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High-throughput liquid chromatography–mass spectrometry based targeted metabolomics for separation and quantitation of ~250 cellular metabolites

Fatemeh Mirnaghi
University of Toronto, Canada

Abstract

Target-based metabolomics is focused on a subset of metabolites selected from metabolic pathways of interest to measure changes in concentrations of endogenous metabolites. Metabolomics is a valuable tool for assessing metabolic changes in a given disease state and systemic responses to environmental, therapeutic, or genetic interventions.Since hundreds of endogenous metabolites are present, representing diverse chemical structures and properties, the ability to simultaneously analyze and efficiently quantitate of multiple metabolites is challenging. Liquid chromatography–mass spectrometry (LC–MS) is a capable technique for the quantitation of multiple metabolites, because of its potential for high sensitivity and specificity, and the opportunity to confirm the molecular formulas of the specific compounds. However, existing LC-MS based metabolomics methods are usually limited to analysis of only similar classes of metabolites. The numbers of metabolite classes which can be simultaneously measured in one assay are restricted by the choice of chromatographic column, MS detection time, and ionization polarity.

In this study, we report a high-throughput, sensitive, and reproducible method for target-based metabolomics studies of different classes of metabolites (amino acids, sugar, nucleotides, nucleic acids, organic acids, vitamins, lipids and fatty acids). This method combines two different separation conditions coupled through a multiport valve, a dual injection system, optimal ionization polarities, and the most sensitive multiple reaction monitoring acquisition mode. In 25 min, ~250 endogenous metabolites are separated using reversed-phase or HILIC chromatographic systems and are sequentially analyzed on a triple-quadrupole MS system. The optimized method is used for the analysis of cellular metabolites from biological samples.

Biography

Fatemeh Mirnaghi has completed her Ph.D. in 2012 from University of Waterloo in Analytical Chemistry and she is doing her postdoctoral studies at University of Toronto, Terrence Donnelly Centre for Cellular and Biomolecular Research. She has published more than 15 papers in reputed journals and presented more than 25 talks and poster presentations in several international conferences and seminars. She has serving as a reviewer for the journal of Analytica Chimica Acta since 2009.