

**A metabolomic study of the PPAR δ agonist GW501516 for enhancing
running endurance in Kunming mice**

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Supplementary Figure 1

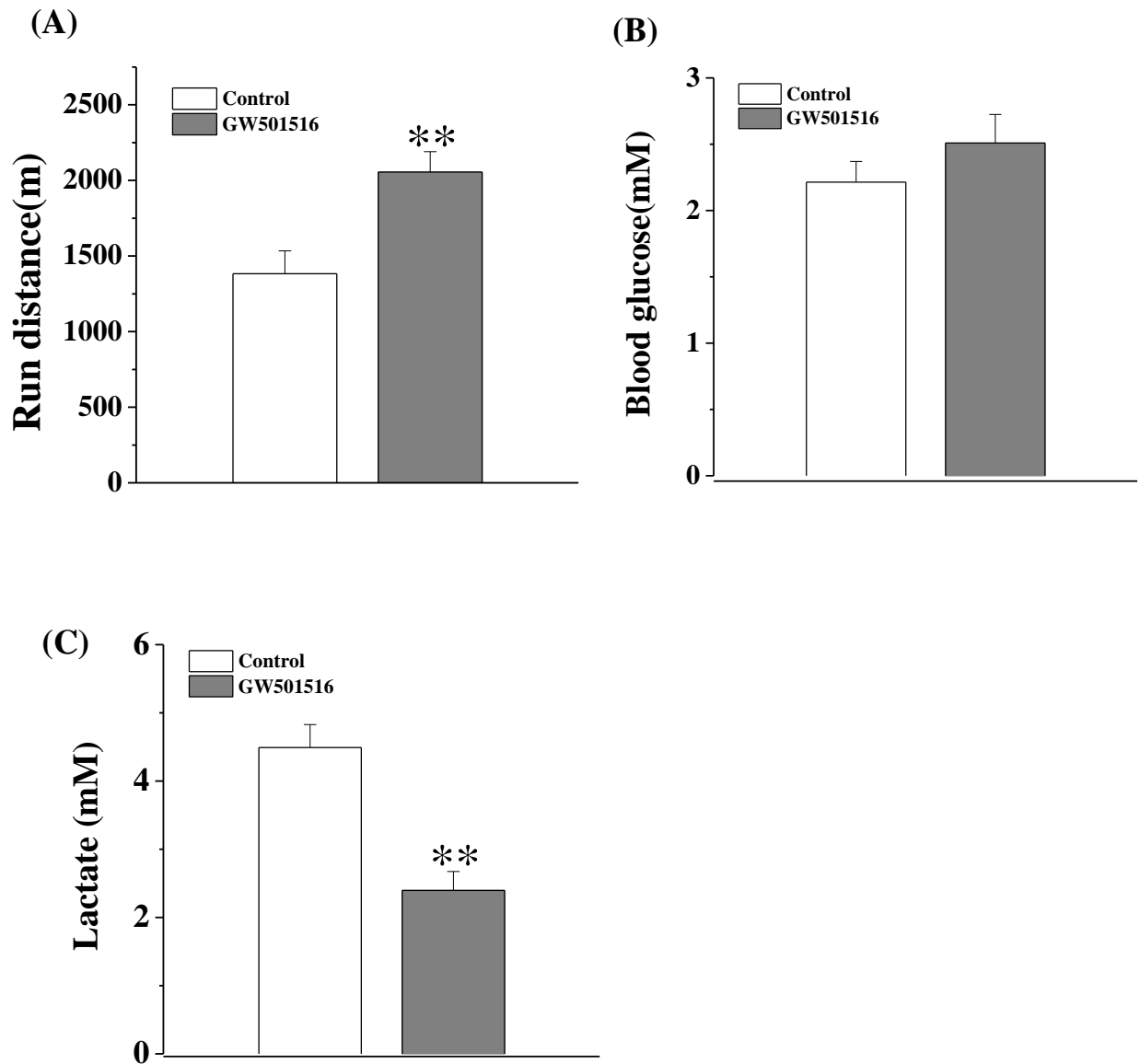


Figure S1. Effects of GW501516 administration for 7 days on running performance in sedentary mice. Forced treadmill running endurance tests were performed after 7 days of GW501516 treatment. Blood glucose and lactate were tested immediately after running (n = 9–10 per group). * $p < 0.05$, ** $p < 0.01$ compared to untreated control mice.

Supplementary Figure 2

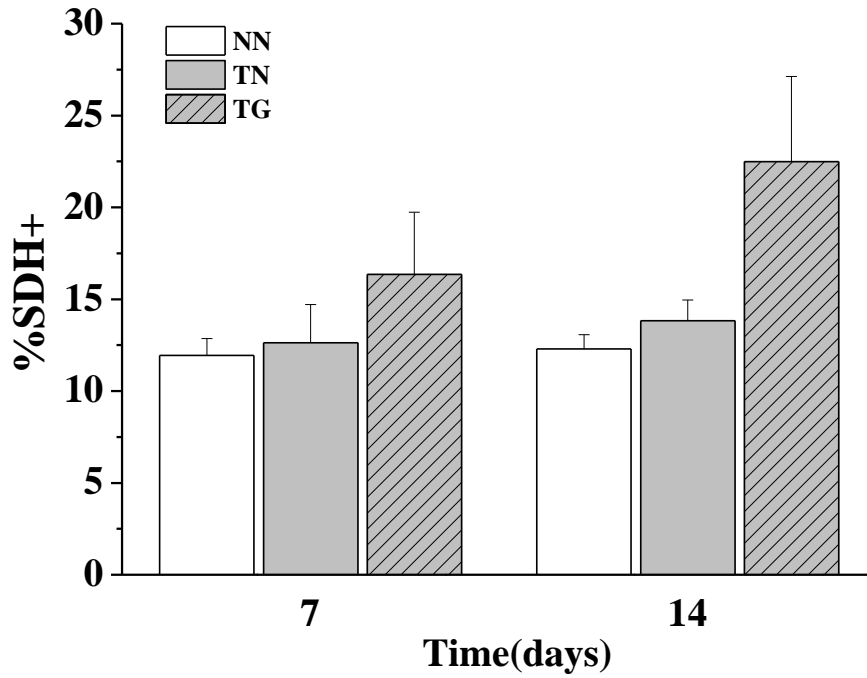


Figure S2. Effects of GW501516 treatment on SDH-positive fibres in trained mice.

Quantification of SDH-positive fibres from the NN, TN, and TG groups after 1 and 2 week of treatment.

Supplementary Figure 3

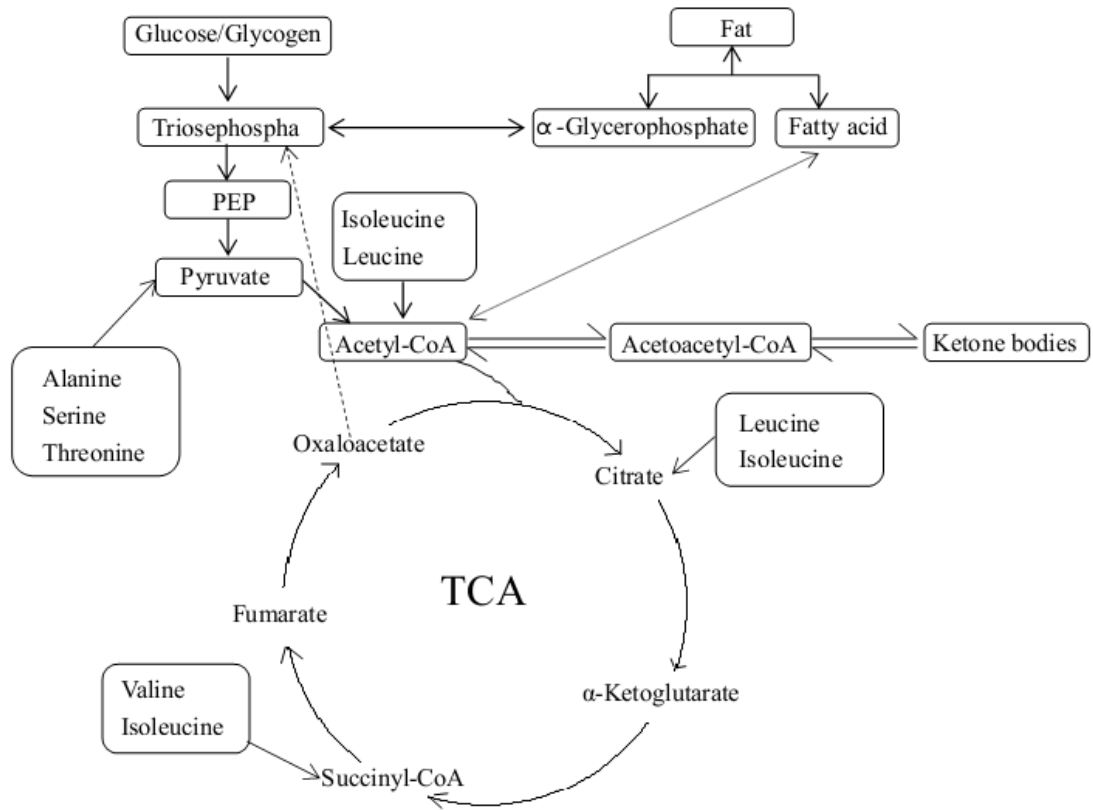


Figure S3. Diagram of branched-chain amino acids (BCCA) in the tricarboxylic acid cycle.

Supplementary Figure 4

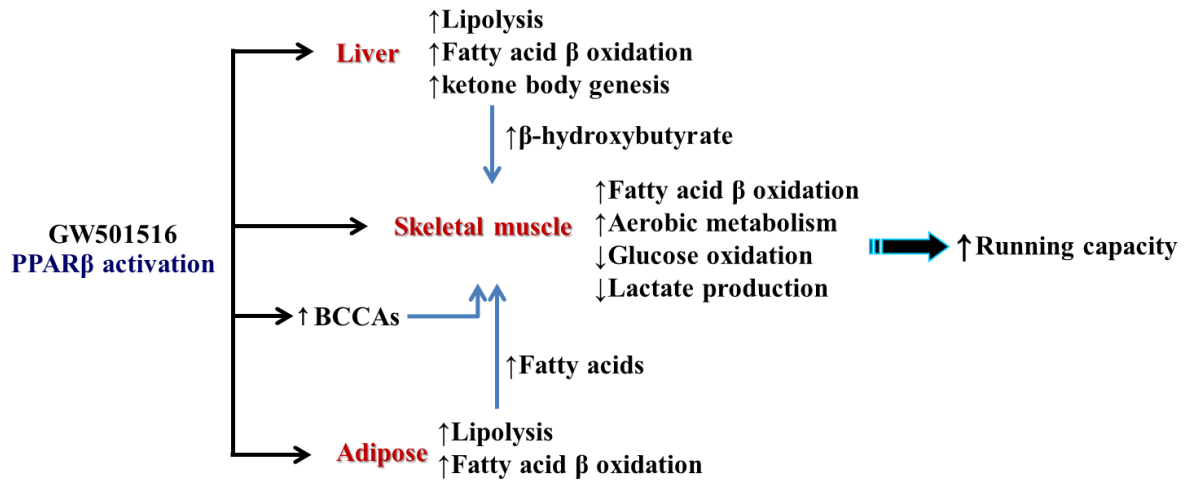


Figure S4. Schematic of the physiological pathways that enhance running endurance after GW501516 treatment. PPAR δ is activated by GW501516 leading to reduced blood glucose metabolism and increased fatty acid metabolism by promoting lipolysis in adipose tissue and the liver, which increases the supply of fatty acids, β -hydroxybutyrate, and BCCAs to skeletal muscle.

Supplement Table 1

Summary of the differentiated serum fatty acids associated with training and/or GW501516 treatment

NO.	Metabolites	<i>P</i>				VIP			
		a	b	c	d	a	b	c	d
1	3-hydroxy-Hexadecanoic acid	0.001	0.002	0.373	0.002	1.48	1.84	0.77	1.36
2	Octanoic acid	0.512	0.001	0.704	0.003	0.34	1.38	0.41	1.17
3	Decanoic acid	0.200	0.010	0.485	0.003	0.65	1.13	0.81	1.28
4	Dodecanoic acid	0.000	0.043	0.608	0.004	1.69	0.89	0.07	1.32
5	Tetradecanoic acid	0.000	0.000	0.050	0.003	1.68	1.48	1.12	1.35
6	Palmitic acid	0.109	0.013	0.003	0.000	0.82	1.19	1.82	1.37
7	15-methyl-Hexadecanoic acid	0.000	0.217	0.720	0.001	1.91	0.74	0.40	1.40
8	Pentadecanoic acid	0.000	0.032	0.197	0.001	1.89	0.97	0.66	1.48
9	Stearic acid	0.000	0.005	0.003	0.000	1.18	0.00	1.84	1.38
10	Eicosanoic acid	0.006	0.377	0.829	0.005	1.34	0.28	0.07	1.29
11	Docosanoic acid	0.002	0.351	0.756	0.016	1.45	0.20	0.11	1.11
12	Tetracosanoic acid	0.001	0.874	0.416	0.007	1.60	0.30	0.30	1.24

13	Palmitoleic acid	0.031	0.924	0.445	0.045	1.03	0.05	0.65	1.18
14	Oleic acid	0.839	0.839	0.018	0.046	0.10	0.58	1.64	1.19
15	Linoleic acid	0.008	0.533	0.358	0.046	1.30	0.36	0.62	0.92
16	α -linolenic acid	0.000	0.417	0.000	0.263	1.78	0.17	2.24	0.51
17	11,14-Eicosadienoic acid	0.628	0.397	0.002	0.004	0.25	0.64	1.94	1.36
18	8,11,14-Eicosatrienoic acid	0.000	0.027	0.043	0.422	1.63	0.94	1.49	0.19
19	Arachidonic acid	0.003	0.112	0.004	0.022	1.40	0.63	1.83	1.06
20	8,11,14,17-Eicosapentaenoic acid	0.179	0.506	0.011	0.042	0.69	0.38	1.13	1.02
21	Eicosapentaenoic acid	0.005	0.036	0.433	0.020	1.42	1.03	0.66	1.12
22	Docosahexaenoic acid	0.906	0.673	0.037	0.010	0.06	0.02	1.54	1.21

1. P means p value obtained from one-way analysis of variance (ANOVA).
2. Variable importance in the projection (VIP) was obtained from PLS-DA.
3. a, b, c, d respectively represents NG vs. NN, TN vs. NN, TG vs. TN, TG vs. NG.