

Metabonomics: Mining for Metabolites in Biofluids

Metabolites are the products and by-products of the many intricate biosynthesis and catabolism pathways that exist in humans and other living systems. Historically, measurement of metabolites in human biofluids has been used for the diagnosis of a number of genetic conditions and for assessing exposure to certain xenobiotics. Traditional analysis approaches have focused on one or a few metabolites.

More recently, advances in analytical separation and detection technologies, coupled with developments in bioinformatics, have made it possible to measure and interpret complex time-related metabolite profiles that are present in biofluids such as urine, plasma, saliva, and cerebrospinal fluid. The terms *metabonomics* and *metabolomics* have been coined to describe metabolic profiling, although the precise nomenclature, including potential distinctions between these terms, is still evolving.

The application of metabonomics to study potential environmental inputs to disease was one of several featured topics at a Division of Extramural Research and Training science planning retreat held 27–28 November 2001 in Southern Pines, North Carolina. This session highlighted the opportunities and challenges afforded by metabolic profiling and will be used to guide anticipated future efforts of the NIEHS to promote and support the application of this approach to environmental health sciences and its integration with ongoing and future genomic and proteomic initiatives.

Metabolic profiling employs a range of analytical approaches (e.g., mass spectrometry and high-resolution ¹H nuclear magnetic resonance spectroscopy) suited to the chemical properties of the metabolite class(es) of interest. Bioinformatic tools are used to maximize information recovery from biofluid samples and to aid interpretation of the very large multivariate metabolite data sets that are created.

Metabolic profiling can be applied to multiple levels of biological organization, ranging from single cells to whole organisms. Perhaps the greatest interest has been on the metabonomic analysis of integrated body pools such as urine and plasma, as these pools reflect systems-wide phenotypic response(s). In such case, metabonomics provides an integrated readout of both primary and secondary perturbations that point to a pathophysiologic process, genetic modification, or xenobiotic exposure.

Significant opportunities exist for the application of metabonomics to the field of environmental health sciences, particularly in the area of biomarkers of exposure and disease. Widespread incorporation of this promising approach will require the development and refinement of appropriate high-throughput technologies to measure chemically diverse subsets of metabolite molecules. Another large challenge will be to create a database of metabolic profiles with linkages to protein and gene expression databases. It is envisioned that a new and fundamental understanding of organismic responses to environmental insult will emerge from the integration of metabonomic data with those obtained from the study of global patterns of gene and protein expression.

The NIEHS encourages the submission of investigator-initiated applications that use metabolic profiling as a novel tool to elucidate mechanisms of environment–disease linkages. Please contact the health science administrator listed below if you have any questions or wish to discuss a potential research proposal.

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