for detecting the level of the one or more FSLMs in the sample from the subject by mass spectrometry.

In some embodiments, the one or more isotopically labeled ether phospholipids comprise one or more isotopically labeled ether diacylglycerophosphocholines (PCO-).

In some embodiments, the one or more isotopically labeled ether diacylglycerophosphocholines (PCO-) comprise PC(O-16:0/18:2), PC(O-16:0/22:6), PC(O-18:0/18:2), PC(O-18:1/20:5), PCO-36:3, PCO-34:2, PCO-40:2, PCO-44:7 and PC(O-17:0/20:4).

In some embodiments, the one or more isotopically labeled ether phospholipids comprise one or more isotopically labeled phosphatidylethanolamine ethers (PEO-).

In another aspect, provided herein is the use of an FXN replacement therapy in the manufacture of a medicament for treating an FXN deficiency, the use comprising: (a) determining an FXN lipid profile in a sample obtained from an FXN deficient subject for one or more FXN-sensitive lipid markers (FSLMs), (b) comparing the FXN lipid profile of the sample with at least one other lipid profile selected from the group consisting of normal FXN lipid profile for the one or more FSLMs, baseline FXN(-) lipid profile for the one or more FSLMs, and FXN replacement lipid profile for the one or more FSLMs, (c) classifying the FXN lipid profile determined in step (a) as corresponding to a normal FXN lipid profile, baseline FXN(-) lipid profile or an FXN replacement lipid profile, and (d) initiating or modulating an FXN replacement therapy based on the classification of the FXN lipid profile of the sample.

In another aspect, provided herein is a method of detecting one or more frataxin-sensitive lipid markers (FSLMs) in a sample from a frataxin (FXN) deficient subject, comprising contacting the sample, or a portion thereof, with one or more reagents specific for detecting the level of each of the one or more FSLMs; or subjecting the sample, or a portion thereof, to analysis by mass spectrometry.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a scatter plot showing the results of principal component analysis (PCA) of all MS signals from all analyzed human plasma samples, with different colors indicating FRDA subjects and healthy subjects.

Figure 2 is a scatter plot showing the results of PCA of all MS signals from all human plasma samples, with different colors indicating subjects of different genders.

Figure 3 is a volcano plot that presents the comparison of human plasma samples from FRDA subjects *vs*. healthy controls. The different lipid subclasses are indicated by different colors. Gray dots represent lipids that are were not identified. The horizontal red line indicates the threshold p-value of 0.04, and the vertical red lines represent fold change of 1.23.

Figure 4 is a boxplot showing log2 fold change in the levels of the most significantly modulated lipids in human plasma samples obtained from FRDA subjects as compared to healthy subjects.

Figure 5, panel A is a PCA loading plot of the 168 features discriminating FRDA subjects from healthy subjects with lipid subclasses for the 111 annotated features (66 unique lipids) using the color code for PC1 vs. PC2.