



EMERGING SCIENCE FOR ENVIRONMENTAL HEALTH DECISIONS

AGENDA

Computational Toxicology: From Data to Analyses to Applications

SEPTEMBER 21-22, 2009, WASHINGTON, DC

MONDAY, 8:00–5:00, TUESDAY, 8:30–NOON*

NAS BUILDING, 2101 CONSTITUTION AVENUE, NW (NOT 500 FIFTH STREET)

Computational toxicology is emerging at the intersection of toxicology, systems biology, biostatistics, and computer science—and that may enhance scientists' capacity to estimate risk or outcomes associated with an organism's exposure to environmental stressors.

A KEY ELEMENT driving the predictive capability is the advancement in computer-based approaches to modeling biological systems at different scales, from molecules to organisms. Equally important are novel technologies derived from computational chemistry, molecular biology and systems biology to produce high dimensional data streams necessary for populating such biological models. Likewise, advances in high-throughput and high-content screening assays provide an unparalleled level of detail for chemical and molecular interactions, cellular pathways, and tissue-level processes under normal physiological condition and upon exposure to environmental stressors.

THE APPLICATION of computational toxicology provides a novel framework for *in silico* modeling and simulation to validate and predict key aspects of biology that are difficult to analyze experimentally due to cost, scale or complexity. Thus, computational modeling of biological systems can begin *in silico* reconstruction of

normal functions and prediction of major disease states. The science of computational toxicology is also expected to reach beyond basic research and into regulatory decision-making and environmental health protection. A major research objective of computational toxicology is improved understanding of transformation and metabolism, better diagnostic/prognostic molecular markers, enhanced characterization of toxicity pathways, and improved systems biology approaches, modeling frameworks, dose metrics, and uncertainty analysis.

THIS MEETING will provide focus by assessing the state-of-the-art in the field and reviewing the practical applications of the new science. The potential and translation of these new technologies will be explored by participants who are leading the way in data collection, mining and modeling the data, and pioneering novel technologies—conferring with scientists from regulatory bodies who are challenged with incorporating new science into decision-making.

COMING IN 2010...

- The Exposome: A Powerful Approach for Evaluating Environmental Exposures and Their Influences on Human Disease

TBD, 2010, Washington, DC

* After the meeting ends, Committee and Government liasons meet until approximately 3:00 p.m.

MONDAY, SEPTEMBER 21, 2009
LECTURE ROOM, NAS BUILDING

Introduction/Overview—*Ivan Rusyn, *University of North Carolina, Chapel Hill, Department of Environmental Science and Engineering*

EMERGING DATA STREAMS AMENABLE TO COMPUTATIONAL MODELING AND DATA MINING

Molecular and Cellular Scale Data—Chris Austin, *Director, NIH Chemical Genomics Center*

Tissue Scale Data: Co-culture Systems, 3D Cultures, Tissues Slices—Linda Griffith, *Massachusetts Institute of Technology, Department of Biological Engineering*

Organism Scale Data (Zebrafish)—Robert Tanguay, *Oregon State University, Department of Environmental and Molecular Toxicology*

EXISTING DIGITALIZED DATA TO GENERATE NEW INSIGHTS WITH NEW ANALYSIS OR TO PHENOTYPICALLY ANCHOR NEW DATA

Digitalized Traditional Toxicity Data: Database Efforts at EPA and Beyond—Richard Judson, *US Environmental Protection Agency, National Center for Computational Toxicology*

Genetic/Sequence Data: Data for Insight into Human Variability and/or Cross Species Comparison—Carolyn J. Mattingly, *Mount Desert Biological Laboratory*

Panel Discussion to integrate morning presentations

EMERGING DATA ANALYSIS AND MODELING TOOLS

Combining High Throughput Screening Data and QSAR to Improve Hazard Predictions—Alex Tropsha, *University of North Carolina, Chapel Hill, School of Pharmacy*

Predictive Model Screening and Learning Curves in Computational Toxicology—Russel Wolfinger, *SAS Institute*

Tools for Network Analysis: “Biologically-Driven” In Silico Models—H. Steve Wiley, *Pacific Northwest National Laboratory*

In Silico Modeling with Virtual Tissues—Richard Superfine, *University of North Carolina, Chapel Hill, Department of Physics and Astronomy*

* The Standing Committee on Use of Emerging Science for Environmental Health Decisions

SCIENTIFIC QUESTIONS ABOUT COMPUTATIONAL TOXICOLOGY APPLICATIONS

- Which computational approaches are robust, scientifically valid, and interpretable now?
- Are there specific areas that require large scale investment to achieve scientific acceptance of the technology?
- How will these approaches/technologies be validated?

Panelists: Deborah Cory-Slechta, The Environmental and Occupational Health Sciences Institute; Bennett van Houten, University of Pittsburgh, Department of Pharmacology and Chemical Biology; Abigail Li, Exponent, Toxicology and Mechanistic Biology; Committee Members TBD.

TUESDAY, SEPTEMBER 22, 2009
LECTURE ROOM, NAS BUILDING

DECISION-MAKER DISCUSSION OF POTENTIAL USE

Structured Roundtable Discussion with Practitioners about Time Horizons, Translational Potential, Decision-Making Potential

1. Which applications are short-term, medium-term or long term? Where are we with each?
 - A. Identification of Substances [Chemical and Other] in the Environment that May Impact Human Health
 - B. Dose-response Assessment
 - C. Comparing Safety of Chemicals and Other Substances
 - D. Prioritizing Testing Needs
2. When and what needs to be communicated about the emerging science? At what level is public engagement appropriate?
3. What are the appropriate decision rules?
4. Are there expectation management issues to consider?

Discussants:

Roundtable discussion will include liaisons and committee members, as well as speakers and panelists from previous sessions. Additional discussants TBD are invited to drive the discussion towards application and practice questions.

At the request of the National Institute for Environmental Health Sciences, the National Academies formed the *Standing Committee on Use of Emerging Science for Environmental Health Decisions* to facilitate communication among government, industry, environmental groups, and the academic community about scientific advances that may be used in the identification, quantification, and control of environmental impacts on human health.

