

Table S1. The ROC AUC.

	AUC
LPE(0:0/16:0)	0.889
Deoxycholic acid glycine conjugate	0.889
Equol 4'-O-glucuronide	1.000
Glycocholic acid	0.917
m-Methylhippuric acid	0.917
p-Cresol sulfate	0.736
10-Hydroxy-9-(phosphonoxy)octadecanoate	0.972
Argininic acid	0.889
Sphinganine 1-phosphate	1.000
Estriol 3-sulfate 16-glucuronide	0.917
3-Hydroxyoctanoic acid	0.861
3-Dehydrocarnitine	0.889
Docosahexaenoic acid	1.000
3-Hexenedioic acid	0.944
LPE(0:0/20:3)	0.944
Erythrose	0.778
LPC(15:0)	0.972
2-Ketobutyric acid	1.000
Glycocholic acid	0.889
Alanine	0.917
Lactic acid	0.917
LPE(0:0/16:0)	0.889

Chromatographic and mass spectrometric conditions

HPLC analysis was performed using a Waters UHPLC-Q-TOF/MS system (Waters, USA). Plasma samples (5 mL) were injected into an ACQUITY UPLC BEH C18 column (2.1×100 mm×1.7 μm, Waters), The column temperature was 40°C, and the flow rate was 0.3 mL min⁻¹. Q-TOF/MS was equipped with electrospray ionisation in negative mode. The MS parameters were as follows: drying gas temperature, 450°C; drying gas flow, 10mL /min; desolvation gas flow, 800 L/h; capillary voltage, 2.5kV; Ionization source temperature, 100°C; reference ions [M-H]⁻=554.2615; data acquisition range, m/z 50-1000Da.

Table S2. The correlation matrix of 22 Biomarkers

	Lactic acid	2-Ketobutyric acid	3-Hexenedioic acid	Galactonic acid	Sphinganine 1-phosphate	LysoPE(0:0/16:0)	Glycocolic acid	LysoPE(0:0/20:3)	Argininc acid	But-2-enoiac acid	Deoxyglycine conjugate	LysolPC (15:0)	Equol 4-O-glucuronide	3-Dehydrocarnitine	Docosahexaenoic acid	10-hydroxy-9-(phosphonoxy)octadecanoate	Alanine	Erythrose	3-Hydroxyoctanoic acid	Estradiol 3-sulfate 16-glucuronide	p-Cresol sulfate	m-Methylpuric acid
Lactic acid	1	0.76006	0.60195	0.72027	0.42614	0.24551	0.435	0.62007	0.52683	0.04730	0.1727	0.2287	0.31871	-0.31238	-0.61055	-0.73166	-0.49468	-0.67904	-0.10204	-0.45991	-0.043661	-0.33435
2-Ketobutyric acid	0.76006	1	0.81768	0.89191	0.62667	0.61978	0.66733	0.58354	0.58128	0.07124	0.42247	0.53664	0.5976	-0.36412	-0.65499	-0.69317	-0.62601	-0.60503	-0.48571	-0.52439	-0.062021	-0.55234
3-Hexenedioic acid	0.60195	0.81768	1	0.81701	0.49742	0.56108	0.43689	0.44062	0.57246	0.03551	0.24776	0.43123	0.3943	-0.42436	-0.79982	-0.82513	-0.53913	-0.50894	-0.44627	-0.34001	-0.055416	-0.55277
Galactonic acid	0.72027	0.89191	0.81701	1	0.42265	0.4062	0.38696	0.39454	0.60067	0.05803	0.26351	0.33095	0.42436	-0.33572	-0.67072	-0.78913	-0.60149	-0.48179	-0.33997	-0.49435	-0.052588	-0.46075
Sphinganine	0.42614	0.62667	0.49742	0.42265	1	0.679	0.62	0.6310	0.3	0.0	0.56	0.69	0.61	-	-	-0.48426	-	-	-	-	-	-

ne 1-phosphate	42 61 4	667	742	226 5		84	778	5	12 37	71 99 6	69	15	316	0.369 94	0.685 42		0. 49 03 8	0.59 467	0.500 49	0.63 236	0. 45 10 3	0.571 4
LysoPE(0:0/16:0)	0. 24 55 1	0.61 978	0.56 108	0.4 062	0.67 984	1	0.70 81	0.6350 1	0.4 41 4	0. 62 05 8	0.65 911	0.83 91	0.70 579	- 0.283 95	- 0.439 03	-0.2654	- 0. 18 08 7	- 0.14 222	- 0.625 73	- 0.58 924	- 0. 78 21 5	- 0.761 61
Glycocholic acid	0. 43 5	0.66 733	0.43 689	0.3 869 6	0.62 778	0.708 1	1	0.7486 4	0.6 05 36	0. 71 99	0.81 189	0.76 019	0.84 166	- 0.566 09	- 0.352 22	-0.24902	- 0. 44 35 2	- 0.31 261	- 0.602 94	- 0.64 718	- 0. 64 32 4	- 0.506 12
LysoPE(0:0/20:3)	0. 62 00 7	0.58 354	0.44 062	0.3 945 4	0.63 105	0.635 01	0.74 864	1	0.6 47 89	0. 60 68 4	0.57 166	0.59 167	0.64 399	- 0.508 93	- 0.521 91	-0.4969	- 0. 31 10 5	- 0.32 43	- 0.516 86	- 0.56 775	- 0. 55 26 2	- 0.501 54
Argininic acid	0. 52 68 3	0.58 128	0.57 246	0.6 006 7	0.31 237	0.441 4	0.60 536	0.6478 9	1	0. 54 25 5	0.63 389	0.63 256	0.77 07	- 0.471 01	- 0.472 11	-0.6604	- 0. 22 32 8	- 0.05 739 2	- 0.562 18	- 0.56 929	- 0. 39 59 8	- 0.240 36
But-2-enoic acid	0. 47 30 3	0.71 246	0.35 551	0.5 803 6	0.71 996	0.620 58	0.71 99	0.6068 4	0.5 42 55	1	0.78 914	0.71 211	0.85 061	- 0.220 21	- 0.462 87	-0.38922	- 0. 32 49 1	- 0.24 632	- 0.647 97	- 0.65 706	- 0. 42 82 4	- 0.311 57
Deoxycholic acid glycine conjugate	0. 17 27	0.42 247	0.24 776	0.2 635 1	0.56 69	0.659 11	0.81 189	0.5716 6	0.6 33 89	0. 78 91 4	1	0.88 072	0.94 122	- 0.471 42	- 0.357 8	-0.19718	- 0. 20 82	0.00 642 01	- 0.763 87	- 0.63 446	- 0. 41 35	- 0.255 72

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LysoPC(15:0)	0.2287	0.53664	0.43123	0.33095	0.6915	0.8391	0.76019	0.59167	0.63256	0.07121	0.88072	1	0.90448	-0.42246	-0.46184	-0.32103	-0.22163	-0.14652	-0.75488	-0.64629	-0.51726	-0.46464	
Equol 4'-O-glucuronide	0.31871	0.5976	0.3943	0.42436	0.61316	0.70579	0.84166	0.64399	0.7707	0.08506	0.94122	0.90448	1	-0.37502	-0.39163	-0.3524	-0.20182	-0.05446	-0.77329	-0.66208	-0.45246	-0.30373	
3-Dehydrocarnitine	-0.31238	-0.36412	-0.42436	-0.33572	-0.36994	-0.28395	-0.56609	-0.50893	-0.47101	-0.02202	-0.47142	-0.42246	-0.37502	1	0.5457	0.41411	0.77368	0.4698	0.42224	0.40362	0.3439	0.35512	
Docosaheaxaenoic acid	-0.61055	-0.65499	-0.79982	-0.67072	-0.68542	-0.43903	-0.35222	-0.52191	-0.47211	-0.04628	-0.3578	-0.46184	-0.39163	0.5457	1	0.88471	0.61073	0.63126	0.54096	0.3365	0.2884	0.34854	
10-hydroxy-9-(phosphonoxy)octadecanoate	-0.73166	-0.69317	-0.82513	-0.78913	-0.48426	-0.2654	-0.24902	-0.4969	-0.6604	-0.03892	-0.19718	-0.32103	-0.3524	0.41411	0.88471	1	0.50878	0.54689	0.40371	0.30975	0.34547	0.23862	
Alanine	-0.49468	-0.62601	-0.53913	-0.60149	-0.49038	-0.18087	-0.44352	-0.31105	-0.22328	-0.03249	-0.20821	-0.22163	-0.20182	0.77368	0.61073	0.50878	1	0.81552	0.25199	0.3397	0.30608	0.38127	

Erythrulose	- 0. 67 90 4	- 0.60 503	- 0.50 894	- 0.4 817 9	- 0.59 467	- 0.142 22	- 0.31 261	- 0.3243	- 0.0 57 39 2	- 0. 24 63 2	0.00 642 01	- 0.14 652	- 0.05 446 2	0.469 8	0.631 26	0.54689	0. 81 55 2	1	0.029 764	0.26 736	0. 23 42 5	0.359 27
3-Hydroxyoctanoic	- 0. 10 20 4	- 0.48 571	- 0.44 627	- 0.3 399 7	- 0.50 049	- 0.625 73	- 0.60 294	- 0.5168 6	- 0.5 62 18	- 0. 64 79 7	- 0.76 387	- 0.75 488	- 0.77 329	0.422 24	0.540 96	0.40371	0. 25 19 9	0.02 976 4	1	0.17 482	0. 15 50 9	0.089 025
Estriol 3-sulfate 16-glucuronide	- 0. 45 99 1	- 0.52 439	- 0.34 001	- 0.4 943 5	- 0.63 236	- 0.589 24	- 0.64 718	- 0.5677 5	- 0.5 69 29	- 0. 65 70 6	- 0.63 446	- 0.64 629	- 0.66 208	0.403 62	0.336 5	0.30975	0. 33 97	0.26 736	0.174 82	1	0. 74 18 1	0.693 73
p-Cresol sulfate	- 0. 43 66 1	- 0.62 021	- 0.55 416	- 0.5 258 8	- 0.45 103	- 0.782 15	- 0.64 324	- 0.5526 2	- 0.3 95 98	- 0. 42 82 4	- 0.41 351	- 0.51 726	- 0.45 246	0.343 9	0.288 4	0.21547	0. 30 60 8	0.23 425	0.155 09	0.74 181	1	0.922 43
m-Methylhippuric acid	- 0. 33 43 5	- 0.55 234	- 0.55 277	- 0.4 607 5	- 0.57 14	- 0.761 61	- 0.50 612	- 0.5015 4	- 0.2 40 36	- 0. 31 15 7	- 0.25 572	- 0.46 464	- 0.30 373	0.355 12	0.348 54	0.23862	0. 38 12 7	0.35 927	0.089 025	0.69 373	0. 92 24 3	1

Table S3. UHPLC–Q–TOF/MS gradient elution method

T(min)	Phase A (0.1% formic acid) in water	Phase B (0.1% formic acid) in acetonitrile
0	98	2
5	94	6
10	87	13
15	85	15
20	80	20
25	72	28
30	60	40
35	15	85
40	15	85
42	98	2
45	98	2

spectrometric conditions:

The MS parameters were as follows: drying gas temperature, 450°C; drying gas flow, 10mL /min; desolvation gas flow, 800 L/h; capillary voltage, 2.5kV; Ionization source temperature, 100°C.