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Targeted metabolite analysis of central carbon metabolism by LC-MS

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Central carbon metabolism (CCM) is a complex metabolic network that consists of several sub-pathways: glycolysis, gluconeogenesis, the pentose phosphate pathway, and the tri-carboxylic acid cycle. As the central hub of energy metabolism in a cell or an organism, multiple enzymes are involved in CCM to convert the low-molecular weight energy precursors such as glucose into various small-molecule metabolizing products as the metabolic intermediates. Some of these compounds also act as the substrates to synthesize other biomolecules such as amino acids. During the metabolic processesof CCM, cell usable energy is produced in the form of ATP for maintaining regular cellular function. Thus, reliable and sensitive measurement of the CCM-related metabolites can provide essential information about the catabolic and anabolic state of a biological system and is of important interest.

The CCM-related metabolites include low-molecular weight sugars, sugar phosphates, nucleotides, co-factors, phosphocarboxylic and free carboxylic acids. Determination of these compounds in biological matrices by liquid chromatography-mass spectrometry (LC/MS) remains challenging. To perform comprehensive metabolomic analysis of the whole CCM pathway, we developed several new and improved chemical derivatization-reversed-phase UPLC and ion-pairing UPLC methods, and combined them with high-resolution MS for isotope-resolved metabolic profiling, and with high-sensitivity tandem MS for reliable quantitation of the full pathway metabolites. With the optimization of chemical derivatization, chromatographic separation and MS detection, precise and accurate quantitation of >50 CCM metabolites were achieved with assay validation. These well-developed methods are being applied for tissue and cell metabolomics in the metabolic pathway-specific way.

Biography

Christoph H Borchers received his B.S., M.S. and Ph.D. from the University of Konstanz, Germany. After his post-doctoral training and employment as a staff scientist at NIEHS/NIH/RTP, in North Carolina, he became the director of the UNC-Duke Proteomics Facility and held a faculty position at the UNC Medical School in Chapel Hill, NC (2001-2006). Since then, Borchers has been employed at the University of Victoria (UVic), Canada and holds the current positions of Professor in the Department of Biochemistry and Microbiology and the Don and Eleanor Rix BC Leadership Chair in Biomedical and Environmental Proteomics. He is also the Director of the UVic-Genome BC Proteomics Centre, which is one out of five Genome Canada funded Science & Technology Innovation Centers and the only one devoted to proteomics.

His research is centred around the improvement, development and application of proteomics technologies with a major focus on techniques for quantitative targeted proteomics for clinical diagnostics. Multiplexed LC-MRM-MS approaches and the immuno-MALDI (iMALDI) technique are of particular interest. Another focus of his research is on technology development and application of the combined approach of protein chemistry and mass spectrometry for structural proteomics. Dr. Borchers has published over 145 peer-reviewed papers in scientific journals and is the founder and CSO of two companies, Creative Molecules Inc., and MRM Proteomics Inc. He is also involved in promoting proteomic research and education through his function as HUPO International Council Member, Scientific Director of the BC Proteomics Network and President of the Canadian National Proteomics Network.

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