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**Lipids profiling in serum from apolipoprotein E-knock out mice fed with different diets and its application on the
research of regulatory effect on lipid metabolism**

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Hong Chen¹, Fenghong Huang¹**

Table of contents:

- 1) Fig S1-S2
- 2) Table S1-S15

Fig S1 The PCA of QC samples

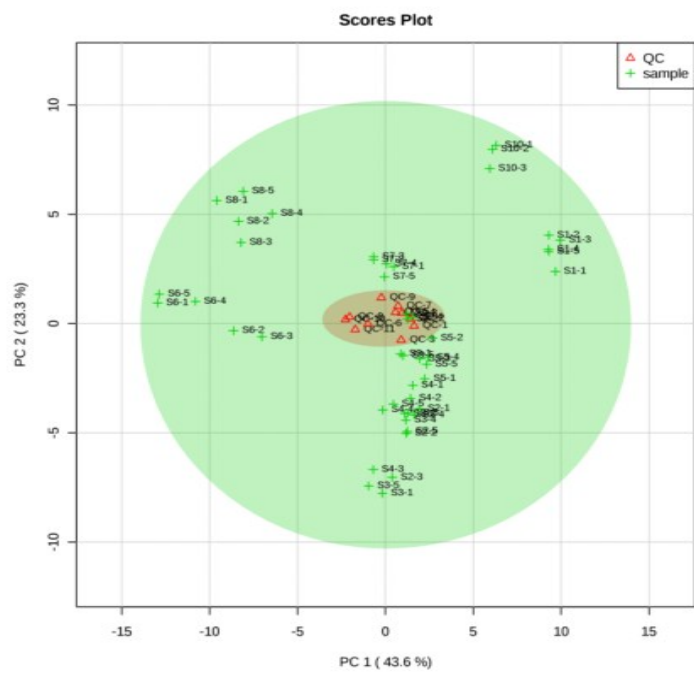


Fig S2 Heatmap visualization of differential metabolites and related pathways. a) M to C, b) YR+M to C, c) APP+M to C, d) LAV+M to C and e) SO+M to C. The color scale (right) illustrates the relative expression level of metabolites across all samples: red color represents an expression level above mean, green color represents expression lower than the mean.

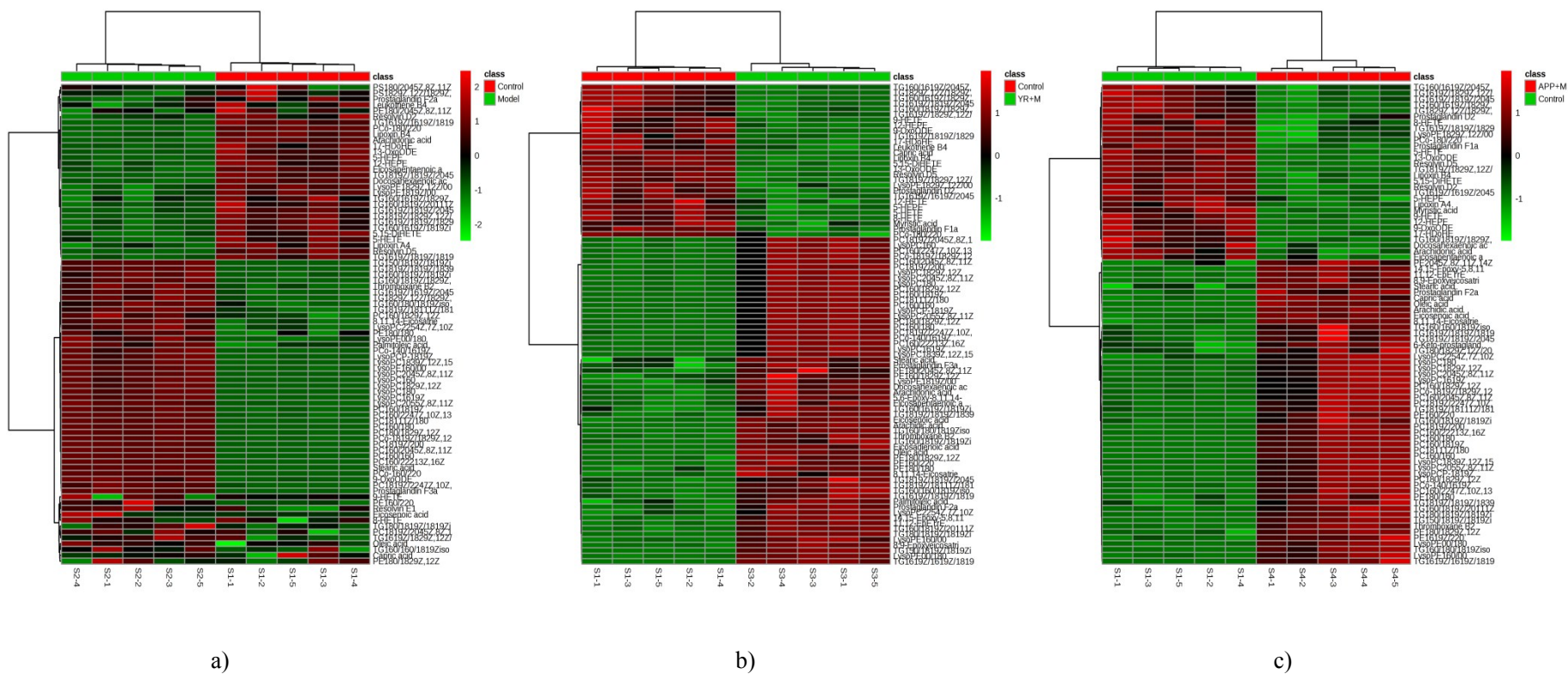


Table S1 The ingredient of each diets

Ingredient	D12102C		D12108C		OD16070802	
	gm	kcal	gm	kcal	gm	kcal
Casein	200	800	200	800	200	800
L-Cystine	3	12	3	12	3	12
Corn Starch	375	1500	212	848	212	848
Maltodextrin 10	125	500	71	284	71	284
Sucrose	200	800	113	452	113	452
Cellulose, BW200	50	0	50	0	50	0
Soybean Oil	25	225	25	225	25	225
Seal oil	0	0	0	0	36	324
Cocoa Butter	20	180	155	1395	119	1071
Mineral Mix S10021	10	0	10	0	10	0
Dicalcium Phosphate	13	0	13	0	13	0
Calcium Carbonate	5.5	0	5.5	0	5.5	0
Potassium Citrate	16.5	0	16.5	0	16.5	0
Vitamin Mix V10001	10	40	10	40	10	40
Choline Bitartrate	2	0	2	0	2	0
Cholesterol	0	0	11.25	0	11.25	0

Table S2 The composition of each diets

Diet NO.	D12102C		D12108C		OD16070802	
	gm%	kcal%	gm%	kcal%	gm%	kcal%
Protein	19.2	20	23	20	23	20
Carbohydrate	67.3	70	45	40	45	40
Fat	4.3	10	20	40	20	40
Total		100		100		100
kcal/gm		3.85		4.5		4.5

Table S3 The optimal parameters of PL

Classes	Scan mode	Declustering potential (V)	Collision energy (V)
PC	+PIS 184	166.8	47.7
PE	+NLS 141	139.9	35.3
PS	+NLS 185	127.7	38.8
PG	+NLS 189	64.6	28.5
PA	+NLS 115	71.3	25.7
PI	+NLS 277	120.4	32.6

Table S4 The optimal parameters of LM

Compounds	Scan mode	Precursor ion (m/z)	Product ion (m/z)	Declustering potential (V)	Collision energy (V)	IS	Retention time (min)
AA	(-)	303.2	259.3	-89	-20	d4-PGE ₂	13.70
LXB ₄	(-)	351.3	221.2	-70	-23	d ₄ -LTB ₄	3.12
5,15-DIHETE	(-)	335.3	115	-43	-20	d ₈ -5S-HETE	5.36
EPA	(-)	301.3	257.3	-90	-19	d4-PGE ₂	12.30
LXA ₅	(-)	349.3	215.2	-48	-26	d ₄ -LTB ₄	3.08
5-HEPE	(-)	317.2	115	-53	-20	d ₈ -5S-HETE	8.94
12-HEPE	(-)	317.2	179.1	-64	-20	d ₈ -5S-HETE	8.73
15-HEPE	(-)	317.2	219.2	-63	-19	d ₈ -5S-HETE	8.46
18-HEPE	(-)	317.2	259.2	-84	-18	d ₈ -5S-HETE	8.03
DHA	(-)	327.3	283.3	-90	-17	d4-PGE ₂	13.20
RvD5	(-)	359.2	199.2	-40	-22	d5-RVD1	5.38
1-Mar	(-)	359.2	250.2	-65	-22	d ₄ -LTB ₄	5.31
PDX	(-)	359.2	153.1	-55	-24	d ₄ -LTB ₄	5.28
4-HDHA	(-)	343.2	101	-46	-21	d ₈ -5S-HETE	10.30
7-HDHA	(-)	343.3	141	-50	-19	d ₈ -5S-HETE	9.82
14-HDHA	(-)	343.3	205.2	-74	-18	d ₈ -5S-HETE	9.51
17-HDHA	(-)	343.2	245.2	-83	-17	d ₈ -5S-HETE	9.32
9-HETE	(-)	319.2	151	-70	-21	d ₈ -5S-HETE	9.98
19-HETE	(-)	319.2	231.2	-91	-23	d ₈ -5S-HETE	8.25
18-HETE	(-)	319.3	261.2	-61	-23	d ₈ -5S-HETE	8.73
17-HETE	(-)	319.3	247.2	-84	-22	d ₈ -5S-HETE	8.80
16-HETE	(-)	319.2	189.2	-72	-22	d ₈ -5S-HETE	8.90
PGJ ₂	(-)	333.2	189.2	-36	-24	d ₄ -PGE ₂	4.57
PGK ₁	(-)	351.3	251.2	-60	-27	d4-PGE ₂	3.19
PGD ₂	(-)	351.3	271.2	-52	-24	d4-PGE ₂	3.38

PGF _{2α}	(-)	353.2	193.1	-90	-39	d4-PGE ₂	3.17
11,12-EET	(-)	319.2	167.2	-61	-19	d11-11,12-EET	10.90
5-HETE	(-)	319.3	115	-58	-21	d ₈ -5S-HETE	10.20
LTB ₄	(-)	335.3	195.2	-70	-22	d ₄ -LTB ₄	5.67
15-HETE	(-)	319.3	219.2	-73	-18	d ₈ -5S-HETE	9.36
PGE ₂	(-)	351.3	271.2	-56	-24	d4-PGE ₂	3.22
PGF _{1α}	(-)	355.2	293.3	-95	-33	d4-PGE ₂	2.99
6-Keto-PGF _{1α}	(-)	369.3	163.1	-110	-42	d4-PGE ₂	2.70
8-HETE	(-)	319.3	155	-66	-20	d ₈ -5S-HETE	9.84
11-HETE	(-)	319.2	167.1	-68	-22	d ₈ -5S-HETE	9.62
12-HETE	(-)	319.2	179	-84	-20	d ₈ -5S-HETE	9.83
20-HETE	(-)	319.3	289.3	-78	-25	d ₈ -5S-HETE	8.36
5,6-EET	(-)	319.2	191.2	-85	-16	d11-11,12-EET	11.20
8,9-EET	(-)	319.2	155	-66	-17	d11-11,12-EET	11.00
14,15-EET	(-)	319.2	219	-64	-16	d11-11,12-EET	10.50
PGF _{3α}	(-)	351.2	307.2	-63	-26	d4-PGE ₂	2.88
TXB ₂	(-)	369.3	169.1	-68	-24	d4-PGE ₂	2.94
TXB ₃	(-)	367.3	169.1	-62	-23	d4-PGE ₂	2.73
LXA ₄	(-)	351.2	115	-63	-21	d ₄ -LTB ₄	3.52
RVE1	(-)	349.2	195.1	-78	-23	d ₄ -LTB ₄	2.57
RVD1	(-)	375	141	-45	-20	d5-RVD1	3.44
RVD2	(-)	375.2	141.2	-80	-23	d5-RVD1	3.10
RVD3	(-)	375.2	147.1	-80	-28	d5-RVD1	3.07
5s,6r-DIHETE	(-)	335.3	114.9	-71	-22	d ₈ -5S-HETE	7.96
5s,6s-DIHETE	(-)	335	115	-50	-29	d ₈ -5S-HETE	8.22
13-oxoODE	(-)	293	113	-70	-30	d4-9s-HODE	9.48
9-oxoODE	(-)	293.2	185.2	-68	-29.24	d4-9s-HODE	9.74

Table S5 The quantitative result of free fatty acids (FFA) in each groups (n=5, Concentration: nmol/L)

Metabolites	C	M	YR+M	APP+M	LAV+M	SO+M
C10:0	404.3±16.9	nd	nd	610.5±36.4	543.1±70	219.4±24.2
C12:0	1413.3±271.5	1376.9±72.2	1165±57.4	1154±220.6	1411.6±56.1	919.9±175.1
C14:0	15430.3±975.3	13434.2±484.7	12188.9±823.2	11766.1±237.5	10467±530.2	7280.9±871.4
C16:0	35653.1±2286.4	35012.1±915.4	33123.7±5325.6	34904.9±2403.7	36786.2±3328.3	13718.5±1695.7
C16:1	10133.6±1635.6	18116.3±1505.1	16447±1038.9	9829.2±622.6	9715.8±835.6	1849.9±419.9
C18:0	9008.1±896.4	12375.4±701.9	11122.4±355.8	11520.4±153.7	10859±1159.6	6302.9±529.4
C18:1	22920±327	60517.1±862.8	53987.9±3695.3	47715.5±2268.8	46168±1864	11896.5±2255.3
C18:2	22984.1±2538.4	25399.9±1022	19089.6±2317.7	18799.7±1718.2	15604.5±616.9	4966.6±1326.2
C18:3	1999.1±619	1905.9±57.7	1970.8±42.3	3079.3±67.5	2364.5±74.7	236.6±29.1
C20:0	nd	314.1±448.5	805.9±93.9	820.1±67.7	1067.9±42.2	81.9±24.8
C20:1	542.1±53.3	1897.5±57.4	1631.3±32.4	1690.4±94.9	1494.7±12.9	230.6±12.6
C20:2	nd	284.1±390.3	552.9±83.3	nd	nd	nd
C20:3	463.7±41.4	1724.7±51.1	1021.1±163.1	838.7±4.3	496±681.1	80.5±49.7
C20:4	3217±546	6693.5±363.7	3725.3±8.3	1632.5±1499.1	1873.5±1729.5	422.8±138.3
C20:5	444.3±34.3	236.8±324.2	812.2±125.9	395.3±367.4	454.8±259.1	207.6±86.3
C22:0	nd	180.8±404.3	nd	nd	nd	nd
C22:1	nd	nd	nd	1011.1±932.7	288±394.8	50.4±49.1
C22:6	2250.8±156	3767.5±62.5	2076.8±276.3	nd	550.6±759.5	717.6±170.8

"nd" stand for " not detected because concentrations were lower than LOQ"

Table S6 The quantitative result of phospholipid (PL) in each groups (n=5, Concentration: nmol/mL)

Metabolites	C	M	YR+M	APP+M	LAV+M	SO+M
LPC(16:0)	81.1±1.88	131.67±7.42	108.2±34.84	114.99±20.15	122.23±2.26	113.45±3.48
LPC(16:1)	2.04±0.03	4.64±0.31	3.69±1.24	3.82±0.76	3.88±0.12	3.79±0.15
LPC(18:0)	45.01±1.43	99.01±4.63	85.61±26.02	88.26±14.93	95.76±1.63	91.21±2.22
LPC(18:1)	21.2±0.76	89.05±5.68	75.13±25.68	78.51±14.21	80.27±0.95	77.39±2.22
LPC(18:2)	45.52±2.09	92.33±6.58	81.84±28.1	84.63±15.55	86.95±1.47	89.37±3.14
LPC(18:3)	0.65±0.01	2.12±0.15	1.93±0.64	1.9±0.37	1.83±0.08	1.43±0.06
LPC(20:4)	16.71±0.76	42.14±3.08	31.17±10.39	36.31±7.07	40.53±1.06	17.7±0.6
LPC(20:5)	0.32±0.02	1.3±0.08	1.34±0.45	1.14±0.23	1.2±0.04	6.66±0.27
PC(O-30:1)	0.29±0.02	0.92±0.05	0.77±0.29	0.71±0.11	0.81±0.06	0.79±0.03
LPC(O-16:0)	0.61±0.01	1.14±0.09	0.93±0.35	1.01±0.1	1.09±0.03	0.93±0.04
LPC(O-18:0)	1.34±0.03	1.7±0.06	1.38±0.45	1.48±0.26	1.64±0.07	1.51±0.06
LPC(O-18:1)	0.29±0.02	0.8±0.06	0.61±0.23	0.64±0.12	0.72±0.02	0.6±0.02
PC(O-18:0/14:2)	nd	1.1±0.03	0.92±0.28	0.99±0.16	1.02±0.05	1.02±0.05
PC(O-16:1/18:0)	2.97±0.21	60.9±1.92	50.65±14.25	55.42±8.36	61.2±1.88	52.33±1.63
PC(O-16:1/18:1)	3.11±0.05	15.19±0.33	13.33±3.61	13.65±2.14	14.96±0.42	14.56±0.29
PC(18:1/18:0)	13.27±0.32	103.97±1.33	98.61±10.82	92.05±13.82	97.12±3.4	115.25±2.79
PC(18:0/18:2)	128.7±3	311.44±6.12	328.32±11.56	288.52±42.81	298.51±9.39	361.22±5.77
PC(18:1/18:2)	47.54±1.05	88.08±1.96	84.39±3.57	74.47±11.73	77.28±2.36	81.66±1.63
PC(16:0/20:4)	114.7±2.75	223.49±4.12	188.05±11.69	186.74±30.13	203.13±5.14	106.98±1.78
PC(18:1/20:0)	0.75±0.06	4.01±0.12	3.56±0.98	3.82±0.58	3.82±0.22	4.31±0.33
PC(16:0/22:2)	2.41±0.1	11.45±0.42	10.66±2.48	11.63±2.02	12.6±0.88	13.85±0.51
PC(16:0/22:3)	9.94±0.21	29.58±0.5	32.24±6.74	26.57±4.22	30.23±1.19	31.18±0.98
PC(16:0/22:4)	56.61±1.21	132±2.12	116.18±5.34	115.49±17.42	126.07±3.57	62.02±1.28
PC(18:1/20:4)	19.66±0.47	30.12±0.35	27.69±0.99	25.66±4.06	27.07±0.85	35.7±1
PC(16:0/22:6)	95.16±2.25	97.61±1.54	106.57±24.49	84.49±13.4	84.94±2.68	104.75±2.09
PC(18:2/22:1)	nd	0.83±0.04	0.76±0.13	0.79±0.1	0.84±0.05	0.75±0.05
PC(18:1/22:4)	1.81±0.09	3.42±0.18	3.01±0.49	3.09±0.42	3.2±0.08	3.19±0.1
PC(O-20:0/20:1)	2.11±0.05	1.81±0.07	1.53±0.32	1.67±0.22	1.79±0.06	1.96±0.07
PC(O-20:1/20:1)	0.29±0.02	0.92±0.02	0.77±0.2	0.85±0.13	0.97±0.06	1.02±0.04
LPC(22:5)	1.13±0.19	2.16±0.21	2.07±0.63	2.24±0.44	2.29±0.21	2.18±0.39
PC(O-16:0/16:0)	0.93±0.04	15.56±0.51	13.12±3.71	13.8±2.17	16±0.55	13.89±0.24

PC(O-16:1/16:0)	0.55±0.04	6.2±0.22	5.13±1.46	5.53±0.78	6.13±0.2	6.41±0.16
PC(16:0/16:0)	7.44±0.23	61±0.61	58.02±2.52	53.79±8.17	56.23±2.18	65.72±1.24
PC(16:0/16:1) PC(14:1/18:0)	3.58±0.11	30.9±0.7	26.45±3.17	25.29±3.97	24.6±1.22	28.13±0.71
PC(14:0/18:2) PC(14:2/18:0)	0.89±0.03	2.51±0.08	2.11±0.58	2.08±0.37	2.11±0.1	2.1±0.03
PC(O-18:0/18:0)	nd	2.54±0.06	2.26±0.54	2.42±0.35	2.83±0.12	3.03±0.06
PC(O-18:0/18:2)	6.37±0.33	17.55±0.45	15.44±3.82	15.93±2.4	17.19±0.53	16.34±0.41
PC(O-18:2/18:1)	1.69±0.11	8.09±0.19	7.32±1.93	7.19±1.18	7.99±0.31	7.11±0.19
PC(O-16:0/20:4)	3.76±0.16	34.55±0.97	27.25±7.57	30.05±4.94	33.83±1.31	17.5±0.52
PC(16:0/18:0)	1.75±0.07	13.87±0.57	13.13±0.57	12.44±2.07	12.79±0.61	15.06±0.3
PC(16:0/18:1)	78.81±1.94	362.52±9.53	341.5±13.42	325.28±47.03	328.31±11.52	346.25±7.59
PC(16:0/18:2)	293.35±7.11	472.89±10.32	467.66±17.44	439.01±64.07	440.92±15.5	505.52±8.55
PC(O-16:0/22:0)	2.69±0.08	2.99±0.08	2.77±0.45	2.67±0.36	2.82±0.12	4.05±0.13
PC(O-20:0/18:1)	0.71±0.03	5.02±0.07	4.17±1.18	4.7±0.62	4.92±0.1	5.09±0.11
PC(O-18:0/20:4)	3.45±0.18	25.65±0.8	20.71±5.49	22.89±3.63	26.38±0.65	12.98±0.28
PC(O-16:0/22:6)	2.64±0.13	11.37±0.25	10.32±2.89	9.92±1.59	11.08±0.32	16.21±0.28
PC(O-18:0/22:0)	9.2±0.2	6.27±0.03	6.5±0.49	5.24±0.86	5.32±0.17	6.47±0.26
LPE(16:0)	1.53±0.08	3.24±0.24	2.97±0.33	3.13±0.48	3.19±0.26	3.53±0.31
LPE(18:0)	1.53±0.12	4.78±0.3	4.48±0.2	4.45±0.62	4.73±0.24	5.51±0.36
LPE(18:1)	0.79±0.07	1.33±0.12	1.18±0.08	1.11±0.15	1.28±0.18	1.49±0.35
LPE(18:2)	3.28±0.14	2.37±0.18	2.39±0.17	1.88±0.38	1.97±0.07	2.22±0.23
LPE(20:3)	0.21±0.04	0.27±0.03	0.22±0.05	0.24±0.06	0.24±0.05	0.3±0.12
LPE(22:5)	0.26±0.05	0.24±0.07	nd	nd	0.24±0.1	nd
LPE(O-16:0)	0.36±0.04	0.37±0.05	0.48±0.04	0.47±0.07	0.41±0.04	0.49±0.07
LPE(O-18:0)	nd	0.2±0.02	0.21±0	0.23±0.05	0.17±0.04	0.28±0.09
LPG(O-16:1)	0.49±0.08	nd	1.16±0.44	0.87±0.14	1.12±0.17	1.75±0.37
LPS(16:0)	3.15±0.27	3.79±0.45	3.22±0.38	3.47±1.5	3.88±0.41	2.59±0.43
LPS(18:0)	1.17±0.17	1.71±0.39	1.61±0.48	1.38±0.55	1.9±0.24	1.27±0.23
LPS(18:1)	0.73±0.13	2.84±0.27	2.12±0.28	2.09±0.76	2.7±0.36	1.99±0.34
LPS(18:2)	1.91±0.14	2.72±0.44	2.25±0.29	2.16±0.85	2.54±0.38	2.12±0.39
PA(O-16:0/18:2)	nd	4.15±0.73	4.78±1.49	3.8±1.2	7.89±0.69	9.17±4.38
PE(O-16:0/16:0)	nd	nd	nd	0.23±0.08	0.18±0.02	nd
PE(O-16:0/18:0)	nd	0.65±0.16	0.47±0.12	0.66±0.08	0.63±0.08	0.61±0.14
PE(18:0/18:0)	0.51±0.13	1.28±0.19	1.25±0.09	1.39±0.26	1.13±0.08	1.5±0.22

PE(18:0/18:1)	0.2±0.03	0.68±0.09	0.66±0.12	0.61±0.13	0.65±0.1	0.71±0.12
PE(18:0/18:2)	0.86±0.1	1.71±0.09	2.01±0.14	1.46±0.09	1.61±0.23	1.85±0.14
PE(18:1/18:2)	0.34±0.05	0.35±0.06	0.47±0.08	0.4±0.06	0.29±0.1	0.37±0.05
PE(18:2/18:2)	0.9±0.11	0.92±0.08	1.07±0.2	1.14±0.24	0.89±0.13	0.52±0.05
PE(16:1/20:5)	nd	0.3±0.06	0.29±0.05	0.27±0.01	0.27±0.08	0.34±0.07
PE(O-18:1/18:1)	1.05±0.08	5.09±0.3	4.83±0.32	4.7±0.71	4.51±0.27	4.54±0.19
PE(16:0/22:0)	0.61±0.04	2.34±0.23	2.44±0.26	2.01±0.44	1.89±0.22	3.1±0.25
PE(16:1/22:0)	0.18±0.04	0.48±0.14	0.43±0.16	0.46±0.08	0.36±0.07	0.67±0.13
PE(O-18:0/20:4)	2.44±0.14	9.6±0.19	8.16±0.56	9.01±1.36	7.85±0.41	5.26±0.29
PE(14:1/24:1)	0.2±0.03	0.31±0.03	0.32±0.06	0.35±0.14	0.28±0.02	0.51±0.12
PE(18:0/20:3)	0.25±0.05	0.37±0.05	0.41±0.17	0.43±0.1	0.39±0.13	0.69±0.17
PE(18:0/20:4)	1.59±0.14	2.19±0.21	2.35±0.31	2.33±0.35	2.1±0.21	1.19±0.14
PE(18:1/20:4)	0.71±0.16	0.57±0.1	0.68±0.12	0.67±0.1	0.56±0.15	0.82±0.13
PE(O-20:1/18:1)	0.63±0.08	2.66±0.2	2.73±0.28	2.51±0.39	2.6±0.13	2.72±0.16
PE(P-20:0/20:4)	0.88±0.1	3.4±0.4	3.41±0.29	3.51±0.81	3.24±0.29	8.08±0.36
PE(20:4/20:4)	0.21±0.04	0.45±0.09	0.47±0.1	0.48±0.07	0.48±0.02	0.52±0.16
PE(O-20:4)	3.69±0.28	2.66±0.12	2.52±0.32	2.3±0.31	2.52±0.36	1.3±0.13
PE(O-20:5)	0.21±0.05	nd	nd	nd	nd	0.4±0.08
PE(O-22:6)	5.59±0.18	2.91±0.32	2.54±0.2	2.19±0.29	2.7±0.22	2.48±0.24
PE(O-16:0/18:1)	0.19±0.04	1.6±0.26	1.56±0.26	1.59±0.24	1.51±0.14	1.48±0.16
PE(P-16:0/18:1)	0.21±0.02	0.87±0.11	0.92±0.19	0.89±0.23	0.62±0.04	0.75±0.14
PE(16:0/18:0)	nd	0.21±0	nd	nd	nd	nd
PE(16:0/18:1)	0.19±0.03	0.45±0.13	0.56±0.06	0.53±0.07	0.5±0.08	0.51±0.05
PE(16:0/18:2)	0.63±0.1	0.83±0.06	1.13±0.2	0.85±0.12	0.74±0.06	0.84±0.2
PE(O-18:1/20:5)	2.11±0.18	8.69±0.33	8.03±0.66	7.76±1.15	6.14±0.53	10.1±0.83
PG(O-14:1/20:1)	nd	1.69±0.14	nd	nd	nd	2.11±1.11
PG(20:4/22:0)	nd	nd	1.52±0.4	1.68±0.57	nd	2.71±0.96
PS(18:0/18:0)	0.79±0.41	1.91±0.36	2.16±0.53	2.48±0.7	2.35±0.49	1.44±0.16
PS(18:0/18:1)	0.63±0.2	0.86±0.13	0.78±0.14	0.98±0.39	1.01±0.19	1.04±0.2
PS(18:1/18:1)	0.61±0.06	0.94±0.21	0.86±0.01	0.85±0.2	0.77±0.11	0.75±0.13
PS(18:0/18:3)	nd	0.84±0.21	0.74±0.3	0.94±0.32	1.21±0.22	1.05±0.07
PS(18:2/18:2)	10.31±3.62	19.7±2.32	17.53±1.31	18.83±3.51	22.01±4.94	24.01±1.78
PS(14:1/22:5)	2.82±0.9	1.67±0.44	1.36±0.17	1.49±0.38	1.77±0.74	1.6±0.38

PS(16:0/22:0)	0.69±0.15	1.35±0.36	1.51±0.18	2.01±0.62	1.56±0.55	1.08±0.32
PS(18:0/20:4)	2.05±0.45	5.19±0.85	4.57±1.09	4.51±1.16	6.24±2.89	7.08±0.96
PS(18:1/20:4)	22.19±9.04	20.03±2.11	19.47±1.63	19.43±3.98	23.19±6.55	27.8±2.66
PS(18:0/22:0)	nd	nd	0.77±0.2	0.7±0.13	0.83±0.04	nd
PS(18:1/22:0)	nd	nd	0.81±0.04	0.85±0.34	0.91±0.23	0.83±0.22
PS(18:0/22:6)	2.36±0.9	2.15±0.77	2.05±0.39	2.03±0.73	2.59±0.48	2.31±0.2
PS(20:4/20:4)	4.49±1.19	2.34±0.57	2.33±0.5	2.24±0.55	3.16±0.91	4.17±0.88
PS(10:0/18:0)	0.69±0.1	0.74±0.1	0.78±0.08	0.94±0.38	0.88±0.2	0.67±0.21
PS(16:0/18:1)	nd	0.92±0.18	0.77±0.07	0.73±0.24	0.9±0.17	0.72±0.11
PS(16:0/18:2)	0.81±0.16	0.72±0.12	0.97±0.15	0.82±0.27	0.81±0.19	nd
PS(O-20:0/18:0)	26.7±9.81	18.51±2.46	14.26±1.49	16.56±3.23	21.27±5.53	11.11±1.3

"nd" stand for " not detected because concentrations were lower than LOQ"

Table S7 The quantitative result of lipid mediators (LM) in each groups (n=5, Concentration: nmol/L)

Metabolites	C	M	YR+M	APP+M	LAV+M	SO+M
AA	1986±257.35	1046±137.77	4943.6±728.68	1154.4±203.97	1962±246.52	2200±281.78
LXB ₄	12.02±0.94	3±0.37	3.12±0.44	5.86±0.93	2.44±0.34	1.78±0.33
5,15-DIHETE	3.96±0.28	1.49±0.23	0.9±0.25	1.39±0.25	1.86±0.28	0.43±0.07
EPA	496.6±62.97	271±37.37	1091.8±176.2	322.2±54.01	487.8±41.55	4024±499.58
LXA ₅	3.22±0.24	1.66±0.19	0.99±0.2	1.68±0.35	0.89±0.27	1.55±0.26
12-HEPE	1726±110.82	1168±110.71	961.8±147.39	1081.8±151.03	1152±170.21	4830±573.8
5-HEPE	8.67±1.58	1.39±0.28	3.54±0.54	2.48±0.31	2.74±0.13	24.56±3.42
15-HEPE	12.03±1.87	5.2±0.88	6.6±1	6.04±0.41	7.73±0.93	54.52±4.69
18-HEPE	12.06±2.11	1.93±0.23	3.65±0.38	3.4±0.86	3.68±0.19	40.18±2.85
DHA	1266±238.18	749.4±94.9	4162±457.68	691.6±113.79	1460±241.87	4360±601.12
RvD5	2.05±0.16	0.53±0.1	0.6±0.09	0.33±0.07	0.45±0.13	0.51±0.15
1-Mar	4.9±0.66	0.46±0.09	0.55±0.1	0.48±0.09	0.45±0.08	1.55±0.26
PD1	2.84±0.35	0.81±0.08	0.56±0.08	0.45±0.11	0.84±0.13	1.39±0.33
4-HDHA	40.92±5.76	7.64±0.45	10.6±1.44	7.62±0.91	9.97±1.51	47.48±5.92
7-HDHA	16.28±2.32	1.21±0.1	2.58±0.44	2.86±0.44	2.94±0.55	12.2±1.57
14-HDHA	2008±84.68	1784±189.42	1882±265.93	1796±240.27	2352±280.12	3265±324.6
17-HDHA	352.6±47.44	225.4±31.57	162.6±15.04	158.8±15.99	183.8±19.59	354.8±21.53
9-HETE	65.52±10.41	35.22±1.43	27.85±2.62	26.33±2.28	33.6±1.71	18.78±2.34
19-HETE	11.28±0.16	11.29±1.43	8.58±1.49	11.53±1.43	11.1±0.97	5.79±0.39
18-HETE	8.27±0.55	5.54±0.47	5.15±0.7	5.32±0.79	5.33±0.46	2.27±0.33
17-HETE	1.78±0.06	1.66±0.14	1.15±0.13	1.2±0.14	1.36±0.23	0.94±0.18
16-HETE	4.47±0.34	4.09±0.59	4.9±0.68	3.22±0.7	2.56±0.41	1.54±0.25
PGJ ₂	0.33±0.08	0.37±0.08	0.37±0.06	0.4±0.11	0.55±0.11	0.42±0.04
PGK ₁	2.16±0.25	0.61±0.15	0.88±0.17	1.17±0.22	1.06±0.09	1.08±0.29
PGD ₂	6.8±0.46	6.52±0.75	4.84±0.24	5.13±0.67	6.34±0.63	4.1±0.74
PGF _{2α}	1.38±0.07	1.93±0.13	1.93±0.13	2.09±0.2	2.54±0.35	1.61±0.25
11,12-EET	233.2±26.29	192.4±22.2	713.6±54.84	796.2±85.83	297.8±56.41	236.4±31.14
5-HETE	82.4±12.27	23.11±3.05	22.64±3.04	26.58±1.84	26.95±2.95	20.97±3.15
LTB ₄	1.66±0.28	0.76±0.17	0.94±0.13	1.25±0.17	1.15±0.16	0.79±0.11
15-HETE	160.4±23.95	136.4±17.17	76.06±6.15	98±9.28	110.24±14.29	85.2±7.55
PGE ₂	4.9±0.49	5.09±0.31	4.13±0.37	4.16±0.59	4.35±0.18	4.55±0.48

PGF _{1α}	3.54±0.31	4.15±0.52	1.88±0.27	1.33±0.22	1.47±0.11	2.03±0.27
6-Keto-PGF _{1α}	0.43±0.14	0.54±0.06	0.74±0.07	0.95±0.14	1.05±0.12	0.87±0.24
8-HETE	59.21±6.58	40.76±4.99	31.37±4.44	37.54±6.54	57.35±5.6	42.57±6.2
11-HETE	41.28±6.65	42.58±4.39	50.38±5.2	59.78±7.91	77.86±8.98	44.52±0.77
12-HETE	9562±1272.6	9876±561.36	6210±843.71	11400±758.29	11008±1599.97	6652±1108.27
20-HETE	9.44±0.88	12.1±1.64	9.97±1.23	10.64±0.94	13.34±1.51	8.29±0.3
5,6-EET	5848±748.18	5596±1013.18	14640±1722.79	4632±560.95	2144±242.24	7078±1314.96
8,9-EET	286.6±26.67	390.2±60.78	775.2±57.54	766.2±90.06	329.6±45.2	266.8±28.73
14,15-EET	337.4±38.93	388±60.25	952±113.23	1132.6±86.71	402.4±61.33	357.8±47.04
PGF _{3α}	1.66±0.23	5.27±0.69	2.43±0.2	1.04±0.36	0.58±0.12	2.51±0.43
TXB ₂	125.4±8.35	394.2±22.93	260.4±24.64	298.6±30.81	287±9.87	233.2±19.9
TXB ₃	3.94±0.37	7.06±0.53	6.3±0.66	6.05±0.49	6.07±0.68	30.88±4.46
LXA ₄	2.39±0.59	0.58±0.21	2.27±0.52	0.5±0.19	0.58±0.24	1.17±0.49
RVE1	8.37±0.85	5.97±0.64	6.43±0.83	5.81±1.12	5.27±0.51	2.9±0.51
RVD1	0.85±0.18	1.07±0.14	0.9±0.21	0.48±0.08	0.53±0.18	0.69±0.14
RVD2	5.17±0.61	1.33±0.19	4.07±0.49	1.84±0.3	5.51±1.1	3.94±0.61
RVD3	0.57±0.18	0.23±0.08	0.31±0.07	0.12±0.01	0.33±0.15	nd
5s,6r-DIHETE	0.17±0.04	0.14±0.03	0.08±0.02	0.15±0.08	0.18±0.02	0.09±0.05
5s,6s-DIHETE	1.14±0.13	1.36±0.17	0.4±0.11	0.34±0.06	0.38±0.03	0.3±0.08
13-oxoODE	89.5±7.41	14.94±2.45	27.62±2.3	31.58±3.81	52.44±6.26	82.38±6.31
9-oxoODE	82.84±18.28	13.86±2.95	17.14±1.59	14.1±1.29	13.9±2.16	24.4±3.87

"nd" stand for " not detected because concentrations were lower than LOQ"

Table S8 The quantitative result of triacylglycerol (TAG) in each groups (n=5, Concentration: nmol/mL)

Metabolites	C	M	YR+M	APP+M	LAV+M	SO+M
ArPoPo	0.6±0.1	0.2±0	0.3±0	0.2±0	0.2±0	0.2±0
DhPPo	2.2±0.5	1±0.2	1.2±0.3	0.8±0.2	0.8±0.2	1.6±0.4
ArLPo	3.1±0.6	1.1±0.2	1.1±0.3	1±0.3	0.9±0.2	0.5±0.1
EpOPo+EpLP	5.5±0.9	1.4±0.3	1.9±0.5	1.3±0.4	1.1±0.3	8±1.3
LnPPo+LnMO	0.5±0.1	0.2±0.1	0.3±0.1	0.2±0.1	0.2±0	0.1±0
LPoPo+LLM	0.3±0.1	0.3±0.1	0.4±0.1	0.3±0.1	0.2±0	0.2±0
ArPPo	0.8±0.1	0.5±0.1	0.4±0.1	0.4±0.1	0.4±0.1	0.2±0
PaPO	0.6±0.1	0.7±0.1	0.9±0.1	0.6±0.2	0.5±0.1	0.4±0.1
LnPoO+PLLn	7.6±1.6	2.1±0.4	2.5±0.4	1.9±0.5	1.4±0.3	0.9±0.1
DpPPo	0.5±0.1	0.3±0.1	0.3±0	0.2±0	0.2±0	0.2±0
EpPO	2.4±0.4	2±0.4	2.7±0.3	2.1±0.5	1.5±0.2	13.1±2.4
ArPoO	12.2±1.8	5.4±1	5.2±0.5	5.2±1.2	4.2±0.5	2.4±0.4
LLL	5.1±0.9	0.8±0.2	0.9±0.1	0.8±0.2	0.7±0.2	0.4±0.1
MOL	0.9±0.1	0.4±0.1	0.5±0.1	0.4±0.1	0.3±0.1	0.2±0
MoOO	0.1±0	0.4±0	0.6±0	0.4±0.1	0.3±0	0.2±0
PPoL	8.2±1.4	2.6±0.5	3±0.4	2.3±0.5	1.8±0.4	1.3±0.2
PoPoO	0±0	0.5±0.1	0.6±0	0.5±0.1	0.4±0	0.2±0
PoOL	6.4±0.4	4.4±0.2	5.3±0.1	4.3±0.7	3.2±0.3	2.2±0.3
LnPO	35.9±3.5	6.9±0.7	8.5±0.3	7±1.2	5.5±0.5	4±0.6
LLO	21±1.9	7±0.4	8.5±0.6	6.9±0.8	6.1±1.3	4.3±0.6
LnOO	2±0.2	3.2±0.2	3.9±0.4	3.1±0.4	2.4±0.3	1.6±0.2
DpPO	2.8±0.4	4.1±0.5	3.3±0.5	3.5±0.7	2.9±0.5	3.3±0.5
EtOL	1.3±0.2	2.4±0.4	1.9±0.4	2.1±0.5	1.8±0.3	0.6±0
ArOO	6.9±1.3	20.7±2.7	16.7±3.8	16.7±3.8	12.1±2.4	5.2±0.3
MOO	0.9±0.2	2.6±0.8	2.2±0.3	2.3±0.4	1.6±0.3	0.8±0.1
PPoO	3.9±0.6	6.3±0.5	6.3±0.6	5.4±0.7	4.1±0.5	3.2±0.4
PLO	76.1±15.2	38.3±4.8	36.5±5.3	26.8±4.2	19.3±3	14.5±2.1
PoOO	4.8±1.1	16.8±2	15.5±2.8	11.6±2.8	7.5±1.6	4±0.3
OOL	21±4.9	27.4±4	30.6±5.5	23.5±5.6	18.2±4.4	9.1±0.5
PEtO	1.1±0.3	4.7±1	4.3±0.8	4.1±1.6	4.2±0.8	1.4±0.1
LLS	3.3±0.6	2.7±0.5	3.4±0.7	2.6±0.6	1.5±0.5	1.6±0.2

MSO	0.1±0	0.1±0	0.2±0.1	0.1±0	0.1±0	0.2±0
PPO	5±1	14±2	18.5±3.5	15.1±4	8.7±1.6	8.1±0.4
POO	20.9±3.1	65.6±10.7	74.2±13.2	59.5±14	51.8±5	38.2±4.5
OOO	7.5±2.9	42.9±6	43.9±6.7	35.5±9	32.3±5.4	17.8±4.1
EdPO	1.7±0.3	1.4±0.2	1.2±0.2	1.2±0.3	1.1±0.1	1.1±0.1
POS	1.5±0.3	16.9±0.5	20.5±1.5	19.7±4.1	10.4±2	23.3±4
GPP	0.4±0.1	0.4±0	0.3±0	0.3±0.1	0.4±0.1	0.5±0.1
GPO	0.9±0.1	2.7±0.4	2.4±0.2	2.7±0.5	2.5±0.4	3.5±1.1
SOO	2.2±0.5	20.2±2.6	24.9±2.1	25.8±5.4	14.8±2	32.7±9.6
OOG+OLA	0.6±0.2	3.8±0.8	4.9±1.5	6.3±2	6±1.1	5.3±0.7
SLG	0.3±0.1	0.5±0.2	0.6±0.1	0.5±0.1	0.5±0	0.8±0.2
DhHP	0.3±0.1	11.2±1.7	8.1±1.1	8.5±2.2	9.1±1.7	18.7±2.1
DhHO	0.1±0	4.2±0.3	3.5±0.2	3.6±0.9	3.1±0.6	9±2.2
DhSH	0.1±0	4±0.7	3.8±1.2	5.7±2	7.9±1.8	19.2±3
PdOO	0±0	3±0.2	2.5±0.3	2.8±0.5	2.7±0.3	4±0.9

"nd" stand for " not detected because concentrations were lower than LOQ"

Table S9 The potential active metabolites between model group (M) and control group (C) (VIP>1, p<0.05)

Metabolites	VIP	Fold change	P value	Regulation (up or down)
M vs. C				
PC(16:0/16:0)	1.19	8.63	***	↑
PC(18:1(11Z)/18:0)	1.19	2.42	***	↑
Oleic acid	1.19	1.11	***	↑
PC(16:0/22:4(7Z,10Z,13Z,16Z))	1.19	1.53	***	↑
TG(16:0/18:0/18:1(9Z))[iso6]	1.19	1.60	***	↑
PC(16:0/18:1(9Z))	1.19	1.61	***	↑
PC(18:0/18:2(9Z,12Z))	1.18	1.85	***	↑
Capric acid	1.18	0.97	***	↓
PC(18:1(9Z)/20:0)	1.18	4.76	***	↑
PC(16:0/20:4(5Z,8Z,11Z,14Z))	1.18	5.33	***	↑
PC(16:0/22:2(13Z,16Z))	1.18	2.98	***	↑
PC(16:0/18:0)	1.18	4.60	***	↑
8,11,14-Eicosatrienoic acid	1.18	2.08	***	↑
PC(o-18:1(9Z)/18:2(9Z,12Z))	1.18	1.95	***	↑
PC(18:1(9Z)/20:4(5Z,8Z,11Z,14Z))	1.18	1.03	***	↑
Eicosenoic acid	1.18	/	***	↑
PC(o-18:0/22:0)	1.18	/	***	↓
PC(16:0/18:2(9Z,12Z))	1.18	1.11	***	↑
LysoPC(20:5(5Z,8Z,11Z,14Z,17Z))	1.18	3.20	***	↑
TG(15:0/18:1(9Z)/18:1(9Z))[iso3]	1.18	67.85	***	↑
LysoPC(P-18:1(9Z))	1.18	2.03	***	↑
PC(o-14:0/16:1(9Z))	1.18	1.86	***	↑
Thromboxane B2	1.18	1.79	***	↑
LysoPC(18:0)	1.18	4.20	***	↑
LysoPE(0:0/18:0)	1.18	1.69	***	↑
LysoPC(18:3(9Z,12Z,15Z))	1.18	2.52	***	↑
13-OxoODE	1.18	0.17	***	↓
Lipoxin B4	1.17	0.38	***	↓
TG(16:1(9Z)/16:1(9Z)/18:1(9Z))[iso3]	1.17	0.29	***	↓
LysoPC(16:1(9Z))	1.17	2.20	***	↑

PC(18:1(9Z)/22:4(7Z,10Z,13Z,16Z))	1.17	1.89	***	↑
Resolvin D5	1.17	0.09	***	↓
LysoPC(20:4(5Z,8Z,11Z,14Z))	1.17	4.06	***	↑
PE(16:0/22:0)	1.17	2.58	***	↑
TG(18:1(9Z)/18:2(9Z,12Z)/18:2(9Z,12Z))[iso3]	1.17	0.16	***	↓
TG(18:0/18:1(9Z)/18:1(9Z))[iso3]	1.17	1.56	***	↑
5,15-DiHETE	1.17	0.55	***	↓
LysoPC(18:2(9Z,12Z))	1.17	3.27	***	↑
LysoPE(16:0/0:0)	1.17	3.12	***	↑
LysoPC(16:0)	1.16	2.27	***	↑
PE(18:0/18:2(9Z,12Z))	1.16	1.02	***	↑
Resolvin D2	1.16	0.40	***	↓
TG(16:1(9Z)/18:1(9Z)/18:1(9Z))[iso3]	1.15	0.68	***	↓
TG(18:1(9Z)/18:1(11Z)/18:1(9Z))[iso3]	1.15	1.65	***	↑
TG(16:1(9Z)/16:1(9Z)/20:4(5Z,8Z,11Z,14Z))[iso3]	1.15	3.48	***	↑
Prostaglandin F3a	1.15	3.14	***	↑
TG(16:0/18:1(9Z)/20:1(11Z))[iso6]	1.15	0.50	***	↓
5-HETE	1.15	0.46	***	↓
TG(18:1(9Z)/18:1(9Z)/20:4(5Z,8Z,11Z,14Z))[iso3]	1.14	0.33	***	↓
12-HEPE	1.14	0.43	***	↓
TG(18:2(9Z,12Z)/18:2(9Z,12Z)/18:2(9Z,12Z))	1.14	5.75	***	↑
TG(16:1(9Z)/18:1(9Z)/18:2(9Z,12Z))[iso6]	1.14	0.44	***	↓
TG(18:1(9Z)/18:1(9Z)/18:3(9Z,12Z,15Z))[iso3]	1.14	67.85	***	↑
LysoPE(18:2(9Z,12Z)/0:0)	1.13	0.72	***	↓
TG(16:0/18:1(9Z)/18:1(9Z))[iso3]	1.13	2.90	***	↑
TG(16:0/16:0/18:1(9Z))[iso3]	1.13	1.16	***	↑
LysoPE(18:1(9Z)/0:0)	1.13	0.72	***	↓
9-OxoODE	1.12	2.11	***	↑
Prostaglandin F2a	1.12	0.83	***	↓
LysoPC(22:5(4Z,7Z,10Z,13Z,16Z))	1.12	1.90	***	↑
Palmitoleic acid	1.12	1.37	***	↑
TG(16:0/16:1(9Z)/18:2(9Z,12Z))[iso6]	1.12	0.67	***	↓
5-HEPE	1.12	0.16	***	↓

PE(18:0/18:0)	1.11	3.46	***	↑
TG(16:1(9Z)/18:1(9Z)/20:4(5Z,8Z,11Z,14Z))[iso6]	1.11	0.35	***	↓
Arachidonic acid	1.10	0.25	***	↓
TG(16:0/16:1(9Z)/18:1(9Z))[iso6]	1.10	0.32	***	↓
Eicosapentaenoic acid	1.10	0.51	***	↓
TG(16:1(9Z)/18:2(9Z,12Z)/20:4(5Z,8Z,11Z,14Z))[iso6]	1.09	1.31	***	↑
Stearic acid	1.09	2.64	***	↑
9-HETE	1.09	1.00	***	↑
Lipoxin A4	1.09	0.71	***	↓
Leukotriene B4	1.08	0.85	***	↓
PC(o-16:0/22:0)	1.07	7.04	***	↑
PE(18:0/20:4(5Z,8Z,11Z,14Z))	1.05	0.80	***	↓
TG(16:0/18:1(9Z)/18:2(9Z,12Z))[iso6]	1.05	9.21	***	↑
PS(18:0/20:4(5Z,8Z,11Z,14Z))	1.04	0.90	***	↓
Resolvin E1	1.04	1.26	**	↑
8-HETE	1.03	1.03	**	↑
17-HDoHE	1.03	0.54	**	↓
PS(18:2(9Z,12Z)/18:2(9Z,12Z))	1.03	0.59	**	↓
Docosahexaenoic acid	1.01	0.26	**	↓

“↑” for up-regulation and “↓” for down-regulation. “*”, “**” and “***” indicate the difference is significant ($P<0.05$), ($P<0.01$) and ($P<0.001$). VIP, variable importance for projection.

Table S10 The potential active metabolites between Yirui capsule group (YR+M) and control group (C) (VIP>1, p<0.05)

Metabolites	VIP	Fold change	P value	Regulation (up or down)
YR+M vs. C				
Capric acid	1.16	/	***	↓
Eicosenoic acid	1.16	3.01	***	↑
TG(16:0/18:0/18:1(9Z))[iso6]	1.16	13.93	***	↑
TG(16:1(9Z)/16:1(9Z)/18:1(9Z))[iso3]	1.15	/	***	↑
LysoPE(0:0/18:0)	1.15	2.92	***	↑
Oleic acid	1.15	2.36	***	↑
Arachidic acid	1.15	/	***	↑
TG(18:0/18:1(9Z)/18:1(9Z))[iso3]	1.15	11.34	***	↑
TG(15:0/18:1(9Z)/18:1(9Z))[iso3]	1.15	56.96	***	↑
Lipoxin B4	1.15	0.26	***	↓
Resolvin D5	1.15	0.3	***	↓
13-OxoODE	1.14	0.31	***	↓
5,15-DiHETE	1.14	0.23	***	↓
11,12-EpETrE	1.14	3.06	***	↑
8,9-Epoxyeicosatrienoic acid	1.14	2.7	***	↑
Eicosadienoic acid	1.14	/	***	↑
PE(16:0/22:0)	1.14	3.98	***	↑
PE(18:0/18:2(9Z,12Z))	1.14	2.32	***	↑
TG(18:1(9Z)/18:2(9Z,12Z)/18:2(9Z,12Z))[iso3]	1.14	0.4	***	↓
TG(16:0/18:1(9Z)/20:1(11Z))[iso6]	1.14	2.58	***	↑
Thromboxane B2	1.13	2.08	***	↑
Docosahexaenoic acid	1.13	3.29	***	↑
PE(18:0/18:0)	1.12	2.43	***	↑
14,15-Epoxy-5,8,11-eicosatrienoic acid	1.12	2.82	***	↑
TG(18:1(9Z)/18:1(11Z)/18:1(9Z))[iso3]	1.12	5.89	***	↑
5-HETE	1.12	0.27	***	↓
5,6-Epoxy-8,11,14-eicosatrienoic acid	1.12	2.5	***	↑
TG(18:2(9Z,12Z)/18:2(9Z,12Z)/18:2(9Z,12Z))	1.11	0.18	***	↓
TG(16:1(9Z)/16:1(9Z)/20:4(5Z,8Z,11Z,14Z))[iso3]	1.11	0.39	***	↓
LysoPE(16:0/0:0)	1.11	1.94	***	↑

5-HEPE	1.11	0.56	***	↓
LysoPE(18:2(9Z,12Z)/0:0)	1.11	0.73	***	↓
TG(16:0/18:1(9Z)/18:1(9Z))[iso3]	1.11	3.54	***	↑
TG(18:1(9Z)/18:1(9Z)/18:3(9Z,12Z,15Z))[iso3]	1.11	1.99	***	↑
Prostaglandin F1a	1.10	0.53	***	↓
Arachidonic acid	1.10	2.49	***	↑
Prostaglandin F2a	1.10	1.4	***	↑
17-HDoHE	1.10	0.46	***	↓
Prostaglandin D2	1.10	0.71	***	↓
TG(16:0/16:0/18:1(9Z))[iso3]	1.10	3.67	***	↑
TG(16:1(9Z)/18:1(9Z)/20:4(5Z,8Z,11Z,14Z))[iso6]	1.09	0.43	***	↓
LysoPE(18:1(9Z)/0:0)	1.09	1.5	***	↑
PC(18:1(11Z)/18:0)	1.09	7.78	***	↑
PC(16:0/18:1(9Z))	1.09	4.39	***	↑
PC(16:0/16:0)	1.09	7.68	***	↑
LysoPC(20:5(5Z,8Z,11Z,14Z,17Z))	1.09	4.84	***	↑
LysoPC(P-18:1(9Z))	1.09	4.08	***	↑
PC(18:0/18:2(9Z,12Z))	1.09	2.53	***	↑
PC(16:0/18:0)	1.09	7.48	***	↑
PC(16:0/22:2(13Z,16Z))	1.09	4.88	***	↑
LysoPC(18:0)	1.09	2.16	***	↑
LysoPC(18:3(9Z,12Z,15Z))	1.09	3.41	***	↑
8,11,14-Eicosatrienoic acid	1.09	2.2	***	↑
PC(o-14:0/16:1(9Z))	1.09	3.13	***	↑
TG(16:1(9Z)/18:1(9Z)/18:1(9Z))[iso3]	1.09	3.22	***	↑
LysoPC(20:4(5Z,8Z,11Z,14Z))	1.09	2.14	***	↑
9-OxoODE	1.09	0.21	***	↓
PC(18:1(9Z)/20:0)	1.09	5.3	***	↑
LysoPC(18:2(9Z,12Z))	1.09	2.07	***	↑
PC(16:0/18:2(9Z,12Z))	1.09	1.61	***	↑
LysoPC(16:1(9Z))	1.09	2.08	***	↑
PC(o-18:1(9Z)/18:2(9Z,12Z))	1.09	1.8	***	↑
8-HETE	1.09	0.53	***	↓

TG(16:0/16:1(9Z)/18:2(9Z,12Z))[iso6]	1.09	0.37	***	↓
PC(16:0/20:4(5Z,8Z,11Z,14Z))	1.09	1.6	***	↑
9-HETE	1.09	0.43	***	↓
PC(16:0/22:4(7Z,10Z,13Z,16Z))	1.09	2.04	***	↑
PC(18:1(9Z)/22:4(7Z,10Z,13Z,16Z))	1.09	1.78	***	↑
LysoPC(16:0)	1.09	1.52	***	↑
PC(18:1(9Z)/20:4(5Z,8Z,11Z,14Z))	1.08	1.41	***	↑
Palmitoleic acid	1.08	1.62	***	↑
Eicosapentaenoic acid	1.08	2.2	***	↑
PC(o-18:0/22:0)	1.07	0.69	***	↓
LysoPC(22:5(4Z,7Z,10Z,13Z,16Z))	1.07	2.07	***	↑
12-HEPE	1.07	0.41	***	↓
TG(16:1(9Z)/18:2(9Z,12Z)/20:4(5Z,8Z,11Z,14Z))[iso6]	1.07	0.36	***	↓
TG(16:0/16:1(9Z)/18:1(9Z))[iso6]	1.06	1.6	***	↑
TG(16:1(9Z)/18:1(9Z)/18:2(9Z,12Z))[iso6]	1.05	0.82	***	↓
TG(16:0/16:1(9Z)/20:4(5Z,8Z,11Z,14Z))[iso6]	1.05	0.54	***	↓
Myristic acid	1.04	0.79	***	↓
Prostaglandin F3a	1.03	1.46	***	↑
TG(16:0/18:1(9Z)/18:2(9Z,12Z))[iso6]	1.03	0.48	***	↓
TG(18:1(9Z)/18:1(9Z)/20:4(5Z,8Z,11Z,14Z))[iso3]	1.03	2.42	***	↑
Leukotriene B4	1.02	0.57	***	↓
PE(18:0/20:4(5Z,8Z,11Z,14Z))	1.01	1.48	***	↑
PE(16:0/18:2(9Z,12Z))	1.01	1.79	**	↑
12-HETE	1.00	0.65	**	↓
Stearic acid	1.00	1.23	**	↑

“↑” for up-regulation and “↓” for down-regulation. “*”, “**” and “***” indicate the difference is significant ($P<0.05$), ($P<0.01$) and ($P<0.001$). VIP, variable importance for projection.

Table S11 The potential active metabolites between antihypertensive peptides capsule group (APP+M) and control group (C) (VIP>1, p<0.05)

Metabolites	VIP	Fold change	P value	Regulation (up or down)
APP+M vs. C				
Oleic acid	1.18	2.08	***	↑
Arachidic acid	1.18	/	***	↑
Eicosenoic acid	1.17	3.12	***	↑
Resolvin D5	1.17	0.16	***	↓
8,11,14-Eicosatrienoic acid	1.17	1.81	***	↑
14,15-Epoxy-5,8,11-eicosatrienoic acid	1.17	3.36	***	↑
5,15-DiHETE	1.17	0.35	***	↓
TG(18:1(9Z)/18:2(9Z,12Z)/18:2(9Z,12Z))[iso3]	1.16	0.33	***	↓
13-OxoODE	1.16	0.35	***	↓
Prostaglandin F1a	1.16	0.37	***	↓
11,12-EpETrE	1.16	3.41	***	↑
PC(18:1(11Z)/18:0)	1.15	6.93	***	↑
Capric acid	1.15	1.51	***	↑
PC(16:0/16:0)	1.15	7.23	***	↑
TG(15:0/18:1(9Z)/18:1(9Z))[iso3]	1.15	63.18	***	↑
PC(o-18:0/22:0)	1.15	0.57	***	↓
Thromboxane B2	1.15	2.38	***	↑
PC(16:0/18:1(9Z))	1.15	4.13	***	↑
PC(18:1(9Z)/20:0)	1.15	5.09	***	↑
TG(16:1(9Z)/16:1(9Z)/20:4(5Z,8Z,11Z,14Z))[iso3]	1.15	0.28	***	↓
PC(16:0/18:0)	1.15	7.11	***	↑
8,9-Epoxyeicosatrienoic acid	1.15	2.67	***	↑
Lipoxin B4	1.15	0.49	***	↓
Resolvin D2	1.14	0.36	***	↓
TG(18:2(9Z,12Z)/18:2(9Z,12Z)/18:2(9Z,12Z))	1.14	0.15	***	↓
LysoPE(0:0/18:0)	1.14	2.91	***	↑
PC(16:0/22:2(13Z,16Z))	1.14	4.83	***	↑
5-HETE	1.14	0.32	***	↓
PE(18:0/18:2(9Z,12Z))	1.14	1.69	***	↑

TG(16:0/18:0/18:1(9Z))[iso6]	1.14	13.42	***	↑
TG(18:0/18:1(9Z)/18:1(9Z))[iso3]	1.13	11.77	***	↑
LysoPC(P-18:1(9Z))	1.13	3.7	***	↑
LysoPE(18:2(9Z,12Z)/0:0)	1.12	0.57	***	↓
TG(16:0/16:1(9Z)/18:2(9Z,12Z))[iso6]	1.12	0.29	***	↓
17-HDoHE	1.12	0.45	***	↓
12-HEPE	1.12	0.29	***	↓
9-OxoODE	1.12	0.17	***	↓
PC(18:0/18:2(9Z,12Z))	1.12	2.24	***	↑
PC(o-14:0/16:1(9Z))	1.12	2.48	***	↑
Myristic acid	1.12	0.76	***	↓
9-HETE	1.12	0.4	***	↓
LysoPC(20:5(5Z,8Z,11Z,14Z,17Z))	1.11	3.57	***	↑
TG(16:1(9Z)/16:1(9Z)/18:1(9Z))[iso3]	1.11	/	***	↑
PC(16:0/22:4(7Z,10Z,13Z,16Z))	1.11	2.04	***	↑
5-HEPE	1.11	0.63	***	↓
Prostaglandin F2a	1.11	1.51	***	↑
LysoPC(18:3(9Z,12Z,15Z))	1.11	2.94	***	↑
TG(16:1(9Z)/18:1(9Z)/20:4(5Z,8Z,11Z,14Z))[iso6]	1.11	0.43	***	↓
LysoPE(16:0/0:0)	1.10	2.04	***	↑
TG(16:0/18:1(9Z)/20:1(11Z))[iso6]	1.10	2.93	***	↑
PE(16:0/22:0)	1.10	3.28	***	↑
PE(16:1(9Z)/22:0)	1.10	2.5	***	↑
TG(16:0/18:1(9Z)/18:2(9Z,12Z))[iso6]	1.10	0.35	***	↓
Lipoxin A4	1.10	0.21	***	↓
TG(16:1(9Z)/18:2(9Z,12Z)/20:4(5Z,8Z,11Z,14Z))[iso6]	1.09	0.32	***	↓
PE(18:0/18:0)	1.09	2.7	***	↑
PC(18:1(9Z)/22:4(7Z,10Z,13Z,16Z))	1.09	1.71	***	↑
TG(18:1(9Z)/18:1(11Z)/18:1(9Z))[iso3]	1.09	4.76	***	↑
LysoPC(18:0)	1.09	1.96	***	↑
TG(16:1(9Z)/18:1(9Z)/18:2(9Z,12Z))[iso6]	1.08	0.67	***	↓
LysoPC(20:4(5Z,8Z,11Z,14Z))	1.08	2.17	***	↑
Stearic acid	1.08	1.28	***	↑

TG(16:0/18:1(9Z)/18:1(9Z))[iso3]	1.07	2.84	***	↑
6-Keto-prostaglandin F1a	1.06	2.19	***	↑
LysoPC(18:2(9Z,12Z))	1.06	1.86	***	↑
TG(18:1(9Z)/18:1(9Z)/18:3(9Z,12Z,15Z))[iso3]	1.06	1.59	***	↑
Arachidonic acid	1.06	0.58	***	↓
TG(16:0/16:0/18:1(9Z))[iso3]	1.05	3.01	***	↑
8-HETE	1.05	0.63	***	↓
PC(16:0/20:4(5Z,8Z,11Z,14Z))	1.05	1.63	***	↑
TG(18:1(9Z)/18:1(9Z)/20:4(5Z,8Z,11Z,14Z))[iso3]	1.05	2.42	***	↑
Prostaglandin D3	1.05	0.48	***	↓
LysoPC(16:1(9Z))	1.05	1.87	***	↑
LysoPC(22:5(4Z,7Z,10Z,13Z,16Z))	1.05	1.98	***	↑
PC(α -18:1(9Z)/18:2(9Z,12Z))	1.04	1.57	***	↑
PC(16:0/18:2(9Z,12Z))	1.04	1.5	***	↑
TG(16:0/16:1(9Z)/20:4(5Z,8Z,11Z,14Z))[iso6]	1.03	0.55	**	↓
PE(20:4(5Z,8Z,11Z,14Z)/20:4(5Z,8Z,11Z,14Z))	1.03	2.26	***	↑
TG(16:1(9Z)/18:1(9Z)/18:1(9Z))[iso3]	1.03	2.41	***	↑
Docosahexaenoic acid	1.02	0.55	**	↓
Prostaglandin D2	1.02	0.76	**	↓
Eicosapentaenoic acid	1.01	0.65	**	↓
TG(18:0/18:2(9Z,12Z)/20:1(11Z))[iso6]	1.00	1.84	**	↑

“↑” for up-regulation and “↓” for down-regulation. “*”, “**” and “***” indicate the difference is significant ($P<0.05$), ($P<0.01$) and ($P<0.001$). VIP, variable importance for projection.

Table S12 The potential active metabolites between lemon apple vinegar drink group (LAV+M) and control group (C) (VIP>1, p<0.05)

Metabolites	VIP	Fold change	P value	Regulation (up or down)
LAV+M vs. C				
LysoPC(P-18:1(9Z))	1.21	3.79	***	↑
Arachidic acid	1.21	/	***	↑
PC(18:1(11Z)/18:0)	1.21	7.32	***	↑
LysoPC(18:0)	1.21	2.13	***	↑
PC(16:0/16:0)	1.21	7.56	***	↑
PC(16:0/18:1(9Z))	1.21	4.17	***	↑
LysoPC(20:5(5Z,8Z,11Z,14Z,17Z))	1.21	3.77	***	↑
PC(16:0/22:4(7Z,10Z,13Z,16Z))	1.20	2.23	***	↑
LysoPC(20:4(5Z,8Z,11Z,14Z))	1.20	2.43	***	↑
PC(16:0/18:0)	1.20	7.31	***	↑
Eicosenoic acid	1.20	2.76	***	↑
PC(18:0/18:2(9Z,12Z))	1.20	2.32	***	↑
LysoPC(18:2(9Z,12Z))	1.20	1.91	***	↑
PC(16:0/20:4(5Z,8Z,11Z,14Z))	1.20	1.77	***	↑
LysoPC(18:3(9Z,12Z,15Z))	1.20	2.82	***	↑
LysoPC(16:1(9Z))	1.20	1.9	***	↑
PC(o-18:0/22:0)	1.20	0.58	***	↓
LysoPC(16:0)	1.20	1.51	***	↑
PC(18:1(9Z)/20:0)	1.20	5.09	***	↑
Thromboxane B2	1.20	2.29	***	↑
Oleic acid	1.20	2.01	***	↑
LysoPE(0:0/18:0)	1.20	3.09	***	↑
PC(18:1(9Z)/22:4(7Z,10Z,13Z,16Z))	1.20	1.77	***	↑
PC(16:0/22:2(13Z,16Z))	1.20	5.24	***	↑
PC(o-18:1(9Z)/18:2(9Z,12Z))	1.20	1.63	***	↑
Lipoxin B4	1.20	0.2	***	↓
PC(16:0/18:2(9Z,12Z))	1.19	1.5	***	↑
TG(16:1(9Z)/16:1(9Z)/18:1(9Z))[iso3]	1.19	/	***	↑
LysoPE(18:2(9Z,12Z)/0:0)	1.19	0.6	***	↓
TG(15:0/18:1(9Z)/18:1(9Z))[iso3]	1.19	60.69	***	↑

Resolvin D5	1.19	0.22	***	↓
PC(18:1(9Z)/20:4(5Z,8Z,11Z,14Z))	1.19	1.38	***	↑
PC(o-14:0/16:1(9Z))	1.19	2.83	***	↑
TG(18:1(9Z)/18:2(9Z,12Z)/18:2(9Z,12Z))[iso3]	1.19	0.29	***	↓
TG(16:1(9Z)/18:1(9Z)/18:2(9Z,12Z))[iso6]	1.18	0.5	***	↓
Prostaglandin F1a	1.18	0.42	***	↓
LysoPE(16:0/0:0)	1.18	2.08	***	↑
TG(18:0/18:1(9Z)/18:1(9Z))[iso3]	1.18	6.73	***	↑
PE(16:0/22:0)	1.18	3.09	***	↑
TG(16:1(9Z)/16:1(9Z)/20:4(5Z,8Z,11Z,14Z))[iso3]	1.18	0.23	***	↓
5,15-DiHETE	1.17	0.47	***	↓
TG(16:0/18:1(9Z)/18:1(9Z))[iso3]	1.17	2.47	***	↑
5,6-Epoxy-8,11,14-eicosatrienoic acid	1.17	0.37	***	↓
TG(18:2(9Z,12Z)/18:2(9Z,12Z)/18:2(9Z,12Z))	1.16	0.14	***	↓
TG(16:0/18:0/18:1(9Z))[iso6]	1.16	7.1	***	↑
Myristic acid	1.16	0.68	***	↓
5-HETE	1.16	0.33	***	↓
TG(16:0/16:1(9Z)/18:2(9Z,12Z))[iso6]	1.16	0.22	***	↓
TG(16:1(9Z)/18:1(9Z)/20:4(5Z,8Z,11Z,14Z))[iso6]	1.16	0.34	***	↓
Prostaglandin F3a	1.16	0.35	***	↓
LysoPC(22:5(4Z,7Z,10Z,13Z,16Z))	1.15	2.02	***	↑
TG(18:1(9Z)/18:1(11Z)/18:1(9Z))[iso3]	1.15	4.32	***	↑
PE(18:0/18:0)	1.15	2.2	***	↑
TG(16:0/18:1(9Z)/20:1(11Z))[iso6]	1.15	2.67	***	↑
13-OxoODE	1.15	0.59	***	↓
9-OxoODE	1.14	0.17	***	↓
12-HEPE	1.14	0.32	***	↓
TG(16:0/18:1(9Z)/18:2(9Z,12Z))[iso6]	1.14	0.25	***	↓
TG(16:1(9Z)/18:2(9Z,12Z)/20:4(5Z,8Z,11Z,14Z))[iso6]	1.13	0.28	***	↓
17-HDoHE	1.13	0.52	***	↓
6-Keto-prostaglandin F1a	1.13	2.44	***	↑
Prostaglandin F2a	1.12	1.84	***	↑
Resolvin E1	1.12	0.63	***	↓

PE(20:4(5Z,8Z,11Z,14Z)/20:4(5Z,8Z,11Z,14Z))	1.12	2.25	***	↑
9-HETE	1.11	0.51	***	↓
PE(18:0/18:2(9Z,12Z))	1.11	1.86	***	↑
Prostaglandin D3	1.11	0.36	***	↓
PC(16:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	1.11	0.89	***	↓
Lipoxin A4	1.11	0.24	***	↓
Linoleic acid	1.10	0.68	***	↓
5-HEPE	1.10	0.67	***	↓
TG(16:0/16:1(9Z)/20:4(5Z,8Z,11Z,14Z))[iso6]	1.08	0.52	***	↓
LysoPE(18:1(9Z)/0:0)	1.08	1.63	***	↑
TG(18:0/18:2(9Z,12Z)/20:1(11Z))[iso6]	1.07	1.58	***	↑
TG(18:0/18:2(9Z,12Z)/18:2(9Z,12Z))[iso3]	1.06	0.45	***	↓
PE(16:1(9Z)/22:0)	1.06	1.93	***	↑
20-Hydroxyeicosatetraenoic acid	1.05	1.41	**	↑
PE(18:0/20:4(5Z,8Z,11Z,14Z))	1.02	1.32	**	↑
TG(16:0/16:0/18:1(9Z))[iso3]	1.02	1.73	**	↑
TG(18:1(9Z)/18:1(9Z)/20:4(5Z,8Z,11Z,14Z))[iso3]	1.01	1.76	**	↑
Capric acid	1.01	1.34	**	↑
PS(18:2(9Z,12Z)/18:2(9Z,12Z))	1.01	2.14	**	↑

“↑” for up-regulation and “↓” for down-regulation. “*”, “**” and “***” indicate the difference is significant ($P<0.05$), ($P<0.01$) and ($P<0.001$). VIP, variable importance for projection.

Table S13 The potential active metabolites between seal oil capsule group (SO+M) and control group (C) (VIP>1, $p<0.05$)

Metabolites	VIP	Fold change	P value	Regulation (up or down)
SO+M vs. C				
PC(16:0/16:0)	1.17	8.83	***	↑
PC(16:0/18:0)	1.17	8.6	***	↑
PC(18:1(11Z)/18:0)	1.17	8.68	***	↑
PC(18:0/18:2(9Z,12Z))	1.17	2.81	***	↑
PC(16:0/18:1(9Z))	1.17	4.39	***	↑
LysoPC(P-18:1(9Z))	1.17	3.65	***	↑
LysoPC(20:5(5Z,8Z,11Z,14Z,17Z))	1.17	20.84	***	↑
PC(16:0/22:2(13Z,16Z))	1.17	5.76	***	↑
PC(16:0/18:2(9Z,12Z))	1.17	1.72	***	↑
PC(o-18:1(9Z)/18:2(9Z,12Z))	1.17	1.72	***	↑
LysoPC(18:0)	1.17	2.03	***	↑
PC(18:1(9Z)/20:4(5Z,8Z,11Z,14Z))	1.17	1.82	***	↑
PC(o-14:0/16:1(9Z))	1.17	2.76	***	↑
19(S)-HETE	1.17	0.51	***	↓
LysoPC(18:3(9Z,12Z,15Z))	1.17	2.2	***	↑
5,15-DiHETE	1.17	0.11	***	↓
LysoPC(18:2(9Z,12Z))	1.17	1.96	***	↑
LysoPC(16:1(9Z))	1.17	1.86	***	↑
PC(18:1(9Z)/20:0)	1.17	5.74	***	↑
LysoPE(0:0/18:0)	1.17	3.59	***	↑
Lipoxin B4	1.17	0.15	***	↓
PC(18:1(9Z)/22:4(7Z,10Z,13Z,16Z))	1.16	1.76	***	↑
PE(16:0/22:0)	1.16	5.05	***	↑
PC(o-16:0/22:0)	1.16	1.51	***	↑
TG(18:1(9Z)/18:2(9Z,12Z)/18:2(9Z,12Z))[iso3]	1.16	0.2	***	↓
PC(o-18:0/22:0)	1.16	0.7	***	↓
LysoPC(16:0)	1.16	1.4	***	↑
TG(16:1(9Z)/18:1(9Z)/18:2(9Z,12Z))[iso6]	1.16	0.34	***	↓
Palmitic acid	1.16	0.38	***	↓
Eicosapentaenoic acid	1.16	8.1	***	↑
Resolvin D5	1.16	0.25	***	↓

Linoleic acid	1.15	0.22	***	↓
LysoPE(16:0/0:0)	1.15	2.3	***	↑
Myristic acid	1.15	0.47	***	↓
8,11,14-Eicosatrienoic acid	1.15	0.17	***	↓
PE(18:0/18:2(9Z,12Z))	1.15	2.14	***	↑
Resolvin E1	1.14	0.35	***	↓
5-HEPE	1.14	2.8	***	↑
TG(16:0/18:0/18:1(9Z))[iso6]	1.14	15.83	***	↑
TG(16:1(9Z)/18:1(9Z)/20:4(5Z,8Z,11Z,14Z))[iso6]	1.14	0.2	***	↓
TG(16:1(9Z)/16:1(9Z)/18:1(9Z))[iso3]	1.14	/	***	↑
Palmitoleic acid	1.14	0.18	***	↓
Thromboxane B2	1.14	1.86	***	↑
TG(18:2(9Z,12Z)/18:2(9Z,12Z)/18:2(9Z,12Z))	1.14	0.09	***	↓
Oleic acid	1.14	0.52	***	↓
5-HETE	1.14	0.25	***	↓
Docosahexaenoic acid	1.14	3.44	***	↑
TG(16:0/16:1(9Z)/18:2(9Z,12Z))[iso6]	1.13	0.16	***	↓
TG(16:0/16:1(9Z)/20:4(5Z,8Z,11Z,14Z))[iso6]	1.13	0.24	***	↓
9-HETE	1.13	0.29	***	↓
TG(15:0/18:1(9Z)/18:1(9Z))[iso3]	1.13	90.57	***	↑
12-HEPE	1.13	2.83	***	↑
TG(16:1(9Z)/16:1(9Z)/20:4(5Z,8Z,11Z,14Z))[iso3]	1.13	0.39	***	↓
Eicosenoic acid	1.12	0.33	***	↓
TG(16:0/18:1(9Z)/18:2(9Z,12Z))[iso6]	1.12	0.19	***	↓
TG(16:1(9Z)/18:2(9Z,12Z)/20:4(5Z,8Z,11Z,14Z))[iso6]	1.12	0.17	***	↓
LysoPE(18:2(9Z,12Z)/0:0)	1.12	0.68	***	↓
PE(18:0/18:0)	1.11	2.91	***	↑
Prostaglandin F1a	1.11	0.57	***	↓
PE(16:1(9Z)/22:0)	1.11	3.62	***	↑
PS(18:2(9Z,12Z)/18:2(9Z,12Z))	1.10	2.33	***	↑
Capric acid	1.10	0.34	***	↓
TG(18:0/18:1(9Z)/18:1(9Z))[iso3]	1.09	14.88	***	↑
TG(16:0/18:1(9Z)/18:1(9Z))[iso3]	1.09	1.83	***	↑

9-OxoODE	1.09	0.29	***	↓
PC(16:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	1.09	1.1	***	↑
Prostaglandin D2	1.09	0.6	***	↓
PE(18:2(9Z,12Z)/18:2(9Z,12Z))	1.09	0.58	***	↓
PC(16:0/22:4(7Z,10Z,13Z,16Z))	1.09	1.1	***	↑
TG(16:0/16:0/18:1(9Z))[iso3]	1.08	1.62	***	↑
Leukotriene B4	1.08	0.48	***	↓
Alpha-Linolenic acid	1.07	0.13	***	↓
PS(18:0/20:4(5Z,8Z,11Z,14Z))	1.07	3.45	***	↑
TG(18:0/18:2(9Z,12Z)/20:1(11Z))[iso6]	1.06	2.67	***	↑
TG(18:0/18:2(9Z,12Z)/18:2(9Z,12Z))[iso3]	1.06	0.48	***	↓
Stearic acid	1.06	0.7	***	↓
LysoPC(22:5(4Z,7Z,10Z,13Z,16Z))	1.04	1.92	***	↑
TG(18:1(9Z)/18:1(9Z)/18:2(9Z,12Z))[iso3]	1.04	0.43	***	↓
PC(16:0/20:4(5Z,8Z,11Z,14Z))	1.03	0.93	***	↓
TG(16:0/18:1(9Z)/20:1(11Z))[iso6]	1.03	3.75	***	↑
TG(18:1(9Z)/18:1(11Z)/18:1(9Z))[iso3]	1.01	2.39	**	↑

“↑” for up-regulation and “↓” for down-regulation. “*”, “**” and “***” indicate the difference is significant ($P<0.05$), ($P<0.01$) and ($P<0.001$). VIP, variable importance for projection.

Table S14 Concentration of lipid mediators in mice serum samples.

C	M	YR+M	APP+M	LAV+M	SO+M
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Cyclooxygenase pathway	PGD ₂	6.8±0.46a	6.52±0.75a	4.84±0.24bc	5.13±0.67b	6.34±0.63a	4.1±0.74c
	PGE ₂	4.9±0.49ab	5.09±0.31a	4.13±0.37c	4.16±0.59c	4.35±0.18bc	4.55±0.48abc
	TXB ₂	125.4±8.35e	394.2±22.93a	260.4±24.64cd	298.6±30.81b	287±9.87bc	233.2±19.9d
	TXB ₃	3.94±0.37c	7.06±0.53b	6.3±0.66bc	6.05±0.49bc	6.07±0.68bc	30.88±4.46a
	RvE1	8.37±0.85a	5.97±0.64bc	6.43±0.83b	5.81±1.12bc	5.27±0.51c	2.9±0.51d
5-lipoxygenase pathway	5-HETE	82.4±12.26a	23.11±3.05b	22.64±3.04b	26.58±1.84b	26.95±2.95b	20.97±3.15b
	LTB ₄	1.66±0.28a	0.76±0.17d	0.94±0.13cd	1.25±0.17b	1.15±0.16bc	0.79±0.11d
	LXA ₄	2.39±0.59a	0.58±0.21c	2.27±0.52a	0.5±0.19c	0.58±0.24c	1.17±0.49b
	LXB ₄	12.02±0.94a	3±0.37c	3.12±0.44c	5.86±0.93b	2.44±0.34cd	1.78±0.33d
12-lipoxygenase pathway	12-HETE	9562±1272.6c	9876±561.36bc	6210±843.71d	11400±758.29a	11008±1599.98ab	6652±1108.27d
	14-HDHA	2008±84.68c	1784±189.42c	1882±265.93c	1796±240.27c	2352±280.12b	3266±281.12a
	RvD1	0.85±0.18b	1.07±0.14a	0.9±0.21ab	0.48±0.08c	0.53±0.18c	0.64±0.13c
	RvD2	5.17±0.61a	1.33±0.19c	4.07±0.49b	1.84±0.3c	5.51±1.1a	3.92±0.43b
	RvD3	0.57±0.18a	0.23±0.08cd	0.31±0.07bc	0.12±0.01d	0.33±0.15bc	0.45±0.15ab
	RvD5	2.05±0.16a	0.53±0.1b	0.6±0.09b	0.33±0.07c	0.45±0.13bc	0.51±0.15b
	MaR1	4.9±0.66a	0.46±0.09b	0.55±0.1bc	0.48±0.09bc	0.45±0.08bc	1.56±0.19a
15-lipoxygenase pathway	15-HETE	160.4±23.95a	136.4±17.17b	76.06±6.15e	98±9.28cd	110.24±14.29c	85.2±7.55de
	17-HDHA	352.6±47.44a	225.4±31.57b	162.6±15.04c	158.8±15.99c	183.8±19.59c	354.8±21.53a
	9-oxoODE	82.84±18.28a	13.86±2.95c	17.14±1.59bc	14.1±1.29c	13.9±2.16c	24.4±3.87b
	13-oxoODE	89.5±7.41a	14.94±2.45e	27.62±2.3d	31.58±3.81d	52.44±6.26c	82.38±6.31b
	PDX	2.84±0.35a	0.81±0.08cd	0.56±0.08de	0.45±0.11e	0.84±0.13c	1.39±0.33b
Alternative pathway	20-HETE	9.44±0.88cd	12.1±1.64ab	9.97±1.23c	10.64±0.94bc	13.34±1.51a	8.29±0.3d
	5,6-EET	5848±748.18bc	5596±1013.18c	14640±1722.79a	4632±560.95c	2144±242.24d	7078±1314.96bc
	8,9-EET	286.6±26.67c	390.2±60.78b	775.2±57.54a	766.2±90.06a	329.6±45.2bc	266.8±28.73c
	11,12-EET	233.2±26.29cd	192.4±22.2d	713.6±54.84b	796.2±85.83a	297.8±56.41c	236.4±31.14cd
	14,15-EET	337.4±38.93c	388±60.25c	952±113.23b	1132.6±86.71a	402.4±61.33c	357.8±47.04c
	18-HEPE	12.06±2.11b	1.93±0.23c	3.65±0.38c	3.4±0.86c	3.68±0.19c	40.18±2.85a
PUFA-ratios	EPA/AA	0.25±0.02b	0.27±0.07b	0.22±0.02b	0.28±0.05b	0.25±0.04b	1.85±0.34a
	DHA/AA	0.64±0.09c	0.73±0.17bc	0.85±0.07b	0.6±0.06c	0.75±0.1bc	2±0.3a
HEPE or HDHA/HETE ratios	HEPE/HETE ratio	0.18±0.01b	0.12±0.01c	0.15±0.02b	0.09±0.01c	0.11±0.03c	0.72±0.04a
	HDHA/HETE ratio	0.24±0.03c	0.2±0.02de	0.32±0.03b	0.17±0.03e	0.23±0.02cd	0.54±0.05a

(a, b, c, d, e (p<0.05)); there is no significant difference when the mark contains the same letter

Table S15 Concentration of FFA,PL and TAG in mice serum samples.

		C	M	YR+M	APP+M	LAV+M	SO+M
FFA	Total FFA(nmol/mL)	126.86±5.86d	183.24±1.96a	159.72±9.52b	145.77±2.78c	140.15±1.81c	48.07±5.61e
	EPA(pmol/mL)	496.6±62.97c	271±37.37c	1091.8±176.2b	322.2±54.01c	487.8±41.55c	4024±499.58a
	DHA(pmol/mL)	1266±238.18b	749.4±94.9c	4162±457.68a	691.6±113.79c	1460±241.87b	4360±601.12a
PL	Total PL(nmol/mL)	1247.24±37.87c	2819.89±68.15a	2708.81±84.25ab	2527.39±392.02b	2646.1±62.93ab	2640.68±54.58ab
	PC(16:0/20:4)(nmol/mL)	114.7±2.75c	223.4±4.12a	188±11.6bc	186.7±30.1ab	203.1±5.14a	106.9±1.78c
	DHA-PL(nmol/mL)	105.75±3.46bc	114.04±2.88abc	121.48±27.97ab	98.63±16.01c	101.31±3.7c	125.75±2.81a
	EPA-PL(nmol/mL)	2.64±0.25d	10.29±0.47b	9.66±1.16b	9.17±1.39b	7.61±0.65c	17.5±1.25a
TAG	Total TAG(nmol/mL)	279.57±41.42bc	358.24±33.29a	379.01±45.44a	325.86±64.05ab	256.87±29.04c	268.25±32.11c
	n-6 PUFA-TAG	169.37±26.93a	120.3±13.76b	120.15±17.48b	98.86±19.37b	76.38±12.48c	45.99±3.97d
	n-3 PUFA-TAG	60.49±7.22b	41.22±4.5c	40.9±3.96c	38.58±8.34c	36.75±5.34c	80.04±10.13a
	MUFA-TAG	57.96±11.96d	183.16±18.99ab	199.89±26.85a	168.06±35.08b	135.46±13.63c	112.37±15.61c
	SFA-TAG	167.65±24.44bc	194.69±16.45ab	215.17±23.38a	185.38±34.91ab	140.06±11.87c	170.33±23.3bc

(a, b, c, d, e (p<0.05)); there is no significant difference when the mark contains the same letter