Supporting Information

Identification of GPR35 involved metabolic characteristics using LC-MS/MS-based metabolomics and lipidomics

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Extended Methods

Chemical derivatization

For amino and phenol metabolite derivatization, 20 μL of ACN-H_2O (1:1, v/v), 100 μL of carbonate buffer (pH 10), and 100 μL of Dns-Cl solution (20 mM) were pipetted into each dried sample. The resulting mixture was incubated at 35 °C for 15 min. After that, 40 μL of NaOH solution (100 mM) was added to the sample and incubated at 35 °C for 10 min to quench the reaction. The excessive alkaline was removed by adding 40 μL of formic acid (425 mM). For carboxyl submetabolome derivatization, the dried sample was mixed with 20 μL of ACN-MeOH-H_2O (2:2:1, v/v/v), 40 μL of MeOH, 20 μL of HATU solution (6 mM), and 20 μL of Dns-PP solution (12 mM). After mixing, the derivatization reaction solution was incubated at 55 °C for 20 min.

Instrument analysis

Metabolite quantification was performed on a Shimadzu Nexera UPLC system interfaced with an 8060 triple quadruple mass spectrometer (Shimadzu, Kyoto, Japan) equipped with an electrospray ionization (ESI) source. The autosampler was kept at 4 °C. The chromatography separation was performed on an Agilent Zorbax Eclipse XDB-C18 column (2.1 × 100 mm, 1.8 μm, Agilent Technologies, Santa Clara, CA) at 50 °C. Mobile phase A was 0.1% formic acid in the water, and mobile B was methanol. The chromatographic gradient was run at a flow rate of 0.40 mL/min as follows: for Dns-Cl derivatized products, 0-2 min (30% B), 2-5 min (30%-52% B), 5-15 min (52%-65% B), 15-20 min (65%-78% B), 20-23 min (78% B), 23-27 min (100% B), and 27-29 min (30% B); for Dns-PP derivatized products, 0-2 min (30% B), 2-5 min (30%-52% B), 5-15 min (52%-65% B), 15-20 min (65%-78% B), 20-22.5 min (78% B), 22.5-29 min (90% B), 29-38 min (100% B), and 38-40 min (30% B). The mass spectrometer was operated by scheduled multiple reaction monitoring (MRM) in positive ion mode with the optimal parameters as follows: spray voltage, 4.5 kV; nebulizing gas, 3 L/min; drying gas, 15 L/min; heat block temperature, 400 °C; desorption line temperature, 250 °C. The optimized MRM transitions are listed in Table S4.

Table S1. The oligonucleotide sequences for lentiviral vectors.

Virus type		Sequence
Knock-down	Forward	GATCCGCATCTACATGACCAACCTGGTTCAAGAGACCAG GTTGGTCATGTAGATGCTTTTTTG
	Reverse	AATTCAAAAAAGCATCTACATGACCAACCTGGTCTCTTGA ACCAGGTTGGTCATGTAGATGCG
Over-expression	>NM_001195381.3:851-1873 Homo G protein-coupled receptor 35 (GPR35), transcript variant 2, mRNA	

Table S2. The primer sequences for RT-PCR.

Oligo	Primer sequences		Source
Human GPR35	Forward primer	5’-AACCTCCTGGTGTTCGTGGTCT-3’	Takara
	Reverse primer	5’-GCAGTTGGCATCTGAGAGCTTG-3’	Takara
Human GAPDH	Forward primer	5’-GGAGCGAGATCCCTCCAAAAT-3’	Takara
	Reverse primer	5’-GGCTGTTGTCATACTTCTCATGG-3’	Takara

Table S3. The antibodies used for western blot analysis.

Antibody	Dilution rate	catalog number	manufacturer
GPR35	1:1000	55248-1-AP	Proteintech
ERK1/2	1:1000	4695	Cell Signaling Technology
pERK1/2	1:1000	AF1015	Affinity
α-Tubulin	1:8000	66031-1	Proteintech
HRP-conjugated Affinipure Goat Anti-Mouse IgG(H+L)	1 :8000	SA00001-1	Proteintech
HRP-conjugated Affinipure Goat Anti-Rabbit IgG(H+L)	1 :8000	SA00001-2	Proteintech

Table S4. The optimized MRM transitions and parameters for the analysis of Dns-Cl and Dns-PP labeled metabolites.

No.	Dns-Compound	Abbreviation	MW	Class	RT (min)	CE (V)	Parent ion (m/z)	Fragment (m/z)	Derivatization
1	Ethanolamine	EA	61.08	Amines	5.75	-15	295.00	156.60	Dns-Cl
2	Putrescine	Put	88.15	Amines	17.40	-37	555.20	170.10	Dns-Cl
3	L-Histidine	His	155.15	Amino acids	18.45	-35	622.70	169.70	Dns-Cl
4	L-Arginine	Arg	174.20	Amino acids	3.75	-36	408.10	170.20	Dns-Cl
5	L-Asparagine	Asn	132.12	Amino acids	3.95	-35	366.10	170.10	Dns-Cl
6	L-Glutamine	Gln	146.14	Amino acids	4.52	-25	380.20	169.50	Dns-Cl
7	L-Serine	Ser	105.09	Amino acids	5.09	-15	338.70	169.50	Dns-Cl
8	L-Glycine	Gly	75.07	Amino acids	5.71	-15	309.00	156.50	Dns-Cl
9	L-Threonine	Thr	119.12	Amino acids	6.08	-20	353.20	157.20	Dns-Cl
10	L-Alanine	Ala	89.09	Amino acids	6.53	-15	323.20	156.50	Dns-Cl
11	L-Proline	Pro	115.13	Amino acids	8.09	-18	349.00	169.50	Dns-Cl
12	L-Methionine	Met	149.21	Amino acids	8.75	-15	383.00	169.50	Dns-Cl
13	L-Valine	Val	117.15	Amino acids	9.04	-15	351.10	156.70	Dns-Cl
14	L-Tryptophan	Trp	204.23	Amino acids	9.61	-29	438.20	170.10	Dns-Cl
15	L-Isoleucine	Ile	131.17	Amino acids	11.18	-15	365.00	156.50	Dns-Cl
16	L-Leucine	Leu	131.17	Amino acids	11.42	-15	365.00	156.50	Dns-Cl
17	L-Phenylalanine	Phe	165.19	Amino acids	11.50	-25	399.10	169.50	Dns-Cl
18	Ornithine	Orn	132.16	Amino acids	14.99	-25	599.20	170.00	Dns-Cl
19	L-Lysine	Lys	146.19	Amino acids	15.91	-25	613.20	170.10	Dns-Cl
20	L-Tyrosine	Tyr	181.19	Amino acids	20.11	-25	648.20	170.10	Dns-Cl
21	L-Aspartic acid	Asp	133.10	Amino acids	3.95	-35	367.37	170.10	Dns-Cl

No.	Dns-Compound	Abbreviation	MW	Class	RT (min)	CE (V)	Parent ion (m/z)	Fragment (m/z)	Derivatization
22	L-Glutamic acid	Glu	147.13	Amino acids	5.30	-35	381.40	169.50	Dns-Cl
23	L-Citrulline	Cit	175.19	Amino acids	4.91	-35	409.45	170.10	Dns-Cl
24	Nε-Methyl-L-lysine	MeLys	160.21	Amino acids	18.41	-41	626.85	170.15	Dns-Cl
25	Nε-Nε-Nε-Trimethyl-L-lysine	TMeLys	188.27	Amino acids	3.46	-32	422.05	170.15	Dns-Cl
26	Nε-Acetyl-L-lysine	AceLys	188.22	Amino acids	6.16	-32	421.75	170.15	Dns-Cl
27	NG-NG'-Dimethyl-L-arginine	SDMA	202.25	Amino acids	4.49	-35	435.80	170.15	Dns-Cl
28	NG,NG-Dimethy-L-arginine	ADMA	202.25	Amino acids	4.33	-36	435.80	170.15	Dns-Cl
29	NG-Methyl-L-arginine	MeArg	188.23	Amino acids	4.12	-34	422.00	170.15	Dns-Cl
30	Cholic acid	CA	408.58	Bile acids	23.59	-36	710.00	320.10	Dns-PP
31	Chenodeoxycholic acid	CDCA	392.57	Bile acids	24.17	-37	693.80	320.20	Dns-PP
32	Deoxycholic Acid	DCA	392.57	Bile acids	24.38	-36	694.20	320.20	Dns-PP
33	Lithocholic acid	LCA	376.57	Bile acids	25.26	-33	678.05	320.15	Dns-PP
34	Glycocholic acid	GCA	465.62	Bile acids	21.97	-34	767.55	320.20	Dns-PP
35	Ursodeoxycholic acid	UDCA	392.57	Bile acids	21.89	-36	694.60	320.20	Dns-PP
36	Glycodeoxycholic acid	GDCA	449.62	Bile acids	23.89	-33	751.25	320.20	Dns-PP
37	Glycochenodeoxycholic Acid	GCDCA	449.62	Bile acids	23.72	-36	751.05	320.10	Dns-PP
38	Glycoursodeoxycholic acid	GUDCA	449.62	Bile acids	20.48	-34	751.55	320.20	Dns-PP
39	L-Carnitine	Car	161.20	Acylcarnitines	4.99	-31	463.10	386.15	Dns-PP
40	L-Acetylcarnitine	Car2	203.24	Acylcarnitines	5.43	-27	505.25	386.15	Dns-PP
41	3-Hydroxybutyryl-carnitine	Car4-OH	247.29	Acylcarnitines	5.72	-28	549.30	386.05	Dns-PP
42	Butyrylcarnitine	Car4	231.29	Acylcarnitines	6.60	-27	533.30	386.15	Dns-PP
43	Tiglylcarnitine	Car5:1	243.30	Acylcarnitines	6.96	-25	545.10	386.15	Dns-PP

No.	Dns-Compound	Abbreviation	MW	Class	RT (min)	CE (V)	Parent ion (m/z)	Fragment (m/z)	Derivatization
44	Isovaleryl-L-carnitine	isoCar5	245.32	Acylcarnitines	7.49	-27	547.35	386.15	Dns-PP
45	Valerylcarnitine	Car5	245.32	Acylcarnitines	7.78	-26	547.15	386.15	Dns-PP
46	3-Hydroxyhexanoyl carnitine	Car6-OH	275.34	Acylcarnitines	7.25	-29	577.15	386.15	Dns-PP
47	Hexanoylcarnitine	Car6	259.34	Acylcarnitines	9.33	-27	561.15	386.15	Dns-PP
48	L-Octanoylcarnitine	Car8	287.40	Acylcarnitines	13.45	-29	588.90	386.15	Dns-PP
49	3-Hydroxydodecanoyl-L- carnitine	Car12-OH	359.50	Acylcarnitines	18.27	-32	661.40	386.15	Dns-PP
50	Decanoyl-L-carnitine	Car10	315.45	Acylcarnitines	17.51	-29	617.35	386.15	Dns-PP
51	trans-2-Dodecenoyl-L-carnitine	Car12:1	341.49	Acylcarnitines	19.31	-29	643.40	386.05	Dns-PP
52	Lauroyl-L-carnitine	Car12	343.50	Acylcarnitines	19.84	-30	645.40	386.15	Dns-PP
53	cis,cis-5,8-Tetradecandienoyl-L-carnitine	Car14:2	367.52	Acylcarnitines	19.73	-30	669.55	386.15	Dns-PP
54	trans-2-Tetradecenoyl-L-carnitine	Car14:1	369.54	Acylcarnitines	21.05	-28	671.55	386.15	Dns-PP
55	Myristoyl-L-carnitine	Car14	371.55	Acylcarnitines	21.50	-30	673.45	386.05	Dns-PP
56	cis,cis-9,12-Octadecadienoyl-L-carnitine	Car18:2	423.63	Acylcarnitines	23.03	-31	725.55	386.15	Dns-PP
57	trans-2-Hexadecenoyl-L-carnitine	Car16:1	397.59	Acylcarnitines	23.09	-30	699.60	386.15	Dns-PP
58	3-Hydroxyoctadecanoyl-L-carnitine	Car18-OH	443.66	Acylcarnitines	23.76	-33	745.60	386.15	Dns-PP
59	Palmitoyl-L-carnitine	Car16	399.61	Acylcarnitines	23.70	-33	702.25	386.15	Dns-PP
60	Oleoyl-L-carnitine	Car18:1	425.64	Acylcarnitines	23.77	-32	727.65	386.15	Dns-PP
61	Stearoyl-L-carnitine	Car18	427.66	Acylcarnitines	23.87	-33	729.10	386.05	Dns-PP
62	Acetic acid	C2	60.05	Fatty acids	7.47	-28	362.20	320.00	Dns-PP
63	Propionic acid	C3	74.08	Fatty acids	8.91	-23	376.20	320.10	Dns-PP
64	Isobutyric acid	C4-2	88.11	Fatty acids	10.53	-20	390.30	320.10	Dns-PP
65	Butyric acid	C4-1	88.11	Fatty acids	10.89	-20	390.30	320.10	Dns-PP

No.	Dns-Compound	Abbreviation	MW	Class	RT (min)	CE (V)	Parent ion (m/z)	Fragment (m/z)	Derivatization
66	2-Methylbutyric acid	C5-1	102.13	Fatty acids	12.67	-19	403.80	320.10	Dns-PP
67	Isovaleric acid	C5-2	102.13	Fatty acids	13.03	-20	404.10	320.20	Dns-PP
68	Valeric acid	C5-3	102.13	Fatty acids	13.54	-19	404.10	320.10	Dns-PP
69	3-Methylvaleric acid	C6-2	116.16	Fatty acids	15.66	-19	418.10	320.1	Dns-PP
70	Isocaproic acid	C6-3	116.16	Fatty acids	16.08	-20	418.10	320.20	Dns-PP
71	Hexanoic acid	C6-1	116.16	Fatty acids	16.45	-30	418.10	320.00	Dns-PP
72	2-Methylhexanoic acid	C7-2	130.18	Fatty acids	17.93	-19	432.1	320.20	Dns-PP
73	Heptanoic acid	C7-1	130.18	Fatty acids	18.78	-20	432.10	320.20	Dns-PP
74	2-Ethylhexanoic acid	C8-3	144.21	Fatty acids	19.29	-18	446.10	320.20	Dns-PP
75	2-Methylheptanoic Acid	C8-2	144.21	Fatty acids	19.79	-20	446.10	320.10	Dns-PP
76	Octanoic acid	C8-1	144.21	Fatty acids	20.52	-21	446.10	320.20	Dns-PP
77	4-Methyloctanoic acid	C9-2	158.24	Fatty acids	21.60	-21	460.10	320.10	Dns-PP
78	Nonanoic acid	C9-1	158.24	Fatty acids	22.03	-21	460.10	170.00	Dns-PP
79	Decanoic acid	C10	172.26	Fatty acids	23.70	-22	473.60	170.00	Dns-PP
80	Dodecanoic acid	C12	200.32	Fatty acids	24.79	-22	501.70	320.30	Dns-PP
81	Tridecanoic acid	C13	214.34	Fatty acids	25.43	-24	515.90	320.10	Dns-PP
82	Myristic acid	C14	228.37	Fatty acids	26.21	-40	530.40	320.00	Dns-PP
83	cis-5,8,11,14,17-Eicosapentaenoic acid	C20:5	302.45	Fatty acids	26.34	-38	604.20	320.00	Dns-PP
84	γ-Linolenic acid	C18:3	278.43	Fatty acids	26.41	-44	580.00	320.10	Dns-PP
85	Palmitoleic acid	C16:1	254.41	Fatty acids	26.71	-23	556.50	320.10	Dns-PP
86	Pentadecanoic acid	C15	242.40	Fatty acids	27.17	-35	544.20	320.00	Dns-PP
87	cis-4,7,10,13,16,19- Docosahexaenoic acid	C22:6	328.49	Fatty acids	27.19	-21	630.30	157.00	Dns-PP

No.	Dns-Compound	Abbreviation	MW	Class	RT (min)	CE (V)	Parent ion (m/z)	Fragment (m/z)	Derivatization
88	Arachidonic acid	C20:4	304.47	Fatty acids	27.39	-24	606.20	157.00	Dns-PP
89	Linoleic acid	C18:2	280.45	Fatty acids	27.45	-24	582.30	263.45	Dns-PP
90	Palmitic acid	C16	256.42	Fatty acids	28.40	-45	558.20	320.00	Dns-PP
91	Oleic acid	C18:1	282.46	Fatty acids	29.13	-37	584.30	319.50	Dns-PP
92	Stearic acid	C18	284.48	Fatty acids	30.65	-26	586.30	320.10	Dns-PP
93	cis-11-Eicosenoic acid	C20:1	310.51	Fatty acids	30.84	-37	612.30	320.00	Dns-PP
94	Nonadecanoic acid	C19	298.50	Fatty acids	31.12	-26	600.50	320.10	Dns-PP
95	Erucic acid	C22:1	338.57	Fatty acids	31.74	-27	640.50	320.10	Dns-PP
96	Heneicosanoic acid	C21	326.56	Fatty acids	32.07	-27	628.40	320.20	Dns-PP
97	Behenic acid	C22	340.58	Fatty acids	32.54	-29	642.00	320.20	Dns-PP
98	Nervonic acid	C24:1	366.62	Fatty acids	32.67	-29	668.30	320.20	Dns-PP
99	elaidic acid	isoC18:1	282.46	Fatty acids	29.48	-27	584.88	320.10	Dns-PP
100	Kynurenine	KYN	208.21	Indole derivatives	8.89	-33	442.20	170.15	Dns-Cl
101	Xanthurenic Acid	XA	205.17	Indole derivatives	9.51	-25	439.10	170.10	Dns-Cl
102	6-Hydroxymelatonin	6-HMT	248.28	Indole derivatives	11.74	-33	482.20	170.05	Dns-Cl
103	5-Hydroxyindoleacetate	HIAA	191.18	Indole derivatives	11.92	-27	425.10	170.10	Dns-Cl
104	N-Acetyl-Serotonin	NAS	218.25	Indole derivatives	12.02	-24	452.15	170.05	Dns-Cl
105	Tryptamine	Trpm	160.22	Indole derivatives	13.25	-30	394.20	170.05	Dns-Cl
106	3-Hydroxyanthranilic Acid	HAA	153.14	Indole derivatives	15.54	-19	387.20	170.10	Dns-Cl
107	Kynurenic Acid	KA	189.17	Indole derivatives	17.14	-28	423.15	170.15	Dns-Cl
108	3-Hydroxy-DL-Kynurenine	HK	224.21	Indole derivatives	20.62	-44	691.20	170.05	Dns-Cl
109	Serotonin	5-HT	176.22	Indole derivatives	20.79	-27	643.20	170.05	Dns-Cl

No.	Dns-Compound	Abbreviation	MW	Class	RT (min)	CE (V)	Parent ion (m/z)	Fragment (m/z)	Derivatization
110	Indole-3-carboxaldehyde	IAld	145.16	Indole derivatives	18.68	-37	379.15	169.50	Dns-Cl
111	5-Hydroxy-L-tryptophan	5-HTP	220.23	Indole derivatives	18.48	-44	687.30	170.20	Dns-Cl
112	2-Oxoadipic Acid	2-OAA	160.12	Indole derivatives	19.62	-47	763.45	170.10	Dns-PP
113	Indolelactic acid	ILA	205.21	Indole derivatives	11.19	-30	507.15	170.10	Dns-PP
114	5-Methoxyindoleacetic Acid	5-MIAA	205.22	Indole derivatives	11.20	-23	507.00	320.10	Dns-PP
115	Indole-3-Acetic Acid	IAA	175.18	Indole derivatives	12.43	-21	477.20	320.20	Dns-PP
116	3-Indolepropionic acid	IPA	189.21	Indole derivatives	13.60	-22	491.65	320.10	Dns-PP
117	2-Picolinic acid	PA	123.11	Indole derivatives	8.95	-29	425.05	170.10	Dns-PP
118	Xanthine	Xan	152.11	Nucleotide Metabolism	7.26	-35	386.30	170.00	Dns-Cl
119	Hypoxanthine	Hyp	136.11	Nucleotide Metabolism	8.45	-22	369.90	169.70	Dns-Cl
120	cytosine	Cyt	111.10	Nucleotide Metabolism	6.87	-22	345.00	170.15	Dns-Cl
121	5-Methylcytosine	MeCyt	125.13	Nucleotide Metabolism	7.73	-20	358.95	170.20	Dns-Cl
122	2'-Deoxycytidine	dC	227.22	Nucleotide Metabolism	6.46	-21	461.00	112.15	Dns-Cl
123	5-Methyl-2'-deoxycytidine	MedC	241.24	Nucleotide Metabolism	6.65	-21	475.00	126.20	Dns-Cl
124	Cytidine	Cyd	243.22	Nucleotide Metabolism	5.75	-20	477.10	112.10	Dns-Cl
125	5-Methylcytidine	MeCyd	257.24	Nucleotide Metabolism	5.92	-23	491.00	126.20	Dns-Cl
126	Adenine	Ade	135.13	Nucleotide Metabolism	9.33	-24	369.00	170.20	Dns-Cl
127	1-Methyladenine	MeAde	149.15	Nucleotide Metabolism	5.91	-27	382.70	170.10	Dns-Cl
128	Adenosine	Ado	267.24	Nucleotide Metabolism	5.33	-33	500.95	136.20	Dns-Cl
129	1-Methyladenosine	MeAdo	281.27	Nucleotide Metabolism	3.50	-30	514.80	150.10	Dns-Cl
130	2′-Deoxyadenosine	dA	251.24	Nucleotide Metabolism	8.89	-55	485.00	119.20	Dns-Cl
131	Guanine	Gua	151.13	Nucleotide Metabolism	7.81	-25	384.90	170.10	Dns-Cl

No.	Dns-Compound	Abbreviation	MW	Class	RT (min)	CE (V)	Parent ion (m/z)	Fragment (m/z)	Derivatization
132	Guanosine	Guo	283.24	Nucleotide Metabolism	4.33	-57	517.00	135.10	Dns-Cl
133	2′-Deoxyguanosine	dG	267.24	Nucleotide Metabolism	8.10	-21	501.00	152.10	Dns-Cl
134	Uracil	Ura	112.09	Nucleotide Metabolism	8.43	-15	345.95	169.70	Dns-Cl
135	Uridine	Urd	244.20	Nucleotide Metabolism	6.88	-24	477.95	113.20	Dns-Cl
136	2′-Deoxyuridine	dU	228.20	Nucleotide Metabolism	8.25	-30	461.95	113.20	Dns-Cl
137	Thymine	Thy	126.12	Nucleotide Metabolism	10.40	-18	359.90	169.50	Dns-Cl
138	Thymidine	Thd	242.23	Nucleotide Metabolism	9.20	-29	476.00	127.10	Dns-Cl
139	4-Aminobutyric acid	GABA	103.12	Organic acids	6.52	-20	337.00	169.50	Dns-Cl
140	α-Ketoglutaric acid	KGA	146.10	Organic acids	19.69	-35	748.95	320.20	Dns-PP
141	Succinic acid	SAD	118.09	Organic acids	18.52	-60	721.45	170.20	Dns-PP
142	Fumaric acid	FC 33	116.07	Organic acids	18.87	-51	719.10	170.00	Dns-PP
143	Malic acid	MalA	134.09	Organic acids	17.87	-59	737.40	170.20	Dns-PP
144	Pyruvic acid	PyrA	88.06	Organic acids	8.71	-40	390.00	170.20	Dns-PP
145	Citric acid	CitrA	192.12	Organic acids	23.88	-57	1096.90	320.20	Dns-PP
146	Ketoleucine	KICA	130.14	Organic acids	16.09	-26	432.25	170.20	Dns-PP
147	3-Methyl-2-oxovaleric acid	KMVA	130.14	Organic acids	15.65	-24	432.25	170.00	Dns-PP
148	alpha-Ketoisovaleric acid	KIVA	116.12	Organic acids	12.73	-24	418.25	170.20	Dns-PP
149	3-Hydroxybutyric acid	BHB	104.10	Organic acids	7.68	-43	406.00	320.20	Dns-PP
150	Isocitric acid	isoCitrA	192.12	Organic acids	23.68	-83	1096.80	170.10	Dns-PP

Table S5. The optimized MRM transitions and parameters for the analysis of lipids

No.	Compound	Parent ion (m/z)	Fragment (m/z)	RT (min)	CE (V)	No.	Compound	Parent ion (m/z)	Fragment (m/z)	RT (min)	CE (V)
1	DG 16:0_14:0	558.51	285.24	15.22	-30	25	DG 22:6_16:0	658.54	313.27	15.01	-30
2	DG 16:0_16:0	586.54	313.27	16.14	-30	26	DG 22:6_16:1	656.53	311.26	15.87	-30
3	DG 16:1_16:0	584.52	313.27	15.27	-30	27	DG 22:6_18:0	686.57	341.30	15.98	-30
4	DG 18:0_16:0	614.57	313.27	16.94	-30	28	TG 14:0_14:0_18:3	790.69	545.46	18.46	-30
5	DG 18:0_18:0	642.60	341.31	17.59	-30	29	TG 14:0_18:2_20:5	866.72	621.49	18.51	-30
6	DG 18:1_14:0	584.52	285.24	15.25	-30	30	TG 15:1_18:2_18:3	854.72	597.49	19.28	-30
7	DG 18:1_16:0	612.56	313.27	16.15	-30	31	TG 16:0_12:0_17:1	780.71	507.44	18.77	-30
8	DG 18:1_16:1	610.54	311.26	15.38	-30	32	TG 16:0_14:0_18:3	818.72	545.46	18.75	-30
9	DG 18:1_18:0	640.59	341.31	16.99	-30	33	TG 16:0_15:1_16:1	806.72	533.46	18.81	-30
10	DG 18:1_18:1	638.57	339.29	16.15	-30	34	TG 16:0_18:1_20:3	900.80	627.53	19.33	-30
11	DG 18:2_16:0	610.54	313.27	15.54	-30	35	TG 17:1_12:0_18:2	804.71	519.44	18.58	-30
12	DG 18:2_17:0	624.56	327.29	15.97	-30	36	TG 17:1_18:2_20:4	908.77	623.50	18.92	-30
13	DG 18:2_18:0	638.57	341.31	16.39	-30	37	TG 18:0_14:0_16:0	824.77	523.47	19.26	-30
14	DG 18:2_18:1	636.56	339.29	15.59	-30	38	TG 18:0_16:0_18:2	876.80	575.50	19.49	-30
15	DG 20:3_18:0	664.59	341.31	16.67	-30	39	TG 18:0_17:1_18:1	890.82	589.52	19.62	-30
16	DG 20:3_18:1	662.57	339.29	15.90	-30	40	TG 18:0_18:0_22:6	952.84	651.53	19.45	-30
17	DG 20:4_16:0	634.54	313.27	15.29	-30	41	TG 18:1_18:1_22:0	960.90	661.61	20.17	-30
18	DG 20:4_18:0	662.57	341.31	16.23	-30	42	TG 18:1_18:2_22:3	952.84	653.54	19.40	-30
19	DG 20:4_18:1	660.56	339.29	15.44	-30	43	TG 18:1_18:2_24:0	986.91	687.63	20.24	-30
20	DG 20:5_16:0	632.52	313.27	16.13	-30	44	TG 18:1_19:0_19:0	934.88	635.60	19.44	-30
21	DG 22:4_18:0	690.60	341.31	16.81	-30	45	TG 18:1_20:2_22:5	976.83	677.55	19.76	-30
22	DG 22:4_18:1	688.59	339.29	16.07	-30	46	TG 16:0e_16:0_16:0	810.79	537.52	19.28	-30
23	DG 22:5_16:0	660.56	313.27	15.33	-30	47	TG 20:0e_18:1_18:1	918.88	619.60	19.73	-30
24	DG 22:5_18:1	686.57	339.29	15.48	-30	48	TG 16:0p_16:0_16:0	808.77	535.51	19.06	-30
49	TG 20:0p_16:0_18:1	890.85	617.59	19.60	-30	76	PE 37:6	750.51	609.49	13.78	-30

No.	Compound	Parent ion (m/z)	Fragment (m/z)	RT (min)	CE (V)	No.	Compound	Parent ion (m/z)	Fragment (m/z)	RT (min)	CE (V)
50	TG 20:0p_18:1_18:1	916.87	617.59	19.66	-30	77	PE 38:1	774.60	633.58	16.23	-30
51	CE 20:3	692.63	369.35	16.81	-30	78	PE 38:2	772.59	631.57	15.36	-30
52	CE 20:4	690.62	369.35	17.05	-30	79	PE 38:3	770.57	629.55	14.77	-30
53	CE 20:5	688.60	369.35	19.13	-30	80	PE 38:4	768.55	627.53	14.40	-30
54	CE 22:6	714.62	369.35	19.25	-30	81	PE 38:5	766.54	625.52	13.38	-30
55	PE 32:0	692.52	551.50	13.49	-30	82	PE 38:6	764.52	623.50	12.58	-30
56	PE 32:1	690.51	549.49	13.12	-30	83	PE 38:7	762.51	621.49	11.77	-30
57	PE 33:1	704.52	563.50	15.01	-30	84	PE 39:4	782.57	641.55	15.61	-30
58	PE 33:2	702.51	561.49	13.29	-30	85	PE 39:5	780.55	639.53	15.14	-30
59	PE 34:1	718.54	577.52	14.26	-30	86	PE 39:6	778.54	637.52	14.83	-30
60	PE 34:2	716.52	575.50	13.30	-30	87	PE 40:1	802.63	661.61	17.09	-30
61	PE 34:3	714.51	573.49	12.32	-30	88	PE 40:2	800.62	659.60	16.27	-30
62	PE 35:1	732.55	591.53	14.75	-30	89	PE 40:3	798.60	657.58	15.70	-30
63	PE 35:2	730.54	589.52	13.84	-30	90	PE 40:4	796.59	655.57	15.09	-30
64	PE 35:4	726.51	585.49	13.99	-30	91	PE 40:5	794.57	653.55	14.45	-30
65	PE 36:0	748.59	607.57	15.29	-30	92	PE 40:6	792.55	651.53	14.04	-30
66	PE 36:1	746.57	605.55	15.26	-30	93	PE 40:7	790.54	649.52	13.06	-30
67	PE 36:2	744.55	603.53	14.43	-30	94	PE 42:1	830.66	689.64	17.76	-30
68	PE 36:3	742.54	601.52	13.58	-30	95	PE 42:4	824.62	683.60	16.36	-30
69	PE 36:4	740.52	599.50	13.23	-30	96	PE 42:6	820.59	679.57	14.60	-30
70	PE 36:5	738.51	597.49	12.23	-30	97	PE 42:7	818.57	677.55	14.12	-30
71	PE 37:1	760.59	619.57	15.73	-30	98	PE O-32:1	676.53	535.51	13.92	-30
72	PE 37:2	758.57	617.55	14.86	-30	99	PE O-33:2	688.53	547.51	12.01	-30
73	PE 37:3	756.55	615.53	14.40	-30	100	PE O-34:1	704.56	563.54	14.33	-30
74	PE 37:4	754.54	613.52	14.84	-30	101	PE O-35:2	716.56	575.54	13.31	-30
75	PE 37:5	752.52	611.50	14.05	-30	102	PE O-35:3	714.54	573.52	12.30	-30

No.	Compound	Parent ion (m/z)	Fragment (m/z)	RT (min)	CE (V)	No.	Compound	Parent ion (m/z)	Fragment (m/z)	RT (min)	CE (V)
103	PE O-36:1	732.59	591.57	14.76	-30	130	Cer d18:0/16:0	540.54	266.28	14.68	-30
104	PE O-36:2	730.57	589.55	13.85	-30	131	Cer d18:0/22:0	624.63	266.28	17.74	-30
105	PE O-36:4	726.54	585.52	13.98	-30	132	Cer d18:1/14:0	510.49	264.26	13.03	-30
106	PE O-36:5	724.53	583.51	13.81	-30	133	Cer d18:1/16:0	538.52	264.26	14.26	-30
107	PE O-37:2	744.59	603.57	14.43	-30	134	Cer d18:1/22:0	622.61	264.26	17.06	-30
108	PE O-37:3	742.57	601.55	13.59	-30	135	Cer d18:1/22:1	620.60	264.26	16.29	-30
109	PE O-38:1	760.62	619.60	15.69	-30	136	Cer d18:1/24:0	650.64	264.26	17.69	-30
110	PE O-38:2	758.61	617.59	14.85	-30	137	Cer d18:1/24:1	648.63	264.26	17.08	-30
111	PE O-38:3	756.59	615.57	14.26	-30	138	Cer d18:2/16:0	536.50	262.25	13.31	-30
112	PE O-38:4	754.57	613.55	14.06	-30	139	Cer d18:2/20:0	592.57	262.25	15.53	-30
113	PE O-38:5	752.56	611.54	14.09	-30	140	Cer d18:2/22:0	620.60	262.25	16.42	-30
114	PE O-38:6	750.54	609.52	13.79	-30	141	Cer d18:2/24:0	648.63	262.25	17.23	-30
115	PE O-38:7	748.53	607.51	15.28	-30	142	Cer d18:2/24:1	646.61	262.25	16.45	-30
116	PE O-40:2	786.64	645.62	15.88	-30	143	Cer d18:2/26:0	676.66	262.25	17.85	-30
117	PE O-40:3	784.62	643.60	15.29	-30	144	HexCer d18:0/18:0	730.62	266.28	15.81	-30
118	PE O-40:4	782.61	641.59	15.43	-30	145	HexCer d18:1/14:0	672.54	264.26	11.53	-30
119	PE O-40:5	780.59	639.57	15.00	-30	146	HexCer d18:1/16:0	700.57	264.26	12.89	-30
120	PE O-40:6	778.57	637.55	14.72	-30	147	HexCer d18:1/24:0	812.70	264.26	16.83	-30
121	PE O-42:5	808.62	667.60	14.99	-30	148	HexCer d18:1/24:1	810.68	264.26	16.00	-30
122	LPE 16:0	454.29	313.27	2.97	-30	149	HexCer d18:2/16:0	698.56	262.25	11.82	-30
123	LPE 17:0	468.31	327.29	3.79	-30	150	HexCer d18:2/22:0	782.65	262.25	15.32	-30
124	LPE 18:0	482.33	341.31	4.62	-30	151	HexCer d18:2/24:0	810.68	262.25	16.19	-30
125	LPE 18:1	480.31	339.29	3.08	-30	152	Hex_2Cer d18:1/16:0	862.63	264.26	12.18	-30
126	LPE 18:2	478.29	337.27	2.31	-30	153	Hex_2Cer d18:1/24:1	972.73	264.26	15.48	-30
127	LPE 24:0	566.42	425.40	10.97	-30	154	Hex_2Cer d18:2/16:0	860.61	262.25	12.17	-30
128	Cer d16:1/24:0	622.61	236.24	17.12	-30	155	Hex_2Cer d18:2/24:0	972.73	262.25	15.68	-30

No.	Compound	Parent ion (m/z)	Fragment (m/z)	RT (min)	CE (V)	No.	Compound	Parent ion (m/z)	Fragment (m/z)	RT (min)	CE (V)
129	Cer d16:1/24:1	620.60	236.24	16.32	-30	156	PC 28:0	678.51	184.07	11.48	-40
157	PC 32:0	734.57	184.07	14.02	-40	184	PC 37:1	802.63	184.07	17.14	-40
158	PC 32:2	730.54	184.07	12.01	-40	185	PC 37:2	800.62	184.07	14.99	-40
159	PC 32:3	728.52	184.07	11.14	-40	186	PC 37:3	798.60	184.07	15.80	-40
160	PC 33:0	748.59	184.07	15.16	-40	187	PC 37:4	796.59	184.07	14.95	-40
161	PC 33:1	746.57	184.07	15.16	-40	188	PC 37:5	794.57	184.07	13.96	-40
162	PC 33:2	744.55	184.07	12.62	-40	189	PC 37:6	792.55	184.07	13.76	-40
163	PC 33:3	742.54	184.07	13.91	-40	190	PC 38:1	816.65	184.07	16.68	-40
164	PC 34:0	762.60	184.07	15.37	-40	191	PC 38:2	814.63	184.07	16.20	-40
165	PC 34:1	760.59	184.07	14.21	-40	192	PC 38:3	812.62	184.07	14.79	-40
166	PC 34:2	758.57	184.07	13.30	-40	193	PC 38:4	810.60	184.07	13.89	-40
167	PC 34:3	756.55	184.07	12.49	-40	194	PC 38:5	808.59	184.07	13.29	-40
168	PC 34:4	754.54	184.07	11.81	-40	195	PC 38:6	806.57	184.07	12.65	-40
169	PC 34:5	752.52	184.07	10.82	-40	196	PC 38:7	804.55	184.07	11.70	-40
170	PC 35:0	776.62	184.07	16.26	-40	197	PC 39:2	828.65	184.07	17.71	-40
171	PC 35:1	774.60	184.07	14.98	-40	198	PC 39:4	824.62	184.07	16.09	-40
172	PC 35:2	772.59	184.07	13.86	-40	199	PC 39:6	820.59	184.07	14.91	-40
173	PC 35:3	770.57	184.07	14.83	-40	200	PC 40:0	846.70	184.07	16.59	-40
174	PC 35:4	768.55	184.07	13.91	-40	201	PC 40:1	844.68	184.07	17.85	-40
175	PC 36:0	790.63	184.07	15.50	-40	202	PC 40:2	842.66	184.07	16.75	-40
176	PC 36:1	788.62	184.07	15.51	-40	203	PC 40:4	838.63	184.07	15.13	-40
177	PC 36:2	786.60	184.07	14.45	-40	204	PC 40:5	836.62	184.07	14.50	-40
178	PC 36:3	784.59	184.07	13.57	-40	205	PC 40:6	834.60	184.07	13.49	-40
179	PC 36:4	782.57	184.07	12.99	-40	206	PC 40:7	832.59	184.07	12.81	-40
180	PC 36:5	780.55	184.07	12.33	-40	207	PC 41:1	858.70	184.07	16.69	-40
181	PC 36:6	778.54	184.07	11.11	-40	208	PC 42:1	872.71	184.07	19.01	-40

No.	Compound	Parent ion (m/z)	Fragment (m/z)	RT (min)	CE (V)	No.	Compound	Parent ion (m/z)	Fragment (m/z)	RT (min)	CE (V)
182	PC 36:7	776.52	184.07	14.83	-40	209	PC 42:10	854.57	184.07	18.23	-40
183	PC 37:0	804.65	184.07	11.67	-40	210	PC 42:11	852.55	184.07	17.61	-40
211	PC 42:2	870.70	184.07	17.84	-40	238	PC O-36:3	770.61	184.07	15.06	-40
212	PC 42:4	866.66	184.07	16.10	-40	239	PC O-36:4	768.59	184.07	13.91	-40
213	PC 42:5	864.65	184.07	15.51	-40	240	PC O-36:5	766.57	184.07	13.74	-40
214	PC 42:6	862.63	184.07	14.59	-40	241	PC O-36:6	764.56	184.07	12.76	-40
215	PC 42:7	860.62	184.07	14.03	-40	242	PC O-38:0	804.68	184.07	11.70	-40
216	PC 44:1	900.74	184.07	20.47	-40	243	PC O-38:1	802.67	184.07	16.20	-40
217	PC 44:11	880.59	184.07	18.54	-40	244	PC O-38:2	800.65	184.07	14.99	-40
218	PC 44:12	878.57	184.07	17.60	-40	245	PC O-38:3	798.64	184.07	15.81	-40
219	PC 44:2	898.73	184.07	18.90	-40	246	PC O-38:4	796.62	184.07	15.00	-40
220	PC 46:5	920.71	184.07	17.75	-40	247	PC O-38:5	794.61	184.07	13.96	-40
221	PC O-29:0	678.54	184.07	11.47	-40	248	PC O-38:6	792.59	184.07	13.76	-40
222	PC O-30:0	692.56	184.07	13.76	-40	249	PC O-40:0	832.72	184.07	12.81	-40
223	PC O-31:0	706.57	184.07	12.75	-40	250	PC O-40:1	830.70	184.07	16.68	-40
224	PC O-32:0	720.59	184.07	15.06	-40	251	PC O-40:4	824.65	184.07	16.08	-40
225	PC O-32:1	718.57	184.07	13.78	-40	252	PC O-40:5	822.64	184.07	15.20	-40
226	PC O-32:2	716.56	184.07	13.76	-40	253	PC O-40:6	820.62	184.07	14.91	-40
227	PC O-33:1	732.59	184.07	13.00	-40	254	PC O-40:7	818.61	184.07	13.83	-40
228	PC O-33:2	730.57	184.07	12.00	-40	255	PC O-42:1	858.73	184.07	17.95	-40
229	PC O-34:0	748.62	184.07	15.16	-40	256	PC O-42:7	846.64	184.07	16.35	-40
230	PC O-34:1	746.61	184.07	15.17	-40	257	LPC 14:0	468.31	184.07	1.95	-40
231	PC O-34:2	744.59	184.07	12.85	-40	258	LPC 15:0	482.33	184.07	3.68	-40
232	PC O-34:3	742.57	184.07	13.91	-40	259	LPC 15:1	480.31	184.07	3.56	-40
233	PC O-34:4	740.56	184.07	12.65	-40	260	LPC 16:0	496.34	184.07	2.94	-40
234	PC O-35:2	758.61	184.07	13.29	-40	261	LPC 16:1	494.33	184.07	2.06	-40

No.	Compound	Parent ion (m/z)	Fragment (m/z)	RT (min)	CE (V)	No.	Compound	Parent ion (m/z)	Fragment (m/z)	RT (min)	CE (V)
235	PC O-36:0	776.65	184.07	16.14	-40	262	LPC 18:0	524.37	184.07	4.66	-40
236	PC O-36:1	774.64	184.07	15.16	-40	263	LPC 18:1	522.36	184.07	2.96	-40
237	PC O-36:2	772.62	184.07	13.99	-40	264	LPC 18:2	520.34	184.07	2.30	-40
265	LPC 20:0	552.40	184.07	6.85	-40	292	SM 36:0	733.62	184.07	13.01	-40
266	LPC 20:3	546.36	184.07	2.64	-40	293	SM 36:1	731.61	184.07	12.01	-40
267	LPC 20:4	544.34	184.07	2.18	-40	294	SM 36:2	729.59	184.07	12.75	-40
268	LPC 22:0	580.43	184.07	9.10	-40	295	SM 36:3	727.58	184.07	11.51	-40
269	LPC 22:1	578.42	184.07	7.06	-40	296	SM 37:1	745.62	184.07	13.09	-40
270	LPC 22:4	572.37	184.07	2.58	-40	297	SM 37:2	743.61	184.07	13.91	-40
271	LPC 22:6	568.34	184.07	2.10	-40	298	SM 38:0	761.65	184.07	14.21	-40
272	LPC 24:0	608.47	184.07	10.96	-40	299	SM 38:1	759.64	184.07	13.29	-40
273	LPC 24:1	606.45	184.07	9.19	-40	300	SM 38:2	757.62	184.07	12.50	-40
274	LPC 26:0	636.50	184.07	10.85	-40	301	SM 38:3	755.61	184.07	11.83	-40
275	LPC 26:1	634.48	184.07	11.01	-40	302	SM 39:1	773.65	184.07	15.28	-40
276	LPC O-16:0	482.36	184.07	3.54	-40	303	SM 39:2	771.64	184.07	14.82	-40
277	LPC O-16:1	480.34	184.07	3.54	-40	304	SM 40:0	789.69	184.07	15.51	-40
278	SM 31:1	661.53	184.07	10.27	-40	305	SM 40:2	785.65	184.07	13.58	-40
279	SM 32:0	677.56	184.07	11.70	-40	306	SM 40:3	783.64	184.07	13.01	-40
280	SM 32:1	675.54	184.07	11.01	-40	307	SM 41:0	803.70	184.07	16.21	-40
281	SM 32:2	673.53	184.07	9.77	-40	308	SM 42:0	817.72	184.07	16.67	-40
282	SM 33:0	691.58	184.07	13.54	-40	309	SM 42:1	815.70	184.07	15.69	-40
283	SM 33:1	689.56	184.07	11.88	-40	310	SM 42:2	813.69	184.07	16.30	-40
284	SM 33:2	687.54	184.07	10.69	-40	311	PI 32:1	807.50	241.01	10.47	60
285	SM 34:0	705.59	184.07	11.82	-40	312	PI 34:1	835.53	241.01	11.70	60
286	SM 34:1	703.58	184.07	12.57	-40	313	PI 34:2	833.52	241.01	10.74	60
287	SM 34:2	701.56	184.07	11.41	-40	314	PI 35:2	847.53	241.01	12.58	60

No.	Compound	Parent ion (m/z)	Fragment (m/z)	RT (min)	CE (V)	No.	Compound	Parent ion (m/z)	Fragment (m/z)	RT (min)	CE (V)
288	SM 34:3	699.54	184.07	10.43	-40	315	PI 36:1	863.57	241.01	12.76	60
289	SM 35:1	717.59	184.07	13.75	-40	316	PI 36:2	861.55	241.01	12.52	60
290	SM 35:2	715.58	184.07	12.52	-40	317	PI 36:3	859.53	241.01	11.14	60
291	SM 35:3	713.56	184.07	11.23	-40	318	PI 36:4	857.52	241.01	10.68	60
319	PI 37:2	875.57	241.01	12.56	60	335	PS 38:2	814.56	727.56	12.98	35
320	PI 37:3	873.55	241.01	12.58	60	336	PS 38:3	812.54	725.54	12.76	35
321	PI 37:4	871.53	241.01	12.58	60	337	PS 38:4	810.53	723.53	12.56	35
322	PI 38:2	889.58	241.01	12.56	60	338	PS 40:2	842.59	755.59	12.77	35
323	PI 38:4	885.55	241.01	12.27	60	339	PS 40:5	836.54	749.54	12.59	35
324	PI 38:5	883.53	241.01	10.91	60	340	PG 32:1	719.49	153.00	10.90	45
325	PI 39:4	899.57	241.01	12.55	60	341	PG 34:0	749.53	153.00	12.54	45
326	PI 39:5	897.55	241.01	12.59	60	342	PG 34:1	747.52	153.00	12.54	45
327	PI 40:4	913.58	241.01	12.66	60	343	PG 34:2	745.50	153.00	11.18	45
328	PI 40:5	911.57	241.01	12.51	60	344	PG 36:1	775.55	153.00	13.12	45
329	PI 40:6	909.55	241.01	11.65	60	345	PG 36:2	773.53	153.00	12.49	45
330	PS 34:1	760.51	673.51	12.59	35	346	PG 38:2	801.57	153.00	12.67	45
331	PS 35:1	774.53	687.53	12.99	35	347	PG 40:7	819.52	153.00	10.42	45
332	PS 36:1	788.54	701.54	13.39	35	348	PG 40:8	817.50	153.00	11.59	45
333	PS 36:2	786.53	699.53	12.57	35	349	PG 44:12	865.50	153.00	12.77	45
334	PS 37:2	800.54	713.54	12.98	35	350	PG 44:9	871.55	153.00	12.89	45

Table S6. GPR35-related metabolites and their relative levels in each intervention group

Level	No.	Compound	C		ML		PA		KDNC		KD		OENC		OE	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
1	1	KA	1.00	0.00	1.35	0.04	0.67	0.01	1.00	0.01	1.05	0.01	1.00	0.03	0.76	0.02
2	1	Ado	1.00	0.00	2.12	0.04	0.92	0.04	1.00	0.02	0.84	0.03	1.00	0.03	1.51	0.04
3	1	Ile	1.00	0.00	1.09	0.01	0.67	0.09	1.00	0.02	1.17	0.01	1.00	0.02	0.72	0.01
3	2	C8-1	1.00	0.03	1.26	0.03	0.94	0.04	1.00	0.03	1.53	0.04	1.00	0.03	0.75	0.01
3	3	Asp	1.00	0.01	0.91	0.08	1.08	0.02	1.00	0.06	0.45	0.01	1.00	0.08	1.46	0.04
4	1	Asn	1.00	0.05	0.84	0.00	0.72	0.05	1.00	0.07	0.79	0.01	1.00	0.03	1.71	0.05
4	2	C3	1.00	0.01	0.91	0.07	0.75	0.03	1.00	0.05	1.24	0.03	1.00	0.02	0.66	0.05
4	3	DCA	1.00	0.01	1.01	0.01	1.01	0.00	1.00	0.04	1.09	0.01	1.00	0.11	0.54	0.02
4	4	GABA	1.00	0.18	1.19	0.05	1.38	0.06	1.00	0.03	1.35	0.02	1.00	0.04	0.61	0.02
4	5	MeCyd	1.00	0.03	2.28	0.18	0.92	0.03	1.00	0.06	1.18	0.06	1.00	0.17	1.30	0.08
4	6	Guo	1.00	0.07	4.20	0.25	0.89	0.02	1.00	0.15	1.34	0.11	1.00	0.05	1.26	0.02
4	7	Gln	1.00	0.12	0.63	0.01	0.61	0.01	1.00	0.05	1.48	0.03	1.00	0.09	1.11	0.03
4	8	Ser	1.00	0.08	0.62	0.02	0.83	0.00	1.00	0.01	0.82	0.02	1.00	0.01	0.89	0.01
4	9	C2	1.00	0.06	0.48	0.00	0.57	0.02	1.00	0.05	0.88	0.05	1.00	0.00	0.90	0.01
4	10	Met	1.00	0.11	0.70	0.00	0.45	0.01	1.00	0.03	0.78	0.02	1.00	0.01	1.31	0.02
4	11	KYN	1.00	0.12	0.58	0.01	0.62	0.00	1.00	0.02	0.65	0.02	1.00	0.01	0.92	0.02
4	12	Val	1.00	0.01	0.94	0.00	0.64	0.05	1.00	0.01	1.05	0.02	1.00	0.01	0.85	0.02
4	13	Leu	1.00	0.01	1.06	0.02	1.04	0.00	1.00	0.01	0.82	0.02	1.00	0.01	0.67	0.00
4	14	C4-1	1.00	0.08	0.51	0.01	0.49	0.01	1.00	0.02	1.18	0.01	1.00	0.00	0.94	0.00

Level	No.	Compound	C		ML		PA		KDNC		KD		OENC		OE	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
4	15	Phe	1.00	0.00	0.74	0.05	0.64	0.04	1.00	0.01	1.09	0.02	1.00	0.04	0.91	0.03
4	16	ILA	1.00	0.15	5.39	0.05	2.24	0.14	1.00	0.02	0.91	0.03	1.00	0.07	1.84	0.04
4	17	5-MIAA	1.00	0.03	1.88	0.10	1.13	0.02	1.00	0.01	1.01	0.02	1.00	0.04	0.99	0.02
4	18	NAS	1.00	0.12	0.79	0.07	0.66	0.04	1.00	0.01	1.15	0.01	1.00	0.11	1.02	0.02
4	19	C5-2	1.00	0.05	1.51	0.06	1.43	0.06	1.00	0.00	1.00	0.00	1.00	0.06	1.72	0.13
4	20	HAA	1.00	0.03	0.49	0.02	0.62	0.02	1.00	0.08	2.12	0.32	1.00	0.01	2.11	0.12
4	21	C6-1	1.00	0.03	1.73	0.01	1.81	0.02	1.00	0.01	1.11	0.00	1.00	0.02	0.81	0.00
4	22	C8-3	1.00	0.01	1.50	0.04	1.41	0.01	1.00	0.02	1.25	0.01	1.00	0.03	0.94	0.01
4	23	5-HT	1.00	0.06	0.72	0.07	0.63	0.02	1.00	0.00	1.13	0.04	1.00	0.01	0.94	0.01
4	24	C9-1	1.00	0.05	1.18	0.03	1.28	0.03	1.00	0.15	0.65	0.01	1.00	0.00	0.95	0.03
4	25	CDCA	1.00	0.01	1.01	0.00	1.04	0.00	1.00	0.00	0.94	0.01	1.00	0.18	0.46	0.00
4	26	C14	1.00	0.33	1.90	0.26	1.46	0.19	1.00	0.03	0.71	0.01	1.00	0.01	1.79	0.04
4	27	C16:1	1.00	0.01	2.85	0.14	1.10	0.00	1.00	0.05	0.32	0.02	1.00	0.11	0.36	0.04
4	28	C15	1.00	0.00	1.00	0.00	1.00	0.00	1.00	0.00	1.31	0.83	1.00	0.00	3.09	0.40
4	29	C22:6	1.00	0.04	2.17	0.15	1.32	0.02	1.00	0.01	0.62	0.02	1.00	0.06	0.74	0.01
4	30	C18:1	1.00	0.04	0.89	0.02	1.13	0.03	1.00	0.01	0.50	0.02	1.00	0.01	0.94	0.10
4	31	C20:1	1.00	0.17	3.26	0.20	2.78	0.06	1.00	0.08	0.86	0.08	1.00	0.01	0.69	0.00
4	32	C19	1.00	0.01	0.55	0.02	0.63	0.04	1.00	0.07	3.36	0.18	1.00	0.03	0.88	0.02
4	33	C22:1	1.00	0.35	4.18	0.60	2.04	1.41	1.00	0.06	1.34	0.06	1.00	0.11	1.13	0.05
4	34	C22	1.00	0.18	4.14	0.13	1.43	0.22	1.00	0.03	1.62	0.05	1.00	0.04	0.91	0.02

Level	No.	Compound	C		ML		PA		KDNC		KD		OENC		OE	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
4	35	C24:1	1.00	0.00	1.14	0.14	1.00	0.00	1.00	0.04	0.38	0.03	1.00	0.00	0.58	0.01
4	36	Glu	1.00	0.06	0.65	0.02	0.84	0.02	1.00	0.02	1.46	0.05	1.00	0.01	1.26	0.01
4	37	MeLys	1.00	0.11	0.84	0.05	0.52	0.03	1.00	0.01	1.01	0.02	1.00	0.02	0.79	0.01
4	38	SDMA	1.00	0.07	0.52	0.07	0.45	0.01	1.00	0.01	0.96	0.01	1.00	0.06	0.74	0.02
4	39	ADMA	1.00	0.02	0.60	0.01	0.51	0.00	1.00	0.05	0.92	0.01	1.00	0.06	0.71	0.02
4	40	MeArg	1.00	0.08	0.86	0.05	0.66	0.03	1.00	0.01	0.91	0.02	1.00	0.00	0.97	0.02
4	41	GDCA	1.00	0.05	1.05	0.00	1.41	0.19	1.00	0.00	0.60	0.05	1.00	0.00	0.37	0.00
4	42	GCDCA	1.00	0.13	0.57	0.11	0.71	0.00	1.00	0.00	0.99	0.00	1.00	0.00	2.90	0.50
4	43	Car	1.00	0.03	0.47	0.02	1.19	0.06	1.00	0.06	0.86	0.04	1.00	0.05	0.57	0.02
4	44	Car2	1.00	0.02	1.67	0.03	2.30	0.14	1.00	0.04	0.84	0.01	1.00	0.01	0.69	0.01
4	45	Car4-OH	1.00	0.07	2.95	0.07	4.39	0.18	1.00	0.07	0.79	0.02	1.00	0.02	0.78	0.02
4	46	Car4	1.00	0.01	3.18	0.05	2.73	0.01	1.00	0.02	0.75	0.01	1.00	0.03	0.61	0.01
4	47	Car5:1	1.00	0.00	1.49	0.00	2.04	0.00	1.00	0.00	0.79	0.00	1.00	0.07	0.70	0.06
4	48	isoCar5	1.00	0.08	3.11	0.00	3.01	0.08	1.00	0.03	0.74	0.03	1.00	0.00	0.57	0.03
4	49	Car5	1.00	0.07	2.65	0.05	2.24	0.14	1.00	0.02	0.94	0.02	1.00	0.05	0.52	0.01
4	50	Car6-OH	1.00	0.00	0.99	0.00	0.51	0.00	1.00	0.00	0.86	0.00	1.00	0.00	1.00	0.00
4	51	Car6	1.00	0.00	7.13	0.29	4.59	0.00	1.00	0.08	0.82	0.07	1.00	0.05	0.61	0.04
4	52	Car8	1.00	0.00	6.96	0.00	4.08	0.00	1.00	0.22	0.74	0.00	1.00	0.12	0.36	0.00
4	53	Car12-OH	1.00	0.00	1.19	0.00	2.45	0.00	1.00	0.00	0.99	0.00	1.00	0.00	0.83	0.00
4	54	Car12:1	1.00	0.00	5.14	0.14	4.25	0.39	1.00	0.00	0.86	0.00	1.00	0.00	0.72	0.05

Level	No.	Compound	C		ML		PA		KDNC		KD		OENC		OE	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
4	55	Car12	1.00	0.01	1.33	0.01	1.14	0.00	1.00	0.00	0.98	0.01	1.00	0.03	0.58	0.00
4	56	Car14:1	1.00	0.00	24.86	1.72	8.16	0.00	1.00	0.00	0.99	0.00	1.00	0.11	0.75	0.09
4	57	Car14	1.00	0.08	6.25	0.19	3.24	0.09	1.00	0.01	0.90	0.02	1.00	0.01	0.69	0.02
4	58	Car18:2	1.00	0.00	2.98	0.09	2.41	0.25	1.00	0.00	0.96	0.04	1.00	0.00	0.83	0.00
4	59	Car16:1	1.00	0.06	6.51	0.05	3.71	0.02	1.00	0.07	0.86	0.02	1.00	0.02	0.92	0.01
4	60	Car16	1.00	0.03	7.15	0.10	5.82	0.38	1.00	0.01	0.75	0.02	1.00	0.10	1.16	0.03
4	61	Car18:1	1.00	0.03	6.29	0.19	4.98	0.18	1.00	0.03	0.87	0.00	1.00	0.01	0.70	0.01
4	62	Car18	1.00	0.00	5.97	0.00	4.89	0.74	1.00	0.03	0.75	0.03	1.00	0.00	0.76	0.00
4	63	KIVA	1.00	0.05	1.53	0.03	1.51	0.01	1.00	0.01	0.63	0.02	1.00	0.03	0.97	0.01
4	64	BHB	1.00	0.02	0.55	0.01	0.49	0.01	1.00	0.05	0.67	0.04	1.00	0.04	0.74	0.01
4	65	Xan	1.00	0.02	0.77	0.01	0.57	0.01	1.00	0.07	0.56	0.07	1.00	0.03	0.95	0.02
4	66	Cyd	1.00	0.02	2.40	0.01	1.43	0.04	1.00	0.05	0.54	0.07	1.00	0.11	3.47	0.11
4	67	Ade	1.00	0.02	0.70	0.02	0.64	0.01	1.00	0.02	0.92	0.01	1.00	0.02	0.86	0.02
4	68	Ura	1.00	0.08	0.29	0.03	0.37	0.00	1.00	0.09	1.51	0.06	1.00	0.00	1.80	0.05
4	69	Urd	1.00	0.06	2.07	0.02	0.94	0.01	1.00	0.01	1.71	0.14	1.00	0.04	1.18	0.08
4	70	Thy	1.00	0.09	0.45	0.01	0.52	0.02	1.00	0.02	0.80	0.01	1.00	0.04	0.90	0.03

Note: Data was normalized to corresponding controls.

Table S7. GPR35-related lipids and their relative levels in each intervention group

Level	No	Compound	C		ML		PA		KDNC		KD		OENC		OE	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
1	1	DG 16:0_14:0	1.00	0.02	1.21	0.05	0.45	0.01	1.00	0.07	1.21	0.05	1.00	0.09	0.67	0.09
1	2	DG 16:0_16:0	1.00	0.02	1.28	0.15	0.44	0.03	1.00	0.13	1.22	0.07	1.00	0.08	0.89	0.05
1	3	PE 32:0	1.00	0.07	1.28	0.07	0.56	0.05	1.00	0.09	1.29	0.10	1.00	0.12	0.78	0.02
1	4	PE 33:1	1.00	0.11	1.30	0.11	0.51	0.04	1.00	0.11	1.81	0.14	1.00	0.08	0.91	0.03
1	5	PE 34:1	1.00	0.06	1.18	0.06	0.51	0.03	1.00	0.06	1.32	0.10	1.00	0.03	0.87	0.01
1	6	PE 34:2	1.01	0.08	1.33	0.12	0.59	0.02	1.00	0.07	1.20	0.11	1.00	0.14	0.75	0.01
1	7	PE 35:2	1.00	0.04	1.31	0.05	0.54	0.01	1.00	0.01	1.45	0.05	1.00	0.04	0.73	0.08
1	8	PE 36:3	1.00	0.08	1.37	0.05	0.57	0.05	1.00	0.12	1.33	0.09	1.00	0.06	0.86	0.12
1	9	PE 36:4	1.00	0.05	1.38	0.08	0.52	0.02	1.00	0.08	1.25	0.14	1.00	0.04	0.69	0.05
1	10	PE 36:5	1.00	0.05	1.29	0.14	0.58	0.02	1.00	0.05	1.27	0.10	1.00	0.08	0.69	0.08
1	11	PE 37:5	1.00	0.11	1.36	0.08	0.46	0.03	1.00	0.09	2.07	0.06	1.00	0.11	0.94	0.08
1	12	PE 38:1	1.00	0.09	1.04	0.06	0.36	0.04	1.00	0.14	1.31	0.18	1.00	0.03	1.00	0.11
1	13	PE 38:5	1.00	0.06	1.41	0.04	0.56	0.06	1.00	0.10	1.56	0.07	1.00	0.03	0.76	0.10
1	14	PE 38:7	1.00	0.05	1.02	0.15	0.33	0.02	1.00	0.02	1.32	0.12	1.00	0.13	0.81	0.05
1	15	PE 40:1	1.00	0.10	1.28	0.06	0.49	0.05	1.00	0.02	1.35	0.03	1.00	0.14	0.75	0.04
1	16	PE 40:3	1.00	0.05	1.05	0.05	0.33	0.03	1.00	0.13	1.37	0.06	1.00	0.01	0.96	0.11
1	17	PE O-33:2	1.00	0.11	1.79	0.07	0.83	0.06	1.00	0.12	1.07	0.05	1.00	0.13	0.75	0.01
1	18	PE O-35:2	1.00	0.04	1.39	0.07	0.56	0.05	1.00	0.07	1.31	0.02	1.00	0.09	0.73	0.01
1	19	PE O-36:2	1.00	0.07	1.23	0.06	0.48	0.01	1.00	0.06	1.38	0.12	1.00	0.06	0.75	0.10
1	20	PE O-38:7	1.00	0.13	1.01	0.06	0.43	0.04	1.00	0.09	1.42	0.13	1.00	0.03	0.94	0.10
1	21	LPE 18:0	1.00	0.02	1.65	0.14	0.61	0.09	1.00	0.06	1.34	0.08	1.00	0.10	0.90	0.03
1	22	LPE 18:1	1.00	0.13	1.16	0.16	0.63	0.06	1.00	0.12	1.58	0.17	1.00	0.08	0.79	0.11
1	23	Cer d18:2/24:1	1.00	0.07	1.56	0.16	0.44	0.02	1.00	0.14	1.08	0.02	1.00	0.07	0.97	0.02

Level	No	Compound	C		ML		PA		KDNC		KD		OENC		OE	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
1	24	Hex_2Cer d18:1/16:0	1.00	0.07	1.12	0.07	0.47	0.04	1.00	0.13	1.21	0.07	1.00	0.13	0.94	0.11
1	25	Hex_2Cer d18:2/16:0	1.00	0.12	1.99	0.14	0.66	0.07	1.00	0.13	1.01	0.13	1.00	0.08	0.99	0.03
1	26	PC 32:2	1.00	0.14	1.24	0.06	0.49	0.05	1.00	0.06	1.36	0.10	1.00	0.06	0.81	0.05
1	27	PC 34:4	1.00	0.06	1.46	0.09	0.60	0.05	1.00	0.07	1.50	0.09	1.00	0.13	1.00	0.06
1	28	PC 34:5	1.00	0.10	1.51	0.10	0.36	0.03	1.00	0.13	1.76	0.06	1.00	0.08	0.72	0.07
1	29	PC 36:6	1.00	0.03	1.15	0.06	0.42	0.04	1.00	0.11	1.68	0.11	1.00	0.07	0.84	0.09
1	30	PC 38:3	1.00	0.11	1.05	0.05	0.39	0.01	1.00	0.06	1.24	0.07	1.00	0.08	0.99	0.14
1	31	PC 38:7	1.00	0.07	1.14	0.11	0.43	0.02	1.00	0.10	1.62	0.21	1.00	0.07	0.96	0.05
1	32	PC 39:2	1.00	0.12	1.34	0.16	0.40	0.06	1.00	0.12	1.18	0.01	1.00	0.04	0.76	0.04
1	33	PC 42:10	1.00	0.11	1.32	0.08	0.38	0.05	1.00	0.08	1.09	0.07	1.00	0.08	0.81	0.07
1	34	PC O-33:2	1.00	0.10	1.35	0.08	0.53	0.07	1.00	0.07	1.38	0.05	1.00	0.06	0.74	0.04
1	35	PC O-38:0	1.00	0.10	1.07	0.07	0.39	0.01	1.00	0.09	1.72	0.20	1.00	0.02	0.77	0.10
1	36	PC O-40:4	1.00	0.03	1.43	0.14	0.41	0.04	1.00	0.14	1.57	0.08	1.00	0.09	0.99	0.13
1	37	LPC 20:3	1.00	0.13	1.66	0.07	0.96	0.07	1.00	0.10	1.31	0.08	1.00	0.03	0.66	0.06
1	38	LPC 26:1	1.00	0.14	1.12	0.05	0.47	0.04	1.00	0.09	1.75	0.09	1.00	0.13	0.98	0.12
1	39	SM 31:1	1.00	0.04	3.07	0.33	0.90	0.07	1.00	0.00	11.00	1.60	1.00	0.09	0.07	0.00
1	40	SM 34:0	1.00	0.10	1.25	0.11	0.53	0.03	1.00	0.03	1.32	0.05	1.00	0.11	0.97	0.08
1	41	SM 36:1	1.00	0.06	1.30	0.10	0.52	0.06	1.00	0.05	1.33	0.04	1.00	0.07	0.74	0.05
1	42	SM 36:2	1.00	0.10	1.22	0.12	0.44	0.05	1.00	0.13	1.40	0.11	1.00	0.12	0.97	0.05
1	43	SM 38:0	1.00	0.07	1.27	0.09	0.47	0.06	1.00	0.08	1.44	0.08	1.00	0.01	0.75	0.07
1	44	SM 38:2	1.00	0.05	1.30	0.06	0.51	0.04	1.00	0.11	1.36	0.09	1.00	0.09	0.90	0.02
1	45	SM 38:3	1.00	0.08	1.32	0.08	0.50	0.04	1.00	0.11	1.60	0.09	1.00	0.03	0.85	0.05
1	46	SM 40:0	1.00	0.11	1.11	0.08	0.44	0.06	1.00	0.08	1.24	0.09	1.00	0.07	0.92	0.01
1	47	SM 40:2	1.00	0.05	1.15	0.10	0.44	0.02	1.00	0.05	1.25	0.06	1.00	0.07	0.92	0.01
1	48	PI 34:1	1.00	0.06	1.27	0.15	0.38	0.05	1.00	0.03	1.65	0.08	1.00	0.06	0.84	0.11

Level	No	Compound	C		ML		PA		KDNC		KD		OENC		OE	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
1	49	PI 36:2	1.00	0.08	1.22	0.05	0.31	0.03	1.00	0.15	1.20	0.09	1.00	0.04	0.96	0.05
1	50	PI 38:2	1.00	0.02	1.37	0.06	0.25	0.03	1.00	0.01	1.05	0.12	1.00	0.08	0.94	0.11
1	51	PI 38:4	1.00	0.02	1.31	0.14	0.26	0.01	1.00	0.04	1.36	0.08	1.00	0.08	0.86	0.09
1	52	PI 38:5	1.00	0.02	1.36	0.12	0.26	0.03	1.00	0.00	1.31	0.10	1.00	0.05	0.85	0.07
1	53	PI 40:4	1.00	0.09	2.05	0.18	0.44	0.02	1.00	0.03	1.25	0.04	1.00	0.07	0.86	0.05
1	54	PS 36:1	1.00	0.07	1.89	0.17	0.49	0.05	1.00	0.12	1.49	0.16	1.00	0.09	0.84	0.04
1	55	PG 34:0	1.00	0.07	1.97	0.08	0.70	0.06	1.00	0.15	1.14	0.15	1.00	0.09	0.92	0.06
1	56	PG 34:2	1.00	0.07	1.87	0.02	0.85	0.12	1.00	0.14	1.10	0.12	1.00	0.06	0.77	0.04
2	1	TG 18:1_18:2_22:3	1.00	0.09	1.07	0.02	0.81	0.04	1.00	0.08	0.18	0.00	1.00	0.00	7.01	0.10
2	2	PE O-36:5	1.00	0.04	1.57	0.10	0.60	0.08	1.00	0.07	0.95	0.11	1.00	0.07	1.15	0.11
2	3	Cer d18:2/22:0	1.00	0.07	1.47	0.20	0.37	0.04	1.00	0.03	0.85	0.01	1.00	0.06	1.10	0.03
2	4	HexCer d18:1/16:0	1.00	0.06	1.13	0.11	0.46	0.02	1.00	0.07	0.91	0.04	1.00	0.09	1.39	0.08
2	5	PC 33:1	1.00	0.10	1.19	0.09	0.45	0.02	1.00	0.04	1.00	0.07	1.00	0.04	1.16	0.02
2	6	PC O-34:1	1.00	0.12	1.20	0.10	0.44	0.02	1.00	0.00	0.99	0.06	1.00	0.03	1.11	0.05
2	7	PC O-34:3	1.00	0.13	1.05	0.07	0.39	0.02	1.00	0.07	0.76	0.04	1.00	0.12	1.47	0.06
2	8	SM 37:2	1.00	0.04	1.22	0.11	0.45	0.02	1.00	0.13	0.81	0.05	1.00	0.05	1.23	0.05
3	1	DG 22:6_18:0	1.00	0.12	1.51	0.11	0.36	0.00	1.00	0.06	0.77	0.04	1.00	0.12	0.91	0.07
3	2	PE 40:7	1.00	0.09	1.01	0.03	0.43	0.05	1.00	0.11	1.31	0.07	1.00	0.08	1.20	0.11
3	3	PE O-42:5	1.00	0.00	1.00	0.00	1.00	0.00	1.00	0.07	0.23	0.00	1.00	0.00	2.51	0.26
3	4	Cer d18:2/24:0	1.00	0.12	1.36	0.11	0.34	0.02	1.00	0.11	1.11	0.07	1.00	0.13	1.17	0.02
3	5	PC 34:0	1.00	0.13	1.03	0.03	0.38	0.01	1.00	0.07	1.23	0.07	1.00	0.05	1.06	0.07
3	6	PC 34:1	1.00	0.07	1.06	0.06	0.40	0.01	1.00	0.04	1.14	0.08	1.00	0.04	1.07	0.04
3	7	PC 35:0	1.00	0.14	1.21	0.13	0.40	0.05	1.00	0.12	1.25	0.04	1.00	0.13	1.15	0.17
3	8	PC 35:1	1.00	0.04	1.14	0.09	0.38	0.03	1.00	0.07	1.25	0.07	1.00	0.13	1.01	0.06
3	9	PC 35:3	1.00	0.13	1.13	0.10	0.42	0.00	1.00	0.08	1.05	0.09	1.00	0.04	1.26	0.06

Level	No	Compound	C		ML		PA		KDNC		KD		OENC		OE	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
3	10	PC 35:4	1.00	0.09	1.12	0.05	0.44	0.02	1.00	0.12	1.18	0.06	1.00	0.09	1.26	0.13
3	11	PC 36:7	1.00	0.04	1.11	0.10	0.37	0.03	1.00	0.08	1.21	0.07	1.00	0.13	1.15	0.15
3	12	PC 37:1	1.00	0.08	1.49	0.17	0.48	0.07	1.00	0.10	1.18	0.04	1.00	0.07	1.10	0.09
3	13	PC 37:2	1.00	0.02	1.27	0.07	0.40	0.03	1.00	0.14	1.07	0.11	1.00	0.02	1.23	0.10
3	14	PC 37:4	1.00	0.12	1.23	0.13	0.43	0.03	1.00	0.07	1.19	0.06	1.00	0.06	1.28	0.06
3	15	PC 37:5	1.00	0.13	1.18	0.07	0.43	0.03	1.00	0.13	1.34	0.08	1.00	0.09	1.22	0.05
3	16	PC 38:2	1.00	0.09	1.12	0.05	0.40	0.01	1.00	0.05	1.22	0.06	1.00	0.10	1.08	0.08
3	17	PC 39:4	1.00	0.12	1.13	0.10	0.39	0.05	1.00	0.12	1.27	0.05	1.00	0.10	1.14	0.05
3	18	PC 39:6	1.00	0.13	1.03	0.08	0.36	0.02	1.00	0.07	1.34	0.13	1.00	0.07	1.14	0.08
3	19	PC 40:0	1.00	0.12	1.07	0.09	0.32	0.02	1.00	0.04	1.18	0.13	1.00	0.01	1.07	0.09
3	20	PC 40:1	1.00	0.14	1.17	0.14	0.29	0.01	1.00	0.10	0.84	0.11	1.00	0.11	0.96	0.04
3	21	PC 42:11	1.00	0.08	1.29	0.15	0.45	0.01	1.00	0.13	1.20	0.09	1.00	0.06	1.07	0.04
3	22	PC 44:11	1.00	0.13	1.27	0.13	0.38	0.04	1.00	0.03	1.03	0.05	1.00	0.06	1.13	0.05
3	23	PC 44:12	1.00	0.14	1.52	0.16	0.45	0.04	1.00	0.06	1.11	0.07	1.00	0.13	1.29	0.13
3	24	PC O-29:0	1.00	0.09	1.15	0.10	0.46	0.02	1.00	0.12	1.12	0.14	1.00	0.06	1.01	0.08
3	25	PC O-30:0	1.00	0.10	1.10	0.14	0.43	0.03	1.00	0.08	1.08	0.07	1.00	0.14	1.29	0.05
3	26	PC O-31:0	1.00	0.02	1.15	0.10	0.36	0.04	1.00	0.09	1.14	0.12	1.00	0.11	1.05	0.05
3	27	PC O-32:0	1.00	0.06	1.29	0.10	0.50	0.02	1.00	0.04	1.02	0.12	1.00	0.12	1.12	0.08
3	28	PC O-32:1	1.00	0.07	1.10	0.06	0.41	0.05	1.00	0.08	1.03	0.11	1.00	0.11	1.20	0.03
3	29	PC O-34:0	1.00	0.03	1.20	0.07	0.45	0.02	1.00	0.15	1.17	0.10	1.00	0.03	1.24	0.08
3	30	PC O-34:2	1.00	0.08	1.11	0.09	0.43	0.05	1.00	0.10	1.36	0.17	1.00	0.09	1.11	0.16
3	31	PC O-36:0	1.00	0.07	1.40	0.09	0.41	0.03	1.00	0.07	1.22	0.05	1.00	0.09	1.30	0.09
3	32	PC O-36:1	1.00	0.04	1.12	0.05	0.37	0.03	1.00	0.06	1.24	0.07	1.00	0.13	1.38	0.04
3	33	PC O-36:2	1.00	0.06	1.06	0.08	0.36	0.05	1.00	0.01	1.28	0.13	1.00	0.09	1.21	0.09
3	34	PC O-36:4	1.00	0.07	1.43	0.11	0.53	0.03	1.00	0.04	1.04	0.11	1.00	0.08	1.29	0.06

Level	No	Compound	C		ML		PA		KDNC		KD		OENC		OE	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
3	35	PC O-38:1	1.00	0.09	1.14	0.08	0.36	0.05	1.00	0.11	1.10	0.01	1.00	0.09	1.26	0.06
3	36	PC O-38:2	1.00	0.04	1.22	0.10	0.41	0.02	1.00	0.10	1.10	0.05	1.00	0.04	1.27	0.06
3	37	PC O-38:3	1.00	0.06	1.23	0.16	0.41	0.06	1.00	0.15	1.06	0.14	1.00	0.08	1.10	0.09
3	38	PC O-38:4	1.00	0.10	1.23	0.11	0.46	0.03	1.00	0.04	1.15	0.03	1.00	0.07	1.26	0.07
3	39	PC O-38:5	1.00	0.14	1.18	0.05	0.42	0.03	1.00	0.05	1.28	0.14	1.00	0.08	1.25	0.04
3	40	PC O-40:0	1.00	0.03	1.29	0.02	0.43	0.06	1.00	0.07	1.31	0.07	1.00	0.08	1.12	0.05
3	41	PC O-40:1	1.00	0.05	1.04	0.05	0.32	0.02	1.00	0.04	1.13	0.02	1.00	0.09	1.10	0.10
3	42	PC O-40:5	1.00	0.06	1.19	0.10	0.36	0.05	1.00	0.05	1.40	0.07	1.00	0.05	1.12	0.05
3	43	PC O-40:6	1.00	0.08	1.07	0.11	0.37	0.01	1.00	0.14	1.27	0.11	1.00	0.13	1.28	0.09
3	44	PC O-40:7	1.00	0.04	1.04	0.11	0.28	0.02	1.00	0.08	1.24	0.10	1.00	0.13	1.15	0.08
3	45	LPC 18:0	1.00	0.03	2.32	0.24	0.86	0.06	1.00	0.13	1.29	0.13	1.00	0.12	1.06	0.07
3	46	LPC 18:2	1.00	0.11	0.92	0.10	0.91	0.04	1.00	0.08	1.39	0.10	1.00	0.06	0.65	0.04
3	47	SM 32:0	1.00	0.11	1.07	0.04	0.35	0.04	1.00	0.06	1.33	0.16	1.00	0.15	1.34	0.03
3	48	SM 34:1	1.00	0.07	1.22	0.08	0.39	0.03	1.00	0.13	1.20	0.10	1.00	0.06	1.25	0.07
3	49	SM 34:2	1.00	0.06	1.01	0.04	0.30	0.00	1.00	0.10	1.01	0.12	1.00	0.05	1.44	0.11
3	50	SM 37:1	1.00	0.06	1.07	0.12	0.33	0.01	1.00	0.11	1.48	0.11	1.00	0.08	1.20	0.00
3	51	SM 39:2	1.00	0.06	1.08	0.10	0.38	0.02	1.00	0.04	1.01	0.13	1.00	0.14	1.40	0.02
3	52	SM 41:0	1.00	0.07	1.14	0.03	0.33	0.02	1.00	0.11	1.04	0.09	1.00	0.13	1.15	0.14
3	53	SM 42:1	1.00	0.14	1.12	0.05	0.42	0.02	1.00	0.05	1.34	0.05	1.00	0.08	1.09	0.08
3	54	SM 42:2	1.00	0.13	1.15	0.08	0.39	0.03	1.00	0.05	1.39	0.03	1.00	0.15	1.18	0.09
3	55	PG 32:1	1.00	0.03	1.72	0.07	0.57	0.02	1.00	0.14	0.92	0.09	1.00	0.10	0.78	0.08
3	56	PG 34:1	1.00	0.09	2.18	0.15	0.88	0.07	1.00	0.11	1.09	0.14	1.00	0.03	1.20	0.05
4	1	DG 18:0_18:0	1.00	0.10	3.09	0.45	1.01	0.04	1.00	0.08	1.46	0.12	1.00	0.12	1.09	0.12
4	2	DG 18:1_16:0	1.00	0.06	0.58	0.03	0.14	0.02	1.00	0.09	0.96	0.04	1.00	0.04	1.29	0.15
4	3	DG 18:1_16:1	1.00	0.04	0.75	0.10	0.26	0.01	1.00	0.11	1.57	0.06	1.00	0.11	0.81	0.05

Level	No	Compound	C		ML		PA		KDNC		KD		OENC		OE	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
4	4	DG 18:1_18:1	1.00	0.09	0.92	0.03	0.37	0.04	1.00	0.15	1.28	0.15	1.00	0.12	0.84	0.06
4	5	DG 18:2_16:0	1.00	0.11	0.74	0.05	0.29	0.02	1.00	0.06	1.20	0.06	1.00	0.11	0.77	0.07
4	6	DG 20:4_18:0	1.00	0.09	1.41	0.13	0.46	0.05	1.00	0.09	1.85	0.24	1.00	0.07	1.13	0.13
4	7	DG 22:5_18:1	1.00	0.00	1.00	0.00	1.00	0.00	1.00	0.00	1.00	0.00	1.00	0.00	4.31	0.43
4	8	TG 16:0e_16:0_16:0	1.00	0.06	1.41	0.09	0.34	0.03	1.00	0.12	0.09	0.00	1.00	0.13	0.10	0.00
4	9	PE 35:1	1.00	0.08	0.99	0.02	0.36	0.03	1.00	0.12	1.40	0.01	1.00	0.09	1.32	0.07
4	10	PE 35:4	1.00	0.11	1.20	0.05	0.62	0.08	1.00	0.00	26.27	1.78	1.00	0.09	1.14	0.11
4	11	PE 36:0	1.00	0.02	0.89	0.05	0.34	0.03	1.00	0.07	1.30	0.05	1.00	0.08	0.89	0.10
4	12	PE 36:1	1.00	0.08	0.84	0.05	0.32	0.05	1.00	0.05	1.53	0.04	1.00	0.06	0.88	0.07
4	13	PE 36:2	1.00	0.10	0.82	0.05	0.28	0.03	1.00	0.05	1.21	0.11	1.00	0.06	1.03	0.03
4	14	PE 37:2	1.00	0.08	0.74	0.11	0.29	0.01	1.00	0.11	1.23	0.12	1.00	0.14	1.07	0.08
4	15	PE 37:3	1.00	0.13	1.17	0.07	0.42	0.03	1.00	0.08	1.75	0.07	1.00	0.09	1.06	0.09
4	16	PE 37:4	1.00	0.13	1.29	0.16	0.46	0.06	1.00	0.06	2.23	0.12	1.00	0.12	1.09	0.03
4	17	PE 38:3	1.00	0.13	0.84	0.04	0.29	0.03	1.00	0.10	1.19	0.06	1.00	0.14	0.96	0.06
4	18	PE 39:4	1.00	0.04	1.02	0.09	0.35	0.01	1.00	0.06	1.87	0.13	1.00	0.11	1.10	0.03
4	19	PE 40:4	1.00	0.12	0.66	0.02	0.17	0.01	1.00	0.03	1.69	0.04	1.00	0.05	1.01	0.02
4	20	PE 40:5	1.00	0.09	0.74	0.02	0.28	0.01	1.00	0.10	1.50	0.19	1.00	0.11	1.13	0.07
4	21	PE 40:6	1.00	0.06	0.76	0.04	0.28	0.02	1.00	0.10	1.54	0.13	1.00	0.12	0.80	0.05
4	22	PE 42:1	1.00	0.15	0.94	0.11	0.40	0.01	1.00	0.08	1.60	0.18	1.00	0.14	0.77	0.05
4	23	PE 42:4	1.00	0.04	0.96	0.07	0.31	0.04	1.00	0.11	1.36	0.19	1.00	0.12	1.04	0.10
4	24	PE O-32:1	1.00	0.00	1.00	0.00	1.00	0.00	1.00	0.00	5.34	0.37	1.00	0.00	1.00	0.00
4	25	PE O-36:1	1.00	0.00	0.90	0.02	0.34	0.05	1.00	0.04	1.57	0.02	1.00	0.03	0.96	0.02
4	26	PE O-36:4	1.00	0.09	2.35	0.07	0.81	0.11	1.00	0.00	4.36	0.48	1.00	0.11	1.05	0.09
4	27	PE O-37:2	1.00	0.11	0.83	0.04	0.29	0.03	1.00	0.06	1.26	0.03	1.00	0.04	1.01	0.03
4	28	PE O-38:2	1.00	0.15	0.82	0.07	0.28	0.02	1.00	0.09	1.06	0.10	1.00	0.03	1.22	0.12

Level	No	Compound	C		ML		PA		KDNC		KD		OENC		OE	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
4	29	PE O-38:4	1.00	0.11	0.99	0.11	0.33	0.05	1.00	0.04	1.88	0.06	1.00	0.05	1.12	0.07
4	30	PE O-38:5	1.00	0.10	1.29	0.08	0.43	0.06	1.00	0.09	1.81	0.08	1.00	0.07	1.04	0.10
4	31	PE O-38:6	1.00	0.08	1.59	0.16	0.71	0.05	1.00	0.07	2.12	0.01	1.00	0.07	1.46	0.11
4	32	PE O-40:4	1.00	0.07	0.97	0.09	0.30	0.04	1.00	0.07	1.88	0.10	1.00	0.12	1.10	0.04
4	33	PE O-40:5	1.00	0.08	0.96	0.09	0.38	0.01	1.00	0.09	1.93	0.13	1.00	0.07	1.04	0.04
4	34	PE O-40:6	1.00	0.07	1.06	0.12	0.39	0.04	1.00	0.07	1.53	0.11	1.00	0.15	1.04	0.03
4	35	Cer d18:1/22:0	1.00	0.10	0.96	0.10	0.20	0.02	1.00	0.08	1.30	0.09	1.00	0.11	0.87	0.02
4	36	Cer d18:1/24:0	1.00	0.11	0.83	0.02	0.23	0.03	1.00	0.14	1.21	0.10	1.00	0.05	1.38	0.12
4	37	HexCer d18:2/16:0	1.00	0.08	1.09	0.02	0.46	0.04	1.00	0.13	1.16	0.11	1.00	0.12	1.63	0.06
4	38	PC 32:0	1.00	0.11	0.95	0.05	0.34	0.04	1.00	0.09	1.21	0.14	1.00	0.06	0.99	0.04
4	39	PC 34:2	1.00	0.08	0.79	0.04	0.29	0.02	1.00	0.03	1.20	0.13	1.00	0.02	1.04	0.02
4	40	PC 36:0	1.00	0.12	0.90	0.04	0.32	0.03	1.00	0.09	1.22	0.15	1.00	0.00	1.11	0.16
4	41	PC 36:1	1.00	0.07	0.80	0.04	0.29	0.02	1.00	0.02	1.23	0.10	1.00	0.06	1.14	0.02
4	42	PC 36:2	1.00	0.11	0.94	0.05	0.34	0.01	1.00	0.05	1.25	0.06	1.00	0.00	1.12	0.04
4	43	PC 36:3	1.00	0.14	0.83	0.05	0.29	0.03	1.00	0.04	1.27	0.06	1.00	0.07	1.14	0.02
4	44	PC 36:4	1.00	0.01	1.00	0.06	0.39	0.05	1.00	0.04	1.54	0.09	1.00	0.12	1.10	0.11
4	45	PC 37:3	1.00	0.12	1.35	0.03	0.43	0.06	1.00	0.06	1.16	0.04	1.00	0.14	1.60	0.12
4	46	PC 37:6	1.00	0.06	0.96	0.06	0.37	0.02	1.00	0.07	0.89	0.09	1.00	0.04	1.19	0.07
4	47	PC 38:1	1.00	0.09	0.98	0.05	0.29	0.02	1.00	0.09	1.44	0.05	1.00	0.07	1.16	0.09
4	48	PC 38:4	1.00	0.11	0.95	0.07	0.36	0.02	1.00	0.10	1.54	0.15	1.00	0.10	1.10	0.14
4	49	PC 38:5	1.00	0.06	0.93	0.05	0.33	0.02	1.00	0.08	1.47	0.10	1.00	0.07	1.07	0.15
4	50	PC 38:6	1.00	0.03	0.98	0.07	0.36	0.05	1.00	0.07	1.63	0.13	1.00	0.10	1.12	0.07
4	51	PC 40:2	1.00	0.12	0.80	0.09	0.24	0.02	1.00	0.07	1.24	0.09	1.00	0.03	1.15	0.14
4	52	PC 40:5	1.00	0.07	0.84	0.11	0.33	0.03	1.00	0.13	1.50	0.09	1.00	0.06	1.08	0.08
4	53	PC 40:6	1.00	0.14	0.87	0.05	0.31	0.01	1.00	0.07	2.24	0.08	1.00	0.09	1.10	0.07

Level	No	Compound	C		ML		PA		KDNC		KD		OENC		OE	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
4	54	PC 42:2	1.00	0.08	0.67	0.10	0.25	0.01	1.00	0.08	1.27	0.03	1.00	0.08	1.01	0.06
4	55	PC 42:4	1.00	0.08	0.98	0.07	0.27	0.03	1.00	0.10	1.27	0.12	1.00	0.07	1.11	0.04
4	56	PC 42:5	1.00	0.15	0.96	0.12	0.36	0.01	1.00	0.08	1.69	0.08	1.00	0.14	1.01	0.08
4	57	PC 42:7	1.00	0.02	0.96	0.13	0.37	0.01	1.00	0.10	1.04	0.10	1.00	0.10	1.24	0.10
4	58	PC 44:2	1.00	0.08	0.62	0.05	0.18	0.02	1.00	0.13	1.32	0.09	1.00	0.05	1.03	0.10
4	59	PC 46:5	1.00	0.08	0.49	0.03	0.17	0.01	1.00	0.08	1.67	0.19	1.00	0.13	0.89	0.02
4	60	PC O-32:2	1.00	0.12	0.92	0.09	0.35	0.02	1.00	0.11	0.83	0.07	1.00	0.08	1.27	0.07
4	61	PC O-33:1	1.00	0.10	0.92	0.06	0.35	0.01	1.00	0.04	1.16	0.11	1.00	0.05	0.97	0.01
4	62	PC O-34:4	1.00	0.03	1.32	0.15	0.36	0.04	1.00	0.03	1.71	0.23	1.00	0.04	1.17	0.05
4	63	PC O-35:2	1.00	0.15	0.83	0.04	0.31	0.03	1.00	0.03	1.19	0.13	1.00	0.04	1.17	0.05
4	64	PC O-36:5	1.00	0.06	0.85	0.04	0.25	0.02	1.00	0.01	1.10	0.10	1.00	0.09	1.44	0.13
4	65	PC O-38:6	1.00	0.06	0.99	0.08	0.38	0.01	1.00	0.08	0.95	0.10	1.00	0.01	1.63	0.06
4	66	PC O-42:7	1.00	0.13	0.91	0.04	0.31	0.04	1.00	0.10	1.19	0.10	1.00	0.13	1.04	0.14
4	67	LPC 15:0	1.00	0.12	2.53	0.36	1.12	0.06	1.00	0.04	1.58	0.07	1.00	0.00	5.00	0.56
4	68	LPC 15:1	1.00	0.08	5.72	0.41	1.02	0.03	1.00	0.04	1.26	0.13	1.00	0.08	1.28	0.18
4	69	LPC 16:0	1.00	0.12	2.42	0.19	1.28	0.07	1.00	0.03	1.56	0.20	1.00	0.11	0.97	0.11
4	70	LPC 18:1	1.00	0.07	2.05	0.10	1.45	0.12	1.00	0.08	1.42	0.19	1.00	0.13	0.76	0.05
4	71	LPC 20:0	1.00	0.10	6.04	0.74	1.57	0.19	1.00	0.06	1.07	0.07	1.00	0.12	1.03	0.09
4	72	LPC 22:1	1.00	0.11	6.73	0.34	1.44	0.09	1.00	0.14	1.37	0.06	1.00	0.00	2.32	0.34
4	73	LPC 24:0	1.00	0.11	0.93	0.06	0.40	0.04	1.00	0.07	1.74	0.11	1.00	0.07	1.22	0.05
4	74	LPC 26:0	1.00	0.07	0.96	0.06	0.28	0.03	1.00	0.12	2.20	0.29	1.00	0.05	0.91	0.02
4	75	LPC O-16:1	1.00	0.06	4.71	0.33	1.22	0.06	1.00	0.06	1.15	0.09	1.00	0.10	0.98	0.02
4	76	SM 34:3	1.00	0.13	2.73	0.16	0.81	0.03	1.00	0.12	1.89	0.15	1.00	0.10	1.07	0.15
4	77	SM 35:1	1.00	0.14	0.93	0.09	0.32	0.02	1.00	0.11	1.03	0.13	1.00	0.12	1.20	0.18
4	78	SM 36:0	1.00	0.14	0.78	0.06	0.30	0.00	1.00	0.03	1.14	0.13	1.00	0.04	1.00	0.02

Level	No	Compound	C		ML		PA		KDNC		KD		OENC		OE	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
4	79	SM 38:1	1.00	0.07	0.93	0.06	0.34	0.03	1.00	0.03	1.18	0.14	1.00	0.02	1.04	0.04
4	80	SM 39:1	1.00	0.08	1.46	0.08	0.50	0.06	1.00	0.14	1.09	0.03	1.00	0.06	1.68	0.01
4	81	SM 40:3	1.00	0.10	0.98	0.07	0.34	0.02	1.00	0.04	1.47	0.22	1.00	0.06	0.51	0.06
4	82	SM 42:0	1.00	0.10	0.97	0.09	0.30	0.03	1.00	0.05	1.28	0.08	1.00	0.07	1.24	0.12
4	83	PI 36:1	1.00	0.07	2.30	0.19	1.08	0.06	1.00	0.15	1.91	0.18	1.00	0.08	0.73	0.02
4	84	PI 37:2	1.00	0.12	0.94	0.04	0.27	0.01	1.00	0.09	0.85	0.10	1.00	0.06	1.41	0.07

Note: Data was normalized to corresponding controls.

Table S8. GPR35-related lipid subclasses and their variation trends

Compound	KD	OE	ML	PA
DG	↑	↓	↑**	↓***
TG	↓***	↑***	↑	↓*
PE	↑***	↓**	↑***	↓***
PE(O)	↑***	↓**	↑***	↓***
LPE	↑**	↓	↑***	↓***
Cer	↑	↑	↑**	↓***
HexCer	↓	↑***	↑	↓***
Hex_2Cer	↑	↑	↑***	↓***
PC	↑*	↑	↑*	↓***
PC(O)	↑*	↑	↑*	↓***
LPC	↑***	↓	↑***	↓*
SM	↑***	↑	↑*	↓***
PI	↑***	↓	↑**	↓***
PS	↑**	↓	↑***	↓**
PG	↑	↑	↑***	↓**

Note: The arrows represent the lipid subclasses in the model groups were up/down-regulated (↑/↓). KD, knock-down; OE, over-expression; ML, ML194; PA, pamoic acid. *P < 0.05, **P < 0.01, and ***P < 0.001.

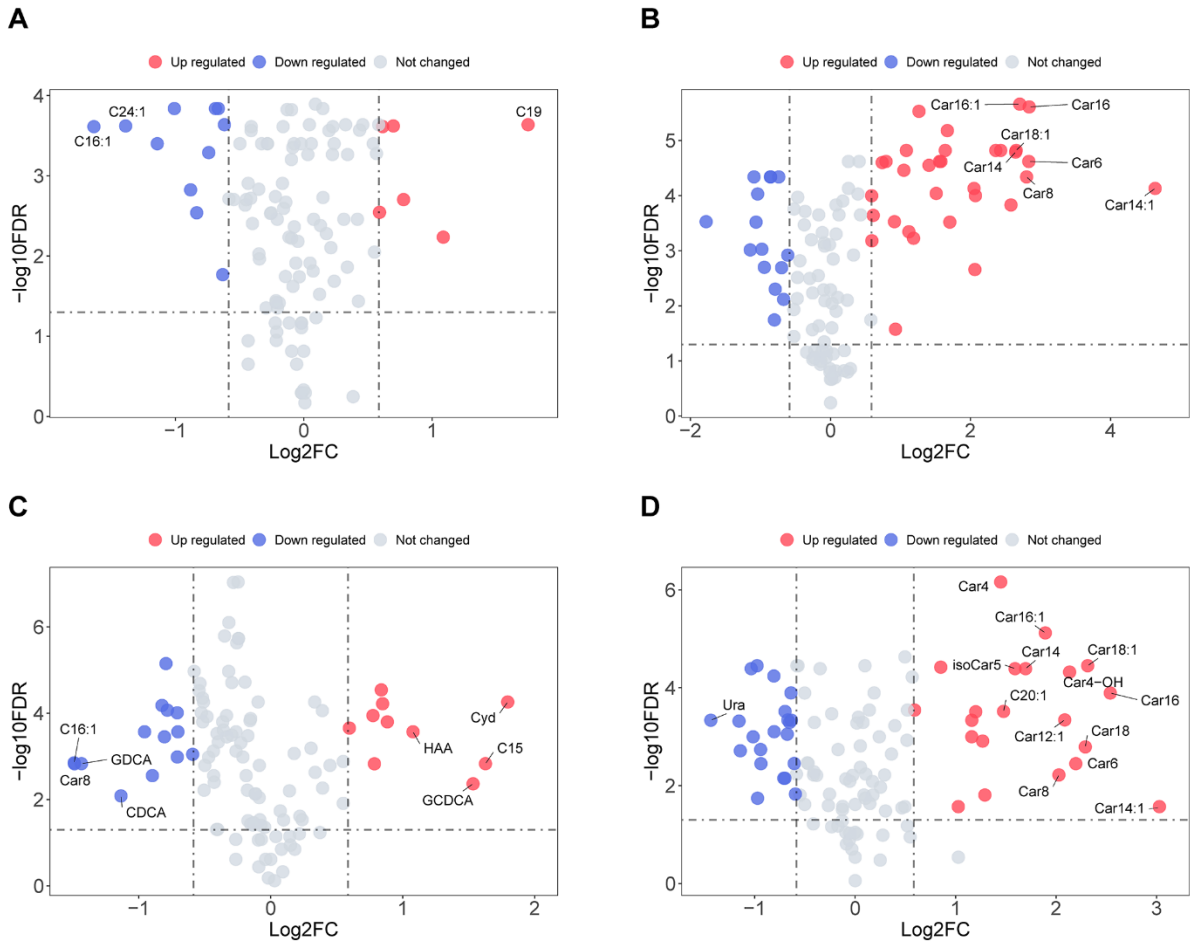

Figure S1. The significant changes of metabolites caused by GPR35 interventions. The volcano plots of metabolites under different GPR35 interventions including (A) knock-down, (B) over-expression, (C) inhibition and (D) activation respectively. The red dots in the figure represent upregulated metabolites, the blue dots represent downregulated metabolites, and the gray dots represent no significant difference. X-axis corresponds to log2 (fold change) and y-axis corresponds to –log10 (adjusted p value).

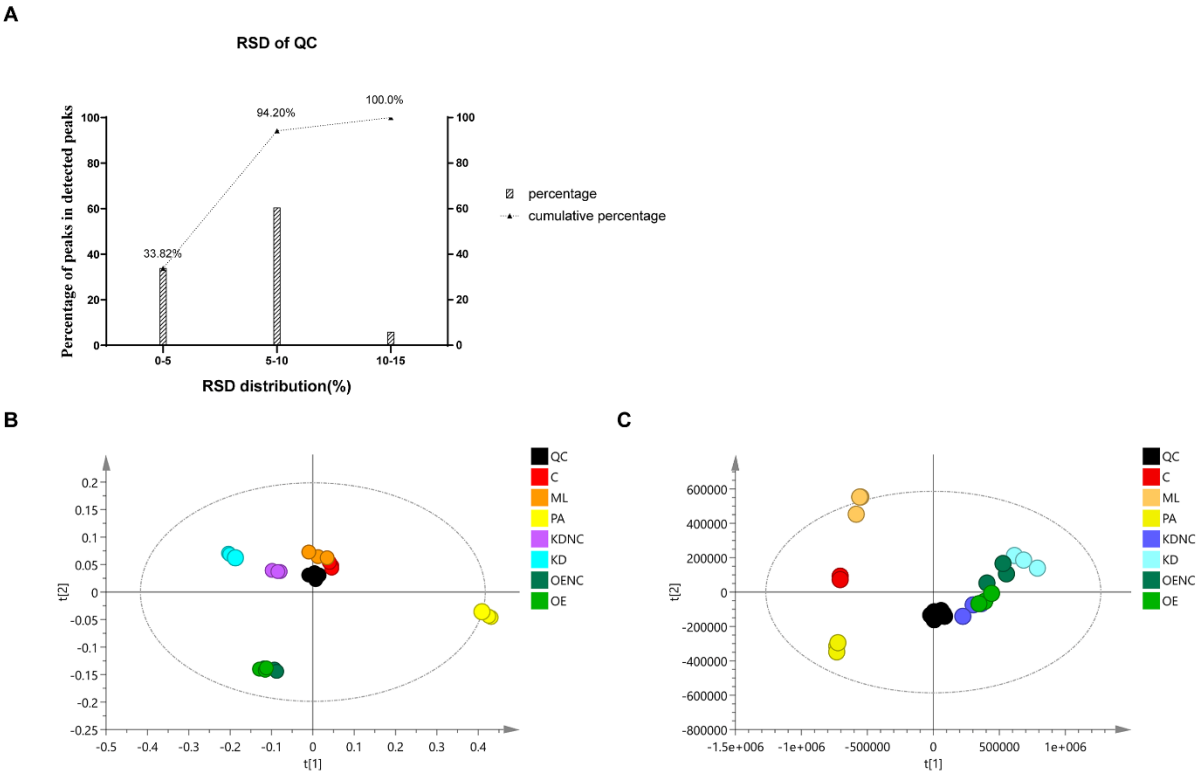

Figure S2. Data quality evaluation of pseudotargeted lipidomics. (A) RSD distribution of detected lipids in QC samples (n=10). (B) PCA (+) and (C)PCA (-) score plots of samples and QC samples (n=3).

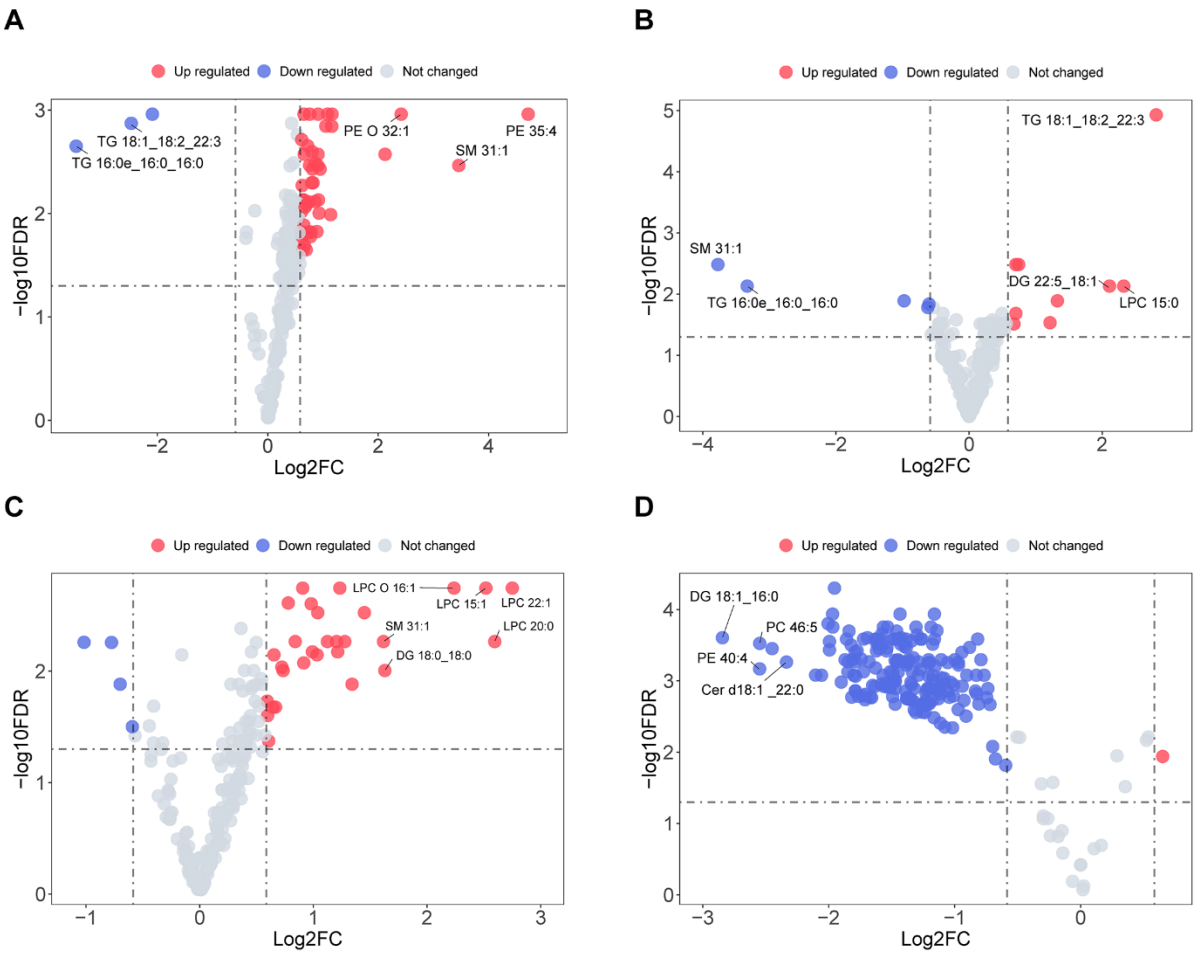

Figure S3. The significant changes of lipids caused by GPR35 interventions. The volcano plots of lipids under different GPR35 interventions including (A) knock-down, (B) over-expression, (C) inhibition and (D) activation respectively. The red dots in the figure represent upregulated lipids, the blue dots represent downregulated lipids, and the gray dots represent no significant difference. X-axis corresponds to log2 (fold change) and y-axis corresponds to –log10 (adjusted p value).