

Supplementary Data

Table S1: Metabolites identified in control cells, corresponding to the chromatogram in Fig 5A.

COMPOUND NAME	MOL. WEIGHT	RETENTION TIME	% Abundance
2,4-Pentanediol	104	7.335	0.02
N,N-Dimethylacetamide	87	7.3605	0.17
Propanoic acid	74	7.3715	0.02
1,3-Pentadiene	68	7.501	0.27
Benzo[b]thiophene, 2-ethyl-	162	7.5375	0.28
3-Methyl-3-pentanol	102	7.5525	0.22
2-Amino-4-tertbutylthiazole	156	7.565	0.10
4-Methoxy-2-allylphenol	164	7.63	0.02
2-Propanone	58	7.7235	0.03
2-Butanone	72	7.7625	0.03
Quinazolinone	141	7.8245	0.10
Pyrrolidine-2-carboxylic acid	115	7.9215	0.36
Acetamide	59	7.927	0.40
Phosphorodichloridic acid	134	7.9505	0.09
Isoquinoline	129	7.97	0.01
Ursan-3-one, 16-hydroxy-, (16 β ,18 α ,19 α ,20 β)-	442	7.9975	0.02
Tripyrrolidinophosphine oxide	257	8.025	0.14
Thiazole, 4-methyl-2-phenyl	175	8.1	0.01
1,4-Pentadien-3-ol	84	8.1655	0.02
Cyclopentene	68	8.18	0.07
3-Phenylindole	193	8.376	0.16
5-Nonanol	144	8.4065	0.02
Benzo(b)thiophene-3-acetamide	191	8.4775	0.12
2,4,6-trimethyl Pyridine	121	8.686	0.58
m-Aminobenzenesulfonyl fluoride	175	8.7125	0.03
Allyl dithiopropanoate	146	8.7755	0.01
N-Trifluoroacetylmorpholine	183	8.82	0.03
Benzaldehyde	106	9.1995	0.11
2-oxo-Pentanoic acid	116	9.234	0.05
8-Chloro-5-quinolinecarboxylic acid	207	9.4815	0.01
D-(-)-Lactic acid	90	9.7975	45.35
Dodecane	170	9.8265	0.98

Egenine	369	9.8885	0.05
9,10-Anthracenedione	208	9.954	0.01
Hexanoic acid	116	10.0705	0.04
2-Propenoic acid	72	10.2845	0.22
2-Undecene, 2,5-dimethyl	182	10.2915	0.05
2H-Pyranmethanol, tetrahydro-2,5-dimethyl-	144	10.497	0.02
Octane, 2,3,6,7-tetramethyl	170	10.5095	0.07
L-Alanine	89	10.5615	0.33
5-methyl Dodecane	184	10.5945	0.08
Undecane	156	10.723	0.26
2,5-dimethyl Nonane	156	10.7355	0.29
2-Ketoisocaproic acid	130	10.789	0.14
Glycine	75	10.9035	0.06
3-Amino-1-propanol	75	11.0365	0.12
2H-1,3-Oxazine, tetrahydro-2-(4-methylphenyl	225	11.4815	0.01
2-Ketobutyric acid	102	11.792	0.01
Ala-Pro	343	12.259	0.04
Oxanilic acid	165	12.2695	0.11
Nonane	128	12.3205	0.02
L-Valine	117	12.4665	1.92
Butanoic acid	88	12.627	0.05
Pyrazolidine-1-carbothioic acid, 2-phenyl-, methanamide	221	12.689	0.01
Pentanoic acid	102	12.9375	0.09
Octanoic acid	144	13.2745	0.03
Glycerol	92	13.3375	2.32
L-Leucine	131	13.346	3.64
Pentadecane	212	13.5175	0.44
Undecane, 2-methyl	170	13.6505	0.11
L-Isoleucine	131	13.6925	1.76
Hexadecane	226	13.743	0.11
Citrazinic acid	155	13.8415	0.02
2-methyl Undecane	170	13.8585	0.14
2-Hexenoic acid	114	13.8965	0.05
Fumaric acid	116	13.9235	0.15
Butanedioic acid	118	14.0105	0.16
2-Hexyl-1-octanol	214	14.0475	0.03
Pyridine, 2-methyl-5-phenyl-	169	14.2535	0.01
Acetic acid	60	14.5565	0.23
Decane, 3,6-dimethyl	170	14.653	0.05

Serine	105	14.664	0.18
Nonanoic acid	158	14.7435	0.06
Dodecanedioic acid	230	14.7595	0.12
Benzene, 1,3,5-trimethyl	120	14.913	0.05
L-threonine	119	15.036	0.37
Isophthalic acid	166	16.1715	0.01
Hexanedioic acid	256	16.752	0.25
2-Butenedioic acid	116	17.003	0.04
L-Proline	115	17.01	2.66
Dodecane, 1-iodo	296	17.083	0.05
Benzoic acid	122	17.205	1.19
Quinoline	129	17.3485	0.03
Undecanoic acid	186	17.61	0.01
Anthraquinone, 1-(m-methoxyphenyl)	314	17.7635	0.01
5-Androsten-3 β -ol-17-one, semicarbazone	274	18.002	0.01
L-Glutamic acid	147	18.2025	0.15
L-phenylalanine	165	18.375	0.42
Octanedioic acid	69	19.2	0.12
Uridine, 5-tridecafluorohexyl-2'-deoxy	244	19.3785	0.10
Octadecane	254	19.329	0.18
9-hexyl-Heptadecane	324	20.079	0.04
β -D-Galactofuranose	180	20.336	0.44
Azelaic acid	188	20.34	1.42
1,2,3-Propanetricarboxylic acid	176	20.54	0.07
D-(+)-Talofuranose	176	20.7845	0.33
D-(-)-Ribofuranose	150	20.876	2.84
Sebacic acid	202	21.4455	0.22
β -D-Galactopyranoside	194	21.483	0.47
Levogluconan	162	21.5685	1.19
Decanoic acid	172	21.7055	0.02
β -D-Glucopyranose	180	22.2315	5.98
4-Azaphenanthrene, 1-methyl-3-phenylethynyl	295	22.6175	0.11
Hexadecanoic acid	256	23.0895	1.52
Oleanitrile	263	23.5705	0.11
Hexadecenitrile	235	23.5755	0.06
9,12-Octadecadienoic acid	280	24.736	1.55
Ethyl iso-allocholate	436	24.787	4.94
Oleic acid	282	24.7905	8.82
Octadecanoic acid	284	25.0065	0.19

Table S2: Metabolites identified in LPS-treated cells, corresponding to the chromatogram in Fig 5B.

COMPOUND NAME	MOL. WEIGHT	RETENTION TIME	% Abundance
Sarcosylserine	89	7.678	0.13
2,6-Dimethylbenzenethiol, S-acetyl-	210.41	7.9135	0.43
α -D-Glucopyranoside	194	8.3015	0.00
β -Hydroxypyruvic acid	104	8.3305	0.47
N-ethyl-butanamide	115	8.3325	0.19
Thiazole, 5-methyl-2-phenyl	175	8.089	0.02
2-Hydroxyoctanoic acid	160	8.066	0.29
Acetaldehyde, 3H-1,2-dithiol-3-ylidene	144	8.117	0.05
Ethyl 2-acetylbutyrate	158	8.1405	0.10
s-Triazine	81	8.3685	0.23
Fumaric acid	116	8.3665	0.10
Pyridine, 2,4,6-trimethyl	121	8.6775	0.61
Nonane, 5-(2-methylpropyl	184	9.709	0.03
Phthalimide	147	9.7345	0.73
γ -(Diethylamino)propylamine	130	9.742	0.82
Propanoic acid	74	9.789	18.14
Lactic acid	90	9.7865	13.82
Undecane, 4,7-dimethyl-	184	9.8275	0.53
Dodecane	170	9.9325	0.28
2-Propenoic acid	72	10.286	0.31
2H-Pyranmethanol, tetrahydro-2,5-dimethyl	144	10.4985	0.03
L-Alanine	89	10.5645	0.31
Undecane, 4,7-dimethyl	184	10.625	0.59
Epinephrine	183	11.105	0.28
1,2-Diacetoxy-1-ethoxyethane	190	11.8245	0.02
Oxanilic acid	165	12.27	0.13
Octanoic acid	144	13.2755	0.29
4-Propylacridine	221	13.3375	0.72
L-Leucine	131	13.3465	3.03
Pentadecane	212	13.5185	0.48
L-Isoleucine	131	13.6935	1.27
Undecane, 2-methyl	170	13.859	0.16
Palmitic acid	256	13.9245	0.15
Butanedioic acid	118	14.0115	0.12

Pentanoic acid	102	14.017	0.09
Dodecane, 4,6-dimethyl-	198	14.229	0.45
Acetic acid	60	14.557	0.25
α -D-Glucopyranoside	194	14.559	0.20
Serine	105	14.6655	0.21
Dodecanedioic acid	230	14.7605	0.13
6,7-Dimethyl-3H-isobenzofuran-1-one	162	14.917	0.15
L-threonine	119	15.038	0.48
Pentanedioic acid	132	15.3565	0.05
Hexanedioic acid	146	16.756	0.17
5-Bromonicotinic acid	202	17.009	0.31
4-Acetylpyrimidine	122	17.021	0.00
L-Proline	115	17.012	2.30
Benzoic acid	122	17.208	1.38
Undecane	156	17.7755	0.08
L-phenylalanine	165	18.39	0.34
Mannose	180	20.875	0.60
D-(-)-Ribofuranose	150	20.8785	3.94
Sebacic acid	202	21.335	0.00
D-(+)-Mannopyranose	180	21.3625	10.28
L-Tyrosine	181	21.9505	0.28
β -D-Glucopyranose	180	22.236	14.14
Hexadecanoic acid	256	23.096	3.76
Oleic acid	282	24.787	4.62
17-Octadecynoic acid	280	24.8525	0.52
9,12-Octadecadienoic acid	280	24.739	1.96
1-Iodo-2-methylundecane	296	22.2055	0.15
trans-9-Octadecenoic acid	282	24.7905	7.70
1-Methyl-3-ethyladamantane	178	24.816	0.03
Tetradecanoic acid	228	21.016	0.57

Table S3: Metabolites identified in FFA-treated cells, corresponding to the chromatogram in Fig 5C.

COMPOUND NAME	MOL. WEIGHT	RETENTION TIME	% Abundance
D-(+)-Arabitol	152	7.409	0.04
Acetamide	59	7.49	0.63
Benzo[b]thiophene, 2-ethyl	162	7.495	0.24
Pyrazine	80	7.5895	0.03
Butanoic acid	88	7.6155	0.63

Formamide	45	7.811	0.54
Propanoic acid	74	7.8865	0.17
4-Methyl-1-hexanol	116	8.314	0.20
3-Phenylindole	193	8.3495	0.16
Butane	58	9.266	0.04
4-Mercaptophenol	126	9.4815	0.02
D-Lactic acid	90	9.784	66.29
Decane, 2,3,5,8-tetramethyl	198.39	9.787	1.44
Hexanoic acid	116.0837	10.051	0.02
Norephedrine	151.2056	10.185	0.01
2-Propenoic acid	72.0627	10.2695	0.09
2-(octyloxy)-Ethanol	174	10.2755	0.06
Sulfurous acid	82	10.491	0.03
5-methyl-Dodecane	184	10.495	0.08
L-Alanine	89	10.5565	0.02
Undecane	156	10.6105	0.48
Dodecane	170	10.709	0.27
Benzenamine	93	10.7985	0.02
Benzofuran	118	10.815	0.00
Glyoxylic oxime acid	233	11.021	0.10
6-Aminocaproic acid	131	11.188	0.04
Propiolic acid	70	11.9165	0.01
Pentanoic acid	102	12.7315	1.59
1,2-Benzenediol	110	12.7375	0.07
Urea	60	12.9765	0.41
3-Fluoro-5-(trifluoromethyl)benzaldehyde	192	13.083	0.05
2-Bromo dodecane	248	13.4305	0.04
Undecane, 2-methyl-	170	13.647	0.12
Hexadecane	226	13.8485	0.11
Indole, 3-imidazolo[2,1-b]thiazole-5-yl-	239	13.9145	0.04
1-Octanol, 2-butyl-	186	13.9195	0.11
Butanedioic acid	118	14.006	0.52
Pentadecane	212	14.2245	0.40
Pyrimidine	80	14.3695	0.27
Acetic acid	60	14.566	0.21
Undecane, 4,7-dimethyl-	184	14.6485	0.03
Nonanoic acid	158	14.74	0.04
Dodecanedioic acid	230	14.7475	0.11
6,7-Dimethyl-3H-isobenzofuran-1-one	162	14.917	0.14
Pentanedioic acid	132	15.353	0.05
Calycanthidine	360	15.8345	0.01

2-Piperidone	99	16.115	0.05
3-Ethyl-3-methylheptane	142	16.43	0.02
Carotene	536	16.617	0.09
2-aminobenzoate	137	16.6655	0.01
Hexanedioic acid	146	16.7505	0.26
L-Methionine	149	16.959	0.22
Dodecane, 5,8-diethyl	226	17.003	0.08
L-Proline	115	17.0085	1.88
Phosphine, 1,2-ethanediylbis[dicyclohexyl]	422	17.1665	0.00
Benzoic acid	122	17.2095	1.67
Heptadecane	240	17.362	0.13
Benzenepropanoic acid	150	17.8145	0.15
cis-9-Octadecenoic acid	282	17.834	0.02
Heptanedioic acid	160	18.0325	0.13
Glutamic acid	147	18.202	0.06
Heptacosane	380	19.3305	0.22
Phosphoric acid	97	19.861	0.08
Azelaic acid	188	20.3655	2.93
Z-10-Pentadecen-1-ol	226	21.113	0.04
Sebacic acid	202	21.4545	6.27
n-Pentadecanoic acid	242	21.6745	0.04
L-Lysine	146	21.7385	0.34
Tetracosane	338	21.749	0.14
L-Tyrosine	181	21.9535	0.50
n-Pentadecanoic acid	242	22.062	0.03
2-Ethylbutyric acid	116	22.824	0.03
cis, 6-Octadecenoic acid	282	22.847	0.01
Palmitelaidic acid	254	22.894	0.06
Hexadecanoic acid	256	23.095	2.14
Oleanitrile	263	23.581	0.35
Heptadecanoic acid	270	23.7195	0.02
Decanedioic acid	202	24.437	0.10
9,12-Octadecadienoic acid	280	24.743	0.43
Oleic acid	282	24.795	4.80
Octadecanoic acid	284	25.0205	0.61
Citronellol epoxide	172	26.266	0.08
Eicosenoic acid	310	26.5995	0.09
Terephthalic acid	166	27.34	0.01
Iodosobenzoic acid	220	35.5845	0.01

Table S4: Metabolite sub-class identified in control cells. Data corresponds to Fig 6A.

Metabolite Set	Total	Hits	Expected	P value	Holm P	FDR
Saturated Fatty Acids	38	10	0.0115	1.35000000 00000001E- 27	1.409999999 9999999E- 24	1.409999999 9999999E- 24
Amino acids	277	10	0.0837	1.68E-18	1.75E-15	8.77E-16
Alkanes	42	5	0.0127	1.79E-12	1.87E-9	6.24E-10
Dicarboxylic acids	140	5	0.0423	8.58E-10	8.94E-7	2.24E-7
Hydrocarbons	52	4	0.0157	2.02E-9	2.1E-6	3.83E-7
TCA acids	9	3	0.00272	2.2E-9	2.29E-6	3.83E-7
Organic dicarboxylic acids	23	3	0.00695	4.62E-8	4.81E-5	6.91E-6
Ketones	4	2	0.00121	5.38E-7	5.59E-4	7.04E-5
Straight chain Fatty Acids	6	2	0.00181	1.35E-6	0.0014	1.56E-4
Isoquinolines	1	1	3.02E-4	3.02E-4	0.313	0.0287
Benzoyl derivatives	1	1	3.02E-4	3.02E-4	0.313	0.0287
Carboximidic acids	2	1	6.04E-4	6.04E-4	0.625	0.0527
Oxepanes	3	1	9.06E-4	9.06E-4	0.937	0.0729
Quinolines	4	1	0.00121	0.00121	1.0	0.0903
Short-chain keto acids	5	1	0.00151	0.00151	1.0	0.0987
Benzyl cyanides	5	1	0.00151	0.00151	1.0	0.0987
Pyrimidine deoxyribonucleosides	6	1	0.00181	0.00181	1.0	0.0997
Tricarboxylic acids	6	1	0.00181	0.00181	1.0	0.0997
Heteroaromatic compounds	6	1	0.00181	0.00181	1.0	0.0997
Carboxylic acids	8	1	0.00242	0.00241	1.0	0.115
Quinoline carboxylic acids	8	1	0.00242	0.00241	1.0	0.115
Phosphate esters	8	1	0.00242	0.00241	1.0	0.115
Unsaturated Fatty Acids	267	2	0.0807	0.00303	1.0	0.138
Sugar alcohols	12	1	0.00363	0.00362	1.0	0.158
Benzoic acids	24	1	0.00725	0.00723	1.0	0.302
Oxo Fatty Acids	43	1	0.013	0.0129	1.0	0.519
Oxo Fatty Acids	150	1	0.0453	0.0443	1.0	1.0
Hydroxy Fatty Acids	274	1	28	0.0795	1.0	1.0
C15 isoprenoids	333	1	1	58	1.0	
Unsaturated Fatty Acids	911	1	5	1	1.0	

Table S5: Metabolite sub-class identified in LPS-treated cells. Data corresponds to Fig 6B.

Metabolite Set	Total	Hits	Expect	P value	Holm P	FDR
Saturated Fatty Acids	38	5	0.00746	1.12E-13	1.17E-10	7.37E-11
Amino acids	277	7	0.0544	1.41E-13	1.47E-10	7.37E-11
Dicarboxylic acids	140	4	0.0275	1.91E-8	1.99E-5	6.65E-6
Straight chain Fatty Acids	6	2	0.00118	5.63E-7	5.88E-4	1.47E-4
TCA acids	9	2	0.00177	1.35E-6	0.00141	2.83E-4

Aryl alkyl ketones	10	2	0.00196	1.69E-6	0.00176	2.95E-4
Unsaturated Fatty Acids	267	3	0.0524	2.12E-5	0.022	0.00299
Hydroxy Fatty Acids	274	3	0.0538	2.29E-5	0.0238	0.00299
Alkanes	42	2	0.00825	3.22E-5	0.0334	0.00374
Hydrocarbons	52	2	0.0102	4.95E-5	0.0514	0.00518
1,3,5-triazine-2,4-diamines	1	1	1.96E-4	1.96E-4	0.203	0.0187
Carboximidic acids	2	1	3.93E-4	3.93E-4	0.406	0.0342
Pyrimidine deoxyribonucleosides	6	1	0.00118	0.00118	1.0	0.0948
Disaccharides	9	1	0.00177	0.00177	1.0	0.132
Catechols	11	1	0.00216	0.00216	1.0	0.15
Pyridinecarboxylic acids	14	1	0.00275	0.00275	1.0	0.18
Phenylacetic acids	15	1	0.00295	0.00294	1.0	0.181
Monosaccharides	18	1	0.00353	0.00353	1.0	0.205
Organic dicarboxylic acids	23	1	0.00452	0.00451	1.0	0.246
Benzoic acids	24	1	0.00471	0.0047	1.0	0.246
Unsaturated Fatty Acids	911	1	0.179	0.164	1.0	1.0

Table S6: Metabolite sub-class identified in FFA-treated cells. Data corresponds to Fig 6C.

Metabolite Set	Total	Hits	Expect	P value	Holm P	FDR
Saturated Fatty Acids	38	10	0.00976	2.29E-28	2.39E-25	2.39E-25
Amino acids	277	6	0.0711	1.19E-10	1.25E-7	6.23E-8
Hydrocarbons	52	4	0.0134	1.03E-9	1.08E-6	3.61E-7
Organic dicarboxylic acids	23	3	0.00591	2.82E-8	2.94E-5	7.36E-6
Dicarboxylic acids	140	4	0.036	5.76E-8	6.0E-5	1.21E-5
Alkanes	42	3	0.0108	1.82E-7	1.89E-4	3.17E-5
Unsaturated Fatty Acids	267	4	0.0686	7.6E-7	7.9E-4	1.13E-4
Straight chain Fatty Acids	6	2	0.00154	9.69E-7	0.00101	1.27E-4
Carboxylic acids	8	2	0.00205	1.81E-6	0.00188	2.1E-4
Non-metal phosphates	1	1	2.57E-4	2.57E-4	0.266	0.0244
P-phthalic acids	1	1	2.57E-4	2.57E-4	0.266	0.0244
Carboximidic acids	2	1	5.14E-4	5.14E-4	0.532	0.0413
Benzofurans	2	1	5.14E-4	5.14E-4	0.532	0.0413
Piperidinones	3	1	7.7E-4	7.7E-4	0.796	0.0575
Anilines	4	1	0.00103	0.00103	1.0	0.0716
Ureas	6	1	0.00154	0.00154	1.0	0.0947
Pyrazines	6	1	0.00154	0.00154	1.0	0.0947
Aminobenzoic acids	7	1	0.0018	0.0018	1.0	0.104
Phenylpropanes	8	1	0.00205	0.00205	1.0	0.113
TCA acids	9	1	0.00231	0.00231	1.0	0.115
Pyrimidines	9	1	0.00231	0.00231	1.0	0.115
Catechols	11	1	0.00282	0.00282	1.0	0.134
Amino Fatty Acids	23	1	0.00591	0.00589	1.0	0.268

Benzoic acids	24	1	0.00616	0.00615	1.0	0.268
Branched Fatty Acids	372	1	0.0955	0.0912	1.0	1.0
Unsaturated Fatty Acids	911	1	0.234	0.209	1.0	1.0
Hippuric acids	1470	1	0.377	0.315	1.0	1.0

Table S7: Pathway enrichments for control cells. Data corresponds to Fig 7A.

Metabolite Set	Total	Hits	Expected	P value	Holm P	FDR
Fatty Acid Biosynthesis	35	5	0.99	0.00227	0.225	0.225
Valine, Leucine and Isoleucine Degradation	60	6	1.7	0.00516	0.505	0.255
Alanine Metabolism	17	3	0.481	0.0106	1.0	0.309
Arginine and Proline Metabolism	53	5	1.5	0.014	1.0	0.309
Glutathione Metabolism	21	3	0.594	0.0192	1.0	0.309
Glycine and Serine Metabolism	59	5	1.67	0.0217	1.0	0.309
Carnitine Synthesis	22	3	0.622	0.0218	1.0	0.309
Propanoate Metabolism	42	4	1.19	0.0275	1.0	0.34
Phenylalanine and Tyrosine Metabolism	28	3	0.792	0.0415	1.0	0.379
Glutamate Metabolism	49	4	1.39	0.0453	1.0	0.379
Urea Cycle	29	3	0.82	0.0454	1.0	0.379
Ketone Body Metabolism	13	2	0.368	0.0497	1.0	0.379
Glucose-Alanine Cycle	13	2	0.368	0.0497	1.0	0.379
Citric Acid Cycle	32	3	0.905	0.0582	1.0	0.412
Aspartate Metabolism	35	3	0.99	0.0726	1.0	0.47
Warburg Effect	58	4	1.64	0.076	1.0	0.47
Beta Oxidation of Very Long Chain Fatty Acids	17	2	0.481	0.0809	1.0	0.471
Butyrate Metabolism	19	2	0.538	0.0982	1.0	0.512
Mitochondrial Electron Transport Chain	19	2	0.538	0.0982	1.0	0.512
Threonine and 2-Oxobutanoate Degradation	20	2	0.566	0.107	1.0	0.531
Glycerolipid Metabolism	25	2	0.707	0.155	1.0	0.733
Selenoamino Acid Metabolism	28	2	0.792	0.186	1.0	0.827
Biotin Metabolism	8	1	0.226	0.206	1.0	0.827
Lysine Degradation	30	2	0.849	0.207	1.0	0.827
Ammonia Recycling	32	2	0.905	0.228	1.0	0.827
Homocysteine Degradation	9	1	0.255	0.228	1.0	0.827
Tryptophan Metabolism	60	3	1.7	0.238	1.0	0.827
Amino Sugar Metabolism	33	2	0.934	0.239	1.0	0.827
Malate-Aspartate Shuttle	10	1	0.283	0.25	1.0	0.827
Pyruvaldehyde Degradation	10	1	0.283	0.25	1.0	0.827
Trehalose Degradation	11	1	0.311	0.272	1.0	0.868
Vitamin K Metabolism	14	1	0.396	0.333	1.0	1.0
Methionine Metabolism	43	2	1.22	0.346	1.0	1.0
Purine Metabolism	74	3	2.09	0.35	1.0	1.0
Pyruvate Metabolism	48	2	1.36	0.398	1.0	1.0
Alpha Linolenic Acid and Linoleic Acid	19	1	0.538	0.423	1.0	1.0

Metabolism						
Ethanol Degradation	19	1	0.538	0.423	1.0	1.0
Glycolysis	25	1	0.707	0.516	1.0	1.0
Cysteine Metabolism	26	1	0.736	0.53	1.0	1.0
Oxidation of Branched Chain Fatty Acids	26	1	0.736	0.53	1.0	1.0
Phytanic Acid Peroxisomal Oxidation	26	1	0.736	0.53	1.0	1.0
Plasmalogen Synthesis	26	1	0.736	0.53	1.0	1.0
Mitochondrial Beta-Oxidation of Short Chain Saturated Fatty Acids	27	1	0.764	0.544	1.0	1.0
Mitochondrial Beta-Oxidation of Long Chain Saturated Fatty Acids	28	1	0.792	0.557	1.0	1.0
Bile Acid Biosynthesis	65	2	1.84	0.56	1.0	1.0
Pentose Phosphate Pathway	29	1	0.82	0.57	1.0	1.0
Folate Metabolism	29	1	0.82	0.57	1.0	1.0
Tyrosine Metabolism	72	2	2.04	0.618	1.0	1.0
Beta-Alanine Metabolism	34	1	0.962	0.629	1.0	1.0
Fatty Acid Elongation In Mitochondria	35	1	0.99	0.64	1.0	1.0
Gluconeogenesis	35	1	0.99	0.64	1.0	1.0
Nicotinate and Nicotinamide Metabolism	37	1	1.05	0.661	1.0	1.0
Galactose Metabolism	38	1	1.08	0.671	1.0	1.0
Porphyrin Metabolism	40	1	1.13	0.69	1.0	1.0
Histidine Metabolism	43	1	1.22	0.716	1.0	1.0
Fatty acid Metabolism	43	1	1.22	0.716	1.0	1.0
Steroid Biosynthesis	48	1	1.36	0.756	1.0	1.0
Pyrimidine Metabolism	59	1	1.67	0.825	1.0	1.0
Arachidonic Acid Metabolism	69	1	1.95	0.871	1.0	1.0

Table S8: Pathway enrichments for LPS-treated cells. Data corresponds to Fig 7B.

Metabolite Set	Total	Hits	Expected	P value	Holm P	FDR
Phenylalanine and Tyrosine Metabolism	28	3	0.601	0.0199	1.0	0.891
Trehalose Degradation	11	2	0.236	0.0215	1.0	0.891
Warburg Effect	58	4	1.24	0.0314	1.0	0.891
Fatty Acid Biosynthesis	35	3	0.751	0.036	1.0	0.891
Mitochondrial Electron Transport Chain	19	2	0.408	0.0603	1.0	0.936
Tyrosine Metabolism	72	4	1.55	0.0624	1.0	0.936
Catecholamine Biosynthesis	20	2	0.429	0.0662	1.0	0.936
Arginine and Proline Metabolism	53	3	1.14	0.1	1.0	1.0
Urea Cycle	29	2	0.622	0.126	1.0	1.0
Glycine and Serine Metabolism	59	3	1.27	0.128	1.0	1.0
Valine, Leucine and Isoleucine Degradation	60	3	1.29	0.133	1.0	1.0
Citric Acid Cycle	32	2	0.687	0.148	1.0	1.0
Aspartate Metabolism	35	2	0.751	0.171	1.0	1.0
Gluconeogenesis	35	2	0.751	0.171	1.0	1.0
Ketone Body Metabolism	13	1	0.279	0.247	1.0	1.0
Glucose-Alanine Cycle	13	1	0.279	0.247	1.0	1.0
Thyroid hormone synthesis	13	1	0.279	0.247	1.0	1.0

Vitamin K Metabolism	14	1	0.3	0.263	1.0	1.0
Pyruvate Metabolism	48	2	1.03	0.275	1.0	1.0
Glutamate Metabolism	49	2	1.05	0.284	1.0	1.0
Alanine Metabolism	17	1	0.365	0.311	1.0	1.0
Alpha Linolenic Acid and Linoleic Acid Metabolism	19	1	0.408	0.34	1.0	1.0
Butyrate Metabolism	19	1	0.408	0.34	1.0	1.0
Ethanol Degradation	19	1	0.408	0.34	1.0	1.0
Threonine and 2-Oxobutanoate Degradation	20	1	0.429	0.355	1.0	1.0
Glutathione Metabolism	21	1	0.451	0.369	1.0	1.0
Carnitine Synthesis	22	1	0.472	0.383	1.0	1.0
Glycerolipid Metabolism	25	1	0.537	0.422	1.0	1.0
Glycolysis	25	1	0.537	0.422	1.0	1.0
Oxidation of Branched Chain Fatty Acids	26	1	0.558	0.435	1.0	1.0
Phytanic Acid Peroxisomal Oxidation	26	1	0.558	0.435	1.0	1.0
Selenoamino Acid Metabolism	28	1	0.601	0.46	1.0	1.0
Pentose Phosphate Pathway	29	1	0.622	0.472	1.0	1.0
Fructose and Mannose Degradation	32	1	0.687	0.506	1.0	1.0
Amino Sugar Metabolism	33	1	0.708	0.517	1.0	1.0
Fatty Acid Elongation In Mitochondria	35	1	0.751	0.538	1.0	1.0
Galactose Metabolism	38	1	0.816	0.568	1.0	1.0
Propanoate Metabolism	42	1	0.901	0.606	1.0	1.0
Fatty acid Metabolism	43	1	0.923	0.614	1.0	1.0
Steroid Biosynthesis	48	1	1.03	0.656	1.0	1.0
Pyrimidine Metabolism	59	1	1.27	0.732	1.0	1.0
Tryptophan Metabolism	60	1	1.29	0.738	1.0	1.0
Bile Acid Biosynthesis	65	1	1.4	0.767	1.0	1.0
Purine Metabolism	74	1	1.59	0.811	1.0	1.0

Table S9: Pathway enrichments for FFA-treated cells. Data corresponds to Fig 7C.

Metabolite Set	Total	Hits	Expect	P value	Holm P	FDR
Urea Cycle	29	4	0.538	0.0015	0.148	0.101
Arginine and Proline Metabolism	53	5	0.982	0.00204	0.2	0.101
Fatty Acid Biosynthesis	35	4	0.649	0.00307	0.298	0.101
Glutathione Metabolism	21	3	0.389	0.00582	0.559	0.144
Glutamate Metabolism	49	4	0.908	0.0105	0.999	0.208
Glucose-Alanine Cycle	13	2	0.241	0.0225	1.0	0.371
Alanine Metabolism	17	2	0.315	0.0375	1.0	0.486
Propanoate Metabolism	42	3	0.779	0.0392	1.0	0.486
Butyrate Metabolism	19	2	0.352	0.0462	1.0	0.508
Pyruvate Metabolism	48	3	0.89	0.0551	1.0	0.543
Carnitine Synthesis	22	2	0.408	0.0603	1.0	0.543
Cysteine Metabolism	26	2	0.482	0.0812	1.0	0.551
Warburg Effect	58	3	1.08	0.0874	1.0	0.551
Glycine and Serine Metabolism	59	3	1.09	0.091	1.0	0.551
Phenylalanine and Tyrosine Metabolism	28	2	0.519	0.0924	1.0	0.551
Selenoamino Acid Metabolism	28	2	0.519	0.0924	1.0	0.551

Tryptophan Metabolism	60	3	1.11	0.0947	1.0	0.551
Lysine Degradation	30	2	0.556	0.104	1.0	0.572
Ammonia Recycling	32	2	0.593	0.116	1.0	0.605
Amino Sugar Metabolism	33	2	0.612	0.122	1.0	0.605
Aspartate Metabolism	35	2	0.649	0.135	1.0	0.609
Biotin Metabolism	8	1	0.148	0.139	1.0	0.609
Tyrosine Metabolism	72	3	1.33	0.143	1.0	0.609
Nicotinate and Nicotinamide Metabolism	37	2	0.686	0.148	1.0	0.609
Malate-Aspartate Shuttle	10	1	0.185	0.171	1.0	0.652
Pyruvaldehyde Degradation	10	1	0.185	0.171	1.0	0.652
D-Arginine and D-Ornithine Metabolism	11	1	0.204	0.187	1.0	0.661
Glycerol Phosphate Shuttle	11	1	0.204	0.187	1.0	0.661
Ketone Body Metabolism	13	1	0.241	0.217	1.0	0.716
Thyroid hormone synthesis	13	1	0.241	0.217	1.0	0.716
Vitamin K Metabolism	14	1	0.26	0.232	1.0	0.74
Beta Oxidation of Very Long Chain Fatty Acids	17	1	0.315	0.274	1.0	0.779
Spermidine and Spermine Biosynthesis	18	1	0.334	0.288	1.0	0.779
Alpha Linolenic Acid and Linoleic Acid Metabolism	19	1	0.352	0.301	1.0	0.779
Mitochondrial Electron Transport Chain	19	1	0.352	0.301	1.0	0.779
Ethanol Degradation	19	1	0.352	0.301	1.0	0.779
Valine, Leucine and Isoleucine Degradation	60	2	1.11	0.307	1.0	0.779
Catecholamine Biosynthesis	20	1	0.371	0.315	1.0	0.779
Vitamin B6 Metabolism	20	1	0.371	0.315	1.0	0.779
Lactose Synthesis	20	1	0.371	0.315	1.0	0.779
Betaine Metabolism	21	1	0.389	0.328	1.0	0.791
Glycerolipid Metabolism	25	1	0.463	0.377	1.0	0.816
Glycolysis	25	1	0.463	0.377	1.0	0.816
Oxidation of Branched Chain Fatty Acids	26	1	0.482	0.389	1.0	0.816
Phytanic Acid Peroxisomal Oxidation	26	1	0.482	0.389	1.0	0.816
Inositol Phosphate Metabolism	26	1	0.482	0.389	1.0	0.816
Plasmalogen Synthesis	26	1	0.482	0.389	1.0	0.816
Mitochondrial Beta-Oxidation of Short Chain Saturated Fatty Acids	27	1	0.5	0.401	1.0	0.816
Purine Metabolism	74	2	1.37	0.404	1.0	0.816
Mitochondrial Beta-Oxidation of Long Chain Saturated Fatty Acids	28	1	0.519	0.412	1.0	0.816
Folate Metabolism	29	1	0.538	0.423	1.0	0.821
Citric Acid Cycle	32	1	0.593	0.456	1.0	0.845
Fructose and Mannose Degradation	32	1	0.593	0.456	1.0	0.845
Inositol Metabolism	33	1	0.612	0.466	1.0	0.845
Beta-Alanine Metabolism	34	1	0.63	0.476	1.0	0.845
Fatty Acid Elongation In Mitochondria	35	1	0.649	0.486	1.0	0.845
Gluconeogenesis	35	1	0.649	0.486	1.0	0.845
Methionine Metabolism	43	1	0.797	0.56	1.0	0.925
Histidine Metabolism	43	1	0.797	0.56	1.0	0.925

Fatty acid Metabolism	43	1	0.797	0.56	1.0	0.925
Steroid Biosynthesis	48	1	0.89	0.601	1.0	0.976
Pyrimidine Metabolism	59	1	1.09	0.679	1.0	1.0
Bile Acid Biosynthesis	65	1	1.2	0.715	1.0	1.0
Arachidonic Acid Metabolism	69	1	1.28	0.737	1.0	1.0

Table S10: Intracellular metabolic pathway impacts of control cells. Data corresponds to Fig 7E.

Pathway Name	Match Status	p	-log(p)	Holm p	FDR	Impact
Carnitine Synthesis	3/16	0.0054105	2.2668	0.53564	0.31455	0.13235
Fatty Acid Biosynthesis	4/33	0.0063545	2.1969	0.62274	0.31455	0.067308
Citric Acid Cycle	3/26	0.021473	1.6681	1.0	0.58429	0.08
Valine, Leucine and Isoleucine Degradation	4/51	0.029047	1.5369	1.0	0.58429	0.028571
Threonine and 2-Oxobutanoate Degradation	2/13	0.036057	1.443	1.0	0.58429	0.175
Mitochondrial Electron Transport Chain	2/15	0.047154	1.3265	1.0	0.58429	0.037383
Butyrate Metabolism	2/16	0.05317	1.2748	1.0	0.58429	0.078125
Glycerolipid Metabolism	2/23	0.10127	0.99452	1.0	0.87748	0.1
Arginine and Proline Metabolism	3/48	0.10147	0.99394	1.0	0.87748	0.018868
Warburg Effect	3/49	0.10636	0.97322	1.0	0.87748	0.044444
Phenylalanine and Tyrosine Metabolism	2/25	0.1167	0.93292	1.0	0.88873	0.10145
Biotin Metabolism	1/7	0.15557	0.80824	1.0	0.99529	0.1
Homocysteine Degradation	1/7	0.15557	0.80824	1.0	0.99529	0.1
Bile Acid Biosynthesis	3/59	0.16086	0.79356	1.0	0.99529	0.016634
Porphyrin Metabolism	2/36	0.20974	0.67831	1.0	1.0	0.033835
Trehalose Degradation	1/11	0.23367	0.63139	1.0	1.0	0.034483
Methionine Metabolism	2/39	0.23655	0.62608	1.0	1.0	0.033149
Alanine Metabolism	1/14	0.28769	0.54107	1.0	1.0	0.028571
Glutamate Metabolism	2/45	0.29075	0.53649	1.0	1.0	0.017442
Plasmalogen Synthesis	1/16	0.32166	0.49261	1.0	1.0	0.05

Table S11: Intracellular metabolic pathway impacts of LPS-treated cells. Data corresponds to Fig 7F.

Pathway Name	Match Status	p	-log(p)	Holm p	FDR	Impact
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Phenylalanine and Tyrosine Metabolism	3/25	0.0072725	2.1383	0.71998	0.44378	0.19565
Tyrosine Metabolism	4/55	0.011069	1.9559	1.0	0.44378	0.043902
Trehalose Degradation	2/11	0.013448	1.8713	1.0	0.44378	0.068966
Catecholamine Biosynthesis	2/14	0.021597	1.6656	1.0	0.48855	0.10417
Mitochondrial Electron Transport Chain	2/15	0.024674	1.6078	1.0	0.48855	0.037383
Warburg Effect	3/49	0.045275	1.3441	1.0	0.74704	0.044444
Citric Acid Cycle	2/26	0.068509	1.1643	1.0	0.96891	0.066667
Fatty Acid Biosynthesis	2/33	0.10391	0.98336	1.0	1.0	0.028846
Ketone Body Metabolism	1/12	0.18538	0.73194	1.0	1.0	0.055556
Arginine and Proline Metabolism	2/48	0.1918	0.71715	1.0	1.0	0.012579
Threonine and 2-Oxobutanoate Degradation	1/13	0.19927	0.70056	1.0	1.0	0.05
Valine, Leucine and Isoleucine Degradation	2/51	0.21059	0.67655	1.0	1.0	0.011429
Butyrate Metabolism	1/16	0.23961	0.62049	1.0	1.0	0.03125
Carnitine Synthesis	1/16	0.23961	0.62049	1.0	1.0	0.088235
Bile Acid Biosynthesis	2/59	0.26166	0.58227	1.0	1.0	0.0088063
Phytanic Acid Peroxisomal Oxidation	1/19	0.27804	0.55589	1.0	1.0	0.05
Glycolysis	1/20	0.29044	0.53695	1.0	1.0	0.027273
Oxidation of Branched Chain Fatty Acids	1/22	0.31463	0.50219	1.0	1.0	0.022388
Urea Cycle	1/23	0.32644	0.4862	1.0	1.0	0.0075758
Glycerolipid Metabolism	1/23	0.32644	0.4862	1.0	1.0	0.0625

Table S12: Intracellular metabolic pathway impacts of FFA-treated cells. Data corresponds to Fig 7G.

Pathway Name	Match Status	p	-log(p)	Holm p	FDR	Impact
Fatty Acid Biosynthesis	3/33	0.011099	1.9547	1.0	0.72466	0.048077
Butyrate Metabolism	2/16	0.021959	1.6584	1.0	0.72466	0.078125
Carnitine Synthesis	2/16	0.021959	1.6584	1.0	0.72466	0.11765
Cysteine Metabolism	2/24	0.047154	1.3265	1.0	1.0	0.069767
Biotin Metabolism	1/7	0.09982	1.0008	1.0	1.0	0.1
Arginine and Proline Metabolism	2/48	0.15707	0.80389	1.0	1.0	0.015723
Ketone Body Metabolism	1/12	0.16534	0.78163	1.0	1.0	0.055556
Catecholamine Biosynthesis	1/14	0.19028	0.72061	1.0	1.0	0.0625

Tyrosine Metabolism	2/55	0.19491	0.71016	1.0	1.0	0.039024
Mitochondrial Electron Transport Chain	1/15	0.20248	0.69361	1.0	1.0	0.018692
Plasmalogen Synthesis	1/16	0.21452	0.66854	1.0	1.0	0.05
Bile Acid Biosynthesis	2/59	0.21714	0.66327	1.0	1.0	0.008806 3
Mitochondrial Beta-Oxidation of Short Chain Saturated Fatty Acids	1/17	0.22638	0.64515	1.0	1.0	0.027273
Sulfate/Sulfite Metabolism	1/19	0.24961	0.60273	1.0	1.0	0.029412
Phytanic Acid Peroxisomal Oxidation	1/19	0.24961	0.60273	1.0	1.0	0.05
Lysine Degradation	1/20	0.26098	0.58339	1.0	1.0	0.069307
Oxidation of Branched Chain Fatty Acids	1/22	0.28324	0.54784	1.0	1.0	0.022388
Urea Cycle	1/23	0.29413	0.53145	1.0	1.0	0.015152
Glycerolipid Metabolism	1/23	0.29413	0.53145	1.0	1.0	0.0625
Mitochondrial Beta-Oxidation of Long Chain Saturated Fatty Acids	1/24	0.30487	0.51588	1.0	1.0	0.015