

Metabolic Profiling: Application to Toxicology and Risk Reduction An International Conference

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The NIEHS hosted an international conference on *Metabolic Profiling: Application to Toxicology and Risk Reduction* on May 14-15, 2003. Meeting sponsors included the NIEHS and Office of Rare Disease of the NIH; Food and Drug Administration; Paradigm Genetics and Waters Corporation. The conference was designed to define the state of the science for the emerging technology of metabolic profiling, also called *metabonomics* or *metabolomics*, and its application in basic and applied health research. Three scientific sessions focused on the application of metabolic profiling to *toxicology*, *risk reduction*, and *computational and systems biology*. The conference was instrumental in identifying future directions for technology and research in metabolic profiling to significantly advance exposure assessment, predictive and mechanistic toxicology and clinical medicine.

The concept of metabolic profiling is not a new. It is essentially “biochemistry grown up” or what biochemistry would have been had methods now available been around in the 1930s when the components and dynamics of the Krebs cycle were being worked out. Previously, one at a time measurements, isolated tissue preparations and interspecies extrapolation often founded on hope, were successfully used to describe basal intermediary metabolism, but did not provide the flexibility and sensitivity to gain a whole-organism look at biological responses. A variety of approaches currently being used for metabolic profiling of biosamples (blood, urine, tissue) will be discussed. These approaches build on basic science technologies such nuclear magnetic resonance (NMR) spectroscopy, liquid and gas chromatography, tandem mass spectroscopy (MS/MS), and time-of-flight mass spectroscopy (MS-TOF).

Industry has played a leadership role in advancing metabolic profiling technologies as a means of streamlining and accelerating chemical toxicity testing and drug discovery and development. Thus, current applications focus largely on the identification and validation of predictive markers of liver, renal, cardiovascular and neurodegenerative toxicity and disease in animals and humans exposed to a variety of chemicals, drugs and nutritional agents. Currently with technology development, new computational, database and visualization tools are being developed to facilitate data mining, pattern recognition and information recovery from the vast amount of metabolic profiling data generated using high throughput approaches. Several example applications with relevance to environmental health science research will be discussed.

Metabonomics represents a new approach for environmental science research but realization of this potential will require new initiatives that focus on technology development and application to environmentally relevant exposures and disease. The conference provided a needed forum for information exchange and scientific partnering amongst academic, industry and government scientists, engineers, statisticians and information technologists. An emerging area of shared interest is

in systems biology: the integration of “omics” data in order to define and model dynamic, systems level responses to exogenous agents (chemicals, drugs, and nutritional factors). Systems biology approaches have been successfully used to model functional pathways and metabolic regulation in simple biological systems such as yeast. An important challenge in this post-genomic era will be the development of comparable model approaches for complex mammalian systems. This is critical for placing “omics” information in a real world disease context which links genetic composition and functional genomics with risk of prognosis for future disease.

Several collaborative efforts are underway to stimulate technology development, collaborative research, and communication about metabolic profiling programs on a global scale. These include the Consortium for Metabonomics in Toxicology (COMET), the European Nutrigenomics Organization (NuGO) and the NIEHS National Center for Toxicogenomics (NCT). Each of these forums will merge research and technology interests in metabolic profiling and systems biology and serve to advance the field in a positive direction in this post-genomic era.