a one-stop shop for all your questions and member needs. The Pavilion is located in the Exhibit Hall, Booth 1901, and open the following hours:

Monday ..... 9:00 AM-4:30 PM  
 Tuesday ..... 8:30 AM-4:30 PM  
 Wednesday ..... 8:30 AM-4:30 PM

### Sponsorship

SOT would like to invite your organization to be a sponsor of the 2010 Annual Meeting. SOT appreciates the generous contributions of sponsors that make the SOT Annual Meeting possible. Sponsor names are prominently displayed on the Annual Meeting Web site, as well as in print materials that are distributed before and during

the Annual Meeting. Sponsorship is also recognized through colorful banners and signage displayed around the Convention Center during the Annual Meeting.

### Tours

SOT is proud to offer all attendees and their guests a wide range of tours to make your visit to Salt Lake City more enjoyable. A tour desk will be located in the South Foyer of the Salt Palace Convention Center. Tour desk hours will be listed in the *Program*, or you may visit the Annual Meeting section of the SOT Web site for details.

### Tour Registration

To register for tours, please either fax, mail, or e-mail your tour registration form, found on the SOT Web site, to Western Leisure/SOT. For more information go to [www.societyoftoxicology.westernleisure.com](http://www.societyoftoxicology.westernleisure.com). If you have any questions, please call Western Leisure at (801) 233-0600 or e-mail at [info@westernleisure.com](mailto:info@westernleisure.com). Register now to ensure your reservation for tours. On-site registration will be limited and will be accommodated on a space-available basis only.

- The registration deadline is February 28, 2010, for all tours. Western Leisure reserves the right to cancel tours if minimums are not met.
- If a tour is cancelled due to insufficient registration, customers will be given the opportunity to either receive a full refund or to select another tour, if seating is available.
- Full payment to Western Leisure must accompany your registration form. All payments are due in U.S. dollars, VISA, MasterCard, American Express, checks, and cash (on-site sales only) are accepted. Discover is not accepted.
- Refunds will only be made if written notice is received in writing to Western Leisure and faxed to (801) 233-0900 by February 28, 2010, for all tours. No refunds will be made after this date.

- Beginning Sunday, March 7, prepaid tickets may be picked up at the Tour Desk located in the South Foyer near SOT registration of the Salt Palace Convention Center.

### Sunday Morning with the Mormon Tabernacle Choir & City Tour

**Sunday, March 7, 2010**  
**8:30 AM-12:00 NOON**  
*\$35 per person*  
*Minimum of 30 people*

Begin the morning with a short downtown tour followed by a 30 minute nationally broadcast session at Temple Square with the world renown, Mormon Tabernacle Choir. This is the longest continuously running radio broadcast in the world. After the broadcast, the tour will take a complete look at what makes Salt Lake City so unique. Stops include Union Pacific Depot, which includes the Olympic Legacy Plaza, a residential section called *Avenues*, Fort Douglas, and the Olympic Cauldron Park at Rice Eccles Stadium, and Rice Eccles, which was the site of the Opening and Closing 2002 Winter Olympic Ceremonies.

### Utah Olympic Park and Park City

**Monday, March 8, 2010**  
**10:00 AM-2:00 PM**  
*\$48 per person*  
*Minimum of 30 people*

In February of 2002, world-class athletes from every country gathered in Salt Lake City for the 2002 Winter Olympics. Now is your chance to see what all the excitement was about. Tour the Utah Olympic Park. This venue was the site for the Bobsled, Ski Jumping, Luge, and Skeleton events. On the tour you have the chance to learn about those events from those who actually participated. We are lucky enough to have an athlete get on our bus and take us to the top of those events, and let you look over the edge! When we're done at the park, you will also tour Park City (Home of the Sundance Film Festival) and learn its fascinating

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## GENERAL INFORMATION

history as a mining boomtown. Today, Park City is a skiing mecca and get-away for the rich and famous—yet still retains the charming qualities of a quaint mountain town. You will get a chance to explore the shops, boutiques, and art galleries lined along Main Street with plenty of time to grab a bite to eat before heading back down Parley's Canyon into Salt Lake.

### Lakes, Mines & Mills

Tuesday, March 9, 2010

10:00 AM–4:00 PM

\$65 per person

Minimum of 30 people

This tour will be an exciting day, full of contrasts. Begin your tour by visiting the Great Salt Lake, known as "America's Dead Sea." The Great Salt Lake is many times saltier than the ocean, making it impossible to sink while swimming there. Hear tales of its origin, its discovery, and of the many legends it has spawned. See the Saltair Pavilion, and have a chance to touch the salty water. Our next stop will be historic Gardner Village. Nestled beneath hillside pastures on the banks of the Jordan River, the Village offers vintage pioneer architecture, antique fixtures, cobblestone paths and ponds along with proprietor's who render personalized service straight from the heart. The Village was estab-

lished in honor of Mormon Pioneer and polygamist Archibald Gardner. Today, this land contains the outlines of the once bustling Utah mill industry and history. It is complete with historic cabins, houses and buildings that have been restored into quaint and unique shops. There will be plenty of time to explore and shop in the village before we meet in the mill for lunch. We'll re-board the coach and continue along the base of the Oquirrh Mountains as you make your way to Kennecott's Bingham Canyon Copper Mine. The largest mining operation ever undertaken, the pit is 2 1/2 miles from rim to rim and over 1/2 mile deep. You will have time to visit the observation deck and see the workings of the mine.

### Antelope Island & Ogden's Union Station

Wednesday, March 10, 2010

10:00 AM–3:00 PM

\$65 per person

Minimum of 30 people

We begin our tour by heading North as we travel to Ogden's Union Station, a monument to the state's railroading history. Though it is no longer a train depot, the Station continues to attract people from all over the world. Most come to see the John M. Browning Firearms Museum and the Utah State Railroad Museum/Eccles Rail

Center with its display of two of the largest locomotives ever manufactured. Stay to see the Natural History Museum and the Browning Kimball Car Museum. Next we will head due West across the Great Salt Lake to visit Antelope Island, home to a unique ecosystem which reflects what the pioneers encountered when they arrived in the Salt Lake Valley. Our tour will stop at Buffalo Point, which provides a stunning view of the Great Salt Lake.

### The Toxicologist/ Program

1. SOT Members in the U.S. and Canada will receive the printed *Program* and *The Toxicologist* on CD-ROM (with *Itinerary Planner*) prior to the Annual Meeting, as will U.S. and Canadian non-members who register by January 22, 2010.

Non U.S. SOT Members may pick up the printed *Program* and *The Toxicologist* on CD-ROM at the meeting or may request that these be mailed following the Annual Meeting. Send e-mail requests to jimd@toxicology.org.

2. Non-members in the U.S. who register after January 22 will receive the *Program* and *The Toxicologist* on CD-ROM (with *Itinerary Planner*) at the registration area on-site.

3. Registrants will receive the Annual Meeting abstracts in *The Toxicologist* on CD-ROM as part of the Annual Meeting registration fee. Annual Meeting attendees may purchase a printed version of *The Toxicologist* for \$20 per copy. You may preorder on the Registration Form and pick up a copy on-site or wait to purchase a copy on-site (available while supplies last). *The Toxicologist* will be available for download (February 2010) free-of-charge on the SOT Web site.

4. The Annual Meeting *Itinerary Planner* is available on the SOT Web site January–April.

NOTE: Please bring your copy of the *Program* with you to the meeting.

### On-line Itinerary Planning Tool Enhancements

SOT is excited about the improved functionality of the on-line customizable *Itinerary Planner*. We invite you to use this tool to plan your Annual Meeting experience using iCal technology.

Choose the presentations, featured lectures, meetings, or special event functions you wish to add to your personal itinerary. After you've selected your schedule of sessions, you'll be able to export this information to your default calendar program for reference using iCal. The downloaded information will contain specific details for these sessions or events such as date, time, and the location. Additionally, each presentation downloaded provides you with access to detailed abstract information including authors, institutions, and the full abstract.

Look for more information to be made available soon on the SOT Web site.



## GENERAL INFORMATION

### Transportation

#### Air Transportation

Salt Lake City International Airport is located five miles northwest of downtown Salt Lake City or about a 10-minute drive. It serves more than 20 million passengers annually and ranks as the 23rd largest airport in the United States. The airport ranks as one of the most cost-effective, large hub airports in the nation and is situated within a two and a half hour flight from half of the United States population.

Airlines serving Salt Lake City operate over 300 daily departures to 71 nonstop destinations throughout the U.S. and Canada. The U.S. Department of Transportation typically ranks Salt Lake City International Airport in the top 10 U.S. airports for on-time performance.

Nine airlines and their affiliates serve Salt Lake City International Airport and include American, Continental, Delta, Frontier, JetBlue, Southwest, United and US Airways. It is Delta's third largest hub. For more information, call (801) 575-2400 or (800) 595-2442, or visit [www.slcairport.com](http://www.slcairport.com).

#### Special Airfare Discounts

SOT has established discounted rates through American, Delta, and JetBlue Airlines originating in the United States and Canada. Be sure to use the discounted reference numbers when making your reservations. You may purchase your ticket on-line, call the airline directly using the toll-free numbers, or provide your travel agent with the reference/discount numbers listed below to receive the discount.

#### American Airlines

(800) 433-1790

[www.aa.com](http://www.aa.com)

**Discount Code: 5130AC**

American Airlines is offering a 5% discount off the lowest applicable fare. The discount is valid March 4–14, 2010, for travel to Salt Lake City. You may make reservations by

calling the Meeting Services Desk at (800) 433-1790 from anywhere in the United States or Canada and refer to discount code 5130AC. A \$20 service fee per ticket will apply for each ticket booked over the phone. You may also book your ticket on-line at [www.aa.com](http://www.aa.com) (no service fee applies) and under the promotion code section, type 5130AC to receive the SOT discount.

#### Delta Airlines

(800) 328-1111

[www.nwa.com](http://www.nwa.com)

**Discount Code: NY299**

Delta Airlines is offering up to a 5% discount off full/non-restricted fares to Salt Lake City. The discount is valid March 2–17, 2010, applicable to U.S./Canada originating passengers. You may make reservations by calling (800) 328-1111 from anywhere in the United States or Canada and refer to file number NY299. The \$20 service fee per ticket has been waived for SOT. You may also book your ticket on-line at [www.nwa.com](http://www.nwa.com) (no service fee applies) and under the promotion code section, type NY299 to receive the SOT discount.

#### JetBlue

(800) 328-1111

[www.jetblue.com/promo](http://www.jetblue.com/promo)

**Discount Code: SOT2010**

JetBlue is offering a 5% discount off the lowest available fare. The discount is valid March 5–13 for travel to Salt Lake City. To use the discount, book your flight on-line at [www.jetblue.com/promo](http://www.jetblue.com/promo) and use the discount code SOT2010.

#### SOT Travel Agent— Carlson Wagonlit

Carlson Wagonlit is the official travel management firm for SOT's 49<sup>th</sup> Annual Meeting. To take advantage of their services and savings, call toll-free (800) 535-9117 Monday through Friday, 9:00 AM–5:30 PM (Eastern Standard Time) and ask to speak to anyone on our SOT dedicated team or e-mail:

[washington.remote@carlsonwagonlit.com](mailto:washington.remote@carlsonwagonlit.com). To obtain the maximum discounted fares, call at least 60 days prior to departure. Lower fares are still obtainable up to 14 days in advance. Please note that Carlson Wagonlit charges a \$40 service fee per ticket.

*Before calling Carlson Wagonlit, please gather the following information:*

- The desired dates of arrival to and departure from Salt Lake City.
- Your home city or originating airport.
- Your approximate time of departure from the originating airport.
- The number of persons traveling (adults/children).
- Your method of payment, either credit card or check.
- Your airline frequent flyer number(s).

Identify yourself as a Society of Toxicology attendee. Carlson Wagonlit will find the best fare for you and e-mail an itinerary to you.

#### Ground Transportation

Arrive at the Salt Lake City International Airport and be downtown in minutes! Taxis, limos, buses, car rentals, and shuttles supply service to downtown and the ski resorts. For more information on ground transportation from the airport visit [www.slcairport.com](http://www.slcairport.com), or call the Ground Transportation Desk at (801) 575-2477.

#### Car Rental

**Avis Rent A Car Systems, Inc.**

(800) 331-1600

[www.avis.com](http://www.avis.com)

**Discount Number: T534999**

Avis Rent A Car Systems is the official car rental company for the 49<sup>th</sup> Annual Meeting. SOT discounted rates, including unlimited mileage, begin at \$43.99 per day. These special group rates are good one week before and after the SOT Annual Meeting, so you can take in the sights and explore the surroundings at your own pace. To reserve your car on-line go to [www.avis.com](http://www.avis.com).

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You may also call Avis directly at (800) 331-1600 to reserve your car. Be sure to mention the SOT Avis Worldwide Discount Number (AWD) T534999.

### Express Shuttle Utah

The Express Shuttle Utah will transport you from Salt Lake City Airport to your downtown hotel for a discounted price of \$7 per person one way (prices subject to change). Reservations are not required for transfers from the airport. Upon arrival at the airport, proceed to one of two Express Shuttle desks, located in the baggage claim areas of both terminals. Let the desk agent know you are with The Society of Toxicology Annual Meeting.

Reservations are required for transfers to the airport and must be made at least 24 hours in advance. You must mention that you are with the conference in order to receive the \$7 rate.

You may make your reservations by calling (800) 397-0773, or you may make them on-line at [www.xpressshuttleutah.com](http://www.xpressshuttleutah.com). If you would like to make reservations on-line, please type the name of our meeting in the comments sections, and they will adjust the price.

### Taxi Service

There are three main taxi companies in Salt Lake City, and each offers 24-hour service:

- City Cab (801) 363-5550
- Yellow Cab (801) 521-2100
- Ute Cab (801) 359-7788

You can call for service or hail them in the street, but they are not as plentiful as in other major cities. Some downtown hotels like the Salt Lake Hilton have taxi stands. A one-way taxi from the airport to downtown is usually around \$10–\$15.

Taxi service booths are located in the baggage claim areas outside of door #7 in Terminal One and door #11 in Terminal Two.

### Utah Transit Administration (UTA)

UTA provides more than 100 bus routes throughout a 1,800 square mile area. UTA also provides light-rail service (TRAX), airport transportation, service to ski resorts in winter, and door-to-door transportation for disabled passengers. Fares are approximately \$2 one-way or \$5 for an all-day pass. A free fare zone allows passengers to navigate easily downtown. The closest TRAX stop to the South Foyer entrance of the Salt Palace Convention Center is Gallivan Plaza at 239 South Main Street.

A UTA bus leaves the airport for the City Center Station every 30 minutes during the day and every 60 minutes after 7:00 PM. Bus stops are located in the parking structure between Terminal One and Terminal Two. Limited service is available on weekends and holidays.

Call (801) 743-3882 for more information, or visit [www.rideuta.com](http://www.rideuta.com).

### Amtrak

**340 South 600 West  
Salt Lake City, UT 84101**

There is currently one Amtrak train route that runs through Salt Lake City. This route, California Zephyr, runs from the San Francisco area to Chicago and is believed to be one of the most scenic train rides in all of North America. The train station is located downtown and is approximately one mile from the Salt Palace Convention Center. For more information, visit [www.amtrak.com](http://www.amtrak.com) or call (800) 872-7245.

### Driving

Driving to Salt Lake or the resorts is a breeze on Interstate 15, recently rebuilt, making it easier to go anywhere. In Salt Lake City, wide streets are laid out in a grid system, starting downtown at the intersection of Main Street and South Temple. From there the streets are numbered in increments of 100. If you go 4 blocks south,

you are on 400 South. If you then turn left and go 4 blocks, you are on 400 South and 400 East, called 4th South and 4th East. If you end up at 3900 South and 2700 East, you are 39 blocks South and 27 blocks East of the downtown marker.

### SOT Ride Share

SOT is offering a Ride Sharing Program in conjunction with the Annual Meeting. For those who live close enough to the Salt Lake City area or those who do not wish to fly, consider the Ride Share Program. Avoid airport hassles by driving and make it easier for other scientists to attend by sharing rides. Students especially appreciate ways to make the meeting even more economical.

Once you have registered for the Annual Meeting, you can access the Ride Sharing Program on-line at the Annual Meeting Web site. You can indicate whether you want to drive or be a passenger, and then see a list of others who have signed up. It will be up to you to match your plans with another registrant, and then to remove your names when you have travel plans in place.

## REGISTRATION

Registration for the Annual Meeting is available now. Register by January 22 to get the Early Bird Rate and avoid on-site registration lines by insuring that you receive your registration materials before meeting. Registration is available on-line, *via* fax, or can be mail to SOT Headquarters.

### On-Line Registration

SOT members and non-members are invited to register for the 2010 SOT Annual Meeting using the SOT On-Line Registration system. The system is designed for those who will be paying their registration fee by credit card and who have access to the Internet.

Registration information can be accessed *via* the SOT Web site at [www.toxicology.org/register](http://www.toxicology.org/register). After registration, you will receive an electronic confirmation. If you do not, please send an e-mail to [jimd@toxicology.org](mailto:jimd@toxicology.org).

### Mail or Fax Registration

Registrants may fax or mail their registration payments using the Registration Form located on pages 19 and 21.

*Please type or print clearly.*

**REGISTRATION:** No phone registrations will be accepted.

**Please send Registration Forms to:**

SOT Registration  
P.O. Box 91895  
Washington, DC 20090-1895

*or*

SOT Headquarters (Faxes require credit card payment)  
Fax: (703) 438-3113

**USPS Express packages must be mailed to:**

SOT Headquarters  
1821 Michael Faraday Drive, Suite 300  
Reston, VA 20190

Forms will be date-stamped as they arrive. This is your date of registration. Faxes will be accepted by SOT Headquarters only if a credit card number is clearly listed in the appropriate area.

**NOTE:** To prevent double-billing, if you are registering by fax, **DO NOT** mail your original registration form. SOT needs only one copy for processing. All mailed and faxed registration forms will be processed on-line by SOT staff.

### Registration Materials:

Badges and event tickets are mailed in advance if you register before January 22. When you arrive at the Salt Palace Convention Center, please go to the registration area located in the South Lobby to pick up your registration materials (i.e., *The Toxicologist* on CD-ROM, the *ToxExpo™ Directory* and other supplementary materials). You must present your 2010 Annual Meeting badge to obtain the registration materials. The materials will be available in bins near the registration area. If you have not already registered or have not received your badge, please go to the registration counters. **NOTE:** If you are registered and have your badge, you do not need to stand in the registration line.

### Registration Guidelines:

**PAYMENT:** Registration Forms will be returned if not accompanied by one of the following methods of payment:

- Check (company or personal); U.S. Currency only. Please list all registrants on check memo or check stub.
- Government Purchase Order. (Check must be drawn from the U.S. Department of Treasury.)
- Money Order.
- Visa, MasterCard, Discover, Diner's Club, or American Express.

### Registration Deadlines:

- Early Bird Registration until **January 22, 2010**
- Standard Registration until **February 12, 2010**
- Final Registration after **February 12, 2010**

**DO NOT** mail your Registration Form to SOT if it will arrive after March 2, 2010. SOT will accept Annual Meeting Registrations until March 2. After March 2, registrations not processed on-line will only be accepted on-site at the Annual Meeting. The on-line registration system will be open throughout the meeting and if you register on-line after March 2, 2010, you can easily pick up your badge at the "Badge Pick Only" registration counter.

**GUEST/SPOUSE REGISTRATION:** The SOT Guest/Spouse Hospitality Center provides guest participants (non-scientists) with a place to meet and socialize with other guests. The Center will be open Sunday through Thursday and information on local attractions, rental cars, and tours will be available there.

Guests and Spouses must be registered for Annual Meeting to access the Hospitality Center. Guests must register with the person they are accompanying and are welcome to attend the Welcoming Reception. **Reminder:** Children under the age of 15 are not permitted in the Exhibit Hall at any time or in scientific sessions unless consent is given by the session chair.

**ONE-DAY REGISTRATION:** There is no reduced fee for one-day registration.

**TICKETS:** Tickets for Continuing Education courses and other events may be required. These tickets will be issued with your meeting badge. Annual Meeting registration is required to participate.



# Registration Form (Part 1)

## 49<sup>th</sup> SOT Annual Meeting

March 7–11, 2010

R2010

**FOR OFFICE USE ONLY**

Date Received: \_\_\_\_\_

Input:  Initials: \_\_\_\_\_

(Required: Please check the appropriate box)

PLEASE PRINT CLEARLY OR TYPE

SOT Member  Non-Member Badge Name: \_\_\_\_\_

First Name/Middle Initial: \_\_\_\_\_

Last Name: \_\_\_\_\_ Professional Degree(s): \_\_\_\_\_

Organization Name: \_\_\_\_\_

(Is this a new employer and/or new address?  Yes  No)

Company (second line): \_\_\_\_\_

Department: \_\_\_\_\_

Street Address: \_\_\_\_\_

City: \_\_\_\_\_ Prov/State: \_\_\_\_\_ Zip: \_\_\_\_\_ Country: \_\_\_\_\_

Area Code/Phone Number: \_\_\_\_\_ Fax Number: \_\_\_\_\_

E-mail Address: \_\_\_\_\_

Special Accessibility Requirements: \_\_\_\_\_

If you are a Student or Postdoc registrant, please provide the following information:

Postdoc  Graduate Student  Undergraduate Student (Fax Student ID)

Institution: \_\_\_\_\_ Advisor's Name: \_\_\_\_\_

Advisor's Phone Number: \_\_\_\_\_ Advisor's E-mail: \_\_\_\_\_

**REGISTRATION FEES:**

	Early Bird Registration (Received by Jan. 22)	Standard Registration (Jan. 23 to Feb. 12)	Final Registration (After Feb. 12*)	
SOT Member	\$295	\$345	\$395	\$ _____
Non-Member**	\$590	\$640	\$690	\$ _____
SOT Retired Member	\$ 65	\$105	\$145	\$ _____
Postdoctoral SOT Member	\$ 80	\$120	\$160	\$ _____
Postdoctoral Non-Member**	\$160	\$200	\$240	\$ _____
Graduate Student Member	\$ 60	\$100	\$140	\$ _____
Graduate Student Non-Member**	\$120	\$160	\$200	\$ _____
Undergraduate Student	\$ 0	\$ 0	\$ 0	\$ _____
SOT Affiliate	\$ 0	\$ 0	\$ 0	\$ _____
Press	\$ 0	\$ 0	\$ 0	\$ _____
Guest/Spouse (Non-Scientist)	\$ 70	\$ 85	\$100	\$ _____

Guest/Spouse Name: \_\_\_\_\_

**METHOD OF PAYMENT:**

All registrations submitted by hard copy or fax will be processed on-line by SOT staff.

Check or Money Order # \_\_\_\_\_

Government Purchase Order # \_\_\_\_\_

(U.S. GOVERNMENT P.O. FORM MUST BE ATTACHED)

American Express  Diner's Club  Discover  MasterCard  Visa

Credit Card #: \_\_\_\_\_ Expiration Date: \_\_\_\_\_

Signature: \_\_\_\_\_ Cardholder's Printed Name: \_\_\_\_\_

Registration Fee(s) (from part 1) \$ \_\_\_\_\_  
 Continuing Education Courses (from part 2) \$ \_\_\_\_\_  
 Student Functions (from part 2) \$ \_\_\_\_\_  
 Optional Abstract Material (from part 2) \$ \_\_\_\_\_  
**TOTAL DUE \$ \_\_\_\_\_**

\*After February 12, Final Registration rates apply. SOT will accept faxed Registration Forms until March 2. On-line registration will be open until March 11. On-Site Registration Forms will be available at the Annual Meeting Registration Desk.

\*\*Special offer to non-member 2010 Annual Meeting attendees: apply for membership by May 1, 2010, and, if accepted, SOT will waive your 2010 dues.

**RETURN THIS TWO-PAGE FORM WITH PAYMENT TO:**  
 Society of Toxicology • P.O. Box 91895 • Washington, DC 20090-1895  
 Faxed forms are accepted only if using a credit card. Fax form to: (703) 438-3113.  
**U.S. GOVERNMENT PURCHASE ORDERS MAY BE FAXED OR MAILED WITH THE REGISTRATION FORM.**  
 Express packages may be mailed to:  
 SOT Headquarters Registration Dept., 1821 Michael Faraday Drive, Suite 300, Reston, VA 20190-5332  
 Questions? Contact SOT • Tel: (703) 438-3115 • E-mail: sothq@toxicology.org

# SOCIETY OF TOXICOLOGY 2010

## REGISTRATION

Registration

**CONFIRMATION:** You will be mailed a registration confirmation, name badge and Continuing Education and/or event ticket(s) before the meeting if your Registration Form is received by January 22, 2010. If your registration is received after January 22, you can pick up your badge and tickets at the "Badge Pick-up Only" registration counters on-site.

**CANCELLATION REFUND POLICY:** All requests for cancellations and/or refunds must be received in writing to SOT Headquarters by February 12, 2010. These refunds will be processed, less a

\$50 cancellation fee, following the Annual Meeting. **Refund requests received after February 12, 2010, will not be processed.**

**EXHIBITORS:** Please go to the Exhibitor Service Center on-line to register. If your company would like more information on exhibit opportunities, go to [www.toxexpo.com](http://www.toxexpo.com). To request a booth, use the "Become an Exhibitor" tab and follow the easy steps from there. You may also contact Liz Kasabian at SOT Headquarters: (703) 438-3115, fax: (703) 438-3113, or e-mail: [liz@toxicology.org](mailto:liz@toxicology.org).

**AMERICANS WITH DISABILITIES ACT (ADA):** The Salt Palace Convention Center is accessible to persons with special needs. If you have special needs, please check the special accessibility requirement box or contact Heidi Prange at SOT Headquarters: (703) 438-3115 ext. 1424 or e-mail: [heidi@toxicology.org](mailto:heidi@toxicology.org).

## Post Convention Package Now Available

SOT is pleased to offer Annual Meeting attendees a post conference weekend package get-away that includes discounted suites and ski packages at the award-winning Hotel Park City. The hotel offers luxurious suite accommodations, mountain base skiing with shuttle, a world-class spa, and fine dining.

*For more information please contact Heidi Prange at [heidi@toxicology.org](mailto:heidi@toxicology.org).*





# Registration Form

## 49<sup>th</sup> SOT Annual Meeting

(Part 2 continued from page 19)

March 7–11, 2010

### CONTINUING EDUCATION COURSES:

Yes, I would like to attend the following CE courses. (Only meeting registrants may enroll in a CE course.) AM # \_\_\_\_\_ PM # \_\_\_\_\_

	Early Bird Registration (Received by Jan. 22)	Standard Registration (Jan. 23 to Feb. 12)	Final Registration (After Feb. 12)	# of Courses	
SOT Member/Corp Affiliate	\$150 each	\$175 each	\$200 each	x _____	\$ _____
Retired Member	\$110 each	\$135 each	\$160 each	x _____	\$ _____
Non-Member	\$300 each	\$325 each	\$350 each	x _____	\$ _____
Postdoctoral (SOT Member/Non-Member)	\$ 90 each	\$115 each	\$140 each	x _____	\$ _____
Graduate or Undergraduate Student (SOT Member/Non-Member)	\$ 45 each	\$ 70 each	\$ 95 each	x _____	\$ _____
Press	\$ 0 each	\$ 0 each	\$ 0 each	x _____	\$ _____

Yes, I would like to attend the Sunrise Continuing Education Mini-Course (includes continental breakfast)

	Early Bird Registration (Received by Jan. 22)	Standard Registration (Jan. 23 to Feb. 12)	Final Registration (After Feb. 12)	
SOT Member/Corp Affiliate	\$ 55 each	\$ 80 each	\$105 each	\$ _____
Retired Member	\$ 55 each	\$ 80 each	\$105 each	\$ _____
Non-Member	\$ 75 each	\$100 each	\$125 each	\$ _____
Postdoctoral (SOT Member/Non-Member)	\$ 55 each	\$ 80 each	\$105 each	\$ _____
Graduate or Undergraduate Student (SOT Member/Non-Member)	\$ 25 each	\$ 50 each	\$ 75 each	\$ _____
Press	\$ 0 each	\$ 0 each	\$ 0 each	\$ _____

### STUDENT AND POSTDOCTORAL FUNCTIONS:

- Yes, I am an undergraduate student and would like to attend the Sunday Undergraduate Education Program. (Limited seating) \$ Complimentary
- Yes, I am a student or postdoc registrant and would like to attend the complimentary Student/Postdoctoral Reception. \$ Complimentary
- Yes, I am a student or postdoc registrant and would like to attend the *In Vitro* Lecture and Luncheon. (A \$5 deposit is required and will be exchanged for the ticket at the luncheon. Limited seating.) \$ \_\_\_\_\_
- Yes, I am a postdoc registrant and would like to attend the Postdoc Luncheon on Tuesday. (Limited seating) \$ Complimentary

### OPTIONAL ABSTRACT MATERIAL:

2010 registrants will receive the abstracts, *The Toxicologist* on CD-ROM, as part of the Annual Meeting registration fee. A printed version of *The Toxicologist* will be available for purchase at \$20 per copy (available while supplies last).

Yes, I want to purchase the printed version of *The Toxicologist*. \$20 each x \_\_\_\_\_ \$ \_\_\_\_\_

### REGISTRANT—CIRCLE ALL THAT APPLY: (YOU MUST MAKE ONE SELECTION/CATEGORY)

<b>A. Type of Organization:</b>	14. Quality Assurance	28. Mechanisms	a. Analytical	g. Lab Animal
1. Academia	15. Regulatory	29. Metals	b. Aquatic Tox.	h. Neurotoxicology
2. Government	16. R&D-Admin.	30. Molecular Biology	c. Clinical Tox.	i. Pathology
3. Military	17. R&D-Operations	31. Mutagenicity	d. Computer	44. Other _____
4. Private Industry	18. R&D-Technical	32. Neurotoxicology	e. <i>In Vitro</i> Tox.	<b>E. Purchasing Responsibilities:</b>
5. Other _____	19. Teaching	33. Pathology	f. Pathology	45. a. I make purchasing decisions
<b>B. Job Function:</b>	20. Other _____	34. Pharmacokinetics	g. Preclinical Tox.	b. I influence purchasing decisions
6. Analytical	<b>C. Field of Work:</b>	35. Pharmacology	h. Quality Assurance	c. I do not participate in purchasing decisions
7. Financial/Purch.	21. Biotechnology	36. Occup. Health	i. Wildlife Tox.	
8. Health and Safety	22. Carcinogenesis	37. Risk Assessment	43. Supplies/Equipment	
9. Computer/Statistics	23. Epidemiology	38. Repro. & Dev. Tox.	a. Analytical	
10. Mgmt-Corporate	24. Immunotoxicology	39. General Tox.	b. Clinical Chem.	
11. Mgmt-Facilities	25. Infusion Tox.	40. Other _____	c. Hardware	
12. Mgmt-Personnel	26. Inhalation Tox.	<b>D. Product Interest:</b>	d. Software	
13. Marketing/Sales	27. Genetic Tox.	41. Publications	e. <i>In Vitro</i>	
		42. Contract Services:	f. <i>In Vivo</i>	

SOT Annual Meeting registrants grant SOT permission to reproduce, copy, and publish photographs taken at the Annual Meeting unless written notification by the registrant, stating otherwise, is submitted to SOT Headquarters prior to the Annual Meeting or while registering on-site.

**There will be no refunds for cancellations received at SOT Headquarters after February 12, 2010.**

SOT will accept faxed Registration Forms until March 2. On-line registration will be open until March 11. On-Site Registration Forms will be available at the Annual Meeting Registration Desk. There will be no refunds after February 12, 2010.



# SOT Job Bank

## THE ULTIMATE RECRUITMENT AND EMPLOYMENT RESOURCE

**Job Seekers—Your Dream Job Awaits You in the SOT Job Bank!!!**

**Employers Are Looking for Candidates through this Service  
and You Don't Want to Be Left Out**

- All SOT Members can utilize the SOT Job Bank as a job seeker **free-of-charge**.
- Register and enter your candidate profile; it only takes 15 minutes to complete.
- Post your resume.
- Review the positions posted by major corporations, academic institutions, government agencies, and private research organizations; positions range from junior to senior level.
- Search by geographic location, employer name, salary, and other criteria.
- Find potential matches to your skills and training at any stage of your career.
- Apply for positions.
- Gain access to information that will help you plan your near-term and long-term goals and objectives.
- See which sectors are hiring.
- Stay abreast of new and emerging areas.

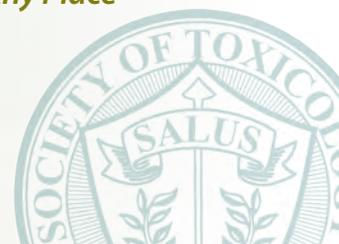
**Employers—Recruit Highly Qualified Candidates  
through the SOT Job Bank!!!**

**The SOT Job Bank is the Ideal Place to Streamline Your Recruitment Process and  
Provides Your Organization with a Valuable Tool**

- Search from a pool of distinguished candidates.
- Join the many employers who rely on this cost effective and efficient database to assist with their employment needs.
- Find the right candidate from among scientists trained in toxicology and the biological sciences with the expertise and right work experience for your position.
- Schedule interviews to hold during the SOT Annual Meeting at the on-site Job Bank Center.
- Reserve interview rooms in advance or on-site.
- SOT Affiliate Members receive a reduced registration rate in appreciation for supporting the Society in achieving its objectives.

*The On-Line SOT Job Bank Is Available Any Time, from Any Place  
at [www.toxicology.org](http://www.toxicology.org).*

**SOT** | Society of  
Toxicology



# 49<sup>TH</sup> ANNUAL MEETING AND TOXEXPO™

## CAREER RESOURCE AND DEVELOPMENT SERVICES

### Streamline Your Job Search: Use SOT Job Bank Services

#### Free Job Search for SOT Members!

The SOT Annual Meeting, with over 6,500 attendees including the best toxicologists, early career scientists, and toxicology-related employers, is the best place to make your connection, whether you are looking for a position or searching for the right candidate. To facilitate job searches, the SOT on-line Job Bank is available at all times, and provides you the opportunity to prepare to take full advantages of the on-site Job Bank Center in Salt Lake City.

### Job Bank

#### Access available any time, any place!

The on-line Job Bank includes positions available at corporations, academic institutions, government agencies, and private research organizations. Last year over 200 hundred positions were posted at the time of the Annual Meeting. Employers rely on this service to provide them with a robust database of candidates available for career opportunities, ranging from junior to senior level positions. As a member benefit, SOT members can search Job Bank listings at no cost. **SOT Affiliates use this system at a reduced rate in appreciation of their commitment to helping further the objectives of the Society.** Candidates and employers alike can access this year-round service any time, any place at [www.toxicology.org](http://www.toxicology.org).

#### The SOT on-line Job Bank allows you to:

- Register as a candidate or employer
- Post employment positions or resumes
- Search the Job Bank database
- Contact employers or candidates

Once registered, candidates may search the listing of available jobs and employers may browse candidate profiles. Both employers and candidates have the option of making a confidential posting, in which no identifying information is displayed. Communication with a desired employer or candidate can even be made *via* e-mail messages created within the system to protect confidentiality. Candidates want to have their CV and contact information up-to-date with the increased traffic to the Job Bank at the time of the Annual Meeting.

### Annual Meeting Job Bank Center

Located in the Salt Palace Convention Center in rooms 155 A and 155 D, the on-site Job Bank Center provides access to the SOT Job Bank as well as assistance in facilitating interviews at the SOT Annual Meeting. We offer personalized assistance if you are new to the Job Bank or have questions. For your convenience, printers will be available for producing hard copies of candidate profiles and position descriptions. All candidates and positions must be sought on-line.

The Center is available during the following hours of operation:

Sunday.....	10:00 AM–4:30 PM
Monday .....	9:00 AM–4:30 PM
Tuesday .....	8:30 AM–4:30 PM
Wednesday .....	8:30 AM–4:30 PM

Employers recognize and appreciate that the Annual Meeting Job Bank Center provides a cost-effective and efficient way to interview a distinguished pool of candidates. For your convenience, we provide six interview rooms on-site during the hours listed above. **New this year:** In advance of the meeting, employers will be able to make reservations for these interview rooms, allowing better scheduling for employers and candidates.

As with the on-line Job Bank, SOT Members have free access to the Center. **All users with current registration at the time of the Annual Meeting will be permitted to use this service.** Although you are encouraged to preregister before entering the Job Bank Center, you can register on-site.

Job Bank access will be available—always—through your personal computer and at the Annual Meeting E-mail Center. Access to the on-line Job Bank in the Job Bank Center is limited to short searches for updates or new information. For additional information, contact Kristen Meletti at SOT Headquarters: (703) 438-3115 ext. 1660 or e-mail: [kristen@toxicology.org](mailto:kristen@toxicology.org).

### Mentor Match

#### On-Line Mentoring Program

The Society of Toxicology recognizes the importance of mentoring in the scientific and professional development of its members. The objective of the on-line mentoring program, Mentor Match, is to provide a service that matches mentees with potential mentors from the SOT membership to provide advice on career path selection, professional development, and life/work balance issues. SOT members are encouraged to share their professional knowledge and experience by serving as mentors for colleagues and for the next generation of toxicologists. The SOT Annual Meeting provides a great opportunity for the mentor and mentee to meet in person. We strongly encourage members of the Society to visit the Mentor Match site and register on-line as mentors and/or mentees. The Mentor Match program will develop as individuals register, allowing the quantity of profiles to increase to a robust combination of both mentors and mentees. The Mentor Match program is accessible to all active SOT members by visiting [www.toxicology.org](http://www.toxicology.org).

*Be a member of the premier group that is creating a safer and healthier world by advancing the science of toxicology*

## As an SOT member you can . . .

**Stay connected at [www.toxicology.org](http://www.toxicology.org)**  
Access member-restricted information  
Use the on-line Member Directory

**Pay Reduced Registration Fees**  
for SOT meetings

**Receive SOT Publications**  
*The Toxicologist* (CD-Rom)  
*Toxicological Sciences*  
*Communiqué*  
Others

**Communicate the Importance of Our Discipline**

**Utilize Career Resources**

**Register for Mentor Match**

**Nominate for Awards**

**Volunteer and Demonstrate Your Leadership Skills**

**Find Products and Services Easily at ToxExpo™**

### Membership Fees:

Full Membership .....	\$135
Associate Membership .....	\$135
Postdoctoral Membership.....	\$35
Student Membership .....	\$20
Retired Membership.....	\$0

*Easy on-line membership application takes approximately 15 minutes to complete.*

### Participate in Your Regional SOT Chapter

Join one of 18 Regional Chapters that foster scientific exchange at a local level, organize regular meetings throughout the year, and sponsor awards.

### Join a Specialty Section

Choose from 25 SOT Specialty Sections that provide forums for networking and exchanging information with peers who share an interest in your area of toxicology. The annual receptions and meetings of the Specialty Sections at the Annual Meeting are ideal opportunities to network with colleagues. Each Specialty Section membership is \$15. Student and postdoctoral members receive the first Specialty Section at no cost.

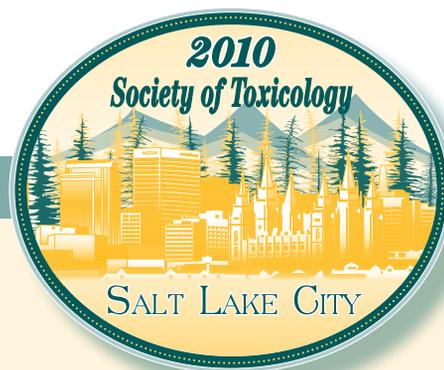
### Choose a Special Interest Group

SOT is committed to increasing the diversity and inclusiveness of the Society. Join one of six established groups that provide forums for networking, education, and recognition of achievement. Each Special Interest Group is \$15. Student and postdoctoral members receive the first Special Interest Group at no cost.

# Membership

**[www.toxicology.org](http://www.toxicology.org)**

For complete information about membership in the Society of Toxicology, visit the SOT Web site at [www.toxicology.org](http://www.toxicology.org) and select Member Information.



**March 7-11, 2010**

## RECOGNITION AND SOCIAL EVENTS

### Awards Ceremony

**Sunday, March 7, 5:15 PM–6:30 PM**  
**Ballroom J**  
**Salt Palace Convention Center**

*Open to all attendees*

Join us as SOT honors our prestigious award winners at the SOT Awards Ceremony (pages 28–29). Please refer to the Awards and Fellowships section of the SOT Web site for complete details about the awards and submitting nominations for the 2011 Annual Meeting.

### Welcoming Reception

**Sunday, March 7, 6:30 PM–7:30 PM**  
**Hall E**  
**Salt Palace Convention Center**

Continue the celebration by attending the Welcoming Reception following the Awards Ceremony. The Welcoming Reception is a great opportunity to renew old friendships and to make new acquaintances. Please join the Society in this kick-off of the Annual Meeting.

### 25-Year (Or More) Member Reception

**Sunday, March 7, 7:00 PM–8:00 PM**  
**Ballroom A**  
**Salt Palace Convention Center**

If you have been a member of the Society of Toxicology for 25 years or more, please join your colleagues to celebrate and recognize the scientists who established the Society. Be sure to sport your 25-year, 35-year, or the new 45-year member pin.

### Student/Postdoctoral Fellow Mixer

**Sunday, March 7, 7:30 PM–8:30 PM**  
**Room 355**  
**Salt Palace Convention Center**

*Ticket Required*

All students and postdoctoral fellows are invited to attend this reception. Refreshments will be provided by SOT and sponsors. A cash bar will also be available. Ticket and Meeting Badge required.

### In Vitro Toxicology Lecture and Luncheon for Students

**Monday, March 8, 12:15 PM–1:30 PM**  
**Room 255 E**  
**Salt Palace Convention Center**

*Ticket Required*

**Lecturer: TBA**  
**Title: TBA**

Graduate students, undergraduates, post-doctoral scholars, and recipients of Colgate-Palmolive awards are among the guests at the *In Vitro* Lecture and Luncheon. The goal of the *In Vitro* Lecture series is to feature important research using *in vitro* and alternative techniques to study basic mechanisms and to illustrate how these test methods benefit animal welfare by refining and reducing animal use. Students and post-docs can reserve a ticket for the luncheon with a \$5 deposit when they register for the SOT Annual Meeting.

### Postdoctoral Assembly Luncheon

**Tuesday, March 9, 12:00 NOON–1:15 PM**  
**Room 255 E**  
**Salt Palace Convention Center**

*Ticket Required*

Amidst scrambling to attend all of the events at the meeting, this will be time for postdocs to kick back and relax! All postdoctoral fellows are invited to a casual luncheon organized by the Postdoctoral Assembly (PDA). We will announce the recipients of the Best Postdoctoral Publication Awards and acknowledge the postdocs who received awards this year from Regional Chapters, Special Interest Groups, and Specialty Sections. The PDA Board members will present an overview of accomplishments and future directions for the PDA and will introduce the new board members for 2010–2011. There will be a drawing for prizes. Postdocs can reserve a ticket when registering for the Annual Meeting.

### Regional Chapter Receptions

**Monday, March 8 through Wednesday, March 10, Various Times**

*(Refer to the Annual Meeting Program and Itinerary Planner for more details.)*

Many of the SOT Regional Chapters meet during the SOT Annual Meeting. A list of Regional Chapter receptions will be listed in the *Program* Event Calendar.

### Special Interest Group Receptions

**Monday, March 8 through Wednesday, March 10, Various Times**

*(Refer to the Annual Meeting Program and Itinerary Planner for more details.)*

Each of the 6 Special Interest Groups will hold a meeting/reception during the 2010 SOT Annual Meeting at the Hilton Hotel or at a local venue. All current and prospective SOT Special Interest Group members are encouraged to attend. The Event Calendar in the *Program* will have a listing of locations and function times.

### Specialty Section Receptions

**Monday, March 8 through Wednesday, March 10, Various Times**

*(Refer to page 26 for details.)*

Each of the 25 SOT Specialty Sections will hold either a luncheon or early evening meeting/reception during the 2010 SOT Annual Meeting. All current and prospective SOT Specialty Section members are encouraged to attend. Dates for the Specialty Section Receptions are listed on the following page.

## RECOGNITION AND SOCIAL EVENTS

### Specialty Section Receptions

<b>Event</b>	<b>Date</b>	<b>Time</b>
Biological Modeling Specialty Section Reception	Tuesday, March 9	6:00 PM–7:30 PM
Biotechnology Specialty Section Reception	Wednesday, March 10	6:00 PM–7:30 PM
Carcinogenesis Specialty Section Reception	Monday, March 8	6:00 PM–7:30 PM
Cardiovascular Toxicology Specialty Section Reception	Monday, March 8	12:00 NOON–1:30 PM
Comparative and Veterinary Specialty Section Reception	Tuesday, March 9	6:00 PM–7:30 PM
Dermal Toxicology Specialty Section Reception	Monday, March 8	6:00 PM–7:30 PM
Drug Discovery Toxicology Specialty Section Reception	Tuesday, March 9	6:00 PM–7:30 PM
Ethical, Legal, and Social Issues Specialty Section Reception	Wednesday, March 10	6:00 PM–7:30 PM
Food Safety Specialty Section Reception	Monday, March 8	6:00 PM–7:30 PM
Immunotoxicology Specialty Section Reception	Tuesday, March 9	6:00 PM–8:00 PM
<i>In Vitro</i> and Alternative Methods Specialty Section Luncheon	Tuesday, March 9	12:00 NOON–1:30 PM
Inhalation and Respiratory Specialty Section Reception	Tuesday, March 9	6:00 PM–7:30 PM
Mechanisms Specialty Section Reception	Tuesday, March 9	6:00 PM–7:30 PM
Medical Device Specialty Section Reception	Monday, March 8	6:00 PM–7:30 PM
Metals Specialty Section Reception	Monday, March 8	6:00 PM–7:30 PM
Mixtures Specialty Section Reception	Tuesday, March 9	6:00 PM–7:30 PM
Molecular Biology Specialty Section Reception	Monday, March 8	6:00 PM–7:30 PM
Nanotoxicology Specialty Section Reception	Monday, March 8	6:00 PM–7:30 PM
Neurotoxicology Specialty Section Reception	Wednesday, March 10	6:00 PM–7:30 PM
Occupational and Public Health Specialty Section Luncheon	Monday, March 8	12:00 NOON–1:30 PM
Ocular Toxicology Specialty Section Reception	Monday, March 8	6:30 PM–7:30 PM
Regulatory and Safety Evaluation Specialty Section Reception	Tuesday, March 9	6:30 PM–7:30 PM
Reproductive and Developmental Toxicology Specialty Section Reception	Wednesday, March 10	6:30 PM–7:30 PM
Risk Assessment Specialty Section Reception	Monday, March 8	6:30 PM–7:30 PM
Toxicologic and Exploratory Pathology Specialty Section Luncheon	Wednesday, March 10	12:00 NOON–1:30 PM

# Thank You

### Council

Cheryl Lyn Walker ..... President  
 Michael P. Holsapple..... Vice President  
 Jon C. Cook ..... Vice President-Elect  
 Lawrence R. Curtis ..... Treasurer  
 Martin A. Philbert ..... Secretary  
 Peter L. Goering..... Secretary-Elect  
 Kenneth S. Ramos ..... Past President  
 Matthew S. Bogdanffy ..... Councilor  
 Susan J. Borghoff ..... Councilor  
 Patricia E. Ganey ..... Councilor  
 Ronald N. Hines ..... Councilor

### Scientific Program Committee

Michael P. Holsapple..... Council Contact,  
 Chair, Member  
 Jon C. Cook ..... Co-Chair, Member  
 Cynthia A. Afshari ..... Member  
 Michael Aschner ..... Member  
 William J. Brock..... Member  
 Leigh Ann Burns Naas..... Member  
 Myrtle A. Davis..... Member  
 Paul M. D. Foster..... Member  
 Annie M. Jarabek ..... Member  
 Charlene A. McQueen ..... Member  
 Terrence J. Monks ..... Member  
 Richard S. Pollenz ..... Member  
 Hollie I. Swanson..... Member  
 David B. Warheit..... Member

### Continuing Education Committee

John C. Lipscomb ..... Chair, Member  
 Hadi Falahatpisheh ..... Member  
 Kathleen Gabrielson ..... Member  
 Michelle J. Hooth ..... Member  
 Debra L. Laskin ..... Member  
 Christopher A. Reilly ..... Member  
 Stephen H. Safe ..... Member  
 Courtney E. W. Sulentic..... Member  
 Yanan Tian ..... Member  
 Anne Elizabeth Loccisano ..... Postdoctoral  
 Representative  
 Sarah J. Gilpin..... Student Representative  
 Ronald N. Hines ..... Council Contact

# AWARDS CEREMONY

## SUNDAY, MARCH 7, 2010

The Society of Toxicology will present these Awards 5:15 PM–6:30 PM at the Salt Palace Convention Center, Ballroom J.

### SOCIETY OF TOXICOLOGY AWARDS



#### ACHIEVEMENT AWARD

**Gary W. Miller, Ph.D.**  
*Emory University*



#### ARNOLD J. LEHMAN AWARD

**Edward V. Ohanian, Ph.D.**  
*U.S. EPA*



#### DISTINGUISHED TOXICOLOGY SCHOLAR AWARD

**Harihara M. Mehendale, M.S., Ph.D., DABT**  
*University of Louisiana at Monroe*



#### EDUCATION AWARD

**Tetsuo Satoh, Ph.D., ATS**  
*Chiba University, NPO-HAB Research Laboratories, and Showa University*



#### ENHANCEMENT OF ANIMAL WELFARE AWARD

**Leonard M. Schechtman, B.S., M.S., Ph.D.**  
*Innovative Toxicology Consulting, LLC*



#### FOUNDERS AWARD

**James S. Bus, Ph.D., DABT, ATS**  
*Dow Chemical Company*



#### LEADING EDGE IN BASIC SCIENCE AWARD

**Richard S. Paules, Ph.D.**  
*National Institute of Environmental Health Sciences*



#### MERIT AWARD

**Marion F. Ehrich, Ph.D., DABT, ATS**  
*Virginia-Maryland Regional College of Veterinary Medicine*



#### PERRY J. GEHRING DIVERSITY STUDENT TRAVEL AWARD

**Nygerma L. Dangleben**  
*University of California Berkeley*



SOT Sponsored Awards



#### PUBLIC COMMUNICATIONS AWARD

**Philip Wexler, B.S., M.L.S.**  
*National Library of Medicine*



#### TRANSLATIONAL IMPACT AWARD

**Kenneth E. McMartin, Ph.D.**  
*Louisiana State University Health Science Center*



#### BOARD OF PUBLICATIONS BEST PAPER IN TOXICOLOGICAL SCIENCES AWARD



Identification and Characterization of Toxicity of Contaminants in Pet Food Leading to an Outbreak of Renal Toxicity in Cats and Dogs (*ToxSci*, November 2008, Vol. 106, No. 1: 251–262)

**Roy L. M. Dobson, Safa Motlagh, Mike Quijano, R. Thomas Cambron, Timothy R. Baker, Aletha M. Pullen, Brian T. Regg, Adrienne S. Bigalow-Kern, Thomas Vennard, Andrew Fix, Renate Reimschuessel, Gary Overmann, Yuching Shan, and George P. Daston**



#### BEST POSTDOCTORAL PAPER AWARD

**Bret Bessac, Ph.D.**  
*Yale University School of Medicine*  
Transient Receptor Potential Ankyrin 1 Antagonists Block the Noxious Effects of Toxic Industrial Isocyanates and Tear Gases, *The FASEB Journal* (2009) Vol. 23 1102-1114

**Manabu Nukaya, Ph.D.**  
*University of Wisconsin-Madison*  
The Role of the Dioxin Responsive Elements Cluster Between Cyp1a1 and Cyp1a2 Loci in Aryl Hydrocarbon Receptor Biology, *Proc. Natl. Acad. Sci. USA* (2009) 106, 4923-8

**Nicholas Radio, Ph.D.**  
*Cellumen*  
Assessment of Chemical Effects on Neurite Outgrowth in PC12 Cells Using High Content Screening, *Toxicol Sci.* (2008) 105(1), 106-118

# CONGRATULATIONS!

## SPONSORED AWARDS

### ASTRAZENECA TRAVELING LECTURESHIP AWARD

**Jon Christopher Corton, Ph.D.**  
*U.S. EPA*

### COLGATE-PALMOLIVE AWARDS FOR STUDENT RESEARCH TRAINING IN ALTERNATIVE METHODS

**Natalia VanDuyn, B.S.**  
*Indiana University School of Medicine*

**David T. Szabo, M.S.**  
*University of North Carolina at Chapel Hill*

### COLGATE-PALMOLIVE GRANTS FOR ALTERNATIVE RESEARCH

**Duncan Craig Ferguson, V.M.D., Ph.D., B.A.**  
*University of Illinois Urbana-Champaign*

**Patrick Allard, M.S., Ph.D.,**  
*Harvard Medical School*

**Mehmet Uzumcu, D.V.M, Ph.D.**  
*Rutgers University*

### PFIZER UNDERGRADUATE STUDENT TRAVEL AWARDS

**Annie Carlton**  
*Bates College*

**Alisha Chitrakar**  
*Saint Peters College*

**Megan Culbreth**  
*North Carolina State University*

**Chang Woo Lee**  
*University of Texas MD Anderson*

**Sharon Ochs**  
*Wright State University*

### SYNGENTA FELLOWSHIP AWARD IN HUMAN HEALTH APPLICATIONS OF NEW TECHNOLOGIES

**Haitian Lu, M.S.**  
*Michigan State University*

## SOT AWARD LECTURES

### Leading Edge in Basic Science Award Lecture: Toxicogenomics at NIEHS: How Genomics Is Impacting the Science of Toxicology

Monday, March 8, 12:30 PM–1:20 PM

*Lecturer: Richard S. Paules, National Institute of Environmental Health Sciences*

### Translational Impact Award Lecture: Translating Mechanism-Based Research into Antidotes: Trials, Tribulations, and Triumphs

Tuesday, March 9, 8:00 AM–8:50 AM

*Lecturer: Kenneth E. McMartin, Louisiana State University Health Science Center*

### Distinguished Toxicology Scholar Award Lecture: Toxic Injury: Initiation, Expansion, and Repair

Tuesday, March 9, 12:30 PM–1:20 PM

*Lecturer: Harihara M. Mehendale, University of Louisiana at Monroe*

### Merit Award Lecture: Living with Passion—Opening Doors in Research, Teaching, and Service

Wednesday, March 10, 12:30 PM–1:20 PM

*Lecturer: Marion Ehrich, Virginia-Maryland Regional College of Veterinary Medicine*

SOT/AstraZeneca IUTOX Fellowships for individuals from developing countries selected in December 2009 will be honored at the Awards Ceremony.

Regional Chapters, Special Interest Groups, and Specialty Sections offer awards throughout the year—Check the Web site for full details at [www.toxicology.org](http://www.toxicology.org).

The Novartis Graduate Student Fellowship Award recipients selected in March 2010 will be honored at the Awards Ceremony.

## CONTINUING EDUCATION

### Continuing Education Courses

The Continuing Education Program offers a wide range of courses that cover established knowledge in toxicology, as well as new developments in toxicology and related disciplines. Courses can be applied toward certifying and licensing board requirements and may also be used for recertification with the American Board of Toxicology (ABT). Both basic and advanced course topics are offered. The basic course is intended to provide a broad overview of an area or to assist individuals in learning new techniques or approaches. The advanced course is intended to be of interest to individuals with previous knowledge of the subject or already working in the field.

All courses will be held on Sunday, March 7, 2010, at the Salt Palace Convention Center. Please check the signage in the registration area and at the CE Booth for room assignments. Note: Your course materials will be available in the room immediately prior to the course (they will not be available at the registration area). If you have your course ticket, go directly to the assigned course room. If you have not received your course ticket or have not registered, please go to the registration area on Saturday afternoon/evening or on Sunday morning. If you have misplaced your ticket, please go to a Continuing Education Booth at the Convention Center on Sunday. The booths will be open from 6:30 AM–5:30 PM.

**Please Note:** Each Continuing Education Course is offered in one of three time blocks:

**Sunrise (7:00 AM–7:45 AM)**

**Morning (8:15 AM–12:00 NOON)**

**Afternoon (1:15 PM–5:00 PM)**

Registration for the Annual Meeting and a separate CE course ticket are required.

### Continuing Education Target Areas

In addition to the thematic approach topics selected by the Scientific Program Committee, the Continuing Education Committee has chosen two specific target areas to highlight in the courses offered this year. The target area is noted following the course title.

#### Biologicals

This topic provides an integrated discussion of the regulatory and risk assessment processes for the development of human monoclonal antibodies, siRNA molecules, vaccines, and other biological materials to be used as new disease modifying therapies, including the evolving and emerging regulations for FDA approval and regulatory aspects of biologicals *versus* small molecules.

#### Cytokine Biology

Cytokines, molecules important in mediating toxicant-induced responses, emanate from multiple sources. Their release is in response to different stimuli and they interact to produce distinct and defined cellular and organismic responses. These responses are deterministic in autoimmune diseases and in response to toxicant exposure. This theme includes elucidation of their roles in diseases (including cancer), response to injury from exposure to chemical or biological agents (including infections), analytical approaches for quantification of cytokine release, presentation of examples of cytokine involvement in toxic responses, cytokine effects on xenobiotic metabolism, and emerging issues in the area.

#### Biological Pathway Analysis: An Introduction to the Pathway Knowledge Bases for Toxicological Research

SR01

CE SUNRISE

*Chairperson(s): Marc E. Gillespie, St. John's University, Queens, NY*

*Sponsor:*

**Molecular Biology Specialty Section**

Genomic and proteomic datasets are a complex and information rich resource. Toxicology is expanding to new omics-based technologies to identify important gene and protein expression changes. A critical step in such studies is the analysis of the data set to derive reasonable mechanistic meaning and testable hypothesis. Additionally, the use of genomic and proteomic approaches to identify new lead molecules for biologically relevant targets is rapidly expanding. A challenge for scientists is how to properly and effectively incorporate high-throughput omics technologies into their research programs. This course will present practical cases demonstrating how the Reactome pathway analysis tools can be used to identify relevant biological pathways within large and immensely complex data sets derived from multiple high-throughput technology platforms. The course will begin with an overview of how genomic and proteomic data sets are generated including, but not limited to, microarray gene expression data, mass-spectrometry data, protein interaction data, and RNAi screening. All of these methods share a common endpoint, the generation of large datasets that the toxicologist must analyze without prior knowledge of a reasonable mechanistic basis or outcome. Often the analysis of such data can be biased by focusing on known genes and pathways. The creation of new knowledge bases, often called pathway databases, incorporates information on protein, gene, and literature databases to facilitate the identification of relevant schemes using combinations of data, resulting in predictions that more closely approximate biological networks. The course will review how available knowledge bases

# 49<sup>TH</sup> ANNUAL MEETING AND TOXEXPO™

## CONTINUING EDUCATION

such as Reactome and PharmGKB can be used to interrogate large and complex datasets to identify the contributions of specific pathways in a given biological response to toxicant exposure.

- **Biological Pathway Analysis: An Introduction to the Pathway Knowledge Bases for Toxicological Research**, Marc E. Gillespie, St. John's University, Queens, NY

### Biologicals: Introduction to Drug Development/Biologicals

AM02

CE BASIC

*Chairperson(s): James D. Green, Biogen Idec, Inc., Cambridge, MA, and Laura Andrews, Genzyme Corporation, Framingham, MA*

*Sponsor:*

Regulatory and Safety Evaluation Specialty Section

*Endorsed by:*

Comparative and Veterinary Specialty Section  
Drug Discovery Toxicology Specialty Section  
Immunotoxicology Specialty Section

Toxicologists and other preclinical scientists have developed an extensive experience base with a wide range of product classes of biologics over the last two decades. These product classes include proteins, monoclonal antibodies, vaccines, cell therapies, gene therapy products, peptides, and oligonucleotides. These product classes are diverse in origin and are manufactured by a variety of production methods. For example, host cells (e.g., *E. coli*, yeast, CHO cells) are used in the production of antibodies and proteins; various solid and liquid state chemical syntheses have been used for the production of peptides, siRNA's and oligonucleotides, and a variety of vectors (e.g., retrovirus, AAV) have been used to produce gene therapy products. The historical information that has set the ground work for current practices will be reviewed and important global regulatory requirements will be identified that should be considered collectively when designing the battery of nonclinical safety studies. Unique considerations for each of these product classes will be highlighted as well as the timing of the considerations. Emphasis will be placed on two distinct phases; in particular, those that occur prior to the conduct of human clinical trials and those that occur during clinical development. The course will be an integrated discussion of the scientific, risk/benefit, and regulatory considerations that should be considered for the development and human testing of biotherapeutics. We intend to address evolving regulatory requirements in each specific product area and, as appropriate, discuss important differences from the development of small molecule drugs. Students with little or no experience in this area, as well as toxicologists working in pharmaceutical drug development will benefit from taking this course.

- **Introduction**, James D. Green, Biogen Idec, Inc., Cambridge, MA
- **Principles for Development of Proteins**, Shawn M. Heidel, Eli Lilly & Company, Indianapolis, IN
- **Principles for Development of Monoclonal Antibodies and Related Forms**, Randy Soltys, Genentech Inc., South San Francisco, CA
- **Principles for Development of Novel Biologics: siRNA, Oligonucleotides, Anti-Sense, and Aptamers**, Arthur A. Levin, Santaris Pharma A/S, San Diego, CA
- **Principles for Development of Vaccines, Cell and Gene Therapies, and Blood Products (CBER-Regulated Products)**, Timothy MacLachlan, Genzyme Corporation, Framingham, MA

### Comparative Biology of the Lung

AM03

CE BASIC

*Chairperson(s): Richard Parent, Consultox Ltd., Damariscotta, ME, and Daniel Costa, U.S. EPA, Research Triangle Park, NC*

*Sponsor:*

Inhalation and Respiratory Specialty Section

*Endorsed by:*

Drug Discovery Toxicology Specialty Section  
Immunotoxicology Specialty Section  
Regulatory and Safety Evaluation Specialty Section

All mammals have evolved respiratory structures to ensure that the principal function of the lung, gas exchange, is met under varying physiological conditions. However, this essential function is achieved despite significant differences in the structural organization, cellular composition, and related functions mediated through the respiratory system and across mammalian species. Translational toxicology requires that one understand these innate differences in fundamental respiratory biology if one is to appropriately interpret and extrapolate findings in animal models. On a gross level, the nasal passages, pleural thickness, vascularity, and connective tissue structure vary between species. Quantitative evaluation of the tracheobronchial airway tree demonstrates few consistent features between species. The epithelial cell populations lining the lung differ in cell type, location, and abundance. The metabolic enzymes, cytokines, chemokines, protease, and anti-oxidant potential, although showing some similarities, also demonstrate vast differences. Similarly, basic immunological functions in laboratory animals must be understood and related to those in humans to enable appropriate species translation. We will illustrate many of these fundamental differences, describe methods for making measurements in different species, and most importantly, focus on the fundamentals of appropriate interpretation of

## CONTINUING EDUCATION

study data derived in animals for human use. Attendees will gain a basic understanding of the value and pitfalls extending from these species differences, which will enable improved study design and extrapolation of research data for efficacy, safety pharmacology, and toxicology studies. This course is intended to provide attendees with a basic understanding of lung structure-function relationships and associated immunological and metabolic functions in laboratory animals that will aid in the extrapolation of inhalation or respiratory data to humans.

- **Introduction**, Richard Parent, Consultox Ltd., Damariscotta, ME, and Daniel Costa, U.S. EPA, Research Triangle Park, NC
- **Comparative Anatomy of Mammalian Respiratory Systems**, Kent Pinkerton, University of California, Davis, CA
- **Interpretation and Limitations in the Assessment of Lung Function in Laboratory Mammals**, Jeffrey Tepper, Tepper Nonclinical Consulting, San Carlos, CA
- **Metabolism and Enzymatic Balance in the Respiratory Tract**, Laura Van Winkle, University of California, Davis, CA
- **Pulmonary Immune Functions Important for Translational Toxicology and Predictive of Risk in Humans**, Gary R. Burleson, BRT—Burleson Research Technologies, Inc., Morrisville, NC
- **Concluding Remarks**, Daniel Costa, U.S. EPA, Research Triangle Park, NC

### Cytokines: Balancing Therapeutic Utility and Immune System-Mediated Toxicities/ Cytokine Biology

AM04

CE BASIC

*Chairperson(s): Lynne A. LeSauter, Charles River, Montreal, Quebec, Canada, and Rafael Ponce, Amgen, Inc., Seattle, WA*

*Sponsor:*

**Immunotoxicology Specialty Section**

Direct and indirect modulation of cytokines *via* therapeutics, either increasing or decreasing cytokines, is a central factor in the success of current therapies targeting cancer, autoimmunity, inflammation, and infection. However, nonclinical and clinical data demonstrate that these therapies can overwhelm compensatory mechanisms designed to protect the host, resulting in toxicity. The therapeutic benefits and potential toxicities can be best understood through an understanding of the central role of cytokines in modulating cellular function. To address these specific issues, we will define the central toxicities and syndromes that have been identified as arising from cytokine-mediated immunomodulation; establish the immunological basis for these toxicities using in-depth exploration where possible, including useful biological markers that can inform

clinicians and toxicologists; develop an understanding of cytokine modulation in the treatment of cancer, autoimmunity, inflammation, and infection; and identify deficiencies in current toxicological practice for predicting certain immune system-mediated risks arising from cytokine-mediated immunomodulation in humans. Finally, we will explore specific case studies where these principles have been applied to reinforce these central concepts.

- **Introduction**, Lynne A. LeSauter, Charles River, Montreal, Quebec, Canada
- **Cytokine Modulation: The Yin and the Yang**, Rafael Ponce, Amgen, Inc., Seattle, WA
- **Immunomodulators That Inhibit Cytokines**, Theodora W. Salcedo, Bristol-Myers Squibb, Syracuse, NY
- **Immunomodulators That Are Pro-Inflammatory Cytokines**, Dennis M. Miller, ZymoGenetics, Inc., Seattle, WA
- **Cytokine Storms: It's Not Nice to Fool with Mother Nature**, Christopher Horvath, Taligen Therapeutics, Cambridge, MA

### CELL SIGNALING

#### Nuclear Receptors: Role in Chemical Mode of Action and Targets for Toxicity Testing

AM05

CE BASIC

*Chairperson(s): Chris Corton, U.S. EPA, Research Triangle Park, NC, and Jack Vanden Heuvel, Pennsylvania State University, University Park, PA*

*Sponsor:*

**Molecular Biology Specialty Section**

*Endorsed by:*

**Drug Discovery Toxicology Specialty Section**

Nuclear receptors (NR) are one of the most abundant classes of transcriptional regulators in animals and function as ligand-activated transcription factors. They provide a direct link between signaling molecules and transcriptional responses that impact diverse functions including development, metabolic homeostasis, and reproduction. NR are not only promising pharmacological targets but can be activated inappropriately by environmentally relevant chemicals leading to a broad spectrum of adverse effects. Thus the intent of this basic course is to provide an overview of the biology of nuclear receptors, the pathways and modes of action of a subset of nuclear receptors involved in chemical toxicity, and strategies for screening chemicals for nuclear receptor interactions as well as placement in mode-of-action categories. To begin with, we will cover the structure, function and general mechanisms of activation as well as basic biological roles of NR that are targets of xenobiotics in different tissues and cell types. We will then explore

the role of nuclear receptors in both augmenting and suppressing chemical carcinogenesis, which will include a summary of mode of action and human relevance of those NR (CAR, PPAR, PXR, RXR) commonly associated with liver cancer. Following this summary, the adverse effects of xenobiotics on the endocrine system associated with activation or modulation of estrogen, androgen, and thyroid hormone receptors will be addressed. Finally, both the primary and secondary screening strategies to define effects of chemicals on NRs and the pathways that mediate their adverse effects will conclude this course. The intended audience for this course includes those who desire a basic knowledge of the state of the science of nuclear receptors in chemical mode of action and strategies for accelerating the placement of chemicals into mode-of-action pathways. The course will be of interest to many who are engaged in wider aspects of carcinogenesis, reproductive biology and risk assessment.

- **Introduction**, Chris Corton, U.S. EPA, Research Triangle Park, NC, and Jack Vanden Heuvel, Pennsylvania State University, University Park, PA
- **The Structure and Function of Nuclear Receptors**, Jack Vanden Heuvel, Pennsylvania State University, University Park, PA
- **Role of Nuclear Receptors in Chemical Carcinogenesis**, Chris Corton, U.S. EPA, Research Triangle Park, NC
- **Role of Nuclear Receptors in Endocrine Disruption**, Stephen Safe, Texas A&M University, College Station, TX
- **Nuclear Receptors and High-Throughput Screening**, Keith Houck, U.S. EPA, Research Triangle Park, NC

### Predictive Power of Novel Technologies (Cells to 'Omics): Promises, Pitfalls, and Potential Applications

AM06

CE BASIC

**Chairperson(s):** Srikanth S. Nadadur, NIEHS, Research Triangle Park, NC, and Mary Jane Cunningham, Nanomics Biosciences, Inc., Cary, NC

**Sponsor:**

Molecular Biology Specialty Section

**Endorsed by:**

Inhalation and Respiratory Specialty Section  
Mechanisms Specialty Section

Advances in the disciplines of cell and molecular biology have led to the development of novel biotechnologies capable of generating “global molecular profiles” for *in situ* toxicological assessment. These technologies should accelerate our understanding of the

molecular basis for susceptibility to toxicants and provide new insights into mechanisms of action. Both theoretical and practical information on these emerging high-throughput technologies and their applicability, interpretation, and integration will present a more comprehensive understanding of cellular responses to chemical/toxicant stress. To begin, the course will highlight the utility of laser capture microdissection in isolating specific cell populations for toxicological assessment at the level of RNA and proteins. An overview of proteomic technologies in protein interaction studies and their relevance to changes in downstream signaling mediators involved in toxic response pathways will be presented, followed by an update of gene expression profiling approaches in toxicogenomics and systems biology research. Focus will be placed on the examination of the capabilities of high-throughput technologies for identifying single nucleotide polymorphisms (SNPs) and their value for identifying and characterizing underlying genetic susceptibilities to toxicants. Finally, high-throughput technologies available to identify genome-wide epigenetic alterations will be presented, including their role in epigenetic alterations in health, disease, and toxicant-induced biological outcomes. The goal of this course is to educate toxicologists on the array of ever-growing technologies available to gain a comprehensive understanding of the underlying mechanisms mediating complex biological responses. Using these technologies, investigators can move towards a better and more reliable prediction and extrapolation of toxic responses. This course is relevant to scientific technical and regulatory staff involved in various stages of compound development.

- **‘Omics to Predict Specific Interaction(s) in Complexity**, Srikanth S. Nadadur, NIEHS, Research Triangle Park, NC
- **Integrating Transgenic Animal Models and Laser Capture Microdissection Applications with Micro-‘Omic Based Analyses for *In Vivo* Toxicological Assessments**, Kevin L. Dreher, U.S. EPA, Research Triangle Park, NC
- **Clinical Proteomics: Mapping Molecular Networks in Clinical Specimens Using Reverse Phase Protein Microarrays**, Emanuel F. Petricoin, George Mason University, Manassas, VA
- **Gene Expression Profiling for Toxicity Assessment Using Systems Biology**, Mary Jane Cunningham, Nanomics Biosciences, Inc., Cary, NC
- **The Role of DNA Variation in Human Drug Response**, Steven P. Hamilton, University of California, San Francisco, CA
- **Epigenome Profiling: Mapping Epigenetic Alterations in Health and Disease**, Steven A. Belinsky, Lovelace Respiratory Research Institute, Albuquerque, NM

## CONTINUING EDUCATION

### Reproduction and Regulatory Impact

AM07

CE BASIC

**Chairperson(s):** Robert E. Chapin, Pfizer Global Research & Development, Groton, CT, and Jeffrey S. Moffit, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT

**Sponsor:**

Reproductive and Developmental Toxicology Specialty Section

**Endorsed by:**

Regulatory and Safety Evaluation Specialty Section

Most new compounds destined for commerce, and all compounds intended for human consumption, need to be assessed for developmental and reproductive toxicity (DART). However, the underlying biology can be confusing because the jargon employed by the cognoscenti can be impenetrable and the implications of findings in these studies are often difficult to appreciate quickly. Our panel will begin this course with an open dialogue designed to lift the veil of uncertainty around many of these issues. After a quick review of some of the key biology, we will touch on the characteristic study designs which generate the necessary data. A point of focus will have the panel examine the typical effects seen in adults and juveniles, and what impact these can have on the registration and use of the compound in Europe and the U.S., respectively. Although the focal point for this course will be on environmental compounds, the final presentation will highlight drug candidates and how reproductive or developmental findings affect their journey to the marketplace. It is our goal to leave students with a better understanding of the impacts that reproductive or developmental findings have on the registration and use of environmental and pharma compounds.

- **Basic Biology and Study Designs**, Chad Blystone, NIEHS/NTP, Research Triangle Park, NC
- **The Regulatory Impact of Effects on Reproduction and Development**, Aldert Piersma, RIVM, Bilthoven, Netherlands
- **The Impact of DART Findings on Regulating Environmental and Occupational Exposures in the U.S.**, Vicki Dellarco, U.S. EPA, Washington, DC
- **The Impact of DART Findings on Drug Development and Approval in the U.S.**, Tracey Zoetis, Sciluent, Herndon, VA

### Assessment of Ocular Toxicity in Toxicology Studies Conducted for Regulatory Purposes

PM08

CE BASIC

**Chairperson(s):** Margaret Collins, Charles River Laboratories, Reno, NV, and Andrea Weir, Charles River Laboratories, Reno, NV

**Sponsor:**

Toxicologic and Exploratory Pathology Specialty Section

**Endorsed by:**

Comparative and Veterinary Specialty Section  
Regulatory and Safety Evaluation Specialty Section

Ocular toxicity is known to occur following intended or unintended exposure of ocular tissues to xenobiotics. It can occur following local exposure of the eye to an agent or after exposure *via* oral or other routes of administration. In order to define the risks that pharmaceuticals, pesticides, and other toxic substances pose to the eye, an assessment of ocular toxicity is routinely included in general toxicology studies conducted for regulatory purposes. Because anatomical and physiological differences between species can impact the nature of the ocular effects observed, understanding species differences is important. Although it is possible to detect some ocular effects, such as conjunctivitis, with the naked eye, more sensitive techniques are routinely used to assess ocular toxicity. Slit lamp biomicroscopy and indirect ophthalmoscopy are routinely utilized to more closely evaluate the anterior and posterior chambers of the eye, respectively, during the course of toxicology studies. At the time of necropsy, ocular tissues are collected and processed for histopathological evaluation. More specialized endpoints, such as electroretinography, can be incorporated, as needed. Ocular anatomy and physiology and the assessment of ocular toxicity can be challenging to scientists involved in the safety assessment of pharmaceuticals, pesticides, and other agents. This basic course will cover ocular anatomy and physiology in laboratory animals, established methods used to assess ocular toxicity, as well as more novel techniques for toxicity assessment. Examples of ocular toxicity that can occur following different routes of exposure will be discussed.

- **Introduction and Overview**, Margaret Collins, Charles River Laboratories, Reno, NV
- **Comparative Ocular Anatomy and Physiology in Laboratory Animals**, Mark Vezina, Charles River Laboratories, Montreal, Quebec, Canada
- **Diagnostics in Ocular Toxicology**, Robert Munger, Animal Ophthalmology Clinic, Dallas, TX

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## CONTINUING EDUCATION

- **Diagnostics and Ocular Imaging in the 21<sup>st</sup> Century**, Christopher Murphy, University of California, Davis, CA
- **Ocular Pathology: Looking at the Eye**, Ken Schafer, Vet Path Services, Inc., Greenfield, IN

### GENE-ENVIRONMENT INTERACTIONS

#### Gene-Environment Interactions Influence Cytokine Biology in Immunotoxicity and Disease: Genomic, Genetic, and Epigenetic Perspectives/Cytokine Biology

PM09

CE ADVANCED

*Chairperson(s): Berran Yucesoy, CDC/NIOSH, Morgantown WV, and Victor J. Johnson, CDC/NIOSH, Morgantown WV*

*Sponsor:*

Immunotoxicology Specialty Section

*Endorsed by:*

Inhalation and Respiratory Specialty Section  
Occupational and Public Health Specialty Section

Cytokines are key signaling and effector molecules that regulate many aspects of host response to exogenous stressors. To date, animal and human studies have identified individual and interacting effects of cytokines at different stages in the pathogenesis of chronic inflammatory and immune-mediated diseases. Animal studies utilizing gene knock-out and transgenic animals and expression microarrays have identified disease-related cytokine networks. Human studies using various genome screening efforts have also uncovered potential candidate genes for disease development and progression. Cytokine genes and their receptors are highly polymorphic and variations in these genes have been associated with the course of and susceptibility to a variety of diseases including infectious, inflammatory, and autoimmune. In addition, epigenetic changes including altered DNA methylation and histone acetylation can control cytokine gene expression by changing the transcription-permissive nature of chromatin structure. Environmental factors are known to modify the direction and magnitude of disease risk in an environment-specific manner. In this respect, genetic association studies have identified interactions between cytokine gene variations and environmental/occupational exposures as shown in the case of silicosis and asthma. In addition, recent studies demonstrated that environmental exposures might alter methylation states of key cytokines genes supporting an epigenetic gene-environment interaction. This course will address aspects of the current state of knowledge with respect to genomic, genetic, and epigenetic approaches in the investigation of cytokine genes associated with occupational and environmental-related diseases.

- **Exploring Gene-Environment Interactions and the Role of Cytokines in Occupational Allergic Respiratory Disease: Whole-Genome Expression and Beyond**, Victor J. Johnson, CDC/NIOSH, Morgantown, WV
- **Influence of Cytokine Gene Variations on Chronic Inflammatory/Immune Diseases: Importance of Gene-Environment Interactions**, Berran Yucesoy, CDC/NIOSH, Morgantown, WV
- **Genetic Regulation of Cytokines in Risk of Beryllium Sensitization and CBD: A Model for Gene-Environment Interaction**, Lisa A. Maier, National Jewish Health, Denver, CO
- **Environmental Epigenomics and Disease Susceptibility**, Randy L. Jirtle, Duke University Medical Center, Durham, NC

### MITOCHONDRIAL BASIS OF DISEASE

#### Mitochondrial Toxicity: Animal Models and Screening Methods in Drug Development

PM10

CE BASIC

*Chairperson(s): Yvonne Will, Pfizer Global Research & Development, Groton, CT, and Carlos Palmeira, University of Coimbra, Coimbra, Portugal*

*Sponsor:*

Drug Discovery Toxicology Specialty Section

*Endorsed by:*

Regulatory and Safety Evaluation Specialty Section

Mitochondria produce almost all the energy in cells, but also chronically expose the cell to cytotoxic free radicals. Mitochondrial disease and toxicity is a rapidly advancing field and the consequences of mitochondrial impairment should be appreciated by scientists in all disciplines. It is estimated that more than 75 diseases and metabolic disorders are attributable, at least in part, to mitochondrial dysfunction. Mitochondrial dysfunction can lead to many different pathologies of the liver, heart, muscle, kidney, and CNS through diverse mechanisms. Numerous widely prescribed therapeutics can undermine mitochondrial function by interfering with DNA replication or expression, and more acutely, by uncoupling or inhibiting oxidative phosphorylation, leading to organ dysfunction and damage. In addition, numerous environmental agents can contribute to diseases and toxicity through modifications of mitochondrial function, leading for example to Parkinson's Disease and Autism. This course will review fundamental concepts of mitochondrial biology and the many different mechanisms by which xenobiotics interfere with mitochondrial function. Both common and novel *in vitro* screening approaches will be described, as well as *in vivo* animal models used to study mitochondrial-mediated

## CONTINUING EDUCATION

toxicities and pathologies, with an emphasis on both their utility and limitations. The course will also introduce Structure-Activity Relationship and systems biology approaches to reveal common factors and novel mechanisms of mitochondrial toxicity. Upon completion of this course, participants will have a deeper understanding of how xenobiotics can alter the basic biochemistry and physiology of mitochondria, how minute changes in mitochondrial processes translate into complex toxicities, organ pathologies, and diseases, as well as a basic understanding of how to study mitochondria and mitochondrial dysfunction.

- **Mitochondrial Function and Dysfunction in Disease and Drug-Induced Toxicity**, James Dykens, Pfizer Global Research & Development, Sandwich, United Kingdom
- **Animal Models of Mitochondria-Mediated Drug Toxicity**, Urs A. Boelsterli, University of Connecticut School of Pharmacy, Storrs, CT
- **In Vitro Approaches to Assess Mitochondria-Mediated Drug Toxicity and Possible Biomarker Development: Advantages and Limitations**, Yvonne Will, Pfizer Global Research and Development, Groton, CT
- **Integrated Mitochondrial and Nuclear Genomic Regulation of Oxidative Phosphorylation in the Study of Mitochondrial Toxicity and Function**, Toshimori Kitami, Broad Institute of MIT and Harvard University, Cambridge, MA

### ICH Initiatives for Conducting Pharmaceutical Preclinical Safety Studies: New and Revised Guidelines and Challenges

PM11

CE ADVANCED

**Chairperson(s):** Tao Wang, Novartis Pharmaceuticals Corporation, Emeryville, CA, and David McGuinn, U.S. FDA, Silver Spring, MD

**Sponsor:**

Regulatory and Safety Evaluation Specialty Section

**Endorsed by:**

Carcinogenesis Specialty Section  
Reproductive and Developmental Toxicology Specialty Section  
Women in Toxicology Special Interest Group

In recent years, the International Conference of Harmonization (ICH) Expert Working Groups have been developing new guidelines and revising some of the existing guidelines on preclinical safety requirements. Some of the important recent initiatives include new guidance, ICH S9, for preclinical evaluation of anticancer pharmaceuticals, revision of ICH M3 guidance that addresses the timing of preclinical studies in relation to various stages of clinical development, and new guidelines on genotoxicity testing (ICH S2) that replaces and combines the ICH S2A and S2B guidelines. Over

the past decade, substantial experience regarding preclinical safety evaluation of biologics (ICH S6) has been gained and based on this experience revision of S6 is underway. The latest rationale behind the new initiatives at ICH will be discussed, while a panel of experts will present new developments and key challenges in each of the areas mentioned above and will provide expert commentary and perspective on the potential impact on preclinical safety evaluation programs these guidelines may have. Case studies will be used to highlight detailed examples, experience in conducting non-clinical ICH safety studies, and the acceptance of the ICH guidelines by the practicing regulatory organizations and reviewers. Our panel experts have years of experience in preclinical toxicology testing from either an industry or regulatory perspective. In addition, several have represented the United States on the ICH Expert Working Groups, and participated in writing or revising these ICH guidelines. This panel will be available to answer questions that will allow participants to obtain valuable information on this topic.

- **Introduction**, Tao Wang, Novartis Pharmaceuticals Corporation, Emeryville, CA
- **Fundamentals of Nonclinical Drug Development**, David McGuinn, U.S. FDA, Silver Spring, MD
- **Preclinical Development of Oncology Therapeutics: An Industry Perspective**, Daniel Lapadula, Novartis Pharmaceuticals Corporation, East Hanover, NJ
- **Use of Genotoxicity and Carcinogenicity Data in U.S. FDA Center for Drug Evaluation and Research**, David Jacobson-Kram, U.S. FDA, Silver Spring, MD
- **Nonclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals: FDA Regulatory Perspective on the ICH S6 Guidance and Updates**, Anne M. Pilaro, U.S. FDA, Silver Spring, MD

### Segment-Specific Renal Pathology for the Non-Pathologist

PM12

CE BASIC

**Chairperson(s):** Debie Hoivik, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, and Susan G. Emeigh Hart, Auxilium Pharmaceuticals, Inc., Malvern, PA

**Sponsor:**

Toxicologic and Exploratory Pathology Specialty Section

**Endorsed by:**

Regulatory and Safety Evaluation Specialty Section

The structural and functional complexity of the kidney uniquely predisposes it to be a sensitive target organ for a number of toxicants. By taking a segment-specific approach to the kidney, participants will gain a broad understanding of structure and func-

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tion, spontaneous changes, the utility of biomarkers for injury, and morphological changes associated with injury. The different segments of the nephron will be reviewed. Species and gender-related differences in renal structure and function will be emphasized, especially where these contribute to differences in nephrotoxic responses. These differences need to be considered when determining the relevance of findings seen in animal studies to humans. We will review some of the more commonly noted spontaneous lesions and their overall incidences, variance by strain (rodents) and age, all of which can impact study outcome. Lesions such as renal amyloidosis in the mouse and chronic progressive nephropathy in the rat are just two examples of spontaneous lesions which may adversely impact the outcome of a study or may be enhanced by chemical administration, often complicating findings and interpretation. Representative examples of segment-specific morphological changes that occur as a direct response to toxicant exposure will be provided, focusing on those changes evident in laboratory animals used for regulatory testing of new chemical entities. For each morphological change, a corresponding control will be provided to clearly depict the nature of the change. Finally, when choosing a biomarker to monitor for kidney effects, it is critical to understand the utility and limitations of traditional and novel serum and urinary markers of renal injury. Participants will gain a broader perspective on selection and implementation of biomarkers, particularly of the newer urinary markers which provide insight into segment specificity or mechanisms of nephrotoxic injury. Moreover, the participants will understand the specificity of each biomarker as a predictor of injury for specific parts of the nephron.

- **The Kidney: Anatomic and Physiologic Features of Mechanistic Relevance**, Susan G. Emeigh Hart, Auxilium Pharmaceuticals, Inc., Malvern, PA
- **Spontaneous and Background Changes in Laboratory Animals**, John Seely, Experimental Pathology Laboratories, Inc., Research Triangle Park, NC
- **Renal Toxicant Induced Lesions by Nephron Segment**, Jim Stoltz, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT
- **Biomarkers of Renal Injury**, Daniela Ennulat, GlaxoSmithKline, King of Prussia, PA

### TOXICITY TESTING IN THE 21<sup>ST</sup> CENTURY

#### Technologies and Tools for Toxicity Testing in the 21<sup>st</sup> Century

PM13

CE BASIC

**Chairperson(s):** Robert Kavlock, U.S. EPA, Research Triangle Park, NC, and Dan Wilson, Dow Chemical Company, Midland, MI

**Sponsor:**

*In Vitro* and Alternative Methods Specialty Section

**Endorsed by:**

Risk Assessment Specialty Section

Toxicology testing has traditionally been associated with defined and tiered testing around dedicated endpoints (i.e., acute, reproductive and developmental, chronic and cancer, etc.). Over time, validated surrogates or refined alternatives for some of the endpoints have come into acceptance for screening and international regulatory use. Coinciding with the release of the NAS report on *Toxicity Testing in the 21<sup>st</sup> Century: A Vision and a Strategy*, a dedicated and rapid shift towards use of more non-whole animal testing is underway. Also, *in vitro* methods are expected to play a major role under REACH and to address the European Union-wide ban on animal use in cosmetics development. Inherent in this shift is a necessary understanding of the critical aspects of cellular, metabolic, and genetic functions effected in response to chemical and drug-induced toxicity as well the dose-response attributes of the responses. Towards this end, elaboration of predictive toxicity pathways by integration of information from *in vitro* assays, surrogate organisms, 'omics technologies, *in silico* approaches, and bioinformatics is ongoing. A review of how the classic approaches for toxicity testing are evolving into sophisticated molecular/mechanistic based approaches and the nature and implementation of *in vitro* high-throughput screening assays, with some mention of implementation of informatics approaches will be addressed. Further insight into how the information will be considered in the context of animal use, testing prioritization, dose-response considerations, and human health risks will be explored. This basic course should be of interest to classically trained toxicologists and investigators and regulators wanting to understand the latest technologies and tools that will be the necessary repertoire for card-carrying mammalian toxicologists.

- **From Classical Mammalian Toxicology and Pathology to the Land of *In Vitro*, Molecular, Genomics, and Other Tools**, Kevin Morgan, sanofi-aventis, Research Triangle Park, NC

## CONTINUING EDUCATION

- **Whole Genome Technologies: Integrating Human Genetic Variability into Toxicology**, Douglas A. Bell, NIEHS-NIH, Research Triangle Park, NC
- **Considerations When Utilizing High-Throughput Technologies and Cells of Different Target Organs to Evaluate Toxicity Endpoints of Large Sets of Chemicals**, Jon Inglefield, Emergent Biosolutions, Gaithersburg, MD
- **New Tools—How Do They Affect the Bottom Line Decisions?** Paul Price, Dow Chemical Company, Midland, MI



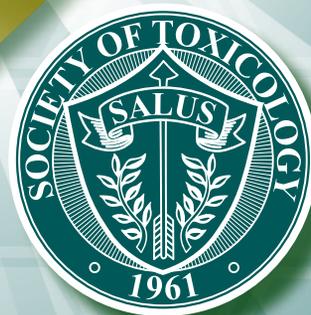
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## FEATURED SESSIONS

### Plenary Opening Lecture: Discovery of Nitric Oxide and Cyclic GMP Cell Signaling and Their Role in Drug Development

Monday, March 8, 8:00 AM–9:00 AM



**Lecturer:** Nobel Laureate Ferid Murad, John S. Dunn, Sr., Distinguished Chair, University of Texas Health Science Center at Houston, Houston, TX

The role of nitric oxide in cellular signaling in the past three decades has become one of the most rapidly growing areas in biology. Nitric oxide is a gas and a free radical with an unshared electron that can regulate an ever-growing list of biological processes. Nitric oxide is formed from L-arginine by a family of enzymes called nitric oxide synthases. These enzymes have a complex requirement for a number of cofactors and regulators including NADPH, tetrahydrobiopterin, flavins, calmodulin, and heme. The enzymes are present in most cells and tissues.

In many instances, nitric oxide mediates its biological effects by activating the soluble isoform of guanylyl cyclase and increasing cyclic GMP synthesis from GTP. Cyclic GMP, in turn, can activate cyclic GMP-dependent protein kinase (PKG) and can cause smooth muscles and blood vessels to relax, decrease platelet aggregation, alter neuron function, etc. These effects can decrease blood pressure, increase blood flow to tissues, alter memory and behavior, decrease blood clotting, etc.

The list of effects of nitric oxide that are independent of cyclic GMP formation is also growing at a rapid rate. For example, nitric oxide can interact with transition metals such as iron, thiol groups, other free radicals, oxygen, superoxide anion, unsaturated fatty acids, and other molecules. Some of these reactions result in the oxidation of nitric oxide to nitrite and nitrate to terminate the effect, while other reactions can lead to altered protein structure function and/or catalytic capacity. These effects probably regulate bacterial infections, inflammation of tissues, tumor growth, and other disorders. These diverse effects of nitric oxide that are cyclic GMP dependent or independent can alter and regulate numerous important physiological events in cell regulation and function. Nitric oxide can function as an intracellular messenger, an antacid, a paracrine substance, a neurotransmitter, or as a hormone that can be carried to distant sites for effects. Thus, it is a unique molecule with an array of signaling functions.

However, with any messenger molecule, there can be too little or too much of the substance, resulting in pathological events. Some of the methods to regulate either nitric oxide formation, metabolism, or function have been in clinical use for more than a century, as

with the use of organic nitrates and nitroglycerin in angina pectoris that was initiated in the 1870s. Inhalation of low concentrations of nitric oxide can be beneficial in premature infants with pulmonary hypertension and increase survival rates. Ongoing clinical trials with nitric oxide synthase inhibitors and nitric oxide scavengers are examining the effects of these agents in septic shock, hypotension with dialysis, inflammatory disorders, cancer therapy, etc. Recognition of additional molecular targets in the areas of nitric oxide and cyclic GMP research will continue to promote drug discovery and development programs in this field. Current and future research will undoubtedly expand the clinician's therapeutic armamentarium to manage a number of important diseases by perturbing nitric oxide formation and metabolism.

Such promise and expectations have obviously fueled the interests in nitric oxide research for a growing list of potential therapeutic applications. There have been and will continue to be many opportunities from nitric oxide and cyclic GMP research to develop novel and important therapeutic agents. There are presently more than 80,000 publications in the area of nitric oxide research.

The lecture will discuss our discovery of the first biological effects of nitric oxide and how the field has evolved since our original reports in 1977. The possible utility of this signaling pathway to facilitate novel drug development and the creation of numerous projects in the pharmaceutical and biotechnology industries will also be discussed.

### SOT/EUROTOX Debate

Monday, March 8, 4:35 PM–5:55 PM

**Threshold of Toxicological Concern (TTC): Is Based on Science or Politics?**

**Chairperson(s):** Jon C. Cook Pfizer Global Research and Development, Groton, CT, and Nancy Claude Institut de Recherches Internationales Servier, Courbevois, France

**SOT Debater:** Michael Cheeseman, U.S. FDA, Center for Food Safety and Applied Nutrition, College Park, MD

**EUROTOX Debater:** Sue Barlow, Independent Consultant in Toxicology, Brighton, Great Britain

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European Societies of Toxicology (EUROTOX)

# 49<sup>TH</sup> ANNUAL MEETING AND TOXEXPO™



## FEATURED SESSIONS

### U.S. FDA Advisory Panel Appointments

Wednesday, March 10, 7:30 AM–8:50 AM

**Chairperson(s):** James A. Popp, Stratoxon, LLC., Lancaster, PA and Margaret A. Miller, U.S. FDA National Center for Toxicology Research, Rockville, MD



### Keynote Medical Research Council (MRC) Lecture: The Interplay between Phosphorylation and Ubiquitination in Regulating the Innate Immune System

Wednesday, March 10, 8:00 AM–9:00 AM

**Lecturer:** Sir Philip Cohen, Medical Research Council Protein Phosphorylation Unit, University of Dundee, The Sir James Black Centre, Dundee, United Kingdom

Infection by bacteria and viruses triggers cells of the innate immune system to produce pro-inflammatory cytokines and interferons that mount the responses to fight the invading pathogens. However these defence mechanisms are a double-edged sword because the uncontrolled production of these substances causes chronic inflammatory and autoimmune diseases. This talk will focus on the signaling pathways downstream of Toll-Interleukin Receptors. The engagement of these receptors by their agonists triggers the formation of Lys63-linked polyubiquitin chains and polyubiquitylated proteins, which then recruit and activate the key protein kinases that drive the production of pro-inflammatory cytokines and type 1 interferons. The mechanisms that initiate the formation of Lys63-linked polyubiquitin chains and the proteins that interact with them (NEMO, OPTN, ABIN1 and ABIN2) will be discussed. Finally, the characterization of mice that express an ABIN1 mutant unable to bind to Lys63-linked polyubiquitin chains will be described and a model that accounts for the striking phenotype displayed by these knock-in mice will be presented.

### Issues Sessions: National Academy of Sciences Vision for Toxicity Testing in the 21<sup>st</sup> Century

Thursday, March 11, 7:30 AM–8:50 AM

**Chairperson(s):** Jon C. Cook, Pfizer Inc., Groton, CT

This Issues Session will continue the dialog begun at the highly successful 2008 NRC session in which the Annual Meeting participants were provided an overview of the three National Academy reports addressing key issues impacting the Society and the profession of toxicology. These reports included Toxicity Testing in the 21<sup>st</sup> Century: A Vision and Strategy, Application of Toxicogenomics Technologies to Predictive Toxicology and Risk Assessment, and Models in Environmental Regulatory Decision Making. For the past two years, *Toxicological Sciences* has published a Forum Series on the Vision for Toxicology Testing in the 21<sup>st</sup> Century. This is the third year we have had an Issues Session at the Annual Meeting dedicated to this discussion. In this installment, the Dr. Boekelheide will provide his perspective on distinguishing adaptive from adverse responses in *in vitro* systems, Dr. Hubal will introduce the concept of the exposome, and Dr. Wogan will describe the scientific challenges to the exposome approach. Dr. Chris Wild has argued that we need to complement the efforts around the genome with an exposome, which he defined as representing all environmental exposures from conception onwards including exposures from diet, lifestyle, and endogenous sources as a critical interest to disease etiology as well as influencing toxicological outcome.

- **Distinguishing Adaptive from Adverse Responses in the New Testing Paradigm**, Kim Boekelheide, Brown University, Providence, RI
- **Does Exposure Imitate Art: Exposure Science for 21<sup>st</sup> Century Toxicity Testing**, Elaine Cohen Hubal, U.S. EPA, Research Triangle Park, NC
- **Scientific Challenges to the Exposome Approach**, Gerald N. Wogan, Massachusetts Institute of Technology (MIT), Cambridge, MA

## FEATURED SESSIONS

### **NIH Brown Bag Lunch**

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**Tuesday, March 9, 12:00 NOON–1:15 PM**

*Chairperson(s): Joel G. Pounds, Pacific Northwest National Laboratory, Richland, WA*

*Sponsored by: Research Funding Committee*

Join staff from the NIH Center for Scientific Review (CSR) and the NIEHS program officers for lunch and informal discussions about review and grant opportunities at NIEHS. There will be time for questions and discussion, and you can make arrangements to meet these representatives later in the NIH Resource Room. Bag lunches will be available for the first 75 participants.

### **NIH Resource Room**

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**Tuesday, March 9, 9:00 AM–4:30 PM**

**Wednesday, March 10, 9:00 AM–4:30 PM**

*Chairperson(s): Joel G. Pounds, Pacific Northwest National Laboratory, Richland, WA*

*Sponsored by: Research Funding Committee*

NIH program and review staff of the Center for Scientific Review and NIEHS will be available in the NIH Resource Room for individual conversations. Attend the NIH Brown Bag Lunch on Tuesday to make an appointment or check the posted schedule to meet with the NIH staff member who can discuss with you aspects of scientific review or specific grant opportunities. New investigators are especially encouraged to meet with program staff. Handouts will be available.

# 50 Endowment Awardees for SOT's 50<sup>th</sup> Anniversary



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In 2009, there were 22 Endowment Award Recipients.

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- Educational Activities Fund
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## INDIVIDUAL CONTRIBUTIONS

Recognition Level	Contribution in a Fiscal Year
Paracelsus Circle	\$500 or more
Gold	\$250-\$499
Silver	\$100-\$249
Bronze	\$40-\$99



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## SYMPOSIA

### MONDAY

#### Mechanistic Role of Reactive Intermediate Protein Covalent Binding in Target Organ Toxicity: Past, Present, and Future

March 8, 9:15 AM–12:00 NOON

**Chairperson(s):** Jose E. Manautou, University of Connecticut, Storrs, CT, and George B. Corcoran, Wayne State University, Detroit, MI

**Sponsor:**

Mechanisms Specialty Section

**Endorsed by:**

Drug Discovery Toxicology Specialty Section

Molecular Biology Specialty Section

The pioneering work of Brodie and co-workers in the early 1970's demonstrated that protein covalent binding of a reactive metabolite of acetaminophen, N-acetyl-p-benzoquinoneimine, was strongly associated with hepatotoxicity. Over the last three decades, immunological, biochemical, molecular biological, and proteomic approaches have been used to identify specific proteins adducted by reactive electrophilic metabolites. Although the identity of a number of protein targets, and the effects of covalent adduction on protein structure and function are known, the precise role of protein covalent binding in chemical-induced toxicities remains a subject of contention. Indeed, the importance of reactive intermediate protein binding has been challenged by multiple studies employing experimental manipulations that reduce toxicity in the absence of an effect on protein binding. To adequately address these findings state-of-the-knowledge of reactive intermediate protein binding and its toxicological consequences will be presented. The specific topics to be discussed include current views on the importance of protein covalent binding, latest *in vivo* and *in vitro* approaches to study covalent binding, the pharmaceutical industry's perspective on the role of reactive intermediate binding in toxicity and the current safety assessment guidelines for drug candidates with covalent binding liability. Finally, current and future tools and technologies for studying reactive intermediate biology will be highlighted.

- **Reactive Intermediates and Their Interaction with Cellular Proteins: Historical Perspective**, Peter Moldeus, AstraZeneca, Sodertalje, Sweden
- **The Enigma of Reactive Metabolites**, Jack Uetrecht, University of Toronto, Toronto, Ontario, Canada
- **Bioactivation and Covalent Binding Applied in a Drug Research Setting**, R. Scott Obach, Pfizer Inc., Groton, CT
- **Knowns and Known Unknowns in Protein Covalent Binding and Toxicity**, Robert Hanzlik, University of Kansas, Lawrence, KS

#### Neurological Responses After Exposure to Inhaled Metal Particles

Monday, March 8, 9:15 AM–12:00 NOON

**Chairperson(s):** James Antonini, CDC-NIOSH, Morgantown, WV, and Lung-Chi Chen, New York University School of Medicine, Tuxedo Park, NY

**Sponsor:**

Inhalation and Respiratory Specialty Section

**Endorsed by:**

Immunotoxicology Specialty Section

Metals Specialty Section

Most studies examining the toxicology of inhaled metal particles have focused on responses in the target organ, the respiratory system. Less information exists regarding the effects associated with the inhalation of metals in extrapulmonary organs, specifically the central nervous system. There is increasing interest in the health effects of airborne incidental and manufactured metal nanoparticles (particles with one dimension <100 nm) in the environment and workplace. These smaller particles may translocate more easily from deposited sites in the respiratory tract to brain structures after inhalation. Mechanisms of particle translocation include uptake and transport along olfactory and sensory neurons, transcellular transport across respiratory epithelium to the circulation, and lymphatic clearance. Chemical composition, oxidation state, and solubility all may affect metal transport and biological responses to inhaled metals. Both animal and human studies have demonstrated that inhaled metals can translocate to the central nervous system, as well as, induce neurofunctional changes. Alterations in markers of neuroinflammation and cellular toxicity have been observed in specific brain regions using animal models after exposure to a variety of occupational particles and ambient air pollution. Cognitive deficits, brain abnormalities, and neurodevelopmental effects have been associated with exposure to metals in healthy children in Europe and North America. Our panel of experts from the fields of inhalation, neurological, metal, and occupational toxicology will highlight neurological findings of animal and human studies after occupational and environmental lung exposures. All aspects of the topic, such as metal chemistry, inhalation exposure of metal particles, metal translocation from the respiratory system to the central nervous system, and neurological responses, will be examined. An increase in the understanding of metal particle inhalation and neurotoxicity may allow for the development of prevention strategies to better protect susceptible populations in the workplace and environment.

- **Olfactory Transport of Inhaled Particles and Metals**, David Dorman, North Carolina State University, Raleigh, NC
- **Dopaminergic Neurotoxicity Following Exposure to Manganese-Containing Welding Fumes**, Krishnan Sriram, CDC-NIOSH, Morgantown, WV

- **Central Nervous System Effects after Exposures to Nanosized Particles**, Patricia Gillespie, New York University School of Medicine, Tuxedo, NY
- **Neurobehavioral Effects in Adolescents Exposed to Metals**, Roberto Lucchini, University of Brescia, Brescia, Italy
- **Neuroinflammation, Severe Air Pollution, and Children**, Lilian Calderon-Garciduenas, The University of Montana, Instituto Nacional de Pediatría, Mexico City, Mexico

### Ovarian Toxicity: Current Concepts in Toxicology, Pathology, and Mechanisms

Monday, March 8, 9:15 AM–12:00 NOON

**Chairperson(s):** William J. Brock, Brock Scientific Consulting, LLC, Montgomery Village, MD, and Ali Faqi, MPI Research, Mattawan, MI

**Sponsor:**

Reproductive and Developmental Toxicology Specialty Section

**Endorsed by:**

Regulatory and Safety Evaluation Specialty Section  
Reproductive and Developmental Toxicology Specialty Section  
Women in Toxicology Special Interest Group

The ovary is responsible for the differentiation and release of a mature oocyte for fertilization and for synthesizing and secreting hormones that are essential for follicle development, estrous cyclicity, and maintenance of the reproductive tract and its function. Reproductive toxicity studies are important components of the regulatory approval of drugs and chemicals. The identification of ovarian toxicity and determination of its cause requires familiarity with ovarian anatomy, physiology, relationships with other components of the female reproductive tract, and the neuroendocrine regulation of the estrous cycle. A mechanistic approach at the morphologic, biochemical, and molecular level demonstrate that various factors are involved in ovarian toxicity. Therefore, our focus will be on the basic concepts of ovarian anatomy, histopathology, and potential mechanisms of toxicity. We will begin by discussing the importance of assessing fertility that utilizes a combination of methods including evaluation of estrous cycle length, fertility endpoints, and ovarian weights. Recent collaborative work suggests a 2-week rodent study may be sufficient to elucidate the effect of pharmaceuticals on ovarian function and its impact on the revised ICH M3 will be presented. Better interpretation of drug induced ovarian toxicity will be highlighted as fertility effects in rodents, especially when both sexes are treated do not often distinguish between male or female mediated effects. A mechanistic model of ovarian toxicity of 4-vinylcyclohexene

diepoxide provides an understanding of the potential risk of human exposure to environmental ovarian toxicants and greater insight of toxicants on reproductive health in women will also be discussed.

- **Ovarian Toxicity: Anatomy, Pathophysiology, and the Illusion of Simplicity**, Michael Mirsky, Pfizer, Groton, CT
- **Ovarian Toxicity Induced by Pharmaceuticals and Chemicals**, Ali Faqi, MPI Research, Mattawan, MI
- **Ovotoxicity Caused by 4-Vinylcyclohexene Diepoxide: Mechanistic Insights**, Patricia Hoyer, University of Arizona, Tucson, AZ
- **Collaborative Work on Evaluation of Ovarian Toxicity by Repeated-Dose and Fertility Studies in Female Rats**, Atsushi Sambuissu, Daiichi Sankyo Co., Ltd., Fukuroi, Shizuoka, Japan

### Silica and Asbestos Immunotoxicity: Mechanisms to Fibrosis, Autoimmunity, and Modified Tumor Resistance

Monday, March 8, 9:15 AM–12:00 NOON

**Chairperson(s):** Andrij Holian, University of Montana, Missoula, MT, and Takemi Otsuki, Kawasaki Medical School, Kurashiki, Okayama, Japan

**Sponsor:**

Immunotoxicology Specialty Section

**Endorsed by:**

Inhalation and Respiratory Specialty Section  
Mechanisms Specialty Section  
Occupational and Public Health Specialty Section

Effects of silica/asbestos on local and systemic immune system components are very important in the cascade of events in a host that evolve over the course of time from the point of initial exposure to the ultimate onset of lung fibrosis (i.e., silicosis, asbestosis), malignant tumors (i.e., lung cancer, mesothelioma), or autoimmune disorders (e.g., systemic sclerosis, rheumatoid arthritis—Caplan syndrome). In particular, mechanisms used by immune competent cells to process the entrained *silica* or asbestos may affect induction of these pathologies. With regard to asbestos specifically, there may also be a reduction in local/general anti-tumor immune responses that serves to amplify its own carcinogenic potential *in situ*. We will begin with an up-to-date overview of emerging topics in the field of silica/asbestos toxicology that can, in turn, serve as a basis to understand mechanistic interpretations that link development of pneumoconioses to fibrotic diseases, autoimmunity, and cancer. To better understand these issues the latest findings on the roles that particle recognition, inflammasome formation, cytokine-driven inflammation, or immune dysfunction have in eventual induction of fibrosis, altered autoimmunity, and/or modified tumor resistance

## SYMPOSIA

*in silico*/asbestos-exposed hosts. It is anticipated that with an enhanced understanding of the molecular pathological mechanisms underlying the immunotoxicologic effects of silica/asbestos, researchers in many fields (including immunology, immunotoxicology, pulmonary biology and medicine, occupational medicine) will be better able to develop therapeutic tools for the prevention, mitigation, or treatment of debilitating diseases induced by these agents.

- **Tumor Necrosis Factor (TNF) Protects Macrophages from Silica-Induced Apoptosis**, Luis Ortiz, University of Pittsburgh, Pittsburgh, PA
- **Scavenger Receptors and Macrophage Subpopulations in the Development of Silicosis**, Andrij Holian, University of Montana, Missoula, MT
- **Sensing of Cell Stress and Cytoplasmic DNA by the NLRP3 and AIM2 Inflammasomes**, Eicke Latz, University of Massachusetts Medical School, Worcester, MA
- **Asbestos-Induced Autoimmunity: The Possible Role of System XC- In Macrophage Signaling**, Jean Pfau, Idaho State University, Pocatello, ID
- **Effects of Asbestos on T-Lymphocytes and NK Cells in the Alteration of Tumor Immunity**, Takemi Otsuki, Kawasaki Medical School, Kurashiki, Okayama, Japan

producing Tr-1 cells as well as Foxp3 expressing IL-10 T cells, with resulting suppression of the Th2 cytokine signaling pathways and products. Activation, expansion or suppression of CD4(+)CD25(+) T(Regs) *in vivo* by xenobiotics, including drugs, may therefore represent a relevant mechanism underlying immunotoxicity, including allergic asthma, autoimmune disease, and immunosuppression.

- **Introduction to the Role of T(Regs) in Immunity**, Mohamed Oukka, Harvard Institutes of Medicine, Cambridge, MA
- **Role of Immunoregulatory Cells in Chemical and Protein Allergy**, Raymond Pieters, Utrecht University, University of Applied Sciences, Utrecht, Netherlands
- **Induction of AHR-Dependent (T(Regs): A Novel Pathway for TCDD Immunotoxicity**, Nancy Kerkvliet, Oregon State University, Corvallis, OR
- **Safety Assessment of Immunomodulatory Biologics: The Promise and Challenges of Regulatory T Cell Modulation**, Rafael Ponce, Amgen, Seattle, WA

### Faster Science for Better Decisions: Characterizing Environmental Contaminant Risk from High-Throughput Data

Monday, March 8, 1:40 PM–4:25 PM

*Chairperson(s):* David Dix, U.S. EPA, Research Triangle Park, NC, and Russell S. Thomas, The Hamner Institutes for Health Sciences, Research Triangle Park, NC

*Sponsor:*  
Molecular Biology Specialty Section

*Endorsed by:*  
Biological Modeling Specialty Section  
In Vitro and Alternative Methods Specialty Section  
Risk Assessment Specialty Section

Tens of thousands of chemicals and other man-made contaminants exist in our environment, but only a fraction of these have been characterized for their potential risk to humans and there is widespread interest in closing this data gap in order to better manage contaminant risk. Current practice of exposure estimation, toxicity testing, and risk characterization for environmental contaminants is too slow to support high quality science-based regulatory decisions for thousands of contaminants. We will address the various components required for performing rapid, quantitative, and high-quality risk characterizations on thousands of contaminants. Approaches and technologies well suited to address specific

### CELL SIGNALING

#### Alterations in Regulatory T Cells: Novel Pathways to Immunotoxicology

Monday, March 8, 1:40 PM–4:25 PM

*Chairperson(s):* Emanuela Corsini, University of Milan, Milan, Italy, and Dori Germolec, NIEHS, Research Triangle Park, NC

*Sponsor:*  
Immunotoxicology Specialty Section

Regulatory T cells (T(Regs)) have been shown to be critical in the maintenance of immune responses and T cell homeostasis. For example, depletion of CD4(+)CD25(+) T(Regs) from mice resulted in the development of multiorgan autoimmune diseases. CD4(+)CD25(+) T(Regs) and/or IL-10-producing Tr-1 cells are capable of modulating cell signaling thereby suppressing or attenuating Th2 responses to allergens. Moreover, adoptive transfer of CD4(+)CD25(+) T(Regs) from healthy to diseased animals resulted in the prevention or cure of certain autoimmune diseases, and was able to induce transplantation tolerance. Clinical improvement seen after allergen immunotherapy for allergic diseases such as rhinitis and asthma is associated with the induction of IL-10 and TGF-beta

aspects of this process include high-throughput hazard assessments addressing the complex biology associated with environmental toxicity; using reverse dosimetry, pharmacokinetics, and biomonitoring equivalents to account for dose and exposure in evaluating high-throughput screening results; defining and quantifying the uncertainty associated with high-throughput data; and finally, breaking from the current paradigm and using high-throughput chemical risk characterization for screening, prioritization, and other regulatory applications.

- **High-Throughput Screening for Hazard and Risk of Environmental Contaminants**, David Dix, U.S. EPA, Research Triangle Park, NC
- **Defining the Exposure-Dose-Toxicity Relationships in High-Throughput Screens Using *In Vitro* Pharmacokinetic Assays and Reverse Dosimetry**, Russell Thomas, The Hamner Institutes for Health Sciences, Research Triangle Park, NC
- **Consideration of Dose in Evaluation of Toxicity Data: Use of Biomonitoring and Pharmacokinetic Data**, Sean Hays, Summit Toxicology, L.L.P., Lyons, CO
- **Accounting for Uncertainty in the Application of High-Throughput Datasets**, R. Woodrow Setzer, U.S. EPA, Research Triangle Park, NC
- **Putting High-Throughput Chemical Risk Characterization Into Real-World Practice**, Stanley Barone, U.S. EPA, Washington, DC

### Genotoxic Impurities in Drugs and Drug Products: What is the Right Way to Deal with Impurities in R&D Versus Regulatory Guidance?

Monday, March, 1:40 PM–4:25 PM

**Chairperson(s):** Saryu Goel, Supernus Pharmaceuticals Inc, Rockville, MD, and Lutz Mueller, Hoffmann La Roche Inc, Basel, Sweden

**Sponsor:**

Carcinogenesis Specialty Section

**Endorsed by:**

Drug Discovery Toxicology Specialty Section

*In Vitro* and Alternative Methods Specialty Section

Regulatory and Safety Evaluation Specialty Section

The process of chemical drug synthesis necessitates the use of highly reactive starting materials and/or intermediates that have the potential to be present as low level residues within the final drug/

drug product. These materials often have the potential to react with DNA (genotoxic), with adverse health consequences to humans. Additionally, the quality of starting materials used in drug manufacture is not regulated and may inadvertently introduce genotoxic contaminants in final product. To minimize inadvertent health risks, the European Medicines Agency (EMA) issued guidance in June 2006 and subsequently the U.S. Food and Drug Administration (FDA) issued draft guidance in December 2008 mandating pharmaceutical companies to closely monitor, evaluate, and mitigate risks associated with potential genotoxic impurities in drugs and drug products. The new genotoxic impurity guidance's interject stringent requirements to Q3A, B, and C guidances. As with all guidances the burden of developing appropriate strategies to implement such guidances remains with the scientists at pharmaceutical companies with practical considerations. To better understand this new guidance, attendees will be provided with current state of the science and regulations and approaches to identify potential impurities in drug/drug products; an overview of evolving strategies to determine genotoxic potential of identified impurities during product development cycle; and, an opportunity to discuss strategies to mitigate risks using case studies. To gain a balanced perspective, representatives from industry, regulatory agencies, and others from the expert scientific community will address these issues as outlined. To begin, a brief preview of the genotoxic impurities issue in drugs will be provided and followed by presentations on the historical development and implementation of this guidance around the globe. Finally, the panelists will discuss lessons learned from previously approved drugs, a now well known case of contamination of an approved drug, review of SAR software's available to aid initial assessment, and the impact of regulation on the future of the drug development research and development process.

- **Science and Regulation of Genotoxic Impurities in Drug Substances and Products**, David Jacobson-Kram, U.S. FDA, College Park, MD
- **Regulation of Genotoxic Impurities Identified During Clinical Development: A Regulator's Experience**, Roland Froetschl, BfArM, Bonn, Germany
- **Qualification Strategies-Genotoxicity Study Designs and Evaluation of Data for Regulatory Submission: A Case Study**, Gopala Krishna, Enzon Pharmaceuticals, Inc., Piscataway, NJ
- **Moving Genotoxic Compounds from TTC Considerations to a Permitted Daily Intake Calculation—How to Do and What Information Do You Need?** Elmar Gocke, F. Hoffmann La Roche Ltd., Basel, Switzerland
- **The Role of Data Sharing in Developing (Q)SAR Models for the Evaluation of Genotoxic Impurities**, Scott McDonald, Lhasa Ltd., Leeds, West Yorkshire, United Kingdom

## SYMPOSIA

### METABOLIC DISEASE

#### Metabolic Syndrome and Increased Sensitivity to Drug-Induced Liver Injury (DILI): Nonclinical Models and Clinical Implications

Monday, March 8, 1:40 PM–4:25 PM

**Chairperson(s):** John W. Davis II, Pfizer Global Research & Development, Chesterfield, MO, and George B. Corcoran, Wayne State University, Detroit, MI

**Sponsor:**

Drug Discovery Toxicology Specialty Section

**Endorsed by:**

In Vitro and Alternative Methods Specialty Section

Mechanisms Specialty Section

Toxicologic and Exploratory Pathology Specialty Section

Metabolic Syndrome can be described as a constellation of interrelated factors that increase the risk for cardiovascular disease. These factors, which include central obesity/elevated body mass index, hyperinsulinemia and/or insulin resistance (Type-2 diabetes), hyperlipidemia (elevated triacylglycerols +/- low high-density lipoprotein), hypertension and hepatic steatosis (non-alcoholic fatty liver disease/NAFLD) may also place humans at a higher level of risk for developing DILI. It is estimated that 76%–100% of obese individuals (30% of general population) have hepatic steatosis. Although hepatic steatosis is considered to be a reversible form of cell injury, the hepatocytes are more prone to irreversible cell injury and ultimately, cell death. Therefore, hepatic steatosis, and the hyperinsulinemia which is believed to be the catalyst for its development, is not considered a toxic endpoint, but rather, a first hit. Patients with steatosis may also present with an inflammatory response to the injury (non-alcoholic steatohepatitis/NASH), and if allowed to progress unchecked, additional hepatocellular damage/cell loss may outpace the liver's ability to repopulate itself and fibrous connective tissue may be laid down (hepatic fibrosis). Given that subjects with a first hit are presumably allowed to enroll in clinical trials, the need for developing both *in vivo* and *in vitro* models for studying the safety of compounds in an environment relevant to the obese state prior to clinical trials is critical. We will begin by providing an overview of metabolic syndrome, followed by discussions regarding the development of both *in vivo* and *in vitro* testing systems that may help both scientists and clinicians better understand the relevance of this clinical scenario to DILI. Finally, a discussion of the clinical implications of patients with

symptoms of this syndrome will provide the perspective necessary for tackling this significant issue.

- **Metabolic Syndrome and Increased Sensitivity to Drug-Induced Liver Injury (DILI): Historic Perspective**, George Corcoran, Wayne State University, Detroit, MI
- **In Vivo Modeling of Non-Alcoholic Fatty Liver Disease (NAFLD) in Zucker Rats for the Purpose of Predicting Drug-Induced Liver Injury**, Timothy LaBranche, Pfizer Global Research & Development, Chesterfield, MO
- **Development of a Hepatocyte Culture Model of Non-Alcoholic Fatty Liver Disease (NAFLD) for Predicting Drug-Induced Liver Injury (DILI) Using Zucker Rats**, Julio Davila, Pfizer Global Research & Development, Chesterfield, MO
- **ADME in Metabolic Syndrome: Increased Risk of Drug-Induced Toxicity**, Nathan Cherrington, University of Arizona, Tucson, AZ
- **A Prospective Study of Acute Drug-Induced Liver Injury in Patients Suffering from Non-Alcoholic Fatty Liver Disease**, Giovanni Tarantino, University of Naples Federico II Medical School, Naples, Italy

#### Phthalate Reproductive and Developmental Toxicity: Implications for Cumulative Risk Assessment

Monday, March 8, 1:40 PM–4:25 PM

**Chairperson(s):** Susan Makris, U.S. EPA, Washington, DC, and Paul Foster, NIEHS, Research Triangle Park, NC

**Sponsor:**

Reproductive and Developmental Toxicology Specialty Section

**Endorsed by:**

Mixtures Specialty Section

Regulatory and Safety Evaluation Specialty Section

Phthalates, a group of chemicals with many commercial uses (e.g., solvents, additives, plasticizers), have been associated with effects on the male reproductive system of laboratory animals following exposures during development and in adults. Studies have shown widespread human exposure to phthalates, and there are concerns for phthalate-related reproductive and developmental toxicity to humans. Since humans are generally exposed to mixtures of phthalates, rather than to single chemical entities, the importance of conducting a cumulative human health risk assessment has been recognized. We will highlight important reviews relative to the effects of phthalate exposures in laboratory animals and humans,

and the use of biomarkers to quantify human exposure to phthalates, including for susceptible populations. The ground-breaking 2008 National Research Council (NRC) recommendations regarding the assessment of cumulative risk of human exposures to phthalates, and other chemicals, will be discussed. Finally, an overview will be provided that will address the conduct and status of phthalate risk assessment at the U.S. EPA including the consideration of cumulative risk in response to the NRC report.

- **Biomonitoring for Exposure Assessment to Phthalates**, Antonia Calafat, Centers for Disease Control and Prevention, Atlanta, GA
- **Phthalate Exposures and Potential Impact on Human Reproductive Health**, Russ Hauser, Harvard School of Public Health, Boston, MA
- **Effects of Mixtures of Phthalates and Other Toxicants on Sexual Differentiation in Rats: A Risk Framework Based Upon Disruption of Common Developing Systems**, Leon Gray, U.S. EPA, Research Triangle Park, NC
- **The NRC Report on Phthalates and Cumulative Risk Assessment: Focus on Cumulative Risk and Common Adverse Outcomes**, Deborah Cory-Slechta, University of Rochester Medical Center, Rochester, NY
- **U.S. Environmental Protection Agency's (EPA) Cumulative Risk Assessment of the Phthalates**, Jamie Strong, ORD/NCEA, Washington, DC

## TUESDAY

### TRANSLATIONAL TOXICOLOGY

#### **Anti-Drug Antibody-Mediated Toxicity in Nonclinical Toxicity Studies: Impact and Relevance to Human Safety**

**Tuesday, March 9, 9:00 AM–11:45 AM**

*Chairperson(s): Barbara Mounho, Amgen, Inc, Thousand Oaks, CA, and Marque Todd, Pfizer Inc, San Diego, CA*

**Sponsor:**

Regulatory and Safety Evaluation Specialty Section

**Endorsed by:**

Immunotoxicology Specialty Section

Toxicologic and Exploratory Pathology Specialty Section

Immunogenicity is a unique property of biotherapeutics thus it is accepted that the administration of a biotherapeutic to humans or animals has the potential to elicit an antibody response against the drug if the biotherapeutic is perceived as foreign. Most biologics are human-specific proteins or monoclonal antibodies and it is not unexpected that the administration these drugs may result in the production of anti-drug antibodies (ADA). ADA responses are a common challenge during the conduct of nonclinical toxicity studies for biologics, and these responses can potentially affect the outcome and interpretation of a toxicity study. The impact of ADA on toxicology studies can vary having no affect, an alteration of the pharmacokinetic profile resulting in decreased/increased systemic exposure, an abrogation of the pharmacological activity, or neutralization of the biological activity of an endogenous protein that mediates a critical biological function. Another potential consequence of the production of ADA is ADA-drug immune complex formation with deposition in various organs and tissues. These immune complexes can result in significant inflammation and tissue damage with resultant organ dysfunction. A common example of immune complex-mediated toxicity is immune complex-mediated glomerulonephritis. Immune complex formation has also been associated with "anaphylactoid-like" hypersensitivity reactions and serum sickness. In addition, although rare, ADA have been associated with classical IgE-mediated acute hypersensitivity reactions and autoimmunity. These various ADA-associated toxicities can confound the conduct and interpretation of toxicity studies. This session will highlight case studies to explore potential ADA-mediated toxicities including hypersensitivity reactions and immune complex formation/deposition and impact on clinical development/safety will be discussed.

- **Introduction: General Review of the Types of Anti-Drug Antibody-Mediated Responses That Can Occur in Toxicology Studies**, Barbara Mounho, Amgen, Thousand Oaks, CA
- **Mechanisms of Anti-Drug Mediated Toxicities Observed in Nonclinical Toxicology Studies and Impact on Clinical Trial Design and Human Safety**, Andrea Weir, Navigator Services Charles River Laboratories, Reno, NV
- **Atypical Hypersensitivity Reactions Elicited by a mAb Targeting a Human Fc Receptor**, Meghan Flaherty, Genzyme, Framingham, MA
- **Case Study on the Impact of Immunogenicity on Adverse Effects in Toxicology Studies and Consequences for the Clinical Development Program**, Jeanine Bussiere, Amgen Inc., Thousand Oaks, CA
- **Characterization of Potential Immune Complexes Observed in Cynomolgus Monkeys and Relationship to Observed Toxicities of Monoclonal Antibody Drug Candidates**, Marque Todd, Pfizer, Inc., San Diego, CA

## SYMPOSIA

### Bile Salt Transport and Liver Injury

Tuesday, March 9, 9:00 AM–11:45 AM

**Chairperson(s):** Hisham K. Hamadeh, Amgen, Inc., Thousand Oaks, CA, and John W. Davis II, Pfizer Global Research & Development, Chesterfield, MO

**Sponsor:**

Drug Discovery Toxicology Specialty Section

**Endorsed by:**

Mechanisms Specialty Section

Toxicologic and Exploratory Pathology Specialty Section

Bile formation is one of the key functions of mammalian liver. It involves vectorial transport of bile acids and other cholephilic compounds across hepatocytes from the sinusoidal blood into bile. Thereby, bile acids are concentrated more than 500-fold in bile as compared to sinusoidal blood. This concentrative, energy driven process is dependent on the bile salt export pump BSEP. Pathophysiological alterations in BSEP function by inherited mutations, inhibition of function by drugs, or disease-related down regulation may lead to a wide spectrum of mild to severe forms of liver disease. Furthermore, many genetic variants of BSEP are known, some of which potentially render individuals susceptible to certain acquired forms of liver disease. Drug-induced disruption in BSEP-mediated bile acid excretion has been implicated in the development of clinical liver injury for several marketed or withdrawn compounds. Unfortunately, nonclinical species are not reliable predictors of drug-induced liver injury routinely seen in clinical trials and attributed to BSEP inhibition. The challenge for the pharmaceutical industry is to understand the relationship between perturbation of bile acid flow and development of liver injury in humans. Investigations on the potential involvement of disruption of BSEP function in the manifestation of clinical liver injury are very timely in drug development. This session will focus on both nonclinical models and clinical manifestations of perturbation of hepatobiliary transporters in drug-induced liver injury.

- **Bile Salt Export Pump (BSEP) Regulation in Acquired Cholestatic Liver Diseases**, Michael Trauner, Medical University of Graz, Graz, Styria, Austria
- **BSEP Inhibition As a Contributor to Drug-Induced Liver Injury in Humans**, Hisham Hamadeh, Amgen Inc, Thousand Oaks, CA
- **Impaired Hepatic Bile Acid Transport and Drug-Induced Hepatotoxicity: Mechanisms and Model Systems**, Kim Brouwer, University of North Carolina at Chapel Hill, Chapel Hill, NC

- **Inhibition of Hepatobiliary Transporters by a Novel Kinase Inhibitor Contributes to Liver Toxicity in Nonclinical Species**, John Daniels, Pfizer, Inc., Groton, CT
- **Understanding the Cross-Talk Between Bile Salt Export Pump (BSEP) and Other Efflux Transporters in the Manifestation of Drug-Induced Liver Injury**, Jose Manautou, University of Connecticut, Storrs, CT

### CELL SIGNALING

### MAP Kinase Signaling: A Common Target Eliciting Unique Tissue Responses

Tuesday, March 9, 9:00 AM–11:45 AM

**Chairperson(s):** Haitian Lu, Michigan State University, East Lansing MI, and Sarah Campion, Brown University, Providence, RI

**Sponsor:**

Student Advisory Council and Postdoctoral Assembly

**Endorsed by:**

Mechanisms Specialty Section

Molecular Biology Specialty Section

The mitogen-activated protein kinase (MAPK) signal transduction pathways are triggered by a variety of extracellular stimuli. Upon activation, MAPKs phosphorylate downstream targets, transducing these extracellular stimuli into cellular responses. Since their identification, MAPK signal transduction pathways have been found to regulate diverse and critical cellular processes such as gene expression, cell proliferation, differentiation, motility, survival and apoptosis, by altering the phosphorylation status of key regulatory proteins. Numerous studies have revealed that activation of MAPK signaling cascades also occurs in response to a variety of chemical and physical stresses. The activation status of critical MAPKs, including extracellular signal-related kinase (ERK), p38 and c-Jun N-terminal kinase (JNK), may be modulated by exposure to xenobiotics. Ongoing research continues to elucidate the role of MAPK signaling alterations during chemical-induced toxicity. Despite the ubiquitous nature of MAPK signal transduction pathways, the modulation and function of each individual MAPK has been suggested to be highly cell type and context dependent. Therefore, in-depth studies are needed to understand the mechanisms underlying tissue-specific toxicity involving alterations of MAPK signaling pathways. This session will highlight the most recent research progress made to characterize the alterations of MAPK signaling pathways in response to toxicant exposures, and how these alterations contribute to toxicity and/or pathogenesis in different tissues and cell types. The qualitative comparison among

data presented in this session will either suggest a paradigm of

MAPK response to various toxicants, or illustrate the cell type/tissue specific difference in the role of MAPK signaling alterations during toxic responses.

- **Gene Expression Studies Demonstrate That the K-ras/Erk MAP Kinase Signal Transduction Pathway Contributes to the Pathogenesis of Cumene-Induced Lung Tumors**, Stephanie Lahousse, NIEHS, Research Triangle Park, NC
- **Role of MAP Kinases and Phosphatidylinositol-3 Kinase/Akt in Regulating Keratinocyte Antioxidant Expression in Response to 4-Hydroxynonenal, a Lipid Peroxidation End Product**, Ruijin Zheng, Rutgers University, Piscataway, NJ
- **Activation of c-Jun N-Terminal Protein Kinase Is a Common Mechanism Underlying Paraquat- and Rotenone-Induced Dopaminergic Cell Apoptosis**, Heather Klintworth, University of Washington, Seattle, WA
- **Toxicant Mediated Anti-Inflammatory Effects and the Role of MAP Kinase**, Wei Tan, Mississippi State University, Mississippi State, MS
- **Multiparametric Single Cell Analysis of Toll-Like Receptor Activated Kinase Phosphorylation Alteration by 2, 3, 7, 8-Tetrachlorodibenzo-p-dioxin**, Colin North, Michigan State University, East Lansing, MI

### MITOCHONDRIAL BASIS OF DISEASE

#### Molecular Determinants of Mitochondrial Disease

**Tuesday, March 9, 9:00 AM–11:45 AM**

**Chairperson(s):** Kendall B. Wallace, University of Minnesota Medical School, Duluth, MN, and Rick G. Schnellmann, Medical University of South Carolina, Charleston, SC

**Sponsor:**

Mechanisms Specialty Section

**Endorsed by:**

Molecular Biology Specialty Section

Metabolic disorders have gained increasing recognition as important outcomes to many toxicities, the etiologies of which include environmental and occupational exposures, as well as adverse drug reactions. Because of its fundamental role in cell bioenergetics and intermediary metabolism, the mitochondrion is implicated in the pathogenesis of many of these disease states. While the majority of studies have been directed at understanding the acute response

to mitochondrial toxicity, only recently have investigators come to realize the significance of subtle molecular changes that occur in response to mitochondrial injuries that define the metabolically compensated state of the cell. Such changes are essential to the cell being able to withstand low doses and chronic exposures to agents that interfere with mitochondrial function. Collectively, it is these events that define the biological response to sub-lethal exposures and that offer unique opportunities for identifying exposures that may otherwise go unrecognized as a potential metabolic liability for the individual. To adequately address these issues, a general overview of mitochondrial metabolism followed by a series of focused discussions of the molecular changes that define the biological response will be highlighted. The session concludes by leveraging this understanding of the molecular response to the identification of potential biomarkers for reporting subtle, non-clinical cases of mitochondrial toxicity.

- **Mitochondrial Toxicity and the Compensated Metabolic State**, Kendall B. Wallace, University of Minnesota, Duluth, MN
- **Transcriptional Profiling of Mitochondrial Toxicity**, Varsha Desai, NCTR, U.S. FDA, Jefferson, AR
- **Metabonomic and Fluxomic Fingerprinting of Metabolic and Mitochondrial Stress**, Petras Dzeja, Mayo Clinic, Rochester, MN
- **Mitochondrial Biogenesis—Rescue from Metabolic Disorders**, Rick Schnellmann, Medical University of South Carolina, Charleston, SC

#### POPs: What's New and Why Should We Care?

**Tuesday, March 9, 9:00 AM–11:45 AM**

**Chairperson(s):** Arnold Schechter, University of Texas at Dallas, Dallas, TX, and Linda Birnbaum, NIEHS, Research Triangle Park, NC

**Sponsor:**

Occupational and Public Health Specialty Section

The persistent organic pollutants, or POPs, are of increasing concern among the general public, health care providers, and scientists. These synthetic pollutants are characterized as being very persistent in biota and the environment, toxic, undergo trans-boundary migration, and are bioaccumulative. Legacy or classical POPs include PCBs, organochlorine pesticides, and chlorinated dioxins/furans. Presently, considerable interest is focused on newly emerging POPs such as brominated flame retardants (BFRs), including polybrominated diphenyl ethers or PBDEs, and polyfluoroalkyl chemicals (PFCs) which include PFOS and PFOA. Tremendous improvements in analytical chemistry have improved the rates of detection of these compounds in the environment and in humans. Increasing levels of many of the emerging POPs measured in human and environ-

## SYMPOSIA

mental samples has become cause for concern. Questions regarding these compounds include exposure assessment, toxicity, possible substitutes, interactions, metabolism, and regulations. Therefore, this session will provide a current overview from leaders in these important areas and will be followed by detailed recent findings from the scientists actively researching these compounds.

- **Legacy and Emerging POPs**, Linda Birnbaum, National Institute of Environmental Health Sciences, Research Triangle Park, NC
- **Are Concentrations of Polyfluoroalkyl Chemicals in the General U.S. Population Declining? Data from the National Health and Nutrition Examination Surveys (NHANES)**, Antonia Calafat, Centers for Disease Control and Prevention, Atlanta, GA
- **POPs in the U.S. Population and in U.S. Food**, Arnold Schechter, University of Texas School of Public Health, Dallas, TX
- **Levels and Trends of Historic POPs (PCDD/Fs and PCBs) and Newer POPs (PBDEs) in U.S. Meat and Poultry and Implications for Human Exposure**, Janice Huwe, U.S. Department of Agriculture, Fargo, ND
- **Emerging POPs in Edible Tissues: ADME Study of BDE-47 in Chickens**, Heldur Hakk, U.S. Department of Agriculture, Fargo, ND
- **PBDE Exposure from Products to Person**, Tom Webster, Boston University School of Public Health, Boston, MA

### GENE-ENVIRONMENT INTERACTIONS

#### Genetics: The Link between Exposures, Gene x Environment Interaction, and Toxicity

Tuesday, March 9, 1:30 PM–4:15 PM

*Chairperson(s):* John E. French, NIEHS, Research Triangle Park, NC, and David W. Threadgill, North Carolina State University, Raleigh, NC

**Sponsor:**

Carcinogenesis Specialty Section

**Endorsed by:**

Drug Discovery Toxicology Specialty Section  
Risk Assessment Specialty Section  
Toxicologic and Exploratory Pathology Specialty Section

Exposure to drugs and/or environmental toxicants that exceed an individual's capacity or ability to metabolize and eliminate active metabolites may have a significant impact on toxicity and the dysregulation of homeostasis and the development of exposure-related human disease. Significant differences exist between

individuals at the population level based upon their inherited genetic (single nucleotide polymorphisms and copy number variants) and/or epigenetic differences in environmentally responsive genic and non-genic sequences and pathways. To better understand these differences, will be begin with an overview of the current research, new strategies, and models for pharmacology and toxicology using genetically defined and/or genetically altered inbred mouse models. These genetically diverse cell or tissue based models will be used to highlight acute or chronic human disease in large genetically-diverse human populations. Together, the speakers will provide both insight and new hypotheses for the role of individual (heritable SNPs, CNV, methylated sequences, RNAi, etc.) and environmental factors that affect the development of major polygenic human diseases including asthma, drug induced liver injury, respiratory, cancer, and cardiovascular diseases.

- **The NTP Host Susceptibility Initiative: A New Strategy and Paradigm for Hazard Identification and Risk Characterization**, John E. French, NIEHS, Research Triangle Park, NC
- **Affect of Genetic Variation on Drug Metabolism and Toxicities in Inbred Mouse Strains**, Matthew Pletcher, Pfizer Global Research & Development, Groton, CT
- **Genetic Variation in Mice: Modeling Disease, Pharmacogenetics, and Basic Biology**, Tim Wiltshire, University of North Carolina at Chapel Hill, Chapel Hill, NC
- **Mouse Model of the Human Opulation (MMHP) for Systems Biology and Toxicology**, David Threadgill, North Carolina State University, Raleigh, NC

### CELL SIGNALING

#### It's Not Your Father's Aryl Hydrocarbon Receptor: New Biological Roles for a Misunderstood Receptor

Tuesday, March 9, 1:30 PM–4:15 PM

*Chairperson(s):* Russell S. Thomas, The Hamner Institutes for Health Sciences, Research Triangle Park, NC, and J. Craig Rowlands, The Dow Chemical Company, Midland, MI

**Sponsor:**

Molecular Biology Specialty Section

**Endorsed by:**

Mechanisms Specialty Section

The aryl hydrocarbon receptor (AhR) has been traditionally associated with regulating responses to a variety of environmental chemicals. However, the AhR has been highly conserved throughout evolution and there is a growing body of evidence that the receptor

modulates critical aspects of cellular function that are independent of its response to xenobiotics. The modulation of cell responses are highly context specific resulting in growth promotion in certain cell types and growth arrest and differentiation in other cells. Endogenous chemicals have been identified in animals with AhR agonist activity indicating they are endogenous ligands for this receptor. These results suggest that the AhR should be viewed in the same light as other cellular receptors (e.g., ER, AR, and PPAR) with a physiological role that can be disrupted by xenobiotic chemicals rather than a receptor that evolved primarily as a xenobiotic sensor. Therefore, we will address new research on the biological roles for the AhR in cell growth, death, and differentiation and the potential human health risks and therapeutic benefits associated with exposure to exogenous AhR ligands. Molecular aspects of AhR signaling are conserved across other nuclear receptor pathways and therefore the issues discussed may have relevance to the modes-of-action for xenobiotics mediated by other nuclear receptors. This session will be of interest to investigators and regulators wanting to understand the latest research on the underlying biological roles for this remarkable pleiotropic receptor.

- **The Role of the Aryl Hydrocarbon Receptor in Mammary Differentiation and Disease**, Julie Hall, The Hamner Institutes for Health Sciences, Research Triangle Park, NC
- **Direct Regulation of Aryl Hydrocarbon Receptor Function by Selective Estrogen Receptor Modulators (SERMs)**, Donald McDonnell, Duke University, Durham, NC
- **Functional Cross-Talk Between AHR and WNT Signaling: Opportunities to Modulate Epithelial and Mesenchymal Interactions**, Robert Tanguay, Oregon State University, Corvallis, OR
- **The Aryl Hydrocarbon Receptor Has a Novel Role in the Maintenance and Function of Hematopoietic Stem Cells and Possibly other Stem Cell Populations**, Thomas Gasiewicz, University of Rochester, Rochester, NY
- **Development of Selective AhR Modulators (SAhRMs) for Treatment of Disease**, Stephen Safe, Texas A&M University, College Station, TX

### Mechanisms of Chemical-Induced Liver Cancer: Putting the Pieces Together

Tuesday, March 9, 1:30 PM–4:15 PM

**Chairperson(s):** Chris Corton, U.S. EPA, Research Triangle Park, NC, and Jay Goodman, Michigan State University, East Lansing, MI

**Sponsor:**

Carcinogenesis Specialty Section

**Endorsed by:**

Mechanisms Specialty Section

Molecular Biology Specialty Section

A large number of chemicals, including non-genotoxic compounds, increase the incidence of liver tumors in mice and rats. Key events in liver tumor formation include perturbation of gene expression homeostasis, increases in oxidative stress, and activation of cell growth pathways. The mechanisms that underlie these events may include activation of pathways under control of nuclear receptors. Although hepatocellular carcinoma (HCC) in humans is the fifth most common neoplasm worldwide and the third most common cause of cancer-related death, the human relevance of the rodent liver tumor response remains controversial. Differences in nuclear receptor levels and down-stream responses between rodents and humans might contribute to a species difference in sensitivity. A number of new techniques that interrogate changes in the epigenome have been applied to rodent liver carcinogenesis and are illuminating the molecular events in the “black box” between nuclear receptor activation and liver tumor induction. These techniques can assess changes in the methylation status of the DNA, gene expression, alternative splicing, and miRNA levels. Information from these data streams can be integrated into mathematical models of the structure and function of the liver to identify genetic networks required for liver tumor induction and allow prediction of the ability of chemicals to induce liver cancer through different modes of action. Our panel of experts will discuss how the assessment of genetic and genomic changes have increased our understanding of the key events and human relevance of rodent liver tumors. We will conclude with a discussion of computational strategies to integrate different types of data in biologically-relevant models of hepatic functions that can be used to predict liver cancer after chemical exposure. This session will be of interest to those in systems biology, liver toxicity, nuclear receptors, and the impact of modulation of stress pathways on chemical toxicity.

- **Identification of Genetic Determinants of Susceptibility to Liver Tumor Induction**, Norman Drinkwater, University of Wisconsin, Madison, WI
- **Identification of Genes Involved in Phenobarbital-Induced Carcinogenesis: Emphasis on Altered DNA Methylation, Expression, and Pathways**, Jay Goodman, Michigan State University, East Lansing, MI
- **The Other World of the Transcriptome: Role of Nuclear Receptors in Chemical Induced Effects on Alternative Splicing in the Liver**, Chris Corton, U.S. EPA, Research Triangle Park, NC
- **Impact of Altered MicroRNA Expression in Liver Carcinogenesis**, Igor Pogribny, National Center for Toxicological Research, Jefferson, AR
- **Predictive Models of Liver Cancer**, Imran Shah, U.S. EPA, Research Triangle Park, NC

## SYMPOSIA

### New Strategies for the Use of Genetic Toxicology Data in Human Risk Assessment

Tuesday, March 9, 1:30 PM–4:15 PM

**Chairperson(s):** B. Bhaskar Gollapudi, Dow Chemical Company, Midland, MI, and James Kim, ILSI Health and Environmental Sciences Institute, Washington, DC

**Sponsor:**

Carcinogenesis Specialty Section

**Endorsed by:**

Regulatory and Safety Evaluation Specialty Section  
Risk Assessment Specialty Section

The field of genetic toxicology is in need of new approaches in experimental design and data interpretation to improve the scientific basis of its utility for the purpose of accurate human risk assessment. Furthermore, there is an urgent need for a framework for the integration of the *in vitro* testing results into a risk-based assessment of the effects of chemical exposures to human health. A tripartite initiative under the auspices of the ILSI Health and Environmental Institute involving scientists from regulatory, academic, and industrial sectors was initiated to address and make recommendations on these issues. The scientists involved in this initiative were charged with systematically examining the state of the science in genotoxicity assessment, assessing the utility of new and emerging genetic toxicology tools, and addressing a shift away from qualitative genotox assessment to a quantitative approach. The recommendations emerging from this initiative as well as those advanced by others are expected to advance the field of genetic toxicology into the 21<sup>st</sup> century.

- **Introduction to the HESI IVGT Project Committee**, James Kim, ILSI Health and Environmental Sciences Institute, Washington, DC
- **Current Strategies in Assessing Genotoxic Risk**, Kerry Dearfield, U.S. Department of Agriculture, Washington, DC
- **Need for a New Approach to Genetic Toxicity Assessment: Lessons Learned and New Opportunities**, James MacGregor, Toxicology Consulting Services, Arnold, MD
- **Approaches to Follow-up on Positive Results in Genetic Toxicology Tests in the Context of Human Risk Assessment**, Veronique Thybaud, sanofi-aventis, Paris, France
- **New Technologies to Predict Genotoxic Risk in Humans**, David Jacobson-Kram, U.S. FDA, College Park, MD
- **Beyond Positive or Negative: A Quantitative Approach for Interpreting Genotoxicity Data**, B. Bhaskar Gollapudi, Dow Chemical Company, Midland, MI
- **Optimal Design for *In Vivo* Mutation Studies to Inform Cancer Mode-of-Action Assessment**, Martha Moore, U.S. FDA, Jefferson, AR

### METABOLIC DISEASE

### Recent Knowledge of Critical Regulators of Lipid Homeostasis in Metabolic Disease

Tuesday, March 9, 1:30 PM–4:15 PM

**Chairperson(s):** Shashi Ramaiah, Pfizer Global Research and Development, St. Louis, MO, and Mayurranjan Mitra, Washington University School of Medicine, Monroe, LA

**Sponsor:**

Mechanisms Specialty Section

**Endorsed by:**

Comparative and Veterinary Specialty Section  
Molecular Biology Specialty Section

Modifications in human lifestyle and nutritional status over the recent decades have led to an increase in the incidence of obesity and insulin resistance, leading to metabolic syndrome. Metabolic syndrome is a culmination of risk factors for diseases such as diabetes, hepatic steatosis, cardiovascular disorders, stroke, and drug-induced toxicities. Insulin resistance, a hallmark of metabolic syndrome, is thought to play an important role in the development of hyperglycemia, hyperlipidemia, and lipotoxicity. Metabolic abnormalities such as insulin resistance, lipotoxicity, and hypertriglyceridemia are not only associated with lifestyle changes but also by consumption of xenobiotics such as ethanol. The accumulation of highly toxic lipid metabolites has been shown to contribute towards ER stress and organ toxicities. In the past, various strategies for increasing tissue glucose uptake and metabolism and fatty acid oxidation have been devised for normalizing the elevated blood glucose and lipid levels thereby improving insulin sensitivity and the metabolic syndrome. There is a greater need for precise understanding of the molecular basis of metabolic syndrome so that effective therapies can be developed. Cell surface receptors were shown to transport glucose and fatty acids into the tissue thereby lower blood glucose and fatty acid levels. The nuclear hormone receptor PPAR $\alpha$  and its binding partner PPAR $\gamma$  coactivator-1 (PGC-1) were shown to induce the cellular fatty acid oxidation machinery thereby prevent accumulation of excess fat in the body. Recently, significant progress has been made in identifying novel molecules and their unique mechanisms that play a critical role in regulating and maintaining lipid homeostasis. Novel molecules such as lipin 1, PPAR $\gamma$  binding protein (PBP), SIRT 1, and PAS kinase have been recently added to the list of critical regulators of lipid homeostasis. This session will introduce the latest advancements in the field of metabolic research and discuss the functions of these novel mediators of lipid homeostasis.

- **PAS Kinase and the Control of Lipid Metabolism**, Jared Rutter, University of Utah School of Medicine, Salt Lake City, UT

- **The Role of SIRT1 in Alcoholic Fatty Liver**, Min You, University of South Florida, Tampa, FL
- **Role of PPAR Binding Protein (PBP) in Cardiac Mitochondrial Biology**, Philip Barger, Washington University School of Medicine, St. Louis, MO
- **Role of Lipin 1 Protein in Lipid Homeostasis**, Mayurranjan Mitra, Washington University School of Medicine, St. Louis, MO

### METABOLIC DISEASE

#### Zinc, Copper, and Their Metabolic Effect: Myths and Musts

Tuesday, March 9, 1:30 PM–4:15 PM

**Chairperson(s):** Lu Cai, University of Louisville, Louisville, KY, and Karl T. Weber, University of Tennessee Health Science Center, Memphis, TN

**Sponsor:**

Metals Specialty Section

**Endorsed by:**

Food Safety Specialty Section

Mechanisms Specialty Section

Molecular Biology Specialty Section

Metabolic syndromes are featured by a group of metabolic risk factors in one person, including abdominal obesity, atherogenic dyslipidemia, elevated blood pressure, insulin resistance, and proinflammatory state. While the exact mechanism remains elusive, an altered homeostasis of essential metals such as zinc (Zn) and copper (Cu) is known to contribute to the etiology of metabolic syndromes. Zn and Cu are the metals indispensable for the structure and activity of many enzymes and proteins; their deficiency and overload have been associated to numerous patho-physiological changes, including insulin resistance syndrome. Zn deficiency is closely related to the metabolic syndrome, cardiovascular diseases, and insulin resistance, while increased systemic Cu levels may be related to the risk of cardiovascular disease, brain diseases, and other metabolic syndromes. The current understanding of the roles of Zn and Cu homeostasis in the insulin signaling, cardiovascular inflammation, diabetes, and diabetic complications will be explored. A brief overview highlighting the association of Zn and Cu with inflammation, diabetes, and diabetic complications will begin this session. Important components of this exploration will cover how Zn sensitizes insulin function and protects endothelial cells from oxidative stress. The effect of Zn dyshomeostasis on cardiac mitochondrial dysfunction, oxidative stress, and pathogenic remodeling will then be examined. The dysregulation of Cu homeostasis in brain and cerebrospinal fluid as the consequence of iron (Fe) meta-

bolic disorders will also be discussed. Given that metallothionein (MT) plays a critical role in Zn homeostasis, therefore, how Zn *via* MT's gene upregulation was used to prevent diabetes and diabetic complications will be addressed in the final presentation.

- **Role of Zinc in Endothelial Cell Function: Implications in Atherosclerosis**, Bernhard Hennig, University of Kentucky, Lexington, KY
- **Coupled Calcium and Zinc Dyshomeostasis in Cardiac Myocytes and Mitochondria During Chronic Aldosteronism**, Karl T. Weber, University of Tennessee Health Science Center, Memphis, TN
- **Regulation of Copper Homeostasis in Brain and Cerebrospinal Fluid: Effect of Iron Deficiency and Overload**, Wei Zheng, Purdue University, West Lafayette, IN
- **Modulation of the Metabolic Effects of GSK-3 Isoforms by Zn and/or Cu Implications for Diabetes**, Thomas Force, Thomas Jefferson University, Philadelphia, PA
- **Potential Effects of Zinc on Diabetic Complications: Role of Metallothionein**, Lu Cai, University of Louisville, Louisville, KY

## WEDNESDAY

### Gender Divergent Xenobiotic Responses

Wednesday, March 10, 9:00 AM–11:45 AM

**Chairperson(s):** Kathleen Gabrielson, Johns Hopkins Medical Institutions, Baltimore, MD, and DeLisa Fairweather, The Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD

**Sponsor:**

Comparative and Veterinary Specialty Section

**Endorsed by:**

Immunotoxicology Specialty Section

Metals Specialty Section

Molecular Biology Specialty Section

Differences in exposure, anatomy, physiology, biochemistry, and behavior between males and females dramatically affect the biological response; yet gender differences have not received adequate attention in toxicology. This session will highlight cutting edge discoveries within gender divergent biology that have a major impact on the toxicological response. Both mechanisms and relevant examples of gender-dependent toxicities will be provided. To fully understand these issues, an overview will be provided that will allow participants to review recent findings on the divergence of gene expression between males and females in response to toxic

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insults influenced by gender specific drug elimination and cellular efflux. Elegant studies that demonstrate sex and growth hormonal dependence reveal the importance of these factors in toxic and therapeutic responses. Further exploration will allow us to focus on the mechanisms behind gender differences in cation transporter expression in the GI tract and kidney. Interplay between gender and the underlying nutritional status of zinc, iron, and calcium, as well as the influence of transporter expression and toxicity. Essential element deficiencies result in gender specific up-regulation of transporters, thereby facilitating the transport of toxic metals such as lead and cadmium. Adequate focus will be provided on the immune system and how steroid hormones influence immunomodulatory proteins of the toll-like receptor family. These findings have relevance not only to the toxic response, but also to the pathogenesis and severity of infectious disease influenced by concurrent toxin exposure. Finally, gender divergence in gene expression in the heart during cancer therapy will be addressed and how it affects signal transduction pathways controlling mitochondrial function and protein translation differently in males and females which will explain why females are better protected from the cardiotoxic effects of the chemotherapy.

- **Mechanism of Gender-Divergent Expression of Phase II Enzymes and Multi-Drug Resistance (MDR) Transporters: Implications to Toxicology**, Curtis Klaassen, University of Kansas Medical Center, Kansas City, KS
- **Sex and Transporters in the GI Tract and Kidney**, Michael Gochfeld, Robert Wood Johnson Medical School, Piscataway, NJ
- **Sex Differences, Cigarette Smoke, and Inflammatory Heart Disease: Role of Alternatively Activated Macrophages**, DeLisa Fairweather, The Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD
- **Mechanisms of Gender Differences in Chemotherapy Induced Cardiac Toxicity**, Kathleen Gabrielson, Johns Hopkins Medical Institutions, Baltimore, MD

## MITOCHONDRIAL BASIS OF DISEASE

### Mitochondrial Toxicity in Disease and Death

Wednesday, March 10, 9:00 AM–11:45 AM

*Chairperson(s): Boris Zhivotovsky, Karolinska Institutet, Stockholm, Sweden, and Dean P. Jones, Emory University, Atlanta, GA*

*Sponsor:*

**Mechanisms Specialty Section**

*Endorsed by:*

**Drug Discovery Toxicology Specialty Section**

**Molecular Biology Specialty Section**

Mitochondria play a central role in cell life and death and are known to be important in a wide range of diseases. Many attempts were undertaken to develop drugs that target mitochondria and suggested to be used to treat mitochondrial dysfunctions associated with various disease. However, it is known that such drugs induce mitochondrial toxicity. At the same time mitochondria are central to many chronic toxicities the details of the mechanisms remain unknown and effective preventive strategies have not been established. Therefore our approach to explore these issues will be to delineate therapy-related toxicities, which are essential to understanding the mechanisms behind the role of mitochondria in disease and death. To achieve this goal, an interaction between both fundamental and applied research is important. Our panel of experts represent different areas of toxicology, from academia to and industry, which will provide attendees a varying perspectives on this important issue which will lend itself to broad and deep discussions relative to where the field of toxicology is headed.

- **Mitochondria As a Target for Chemotherapy**, Boris Zhivotovsky, Karolinska Institutet, Stockholm, Sweden
- **Mitochondrial Redox Proteome: Susceptible Site of Chronic Toxicity**, Dean P. Jones, Emory University, Atlanta, GA
- **Iron, Lysosomal Fragility, and Mitochondrial Dysfunction**, John Lemasters, Medical University of South Carolina, Charleston, SC
- **Mitochondrial Oxidative Stress: Implications for Cell Death**, Sten Orrenius, Karolinska Institutet, Stockholm, Sweden
- **Methods to Detect Mitochondrial Toxicity Caused by Anti-Retroviral and Antibacterial Therapy**, Sashi Nadanaciva, Pfizer Research and Development, Groton, CT

### The Fetal Basis of Adult Disease

Wednesday, March 10, 9:00 AM–11:45 AM

**Chairperson(s):** Don A. Delker, University of Utah School of Medicine, Salt Lake City, UT, and Erik J. Tokar, NCI at NIEHS, Research Triangle Park, NC

**Sponsor:**

Metals Specialty Section

**Endorsed by:**

In Vitro and Alternative Methods Specialty Section

Mechanisms Specialty Section

Molecular Biology Specialty Section

Recent studies provide convincing evidence for the fetal basis of adult disease. Gestation is a period of high sensitivity to toxicants, with a variety of maternal exposures leading to consequent diseases such as cancer, atherosclerosis, hypertension, obesity, and diabetes in the offspring often much later in adulthood. There is strong suspicion that embryonic/fetal stem cells (SCs) are key targets in the transplacental chemical attack that is the etiological basis of these diseases, in part because of their relative abundance and their role in organogenesis and differentiation. The long latency period between *in utero* exposure and development of adulthood diseases is consistent with lesions in conditionally immortal SC populations with their limitless capacity for self-renewal. Beginning with the theory of the fetal basis of adult disease (the Barker Hypothesis) and how it relates to alterations in SCs and SC numbers, the symposium will then describe the impact of transplacental arsenic exposure on skin SC dynamics, illustrating how early life arsenic exposure plays a role in skin cancer much later in life. The transplacental arsenic-induced changes in liver programming associated with accelerated atherosclerosis in adulthood, and the effects of maternal lead (Pb) exposure on the hypothalamic-pituitary-adrenal axis and development of Pb-associated adult diseases will then be covered. Next, *in vitro* SC model systems demonstrating arsenic transforms SCs into a pluripotent cancer SC (CSC) phenotype and how this phenomenon may be specific to arsenic as opposed to other carcinogenic metals (e.g. cadmium) are described. Concluding this session, our panel of experts will discuss genomic profiling of SC signaling pathways in adult animals following environmental chemical exposure and how the activation of these pathways *in vivo* may predict tumor outcome. This session will be of interest to those researching developmental exposure to metals and other toxicants, metal toxicology, molecular mechanisms involved the regulation of SCs, and the initiation of CSCs, as well as those interested in the fetal basis of adult disease.

- **Modulation of Human Stem Cells During *In Utero* Exposures to Toxicants: A Mechanistic Explanation to the Barker Hypothesis**, James Trosko, Michigan State University, East Lansing, MI

- **Fetal Arsenic Exposure Enhances Skin Cancer in Adulthood with Contemporaneous Distortion of Tumor Stem Cell Dynamics**, Michael Waalkes, NCI at NIEHS, Research Triangle Park, NC
- **Transplacental Arsenic Exposure Induced Changes in Liver Programming Associated with Accelerated Atherosclerosis**, J. Christopher States, University of Louisville, Louisville, KY
- **Permanent Effects of Maternal Lead (Pb) Exposure on the HPA Axis: A Biological Unifying Mechanism for Pb-Associated Adult Diseases**, Deborah Cory-Slechta, University of Rochester School of Medicine, Rochester, NY
- **Arsenic-Induced Stem Cell Initiation Produces a Cancer Stem Cell Phenotype During Malignant Transformation**, Erik J. Tokar, NCI at NIEHS, Research Triangle Park, NC
- **Epigenetic Signaling As a Target for Chemical Toxicity and Carcinogenesis**, Don A. Delker, University of Utah School of Medicine, Salt Lake City, UT

### Aging as a Determinant of Xenobiotic Toxicity

Wednesday, March 10, 1:30 PM–4:15 PM

**Chairperson(s):** Chris Corton, U.S. EPA, Research Triangle Park, NC, and Harihara Mehendale, University of Louisiana at Monroe, Monroe, LA

**Sponsor:**

Mechanisms Specialty Section

**Endorsed by:**

Carcinogenesis Specialty Section

Molecular Biology Specialty Section

One of the greatest achievements of the last eight decades is better health care which has led to a burgeoning aging population. By 2030, the number of individuals older than 65 will more than double to 72 million and one of every five Americans will be older than 65. The rapid growth in the number of older Americans has many implications for public health including the need to better understand the risks posed to older adults by environmental exposures to chemicals. The capacity to appropriately respond to toxicant exposure declines with normal aging and may be exacerbated in individuals with pre-existing conditions. This decline can result in compromised pharmacokinetic and pharmacodynamic responses to environmental exposures encountered in daily activities. Thus our objectives will be to highlight recent studies of altered sensitivities to xenobiotic exposure by aging in a number of tissues and to bring forward substantial new information on what is known about their mechanisms. We will include an overview of molecular pathways that are altered in aging including those involved in xenobiotic

## SYMPOSIA

metabolism that will include important examples of how aging alters chemical sensitivity in the liver, lung, and brain. This session will be of interest to those studying the impact of modulation of stress pathways on chemical toxicity and risk assessors interested in incorporating data on sensitive subpopulations.

- **Evidence for Genetic Pathways in Humans Similar to Those That Regulate Aging in Model Organisms**, Russell Bell, Prolexys Pharmaceuticals, Salt Lake City, UT
- **Divergent Gender-Dependent Genetic Networks in the Aging Mammalian Liver: Alteration of Xenobiotic Metabolism Genes**, Chris Corton, U.S. EPA, Research Triangle Park, NC
- **Aging Rats are Protected from Chlordecone Amplified Progression of Carbon Tetrachloride Hepatotoxicity**, Harihara Mehendale, University of Louisiana at Monroe, Monroe, LA
- **Comparative Effects of the Organophosphorus Insecticides Chlorpyrifos and Parathion in Adult and Aging Rats**, Carey Pope, Oklahoma State University, Stillwater, OK
- **Pulmonary Effects of Inhaled Air Pollutants in Elderly Mice, Role of Oxidative Stress, and Inflammatory Cytokines**, Debra Laskin, Rutgers University, Piscataway, NJ

### CELL SIGNALING

#### TRPing the Sensor: The Role of TRP Channel Signaling in Cardiopulmonary Toxicity

Wednesday, March 10, 1:30 PM–4:15 PM

*Chairperson(s):* Sven-Eric Jordt, Yale University, New Haven, CT, and Daniel J. Conklin, University of Louisville, Louisville, KY

**Sponsor:**

Inhalation and Respiratory Specialty Section

**Endorsed by:**

Mechanisms Specialty Section

Occupational and Public Health Specialty Section

Transient receptor potential (TRP) ion channels comprise a large family of cationic (calcium) conducting channels (TRP A, C, M, V) responsive to environmental and endogenous stimuli. TRP channels are activated by noxious airborne compounds such as tear gas and reactive aldehydes, as well as endogenously generated unsaturated aldehydes associated with tissue injury and inflammation, including  $\alpha$ ,  $\beta$ -unsaturated aldehydes like acrolein and 4-hydroxynonenal. The TRP receptor channels transduce a variety of chemical signals *via* neural afferents (C-fibers) into sensory signals, including pain (nociceptive) responses. Increasingly, these channels are being found in other cell types, including airway epithelial and cardiovascular endothelium. The TRPA1 and TRPV1 (vanilloid- or capsaicin-sensitive) channels are implicated in

pulmonary inflammation and asthma associated with exposure to noxious stimuli including chlorine, tear gases, isocyanates, tobacco smoke, and aldehydes. TRP channel activation triggers the release of neuropeptides such as substance P and CGRP, which stimulate local inflammatory responses, vasodilation, and edema. Recent work extends these findings to include complex cardiovascular responses, such as circulatory collapse and hypotension. These responses are triggered by specific TRP agonists, as well as by unsaturated aldehydes, which implicate a role of TRP channels located in cardiovascular cells or sensory afferents in these tissues in these effects. This session will explore several pathophysiological models that implicate various TRP channels in deleterious effects of noxious stimuli in cardiopulmonary toxicity and probe the mechanisms that connect channel activation/inhibition in these responses to exogenous and endogenous stimuli. The relevance of TRP signaling to human health and the potential for therapeutic targeting will be addressed.

- **TRPA1 Mediates the Noxious Effects of Tear Gases and Industrial Isocyanates**, Sven-Eric Jordt, Yale University, New Haven, CT
- **Tobacco Smoke, TRPA1, and Endothelium Dysfunction: Role of Acrolein**, Daniel J. Conklin, University of Louisville, Louisville, KY
- **TRP Receptors and Sensory Irritation**, John Morris, University of Connecticut, Storrs, CT
- **Role of TRPA1 in Airway Inflammation and Hyper-reactivity**, Ana Caceres, Yale University, New Haven, CT
- **Role of TRPV1 in Airway Hypersensitivity Induced by Mucosal Inflammation**, Lu-Yuan Lee, University of Kentucky, Louisville, KY
- **The Endothelial TrpV4 Channel: Pharmacology, Toxicology, and Therapeutic Target**, Robert Willette, GlaxoSmithKline Pharmaceuticals, Upper Merion, PA

### Zebrafish Models for Developmental Neurobehavioral Toxicology

Wednesday, March 10, 1:30 PM–4:15 PM

*Chairperson(s):* Edward D. Levin, Duke University Medical Center, Durham, NC, and Stephanie Padilla, U.S. EPA, Durham, NC

*Sponsor:*

Neurotoxicology Specialty Section

*Endorsed by:*

*In Vitro* and Alternative Methods Specialty Section

Reproductive and Developmental Toxicology Specialty Section

With the emerging techniques for toxicology in the 21<sup>st</sup> century, zebrafish can provide a key mechanistic model for developmental neurobehavioral toxicology because they have already become the predominant aquatic model for the study of molecular aspects of development in general and neurodevelopment in particular. Developmental neurobehavioral toxicology can benefit enormously from using the zebrafish model for higher throughput screening as well as to identify critical molecular and cellular interaction mechanisms of functional behavioral impairment. To use zebrafish for neurobehavioral toxicity research, we must develop sensitive, efficient, valid, and reliable behavioral test methods. Recently, a variety of researchers have been doing just that. In this symposium several investigators representing the field will describe how they have developed neurobehavioral tests for zebrafish and used them for the assessment of the adverse effects of environmental toxicants, including pesticides and metals. The advantages of computerized video tracking systems for behavioral analysis in zebrafish will be assessed. The complementary relationships of developmental neurobehavioral toxicology studies using zebrafish and classic rodent models will be discussed. Each paradigm has its own set of advantages and limitations. In concert, complementary fish and rodent models as well other developmental model systems can answer a broad array of pressing questions in neurobehavioral toxicology. The use of these neurobehavioral behavioral paradigms for both screening of functional effects and mechanistic studies of the neurotoxic events underlying the behavioral impairments will be presented. Future directions for zebrafish models for developmental neurobehavioral toxicology will be discussed.

- **A Zebrafish Model for What Ails, and Possibly Cures, Us: A Behavioral Perspective of Developmental Lead and Mercury Toxicity**, Daniel Weber, University of Wisconsin Milwaukee, Milwaukee, WI
- **The Zebrafish As a Model for Developmental Exposure to Pyrethroid Pesticides**, Lori White, Rutgers University, New Brunswick, NJ
- **Persisting Effects of Early Developmental OP Pesticide Exposure on Cognitive and Sensorimotor Function**, Edward D. Levin, Duke University Medical Center, Durham, NC
- **The Benefits of Zebrafish As a Complementary Model for Studying the Molecular Bases of Developmental Neurotoxicology**, Elwood Linney, Duke University Medical Center, Durham, NC
- **Behavioral Screens for Detecting Developmental Neurotoxicity in Larval Zebrafish**, Stephanie Padilla, U.S. EPA, Research Triangle Park, NC

## WORKSHOPS

### MONDAY

#### TRANSLATIONAL TOXICOLOGY

##### Does Background Disease Lead to Low Dose Linearity?

Monday, March 8, 9:15 AM–12:00 NOON

**Chairperson(s):** Lorenz Rhomberg, Gradient Corporation, Cambridge, MA, and Rory Conolly, U.S. EPA, Research Triangle Park, NC

**Sponsor:**

Risk Assessment Specialty Section

**Endorsed by:**

Biological Modeling Specialty Section

The additivity-to-background argument was first applied to genotoxic carcinogens by Crump *et al.* (*Cancer Res* 36:2973, 1976), but application to noncancer toxicity has recently been advocated in a report by White *et al.* (2009, *Environ Health Perspect* 117:283) and by the National Research Council (*Science and Decisions: Advancing Risk Assessment*, NRC Press 2009). Adoption of this approach would suggest the lack of thresholds for noncancer toxicity, in contrast to longstanding practice and established tenets. Proponents of additivity-to-background for such endpoints argue that heterogeneity in the human population leads some individuals to be at the margins of acceptable levels of such underlying physiological variables, and that the background rates of disease are explicable, at least in part, by individuals who, even without chemical stressors, have values of the underlying variables that are insufficient to maintain health. The emerging application of systems biology to characterizing normal control processes and their alteration by chemical stressors may provide an avenue for investigating these hypotheses. A deeper discussion of the issues and identification of research approaches to help resolve them is warranted. Our panel of experts, each with their own perspectives, will begin the dialogue aimed at producing theoretical arguments that additivity produces low dose linearity to reflect our understanding of the relevant biology on background disease, population heterogeneity, and the incremental effects of toxicants. We will examine prospects for new research to illuminate and perhaps resolve, what, are at times, contentious issues with large impacts on the use of toxicological data in regulation and public health protection.

- **The Additivity to Background Argument for Low Dose Linearity: Is It Viable?** Kenny Crump, Louisiana Tech University, Ruston, LA
- **Linearity and Non-Linearity in Individual and Population Dose-Response Relationships**, Lauren Zeise, California EPA, Oakland, CA

- **Empirical Approaches and Key Events Analysis to Understand the Relevance of Background in Dose-Response**, George Daston, Procter & Gamble, Cincinnati, OH
- **Noncancer Toxicity Potential at Low Doses: Background Processes Considered Statistically and Biologically**, Lorenz Rhomberg, Gradient Corporation, Cambridge, MA

##### Heart Smart: Innovative Approaches for Improving Cardiovascular Safety Through Collaboration

Monday, March 8, 9:15 AM–12:00 NOON

**Chairperson(s):** Cyril D. Pettit, HESI, Washington, DC, and Jean-Pierre Valentin, AstraZeneca UK, Macclesfield, Cheshire, United Kingdom

**Sponsor:**

Regulatory and Safety Evaluation Specialty Section

**Endorsed by:**

Drug Discovery Toxicology Specialty Section

Nonclinical and clinical safety is a major cause of drug attrition. A recent Association of the British Pharmaceutical Industry (ABPI) review of more than 225 drugs revealed that cardiovascular toxicities account for at least 28% of compound discontinuation. Although research and development expenditure continues to rise, the number of new drug applications is still declining. A strategy is therefore required to detect drugs with potential liabilities earlier in drug discovery in order to progress only the real winners. Pharmaceutical companies and regulatory bodies alike have recognized this challenge and have realized the need for scientists from different institutions—industry, academia, and government—to share their proprietary data more widely. This session will highlight collaborative projects that have been initiated to tackle various aspects of cardiovascular toxicities. We will begin with an introduction of the role of collaborations within translational toxicology, highlighting the benefit gained from large, diverse data sets. Further information will be provided as we progress in describing an ABPI program—the animal model framework—utilizing hemodynamic and ECG data from conscious telemetered dogs in addition to *in vitro* human ion channel data, in line with ICH S7B guidelines to predict Phase I clinical trial outcome. Participants will be provided an overview of the FDA-HESI seminar that was designed to assess in more detail predictability of nonclinical cardiac repolarization data for assessing QT liability in the clinic through retrospective analysis of data from the FDA, contributing companies, and the literature. We will move on to explore what more can be done to understand cardiac toxicities by reviewing a HESI initiative that aims to integrate structure and function relationships. Finally, participants will be asked what additional data can be exploited

from the animal model framework to address compound attrition due to non-cardiovascular toxicities.

- **Using the Animal Model Framework to Predict Non-Cardiovascular Toxicities—An ABPI Program**, Lorna Ewart, AstraZeneca Pharmaceuticals, Macclesfield, Cheshire, United Kingdom
- **Animal Model Framework: Translation of Nonclinical Functional Cardiovascular Data to Humans—An ABPI Program**, Rob Wallis, Pfizer, Groton, CT
- **Predictivity of Nonclinical Data for Assessing QT Liability in the Clinic—An FDA-HESI Joint Program**, John Koerner, U.S. FDA, Silver Spring, MD
- **Current Practices and New Opportunities in Assessing Structural-Functional Cardiovascular Toxicities—A HESI Initiative**, Dustan Sarazan, Covance, Madison, WI
- **The Cardiac Safety Research Consortium (CSRC): A Critical Path Initiative for Cardiac Safety Evaluation Through a New Paradigm of Pre-Competitive Public-Private Partnering**, Mitchell Krucoff, Duke University, Durham, NC

### TOXICITY TESTING IN THE 21<sup>ST</sup> CENTURY

#### Toxicology in the 21<sup>st</sup> Century: Stem Cells in Drug Discovery and Development

Monday, March 8, 9:15 AM–12:00 NOON

**Chairperson(s):** Kyle Kolaja, Hoffmann-LaRoche, Inc., Nutley, NJ, and Chris Kendrick-Parker, Cellular Dynamics International, Madison, WI

**Sponsor:**

Drug Discovery Toxicology Specialty Section

**Endorsed by:**

*In Vitro* and Alternative Methods Specialty Section  
Mechanisms Specialty Section

Pluripotent stem cells have the potential to differentiate into any cell type in the body. This biological paradigm is being leveraged to change the way drugs are discovered, assessed, designed, and delivered. Stem cell derived models of various tissues including inflammatory cells, cardiomyocytes, neurons, beta-islet cells, etc., have demonstrated utility in understanding disease processes as well as predicting toxicological outcomes. As our understanding of genetic reprogramming into a stem cell and subsequent differentiation into terminal cell types increases, it will enable a variety of applications in the pharmaceutical and chemical industries. *In vitro* models will be followed by individual understanding of biology

through inducible pluripotent (iPS) technology and ultimately cellular therapies will be brought to the clinic. In this session, we will cover a series of presentations that will expound upon our understanding of pluripotent cells and their utility in providing cellular models, how they are being used to understand pharmaceutical mechanisms of efficacy and toxicity, and the practical issues and obstacles that will need to be addressed to make regenerative, cellular therapy a reality.

- **Human Inducible Pluripotent Stem Cell Derived *In Vitro* Models —The Path to a Better Understanding of Individual Biology and Their Utility in Drug Discovery and Development**, Chris Kendrick-Parker, Cellular Dynamics International, Madison, WI
- **Application of Stem Cell-Derived Cardiomyocytes in Toxicology and Safety Pharmacology**, Kyle Kolaja, Hoffmann-LaRoche, Nutley, NJ
- **Pharmaceutical Perspectives on Introduction of Regenerative Medicine Concepts into the Existing Pharmaceutical Paradigm**, Ruth McKernan, Pfizer, Groton, CT
- **Developing Stem Cell-Based Therapies: FDA Product and Preclinical Regulatory Considerations**, Mercedes Serabian, U.S. FDA, Silver Spring, MD
- **How the Understanding of the Biology of Inducible Pluripotent Stem Cells Will Evolve: Predictions on Methods of Stem Cell Induction and the Impact on Cell-Based Therapy**, James Thomson, University of Wisconsin, Madison, WI

#### Determination of the Contribution of Individual Stressors in Cumulative Risk Assessments

Monday, March 8, 1:40 PM–4:25 PM

**Chairperson(s):** Michael Dourson, Toxicology Excellence for Risk Assessment, Cincinnati, OH, and Paul Price, The Dow Chemical Company, Midland, MI

**Sponsor:**

Mixtures Specialty Section

**Endorsed by:**

Biological Modeling Specialty Section

In the NRC reports *Science and Decisions: Advancing Risk Assessment* and *Phthalates and Cumulative Risk Assessment: The Task Ahead* the U.S. EPA is challenged to move towards cumulative risk assessment and away from chemical-by-chemical approaches to determining public health. The U.S. EPA has more than decade of experience in assessing cumulative risks and has recently release a significant resource documents on cumulative risk assessment.

## WORKSHOPS

Despite the importance of cumulative risk assessments, there are major challenges that have limited the number of cumulative assessments performed. Cumulative risk assessments are population based, thus separate assessments are required for different populations. Site-specific information will play a critical role in such assessments. In any population the combination of exposures to chemical and non-chemical stressors varies from person-to-person and from moment-to-moment. These complexities affect both the determination of the cumulating risks and the contributions of any one stressor. Simulation modeling is expected to play a major part in the assessment of cumulative risks. Modeling provides an effective means of tracking and combining the impacts of exposures to stressors that occur by multiple routes and sources. These models include exposure, PBPK, and biologically-based dose-response models (BBDR) which become more effective when they are linked so that data and assumptions in exposure models are passed on to PBPK and BBDR models. This session will present a review of the technical issues for each step of the cumulative risk assessment process. Therefore it is important that we begin with an overview from an NRC committee member who authored the report and follow up with presentations from leading speakers on the various phases of the dose-to-response modeling process—exposure, kinetics, and dose-response. Finally, we will present a statistical model for the evaluation of the impact of cumulative risks that can assist in ranking or screening cumulative risks.

- **Advancing Cumulative Risk Assessment and Impact Evaluation**, Lauren Zeise, California EPA, Oakland, CA
- **Key Characteristics of a Cumulative Exposure Assessment**, Claire Franklin, The LifeLine Group, Ottawa, Ontario, Canada
- **Use of PBPK Models to Assess the Cumulative Effects of Chemical Mixtures and Non-Chemical Stressors**, Kannan Krishnan, University of Montreal, Montreal, Quebec, Canada
- **Developing Models of Cumulative Response to Multiple Chemical Stressors and the Determination of the Contributions of Individual Stressors**, Jason Lambert, U.S. EPA, Cincinnati, OH
- **Predicting the Magnitude of Cumulative Chemical Exposures from Source-Specific Data**, Paul Price, The Dow Chemical Company, Midland, MI

Scientific

## TUESDAY

### TOXICITY TESTING IN THE 21<sup>ST</sup> CENTURY

#### Opportunities to Modify Current Regulatory Testing Guidelines and Advance the Assessment of Carcinogenicity Risk in the 21<sup>st</sup> Century

Tuesday, March 9, 9:00 AM–11:45 AM

*Chairperson(s):* Frank D. Sistare, Merck and Co., Inc., West Point, PA, and David Jacobson-Kram, U.S. FDA, Silver Spring, MD

*Sponsor:*

Regulatory and Safety Evaluation Specialty Section

*Endorsed by:*

Carcinogenesis Specialty Section

Drug Discovery Toxicology Specialty Section

In Vitro and Alternative Methods Specialty Section

The two-year rodent bioassay is currently the most expensive and time-consuming animal test required for pharmaceutical and chemical carcinogenicity assessment. A vision for the 21<sup>st</sup> century is proposed for a staged approach to altering the current pharmaceutical carcinogenicity testing paradigm that reduces the timeline, animal and human resources, and improves human risk assessment. Analyses of decades of shared data from pharmaceutical carcinogenicity testing are helping to define an approach to preserve protections and benefits afforded to patients, while providing support for a near-term significant modification to testing guidelines. These data are also helping to define a research strategy that will deliver further improved testing. In the past decade, genetically modified animal models have been introduced and incorporated as an addition to the pharmaceutical test battery option. A new paradigm supported by decades of test data proposes to maximize the value of such mouse models to minimize the need for two-year rat carcinogenicity studies. Furthermore, advances are being made through collaborative research initiatives that point to anticipated growth in qualified biomarkers for monitoring in both animal models, and *in vitro* test systems that may allow quicker resource sparing approaches to improved cancer risk identification. These approaches promise not only to allow earlier identification of rodent tumorigenic chemicals, but also to provide deeper insights into mode-of-action and better understanding of human relevance. Therefore it is a goal of this session to provide new understanding of key lessons learned from decades of pharmaceutical testing experience, of emerging carcinogenic based biomarkers, of development of *in vitro* screening and mechanistic models, of

integrated mode-of-action systems biology based approaches to identify and assess genotoxic and nongenotoxic mechanisms, and offer regulatory perspectives on the impact of these developments on the near-term and long-term future of carcinogenicity testing.

- **Lessons Learned from an Analysis of Pharmaceutical Experience with Decades of Rat Carcinogenicity Testing**, Frank D. Sistare, Merck and Co Inc., West Point, PA
- **A Proposed Vision on the Future of Carcinogenicity Testing**, David Jacobson-Kram, U.S. FDA, Silver Spring, MD
- **Integrating Predictive and Mechanistic Carcinogenicity Biomarker into Drug Discovery and Development**, Mark Fielden, Amgen, South San Francisco, CA
- **Improving Cancer Risk Assessment of Drug Candidates by Integrating Systems Biology to Define Mode-of-Action of Carcinogens**, Jiri Aubrecht, Pfizer Inc, Groton, CT
- **Using *In Vitro* Hazard Identification Approaches for Improving Human Cancer Risk Assessment and Preclinical Testing**, Joost van Delft, Maastricht University, Maastricht, Netherlands

### Research Advances and Enduring Needs in Children's Environmental Health Protection

**Tuesday, March 9, 9:00 AM–11:45 AM**

**Chairperson(s):** Sally P. Darney, U.S. EPA, Research Triangle Park, NC, and Allen Dearry, NIEHS, Research Triangle Park, NC

**Sponsor:**

Reproductive and Developmental Toxicology Specialty Section

**Endorsed by:**

Occupational and Public Health Specialty Section  
Risk Assessment Specialty Section  
Women in Toxicology Special Interest Group

Children may be more vulnerable and susceptible to health impacts of environmental contaminants based upon age-specific behaviors that increase exposure; developmental processes that are differentially susceptible to disruption; and genetic variables that alter biological responses to toxicants. Federal laws require consideration of children's unique vulnerability in rule making activities. Recent research about how children are exposed and react to environmental contaminants helps decision makers set environmental standards based on scientific information rather than default assumptions. In 1998, the U.S. EPA and NIEHS partnered to fund the Centers for Children's Environmental Health and Disease Prevention Research Program. These centers are examining interactions between key environmental exposures and a range of child prevalent diseases such as asthma and autism. Emphasizing multidisciplinary basic, applied, and community-based participatory approaches, their

common goal is to reduce children's health risks from environmental contaminants, prevent childhood diseases, and share findings with the affected communities and the broader public. In 2009, NIH launched the National Children's Study (NCS) in partnership with CDC, U.S. EPA, and NIEHS. NCS will recruit and follow 100,000 children from before birth to adulthood, gathering both exposure and health outcome information and evaluating how early life exposures may affect their subsequent health. Therefore it is important that we seize the opportunity through these initiatives to synthesize recent research advances in child-specific exposure science and health effects, including lessons learned from the Children's Centers, illustrate how these advances are being integrated into new studies such as the NCS, consider how this new knowledge can be used in risk assessment, and address ongoing challenges. Specifically, these challenges include interpreting biomonitoring data, finding and eliminating exposure sources, predicting health effects, communicating the findings to regulators and the public in meaningful ways, and informing policy decisions.

- **Federal Efforts to Address Children's Environmental Health**, Allen Dearry, NIEHS, Research Triangle Park, NC
- **Children's Exposures to Chemicals**, Linda Sheldon, U.S. EPA, Durham, NC
- **Gene-Environment Interactions and Children's Susceptibility**, Elaine Faustman, University of Washington, Seattle, WA
- **Unique Opportunities in the National Children's Study**, Edward Clark, University of Utah, Salt Lake City, UT
- **How Can Science Inform Risk-Based Decisions and Protect Children's Health?** Stanley Barone, U.S. EPA, Washington, DC

### Immunotoxicity and Other Safety Considerations in the Development of Therapeutic Vaccines

**Tuesday, March 9, 1:30 PM–4:15 PM**

**Chairperson(s):** Michaela Sharpe, Pfizer Limited, Sandwich, United Kingdom, and Ken Draper, Draper Consulting, LLC, Reno, NV

**Sponsor:**

Immunotoxicology Specialty Section

**Endorsed by:**

Regulatory and Safety Evaluation Specialty Section  
Reproductive and Developmental Toxicology Specialty Section  
Toxicologic and Exploratory Pathology Specialty Section

Prophylactic vaccination has proven highly effective against many highly virulent infectious diseases and has reduced the medical burden from these infections throughout the world. Despite these

## WORKSHOPS

successes, many infectious agents, such as human immunodeficiency virus (HIV), herpes simplex virus (HSV), and Epstein Barr Virus (EBV) establish chronic latent infections and create considerable morbidity upon reactivation following immunosuppression. Traditional vaccines that generate antibody-mediated immunity have limited effects on chronic quiescent infections and do little to inhibit the spread of these viruses. While monoclonal antibody therapy can provide limited passive vaccination for these maladies, the cost is great and patient compliance is low. A therapeutic vaccination that induces both humoral (antibody-mediated) and cellular (T cell-mediated) immunity holds promise in combating these latent infections, as well reducing the medical impact for other chronic human maladies, including cancer, addiction, and genetic/metabolic disease. In addition to cost and compliance issues, successful therapeutic vaccination will need to overcome immune tolerance while controlling dysregulation and/or deleterious effects of immune activation (i.e., unwanted T cell activation and undesirable off-target effects will need to be minimized). An overview of clinical indications under consideration for therapeutic vaccination (HIV, caffeine and nicotine addiction, cancer, etc.), approaches to development of therapeutic vaccines (adjuvant use, dendritic cell activation, viral vectors, etc.), and safety concerns of therapeutic immune activation (induction of autoimmunity, unregulated T cell activation, etc.) will be presented.

- **Overview of Therapeutic Vaccines**, Ken Draper, Draper Consulting, LLC, Reno, NV
- **Safety Considerations in the Development of Therapeutic Vaccines—Introduction**, Michaela Sharpe, Pfizer Limited, Sandwich, United Kingdom
- **Mechanisms for Maintaining and Breaking Immunological Tolerance: Applications and Potential Consequences in the Development of Therapeutic Vaccines**, Brian Champion, Pfizer Limited, Sandwich, United Kingdom
- **Safety Assessment of Therapeutic Vaccines and Adjuvants for Non-Infectious Diseases: CBER Perspective**, Theresa Chen, U.S. FDA, Silver Spring, MD
- **Safety Assessment of Therapeutic Vaccines and Adjuvants—An Industry Perspective**, Lawrence Segal, GlaxoSmithKline Biologicals, Wavre, Belgium
- **Case Study—Issues in Nonclinical Safety Testing and Immune-Related Clinical Toxicity Impacting the Development of a Vaccine for Alzheimer's Disease**, Garvin Warner, Wyeth Research, Andover, MA

### Widely Varying Strategies Implemented in Discovery to Reduce the Failure Rate of Clinical Lead Candidates in Development

Tuesday, March 9, 1:30 PM–4:15 PM

**Chairperson(s):** Alan S. Bass, Schering-Plough Research Institute, Kenilworth, NJ, and Mark E. Cartwright, Schering-Plough Research Institute, Lafayette, NJ

**Sponsor:**

**Drug Discovery Toxicology Specialty Section**

The current discovery screening paradigm for the selection of novel molecular candidates to progress into development is fraught with a high level of failure in the early-to-late stages of development. The relationship of the number of candidates entering Phase I to achieve one successful registration varies from one pharmaceutical company to another. However, published data suggests that for every 12 new molecular entities entering Phase I, only one successfully achieves marketing authorization. The significant cost of such an endeavor in terms of operating expenses, lost time, and missed opportunities to advance the best candidates for the treatment of devastating diseases is too great to justify continuing with the status quo. As a result, there has been significant effort devoted across the pharmaceutical industry to early identification of potential liabilities of promising lead candidates that may lead to failure of those candidates in development. A goal of this session will be to advance the topic of discovery risk mitigation introduced in recent years in an attempt to reduce the number of failures being witnessed in early-to-late development. Topics include, identifying the potential on-target-related toxicities during lead finding, deselecting those candidates likely to fail in development due to on-target or off-target related toxicities, staged approaches to evaluating the pharmacodynamic safety (safety pharmacology) of potential lead candidates, integrating safety endpoints into proof of concept studies, and application of structure activity toxicology (SAT) identifying and mitigating the risk of metabolite-related toxicity. Presenters will share their experiences in each of these emerging areas of safety science and engage the audience in a debate of best practices. Important deliverables will include advancing knowledge in the conceptual and practical approaches to mitigating the risk of failure of promising new drugs progressing towards marketing authorization.

- **Mitigation Strategies during Early Research: Evaluation of Novel Therapeutic Targets for Potential On-Target Toxicity**, John Davis, Procter & Gamble Research and Development, Chesterfield, MO
- **Mitigation Strategies Carried Out in Discovery to Assess the Pharmacodynamic Safety of Promising New Molecules**, Alan S. Bass, Schering-Plough Research Institute, Kenilworth, NJ

- **Managing Resource Limitations in Discovery Toxicology: Integration of Risk Mitigation Approaches Into Efficacy Studies and Other Strategies for Novel Therapeutic Targets**, Bruce Car, Bristol-Myers Squibb Inc., Princeton, NJ
- **Structure Activity Toxicology (SAT) As a Means of De-Risking Compound Failure**, Mark Cartwright, Schering-Plough Research Institute, Lafayette, NJ
- **Mitigation Strategies during Discovery Lead Optimization: Management of a Preclinical Off-Target Adrenal Finding**, Bruce Homer, Pfizer, Chesterfield, MO

## WEDNESDAY

### Current Thinking and Experiences Related to Developmental and Reproductive Safety Assessment of Biotherapeutics

Wednesday, March 10, 9:00 AM–11:45 AM

*Chairperson(s): Christopher J. Bowman, Pfizer Global Research and Development, Groton, CT, and Tacey E. White, GlaxoSmithKline, King of Prussia, PA*

**Sponsor:**

Reproductive and Developmental Toxicology Specialty Section

**Endorsed by:**

Comparative and Veterinary Specialty Section

As scientific thinking and regulatory expectations around highly target-specific biotherapeutics have evolved, it has become increasingly difficult to design meaningful nonclinical strategies that reduce uncertainty around the risk of effects on human reproduction and development. Importantly, these nonclinical studies are likely the most reliable method available to prevent drug-induced birth defects and infertility since clinical evaluation of these endpoints is unethical or rare. These studies should generally be in compliance with ICH S5, which is designed primarily to detect toxicity to reproduction and development (hazard identification). From ICH S5 relatively standard nonclinical strategies for small molecules have evolved, but for practical, technical, and sometimes ethical reasons may have limited value for large molecules or vaccines (issues ranging from placental transfer to limited off-target toxicity). Although most biological effects of biotherapeutics have an origin in modification of a target or target signaling, it is not uncommon to have unexpected effects on reproduction and/or development since regulation/function of the target during these lifestages is often not well understood, particularly for novel drug targets. As described in ICH S6, for biotherapeutics careful scrutiny of the nonclinical strategy and conduct of specific studies is necessary to appropriately account for many issues, particularly species specificity,

immunogenicity, biological activity and/or elimination half-life. In order to adhere to ever-changing regulatory expectations, minimize the use of animals; and improve the performance of safety assessment/toxicology around potential treatment-related effects on reproduction and development; innovative strategies using a combination of animal models (e.g., transgenic) and study designs (e.g., use of homologues or combined pre/postnatal development in nonhuman primate) are currently being developed and applied by many companies.

- **Current Regulatory Experience and Proposed Modifications to ICH S6**, Jan Willem Van Der Laan, National Institute for Public Health and the Environment, Bilthoven, Netherlands
- **Preclinical Strategy Considerations for Assessing the Reproductive and Developmental Toxicity Potential of Biopharmaceuticals**, Joy Cavagnaro, Access BIO, Leesburg, VA
- **Challenges and Solutions for Evaluating the Developmental Toxicity Potential of Biotherapeutics**, Laura Andrews, Genzyme Corporation, Framingham, MA
- **Case Studies: Developmental and Reproductive Toxicity (DART) Strategies Employed to Support the Registration of Golimumab and Ustekinumab**, Clifford Sachs, Centocor R&D, Inc., Radnor, PA
- **State of the Science on Reproductive and Developmental Safety Assessment on Vaccines and Adjuvants**, Sarah Gould, Sanofi Pasteur, Lyon Marcy L'Etoile, France

## TRANSLATIONAL TOXICOLOGY

### Novel Research Approaches and Animal Models in Translational Toxicology

Wednesday, March 10, 9:00 AM–11:45 AM

*Chairperson(s): Shashi K. Ramaiah, Pfizer Global Research and Development, St. Louis, MO, and Benjamin D. Humphreys, Harvard University, Boston, MA*

**Sponsor:**

Toxicologic and Exploratory Pathology Specialty Section

**Endorsed by:**

Drug Discovery Toxicology Specialty Section

Regulatory and Safety Evaluation Specialty Section

Translational toxicology is defined by the ability to translate preclinical animal safety findings to human is integral to successful drug development. Preclinical safety studies are mostly carried out in both rodent and a non-rodent species, with the primary goal to demonstrate or identify target organ effects translatable to human health. In addition these studies also enable selection of the dose for first-in-human studies, demonstrate a margin of safety between

## WORKSHOPS

the efficacious and toxic doses, and establish mechanisms for monitoring safety during clinical trials such as biomarkers. In order to demonstrate translatability, it is critical to develop the most relevant animal model and to select the appropriate endpoints that can accurately predict human toxicity. If a safety issue is identified, it is of utmost importance to have the most sensitive and specific translatable biomarker of organ toxicity in addition to the ideal assay platform to monitor such biomarkers clinically. Without these, the incidence of drug failure due to toxicity during clinical development and the occurrence of morbidity and mortality in human patients will continue to increase. The goal of this session will be to provide novel research approaches and examples to address certain gaps in drug development to ensure clinical translatability. The application of novel research approaches, animal models, and biomarker platforms will be discussed from clinical and nonclinical scientists actively engaged in these areas.

- **Why Do Animal Models Fail to Predict Idiosyncratic Hepatotoxicity in Humans**, Arie Regev, Eli Lilly, Indianapolis, IN
- **Novel Translational Research Approaches to Understand and Predict Drug Induced Liver Injury**, Paul Watkins, University of North Carolina, Chapel Hill, NC
- **Kidney and Vascular Toxicities of VEGF Signaling Pathway Inhibitors: Mechanism-Dependent Biomarkers for Treatment Efficacy?** Benjamin Humphreys, Harvard University, Boston, MA
- **Lead Optimization Strategies and Novel Biomarker Technologies to Ensure Drug Safety**, Josef Ozer, Pfizer Global Research and Development, St. Louis, MO

### TOXICITY TESTING IN THE 21<sup>ST</sup> CENTURY

#### **Toxicity Testing in the 21<sup>st</sup> Century for Ecotoxicology**

**Wednesday, March 10, 9:00 AM–11:45 AM**

*Chairperson(s): Stephen Edwards, U.S. EPA, Research Triangle Park, NC, and Gerald Ankley, U.S. EPA, Duluth, MN*

*Sponsor:*  
Biological Modeling Specialty Section

*Endorsed by:*  
Immunotoxicology Specialty Section  
Risk Assessment Specialty Section

The National Research Council (NRC) report, *Toxicity Testing in the Twenty-first Century: A Vision and a Strategy* has relevance for ecological as well as human health risk assessment. In April 2009,

the Society of Environmental Toxicology and Chemistry (SETAC) held a workshop that considered key elements of the scientific foundation that would be needed to implement the vision of toxicity pathway-based testing in support of ecological risk assessment. The term adverse outcome pathway (AOP) was used to describe the linkage of molecular events modeled in a toxicity pathway assay to downstream biologic effects considered adverse from an ecotoxicological perspective (i.e., effects on survival, reproduction). Five challenges related to the elucidation and description of AOPs were considered. First, consistent with the NRC strategy concerning toxicity pathway elucidation and linkage to adversity, the challenge of describing AOPs from the extant literature and quantitatively modeling key components was addressed. Second, approaches for reverse engineering AOPs from combinations of transcriptomic, proteomic, metabolomic, and/or phenotypic data were examined. Because adversity in an ecological risk context is typically considered at the population level, approaches for translating toxicity pathway outputs into appropriate parameters for population modeling was a third challenge discussed. The fourth related to the challenge of discriminating adaptive (i.e., homeostatic, allostatic) responses from adverse ones and incorporating that knowledge into AOP models. Finally, because species extrapolation is a central challenge in ecological risk assessment, the workshop examined how to determine conservation of AOPs among species and use this information in predicting species sensitivity to support ecological risk assessments. This session will summarize the results of the SETAC effort and invite discussion with SOT members regarding development of an integrated toxicity testing paradigm that supports both human health and ecological risk assessment.

- **Adverse Outcome Pathway (AOP) Modeling of Known Pathways**, Melvin Andersen, The Hamner Institutes, Research Triangle Park, NC
- **Reverse Engineering Adverse Outcome Pathways from ‘Omics Data**, Edward Perkins, U.S. Army ERDC, Vicksburg, MS
- **Adverse Outcome Pathways and Ecological Risk Assessment: Bridging to Population Level Effects**, Gerald Ankley, U.S. EPA, Duluth, MN
- **Testing and Risk Assessment of Chemicals That Impact Highly Adaptive Biological Systems: The Case of Endocrine Systems**, John Nichols, U.S. EPA, Duluth, MN
- **Species Extrapolation for the 21<sup>st</sup> Century**, Jared Goldstone, Woods Hole Oceanographic Institution, Woods Hole, MA
- **Predictive Ecotoxicology in the 21<sup>st</sup> Century**, Daniel Villeneuve, U.S. EPA, Duluth, MN

### Understanding Nonlinearities at the Low-End of the Dose-Response Curve: Insights from Molecular Network Analysis

Wednesday, March 10, 9:00 AM–11:45 AM

**Chairperson(s):** Sally P. Darney, U.S. EPA, Research Triangle Park, NC, and Robert E. Chapin, Pfizer, Inc., Groton, CT

**Sponsor:**

Reproductive and Developmental Toxicology Specialty Section

**Endorsed by:**

Molecular Biology Specialty Section

As we move more and more into predictive toxicology, there will be a pressing need to more fully understand the world of *in vivo* effects and how (or if, or when) those translate into measurable impacts on health. This includes responses seen at very low doses or internal concentrations. We will explore the world of low dose effects reported for endocrine disrupting chemicals thought to exert health effects primarily by interfering with steroid hormone receptor function. Participants will learn the latest details of steroid hormone action including binding of endogenous hormone and/or hormone mimics to steroid receptors and the possibility of non-receptor-mediated actions. This will set the stage for examining mechanisms by which low levels of exogenous ligand may alter endogenous responses or developmental processes. With this foundation, diverse effects reported for the weakly estrogenic compound Bisphenol A will be reviewed, particularly surprises seen at very low doses where the dose-response deviates from the expected linear relationship. Recent explorations of gene regulatory networks suggest explanations for these unexpected nonlinearities, especially at very low levels of signal. Discussants will add perspectives on the mechanistic and risk assessment implications provided by the new science of steroid signaling and gene regulatory networks. By providing this information, we hope that the audience will come away from this session with a better understanding of the biological plausibility of low dose effects of endocrine disrupting chemicals as well as implications for risk assessment and predictive toxicology. Additionally participants will gain insights on how to focus on nonlinear biological networks, as opposed to our accustomed linear pathways, and how to leverage all available biological data to translate very low dose effects into outcomes more conventionally measured in toxicity studies.

- **Understanding Nonlinearities at the Low-End of the Dose-Response Curve: Insights from Molecular Network Analysis**, Sally P. Darney, U.S. EPA, Research Triangle Park, NC
- **Estrogen Receptors as Sensors and Mediators of Diverse Ligand Responses**, Geoffrey Greene, University of Chicago, Chicago, IL

- **Low Dose Effects of Bisphenol A in Animal Studies**, Kristina Thayer, NIEHS, Research Triangle Park, NC
- **Dose-Response Relationships in Gene Regulatory Networks and Lack of Linearity at Low Dose**, Qiang Zhang, The Hamner Institutes, Durham, NC

### TOXICITY TESTING IN THE 21<sup>ST</sup> CENTURY

#### High-Throughput Electrophysiology—21<sup>st</sup> Century Toxicity Testing Approaches with Functional Outcomes

Wednesday, March 10, 1:30 PM–4:15 PM

**Chairperson(s):** Timothy J. Shafer, U.S. EPA, Research Triangle Park, NC, and Glenn E. Kirsch, ChanTest Corporation, Cleveland, OH

**Sponsor:**

Neurotoxicology Specialty Section

**Endorsed by:**

Drug Discovery Toxicology Specialty Section  
In Vitro and Alternative Methods Specialty Section  
Regulatory and Safety Evaluation Specialty Section

The NAS report on Toxicity Testing in the 21<sup>st</sup> Century envisions a future approach to toxicity testing that relies on *in vitro*, high-throughput approaches to identify and characterize toxicity hazards of environmental chemicals. These approaches are expected to replace or reduce the number of animals needed for toxicity testing. However, description of adverse effects for the purpose of hazard identification has relied predominantly on changes in structure and/or function in animals. In addition, many endpoints measured in high-throughput or high-content assays are biochemical and difficult to link directly to functional changes. For excitable tissues such as in the nervous and cardiac system, *in vivo* electrophysiological assessments have been widely and successfully utilized to describe adverse effects, whereas *in vitro* electrophysiological approaches have provided important information on mechanisms-of-actions of pesticides, metals, and other compounds. In recent years, new high-throughput/high-content electrophysiological assays have been developed and widely utilized for drug target screening and/or safety pharmacology—for example, screening of compound effects on HERG channels to identify those that produce *torsades de pointes*, a lethal cardiac side-effect of some drugs. Many of these electrophysiological approaches can be readily adapted to toxicity testing and will provide high-content information in addition to their throughput capabilities. Thus, these approaches can provide not only information on functional changes in electrically excitable tissues, but also information regarding potential toxicity

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pathways by which compounds may disrupt function. This session will describe a number of these HTS approaches for electrophysiology, and discuss their use for safety and toxicity testing. More importantly, it will focus on how these approaches can be further adapted for use in 21<sup>st</sup> century toxicity testing for toxicity pathway and hazard identification.

- **Use of Cell and Tissue-Based Methods for Rapid Identification of Cardiovascular Toxicity Pathways in Discovery Toxicology**, Paul Levesque, Bristol-Myers Squibb, Pennington, NJ
- **Automated Patch Clamp Assessment of Pyrethroid Insecticide Interactions with Cloned Human Na<sup>+</sup> Channels**, Glenn Kirsch, ChanTest Corporation, Cleveland, OH
- **The Promise of Microelectrode Array Approaches for Toxicity Testing: Examples with Neuroactive Chemicals**, Andrew F.M. Johnstone, U.S. EPA, Research Triangle Park, NC
- **FDA Use of Data from *In Vitro* Electrophysiology in a Regulatory Environment; Applying Lessons Learned in Safety Pharmacology to Toxicity Testing**, John Koerner, U.S. FDA, Silver Spring, MD

### Minerals and Metals: Pros and Cons of Deliberate Exposure

Wednesday, March 10, 1:30 PM–4:15 PM

**Chairperson(s):** Ruth A. Roberts, Astra Zeneca UK, Macclesfield, United Kingdom, and Jonathan Powell, MRC Centre for Human Nutrition UK, Cambridge, United Kingdom

**Sponsor:**  
Metals Specialty Section

**Endorsed by:**  
Carcinogenesis Specialty Section  
Drug Discovery Toxicology Specialty Section  
Neurotoxicology Specialty Section

Metals and minerals are known to induce adverse effects ranging from oxidative stress to carcinogenesis. However, some are administered or are under consideration for therapeutic intent either as direct administration or as a consequence of metal-to-metal joint replacement. For example, oral iron can reduce the incidence of anemia—number 11 on the World Health Organization's top 20 list of global disease burden. On the other hand, there is a risk of increasing infection and morbidity/mortality in developing countries or risk of chronic subclinical inflammation and colon cancer in the developed world. We will explore the potential of metals

and minerals in therapy and in parallel will consider the potential adverse effects that need to be considered. The presentations are designed to provide attendees with important and biologically relevant issues related to *in vivo* exposures to metals and minerals, a comprehensive and stimulating state-of-the-art update on innovative testing methods, and a vision of expected scientific advances in the understanding of how minerals and metals can affect developmental, degenerative, and carcinogenic processes. The focus of this session encompasses concepts and themes from cell physiology through to molecular biology with an overall goal of ensuring a better understanding of the assessment of hazard and risk associated with exposures to minerals and metals. As such, it is intended for basic and applied scientists in academia, government, and industry.

- **Therapeutic Uses of Metals and Minerals: The Risk-Benefit Interface**, Jonathan Powell, MRC Centre for Human Nutrition UK, Cambridge, United Kingdom
- **Protection Against Chromium (VI)-Induced Oxidative Stress and Apoptosis by Nrf2**, Qiang Ma, NIOSH, Morgantown, WV
- **Functional Profiling to Identify Metal Toxicity Pathways in Yeast**, Chris Vulpe, University of California Berkeley, Berkeley, CA
- **Metals and Oxidative Impairment in Neurodegenerative Disorders**, Michael Aschner, Vanderbilt University, Nashville, TN

### CELL SIGNALING

#### 'Omics Profiling of Cell and Tissue Interactions of Nanomaterials: Insight into Mechanisms of Action

Wednesday, March 10, 1:30 PM–4:15 PM

**Chairperson(s):** Mary Jane Cunningham, Nanomics Biosciences Inc, Cary, NC, and Frank Witzmann, Indiana University School of Medicine, Indianapolis, IN

**Sponsor:**  
Molecular Biology Specialty Section

**Endorsed by:**  
Nanotoxicology Specialty Section

Nanomaterials (NMs) are nano-scale materials which are engineered or naturally-occurring. NMs are being developed for a variety of products ranging from medical therapies to consumer goods and often exhibit novel properties not seen with other large scale materials of similar chemical composition. However, the

adverse effects, if any, of NMs have not been adequately tested. Future testing assays for the 21<sup>st</sup> century include high-throughput screening technologies to identify cellular interactions with NMs for efficacy and safety. This session will present ongoing genomics, proteomics, and metabolomics studies of interactions between natural and engineered NMs and biological systems. Findings of novel interactions of NMs and biological systems will be highlighted and the feasibility of these approaches for future comprehensive studies of NM efficacy and safety will be discussed. Examples of *in vitro* cellular interactions with a variety of NMs will be provided which include mRNA, miRNA, and proteomic expression profiles of human and mammalian cells exposed to nanotubes, nanocrystals (quantum dots), dendrimers and nano-scale particles of both terrestrial and extra-terrestrial origin. Selective activation of specific genes, proteins, and cellular signaling pathways will be related to possible mechanisms of action. We will highlight how the addition of metabolomics to other 'omics based studies can further define the effects of NMs on biological systems after environmental exposures. The final presentation will expand upon the systems biology approach and show how multiple 'omics technologies can provide mechanistic meaning when individual data sets are analyzed ranging from a global to subcellular view. This session should be of interest to all investigators interested in state-of-the-art 'omics technologies for screening the effects of foreign materials, including NMs, in humans and other organisms.

- **Messenger RNA and MicroRNA Expression Profiling of Nanomaterial Interactions with Primary Human Skin and Lung Cells**, Mary Jane Cunningham, Nanomics Biosciences, Inc., Cary, NC
- **Carbon Nanoparticle Exposure Alters Barrier Epithelial Cell Function: Proteomic and Electrophysiological Analyses**, Frank Witzmann, Indiana University School of Medicine, Indianapolis, IN
- **Genomic Signatures for Size-Dependent Biological Effects of Gold Nanoparticles**, Fanqing Chen, Lawrence Berkeley National Lab, Berkeley, CA
- ***In Vitro* and *In Vivo* Metabolomic and Proteomic Biomarker Studies of III-V Semiconductors on Renal Proximal Tubule Cells**, Bruce Fowler, ATSDR/CDC, Atlanta, GA
- **Dynamic Network Analysis of Nanosilica-Induced Toxicity Pathways Using Microarray and Proteomic Data**, Katrina Waters, Pacific Northwest National Laboratory, Richland, WA

## The Process of Defining Risk for Environmental Chemicals Having Significant Skin Exposure and Absorption Potential

Wednesday, March 10, 1:30 PM–4:15 PM

**Chairperson(s):** William G. Reifenrath, Stratacor, Inc., Richmond, CA, and, John H. Ross, Gem Quality Risk Inc, Carmichael, CA

**Sponsor:**

Dermal Toxicology Specialty Section

**Endorsed by:**

Regulatory and Safety Evaluation Specialty Section  
Risk Assessment Specialty Section

Skin exposure and subsequent absorption of environmental contaminants are often critical issues for regulatory decisions concerning the treatment of contaminants or remediation at hazardous waste sites. Likewise, these issues are important in the registration or re-registration of pesticides. To address these points, laboratory studies are generally conducted with excised skin or animal models to determine the extent (percent absorption) or rate of penetration (permeability constant) of a chemical in question. In addition, exposure determinations, often based on field studies, determine the form and amount of chemical that can potentially reach the skin. Biomonitoring studies can integrate the processes of skin exposure and systemic absorption. The forgoing studies generate numbers, which require a translation into the potential for bioeffect, and the significance of that effect, which leads to a risk assessment. Regulators, such as the U.S. EPA, then make decisions based on the assembled data. The process works best when there is communication between all parties, starting with the design of experimental protocols. In recent years, there has been an increasing reliance on *in vitro* permeation data. While test guidelines are available for percutaneous absorption, actual studies have unique aspects that need to be addressed or negotiated. Decisions on seemingly small details at any level can ultimately have major impacts. Therefore, it is our intent to give a vertical perspective on the process by which safety assessments are made, starting at the laboratory and ending with a regulatory decision, and highlighting those aspects that can shape the outcome.

- **Dermal Absorption in the Exposure Assessment Process**, John H. Ross, Gem Quality Risk Inc., Carmichael, CA
- **Translating *In Vitro* Skin Absorption Data into Estimates of Human Skin Absorption**, William G. Reifenrath, Stratacor, Inc., Richmond, CA
- ***In Vitro* Dermal Absorption of Soil Contaminants: Importance of Modeling Field Exposure Conditions**, Richard Moody, Health Canada, Ottawa, Ontario, Canada

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- **Surface Deposition of Pesticides and Dermal Absorption of Residues in Agricultural and Urban Environments, Determinants of Pesticide Absorption in Agricultural and Residential Settings**, Robert Krieger, University of California Riverside, Riverside, CA
- **Regulatory Perspectives on the Use of Dermal Absorption Data for Risk Assessment**, P.V. Shah, U.S. EPA, Washington, DC
- **EU/OECD Guidelines—A Perspective from Bayer CropScience**, Philip Fisher, Bayer CropScience, Sophia Antipolis, France

### TRANSLATIONAL TOXICOLOGY

#### Translation of Nonclinical Models to Clinical Risk Management Strategies of Severe Infectious Diseases with Immunomodulatory Drugs

Wednesday, March 10, 1:30 PM–4:15 PM

*Chairperson(s): Wendy J. Komocsar, Eli Lilly and Company, Indianapolis, IN, and Thomas T. Kawabata, Pfizer, Inc., Groton, CT*

*Sponsor:*

Immunotoxicology Specialty Section

The recent development of immunomodulatory drugs to treat autoimmune and inflammatory diseases has resulted in significant patient benefit. However, modulation of immune responses may also result in decreased host resistance mechanisms and increased risk for infectious diseases and cancer. Some infrequent, but severe infectious diseases such as Progressive Multi-Focal Leukoencephalopathy (PML) and tuberculosis, have had significant impact on public health and the development of immunomodulatory therapies. The mechanism for the development of these diseases with drugs of different mechanisms of action and the susceptibility factors of certain patients is not clear. Currently, knowledge of the mechanism-of-action of the drug being developed, findings from standard toxicology studies and studies of immune function assessment may help determine potential risk for PML or tuberculosis, but do not provide decision making information on relative risk in the early stages of drug development. Given the low incidence of these severe infectious diseases and strict inclusion criteria of clinical trials, it is difficult to determine if severe infections will be a risk until larger populations are treated. Moreover, clinical monitoring to assess changes in immune function that may lead to decreased host resistance or biomarkers of recrudescence of microbes have not been adequately developed and validated. Application of approaches used in infection monitoring/prevention in the setting of clinical transplantation may provide some additional insight for the development of less suppressive immunomodulators. To address

these significant gaps, research across many disciplines is needed to better predict and risk manage severe infectious diseases. The goal of this session is to increase awareness of this issue and stimulate discussion on approaches to develop translatable nonclinical and clinical assays/biomarkers for better risk assessment and management of infection liability in the clinic.

- **Clinical Consequences of Adverse Unintended Immunomodulation**, Ian Gourley, Wyeth Research, Collegeville, PA
- **Risk Management of Infections with Transplantation**, Camille Nelson Kotton, Massachusetts General Hospital, Boston, MA
- **Progressive Multifocal Leukoencephalopathy and Immunomodulatory Drugs**, Thomas T. Kawabata, Pfizer Inc., Groton, CT
- **Mycobacterium Tuberculosis Overview and the Reactivation of Latent Tuberculosis**, Wendy J. Komocsar, Eli Lilly and Company, Indianapolis, IN
- **The Use of Nonclinical Assessment Strategies in the Prediction of Clinical Risks of Immunomodulatory Molecules: Case Study for Abatacept—A Selective Co-Stimulation Modulator**, Helen Haggerty, Bristol-Myers Squibb, East Syracuse, NY

## THURSDAY

### INNOVATIONS OF APPLIED TOXICOLOGY (IAT)

#### Blood-Based Genomic Profiles as Biomarkers of Exposure and Effect

Thursday, March 11, 9:00 AM–11:45 AM

*Chairperson(s): Russell S. Thomas, The Hamner Institutes for Health Sciences, Research Triangle Park, NC, and Richard S. Paules, NIEHS, Research Triangle Park, NC*

*Sponsor:*

Molecular Biology Specialty Section

*Endorsed by:*

Drug Discovery Toxicology Specialty Section

Regulatory and Safety Evaluation Specialty Section

Over the past decade, advances in genomic technology have transitioned its application from a specialized research tool to a robust, off-the-shelf commodity for both research and clinical use. Current technology has become more reliable and reproducible with broad-

coverage of genomic analytes thereby providing an ideal platform for biomarker discovery, validation, and application. However, identifying genomic-based biomarkers of chemical exposure and, in particular, biomarkers of effect from most target tissues (e.g., liver, kidney) would require biopsy samples from human subjects that would be difficult, if not impossible to obtain. As a result, recent research has focused on deriving blood-based genomic biomarkers that can predict exposure and organ-specific toxicity. This session will provide an overview of the new research on the identification and validation of genomic biomarkers from peripheral blood mononuclear cells, exosomal microparticles, and circulating miRNA and mRNA with application to predicting chemical exposure and effects. This session should be of wide-ranging interest to those involved in drug development, biomonitoring interpretation, and risk assessment.

- **Isolation and Characterization of Blood-Borne Free and Microparticle-Associated mRNAs to Predict Drug-Induced Liver Injury**, Barbara Wetmore, The Hamner Institutes for Health Sciences, Research Triangle Park, NC
- **Blood Transcriptomic Findings in Acute Liver Injury**, Richard S. Paules, NIEHS, Research Triangle Park, NC
- **Application of Circulating miRNAs to Predict Drug Induced Liver Injury**, David Galas, Institute for Systems Biology, Seattle, WA
- **Blood-Based Genomic Profiles of Humans Exposed to Carcinogens**, Martyn Smith, University of California, Berkeley, CA

### TRANSLATIONAL TOXICOLOGY

#### Humanized Models in Toxicology and Their Application to Hazard Characterization and Risk Assessment

Thursday, March 11, 9:00 AM–11:45 AM

**Chairperson(s):** Darrell R. Boverhof, Dow Chemical Company, Midland, MI, and Cliff Elcombe, CXR Biosciences Ltd., Dundee, United Kingdom

**Sponsor:**  
Mechanisms Specialty Section

**Endorsed by:**  
Risk Assessment Specialty Section

The toxicity testing paradigm is at a turning point. Many are calling for the implementation of new approaches, models, and technologies in order to enhance and refine the hazard and risk assessment process. Important components to the emerging views are implementation of mode/mechanism-of-action data, a greater focus on

human models/relevance, and a reduction in the use of animals. One important emerging tool that has the potential to advance the field is the use of humanized mouse models. Humanized models clearly offer the potential for increased use of mechanism/mode-of-action while inherently providing data on the potential human risk. Furthermore, if implemented strategically into the hazard and risk assessment paradigms, such models could obviate the need for large-scale animal testing thereby reducing animal use. However, the application of these data to human risk assessment requires appropriate and consistent interpretation of the data and acceptance of a given mode-of-action and its relevance to humans. Such acceptance requires discussion and consensus among all relevant stakeholders. The goal of this session is to provide examples of humanized models that are being used in toxicology and to initiate discussions on the use of these data in the evaluation of hazard relevance and risk assessment in humans.

- **Transgenic Human AHR Mouse and Human Risk Assessment**, Gary Perdew, The Pennsylvania State University, University Park, PA
- **Nuclear Receptor (CAR/PXR) Humanized Mouse Models to Investigate Nongenotoxic Hepatocarcinogenesis**, Clifford Elcombe, CXR Biosciences Ltd, Dundee, United Kingdom
- **Humanized Drug Metabolizing Enzyme Mouse Models-Potential Application in Safety Assessment of Drug Metabolites**, Alema Galijatovic-Idrizbegovic, Merck, West Point, PA
- **PPAR $\alpha$ -Humanized Mice and Human Risk Assessment**, Frank Gonzalez, National Cancer Institute, Bethesda, MD
- **Humanized Models in the Assessment of Novel Products Used Under Investigational New Drugs**, Martin Green, U.S. FDA, Rockville, MD

### CELL SIGNALING

#### Systems Biology Approaches to Understanding Cell Signaling in Dermal and Ocular Toxicology

Thursday, March 10, 9:00 PM–11:45 PM

**Chairperson(s):** Carol L. Sabourin, Battelle, Columbus, OH, and Jeffrey Yourick, Joint Science & Technology, Fort Belvoir, VA

**Sponsor:**  
Dermal Toxicology Specialty Section

**Endorsed by:**  
Ocular Toxicology Specialty Section

Transcriptomics, proteomics, and metabolomics provide high-throughput global analysis of the genome and associated interactive players. These approaches are colloquially described as ‘omics

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technologies and have been used to enhance the understanding of function, toxicological mechanisms, and risk assessment by identifying novel biomarkers of exposure including alterations in biological processes, cell signaling pathways, and specific genes. These 'omics studies typically generate large data sets in which bioinformatic interpretation requires unique and evolving computer-based analytical approaches, including large databases and an assortment of analytical tools. As the largest organ of the body, the skin performs multifunctional roles as a physical barrier, physiological mediator, communicator between the external environment and internal biological processes, and a vehicle for drug delivery. The skin consists of the epidermis and dermis composed of a multitude of cell types separated by a basement membrane. The eye consists of many diverse components such as the cornea, iris, pupil, lens, retina, macula, optic nerve, choroid, and vitreous. The corneal epithelium functions as a barrier to the environment and is susceptible to toxicant injury. The cornea must remain intact and transparent to refract light properly and disruption or disorganization of this structure can interfere with this process. The dynamic cell types of the skin and eye control multicellular processes through extensive networks of cell-to-cell communication that ultimately influence gene transcription and protein expression. Elucidating the complex molecular events underlying dermal and ocular responses to toxicants and drugs will assist in identifying biomarkers, developing safety assessment strategies, and accelerating the development of effective medical countermeasures. The practical applications of 'omics to understanding the toxic responses will be discussed.

- **Transcriptomics in Chemical-Exposed Skin: Current Status and Future Directions**, James Rogers, Battelle Memorial Institute, Columbus, OH
- **Cutting the Mustard: Application of Systems Biology Approaches to Identify Therapeutic Strategies for Treating Dermal Sulfur Mustard Injuries**, James Dillman, USAMRICD, Aberdeen Proving Ground, MD
- **Using Gene Expression Profiling of Nano-Scale Materials in Primary Human Epidermal Keratinocytes to Understand Cellular Interactions**, Mary Jane Cunningham, Nanomics Biosciences, Inc., Cary, NC
- **Ocular Toxicity Proteomics: Approaches for Differential Corneal Protein Identification**, John Schlager, Wright Patterson Air Force Base, Dayton, OH
- **Metabolomics: A Novel Tool for Understanding the Early-Stage Mechanistic Underpinnings of Safety**, Michael Milburn, Metabolon, Inc., Research Triangle Park, NC

## Toxicological Challenges in Green Product Development

Thursday, March 11, 9:00 AM–11:45 AM

**Chairperson(s):** Erica L. Dahl, Institute for In Vitro Sciences, Gaithersburg, MD, and David G. Allen, Integrated Laboratory Systems, Inc., Research Triangle Park, NC

**Sponsor:**  
In Vitro and Alternative Methods Specialty Section

**Endorsed by:**  
Occupational and Public Health Specialty Section

In recent years there has been a tremendous increase in the demand for products that are green. However, this claim can be difficult to define, and in some cases (e.g. restrictions on reproductive toxins or carcinogens) conflicts with the equally desirable claim that a product was not tested on animals. A number of independent organizations have emerged with the stated goal of validating these claims to help consumers navigate a bewildering array of products in their efforts to shop conscientiously. A closer examination of the safety testing required by these certifying organizations reveals some apparent conflicts. For example, organizations offering green certification forbid carcinogens or reproductive toxins in cleaning products, while organizations offering not tested on animal certifications forbid the *in vivo* testing that would be required to detect these endpoints. The purpose of this session is to bring together toxicologists who are working to reduce the environmental impacts of household and institutional cleaning products with those who are working to reduce animal testing. Our panel of experts includes toxicologists from industry, non-governmental organizations, and the government. It is our intent to identify strategies to reconcile apparent conflicts between green and not tested on animal claims while maintaining the high standards of safety testing required to protect human health and the environment. The overall goal is to begin building a consensus regarding a definition of green that is scientifically sound and minimizes reliance on animal testing.

- **The Role of Toxicology in Setting Green Product Standards**, Sarah Willems, JohnsonDiversey, Inc., Sturtevant, WI
- **Developing and Using Non-Animal Tests for the Consumer Products Industry**, Hans Raabe, Institute for In Vitro Sciences, Gaithersburg, MD
- **Evaluating and Certifying Green Claims**, Clif McLellan, NSF International, Ann Arbor, MI
- **The U.S. EPA Design for the Environment Program**, Emma Lavoie, U.S. EPA, Washington, DC
- **Incorporating Not Tested on Animals into Safety Assessment of Natural Cleaning Products**, Noe Galvan, The Clorox Company, Pleasanton, CA



## ROUNDTABLES

### MONDAY

#### Combination Toxicology Studies for Pharmaceutical Agents: Design Considerations and Impact on Clinical Development

Monday, March 8, 12:10 PM–1:30 PM

*Chairperson(s): Sushmita Chanda, Roche Palo Alto, Palo Alto, CA, and Hanan N. Ghantous, U.S. FDA, Silver Spring, MD*

**Sponsor:**

Regulatory and Safety Evaluation Specialty Section

**Endorsed by:**

Toxicologic and Exploratory Pathology Specialty Section

Drugs or biotherapeutics are often combined in the clinic to maximize efficacy. The impact of such combination therapies are well known in the field of oncology and viral therapy, specifically HIV. The benefits of combination therapies have influenced pharmaceutical industries to explore development of new molecular entities (NME) with either NMEs or marketed products, or the combination of marketed products. In 2006, the Committee for Medicinal Products for Human Use (CHMP) and the U.S. FDA issued guidelines for nonclinical safety evaluation for combination products. The need for combination toxicity studies are dependent on the existing clinical and nonclinical data for each individual compound that is used to support the proposed dose and duration in patients. Nonclinical combination toxicity studies are generally conducted to evaluate whether combination of two or more agents cause a potentiation, synergistic, or additive effects on target organ toxicities that were identified for individual compounds. Design of such studies is critical in hazard identification as it impacts clinical monitoring. Usually the most sensitive species is used. Dose selection for individual compounds should consider levels that have some minimal effect so that exacerbation or additive effects can be clearly evaluated. Usually establishment of a NOAEL is not necessary, unless it is being developed as a co-formulation and there is lack of clinical/nonclinical data on individual compounds. Duration of studies depends on the type of toxicity profile that is seen with individual compounds and usually does not exceed more than 90 days of dosing. Integration of data from ADME, PK, and clinical studies for individual compounds is important for designing successful combination toxicity studies. The roundtable will discuss general considerations for when and how to conduct combination toxicity studies with special focus on design considerations and challenges. Case examples and shared learning from combination toxicity studies and the impact on clinical monitoring will be discussed.

- **Regulatory Perspective on Combination Toxicity Studies,** Hanan N. Ghantous, U.S. FDA, Silver Spring, MD

- **Points to Consider in Designing Combination Toxicity Studies,** Sushmita M. Chanda, Roche Palo Alto, Palo Alto, CA
- **Case Studies: Selection of Doses, Species and Duration for Combination Toxicity Studies,** Lorrene A. Buckley, Eli Lilly & Company, Indianapolis, IN
- **Impact of Combination Toxicity Findings on Clinical Monitoring,** Leigh Ann Burns Naas, Pfizer Global Research and Development, San Diego, CA

#### Melamine Contamination of Infant Formulas: Lessons Learned

Monday, March 8, 12:10 PM–1:30 PM

*Chairperson(s): Wilson K. Rumbeiha, Michigan State University, Lansing, MI, and Madhusudan G. Soni, Soni & Associates Inc., Vero Beach, FL*

**Sponsor:**

Food Safety Specialty Section

**Endorsed by:**

Comparative and Veterinary Specialty Section  
Risk Assessment Specialty Section

In September 2008, officials in China acknowledged that illegal use of a fraudulent protein substitute, melamine, for months had contaminated powdered infant formula that was sold throughout the country. The tainted formulas also entered the market in several countries, in South East Asia and Africa. In the Peoples Republic of China alone at least 51,900 children are believed to have been affected by tainted food products, of whom 6 died. Some milk products contained > 2000 ppm melamine. In 2007 pet food contaminated with melamine, cyanuric acid, ammelide, and ammeline affected thousands of cats and dogs in North America. In the pet food outbreak, the pathogenesis involved co-precipitation of melamine and cyanuric acid in renal distal tubules and collecting ducts, causing acute renal failure. In the infant formula outbreak, the cardinal toxic effect of melamine in these children was the presence of kidney calculi, leading to acute kidney injury. Unlike in pets where melamine-cyanurate interaction was a significant phenomenon in pathogenesis of acute renal failure, in infants the crystals consisted of melamine alone. The mechanism of melamine-induced nephrotoxicity in infants remains unknown. This emerging disease is likely to occur again because of the widespread use and availability of melamine and its analogues in the environment. The objectives of this session are to offer the current scientific status of this tragedy arising from the unscrupulous use of melamine in infant formula and how to use this knowledge to develop better public health and safety policies. Presentations will cover comparison between renal failure in pet food and infant formula outbreaks, dose-response, and risk assessment considerations of melamine

## ROUNDTABLES

in infants, the chemistry and analysis of melamine and analogues in food for risk assessment purposes, guidance on levels of health concern in foods, and regulatory aspects.

- **A Comparison between Pet Food Recall and Infant Formula Incidence in China**, Renate Reimschuessel, U.S. FDA, College Park, MD
- **Dose-Response and Risk Assessment Considerations of Melamine in Infants**, Christopher Portier, NIH, Research Triangle Park, NC
- **Risk/Safety Assessment of Melamine and Its Congeners in Food Products**, David Hattan, U.S. FDA, College Park, MD
- **Analysis of Melamine and Analogues in Food for Exposure and Risk Assessment**, Sheryl Tittlemier, Health Canada, Ottawa, Ontario, Canada

### Inhaled Particles: From the Nose to the Brain?

**Monday, March 8, 4:35 PM–5:55 PM**

**Chairperson(s):** *Flemming Cassee, National Institute for Public Health and the Environment, Bilthoven, Netherlands, and Alison Elder, University of Rochester Medical Center, Rochester, NY*

**Sponsor:**

Inhalation and Respiratory Specialty Section

**Endorsed by:**

Nanotoxicology Specialty Section  
Neurotoxicology Specialty Section  
Risk Assessment Specialty Section

Particle toxicology has come a long way from revealing the prominent role for coal and silica-induced diseases in the early 20<sup>th</sup> century, to investigating the infamous asbestos fibers, to the more recent discussion on man made mineral fibers, ambient particulate matter, and engineered nanoparticles. The focus has gradually expanded from the traditional target organ, the respiratory system, to extra-pulmonary organs such as the heart, vascular system, and more recently the brain. While particle translocation into the brain occurs under certain conditions, the specific mechanisms linking particle exposures to physiological responses in the central nervous system remain to be investigated. The same is true for the functional effects noted in volunteers exposed to (combustion derived) ultra-fine or nanoparticles. This session will present the latest findings regarding nose-particle-brain interactions both from the viewpoint of ambient (ultrafine) particles and engineered nanoparticles.

- **Inhaled Particles: From the Nose to the Brain: An Overview**, Flemming Cassee, National Institute for Public Health and the Environment, Bilthoven, Netherlands
- **Translocation of Nano-Sized Particles to the Central Nervous System: Physicochemical Considerations**, Alison Elder, University of Rochester Medical Center, Rochester, NY
- **Nanoparticle Transport from the Lungs to the Brain: Role of the Circulatory Pathway**, Wolfgang G. Kreyling, Helmholtz Center, Munich, Germany
- **Concentrated Particulate Matter, Oxidative Stress, and Neurodegeneration: *In Vivo* and *In Vitro* Models**, Bellina Veronesi, U.S. EPA, Research Triangle Park, NC
- **Effects of Diesel Engine Exhaust and Carbon Nanoparticle Inhalation in Rat and Mouse Brain**, Roel P.F. Schins, Institut for Umweltmedizinische Forschung, Dusseldorf, Germany
- **Brain Regions Show Variation in Response after Diesel Engine Exhaust and Traffic-Derived Particulate Matter**, Arezoo Campbell, Western University, Pomona, CA
- **Exposure to Diluted Diesel Engine Exhaust Causes Changes in Brain Activity but not in Cognitive Performance in Human Volunteers or Rats**, Paul J.A. Borm, Centre of Expertise Life Sciences, Heerlen, Netherlands

### Safety of Vitamins and Minerals: Controversies and Perspectives

**Monday, March 8, 4:35 PM–5:55 PM**

**Chairperson(s):** *Madhusudan G. Soni, Soni & Associates Inc., Vero Beach, FL, and Stanley Omaye, University of Nevada Reno, Reno, NV*

**Sponsor:**

Food Safety Specialty Section

**Endorsed by:**

Carcinogenesis Specialty Section  
Regulatory and Safety Evaluation Specialty Section  
Risk Assessment Specialty Section

Available information suggests that currently over 47% of males and 59% of females use dietary supplements for health benefits, and the number of users is rapidly increasing. However, numerous studies published over more than a decade have linked some supplements (including vitamins E, C, D, A, and B, as well as selenium) to no health benefits or even to adverse health effects. The recent studies with negative results to draw media attention include: a 2008 study on the ability of vitamin E and selenium to lower prostate cancer



## ROUNDTABLES

risk that was halted amidst fear of potential harm; vitamin C may do more harm than good as it may protect cancer cells; intake of vitamins E and C by 15,000 male physicians for 10 years had no health benefits. In contrast, there are compelling cause and effect data linking use of folic acid containing multivitamins with consistent and significant reductions in adverse pregnancy outcomes; benefits of calcium and vitamin D supplements in improving bone strength and reducing fractures. These conflicting findings have left consumers confused about the benefits and wary of the possible adverse effects of vitamin and mineral supplementation. The objectives of this session are to characterize the current state of the science as it relates to the impact of vitamin and mineral supplementation on human health; review the statutory and regulatory perspective on vitamin use from a safety perspective; assess the credibility of meta-analysis in the safety assessment of vitamins; and elicit the mechanisms of these interactions—prooxidant vs. antioxidant effects or beneficial vs. adverse effects.

- **Are Vitamins and Minerals Used for Prevention or Treatment? Statutory and Regulatory Perspective**, Thane S. Thurmond, U.S. FDA, College Park, MD
- **Meta-Analysis: High-Dosage Vitamin E Supplementation May Increase All-Cause Mortality**, Edgar R. Miller, The Johns Hopkins Medical Institutions, Baltimore, MD
- **Beta-Carotene Supplementation: Example of When Lifestyle Habits Can Increase Risk Factors**, Adrienne Bendich, GSK Consumer Healthcare, Parsippany, NJ
- **Supplements: Pro-Oxidant Versus Antioxidant Effects or Beneficial Versus Adverse Effects**, Stanley T. Omaye, University of Nevada Reno, Reno, NV

### **The Evolution of the Extended One-Generation Study Design for Agricultural and Industrial Chemical Hazard Identification**

**Monday, March 8, 4:35 PM–5:55 PM**

*Chairperson(s): Edward Carney, The Dow Chemical Company, Midland, MI, and James Lamb, Exponent, Inc., Alexandria, VA*

**Sponsor:**

Reproductive and Developmental Toxicology Specialty Section

**Endorsed by:**

Immunotoxicology Specialty Section

In 2006, the International Life Sciences Institute (ILSI) Health and Environmental Sciences Institute (HESI) recommended a new approach to the safety assessment of agricultural chemicals (36:37, 2006). This approach modified the testing required for agricultural

chemicals and emphasized the use of pharmacokinetics in dose level selection. Among the most significant changes is the inclusion of an extended one-generation study design in which chemicals can be evaluated for effects on the developing nervous, reproductive, and immune systems. Since its inception in 2006, several laboratories have worked with the extended one-generation study design. Based on the experiences of these laboratories, modifications to the study design have been introduced. Furthermore, the extended one-generation study is being developed as an OECD test guideline with some additional design modifications. Therefore, the implementation has reached a critical nexus, where for the first time data are available to assess the practicality of the design and remaining challenges. This roundtable session will present experiences with the extended one-generation study and opinions on its use from both laboratory scientists and regulators. The goal of this session will be to discuss the strengths and weaknesses of the extended one-generation study approach proposed for the hazard assessment of both agricultural and industrial chemicals.

- **The Extended One-Generation Study Design: A New Approach to Life Stages Toxicity Testing**, Ralph Cooper, U.S. EPA, Research Triangle Park, NC
- **European Chemical Producers Association (ECPA) Demonstration Studies: Positive Control Studies for Developmental Neurotoxicity, Developmental Immunotoxicity, and Reproductive Toxicity Using the Extended One-Generation Study Design**, Larry Sheets, Bayer CropScience, Stilwell, KS
- **Using the Extended One-Generation Study to Fulfill Data Requirements: A Case Study with 2,4-D**, Sue Marty, The Dow Chemical Company, Midland, MI, and Barbara Neal, Exponent, Alexandria, VA
- **Development of an OECD Test Guideline on the Extended One-Generation Study**, Liz Mendez, U.S. EPA, Washington, DC

## ROUNDTABLES

### TUESDAY

#### TRANSLATIONAL TOXICOLOGY

##### Can Animal Neurotoxicity Predict Human Dysfunction?

Tuesday, March 9, 7:30 AM–8:50 AM

*Chairperson(s): Philip J. Bushnell, U.S. EPA, Research Triangle Park, NC, and William K. Boyes, U.S. EPA, Research Triangle Park, NC*

**Sponsor:**

Neurotoxicology Specialty Section

**Endorsed by:**

Risk Assessment Specialty Section

An important purpose of animal toxicity studies is to predict human disease, with the goal of minimizing the impact of chemical exposures on public health. Animal experiments can assert causal relationships between exposure and effect, characterize profiles of effects and, in conjunction with pharmacokinetic and empirical models, quantify dose-response relationships and their impact on public health. This discussion will evaluate the ability of animal models to predict effects on public health, including advantages and disadvantages of several approaches, by addressing the following. What aspects of an animal model enable one to predict impacts on human health? What information is needed to make such predictions quantitative? Can animal models account for differences in sensitivity to chemical toxicants? What is the role of behavioral and other whole-animal tests in toxicology in the 21<sup>st</sup> century? How can animal models facilitate the development of biomarkers of neurotoxicity? These questions will be explored using four cases in which animal models have revealed significant characteristics of exposure to neurotoxic chemicals.

- **Introduction: Raising the Issues**, William K. Boyes, U.S. EPA, Research Triangle Park, NC
- **Worms, Metals, and Parkinson's Disease**, Richard Nass, Indiana University School of Medicine, Indianapolis, IN
- **PCBs, Attention, and Impulsivity: Studies in Animals and Humans and Parallels with Attention Deficit Hyperactivity Disorder (ADHD)**, Susan L. Schantz, University of Illinois Urbana Champaign, Urbana, IL
- **Translational Studies of Organophosphorus Pesticide-Induced Neurobehavioral Deficits**, K. Matthew Lattal, Oregon Health Science University, Portland, OR
- **Modeling Acute Neurobehavioral Effects of Inhaled Volatile Organic Solvents**, Philip J. Bushnell, U.S. EPA, Research Triangle Park, NC

##### Weighing Complex Data in Risk Decisions: Concepts of Evidence-Based Toxicology

Tuesday, March 9, 7:30 AM–8:50 AM

*Chairperson(s): James Bus, The Dow Chemical Company, Midland, MI, and Barbara D. Beck, Gradient Corporation, Cambridge, MA*

**Sponsor:**

Academy of Toxicological Sciences

**Endorsed by:**

Mechanisms Specialty Section  
Occupational and Public Health Specialty Section  
Risk Assessment Specialty Section

One of the most significant challenges facing toxicology today is how the regulatory community can incorporate complex mode-of-action information into science-based decision making. Toxicology has made significant progress in developing and promoting use of mode-of-action frameworks as tools to transparently organize complex toxicology datasets for regulatory evaluations. However, implementation of framework approaches continues to be hindered by a lack of understanding and agreement as to how to efficiently and effectively weigh the data used in ultimate decision-making, i.e., when is it known how much is enough. The medical community has initiated the practice of Evidence-Based Medicine (EBM), a data evaluation approach that has been successfully used to improve translation of complex clinical information into effective medical practice. The principles and approaches of EBM offer significant opportunity for parallel application to complex problems in toxicology, and in recent years active discussion has emerged within the field of toxicology on the potential value of incorporating EBM into what has been termed Evidence-Based Toxicology (EBT). The exploration and discussion of EBT is of great importance to toxicology in that the ability to sustain core support for mode-of-action research is in part dependent on its efficient and reasoned incorporation into regulatory decision-making. Therefore the goal of this roundtable will be to introduce the topic of EBT and to discuss its potential as a tool for moving complex toxicology mode-of-action datasets into regulatory decision-making.

- **Evidence-Based Toxicology: Learnings from Evidence-Based Medicine**, Phil Guzelian, University of Colorado Health Sciences Center, Centennial, CO
- **Evidence-Based Toxicology: Improving the Reliability of Data and Tool Appraisal in Toxicological Practice**, Thomas Hartung, Johns Hopkins Medical Institutions, Baltimore, MD



## ROUNDTABLES

- **Hypothesis-Based Approaches to Weighing Information of Complex Datasets**, Lorenz Rhomberg, Gradient Corporation, Cambridge, MA
- **Incorporation of Complex Mode-of-Action Information into Mode-of-Action Framework Analyses**, Vicki Dellarco, U.S. EPA, Washington, DC

### TRANSLATIONAL TOXICOLOGY

#### The Ying and Yang of Immunomodulatory Biopharmaceuticals: What Have We Learned since MABEL and How Close Are We to the Clinical Dose?

Tuesday, March 9, 12:00 NOON–1:20 PM

*Chairperson(s):* Joy A. Cavagnaro, Access BIO LLC, Boyce, VA, and Tony R. Arulanandam, Regeneron Pharmaceuticals, Tarrytown, NY

*Sponsor:*

Immunotoxicology Specialty Section

*Endorsed by:*

Comparative and Veterinary Specialty Section  
Drug Discovery Toxicology Specialty Section

Given the fine balance between achieving the desired pharmacology *versus* unintended pharmacology, immunomodulatory biopharmaceuticals present significant challenges for identification of risks from preclinical models to estimation of First in Human (FIH) doses. As an extension to last year's biotherapeutics roundtable discussion on the concepts of when a Minimal Anticipated Biological Effect Level (MABEL), a Pharmacologically Active Dose (PAD), or No Observable Adverse Effect Level (NOAEL) approach should be considered for setting FIH doses, this session will discuss application and clinical validation of the various approaches. Selection of the most appropriate approach is dependent on a clear understanding of the target biology and pharmacology of the biopharmaceutical in question in pharmacologically relevant animal species and/or animal models of disease and appropriate human *in vitro* systems that can better predict the outcome in humans. In cases where immune activation is desired, exaggerated immune responses could lead to adverse immune related events (e.g. cytokine release, systemic inflammatory response, and organ failure) that in some cases may have serious consequences. Similarly in cases where immune modulation is desired to combat autoimmune inflammatory disease the exaggerated pharmacology can result in immunosuppression resulting in serious infections that in some cases have also been fatal. Immune antagonist targets may also be considered high risk in causing unintended immune activation and may warrant MABEL or alternate preclinical strategies for

estimating FIH dosing. A retrospective analysis of estimated FIH doses for both immune agonist and antagonist classes of immunomodulator biopharmaceuticals in clinical development will be presented and compared to the eventual dose used in the clinical trial to demonstrate safety and efficacy. Case examples of when MABEL *vs.* NOAEL *vs.* PAD approach was relevant to FIH dosing will be discussed.

- **Introduction**, Joy Cavagnaro, Access BIO LLC, Boyce, VA, and Tony R. Arulanandam, Regeneron Pharmaceuticals, Tarrytown, NY
- **Antagonizing the Suppressor, the Anti-CTLA4 mAb Experience in Cancer**, Jesus Gomez-Navarro, Pfizer, Inc., Groton, CT
- **IL-21 Case Study for Cancer: Retrospective Analysis of the MABEL Approach**, Dennis Miller, ZymoGenetics Inc, Seattle, WA
- **Anti-IL12 mAb a Potent Inhibitor of IL-12 and IL-23 Responses for Autoimmune Disease Indications**, William Bracken, Abbott Laboratories, Abbott Park, IL
- **FIH Dose Estimation Strategies for High Risk Immune Antagonist Targets: Anti-OX40L mAb and Anti-Beta7 integrin mAb Experiences in Clinical Dose Evaluation**, Tom Gelzleichter, Genentech, Inc., South San Francisco, CA
- **MABEL vs NOAEL: What the Food and Drug Administration has Learned About from Their Review of Immunomodulatory Biologic Drugs**, Carmen Booker, U.S. FDA, Silver Spring, MD

#### Women's Health: Toxicology and Safety of Complementary and Alternative Medicine

Tuesday, March 9, 12:00 NOON–1:20 PM

*Chairperson(s):* Brinda Mahadevan, Schering-Plough Research Institute, Summit, NJ, and Diana J. Auyeung-Kim, Charles River Preclinical Services, Reno, NV

*Sponsor:*

Women in Toxicology Special Interest Group

*Endorsed by:*

Food Safety Specialty Section  
Molecular Biology Specialty Section  
Regulatory and Safety Evaluation Specialty Section

The World Health Organization estimates that 65–80% of the world's population use traditional medicine as their primary form of health care. As the incidence in disease states affecting women increases, a corresponding increase in the use of complementary and alternative medicines (CAM) has been observed. In the Asian cultures, CAM has had a long history of development and appli-

## ROUNDTABLES

cation in the treatment of many diseases affecting multiple organ systems. Approximately 38% of adults in the U.S. currently use some form of CAM therapy (20% of women in the U.S. use some form of CAM therapy for control of menopausal symptoms or other related health concerns alone), some of which are used in conjunction with conventional medicine. In 21<sup>st</sup> century medicine, the value of CAM has been considered and questioned due in part to the use of advanced technologies in bringing novel insights into the unique features of CAM. However, there are safety concerns in the use of CAM that may interfere with conventional medicine or pose unique safety risks for susceptibility to other disease states. Presenters in this session will discuss the use of CAM to improve women's health. Specific topics that will be addressed are the impact of CAM on breast and endometrial cancers and menopause in addition to the advantages and disadvantages of CAM in each health related paradigm. The overall goal of this session is to highlight the current status of toxicology issues in the use of CAM in women's health. In addressing these issues, we are hopeful that attendees will develop a better appreciation of the use of CAM and the challenges that arise with their use with respect to safety.

- **Introduction**, Diana J. Auyeung-Kim, Charles River Preclinical Services, Reno, NV
- **Current Status and Toxicology Issues in CAM Used for Women's Health**, Jie Liu, NIEHS, Research Triangle Park, NC
- **Breast and Endometrial Safety of CAM Interventions**, J. Mark Cline, Wake Forest University School of Medicine, Winston-Salem, NC
- **Dietary Phytoestrogens and Breast Cancer: A Complex Safety Issue Involving Dose and Timing of Exposure**, Bill Helferich, University of Illinois at Urbana-Champaign, Urbana, IL

The field of oligonucleotide (ON) therapeutics is expanding rapidly, with applications to a broad array of molecular targets and disease indications. In general, various classes of ONs are categorized by their mechanism of action. Historically, the most familiar subclass is comprised of single-stranded DNA antisense ON, where hybridization to specific mRNA sequences inhibits expression of targeted proteins. Antisense ONs have been intensively investigated for nearly two decades, with one approved product and numerous other undergoing clinical development, several of which have recently been reported to exhibit compelling clinical pharmacology. Another type of application is the aptamer subclass. These molecules are identified through an elaborate screening process that selects for high affinity binding of a target protein. Thus far, one ON aptamer has been approved, and several other are undergoing clinical evaluation. As more is learned about RNA biology, the field has expanded to include therapeutic ONs that work through novel molecular mechanisms. An example is the emerging subclass of small interfering RNAs (siRNAs), which are double-stranded RNA molecules that act through RNA interference (RNAi). These siRNA also inhibit expression of proteins *via* targeted hybridization to specific mRNA sequences. The pharmacologic potency of these molecules has been impressive in nonclinical investigations, and several have entered the clinic. On the horizon are several new applications of ONs involving modulation of gene expression, and the one that has garnering most attention is the microRNA subclass. The expansion of the potential therapeutic utility of ONs is driven by a boom in the appreciation of the native role that RNA plays in regulation of the production of proteins through endogenous antisense, RNAi or micro-RNA interactions. This session will provide an overview of the regulatory perspective on development of ON-based therapeutics and will provide several examples of development programs that represent the various subclasses of ONs.

- **Screening and Selection of Antisense Oligonucleotides for Development**, Scott Henry, Isis Pharmaceuticals, Carlsbad, CA
- **Challenges of siRNA Delivery for Therapeutic Application**, Thomas Singer, Hoffman-LaRoche, Inc., Basel, Switzerland
- **Unique Therapeutic Opportunities and Challenges for Micro RNA**, Lisa Hildebrandt-Eriksen, Santaris Pharmaceuticals, Hoersholm, Denmark
- **General Considerations and Toxicology Program Design for Therapeutic Aptamers**, Page Bouchard, Archemix, Lexington, MA

## WEDNESDAY

### Overview of Current Regulatory Expectations for Oligonucleotide-Based Therapeutics: Case Studies for Different Classes of ODNs

Wednesday, March 10, 4:30 PM–5:50 PM

*Chairperson(s):* Scott P. Henry, ISIS Pharmaceuticals, Carlsbad, CA, and Doug Kornbrust, Preclinsight, Reno, NV

*Sponsor:*

Regulatory and Safety Evaluation Specialty Section

*Endorsed by:*

Drug Discovery Toxicology Specialty Section

## HISTORICAL HIGHLIGHTS

### TRANSLATIONAL TOXICOLOGY

#### **Translating Toxicology to Public Health Protection: Lessons Learned from Superfund**

**Monday, March 8, 12:10 PM–1:30 PM**

*Chairperson(s): Michele La Merrill, Mount Sinai School of Medicine, New York, NY, and Claudia Thompson, NIEHS, Research Triangle Park, NC*

**Sponsor:**

**Occupational and Public Health Specialty Section**

**Endorsed by:**

**Postdoctoral Assembly  
Research Funding Committee**

The NIEHS strives to improve human health through the translation of scientific discoveries from bench to policy and bench to public health. The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) defined and refined how toxicology can translate to public health benefits. This includes using the best available science to make health protective decisions at Superfund sites and conversely adapting what is learned at sites to inform new research directions. This two-way communication is exemplified by the NIEHS Superfund Research Program (SRP). The SRP, mandated by Congress to complement the applied nature of the national Superfund program, supports teams of scientists from the biomedical, engineering, environmental, and ecological disciplines to provide fundamental knowledge that could be used by decision-makers. To accelerate the timeframe whereby science is used by decision-makers, each SRP must include translational activities which include technology transfer, community outreach, and partnership with governmental agencies. Superfund responses need to act on the best available science, and not be halted by knowledge gaps in toxicology. This session will examine what lessons have been learned from the SRP; how toxicological research can be translated to remediation decisions; how biomarkers can inform risk assessment; how biomonitoring can reduce exposure at contaminated sites; and how SRP innovation can benefit the multi-agency work at Superfund sites.

- **The NIEHS Superfund Research: Translating Basic Science to Human Health and Environmental Risk Assessment,** William Suk, NIEHS, Research Triangle Park, NC
- **The Use and Development of Biomarkers in Superfund Risk Assessment,** James Swenberg, University of North Carolina, Chapel Hill, NC
- **Translation of Toxicological Mechanisms into Bioassays for Chemical Detection and Site Characterization,** Michael S. Denison, University of California, Davis, CA

- **Integrating Health Promotion into Biomarker Studies,** Thomas McDonald, Bayer HealthCare Pharmaceuticals, Richmond, CA
- **Translating Innovations of the Superfund Research Program into the Future,** Linda Birnbaum, NIEHS, Research Triangle Park, NC

## INFORMATIONAL SESSIONS

### TOXICITY TESTING IN THE 21<sup>ST</sup> CENTURY

#### Human Hepatocytes Derived from Embryonic Stem Cells: A New Tool for *In Vitro* Toxicity Testing

Tuesday, March 9, 7:30 AM–8:50 AM

*Chairperson(s):* Claudia McGinnis, Apredica Inc, Watertown, MA, and Glenn Prestwich, The University of Utah, Salt Lake City, UT

*Sponsor:*

*In Vitro* and Alternative Methods Specialty Section

*In vitro* methods for liver toxicity testing have seen poor acceptance as an alternative to animal testing because of low specificity and sensitivity to *in vivo* outcomes. Hepatocytes are highly differentiated cells with complex functions that are particularly difficult to be maintained over an acceptable timeframe. Recently, some advances have been made to improve hepatocyte longevity and functionality using 3D and co-culture technologies. However, these models rely on the continuous availability of human primary liver cells obtained from a limited number of human donors. As a result, good quality cells are in short supply for research purposes. Generating functional hepatocytes from pluripotent stem cells would provide a continuous cell pool capable of expansion. The use of human embryonic stem cells (hESC) and differentiation into mature cell lineages is a new and rapidly evolving area of research with a great promise in generating alternative *in vitro* models to study human toxicities. However, while considerable advances have been made in recent years to develop hepatocyte-like cells from embryonic and other stem cells, the application of hESC-derived hepatocytes in toxicology still faces several challenges. This session will describe methods, current and, future applications of hESC-derived hepatocytes for the assessment of mechanisms leading to hepatotoxicity. An overview will be given on technology developments necessary to generate an hESC-hepatocyte model which mimic adult liver function *in vitro*, has adequate enzymatic/transporter expression and longevity in long-term culture, and is translatable into higher throughput screening applications for predictive toxicity and ADME testing. Novel support systems will be described which have improved functionality and longevity of hESC-derived hepatocytes.

- **Human Hepatocytes Derived from Embryonic Stem Cells: A New Tool for *In Vitro* Toxicity Testing—Introduction**, Claudia McGinnis, Apredica Inc, Watertown, MA
- **A Polymer Matrix Promotes and Stabilizes hESC-Derived Hepatocyte Function**, David C. Hay, MRC Centre for Regenerative Medicine, Edinburgh, United Kingdom

- **Applications of hESC-Derived Hepatocytes in Toxicity and ADME Testing**, Claudia McGinnis, Apredica Inc, Watertown, MA
- **Engineered Extracellular Matrices for Regenerative Medicine and Drug Evaluation**, Glenn D. Prestwich, The University of Utah, Salt Lake City, UT

#### Recent Advances in Pulmonary Surfactant Toxicological Assessment and Therapeutics

Tuesday, March 9, 7:30 AM–8:50 AM

*Chairperson(s):* Richard A. Parent, Consultox, Limited, Damariscotta, ME, and Michelle A. De Crosta, Discovery Laboratories, Inc., Warrington, PA

*Sponsor:*

Inhalation and Respiratory Specialty Section

*Endorsed by:*

*In Vitro* and Alternative Methods Specialty Section  
Reproductive and Developmental Toxicology Specialty Section

Pulmonary surfactant is critical for proper respiratory function. The primary role of pulmonary surfactant is to reduce surface tension in the lung and prevent collapse of alveoli and distal airways, thereby preserving functional residual capacity and promoting gas exchange. Surfactants are a complex mixture of phospholipids and proteins. Phospholipids lower surface tension, while proteins play a critical role in a variety of functions related to respiratory health and development, including the further lowering of surface tension by maintaining the phospholipid monolayer. The introduction of surfactant replacement therapy (SRT) in the United States (U.S.) in 1990 for the treatment of respiratory distress syndrome (RDS) has led to reduced morbidity and mortality in preterm infants. There is evidence that surfactant dysfunction exists in other lung diseases, and clinical trials have been conducted investigating the use of SRT beyond the treatment of RDS. The initial exogenous pulmonary surfactant introduced in the U.S. was a blend of synthetic phospholipids. However, the exogenous surfactants currently available for therapeutic use all contain proteins extracted from animal sources, raising the possibility for the inclusion of prions and non-target substances into the surfactant. In addition, analyses of these animal-derived surfactants have revealed considerable variability in terms of purity as well as the concentration of the target surfactant proteins. These concern in turn raise questions regarding the potential toxicity of exogenous surfactants.

- **Recent Advances in Pulmonary Surfactant Toxicological Assessment and Therapeutics**, Michelle A. De Crosta, Discovery Laboratories, Inc., Warrington, PA



## INFORMATIONAL SESSIONS

- **Inherent Toxicological Issues Related to Animal-Derived Pulmonary Lung Surfactants for Treatment of RDS**, Michael F. Beers, University of Pennsylvania School of Medicine, Philadelphia, PA
- **Case Studies of *In Vivo* Models for Assessing SRT**, Russell G. Clayton, Discovery Laboratories, Inc., Warrington, PA
- **Utilization of High-Performance Liquid Chromatography with Charged Aerosol Detection (HPLC-CAD) Technology for Assessing Impurity Profiles in Synthetic and Animal-Derived Pulmonary Surfactants**, John G. Nikelly, University of the Sciences in Philadelphia, Philadelphia, PA

### Impact of Tungsten and Tungsten Alloys on Health Risk

Wednesday, March 10, 7:30 AM–8:50 AM

**Chairperson(s):** Palur G. Gunasekar, Naval Health Research Center Detachment, Wright-Patterson Air Force Base, Dayton, OH, and Michelle J. Hooth, NIEHS, Research Triangle Park, NC

**Sponsor:**

Metals Specialty Section

**Endorsed by:**

Carcinogenesis Specialty Section

Metals Specialty Section

Risk Assessment Specialty Section

Debate of the potential human health effects of tungsten (W) is fostered by widespread exposure to naturally occurring W in air, soil, water, and the diet and anthropogenic sources including the use of tungsten alloy (WA) in military munitions. There is particular concern about the exposure of military personnel to retained W-based munitions fragments. The cellular and molecular mechanisms of systemic W toxicity and the role of W speciation in W-induced toxicity remain poorly defined. Intensive research on the characterization of potential adverse health effects associated with tungsten exposure is underway and employs multiple routes of exposure including oral, inhalation and implantation. Other recent studies have characterized W transport mechanisms, pharmacokinetic parameters, and biochemical and pathological indices *in vitro* and *in vivo*. These efforts have identified new biomarkers of exposure and effect as well as new opportunities for therapeutic intervention or management of potential health hazards. This session will review current research programs as well as describe the recent studies examining the toxicity and carcinogenicity of embedded tungsten and heavy metal tungsten alloy pellets and refined corrosion assessments to define the degradation rate of the pellets. Our panel of experts will discuss the absorption/transport, distribution and elimination of tungsten and effects on the nervous system and immune system with particular

emphasis on the mechanisms through which W may produce toxic effects.

- **Tungsten and Tungsten Heavy Alloys: Health Effects and Metallographic Analysis of Tungsten and Tungsten Heavy Alloys Following Implantation in Rat Muscle**, Brian Schuster, AMSRD, Aberdeen Proving Ground, MD
- **Chemical and Microscopy Assessment of Tungsten in Tissues**, Jose Centeno, Armed Forces Institute of Pathology, Washington, DC
- **The Pharmacokinetics of Inhaled Tungsten**, David Dorman, North Carolina State University, Raleigh, NC
- **Rat Serum Antibodies Indicate Oxidative Stress and Renal Toxicity, but not Neurotoxicity Following Subchronic Exposure to Sodium Tungstate**, Wilfred C. McCain, U.S. Army, Aberdeen Proving Ground, MD
- **Immunotoxicity of Tungstate Following Oral Exposure**, Michael Stockelman, Wright-Patterson Air Force Base, Dayton, OH

### The 2009 Tennessee Fly Ash Spill: An Environmental Emergency Case Study

Wednesday, March 10, 7:30 AM–8:50 AM

**Chairperson(s):** Michael E. Otlinger, U.S. EPA, Cincinnati, OH, and Angela Harris, CTEH, North Little Rock, AR

**Sponsor:**

Occupational and Public Health Specialty Section

On December 22, 2008, at approximately 1:00 AM, a retaining wall supporting a surface impoundment of fly ash sludge at the Kingston Fossil Plant in Harriman, Tennessee, breached releasing an estimated 5.4 million cubic yards of material into the Emory and Clinch Rivers and surrounding areas. The release extended over approximately 300 acres of land outside of the containment site. A wave of ash and water destroyed homes, disrupted electrical and natural gas lines, covered roads and rail tracks, and necessitated the evacuation of nearby residents. Responders at the scene pursued a variety of activities intended to assess the extent of both the release and the potential hazard posed by the event and to contain the spread of any hazardous materials released into the environment. The roles, responsibilities, and interactions of various local, state, and federal partners present at the scene had a substantial impact on response activities. This included oversight of the development and initiation of a large program of environmental sampling of the air, soil, and water followed by analysis of the resulting data. The Tennessee fly ash spill is representative of other environmental emergencies, and is therefore an excellent case study in which to provide a framework for discussions concerning the role of toxicology in protecting

## INFORMATIONAL SESSIONS

environmental and human health in affected communities, and in determining the appropriate roles and actions of the various regulators at the scene. Information about the formation and toxicological hazards associated with fly ash will be presented, along with a discussion of the U.S. EPA incident command structure, regulatory issues, sampling strategies and limitations, as well as integration of all of this information into effective public health practice following such emergencies.

- **A Reprise of Fly Ash Chemistry and Toxicity**, Michael E. Ottlinger, U.S. EPA, Cincinnati, OH
- **Fly Ash Radioisotopes and Associated Hazards**, Jeffrey Nemhauser, CDC, Atlanta, GA
- **U.S. EPA Emergency Response to the TVA Fly Ash Release: A Federal On-Scene-Coordinator's Perspective**, David Dorian, U.S. EPA, Atlanta, GA, and Tim Frederick, U.S. EPA, Atlanta, GA
- **Review of the Statutory Basis for Federal Authorities and Discussion of the Status of Fly Ash Under Existing Environmental Law**, John Benitez, Vanderbilt University, Nashville, TN, and Saralyn Williams, Vanderbilt University, Nashville, TN

### Life-Stage Adjustment Five Years Later—Experiences from the Cancer Risk Assessment Field

Wednesday, March 10, 12:00 NOON–1:20 PM

*Chairperson(s):* Michael Dourson, Toxicology Excellence for Risk Assessment, Cincinnati, OH, and Clifton McLellan, NSF International, Ann Arbor, MI

*Sponsor:*  
Risk Assessment Specialty Section

*Endorsed by:*  
Carcinogenesis Specialty Section  
Regulatory and Safety Evaluation Specialty Section

In 2005, the U.S. EPA released the Guidelines for Cancer Risk Assessment (Cancer Guidelines) and the Supplemental Guidance Assessing Susceptibility from Early-Life Exposure to Carcinogens (Supplemental Guidance). The Cancer Guidelines describe the Agency's current methods for conducting cancer risk assessments, and introduce the framework for determining the mode-of-action (MOA) by which the chemical induces cancer. The Supplemental Guidance also considers MOAs and recommends the development of separate cancer potencies, based on early- and later-life exposures, for compounds with mutagenic MOAs. With the issuance of the Supplemental Guidance, the potential for children's risk to carcinogenic chemicals was explicitly addressed for the first time.

During the past several years, risk assessors in the public health field, state governments, and industry, have implemented the MOA framework and addressed the concept of life-stage susceptibility through a variety of approaches. The purpose of this session will be to share experiences and recent developments in the application of potency adjustments for carcinogens acting through a mutagenic or unknown MOA. Setting the stage will be a review from the U.S. EPA of the basis for early-life default factors and the conditions for their use in quantitative assessment. An example life-stage adjustment will be presented to illustrate an application of the guidance in establishing allowable concentrations in drinking water. In the consumer product area, the impact of the guidance on different population groups will be examined. Approaches taken by the Minnesota Department of Health in addressing groundwater contaminants and by the California EPA in addressing life-stage susceptibility will be presented.

- **U.S. EPA's Age-Dependent Adjustment Factors (ADAFs): What's Mode-of-Action (MOA) Got to Do with It?** Rita Schoeny, U.S. EPA, Washington, DC
- **Keeping it Transparent: The Use of Age-Dependent Adjustment Factors in Establishing Allowable Concentrations in Drinking Water**, J. Caroline English, NSF International, Ann Arbor, MI
- **Application of U.S. EPA Supplemental Guidance for Early Life Exposure to Consumer Products**, Susan Felter, Proctor & Gamble Company, Cincinnati, OH
- **Use of Early Life-Stage Cancer Potency Adjustments in Minnesota Groundwater Rules**, Helen Goeden, Minnesota Department of Public Health, St. Paul, MN
- **Potency Distributions for Age-Sensitive Factors Inform Life-Stage Adjustments**, Lauren Zeise, California EPA, Oakland, CA

### TRANSLATIONAL TOXICOLOGY

#### Measuring Immune Responses in Monkeys for Drug Development: Opportunities and Challenges for Predicting Human Efficacy and Immunotoxicity

Wednesday, March 10, 12:00 NOON–1:20 PM

*Chairperson(s):* Cris Kamperschroer, Pfizer Inc., Groton, CT, and Herve Lebec, Amgen, Inc., Seattle, WA

*Sponsor:*  
Immunotoxicology Specialty Section

As drug targets become increasingly diverse, we must adapt the approaches we use to evaluate drug efficacy and safety testing. Immunomodulatory drugs can be challenging to develop because



## INFORMATIONAL SESSIONS

some immunomodulatory targets are only expressed during an immune response, or they are expressed but display no measurable function in the absence of an immune response. In these cases, we must track immune responses in order to evaluate drug effects. In addition, immunomodulatory drugs may cause immunosuppression that can lead to opportunistic infections, creating a need to monitor immune responses against those infections. In recent years, there have been significant advances in methods for tracking immune responses. In drug development, monkeys (eg. macaques) are often used for studies when other species do not express the target or have insufficient homology to the intended human target or relevant biological system. These situations are becoming more common, increasing the need to induce and measure immune responses in monkeys. For human translation, it is desirable to develop and employ methods of immune monitoring that can be used in the clinic. Antigen-specific responses are preferred because they are more physiologically relevant than those driven by polyclonal stimulators or mitogens. However, there are significant challenges to measuring antigen-specific immune responses in monkeys, such as a lack of appropriate antigen, lack of specific reagents, and the inherently variable nature of immune responses in outbred populations. This session will focus on various methods currently being used to track immune responses in monkeys and how those measurements are being used to assess either efficacy or immunotoxic potential of test compounds. The session will include discussion of experiences from scientists in an academic setting, where the most current technologies are being developed, as well as experiences and challenges encountered by those in industry attempting to track immune responses in monkeys to support drug development.

- **Measuring Immune Responses in Monkeys for Drug Development—Opportunities and Challenges for Predicting Human Efficacy and Immunotoxicity**, Cris Kamperschroer, Pfizer Inc., Groton, CT
- **Immunotoxicology Assessment of Tuberculosis Risk**, JoAnne Flynn, University of Pittsburgh, Pittsburgh, PA
- **Monitoring T Cell Responses Against Chronic Viral Infections in Monkeys**, Amitinder Kaur, Harvard Medical School, Boston, MA
- **T-Dependent Antibody Responses and Immunophenotyping in Monkeys—Impact on Study Design and Interpretation**, Herve Lebec, Amgen, Inc., Seattle, WA

### TOXICITY TESTING IN THE 21<sup>ST</sup> CENTURY

#### The Tox21<sup>st</sup> Community and the Future of Toxicology Testing

Wednesday, March 10, 12:00 NOON-1:20 PM

*Chairperson(s):* Raymond Tice, NIEHS, Research Triangle Park, NC, and Robert Kavlock, U.S. EPA, Research Triangle Park, NC

*Sponsor:*

*In Vitro* and Alternative Methods Specialty Section

*Endorsed by:*

Molecular Biology Specialty Section

Regulatory and Safety Evaluation Specialty Section

Risk Assessment Specialty Section

In early 2008, the National Institute of Environmental Health Sciences/National Toxicology Program, the NIH Chemical Genomics Center, and the U.S. EPA's National Center for Computational Toxicology entered into a Memorandum of Understanding to collaborate on the research, development, validation, and translation of new and innovative test methods that characterize key steps in toxicity pathways. A central component is the exploration of high throughput screening assays and tests using phylogenetically lower animal species (e.g., fish, worms), as well as high-throughput whole genome analytical methods, to evaluate mechanisms of toxicity. The goals of the Tox21 Community are to investigate the use of these new tools to prioritize substances for further in-depth toxicological evaluation, identify mechanisms of action for further investigation, and develop predictive models for *in vivo* biological response. Success is expected to result in test methods for toxicity testing that are more mechanistically based and economically efficient; as a consequence, a reduction or replacement of animals in regulatory testing is anticipated to occur in parallel with an increased ability to evaluate the large numbers of chemicals that currently lack adequate toxicological evaluation. The initial focus of this collaboration has been on identifying toxicity-related pathways (and assays for those pathways), establishing a Tox21 library of ~10000 compounds, and developing the databases and bioinformatic tools needed to mine the resulting data. This session will inform the scientific community of progress in meeting the Tox21 goals, successful efforts to expand the collaboration nationally and internationally, novel assay platforms that have been integrated into the screening strategy, and how Tox21 data might be used for hazard identification and risk assessment.

- **The Tox21 Compound Library—Setting the Stage for High-Throughput Testing**, Cynthia Smith, NIEHS, Research Triangle Park, NC

## INFORMATIONAL SESSIONS

- **Predicting Toxicological Effects: Identifying Critical Cellular Pathways and Assays for Those Pathways**, Menghang Xia, NIH, Bethesda, MD
- **Tox21: Databases, Data Mining, and Predictive Patterns**, Richard Judson, U.S. EPA, Research Triangle Park, NC
- **The Tox21 Initiative and the Future of Toxicology**, Linda Birnbaum, NIEHS, Research Triangle Park, NC

### Seeking Funding for Undergraduate Research

**Wednesday, March 10, 4:30 PM–5:50 PM**

*Chairperson(s): Joan B. Tarloff, University of the Sciences in Philadelphia, Philadelphia, PA, and Vanessa Fitsanakis, King College, Bristol, TN*

**Sponsor:**

Education Committee

**Endorsed by:**

Postdoctoral Assembly

Research Funding Committee

Most undergraduate professors are adept at finding teaching and learning resources for their classrooms and students. It is often more difficult, however, for them to readily know where to go for research funding. Additionally, many undergraduate faculty may find the information posted on National Institutes of Health (NIH) or National Science Foundation (NSF) Web sites intimidating and difficult to navigate if the faculty are not used to the language of granting bodies or institutions. Available grants could be in the form of classroom and teaching enhancement, professional development, or research opportunities for faculty and students. Both the NIH and the NSF have grants specifically tailored to the needs of undergraduate students and faculty. This session will provide undergraduate faculty with the opportunity to hear presentations from representatives from both federal programs, and to ask questions of each. The goal is to link toxicology faculty and undergraduate teaching institutions with appropriate contacts at the NIH and NSF, as well as encourage them to apply for funding. Such opportunities will directly benefit the faculty and students, thus strengthening the future applicants for toxicology programs around the nation.

- **Seeking Funding for Undergraduate Research**, Joan B. Tarloff, University of the Sciences in Philadelphia, Philadelphia, PA
- **Academic Research Enhancement Awards (AREA) through NIH**, Michael Humble, NIEHS, Durham, NC
- **Research Experiences for Undergraduates (REU) Awards through NSF**, Sally O'Connor, NSF, Arlington, VA
- **Experiences with the AREA Program**, Eli Hestermann, Furman University, Greenville, SC

## EDUCATION-CAREER DEVELOPMENT SESSIONS

### Where Do I Go Now? Rational Career Development Planning for Early-Career Scientists

Tuesday, March 9, 9:00 AM–11:45 AM

*Chairperson(s):* Betina J. Lew, University of Rochester Medical Center, Rochester, NY, and Amy Wang, U.S. EPA, Research Triangle Park, NC

**Sponsor:**

Postdoctoral Assembly

**Endorsed by:**

Career Resource and Development Committee  
Student Advisory Council  
Research Funding Committee

Toxicology training during graduate school and postdoctoral fellowships provides early-career scientists with a wide array of transferable skills that can be used in many job sectors, but navigating the all of the possible career options can be a daunting task. Additionally, finding and preparing for a career path that is right for yourself is not always easy, particularly when it differs from that of your mentor or is non-traditional. The majority of students and postdocs are trained in academic institutions with resources that prepare them for a career in academia. However, a recent National Postdoctoral Association survey indicated that even though 45% of the postdocs plan on being a tenure-track faculty member, less than 20% will obtain this position. Therefore, it is important for early-career scientists to gather ample information and diverse experiences to better prepare them for multiple career paths. The first step in this process is to identify transferable skills and translate them into realistic paths towards a rewarding job.

With broad coverage of non-traditional career paths in toxicology, this session will provide early-career scientists with insight on how to map a career path that fits their passion and skills. Using an interactive format, speakers will identify tools to utilize in pursuit to navigating different paths. Discussions will include identifying marketable skills, rational career planning, networking, and improving marketability. Grant preparation will also be discussed during a presentation on writing a successful career transition grant application. Specifically, the K99/R00 grant program, which has no citizenship restrictions, provides support to an individual postdoctoral fellow transitioning to an independent faculty position.

- **How to Identify Your Skills and Passions**, Kristen Keefe, University of Utah, Salt Lake City, UT
- **Career Planning and Development for Early-Career Scientists**, Douglas Wolf, U.S. EPA, Research Triangle Park, NC
- **Improving Networking and Communication Skills**, Lori Conlan, NIH, Bethesda, MD

- **Making Yourself More Marketable in Private Industry**, James Popp, Stratoxon LLC, Lancaster, PA
- **The NIH Pathways to Independence Award: A Transition to an Academic Career**, Jerrold Heindel, NIEHS, Research Triangle Park, NC

### Science Communication in 2010: A New Decade in Toxicology and Need for Better Communication

Tuesday, March 9, 12:00 NOON–1:20 PM

*Chairperson(s):* Banalata Sen, NIEHS, Durham, NC, and Sneha Bhatia, Research Institute for Fragrance Materials, Inc., Woodcliff Lake, NJ

**Endorsed by:**

Ethical, Legal, and Social Issues Specialty Section  
Postdoctoral Assembly  
Women in Toxicology Special Interest Group

Scientists do science, writers write. Wrong! Scientists do science and write about it as well. It is imperative that scientists publish their work. Furthermore, publishing is just one aspect of science. Scientists also have to be able to communicate complex scientific concepts to the non-scientific audience. This large group of constituents include the general public, media, policymakers, communities, and individuals. This is an obligation scientists have towards the community-at-large and one that can be accomplished with relative ease once the basic nuances of effective communication are understood. Effective communication is therefore not just an icing on the cake, rather it is fundamental to interpretation and dissemination of science. Yet science communication is not an integral part of science education. Most scientists do not have any formal training in science writing. They learn to write by following the style and approach of their mentors or other authors. Some form of training in science writing becomes even more crucial for authors for whom English is a second language. Laying this basic foundation is important since the public learns about science from many different sources, including newspapers, magazines, books, radio, television, the Internet, electronic news services, and films. Because information is readily available at our finger tips it can easily be distorted with the unfortunate circumstance that bad science sometimes triumphs over good science. Therefore it is important for us to effectively communicate science messages to distinguish the myths from the facts. This session will aim to highlight strategies, techniques, and resources that make the field of good science communication invaluable.

- **Science Writing**, Jane Schroeder, NIEHS, Research Triangle Park, NC

Scientific

## EDUCATION-CAREER DEVELOPMENT SESSIONS

- **Blogs, Podcasts, and More**, Sneha Bhatia, Research Institute of Fragrance Materials, Inc., Woodcliff, NJ
- **Communicating Hazard**, Linda Birnbaum, NIEHS, Research Triangle Park, NC
- **Communication as a Career**, Banalata Sen, NIEHS, Research Triangle Park, NC
- **How Sputnik, Radiation Fallout, Chemical Toxicants, Bioethics for Hippies, Stem Cells, Sushi, Kimchie, and Gelato Led to a “Biological Rosetta Stone” for Human Diseases**, James E. Trosko, Michigan State University, East Lansing, MI
- **From Academia to Biotechnology: Beginning Your Own Company**, Judy Raucy, Puracyp, Inc., Carlsbad, CA

### Career Alternatives in Toxicology: Lessons Learned

Wednesday, March 10, 7:30 AM–8:50 AM

*Chairperson(s): Judy Raucy, Puracyp, Inc., Carlsbad, CA, and Hisham K. Hamadeh, Amgen, Inc., Thousand Oaks, CA*

#### *Sponsor:*

Career Resource and Development Committee

For individuals who desire to take a career break or those set to retire, many options are available. There are many avenues to explore including those that involve technical opportunities for toxicologists and environmental scientists. Of the many opportunities to explore, the Peace Corps and U.N. volunteer programs offer a myriad of opportunities for environmental scientists wishing to practice their trade abroad. In addition to these two examples, other alternatives will be discussed including those available in academia, which provides its own set of unique experiences. For example, just how does one go about leaving a career in cancer research and epigenetic toxicology to become an administrator at the Radiation Effects Research Foundation in Hiroshima, Japan? There are many positive sides to such a decision, including work on a historic project in a foreign country and interactions with scientists who may benefit from your insight; however, there can be disadvantages as well. Experienced panel members will highlight the “price-paid” for such decisions. What about options other than academic research, such as toxicologists with innovative ideas who wish to capitalize on their talents and drive by starting a biotechnology company? Our panel of experts will provide insight and tips on the challenges involved in bringing an idea for a commercial product to the market place. This specific discussion will note the distinct advantages and disadvantages of embarking on a career change from academia to establishing a biotechnology company. This last discussion will highlight the specific and unique challenges of starting a company, including acquisition of intellectual property rights, obtaining funding, and marketing of products. This session should be of interest to anyone looking to explore career alternatives off the beaten path.

- **International Technical Volunteering for Toxicology**, Timothy D. Landry, Peace Corps-Semarnat, Tlaxcala Tlax, Mexico



## REGIONAL INTEREST SESSION

### METABOLIC DISEASE

#### Signaling Mechanisms for Metabolic Dysfunction Following Low-Level Arsenic Exposures: From Mouse to Man

Monday, March 8, 1:40 PM–4:25 PM

**Chairperson(s):** Aaron Barchowsky, University of Pittsburgh, Pittsburgh, PA, and Richard Vaillancourt, University of Arizona, Tucson, AZ

**Sponsor:**

Metals Specialty Section

**Endorsed by:**

Mechanisms Specialty Section

Molecular Biology Specialty Section

Chronic low level arsenic exposure is a major public health concern, since it has been linked to increase risks of cardiovascular and metabolic-related diseases in human populations throughout the world. Epidemiological studies that carefully address arsenic speciation in complex exposure analysis provide evidence of arsenic related increases in atherosclerosis, stroke, and diabetes, even in the heterogeneous United States population. To identify the mechanisms for this disease promotion, recent *in vivo* animal studies have focused investigation on pathogenic responses and signaling in arsenic exposures that are in the low to moderate range of human exposures. These studies revealed that arsenic signals at multiple levels for systemic metabolic changes. Arsenic effects that result in diabetogenic hyperglycemia include redox-dependent suppression of signaling for insulin release from pancreatic beta-cells and direct effects on glucose transport processes. Altered glucose and lipid signaling for cytokine secretion following arsenic exposures have been implicated in generating chronic inflammation. Arsenic effects on macrophages and liver endothelial cells that are responsible for lipid clearance and regulating lipid metabolism, as well as bulk removal of atherogenic modified proteins or glycosaminoglycans, may explain the role of the metalloids in disease promoting deposition of lipids in vessel walls and abdominal fat. Receptor mediated activation of NADPH oxidases is implicated as a rate-limiting step in signaling for inflammation and vascular remodeling following arsenic exposure. Together, these epidemiological and animal studies provide mechanistic insight into molecular pathogenesis of metabolic effects of low level arsenic exposures that may contribute to increased risk of cardiovascular disease and diabetes.

#### Session Introduction

- **Arsenic Contamination in Mines and the Rocky Mountain Region**, Susan Griffin, U.S. EPA, Denver, CO
- **Arsenic Biomonitoring Equivalents in the Rocky Mountain Region**, Sean Hays, Summit Toxicology, Lyons, CO

#### Session Presenters

- **Low-Chronic Arsenic Exposure: Epidemiologic Evidence for Cardiovascular Disease and Diabetes**, Ana Navas-Acien, Johns Hopkins University, Baltimore, MD
- **Antioxidant Response and ROS Signaling in Arsenic-Induced Impairment of Pancreatic Beta-Cell Function**, Jingbo Pi, The Hamner Institutes for Health Sciences, Research Triangle Park, NC
- **Regulation of Glucose Transport Mechanisms by Arsenic**, Richard Vaillancourt, University of Arizona, Tucson, AZ
- **Arsenic as a Pro-Atherogen: Low Dose Effects on Nuclear Receptors and Inflammatory Signaling**, Koren Mann, McGill University, Montreal, Quebec, Canada
- **Arsenic Signaling for Liver Vasculature Remodeling Impacts Protein and Lipid Metabolism**, Aaron Barchowsky, University of Pittsburgh, Pittsburgh, PA

## STUDENT AND POSTDOCTORAL FELLOW EVENTS

### Student/Postdoctoral Fellow Mixer

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**Sunday, March 7, 7:30 PM–8:30 PM**

*Ticket Required*

**Sponsor:**

**Student Advisory Council**

The Student Advisory Council and Graduate Committees host this opportunity for students and postdoctoral fellows to gather, meet new colleagues, and reestablish relationships in an informal atmosphere at the beginning of the meeting. Tickets are obtained at no cost by registering for this event on the Annual Meeting Registration Form. Ticket and meeting badge are required. Complimentary refreshments and a cash bar will be available.

### In Vitro Toxicology Lecture and Luncheon for Students

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**Monday, March 8, 12:15 PM–1:30 PM**

*Ticket Required*

**Sponsor:**

**Colgate-Palmolive Company**

The purpose of this lecture is to discuss the importance of animal research to biomedical sciences and toxicology and the ethical obligations of the scientific community to follow the “3R’s” of animal testing (refine, reduce, replace) whenever it is feasible.

Graduate students, undergraduates, postdoctoral scholars, and recipients of Colgate-Palmolive awards are among the guests at the *In Vitro* Toxicology Lecture and Luncheon. The goal of the *In Vitro* Toxicology Lecture series is to feature important research using *in vitro* and alternative techniques to study basic mechanisms and to illustrate how these test methods benefit animal welfare by refining and reducing animal use. Students and postdocs can reserve a ticket for the luncheon with a \$5 deposit when they register for the SOT Annual Meeting. Lunch is served at the beginning of the event and service concludes before the talk/main program begins. Meal service may not be available to guests who arrive after 12:30 PM.

### MAP Kinase Signaling: A Common Target Eliciting Unique Tissue Responses

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**Tuesday, March 9, 9:00 AM–11:45 AM**

**Chairperson(s):** Haitian Lu, Michigan State University, East Lansing, MI, and Sarah Campion, Brown University, Providence, RI

**Sponsors:**

**Student Advisory Council  
Postdoctoral Assembly**

**Endorsed by:**

**Mechanisms Specialty Section  
Molecular Biology Specialty Section**

This session will highlight the most recent research progress made to characterize the alterations of MAPK signaling pathways in response to toxicant exposures, and how these alterations contribute to toxicity and/or pathogenesis in different tissues and cell types. The qualitative comparison among data presented in this session will either suggest a paradigm of MAPK response to various toxicants, or illustrate the cell type/tissue specific difference in the role of MAPK signaling alterations during toxic responses.

- **Gene Expression Studies Demonstrate That the K-ras/Erk MAP Kinase Signal Transduction Pathway Contributes to the Pathogenesis of Cumene-Induced Lung Tumors**, Stephanie Lahousse, NIEHS, Research Triangle Park, NC
- **Role of MAP Kinases and Phosphatidylinositol-3 Kinase/Akt in Regulating Keratinocyte Antioxidant Expression in Response to 4-Hydroxynonenal, a Lipid Peroxidation End Product**, Ruijin Zheng, Rutgers University, Piscataway, NJ
- **Activation of c-Jun N-Terminal Protein Kinase is a Common Mechanism Underlying Paraquat- and Rotenone-Induced Dopaminergic Cell Apoptosis**, Heather Klintworth, University of Washington, Seattle, WA
- **Toxicant Mediated Anti-Inflammatory Effects and the Role of MAP Kinase**, Wei Tan, Mississippi State University, Mississippi State, MS
- **Multiparametric Single Cell Analysis of Toll-Like Receptor Activated Kinase Phosphorylation Alteration by 2, 3, 7, 8-Tetrachlorodibenzo-p-dioxin**, Colin North, Michigan State University, East Lansing, MI

# 49<sup>TH</sup> ANNUAL MEETING AND TOXEXPO™

## STUDENT AND POSTDOCTORAL FELLOW EVENTS

### Where Do I Go Now? Rational Career Development Planning for Early-Career Scientists

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**Tuesday, March 9, 9:00 AM–11:45 AM**

**Chairperson(s):** *Betina J. Lew, University of Rochester Medical Center, Rochester, NY, and Amy Wang, U.S. EPA, Research Triangle Park, NC*

**Sponsor:**  
Postdoctoral Assembly

**Endorsed by:**  
Career Resource and Development Committee  
Student Advisory Council  
Research Funding Committee

Toxicology training during graduate school and postdoctoral fellowships provides early-career scientists with a wide array of transferable skills that can be used in many job sectors, but navigating the all of the possible career options can be a daunting task. Additionally, finding and preparing for a career path that is right for yourself is not always easy, particularly when it differs from that of your mentor or is non-traditional. With broad coverage of non-traditional career paths in toxicology, this session will provide early-career scientists with insight on how to map a career path that fits their passion and skills.

- **How to Identify Your Skills and Passions**, Kristen Keefe, University of Utah, Salt lake City, UT
- **Career Planning and Development for Early-Career Scientists**, Douglas Wolf, U.S. EPA, Research Triangle Park, NC
- **Improving Networking and Communication Skills**, Lori Conlan, NIH, Bethesda, MD
- **Making Yourself More Marketable in Private Industry**, James Popp, Stratoxon LLC, Lancaster, PA
- **The NIH Pathways to Independence Award: A Transition to an Academic Career**, Carol Shreffler, NIEHS, Research Triangle Park, NC

### Postdoctoral Assembly Luncheon

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**Tuesday, March 9, 12:00 NOON–1:15 PM**

*Ticket Required*

**Chairperson(s):** *Betina Lew, University of Rochester, Rochester, NY*

**Sponsor:**  
Postdoctoral Assembly

Amidst scrambling to attend all of the events at the meeting, this will be time for postdocs to kick back and relax! All postdoctoral fellows are invited to a casual luncheon organized by the Postdoctoral Assembly (PDA). We will announce the recipients of the Best Postdoctoral Publication Awards and acknowledge the postdocs who received awards this year from Regional Chapters, Special Interest Groups, and Specialty Sections. The PDA Board members will present an overview of accomplishments and future directions for the PDA and will introduce the new board members for 2010–2011. There will be a drawing for prizes. Postdocs can reserve a ticket when registering for the Annual Meeting. Lunch is served at the beginning of the event and service concludes before the talk/main program begins. Meal service may not be available to guests who arrive after 12:30 PM.

### Lunch with an Expert

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**Date and time varies by group**

*Meet at the Lunch with an Expert Bulletin Board in Registration Area*

**Sponsor:**  
Student Advisory Council

The purpose of Lunch with an Expert is to provide students and postdoctoral scholars the opportunity to network informally with well-established toxicologists while obtaining career advice and meeting new colleagues. Small groups are composed by matching research interests of students and postdocs with those of an Expert. The Expert for each group identifies a time and place for a meal, and the group meets at the Lunch with an Expert Bulletin Board before proceeding to the restaurant. Sign up *via* the Graduate Student section of the SOT Web site. Details for each group meeting will be sent to participants in advance of the meeting.

## EDUCATION AND PUBLIC OUTREACH ACTIVITIES

### SOT Resource Pavilion

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The SOT Resource Pavilion will feature membership information and items that you can use in outreach related to toxicology. Career brochures and posters, animals in research information, ideas and materials for students in grades K–12, and other resources of interest to toxicologists will be available. Stop by to meet representatives of SOT Special Interest Groups and learn more about their activities.

### Undergraduate Education Program

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**Saturday, March 6, 4:15 PM–9:00 PM**

*Chairperson(s): Adrian Nanez, Amgen, Thousand Oaks, CA*

*Sponsor:*

**Committee for Diversity Initiatives**

This event is for undergraduate students and advisors receiving 2010 MARC and SOT Travel funding and SOT program volunteers.

- **4:15 PM–5:45 PM**—Orientation for SOT Hosts, Peer Mentors, and Advisors
- **5:45 PM–6:00 PM**—Opening Event
- **6:15 PM–6:45 PM**—Introduction to Toxicology—Jose Manautou, University of Connecticut, Storrs, CT
- **6:45 PM–7:15 PM**—Dinner
- **7:30 PM–8:00 PM**—Absorption, Distribution, Metabolism, and Excretion Principles in Toxicology—Nathan Cherrington, University of Arizona, Tucson, AZ
- **8:00 PM–9:00 PM**—Dessert and Networking

### Undergraduate Education Program

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**Sunday, March 7, 8:00 AM–5:00 PM**

*Chairperson(s): Adrian Nanez, Amgen, Thousand Oaks, CA*

*Sponsor:*

**Committee for Diversity Initiatives**

The Sunday program is open to undergraduate students who are registered for this event on the Annual Meeting Registration Form, the undergraduate students receiving MARC, SOT, and Pfizer travel funding, and the SOT program volunteers.

- **8:00 AM**—Welcome
- **8:15 AM–8:55 AM**—Exposure to Cigarette Smoke *In Utero*: Fetal Injury and Life Long Consequences—Judith Zelikoff, New York University School of Medicine, Tuxedo Park, NY
- **9:00 AM–9:45 AM**—Metals, Biocides, and the Environment—Louis Trombetta, St. John's University, Jamaica, NY
- **10:00 AM–10:40 AM**—Optical Nanotechnologies for Imaging of Cellular Processes and Neurosurgery—Martin Philbert, University of Michigan, Ann Arbor, MI
- **10:45 AM–11:30 AM**—Interactive Presentation: Exploring Contemporary Biomedical Problems: Case Studies in Toxicology—Lauren Aleksunes, Rutgers University, Piscataway, NJ
- **11:30 AM–12:45 AM**—Lunch
- **12:45 PM–1:45 PM**—STUDENTS: What Is Graduate School and What Can I Expect?  
How to Get into Graduate School: An Academic Advisor's Perspective
- **12:45 PM–1:30 PM**—ADVISORS: Tips for Advising Prospective Graduate Students or *How to Get Your Students Accepted to Graduate School!!*
- **2:00 PM–2:40 PM**—Career Opportunities in Toxicology—Panel Discussion
- **3:00 PM–5:00 PM**—Open time with Academic Toxicology Program Directors and Internship Sponsors

# 49<sup>TH</sup> ANNUAL MEETING AND TOXEXPO™

## EDUCATION AND PUBLIC OUTREACH ACTIVITIES

### Undergraduate Education Program

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**Monday, March 8, 7:15 AM–2:00 PM**

*Chairperson(s): Adrian Nanez, Amgen, Thousand Oaks, CA*

*Sponsor:*

**Committee for Diversity Initiatives**

This event is for undergraduate students and advisors receiving 2010 MARC and SOT Travel funding and SOT program volunteers.

- **8:00 AM–9:00 AM**—Plenary Lecture
- **9:30 AM–10:50 AM**—Poster Session for Visiting Students
- **11:00 AM–11:50 PM**—Program Wrap-up
- **12:00 NOON–1:15 PM**—*In Vitro* Luncheon
- **1:30 PM–2:00 PM**—Scientific Sessions

### Undergraduate Toxicology Faculty Meeting

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**Tuesday, March 9, 3:30 PM–4:30 PM**

The Education Committee and the Undergraduate Education Subcommittee are hosting the Undergraduate Toxicology Faculty Meeting for all faculty involved in the teaching of toxicology to undergraduates, or for those interested in including toxicology at the undergraduate level. Hear an update on initiatives for undergraduate faculty, provide your input, and network.

### Seeking Funding for Undergraduate Research

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**Wednesday, March 10, 4:30 PM–5:50 PM**

*Chairperson(s): Joan B. Tarloff, University of the Sciences in Philadelphia, Philadelphia, PA, and Vanessa Fitsanakis, Kings College, Bristol, TN*

*Sponsor:*

**Education Committee**

*Endorsed by:*

**Postdoctoral Assembly**

**Research Funding Committee**

It is often difficult for undergraduate professors to readily know where to go for research funding. Both the National Institutes of Health (NIH) and National Science Foundation (NSF) have grants specifically tailored to the needs of undergraduate students and faculty in the form of classroom and teaching enhancement, professional development, or research opportunities for faculty and students. This session will provide undergraduate faculty with the opportunity to hear presentations from representatives from NIH and NSF and to ask questions of each.

- **Seeking Funding for Undergraduate Research**, Joan Tarloff, University of the Sciences in Philadelphia, Philadelphia, PA
- **Academic Research Enhancement Awards (AREA) through NIH**, Michael Humble, NIEHS, Durham, NC
- **Research Experiences for Undergraduates (REU) Awards through NSF**, Sally O'Connor, NSF, Arlington, VA
- **Experiences with the AREA Program**, Eli Hestermann, Furman University, Greenville, SC

# Get Your Research Known More Broadly and Help Advance the Science of Toxicology

## Consider Organizing a Contemporary Concepts in Toxicology (CCT) Meeting

**CCT Meetings expand the opportunities and forums for members to engage in the exchange of ideas and information relevant to toxicology.** CCT meetings are one- to two-day focused, open registration, scientific meetings in contemporary and rapidly progressing areas of toxicological sciences.

If you think that your research area could be enhanced by thought leader collaboration or that public health and safety could be improved by disseminating your research findings more broadly, please consider organizing a SOT CCT. The CCT Committee and the SOT Headquarters staff are prepared to help move your meeting forward.

CCT Meetings focus on a *wide range of topics* and recent CCTs addressed the following:

- PPTOXII: Role of Environmental Stressors in the Developmental Origins of Disease—December 7–10, 2009
- Hemangiosarcoma in Rodents: Mode-of-Action Evaluation and Human Relevance Workshop—December 4–5, 2008
- Perfluorinalkyl Acids and Related Chemistries: Toxicokinetics and Mode-of-Action Workshop—February 14–16, 2007

In order to sustain the quality standards of the Society, only meetings in which SOT maintains scientific and administrative control will be considered. Meetings developed and administered by other organizations may be eligible for Non-SOT Meeting endorsement.



**For additional information,  
visit the SOT Web site**

**[www.toxicology.org](http://www.toxicology.org)**

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## SOT | Society of Toxicology

Exhibits

**You probably know ToxExpo™ as the exhibition associated with the Society of Toxicology's Annual Meeting—it's that—but it's also a great deal more.**

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- A 24/7 comprehensive on-line resource, searchable by company name or by product or service.
- A comprehensive approach to organizing the wealth of ideas and insights in cross-disciplinary areas of toxicology.
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- The place where professionals will learn how to explore a rapidly changing science.
- A chance to think outside the box—find out how your work relates to research in other disciplines.
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### **Exhibit Hall Photography Policy and Protocols for Attendees**

Out of courtesy for the scientific presenters and exhibitors we appreciate your compliance with the following policies:

- Cell phones and other electronic devices should be set on mute.
- Photography of poster presentations is prohibited without the specific consent of the presenter(s)/author(s).
- Photography of exhibitor booths and/or equipment is prohibited.
- Children under the age of 15 are prohibited from accessing the Exhibit Hall at any time.

If you have any questions regarding these policies, please contact the SOT Headquarter staff at the Registration Desk.

### **Exhibit Hours:**

**Monday, March 8**

**9:00 AM–4:30 PM**

**Tuesday, March 9**

**8:30 AM–4:30 PM**

**Wednesday, March 10**

**8:30 AM–4:30 PM**

# 2010 Exhibitor Listing

*It all adds up to an uncommonly rich resource for the scientist, the toxicologist, the policy maker, the educator, the student—anyone looking for the best products and services that toxicology has to offer!*

## **Current 2010 ToxExpo™ Exhibitors** (as of 11/6/09):

### **2010 Annual Meeting sponsors are in yellow.**

See complete listing of sponsors on page 112 and Inside Back Cover.

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 Zoologix, Inc.

## EXHIBITOR HOSTED SESSIONS

### MONDAY

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#### Biological Test Center Capabilities Overview

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Monday, March 8, 9:15 AM–10:15 AM

**Presented by:** Biological Test Center

The Biological Test Center has been providing pharmaceutical, biotechnology, and medical device industries with preclinical contract laboratory services since 1980. Our GLP, AAALAC-accredited facility is located in Irvine, CA. The Center performs a wide-range of biocompatibility, toxicology, pharmacology, pharmacokinetics, ocular, and surgical studies, including innovative ophthalmological and surgical models.

#### Digital Pathology in the 21<sup>st</sup> Century

---

Monday, March 8, 9:15 AM–10:15 AM

**Presented by:** Charles River

Digital pathology is an emerging technology that affords many benefits to pathologists. While pathologists in the clinical area have made good use of this technology, pathologists in the preclinical area have not moved forward as rapidly. The use of digital pathology today and in the future in support of preclinical studies will be reviewed and discussed.

#### An *In Vitro* Method for Measuring Metabolic Stability of Chemicals in Fish

---

Monday, March 8, 10:30 AM–11:30 AM

**Presented by:** CANTEST Ltd.

*In vitro* biotransformation rates were measured using an S9 fraction from rainbow trout incubated with pyrene. Metabolic rates obtained from this study were extrapolated to whole-fish biotransformation rates and used to refine BCF computer model predictions. Our results suggest that this approach can be a potential replacement for *in vivo* measurements of BCF.

#### Choose the Diet Wisely: Purified Diets Vs. Chow in Lab Animal Research

---

Monday, March 8, 10:30 AM–11:30 AM

**Presented by:** Research Diets, Inc.

Grain-based laboratory animal ‘chow’ diets contain measurable and variable levels of toxic heavy metals and bioactive compounds such as phytoestrogens. These can affect the animal’s phenotype. Purified ingredient diets are free of these compounds and can be used to reduce data variability and influence outcome.

#### Demonstration of a Cigarette Smoke Generator in Combination with a Novel Cell Culture Exposure System

---

Monday, March 8, 10:30 AM–11:30 AM

**Presented by:** TSE Systems Inc.

Classic submerged cultures (covered by medium) do not mimic the *in vivo* situation. Lung cells for example are directly exposed to the air. Therefore, dry-wet cultures in combination with cigarette smoke have been chosen to validate our cell culture exposure system.

#### Learn How Genomic Tools Can Be Used to Accelerate Toxicology Decisions, from Discovery to Application

---

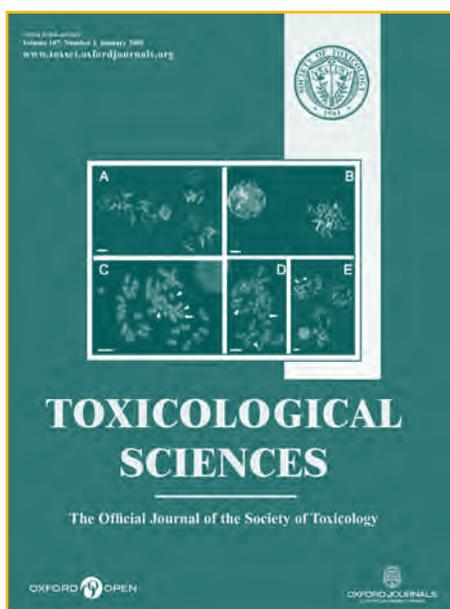
Monday, March 8, 11:45 AM–12:45 PM

**Presented by:** Affymetrix

The use of genomic tools in toxicology and preclinical studies enables researchers to understand mechanisms of toxicity elicited by therapeutic agents, discover biomarkers predictive of treatment responses, and understand how knowledge of genetic variants can be applied to dosing studies.

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\*ISI Journal Citation Reports 2008 Edition, published in 2009



## EXHIBITOR HOSTED SESSIONS

### Analyzing Cells in Real Time: xCELLigence Technology Use in Pharma Research

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Monday, March 8, 11:45 AM–12:45 PM

**Presented by: Roche Applied Science**

The xCELLigence Real-Time Cell Analyzer (RTCA) System allows the label-free, noninvasive dynamic monitoring of cell proliferation and viability in real time by utilizing an impedance read-out. Several cell-based applications have been developed for the system so far. Among them are cellular quality controls, detection of cell proliferation or cytotoxicity.

### Cytokines and Lineage Choice in Stem Cell Differentiation

---

Monday, March 8, 11:45 AM–12:45 PM

**Presented by: STEMCELL Technologies Inc.**

A key feature of hematopoietic stem cells and their progeny is that their proliferation and differentiation is regulated by, and dependent on, external stimulation from cytokines. This session will discuss various assays that offer more biologically relevant screening to determine the mechanism of action on target cells of various pharmaceuticals.

### Predictive *In Vitro* Model for Determining Additive or Synergistic Toxicity of Combinations of New Small Molecule Compounds and Standard Treatments

---

Monday, March 8, 1:00 PM–2:00 PM

**Presented by: ReachBio LLC**

Although certain compounds alone may not exhibit myelotoxicity, they may cause unexpected neutropenia when given to specific patient populations in combination with other drugs. The talk will focus on *in vitro* CFC model for predicting clinical neutropenia of intentional or coincidental combination therapies.

### Interests and Limitations of New *In Vivo* Methodologies to Assess the Potential Cardiovascular Effects of NCEs and Biologics in Large Animal Models

---

Monday, March 8, 1:00 PM–2:00 PM

**Presented by: SNBL USA, Ltd.**

In NHPs, stress induced by manual restraint, complications of anesthesia, and limited data collections can confound Arterial blood pressure and ECG data and interpretation in safety pharmacology/toxicology studies. The physiological and pharmacological validation of the new Jacketed External Telemetry (JET™-BP System) will reveal the advantages and limitations of such methodology.

### DNA Damage, PARP, and the Comet Assay

---

Monday, March 8, 1:00 PM–2:00 PM

**Presented by: Trevigen, Inc.**

The Comet Assay is a valuable tool for monitoring strand breaks in DNA that result from exposure to genotoxic agents. Such exposure may initiate PARP 1 mediated DNA repair and mask DNA strand breaks. Conditions for optimal detection of both double and single strand breaks will be discussed.

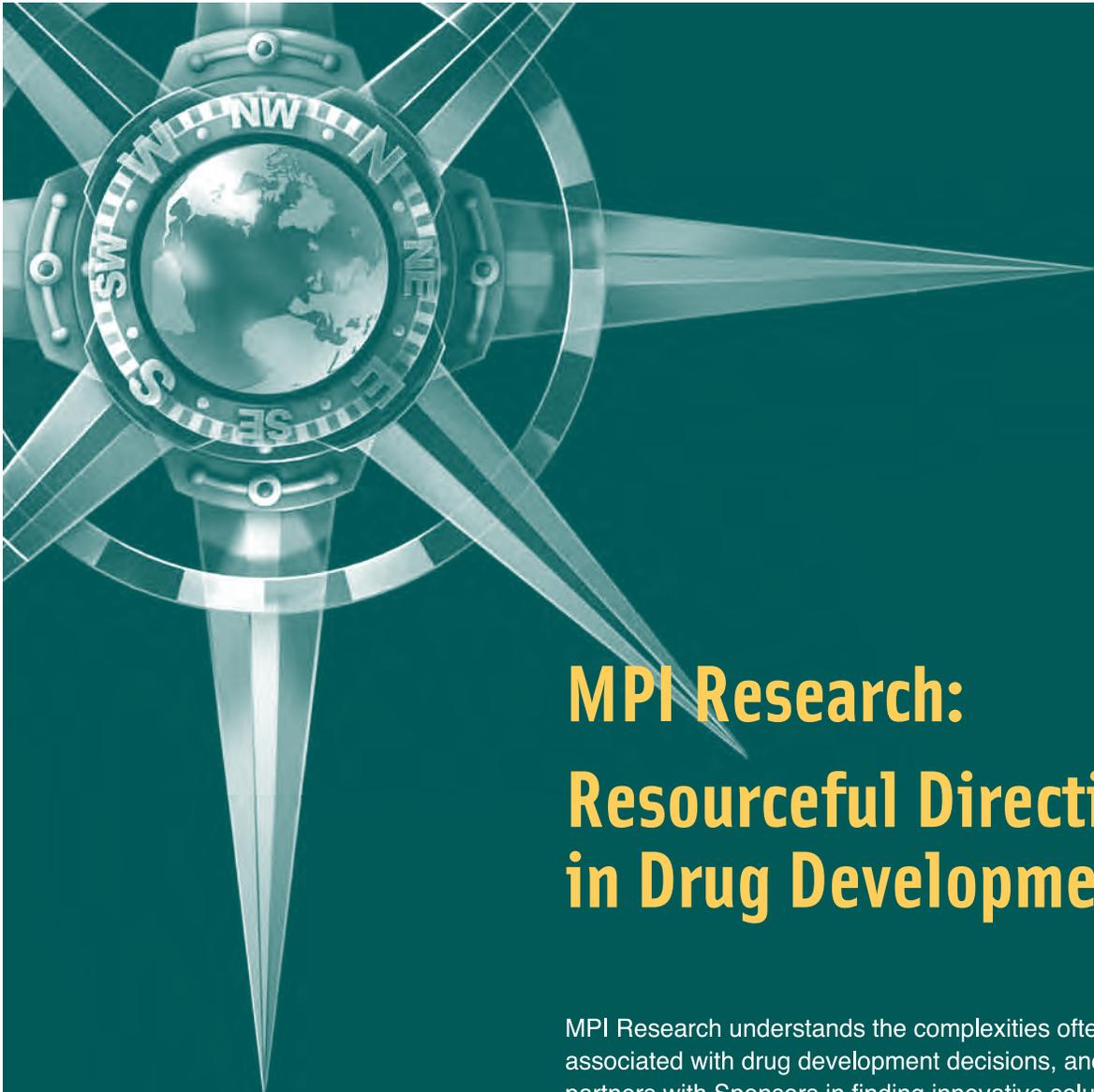
### The Scientific Quest for a New Millennium of Drug Discovery and Development

---

Monday, March 8, 2:15 PM–3:15 PM

**Presented by: Covance, Inc.**

Ten years after starting the Drug Development “New Millennium,” researchers are feeling the impact of new guidelines, an increased emphasis on safety, challenges in the development of biologics, globalization, strategically integrated approaches, and CROs as scientific partners. We invite you to participate in this interactive scientific review of the challenges that have been overcome, those that still exist, and what might lie ahead.



## MPI Research: Resourceful Direction in Drug Development

MPI Research understands the complexities often associated with drug development decisions, and partners with Sponsors in finding innovative solutions to their development challenges. We look forward to greeting you at SOT in **booth 801** and discussing how we can help move your drug development projects forward.

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## EXHIBITOR HOSTED SESSIONS

### Therapeutic Monoclonal Antibodies— Predicting Antibody-Mediated Cytokine Release

---

Monday, March 8, 2:15 PM–3:15 PM

Presented by: **Huntingdon Life Sciences**

Acute cytokine release after clinical dosing has been seen with a small number of therapeutic monoclonal antibodies. The ability to understand this potential in human and toxicity species is essential prior to clinical studies. Understand the mechanisms of cytokine release and the design of *in vitro* and *in vivo* studies.

### The Usefulness of the Minipig in Regulatory Toxicology

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Monday, March 8, 2:15 PM–3:15 PM

Presented by: **LAB Research Inc.**

The seminar will highlight the minipig as the non-rodent species in regulatory studies and how in some cases it is preferable over dogs and primates. In particular, their use in general toxicology testing employing the continuous intravenous infusion and dermal route will be discussed.

## TUESDAY

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### Obese Animal Models of Metabolic Disease

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Tuesday, March 9, 8:30 AM–9:30 AM

Presented by: **Charles River**

Animal models for the assessment of metabolic changes associated with the onset and development of obesity and diabetes are important tools for studying the safety and efficacy of novel therapeutics. This session will focus on how two widely used models (ZDF rat and large animals fed on a high-fat diet) can aid in the development of new drugs to treat insulin resistance, insulin resistance-associated chronic diseases and obesity.

### Preclinical Anticancer Drug Development: Shifting Challenges

---

Tuesday, March 9, 9:45 AM–10:45 AM

Presented by: **Accelera Srl**

Development of oncology treatments involves a unique set of challenges. Learn from the people behind the preclinical development of marketed treatments (Adriamycin, Ellence, Sutent) how to advance your anticancer program smoothly, from screening/lead selection to the development of tailor-made IND packages, and how ICHS9 may impact the future landscape.

### Functional Biomarkers of Renal Injury— Optimizing Interpretive Value in Renal Pharmacology Studies

---

Tuesday, March 9, 9:45 AM–10:45 AM

Presented by: **Huntingdon Life Sciences**

Recognition of adverse renal pharmacodynamic effects requires sophisticated experimental designs and appropriate quantitative evaluations. Biochemistry and histopathology evaluations routinely used have limitations in adequately characterizing drug effects. This session proposes appropriate designs for renal safety pharmacology studies incorporating the use of functional biomarkers for identification and characterization of drug effects.

### Introduction to the Development and Validation Study of the New Technology “Cell able” for New Drug Discovery

---

Tuesday, March 9, 9:45 AM–10:45 AM

Presented by: **Transparent Inc.**

Introduction to the development of and validation study of the new technology “Cell able” for new drug discovery. It is possible to culture human hepatocytes and maintain their functions for a long period using “Cell able.” It could be used for prediction of the toxicity of a large number of drug candidates at one time.



## EXHIBITOR HOSTED SESSIONS

### A System's Toxicology Approach for Drug Discovery and Development

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Tuesday, March 9, 11:00 AM–12:00 NOON

Presented by: **Ingenuity Systems**

Learn how IPA-Tox™ can help you with your research and provide the following:

- An understanding of drug toxicity and mechanism of action
- Identify specific molecular toxicity components
- Industry relevant case study will demonstrate the functionality of the toxicity module

### Predictive Multiparametric *In Vitro* Assay Combinations for Cytotoxicity, Viability, Apoptosis, and ADME Applications with Hepatocytes and Human Stem-Cell Derived Cardiomyocytes

---

Tuesday, March 9, 11:00 AM–12:00 NOON

Presented by: **Promega Corporation**

Combining bioluminescent and fluorescent cell-based assays allows multiparametric measurements from single samples, simplifying mechanistic studies. Multiplex approaches, using human-cell model systems, streamlines data collection, improves data quality, strengthens interpretation, and removes ambiguity. This seminar reviews multiplex applications of viability, cytotoxicity, apoptosis, cytochrome P450 induction/inhibition, and genetic reporter assays.

### SkinEthic Laboratories, Providing You Available, Predictive User Friendly, and Sustainable *In Vitro* Solutions

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Tuesday, March 9, 11:00 AM–12:00 NOON

Presented by: **SkinEthic Laboratories**

SkinEthic models are predictive *in vitro* tools for efficacy and safety screening tests. The usefulness of Episkin and RHE will be discussed within the frame of the GHS classification as well the on-going validation of the HCE—human corneal model. The reproducibility of our production processes for these validated or under validation models will be presented. This updated information will create a forum of information for all scientists and toxicologists on reliable and relevant tools for decision making during preclinical safety phases.

### Higher Throughput *In Vitro* Screening Assays for Drug-Drug Interactions and Organ-Specific Toxicity Using Human Hepatocytes and IdMOC

---

Tuesday, March 9, 12:15 PM–1:15 PM

Presented by: **ADMET Group**

Screening of new chemical entities for adverse drug properties would aid the selection of drug candidates without such liabilities. Higher throughput human hepatocyte P450 inhibition, P450 induction, and cytotoxicity assays and the Integrated Discrete Multiple Organ Co-culture (IdMOC) assay for the evaluation of multiple organ toxicity, will be described.

### Systems Toxicology Data Analysis with GeneGo

---

Tuesday, March 9, 12:15 PM–1:15 PM

Presented by: **GeneGo, Inc.**

GeneGo provides a rich database and powerful suite of tools for analyzing high content molecular toxicology data. Current capabilities of the system and upcoming enhancements for safety assessment will be presented. A guest speaker from industry will present a case study investigating sex and strain differences in toxic response.

### How to Screen for Arrhythmias in Safety Pharmacology When More Than 86,400 Beats are Recorded in One Dog Over 24 Hours

---

Tuesday, March 9, 12:15 PM–1:15 PM

Presented by: **LAB Research Inc.**

Telemetry is essential for continuous monitoring of ECG in safety pharmacology. On the flip side, the amount of data generated presents a challenge during analysis and interpretation, particularly for identification of cardiac arrhythmias. ECG analysis strategies and arrhythmia detection beyond QT interval measurements will be presented and discussed.



## EXHIBITOR HOSTED SESSIONS

### Noninvasive Blood Pressure and Respiration Measurements on Large Animals

---

Tuesday, March 9, 1:30 PM–2:30 PM

Presented by: emka TECHNOLOGIES

This presentation will explain how recent improvements in hardware and in a software algorithm enabled higher efficiency and reliability in the noninvasive study of blood pressure and respiration, as well as the computation of new parameters. Studies done to compare these measurements with those obtained using traditional methods will be presented. Fixed and recurring costs of doing such measurements will also be discussed.

### Tips and Tricks to Maximize Your Literature Search Results

---

Tuesday, March 9, 1:30 PM–2:30 PM

Presented by: Quertle, LLC

The workshop will cover the following:

1. Understanding the difference between relationships *versus* simple occurrence of keywords,
2. Using Power Terms™ such as \$AdverseEffects to enhance results,
3. Constructing efficient queries, including use of capitalization,
4. Searching full-text documents and MEDLINE simultaneously, and
5. Effective filtering to refine results.

### Making New Connections: Networking Strategically

---

Tuesday, March 9, 1:30 PM–2:30 PM

Presented by: Science/AAAS

Find ways to make networking work for you. By being strategic about how you meet people, you can increase your number of contacts with ease. We'll discuss myths and realities surrounding networking and different strategies for networking in various arenas. Learn about informational interviews, business cards, elevator pitches, and more.

### Lead Optimization—What Does the Future Look Like?

---

Tuesday, March 9, 2:45 PM–3:45 PM

Presented by: Covance, Inc.

Now, more than ever, it is crucial to make the right decisions early in the development process. Lead Optimization advancements in the last 10 years have led to the ability to make faster, more concrete decisions, increasing the probability of bringing a successful drug candidate forward. In this session, explore what advancements have been made, why they are important, and what we expect to happen in the next 10 years.

### The Minipig—A Non-Rodent Species in Regulatory Toxicity Testing

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Tuesday, March 9, 4:00 PM–5:00 PM

Presented by: Ellegaard Göttingen Minipigs A/S

This session highlights the relevance of the minipig as a non-rodent model in regulatory toxicity testing, and, in this context, discusses species selection in non-clinical safety studies. The session also provides an overview of marketed drug products (case studies) where minipigs have been used as the non-rodent species.

## WEDNESDAY

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### Innovative Safety Studies and Successful Strategies for an Efficient IND-Enabling Program

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Wednesday, March 10, 8:30 AM–9:30 AM

Presented by: Charles River

Early stage developers need a clear view of the path forward to human trials. Most failures to win FIH trial approval stem from underestimating timelines and the complexity of toxicology programs. Effective planning of toxicology programs and cost-effective innovative approaches to preclinical study design for IND-enabling programs are critical to generating data that will add value to a novel drug or biologic and increase regulatory success.

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### Research | Children's Health

## Influence of Prenatal Lead Exposure on Methylation of Cord Blood DNA

J. Richard Pilsner,<sup>1,4</sup> Howard Hu,<sup>2,4</sup> Adeline Estroff,<sup>3,4</sup> David Cantonwine,<sup>2</sup> Alicia Lazarus,<sup>2</sup> Hector Lora,<sup>2</sup> Martha Maria Tiller-Rob,<sup>2</sup> and Mauricio Hernandez-Avila<sup>1,4</sup>

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**BACKGROUND:** Prenatal lead exposure is associated with adverse pregnancy outcomes and developmental and cognitive deficits because, like tobacco, the mechanism by which lead-induced toxicity occurs involves epigenetic DNA programming via DNA methylation and possibly by other mechanisms.

**OBJECTIVE:** This study was designed to determine whether prenatal lead exposure is associated with alterations in genomic methylation of endogenous DNA levels from umbilical cord samples.

**METHODS:** We measured genomic DNA methylation, as assessed by 450k and LINE-1 (long interspersed nuclear element) methylation via pyrosequencing, on 103 umbilical cord blood (CBL) samples from the Bioprospect of the Early Life Exposure in Mexico to Environmental Toxins (ELEMENT) study group. Prenatal lead exposure had been assessed by measuring cord blood lead levels at the mid-gestational visit and the results using a previously validated method.

**RESULTS:** We found an inverse dose-response relationship in which quartile of prenatal lead reduced with cord LINE-1 methylation ( $p$  for trend = 0.01) and this lead correlated with 450k methylation ( $p$  for trend = 0.05). In mixed effects regression models, maternal blood lead levels were inversely associated with umbilical cord genomic DNA methylation of 450k ( $-0.027$ ,  $p < 0.01$ ) but not LINE-1.

**CONCLUSIONS:** Prenatal lead exposure is inversely associated with genomic DNA methylation in cord blood. These data suggest that the epigenome of the developing fetus can be influenced by maternal cumulative lead burden, which may influence long-term epigenetic programming and disease susceptibility throughout the life course.

**KEY WORDS:** blood lead, cord blood, DNA methylation, early life, epigenetics, lead programming, genomic DNA methylation, intergenerational, lead exposure, life course, Mexico, prenatal blood exposure, susceptibility throughout the life course.

As of 2006, an estimated 275,000 children in the United States continue to have blood lead levels exceeding the U.S. Centers for Disease Control and Prevention (CDC) limit of concern of 10 µg/dL. CDC 2006. Major concern of elevated blood lead levels greatly surpasses U.S. members and signifies a public health priority of global magnitude (Toussaint and Gilliland 2005). Lead exposure produces a wide spectrum of health outcomes, most notably neurocognitive and behavioral deficits in response to pre- and/or postnatal exposure (Needham et al. 1990). Lead exposure has also been associated with spontaneous abortion (Burdette et al. 1999) and other adverse birth outcomes, such as preterm delivery (Anderson et al. 1996; Joffe-Parkinson et al. 2006) and low birth weight (Belfrage et al. 1991; Gonzalez-Casado et al. 1997; et al. 1991). Gonzalez-Casado et al. 1997, which are risk factors for adverse health outcomes over the life course (Baker et al. 1980;

Rich-Edwards et al. 1997). Recently, blood lead levels < 10 µg/dL during early childhood have been reported to confer elevated risk for later life outcomes (Lanphear et al. 2005), further questioning whether a safe level exists for the adverse consequences of exposure. Despite the well-documented health effects of lead, the biological mechanisms underlying these effects have long been elusive (Baker 1980). Lead acts on the placenta during pregnancy (1990) and therefore represents a significant route of exposure to the developing fetus (Needham et al. 1990). Conceptually, pregnancy and lactation are also associated with a marked increase in maternal blood lead levels (Needham et al. 1990). Conceptually, pregnancy and lactation are also associated with a marked increase in maternal blood lead levels (Needham et al. 1990). Conceptually, pregnancy and lactation are also associated with a marked increase in maternal blood lead levels (Needham et al. 1990).

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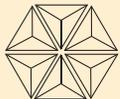
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