



Metabolomics

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RTI International

Eastern Regional Metabolomics
Resource Core

Metabolomics

- Metabolomics involves the broad spectrum analysis of the low molecular weight complement of cells, tissues, or biological fluids.
- Metabolomics makes it feasible to uniquely profile the biochemistry of an individual, or system, apart from, or in addition to, the genome.
 - Metabon(l)omics is used to determine the pattern of changes (and related metabolites) arising from disease, dysfunction, disorder, or from the therapeutic or adverse effects of xenobiotics; including applications in plant and mammalian studies.
- This leading-edge method is now coming to the fore to reveal biomarkers for the early detection and diagnosis of disease, to monitor therapeutic treatments, and to provide insights into biological mechanisms.

NIH Common Fund is Investing in Metabolomics

- NIH Funded Six Regional Comprehensive Metabolomics Resource Cores to
- increase our National capacity to provide metabolomics profiling and data analysis services to basic, translational, and clinical investigators
 - foster collaborative efforts that will advance translational research using metabolomics approaches
 - facilitate institutional development of pioneering research, metabolomics training, and outreach
 - establish National standards
- RTI (Susan Sumner), UC Davis (Oliver Fiehn) and U Michigan (Chuck Burant), UK (Rick Higashi), UF (Art Edison), Mayo Clinic (Sree Nair)
 - Metabolomics DRCC (Shankar Subramaniam, PI, UCSD)
 - Metabolomics Training (Martin Kohlmeier, UNC-CH; Stephen Barnes, UAB)
 - Metabolite Standards Synthesis Cores (Herb Seltzman, RTI; Mary Tang, SRI)

Why Metabolomics?

Specific genes can be identified that define individuals' at risk for a disease, dysfunction, or disorder, or response to treatments.

Some diseases or responses can occur at the level of the proteome; and proteins and metabolites can inform us about the state of a disease, dysfunction or disorder at any given time.

NMR Metabolomics of Urine Benzene dosed for 28 days in Rats

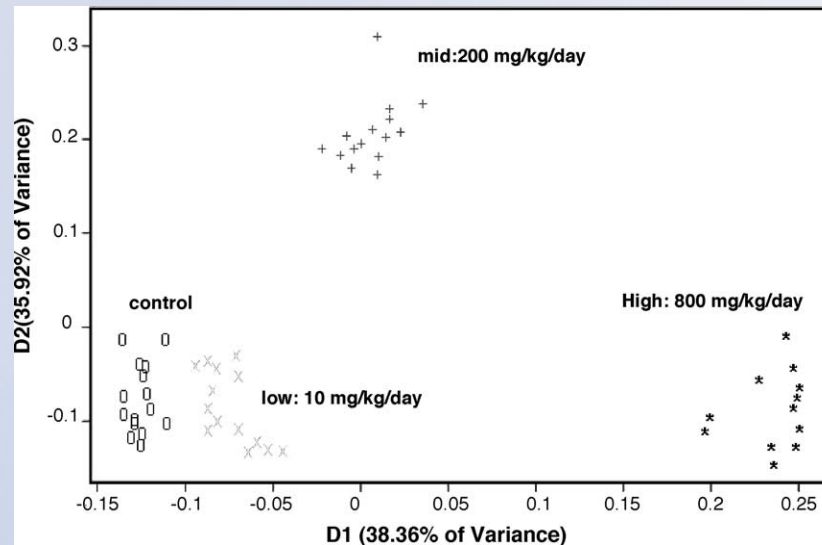


Fig. 1. Urine metabolomics: PCDA Score plot. Score plot of principal component analysis with discriminant (PCDA) of NMR spectra, reflecting the metabolite profiles of urine. Each symbol in the score plot represents an individual NMR spectrum. Per group, samples of five rats were measured in triplicate. The symbols represent: 0, controls; x, exposure to low dose of benzene (10 mg/kg/day); +, mid dose of benzene (200 mg/kg/day); and *, high dose of benzene (800 mg/kg/day).

Benzene 30-Day Study C3H/He Mice, 150 or 300 mg/kg/day sc

TABLE 4. Potential Biomarkers and Related Metabolic Pathways

Accuracy mass (m/z)	Retention time (min)	ESI mode	Benzene exposure group					Metabolites	Related pathway
			5 d	15 d	20 d	25 d	30 d		
137.0485	1.71	+	↓	-	↑	-	↑	Hypoxanthine	Purine metabolism
146.165	0.872	+	↓	↓	↓	↓	↓	Spermidine	Methionine metabolism Spermidine and spermine biosynthesis
195.0768	4.859	+	↓	↓	↓	↓	↑	4-Aminohippuric acid	Minor metabolites of fatty acids
206.0812	7.486	+	-	↓	↓	↓	↑	Indolelactic acid	Tryptophan metabolite
295.1298	5.02	+	↓	↓	↓	↓	↑	Glutamylphenylalanine	Peptides, gamma-glutamyl derivative

Variations compared to control samples: ↑, indicates relative increase in signal; ↓, relative decrease in signal; -, no change.

Sun et al., Journal of Toxicology and Environmental Health, Part A, 75:18, 1163 -1173

Pilot and Feasibility Studies Program

- Consistent with an objective of the NIH Common Fund, an aim of the pilot and feasibility program is to foster collaborations and promote the use of metabolomics.
- Applications will be accepted at least once per year
 - Up to \$50K in RTI RCMRC metabolomics collaboration.
- Awardees must agree to deposit data into the DRCC.
- Studies are selected based on innovation, relevancy, investigator merit, and collaborative potential for future funding.
- Applications may include technology development with RTI RCMRC.
- RTI RCMRC will use the P&F studies program as a means to ensure a sustainability model.
- For more information, go to: www.rti.org/rcmrc

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“NIH Eastern Regional Comprehensive Metabolomics Resource Core”

RTI RCMRC

PI: Susan Sumner

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