Supplementary materials：

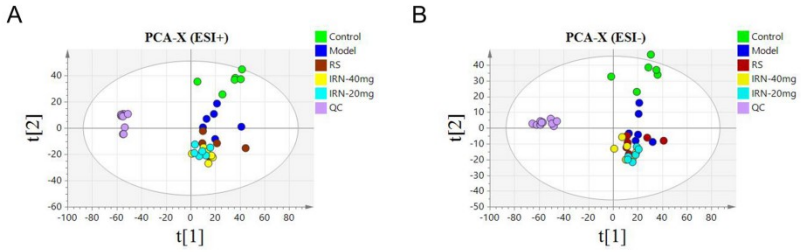

Fig. S1. PCA statistical analysis of serum data. A：PCA score plots for control, model, RS, IRN-20mg/kg, IRN-40mg/kg and QC groups based on LC-MS data in the positive mode. B: PCA score plots for control, model, RS, IRN-20mg/kg, IRN-40mg/kg and QC groups based on LC-MS data in the negative mode.

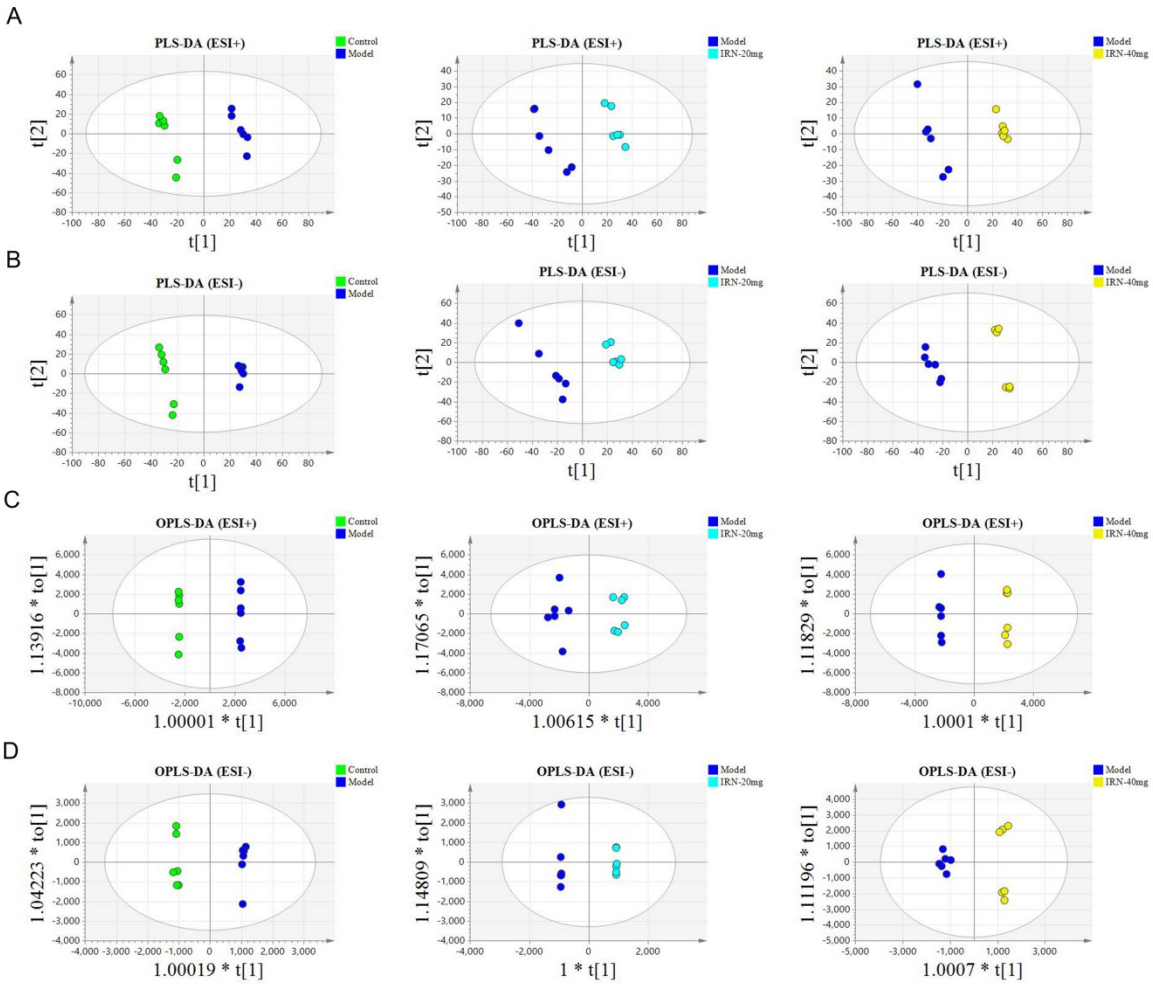

Fig S2. PLS-DA and OPLS-DA score plot of the serum data. A: PLS-DA score plot in positive ion mode. B: PLS-DA score plot in negative ion mode. C: OPLS-DA score plot in positive ion mode. B: OPLS-DA score plot in negative ion mode.

Table 1. Identified potential biomarkers between the control animal group and model animal group in both positive (+) and negative (-) ion modes.

Biomarkers	[M±X] $^{+/-}$	Chemical formula	Model/Control			
			VIP	P	FC	CT
4-Hepteneoylglycine	184.09673	$C_9H_{15}NO_3$	1.4926	0.0002	2.4327	↑
(2Z)-5-hydroxydec-2-enoic acid	185.11731	$C_{10}H_{18}O_3$	1.215	0.0084	-2.2849	↓
3-Hydroxysebacic acid	217.10802	$C_{10}H_{18}O_5$	1.0313	0.0046	-2.5101	↓
Methyl 4-chloro-1H-indole-3-acetate	222.0324	$C_{11}H_{10}ClNO_2$	1.2528	0.001	-3.7776	↓
Galactosylglycerol	253.0926	$C_9H_{18}O_8$	1.2415	0.0000	2.3506	↑
(2E,4Z)-tetradeca-2,4-dienedioic acid	253.14421	$C_{14}H_{22}O_4$	1.4826	0.0011	-4.3766	↓
5-Acetoxydihydrotheaespirane	253.18126	$C_{15}H_{26}O_3$	1.2266	0.0028	-2.297	↓
Dibutyl adipate	257.17563	$C_{14}H_{26}O_4$	1.1111	0.001	-5.449	↓
Acoric acid	267.16025	$C_{15}H_{24}O_4$	1.1604	0.0004	-6.6071	↓
9-HOTE	293.2124	$C_{18}H_{30}O_3$	1.1449	0.0001	-2.232	↓
13-HODE	295.22803	$C_{18}H_{32}O_3$	1.1903	0.0001	-2.5723	↓
Icosa-2,4,6,8,10-pentaenoic acid	301.218	$C_{20}H_{30}O_2$	1.084	0.0000	-3.3066	↓
12,13-DHOME	313.23914	$C_{18}H_{34}O_4$	1.064	0.0001	-2.4426	↓
12-KETE	317.21265	$C_{20}H_{30}O_3$	1.1378	0.0002	-2.568	↓
8-HDoHE	343.22797	$C_{22}H_{32}O_3$	1.1504	0.0002	-2.5679	↓
Siderol	345.24338	$C_{22}H_{34}O_3$	1.1647	0.0028	-2.1641	↓
Blumenol C glucoside	371.20737	$C_{19}H_{32}O_7$	1.1689	0.0002	-3.8063	↓
N-Oleoyl phenylalanine	428.31665	$C_{27}H_{43}NO_3$	1.1221	0.0325	7.3276	↑
LysoPE(P-18:0/0:0)	464.31345	$C_{23}H_{48}NO_6P$	1.1499	0.0001	2.0051	↑
LysoPC(0:0/16:0)	494.32593	$C_{24}H_{50}NO_7P$	1.2757	0.0000	-2.5816	↓
Taurochenodesoxycholic acid	498.28925	$C_{26}H_{45}NO_6S$	1.074	0.0011	2.1914	↑
LysoPE(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)	524.2783	$C_{27}H_{44}NO_7P$	1.0351	0.0000	-2.0565	↓
LysoPE(22:5(7Z,10Z,13Z,16Z,19Z)/0:0)	526.29474	$C_{27}H_{46}NO_7P$	1.211	0.0000	-2.5091	↓
PC(18:1(12Z)-2OH(9,10)/15:0)	776.5592	$C_{45}H_{80}NO_7P$	1.0281	0.0049	2.1755	↑
Indoleacetaldehyde	160.07585	$C_{10}H_9NO$	1.1903	0.0000	-2.1228	↓
N-Hydroxyl-tryptamine	177.1023	$C_{10}H_{12}N_2O$	1.2296	0.0000	-2.0375	↓
Diphenyl sulfide	187.05377	$C_{12}H_{10}S$	1.2969	0.0000	2.1235	↓
S-nirvanol	205.09721	$C_{11}H_{12}N_2O_2$	1.2509	0.0000	-2.0293	↓
2-Phenylethyl hexanoate	221.15352	$C_{14}H_{20}O_2$	1.1662	0.0000	3.8974	↑
3,4-Dimethyl-5-pentyl-2-furanpropanoic acid	239.16441	$C_{14}H_{22}O_3$	1.3571	0.0000	4.5111	↑
2-hydroxytetradeca-4,6-dienoic acid	241.17783	$C_{14}H_{24}O_3$	1.1897	0.001	-4.3718	↓
Vidarabine	268.10394	$C_{10}H_{13}N_5O_4$	1.4129	0.0249	-7.3688	↓
all-trans-Retinoic acid	301.2159	$C_{20}H_{28}O_2$	1.2395	0.000	-3.1031	↓
Docosahexaenoicacid(DHA)	329.24765	$C_{22}H_{32}O_2$	1.0449	0.0004	-2.058	↓

3, 5-Tetradecadiencarnitine	368.27948	$C_{21}H_{37}NO_4$	1.0624	0.0003	-2.1298	↓
Adrenoyl ethanolamide	376.32166	$C_{24}H_{41}NO_2$	1.0334	0.0071	-2.619	↓
Persicachrome	385.27475	$C_{25}H_{36}O_3$	1.1432	0.0000	-3.78	↓
(7Z,10Z)-Hexadecadienoylcarnitine	396.3107	$C_{23}H_{41}NO_4$	1.3817	0.0001	-2.0546	↓
Heptadecanoyl carnitine	414.358	$C_{24}H_{47}NO_4$	1.2527	0.0000	2.5583	↑
Vaccenyl carnitine	426.35812	$C_{25}H_{47}NO_4$	1.7456	0.0000	2.775	↑
Stearoylcarnitine	428.3734	$C_{25}H_{49}NO_4$	1.6698	0.0000	3.3237	↑
Arachidyl carnitine	456.4053	$C_{27}H_{53}NO_4$	1.2024	0.0000	3.9902	↑
LysoPE(20:5(5Z,8Z,11Z,14Z,17Z)/0:0)	500.2769	$C_{25}H_{42}NO_7P$	1.2186	0.0000	-2.4278	↓
LysoPC(P-18:0/0:0)	508.37665	$C_{26}H_{54}NO_6P$	1.5581	0.0000	3.5131	↑
LysoPC(O-18:0/0:0)	510.39175	$C_{26}H_{56}NO_6P$	1.2237	0.0000	3.5646	↑
LysoPE(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)	526.29254	$C_{27}H_{44}NO_7P$	1.1346	0.0000	-2.6473	↓
LysoPE(22:0/0:0)	538.38763	$C_{27}H_{56}NO_7P$	1.0763	0.0000	-2.2849	↓
LysoPC(20:3(8Z,11Z,14Z)/0:0)	546.35516	$C_{28}H_{52}NO_7P$	1.317	0.0000	2.1834	↑
LysoPC(22:5(4Z,7Z,10Z,13Z,16Z)/0:0)	570.35657	$C_{30}H_{52}NO_7P$	1.3492	0.0003	2.3171	↑
LysoPC(22:4(7Z,10Z,13Z,16Z)/0:0)	572.371	$C_{30}H_{54}NO_7P$	1.0413	0.0001	2.1997	↑
Cer(d18:0/20:0)	596.5973	$C_{38}H_{77}NO_3$	1.1485	0.0114	72.9991	↑
PC(18:2(9Z,12Z)/14:0)	730.53894	$C_{40}H_{76}NO_8P$	1.7583	0.0068	51.7614	↑
PC(18:2(9Z,12Z)/15:0)	744.554	$C_{41}H_{78}NO_8P$	1.5304	0.0001	113.0833	↑
PC(22:5(7Z,10Z,13Z,16Z,19Z)/14:0)	780.5541	$C_{44}H_{78}NO_8P$	1.5597	0.0014	64.6053	↑
PC(20:4(8Z,11Z,14Z,17Z)/16:0)	782.56836	$C_{44}H_{80}NO_8P$	1.0624	0.0007	60.1143	↑
PC(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/18:3(9Z,12Z,15Z))	828.55145	$C_{48}H_{78}NO_8P$	1.1074	0.0006	89.3566	↑
PC(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/18:2(9Z,12Z))	830.5686	$C_{48}H_{80}NO_8P$	1.1884	0.007	24.8392	↑
PC(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/20:4(8Z,11Z,14Z,17Z))	854.57025	$C_{50}H_{80}NO_8P$	1.5231	0.0034	30.4044	↑

Table 2 Detailed information on metabolic pathways.

Pathway Name	Match Status	P	-log(p)	FDR	Impact
Glycerophospholipid metabolism	2/36	0.0016426	2.7845	0.13798	0.11182
Linoleic acid metabolism	1/5	0.0099337	2.0029	0.8245	0.0
alpha-Linolenic acid metabolism	1/13	0.02569	1.5902	1.0	0.0

Arachidonic acid metabolism	1/36	0.070058	1.1545	1.0	0.0
Primary bile acid biosynthesis	1/46	0.08892	1.051	1.0	0.02285