Supplementary Material

1 Serum Pretreatment and Instrument Condition of Organic Acid, Free Fatty Acid and Amino acid

1.1 Organic acids detection with GC-MS

Serum samples (100 μL) were placed in an EP tube and 9 μL succinate-2,2,3, 3-D4 solution (100 g/mL) was added as internal standard. 300 μL methanol was added as the protein extraction reagent. Vortex-mixed for 4 min, and the supernatant was centrifuged at 14000 rpm/min at 4 °C for 15 min. The supernatant was extracted and centrifuged at 14000 rpm/min at 4 °C for 10min for a second time. Nitrogen was blown for 45 min until completely dry. Subsequently, 30 μL methoxide pyridine solution (33 mg/ml) was added. After vortexed for 1.5min, the product was placed in a constant temperature oscillator box at 180 r/min and oximation reaction was conducted at 37 °C for 1.5 h. 45μL of MSTFA derivative reagent was added to the oxime-treated samples. After fully eddy, the samples were further set in a constant temperature oscillating chamber at 40 °C. Afterwards, oscillation at 180 r /min for 10 min, the samples were left for 1h, and the supernatant was transferred to the injection bottle. Per 2μL supernatant preprocessed was transferred to the injection bottle for need.

Chromatographic conditions were tested using the TRACE1310 gas chromatograph and the TSQ9000Evo mass spectrometer (Thermo Finnigan, Austin, TX, USA). The TG-WAX capillary column (30 m × 0.25 mm, 0.25 μm film thickness) was used. The

measured temperature was as follows: (1) the initial temperature was 70 °C, which was increased to 155 °C at a rate of 5 °C/min for 2 min; (2) increased to 170 °C at a rate of 5 °C/min and kept for 2 min; (3) increased to 220 °C at a rate of 5 °C /min for 2 min. Mass spectrometry detection conditions: Delivery line temperature maintained at 250 °C. The solvent delay time was 6 min. The source temperature was 250 °C, the electron energy was 70 eV, and the selective reaction was detected by SRM scanning.

1.2 Free-fatty acids detection with GC-MS

Serum samples were thawed in 4 ℃ and fully mixed about 20 s. A volume of 200 μL thawed serum was transferred into a 10 mL glass tube, then 200 μL internal standard solution (200 μg/mL heptadecanoic acid) and 2 mL KOH-CH3OH were added into each sample, vortex-mixed for 30 s and placed at room temperature for 10 min. A certain amount of anhydrous sodium sulfate and 1mL hexane was added into the test tube, vortex-mixed for 1 min. The solution was centrifuged at 3500 rpm for 5 min and the hexane layer was placed into a 4 mL Eppendorf tube. Then another 1 mL hexane was added into the same tube and extracted the hexane layer again based on the same operation. The collection was discarded. Subsequently, 2 mL 10% H_2SO_4-CH_3OH was added into the residuary serum, reacted at 62 °C water bath for 2 h. After the solution cooled to the room temperature, some anhydrous sodium sulfate was added to remove traces of water. After adding 2 mL hexane and mixing for 1 min, the hexane layer was collected and transferred to a new tube after centrifuging at 3500 rpm for 5 min. Then collection was evaporated to dryness under N2 by Bath Nitrogen Blow Instrument

(TTL-DCI, Beijing, China) and reconstituted in 100 μL hexane. The solution was centrifuged at 3500 rpm for 30 s and placed into a sampling vial pending for free fatty acids (FFA) analysis by GC-TQ-MS/MS.

For GC-TQ-MS/MS analysis, a TRACE 1310 gas chromatograph coupled with a TSQ 8000 Evo mass spectrometer (Thermo Finnigan, Austin, Texas, USA) was used. Helium was used as the carrier gas. A split injector (the split ratio being 1:10) was used to add the sample (1.0 μL) onto a Thermo TG-WAX MS (30 m×0.25 mm I.D., 0.25 μm film thickness) capillary column at 230 ℃. Free fatty acid methyl esters were separated in constant flow by the following oven program: (1) after the initial temperature is 50 ℃ for 1 min, the temperature was raised to 200 ℃ at the speed of 10 ℃/min and kept for 10 min; (2) raised the temperature to 220 ℃ at a speed of 5 ℃/min and kept it for 11 min. Mass spectrometry detection conditions: the temperature of the transmission line was maintained at 230 ℃. The solvent delay time was 5 min. The source temperature was 230 ℃ and the electron energy was 70eV. The triple quadrupole mass spectrometer was operated under electron impact ionization mode. The Mass spectra of m/z 30-450 was collected by multiple reaction monitoring for MS/MS measurement.

1.3 Amino acid detection with UPLC-TQ-MS

As usual, our sample needed pretreatment. We took the serum to be tested out of the refrigerator at □80 °C and put it into the refrigerator at 4 °C for melting. The serum and additives were vortexed, and 30 μL of the serum mixture was added into an EP tube

with 10 μL (100 μg/mL) of stable isotope labeled valine-d8 and phenylalanine-d8 as a mixed internal standard solution. 80 μL of sample treatment solution (74.9% methanol, 24.9% acetonitrile, 0.2% formic acid), swirled for 30 s, and let it stand on ice for 30 min. Centrifuged (4 °C, 15000 rmp/min, 20 min), and the supernatant was put into a new EP tube. Overnight at- 20 °C (12 h), and the second centrifugation (4 °C, 15000 rmp/min, 15 min). Later the supernatant prepared at the inner liner tube was placed 2 μL of it into the liquid injection tray for detecting.

ACQUITYTM UPLC system (Waters Corporation, Mil-ford, USA) and the HILIC column (100 mm × 2.1 mm × 1.7 μm, Waters Corporation, Milford, USA) were prepared. The flow rate was 0.30 mL/min, and the injection volume per needle was 2 μL. The mobile phase A was 0.2% formic acid, 5% acetonitrile and 2.5 mmoL/L ammonium formate dissolved in water. The mobile phase B was 0.2% formic acid, 5% water and 2.5 mmoL/L ammonium formate dissolved in acetonitrile. Gradient elution procedure was as follows: (1) 5% A concentration for 0 - 0.5 min; (2) increased to 40% within 6 min; (3) increased to 50% within 6-7 min; (4) 50% A kept for 7-8 min, and balanced to initial conditions within 8-15 min. Mass spectrometry detection conditions: Waters Xevo TQD mass spectrometer (Waters Corporation, Manchester, UK) was used. The flow rate was 650 L/h and the cone gas flow rate was 50 L/h. The temperature of desolvation gas was 400 °C, and the temperature of ion source was 150 °C. The capillary voltage was 3200 V.

Table S1 The organic acid profiles of rat serum.

Organic acid (μg/mL)	HC (n = 7)	HP (n = 7)	HF (n = 7)	VIP			*P*		
				HC-HP	HC-HF	HF-HP	HC-HP	HC-HF	HF-HP
Pyruvic acid	69.52 ± 17.35	30.70 ± 10.80	57.02 ±12.87	1.23785	1.21043	1.29716	0.001	0.064	0.008
Lactic acid	26644.20 ± 4611.28	15410.69 ± 4455.62	21440.60±3167.11	1.21156	0.917632	1.21052	0.002	0.294	0.019
Caproic acid	34.27 ±6.18	36.89 ± 6.94	26.74 ±10.64	0.866183	0.921029	0.916971	0.556	0.164	0.055
Glycolic acid	5.48 ± 1.30	4.02 ± 1.51	4.78 ±2.22	0.88518	0.915384	0.923306	0.225	0.866	0.17
2-Hydroxybutyric acid	59.35 ± 34.28	174.45± 119.97	93.95 ±50.70	0.843044	0.817649	0.889678	0.117	0.616	0.27
Oxalic acid	450.36 ± 83.07	350.12 ± 67.53	336.21 ±117.96	1.27358	1.26238	1.10404	0.003	0.01	0.546
3-Hydroxybutyrate acid	87.11 ± 35.46	212.80 ± 118.06	98.45 ±60.56	1.01037	1.10415	1.0941	0.081	0.889	0.146
Malonic	1.94 ±0.11	1.92 ± 0.05	1.94 ±0.05	0.83816	0.809676	1.00941	0.587	0.958	0.624
Methylmalonic acid	2.63 ±1.05	2.31 ± 0.59	2.73 ±0.46	0.336962	0.609782	0.866545	0.41	0.825	0.299
2-Hydroxyisocaproic acid	13.43 ± 4.97	9.62 ± 2.07	8.32 ±1.72	0.84197	1.3258	0.887196	0.042	0.023	0.776
Caprylic acid	3.59 ± 0.31	4.17 ± 0.60	3.46 ±0.61	1.29128	1.19041	1.12712	0.082	0.973	0.076
Ethylmalonic acid	0.26 ± 0.06	0.20 ± 0.06	0.20 ±0.04	0.933676	1.10223	0.811634	0.089	0.135	0.816
Succinic acid	2.57 ± 1.30	2.90 ± 0.65	3.48 ±1.32	0.751256	0.700072	0.816278	0.619	0.374	0.69
Fumaric acid	0.55 ± 0.12	0.38 ± 0.14	0.74 ±0.37	1.16862	1.07658	1.13951	0.167	0.172	0.01
Glutaric acid	0.25 ± 0.06	0.22 ± 0.02	0.26 ±0.08	0.653998	0.673453	0.891476	0.288	0.825	0.204
Capric acid	6.62 ± 0.68	8.63 ± 0.78	6.69 ±1.69	1.34921	1.24632	1.22886	0.008	0.719	0.017
Oxaloacetic acid	1.77 ± 0.04	1.69± 0.08	1.69 ±0.08	1.07693	1.12574	0.651609	0.037	0.053	0.866
Malic acid	54.57 ± 19.38	29.73± 14.83	66.77 ±34.51	1.17783	1.03169	1.16799	0.057	0.393	0.009
Adipic acid	0.14 ± 0.05	0.13± 0.02	0.12 ±0.02	0.828515	0.966121	0.876401	0.717	0.276	0.46
Pyroglutamic acid	21.44 ± 6.75	12.56 ± 2.81	15.11 ± 4.28	1.27183	1.18275	1.17431	0.034	0.012	0.628
a-ketoglutaric acid	17.72 ± 3.63	7.76 ± 2.13	15.16 ± 6.03	1.30038	1.17334	1.16604	0.001	0.45	0.013

Phospho-pyruvic acid monopotassium salt	3.25 ± 0.62	2.78 ± 0.28	2.66 ± 0.11	0.6892	1.06697	0.892745	0.196	0.081	0.658
Pimelic acid	0.51 ± 0.05	0.47 ± 0.02	0.49 ± 0.02	1.04242	0.91206	1.08046	0.035	0.331	0.215
Suberic acid	0.32 ± 0.08	0.23 ± 0.05	0.27 ± 0.07	1.36558	1.14055	1.23726	0.038	0.462	0.155
Orotic acid	0.66 ± 0.24	0.41 ± 0.11	0.61 ± 0.37	0.750576	0.494449	0.809244	0.196	0.507	0.514
Cis-aconitic acid	0.45 ± 0.23	0.43 ± 0.14	0.52 ± 0.13	0.729388	0.886351	0.913829	0.884	0.204	0.16
Citric acid	133.14 ± 126.97	112.04 ± 169.08	86.44 ± 57.49	0.814358	0.887027	0.728824	0.753	0.448	0.654
Isocitric acid	0.77 ± 0.30	0.72 ± 0.29	0.70 ± 0.18	0.827946	0.75115	0.721688	0.75	0.516	0.739
Sebacic acid	8.53 ± 4.36	6.66 ± 2.49	7.85 ± 2.62	0.67651	0.871321	0.928944	0.281	0.534	0.638

Table S2 The amino acid profiles of rat serum.

Amino acid (μg/mL)	**HC (n = 5)**	**HP (n = 5)**	**HF (n = 5)**	**VIP**			***P***		
				HC-HP	HC-HF	HF-HP	HC-HP	HC-HF	HF-HP
Glycine	118.62 ± 44.91	88.24 ± 20.69	191.04 ± 54.69	0.904306	0.6487	1.08118	0.002	0.02	0.281
Creatinine	33.80 ± 5.43	547.30 ± 7.34	99.38 ± 34.37	0.929164	0.92403	0.95679	0.033	0.031	0.065
Threonine	99.42 ± 12.06	98.10 ± 26.39	121.30 ± 24.81	0.940785	1.02503	0.92603	0.122	0.142	0.926
Valine	61.44 ± 7.92	75.34 ± 5.40	67.22 ± 8.76	1.06361	0.6487	1.19068	0.113	0.246	0.013
Proline	93.80 ± 38.51	82.82 ± 16.43	100.34 ± 19.05	1.24832	1.18757	1.10484	0.318	0.704	0.526
Methionine	7.16 ± 0.77	6.96 ± 1.10	9.64 ± 1.84	0.93963	0.963905	0.888761	0.007	0.011	0.814
Isoleucine	31.24 ± 4.19	34.38 ± 2.84	49.26 ± 7.96	1.01448	1.0456	0.977565	0.001	0.001	0.38
Phenylalanine	41.22 ± 5.08	43.06 ± 3.34	49.10 ± 7.77	0.979714	0.942462	0.917213	0.133	0.057	0.632
Tyrosine	20.32 ± 3.77	21.08 ± 7.57	23.90 ± 7.31	0.888107	0.898562	0.861632	0.503	0.398	0.855
Bingansuan	529.18 ± 141.16	419.3 ± 152.73	873.44 ± 173.62	0.993592	0.995617	1.00708	0.001	0.005	0.288
Trimethy	5.02 ± 3.24	3.76 ± 2.28	39.68 ± 31.03	0.976149	0.805781	0.95831	0.146	0.16	0.855
Aminbutyric acid	2.28 ± 1.23	2.30 ± 0.69	9.60 ± 1.51	1.11443	1.12952	1.08921	0.001	0.001	0.979
Dimethylglycine	4.42 ± 2.46	4.94 ± 1.53	19.88 ± 4.17	1.07147	1.11894	1.08658	0.001	0.001	0.784
Serine	138.88± 30.82	152.08 ± 30.07	258.84 ± 50.10	0.976695	1.02426	0.935963	0.001	0.001	0.594
43-Homs	3.76 ± 1.33	4.66 ± 1.36	3.86 ± 1.07	1.04806	0.844579	0.966205	0.336	0.902	0.282
Lysine	6532.42 ± 1155.228	5863.72 ± 749.27	9840.08 ± 1701.56	1.1979	1.22654	1.09102	0.001	0.001	0.419
Glutamine	155.76 ± 34.59	162.9 ± 38.78	238.22 ± 65.39	1.01299	1.13029	0.9747	0.03	0.019	0.819
Tryptophan	16.54 ± 3.78	19.14 ± 3.97	14.10 ± 3.65	0.845137	0.870829	1.11627	0.058	0.33	0.301
Arginine	19.80 ± 17.38	33.38 ± 14.87	68.26 ± 33.64	0.749796	1.01637	0.877524	0.203	0.076	0.498
Glutamic acid	45.84 ± 9.56	47.16 ± 11.28	85.72 ± 17.19	0.977149	1.04344	0.946167	0.001	0.001	0.876
Creatine	59.74 ± 10.17	74.94 ± 11.98	91.10 ± 37.62	0.870227	0.870011	0.853383	0.748	0.316	0.165

Taurine	14.34 ± 1.33	14.86 ± 1.16	20.04 ± 1.81	0.96698	1.00481	0.951494	0.001	0.001	0.583
4-hydro	6.60 ± 3.30	6.46 ± 1.99	7.70 ± 1.11	1.17365	1.23288	1.13028	0.414	0.467	0.925
Leucine	16.26 ± 1.13	18.40 ± 1.30	25.52 ± 4.20	1.02376	1.04061	0.980091	0.001	0.001	0.221
Histidine	62.66 ± 18.48	65.98 ± 10.05	62.42 ± 9.54	0.94503	1.00985	0.962516	0.68	0.978	0.701
Citrulline	11.18 ± 5.39	16.24 ± 6.25	38.14 ± 8.40	1.02858	1.07118	1.05565	0.001	0.001	0.262
Asparagine	25.40 ± 7.17	19.64 ± 4.88	31.00 ± 6.91	0.956942	0.841981	1.00882	0.016	0.192	0.18
γ-aminobutyric acid	7687.66 ± 1111.88	6393.06 ± 864.26	10904.70 ± 1187.82	1.01196	1.07901	0.999655	0.001	0.001	0.078

Table S3 The fatty acid profiles of rat serum.

Fatty acid (μg/mL)	**HC (n = 5)**	**HP (n = 5)**	**HF (n = 5)**	**VIP**			***P***		
				HC-HP	HC-HF	HF-HP	HC-HP	HC-HF	HF-HP
C14:0	2.63 ± 0.55	3.13 ± 0.39	1.33 ± 0.60	0.84174	1.10025	0.977107	0.219	0.001	<0.001
C16:1	65.95 ± 15.31	92.51 ± 5.11	81.94 ± 36.05	0.88343	0.80905	0.933852	0.056	0.827	883
C16:0	36.32 ± 5.25	46.60 ± 1.88	34.21 ± 4.51	1.0284	0.917552	0.984831	0.005	0.225	<0.001
C18:0	327.09 ± 111.19	440.14 ± 20.51	300.71 ± 118.68	1.02625	0.854206	0.898268	0.042	0.0954	0.038
C18:1	184.65 ± 59.71	239.92 ± 10.34	180.46 ± 76.98	0.998138	0.858086	0.864704	0.083	0.82	0.122
C18:2	542.55 ± 102.33	878.45 ± 185.39	452.32 ± 169.42	0.98534	0.962649	0.974098	0.008	0.282	0.001
C18:3γ	16.91 ± 1.92	22.87 ± 14.37	11.22 ± 6.52	0.82948	0.928352	0.88439	0.681	0.385	0.357
C18:4	0.66 ± 0.02	0.66 ± 0.02	0.62 ± 0.02	1.24072	0.917561	0.981023	0.982	0.021	0.02
C18:3α	1.95 ± 0.71	2.54 ± 0.80	1.20 ± 0.56	1.03335	0.922909	0.931788	0.4	0.05	0.01
C20:2	19.29 ± 6.87	12.91 ± 4.51	41.16 ± 38.99	0.770267	0.975902	0.903358	0.146	0.636	0.398
C20:3	11.60 ± 1.58	14.43 ± 4.95	10.57 ± 5.95	1.05444	0.964084	1.09729	0.346	0.727	0.206
C20:4	1850.20 ± 234.11	2745.10 ± 635.40	1165.05 ± 530.33	0.987674	0.928787	0.962419	0.007	0.105	<0.001
C20:5	3.71 ± 0.46	2.96 ± 0.23	2.39 ± 0.12	0.767307	1.79396	1.36398	0.135	0.011	0.006
C22:4	41.39 ± 5.72	66.89 ± 15.09	42.62 ± 15.98	1.28775	0.75144	1.08524	0.026	0.704	0.013
C22:5	66.68 ± 10.27	80.49 ± 13.14	51.44 ± 22.93	1.0885	0.946653	1.04308	0.305	0.108	0.016
C22:6	1262.06 ± 232.62	2068.11 ± 363.92	1065.98 ± 526.86	1.01257	0.959795	1.00721	0.004	0.685	0.002

Table S4 Reagents.

REAGENT or RESOURCE	SOURCE	IDENTIFIER
SirT1 (D1D7) Rabbit mAb	Cell Signaling Technology	Cst #9475S
Rabbit polyclonal anti- NQO1	Cell Signaling Technology	Affinity#DF6437,RRID: AB_2838400
Rabbit polyclonal anti-GPX4	Cell Signaling Technology	Affinity#DF6701,RRID: AB_2838663
Rabbit polyclonal anti-FOXO3A	Cell Signaling Technology	Affinity#AF6020,RRID: AB_2834954
Rabbit polyclonal anti-beta Actin	Cell Signaling Technology	Affinity#AF7018,RRID: AB_2839420
Rabbit polyclonal anti-SIRT3	Cell Signaling Technology	Affinity#AF5135 RRID:AB_2837621

Table S5 Kit indicators

Name of reagent	Source	IDENTIFIER
GCL Assay Kit	Solarbio	BC1215
GR Assay Kit	Solarbio	BC1165
CAT Assay Kit	Solarbio	BC0205
SOD Assay Kit	Solarbio	BC0175
Gpx Assay Kit	Beyotime	S0056
GSH and GSSG Assay Kit	Beyotime	S0053
MDA Assay Kit	Solarbio	BC0025
ROS Assay Kit	JINGMEI	JM-10531R1
IL-6 Assay Kit	MEIMIAN	3914
GSH Assay Kit	Solarbio	BC1175
TNF-α Assay Kit	MEIMIAN	1112