

# DISCOVERY OF DISEASE AND TOXICITY BIOMARKERS USING HIGH RESOLUTION METABOLOMICS

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## **Abstract**

Metabolomics is being used to identify biomarkers for diseases such as diabetes and diabetic complications, alcoholic-induced liver disease, and cancer, using mouse and monkey models and samples taken from normal and diseased human patients. This approach has provided novel, relevant, and translatable perspectives of these diseases and given unprecedented insights into their mechanisms of pathogenesis and progression. Using high-end platforms including ultra-performance liquid chromatography (UPLC) and 4-dimensional gas chromatography (4D-GC) as the front ends of highly-sensitive quadrupole time-of-flight and triple quadrupole mass spectrometers, cells and tissue extracts, serum, and urine can be successfully probed using to discover and develop chemical fingerprints left from various biological processes. Biomarkers can be identified in easily obtainable biofluids such as urine or serum for cancer diagnosis with the promise of developing early-stage prognostic and diagnostic indicators. Biomarkers can be used to monitor cancer therapy to determine drug efficacy and distinguish responders from non-responders. In many cases, biomarkers can provide mechanistic insight into disease pathogenesis, where an enrichment or depletion of a certain metabolite or metabolites indicates perturbed metabolic processes and therefore point to alterations at the genomic, epigenomic, transcriptomic, and/or proteomic levels. The metabolome might be the most accurate indicator of cellular physiology. Metabolomics can be used to study the metabolism of cancer drugs and identify the full profile of metabolites produced in humans and determine which metabolite leads to efficacy and which leads to toxicity. Metabolomics can be used to study the mechanism of chemical carcinogenesis by establishing the metabolite profile of various carcinogens. The current state of the field and an update on recent developments will be discussed.