Supplementary Information

A single in-vial dual extraction strategy for the simultaneous lipidomics and proteomics analysis of HDL and LDL fractions

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Tables:

Figures:

Lipoprotein isolation

Lipoproteins were isolated from individual or pooled EDTA plasma by ultracentrifugation. In brief, plasma density was adjusted to *d*=1.063 g/mL with KBr and overlaid with KBr saline solution (*d*=1.063 g/mL). Ultracentrifugation was performed at 10,800 × *g* for 18 h at 4 °C using a TLA-100 rotor (Beckman-Coulter, USA). After centrifugation, the upper fraction, ApoB-containing lipoproteins, was recovered and stored. The density of the bottom fraction containing HDLs was adjusted to *d*=1.250 g/mL with KBr and overlaid with KBr saline solution (*d*=1.220 g/mL). The second ultracentrifugation was performed at 15,300 × *g* for 24 h at 4 °C. After this step, HDL fractions, representing the top layer of the tube, were recovered as a single band. HDL and LDL fractions were desalted and concentrated using a centrifugal device (cut-off 10 kDa).

Data re-processing

The molecular feature extraction (MFE) tool in Mass Hunter Qualitative Analysis (B.06.00, Agilent) was employed to clean data of background noise and to provide a list of all possible features in each sample. Features were created using the accuracy of mass measurements to group ions related to the charge-state envelope, isotopic distribution, and/or the presence of adducts and dimers, as well as potential neutral losses. The MFE algorithm finds co-eluting ions that are linked and sums all ion signals into one value defined as a feature. Compound abundance is assigned as a sum of volume for each related ion/peak. Data were reprocessed considering such ions as $[M+H]^+$, $[M+Na]^+$ and $[M+NH_4]^+$ for positive ionisation mode and $[M-H]^-$, $[M+HCOO]^-$ and $[M+Cl]^-$ for negative ionisation mode. Both sets were reprocessed permitting neutral water loss and the maximum permitted charge-state double.

Following this, data were aligned in Mass Profiler Professional (12.6.1, Agilent). Alignment was performed based on *m*/*z* and RT similarities within the samples. No shifts were observed in peaks over the analysis; therefore, alignment was performed without prior RT correction. Parameters applied were 1 % for RT window and 20 ppm for mass tolerance. Alignment was performed by restricting the number of ions and charge-states defined previously during extraction of features.

Data pre-treatment

Aligned data were subjected to Quality Assurance (QA) procedure[1]. This procedure aims to remove random and un-reproducible signals from the data matrix based on the quality

of the signal across QC samples. To achieve this, two-step filtration was performed based on the feature frequency and sample variability. Features present in at least *n*-1 QC samples were kept for the subsequent filtration which allowed only features with RSD<30 % across the QCs (not considering the possible one missing value in the calculation). These data were visualised by means of Principal Components Analysis (PCA) to inspect the quality of data obtained. The list of entities, which passed the QA procedure, was used to build an unsupervised model to observe spontaneous samples clustering and/or spread. Two models were built: for data acquired in positive and negative ionisation mode. To both models, logarithmic transformation and Pareto scaling were applied. Subsequently blank subtraction was performed. Features present in the blank samples (four blanks were considered) were removed from the dataset.

To narrow down the list of variables to biologically relevant signals, filtration based on the frequency across comparable samples was performed. This was performed keeping only those variables that were present in at least 75 % of the samples in at least one of the compared groups (WT *vs* ApoE-KO). All these steps: QA procedure, blank subtraction and data filtration were performed in Mass Profiler Professional software (12.6.1, Agilent).

Data treatment

Multivariate statistical analysis was applied only to the validation part (animal model) to select features responsible for the separation between groups. The combination of variable influence in projection (VIP) and correlation coefficient (p(corr)) was performed[2] in SIMCA-P+ (12.0.1, Umetrics, Umea), with an established cut-off of 1.5 for VIP score. Accepted p(corr) values were within the range of -1 and -0.75 and 0.75 and 1. To achieve this Orthogonal Projections to Latent Structures-Discriminant Analysis (OPLS-DA) models were built for comparison between ApoE-KO and WT mice for HDL and LDL samples, for the data acquired in positive and negative ionisation mode. All models were transformed (logarithmic transformation) and scaled (pareto scaling). This resulted in total in four models: *i*) ApoE-KO *vs* WT for HDL sample in positive ionisation mode; *ii*) ApoE-KO *vs* WT for HDL sample in negative ionisation mode; *iii*) ApoE-KO *vs* WT for LDL sample in positive ionisation mode; *iv*) ApoE-KO *vs* WT for LDL sample in negative ionisation mode.

Moreover to visualise multidimensional relation between all samples two Partial Least Squares – Discriminant Analysis (PLS-DA) models were built (for data acquired in positive and negative mode) where WT and ApoE-KO were plotted together for both fractions (HDL and LDL). For both models logarithmic transformation and Pareto scaling were applied.

Lipid identification

Features selected to be statistically significant were forwarded for identification. The list of *m/z* was searched for against online available databases such as METLIN (http://metlin.scripps.edu) and lipidMAPS (http://lipidMAPS.org). The Search was performed considering the same adducts as for features extraction (*Data re-processing*). Features were putatively assigned to lipids obtained from the databases based on: *i)* mass accuracy (maximum error mass 15 ppm); *ii)* isotopic pattern distribution; *iii)* possibility of cation and anion formation and *iv)* adducts formation. The rules followed for ionisation and adduct formation are listed in Table 1S below.

Table S1: Summarised criteria followed during the putative lipids identification.

criteria	description	
RT prediction	Information about lipophilicity/lipophobicity of particular lipids was used to predict RT and to reject identifiers which correspond to unexpected RT (*e.g.* TG eluting on the front of the chromatogram or lysolipids appearing in the last part of gradient).	
Elution order	Lipids from the same category (*e.g.* PC or SM) were sorted by the number of carbons and the grade of unsaturation. Each lipid (with particular ID) not matching the elution order created was rejected and alternative ID (if available) was chosen.	
Formulas	Two hits presenting molecules with different formulas were tested by comparison of proposed formulas with the one generated for the searched feature (by use of Molecular Formula Generator tool in MassHunter software).	
PC and SM	For two hits of PC and SM for the same monoisotopic mass, SM were assigned to odd while PC to even *m/z* (nitrogen rule).	
Ionisation and adducts formation	fatty acids	$[M+H]^+$, $[M+H-H_2O]^+$ // $[M-H]^-$, $[M-H-H_2O]^+$
	PC	$[M+H]^+$, $[M+Na]^+$, $[M+K]^+$ // $[M+HCOO]^-$, $[M+Cl]^-$
	PE	$[M+H]^+$, $[M+Na]^+$, $[M+K]^+$ // $[M-H]^-$, $[M+HCOO]^-$
	PI	$[M+Na]^+$ // $[M-H]^-$, $[M+HCOO]^-$, $[M+Cl]^-$
	PG	$[M-H]^-$, $[M+HCOO]^-$, $[M+Cl]^-$
	PS	$[M-H]^-$, $[M+HCOO]^-$, $[M+Cl]^-$
	PA	$[M-H]^-$, $[M+HCOO]^-$, $[M+Cl]^-$
	MG	$[M+H]^+$, $[M+Na]^+$, $[M+NH_4]^+$
	DG	$[M+H]^+$, $[M+Na]^+$, $[M+NH_4]^+$
	TG	$[M+Na]^+$, $[M+NH_4]^+$
	CER	$[M+H]^+$, $[M+Na]^+$ // $[M-H]^-$, $[M+HCOO]^-$, $[M+Cl]^-$
	SM	$[M+H]^+$, $[M+Na]^+$, $[M+K]^+$ // $[M+HCOO]^-$, $[M+Cl]^-$
	CE	$[M+H]^+$, $[M+Na]^+$, $[M+H-H_2O]^+$

In-gel and on-filter protein digestion

Proteins were digested using two different methods: *i)* in-gel digestion and *ii)* filter-aided sample preparation (FASP). In-gel digestion was performed as described previously[3]. Briefly, the precipitated proteins were re-suspended in 30 µL of 50 mM tris(hydroxymethyl)aminomethane hydrochloride (Tris HCl) pH 6.8 containing 1 mM ditiothreitol (DTT) (w/v) and 1 % sodium dodecyl sulfate (SDS) (w/v). The protein extracts were

then subjected to conventional SDS-PAGE to concentrate proteins in the stacking/resolving gel interface. Prior to digestion, the gel bands were reduced with 10 mM DTT, alkylated with 50 mM iodoacetamide (IAA)[4] and digested overnight at 37 °C with sequencing grade trypsin (Promega, Madison, WI, USA) at 8:1 protein:trypsin (w/w) ratio in 50 mM ammonium bicarbonate, pH 8.8.

On-filter digestion was performed based on the FASP protein digestion kit (Expedeon) previously described[5] with minor modifications. Briefly, the precipitated protein samples were re-suspended in 30 µL of 50 mM Tris HCl pH 6.8 containing 1 mM DTT (w/v) and 0.5 % SDS (w/v), and were incubated at 95 °C for 5 min. Then the protein extracts were centrifuged at 13,000 × *g* for 5 min, mixed with 200 µL of urea sample solution (USS) in the filter unit and centrifuged at 10,000 × *g* for 15 min. The filter was then washed with 200 µL of USS and centrifuged at 10,000 × *g* for 15 min and the proteins were incubated with 90 µL of USS and 10 µL of 10 x IAA solution for 20 min in the darkness. Thereafter the filter was washed three times with 100 µL of USS and three times with 100 µL of ammonium bicarbonate solution (ABC). The filter was then placed in a new tube with trypsin (40:1 protein:trypsin (w/w) ratio) and incubated at 37 °C overnight with gentle shaking. The resulting peptides were recovered in two steps: first by adding 40 µL of ABC to the filter before centrifuging at 10,000 × *g* for 10 min (two times) and subsequently by adding 50 µL of 500 mM NaCl followed by centrifugation at 10,000 × *g* for 10 min (also two times).

In both the in-gel and on-filter procedures the resulting tryptic peptides were finally acidified with 1 % trifluoroacetic acid (TFA) (v/v), desalted on C18 Oasis cartridges (Waters Corporation, Milford, MA, USA) using 50 % acetonitrile (ACN) (v/v) in 0.1 % TFA (v/v) as eluent and vacuum dried.

iTRAQ labelling of peptides and MCX fractionation

iTRAQ labelling was performed essentially according to the manufacturer's instructions, as previously described in detail[6]. The dried peptides were taken up in 15 µL of the iTRAQ solution buffer provided with the iTRAQ kit (ABSciex) and labelled by adding 35 µL of the corresponding iTRAQ reagent in ethanol followed by 1 h incubation at room temperature in 70 % ethanol, 180 mM triethylammonium bicarbonate (TEAB) pH 8.53. HDL and LDL samples from WT mice were labelled with iTRAQ tags 114 and 116, respectively and HDL and LDL samples from ApoE-KO mice with tags 115 and 117, respectively.

After the quenching reaction with 50 µL of 0.5 % TFA (v/v) for 30 min, samples were brought to dryness to completely stop the labelling reaction. The four labelled samples were re-suspended in 100 µL 0.1 % TFA (v/v), combined into one tube and cleaned up with C18

Oasis cartridges using 50 % ACN (v/v) in 0.1 % TFA (v/v) as elution solvent. The pooled peptides were separated by cation exchange using MCX Oasis cartridges into six fractions using ammonium formate pH 3 (FA3) and eluted with 250 µL 25 % (v/v) ACN in 0.5 M FA3, 25 % (v/v) ACN in 1 M FA3, 25 % (v/v) ACN in 1.5 M FA3, 25 % (v/v) ACN in 0.5 M FA3 and 1.5 M KCl, 37.5 % (v/v) ACN in 1.25 M FA3, and 50 % (v/v) ACN in 1 M FA3. Each fraction was desalted and dried down prior to LC-MS/MS analysis.

Peptide identification, protein quantification and statistics

Peptide identification was carried out by searching against a human and mouse Uniprot database (as of July 2014) using the SEQUEST algorithm (Proteome Discoverer 1.4, Thermo Fisher Scientific). The searching conditions were as follows: up to two missed cleavages were allowed; 800 ppm and 0.02 ppm were considered as precursor and fragment mass tolerances, respectively; methionine oxidation was selected as a dynamic modification; and cysteine carbamidomethylation as a fixed modification. In the case of the iTRAQ labelled samples lysine and N-terminal modification of +144.1020 Da were added as fixed modifications. The same collections of MS/MS spectra were searched against inverted databases constructed from the same target databases, and the results provided by SEQUEST were analysed using the refined probability ratio method[7, 8] to assess peptide false discovery rates (FDR). At least three unique peptides identified at 1 % FDR were required for a protein to be considered identified. The statistical model used to analyse the quantitative data has been described before in detail[6]. Briefly, the $\log_2$ ratio of concentrations in the two samples being compared, A and B, determined by spectrum *s* of peptide *p* derived from protein *q* is expressed as $X_{eqps}=\log_2(A/B)$. The $\log_2$-ratio value associated with each peptide, X_{eqp}, is then calculated as a weighted average of the spectra used to quantify the peptide and the value associated with each protein, X_{eq}, is similarly the weighted average of its peptides. In addition, a grand mean, X_e, is calculated in each experiment as a weighted average of the protein values. The global distribution of values at each of the levels is described using a standardised variable (*Z*) that expresses the quantitative values in standard deviation units. Z is expected to follow a N(0.1) normal distribution in null hypothesis testing. A 5 % FDR threshold was considered to detect outliers at the scan and peptide levels as well as significant protein abundance changes.

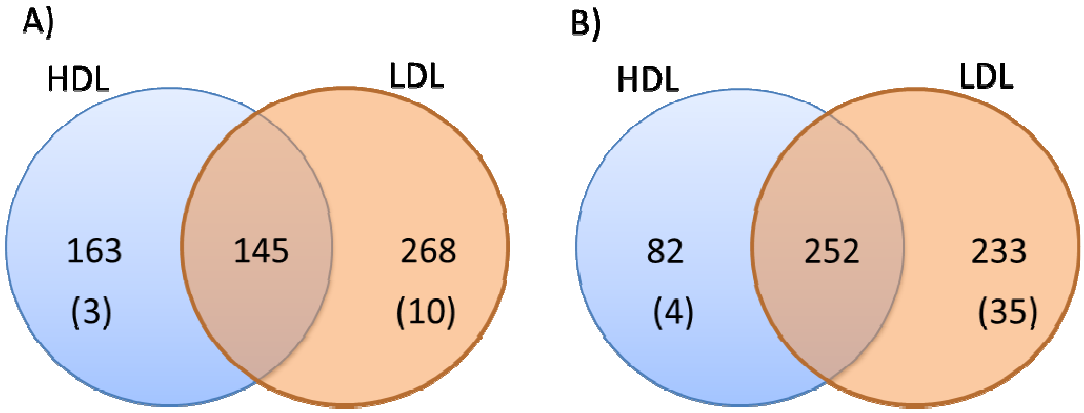

Figure S1: Venn diagrams comparing fully reproducible features for HDL and LDL samples in positive ionisation mode (panel A) and negative ionisation mode (panel B).
The numbers stated in the parentheses indicate molecules found exclusively in one group being absent in the second one.

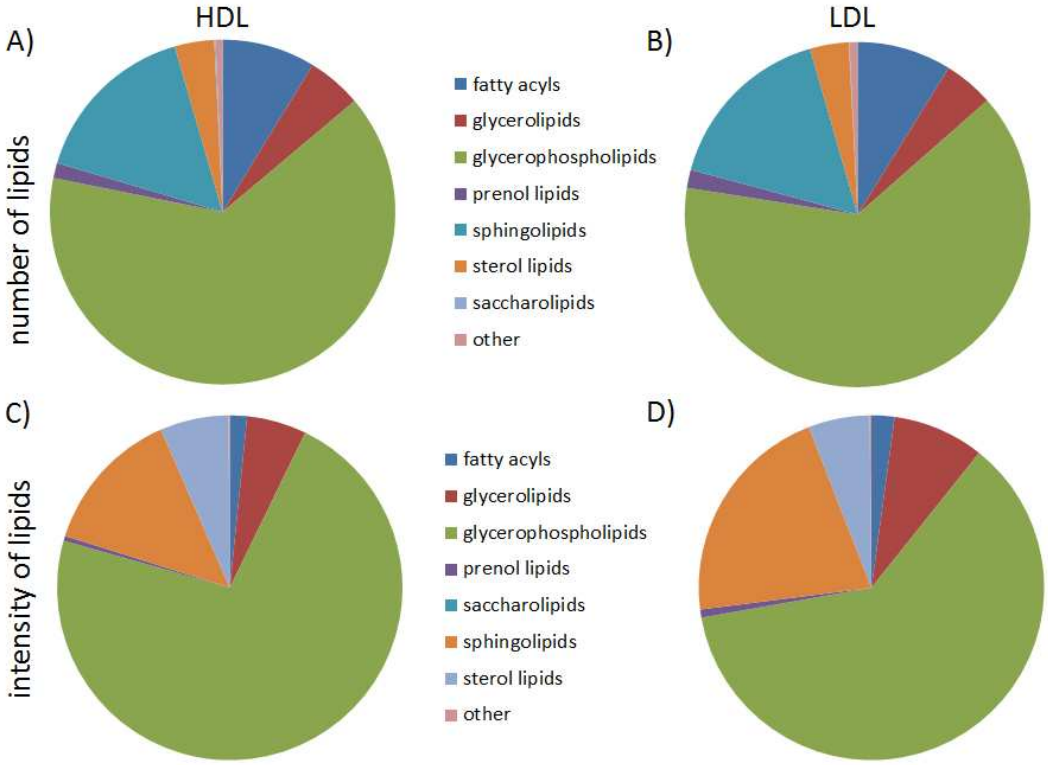

Figure S2: Identified lipids for HDL and LDL samples for method suitability check.
Panels A and B illustrate the proportions between the number of lipids belonging to particular lipid class, while panels C and D show the proportion between the total intensities (abundances) of lipids belonging to particular lipid class.

Suitability check - *Proteomics results*

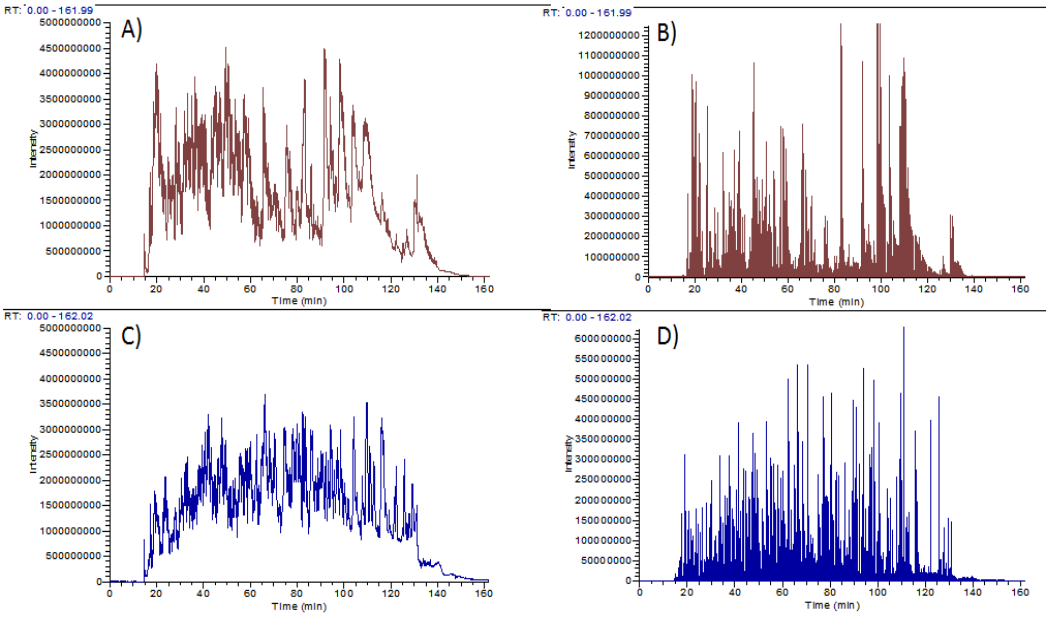

Figure S3: TIC MS (panel A and C) and MS/MS (panel B and D) for HDL (panel A and B) and LDL (panel C and D) samples for method suitability check.

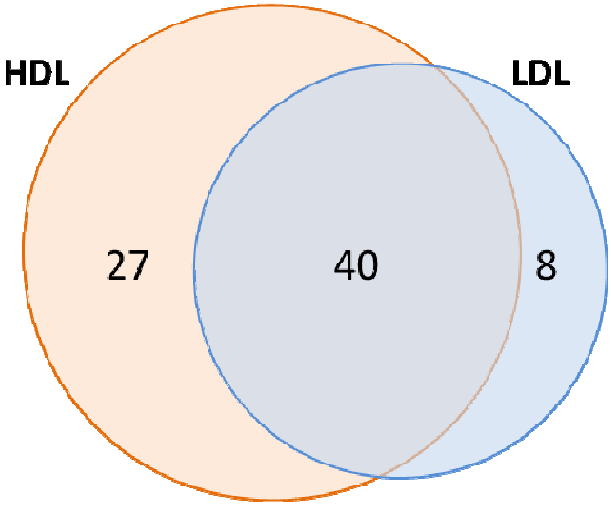

Figure S4: Venn diagram of proteomics data acquired for HDL and LDL samples.
*The total number of identified proteins at 1% FDR and with more than **two peptides** is overlapped.*

Validation - *Lipidomics results*

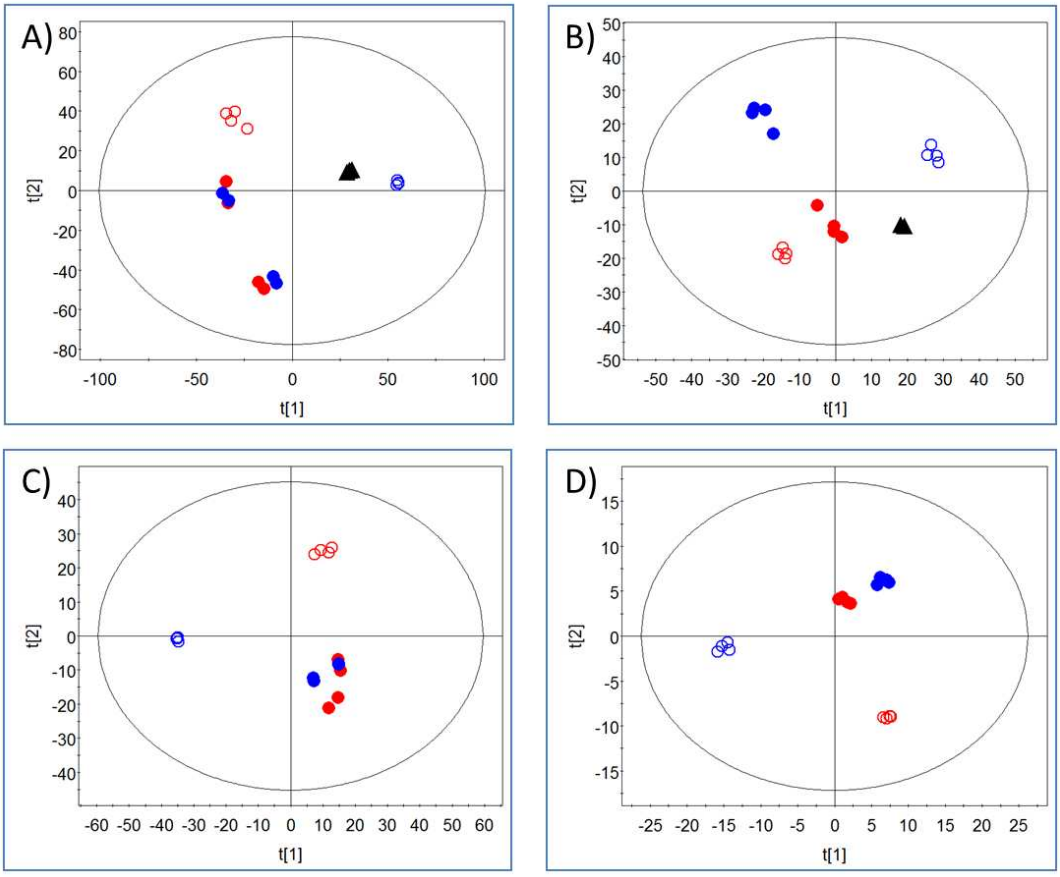

Figure S5: Models built for HDL and LDL samples obtained from wild type and ApoE-KO.
Panels A and B show PCA models built with data after QA procedure, while panels C and D show PLS-DA models built with data after filter by frequency; Cumulative R^2 was calculated as 0.442 for panel A and 0.475 for panel B, while cumulative R^2 and Q^2 were 0.648 and 0.595 for panel C and 0.664 and 0.569 for panel D. Legend: red circle-HDL ApoE-KO; red dot-HDL WT; blue circle-LDL ApoE-KO; blue dot-LDL WT; black triangle-QC.

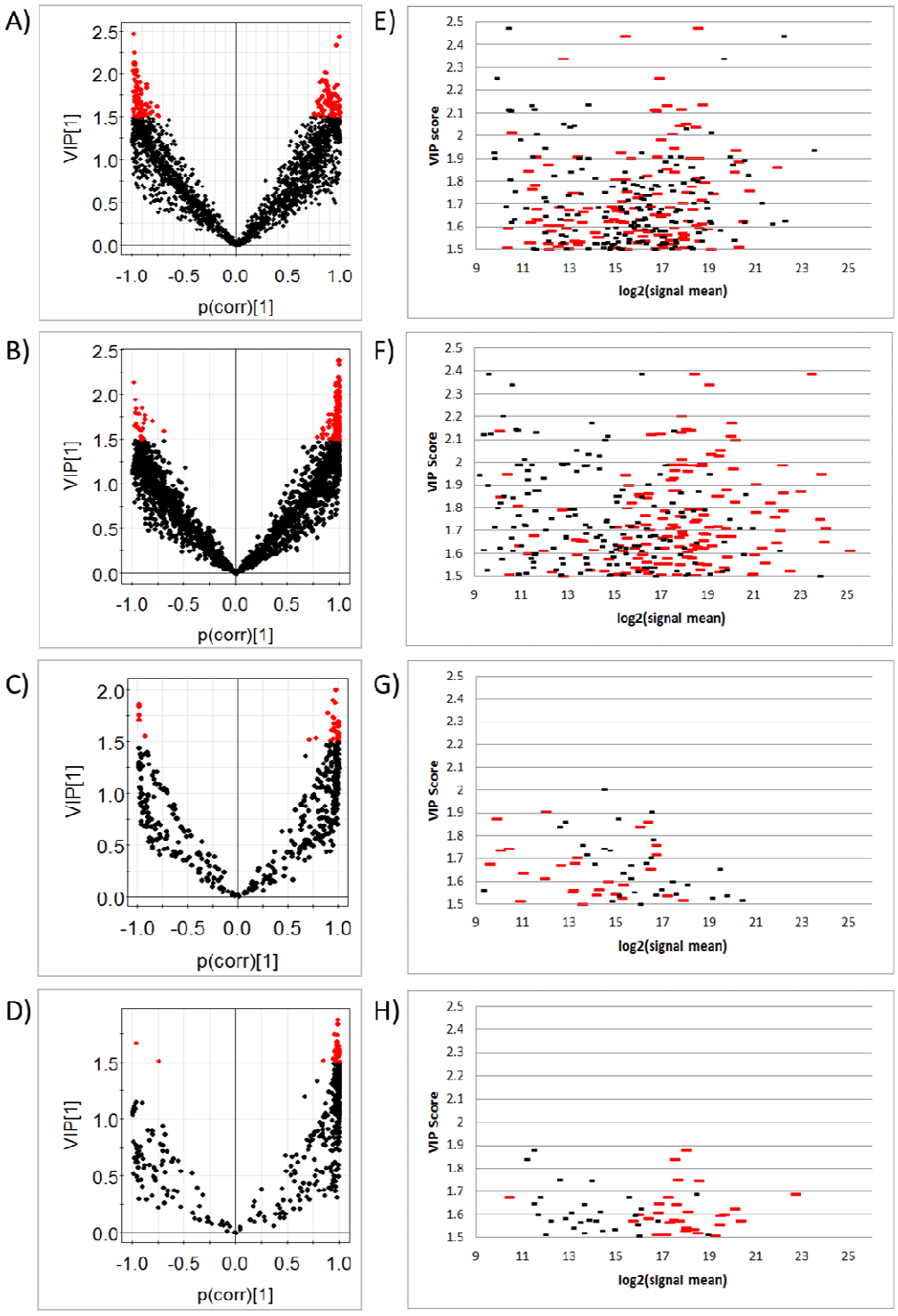

Figure S6: The features responsible for the separation between groups.

Panels A-D show plots combining VIP score and p(corr), where the features considered statistically significant are highlighted in red. Panels E-H show scatters for mean signal against VIP score, where ApoE-KO and WT samples are indicated in red and black, respectively. Panels A and E correspond to the data obtained for HDL samples in positive ionisation mode, B and F for LDL samples in positive ionisation mode, C and G HDL samples in negative ionisation mode and D and H LDL samples in negative ionisation mode.

Validation - *Proteomics results*

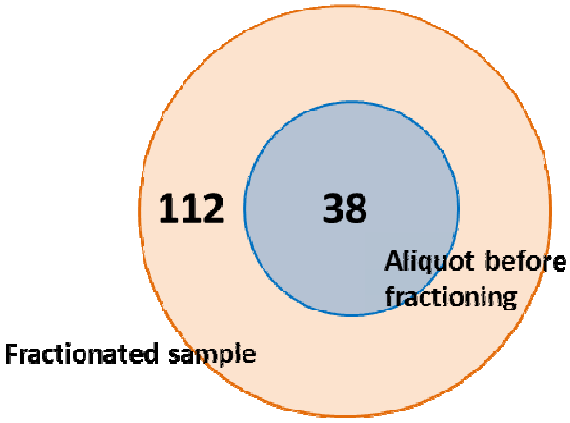

Figure S7: Comparison among proteomics quantitative data acquired for HDL and LDL samples from mice in the iTRAQ experiments. *After iTRAQ labelling experiment for protein quantification one aliquot was analysed directly by LC-MS/MS and the rest of the proteome were fractionated by cation exchange. Protein list were identified and quantified with three or more different peptides.*

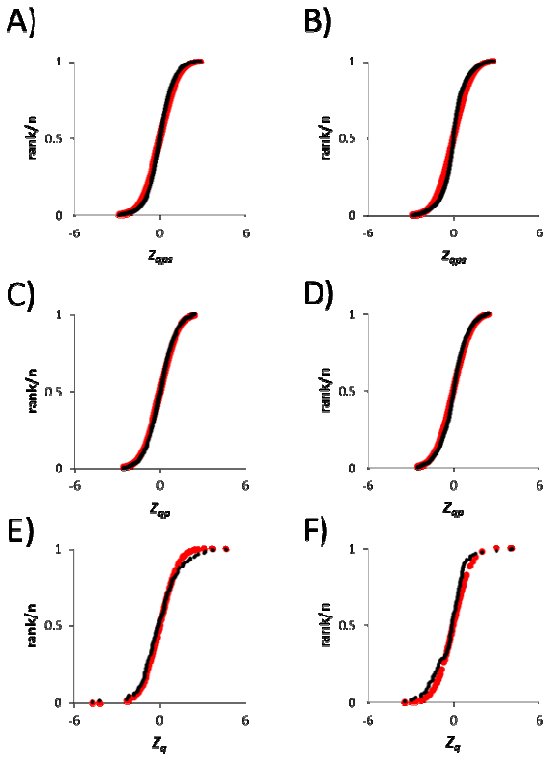

Figure S8: Cumulative distributions of the standardized variables at the spectrum (A, B), peptide (C, D) and protein levels (E, F), in the comparative analysis of HDL samples (A, C, E) and of the LDL samples (B, D, F) among ApoE-KO and WT mice.

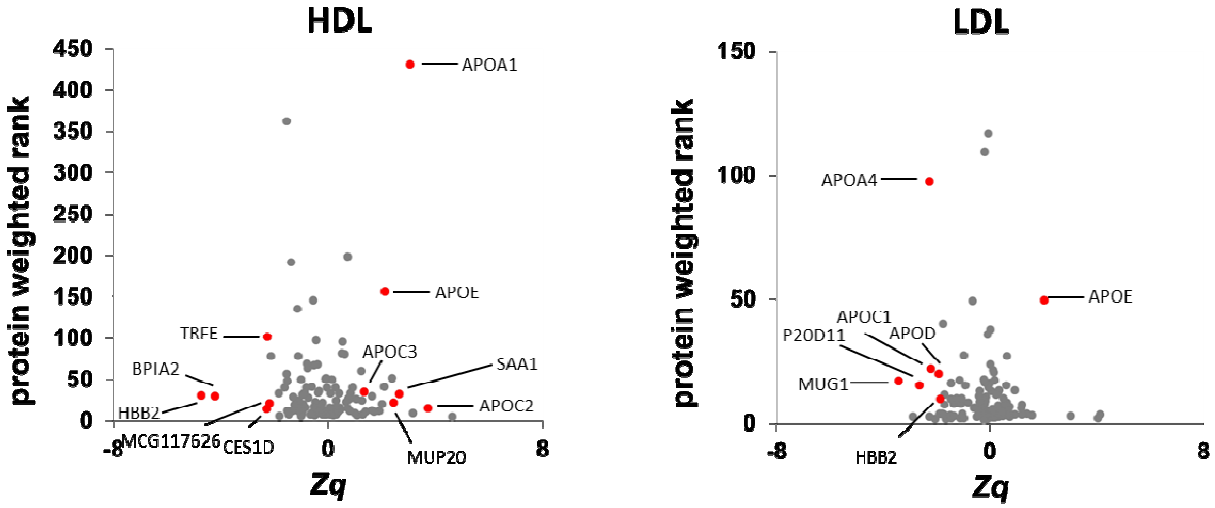

Figure S9: Analysis of statistically significant protein abundance changes in APOE KO related to WT mice.
Weight distributions of protein quantifications around the grand mean obtained by HDL and LDL samples. Negative values signify an increase in protein abundance (toward the left) and positive values, a decrease (toward the right). Outliers at the protein level (p value<0.05) are highlighted in red. Names indicate the entry name of protein abundance changes: ApoA1, Apolipoprotein A-I; ApoA4, Apolipoprotein A-IV; ApoC1, Apolipoprotein C-I; ApoC2, Apolipoprotein C-II ; ApoE, Apolipoprotein E; BPIA2, BPI fold-containing family A member 2; CES1D, Carboxylesterase 1D; HBB2, Hemoglobin subunit beta-2; MUP20, Major urinary protein 20; MCG117626 (GN Obp1a); MUG1, Murinoglobulin-1; TRFE, Serotransferrin; SAA1, Serum amyloid A-1 protein; P20D1, Probable carboxypeptidase PM20D1.

Table S2: Lipids responsible for the separation between ApoE and WT samples in HDL fraction.

MW	RT	Ion	Name	Group	Main class	AV ApoE	AV WT	% change	p(corr)	VIP
294.2195	23.88	[M+H]+	9-OxoODE	octadecanoids	fatty acyls	6,966	772,743	-99	0.96	2.34
294.2195	23.88	[M+H]+	13-HOTE	octadecanoids	fatty acyls	6,966	772,743	-99	0.96	2.34
296.2351	24.67	[M+H]+	9(S)-HODE	octadecanoids	fatty acyls	435,049	44,039	888	-0.96	1.72
367.3086	26.25	[M+NH4]+	PGF2α dimethyl amine	eicosanoids	fatty acyls	136,917	21,646	533	-0.97	1.51
160.1463	24.65	[M+Na]+	1,1-Diethoxypentane	fatty acid esters	fatty acyls	106,035	7,267	1359	-0.93	1.65
182.1307	24.65	[M+H]+	3-undecynoic acid	fatty acids	fatty acyls	106,035	7,267	1359	-0.93	1.65
256.2402	24.71	[M+Na]+	Palmitic acid	fatty acids	fatty acyls	608,386	58,009	949	-0.96	1.74
278.2246	24.71	[M+H]+	α-Linolenic Acid	fatty acids	fatty acyls	608,386	58,009	949	-0.96	1.74
284.2715	15.76	[M+H]+	Stearic acid	fatty acids	fatty acyls	268,134	6,568	3983	-0.96	2.05
340.3341	15.78	[M+H]+	Docosanoic acid	fatty acids	fatty acyls	444,629	13,667	3153	-0.98	2.14
380.3654	8.84	[M+Na]+	pentacosenoic acid	fatty acids	fatty acyls	1,305,095	284,443	359	-0.74	1.51
676.5489	18.92	[M+H]+	1-(O-alpha-D-glucopyranosyl)-(1,3R,29S,31R)-dotriacontanetetraol	fatty acyl glycosides	fatty acyls	399,827	31,200	1182	-0.93	1.60
676.5489	19.19	[M+H]+	1-(O-alpha-D-glucopyranosyl)-(1,3R,29S,31R)-dotriacontanetetraol	fatty acyl glycosides	fatty acyls	357,846	7,962	4395	-0.96	2.04
228.2453	24.65	[M+Na]+	Pentadecan-1-ol // 4-Methyltetradecan-7-ol	fatty alcohols	fatty acyls	166,033	18,487	798	-0.93	1.65
250.2297	24.65	[M+H]+	8,11-Heptadecadienal	fatty aldehydes	fatty acyls	166,033	18,487	798	-0.98	1.68
349.2981	26.28	[M+NH4]+	Anandamide (20:3, n-3)	fatty amides	fatty acyls	154,679	23,369	562	-0.67	0.97
367.3086	26.25	[M+NH4]+	N-oleoyl GABA	fatty amides	fatty acyls	136,917	21,646	533	-0.97	1.51
582.5587	23.27	[M+H]+	DG(34:0)	diacylglycerols	glycerolipids	128,424	3,834	3250	-0.87	1.65
594.5223	21.05	[M+H]+	DG(34:1)	diacylglycerols	glycerolipids	14,526	474,449	-97	0.77	1.68
580.5431	27.05	[M+Na]+	DG(O-34:1)	diacylglycerols	glycerolipids	121,252	6,250	1840	-0.92	1.56
590.4910	18.93	[M+NH4]+	DG(34:3)	diacylglycerols	glycerolipids	ND	57,356	WT	0.89	1.74
607.5257	18.93	[M+H]+	DG(35:2)	diacylglycerols	glycerolipids	ND	57,356	WT	0.89	1.74
586.4597	12.25	[M+Na]+	DG(34:5)	diacylglycerols	glycerolipids	149,127	10,009	1390	-0.94	1.65
608.4441	12.25	[M+H]+	DG(36:8)	diacylglycerols	glycerolipids	149,127	10,009	1390	-0.94	1.65
592.5067	25.44	[M+Na]+	DG(34:2)	diacylglycerols	glycerolipids	1,300	32,903	-96	0.84	1.51
614.4910	25.44	[M+H]+	DG(36:5)	diacylglycerols	glycerolipids	1,300	32,903	-96	0.84	1.51
600.4754	18.40	[M+Na]+	DG(35:5)	diacylglycerols	glycerolipids	113,065	1,350	8275	-0.97	2.11
602.4910	17.81	[M+Na]+	DG(35:4)	diacylglycerols	glycerolipids	152,732	2,542	5909	-0.97	2.13
624.4754	17.81	[M+H]+	DG(37:7)	diacylglycerols	glycerolipids	152,732	2,542	5909	-0.97	2.13
614.491	18.42	[M+Na]+	DG(36:5)	diacylglycerols	glycerolipids	315,925	27,892	1033	-0.92	1.78
636.4754	18.42	[M+H]+	DG(38:8)	diacylglycerols	glycerolipids	315,925	27,892	1033	-0.92	1.78
626.4910	18.24	[M+Na]+	DG(37:6)	diacylglycerols	glycerolipids	234,200	2,742	8443	-0.99	2.12
628.5067	17.85	[M+Na]+	DG(37:5)	diacylglycerols	glycerolipids	63,511	3,647	1642	-0.94	1.73
650.491	17.85	[M+H]+	DG(39:8)	diacylglycerols	glycerolipids	63,511	3,647	1642	-0.94	1.73
690.5223	13.17	[M+H]+	DG(42:9)	diacylglycerols	glycerolipids	92,911	5,997	1449	-0.94	1.69
670.5536	18.00	[M+Na]+	DG(40:5)	diacylglycerols	glycerolipids	376,704	16,593	2170	-0.88	1.33
692.5380	18.00	[M+H]+	DG(42:8)	diacylglycerols	glycerolipids	376,704	16,593	2170	-0.88	1.33

692.5380	21.55	[M+NH4]+	DG(42:8)	diacylglycerols	glycerolipids	68,818	5,906	1065	-0.91	1.63
694.5536	20.18	[M+NH4]+	DG(42:7)	diacylglycerols	glycerolipids	192,463	8,120	2270	-0.96	1.84
696.5693	22.13	[M+NH4]+	DG(42:6)	diacylglycerols	glycerolipids	515,577	73,568	601	-0.99	1.59
692.5380	18.40	[M+Na]+	DG(42:8)	diacylglycerols	glycerolipids	189,840	3,791	4908	-0.98	1.95
714.5223	18.40	[M+H]+	DG(44:11)	diacylglycerols	glycerolipids	189,840	3,791	4908	-0.98	1.95
694.5536	20.46	[M+Na]+	DG(42:7)	diacylglycerols	glycerolipids	366,082	49,401	641	-0.95	1.61
716.5380	20.46	[M+H]+	DG(44:10)	diacylglycerols	glycerolipids	366,082	49,401	641	-0.95	1.61
830.7363	26.60	[M+H]+	TG(50:2)	triacylglycerols	glycerolipids	126,908	1,808	6918	-0.95	1.98
826.7050	27.71	[M+Na]+	TG(50:4)	triacylglycerols	glycerolipids	9,816	407,472	-98	0.74	1.54
848.6894	27.71	[M+H]+	TG(52:7)	triacylglycerols	glycerolipids	9,816	407,472	-98	0.74	1.54
830.7363	24.86	[M+Na]+	TG(50:2)	triacylglycerols	glycerolipids	17,897	369,956	-95	0.82	1.57
852.7207	24.86	[M+H]+	TG(52:5)	triacylglycerols	glycerolipids	17,897	369,956	-95	0.82	1.57
858.7676	27.81	[M+H]+	TG(52:2)	triacylglycerols	glycerolipids	241,193	31,043	677	-0.94	1.55
840.7207	28.39	[M+Na]+	TG(51:4)	triacylglycerols	glycerolipids	ND	112,341	WT	0.85	1.66
862.7050	28.39	[M+H]+	TG(53:7)	triacylglycerols	glycerolipids	ND	112,341	WT	0.85	1.66
850.7050	27.38	[M+NH4]+	TG(52:6)	triacylglycerols	glycerolipids	10,628	944,919	-99	0.80	1.91
850.7050	27.61	[M+NH4]+	TG(52:6)	triacylglycerols	glycerolipids	ND	406,687	WT	0.88	1.82
850.7050	27.40	[M+Na]+	TG(52:6)	triacylglycerols	glycerolipids	ND	355,686	WT	0.88	1.80
872.6894	27.40	[M+H]+	TG(54:9)	triacylglycerols	glycerolipids	ND	355,686	WT	0.88	1.80
862.7989	33.70	[M+NH4]+	TG(52:0)	triacylglycerols	glycerolipids	140,474	17,592	699	-0.88	1.53
862.7989	28.20	[M+Na]+	TG(52:0)	triacylglycerols	glycerolipids	189,906	ND	ApoE	-0.92	1.60
884.7833	28.20	[M+H]+	TG(54:3)	triacylglycerols	glycerolipids	189,906	ND	ApoE	-0.92	1.60
866.7363	28.86	[M+Na]+	TG(55:5)	triacylglycerols	glycerolipids	ND	72,234	WT	0.89	1.72
888.7207	28.86	[M+H]+	TG(55:8)	triacylglycerols	glycerolipids	ND	72,234	WT	0.89	1.72
868.7520	29.86	[M+Na]+	TG(53:4)	triacylglycerols	glycerolipids	ND	114,530	WT	0.92	1.58
890.7363	29.86	[M+H]+	TG(55:7)	triacylglycerols	glycerolipids	ND	114,530	WT	0.92	1.58
906.7676	30.62	[M+NH4]+	TG(56:6)	triacylglycerols	glycerolipids	ND	1,434,820	WT	0.91	1.62
910.7989	33.63	[M+NH4]+	TG(56:4)	triacylglycerols	glycerolipids	ND	86,560	WT	0.90	1.68
916.7520	28.98	[M+NH4]+	TG(57:8)	triacylglycerols	glycerolipids	ND	64,685	WT	0.90	1.67
926.7363	28.36	[M+NH4]+	TG(58:10)	triacylglycerols	glycerolipids	ND	1,438,434	WT	0.86	1.89
926.7363	28.15	[M+NH4]+	TG(58:10)	triacylglycerols	glycerolipids	ND	1,612,752	WT	0.87	1.83
926.7363	28.15	[M+Na]+	TG(58:10)	triacylglycerols	glycerolipids	ND	301,350	WT	0.87	1.86
948.7207	28.15	[M+H]+	TG(60:13)	triacylglycerols	glycerolipids	ND	301,350	WT	0.87	1.86
926.7363	28.38	[M+Na]+	TG(58:10)	triacylglycerols	glycerolipids	ND	235,782	WT	0.88	1.79
948.7207	28.38	[M+H]+	TG(60:13)	triacylglycerols	glycerolipids	ND	235,782	WT	0.88	1.79
928.752	23.79	[M+Na]+	TG(58:9)	triacylglycerols	glycerolipids	2,486	116,688	-98	0.94	1.84
950.7363	23.79	[M+H]+	TG(60:12)	triacylglycerols	glycerolipids	2,486	116,688	-98	0.94	1.84
930.7676	29.64	[M+Na]+	TG(58:8)	triacylglycerols	glycerolipids	3,155	74,211	-96	0.92	1.63
952.7520	29.64	[M+H]+	TG(60:11)	triacylglycerols	glycerolipids	3,155	74,211	-96	0.92	1.63
936.8146	34.04	[M+NH4]+	TG(58:5)	triacylglycerols	glycerolipids	ND	53,490	WT	0.92	1.60
936.8146	33.58	[M+NH4]+	TG(58:5)	triacylglycerols	glycerolipids	8,030	164,063	-95	0.84	1.50

940.8459	30.17	[M+NH4]+	TG(58:3)	triacylglycerols	glycerolipids	2,626	45,556	-94	0.91	1.53
954.7676	30.08	[M+NH4]+	TG(60:10)	triacylglycerols	glycerolipids	ND	93,408	WT	0.92	1.58
966.8615	30.75	[M+NH4]+	TG(60:4)	triacylglycerols	glycerolipids	ND	22,036	WT	0.91	1.53
978.7676	29.63	[M+NH4]+	TG(62:12)	triacylglycerols	glycerolipids	ND	35,513	WT	0.90	1.69
802.5149	12.26	[M+NH4]+	1-(8-[5]-ladderane-octanoyl)-2-(8-[3]-ladderane-octanyl)-sn-glycero-3-phospho-(1'-sn-glycerol)	glycerophosphoglycerols	glycerophospholipids	10,873	118,914	-91	0.90	1.52
396.2641	7.31	[M+H]+	LPA(O-16:0)	lyso-phosphatidic acids	glycerophospholipids	3,181	119,961	-97	0.86	1.68
567.3325	2.75	[M+HCOO]-	LPC(22:6)	lyso-phosphatidylcholines	glycerophospholipids	26,323	168,933	-84	0.98	1.60
479.3012	3.91	[M-H]-	LPE(18:1)	lyso-phosphatidylethanolamines	glycerophospholipids	10,500	87,992	-88	1.00	1.70
501.2855	2.89	[M-H]-	LPE(20:4)	lyso-phosphatidylethanolamines	glycerophospholipids	4,139	89,450	-95	0.95	1.90
620.2962	2.68	[M-H]-	LPI(20:4)	lyso-phosphatidylinositols	glycerophospholipids	ND	34,197	WT	0.94	1.54
564.4519	18.09	[M+HCOO]-	PA(O-14:0/O-14:0)	phosphatidic acids	glycerophospholipids	85,384	6,823	1151	-0.99	1.86
716.572	17.85	[M-H]-	PA(O-38:1) // PA(P-40:0)	phosphatidic acids	glycerophospholipids	9,278	604	1437	-0.94	1.56
578.4311	18.45	[M+H]+	PA(O-28:0)	phosphatidic acids	glycerophospholipids	222,436	8,996	2373	-1.00	2.04
648.4730	18.24	[M+H]+	PA(32:0)	phosphatidic acids	glycerophospholipids	234,200	2,742	8443	-0.99	2.12
634.4937	20.51	[M+Na]+	PA(O-32:0)	phosphatidic acids	glycerophospholipids	ND	42,208	WT	0.79	1.66
656.4781	20.51	[M+H]+	PA(P-34:2)	phosphatidic acids	glycerophospholipids	ND	42,208	WT	0.79	1.66
676.5407	18.92	[M+H]+	PA(O-35:0)	phosphatidic acids	glycerophospholipids	399,827	31,200	1182	-0.93	1.60
676.5407	19.19	[M+H]+	PA(O-35:0)	phosphatidic acids	glycerophospholipids	357,846	7,962	4395	-0.96	2.04
714.5200	18.40	[M+H]+	PA(37:2)	phosphatidic acids	glycerophospholipids	189,840	3,791	4908	-0.98	1.95
714.5563	23.11	[M+H]+	PA(O-38:2) // PA(P-38:1)	phosphatidic acids	glycerophospholipids	84,950	4,878	1642	-0.92	1.82
716.5356	20.46	[M+H]+	PA(37:1)	phosphatidic acids	glycerophospholipids	366,082	49,401	641	-0.95	1.61
704.5720	23.88	[M+Na]+	PA(O-37:0)	phosphatidic acids	glycerophospholipids	3,003	159,337	-98	0.90	1.78
728.5720	22.29	[M+NH4]+	PA(P-39:1)	phosphatidic acids	glycerophospholipids	ND	60,720	WT	0.94	1.53
732.5669	18.01	[M+NH4]+	PA(38:0)	phosphatidic acids	glycerophospholipids	178,482	29,621	503	-0.98	1.53
744.5669	21.14	[M+NH4]+	PA(39:1)	phosphatidic acids	glycerophospholipids	2,660	53,417	-95	0.94	1.62
750.5200	19.40	[M+NH4]+	PA(40:5)	phosphatidic acids	glycerophospholipids	19,413	123,752	-84	1.00	1.55
790.5513	17.86	[M+NH4]+	PA(43:6)	phosphatidic acids	glycerophospholipids	248,055	2,408,637	-90	0.99	1.71
807.5778	17.65	[M+HCOO]-	PC(38:5)	phosphatidylcholines	glycerophospholipids	40,345	545,532	-93	0.70	1.53
819.5778	18.15	[M+HCOO]-	PC(39:6)	phosphatidylcholines	glycerophospholipids	20,307	121,114	-83	1.00	1.57
821.5935	18.75	[M+HCOO]-	PC(39:5)	phosphatidylcholines	glycerophospholipids	434	21,949	-98	0.97	2.00
833.5935	18.94	[M+Cl]-	PC(40:6)	phosphatidylcholines	glycerophospholipids	1,361	22,033	-94	0.94	1.74
831.5778	17.79	[M+HCOO]-	PC(40:7)	phosphatidylcholines	glycerophospholipids	93,841	685,388	-86	1.00	1.65
745.5985	22.29	[M+H]+	PC(O-34:1) // PC(P-34:0)	phosphatidylcholines	glycerophospholipids	ND	60,720	WT	0.94	1.53
761.5935	21.14	[M+H]+	PC(34:0)	phosphatidylcholines	glycerophospholipids	2,660	53,417	-95	0.94	1.62
745.5622	19.40	[M+Na]+	PC(33:1)	phosphatidylcholines	glycerophospholipids	19,413	123,752	-84	1.00	1.55
767.5465	19.40	[M+H]+	PC(35:4)	phosphatidylcholines	glycerophospholipids	19,413	123,752	-84	1.00	1.55
773.6298	21.21	[M+H]+	PC(O-36:1) // PC(P-36:0)	phosphatidylcholines	glycerophospholipids	568,710	100,172	468	-0.97	1.50
803.6768	23.49	[M+H]+	PC(O-38:0)	phosphatidylcholines	glycerophospholipids	39,554	2,670	1381	-0.93	1.50
785.5935	17.86	[M+Na]+	PC(36:2)	phosphatidylcholines	glycerophospholipids	248,055	2,408,637	-90	0.99	1.71

807.5778	17.86	[M+H]+	PC(38:5)	phosphatidylcholines	glycerophospholipids	248,055	2,408,637	-90	0.99	1.71
807.5778	16.78	[M+Na]+	PC(38:5)	phosphatidylcholines	glycerophospholipids	91,077	694,735	-87	0.98	1.58
829.5622	16.78	[M+H]+	PC(40:8)	phosphatidylcholines	glycerophospholipids	91,077	694,735	-87	0.98	1.58
809.5935	17.92	[M+Na]+	PC(38:4)	phosphatidylcholines	glycerophospholipids	432,578	3,297,914	-87	0.99	1.61
831.5778	17.92	[M+H]+	PC(40:7)	phosphatidylcholines	glycerophospholipids	432,578	3,297,914	-87	0.99	1.61
831.6717	27.71	[M+NH4]+	PC(39:0)	phosphatidylcholines	glycerophospholipids	9,816	407,472	-98	0.74	1.54
831.7081	23.29	[M+Na]+	PC(O-40:0)	phosphatidylcholines	glycerophospholipids	107,485	7,186	1396	-0.94	1.50
853.6924	23.29	[M+H]+	PC(P-42:2) // PC(O-42:3)	phosphatidylcholines	glycerophospholipids	107,485	7,186	1396	-0.94	1.50
835.6091	18.41	[M+Na]+	PC(40:5)	phosphatidylcholines	glycerophospholipids	4,463	59,197	-92	0.93	1.61
857.5935	18.41	[M+H]+	PC(42:8)	phosphatidylcholines	glycerophospholipids	4,463	59,197	-92	0.93	1.61
839.6404	20.72	[M+Na]+	PC(40:3)	phosphatidylcholines	glycerophospholipids	3,250	68,266	-95	0.96	1.63
861.6248	20.72	[M+H]+	PC(42:6)	phosphatidylcholines	glycerophospholipids	3,250	68,266	-95	0.96	1.63
845.6873	28.39	[M+NH4]+	PC(40:0)	phosphatidylcholines	glycerophospholipids	ND	112,341	WT	0.85	1.66
847.6455	27.71	[M+NH4]+	PC(O-42:6)	phosphatidylcholines	glycerophospholipids	ND	102,013	WT	0.88	1.78
855.6717	27.40	[M+NH4]+	PC(41:2)	phosphatidylcholines	glycerophospholipids	ND	355,686	WT	0.88	1.80
871.7030	28.86	[M+NH4]+	PC(42:1)	phosphatidylcholines	glycerophospholipids	ND	72,234	WT	0.89	1.72
873.7187	29.86	[M+NH4]+	PC(42:0)	phosphatidylcholines	glycerophospholipids	ND	114,530	WT	0.92	1.58
921.7187	26.17	[M+NH4]+	PC(46:4)	phosphatidylcholines	glycerophospholipids	ND	535,517	WT	0.80	1.62
477.2855	2.92	[M-H]-	PE(18:2)	phosphatidylethanolamines	glycerophospholipids	18,389	102,357	-82	1.00	1.54
715.5152	17.52	[M-H]-	PE(34:2)	phosphatidylethanolamines	glycerophospholipids	9,200	53,488	-83	1.00	1.55
765.5309	18.11	[M-H]-	PE(38:5)	phosphatidylethanolamines	glycerophospholipids	12,378	63,950	-81	0.99	1.50
765.5309	18.11	[M-H]-	PE(P-38:5)	phosphatidylethanolamines	glycerophospholipids	12,378	63,950	-81	0.99	1.50
807.5778	17.65	[M+HCOO]-	PE(41:5)	phosphatidylethanolamines	glycerophospholipids	40,345	545,532	-93	0.70	1.53
819.5778	18.15	[M+HCOO]-	PE(42:6)	phosphatidylethanolamines	glycerophospholipids	20,307	121,114	-83	1.00	1.57
821.5935	18.75	[M+HCOO]-	PE(42:5)	phosphatidylethanolamines	glycerophospholipids	434	21,949	-98	0.97	2.00
833.5935	18.94	[M+Cl]-	PE(43:6)	phosphatidylethanolamines	glycerophospholipids	1,361	22,033	-94	0.94	1.74
833.5935	18.94	[M+HCOO]-	PE(43:6)	phosphatidylethanolamines	glycerophospholipids	250,148	1,331,299	-81	1.00	1.52
673.5046	13.17	[M+NH4]+	PE(P-32:1)	phosphatidylethanolamines	glycerophospholipids	92,911	5,997	1449	-0.94	1.69
675.5203	18.00	[M+NH4]+	PE(O-32:1) // PE(P-32:0)	phosphatidylethanolamines	glycerophospholipids	376,704	16,593	2170	-0.88	1.33
697.5046	18.4	[M+NH4]+	PE(P-34:3) // PE(O-34:4)	phosphatidylethanolamines	glycerophospholipids	189,840	3,791	4908	-0.98	1.95
745.5985	22.29	[M+H]+	PE(O-37:1)) // PE(P-37:0)	phosphatidylethanolamines	glycerophospholipids	ND	60,720	WT	0.94	1.53
761.5935	21.14	[M+H]+	PE(37:0)	phosphatidylethanolamines	glycerophospholipids	2,660	53,417	-95	0.94	1.62
745.5622	19.40	[M+Na]+	PE(36:1)	phosphatidylethanolamines	glycerophospholipids	19,413	123,752	-84	1.00	1.55
767.5465	19.40	[M+H]+	PE(38:4)	phosphatidylethanolamines	glycerophospholipids	19,413	123,752	-84	1.00	1.55
767.5465	19.40	[M+H]+	PE(P-38:4(12OH)	phosphatidylethanolamines	glycerophospholipids	19,413	123,752	-84	1.00	1.55
773.6298	21.21	[M+H]+	PE(O-39:1) // PE(P-39:0)	phosphatidylethanolamines	glycerophospholipids	568,710	100,172	468	-0.97	1.50
803.6768	23.49	[M+H]+	PE(O-41:0)	phosphatidylethanolamines	glycerophospholipids	39,554	2,670	1381	-0.93	1.50
807.5778	17.86	[M+H]+	PE(41:5)	phosphatidylethanolamines	glycerophospholipids	248,055	2,408,637	-90	0.99	1.71
807.5778	16.78	[M+Na]+	PE(41:5)	phosphatidylethanolamines	glycerophospholipids	91,077	694,735	-87	0.98	1.58
809.5935	17.92	[M+Na]+	PE(41:4)	phosphatidylethanolamines	glycerophospholipids	432,578	3,297,914	-87	0.99	1.61
831.6717	27.71	[M+NH4]+	PE(42:0)	phosphatidylethanolamines	glycerophospholipids	9,816	407,472	-98	0.74	1.54

845.6873	28.39	[M+NH4]+	PE(43:0)	phosphatidylethanolamines	glycerophospholipids	ND	112,341	WT	0.85	1.66
855.6717	27.40	[M+NH4]+	PE(44:2)	phosphatidylethanolamines	glycerophospholipids	ND	355,686	WT	0.88	1.80
873.7187	29.86	[M+NH4]+	PE(45:0)	phosphatidylethanolamines	glycerophospholipids	ND	114,530	WT	0.92	1.58
911.7343	23.08	[M+Na]+	PE(48:2)	phosphatidylethanolamines	glycerophospholipids	ND	111,071	WT	0.88	1.78
666.4836	17.76	[M+H]+	PG(O-39:0)	phosphatidylglycerols	glycerophospholipids	106,703	1,272	8290	-0.97	2.11
694.5512	20.18	[M+NH4]+	PG(O-16:0/O-16:0)	phosphatidylglycerols	glycerophospholipids	192,463	8,120	2270	-0.96	1.84
694.5512	20.46	[M+Na]+	PG(O-16:0/O-16:0)	phosphatidylglycerols	glycerophospholipids	366,082	49,401	641	-0.95	1.61
848.6870	27.71	[M+H]+	PG(O-42:0)	phosphatidylglycerols	glycerophospholipids	9,816	407,472	-98	0.74	1.54
888.5728	20.82	[M-H]-	PI(38:3)	phosphatidylinositols	glycerophospholipids	33,026	186,938	-82	0.99	1.54
914.5884	21.02	[M-H]-	PI(40:4)	phosphatidylinositols	glycerophospholipids	1,064	26,037	-96	0.95	1.74
964.6980	20.65	[M+H]+	PI(43:0)	phosphatidylinositols	glycerophospholipids	ND	252,907	WT	0.85	2.03
853.5833	17.65	[M-H]-	PS(41:4)	phosphatidylserines	glycerophospholipids	40,345	545,532	-93	0.70	1.53
865.5833	18.15	[M-H]-	PS(42:5)	phosphatidylserines	glycerophospholipids	20,307	121,114	-83	1.00	1.57
867.5989	18.75	[M-H]-	PS(42:4)	phosphatidylserines	glycerophospholipids	434	21,949	-98	0.97	2.00
823.5727	18.94	[M+HCOO]-	PS(O-40:5)	phosphatidylserines	glycerophospholipids	1,361	22,033	-94	0.94	1.74
877.5833	17.79	[M-H]-	PS(43:6)	phosphatidylserines	glycerophospholipids	93,841	685,388	-86	1.00	1.65
877.5833	18.69	[M+HCOO]-	PS(43:6)	phosphatidylserines	glycerophospholipids	2,083	38,375	-95	0.95	1.64
743.5101	9.29	[M+Na]+	PS(O-34:3) // PS(P-34:2)	phosphatidylserines	glycerophospholipids	1,321	24,558	-95	0.94	1.59
765.4945	9.29	[M+H]+	PS(P-36:5)	phosphatidylserines	glycerophospholipids	1,321	24,558	-95	0.94	1.59
797.5571	12.26	[M+Na]+	PS(O-38:4) // PS(P-38:3)	phosphatidylserines	glycerophospholipids	10,873	118,914	-91	0.90	1.52
819.5414	12.26	[M+H]+	PS(P-40:6)	phosphatidylserines	glycerophospholipids	10,873	118,914	-91	0.90	1.52
805.6197	25.38	[M+NH4]+	PS(O-38:0)	phosphatidylserines	glycerophospholipids	ND	36,660	WT	0.93	1.50
827.6040	14.95	[M+Na]+	PS(O-40:3) // PS(P-40:2)	phosphatidylserines	glycerophospholipids	7,626	102,296	-93	0.92	1.59
849.5884	14.95	[M+H]+	PS(O-42:6)	phosphatidylserines	glycerophospholipids	7,626	102,296	-93	0.92	1.59
847.6302	27.71	[M+NH4]+	PS(40:0)	phosphatidylserines	glycerophospholipids	ND	102,013	WT	0.88	1.78
897.6459	27.64	[M+NH4]+	PS(44:3)	phosphatidylserines	glycerophospholipids	ND	67,394	WT	0.89	1.72
641.4867	16.74	[M+NH4]+	GlcCer(d30:2)	glucosylceramides	neutral glycosphingolipids	48,111	3,778	1173	-0.90	1.57
643.5023	16.22	[M+NH4]+	GlcCer(d30:1)	glucosylceramides	neutral glycosphingolipids	29,633	ND	ApoE	-0.94	1.51
797.6745	21.82	[M+H]+	GlcCer(d41:1)	glucosylceramides	neutral glycosphingolipids	274,352	22,164	1138	-0.95	1.75
813.7057	26.60	[M+NH4]+	GlcCer(d42:0)	glucosylceramides	neutral glycosphingolipids	126,908	1,808	6918	-0.95	1.98
841.7370	27.81	[M+NH4]+	GlcCer(d44:0)	glucosylceramides	neutral glycosphingolipids	241,193	31,043	677	-0.94	1.55
720.1690	27.49	[M+NH4]+	Sagerinic acid	depsides and depsidones	others	12,265	186,609	-93	0.92	1.62
182.1307	24.65	[M+H]+	Linalyl formate	monoterpenes	prenol lipids	106,035	7,267	1359	-0.93	1.65
402.3498	8.84	[M+H]+	δ-Tocopherol	quinone and hydroquinones	prenol lipids	1,305,095	284,443	359	-0.74	1.51
562.4386	18.94	[M+H]+	2-Hexaprenyl-3-methyl-6-methoxy-1,4-benzoquinol	quinone and hydroquinones	prenol lipids	469,768	39,239	1097	-0.99	1.80
638.5427	16.22	[M+Na]+	2-Octaprenylphenol	quinone and hydroquinones	prenol lipids	29,633	ND	ApoE	-0.94	1.51
668.5532	13.17	[M+Na]+	2-Octaprenyl-6-methoxyphenol	quinone and hydroquinones	prenol lipids	92,911	5,997	1449	-0.94	1.69
726.5587	23.88	[M+H]+	Ubiquinone 8	quinone and hydroquinones	prenol lipids	3,003	159,337	-98	0.90	1.78
574.4233	9.91	[M+Na]+	Clerosterol 3-glucoside	terpene glycosides	prenol lipids	31,025	1,509	1956	-0.96	1.63

686.2786	16.10	[M+NH4]+	19-Hydroxydeacetylnomilinic acid 17-beta-D-glucopyranoside	terpene glycosides	prenol lipids	203,744	13,688	1389	-0.93	1.50
946.4773	16.98	[M+NH4]+	1alpha,3beta,22R-Trihydroxyergosta-5,24E-dien-26-oic acid 3-O-b-D-glucoside 26-O-[b-D-glucosyl-(1->2)-b-D-glucosyl] ester	terpene glycosides	prenol lipids	8,031	63,105	-87	0.99	1.63
535.4964	18.95	[M+Na]+	Cer(d34:2)	ceramides	sphingolipids	397,157	13,628	2814	-0.96	1.90
551.4914	14.92	[M+Na]+	Cer(d34:2(2OH))	ceramides	sphingolipids	44,579	1,347	3209	-0.97	1.81
623.6216	22.59	[M+H]+	Cer(d40:0)	ceramides	sphingolipids	63,354	9,247	585	-0.98	1.58
637.6373	23.23	[M+H]+	Cer(d41:0)	ceramides	sphingolipids	77,642	7,670	912	-0.97	1.74
651.6529	23.84	[M+H]+	Cer(d42:0)	ceramides	sphingolipids	116,368	11,145	944	-0.98	1.75
635.5853	31.00	[M+NH4]+	Cer(d40:2(2OH))	ceramides	sphingolipids	34,874	ND	ApoE	-0.82	1.67
835.6021	18.41	[M+Na]+	LacCer(d32:0)	neutral glycosphingolipids	sphingolipids	4,463	59,197	-92	0.93	1.61
861.6177	20.72	[M+H]+	Galbeta1-4Glcbeta-Cer(d34:1)	neutral glycosphingolipids	sphingolipids	3,250	68,266	-95	0.96	1.63
909.6670	25.28	[M+NH4]+	PI-Cer(t42:0)	phosphosphingolipids	sphingolipids	ND	458,399	WT	0.80	1.71
716.5832	17.85	[M-H]-	SM(d35:1)	sphingomyelines	sphingolipids	9,278	604	1437	-0.94	1.56
676.5519	18.92	[M+H]+	SM(d32:0)	sphingomyelines	sphingolipids	399,827	31,200	1182	-0.93	1.60
676.5519	19.19	[M+H]+	SM(d32:0)	sphingomyelines	sphingolipids	357,846	7,962	4395	-0.96	2.04
704.5832	23.88	[M+Na]+	SM(d34:0)	sphingomyelines	sphingolipids	3,003	159,337	-98	0.90	1.78
726.5676	23.88	[M+H]+	SM(d36:3)	sphingomyelines	sphingolipids	3,003	159,337	-98	0.90	1.78
756.6145	21.21	[M+NH4]+	SM(d38:2)	sphingomyelines	sphingolipids	568,710	100,172	468	-0.97	1.50
826.6928	27.71	[M+Na]+	SM(d43:2)	sphingomyelines	sphingolipids	9,816	407,472	-98	0.74	1.54
374.2821	7.31	[M+Na]+	3b-Hydroxy-5-cholenoic acid	bile acids and derivatives	sterol lipids	3,181	119,961	-97	0.86	1.68
402.3498	8.84	[M+H]+	22S-hydroxycholesterol	cholesterol and derivatives	sterol lipids	1,305,095	284,443	359	-0.74	1.51
652.6158	31.00	[M+H]+	CE(18:0)	cholesterol esters	sterol lipids	34,874	ND	ApoE	-0.82	1.67
648.5845	27.28	[M+Na]+	CE(18:2)	cholesterol esters	sterol lipids	44,546	4,631,158	-99	0.99	2.44
670.5689	27.28	[M+H]+	CE(20:5)	cholesterol esters	sterol lipids	44,546	4,631,158	-99	0.99	2.44
674.6002	27.84	[M+Na]+	CE(20:3)	cholesterol esters	sterol lipids	1,200,827	11,424,677	-89	0.82	1.93
696.5845	27.84	[M+H]+	CE(22:6)	cholesterol esters	sterol lipids	1,200,827	11,424,677	-89	0.82	1.93
382.3236	16.62	[M+H]+	25-Dehydrovitamin D3	secosteroids	sterol lipids	258,009	26,447	876	-0.91	1.51
382.3236	25.37	[M+H]+	25-Dehydrovitamin D3	secosteroids	sterol lipids	332,793	36,790	805	-0.98	1.68
382.3236	24.22	[M+H]+	25-Dehydrovitamin D3	secosteroids	sterol lipids	1,789,958	169,647	955	-0.95	1.76
382.3236	24.58	[M+H]+	25-Dehydrovitamin D3	secosteroids	sterol lipids	4,085,436	294,654	1287	-0.95	1.86
384.3392	26.25	[M+H]+	Vitamin D3	secosteroids	sterol lipids	136,917	21,646	533	-0.97	1.51
382.3236	16.62	[M+H]+	1,4-cholestadienone	sterols	sterol lipids	258,009	26,447	876	-0.91	1.51
382.3236	16.62	[M+H]+	Zymosterone	sterols	sterol lipids	258,009	26,447	876	-0.91	1.51
382.3236	25.37	[M+H]+	Zymosterone	sterols	sterol lipids	332,793	36,790	805	-0.98	1.68
382.3236	25.37	[M+H]+	4,6-cholestadienone	sterols	sterol lipids	332,793	36,790	805	-0.98	1.68
382.3236	24.22	[M+H]+	Zymosterone	sterols	sterol lipids	1,789,958	169,647	955	-0.95	1.76
382.3236	24.58	[M+H]+	Zymosterone	sterols	sterol lipids	4,085,436	294,654	1287	-0.95	1.86
384.3392	26.25	[M+H]+	Zymosterol	sterols	sterol lipids	136,917	21,646	533	-0.97	1.51
384.3392	26.25	[M+H]+	Cholestenone	sterols	sterol lipids	136,917	21,646	533	-0.97	1.51

704.5743	23.88	[M+Na]+	Cholesteryl 11-hydroperoxy-eicosatetraenoate	sterols	sterol lipids	3,003	159,337	-98	0.90	1.78
786.6374	23.49	[M+NH4]+	16:0-Glc-Cholesterol	sterols	sterol lipids	39,554	2,670	1381	-0.93	1.50
822.6374	25.38	[M+H]+	18:3-Glc-Campesterol	sterols	sterol lipids	ND	36,660	WT	0.93	1.50
842.7000	24.42	[M+H]+	20:0-Glc-Cholesterol	sterols	sterol lipids	4,804	133,055	-96	0.84	1.58
896.7469	25.66	[M+NH4]+	22:0-Glc-Stigmasterol	sterols	sterol lipids	ND	186,477	WT	0.93	1.54
898.7626	25.97	[M+Na]+	22:0-Glc-Sitosterol	sterols	sterol lipids	10,654	189,271	-94	0.91	1.53

Mass – neutral mass of measured lipid; MW – neutral mass of identifier; AV – average of the signal across the group; % change – negative value means a decrease in ApoE samples in comparison to WT, while positive value means an increase in ApoE sample; ND – not detected; WT – detected only in WT sample; ApoE – detected only in ApoE sample.

Table S3: Lipids found to be responsible for the separation between ApoE and WT samples in LDL fraction.

MW	RT	Ion	Name	Group	Main class	ApoE	WT	% change	p(corr)	VIP
419.3148	6.56	[M+HCOO]-	N-oleoyl histidine	fatty amides	fatty acyls	156,318	3,246	4716	0.97	1.67
465.3219	6.56	[M-H]-	LPE(P-18:0) // LPE(O-18:1)	lyso-phosphatidylethanolamines	glycerophospholipids	156,318	3,246	4716	0.97	1.67
481.3168	5.31	[M-H]-	LPE(18:0)	lyso-phosphatidylethanolamines	glycerophospholipids	1,370,743	108,302	1166	1.00	1.57
501.2855	2.89	[M-H]-	LPE(20:4)	lyso-phosphatidylethanolamines	glycerophospholipids	187,446	13,935	1245	0.97	1.58
505.3168	2.85	[M-H]-	LPE(20:2)	lyso-phosphatidylethanolamines	glycerophospholipids	209,730	5,777	3530	0.95	1.75
525.2855	2.84	[M-H]-	LPE(22:6)	lyso-phosphatidylethanolamines	glycerophospholipids	262,833	20,476	1184	0.96	1.53
509.3481	4.14	[M+HCOO]-	LPE(20:0)	lyso-phosphatidylethanolamines	glycerophospholipids	724,937	59,939	1109	0.98	1.56
509.3845	6.52	[M+HCOO]-	LPAF C-18	lyso-phosphatidylethanolamines	glycerophospholipids	272,449	2,675	10086	0.98	1.88
519.3325	2.83	[M+HCOO]-	LPC(18:2)	lyso-phosphatidylcholines	glycerophospholipids	6,977,307	337,277	1969	0.97	1.69
539.3587	3.54	[M+HCOO]-	LPS(O-20:0)	lyso-phosphatidylserines	glycerophospholipids	119,812	2,707	4326	0.97	1.65
543.3325	2.83	[M+HCOO]-	LPC(20:4)	lyso-phosphatidylcholines	glycerophospholipids	1,150,668	66,192	1638	0.97	1.63
547.3638	4.40	[M+HCOO]-	LPC(20:2)	lyso-phosphatidylcholines	glycerophospholipids	110,811	3,864	2768	0.96	1.52
551.3951	7.65	[M+HCOO]-	PC(O-20:0)	phosphatidylcholines	glycerophospholipids	217,401	17,123	1170	0.99	1.58
567.3325	2.75	[M+HCOO]-	LPC(22:6)	lyso-phosphatidylcholines	glycerophospholipids	827,306	55,433	1392	0.98	1.60
607.4577	13.03	[M+HCOO]-	LPC(24:0)	lyso-phosphatidylcholines	glycerophospholipids	201,138	11,899	1590	0.99	1.65
714.5563	15.73	[M+HCOO]-	PA(O-38:2) // PA(P-38:1)	phosphatidic acids	glycerophospholipids	88,353	6,928	1175	0.99	1.58
760.5618	15.73	[M-H]-	PG(O-36:2 // PG(P-36:1)	phosphatidylglycerols	glycerophospholipids	88,353	6,928	1175	0.99	1.58
717.5672	18.89	[M+HCOO]-	PC(O-32:1) // PC(P-32:0)	phosphatidylcholines	glycerophospholipids	162,341	10,913	1388	0.97	1.57
766.5876	14.94	[M-H]-	PA(O-42:4)	phosphatidic acids	glycerophospholipids	278,381	19,389	1336	1.00	1.61
777.5672	20.11	[M-H]-	PE(P-40:5) // PE(O-40:6)	phosphatidylethanolamines	glycerophospholipids	335,561	30,212	1011	0.94	1.54
788.5356	14.00	[M-H]-	1-(ladderane-octanyl)-2-(ladderane-octanyl)-glycerophosphoglycerol	glycerophosphoglycerols	glycerophospholipids	65,525	3,068	2036	0.95	1.60
743.5829	19.43	[M+HCOO]-	PC(O-36:2) // PC(P-36:1)	phosphatidylcholines	glycerophospholipids	372,423	11,900	3030	0.84	1.52
771.6224	20.15	[M+HCOO]-	GlcCer(d38:1(2OH))	glucosylceramides	neutral glycosphingolipids	630,931	61,732	922	1.00	1.51
781.6432	20.15	[M+Cl]-	GlcCer(d40:2)	glucosylceramides	neutral glycosphingolipids	630,931	61,732	922	1.00	1.51
771.6142	20.15	[M+HCOO]-	PC(P-36:1) // PC(O-36:2)	phosphatidylcholines	glycerophospholipids	630,931	61,732	922	1.00	1.51
782.6302	18.85	[M+HCOO]-	SM(d40:3)	sphingomyelines	sphingolipids	271,974	8,872	2966	0.97	1.54
842.7241	21.76	[M+Cl]-	SM(d44:1)	sphingomyelines	sphingolipids	55,592	4,445	1151	1.00	1.57
878.7000	21.76	[M-H]-	22:3-Glc-Campesterol	sterols	sterol lipids	55,592	4,445	1151	1.00	1.57
282.2559	5.58	[M+H-H2O]+	Oleic Acid	fatty acids	fatty acyls	161,714	6,401	2426	0.96	1.58
242.2610	5.58	[M+Na]+	1-Hexadecanol	fatty alcohols	fatty acyls	161,714	6,401	2426	0.96	1.58
386.3549	7.12	[M+H-H2O]+	Cholesterol	cholesterol and derivatives	sterol lipids	1,995,571	261,069	664	1.00	1.50
351.3137	7.12	[NH4]+	Anandamide (20:2, n-6)	fatty amides	fatty acyls	1,995,571	261,069	664	1.00	1.50
368.3443	7.12	[M+H]+	3-Deoxyvitamin D3	secosteroids	sterol lipids	1,995,571	261,069	664	1.00	1.50
371.3036	1.59	[M+H]+	Tetradecanoylcarnitine	fatty esters	fatty acyls	84,767	2,120	3898	0.97	1.73

354.2770	1.59	[NH4]+	MG(18:2)	monoacylglycerols	glycerolipids	84,767	2,120	3898	0.97	1.73
384.3392	10.19	[M+H]+	Dehydrocholesterol	cholesterol and derivatives	sterol lipids	392,202	36,403	977	1.00	1.63
367.3086	10.19	[NH4]+	PGF2α dimethyl amine	eicosanoids	fatty acyls	392,202	36,403	977	1.00	1.63
367.3086	10.19	[NH4]+	N-oleoyl GABA	fatty amides	fatty acyls	392,202	36,403	977	1.00	1.63
402.3498	10.19	[M+H-H2O]+	δ-Tocopherol	quinone and hydroquinones	prenol lipids	392,202	36,403	977	1.00	1.63
384.3392	10.19	[M+H]+	Previtamin D3	secosteroids	sterol lipids	392,202	36,403	977	1.00	1.63
372.3756	25.21	[M+Na]+	5alpha-Cholestane // Cholestane skeleton	steroids	sterol lipids	37,570	1,785	2004	0.95	1.51
399.3348	2.43	[M+H]+	Palmitoylcarnitine	fatty esters	fatty acyls	741,916	35,234	2006	0.98	1.85
382.3083	2.43	[NH4]+	MG(20:2)	monoacylglycerols	glycerolipids	741,916	35,234	2006	0.98	1.85
386.3549	13.01	[M+Na]+	Cholesterol	cholesterol and derivatives	sterol lipids	14,975,000	949,983	1476	1.00	1.75
402.3498	10.19	[M+Na]+	δ-Tocopherol	quinone and hydroquinones	prenol lipids	860,235	101,508	747	1.00	1.54
424.3341	10.19	[M+H]+	δ-Tocopherol	quinone and hydroquinones	prenol lipids	860,235	101,508	747	1.00	1.54
427.3662	3.93	[M+H]+	DL-Stearoylcarnitine	fatty esters	fatty acyls	233,306	26,670	775	0.99	1.55
410.3396	3.93	[NH4]+	MG(22:2)	monoacylglycerols	glycerolipids	233,306	26,670	775	0.99	1.55
413.3141	12.19	[NH4]+	N-stearoyl glutamic acid	fatty amides	fatty acyls	457,677	7,677	5862	0.97	1.99
408.3603	12.19	[M+Na]+	keto-Hexacosanolide	fatty esters	fatty acyls	457,677	7,677	5862	0.97	1.99
430.3447	12.19	[M+H]+	1α-hydroxy-25-methoxyvitamin D3 / 1α-hydroxy-25-methoxycholecalciferol	secosteroids	sterol lipids	457,677	7,677	5862	0.97	1.99
481.3168	5.43	[M+H]+	LPC(15:0)	lyso-phosphatidylcholines	glycerophospholipids	609,765	55,637	996	0.98	1.63
481.3168	5.43	[M+H]+	LPE(18:0)	lyso-phosphatidylethanolamines	glycerophospholipids	609,765	55,637	996	0.98	1.63
464.2903	5.43	[NH4]+	PA(20:1)	phosphatidic acids	glycerophospholipids	609,765	55,637	996	0.98	1.63
526.4750	23.95	[M+H-H2O]+	Linoleyl linolenate // 36:5	fatty esters	fatty acyls	86,298	2,775	3010	0.83	1.56
509.3845	6.66	[M+H]+	LPAF C-18	lyso-phosphatidylcholines	glycerophospholipids	1,069,096	89,354	1096	0.95	1.68
509.3845	6.66	[M+H]+	PC(O-10:0/O-8:0)	phosphatidylcholines	glycerophospholipids	1,069,096	89,354	1096	0.95	1.68
514.4056	18.29	[M+H]+	Didodecyl thiobispropanoate	fatty acids	fatty acyls	1,868	99,631	-98	-0.97	1.81
519.3325	2.92	[M+H]+	LPC(18:2)	lyso-phosphatidylcholines	glycerophospholipids	36,725,000	4,286,709	757	0.84	1.61
521.3481	3.42	[M+H]+	LPC(18:1)	lyso-phosphatidylcholines	glycerophospholipids	426,770	14,522	2839	0.78	1.53
521.3481	3.42	[M+H]+	PC(O-18:1) // PC(P-18:0)	phosphatidylcholines	glycerophospholipids	426,770	14,522	2839	0.78	1.53
533.3481	10.17	[M+H]+	LPE(22:2)	lyso-phosphatidylethanolamines	glycerophospholipids	1,439	40,310	-96	-0.90	1.51
537.4158	9.31	[M+H]+	PC(O-12:0/O-8:0)	phosphatidylcholines	glycerophospholipids	692,079	32,403	2036	0.97	1.85
539.3587	3.75	[M+H]+	LPS(O-20:0)	lyso-phosphatidylserines	glycerophospholipids	256,386	20,131	1174	0.98	1.68
519.3325	2.25	[M+Na]+	LPC(18:2)	lyso-phosphatidylcholines	glycerophospholipids	471,593	22,210	2023	0.95	1.66
541.3168	2.25	[M+H]+	LPC(20:5)	lyso-phosphatidylcholines	glycerophospholipids	471,593	22,210	2023	0.95	1.66
521.3481	2.91	[M+Na]+	LPC(18:1)	lyso-phosphatidylcholines	glycerophospholipids	6,230,558	763,146	716	0.84	1.52
543.3325	2.91	[M+H]+	LPC(20:4)	lyso-phosphatidylcholines	glycerophospholipids	6,230,558	763,146	716	0.84	1.52
556.5219	25.73	[M+H]+	38:04:00	fatty acids	fatty acyls	35,353	873	3951	0.96	1.72
539.4914	25.73	[NH4]+	Hexacosanoyl carnitine	fatty esters	fatty acyls	35,353	873	3951	0.96	1.72

534.5376	25.73	[M+Na]+	Palmitoleyl arachidate // Stearyl oleate	fatty esters	fatty acyls	35,353	873	3951	0.96	1.72
558.5376	25.32	[M+H]+	Linolenyl arachidate // Palmityl arachidate	fatty esters	fatty acyls	52,690	2,211	2283	0.95	1.72
560.5168	33.04	[M+H]+	1-tetradecanyl-2-(8-[3]-ladderane-octanyl)-sn-glycerol	diradylglycerols	glycerolipids	78,983	5,520	1331	0.93	1.53
562.4386	18.94	[M+H]+	2-Hexaprenyl-3-methyl-6-methoxy-1,4-benzoquinol	quinone and hydroquinones	prenol lipids	2,561	43,485	-94	-0.92	1.60
565.4471	12.01	[M+H]+	PC(O-10:0/O-12:0)	phosphatidylcholines	glycerophospholipids	429,303	12,582	3312	1.00	1.98
545.3481	2.86	[M+Na]+	LPC(20:3)	lyso-phosphatidylcholines	glycerophospholipids	5,053,589	322,568	1467	0.92	1.79
567.3325	2.86	[M+H]+	LPC(22:6)	lyso-phosphatidylcholines	glycerophospholipids	5,053,589	322,568	1467	0.92	1.79
554.4910	14.56	[NH4]+	DG(31:0)	diacylglycerols	glycerolipids	193,708	3,735	5086	0.97	1.93
579.4264	10.48	[M+H]+	PC(O-22:0)	phosphatidylcholines	glycerophospholipids	796,624	64,257	1140	1.00	1.67
562.4022	9.83	[NH4]+	Cholesteryl ferulate	steroid esters	sterol lipids	96,463	3,985	2321	0.96	1.71
565.5070	26.07	[NH4]+	Cer(d35:2(2OH))	ceramides	sphingolipids	16,056	694	2214	0.94	1.53
560.5532	26.07	[M+Na]+	Arachidyl linoleate	fatty esters	fatty acyls	16,056	694	2214	0.94	1.53
562.4233	9.80	[M+Na]+	Campesteryl glucoside	sterols	sterol lipids	449,783	13,253	3294	0.99	1.98
571.5176	33.51	[NH4]+	Cer(t340(2OH))	ceramides	sphingolipids	421,211	46,073	814	0.87	1.56
588.5481	33.51	[M+H]+	1-(methyl-pentadecanyl)-2-(ladderane-octanyl)glycerol	diradylglycerols	glycerolipids	421,211	46,073	814	0.87	1.56
566.5638	33.51	[M+Na]+	Hydroxyphthioceranic acid (C37)	fatty acids	fatty acyls	421,211	46,073	814	0.87	1.56
576.4155	11.81	[NH4]+	PA(P-38:0)	phosphatidic acids	glycerophospholipids	226,673	18,359	1135	1.00	1.67
593.4784	14.57	[M+H]+	PC(O-12:0/O-12:0)	phosphatidylcholines	glycerophospholipids	253,867	2,624	9576	0.98	1.99
576.4390	10.71	[M+Na]+	Schottenol 3-glucoside	sterols	sterol lipids	722,666	50,439	1333	0.99	1.72
576.4390	3.35	[M+Na]+	stigmast-5-en-3beta-ol 3-0-beta-D-glucopyranoside	sterols	sterol lipids	47,790	1,457	3180	0.97	1.67
590.4311	13.10	[NH4]+	PA(P-39:0)	phosphatidic acids	glycerophospholipids	2,164,810	219,730	885	1.00	1.60
590.4335	13.10	[NH4]+	Coenzyme Q6	quinone and hydroquinones	prenol lipids	2,164,810	219,730	885	1.00	1.60
614.3948	10.71	[M+H]+	PA(30:3)	phosphatidic acids	glycerophospholipids	137,668	7,254	1798	0.94	1.67
618.3920	4.11	[NH4]+	3-O-cis-Coumaroylmaslinic acid	triterpenes	prenol lipids	ND	111,667	WT	-0.90	1.62
637.6373	23.23	[M+H]+	Cer(d41:0)	ceramides	sphingolipids	291,714	9,881	2852	0.98	1.96
624.5845	27.66	[M+Na]+	CE(16:0)	cholesterol esters	sterol lipids	11,762,431	69,439	16839	0.99	2.39
646.5689	27.66	[M+H]+	CE(18:3)	cholesterol esters	sterol lipids	11,762,431	69,439	16839	0.99	2.39
649.6373	22.83	[M+H]+	Cer(d42:1)	ceramides	sphingolipids	89,517	11,298	692	0.97	1.52
650.6002	29.93	[M+H]+	CE(18:1)	cholesterol esters	sterol lipids	68,498	1,530,420	-96	-0.90	1.86
651.6529	23.84	[M+H]+	Cer(d42:0)	ceramides	sphingolipids	457,952	13,488	3295	0.99	1.99
660.5094	13.02	[M+H]+	PA(O-34:1) // PA(P-34:0)	phosphatidic acids	glycerophospholipids	178,675	2,337	7547	0.98	1.92
667.6479	22.80	[M+H]+	Cer(t42:0)	ceramides	sphingolipids	501,800	39,623	1166	0.97	1.68
674.5363	14.12	[M+H]+	SM(d32:1)	sphingomyelines	sphingolipids	4,888,493	141,704	3350	1.00	1.99
671.5336	15.15	[NH4]+	GlcCer(d32:1)	glucosylceramides	neutral glycosphingolipids	15,725,000	520,879	2919	1.00	1.95
688.5519	15.15	[M+H]+	SM(d33:1)	sphingomyelines	sphingolipids	15,725,000	520,879	2919	1.00	1.95
666.5798	15.15	[M+Na]+	TG(38:0)	triacylglycerols	glycerolipids	15,725,000	520,879	2919	1.00	1.95

672.5094	16.64	[NH4]+	PA(O-35:2) // PA(P-35:1)	phosphatidic acids	glycerophospholipids	61,579	2,760	2131	0.96	1.54
689.5359	16.64	[M+H]+	PC(O-30:1) // PC(P-30:0)	phosphatidylcholines	glycerophospholipids	61,579	2,760	2131	0.96	1.54
689.5359	16.64	[M+H]+	PE(O-33:1) // PE(P-33:0)	phosphatidylethanolamines	glycerophospholipids	61,579	2,760	2131	0.96	1.54
673.5046	13.17	[NH4]+	PE(P-32:1)	phosphatidylethanolamines	glycerophospholipids	769,398	10,033	7568	0.98	2.05
676.6158	28.52	[M+Na]+	CE(20:2)	cholesterol esters	sterol lipids	ND	97,029	WT	-0.89	1.68
698.6002	28.52	[M+H]+	CE(22:5)	cholesterol esters	sterol lipids	ND	97,029	WT	-0.89	1.68
683.5336	14.82	[NH4]+	GlcCer(d33:2)	glucosylceramides	neutral glycosphingolipids	17,850,000	1,284,072	1290	1.00	1.71
683.5254	14.82	[NH4]+	1-tetradecanyl-2-(8-[3]-ladderane-octanyl)-sn-glycerophosphoethanolamine	glycerophosphoethanolamines	glycerophospholipids	17,850,000	1,284,072	1290	1.00	1.71
700.5519	14.82	[M+H]+	SM(d34:2)	sphingomyelines	sphingolipids	17,850,000	1,284,072	1290	1.00	1.71
678.5798	14.82	[M+Na]+	TG(39:1)	triacylglycerols	glycerolipids	17,850,000	1,284,072	1290	1.00	1.71
685.5493	16.11	[NH4]+	GlcCer(d33:1)	glucosylceramides	neutral glycosphingolipids	106,750,000	14,100,000	657	1.00	1.50
702.5676	16.11	[M+H]+	SM(d34:1)	sphingomyelines	sphingolipids	106,750,000	14,100,000	657	1.00	1.50
680.5955	16.11	[M+Na]+	TG(39:0)	triacylglycerols	glycerolipids	106,750,000	14,100,000	657	1.00	1.50
687.5203	14.23	[NH4]+	PC(P-30:1)	phosphatidylcholines	glycerophospholipids	1,220,727	23,384	5120	1.00	2.10
687.5203	14.23	[NH4]+	PE(P-33:1) // PE(O-33:2)	phosphatidylethanolamines	glycerophospholipids	1,220,727	23,384	5120	1.00	2.10
704.5832	16.87	[M+H]+	SM(d34:0)	sphingomyelines	sphingolipids	8,518,792	373,376	2182	0.99	1.87
704.5743	16.87	[M+H]+	Cholesteryl 11-hydroperoxy-eicosatetraenoate	sterols	sterol lipids	8,518,792	373,376	2182	0.99	1.87
714.5563	15.88	[M+H]+	PA(O-38:2) // PA(P-38:1)	phosphatidic acids	glycerophospholipids	214,702	27,590	678	0.97	1.51
715.5598	16.83	[M+H]+	GlcCer(d34:1(2OH))	glucosylceramides	neutral glycosphingolipids	471,429	13,363	3428	0.97	1.69
698.5250	16.83	[NH4]+	PA(P-37:2)	phosphatidic acids	glycerophospholipids	471,429	13,363	3428	0.97	1.69
715.5516	16.83	[M+H]+	PC(O-32:2) // PC(P-32:1)	phosphatidylcholines	glycerophospholipids	471,429	13,363	3428	0.97	1.69
715.5516	16.83	[M+H]+	PE(O-35:2) // PE(P-35:1)	phosphatidylethanolamines	glycerophospholipids	471,429	13,363	3428	0.97	1.69
693.5696	16.83	[M+Na]+	Cholesteryl nitrolinoleate	sterols	sterol lipids	471,429	13,363	3428	0.97	1.69
694.5536	13.91	[M+Na]+	DG(42:7)	diacylglycerols	glycerolipids	931,128	39,293	2270	1.00	1.88
699.5203	13.91	[NH4]+	PE(P-34:2) // PE(O-34:3)	phosphatidylethanolamines	glycerophospholipids	931,128	39,293	2270	1.00	1.88
716.5720	17.11	[M+H]+	PA(O-38:1) // PA(P-38:0)	phosphatidic acids	glycerophospholipids	5,061,852	225,282	2147	0.99	1.86
716.5832	17.11	[M+H]+	SM(d35:1)	sphingomyelines	sphingolipids	5,061,852	225,282	2147	0.99	1.86
694.5900	17.11	[M+Na]+	3-Hexadecanoyloleanolic acid	triterpenes	prenol lipids	5,061,852	225,282	2147	0.99	1.86
700.5407	19.03	[NH4]+	PA(O-37:2) // PA(P-37:1)	phosphatidic acids	glycerophospholipids	377,594	26,649	1317	0.94	1.50
717.5672	19.03	[M+H]+	PC(O-32:1) // PC(P-32:0)	phosphatidylcholines	glycerophospholipids	377,594	26,649	1317	0.94	1.50
717.5672	19.03	[M+H]+	PE(O-35:1) // PE(P-35:0)	phosphatidylethanolamines	glycerophospholipids	377,594	26,649	1317	0.94	1.50
700.5407	18.36	[NH4]+	PA(O-37:2) // PA(P-37:1)	phosphatidic acids	glycerophospholipids	159,920	6,757	2267	0.96	1.56
717.5672	18.36	[M+H]+	PC(O-32:1) // PC(P-32:0)	phosphatidylcholines	glycerophospholipids	159,920	6,757	2267	0.96	1.56
717.5672	18.36	[M+H]+	PE(O-35:1) // PE(P-35:0)	phosphatidylethanolamines	glycerophospholipids	159,920	6,757	2267	0.96	1.56
700.5519	18.36	[NH4]+	SM(d34:2)	sphingomyelines	sphingolipids	159,920	6,757	2267	0.96	1.56
701.5359	15.24	[NH4]+	PC(P-31:1)	phosphatidylcholines	glycerophospholipids	3,445,934	174,299	1877	1.00	1.82
701.5359	15.24	[NH4]+	PE(O-34:2) // PE(P-34:1)	phosphatidylethanolamines	glycerophospholipids	3,445,934	174,299	1877	1.00	1.82
718.5689	15.24	[M+H]+	Dihydromenaquinone-8	quinone and hydroquinones	prenol lipids	3,445,934	174,299	1877	1.00	1.82

719.5465	17.12	[M+H]+	PC(31:0)	phosphatidylcholines	glycerophospholipids	2,678,643	249,866	972	0.99	1.63
698.5849	15.06	[M+Na]+	DG(42:5)	diacylglycerols	glycerolipids	1,118,487	19,796	5550	0.97	1.97
720.5693	15.06	[M+H]+	DG(44:8)	diacylglycerols	glycerolipids	1,118,487	19,796	5550	0.97	1.97
703.5516	15.06	[NH4]+	PC(O-31:1) // PC(P-31:0)	phosphatidylcholines	glycerophospholipids	1,118,487	19,796	5550	0.97	1.97
703.5516	15.06	[NH4]+	PE(O-34:1) // PE(P-34:0)	phosphatidylethanolamines	glycerophospholipids	1,118,487	19,796	5550	0.97	1.97
726.5676	15.65	[M+H]+	SM(d36:3)	sphingomyelines	sphingolipids	287,906	30,072	857	0.97	1.59
704.5743	15.65	[M+Na]+	Cholesteryl 11-hydroperoxy-eicosatetraenoate	sterols	sterol lipids	287,906	30,072	857	0.97	1.59
726.5587	15.65	[M+H]+	Ubiquinone 8	ubiquinones	prenol lipids	287,906	30,072	857	0.97	1.59
711.5649	16.85	[NH4]+	GlcCer(d35:2)	glucosylceramides	neutral glycosphingolipids	4,076,236	354,107	1051	0.99	1.65
728.5720	16.85	[M+H]+	PA(P-39:1)	phosphatidic acids	glycerophospholipids	4,076,236	354,107	1051	0.99	1.65
728.5832	16.85	[M+H]+	SM(d36:2)	sphingomyelines	sphingolipids	4,076,236	354,107	1051	0.99	1.65
716.5380	14.57	[NH4]+	DG(44:10)	diacylglycerols	glycerolipids	1,072,603	15,613	6770	1.00	2.17
716.5356	14.57	[NH4]+	PA(37:2)	phosphatidic acids	glycerophospholipids	1,072,603	15,613	6770	1.00	2.17
733.5622	14.57	[M+H]+	PE(35:0)	phosphatidylethanolamines	glycerophospholipids	1,072,603	15,613	6770	1.00	2.17
724.6006	17.17	[M+Na]+	DG(44:6)	diacylglycerols	glycerolipids	363,714	24,228	1401	0.99	1.74
746.5826	17.17	[M+H]+	PA(39:0)	phosphatidic acids	glycerophospholipids	363,714	24,228	1401	0.99	1.74
729.5672	17.17	[NH4]+	PC(O-33:2) // PC(P-33:1)	phosphatidylcholines	glycerophospholipids	363,714	24,228	1401	0.99	1.74
729.5672	17.17	[NH4]+	PE(P-36:1) // PE(O-36:2)	phosphatidylethanolamines	glycerophospholipids	363,714	24,228	1401	0.99	1.74
730.5900	20.72	[NH4]+	Ubiquinol 8	ubiquinones	prenol lipids	474,541	43,125	1000	0.99	1.63
732.5305	18.61	[NH4]+	PG(O-34:2) // PG(P-34:1)	phosphatidylglycerols	glycerophospholipids	124,483	13,701	809	0.99	1.56
749.5571	18.61	[M+H]+	PS(O-34:0)	phosphatidylserines	glycerophospholipids	124,483	13,701	809	0.99	1.56
748.6158	22.25	[NH4]+	Plastoquinone-9	ubiquinones	prenol lipids	1,082	182,822	-99	-0.98	2.14
756.5305	12.99	[NH4]+	PG(O-36:4) // PG(P-36:3)	phosphatidylglycerols	glycerophospholipids	70,943	877,248	-92	-0.90	1.53
773.5571	12.99	[M+H]+	PS(O-36:2) // PS(P-36:1)	phosphatidylserines	glycerophospholipids	70,943	877,248	-92	-0.90	1.53
756.6145	21.21	[NH4]+	SM(d38:2)	sphingomyelines	sphingolipids	959,785	99,699	863	0.98	1.59
758.6302	22.19	[NH4]+	SM(d38:1)	sphingomyelines	sphingolipids	360,509	31,786	1034	0.99	1.64
776.4992	12.90	[NH4]+	1-(ladderane-hexanoyl)-2-(ladderane-octanyl)glycerophospho-(glycerol)	glycerophosphoglycerols	glycerophospholipids	560,403	28,756	1849	0.90	1.72
793.5258	12.90	[M+H]+	PS(O-38:6) // PS(P-38:5)	phosphatidylserines	glycerophospholipids	560,403	28,756	1849	0.90	1.72
786.6374	23.490	[NH4]+	16:0-Glc-Cholesterol	sterols	sterol lipids	139,796	4,774	2828	0.96	1.75
808.6217	22.04	[NH4]+	16:2-Glc-Stigmasterol	sterols	sterol lipids	468,285	9,629	4763	0.97	1.77
808.6217	22.04	[NH4]+	18:3-Glc-cholesterol	sterols	sterol lipids	468,285	9,629	4763	0.97	1.77
822.5411	12.05	[NH4]+	PG(40:6)	phosphatidylglycerols	glycerophospholipids	7,069	452,653	-98	-0.94	1.79
822.5258	12.05	[NH4]+	PI(33:1)	phosphatidylinositols	glycerophospholipids	7,069	452,653	-98	-0.94	1.79
817.5833	12.05	[M+Na]+	PS(38:1)	phosphatidylserines	glycerophospholipids	7,069	452,653	-98	-0.94	1.79
839.5676	12.05	[M+H]+	PS(40:4)	phosphatidylserines	glycerophospholipids	7,069	452,653	-98	-0.94	1.79
825.5884	15.09	[M+Na]+	PC(38:4(12OH)	phosphatidylcholines	glycerophospholipids	132,440	6,348	1986	0.95	1.51
825.5884	15.09	[M+Na]+	PS(O-40:4) // PS(P-40:3)	phosphatidylserines	glycerophospholipids	132,440	6,348	1986	0.95	1.51
847.5727	15.09	[M+H]+	PS(P-42:6)	phosphatidylserines	glycerophospholipids	132,440	6,348	1986	0.95	1.51

825.5731	15.09	[M+Na]+	PI-Cer(t36:0)	phosphosphingolipids	sphingolipids	132,440	6,348	1986	0.95	1.51
838.6687	24.35	[NH4]+	20:2-Glc-cholesterol	sterols	sterol lipids	76,544	2,848	2588	0.96	1.60
900.5083	18.47	[NH4]+	(25R)-spirost-5en-3beta-ol 3-O-alpha-L-rhamnopyranosyl-(1-2)-[beta-D-glucopyranosyl-(1-4)]-beta-D-glucopyranoside	sterols	sterol lipids	10,632	133,311	-92	-0.97	1.66
1,023.6700	13.96	[M+H]+	Trihexosylceramide (d34:1)	neutral glycosphingolipids	sphingolipids	98,755	633	15495	0.99	2.12
1,047.3600	5.30	[M+H]+	3-Oxooctadecanoyl-CoA	fatty esters	fatty acyls	2,060,412	275,558	648	0.90	1.51
1,064.7000	13.29	[M+H]+	GlcNAcbeta1-4Manbeta1-4Glcbeta-Cer(d34:1)	neutral glycosphingolipids	sphingolipids	46,516	560	8210	0.98	1.94

Mass – neutral mass of measured lipid; MW – neutral mass of identifier; AV – average of the signal across the group; % change – negative value means a decrease in ApoE samples in comparison to WT, while positive value means an increase in ApoE sample; ND – not detected; WT – detected only in WT sample; ApoE – detected only in ApoE sample.

Table S4: List of HDL proteins quantified in the comparative proteomics experiments of the ApoE-KO mouse model with respect to WT mouse.

Acc Number	Protein name	HDL fraction								Average		
		Replicate 1				Replicate 2						
		Zq	FDR	*p*-value	n pep	Zq	FDR	*p*-value	n pep	Zq	FDR	*p*-value
P02089	Hemoglobin subunit beta-2	-4.70	9.83E-05	2.66E-06	7	-4.85	3.60E-09	1.23E-06	6	-4.77	1.81E-06	1.67E-04
P07743	BPI fold-containing family A member 2	-4.18	7.95E-04	2.86E-05	5	-2.77	3.27E-04	5.66E-03	4	-3.48	5.10E-04	2.35E-02
Q9D3H2	MCG117626	-2.15	2.96E-01	3.13E-02	5	-1.90	9.69E-03	5.73E-02	4	-2.03	4.26E-02	1.31E+00
Q921I1	Serotransferrin	-2.23	2.51E-01	2.54E-02	20	-1.69	1.45E-02	9.13E-02	26	-1.96	4.98E-02	1.15E+00
Q8VCT4	Carboxylesterase 1D	-2.28	2.30E-01	2.28E-02	4	-1.55	3.03E-02	1.22E-01	3	-1.91	5.59E-02	1.03E+00
P23953	Carboxylesterase 1C	-2.11	2.93E-01	3.50E-02	15	-1.54	2.26E-02	1.25E-01	14	-1.82	6.84E-02	1.05E+00
A2AEN9	Protein Gm5938	-1.61	5.17E-01	1.07E-01	7	-1.76	1.39E-02	7.88E-02	5	-1.68	9.20E-02	1.21E+00
P06728	Apolipoprotein A-IV	-1.53	5.86E-01	1.25E-01	47	-1.77	1.15E-02	7.63E-02	49	-1.65	9.84E-02	1.13E+00
A2AEP0	Protein Obp1b	-1.50	5.96E-01	1.34E-01	9	-1.62	1.97E-02	1.06E-01	9	-1.56	1.19E-01	1.22E+00
Q00897	Alpha-1-antitrypsin 1-4	-1.82	4.35E-01	6.86E-02	6	-1.23	5.25E-02	2.19E-01	7	-1.53	1.27E-01	1.17E+00
P07724	Serum albumin	-1.18	8.06E-01	2.38E-01	66	-1.71	1.36E-02	8.66E-02	56	-1.45	1.48E-01	1.24E+00
P21614	Vitamin D-binding protein	-1.09	8.52E-01	2.75E-01	14	-1.35	3.57E-02	1.77E-01	15	-1.22	2.22E-01	1.70E+00
P22599	Alpha-1-antitrypsin 1-2	-1.52	5.89E-01	1.27E-01	7	-0.88	1.03E-01	3.81E-01	7	-1.20	2.30E-01	1.63E+00
Q61247	Alpha-2-antiplasmin	-1.24	7.62E-01	2.16E-01	4	-0.98	8.93E-02	3.27E-01	7	-1.11	2.68E-01	1.64E+00
P07309	Transthyretin	-0.76	9.15E-01	4.45E-01	10	-1.41	3.17E-02	1.58E-01	7	-1.09	2.76E-01	1.59E+00
O35176	Androgen-binding protein	-1.09	8.48E-01	2.77E-01	4					-1.09	2.77E-01	6.89E-01
P07758	Alpha-1-antitrypsin 1-1	-1.12	8.63E-01	2.64E-01	17	-1.00	7.81E-02	3.18E-01	17	-1.06	2.90E-01	1.57E+00
O09043	Napsin-A	-1.32	7.26E-01	1.88E-01	3	-0.67	1.68E-01	5.01E-01	4	-0.99	3.20E-01	1.55E+00
P29621	Serine protease inhibitor A3C	-0.98	8.85E-01	3.29E-01	3					-0.98	3.29E-01	7.21E-01
P01027	Complement C3	-1.37	7.04E-01	1.71E-01	44	-0.51	1.84E-01	6.09E-01	32	-0.94	3.47E-01	1.60E+00
P97336	Odorant binding protein Ia (Fragment)	-0.92	8.99E-01	3.58E-01	4					-0.92	3.58E-01	7.67E-01
P13020	Gelsolin	-1.27	7.32E-01	2.03E-01	7	-0.51	1.89E-01	6.13E-01	10	-0.89	3.74E-01	1.64E+00
P11859	Angiotensinogen	-1.08	8.46E-01	2.80E-01	5	-0.64	1.69E-01	5.24E-01	4	-0.86	3.91E-01	1.63E+00
A6X935	Inter alpha-trypsin inhibitor, heavy chain 4	-0.99	8.81E-01	3.23E-01	8	-0.50	1.89E-01	6.17E-01	7	-0.74	4.57E-01	1.83E+00
Q8C165	Probable carboxypeptidase PM20D1	-0.80	9.19E-01	4.26E-01	9	-0.50	1.88E-01	6.16E-01	9	-0.65	5.16E-01	1.83E+00
P07759	Serine protease inhibitor A3K	-0.75	9.01E-01	4.51E-01	10	-0.54	1.79E-01	5.91E-01	10	-0.65	5.18E-01	1.91E+00
P13634	Carbonic anhydrase 1	-0.71	9.10E-01	4.75E-01	6	-0.56	1.85E-01	5.74E-01	5	-0.64	5.24E-01	1.66E+00
Q61171	Peroxiredoxin-2	-0.94	8.96E-01	3.45E-01	6	-0.32	2.22E-01	7.51E-01	8	-0.63	5.28E-01	1.80E+00
P32848	Parvalbumin alpha	-0.51	9.74E-01	6.12E-01	3	-0.73	1.45E-01	4.68E-01	8	-0.62	5.37E-01	1.65E+00
P97298	Pigment epithelium-derived factor	-0.83	9.14E-01	4.08E-01	4	-0.28	2.58E-01	7.82E-01	3	-0.55	5.81E-01	1.62E+00
O08677	Kininogen-1	-0.60	9.64E-01	5.51E-01	8	-0.41	1.99E-01	6.83E-01	11	-0.50	6.15E-01	1.77E+00
P29699	Alpha-2-HS-glycoprotein	-0.50	9.75E-01	6.19E-01	12	-0.42	1.99E-01	6.72E-01	11	-0.46	6.45E-01	1.75E+00
Q9QXC1	Fetuin-B	-0.46	9.70E-01	6.47E-01	5					-0.46	6.47E-01	1.01E+00
Q8C7G5	Apolipoprotein A-V					-0.43	2.46E-01	6.66E-01	3	-0.43	6.66E-01	3.41E+00
P12399	Protein CTLA-2-alpha					-0.42	2.23E-01	6.73E-01	3	-0.42	6.73E-01	4.42E+00
P02088	Hemoglobin subunit beta-1	-0.53	9.70E-01	5.96E-01	21	-0.14	2.54E-01	8.85E-01	12	-0.34	7.36E-01	1.94E+00
P01029	Complement C4-B	-0.85	9.08E-01	3.93E-01	9	0.26	3.95E-01	7.98E-01	8	-0.30	7.64E-01	1.85E+00
P11588	Major urinary protein 1	-0.28	9.85E-01	7.79E-01	3					-0.28	7.79E-01	1.10E+00

P01942	Hemoglobin subunit alpha	-0.37	9.82E-01	7.12E-01	7	-0.17	2.53E-01	8.67E-01	7	-0.27	7.89E-01	1.86E+00
P21460	Cystatin-C	-0.25	9.86E-01	8.01E-01	3					-0.25	8.01E-01	1.12E+00
Q61207	Sulfated glycoprotein 1	-0.20	9.94E-01	8.39E-01	4	-0.27	2.32E-01	7.87E-01	8	-0.24	8.13E-01	1.82E+00
Q923D2	Flavin reductase (NADPH)	-0.32	9.93E-01	7.49E-01	6	0.05	3.25E-01	9.59E-01	5	-0.13	8.93E-01	1.87E+00
Q00724	Retinol-binding protein 4	-0.33	9.87E-01	7.38E-01	5	0.10	3.60E-01	9.22E-01	4	-0.12	9.06E-01	1.81E+00
P04247	Myoglobin	-0.08	9.93E-01	9.37E-01	9	-0.13	2.78E-01	8.93E-01	5	-0.11	9.15E-01	1.79E+00
E9Q414	Apolipoprotein B-100	0.00	1.01E+00	9.98E-01	288	-0.16	2.46E-01	8.72E-01	265	-0.08	9.35E-01	1.91E+00
Q91X72	Hemopexin	0.08	9.95E-01	9.37E-01	4	-0.23	2.46E-01	8.18E-01	8	-0.08	9.40E-01	1.80E+00
P52430	Serum paraoxonase/arylesterase 1 G	-0.42	9.89E-01	6.77E-01	13	0.33	4.02E-01	7.43E-01	13	-0.04	9.65E-01	1.81E+00
P28665	Murinoglobulin-1	-0.05	1.00E+00	9.62E-01	13	0.04	3.26E-01	9.71E-01	6	-0.01	9.96E-01	1.83E+00
P46412	Glutathione peroxidase 3					0.01	3.42E-01	9.91E-01	4	0.01	9.91E-01	3.80E+00
P19221	Prothrombin					0.08	3.65E-01	9.35E-01	4	0.08	9.35E-01	3.07E+00
P62984	Ubiquitin-60S ribosomal protein L40	0.30	9.91E-01	7.61E-01	4	-0.10	2.85E-01	9.23E-01	6	0.10	9.17E-01	1.66E+00
B5X0G2	Major urinary protein 17	0.56	9.70E-01	5.75E-01	14	-0.29	2.20E-01	7.73E-01	12	0.14	8.91E-01	1.58E+00
A8DUL0	Beta-globin					0.14	3.84E-01	8.87E-01	3	0.14	8.87E-01	2.63E+00
A8DUK4	Beta-globin	0.10	9.84E-01	9.20E-01	5	0.23	3.96E-01	8.21E-01	4	0.16	8.70E-01	1.48E+00
P51910	Apolipoprotein D	0.64	9.48E-01	5.25E-01	12	-0.21	2.42E-01	8.30E-01	10	0.21	8.33E-01	1.39E+00
Q60590	Alpha-1-acid glycoprotein 1	-0.34	9.92E-01	7.31E-01	7	0.79	6.31E-01	4.31E-01	7	0.22	8.25E-01	1.36E+00
Q9CQF9	Prenylcysteine oxidase	-0.03	1.00E+00	9.74E-01	10	0.50	4.95E-01	6.14E-01	4	0.24	8.14E-01	1.31E+00
P32261	Antithrombin-III	0.25	9.87E-01	8.00E-01	4					0.25	8.00E-01	9.69E-01
Q06890	Clusterin	0.16	9.93E-01	8.77E-01	12	0.51	4.76E-01	6.08E-01	11	0.33	7.38E-01	1.17E+00
O70362	Phosphatidylinositol-glycan-specific phospholipase D	0.34	9.91E-01	7.34E-01	3					0.34	7.34E-01	8.55E-01
P63242	Eukaryotic translation initiation factor 5A-1					0.34	4.70E-01	7.33E-01	3	0.34	7.33E-01	1.87E+00
Q01339	Beta-2-glycoprotein 1	0.35	9.89E-01	7.26E-01	3	0.34	4.27E-01	7.33E-01	5	0.35	7.30E-01	1.10E+00
P62204	Calmodulin	0.69	9.23E-01	4.93E-01	4	0.04	3.42E-01	9.66E-01	5	0.36	7.16E-01	1.06E+00
P16301	Phosphatidylcholine-sterol acyltransferase	0.28	9.85E-01	7.76E-01	8	0.45	4.49E-01	6.56E-01	9	0.36	7.15E-01	1.10E+00
B1Q450	Hemoglobin beta chain subunit	0.42	9.86E-01	6.78E-01	3					0.42	6.78E-01	7.70E-01
P62962	Profilin-1	0.45	9.66E-01	6.53E-01	4	0.38	4.96E-01	7.02E-01	3	0.42	6.77E-01	9.74E-01
O55042	Alpha-synuclein					0.46	4.87E-01	6.45E-01	5	0.46	6.45E-01	1.48E+00
P17742	Peptidyl-prolyl cis-trans isomerase A	0.48	9.77E-01	6.34E-01	3					0.48	6.34E-01	7.11E-01
P04939	Major urinary protein 3	0.83	9.17E-01	4.07E-01	3	0.28	4.26E-01	7.81E-01	3	0.55	5.80E-01	7.96E-01
Q9EQI5	Chemokine (C-X-C motif) ligand 7, isoform CRA	0.75	9.03E-01	4.55E-01	3	0.67	5.95E-01	5.02E-01	3	0.71	4.79E-01	6.47E-01
P01887	Beta-2-microglobulin	0.76	9.09E-01	4.48E-01	4					0.76	4.48E-01	4.97E-01
P17897	Lysozyme C-1					0.82	6.80E-01	4.11E-01	3	0.82	4.11E-01	7.14E-01
P31532	Serum amyloid A-4 protein	0.52	9.68E-01	6.00E-01	14	1.13	7.86E-01	2.59E-01	9	0.83	4.09E-01	5.45E-01
P01898	H-2 class I histocompatibility antigen, Q10 alpha chain	0.76	9.03E-01	4.50E-01	27	0.94	6.73E-01	3.50E-01	15	0.85	3.98E-01	5.23E-01
Q91Z73	Beta-2-microglobulin (Fragment)	0.80	9.17E-01	4.21E-01	5	0.97	7.28E-01	3.31E-01	5	0.89	3.74E-01	4.85E-01
Q9Z126	Platelet factor 4	1.07	8.42E-01	2.84E-01	4	0.75	6.32E-01	4.52E-01	3	0.91	3.62E-01	4.56E-01
Q9Z1R3	Apolipoprotein M	1.25	7.60E-01	2.12E-01	9	0.60	5.12E-01	5.49E-01	11	0.92	3.56E-01	4.54E-01
P55065	Phospholipid transfer protein	0.85	9.03E-01	3.95E-01	7	1.04	7.43E-01	3.00E-01	9	0.94	3.45E-01	4.29E-01
G3X9D6	Apolipoprotein N, isoform CRA	1.27	7.37E-01	2.02E-01	3	0.62	5.30E-01	5.38E-01	6	0.95	3.45E-01	4.23E-01
P35441	Thrombospondin-1	0.93	8.94E-01	3.52E-01	9	1.23	8.48E-01	2.18E-01	12	1.08	2.80E-01	3.35E-01
Q61268	Apolipoprotein C-IV	1.66	5.09E-01	9.62E-02	4	0.55	5.39E-01	5.80E-01	3	1.11	2.68E-01	3.08E-01

Q99K47	Fibrinogen, alpha polypeptide					1.15	8.43E-01	2.49E-01	3	1.15	2.49E-01	3.64E-01
P33622	Apolipoprotein C-III	1.37	7.09E-01	1.71E-01	5					1.37	1.71E-01	1.79E-01
P59242	Cingulin					1.74	8.45E-01	8.21E-02	3	1.74	8.21E-02	9.68E-02
P09813	Apolipoprotein A-II	2.11	3.02E-01	3.47E-02	7	1.40	9.26E-01	1.61E-01	6	1.76	7.90E-02	8.65E-02
Q00898	Alpha-1-antitrypsin 1-5	2.04	3.25E-01	4.18E-02	6	1.49	9.78E-01	1.37E-01	5	1.76	7.81E-02	8.46E-02
P34928	Apolipoprotein C-I	2.40	1.80E-01	1.66E-02	9	1.64	9.65E-01	1.01E-01	7	2.02	4.36E-02	4.67E-02
Q5FW60	Major urinary protein 20	2.46	1.63E-01	1.40E-02	5	1.76	8.94E-01	7.83E-02	3	2.11	3.49E-02	3.69E-02
P08226	Apolipoprotein E	2.13	3.03E-01	3.34E-02	38	2.40	6.25E-01	1.66E-02	36	2.26	2.37E-02	2.45E-02
P05366	Serum amyloid A-1 protein	2.66	1.06E-01	7.86E-03	6	1.88	8.48E-01	6.05E-02	4	2.27	2.33E-02	2.39E-02
Q00623	Apolipoprotein A-I	3.06	3.33E-02	2.25E-03	51	1.83	9.15E-01	6.78E-02	43	2.44	1.47E-02	1.48E-02
Q05020	Apolipoprotein C-II	3.73	4.05E-03	1.92E-04	5	2.37	5.70E-01	1.79E-02	4	3.05	2.30E-03	2.30E-03

-3 -1.5 0 1.5 3

Table S5: List of LDL proteins quantified in the comparative proteomics experiments of the ApoE-KO mouse model with respect to WT mouse.

Acc Number	Protein name	LDL fraction								Average		
		Replicate 1				Replicate 2						
		Zq	FDR	*p*-value	n pep	Zq	FDR	*p*-value	n pep	Zq	FDR	*p*-value
P28665	MOUSE Murinoglobulin-1	-3.41	1.16E-02	6.52E-04	13	-2.13	3.90E-01	3.28E-02	6	-2.77	5.13E-01	5.58E-03
P06728	MOUSE Apolipoprotein A-IV	-2.26	1.51E-01	2.41E-02	47	-3.02	1.62E-01	2.54E-03	49	-2.64	3.85E-01	8.36E-03
P34928	MOUSE Apolipoprotein C-I	-2.20	1.62E-01	2.77E-02	9	-2.97	1.60E-01	2.94E-03	7	-2.59	2.96E-01	9.66E-03
Q8C165	MOUSE Probable carboxypeptidase PM20D1	-2.63	6.74E-02	8.66E-03	9	-1.91	4.27E-01	5.64E-02	9	-2.27	5.38E-01	2.34E-02
P02089	MOUSE Hemoglobin subunit beta-2	-1.86	2.91E-01	6.30E-02	7	-2.51	2.73E-01	1.21E-02	6	-2.18	5.32E-01	2.89E-02
P51910	MOUSE Apolipoprotein D	-1.92	2.67E-01	5.48E-02	12	-2.44	2.89E-01	1.46E-02	10	-2.18	4.47E-01	2.92E-02
Q8C7G5	MOUSE Apolipoprotein A-V					-1.95	4.26E-01	5.13E-02	3	-1.95	6.74E-01	5.13E-02
P01898	MOUSE H-2 class I histocompatibility antigen, Q10 alpha chain	-1.76	3.43E-01	7.88E-02	27	-2.11	4.20E-01	3.49E-02	15	-1.93	5.43E-01	5.31E-02
O09043	MOUSE Napsin-A	-1.89	2.78E-01	5.83E-02	3	-1.82	4.13E-01	6.90E-02	4	-1.86	7.30E-01	6.35E-02
O70362	MOUSE Phosphatidylinositol-glycan-specific phospholipase D	-1.73	3.58E-01	8.39E-02	3					-1.73	7.72E-01	8.39E-02
Q61207	MOUSE Sulfated glycoprotein 1	-1.48	5.01E-01	1.38E-01	4	-1.48	5.06E-01	1.40E-01	8	-1.48	1.06E+00	1.39E-01
Q91Z73	MOUSE Beta-2-microglobulin (Fragment)	-1.35	5.88E-01	1.78E-01	5	-1.50	4.93E-01	1.32E-01	5	-1.43	1.01E+00	1.54E-01
P16301	MOUSE Phosphatidylcholine-sterol acyltransferase	-1.24	6.73E-01	2.15E-01	8	-1.53	5.05E-01	1.26E-01	9	-1.38	9.00E-01	1.66E-01
P07743	MOUSE BPI fold-containing family A member 2	-1.70	3.67E-01	8.84E-02	5	-1.06	6.36E-01	2.88E-01	4	-1.38	1.18E+00	1.67E-01
P52430	MOUSE Serum paraoxonase/arylesterase 1	-1.45	5.20E-01	1.47E-01	13	-1.27	5.68E-01	2.06E-01	13	-1.36	1.00E+00	1.74E-01
Q9CQF9	MOUSE Prenylcysteine oxidase	-1.71	3.67E-01	8.77E-02	10	-0.91	6.89E-01	3.63E-01	4	-1.31	1.17E+00	1.91E-01
E9Q414	MOUSE Apolipoprotein B-100	-2.75	5.33E-02	5.88E-03	288	0.16	9.52E-01	8.70E-01	265	-1.30	1.63E+00	1.95E-01
P05366	MOUSE Serum amyloid A-1 protein	-1.07	7.86E-01	2.83E-01	6	-1.49	4.95E-01	1.36E-01	4	-1.28	9.68E-01	2.00E-01
Q61268	MOUSE Apolipoprotein C-IV	-1.16	7.39E-01	2.48E-01	4	-1.39	5.24E-01	1.63E-01	3	-1.27	1.03E+00	2.02E-01
P01887	MOUSE Beta-2-microglobulin	-1.26	6.58E-01	2.09E-01	4					-1.26	9.61E-01	2.09E-01
Q9Z1R3	MOUSE Apolipoprotein M	-1.14	7.39E-01	2.55E-01	9	-1.00	6.59E-01	3.16E-01	11	-1.07	1.19E+00	2.84E-01
P33622	MOUSE Apolipoprotein C-III	-1.05	8.04E-01	2.93E-01	5					-1.05	1.12E+00	2.93E-01

P59242	MOUSE Cingulin					-0.98	6.57E-01	3.26E-01	3	-0.98	1.43E+00	3.26E-01
Q06890	MOUSE Clusterin	-0.91	8.86E-01	3.61E-01	12	-0.95	6.73E-01	3.43E-01	11	-0.93	1.41E+00	3.52E-01
G3X9D6	MOUSE Apolipoprotein N, isoform CRA	-0.58	1.06E+00	5.60E-01	3	-0.65	8.12E-01	5.14E-01	6	-0.62	1.70E+00	5.36E-01
P55065	MOUSE Phospholipid transfer protein	-0.80	9.80E-01	4.24E-01	7	-0.41	8.73E-01	6.80E-01	9	-0.61	1.85E+00	5.44E-01
P01029	MOUSE Complement C4-B	-1.45	5.22E-01	1.48E-01	9	0.36	9.67E-01	7.21E-01	8	-0.54	2.16E+00	5.86E-01
Q9D3H2	MOUSE MCG117626	-0.16	1.03E+00	8.73E-01	5	-0.88	7.10E-01	3.81E-01	4	-0.52	1.74E+00	6.04E-01
Q921I1	MOUSE Serotransferrin	-0.96	8.61E-01	3.36E-01	20	-0.07	9.02E-01	9.45E-01	26	-0.52	1.99E+00	6.06E-01
A2AEN9	MOUSE Protein Gm5938	-0.38	1.07E+00	7.06E-01	7	-0.55	8.20E-01	5.84E-01	5	-0.46	1.91E+00	6.44E-01
P32261	MOUSE Antithrombin-III	-0.44	1.09E+00	6.59E-01	4					-0.44	1.59E+00	6.59E-01
O55042	MOUSE Alpha-synuclein					-0.40	8.80E-01	6.89E-01	5	-0.40	2.44E+00	6.89E-01
Q01339	MOUSE Beta-2-glycoprotein 1	-0.30	1.06E+00	7.63E-01	3	-0.48	8.51E-01	6.33E-01	5	-0.39	1.94E+00	6.97E-01
P97336	MOUSE Odorant binding protein Ia (Fragment)	-0.32	1.05E+00	7.48E-01	4					-0.32	1.64E+00	7.48E-01
Q00623	MOUSE Apolipoprotein A-I	-0.07	1.02E+00	9.44E-01	51	-0.45	8.61E-01	6.55E-01	43	-0.26	1.98E+00	7.96E-01
P17742	MOUSE Peptidyl-prolyl cis-trans isomerase A	-0.23	1.05E+00	8.15E-01	3					-0.23	1.53E+00	8.15E-01
Q61247	MOUSE Alpha-2-antiplasmin	-0.59	1.06E+00	5.57E-01	4	0.13	9.54E-01	8.95E-01	7	-0.23	2.22E+00	8.20E-01
O35176	MOUSE Androgen-binding protein	-0.22	1.05E+00	8.29E-01	4					-0.22	1.44E+00	8.29E-01
P01027	MOUSE Complement C3	-0.65	1.07E+00	5.13E-01	44	0.31	9.77E-01	7.56E-01	32	-0.17	2.27E+00	8.64E-01
Q99K47	MOUSE Fibrinogen, alpha polypeptide					-0.16	9.15E-01	8.74E-01	3	-0.16	2.68E+00	8.74E-01
P09813	MOUSE Apolipoprotein A-II	-0.13	1.03E+00	8.93E-01	7	-0.15	9.16E-01	8.83E-01	6	-0.14	2.10E+00	8.88E-01
P29621	MOUSE Serine protease inhibitor A3C	-0.11	1.02E+00	9.09E-01	3					-0.11	1.27E+00	9.09E-01
P29699	MOUSE Alpha-2-HS-glycoprotein	0.15	1.03E+00	8.82E-01	12	-0.26	9.04E-01	7.96E-01	11	-0.06	2.04E+00	9.56E-01
Q61171	MOUSE Peroxiredoxin-2	-0.37	1.07E+00	7.10E-01	6	0.49	9.90E-01	6.28E-01	8	0.06	2.20E+00	9.55E-01
Q05020	MOUSE Apolipoprotein C-II	0.06	1.02E+00	9.50E-01	5	0.06	9.39E-01	9.52E-01	4	0.06	1.86E+00	9.51E-01
A2AEP0	MOUSE Protein Obp1b	0.34	1.06E+00	7.31E-01	9	-0.21	9.02E-01	8.33E-01	9	0.07	1.56E+00	9.47E-01
P07724	MOUSE Serum albumin	-0.19	1.06E+00	8.48E-01	66	0.34	9.70E-01	7.33E-01	56	0.08	1.97E+00	9.40E-01
P32848	MOUSE Parvalbumin alpha	0.44	1.09E+00	6.61E-01	3	-0.29	8.98E-01	7.74E-01	8	0.08	1.49E+00	9.39E-01
P13020	MOUSE Gelsolin	-0.33	1.06E+00	7.45E-01	7	0.48	9.90E-01	6.33E-01	10	0.08	2.11E+00	9.39E-01
Q00897	MOUSE Alpha-1-antitrypsin 1-4	-0.27	1.06E+00	7.86E-01	6	0.44	9.92E-01	6.58E-01	7	0.09	1.91E+00	9.32E-01
P02088	MOUSE Hemoglobin subunit beta-1	0.02	1.01E+00	9.85E-01	21	0.22	9.67E-01	8.26E-01	12	0.12	1.74E+00	9.05E-01
O08677	MOUSE Kininogen-1	0.04	1.01E+00	9.70E-01	8	0.21	9.70E-01	8.34E-01	11	0.12	1.63E+00	9.02E-01
A8DUL0	MOUSE Beta-globin					0.13	9.58E-01	8.93E-01	3	0.13	2.28E+00	8.93E-01
P07309	MOUSE Transthyretin	-0.01	1.00E+00	9.93E-01	10	0.28	9.85E-01	7.81E-01	7	0.13	1.58E+00	8.93E-01
P62962	MOUSE Profilin-1	-0.24	1.06E+00	8.11E-01	4	0.57	9.79E-01	5.71E-01	3	0.16	1.60E+00	8.70E-01
P07758	MOUSE Alpha-1-antitrypsin 1-1	-0.08	1.02E+00	9.33E-01	17	0.48	9.89E-01	6.30E-01	17	0.20	1.41E+00	8.43E-01
Q60590	MOUSE Alpha-1-acid glycoprotein 1	0.24	1.06E+00	8.08E-01	7	0.16	9.57E-01	8.74E-01	7	0.20	1.31E+00	8.41E-01
P13634	MOUSE Carbonic anhydrase 1	-0.20	1.06E+00	8.42E-01	6	0.61	9.80E-01	5.40E-01	5	0.21	1.43E+00	8.36E-01
P62204	MOUSE Calmodulin	0.60	1.06E+00	5.48E-01	4	-0.18	9.17E-01	8.54E-01	5	0.21	1.10E+00	8.35E-01
P21614	MOUSE Vitamin D-binding protein	0.13	1.03E+00	8.93E-01	14	0.37	9.67E-01	7.14E-01	15	0.25	1.17E+00	8.02E-01
Q8VCT4	MOUSE Carboxylesterase 1D	-0.01	1.00E+00	9.89E-01	4	0.52	9.65E-01	6.00E-01	3	0.26	1.18E+00	7.99E-01
Q91X72	MOUSE Hemopexin	0.10	1.03E+00	9.24E-01	4	0.43	9.86E-01	6.70E-01	8	0.26	1.14E+00	7.94E-01
P31532	MOUSE Serum amyloid A-4 protein	0.02	1.01E+00	9.86E-01	14	0.54	9.78E-01	5.88E-01	9	0.28	1.18E+00	7.80E-01
P22599	MOUSE Alpha-1-antitrypsin 1-2	-0.06	1.01E+00	9.55E-01	7	0.68	9.80E-01	4.98E-01	7	0.31	1.07E+00	7.56E-01
Q9QXC1	MOUSE Fetuin-B	0.32	1.05E+00	7.47E-01	5					0.32	8.59E-01	7.47E-01

P01942	MOUSE Hemoglobin subunit alpha	0.18	1.04E+00	8.60E-01	7	0.53	9.83E-01	5.94E-01	7	0.36	9.36E-01	7.23E-01
P11588	MOUSE Major urinary protein 1	0.36	1.07E+00	7.15E-01	3					0.36	7.93E-01	7.15E-01
P07759	MOUSE Serine protease inhibitor A3K	-0.19	1.05E+00	8.49E-01	10	0.99	1.00E+00	3.24E-01	10	0.40	9.35E-01	6.91E-01
P23953	MOUSE Carboxylesterase 1C	-0.21	1.05E+00	8.31E-01	15	1.02	1.00E+00	3.10E-01	14	0.40	9.45E-01	6.88E-01
Q923D2	MOUSE Flavin reductase (NADPH)	-0.40	1.09E+00	6.86E-01	6	1.30	9.82E-01	1.93E-01	5	0.45	8.71E-01	6.53E-01
P21460	MOUSE Cystatin-C	0.46	1.09E+00	6.47E-01	3					0.46	6.92E-01	6.47E-01
P17897	MOUSE Lysozyme C-1					0.49	9.77E-01	6.21E-01	3	0.49	1.24E+00	6.21E-01
P11859	MOUSE Angiotensinogen	0.40	1.07E+00	6.91E-01	5	0.61	9.76E-01	5.40E-01	4	0.51	7.73E-01	6.13E-01
P04247	MOUSE Myoglobin	0.60	1.06E+00	5.46E-01	9	0.52	9.76E-01	6.00E-01	5	0.56	7.12E-01	5.73E-01
P63242	MOUSE Eukaryotic translation initiation factor 5A-1					0.60	9.79E-01	5.47E-01	3	0.60	8.82E-01	5.47E-01
Q9Z126	MOUSE Platelet factor 4	0.61	1.06E+00	5.44E-01	4	0.67	9.86E-01	5.03E-01	3	0.64	6.33E-01	5.23E-01
B1Q450	MOUSE Hemoglobin beta chain subunit	0.64	1.07E+00	5.22E-01	3					0.64	5.39E-01	5.22E-01
B5X0G2	MOUSE Major urinary protein 17	0.63	1.07E+00	5.30E-01	14	0.77	9.75E-01	4.41E-01	12	0.70	5.79E-01	4.85E-01
P12399	MOUSE Protein CTLA-2-alpha					0.72	9.76E-01	4.72E-01	3	0.72	7.24E-01	4.72E-01
Q9EQI5	MOUSE Chemokine (C-X-C motif) ligand 7, isoform CRA	0.69	1.06E+00	4.89E-01	3	0.76	9.89E-01	4.47E-01	3	0.73	5.45E-01	4.68E-01
A8DUK4	MOUSE Beta-globin	0.50	1.09E+00	6.19E-01	5	0.96	1.00E+00	3.38E-01	4	0.73	5.50E-01	4.66E-01
P97298	MOUSE Pigment epithelium-derived factor	0.47	1.10E+00	6.42E-01	4	1.18	9.82E-01	2.37E-01	3	0.82	4.66E-01	4.10E-01
Q00724	MOUSE Retinol-binding protein 4	0.73	1.04E+00	4.63E-01	5	1.06	9.95E-01	2.88E-01	4	0.90	4.04E-01	3.69E-01
P62984	MOUSE Ubiquitin-60S ribosomal protein L40	0.52	1.08E+00	6.01E-01	4	1.29	9.80E-01	1.96E-01	6	0.91	4.08E-01	3.64E-01
P19221	MOUSE Prothrombin					0.94	1.00E+00	3.48E-01	4	0.94	4.44E-01	3.48E-01
A6X935	MOUSE Inter alpha-trypsin inhibitor, heavy chain 4	0.92	8.85E-01	3.59E-01	8	1.12	9.94E-01	2.61E-01	7	1.02	3.25E-01	3.07E-01
P35441	MOUSE Thrombospondin-1	0.31	1.05E+00	7.57E-01	9	1.83	9.70E-01	6.65E-02	12	1.07	3.07E-01	2.84E-01
P04939	MOUSE Major urinary protein 3	0.93	8.83E-01	3.52E-01	3	1.33	9.69E-01	1.84E-01	3	1.13	2.70E-01	2.58E-01
P46412	MOUSE Glutathione peroxidase 3					1.20	9.88E-01	2.31E-01	4	1.20	2.83E-01	2.31E-01
Q00898	MOUSE Alpha-1-antitrypsin 1-5	1.17	7.28E-01	2.41E-01	6	1.62	9.66E-01	1.05E-01	5	1.40	1.66E-01	1.62E-01
Q5FW60	MOUSE Major urinary protein 20	1.19	7.13E-01	2.33E-01	5	1.91	9.10E-01	5.62E-02	3	1.55	1.22E-01	1.21E-01
P08226	MOUSE Apolipoprotein E	2.04	2.16E-01	4.18E-02	38	3.13	6.51E-01	1.78E-03	36	2.58	9.87E-03	9.87E-03

-3 -1.5 0 1.5 3

Tables S4 and S5: *Proteins in green were increased and proteins in red were decreased in ApoE KO mice samples vs WT samples, considering statistically significant changes in p-values (<0.05) for proteins quantified with two or more peptides. *Accession number and entry name from the Uniprot database (http://www.uniprot.org/). The magnitude of the standardized abundance change (Zq=log2 WT/ApoE-KO) in each comparative analytical replicate experiment and in the averaged statistical analysis are shaded according to the colour scale at the bottom.*

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