Integrative Exposure Biology and Computational Toxicology for Risk Assessment

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Understanding the relationships between environmental exposures and health outcomes requires integration of a wide range of factors—extrinsic (*e.g.* environmental), intrinsic (*e.g.* genotypic), and mechanistic (e.g. toxicolgic)—to assess risk. Application of modern methods in molecular biology and advanced computational tools provide the potential to understand complex exposure-outcome systems. A new generation of scientific tools, including transcriptomics and high throughput assays, is emerging that can rapidly measure signals from cells, tissues, and organisms following exposure to chemicals. Combined with development of widely accessible databases and advances in computational technologies for efficient analysis of multidimensional data, these tools are facilitating a "paradigm shift" in characterization of human-environment interaction for risk assessment. A reverse-engineering or systems-biology approach for holistic study of environmental disease considers coupled networks that span multiple scales of biological organization. Mechanistic understanding is derived by characterization of these networks and impacts of perturbations due to behavioral and environmental influences. This symposium will present recent advances in integrative exposure biology and computational toxicology for risk assessment. Specifically, it will bring together presentations from a team of computational scientists, with diverse backgrounds in biological, chemical and environmental informatics. Presentations will address multiple elements of the toxicant source-to-outcome sequence including: application of informatics tools for toxicant characterization; integration with individual and population exposure modeling tools; and enhancement of current quantitative risk assessment. The proposed presentations highlight progress towards mechanism-based environmental health risk assessments in a person-oriented framework that accounts for simultaneous exposures to contaminants from multiple media, routes and pathways. Application of such a multidisciplinary environmental systems approach to evaluate exposure and hazard is expected to facilitate development of more accurate, and eventually even "personalized," risk assessments.

Elaine Cohen Hubal : ExpoCast: Exposure science for prioritization and toxicity testing
Alan Sasso: Integrated computational models for supporting risk assessment: case studies with chemical mixtures
Sastry Isukapalli: Multiscale mechanistic models in exposure assessment: Case studies with virtual organs
Chris Brinkerhoff: Linking exposure dynamics with health effects through biological modeling: Case study with TCE exposure and oxidative stress

Bill Welsh: Biological Spectra Profile Analysis in Computational Toxicology: Linking the Bioactivities and Molecular Structures of Chemical Datasets
Meric Ovacic et al.: Pathway Modeling of Microarray Data of the Rat Testes after in utero DBP Exposure
Rebecca Fry: Toxicogenomics approaches to understand the impact of prenatal arsenic exposure.
Panos Georgopoulos: Integrative source-to-dose-to-effect modeling for interpreting biomonitoring data in an exposure context