

Targeted metabolomics identifies pharmacodynamic biomarkers for BIO 300 mitigation of radiation-induced lung injury

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Supporting Information

Table S1. List of p180 analytes, ratios and sums.

Table S2. List of significant metabolites comparing 0 w/2 w to 6 w/sham. Significance was calculated by t-test using a FDR of < 5%. The mean values are reported in pmol/mg of tissue. SD=standard deviation, SEM=standard error of the mean, N=number of individual samples

Table S3. List of significant metabolites comparing 6 w to sham. Significance was calculated by t-test using a FDR of < 5%. The mean values are reported in pmol/mg of tissue. SD=standard deviation, SEM=standard error of the mean, N=number of individual samples

Figure S1. Histopathologic damage among BIO 300 treated and untreated male C57L/J mice surviving to day 180 post 12.5 Gy WTLI. Paraffin embedded left lung samples were sectioned at 5 micron thickness and stained with Masson's Trichrome. The lungs of sham-irradiated animals, age matched to the irradiated animals, display normal alveolar architecture with evidence of focal bronchial epithelial hyperplasia in some instances at 180 days. (a). Diffuse inflammation can be observed throughout the untreated, irradiated lung (b) with airway consolidation particularly around the subpleura. High magnification (10x) of the damaged area demonstrates alveolitis with collagen deposition and airway collapse (b.1). Inflammation is characterized by an abundance of foamy macrophages and mononuclear cell lymphocytes (b.2). Bronchial epithelial hyperplasia is also observed (b.2). Parts of the lung were less damaged (b.3) but contained inflammatory cells and displayed interstitial edema with mild to moderately increased alveolar wall thickness. The lungs of male C57L/J mice treated with 2 or 6 weeks of BIO 300 starting 24 hours post exposure

to 12.5 Gy WTLI displayed less damage than the untreated controls. However, 2 weeks of administration was inferior to 6 weeks (c, d). Airway congestion with proteinaceous exudate and mononuclear cell, foamy macrophages, and bronchial epithelial hyperplasia (c.1) along with interstitial inflammation (c.2.) and airway consolidation with fibrous deposition (c.3) were observed in the lungs of animals treated for 2 weeks post-exposure, similar to that of the untreated controls. In contrast, the lungs from surviving animals treated with BIO 300 for 6 weeks displayed less overall damage (D) with focal areas of injury (d.1), but with large volumes of normal, well aerated lung (d.2, d.3). Panels of local damage were taken at 10x magnification.

Figure S2. Multivariate analysis of the four individual cohorts: 0 w, 2 w, 6 w, and sham. A.) PCA plot comparing 0 w (red), 2 w (green), 6 w (purple), and sham (blue). The 95% confidence interval is indicated by the elliptical pattern per group. B.) PLS-DA plot comparing 0 w (red), 2 w (green), 6 w (purple), and sham (blue). The 95% confidence interval is indicated by the elliptical pattern per group. Analysis was performed using MetaboAnalyst 3.0.

Figure S3. Correlation analysis using a dendrogram to compare 0 w (red), 2 w (green), 6 w (purple), and sham (blue). The dendrogram correlation analysis was done using Pearson distance measurement and Ward clustering via MetaboAnalyst 3.0.

Table S1.

	p180 Abbreviation	Common Name	IUPAC Name	Metabolite Class	HMDB ID
1	C0	L-Carnitine	(3R)-3-hydroxy-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB00062
2	C2	L-Acetylcarnitine	3-(acetyloxy)-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB00201
3	C3	Propionylcarnitine	3-(propanoyloxy)-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB00824
4	C3:1	Propenoylcarnitine	(3S)-3-(prop-2-enoyloxy)-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13124
5	C3-OH	Hydroxypropionylcarnitine	(3S)-3-[(3-hydroxypropanoyl)oxy]-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13125
6	C4	Butyrylcarnitine	3-(butanoyloxy)-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB02013
7	C4:1	Butenylcarnitine	(3S)-3-[(2E)-but-2-enoyloxy]-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13126
8	C3-DC (C4-OH)	Hydroxybutyrylcarnitine	(3S)-3-[(3-hydroxybutanoyl)oxy]-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13127
9	C5	Valerylcarnitine	(3S)-3-(pentanoyloxy)-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13128
10	C5:1	Tiglylcarnitine	3-{[(2E)-2-methylbut-2-enoyl]oxy}-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB02366
11	C5:1-DC	Glutaconylcarnitine	(3S)-3-{[(2E)-4-carboxybut-2-enoyl]oxy}-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13129
12	C5-DC (C6-OH)	Glutaryl carnitine	(3S)-3-[(4-carboxybutanoyl)oxy]-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13130
13	C5-M-DC	3-Methylglutaryl carnitine	5-[[1-carboxy-3-(trimethylazaniumyl)propan-2-yl]oxy]-3-methyl-5-oxopentanoate	Acylcarnitine	HMDB00552
14	C5-OH (C3-DC-M)	Hydroxyvalerylcarnitine	(3S)-3-[(1,3-dihydroxypentyl)oxy]-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13132
15	C6:1	2-Hexenoylcarnitine	3-[(2E)-hex-2-enoyloxy]-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13161
16	C6 (C4:1-DC)	Hexanoylcarnitine	3-(hexanoyloxy)-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB00705
17	C7-DC	Pimelylcarnitine	(4S)-4-[(6-carboxyhexanoyl)oxy]-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13328
18	C8	L-Octanoylcarnitine	(3R)-3-(octanoyloxy)-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB00791
19	C9	Nonanoylcarnitine	3-(nonanoyloxy)-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13288
20	C10	Decanoylcarnitine	3-(decanoyloxy)-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB00651
21	C10:1	9-Decenoylcarnitine	3-(dec-9-enoyloxy)-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13205
22	C10:2	linoleoylcarnitine	(3R)-3-[(9Z,12Z)-octadeca-9,12-dienoyloxy]-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB06469
23	C12	Dodecanoylcarnitine	(3R)-3-(dodecanoyloxy)-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB02250
24	C12:1	trans-2-Dodecenoylcarnitine	(4S)-4-(dodec-2-enoyloxy)-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13326
25	C12-DC	Dodecanedioylcarnitine	(4S)-4-[(11-carboxyundecanoyl)oxy]-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13327
26	C14	Tetradecanoylcarnitine	(3R)-3-(tetradecanoyloxy)-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB05066
27	C14:1	cis-5-Tetradecenoylcarnitine	3-[(5Z)-tetradec-5-enoyloxy]-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB02014
28	C14:1-OH	3-Hydroxy-cis-5-tetradecenoylcarnitine	(4S)-4-{[(5Z)-3-hydroxytetradec-5-enoyl]oxy}-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13330
29	C14:2	3, 5-Tetradecadienylcarnitine	(4S)-4-[(3E,5E)-tetradeca-3,5-dienoyloxy]-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13331
30	C14:2-OH	3-Hydroxy-5, 8-tetradecadienylcarnitine	(4S)-4-{[(5E,7E)-3-hydroxytetradeca-5,7-dienoyl]oxy}-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13332
31	C16	9-Hexadecenoylcarnitine	(4S)-4-[(9Z)-hexadec-9-enoyloxy]-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13207

32	C16:1	9-Hexadecenoylcarnitine	(4S)-4-[(9Z)-hexadec-9-enoyloxy]-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13207
33	C16-OH	2-Hydroxyhexadecanoylcarnitine	(4S)-4-[(2-hydroxyhexadecanoyl)oxy]-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13337
34	C16:1-OH	3-Hydroxy-9-hexadecenoylcarnitine	(4S)-4-[[9Z]-3-hydroxyhexadec-9-enoyl]oxy]-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13333
35	C16:2	9,12-Hexadecadienoylcarnitine	(4S)-4-[(9Z,12Z)-hexadeca-9,12-dienoyloxy]-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13334
36	C16:2-OH	3-Hydroxyhexadecadienoylcarnitine	(4S)-4-[(9Z,12Z)-3-hydroxyhexadeca-9,12-dienoyl]oxy]-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13335
37	C18	Stearoylcarnitine	3-(octadecanoyloxy)-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB00848
38	C18:1	11Z-Octadecenylcarnitine	(4S)-4-[(11Z)-octadec-11-enoyloxy]-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13338
39	C18:1-OH	3-Hydroxy-11Z-octadecenoylcarnitine	(4S)-4-[[11Z)-3-hydroxyoctadec-11-enoyl]oxy]-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB13339
40	C18:2	Linoleyl carnitine	(3R)-3-[(9Z,12Z)-octadeca-9,12-dienoyloxy]-4-(trimethylazaniumyl)butanoate	Acylcarnitine	HMDB06469
41	Ala	Alanine	2-aminopropanoic acid	Amino Acid	HMDB00161
42	Arg	Arginine	2-amino-5-carbamimidamidopentanoic acid	Amino Acid	HMDB00517
43	Asn	Asparagine	2-amino-3-carbamoylpropanoic acid	Amino Acid	HMDB00168
44	Asp	Aspartate	2-aminobutanedioic acid	Amino Acid	HMDB00191
45	Cit	Citrulline	2-amino-5-(carbamoylamino)pentanoic acid	Amino Acid	HMDB00904
46	Gln	Glutamine	2-amino-4-carbamoylbutanoic acid	Amino Acid	HMDB00641
47	Glu	Glutamate	2-aminopentanedioic acid	Amino Acid	HMDB00148
48	Gly	Glycine	2-aminoacetic acid	Amino Acid	HMDB00123
49	His*	Histidine	2-amino-3-(1H-imidazol-5-yl)propanoic acid	Amino Acid	HMDB00177
50	Ile	Isoleucine	(3S)-2-amino-3-methylpentanoic acid	Amino Acid	HMDB00172
51	Leu	Leucine	2-amino-4-methylpentanoic acid	Amino Acid	HMDB00687
52	Lys	Lysine	2,6-diaminohexanoic acid	Amino Acid	HMDB00182
53	Met	Methionine	2-amino-4-(methylsulfanyl)butanoic acid	Amino Acid	HMDB00696
54	Orn	Ornithine	2,5-diaminopentanoic acid	Amino Acid	HMDB00214
55	Phe	Phenylalanine	2-amino-3-phenylpropanoic acid	Amino Acid	HMDB00159
56	Pro	Proline	pyrrolidine-2-carboxylic acid	Amino Acid	HMDB00162
57	Ser	Serine	2-amino-3-hydroxypropanoic acid	Amino Acid	HMDB00187
58	Thr	Threonine	(3R)-2-amino-3-hydroxybutanoic acid	Amino Acid	HMDB00167
59	Trp	Tryptophan	2-amino-3-(1H-indol-3-yl)propanoic acid	Amino Acid	HMDB00929
60	Tyr	Tyrosine	2-amino-3-(4-hydroxyphenyl)propanoic acid	Amino Acid	HMDB00158
61	Val	Valine	2-amino-3-methylbutanoic acid	Amino Acid	HMDB00883
62	Ac-Orn*	N-Acetylornithine	5-amino-2-acetamidopentanoic acid	Biogenic Amine	HMDB03357
63	ADMA*	Asymmetric dimethylarginine	2-amino-5-[(E)-[amino(dimethylamino)methylidene]amino]pentanoic acid	Biogenic Amine	HMDB01539
64	SDMA*	Symmetric dimethylarginine	2-amino-5-[(E)-2,3-dimethylcarbamimidamido]pentanoic acid	Biogenic Amine	HMDB03334
65	total DMA	Total dimethylarginine		Biogenic Amine	
66	alpha-AAA	Amino adipic acid	2-aminohexanedioic acid	Biogenic Amine	HMDB00510

67	DOPA*	Dopa	2-amino-3-(3,4-dihydroxyphenyl)propanoic acid	Biogenic Amine	HMDB00181
68	Dopamine*	Dopamine	4-(2-aminoethyl)benzene-1,2-diol	Biogenic Amine	HMDB00073
69	Carnosine*	Carnosine	2-(3-aminopropanamido)-3-(1H-imidazol-5-yl)propanoic acid	Biogenic Amine	HMDB00033
70	Creatinine*	Creatinine	2-imino-1-methylimidazolidin-4-one	Biogenic Amine	HMDB00562
71	Histamine*	Histamine	2-(1H-imidazol-4-yl)ethan-1-amine	Biogenic Amine	HMDB00870
72	Kynurenine	Kynurenine	2-amino-4-(2-aminophenyl)-4-oxobutanoic acid	Biogenic Amine	HMDB00684
73	Met-SO	Methionine sulfoxide	2-amino-4-methanesulfinylbutanoic acid	Biogenic Amine	HMDB02005
74	Nitro-Tyr*	3-Nitrotyrosine	2-amino-3-(4-hydroxy-3-nitrophenyl)propanoic acid	Biogenic Amine	HMDB01904
75	OH-Pro*	4-Hydroxyproline	(4R)-4-hydroxypyrrolidine-2-carboxylic acid	Biogenic Amine	HMDB00725
76	PEA*	Phenylethylamine	2-phenylethan-1-amine	Biogenic Amine	HMDB12275
77	Putrescine*	Putrescine	butane-1,4-diamine	Biogenic Amine	HMDB01414
78	Sarcosine	Sarcosine	2-(methylamino)acetic acid	Biogenic Amine	HMDB00271
79	Serotonin	Serotonin	3-(2-aminoethyl)-1H-indol-5-ol	Biogenic Amine	HMDB00259
80	Spermidine	Spermidine	(4-aminobutyl)(3-aminopropyl)amine	Biogenic Amine	HMDB01257
81	Spermine	Spermine	(3-aminopropyl)({4-[(3-aminopropyl)amino]butyl})amine	Biogenic Amine	HMDB01256
82	Taurine*	Taurine	2-aminoethane-1-sulfonic acid	Biogenic Amine	HMDB00251

	p180 Abbreviation	Common Name	Shorthand	Metabolite Class	HMDB; LMSD ID
83	lysoPC a C14:0	lysoPhosphatidylcholine acyl C14:0	LysoPC(14:0)	Glycerophospholipid	HMDB10379; LMGP01050012
84	lysoPC a C16:0	lysoPhosphatidylcholine acyl C16:0	LysoPC(16:0)	Glycerophospholipid	HMDB10382; LMGP01050018
85	lysoPC a C16:1	lysoPhosphatidylcholine acyl C16:1	LysoPC(16:1)	Glycerophospholipid	HMDB10383; LMGP01050022
86	lysoPC a C17:0	lysoPhosphatidylcholine acyl C17:0	LysoPC(17:0)	Glycerophospholipid	HMDB12108; LMGP01050024
87	lysoPC a C18:0	lysoPhosphatidylcholine acyl C18:0	LysoPC(18:0)	Glycerophospholipid	HMDB10384; LMGP01050026
88	lysoPC a C18:1	lysoPhosphatidylcholine acyl C18:1	LysoPC(18:1)	Glycerophospholipid	HMDB02815; LMGP01050032
89	lysoPC a C18:2	lysoPhosphatidylcholine acyl C18:2	LysoPC(18:2)	Glycerophospholipid	HMDB10386; LMGP01050035
90	lysoPC a C20:3	lysoPhosphatidylcholine acyl C20:3	LysoPC(20:3)	Glycerophospholipid	HMDB10394; LMGP01050133
91	lysoPC a C20:4	lysoPhosphatidylcholine acyl C20:4	LysoPC(20:4)	Glycerophospholipid	HMDB10396; LMGP01050140
92	lysoPC a C24:0	lysoPhosphatidylcholine acyl C24:0	LysoPC(24:0)	Glycerophospholipid	HMDB10405; LMGP01050057
93	lysoPC a C26:0	lysoPhosphatidylcholine acyl C26:0	LysoPC(26:0)	Glycerophospholipid	HMDB29205
94	lysoPC a C26:1	lysoPhosphatidylcholine acyl C26:1	LysoPC(26:1)	Glycerophospholipid	HMDB29220
95	lysoPC a C28:0	lysoPhosphatidylcholine acyl C28:0	LysoPC(28:0)	Glycerophospholipid	HMDB29206
96	lysoPC a C28:1	lysoPhosphatidylcholine acyl C28:1	LysoPC(28:1)	Glycerophospholipid	HMDB29221
97	PC aa C24:0	Phosphatidylcholine diacyl C24:0	PC(24:0)	Glycerophospholipid	
98	PC aa C26:0	Phosphatidylcholine diacyl C26:0	PC(26:0)	Glycerophospholipid	
99	PC aa C28:1	Phosphatidylcholine diacyl C28:1	PC(28:1)	Glycerophospholipid	
100	PC aa C30:0	Phosphatidylcholine diacyl C30:0	PC(30:0)	Glycerophospholipid	
101	PC aa C30:2	Phosphatidylcholine diacyl C30:2	PC(30:2)	Glycerophospholipid	
102	PC aa C32:0	Phosphatidylcholine diacyl C32:0	PC(32:0)	Glycerophospholipid	
103	PC aa C32:1	Phosphatidylcholine diacyl C32:1	PC(32:1)	Glycerophospholipid	
104	PC aa C32:2	Phosphatidylcholine diacyl C32:2	PC(32:2)	Glycerophospholipid	
105	PC aa C32:3	Phosphatidylcholine diacyl C32:3	PC(32:3)	Glycerophospholipid	
106	PC aa C34:1	Phosphatidylcholine diacyl C34:1	PC(34:1)	Glycerophospholipid	
107	PC aa C34:2	Phosphatidylcholine diacyl C34:2	PC(34:2)	Glycerophospholipid	
108	PC aa C34:3	Phosphatidylcholine diacyl C34:3	PC(34:3)	Glycerophospholipid	
109	PC aa C34:4	Phosphatidylcholine diacyl C34:4	PC(34:4)	Glycerophospholipid	
110	PC aa C36:0	Phosphatidylcholine diacyl C36:0	PC(36:0)	Glycerophospholipid	
111	PC aa C36:1	Phosphatidylcholine diacyl C36:1	PC(36:1)	Glycerophospholipid	
112	PC aa C36:2	Phosphatidylcholine diacyl C36:2	PC(36:2)	Glycerophospholipid	
113	PC aa C36:3	Phosphatidylcholine diacyl C36:3	PC(36:3)	Glycerophospholipid	
114	PC aa C36:4	Phosphatidylcholine diacyl C36:4	PC(36:4)	Glycerophospholipid	

115	PC aa C36:5	Phosphatidylcholine diacyl C36:5	PC(36:5)	Glycerophospholipid	
116	PC aa C36:6	Phosphatidylcholine diacyl C36:6	PC(36:6)	Glycerophospholipid	
117	PC aa C38:0	Phosphatidylcholine diacyl C38:0	PC(38:0)	Glycerophospholipid	
118	PC aa C38:1	Phosphatidylcholine diacyl C38:1	PC(38:1)	Glycerophospholipid	
119	PC aa C38:3	Phosphatidylcholine diacyl C38:3	PC(38:3)	Glycerophospholipid	
120	PC aa C38:4	Phosphatidylcholine diacyl C38:4	PC(38:4)	Glycerophospholipid	
121	PC aa C38:5	Phosphatidylcholine diacyl C38:5	PC(38:5)	Glycerophospholipid	
122	PC aa C38:6	Phosphatidylcholine diacyl C38:6	PC(38:6)	Glycerophospholipid	
123	PC aa C40:1	Phosphatidylcholine diacyl C40:1	PC(40:1)	Glycerophospholipid	
124	PC aa C40:2	Phosphatidylcholine diacyl C40:2	PC(40:2)	Glycerophospholipid	
125	PC aa C40:3	Phosphatidylcholine diacyl C40:3	PC(40:3)	Glycerophospholipid	
126	PC aa C40:4	Phosphatidylcholine diacyl C40:4	PC(40:4)	Glycerophospholipid	
127	PC aa C40:5	Phosphatidylcholine diacyl C40:5	PC(40:5)	Glycerophospholipid	
128	PC aa C40:6	Phosphatidylcholine diacyl C40:6	PC(40:6)	Glycerophospholipid	
129	PC aa C42:0	Phosphatidylcholine diacyl C42:0	PC(42:0)	Glycerophospholipid	
130	PC aa C42:1	Phosphatidylcholine diacyl C42:1	PC(42:1)	Glycerophospholipid	
131	PC aa C42:2	Phosphatidylcholine diacyl C42:2	PC(42:2)	Glycerophospholipid	
132	PC aa C42:4	Phosphatidylcholine diacyl C42:4	PC(42:4)	Glycerophospholipid	
133	PC aa C42:5	Phosphatidylcholine diacyl C42:5	PC(42:5)	Glycerophospholipid	
134	PC aa C42:6	Phosphatidylcholine diacyl C42:6	PC(42:6)	Glycerophospholipid	
135	PC ae C30:0	Phosphatidylcholine acyl-alkyl C30:0	PC(O-30:0)	Glycerophospholipid	
136	PC ae C30:1	Phosphatidylcholine acyl-alkyl C30:1	PC(O-30:1); PC(P-30:0)	Glycerophospholipid	
137	PC ae C30:2	Phosphatidylcholine acyl-alkyl C30:2	PC(O-30:2); PC(P-30:1)	Glycerophospholipid	
138	PC ae C32:1	Phosphatidylcholine acyl-alkyl C32:1	PC(O-32:1); PC(P-32:0)	Glycerophospholipid	
139	PC ae C32:2	Phosphatidylcholine acyl-alkyl C32:2	PC(O-32:2); PC(P-32:1)	Glycerophospholipid	
140	PC ae C34:0	Phosphatidylcholine acyl-alkyl C34:0	PC(O-34:0)	Glycerophospholipid	
141	PC ae C34:1	Phosphatidylcholine acyl-alkyl C34:1	PC(O-34:1); PC(P-34:0)	Glycerophospholipid	
142	PC ae C34:2	Phosphatidylcholine acyl-alkyl C34:2	PC(O-34:2); PC(P-34:1)	Glycerophospholipid	
143	PC ae C34:3	Phosphatidylcholine acyl-alkyl C34:3	PC(O-34:3); PC(P-34:2)	Glycerophospholipid	
144	PC ae C36:0	Phosphatidylcholine acyl-alkyl C36:0	PC(O-36:0)	Glycerophospholipid	
145	PC ae C36:1	Phosphatidylcholine acyl-alkyl C36:1	PC(O-36:1); PC(P-36:0)	Glycerophospholipid	
146	PC ae C36:2	Phosphatidylcholine acyl-alkyl C36:2	PC(O-36:2); PC(P-36:1)	Glycerophospholipid	
147	PC ae C36:3	Phosphatidylcholine acyl-alkyl C36:3	PC(O-36:3); PC(P-36:2)	Glycerophospholipid	
148	PC ae C36:4	Phosphatidylcholine acyl-alkyl C36:4	PC(O-36:4); PC(P-36:3)	Glycerophospholipid	

149	PC ae C36:5	Phosphatidylcholine acyl-alkyl C36:5	PC(O-36:5); PC(P-36:4)	Glycerophospholipid	
150	PC ae C38:0	Phosphatidylcholine acyl-alkyl C38:0	PC(O-38:0)	Glycerophospholipid	
151	PC ae C38:1	Phosphatidylcholine acyl-alkyl C38:1	PC(O-38:1); PC(P-38:0)	Glycerophospholipid	
152	PC ae C38:2	Phosphatidylcholine acyl-alkyl C38:2	PC(O-38:2); PC(P-38:1)	Glycerophospholipid	
153	PC ae C38:3	Phosphatidylcholine acyl-alkyl C38:3	PC(O-38:3); PC(P-38:2)	Glycerophospholipid	
154	PC ae C38:4	Phosphatidylcholine acyl-alkyl C38:4	PC(O-38:4); PC(P-38:3)	Glycerophospholipid	
155	PC ae C38:5	Phosphatidylcholine acyl-alkyl C38:5	PC(O-38:5); PC(P-38:4)	Glycerophospholipid	
156	PC ae C38:6	Phosphatidylcholine acyl-alkyl C38:6	PC(O-38:6); PC(P-38:5)	Glycerophospholipid	
157	PC ae C40:1	Phosphatidylcholine acyl-alkyl C40:1	PC(O-40:1); PC(P-40:0)	Glycerophospholipid	
158	PC ae C40:2	Phosphatidylcholine acyl-alkyl C40:2	PC(O-40:2); PC(P-40:1)	Glycerophospholipid	
159	PC ae C40:3	Phosphatidylcholine acyl-alkyl C40:3	PC(O-40:3); PC(P-40:2)	Glycerophospholipid	
160	PC ae C40:4	Phosphatidylcholine acyl-alkyl C40:4	PC(O-40:4); PC(P-40:3)	Glycerophospholipid	
161	PC ae C40:5	Phosphatidylcholine acyl-alkyl C40:5	PC(O-40:5); PC(P-40:4)	Glycerophospholipid	
162	PC ae C40:6	Phosphatidylcholine acyl-alkyl C40:6	PC(O-40:6); PC(P-40:5)	Glycerophospholipid	
163	PC ae C42:0	Phosphatidylcholine acyl-alkyl C42:0	PC(O-42:0)	Glycerophospholipid	
164	PC ae C42:1	Phosphatidylcholine acyl-alkyl C42:1	PC(O-42:1); PC(P-42:0)	Glycerophospholipid	
165	PC ae C42:2	Phosphatidylcholine acyl-alkyl C42:2	PC(O-42:2); PC(P-42:1)	Glycerophospholipid	
166	PC ae C42:3	Phosphatidylcholine acyl-alkyl C42:3	PC(O-42:3); PC(P-42:2)	Glycerophospholipid	
167	PC ae C42:4*	Phosphatidylcholine acyl-alkyl C42:4	PC(O-42:4); PC(P-42:3)	Glycerophospholipid	
168	PC ae C42:5	Phosphatidylcholine acyl-alkyl C42:5	PC(O-42:5); PC(P-42:4)	Glycerophospholipid	
169	PC ae C44:3	Phosphatidylcholine acyl-alkyl C44:3	PC(O-44:3); PC(P-44:2)	Glycerophospholipid	
170	PC ae C44:4	Phosphatidylcholine acyl-alkyl C44:4	PC(O-44:4); PC(P-44:3)	Glycerophospholipid	
171	PC ae C44:5	Phosphatidylcholine acyl-alkyl C44:5	PC(O-44:5); PC(P-44:4)	Glycerophospholipid	
172	PC ae C44:6	Phosphatidylcholine acyl-alkyl C44:6	PC(O-44:6); PC(P-44:5)	Glycerophospholipid	
173	SM (OH) C14:1	Hydroxysphingomyelin C14:1	SM(d18:1/14:1(OH))	Sphingolipid	HMDB13462
174	SM (OH) C16:1	Hydroxysphingomyelin C16:1	SM(d18:1/16:1(OH))	Sphingolipid	HMDB13463
175	SM (OH) C22:1	Hydroxysphingomyelin C22:1	SM(d18:1/22:1(OH))	Sphingolipid	HMDB13466

176	SM (OH) C22:2	Hydroxysphingomyelin C22:2	SM(d18:1/22:2(OH))	Sphingolipid	HMDB13467
177	SM (OH) C24:1	Hydroxysphingomyelin C24:1	SM(d18:1/24:1(OH))	Sphingolipid	HMDB13469
178	SM C16:0	Sphingomyelin C16:0	SM(d18:1/16:0)	Sphingolipid	HMDB10169; LMSP03010003
179	SM C16:1	Sphingomyelin C16:1	SM(d18:1/16:1)	Sphingolipid	HMDB13464; LMSP03010041
180	SM C18:0	Sphingomyelin C18:0	SM(d18:1/18:0)	Sphingolipid	HMDB01348; LMSP03010001
181	SM C18:1	Sphingomyelin C18:1	SM(d18:1/18:1)	Sphingolipid	HMDB12101; LMSP03010029
182	SM C20:2*	Sphingomyelin C20:2	SM(d18:1/20:2)	Sphingolipid	HMDB13465
183	SM C22:3*	Sphingomyelin C22:3	SM(d18:1/22:3)	Sphingolipid	HMDB13468
184	SM C24:0	Sphingomyelin C24:0	SM(d18:1/24:0)	Sphingolipid	HMDB11697; LMSP03010008
185	SM C24:1	Sphingomyelin C24:1	SM(d18:1/24:1)	Sphingolipid	HMDB12107; LMSP03010007
186	SM C26:0*	Sphingomyelin C26:0	SM(d18:1/26:0)	Sphingolipid	HMDB11698; LMSP03010010
187	SM C26:1	Sphingomyeline C26:1	SM(d18:1/26:1)	Sphingolipid	HMDB13461; LMSP03010009
188	H1	Hexose	Total Hexoses	Sugar	

	p180 Abbreviation	Description
189	(C2+C3) / C0	Ratio of short chain acylcarnitines to free carnitine
190	AAA	Sum of the aromatic amino acids
191	ADMA / Arg*	Fraction of asymmetrically dimethylated Arginine of the unmodified Arginine pool
192	BCAA	Sum of branched chain amino acids
193	C2 / C0	Ratio of acetylcarnitine to free carnitine
194	Cit / Arg	Ratio of Citrulline to Arginine
195	Cit / Orn	Ratio of Citrulline to Ornithine
196	CPT-I ratio	Ratio of long chain acylcarnitines to free carnitine ([C16+C18]/C0)
197	Essential AA	Sum of essential amino acids
198	Fisher ratio	Ratio of branched chain amino acids/aromatic amino acids
199	Glucogenic AA	Sum of selected glucogenic amino acids (Alanine, Glycine, Serine)
200	Kynurenine / Trp	Ratio of Kynurenine to Tryptophan
201	Met-SO / Met	Fraction of sulfoxidized Methionine of unmodified Methionine pool
202	MUFA (PC)	Mono-unsaturated glycerophosphocholines
203	MUFA (PC) / SFA (PC)	Ratio of mono-unsaturated to saturated glycerophosphocholines
204	Non essential AA	Sum of the non-essential amino acids
205	Orn / Arg	Ratio of Ornithine to Arginine
206	PUFA (PC)	Sum of poly-unsaturated glycerophosphocholines
207	PUFA (PC) / MUFA (PC)	Ratio of poly-unsaturated to mono-unsaturated glycerophosphocholines

208	PUFA (PC) / SFA (PC)	Ratio of poly-unsaturated to saturated glycerophosphocholines
209	Putrescine / Orn*	Ratio of Putrescine to Ornithine
210	SDMA / Arg*	Fraction of symmetrically dimethylated Arginine of the unmodified Arginine pool
211	Serotonin / Trp	Ratio of Serotonin to Tryptophan
212	SFA (PC)	Sum of saturated glycerophosphocholines
213	Spermidine / Putrescine*	Ratio of Spermidine to Putrescine
214	Spermine / Spermidine	Ratio of Spermine to Spermidine
215	Total (PC+SM)	Sum of choline containing phospholipids
216	Total AA	Sum of all amino acids
217	Total AC / C0	Ratio of esterified to free carnitine
218	Total AC-DC / Total AC	Fraction of dicarboxyacylcarnitines of the total acylcarnitines
219	Total AC-OH / Total AC	Fraction hydroxylated acylcarnitines of the total acylcarnitines
220	Total DMA / Arg*	Fraction of dimethylated Arginine of the unmodified Arginine pool
221	Total lysoPC	Sum of lysoglycerophosphocholines
222	Total lysoPC / Total PC	Ratio of lysoglycerophosphocholines to glycerophosphocholines
223	Total PC	Sum of glycerophosphocholines
224	Total PC aa	Sum of diacyl-glycerophosphocholines
225	Total PC ae	Sum of glycerophosphocholine plasmalogens
226	Total SM	Sum of ceramide phosphocholines (sphingomyelins)
227	Total SM / Total (SM+PC)	Fraction of ceramide phosphocholines (sphingomyelins) of total phospholipid pool
228	Total SM / Total PC	Ratio of total ceramide phosphocholines (sphingomyelins) to total glycerophosphocholines
229	Total SM-non OH	Sum of non-hydroxylated ceramide phosphocholines (sphingomyelins)
230	Total SM-OH	Sum of hydroxylated ceramide phosphocholines (sphingomyelins)
231	Total SM-OH / Total SM-non OH	Ratio of hydroxylated to non-hydroxylated ceramide phosphocholines (sphingomyelins)
232	Tyr / Phe	Ratio of Tyrosine to Phenylalanine

Table S2.

	Metabolite	<i>P value</i> *	0 w and 2 w				6 w and Sham			
			Mean	SD	SE M	N	Mean	SD	SEM	N
1	C0	8.25E-05	39.33	16.4	6.7	6	255.96	92.2	30.7	9
2	C2	5.72E-04	18.37	4.0	1.6	6	60.17	22.1	7.4	9
3	C3	0.0106	1.00	0.5	0.2	6	2.12	0.8	0.3	9
4	Asp	0.0022	273.40	130.3	53.2	6	557.47	148.9	49.6	9
5	Glu	0.0134	737.20	191.0	78.0	6	1056.67	224.0	74.7	9
6	Gly	8.95E-05	490.50	119.9	49.0	6	1625.33	482.8	160.9	9
7	Lys	0.0269	138.50	23.6	9.6	6	92.46	40.6	13.5	9
8	Met-SO	2.95E-04	0.41	0.3	0.1	6	2.77	1.1	0.4	9
9	lysoPC a C18:1	0.0207	8.69	3.2	1.3	6	13.01	3.1	1.0	9
10	lysoPC a C20:3	0.0068	1.07	0.2	0.1	6	2.31	0.9	0.3	9
11	lysoPC a C20:4	0.0041	5.37	2.3	1.0	6	9.70	2.4	0.8	9
12	lysoPC a C24:0	0.0028	0.62	0.2	0.1	6	1.57	0.6	0.2	9
13	lysoPC a C26:0	0.0103	0.60	0.1	0.0	6	0.95	0.3	0.1	9
14	lysoPC a C28:0	1.80E-05	0.60	0.1	0.0	6	1.12	0.2	0.1	9
15	lysoPC a C28:1	0.0115	0.43	0.1	0.0	6	0.61	0.1	0.0	9
16	PC aa C28:1	0.0107	0.70	0.4	0.2	6	1.14	0.2	0.1	9
17	PC aa C30:0	1.93E-04	64.14	48.0	19.6	6	394.53	151.1	50.4	9
18	PC aa C30:2	0.0123	0.69	0.5	0.2	6	1.43	0.5	0.2	9
19	PC aa C32:0	2.05E-07	424.34	346.6	141. 5	6	1795.36	193.4	64.5	9
20	PC aa C32:1	7.84E-04	498.18	383.1	156. 4	6	1214.67	258.5	86.2	9
21	PC aa C32:2	0.0220	42.84	32.1	13.1	6	84.56	29.3	9.8	9
22	PC aa C34:1	1.37E-05	204.13	173.8	71.0	6	689.95	107.0	35.7	9
23	PC aa C34:2	0.0010	273.38	209.3	85.4	6	614.03	103.7	34.6	9
24	PC aa C34:3	0.0026	24.60	18.0	7.3	6	54.68	13.5	4.5	9
25	PC aa C34:4	0.0043	3.07	2.1	0.9	6	8.09	3.1	1.0	9
26	PC aa C36:0	1.25E-05	3.69	2.7	1.1	6	12.19	2.2	0.7	9
27	PC aa C36:1	3.87E-06	15.11	12.7	5.2	6	121.98	32.5	10.8	9
28	PC aa C36:2	5.46E-04	90.60	78.0	31.8	6	224.70	35.8	11.9	9
29	PC aa C36:3	1.92E-04	49.97	39.3	16.0	6	127.97	19.6	6.5	9
30	PC aa C36:4	0.0021	187.70	141.6	57.8	6	469.12	137.8	45.9	9
31	PC aa C36:5	0.0233	12.12	8.3	3.4	6	23.13	8.0	2.7	9
32	PC aa C36:6	0.0224	1.18	0.8	0.3	6	2.25	0.8	0.3	9
33	PC aa C38:0	0.0028	2.32	1.7	0.7	6	5.03	1.2	0.4	9
34	PC aa C38:1	1.96E-05	0.91	0.6	0.2	6	6.54	2.0	0.7	9
35	PC aa C38:3	4.34E-07	13.33	11.3	4.6	6	66.08	10.5	3.5	9
36	PC aa C38:4	1.05E-04	75.79	57.4	23.4	6	249.37	61.6	20.5	9

37	PC aa C38:5	0.0054	38.63	30.0	12.2	6	88.55	27.4	9.1	9
38	PC aa C40:1	1.69E-05	1.08	0.1	0.1	6	3.54	0.9	0.3	9
39	PC aa C40:2	6.37E-06	0.55	0.3	0.1	6	3.65	1.0	0.3	9
40	PC aa C40:3	1.38E-07	0.44	0.3	0.1	6	3.65	0.7	0.2	9
41	PC aa C40:4	2.85E-06	3.12	2.4	1.0	6	20.30	5.0	1.7	9
42	PC aa C40:5	7.27E-05	6.00	4.7	1.9	6	20.81	5.1	1.7	9
43	PC aa C42:0	5.28E-05	0.31	0.1	0.1	6	0.62	0.1	0.0	9
44	PC aa C42:1	2.12E-04	0.16	0.1	0.0	6	1.28	0.5	0.2	9
45	PC aa C42:2	1.29E-04	0.25	0.1	0.0	6	2.14	0.8	0.3	9
46	PC aa C42:4	5.29E-07	0.29	0.2	0.1	6	2.52	0.6	0.2	9
47	PC aa C42:5	1.47E-06	0.55	0.4	0.2	6	3.21	0.7	0.2	9
48	PC aa C42:6	2.75E-05	1.16	0.4	0.2	6	3.01	0.6	0.2	9
49	PC ae C30:0	8.29E-05	1.25	0.7	0.3	6	6.49	2.2	0.7	9
50	PC ae C30:1	7.61E-06	0.58	0.3	0.1	6	2.74	0.7	0.2	9
51	PC ae C30:2	2.29E-05	0.13	0.1	0.0	6	0.30	0.0	0.0	9
52	PC ae C32:1	1.11E-06	12.18	9.9	4.0	6	97.19	22.8	7.6	9
53	PC ae C32:2	3.14E-06	2.34	1.9	0.8	6	9.11	1.5	0.5	9
54	PC ae C34:0	3.65E-05	4.36	3.5	1.4	6	28.02	8.9	3.0	9
55	PC ae C34:1	2.12E-05	18.07	15.2	6.2	6	61.38	10.9	3.6	9
56	PC ae C34:2	6.67E-06	6.77	5.4	2.2	6	28.31	5.8	1.9	9
57	PC ae C34:3	7.87E-06	1.90	1.5	0.6	6	6.92	1.2	0.4	9
58	PC ae C36:0	5.47E-06	0.80	0.4	0.2	6	3.98	1.0	0.3	9
59	PC ae C36:1	1.73E-06	2.81	2.0	0.8	6	12.73	2.5	0.8	9
60	PC ae C36:2	3.76E-05	4.96	3.7	1.5	6	14.02	2.1	0.7	9
61	PC ae C36:3	7.26E-05	2.70	2.1	0.9	6	7.91	1.5	0.5	9
62	PC ae C36:4	2.56E-05	10.40	8.4	3.4	6	40.19	9.2	3.1	9
63	PC ae C36:5	6.14E-07	8.50	6.6	2.7	6	40.46	6.8	2.3	9
64	PC ae C38:1	1.35E-04	0.71	0.3	0.1	6	2.90	1.0	0.3	9
65	PC ae C38:2	1.32E-05	1.38	1.0	0.4	6	4.96	1.0	0.3	9
66	PC ae C38:3	2.57E-06	1.45	0.9	0.4	6	4.42	0.6	0.2	9
67	PC ae C38:4	4.42E-05	5.47	4.0	1.6	6	18.94	4.4	1.5	9
68	PC ae C38:5	0.0020	10.51	8.5	3.5	6	29.26	9.7	3.2	9
69	PC ae C38:6	1.34E-04	5.41	4.2	1.7	6	15.18	2.9	1.0	9
70	PC ae C40:1	0.0277	4.01	2.8	1.1	6	6.93	1.8	0.6	9
71	PC ae C40:2	2.08E-06	0.44	0.2	0.1	6	1.81	0.4	0.1	9
72	PC ae C40:3	2.88E-07	0.43	0.2	0.1	6	1.93	0.3	0.1	9
73	PC ae C40:4	8.53E-07	1.47	0.9	0.4	6	6.71	1.2	0.4	9
74	PC ae C40:5	2.93E-04	1.77	1.3	0.5	6	5.60	1.6	0.5	9
75	PC ae C40:6	0.0115	2.36	1.7	0.7	6	4.75	1.4	0.5	9
76	PC ae C42:0	4.64E-04	3.32	0.5	0.2	6	4.41	0.4	0.1	9
77	PC ae C42:1	7.47E-04	1.09	0.6	0.2	6	2.68	0.8	0.3	9

78	PC ae C42:2	2.77E-04	0.65	0.4	0.2	6	1.53	0.3	0.1	9
79	PC ae C42:5	1.36E-05	1.73	0.3	0.1	6	3.27	0.5	0.2	9
80	PC ae C44:3	9.39E-04	0.28	0.1	0.1	6	0.53	0.1	0.0	9
81	PC ae C44:4	1.21E-05	0.36	0.1	0.0	6	0.63	0.1	0.0	9
82	PC ae C44:6	6.10E-06	0.27	0.1	0.0	6	0.62	0.1	0.0	9
83	SM (OH) C14:1	4.42E-04	1.98	1.5	0.6	6	4.49	0.6	0.2	9
84	SM (OH) C16:1	2.60E-07	0.80	0.6	0.2	6	2.98	0.3	0.1	9
85	SM (OH) C22:1	3.38E-05	0.78	0.7	0.3	6	11.34	4.1	1.4	9
86	SM (OH) C22:2	2.85E-06	0.79	0.7	0.3	6	6.78	1.8	0.6	9
87	SM (OH) C24:1	6.31E-06	0.23	0.2	0.1	6	1.51	0.4	0.1	9
88	SM C16:0	3.85E-06	70.46	55.5	22.7	6	276.08	48.4	16.1	9
89	SM C18:0	4.89E-06	3.07	2.8	1.1	6	33.00	9.5	3.2	9
90	SM C18:1	6.03E-04	1.70	1.5	0.6	6	4.55	1.0	0.3	9
91	SM C24:0	1.17E-06	3.10	2.5	1.0	6	44.20	11.6	3.9	9
92	SM C24:1	5.62E-07	13.15	13.1	5.3	6	138.25	31.8	10.6	9
93	SM C26:1	8.60E-06	0.07	0.1	0.0	6	0.86	0.3	0.1	9
94	(C2+C3) / C0	0.0279	0.58	0.3	0.1	6	0.28	0.1	0.0	9
95	CPT-I ratio	0.0032	0.11	0.1	0.0	6	0.02	0.0	0.0	9
96	Glucogenic AA	7.89E-05	1132.40	293.3	119.7	6	2514.93	544.2	181.4	9
97	Met-SO / Met	0.0013	0.01	0.0	0.0	6	0.06	0.0	0.0	9
98	MUFA (PC)	4.98E-05	758.82	598.7	244.4	6	2219.12	361.4	120.5	9
99	MUFA (PC) / SFA (PC)	1.55E-04	1.39	0.2	0.1	6	0.99	0.1	0.0	9
100	Non essential AA	8.20E-04	3503.15	752.1	307.0	6	5457.45	916.3	305.4	9
101	PUFA (PC)	5.48E-04	1018.49	763.4	311.7	6	2504.19	510.2	170.1	9
102	PUFA (PC) / MUFA (PC)	0.0013	1.41	0.1	0.1	6	1.13	0.1	0.0	9
103	PUFA (PC) / SFA (PC)	5.94E-06	1.94	0.3	0.1	6	1.11	0.2	0.1	9
104	SFA (PC)	3.26E-07	513.26	401.9	164.1	6	2260.84	311.5	103.8	9
105	Total (PC+SM)	1.40E-05	2397.51	1839.6	751.0	6	7522.80	1129.7	376.6	9
106	Total AA	0.0022	4247.32	806.6	329.3	6	6131.29	1012.8	337.6	9
107	Total AC / C0	0.0114	1.55	1.1	0.5	6	0.44	0.3	0.1	9
108	Total AC-DC / Total AC	0.0022	0.13	0.0	0.0	6	0.07	0.0	0.0	9
109	Total AC-OH / Total AC	4.29E-04	0.08	0.0	0.0	6	0.05	0.0	0.0	9
110	Total PC	2.23E-05	2290.56	1755.8	716.8	6	6984.15	1090.1	363.4	9
111	Total PC aa	2.86E-05	2162.99	1664.8	679.7	6	6497.52	1029.2	343.1	9

112	Total PC ae	2.17E-06	127.58	92.2	37.6	6	486.63	80.0	26.7	9
113	Total SM	5.88E-07	106.95	85.3	34.8	6	538.65	94.1	31.4	9
114	Total SM / Total (SM+PC)	1.88E-04	0.05	0.0	0.0	6	0.07	0.0	0.0	9
115	Total SM / Total PC	2.00E-04	0.05	0.0	0.0	6	0.08	0.0	0.0	9
116	Total SM-non OH	6.99E-07	102.37	82.0	33.5	6	511.55	90.6	30.2	9
117	Total SM-OH	3.42E-06	4.58	3.4	1.4	6	27.10	6.6	2.2	9

* all p-values were < 0.05 and had a FDR < 5.0%

Table S3.

	Metabolite	<i>P</i> <i>value</i>	6 w				Sham			
			Mean	SD	SEM	N	Mean	SD	SEM	N
1	Asn*	0.0025	135.48	32.06	14.34	5	56.87	12.09	6.05	4
2	Cit*	0.0067	19.97	8.78	3.93	5	2.53	2.48	1.24	4
3	Lys*	0.0153	118.80	35.35	15.81	5	59.54	11.08	5.54	4
4	Pro	0.0220	149.64	34.15	15.27	5	91.28	22.36	11.18	4
5	Ser*	0.0137	337.56	99.19	44.36	5	161.55	44.03	22.01	4
6	Thr*	0.0136	224.52	53.68	24.01	5	129.60	22.65	11.32	4
7	Trp	0.0374	26.62	7.94	3.55	5	15.18	4.38	2.19	4
8	Tyr*	0.0067	82.20	16.85	7.54	5	46.34	9.06	4.53	4
9	Val	0.0412	105.60	26.93	12.04	5	63.87	21.96	10.98	4
10	Met-SO	0.0184	2.05	0.75	0.33	5	3.68	0.86	0.43	4
11	lysoPC a C14:0	0.0186	12.57	2.15	0.96	5	9.23	0.16	0.08	4
12	lysoPC a C24:0	0.0380	1.92	0.59	0.26	5	1.14	0.15	0.07	4
13	lysoPC a C26:0	0.0253	1.12	0.22	0.10	5	0.74	0.17	0.08	4
14	lysoPC a C26:1*	0.0005	1.02	0.17	0.08	5	0.47	0.05	0.03	4
15	lysoPC a C28:0	0.0293	1.23	0.12	0.05	5	0.98	0.16	0.08	4
16	PC aa C30:0*	0.0024	505.19	104.70	46.82	5	256.20	17.46	8.73	4
17	PC aa C30:2*	0.0016	1.78	0.29	0.13	5	1.00	0.10	0.05	4
18	PC aa C32:1	0.0187	1379.2 2	228.70	102.2 8	5	1008.99	83.31	41.66	4
19	PC aa C32:2*	0.0064	104.91	23.27	10.41	5	59.11	4.21	2.11	4
20	PC aa C32:3*	0.0026	29.06	8.34	3.73	5	9.68	0.39	0.20	4
21	PC aa C34:3	0.0191	63.23	12.33	5.51	5	43.98	2.53	1.26	4
22	PC aa C34:4*	0.0056	10.26	2.42	1.08	5	5.38	0.41	0.20	4
23	PC aa C36:1*	0.0123	100.51	25.57	11.44	5	148.83	14.50	7.25	4
24	PC aa C36:4	0.0210	555.76	126.02	56.36	5	360.81	35.84	17.92	4
25	PC aa C36:5*	0.0122	28.41	6.83	3.05	5	16.52	1.73	0.86	4
26	PC aa C36:6*	0.0113	2.76	0.64	0.29	5	1.61	0.20	0.10	4
27	PC aa C38:1	0.0379	5.35	2.01	0.90	5	8.04	0.61	0.30	4
28	PC aa C38:5	0.0432	104.32	27.58	12.33	5	68.83	7.84	3.92	4
29	PC aa C40:2	0.0449	3.08	0.95	0.42	5	4.37	0.51	0.26	4
30	PC aa C42:1*	0.0016	0.89	0.31	0.14	5	1.78	0.19	0.10	4
31	PC aa C42:2*	0.0073	1.56	0.66	0.30	5	2.87	0.24	0.12	4
32	PC ae C30:0*	0.0036	8.06	1.60	0.71	5	4.52	0.35	0.17	4
33	PC ae C30:1	0.0365	3.15	0.68	0.30	5	2.24	0.17	0.09	4
34	PC ae C34:0	0.0441	33.13	9.02	4.03	5	21.63	2.40	1.20	4
35	PC ae C34:2	0.0330	24.85	5.07	2.27	5	32.64	3.25	1.63	4
36	PC ae C34:3	0.0373	6.20	1.18	0.53	5	7.83	0.48	0.24	4
37	PC ae C38:1	0.0207	2.29	0.74	0.33	5	3.66	0.61	0.30	4

38	PC ae C38:2	0.0338	4.36	0.69	0.31	5	5.71	0.85	0.42	4
39	PC ae C42:5	0.0286	3.58	0.42	0.19	5	2.89	0.29	0.15	4
40	SM (OH) C22:1*	0.0100	8.58	3.17	1.42	5	14.80	1.71	0.85	4
41	SM (OH) C22:2	0.0178	5.65	1.36	0.61	5	8.18	1.01	0.50	4
42	SM C18:0*	0.0038	26.22	6.92	3.09	5	41.47	1.82	0.91	4
43	SM C18:1	0.0162	3.92	0.84	0.37	5	5.33	0.32	0.16	4
44	H1*	0.0123	1887.5 2	424.38	189.7 9	5	995.25	359.02	179.5 1	4
45	AAA	0.0403	191.50	58.25	26.05	5	113.24	22.59	11.29	4
46	Cit / Arg*	0.0092	0.47	0.21	0.09	5	0.08	0.06	0.03	4
47	Essential AA	0.0267	822.34	214.72	96.02	5	488.24	112.37	56.18	4
48	Met-SO / Met*	0.0076	0.04	0.02	0.01	5	0.09	0.02	0.01	4
49	SFA (PC)*	0.0041	2482.8 6	127.14	56.86	5	1983.32	228.98	114.4 9	4
50	Total PC	0.0406	7616.4 2	1036.8 6	463.7 0	5	6193.82	486.44	243.2 2	4
51	Total PC aa	0.0329	7111.9 2	947.82	423.8 8	5	5729.51	459.77	229.8 8	4
52	Total SM / Total (SM+PC)	0.0401	0.07	0.01	0.01	5	0.08	0.00	0.00	4
53	Total SM / Total PC	0.0382	0.07	0.01	0.01	5	0.09	0.00	0.00	4
54	Total SM-OH	0.0195	22.94	5.06	2.26	5	32.30	3.97	1.99	4
55	Total SM-OH / Total SM-non OH*	0.0015	0.05	0.01	0.00	5	0.06	0.00	0.00	4

* FDR < 5.0%

Figure S1.

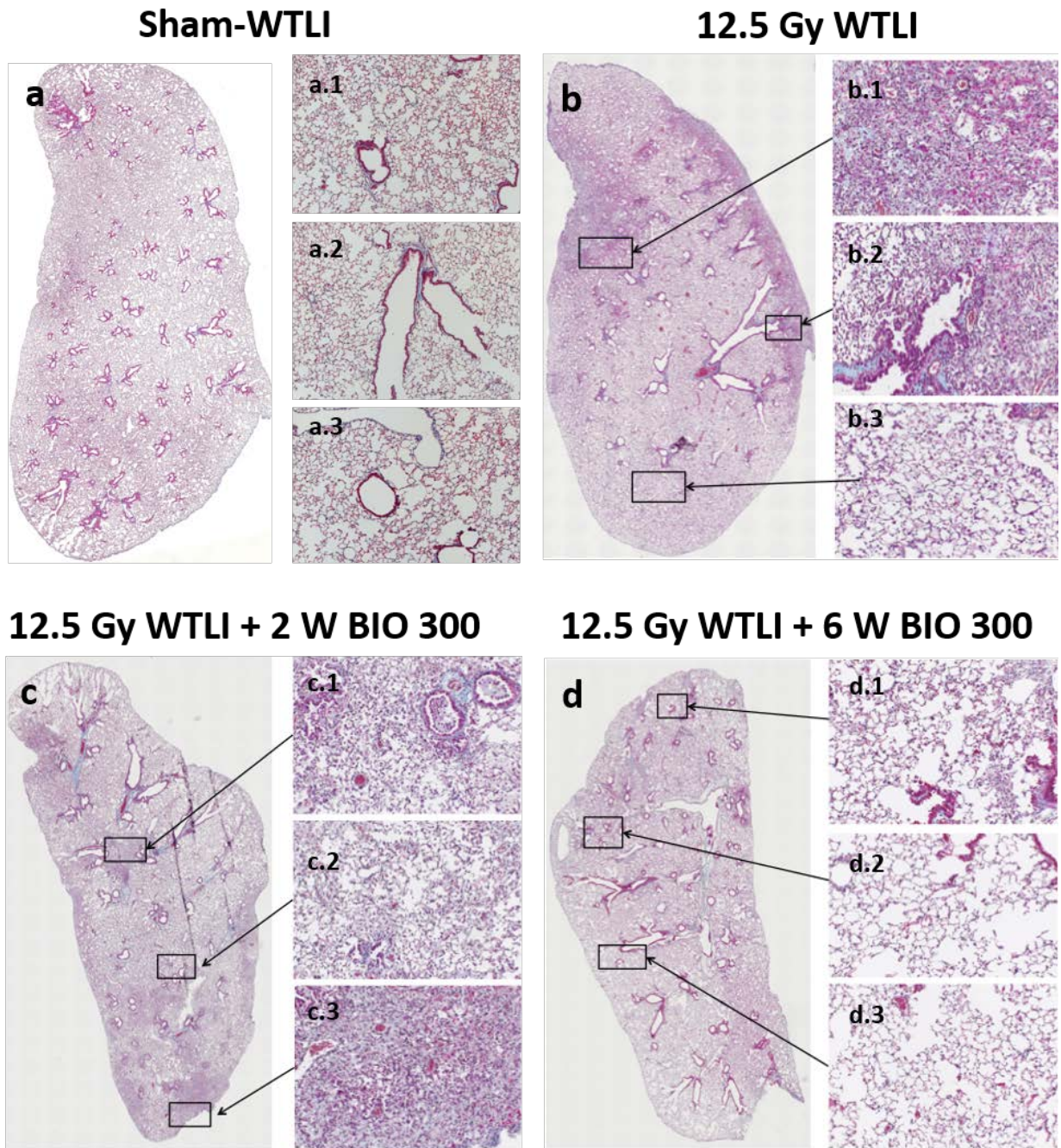


Figure S2.

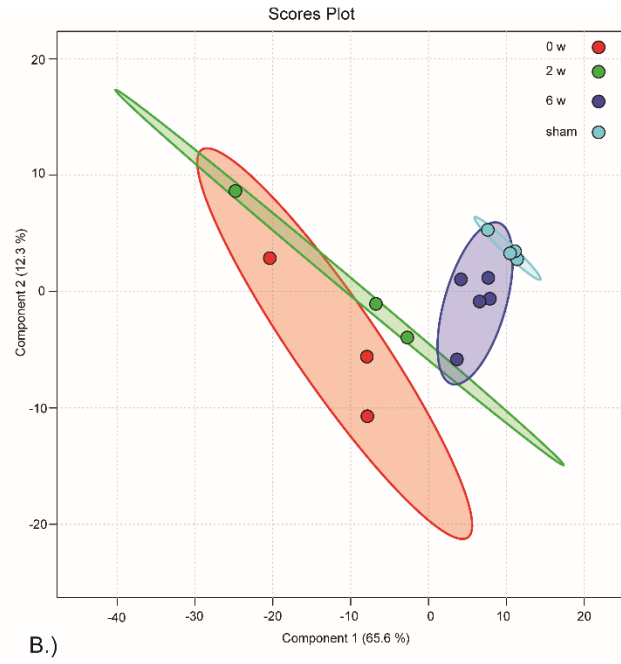
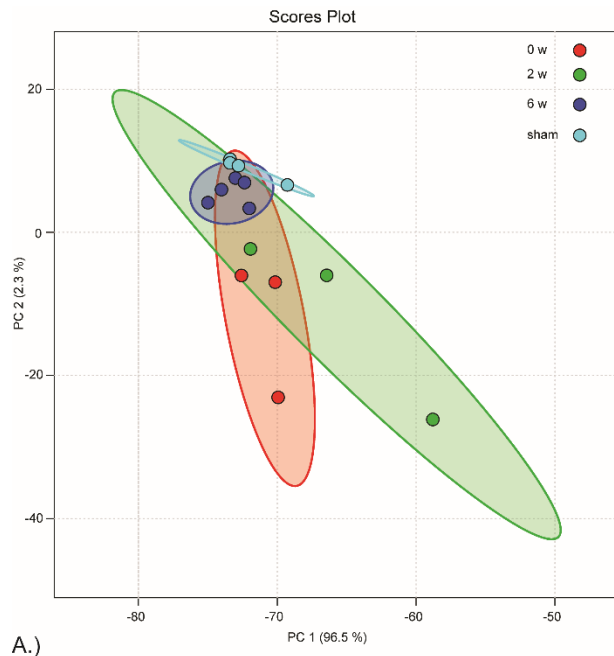


Figure S3.

- 0 w ●
- 2 w ●
- 6 w ●
- sham ●

