SUPPORTING INFORMATION

Comprehensive Metabolomic and Lipidomic Profiling of Human Kidney Tissue: A Platform Comparison

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Overview

Supporting Information - Tables

Supporting Information - Figures

Supporting Information Table S1: Patient and tumor specific data of kidney tissue samples used for platform comparison and proof-of-concept experiment

Patient number	Histology	Matched normal tissue	Nephrectomy	Gender	Age	T	N	M	G	Diameter [cm]
1	ccRCC	Yes	Partial	Male	43	3a	0	0	2	9.5
2	ccRCC	Yes	Partial	Male	37	1a	0	0	1	3.5
3	ccRCC	Yes	Partial	Male	69	1b	0	0	2	4.5
4	ccRCC	Yes	Partial	Male	82	3b	0	0	2	5.5
5	ccRCC	Yes	Partial	Male	49	3a	0	0	2	5.5

Abbreviations: T, primary tumor; N, regional lymph nodes; M, distant metastasis; G, grading; N and M refers to status at primary surgery.

Supporting Information Table S2 List of assigned metabolites in kidney tissue extracts by non-targeted metabolomics

Hydrophilic Interaction Liquid Chromatography (HILIC) Small Molecule Profiling of Aqueous Extracts													
				Positive Ionization Mode					Negative Ionization Mode				
						Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]			Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]
Compound Name	Molecular Formula	Neutral Mass	RT [min]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]
3-Methoxy-4-hydroxyphenylethylene glycol sulfate	C9H12O7S	264.0304	2.33						2	$[M-H]^-$	3.3	3	13
1-Methyladenosine	C11H15N5O4	281.1124	7.96	5	$[M+H]^+$	3.8	7	7	3	$[M+CH_3COO]^-$	3.0	5	5
2-Aminoacetophenone	C8H9NO	135.0684	8.66	2	$[M+H]^+$	5.6	3	1	1	[M+HCOO]-	4.9	6	4
2-Ethylacryloylcarnitine or Tiglylcarnitine	C12H21NO4	243.1471	5.62	2	$[M+H]^+$	2.7	4	5					
3'5'-cyclic AMP	C10H12N5O6P	329.0525	9.08						3	$[M-H]^-$	5.8	17	9
4-Acetamidobutanoate	C6H11NO3	145.0739	2.17						3	$[M-H]^-$	6.3	11	18
4-Hydroxy-L-proline	C5H9NO3	131.0582	9.50	5	$[M+H]^+$	6.5	3	8	5	$[M-H]^-$	6.8	7	7
4-Pyrimidine Methanamine or 2-Aminomethylpyrimidine	C5H7N3	109.0640	11.99	2	$[M+H]^+$	4.0	5	5	1	$[M+HCOO]^-$	1.4	5	9
5-Oxoproline	C5H7NO3	129.0426	8.24	3	$[M+H]^+$	2.7	7	6	3	$[M-H]^-$	4.6	4	11
Acetylcarnitine[e]	C9H17NO4	203.1158	7.56	2	$[M+H]^+$	0.7	2	31					
Acylcarnitine 10:0	C17H33NO4	315.2410	2.90	2	$[M+H]^+$	2.7	6	20					
Acylcarnitine 10:1	C17H31NO4	313.2253	3.01	2	$[M+H]^+$	7.7	12	28					
Acylcarnitine 12:0	C19H37NO4	343.2723	2.61	5	$[M+H]^+$	2.4	8	27					
Acylcarnitine 12:1	C19H35NO4	341.2566	2.65	2	$[M+H]^+$	2.0	8	-					
Acylcarnitine 14:0	C21H41NO4	371.3036	2.40	2	$[M+H]^+$	2.0	7	39					
Acylcarnitine 14:1	C21H39NO4	369.2879	2.42	2	$[M+H]^+$	4.5	8	47					
Acylcarnitine 14:1-OH	C21H39NO5	385.2828	3.82	2	$[M+H]^+$	8.6	14	-					
Acylcarnitine 14:2	C21H37NO4	367.2723	2.50	2	$[M+H]^+$	2.0	6	-					
Acylcarnitine 16:0	C23H45NO4	399.3349	2.26	2	$[M+H]^+$	2.8	9	25					
Acylcarnitine 16:0-OH	C23H45NO5	415.3298	3.51	2	$[M+H]^+$	2.2	10	25					
Acylcarnitine 16:1	C23H43NO4	397.3192	2.28	2	$[M+H]^+$	2.4	7	39					
Acylcarnitine 16:1-OH	C23H43NO5	413.3141	3.55	2	$[M+H]^+$	1.7	6	-					
Acylcarnitine 16:2	C23H41NO4	395.3036	2.36	2	$[M+H]^+$	2.1	8	18					
Acylcarnitine 16:2-OH	C23H41NO5	411.2985	3.69	2	$[M+H]^+$	0.4	7	-					
Acylcarnitine 18:0	C25H49NO4	427.3662	2.16	2	$[M+H]^+$	2.9	8	8					
Acylcarnitine 18:1	C25H47NO4	425.3505	2.17	2	$[M+H]^+$	5.2	8	19					
Acylcarnitine 18:1-OH	C25H47NO5	441.3454	3.31	2	$[M+H]^+$	1.8	8	-					
Acylcarnitine 18:2	C25H45NO4	423.3349	2.22	2	$[M+H]^+$	3.0	8	15					
Acylcarnitine 3:0	C10H19NO4	217.1314	6.63	2	$[M+H]^+$	2.3	8	7					

Table S2 continued

				Positive Ionization Mode					Negative Ionization Mode				
						Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]			Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]
Compound Name	Molecular Formula	Neutral Mass	RT [min]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]
Acylcarnitine 4:0	C11H21NO4	231.1471	5.84	2	$[M+H]^+$	2.6	8	4					
Acylcarnitine 4-OH	C11H21NO5	247.1420	8.22	2	$[M+H]^+$	2.3	7	42					
Acylcarnitine 6:0	C13H25NO4	259.1784	4.33	2	$[M+H]^+$	2.2	7	4					
Acylcarnitine 8:0	C15H29NO4	287.2097	3.38	2	$[M+H]^+$	2.4	7	6					
Acylcarnitine 8:2	C15H27NO4	285.1940	3.85	1	$[M+H]^+$	4.0	6	-					
Adenine	C5H5N5	135.0545	2.76	5	$[M+H]^+$	0.3	7	78	5	$[M-H]^-$	2.2	8	75
Adenosine	C10H13N5O4	267.0968	3.21	5	$[M+H]^+$	2.5	4	54	5	$[M+HCOO]^-$	1.5	5	9
Adenosylhomocysteine	C14H20N6O5S	384.1216	10.91	5	$[M+H]^+$	0.9	9	13	3	$[M-H]^-$	0.7	6	3
Allantoin	C4H6N4O3	158.0440	4.54						5	$[M-H]^-$	3.2	3	5
Betaine[e]	C5H11NO2	117.0790	7.15	2	$[M+H]^+$	4.2	3	3	1	$[M-H]^-$	0.6	3	16
Cefuroxime	C16H16N4O8S	424.0689	5.04	1	$[M+Na]^+$	2.8	6	-	2	$[M-H]^-$	1.1	2	-
Citrulline	C6H13N3O3	175.0957	10.92	4	$[M+H]^+$	0.6	5	9	3	$[M-H]^-$	4.1	11	6
Coumaric acid	C8H8O	120.0575	4.34	2	$[M+H]^+$	1.2	8	7					
Creatine	C4H9N3O2	131.0695	9.55	5	$[M+H]^+$	3.3	2	1	3	$[M-H]^-$	3.1	4	1
Creatinine	C4H7N3O	113.0589	3.11	3	$[M+H]^+$	3.3	4	1	5	$[M-H]^-$	1.5	6	12
Cyclohexylsulfamate	C6H13NO3S	179.0616	2.77						2	$[M-H]^-$	4.3	4	34
Cytosine	C4H5N3O	111.0433	4.48	3	$[M+H]^+$	2.5	8	7					
Dehydroascorbic acid	C6H6O6	174.0164	2.95						5	$[M-H]^-$	4.0	5	37
Deoxycarnitine	C7H15NO2	145.1103	8.43	3	$[M+H]^+$	0.0	7	4					
D-Glucuronic acid	C6H10O7	194.0427	11.37						3	$[M-H]^-$	0.8	6	33
Dimethylarginine	C8H18N4O2	202.1430	11.14	2	$[M+H]^+$	2.8	8	15					
D-Pantothenic acid	C9H17NO5	219.1107	3.07	5	$[M+H]^+$	2.4	7	1	5	$[M-H]^-$	2.2	7	13
Ergothioneine	C9H15N3O2S	229.0885	9.08	2	$[M+H]^+$	2.4	3	3	1	$[M-H]^-$	1.6	7	6
Galactitol	C6H14O6	182.0790	7.91	1	$[M+Na]^+$	0.2	6	6	3	$[M-H]^-$	4.2	9	13
Hexose	C6H12O6	180.0634	8.08	3	$[M+Na]^+$	2.3	9	22	3	$[M-H]^-$	3.5	3	9
Guanidinoacetate	C3H7N3O2	117.0538	9.86	5	$[M+H]^+$	3.1	4	1	3	$[M-H]^-$	3.9	4	2
Guanosine	C10H13N5O5	283.0917	7.43	5	$[M+Na]^+$	2.6	7	1	5	$[M-H]^-$	2.5	8	3
Hippurate	C9H9NO3	179.0582	3.32						5	$[M-H]^-$	2.2	4	14
Histamine	C5H9N3	111.0796	8.59	5	$[M+H]^+$	4.2	6	10					
Homocysteinesulfinic acid	C4H9NO4S	167.0252	5.97	1	$[M+Na]^+$	6.6	8	8	1	$[M-H]^-$	7.4	10	23
Hydroxyisovalerylcarnitine	C12H23NO5	261.1576	7.66	2	$[M+H]^+$	4.1	9	9					

Table S2 continued

				Positive Ionization Mode					Negative Ionization Mode				
						Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]			Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]
Compound Name	Molecular Formula	Neutral Mass	RT [min]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]
Hypotaurine	C2H7NO2S	109.0197	9.41	5	$[M+H]^+$	1.3	3	2	5	$[M-H]^-$	0.7	2	4
Hypoxanthine	C5H4N4O	136.0385	3.33	4	$[M+H]^+$	1.3	5	2	5	$[M-H]^-$	0.3	5	7
Inosine	C10H12N4O5	268.0808	5.51	5	$[M+Na]^+$	3.5	5	2	5	$[M-H]^-$	1.2	5	6
Isovalerylcarnitine	C12H23NO4	245.1627	5.10	2	$[M+H]^+$	4.2	8	4					
Lactate	C3H6O3	90.0317	4.02						3	$[M-H]^-$	0.5	5	3
L-Alanine	C3H7NO2	89.0477	9.55	3	$[M+H]^+$	7.7	6	2	3	$[M-H]^-$	0.4	3	4
L-Arginine	C6H14N4O2	174.1117	12.32	5	$[M+H]^+$	0.1	21	2					
L-Asparagine	C4H8N2O3	132.0535	10.69	3	$[M+H]^+$	5.3	5	2	3	$[M-H]^-$	0.8	7	7
L-Carnitine[e]	C7H15NO3	161.1052	8.89	5	$[M+H]^+$	2.8	3	2					
L-Glutamic acid	C5H9NO4	147.0532	11.14	5	$[M+H]^+$	1.9	15	2	5	$[M-H]^-$	4.6	4	13
L-Glutamine	C5H10N2O3	146.0691	10.44	5	$[M+H]^+$	1.2	1	6	5	$[M-H]^-$	2.8	2	11
L-Isoleucine	C6H13NO2	131.0946	7.58	3	$[M+H]^+$	4.2	2	5	3	$[M-H]^-$	3.4	1	6
L-Leucine	C6H13NO2	131.0946	7.34	3	$[M+H]^+$	4.6	2	2	3	$[M-H]^-$	3.7	5	5
L-Methionine	C5H11NO2S	149.0510	8.05	4	$[M+H]^+$	1.9	8	2	3	$[M-H]^-$	3.0	4	9
L-Phenylalanine	C9H11NO2	165.0790	7.31	5	$[M+H]^+$	3.8	5	6	5	$[M-H]^-$	2.5	5	4
L-Proline	C5H9NO2	115.0633	8.35	3	$[M+H]^+$	2.6	3	2	3	$[M-H]^-$	6.3	18	9
L-Serine	C3H7NO3	105.0426	10.55						5	$[M-H]^-$	0.7	20	8
L-Threonine	C4H9NO3	119.0582	9.81	4	$[M+H]^+$	7.5	3	2	5	$[M-H]^-$	3.9	1	4
L-Tryptophan	C11H12N2O2	204.0899	7.51	3	$[M+H]^+$	3.2	4	2	5	$[M-H]^-$	1.8	5	6
L-Tyrosine	C9H11NO3	181.0739	8.66	5	$[M+H]^+$	3.0	1	2	5	$[M-H]^-$	3.8	11	3
LysoPC 16:0	C24H50NO7P	495.3325	4.65	2	$[M+H]^+$	2.9	13	5	2	$[M+HCOO]^-$	0.2	7	8
LysoPC 18:0	C26H54NO7P	523.3638	4.34	2	$[M+H]^+$	2.8	13	8	2	$[M+HCOO]^-$	0.1	5	7
LysoPC 18:1	C26H52NO7P	521.3481	4.43	2	$[M+H]^+$	9.5	12	5	2	$[M+HCOO]^-$	6.5	6	8
LysoPC 18:2	C26H50NO7P	519.3325	4.57	2	$[M+H]^+$	6.2	12	16	2	$[M+HCOO]^-$	4.7	6	16
LysoPC 16:1	C24H48NO7P	493.3168	4.71	2	$[M+H]^+$	2.5	5	10	1	$[M+HCOO]^-$	0.3	5	11
LysoPC 20:3	C28H52NO7P	545.3481	4.29	2	$[M+H]^+$	2.5	17	12	1	$[M+HCOO]^-$	1.6	5	13
LysoPC 20:4	C28H50NO7P	543.3325	3.79	2	$[M+H]^+$	4.6	12	3	2	$[M+HCOO]^-$	2.6	7	12
LysoPE 16:0	C21H44NO7P	453.2855	5.73	2	$[M+H]^+$	2.3	12	10	2	$[M-H]^-$	0.6	3	7
LysoPE 18:0	C23H48NO7P	481.3168	5.56	2	$[M+H]^+$	3.4	10	7	2	$[M-H]^-$	0.4	5	11
LysoPE 20:4	C25H44NO7P	501.2855	5.17	2	$[M+H]^+$	1.8	13	9	2	$[M-H]^-$	0.4	7	19
Mannitol	C6H14O6	182.0790	7.70	3	$[M+Na]^+$	4.2	6	18	3	$[M-H]^-$	5.1	5	14

Table S2 continued

				Positive Ionization Mode					Negative Ionization Mode				
						Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]			Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]
Compound Name	Molecular Formula	Neutral Mass	RT [min]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]
Metformin	C4H11N5	129.1014	4.31	2	$[M+H]^+$	2.8	7	-					
Methionine sulfoxide	C5H11NO3S	165.0460	10.35	2	$[M+H]^+$	3.7	14	-					
Methylmalonate	C4H6O4	118.0266	2.74	5	$[M+NH_4]^+$	9.9	7	78					
N1-Acetylspermidine	C9H21N3O	187.1685	10.95	2	$[M+H]^+$	1.5	9	30					
N-Acetyl-DL-methionine	C7H13NO3S	191.0616	3.37						3	$[M-H]^-$	1.9	8	32
N-Acetyl-DL-serine	C5H9NO4	147.0532	8.38						3	$[M-H]^-$	3.7	7	25
N-Acetylglycine	C4H7NO3	117.0426	7.02						3	$[M-H]^-$	6.8	6	70
N-Acetyl-L-alanine	C5H9NO3	131.0582	5.00						3	$[M-H]^-$	0.2	7	22
N-Acetyl-L-aspartic acid	C6H9NO5	175.0481	8.78						3	$[M-H]^-$	0.7	2	37
N-Acetylneuraminate	C11H19NO9	309.1060	10.95	5	$[M+Na]^+$	5.7	16	23	3	$[M-H]^-$	3.0	5	11
N-Alpha-Acetyl-L-lysine	C8H16N2O3	188.1161	10.02	4	$[M+H]^+$	8.6	9	7					
Nicotine	C10H14N2	162.1157	2.52	5	$[M+H]^+$	4.5	22	38					
PE 16:0/20:4	C41H74NO8P	739.5152	2.26	2	$[M+H]^+$	8.1	12	9	2	$[M-H]^-$	3.7	6	14
PE 18:0/20:4	C43H78NO8P	767.5465	2.19	2	$[M+H]^+$	4.3	11	10	2	$[M-H]^-$	1.3	6	13
PE P-16:0/18:1	C39H76NO7P	701.5359	2.21	2	[M+H]+	6.7	15	9	2	$[M-H]^-$	6.8	5	13
PI 16:0/20:4	C45H79O13P	858.5258	6.16	2	$[M+Na]^+$	3.9	11	3	2	$[M-H]^-$	1.7	3	9
PI 18:0/18:2 - 18:1/18:1	C45H83O13P	862.5571	6.19	2	$[M+Na]^+$	6.4	8	3	2	$[M-H]^-$	3.0	6	10
PI 18:0/20:4	C47H83O13P	886.5571	6.07	2	$[M+Na]^+$	2.4	11	4	2	$[M-H]^-$	1.1	3	10
PS 18:0/20:4	C44H78NO10P	811.5363	6.09	2	$[M+H]^+$	3.8	8	6	2	$[M-H]^-$	0.6	1	14
PS 36:1	C42H80NO10P	789.5520	6.18	2	$[M+H]^+$	7.6	8	6	1	$[M-H]^-$	14.7	4	11
PS 36:2	C42H78NO10P	787.5363	6.19	2	$[M+H]^+$	9.3	7	4	1	$[M-H]^-$	3.3	7	10
Riboflavin	C17H20N4O6	376.1383	5.37	3	$[M+H]^+$	7.7	22	12					
SM 32:1	C37H75N2O6P	674.5363	3.42	2	$[M+H]^+$	1.8	8	9	2	$[M+HCOO]^-$	2.6	4	15
SM 34:1	C39H79N2O6P	702.5676	3.28	2	$[M+H]^+$	2.9	4	13	2	$[M+HCOO]^-$	0.6	5	22
SM 34:2	C39H77N2O6P	700.5519	3.29	2	$[M+H]^+$	2.2	9	10	1	$[M+HCOO]^-$	0.2	5	2
SM 36:1	C41H83N2O6P	730.5989	3.18	5	$[M+H]^+$	3.1	2	14	3	$[M+HCOO]^-$	2.5	9	22
SM 36:2	C41H81N2O6P	728.5832	3.15	2	$[M+H]^+$	4.5	11	14	1	$[M+HCOO]^-$	0.2	5	13
SM 38:1	C43H87N2O6P	758.6302	3.01	2	$[M+H]^+$	2.9	4	15	1	$[M+HCOO]^-$	0.6	8	14
SM 40:2	C45H89N2O6P	784.6458	2.97	2	$[M+H]^+$	6.1	7	9	2	$[M+HCOO]^-$	3.7	3	3
SM 42:2	C47H93N2O6P	812.6771	2.90	2	$[M+H]^+$	2.3	4	15	2	$[M+HCOO]^-$	0.4	4	11
SN-Glycero-3-phosphocholine	C8H20NO6P	257.1028	10.49	3	$[M+H]^+$	2.9	2	3	5	$[M+HCOO]^-$	2.7	5	10

Table S2 continued

				Positive Ionization Mode					Negative Ionization Mode				
						Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]			Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]
Compound Name	Molecular Formula	Neutral Mass	RT [min]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]
Sorbitol	C6H14O6	182.0790	7.63	3	$[M+Na]^+$	4.1	10	9	3	$[M-H]^-$	5.1	7	28
Succinate	C4H6O4	118.0266	3.71						3	$[M-H]^-$	1.6	5	15
Taurine	C2H7NO3S	125.0147	8.69	5	$[M+H]^+$	1.7	1	3	5	$[M-H]^-$	0.5	1	1
Trigonellinamide	C7H8N2O	136.0637	5.83	2	$[M+H]^+$	2.9	9	4					
Trigonelline	C7H7NO2	137.0477	7.65	5	$[M+H]^+$	0.3	7	4					
Uridine	C9H12N2O6	244.0695	3.37						5	$[M-H]^-$	1.0	5	10
Urocanate	C6H6N2O2	138.0429	2.97	5	$[M+H]^+$	3.2	9	24					
Xanthine	C5H4N4O2	152.0334	4.29	3	$[M+H]^+$	2.0	18	21	5	$[M-H]^-$	4.5	5	16
Xanthosine	C10H12N4O6	284.0757	7.60	5	$[M+Na]^+$	1.5	15	14	5	$[M-H]^-$	0.3	4	8

Table S2 continued

Reversed Phase Liquid Chromatography (RPLC) Lipid Profiling of Organic Extracts

				Positive Ionization Mode					Negative Ionization Mode				
						Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]			Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]
Compound Name	Molecular Formula	Neutral Mass	RT [min]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]	LoA	Adduct	Δppm [b]	CV [%]	CV [%]
Acylcarnitine 14:0	C21H41NO4	371.3036	1.47	2	$[M+H]^+$	6.5	6	-					
Acylcarnitine 16:0	C23H45NO4	399.3349	2.19	2	$[M+H]^+$	5.6	2	13					
Acylcarnitine 16:1	C23H43NO4	397.3192	1.72	2	$[M+H]^+$	4.7	6	-					
Acylcarnitine 18:0	C25H49NO4	427.3662	3.10	2	$[M+H]^+$	5.7	5	7					
Acylcarnitine 18:1	C25H47NO4	425.3505	2.50	2	$[M+H]^+$	5.6	7	13					
Acylcarnitine 18:2	C25H45NO4	423.3349	1.93	2	$[M+H]^+$	7.8	7	-					
Acylcarnitine 20:0	C27H53NO4	455.3975	3.97	2	$[M+H]^+$	4.6	6	12					
Cer d18:1/16:0	C34H67NO3	537.5121	7.60	2	$[M+H-H_2O]^+$	4.5	8	10	2	$[M-H]^-$	1.1	8	6
Cer d18:1/18:0	C36H71NO3	565.5434	8.68	1	$[M+H-H_2O]^+$	3.2	5	11	2	$[M-H]^-$	0.9	8	8
Cer d18:1/20:0	C38H75NO3	593.5747	9.78	1	$[M+H-H_2O]^+$	3.1	8	7	2	$[M-H]^-$	0.4	6	10
Cer d18:1/22:0	C40H79NO3	621.6060	10.90	2	$[M+H-H_2O]^+$	4.2	10	11	2	$[M-H]^-$	0.4	6	10
Cer d18:1/24:0	C42H83NO3	649.6373	12.00	2	$[M+H-H_2O]^+$	4.2	6	6	2	$[M-H]^-$	0.2	9	9
Cer d18:1/24:1	C42H81NO3	647.6216	11.03	2	$[M+H-H_2O]^+$	4.2	7	11	2	$[M-H]^-$	0.5	6	9
Cholesterol sulfate	C27H46O4S	466.3117	3.12						2	$[M-H]^-$	1.5	11	2
Cholesterolester 18:2	C45H76O2	648.5845	15.76	2	$[M+Na]^+$	5.3	4	10					
Cholesterolester 20:4	C47H76O2	672.5845	15.40	2	$[M+Na]^+$	5.1	6	-					
DAG 16:0/18:1	C37H70O5	594.5223	9.78	2	$[M+NH_4]^+$	4.6	7	1					
DAG 16:0/18:2	C37H68O5	592.5067	9.03	2	$[M+NH_4]^+$	5.0	4	5					
DAG 18:0/20:4	C41H72O5	644.5380	10.09	2	$[M+NH_4]^+$	4.9	6	4					
DAG 18:1/18:0	C39H74O5	622.5536	10.90	2	$[M+NH_4]^+$	4.6	5	5					
DAG 18:2/18:1	C39H70O5	618.5223	9.30	2	$[M+NH_4]^+$	4.0	8	1					
Dihexosylceramide d18:1/16:0	C46H87NO13	861.6177	6.78						2	$[M-H]^-$	0.6	4	8
Dihexosylceramide d18:1/22:0	C52H99NO13	945.7116	9.60						2	$[M-H]^-$	2.9	6	7
Dihexosylceramide d18:1/24:0	C54H103NO13	973.7429	10.62						2	$[M-H]^-$	1.2	8	10
Dihexosylceramide d18:1/24:1	C54H101NO13	971.7273	9.70						2	$[M-H]^-$	1.2	8	10
Fatty acid 16:0	C16H32O2	256.2402	2.20						2	$[M-H]^-$	1.4	3	6
Fatty acid 18:0	C18H36O2	284.2715	3.12						2	$[M-H]^-$	1.1	4	5
Fatty acid 18:1	C18H34O2	282.2559	2.48						2	$[M-H]^-$	0.4	3	8
Fatty acid 18:2	C18H32O2	280.2402	1.92						2	$[M-H]^-$	1.0	3	7
Fatty acid 20:4	C20H32O2	304.2402	1.90						2	$[M-H]^-$	1.5	4	9

Table S2 continued

				Positive Ionization Mode					Negative Ionization Mode				
						Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]			Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]
Compound Name	Molecular Formula	Neutral Mass	RT [min]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]
Ganglioside GM3 d18:1/22:0	C63H116N2O21	1236.8071	7.23						2	$[M-H]^-$	2.4	4	13
Ganglioside GM3 d18:1/24:1	C65H118N2O21	1262.8227	7.20						2	$[M-H]^-$	2.6	6	3
Hexosylceramide d18:1/16:0	C40H77NO8	699.5649	6.85						2	$[M-H]^-$	0.4	6	12
Hexosylceramide d18:1/20:0	C44H85NO8	755.6275	8.85						2	$[M-H]^-$	0.5	9	9
Hexosylceramide d18:1/22:0	C46H89NO8	783.6588	9.94						2	$[M-H]^-$	0.0	7	10
Hexosylceramide d18:1/24:0	C48H93NO8	811.6901	11.02						2	$[M-H]^-$	0.2	7	11
Hexosylceramide d18:1/24:1	C48H91NO8	809.6745	10.02						2	$[M-H]^-$	0.7	7	9
LysoPC 16:0	C24H50NO7P	495.3325	2.38	2	$[M+H]^+$	5.1	5	13	2	$[M+CH_3COO]^-$	2.6	5	14
LysoPC 18:0	C26H54NO7P	523.3638	3.26	2	$[M+H]^+$	4.9	5	12	2	$[M+CH_3COO]^-$	1.9	4	12
LysoPC 18:1	C26H52NO7P	521.3481	2.64	2	$[M+H]^+$	4.4	13	12	1	$[M+CH_3COO]^-$	1.1	6	16
LysoPE 16:0	C21H44NO7P	453.2855	2.43	2	$[M+H]^+$	4.7	5	8	2	$[M-H]^-$	0.5	9	7
LysoPE 18:0	C23H48NO7P	481.3168	3.30	2	$[M+H]^+$	5.8	8	14	1	$[M-H]^-$	1.7	7	11
PC 30:0	C38H76NO8P	705.5309	7.12	2	$[M+H]^+$	5.8	7	12	1	$[M+CH_3COO]^-$	4.6	4	9
PC 32:0 - 16:0/16:0	C40H80NO8P	733.5622	8.08	2	$[M+H]^+$	4.6	6	10	2	$[M+CH_3COO]^-$	0.6	4	6
PC 32:1 - 16:1/16:0 - 14:0/18:1	C40H78NO8P	731.5465	7.40	2	$[M+H]^+$	4.7	5	12	2	$[M+CH_3COO]^-$	1.2	4	12
PC 32:2	C40H76NO8P	729.5309	6.73	2	$[M+H]^+$	4.5	7	16					
PC 34:0 - 18:0/16:0	C42H84NO8P	761.5935	9.12	2	$[M+H]^+$	4.7	6	10	2	$[M+CH_3COO]^-$	0.5	5	9
PC 34:1 - 16:0/18:1	C42H82NO8P	759.5778	8.37	2	$[M+H]^+$	4.6	4	6	2	$[M+CH_3COO]^-$	0.6	3	7
PC 34:2 - 16:0/18:2 - 16:1/18:1	C42H80NO8P	757.5622	7.68	2	$[M+H]^+$	4.6	6	5	2	$[M+CH_3COO]^-$	0.5	3	6
PC 34:3 - 18:2/16:1	C42H78NO8P	755.5465	6.99	2	$[M+H]^+$	5.2	6	11	2	$[M+CH_3COO]^-$	0.2	4	11
PC 34:4 A	C42H76NO8P	753.5309	6.75	2	$[M+H]^+$	2.5	6	15					
PC 34:4 B	C42H76NO8P	753.5309	7.40	2	$[M+H]^+$	3.9	5	11					
PC 36:0	C44H88NO8P	789.6248	10.20	2	$[M+H]^+$	5.7	9	14					
PC 36:1 - 18:0/18:1	C44H86NO8P	787.6091	9.43	2	$[M+H]^+$	4.4	5	10	2	$[M+CH_3COO]^-$	1.1	6	9
PC 36:2 - 18:0/18:2 - 18:1/18:1 - 20:2/16:0	C44H84NO8P	785.5935	8.70	2	$[M+H]^+$	4.5	6	6	2	$[M+CH_3COO]^-$	0.5	4	6
PC 36:3 - 18:1/18:2	C44H82NO8P	783.5778	7.93	2	$[M+H]^+$	4.2	7	10	2	$[M+CH_3COO]^-$	0.6	4	7
PC 36:4 - 16:0/20:4	C44H80NO8P	781.5622	7.70	2	$[M+H]^+$	4.2	5	9	2	$[M+CH_3COO]^-$	0.4	4	7
PC 36:4 - 18:2/18:2	C44H80NO8P	781.5622	7.26	2	$[M+H]^+$	4.8	8	11	2	$[M+CH_3COO]^-$	1.7	5	10
PC 36:5 - 16:0/20:5	C44H78NO8P	779.5465	7.12	1	$[M+H]^+$	5.0	6	11	2	$[M+CH_3COO]^-$	4.7	21	13
PC 38:2 - 20:1/18:1 - 20:2/18:0	C46H88NO8P	813.6248	9.63	2	$[M+H]^+$	4.5	5	2	2	$[M+CH_3COO]^-$	1.2	3	9
PC 38:3	C46H86NO8P	811.6091	9.06	2	$[M+H]^+$	4.9	11	18	1	$[M+CH_3COO]^-$	0.6	5	6

Table S2 continued

				Positive Ionization Mode					Negative Ionization Mode				
						Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]			Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]
Compound Name	Molecular Formula	Neutral Mass	RT [min]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]
PC 38:3 - 20:1/18:2 - 20:2/18:1	C46H86NO8P	811.6091	8.90	2	$[M+H]^+$	4.3	12	10	2	$[M+CH_3COO]^-$	3.7	8	11
PC 38:4 - 16:0/22:4 - 18:1/20:3	C46H84NO8P	809.5935	8.40	1	$[M+H]^+$	4.0	10	6	2	$[M+CH_3COO]^-$	3.4	5	7
PC 38:4 - 18:0/20:4	C46H84NO8P	809.5935	8.72	2	$[M+H]^+$	5.1	5	10	2	$[M+CH_3COO]^-$	1.1	4	7
PC 38:5	C46H82NO8P	807.5778	7.95	2	$[M+H]^+$	4.2	5	12	1	$[M+CH_3COO]^-$	1.2	3	7
PC 38:5 - 16:0/22:5	C46H82NO8P	807.5778	7.79	1	$[M+H]^+$	4.7	4	10	2	$[M+CH_3COO]^-$	1.2	20	11
PC 38:6 - 20:4/18:2	C46H80NO8P	805.5622	7.28	2	$[M+H]^+$	5.6	8	14	2	$[M+CH_3COO]^-$	0.5	10	11
PC 38:6 - 22:6/16:0	C46H80NO8P	805.5622	7.55	1	$[M+H]^+$	4.6	6	17	2	$[M+CH_3COO]^-$	6.3	3	15
PC 40:5 - 20:1/20:4	C48H86NO8P	835.6091	8.92	1	$[M+H]^+$	4.6	6	9	2	$[M+CH_3COO]^-$	1.5	3	10
PC O-30:1	C38H76NO7P	689.5359	7.72	2	$[M+H]^+$	9.7	6	13					
PC O-32:1	C40H80NO7P	717.5672	8.72	2	$[M+H]^+$	10.4	6	13					
PC O-32:2	C40H78NO7P	715.5516	7.99	2	$[M+H]^+$	6.8	6	19					
PC O-34:0	C42H86NO7P	747.6142	9.85	2	$[M+H]^+$	4.1	10	15					
PC O-34:1	C42H84NO7P	745.5985	8.99	2	$[M+H]^+$	4.3	7	13					
PC O-34:2	C42H82NO7P	743.5829	8.33	2	$[M+H]^+$	0.0	5	10					
PC O-34:2 - O-18:1/16:0 - O-16:0/18:1	C42H82NO7P	743.5829	8.99	2	$[M+H]^+$	11.1	4	14	2	$[M+CH_3COO]^-$	3.5	6	11
PC O-34:3	C42H80NO7P	741.5672	8.26	2	$[M+H]^+$	6.0	5	11	1	$[M+CH_3COO]^-$	5.6	3	7
PC O-36:4	C44H82NO7P	767.5829	8.35	2	$[M+H]^+$	3.4	8	12					
PC O-36:5	C44H80NO7P	765.5672	8.26	2	$[M+H]^+$	5.8	4	9	2	$[M+CH_3COO]^-$	0.9	4	8
PC O-38:5 A	C46H84NO7P	793.5985	8.59	2	$[M+H]^+$	4.4	8	20					
PC O-38:5 B	C46H84NO7P	793.5985	9.32	2	$[M+H]^+$	4.8	12	13					
PE 16:0/16:1 - 14:0/18:1	C37H72NO8P	689.4996	7.40	2	$[M+H]^+$	5.0	12	12	2	$[M-H]^-$	5.0	12	15
PE 16:0/18:1	C39H76NO8P	717.5309	8.37	2	$[M+H]^+$	4.0	6	11	2	$[M-H]^-$	0.1	10	10
PE 16:0/18:2 - 16:1/18:1	C39H74NO8P	715.5152	7.70	2	$[M+H]^+$	5.1	5	7	2	$[M-H]^-$	1.1	8	11
PE 16:0/20:4	C41H74NO8P	739.5152	7.70	2	$[M+H]^+$	5.2	7	10	2	$[M-H]^-$	0.5	11	12
PE 18:0/20:4	C43H78NO8P	767.5465	8.72	2	$[M+H]^+$	5.6	7	11	2	$[M-H]^-$	0.2	9	9
PE 18:1/18:0 - 16:0/20:1	C41H80NO8P	745.5622	9.41	2	$[M+H]^+$	4.5	7	11	2	$[M-H]^-$	0.4	8	9
PE 18:1/18:1 - 16:0/20:2	C41H78NO8P	743.5465	8.70	2	$[M+H]^+$	4.9	5	8	2	$[M-H]^-$	0.2	9	9
PE 18:1/18:2	C41H76NO8P	741.5309	7.90	2	$[M+H]^+$	4.8	5	8	2	$[M-H]^-$	0.5	9	10
PE 18:2/20:4	C43H74NO8P	763.5152	7.28	2	$[M+H]^+$	5.3	7	11	2	$[M-H]^-$	0.8	10	11
PE 20:3/18:0	C43H80NO8P	769.5622	9.40	2	$[M+H]^+$	1.5	8	10	2	$[M-H]^-$	8.2	9	8
PE P-16:0/18:2	C39H74NO7P	699.5203	8.30	2	$[M+H]^+$	4.7	5	8	2	$[M-H]^-$	1.8	8	9

Table S2 continued

				Positive Ionization Mode					Negative Ionization Mode				
						Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]			Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]
Compound Name	Molecular Formula	Neutral Mass	RT [min]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]
PE P-16:0/20:4	C41H74NO7P	723.5203	8.28	2	$[M+H]^+$	5.4	5	8	2	$[M-H]^-$	0.4	9	7
PE P-16:0/22:4	C43H78NO7P	751.5516	9.01	2	$[M+H]^+$	5.4	7	10	1	$[M-H]^-$	0.4	8	11
PE P-18:0/20:4	C43H78NO7P	751.5516	9.33	1	$[M+H]^+$	4.7	6	10	2	$[M-H]^-$	0.2	9	11
PE P-18:0/22:4	C45H82NO7P	779.5829	10.08	2	$[M+H]^+$	4.8	8	12	2	$[M-H]^-$	0.4	9	10
PE P-18:0/22:6	C45H78NO7P	775.5516	9.14	2	$[M+H]^+$	4.5	9	10	2	$[M-H]^-$	1.3	9	10
PG 16:0/18:1	C40H77O10P	748.5254	6.20	2	$[M+Na]^+$	5.5	5	12	2	$[M-H]^-$	0.5	6	12
PI 16:0/16:0	C41H79O13P	810.5258	5.79						2	$[M-H]^-$	0.3	9	19
PI 16:0/18:0	C43H83O13P	838.5571	6.49						2	$[M-H]^-$	0.6	9	19
PI 16:0/18:1	C43H81O13P	836.5415	5.96						2	$[M-H]^-$	0.0	4	17
PI 16:0/18:2	C43H79O13P	834.5258	5.52						2	$[M-H]^-$	0.2	4	20
PI 16:0/20:4	C45H79O13P	858.5258	5.56						2	$[M-H]^-$	0.4	2	24
PI 16:0/22:5	C47H81O13P	884.5415	5.72						2	$[M-H]^-$	0.0	3	18
PI 16:0/22:6 - 18:1/20:4	C47H79O13P	882.5258	5.47						2	$[M-H]^-$	0.5	6	-
PI 18:0/18:1	C45H85O13P	864.5728	6.70						2	$[M-H]^-$	0.6	4	17
PI 18:0/20:2	C47H87O13P	890.5884	6.86						2	$[M-H]^-$	0.4	9	20
PI 18:0/20:3	C47H85O13P	888.5728	6.45						2	$[M-H]^-$	0.2	5	17
PI 18:0/20:4	C47H83O13P	886.5571	6.20						2	$[M-H]^-$	0.5	5	12
PI 18:0/22:4	C49H87O13P	914.5884	6.76						2	$[M-H]^-$	0.5	6	14
PI 18:0/22:5	C49H85O13P	912.5728	6.37						2	$[M-H]^-$	0.4	13	22
PI 18:1/18:1	C45H83O13P	862.5571	6.20						2	$[M-H]^-$	0.1	6	15
PI 18:1/18:2	C45H81O13P	860.5415	5.69						2	$[M-H]^-$	2.2	4	16
PS 18:0/18:1	C42H80NO10P	789.5520	7.10	2	$[M+H]^+$	4.5	4	17	2	$[M-H]^-$	1.7	4	20
PS 18:0/20:4	C44H78NO10P	811.5363	6.57	2	$[M+H]^+$	5.0	11	16	2	$[M-H]^-$	1.4	2	18
SM 32:1	C37H75N2O6P	674.5363	6.23	2	$[M+H]^+$	5.2	7	14	2	$[M+CH_3COO]^-$	2.0	6	9
SM 34:1	C39H79N2O6P	702.5676	7.10	2	$[M+H]^+$	4.9	5	8	2	$[M+CH_3COO]^-$	0.3	3	8
SM 34:2	C39H77N2O6P	700.5519	6.45	2	$[M+H]^+$	4.9	8	21	2	$[M+CH_3COO]^-$	1.7	9	3
SM 36:1	C41H83N2O6P	730.5989	8.10	2	$[M+H]^+$	4.7	5	10	2	$[M+CH_3COO]^-$	1.2	3	8
SM 36:2	C41H81N2O6P	728.5832	7.40	2	$[M+H]^+$	4.4	6	12	1	$[M+CH_3COO]^-$	0.6	6	3
SM 38:1	C43H87N2O6P	758.6302	9.18	2	$[M+H]^+$	4.5	5	9	2	$[M+CH_3COO]^-$	0.2	4	9
SM 40:1	C45H91N2O6P	786.6615	10.30	2	$[M+H]^+$	5.0	5	8	2	$[M+CH_3COO]^-$	1.6	4	10
SM 42:1	C47H95N2O6P	814.6928	11.40	2	$[M+H]^+$	4.5	6	11	2	$[M+CH_3COO]^-$	0.7	4	11

Table S2 continued

				Positive Ionization Mode					Negative Ionization Mode				
						Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]			Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]
Compound Name	Molecular Formula	Neutral Mass	RT [min]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]
SM 42:2	C47H93N2O6P	812.6771	10.40	2	$[M+H]^+$	4.9	6	10	2	$[M+CH_3COO]^-$	1.5	6	11
SM 42:3	C47H91N2O6P	810.6615	9.60	2	$[M+H]^+$	4.6	5	12	2	$[M+CH_3COO]^-$	1.7	6	11
SM 44:1	C49H99N2O6P	842.7241	12.42	2	$[M+H]^+$	3.6	5	13					
SM 44:2	C49H97N2O6P	840.7084	11.49	2	$[M+H]^+$	3.6	6	11					
TAG 44:0 - 12:0/16:0/16:0	C47H90O6	750.6737	15.09	2	$[M+NH_4]^+$	4.6	5	9					
TAG 44:0 - 14:0/14:0/16:0													
TAG 44:1 - 18:1/12:0/14:0	C47H88O6	748.6581	14.46	2	$[M+NH_4]^+$	5.0	7	9					
TAG 44:1 - 12:0/16:0/16:1													
TAG 44:1 - 14:0/14:0/16:1													
TAG 46:0 - 16:0/14:0/16:0	C49H94O6	778.7050	15.90	2	$[M+NH_4]^+$	5.4	9	11					
TAG 46:1 - 12:0/16:0/18:1	C49H92O6	776.6894	15.30	2	$[M+NH_4]^+$	5.1	6	11					
TAG 46:1 - 14:0/14:0/18:1													
TAG 48:0 - 16:0/16:0/16:0	C51H98O6	806.7363	16.65	2	$[M+NH_4]^+$	5.0	8	10					
TAG 48:1 - 14:0/16:0/18:1	C51H96O6	804.7207	16.07	2	$[M+NH_4]^+$	5.1	8	12					
TAG 48:2 - 14:0/16:0/18:2	C51H94O6	802.7050	15.50	2	$[M+NH_4]^+$	5.3	9	8					
TAG 48:3 - 16:1/16:1/16:1	C51H92O6	800.6894	14.89	2	$[M+NH_4]^+$	5.0	6	17					
TAG 48:3 - 12:0/18:1/18:2													
TAG 48:3 - 14:0/16:1/18:2													
TAG 48:4 - 18:2/18:2/12:0	C51H90O6	798.6737	14.26	2	$[M+NH_4]^+$	4.5	7	-					
TAG 50:1 - 16:0/16:0/18:1	C53H100O6	832.7520	16.80	2	$[M+NH_4]^+$	5.5	9	7					
TAG 50:2 - 16:0/16:0/18:2	C53H98O6	830.7363	16.30	2	$[M+NH_4]^+$	5.4	8	13					
TAG 50:3 - 18:1/18:2/14:0	C53H96O6	828.7207	15.68	2	$[M+NH_4]^+$	5.2	8	9					
TAG 50:4 - 14:0/18:2/18:2	C53H94O6	826.7050	15.09	2	$[M+NH_4]^+$	5.2	7	8					
TAG 50:4 - 16:1/16:1/18:2													
TAG 52:1 - 16:0/16:0/20:1	C55H104O6	860.7833	17.50	2	$[M+NH_4]^+$	4.9	8	11					
TAG 52:2 - 16:0/18:1/18:1	C55H102O6	858.7676	16.98	2	$[M+NH_4]^+$	5.8	6	7					
TAG 52:5 - 18:2/18:2/16:1	C55H96O6	852.7207	15.30	2	$[M+NH_4]^+$	5.1	8	7					
TAG 54:1 - 16:0/18:0/20:1	C57H108O6	888.8146	18.15	2	$[M+NH_4]^+$	5.3	7	8					
TAG 54:2 - 16:0/18:1/20:1	C57H106O6	886.7989	17.70	2	$[M+NH_4]^+$	5.4	9	13					
TAG 54:2 - 18:1/18:0/18:1													
TAG 54:3 - 18:1/18:1/18:1	C57H104O6	884.7833	17.16	2	$[M+NH_4]^+$	6.1	9	12					

Table S2 continued

				Positive Ionization Mode					Negative Ionization Mode				
						Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]			Analytical Reproducibility [c]		Sample Prep. Reproducibility [d]
Compound Name	Molecular Formula	Neutral Mass	RT [min]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]	LoA[a]	Adduct	Δppm [b]	CV [%]	CV [%]
TAG 54:3 - 18:1/16:0/20:2													
TAG 54:4 - 18:1/18:1/18:2	C57H102O6	882.7676	16.60	2	$[M+NH_4]^+$	4.5	9	13					
TAG 54:4 - 18:2/18:2/18:0													
TAG 54:5 - 18:1/18:2/18:2	C57H100O6	880.7520	16.07	2	$[M+NH_4]^+$	5.1	8	14					
TAG 54:6 - 18:2/18:2/18:2	C57H98O6	878.7363	15.50	2	$[M+NH_4]^+$	5.2	8	11					
TAG 56:2 - 16:0/20:1/20:1	C59H110O6	914.8302	18.27	2	$[M+NH_4]^+$	5.0	5	9					
TAG 56:3 - 18:1/18:1/20:1	C59H108O6	912.8146	17.79	2	$[M+NH_4]^+$	5.4	5	8					
TAG 58:3 - 18:1/18:1/22:1	C61H112O6	940.8459	18.40	2	$[M+NH_4]^+$	4.8	13	12					
TAG 58:3 - 18:1/20:1/20:1													
Tetrahexosylceramide d18:1/16:0	C60H110N2O23	1226.7499	6.30						2	$[M-H]^-$	1.3	4	2
Tetrahexosylceramide d18:1/22:0	C66H122N2O23	1310.8438	9.12						2	$[M-H]^-$	2.5	3	10
Tetrahexosylceramide d18:1/24:0	C68H126N2O23	1338.8751	10.20						2	$[M-H]^-$	2.1	5	6
Tetrahexosylceramide d18:1/24:1	C68H124N2O23	1336.8595	9.25						2	$[M-H]^-$	2.2	4	8
Trihexosylceramide d18:1/16:0	C52H97NO18	1023.6706	6.45						2	$[M-H]^-$	1.7	3	8
Trihexosylceramide d18:1/20:0	C56H105NO18	1079.7332	8.30						1	$[M-H]^-$	2.2	7	4
Trihexosylceramide d18:1/22:0	C58H109NO18	1107.7645	9.37						2	$[M-H]^-$	2.5	5	6
Trihexosylceramide d18:1/24:0	C60H113NO18	1135.7958	10.44						2	$[M-H]^-$	1.8	6	8
Trihexosylceramide d18:1/24:1	C60H111NO18	1133.7801	9.45						2	$[M-H]^-$	1.8	5	6

RT, retention time

CV [%], coefficient of variation in percentage

List of abbreviations for lipids can be found below Table S4

[a]LoA (Level of Assignment): LoA 1, accurate mass; LoA 2, accurate mass and MS/MS database or literature; LoA 3, RT standard + accurate mass; LoA 4, accurate mass + RT standard + MS/MS from database or literature; LoA 5, accurate mass + RT + MS/MS standard

[b]Δppm is the difference between calculated and observed mass in parts per million

[c]Analytical Reproducibility describes the average ppm and the CV calculated over 6 QCs analyzed throughout analytical batch A

[d]Sample Prep. Reproducibility describes the CV calculated over 3 independently prepared porcine kidney tissue samples (batch A), if no CV number is provided metabolites could not be detected

[e]Due to saturation, higher expansion values (> ±35ppm) for chromatogram extraction were taken

Note: fatty acid information provided for lipid species do not indicate their stereochemical position (e.g. sn-position at the glycerol backbone)

Supporting Information Table S3: Number of detected and structurally assigned metabolic features by non-targeted metabolomics analysis in the corresponding analytical mode

Analysis mode	Number of metabolic features	Assigned metabolites[a]
HILIC ESI(+)	903	114 (13 %)
HILIC ESI(-)	1149	86 (7 %)
RPLC ESI(+)	1360	120 (9 %)
RPLC ESI(-)	765	107 (14 %)

[a] Percentage of assigned metabolites is related to the corresponding number of features

Supporting Information Table S4: Correlation of targeted and non-targeted metabolomics data

Compound Name (Non-targeted metabolomics)	Compound Name (Targeted metabolomics)	Analysis mode (Non-targeted metabolomics)	Spearman Correlation Coefficient	Classification of Correlation Coefficients
Creatinine	Creatinine	HILIC_POS	1.00	
LysoPC 16:0	lysoPC with acyl residue C16:0	RP_POS	0.99	
PC O-30:1	PC with acyl-alkyl residue sum C30:1	RP_POS	0.98	
PC O-32:2	PC with acyl-alkyl residue sum C32:2	RP_POS	0.98	
Hexose	Hexose	HILIC_POS	0.96	
PC O-32:1	PC with acyl-alkyl residue sum C32:1	RP_POS	0.96	
Acetylcarnitine[a]	Acetylcarnitine	HILIC_POS	0.95	
PC 34:3 - 18:2/16:1	PC with diacyl residue sum C34:3	RP_POS	0.93	
L-Methionine	Methionine	HILIC_POS	0.93	
PC 32:0 - 16:0/16:0	PC with diacyl residue sum C32:0	RP_POS	0.92	
PC 32:2	PC with diacyl residue sum C32:2	RP_POS	0.92	
L-Proline	Proline	HILIC_POS	0.92	
Histamine	Histamine	HILIC_POS	0.92	
PC 34:2 - 16:0/18:2 - 16:1/18:1	PC with diacyl residue sum C34:2	RP_POS	0.90	
LysoPC 18:0	lysoPC with acyl residue C18:0	RP_POS	0.90	
Acylcarnitine 4-OH	Hydroxybutyrylcarnitine	HILIC_POS	0.90	
2-Ethylacryloylcarnitine or Tiglylcarnitine	Tiglylcarnitine	HILIC_POS	0.90	
L-Tyrosine	Tyrosine	HILIC_POS	0.90	
PC O-38:5 A	PC with acyl-alkyl residue sum C38:5[8]	RP_POS	0.89	
Hydroxyisovalerylcarnitine	Hydroxyisovalerylcarnitine	HILIC_POS	0.89	
Acylcarnitine 16:0-OH	Hydroxyhexadecanolycarnitine	HILIC_POS	0.89	
PC 34:4 A	PC with diacyl residue sum C34:4[1]	RP_POS	0.88	
PC 38:6 - 22:6/16:0	PC with diacyl residue sum C38:6[6]	RP_POS	0.88	
PC 34:1 - 16:0/18:1	PC with diacyl residue sum C34:1	RP_POS	0.87	
PC 38:4 - 16:0/22:4 - 18:1/20:3	PC with diacyl residue sum C38:4[4]	RP_POS	0.87	
PC O-38:5 B	PC with acyl-alkyl residue sum C38:5[8]	RP_POS	0.87	
Isovalerylcarnitine	Isovalerylcarnitine	HILIC_POS	0.87	
Acylcarnitine 8:0	Octanoylcarnitine	HILIC_POS	0.87	
SM 36:2	SM with acyl residue sum C18:1	RP_POS	0.85	high ($r \geq 0.7$)
LysoPC 20:4	lysoPC with acyl residue C20:4	HILIC_POS	0.85	
Acylcarnitine 16:2	Hexadecadienoylcarnitine	HILIC_POS	0.85	
PC 36:3 - 18:1/18:2	PC with diacyl residue sum C36:3	RP_POS	0.84	
PC 36:4 - 16:0/20:4	PC with diacyl residue sum C36:4[2]	RP_POS	0.84	
Acylcarnitine 3:0	Propionylcarnitine	HILIC_POS	0.83	
Acylcarnitine 16:0	Hexadecanoylcarnitine	HILIC_POS	0.83	
Acylcarnitine 16:1-OH	Hydroxyhexadecenoylcarnitine	HILIC_POS	0.83	
Dimethylarginine	total-DMA	HILIC_POS	0.83	
SM 34:1	SM with acyl residue sum C16:0	RP_POS	0.82	
PC 30:0	PC with diacyl residue sum C30:0	RP_POS	0.82	
PC O-34:0	PC with acyl-alkyl residue sum C34:0	RP_POS	0.82	
Acylcarnitine 16:1	Hexadecenoylcarnitine	HILIC_POS	0.82	
L-Carnitine[a]	Carnitine (free)	HILIC_POS	0.81	
SM 34:2	SM with acyl residue sum C16:1	RP_POS	0.81	
SM 36:1	SM with acyl residue sum C18:0	RP_POS	0.79	
PC O-34:2 - O-18:1/16:0 - O-16:0/18:1	PC with acyl-alkyl residue sum C34:2[7]	RP_POS	0.79	
L-Isoleucine	Isoleucine	HILIC_POS	0.79	
L-Threonine	Threonine	HILIC_NEG	0.79	
Lactate	Lactate	HILIC_NEG	0.78	
PC 38:5 - 16:0/22:5	PC with diacyl residue sum C38:5[5]	RP_POS	0.78	
LysoPC 20:3	lysoPC with acyl residue C20:3	HILIC_POS	0.77	
Acylcarnitine 4:0	Butyrylcarnitine	HILIC_POS	0.77	
Acylcarnitine 10:0	Decanoylcarnitine	HILIC_POS	0.77	
PC 36:5 - 16:0/20:5	PC with diacyl residue sum C36:5	RP_POS	0.76	
PC O-34:1	PC with acyl-alkyl residue sum C34:1	RP_POS	0.76	
Acylcarnitine 18:1	Octadecenoylcarnitine	HILIC_POS	0.76	
L-Glutamine	Glutamine	HILIC_POS	0.76	
L-Serine	Serine	HILIC_NEG	0.76	

Table S4 continued

Compound Name (Non-targeted metabolomics)	Compound Name (Targeted metabolomics)	Analysis mode (Non-targeted metabolomics)	Spearman Correlation Coefficient	Classification of Correlation Coefficients
SM 44:1	SM with acyl residue sum C26:0	RP_POS	0.75	
PC O-34:2	PC with acyl-alkyl residue sum C34:2[7]	RP_POS	0.75	
LysoPC 18:1	lysoPC with acyl residue C18:1	RP_POS	0.73	high
LysoPC 18:2	lysoPC with acyl residue C18:2	HILIC_POS	0.73	(r ≥ 0.7)
Acylcarnitine 18:1-OH	Hydroxyoctadecenoylcarnitine	HILIC_POS	0.73	
Acylcarnitine 12:0	Dodecanoylcarnitine	HILIC_POS	0.72	
Acylcarnitine 18:0	Octadecanoylcarnitine	HILIC_POS	0.72	
L-Tryptophan	Tryptophan	HILIC_POS	0.70	
Succinate	Succinic acid	HILIC_NEG	0.68	
Acylcarnitine 14:0	Tetradecanoylcarnitine	HILIC_POS	0.68	
Acylcarnitine 16:2-OH	Hydroxyhexadecadienoylcarnitine	HILIC_POS	0.65	
PC 32:1 - 16:1/16:0 - 14:0/18:1	PC with diacyl residue sum C32:1	RP_POS	0.62	
PC O-36:4	PC with acyl-alkyl residue sum C36:4	RP_POS	0.62	
Acylcarnitine 14:1-OH	Hydroxytetradecenoylcarnitine	HILIC_POS	0.62	
Acylcarnitine 14:1	Tetradecenoylcarnitine	HILIC_POS	0.61	
PC 38:5	PC with diacyl residue sum C38:5[5]	RP_POS	0.60	
PC O-34:3	PC with acyl-alkyl residue sum C34:3	RP_POS	0.60	medium
Acylcarnitine 6:0	Hexanoylcarnitine	HILIC_POS	0.59	(0.5 ≤ r < 0.7)
L-Phenylalanine	Phenylalanine	HILIC_POS	0.59	
L-Arginine	Arginine	HILIC_POS	0.58	
SM 42:2	SM with acyl residue sum C24:1	RP_POS	0.55	
SM 44:2	SM with acyl residue sum C26:1	RP_POS	0.55	
PC 38:6 - 20:4/18:2	PC with diacyl residue sum C38:6[6]	RP_POS	0.55	
L-Leucine	Leucine	HILIC_POS	0.53	
Taurine	Taurine	HILIC_POS	0.53	
Acylcarnitine 18:2	Octadecadienoylcarnitine	HILIC_POS	0.52	
Citrulline	Citrulline	HILIC_POS	0.50	
PC O-36:5	PC with acyl-alkyl residue sum C36:5	RP_POS	0.49	
LysoPC 16:1	lysoPC with acyl residue C16:1	HILIC_POS	0.49	
PC 40:5 - 20:1/20:4	PC with diacyl residue sum C40:5	RP_POS	0.48	
SM 42:1	SM with acyl residue sum C24:0	RP_POS	0.43	
PC 38:3	PC with diacyl residue sum C38:3[3]	RP_POS	0.43	weak
PC 36:2 - 18:0/18:2 - 18:1/18:1 - 20:2/16:0	PC with diacyl residue sum C36:2	RP_POS	0.39	(0.3 ≤ r < 0.5)
PC 36:1 - 18:0/18:1	PC with diacyl residue sum C36:1	RP_POS	0.37	
PC 38:4 - 18:0/20:4	PC with diacyl residue sum C38:4[4]	RP_POS	0.37	
Acylcarnitine 10:1	Decenoylcarnitine	HILIC_POS	0.33	
L-Asparagine	Asparagine	HILIC_NEG	0.31	
Acylcarnitine 12:1	Dodecenoylcarnitine	HILIC_POS	0.30	
PC 38:3 - 20:1/18:2 - 20:2/18:1	PC with diacyl residue sum C38:3[3]	RP_POS	0.25	
PC 36:4 - 18:2/18:2	PC with diacyl residue sum C36:4[2]	RP_POS	0.21	
L-Glutamic acid	Glutamate	HILIC_NEG	0.13	low
PC 36:0	PC with diacyl residue sum C36:0	RP_POS	0.03	(r < 0.3)
PC 34:4 B	PC with diacyl residue sum C34:4[1]	RP_POS	0.02	
Acylcarnitine 14:2	Tetradecadienoylcarnitine	HILIC_POS	-0.07	
L-Alanine	Alanine	HILIC_POS	-0.20	

List of abbreviations for lipids can be found below

HILIC_POS, hydrophilic interaction liquid chromatography and positive mode ionization

HILIC_NEG, hydrophilic interaction liquid chromatography and negative mode ionization

RP_POS, reversed phase chromatography and positive mode ionization

[a]Due to saturation in the non-targeted metabolomics assay, $[M2+H]^+$ isotope ions were selected

[1-8] lipid species with the same total carbon numbers and saturation state but different retention times (non-targeted assay) were independently correlated to lipid species from the targeted assay. For example, PC 38:6 – 20:4/18:2 and PC 38:6 – 22:6/16:0 (non-targeted metabolomics) were both individually correlated with the PC with diacyl residue sum C38:6 (targeted metabolomics)

List of abbreviations for lipids

Lipid class	Abbreviation
Ceramide	Cer
Diacylglycerol	DAG
Ether phosphatidylcholine	PC-O
Lysophosphatidylcholine	LysoPC
Lysophosphatidylethanolamine	LysoPE
Phosphatidylcholine	PC
Phosphatidylethanolamine	PE
Phosphatidylglycerol	PG
Phosphatidylinositol	PI
Phosphatidylserine	PS
Plasmalogen phosphatidylethanolamine	PE-P
Sphingomyelin	SM
Triacylglycerol	TAG

Supporting Information Table S5: Comparison of fold changes and p-values (ccRCC and non-tumor tissue) between the non-targeted and the targeted metabolomics assay

	Non-targeted metabolomics					Targeted metabolomics				
Compound Name	Non-tumor tissue (peak area) [mean ± sd (range)]		Tumor tissue (peak area) [mean ± sd (range)]		LogFC p-Value	Non-tumor tissue (pmol/mg) [mean area ± sd (range)]		Tumor tissue (pmol/mg) [mean ± sd (range)]		LogFC p-Value
PC O-32:2[b,c,d]	6.4E+05 ± 3.5E+05	(3.5e+05 - 1.2e+06)	5.8E+04 ± 9.7E+03	(4.2e+04 - 6.5e+04)	3.3 3.02E-04	14.8 ± 3.7	(9.9-20.4)	1.5 ± 0.4	(0.8 - 1.8)	3.1 5.08E-06
PC O-32:1[b,c,d]	3.9E+06 ± 2.2E+06	(1.8e+06 - 6.3e+06)	5.9E+05 ± 1.6E+05	(4.3e+05 - 8.4e+05)	2.6 4.85E-04	36.1 ± 13.4	(21.9-55.4)	6.1 ± 1.7	(3.3 - 8)	2.5 1.01E-04
PC O-34:3[b]	1.4E+06 ± 6.7E+05	(5.8e+05 - 2.0e+06)	7.8E+05 ± 2.4E+05	(3.7e+05 - 9.7e+05)	0.8 2.72E-02	18.5 ± 6.8	(9.2-26.9)	6.5 ± 1.7	(4.3 - 8.2)	1.4 1.90E-04
L-Carnitine[a,b]	1.5E+06 ± 4.8E+05	(8.9e+05 - 2.1e+06)	8.5E+05 ± 1.7E+05	(5.7e+05 - 1.0e+06)	0.8 6.27E-02	383.8 ± 98.2	(240.5-506.9)	205.7 ± 66.3	(115.6 - 272.4)	0.9 2.45E-04
PC O-30:1[b,c,d]	4.4E+05 ± 2.9E+05	(1.6e+05 - 9.2e+05)	5.7E+04 ± 1.2E+04	(4.3e+04 - 6.9e+04)	2.7 9.36E-04	4.3 ± 2.5	(2.3-8.5)	0.2 ± 0.2	(0 - 0.4)	2.7 4.32E-04
Creatinine[b,c,d]	1.6E+07 ± 4.5E+06	(1.1e+07 - 2.3e+07)	5.3E+07 ± 8.9E+06	(4.1e+07 - 6.5e+07)	-1.7 5.38E-04	93.6 ± 19	(61.5-108.5)	482.9 ± 130.2	(298.2 - 656.1)	-2.3 4.46E-04
Hydroxyisovalerylcarnitine[b,c,d]	2.6E+05 ± 8.5E+04	(1.4e+05 - 3.6e+05)	9.0E+05 ± 1.7E+05	(6.9e+05 - 1.1e+06)	-1.9 4.58E-03	0.4 ± 0.1	(0.3-0.6)	1.2 ± 0.2	(1 - 1.4)	-0.9 8.05E-04
Acetylcarnitine[a,b]	2.8E+06 ± 1.4E+06	(8.4e+05 - 3.9e+06)	9.2E+05 ± 3.1E+05	(6.3e+05 - 1.4e+06)	1.5 1.02E-02	445.6 ± 228.8	(145.7-633.8)	109.1 ± 49.7	(64.5 - 189.3)	1.9 1.41E-03
L-Glutamine[b,c,d]	9.1E+05 ± 2.0E+05	(6.0e+05 - 1.1e+06)	4.9E+05 ± 9.0E+04	(4.0e+05 - 6.0e+05)	0.9 1.70E-03	1205.8 ± 326.6	(857.3-1564.4)	354.2 ± 79.5	(276.6 - 455.4)	1.8 2.11E-03
Isovalerylcarnitine[b,c,d]	6.9E+05 ± 2.4E+05	(3.3e+05 - 9.4e+05)	2.9E+06 ± 9.3E+05	(1.7e+06 - 4.1e+06)	-2.1 3.60E-03	0.7 ± 0.2	(0.4-0.9)	2.5 ± 0.8	(1.6 - 3.6)	-1.4 2.14E-03
PC O-34:2	6.4E+05 ± 2.6E+05	(3.5e+05 - 8.9e+05)	3.3E+05 ± 5.7E+04	(2.4e+05 - 3.9e+05)	0.8 3.11E-02	33 ± 8.5	(23.7-43.4)	17.2 ± 3.5	(13.4 - 22.5)	0.9 2.17E-03
PC O-34:2 - O-18:1/16:0 - O-16:0/18:1	1.7E+06 ± 8.1E+05	(1.1e+06 - 3.1e+06)	9.7E+05 ± 1.4E+05	(8.0e+05 - 1.1e+06)	0.7 9.45E-02	33 ± 8.5	(23.7-43.4)	17.2 ± 3.5	(13.4 - 22.5)	0.9 2.17E-03
PC O-38:5 A	2.9E+06 ± 1.6E+06	(1.2e+06 - 5.0e+06)	1.1E+06 ± 2.5E+05	(8.2e+05 - 1.4e+06)	1.3 1.17E-02	54 ± 16.2	(35.9-76.4)	18 ± 5.3	(12.6 - 26.1)	1.6 2.27E-03
PC O-38:5 B	1.3E+06 ± 8.6E+05	(3.8e+05 - 2.2e+06)	2.6E+05 ± 2.5E+04	(2.3e+05 - 2.9e+05)	1.9 1.63E-02	54 ± 16.2	(35.9-76.4)	18 ± 5.3	(12.6 - 26.1)	1.6 2.27E-03
Dimethylarginine	1.0E+05 ± 3.2E+04	(6.9e+04 - 1.5e+05)	2.7E+05 ± 8.2E+04	(1.9e+05 - 3.9e+05)	-1.4 1.41E-02	2.3 ± 0.6	(1.6-3.2)	8.1 ± 1.8	(5.9 - 10.6)	-1.8 2.36E-03
PC 38:3	3.3E+06 ± 1.0E+06	(2.3e+06 - 4.5e+06)	2.6E+06 ± 4.0E+05	(2.1e+06 - 3.1e+06)	0.3 1.98E-01	53.9 ± 6.5	(44.3-60.9)	38.1 ± 7.6	(30.2 - 48.8)	0.5 4.92E-03
PC 38:3 - 20:1/18:2 - 20:2/18:1	8.0E+05 ± 4.0E+05	(3.8e+05 - 1.3e+06)	6.0E+05 ± 1.5E+05	(4.2e+05 - 8.0e+05)	0.3 4.72E-01	53.9 ± 6.5	(44.3-60.9)	38.1 ± 7.6	(30.2 - 48.8)	0.5 4.92E-03
PC 40:5 - 20:1/20:4	8.6E+05 ± 3.5E+05	(5.2e+05 - 1.4e+06)	5.8E+05 ± 9.3E+04	(4.5e+05 - 6.8e+05)	0.5 2.25E-01	13.5 ± 1.7	(11.6-15.6)	7 ± 1.8	(5 - 8.7)	1.0 6.24E-03
PC O-36:5	8.9E+06 ± 4.9E+06	(3.9e+06 - 1.5e+07)	5.0E+06 ± 8.3E+05	(4.0e+06 - 6.1e+06)	0.7 1.69E-01	89.2 ± 31.3	(52.6-129.9)	40.6 ± 4.4	(36.7 - 47.1)	1.1 6.64E-03
2-Ethylacryloylcarnitine or Tiglylcarnitine	8.9E+04 ± 4.7E+04	(3.3e+04 - 1.5e+05)	1.5E+05 ± 3.9E+04	(1.0e+05 - 2.0e+05)	-0.9 7.37E-02	0.1 ± 0	(0.1-0.2)	0.2 ± 0	(0.2 - 0.2)	-0.1 8.54E-03
Acylcarnitine 10:1	1.1E+05 ± 3.2E+04	(5.9e+04 - 1.4e+05)	8.7E+04 ± 2.6E+04	(6.6e+04 - 1.3e+05)	0.4 1.54E-01	0.3 ± 0	(0.2-0.3)	0.2 ± 0	(0.2 - 0.3)	0.1 1.15E-02
Hexose	1.5E+06 ± 9.1E+05	(5.3e+05 - 2.9e+06)	1.5E+05 ± 8.9E+04	(3.8e+04 - 2.6e+05)	3.3 2.08E-02	6341.5 ± 2327.7	(3990.6-9388)	1482.8 ± 741.4	(878.8 - 2717.4)	2.1 1.24E-02
PC O-36:4	3.2E+06 ± 1.6E+06	(1.7e+06 - 5.6e+06)	2.0E+06 ± 5.2E+05	(1.3e+06 - 2.5e+06)	0.6 1.46E-01	45 ± 10.4	(35.6-56.3)	26.3 ± 7.2	(17 - 34.7)	0.8 1.36E-02
PC O-34:1	2.1E+06 ± 5.9E+05	(1.6e+06 - 3.0e+06)	1.2E+06 ± 1.9E+05	(1.0e+06 - 1.5e+06)	0.8 2.64E-02	37.8 ± 12.7	(23.1-54.9)	22.3 ± 4.7	(14.9 - 26.9)	0.7 1.55E-02
PC O-34:0[c]	2.9E+05 ± 9.7E+04	(1.7e+05 - 4.3e+05)	1.6E+05 ± 5.6E+04	(1.2e+05 - 2.5e+05)	0.9 1.92E-03	6.4 ± 3.1	(2.7-10.3)	3.3 ± 0.9	(1.7 - 3.9)	0.9 1.56E-02
PC 38:4 - 16:0/22:4 - 18:1/20:3	1.1E+06 ± 5.3E+05	(7.2e+05 - 2.1e+06)	6.6E+05 ± 8.5E+04	(5.7e+05 - 7.8e+05)	0.7 8.19E-02	210.8 ± 20.5	(182.7-227.3)	145.4 ± 24.1	(120.4 - 170.8)	0.5 1.84E-02
PC 38:4 - 18:0/20:4	2.2E+07 ± 8.6E+06	(1.4e+07 - 3.3e+07)	1.9E+07 ± 3.9E+06	(1.6e+07 - 2.5e+07)	0.1 5.91E-01	210.8 ± 20.5	(182.7-227.3)	145.4 ± 24.1	(120.4 - 170.8)	0.5 1.84E-02
LysoPC 16:0	8.6E+05 ± 6.2E+05	(1.3e+05 - 1.5e+06)	2.2E+06 ± 1.1E+06	(7.4e+05 - 3.5e+06)	-1.6 1.12E-02	26.8 ± 16.2	(10.3-49)	46.9 ± 9.7	(32.8 - 58.4)	-1.0 2.76E-02
Citrulline	9.8E+04 ± 7.3E+03	(9.0e+04 - 1.1e+05)	8.7E+04 ± 6.3E+03	(8.1e+04 - 9.7e+04)	0.2 1.04E-01	23.9 ± 7.3	(12.6-31.2)	11.3 ± 3.3	(6.7 - 14.5)	1.1 3.75E-02
Histamine	2.1E+06 ± 1.4E+06	(1.1e+06 - 4.4e+06)	9.3E+05 ± 1.1E+06	(7.7e+04 - 2.9e+06)	1.9 7.16E-02	25.8 ± 19.7	(11.9-58)	9.7 ± 14	(0.6 - 33.2)	2.5 4.16E-02
PC 32:1 - 16:1/16:0 - 14:0/18:1	1.4E+07 ± 9.2E+06	(6.5e+06 - 2.9e+07)	7.8E+06 ± 1.5E+06	(6.2e+06 - 9.8e+06)	0.6 2.39E-01	131.1 ± 60.1	(83.9-211.6)	66.6 ± 17.5	(41.7 - 83.9)	0.9 4.58E-02
PC 32:0 - 16:0/16:0	2.1E+07 ± 7.0E+06	(1.5e+07 - 3.2e+07)	1.6E+07 ± 2.2E+06	(1.4e+07 - 1.9e+07)	0.3 1.72E-01	133.7 ± 46.9	(64.8-181.8)	85.3 ± 23.7	(56.6 - 120.4)	0.6 6.68E-02
SM 36:2	5.3E+05 ± 2.8E+05	(2.0e+05 - 8.6e+05)	8.9E+05 ± 3.0E+05	(5.8e+05 - 1.2e+06)	-0.9 1.07E-01	10.5 ± 4.2	(5.7-15.7)	17.8 ± 3.7	(11.9 - 21.7)	-0.8 7.26E-02
PC 34:4 A	2.3E+05 ± 1.0E+05	(1.1e+05 - 3.5e+05)	4.5E+05 ± 1.5E+05	(2.8e+05 - 6.0e+05)	-1.0 8.45E-02	4.7 ± 1.3	(2.6-5.8)	7.5 ± 1.8	(5.5 - 10.3)	-0.7 7.51E-02
PC 34:4 B	2.0E+06 ± 1.3E+06	(9.8e+05 - 4.2e+06)	1.2E+06 ± 2.4E+05	(9.1e+05 - 1.5e+06)	0.6 2.36E-01	4.7 ± 1.3	(2.6-5.8)	7.5 ± 1.8	(5.5 - 10.3)	-0.7 7.51E-02
L-Methionine	4.3E+04 ± 2.3E+04	(2.4e+04 - 8.3e+04)	5.6E+04 ± 1.4E+04	(3.8e+04 - 7.0e+04)	-0.5 2.20E-01	67.8 ± 34.8	(36.1-122.8)	131.4 ± 63.7	(74.1 - 227.9)	-1.0 8.00E-02
Acylcarnitine 12:1	1.8E+05 ± 6.9E+04	(8.8e+04 - 2.6e+05)	1.7E+05 ± 1.0E+05	(8.4e+04 - 3.2e+05)	0.2 7.50E-01	0.4 ± 0.1	(0.3-0.4)	0.3 ± 0.1	(0.2 - 0.3)	0.1 8.08E-02
Acylcarnitine 10:0	4.0E+05 ± 2.6E+05	(1.5e+05 - 8.5e+05)	2.9E+05 ± 1.8E+05	(1.3e+05 - 5.7e+05)	0.5 5.18E-01	0.5 ± 0.1	(0.3-0.7)	0.3 ± 0	(0.3 - 0.4)	0.2 9.42E-02
LysoPC 18:1	1.8E+05 ± 1.5E+05	(2.8e+04 - 3.9e+05)	4.6E+05 ± 2.3E+05	(1.2e+05 - 7.2e+05)	-1.6 1.48E-02	11.3 ± 6.9	(3.7-20.4)	17.8 ± 2.8	(13.9 - 21.4)	-0.9 9.89E-02
PC 38:6 - 20:4/18:2	2.5E+06 ± 1.4E+06	(1.0e+06 - 4.2e+06)	2.3E+06 ± 9.3E+05	(1.3e+06 - 3.7e+06)	0.0 9.42E-01	55.9 ± 17.5	(35.1-81.8)	80.9 ± 15.4	(61.4 - 99.2)	-0.6 1.16E-01
PC 38:6 - 22:6/16:0[c]	1.5E+06 ± 6.1E+05	(1.0e+06 - 2.5e+06)	4.7E+06 ± 2.0E+06	(2.7e+06 - 6.8e+06)	-1.6 6.75E-03	55.9 ± 17.5	(35.1-81.8)	80.9 ± 15.4	(61.4 - 99.2)	-0.6 1.16E-01
PC 34:1 - 16:0/18:1	5.2E+07 ± 1.9E+07	(3.7e+07 - 8.4e+07)	7.9E+07 ± 8.7E+06	(6.7e+07 - 8.9e+07)	-0.7 3.93E-02	432 ± 125.3	(296-619.3)	553.3 ± 54.9	(494.4 - 627.4)	-0.4 1.22E-01
LysoPC 18:0	5.4E+05 ± 3.7E+05	(9.7e+04 - 1.0e+06)	9.8E+05 ± 4.3E+05	(4.2e+05 - 1.6e+06)	-1.1 2.56E-02	10.2 ± 6.3	(3.7-19.2)	13.1 ± 3.2	(8.8 - 17.7)	-0.6 1.23E-01
PC 36:2 - 18:0/18:2 - 18:1/18:1 - 20:2/16:0	3.9E+07 ± 1.8E+07	(1.6e+07 - 6.2e+07)	4.0E+07 ± 6.6E+06	(3.0e+07 - 4.7e+07)	-0.2 5.40E-01	321.5 ± 91.1	(185.9-428.1)	247.3 ± 38.3	(194.6 - 287.1)	0.3 1.45E-01
L-Tyrosine	5.2E+05 ± 3.7E+05	(2.6e+05 - 1.2e+06)	6.2E+05 ± 1.9E+05	(4.1e+05 - 8.2e+05)	-0.4 3.56E-01	177.3 ± 102.9	(98-356.3)	253.2 ± 89.3	(161.8 - 369)	-0.6 1.50E-01
Succinate	1.9E+06 ± 2.9E+06	(1.0e+05 - 7.0e+06)	3.3E+05 ± 2.2E+05	(1.8e+05 - 7.1e+05)	1.3 2.78E-01	552.1 ± 406.7	(175.7-1155.9)	215.6 ± 91.7	(121.8 - 338.6)	1.1 1.57E-01
SM 34:1	2.0E+07 ± 9.4E+06	(1.2e+07 - 3.6e+07)	2.4E+07 ± 4.9E+06	(1.8e+07 - 2.9e+07)	-0.3 2.41E-01	274 ± 97.5	(218.5-445.8)	336.1 ± 59.7	(275.7 - 425.7)	-0.3 1.68E-01

Table S5 continued

Compound Name	Non-targeted metabolomics: Non-tumor tissue (peak area) [mean ± sd (range)]	Non-targeted metabolomics: Tumor tissue (peak area) [mean ± sd (range)]	Non-targeted metabolomics: LogFC	Non-targeted metabolomics: p-Value	Targeted metabolomics: Non-tumor tissue (pmol/mg) [mean area ± sd (range)]	Targeted metabolomics: Tumor tissue (pmol/mg) [mean ± sd (range)]	Targeted metabolomics: LogFC	Targeted metabolomics: p-Value
L-Serine	3.0E+05 ± 5.9E+04 (2.5e+05 - 4.0e+05)	3.2E+05 ± 9.7E+03 (3.1e+05 - 3.3e+05)	-0.1	3.50E-01	427.4 ± 318.2 (248.1-993.9)	591.1 ± 233.7 (364 - 909.1)	-0.6	1.78E-01
L-Tryptophan	2.5E+05 ± 2.0E+05 (1.3e+05 - 6.0e+05)	2.4E+05 ± 8.2E+04 (1.5e+05 - 3.3e+05)	-0.1	8.21E-01	76.4 ± 66.2 (30.8-193.1)	94.1 ± 31.6 (53.4 - 123.2)	-0.5	1.87E-01
Acylcarnitine 4-OH	2.1E+07 ± 1.6E+07 (1.3e+06 - 4.0e+07)	8.1E+06 ± 4.9E+06 (3.4e+06 - 1.6e+07)	0.8	3.01E-01	16.4 ± 14 (1.2-33.7)	5.4 ± 5.5 (1.6 - 15.1)	1.2	1.96E-01
SM 36:1	3.3E+06 ± 2.0E+06 (9.6e+05 - 5.8e+06)	4.7E+06 ± 1.6E+06 (3.1e+06 - 6.4e+06)	-0.7	2.10E-01	36.1 ± 16 (18.5-52.2)	53.9 ± 14.5 (39.5 - 76.9)	-0.7	2.02E-01
PC 36:0	7.4E+04 ± 2.3E+04 (5.1e+04 - 1.1e+05)	5.8E+04 ± 5.2E+03 (5.3e+04 - 6.6e+04)	0.3	1.01E-01	4.9 ± 1.3 (3.4-6.6)	3.7 ± 0.6 (3.2 - 4.7)	0.3	2.02E-01
PC 36:4 - 16:0/20:4	3.5E+07 ± 1.5E+07 (2.0e+07 - 5.7e+07)	4.6E+07 ± 9.5E+06 (3.7e+07 - 5.9e+07)	-0.5	1.64E-01	408.4 ± 96.9 (292.5-541.9)	494.3 ± 74.3 (371.6 - 553.2)	-0.3	2.11E-01
PC 36:4 - 18:2/18:2	5.3E+06 ± 3.2E+06 (1.9e+06 - 8.7e+06)	4.1E+06 ± 1.6E+06 (1.6e+06 - 5.9e+06)	0.2	6.27E-01	408.4 ± 96.9 (292.5-541.9)	494.3 ± 74.3 (371.6 - 553.2)	-0.3	2.11E-01
Acylcarnitine 16:2	5.5E+05 ± 6.2E+05 (1.9e+05 - 1.7e+06)	7.4E+05 ± 2.9E+05 (4.0e+05 - 1.1e+06)	-0.8	3.35E-01	0.3 ± 0.2 (0.1-0.5)	0.5 ± 0.3 (0.1 - 0.7)	-0.3	2.55E-01
SM 34:2	1.1E+06 ± 6.5E+05 (4.6e+05 - 2.1e+06)	1.1E+06 ± 2.2E+05 (7.7e+05 - 1.3e+06)	-0.3	4.72E-01	23.5 ± 9.7 (14.7-39.5)	27.9 ± 4 (23.5 - 31.9)	-0.3	2.57E-01
Acylcarnitine 18:0	1.1E+06 ± 2.5E+05 (8.2e+05 - 1.4e+06)	2.1E+06 ± 1.1E+06 (1.2e+06 - 4.0e+06)	-0.8	5.03E-02	2.2 ± 0.6 (1.4-3.1)	3.8 ± 2.2 (1.7 - 7.2)	-0.6	2.66E-01
Acylcarnitine 8:0	6.3E+05 ± 2.4E+05 (3.2e+05 - 9.7e+05)	5.8E+05 ± 2.5E+05 (3.0e+05 - 9.7e+05)	0.1	8.09E-01	0.7 ± 0.2 (0.5-0.9)	0.5 ± 0.1 (0.4 - 0.6)	0.2	2.76E-01
PC 36:1 - 18:0/18:1	9.3E+06 ± 5.1E+06 (6.0e+06 - 1.8e+07)	1.1E+07 ± 9.4E+05 (1.0e+07 - 1.3e+07)	-0.4	2.35E-01	92.1 ± 28.1 (56.9-126.9)	77.8 ± 14.4 (57.3 - 96.7)	0.2	2.79E-01
SM 44:1	4.6E+04 ± 1.8E+04 (2.9e+04 - 6.8e+04)	6.7E+04 ± 1.5E+04 (5.4e+04 - 9.2e+04)	-0.6	4.00E-02	0.2 ± 0.1 (0.1-0.3)	0.3 ± 0.1 (0.2 - 0.3)	-0.1	2.93E-01
Lactate	2.9E+07 ± 9.2E+06 (1.5e+07 - 4.1e+07)	2.3E+07 ± 3.7E+06 (1.8e+07 - 2.8e+07)	0.3	3.69E-01	8527.7 ± 2823.6 (4223.4-11467.7)	6520.7 ± 1794.4 (4934.1 - 9491.9)	0.3	3.02E-01
LysoPC 20:4	5.2E+05 ± 5.1E+05 (9.2e+04 - 1.4e+06)	4.4E+05 ± 1.4E+05 (2.1e+05 - 5.6e+05)	-0.2	8.10E-01	8.2 ± 5.3 (4-16.7)	9.6 ± 2.1 (6.8 - 12.7)	-0.4	3.40E-01
PC 32:2	1.1E+06 ± 8.1E+05 (3.5e+05 - 2.2e+06)	9.3E+05 ± 3.1E+05 (6.1e+05 - 1.4e+06)	0.0	9.41E-01	16.6 ± 9.9 (7.1-27.7)	11.5 ± 3.9 (7.9 - 18.1)	0.4	3.45E-01
L-Phenylalanine	5.4E+05 ± 5.3E+05 (2.5e+05 - 1.5e+06)	3.5E+05 ± 8.0E+04 (2.8e+05 - 4.5e+05)	0.3	5.41E-01	227.2 ± 166 (134.4-519.9)	276.9 ± 102.4 (164.5 - 420.2)	-0.4	3.45E-01
L-Glutamic acid	5.0E+05 ± 8.7E+04 (3.7e+05 - 5.8e+05)	2.6E+05 ± 1.9E+05 (1.4e+05 - 5.8e+05)	1.1	1.95E-02	7857.2 ± 2922.1 (3887.4-11323)	5926.8 ± 886.3 (5098 - 7355.2)	0.3	3.50E-01
SM 42:1	4.4E+06 ± 2.0E+06 (3.0e+06 - 8.0e+06)	6.9E+06 ± 2.2E+06 (4.0e+06 - 9.4e+06)	-0.7	3.41E-02	26.6 ± 4.8 (20.3-32.9)	31 ± 8.6 (24.1 - 43.4)	-0.2	3.53E-01
Acylcarnitine 14:2	2.5E+05 ± 1.9E+05 (1.1e+05 - 5.7e+05)	3.7E+05 ± 1.4E+05 (1.9e+05 - 5.6e+05)	-0.7	2.84E-01	0.1 ± 0 (0.1-0.2)	0.1 ± 0.1 (0 - 0.1)	0.0	3.68E-01
L-Alanine	3.1E+05 ± 1.2E+05 (1.8e+05 - 4.9e+05)	2.9E+05 ± 1.8E+04 (2.6e+05 - 3.0e+05)	0.0	8.64E-01	2983 ± 1843.6 (1041.9-5174.5)	1986 ± 404.1 (1295.6 - 2299.5)	0.3	3.71E-01
L-Leucine	5.6E+05 ± 3.1E+05 (3.1e+05 - 1.1e+06)	4.6E+05 ± 7.5E+04 (3.8e+05 - 5.7e+05)	0.2	5.62E-01	450.7 ± 289.7 (249.2-962.6)	521.7 ± 170.2 (334.4 - 709.3)	-0.3	3.74E-01
L-Isoleucine	1.8E+05 ± 1.2E+05 (1.0e+05 - 4.0e+05)	3.2E+05 ± 1.8E+05 (1.5e+05 - 5.9e+05)	-0.8	9.14E-02	201.2 ± 79.2 (108.4-326)	241.1 ± 60.6 (168.7 - 313.5)	-0.3	3.80E-01
PC 38:5 - 16:0/22:5	1.3E+06 ± 8.5E+05 (6.4e+05 - 2.6e+06)	1.7E+06 ± 6.6E+05 (1.1e+06 - 2.8e+06)	-0.6	3.52E-01	127.9 ± 28.2 (91.2-154.1)	146.2 ± 20.5 (116.8 - 169.2)	-0.2	4.17E-01
PC 38:5	9.0E+06 ± 4.2E+06 (4.8e+06 - 1.4e+07)	1.3E+07 ± 3.0E+06 (9.6e+06 - 1.6e+07)	-0.6	1.90E-01	127.9 ± 28.2 (91.2-154.1)	146.2 ± 20.5 (116.8 - 169.2)	-0.2	4.17E-01
Taurine	1.5E+06 ± 2.6E+05 (1.1e+06 - 1.8e+06)	1.6E+06 ± 3.1E+04 (1.6e+06 - 1.6e+06)	-0.1	4.73E-01	1793.1 ± 235.2 (1585.5-2161.8)	1910.6 ± 237.2 (1529.8 - 2135.1)	-0.1	4.48E-01
Acylcarnitine 4:0	9.0E+06 ± 4.2E+06 (2.6e+06 - 1.3e+07)	1.1E+07 ± 3.9E+06 (5.8e+06 - 1.5e+07)	-0.4	2.94E-01	7.8 ± 3.1 (3.3-10.7)	7.8 ± 5.3 (2.5 - 15.5)	0.2	4.57E-01
PC 36:5 - 16:0/20:5	1.1E+06 ± 5.8E+05 (5.7e+05 - 1.8e+06)	1.6E+06 ± 3.2E+05 (1.0e+06 - 1.8e+06)	-0.7	1.73E-01	27.9 ± 7.7 (18.1-34.8)	32 ± 5.1 (25.9 - 39.1)	-0.2	4.57E-01
SM 42:2	7.2E+06 ± 2.2E+06 (5.2e+06 - 1.1e+07)	1.0E+07 ± 3.7E+06 (6.1e+06 - 1.4e+07)	-0.4	1.79E-01	68.5 ± 12.4 (56.2-88.5)	76.4 ± 24.3 (51.8 - 108)	-0.1	4.71E-01
LysoPC 20:3	2.7E+05 ± 1.8E+05 (1.0e+05 - 4.9e+05)	2.4E+05 ± 4.5E+04 (1.8e+05 - 3.1e+05)	-0.1	8.32E-01	2.1 ± 1.1 (0.8-3.8)	2.2 ± 0.4 (1.6 - 2.6)	-0.2	4.71E-01
Acylcarnitine 14:1	9.7E+05 ± 4.9E+05 (5.2e+05 - 1.7e+06)	1.1E+06 ± 7.6E+05 (5.3e+05 - 2.2e+06)	-0.1	8.65E-01	0.5 ± 0.2 (0.3-0.9)	0.3 ± 0.3 (0.1 - 0.8)	0.2	4.72E-01
L-Threonine	3.1E+05 ± 1.3E+05 (2.0e+05 - 5.3e+05)	3.2E+05 ± 3.5E+04 (2.7e+05 - 3.6e+05)	-0.1	5.78E-01	352.3 ± 324.5 (159.6-930.1)	356.4 ± 171.7 (181.3 - 626.7)	-0.2	4.78E-01
Acylcarnitine 12:0	6.1E+05 ± 3.5E+05 (2.8e+05 - 1.2e+06)	7.7E+05 ± 4.6E+05 (2.9e+05 - 1.3e+06)	-0.3	7.30E-01	0.6 ± 0.2 (0.4-0.9)	0.4 ± 0.3 (0.2 - 0.9)	0.2	4.92E-01
SM 44:2	8.2E+04 ± 2.6E+04 (5.7e+04 - 1.2e+05)	9.0E+04 ± 1.4E+04 (6.9e+04 - 1.0e+05)	-0.2	4.01E-01	0.5 ± 0.2 (0.4-0.7)	0.5 ± 0.1 (0.3 - 0.7)	0.1	5.74E-01
PC 34:2 - 16:0/18:2 - 16:1/18:1	5.8E+07 ± 2.3E+07 (2.8e+07 - 8.1e+07)	6.7E+07 ± 1.2E+07 (4.7e+07 - 7.9e+07)	-0.3	2.70E-01	551.9 ± 155.6 (321.2-706.2)	586.7 ± 98.5 (480.6 - 716.3)	-0.1	5.78E-01
PC 34:3 - 18:2/16:1	2.2E+06 ± 1.5E+06 (7.3e+05 - 4.5e+06)	2.1E+06 ± 5.6E+05 (1.2e+06 - 2.6e+06)	-0.1	7.73E-01	38.6 ± 17.8 (19.5-58.9)	32.3 ± 8.2 (24.1 - 43.5)	0.2	6.01E-01
Acylcarnitine 18:1	7.2E+06 ± 2.5E+06 (4.2e+06 - 1.0e+07)	9.6E+06 ± 3.2E+06 (5.9e+06 - 1.3e+07)	-0.4	3.65E-01	5.6 ± 2.2 (3.3-9.1)	4.8 ± 2.9 (1.7 - 8.7)	0.4	6.07E-01
PC 36:3 - 18:1/18:2	2.8E+07 ± 1.3E+07 (1.4e+07 - 4.5e+07)	3.6E+07 ± 9.3E+06 (2.1e+07 - 4.5e+07)	-0.5	2.03E-01	251.5 ± 69 (162.4-326.7)	266.6 ± 53.9 (209.3 - 328.4)	-0.1	6.29E-01
LysoPC 18:2	1.3E+06 ± 1.1E+06 (1.8e+05 - 2.6e+06)	1.0E+06 ± 4.1E+05 (3.3e+05 - 1.4e+06)	-0.1	7.91E-01	17 ± 11.8 (3.3-28.7)	15.5 ± 2.3 (12.6 - 18.5)	-0.3	6.48E-01
Acylcarnitine 16:1	2.0E+06 ± 9.9E+05 (1.3e+06 - 3.4e+06)	2.6E+06 ± 1.4E+06 (9.6e+05 - 4.3e+06)	-0.3	6.74E-01	1.4 ± 0.7 (0.7-2.3)	1.2 ± 0.9 (0.4 - 2.5)	0.3	6.86E-01
PC 30:0	3.3E+06 ± 2.3E+06 (1.3e+06 - 7.0e+06)	2.9E+06 ± 6.0E+05 (2.3e+06 - 3.7e+06)	0.0	9.96E-01	28.5 ± 14.9 (14.4-47.2)	23.5 ± 5.7 (16.2 - 30.6)	0.2	6.89E-01
LysoPC 16:1	1.1E+05 ± 5.6E+04 (4.6e+04 - 1.9e+05)	1.7E+05 ± 6.2E+04 (7.5e+04 - 2.4e+05)	-0.8	4.32E-02	1.8 ± 1.2 (0.7-3.8)	1.4 ± 0.3 (1.2 - 1.8)	0.1	7.06E-01
L-Proline	2.3E+06 ± 1.7E+06 (1.2e+06 - 5.4e+06)	2.1E+06 ± 5.5E+05 (1.4e+06 - 2.7e+06)	-0.1	8.66E-01	463.9 ± 181.3 (310.1-774.6)	487.7 ± 129.3 (284.2 - 604.1)	-0.1	7.16E-01
L-Arginine	7.1E+04 ± 1.4E+04 (4.9e+04 - 8.3e+04)	6.7E+04 ± 5.1E+03 (6.2e+04 - 7.4e+04)	0.1	7.83E-01	239.3 ± 138.6 (133.9-420.3)	210.6 ± 102.2 (110.1 - 346.2)	0.1	7.75E-01
Acylcarnitine 18:1-OH	1.1E+06 ± 1.2E+06 (4.3e+05 - 3.3e+06)	9.0E+05 ± 4.0E+05 (6.2e+05 - 1.5e+06)	-0.1	9.20E-01	0.6 ± 0.4 (0.3-1.2)	0.5 ± 0.3 (0.3 - 1)	0.1	7.90E-01
Acylcarnitine 16:0-OH	4.5E+05 ± 4.0E+05 (2.0e+05 - 1.1e+06)	3.1E+05 ± 2.0E+05 (1.5e+05 - 6.3e+05)	0.4	6.26E-01	0.3 ± 0.1 (0.2-0.4)	0.3 ± 0.2 (0.1 - 0.6)	0.0	8.48E-01
Acylcarnitine 16:2-OH	1.5E+05 ± 1.6E+05 (5.4e+04 - 4.4e+05)	9.4E+04 ± 2.3E+04 (7.3e+04 - 1.3e+05)	0.2	7.95E-01	0.1 ± 0.1 (0.1-0.2)	0.1 ± 0.1 (0.1 - 0.2)	0.0	8.57E-01

Table S5 continued

Compound Name	Non-targeted metabolomics				Targeted metabolomics					
	Non-tumor tissue (peak area) [mean ± sd (range)]	Tumor tissue (peak area) [mean ± sd (range)]	LogFC	p-Value	Non-tumor tissue (pmol/mg) [mean area ± sd (range)]		Tumor tissue (pmol/mg) [mean ± sd (range)]		LogFC	p-Value
Acylcarnitine 18:2	2.8E+06 ± 1.7E+06 (1.7e+06 - 5.9e+06)	4.8E+06 ± 2.2E+06 (3.1e+06 - 8.4e+06)	-0.8	1.64E-01	1.8 ± 0.9	(0.9-3.1)	1.7 ± 1	(0.7 - 3)	0.1	8.61E-01
L-Asparagine	1.1E+05 ± 4.1E+04 (7.5e+04 - 1.7e+05)	9.9E+04 ± 2.7E+04 (6.2e+04 - 1.4e+05)	0.1	7.18E-01	245.8 ± 220.5	(105.7-633.7)	209.8 ± 62.7	(132.8 - 284.7)	-0.1	8.80E-01
Acylcarnitine 14:0	1.4E+06 ± 8.1E+05 (9.2e+05 - 2.8e+06)	2.3E+06 ± 1.1E+06 (1.1e+06 - 3.8e+06)	-0.7	3.31E-01	1 ± 0.4	(0.6-1.6)	1.1 ± 0.8	(0.3 - 2.3)	0.1	8.89E-01
Acylcarnitine 16:1-OH	6.1E+05 ± 6.0E+05 (2.1e+05 - 1.7e+06)	5.2E+05 ± 2.2E+05 (3.0e+05 - 8.8e+05)	-0.1	8.66E-01	0.4 ± 0.2	(0.2-0.7)	0.4 ± 0.2	(0.2 - 0.7)	0.0	9.19E-01
Acylcarnitine 16:0	3.9E+06 ± 9.6E+05 (2.8e+06 - 4.9e+06)	5.1E+06 ± 2.4E+06 (2.2e+06 - 8.3e+06)	-0.3	5.00E-01	5 ± 1.3	(3.3-6.6)	5.6 ± 3.4	(2 - 9.9)	0.0	9.47E-01
Acylcarnitine 14:1-OH	1.8E+05 ± 7.0E+04 (1.1e+05 - 2.8e+05)	1.5E+05 ± 9.5E+04 (7.8e+04 - 3.0e+05)	0.4	5.06E-01	0.1 ± 0	(0.1-0.2)	0.2 ± 0.1	(0.1 - 0.3)	0.0	9.74E-01
Acylcarnitine 6:0[c]	1.4E+06 ± 2.9E+05 (1.1e+06 - 1.9e+06)	2.3E+06 ± 4.6E+05 (1.8e+06 - 2.9e+06)	-0.7	6.29E-03	1.2 ± 0.1	(1-1.4)	1.3 ± 0.7	(0.5 - 2.4)	0.0	9.74E-01
Acylcarnitine 3:0	4.0E+06 ± 2.4E+06 (1.1e+06 - 7.5e+06)	3.0E+06 ± 7.1E+05 (1.9e+06 - 3.8e+06)	0.2	7.33E-01	5.9 ± 3.2	(2.1-10.8)	5.3 ± 0.7	(4.4 - 6.1)	0.0	9.91E-01

[a]Due to saturation in the non-targeted metabolomics assay, $[M2+H]^+$ isotope ions were selected

[b] Belongs to the top 10 metabolites exhibiting the lowest p-values between ccRCC and non-tumor tissue samples in the targeted metabolomics assay

[c] Belongs to the top 10 metabolites exhibiting the lowest p-values between ccRCC and non-tumor tissue samples in the non-targeted metabolomics assay

[d] Overlap of lowest p-values between targeted and non-targeted metabolomics assay (metabolites are also represented in Figure S9)

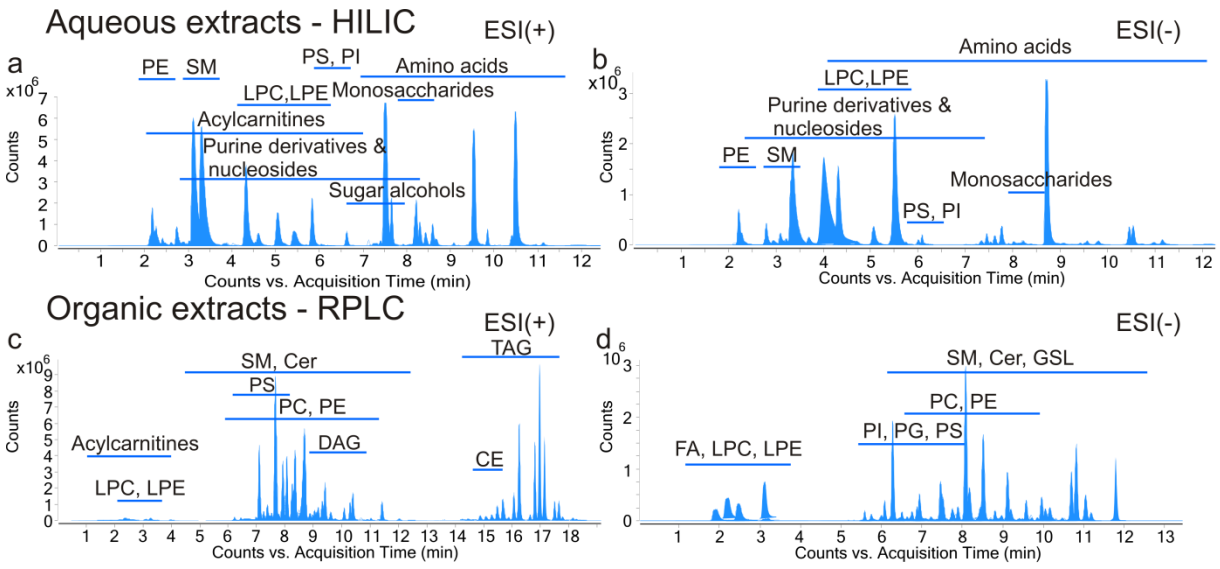
Table is ordered according increasing p-values from the targeted metabolomics assay

p-values are unadjusted for multiple testing

LogFC: mean glog2 fold changes

List of abbreviations for lipids can be found above

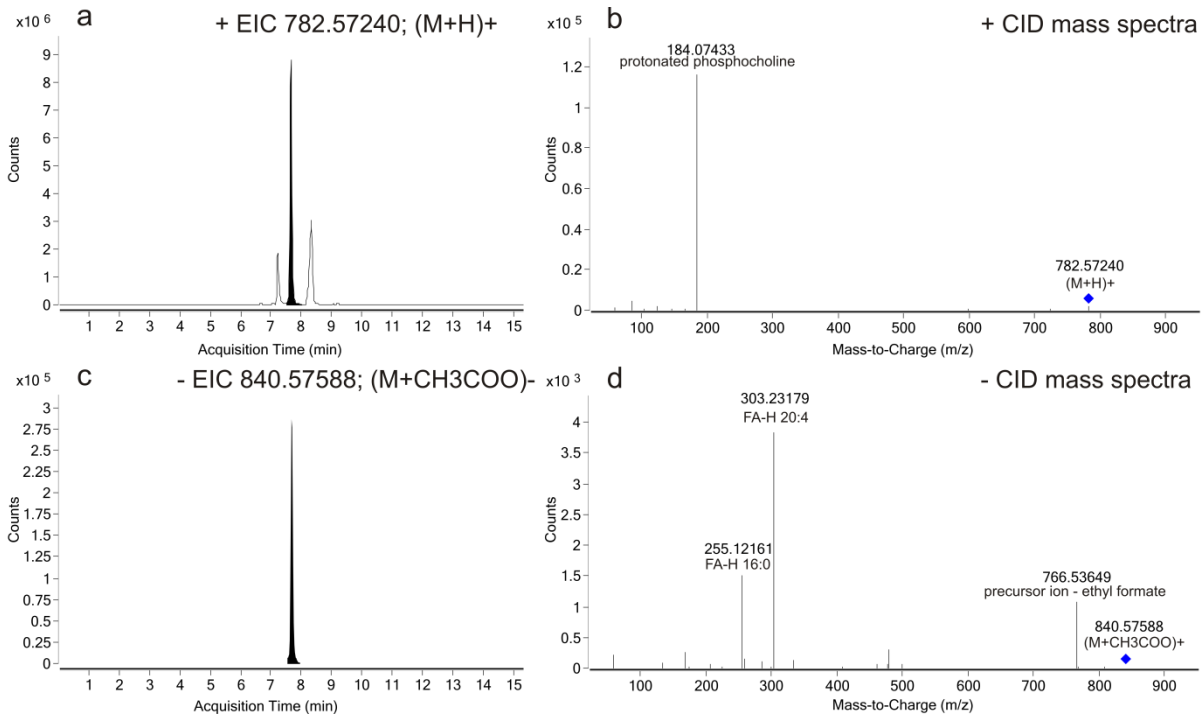
Figure S1



Cer, Ceramides; CE, Cholesterolesters; DAG, Diacylglycerols; FA, Fatty acids; GSL, Glycosphingolipids; LPC, Lysophosphatidylcholines; LPE, Lysophosphatidylethanolamines; PC, Phosphatidylcholines; PE, Phosphatidylethanolamines; PG, Phosphatidylglycerols; PI, Phosphatidylinositols; PS, Phosphatidylserines; SM, Sphingomyelins; TAG, Triacylglycerols

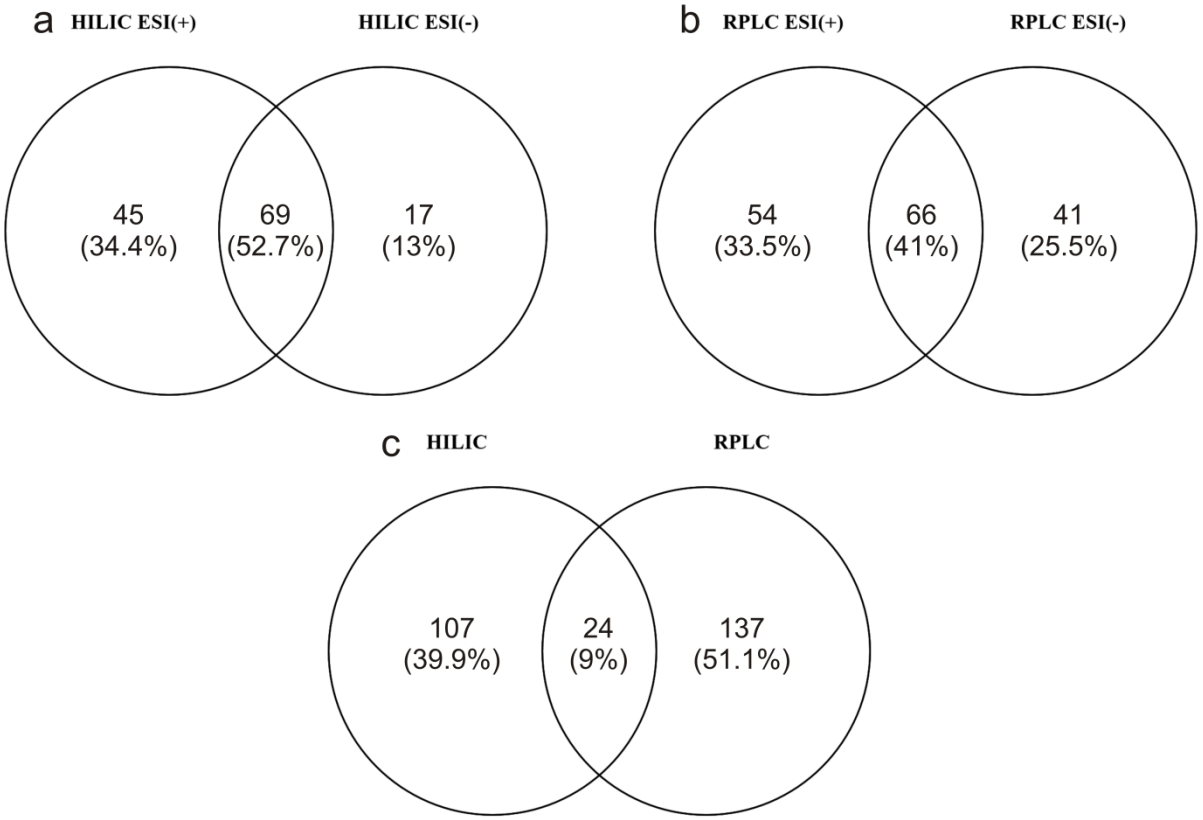
Extracted compound chromatograms (ECCs) demonstrating the elution order of the main metabolite classes that were assigned in aqueous (a, b) and organic (c, d) extracts of kidney tissue. The list of assigned features (Supporting Information Table S2) was used to generate ECCs of the indicated analytical modes.

Figure S2



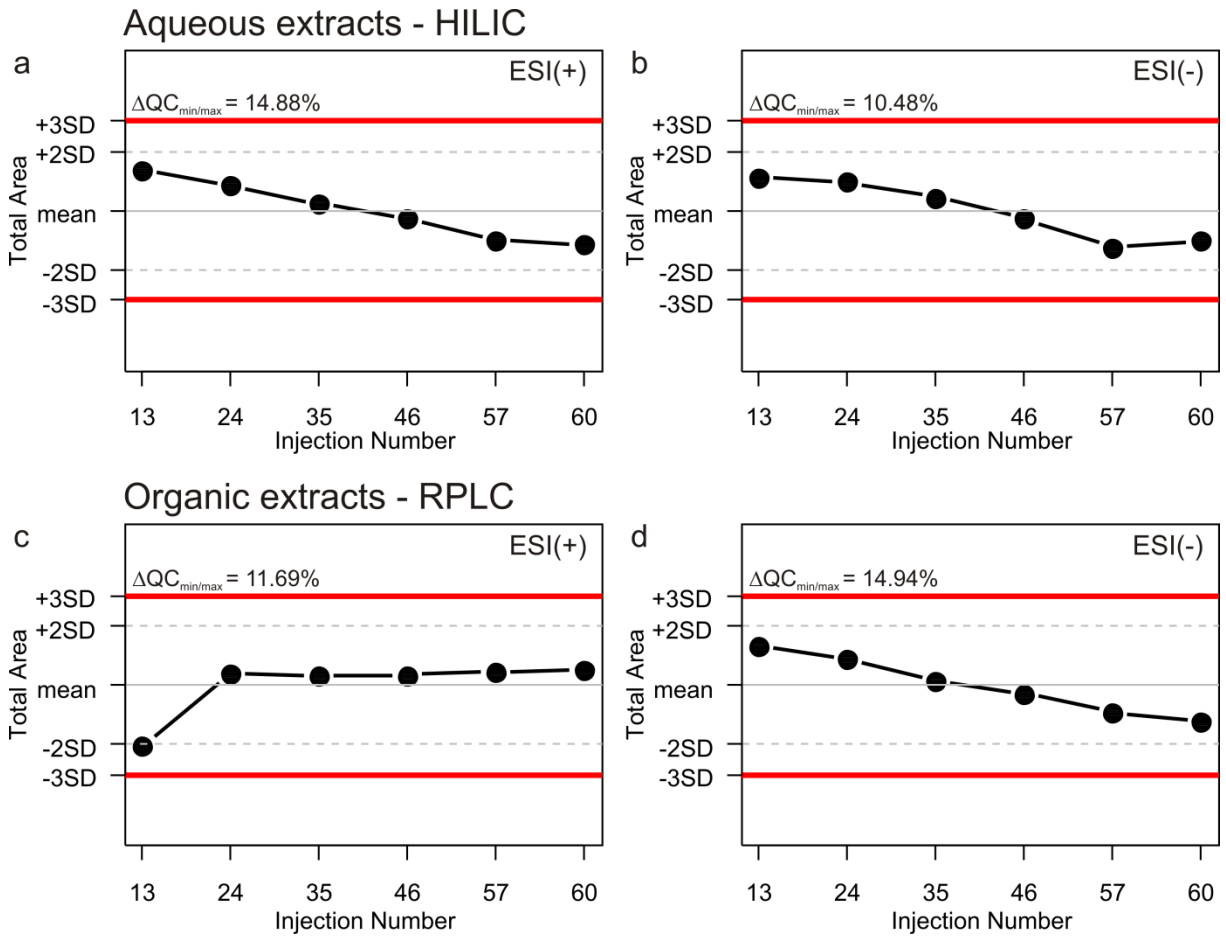
Extracted ion chromatogram (EIC) (a and c) and MS/MS spectra (b and d) of PC (16:0/20:4) analyzed in a kidney tissue organic extract in positive ionization mode (a and b) and negative ionization mode (c and d). (b) illustrates protonated phosphocholine as a main fragment. (d) shows two characteristic, deprotonated fatty acid fragments (FA-H).

Figure S3



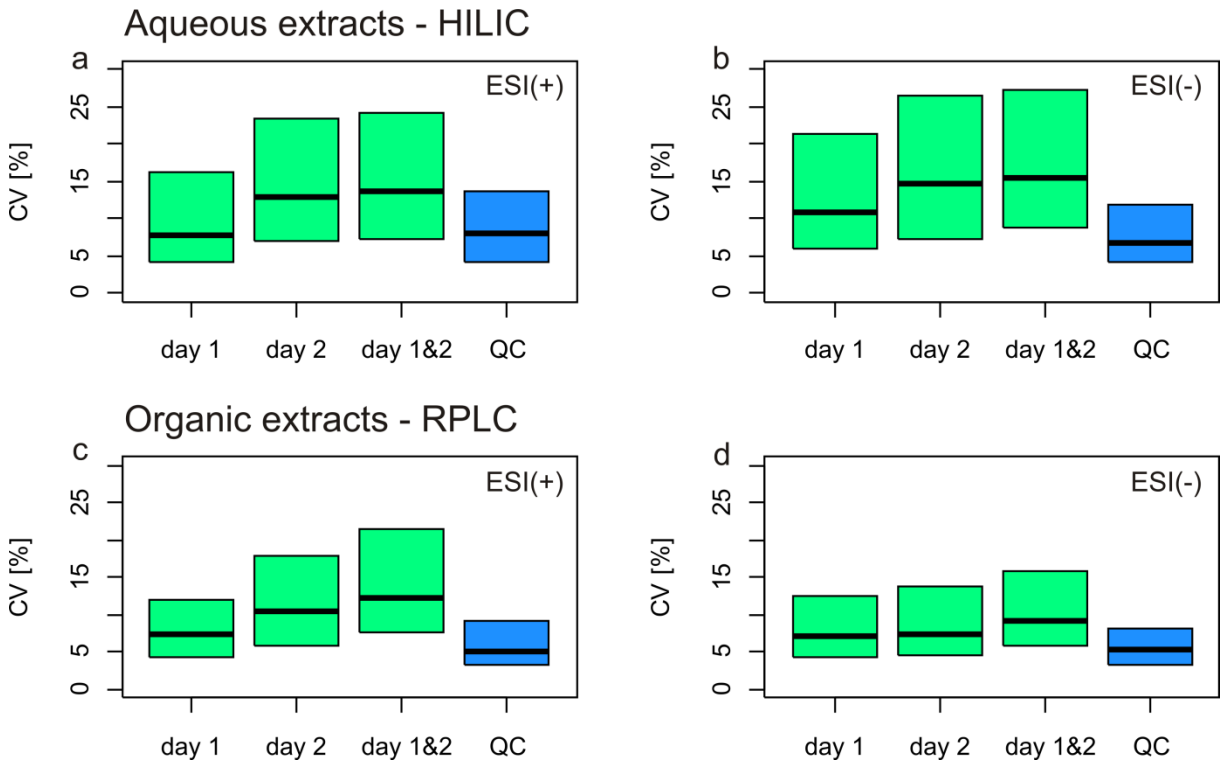
Venn diagrams displaying the extend of overlap of assigned metabolic features (Supporting Information Table S2 and S3) between the different analytical modes of the non-targeted metabolomics assay: (a) HILIC ESI(+) and HILIC ESI(-), (b) RPLC ESI(+) and RPLC ESI(-) and (c) HILIC and RPLC. Percentages are displayed in parentheses and were calculated on the basis of the total number of assigned metabolites for the particular comparison. Venn diagrams were created by using the free available online software Venny 2.1 (http://bioinfogp.cnb.csic.es/tools/venny/index.html).

Figure S4



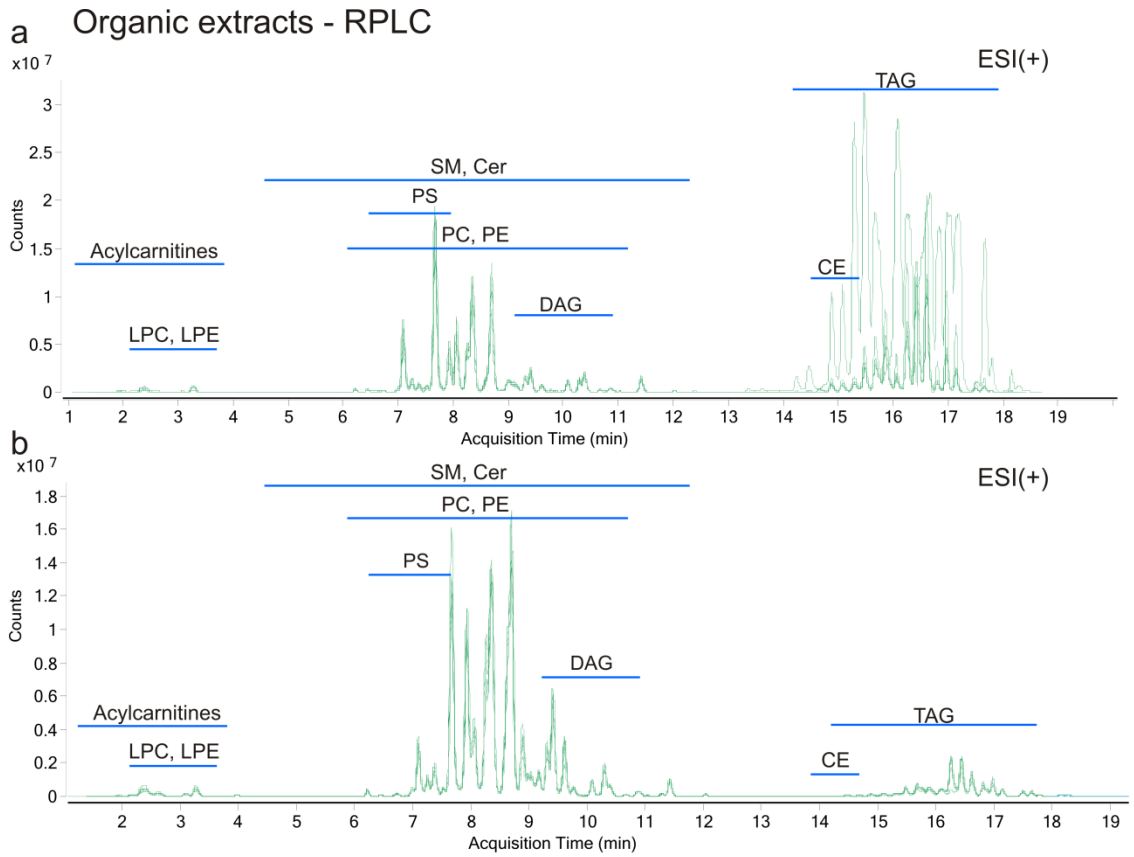
Levey-Jennings chart representing the trend of unnormalized total areas analyzed in QC samples throughout analytical batch A for aqueous (a and b) and for organic (c and d) extracts. QCs are presented in the order of injection. Of note, absolute differences between the highest and the lowest total signal of the QC samples were smaller than 15 %.

Figure S5



Box plots displaying interday sample preparation (green, n=3, for day 1 and day 2, respectively) and analytical reproducibility (blue, n= 6, for QC) calculated as % CVs for sum normalized features found in all replicates in aqueous (a and b) and organic (c and d) extracts. Samples from day 1 and day 2 were prepared on two different days and analyzed together in a single analytical batch (batch A). QC shows the CVs for the analytical reproducibility (n=6) over the whole run. Day 1 & 2 shows the CVs over the six replicates prepared on day 1 and 2.

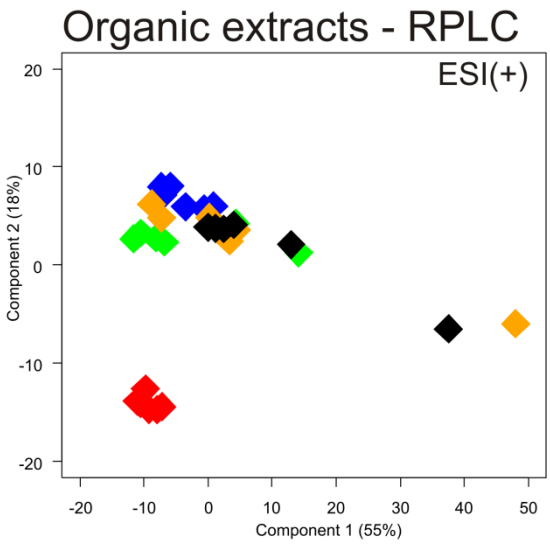
Figure S6



Cer, Ceramides; CE, Cholesterolesters; DAG, Diacylglycerols; LPC, Lysophosphatidylcholines; LPE, Lysophosphatidylethanolamines; PC, Phosphatidylcholines; PE, Phosphatidylethanolamines; PS, Phosphatidylserines; SM, Sphingomyelins; TAG, Triacylglycerols

Total compound chromatogram (TCC) overlay demonstrating variable features observed in human kidney samples. Data acquired in organic extracts (positive mode) of six kidney cortex replicates (green lines) independently prepared from a single kidney tissue sample from patients suffering either interstitial nephritis IN (a) or oncocytoma OC (b) is displayed. Each line represents data from a single kidney cortex replicate. TCC data was extracted based on the list of assigned metabolites (Supporting Information Table S2).

Figure S7



Principle component analysis (PCA) of kidney cortex replicates (n=6, technical replicates) of tumorous samples ccRCC (blue) and OC (red) and the non-tumorous samples UCC, benign area (green), RT (orange) and IN (black) analyzed in organic extracts in positive ionization mode (batch A). Data acquired after RT > 12 minutes were included to demonstrate the contribution of variable features (e.g. TAGs) to the PCA. 426 extracted features, common to all samples were taken for this PCA. OC samples cluster together because in those replicates no variable features after 12 min could be observed (Supporting Information Figure S6). Clustering of all samples under the exclusion of variable features is demonstrated in Figure 2.

Additional comments regarding variable features

Statistical analysis of the positive ion mode data from the organic extract (Figure 2 c) was carried out under exclusion of highly variable features with retention times ≥ 12 min. According to the kidney metabolome characterization (Supporting Information Figure S1 and Table S2) these feature can mainly be assigned to non-polar triacylglycerols (TAGs). Of note, inconsistent TAG levels could not be observed throughout all human replicate kidney samples. For example, among six replicates of IN-derived samples (Supporting Information Figure S6a), one replicate exhibited far higher TAG levels compared to the remaining replicates, whereas the levels of other lipid classes (e.g. phospholipids) remained constant. In contrast, replicate samples derived from an OC patient displayed consistent TAG profiles (Figure S6b). Moreover, reproducibility assessment in porcine kidney demonstrated that TAGs can be analyzed (CVs < 15 %) and recovered (CVs < 20 %) by our protocol with low variability (Table S2). Consequently, the effects exclusively observed in human samples may be explained by regiospecific differences in the abundances of glycerolipids, an observation which is in accordance to several findings in literature. For example, in tissue samples from ccRCC patients highly variable TAG amounts (from 0-6380 mg/g protein) have been reported whereas the neutral lipid content of corresponding normal tissue was low with little fluctuation[1]. Moreover, a noticeable variation of TAG level also within healthy kidney tissue is evident from a recent study employing matrix assisted laser desorption ionization lipid imaging (MALDI)[2]. Here, MALDI images of cross-sections acquired from rat kidney demonstrated that several TAG species (e.g., TAG 50:2, TAG 54:5) display highly variable profiles in the cortex compared to the renal medulla which is characterized by elevated TAG level distributed constantly over the medulla. These observations are in-line with studies[3,4] who also observed elevated TAG amounts in the intact medulla compared to adjacent regions such as cortex or ccRCC.

REFERENCES

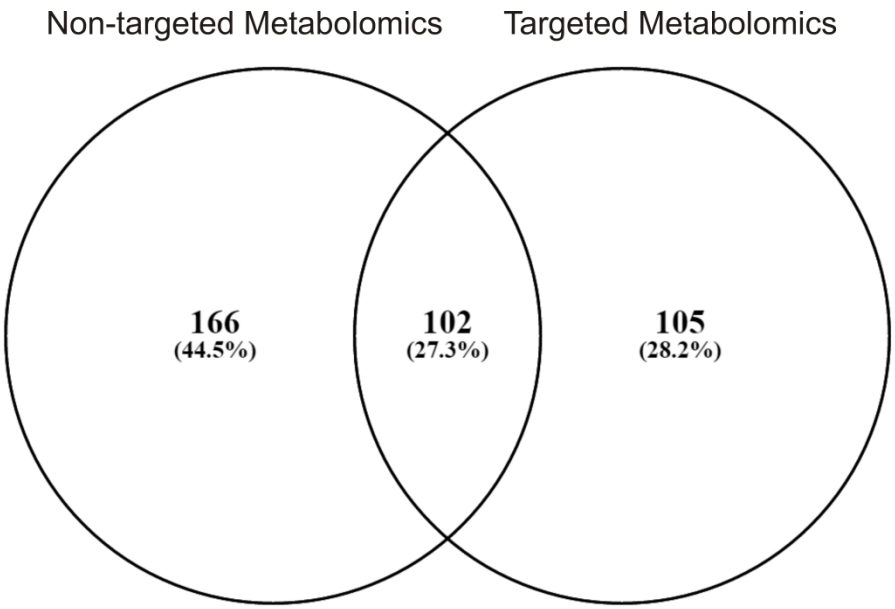
(1) Gebhard, R. L.; Clayman, R. V.; Prigge, W. F.; Figenshau, R.; Staley, N. A.; Reesey, C.; Bear, A. Abnormal cholesterol metabolism in renal clear cell carcinoma. *J. Lipid. Res.* **1987**, *28* (10), 1177-1184.

(2) Muller, L.; Kailas, A.; Jackson, S. N.; Roux, A.; Barbacci, D. C.; Schultz, J. A.; Balaban, C. D.; Woods, A. S. Lipid imaging within the normal rat kidney using silver nanoparticles by matrix-assisted laser desorption/ionization mass spectrometry. *Kidney Int.* **2015**, *88* (1), 186-192.

(3) Tosi, M. R.; Rodriguez-Estrada, M. T.; Lercker, G.; Poerio, A.; Trinchero, A.; Reggiani, A.; Tugnoli, V. Magnetic resonance spectroscopy and chromatographic methods identify altered lipid composition in human renal neoplasms. *Int. J. Mol. Med.* **2004**, *14* (1), 93-100.

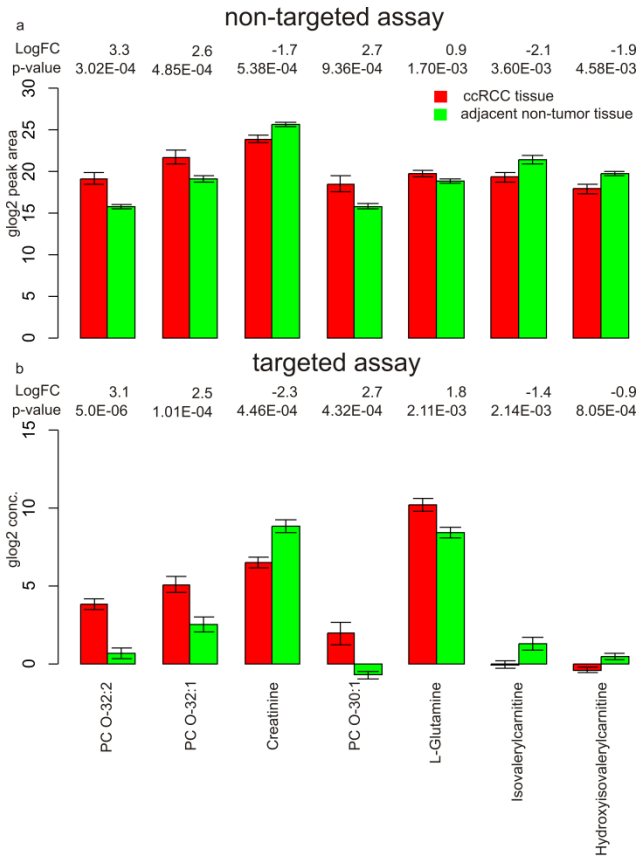
(4) Tugnoli, V.; Poerio, A.; Tosi, M. R. Phosphatidylcholine and cholesteryl esters identify the infiltrating behaviour of a clear cell renal carcinoma: 1H, 13C and 31P MRS evidence. *Oncol. Rep.* **2004**, *12* (2), 353-356.

Figure S8



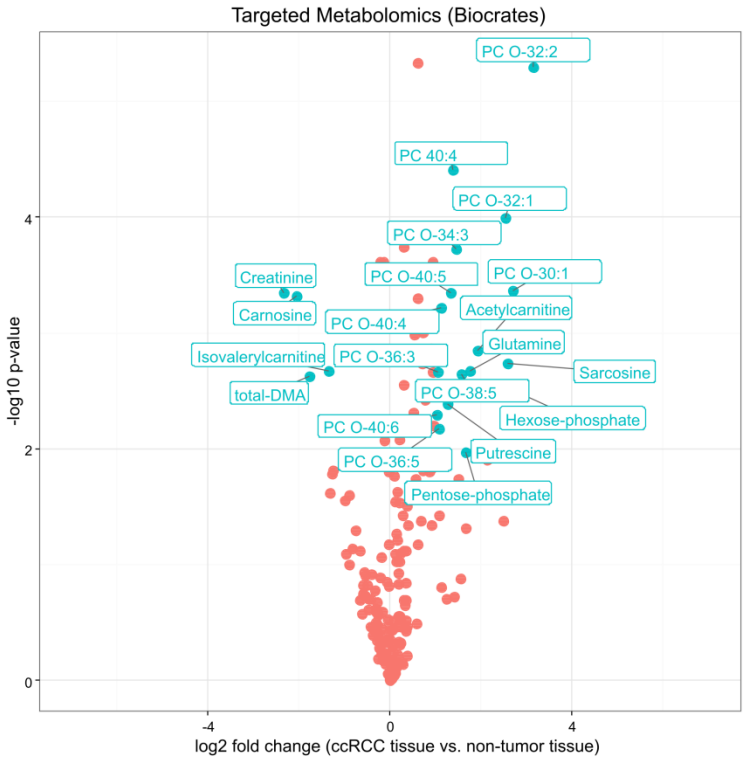
Venn diagrams demonstrating overlapping metabolites between the non-targeted and the targeted metabolomics approach. Of note, the targeted assay comprises 199 metabolites from which 8 were considered as duplicates for comparison (marked with upper case numbers in Supporting Information Table S4) thus resulting in a total number of 207 metabolites in the targeted assay. From the non-targeted assay, a subset of 102 annotated features derived from Table S2, which overlapped with those of the targeted assay, were considered for platform comparison (Supporting Information Table S4). Venn diagrams were created by using the free available online software Venny 2.1 (http://bioinfogp.cnb.csic.es/tools/venny/index.html).

Figure S9



Platform comparison on the basis of most significant marker metabolites determined on the basis of overlapping metabolites (Supporting Information Table S4). Bar-plots represent glog2 transformed peak areas (non-targeted assay) and glog2 transformed concentrations (pmol/mg tissue, targeted assay). Error bars denotes the standard deviation of five biological replicates (see Table S1). Log2 fold changes (FC) and p-values (unadjusted) are indicated above the bars.

Figure S10



Results of the analysis of differentially regulated features between ccRCC and adjacent non-tumor tissue samples derived from five biological replicates (see Table S1) for the targeted metabolomics analysis. The volcano plot displays log2 fold changes versus Benjamini-Hochberg adjusted p-values (-log10 transformed) for 199 metabolites analyzed. Metabolites that exhibited an absolute log2 fold change > 1 and an adjusted p-value < 0.05 are colored in blue and labeled with the corresponding compound name. Red dots represent metabolites that were not significantly altered.