Skyline for small molecules: a flexible tool for cross-platform LC-MS/MS method creation and data analysis for metabolomics.

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The Skyline software package is a powerful open-source and vendor-neutral software tool which has built a strong reputation for promoting collaboration and cross-platform validation of targeted (SRM) and high-resolution proteomics analysis. The software allows direct import of raw mass spectrometry data from all major instrument vendors, speeds method development by allowing direct export of native instrument methods or transition lists, and performs peak integration with a flexible data reporting environment.[1,2] While each instrument vendor does provide data analysis tools for quantitative analysis of small molecules by liquid chromatography – tandem mass spectrometry (LC-MS/MS), there is no software platform for small molecule analysis which allows cross-vendor method creation and data analysis. This presentation will demonstrate the initial implementation of the Skyline software package for the creation of custom LC-MS/MS methods for several classes of metabolites, including targeted LC-MS/MS of hydroxycholesterols, fatty acids, and acylcarnitines among others. The software includes the ability to define precursor and product ions based on empirical formula or m/z, define collision energy specifically by molecule or based on a linear equation, and to define expected retention time. Additionally, we will propose the use of Skyline along with retention time, ion mobility, and accurate mass lipid libraries for the quantification of lipid species from unbiased high-resolution lipidomics datasets, as an alternative to standard metabolomics workflows.[3,4] Enabling Skyline for small molecule method creation and data analysis fills a computational gap by easing the translation and validation of targeted metabolomics methods between instruments and laboratories.

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