Supplementary Materials

Table 1. Comparison of metabolite changes between KOT and KOC, WTT/WTC, KOT/WTT, or KOC/WTC. WTC: Wildtype cells without oxLDL treatment; WTT, Wildtype cells with oxLDL treatment. KOC, *TSPO* knockout cells without oxLDL treatment; KOT, *TSPO* knockout cells with oxLDL treatment.

Mass (m/z)	RT(min)	Putative Metabolite	+/-	KOT/KOC		WTT/WTC		KOT/WTT		KOC/WTC	
Arginine/creatine metabolism				P value	Ratio	P value	Ratio	P value	Ratio	P value	Ratio
89.05	14.3	sarcosine *	+	0.003	2.75	0.001	2.58	0.012	1.55	0.098	1.45
113.06	15.3	Creatinine*	-	0.002	2.68	0.004	3.36	0.044	1.73	0.005	2.17
115.06	13.4	Proline *	-	0.012	1.36	0.012	1.66	0.114	1.16	0.037	1.42
123.99	12.2	Phosphonoacetaldehyde	+	0.972	0.95	0.047	0.81	0.179	0.86	0.19	0.73
131.07	14.2	Creatine *	+	0.007	3.39	<0.001	4.69	0.001	1.74	0.033	2.41
174.11	26.5	Arginine *	+	0.041	0.69	0.04	0.73	0.049	0.71	0.054	0.75
132.05	15.0	Asparagine *	+	0.002	0.65	0.014	0.64	0.046	1.27	0.055	1.25
189.06	14.1	N-Acetyl-L-glutamate	-	0.086	2.17	0.001	2.92	0.012	2.24	0.046	3.02
211.04	15.1	Phosphocreatine*	+	<0.001	2.9	<0.001	7.43	0.002	1.37	<0.001	3.5
Histidine/lysine metabolism											
156.05	11	4-Imidazolone-5-propanoate	+	0.03	1.52	0.01	1.67	0.615	0.94	0.833	1.03
159.09	9.3	5-Acetamidopentanoate	+	0.264	0.13	0.043	0.03	0.063	0.84	0.267	0.21
190.06	16.6	N-Carbamyl-L-glutamate *	-	0.001	1.75	<0.001	1.87	<0.001	1.66	0.002	1.77
188.12	11.6	N6-Acetyl-L-lysine *	+	0.256	1.18	0.016	1.65	0.002	0.58	0.263	0.8
Glycolysis											
88.02	8.3	Pyruvate *	-	0.004	0.69	0.001	0.64	0.043	1.22	0.039	1.12
92.05	10.1	Glycerol	-	0.287	0.14	0.035	0.07	0.426	1.04	0.418	0.47
168.99	16.2	Glyceraldehyde 3-P*	-	0.002	1.668	0.031	1.409	<0.001	3.009	<0.001	2.542
182.08	13.6	Mannitol	-	0.696	0.98	0.011	1.57	0.126	1.17	0.002	1.87
185.99	17.2	3-Phospho-D-glycerate	-	0.03	0.76	0.004	0.81	0.008	1.37	0.005	1.45
260.03	16.8	Glucose 1-phosphate *	-	0.015	1.09	0.042	1.58	0.144	1.07	0.043	1.55
260.03	17.2	Fructose 6-phosphate *	-	0.566	0.94	0.003	1.21	0.047	1.15	0.013	1.48
340	18.5	D-Fructose 1,6-bisphosphate*	-	0.042	1.27	0.039	1.49	0.023	1.63	<0.001	1.92
TCA cycle											
118.03	13.9	Succinate *	-	0.029	1.24	0.18	0.81	0.002	0.67	0.003	0.44
132.01	16.3	Oxaloacetate *	-	0.234	1.01	<0.001	1.21	<0.001	0.86	0.008	1.03
174.02	18.4	cis-Aconitate*	-	0.002	1.44	0.038	1.2	0.003	1.54	0.002	1.28
192.03	18.5	Citrate *	-	0.008	0.85	0.004	0.78	<0.001	1.91	<0.001	1.74
Glutathione homeostasis											

230.02	15.7	Ribose 5-phosphate *	-	0.012	1.24	0.003	1.3	<0.001	1.95	<0.001	2.05
276.02	18.0	6-Phospho-D-gluconate	-	0.048	1.31	0.013	1.52	0.006	1.28	0.038	1.49
307.083	14.1	Glutathione*	+	0.08	1.61	0.43	1.3	0.77	1.03	0.64	0.83
612.63	17.3	Glutathione disulphide *	-	0.005	2.44	0.031	1.84	0.011	2.23	0.036	1.68
745.09	17.3	NADPH *	+	0.003	1.23	0.03	1.16	0.001	1.35	0.007	1.27
		Indicators of oxidative stress									
136.04	9.8	Hypoxanthine *	+	0.573	0.83	0.755	1.03	0.03	1.54	0.059	1.91
152.03	11.2	Xanthine*	-	0.003	0.59	0.002	0.53	0.004	1.57	0.019	1.43
155.07	14.2	Histidine *	+	0.024	1.3	0.015	1.18	0.026	1.19	0.333	1.08
168.03	12.6	Urate*	-	<0.001	1.57	0.021	2.3	0.102	0.61	0.03	0.89
226.106	15.2	carnosine	+	0.06	1.14	0.1	1.32	0.047	1.33	0.01	1.5
240.122	13.6	homocarnosine	+	0.04	1.22	0.28	0.88	0.011	1.85	0.01	1.34
		Taurine/cysteine metabolism									
109.02	14.7	Hypotaurine	+	0.217	1.17	0.016	1.38	0.433	0.97	0.392	1.15
105.04	15.5	Serine *	-	0.014	0.75	0.016	0.71	0.605	0.97	0.435	0.92
125.014	15.0	Taurine*	+	0.44	0.95	0.62	1.02	0.019	1.17	0.03	1.26
125.999	11.0	Hydroxyethansulphonate	-	0.004	1.47	0.006	1.72	0.335	0.93	0.42	1.09
147.05	10.5	O-Acetyl-L-serine	-	0.002	1.7	0.005	2.51	0.313	0.9	0.128	1.33
153.01	14.4	3-Sulfino-L-alanine	-	<0.001	2.9	0.005	2.34	0.001	1.4	0.419	1.12
169	15.8	Cysteic Acid	-	0.001	2.92	<0.001	3.87	0.022	1.49	0.001	1.97
		Pyrimidines and purines									
111.04	11.4	Cytosine *	+	0.954	0.97	0.049	0.79	0.001	0.46	0.004	0.38
114.04	12.0	5,6-Dihydrouracil	+	0.029	0.47	0.008	0.5	0.994	1.02	0.768	1.09
125.06	7.4	5-Methylcytosine	+	0.012	0.58	0.009	0.54	0.435	0.97	0.561	0.9
126.04	12.6	Thymine *	+	<0.001	1.91	0.011	1.4	<0.001	1.48	0.332	1.08
128.06	14.3	5,6-Dihydrothymine	+	<0.001	2.38	0.001	2.59	0.001	1.76	0.003	1.91
146.07	14.7	Glutamine *	+	0.051	0.71	0.007	0.67	0.001	1.39	0.126	1.31
244.11	15.1	dihydrothymidine	+	0.016	1.6	0.013	1.65	0.051	1.26	0.142	1.3
268.08	10.4	Inosine	-	0.001	1.2	0.291	0.95	0.022	0.9	0.001	0.72
		Fatty acids biosynthesis and conjugates									
102.07	12.8	Pentanoate	+	0.255	0.21	0.003	0.17	0.003	0.57	0.183	0.46
144.12	4.2	[FA (8:0)] octanoic acid	-	0.596	0.89	0.008	1.38	0.025	0.84	0.235	1.29
146.09	4.5	hydroxy-heptanoic acid	-	0.077	1.49	0.002	1.52	0.739	1.04	0.853	1.06
174.13	7.3	hydroxy-nonanoic acid	-	0.294	1.17	0.02	1.49	0.106	0.77	0.857	0.98
224.14	3.8	[FA] Methyl jasmonate	-	0.008	2.24	0.001	1.91	0.062	1.45	0.159	1.23
228.14	4.2	Traumatic acid	-	0.004	1.54	0.033	1.25	0.172	1.1	0.294	0.9
228.17	3.9	oxo-tridecanoic acid	-	0.307	1.22	0.028	0.74	0.078	1.43	0.263	0.86

240.17	4.0	oxo-Tetradecenoic acid	-	0.002	5.85	0.003	4.76	0.256	1.24	0.888	1.01
242.19	3.8	oxo-tetradecanoic acid	-	0.014	1.7	0.014	1.69	0.009	1.26	0.27	1.25
246.15	4.6	3-Hydroxydodecanedioicacid	-	<0.001	6.37	0.001	4.76	0.145	1.37	0.721	1.03
278.22	3.5	octadecatrienoic acid	+	<0.001	4.73	0.032	3.03	0.077	0.67	0.092	0.43
284.27	3.6	Octadecanoic acid	-	0.347	1.15	0.041	0.66	0.016	1.97	0.302	1.12
308.27	3.6	Eicosadienoic acid	-	0.853	1.02	0.007	0.83	0.787	0.98	0.107	0.8
312.23	3.8	13S-hydroperoxy-9Z,11E-octadecadienoic acid	-	0.005	3.55	0.015	3.08	0.514	1.11	0.992	0.96
312.27	3.5	oxo-nonadecanoic acid	+	0.011	1.69	0.005	2.04	0.081	1.37	0.009	1.66
328.24	3.6	Docosahexaenoic acid	-	0.492	0.91	0.018	0.69	0.015	1.68	0.08	1.27
330.24	4.1	trihydroxyoctadecenoic acid	-	<0.001	26	<0.001	13.58	0.014	1.47	0.356	0.77
340.3	3.5	oxo-heneicosanoic acid	+	0.005	2.26	0.003	2.39	0.032	1.4	0.085	1.48
368.22	4.2	Prostaglandin G2	-	<0.001	>1000	<0.001	>1000	0.039	1.25	ND	1
		Carnitines									
203.12	10.2	O-Acetylcarnitine*	+	0.029	1.3	0.028	1.42	0.647	1.04	0.263	1.14
231.15	7.9	O-Butanoylcarnitine	+	0.011	0.12	0.001	0.19	0.005	0.32	0.125	0.5
399.33	4.2	L-Palmitoylcarnitine	+	<0.001	7.4	0.002	12.62	0.348	0.69	0.449	1.19
425.35	4.2	Oleoylcarnitine	+	0.004	2.26	0.012	2.78	0.648	0.89	0.547	1.09
427.37	4.1	Stearoylcarnitine	+	0.001	5.57	0.001	7.96	0.6	0.87	0.446	1.24
		Energy metabolism									
347.06	13.4	AMP*	+	<0.001	1.46	<0.001	1.49	0.154	1.05	0.123	1.07
427.03	15.1	ADP *	-	0.237	1.1	0.026	1.23	0.102	1.18	0.002	1.33
443.02	18.2	GDP *	-	0.075	1.33	0.018	1.81	0.748	1.03	0.047	1.41
507	16.7	ATP *	-	0.006	1.18	0.008	1.34	0.145	1.1	0.004	1.25
522.99	19.8	GTP*	-	0.05	1.28	0.08	1.3	0.13	1.11	0.43	1.12
665.12	13.1	NADH *	-	0.005	1.41	0.004	1.6	0.383	1.08	0.018	1.23
		Sphingolipids									
273.27	5.2	Hexadecasphinganine	+	<0.001	23.71	<0.001	35.73	0.197	0.76	0.403	1.15
299.28	7.3	Sphingenine	+	0.372	0.78	<0.001	0.8	0.001	1.75	0.053	1.78
327.31	4.0	N,N-Dimethylsphing-4-enine	+	0.006	2.65	0.003	2.34	0.613	0.92	0.22	0.81
329.33	4.8	dimethylaminooctadecanediol	+	0.003	2.15	0.002	1.91	0.016	1.62	0.016	1.44
535.5	3.7	Cer (d18:2/16:0)	-	0.091	1.4	0.004	2.5	0.139	0.71	0.138	1.26
537.51	3.6	Cer (18:1 16:0)	+	0.204	1.25	0.002	1.78	0.002	0.56	0.192	0.79
699.57	3.7	Glucosylceramide (d18:1/16:0)	-	0.585	1.12	0.01	1.22	0.628	0.94	0.69	1.03
730.6	3.8	SM(d18:1/18:0)	+	0.493	1.1	0.048	1.36	0.114	0.78	0.738	0.97
809.67	3.7	Glucosylceramide (d18:1/24:1)	-	0.024	0.69	0.012	0.61	0.428	0.93	0.207	0.83
		Glycerophospholipids									
105.08	19	diethanolamine	+	0.376	0.76	0.044	0.5	0.569	0.85	0.056	0.56

410.24	4.3	LPA 16:0	-	0.002	2.25	0.031	2.04	0.018	1.61	0.134	1.46
437.29	4.2	LPE 16:0 ether	-	0.002	2.06	0.005	1.97	0.001	2	0.009	1.91
438.27	4.1	LPA 18:0	-	0.001	2.74	0.014	2.31	0.015	1.31	0.588	1.1
453.29	4.3	LPE 16:0	+	0.106	2.05	<0.001	2.89	<0.001	1.53	0.205	2.16
481.35	4.3	Lyso PC 16:2	+	0.194	8.27	<0.001	10.21	0.177	0.82	0.436	1.02
495.33	4.3	LPC 16:0	+	0.059	2.23	0.002	3.65	0.026	1.4	0.112	2.29
509.38	4.2	Lyso PC 18:0 ether	+	0.195	7.88	<0.001	5.04	0.03	0.62	0.307	0.39
523.36	4.2	LPC 18:0	+	0.005	3.74	0.001	4.92	0.573	1.14	0.172	1.5
676.54	3.7	PA O-18:0/17:0	+	<0.001	5.7	0.002	5.19	0.761	1.03	0.886	0.94
678.48	3.5	LPG 30:1 ether	-	0.001	2.64	0.01	2.17	0.111	1.41	0.154	1.16
680.5	3.5	PG 30:0 ether	-	<0.001	4.38	0.008	2.4	0.213	1.26	0.039	0.69
694.48	3.5	PG 30:0	-	0.002	0.46	0.013	0.54	0.008	1.87	0.003	2.22
720.49	3.5	PG 32:1	-	0.008	0.56	0.03	0.65	0.013	1.72	0.005	2
722.51	3.5	PG 32:0	-	0.003	0.49	0.004	0.64	0.001	1.79	0.002	2.32
734.55	3.5	LPG 34:1 ether	-	<0.001	2.38	0.025	1.66	0.56	1.06	0.084	0.74
771.54	3.8	PS 36:3 ether	-	0.05	34.24	0.12	>1000	0.32	2.52	0.37	>1000
773.54	3.6	PE 40:7 ether	-	0.017	0.75	0.001	0.64	0.538	1.06	0.068	0.9
773.557	3.7	PS 36:2 ether	+	0.06	139.3	0.12	19.83	0.19	1.05	0.85	0.15
776.56	3.5	PG 36:1	-	0.071	2.07	0.011	1.79	<0.001	1.23	0.965	1.07
783.58	3.7	PC 36:3	+	<0.001	2.25	<0.001	2.29	0.145	1.12	0.001	1.14
785.52	3.5	PS 36:3	-	<0.001	2.44	0.002	3.01	0.07	0.78	0.855	0.96
797.56	3.7	PS 38:4 ether	+	<0.001	>1000	<0.001	>1000	0.014	1.14	*ND	1
799.57	3.7	PS 38:3 ether	+	<0.001	9.45	<0.001	9.86	0.355	1.08	0.477	1.13
815.57	3.5	PS 38:2	-	0.01	0.66	0.035	0.79	0.052	0.77	0.277	0.92
817.58	3.5	PS 38:1	-	0.042	0.74	0.003	0.74	0.025	0.81	0.08	0.81
831.58	3.7	PC 40:7	+	0.001	0.47	0.05	0.61	0.181	1.2	0.037	1.56
843.6	3.5	PS 40:2	-	0.003	0.52	0.001	0.62	0.017	0.67	0.027	0.81
858.53	3.5	PI 36:4	-	0.002	2.24	<0.001	2.41	0.008	1.36	0.037	1.46
859.61	3.7	PC 42:7	+	0.015	0.55	0.007	0.52	0.1	1.22	0.44	1.16
866.51	3.4	PG 44:12	-	0.003	0.54	0.014	0.66	0.005	1.51	0.006	1.84
871.63	3.5	PS 42:2	-	0.001	0.3	<0.001	0.4	<0.001	0.6	0.127	0.81
879.59	3.6	PI 36:0	+	0.157	0.57	0.038	0.65	0.001	0.4	0.045	0.45
900.57	3.5	PI 17:0/22:4	-	0.013	0.77	0.003	0.7	0.164	1.1	0.895	1.01
		Miscellaneous									
100.05	4.4	glutaraldehyde	-	0.839	1.01	0.002	0.66	<0.001	1.77	0.336	1.15
172.01	13.8	sn-glycerol-1-phosphate	-	0.088	1.52	0.003	2.22	0.08	1.29	0.04	1.88
179.08	10.7	D-Glucosamine or isomer	-	0.634	1.11	0.043	1.42	0.723	0.96	0.152	1.23

187.1	13.3	5-guanidino-3-methyl-2-oxo-pentanoate	+	0.007	0.46	0.031	0.5	<0.001	3.02	0.008	3.3
466.311	3.5	Cholesterolsulfate	-	<0.001	3.47	<0.001	3.49	0.82	1.04	0.75	1.05

*ND: not detected at control samples without oxLDL treatment means there was no sample peak or it was below the range of detection.; m/z: the mass-to-charge ratios; RT: metabolite matches standard retention time.

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W
1	Id	Mass (m/z	RT	Putative n	Map	Pathway	K1C1	K1C2	K1C3	K1T1	K1T2	K1T3	W1C1	W1C2	W1C3	W1T1	W1T2	W1T3	P1	P2	P3	P4	P5
2	116	174.0165	18.4534	cis-Aconita	Carbohydr	Citrate cyc	277201.8	285804.9	283967	370951.5	436722.6	413303.9	205898.1	229285	224589.6	286089.5	263709	241328.5	123973.7	198451.4	161504	178796.9	152199.5
3	253	506.9956	16.70135	ATP	Energy Me	Oxidative	296088.1	312551.1	298400.8	341055	372805.2	354471.6	258816.7	233439.3	232178.5	349988.2	323688.1	297388	364180.5	310809.2	330553.7	353647.1	305366
4	335	260.0297	16.80892	D-Glucose	Carbohydr	Starch anc	18810.05	18719.88	17747.04	19741.98	19994.38	20286.43	14562.92	8555.221	12477.78	17551.41	18727.03	19902.64	24062.64	21674.79	20890.02	20696.19	27204.21
5	365	665.1243	13.11633	NADH	Energy Me	Oxidative	15141.91	13728.67	13628.24	19929.97	18218.88	21863.52	10585.34	11848.03	12091.39	20519.37	18461.3	16403.22	9053.478	16026.06	17586.85	16599.28	21832.55
6	368	132.006	16.38615	Oxaloacet	Carbohydr	Citrate cyc	3401.215	3360.957	3394.325	3403.987	3408.014	3402.365	3318.959	3289.92	3269.056	3959.579	3979.408	3999.237	4017.974	2871.003	3024.384	4332.986	3352.996
7	425	276.0247	18.0255	6-Phospho	Carbohydr	Pentose pl	8244.068	9435.379	6932.648	11474.36	10039.91	10647.94	4806.647	5109.573	6591.383	8745.063	8375.714	8006.364	9362.08	9118.036	8947.48	7307.172	7273.222
8	580	339.996	18.57917	Fructose 1	Energy Me	Carbon fix	6304.875	6381.881	5973.122	6917.875	8990.26	7736.314	3583.249	2942.558	3169.924	5775.322	4821.423	3867.524	11740.59	7481.311	6543.671	7174.382	5577.122
9	592	192.0273	18.55615	Citrate	Carbohydr	Citrate cyc	1437440	1334940	1324176	1125156	1179010	1195760	767843	810610	777958	651349	609372	567395	429664.5	464463.3	313529	386802.1	333173.5
10	671	260.0297	15.95649	Fructose 6	Carbohydr	Pentose pl	20810.05	25917.74	19473.08	21983.24	21069.3	18894.01	14562.92	14476.57	15710.65	17551.41	18008.79	18466.16	16114.53	18158.54	17926.94	18586.49	20616.17
11	694	182.0791	13.65299	Mannitol	Carbohydr	Fructose a	112161.2	111846.5	107914	112128.9	116537.5	95994.21	52029.36	56489.17	68921.07	83880.36	92603.25	101326.1	52966.14	84399.1	85662.32	100817.2	91432.36
12	807	118.0267	13.93982	Succinate	Carbohydr	Citrate cyc	337875.3	324929.6	274233	382493.7	379868.2	401766.8	610007.6	882299.7	655250.8	630796.3	578967.2	527138.1	540805.5	378890.1	318994.4	202570.4	127094.3
13	847	230.019	15.76523	Ribose 5-p	Carbohydr	Pentose pl	4863.99	5267.79	4745.44	5730.64	6135.31	6526.24	2302.17	2340.55	2606.62	3159.78	3140.21	3120.64	4759.002	5799.389	5913.166	4679.298	5131.037
14	866	176.032	15.68773	Ascorbate	Carbohydr	Ascorbate	23802.15	23981.37	17264.16	29687.16	16655.09	21687.72	14850.43	29952.13	19013.32	26239.97	18819.73	11399.5	26215.92	23885.51	19208.66	12110.71	9578.763
15	873	185.9929	17.27585	3-Phospho	Carbohydr	Glycolysis	7750.001	6335.694	7128.477	5583.613	4740.883	5751.232	4751.32	5149.231	4685.215	3774.965	3918.159	4061.352	5610.958	5058.91	4108.764	5382.553	4926.717
16	885	427.0297	15.12579	ADP	Energy Me	Oxidative	20165.82	19232.19	18319.81	18923.05	23086.82	21235.02	15337.52	13966.98	14119.01	19486.76	17862.45	16238.13	18079.41	22021.4	20353.9	21149.62	20438.88
17	960	745.091	17.3333	NADPH	Energy Me	Photosyntl	6880	6530	6960	8760	8000	8340	5080	5140	5810	6420	6070	6136.099	5659.922	6364.469	2303.579	1097.513	772.5307
18	1000	88.01604	8.295672	Pyruvate	Carbohydr	Glycolysis	656931.6	625458.1	632009.3	392505.7	467884.1	469707.3	529035.8	585567.8	590899.3	383695.3	362430.8	341166.3	233989.9	340903.8	323120.9	340932.4	335834.5
19	1116	92.04731	10.1335	Glycerol	Carbohydr	Galactose	1194225	131078	54589.05	64313.63	66605.93	67614.21	351417.2	2332150	238493.1	68310.77	63742.87	59174.96	75691.74	175354	171877.4	201661.6	161495.1
20																							
21	m/z: the mass-to-charge ratios ; RT: metabolite matches standard retention time																						

Figure 1. Some raw data were used for PCA analysis.

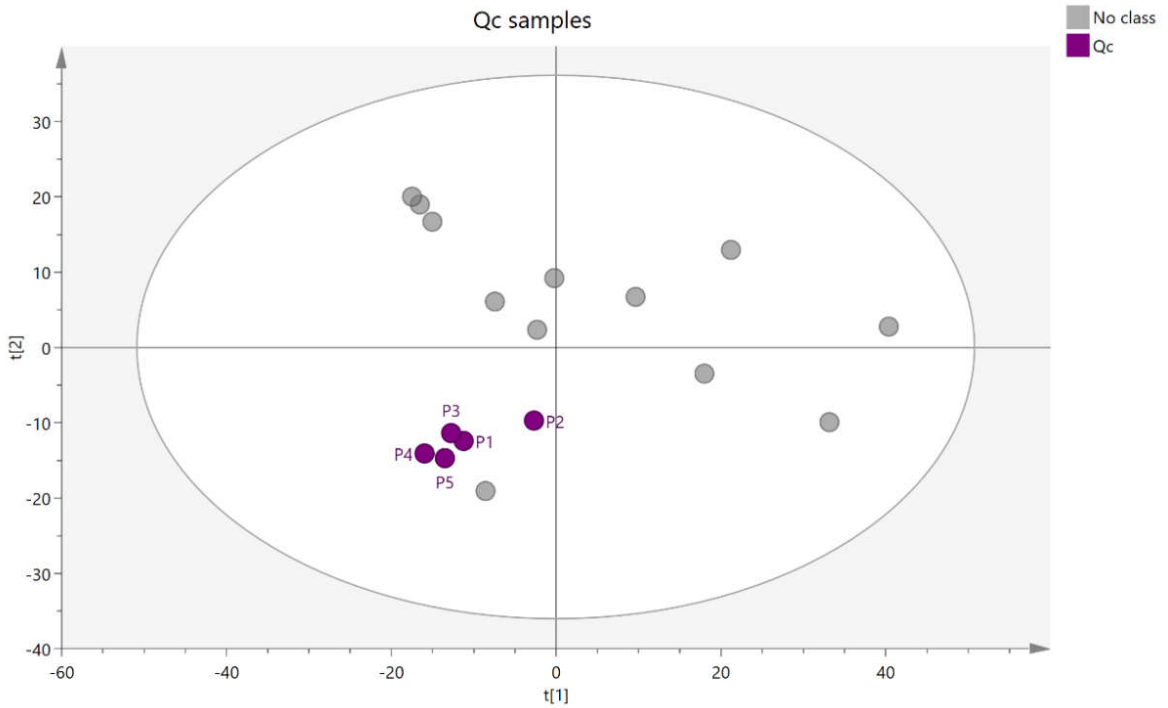

Figure 2. Principle component analysis (PCA) score plot for quality control (QC) (pooled) cell extract samples of wildtype and TSPO knockout RPE cells. P1, P2, P3, P4 and P5 are pooled (QC) sample running throughout the experiment and reflecting the goodness of device sensitivity.

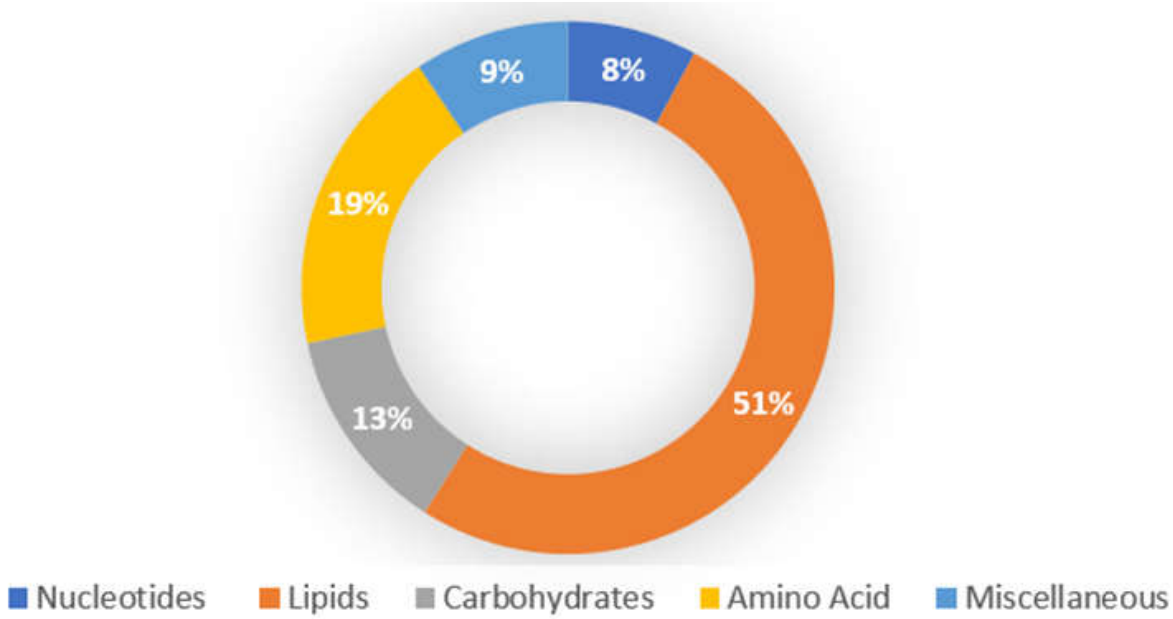

Figure 3. Overveiw for implication of different pathways to all significant affected metabolites. Lipid pathway is the most influenced pathway while nucleotides were the least.