

SCIENTIFIC PROGRAM OVERVIEW

A page reference follows the session information.

Sunday, March 7

CE Target Areas

Course titles related to each theme are color coded in this Program Overview.

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 vs. 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.

7:00 AM–7:45 AM

CONTINUING EDUCATION SUNRISE MINI-COURSE

1. Biological Pathway Analysis: An Introduction to the Pathway Knowledge Bases for Toxicological Research (p86)

8:15 AM–12:00 NOON

CONTINUING EDUCATION MORNING COURSES

2. Biologicals: Introduction to Drug Development (p86)
3. Comparative Biology of the Lung (p87)
4. Cytokines: Balancing Therapeutic Utility and Immune System-Mediated Toxicities (p87)
5. Nuclear Receptors: Role in Chemical Mode of Action and Targets for Toxicity Testing (p88)
6. Predictive Power of Novel Technologies (Cells to 'Omics): Promises, Pitfalls, and Potential Applications (p88)
7. Reproduction and Regulatory Impact (p89)

1:15 PM–5:00 PM

CONTINUING EDUCATION AFTERNOON COURSES

8. Assessment of Ocular Toxicity in Toxicology Studies Conducted for Regulatory Purposes (p89)
9. Gene-Environment Interactions Influence Cytokine Biology in Immunotoxicity and Disease: Genomic, Genetic, and Epigenetic Perspectives (p90)
10. Mitochondrial Toxicity: Animal Models and Screening Methods in Drug Development (p90)
11. ICH Initiatives for Conducting Pharmaceutical Preclinical Safety Studies: New and Revised Guidelines and Challenges (p91)
12. Segment-Specific Renal Pathology for the Non-Pathologist (p91)
13. Technologies and Tools for Toxicity Testing in the 21st Century (p92)

Thematic Approach

Session titles related to each theme are color coded in the Program overview.

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.

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 Interaction theme has been selected to highlight recent advances in this field that are relevant to the toxicological sciences.

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, there is evidence that 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.

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.

Toxicity Testing in the 21st 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.

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.

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 (p102)

9:15 AM–12:00 NOON

SYMPOSIUM SESSIONS

- Mechanistic Role of Reactive Intermediate Protein Covalent Binding in Target Organ Toxicity: Past, Present, and Future (p103)
- Neurological Responses after Exposure to Inhaled Metal Particles (p103)
- Ovarian Toxicity: Current Concepts in Toxicology, Pathology, and Mechanisms (p104)
- Silica and Asbestos Immunotoxicity: Mechanisms to Fibrosis, Autoimmunity, and Modified Tumor Resistance (p104)

WORKSHOP SESSIONS

- **Does Background Disease Lead to Low Dose Linearity?** (p105)
- Heart Smart: Innovative Approaches for Improving Cardiovascular Safety through Collaboration (p105)
- **Toxicology in the 21st Century: Stem Cells in Drug Discovery and Development** (p106)

PLATFORM SESSIONS

- **Biomarkers of Target-Organ Toxicity** (p107)
- Chemical and Biological Weapons—Sulfur Mustard (p107)
- Immunopharmacogenomics and Immune Regulation (p108)
- **Mitochondrial-Mediated Mechanisms of Toxicity of Xenobiotics** (p109)

9:30 AM–12:30 PM

POSTER SESSIONS

- Carcinogenesis I (p112)
- **Epigenetics** (p114)
- Hypersensitivity, Autoimmunity, and Idiosyncratic Drug Reactions (p126)
- Investigations of Chemical Mixtures (p122)
- Mechanistic Aspects of Persistent Organic Chemical Toxicity (p120)
- Nanotoxicology I (p123)
- Neurodevelopmental Toxicity: General (p115)
- **Screening and Predicting Toxicity: Computational Approaches to Identify Targets** (p117)
- **Toxicity Testing—Alternative Models I** (p110)

12:10 PM–1:30 PM

ROUNDTABLE SESSIONS

- Combination Toxicology Studies for Pharmaceutical Agents: Design Considerations and Impact on Clinical Development (p130)
- Melamine Contamination of Infant Formulas: Lessons Learned (p130)

HISTORICAL HIGHLIGHTS SESSION

- **Translating Toxicology to Public Health Protection: Lessons Learned from Superfund** (p131)

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 (p131)

1:00 PM–4:30 PM

POSTER SESSIONS

- Advances in Dermal Toxicology (p145)
- Biotransformation I (p141)
- Carcinogenesis II (p146)
- Chemical and Biological Weapons (p131)
- Environmental Impact of Xenobiotics (p139)
- Genetic Diversity and Response to Xenobiotics (p134)
- Nanotoxicology II (p135)
- Reproductive Toxicology (p136)
- **Toxicity Testing—Alternative Models II** (p142)

1:40 PM–4:25 PM

SYMPOSIUM SESSIONS

- **Alterations in Regulatory T Cells: Novel Pathways to Immunotoxicology** (p148)
- Faster Science for Better Decisions: Characterizing Environmental Contaminant Risk from High-Throughput Data (p149)
- Genotoxic Impurities in Drugs and Drug Products: What Is the Right Way to Deal with Impurities in R&D versus Regulatory Guidance? (p149)
- **Metabolic Syndrome and Increased Sensitivity to Drug-Induced Liver Injury (DILI): Nonclinical Models and Clinical Implications** (p150)
- Phthalate Reproductive and Developmental Toxicity: Implications for Cumulative Risk Assessment (p151)

WORKSHOP SESSION

- Determination of the Contribution of Individual Stressors in Cumulative Risk Assessments (p151)

REGIONAL INTEREST SESSION

- **Signaling Mechanisms for Metabolic Dysfunction Following Low-Level Arsenic Exposures: From Mouse to Man** (p152)

PLATFORM SESSIONS

- Advances in Biomarkers of Renal Injury (p153)
- **Animal Models in the 21st Century** (p153)
- Lipid Metabolism and Apoptosis (p154)
- Methods and Animal Models in Cardiovascular Safety Pharmacology (p154)

4:35 PM–5:55 PM

SOT/EUROTOX DEBATE

Threshold of Toxicological Concern (TTC):
Is It Based on Science or Politics? (p156)

ROUNDTABLE SESSIONS

- Inhaled Particles: From the Nose to the Brain? (p156)
- Safety of Vitamins and Minerals: Controversies and Perspectives (p157)
- The Evolution of the Extended One-Generation Study Design for Agricultural and Industrial Chemical Hazard Identification (p157)

Tuesday, March 9

7:30 AM–8:50 AM

ROUNDTABLE SESSIONS

- **Can Animal Neurotoxicity Predict Human Dysfunction?** (p158)
- Weighing Complex Data in Risk Decisions: Concepts of Evidence-Based Toxicology (p159)

INFORMATIONAL SESSIONS

- **Human Hepatocytes Derived from Embryonic Stem Cells: A New Tool for In Vitro Toxicity Testing** (p159)
- Recent Advances in Pulmonary Surfactant Toxicological Assessment and Therapeutics (p160)

8:00 AM–8:50 AM

TRANSLATIONAL IMPACT AWARD LECTURE

Translating Mechanism-Based Research into Antidotes: Trials, Tribulations, and Triumphs
Lecturer: Kenneth E. McMartin (p160)

9:00 AM–11:45 AM

SYMPOSIUM SESSIONS

- **Anti-Drug Antibody-Mediated Toxicity in Nonclinical Toxicity Studies: Impact and Relevance to Human Safety** (p161)
- Bile Salt Transport and Liver Injury (p161)
- **MAP Kinase Signaling: A Common Target Eliciting Unique Tissue Responses** (p162)
- **Molecular Determinants of Mitochondrial Disease** (p163)
- POPs: What's New and Why Should We Care? (p163)

WORKSHOP SESSIONS

- **Opportunities to Modify Current Regulatory Testing Guidelines and Advance the Assessment of Carcinogenicity Risk in the 21st Century** (p164)
- Research Advances and Enduring Needs in Children's Environmental Health Protection (p164)

EDUCATION-CAREER DEVELOPMENT SESSION

- Where Do I Go Now? Rational Career Development Planning for Early-Career Scientists (p165)

PLATFORM SESSIONS

- Epidemiological Insights: Effects of Environmental and Occupational Exposures (p166)
- **Gene Environmental Interactions in Carcinogenesis** (p166)
- Reproductive and Developmental Effects Using Fish Models (p167)

9:00 AM–12:30 PM

POSTER SESSIONS

- **Animal Models—Emerging Methods** (p185)
- Arsenic I (p188)
- Biological Modeling: Multiple Scales of Parameters, Structures, and Applications (p182)
- Developmental Toxicology (p179)
- DNA Damage and Repair (p169)
- Education (p187)
- Inflammation and the Pathogenesis of Toxicity (p171)
- Kidney I (p177)
- Metal Neurotoxicity: General (p190)
- Mutagenicity (p168)
- Nanotoxicology—Carbon Nanostructures (p175)
- Oxidative Injury and Redox Biology (p173)
- Pharmaceutical Toxicology I (p170)

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?** (p193)
- Women's Health: Toxicology and Safety of Complementary and Alternative Medicine (p194)

EDUCATION—CAREER DEVELOPMENT SESSION

- Science Communication in 2010: A New Decade in Toxicology and Need for Better Communication (p194)

12:30 PM–1:20 PM

DISTINGUISHED TOXICOLOGY SCHOLAR AWARD LECTURE

Toxic Injury: Initiation, Expansion, and Repair—
Lecturer: Harihara M. Mehendale (p195)

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Name: _____

Contact Telephone: _____

1:00 PM–4:30 PM

POSTER SESSIONS

- **Ah Receptor Biology and Toxicology (p209)**
- Apoptosis/Cell Death (p211)
- Biomarkers (p217)
- Biotransformation II (p201)
- **Genotoxicity (p203)**
- Neurodegenerative Disease (p215)
- Neurotoxicity of Pesticides (p212)
- Pharmaceutical Toxicology II (p198)
- Risk Assessment I: New Data and Derivations across Chemicals from A to V (p195)
- Safety Assessment: Commercial and Consumer Products (p207)
- Safety Concerns of Food and Natural Products (p205)

1:30 PM–4:15 PM

SYMPOSIUM SESSIONS

- **Genetics: The Link between Exposures, Gene x Environment Interaction, and Toxicity (p220)**
- **It's Not Your Father's Aryl Hydrocarbon Receptor: New Biological Roles for a Misunderstood Receptor (p220)**
- Mechanisms of Chemical-Induced Liver Cancer: Putting the Pieces Together (p221)
- New Strategies for the Use of Genetic Toxicology Data in Human Risk Assessment (p222)
- **Recent Knowledge on Critical Regulators of Lipid Homeostasis in Metabolic Disease (p222)**
- **Zinc, Copper, and Their Metabolic Effect: Myths and Musts (p223)**

WORKSHOP SESSIONS

- Immunotoxicity and Other Safety Considerations in the Development of Therapeutic Vaccines (p223)
- Widely Varying Strategies Implemented in Discovery to Reduce the Failure Rate of Clinical Lead Candidates in Development (p224)

PLATFORM SESSIONS

- **Emphasis on the Embryo: HTS, PBPK, and Virtual Tissue Technologies (p225)**
- Model Systems in Neurodevelopmental Toxicity (p225)
- Nanotoxicology—Pulmonary Effects (p226)
- **Toxicity Detection—Alternatives to Animal Models (p227)**

Wednesday, March 10

7:30 AM–8:50 AM

INFORMATIONAL SESSIONS

- Impact of Tungsten and Tungsten Alloys on Health Risk (p229)
- The 2009 Tennessee Fly Ash Spill—An Environmental Emergency Case Study (p229)

EDUCATION—CAREER DEVELOPMENT SESSION

- Career Alternatives in Toxicology: Lessons Learned (p230)

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* (p230)

9:00 AM–11:45 AM

SYMPOSIUM SESSIONS

- Gender Divergent Xenobiotic Responses (p231)
- **Mitochondrial Toxicity in Disease and Death (p231)**
- The Fetal Basis of Adult Disease (p232)

9:00 AM–11:45 AM

WORKSHOP SESSIONS

- Current Thinking and Experiences Related to Developmental and Reproductive Safety Assessment of Biotherapeutics (p233)
- **Novel Research Approaches and Animal Models in Translational Toxicology (p233)**
- **Toxicity Testing in the 21st Century for Ecotoxicology (p234)**
- Understanding Nonlinearities at the Low-End of the Dose-Response Curve: Insights from Molecular Network Analysis (p235)

PLATFORM SESSIONS

- Advances in Mycotoxin Toxicity (p235)
- **Impact of Receptors and Gene Regulation in Toxicological Response (p236)**
- Inhalation Toxicology of Ultrafine or Nanoparticles (p236)
- Reproductive and Developmental Toxicity of Phthalates (p237)

9:00 AM–12:30 PM

POSTER SESSIONS

- **Causes and Progression of Hepatic Metabolic Dysfunction (p248)**
- **Gene Regulation (p255)**
- **Hepatotoxicity: Role of Bile Acid Metabolism and Homeostasis (p247)**
- Immunotoxicology: Mechanisms (p240)
- Inhalation Toxicology (p237)
- Nanotoxicology—Gold or Silver Nanoparticles (p254)
- Neurodevelopmental Toxicity of Metals (p246)
- **Signal Transduction (p251)**
- Stem Cell Toxicology (p253)
- Studies in Pharmacokinetics and Disposition (p243)
- **Toxicogenomics—Continuing Advances in Molecular Toxicology (p249)**

12:00 NOON–1:20 PM

INFORMATIONAL SESSIONS

- Life-Stage Adjustment Five Years Later—Experiences from the Cancer Risk Assessment Field (p256)
- **Measuring Immune Responses in Monkeys for Drug Development: Opportunities and Challenges for Predicting Human Efficacy and Immunotoxicity (p257)**
- **The Tox21st Community and the Future of Toxicology Testing (p258)**

12:30 PM–1:20 PM

MERIT AWARD LECTURE

Living with Passion—Opening Doors in Research, Teaching, and Service—Lecturer: *Marion Ehrlich* (p258)

1:00 PM–4:30 PM

POSTER SESSIONS

- Beneficial Effects of Natural Products (p261)
- Carcinogenesis: Breast and Reproductive (p279)
- Cardiovascular Toxicology (p259)
- Exposure Assessment and Emerging Biomonitoring Applications (p268)
- Fetal Basis of Adult Disease (p277)
- Immunotoxicology: Methods and Models (p278)
- Metals I (p265)
- Models and Mechanisms of Hepatotoxicity (p275)
- Pesticides: General (p271)
- Regulations and Policy in Toxicology (p263)
- Risk Assessment II: Methodological Challenges and Metals (p272)

1:15 PM–2:15 PM

FEATURED SESSION

A Conversation with the EPA Office of Research and Development Director: *Paul Anastas* (p280)

1:30 PM–4:15 PM

SYMPOSIUM SESSIONS

- Aging As a Determinant of Xenobiotic Toxicity (p280)
- **TRPing the Sensor: The Role of TRP Channel Signaling in Cardiopulmonary Toxicity (p281)**
- Zebrafish Models for Developmental Neurobehavioral Toxicology (p282)

WORKSHOP SESSIONS

- **High-Throughput Electrophysiology—21st Century Toxicity Testing Approaches with Functional Outcomes (p282)**
- Minerals and Metals: Pros and Cons of Deliberate Exposure (p283)
- **'Omics Profiling of Cell and Tissue Interactions of Nanomaterials: Insight into Mechanisms of Action (p283)**
- The Process of Defining Risk for Environmental Chemicals Having Significant Skin Exposure and Absorption Potential (p284)
- **Translation of Nonclinical Models to Clinical Risk Management Strategies of Severe Infectious Diseases with Immunomodulatory Drugs (p285)**

PLATFORM SESSIONS

- Insights into Polyaromatic Hydrocarbon-Induced Toxicities (p285)
- Nanotoxicology—Metals and Metal Oxide Particles (p286)
- **Predicting Hepatotoxicity: Computational Approaches to a Critical Target (p287)**

2:30 PM–3:30 PM

FEATURED SESSION

A Conversation with the NIEHS Director: *Linda Birnbaum* (p288)

3:45 PM–4:45 PM

FEATURED SESSION

A Conversation with the U.S. FDA National Center for Toxicological Research: *William Slikker, Jr.* (p288)

4:30 PM–5:50 PM

ROUNDTABLE SESSION

- Overview of Current Regulatory Expectations for Oligonucleotide-Based Therapeutics: Case Studies for Different Classes of ODNs (p288)

INFORMATIONAL SESSION

- Seeking Funding for Undergraduate Research (p289)

Thursday, March 11

7:30 AM–8:50 AM

ISSUES SESSION

National Academy of Sciences Vision for Toxicity Testing in the 21st Century (p289)

8:30 AM–12:00 NOON

POSTER SESSIONS

- **Drug-Induced Liver Injury (p293)**
- Endocrine Toxicology (p289)
- Immune System Safety Evaluation/Developmental Immunotoxicology (p297)
- Juvenile Toxicity (p292)
- Metals II (p296)
- **Receptors (p294)**

9:00 AM–11:45 AM

WORKSHOP SESSIONS

- Blood-Based Genomic Profiles As Biomarkers of Exposure and Effect (p299)
- **Humanized Models in Toxicology and Their Application to Hazard Characterization and Risk Assessment (p299)**
- **Systems Biology Approaches to Understanding Cell Signaling in Dermal and Ocular Toxicology (p300)**
- Toxicological Challenges in Green Product Development (p301)