Global Targeted Quantitation for High-Throughput Targeted Lipidomics

LC-MRM and QTRAP® 6500+ System

There are likely more than 150,000 different lipid molecular species present across the biological spectrum. This diversity reflects the different functions lipids fulfill at the cellular, tissue, and organismal levels. The field of lipidomics aims to quantitatively define lipid classes at the molecular species levels in biological systems.

The Challenge:

Direct infusion 'shotgun' lipidomics is an established approach for broad-based lipidomic analysis. It is fast and simple, but it can suffer from inherent ion suppression effects, and due to the extensive isobaric overlap within the lipidome, there is potential for ambiguous identification. Reverse and normal phase LC strategies coupled with MS are also frequently used for lipidomics analyses. These strategies separate lipids based on their physico-chemical properties, but the huge diversity of lipid molecular species makes development of standardized "all-inclusive" methods challenging, especially when quantitation is desired. Furthermore, discovery-based approaches such as information dependent acquisition (IDA) suffer from poor reproducibility, making quantitation unreliable.

The Solution:

An efficient way to maximize sensitivity and specificity is targeted lipidomics using HPLC-triple quadrupole instrumentation in the multiple reaction monitoring (MRM) mode. HILIC separation is an attractive chromatographic strategy that separates lipids into classes and subclasses, which span a very narrow RT window. The QTRAP 6500+ system offers unparalleled sensitivity even at high scan speed (2-5 msec transition time) with rapid Pos/Neg switching (< 5msec). Using qualified MRM transitions and commercially available lipid internal standard mixtures, this method provides quantitative measurement of over 1200 different lipid molecular species (Figure 1).

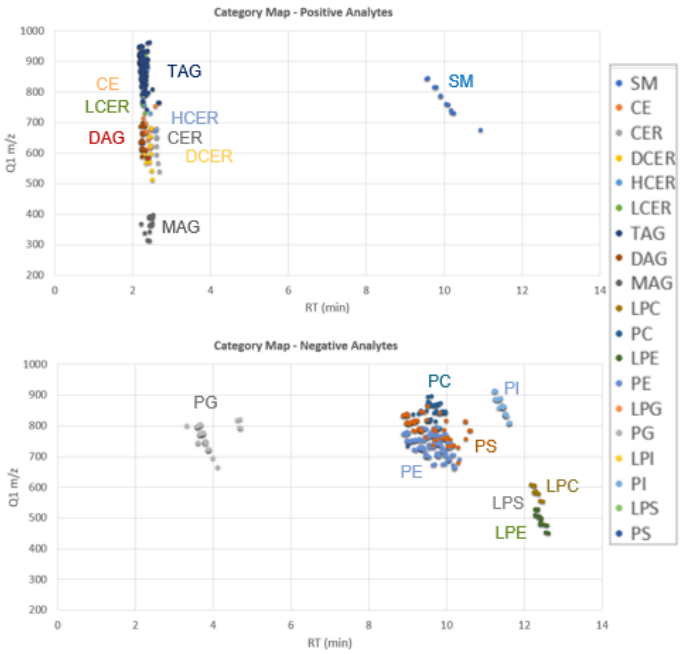

Figure 1. HILIC-Based Separation of Lipids in Plasma. ~1210 MRM transitions of common lipid species and internal standards were used to generate a global profile of lipids in matrix. HILIC separates lipids by class and subclasses, which spans a tight RT window. Additional transitions can be added to the method to allow customization. Easy to use tool available for retention time scheduling and method optimization.

Targeted lipidomics analysis via LC-MRM provides for rapid identification and quantification of a broad spectrum of lipid molecular species. The target list is customizable, works for many different matrices, and data are easily processed using MultiQuant™ Software.

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