

Preliminary Study on Clinical Application of Metabolomics for Laboratory Diagnosis of Inborn Errors of Metabolism

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Metabolomic studies employing small molecular profiling have evolved into a key data-intensive technology for biomarker discovery and customized therapies in medicine. However to date, metabolomic profiling has not been utilized in routine clinical practice.

We present data results of 129 plasma samples collected from patients with a confirmed inborn error of metabolism (IEM) using a rapid metabolomic workflow. In total, 21 different IEMs were represented within our sample set including amino acid, fatty acid oxidation, vitamin cofactor, creatine biosynthesis, and urea cycle disorders. Analysis was performed using a non-targeted multi-mass spectrometry platform. Around 500 small molecule human metabolites (FW <1500 Da) were commonly presented in plasma samples. The analytes detected encompass a number of classes of important small molecule biomarkers such as fatty acids, acylcarnitines, amino acids, bile acids, carbohydrates, lipids and nucleotides, etc. After imputation of controls and internal standards, final standard scores were assigned to each analytes. For the majority of IEM samples studied, classic pathognomonic compounds were among the most significantly elevated analytes detected. Metabolic profiling was able to correctly diagnose 20 of the 21 disorders in our panel for which plasma analysis is informative. We also analyzed plasma specimens from 71 patients who had prior nondiagnostic results. In a subset of these cases, metabolomic analysis uncovered disturbances that pointed to a genetic disorder (e.g., sarcosinemia and trimethyllysine hydroxylase deficiency) or assisted in the interpretation of concurrent DNA analysis. In summary, we have demonstrated the clinical utility in the diagnosis of IEMs as well as functional confirmation of genetic and genomic results of uncertain significance.