TARGETED AND UNTARGETED LIPIDOMICS USING AN INTEGRATED MICROFLUIDICS MASS SPECTROMETRY TECHNOLOGY

Steven Lai; Paul Rainville; Angela Doneanu; Jay Johnson; James Murphy; Robert Plumb; Giuseppe Astarita
Waters Corporation, Milford, MA

OVERVIEW
A fast and robust microfluidics platform for lipidomics analyses with considerable reduction in solvent consumption and increase in sensitivity.

INTRODUCTION
Lipidomics - the screening of lipid species in biological samples - aims to offer a better understanding of health and disease. The need for a fast, comprehensive and sensitive analysis of hundreds of lipid species challenges both the chromatographic separation and mass spectrometry. Here we used a novel microfluidics platform, which integrates the UPLC separation into the course of the mass spectrometer: the platform contains the fluidic connections, electronics, ESI interface, heater, and 1.7 µm particles. Such integrated platforms are suitable for lipidomics analyses with performance comparable to analytical scale LC-MS analysis.

METHODS
A microfluidic MS device was optimized for MS analysis of lipids in complex biological extracts. The integrated microfluidic device was fabricated from resistant ceramic materials that permit operation at high pressure with sub 2 µm particles, leading to highly efficient LC separations of lipid molecules. Lipids were separated using 150 µm ID x 100 mm devices packed with reversed phase C18, 1.7 µm particle at flow rates of 3 µl/min. Analyses were performed using both TOF and QTOF operated in both negative and positive ESI modes. Ion mobility was integrated in the TOF platform to provide collision cross section measurements for lipids for lipid identification.

UNTARGETED LIPIDOMICS
Untargeted data were processed and analyzed using Progenesis QI software, which allowed peak picking, multivariate statistical analysis, and other key lipidomics analysis tools. A microfluidics electrospray increases sampling efficiency.

TARGETED LIPIDOMICS
Targeted lipidomics analysis were conducted using internal standards and TargetLynx for the identification and quantification of selected lipid molecules.

References
1. Targeted Lipidomics Using the IonKey/MS System® Waters App note. 2014. 720004968EN.
4. Isaac G, McDonald S, and Astarita G. “Lipid Separation using IonKey/MS platform for lipidomics analysis in mouse plasma. Samples were analyzed using ionKey/MS system with linear gradient from 0 to 100% solvent B (45 min). Representative extracted ion chromatograms of isobaric glycerophospholipids (19:0/19:0) are shown in Figure 1. The information obtained can be integrated with clinical data to generate testable hypotheses on the functional significance of the lipid abnormalities observed in brains from subjects with Alzheimer’s disease.

CONCLUSIONS
The IonKey/MS system leads to highly efficient LC separation of lipid molecules extracted from biological samples. Chromatographic results were equivalent to using analytical-scale columns [1-4] bringing considerable advantages:

-<20% decrease in solvent consumption, making it convenient for the large-scale analysis and screenings of hundreds or thousands samples.

>-10x increase in sensitivity, which could facilitate the detection of low abundance metabolites.

-4x volumes injection (e.g., 0.2 µl), which makes it ideal when sample limited studies or when multiple injections are required.

-The information obtained can be integrated with clinical data to generate testable hypotheses on the functional significance of the lipid abnormalities observed in brains from subjects with Alzheimer’s disease.

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