

Session title: **Protecting the Consumer: Can "Omics" Keep the Promise?**
When? Sunday, February 21, 2010: 1:30 PM-3:00 PM
Where? Room 5A (San Diego Convention Center)

The Role of Genomics in Mode-of-Action Based Risk Assessment
Ivan Rusyn , University of North Carolina, Chapel Hill, NC

Classical toxicology is traditionally focused on understanding of xenobiotic metabolism, the dose-response relationships between chemicals and adverse health effects, and mode-of-action evaluation for toxicant-induced disease. Novel molecular, biochemical, genetic and genomics approaches are increasingly used to understand the mechanisms of environmental agent-related organ injury and carcinogenesis. Toxicogenomics is a rapidly maturing field which provides the ability to define in greater detail the underlying molecular events preceding or accompanying toxicity. The incorporation of this new information requires careful validation and altered gene expression patterns should be corroborated with conventional indices of toxicity in a dose- and time-dependent manner. Recent efforts by the US EPA advance the process of regulatory acceptance of such data whereby toxicogenomics data is being applied in mode of action analysis. This talk will illustrate the potential steps in risk assessment process that may benefit from the availability of more granular molecular information on toxicity mechanisms, as well as address the challenges inherent in changing the regulatory paradigms.

Mathematical Models for Analyzing Genomic Data Sets: From Equations to Diagnosis

Knut Reinert , Free University of Berlin, Berlin, Germany

Rapid advances in genomics and proteomics have brought such methodologies into sharp focus within the hazard and risk assessment communities. Already in their 2007 paper, "Toxicity Testing in the Twenty-first Century: A Vision and a Strategy", the US National Research Council stressed the upcoming importance of high throughput methods such as functional genomics based on Next Generation sequencing or Proteomics techniques. Three years on, we can produce 10 Gigabases in a couple of days for several thousand dollars, hence it is clear that "omics" techniques could be a viable means for toxicity testing and risk assessment. Having huge data sets and complicated bioinformatics analysis at hand, the focus shifts now to the question of how much we can trust the results of computational analyses using these massive data sets? In addition to modeling the uncertainty and measurement error in the input, we also have to deal with possible mistakes accumulating during the numerous processing steps. Currently there are scarcely any reliable margins of uncertainty computed. In this talk we will give a short introduction to some (simplified) analysis pipelines for high throughput "omics" data that are in use today, and point out what possible effects small changes in parameter settings can have on the outcome of an analysis, and potentially on the result of an associated risk assessment. The goal of the presentation is to make the audience aware of possible pitfalls in the data analysis and to show the need for robust algorithms that are able to assess the accuracy of their results.

Getting More from Your Cell: High-Tech Approaches for In Vitro Testing

Maurice Whelan , JRC Institute for Health and Consumer Protection, Ispra, Italy

Toxicity testing in vitro is undergoing a revolution, and Science and Technology are the drivers - a strong push to embrace a more scientific approach to the understanding of human toxicological hazard, that provides a regulatory decision-making framework where in vitro methods are a critical source of information, coupled with the impact of advanced and converging technologies that are driving the development of a new generation of test systems capable of delivering vast quantities of high quality data. Within this context, the basic approach to developing reliable and relevant in vitro systems for toxicological profiling has to change. Rather than trying to create biological models that mimic the in vivo situation in every way possible, to be able to correlate in vitro data with late-stage pathology data derived from animal studies, we need to take a hypothesis-driven approach to designing tests, that requires a deep theoretical understanding of biological systems, and the requirement of embodiment of specific biological functionality in systems that test against related mechanisms of toxicological action. The ultimate goal is a win-win situation - improved risk assessment methods in the field of consumer safety, with a significantly reduced reliance on animal testing. This talk will describe this change in design philosophy of in vitro systems, and will give some examples of in vitro test systems that reflect the sophistication emerging in modern approaches.