

Table S1. Composition and energy content of the mice diets.

	ND		ND+LA		HFD		HFD+LA	
Ingredients	gm	Kcal	gm	Kcal	gm	Kcal	gm	Kcal
Casein	140.0	560.0	140.0	560.0	233.0	932.2	233.0	932.2
L-Cystine	2.5	10.0	2.5	10.0	2.5	10.0	2.5	10.0
Corn starch	495.0	1983.0	495.0	1983.0	85.0	340.1	85.0	340.1
Maltodextrin	125.0	500.0	125.0	500.0	116.5	466.1	116.5	466.1
Sucrose	100.0	400.0	100.0	400.0	200.0	800.0	200.0	800.0
Cellulose	50.0	-	50.0	-	58.3	-	58.3	-
Potassium	-	-	-	-	19.0	-	19.0	-
Vitamin mix	10.0	40.0	10.0	40.0	10.0	40.0	10.0	40.0
Choline	2.5	-	2.5	-	2.5	-	2.5	-
Mineral mix	35.0	-	35.0	-	11.7	-	11.7	-
Dicalcium phosphate	-	-	-	-	15.2	-	15.2	-
Calcium carbonate	-	-	-	-	6.4	-	6.4	-
Soybean oil	40.0	360.0	20.0	180.0	40.0	360.0	20.0	180.0
Lard	-	-	-	-	200.0	1800.0	200.0	1800.0
tricaprylin	-	-	20.0	180.0	-	-	20.0	180.0
Total	1000.0	3853.0	1000.0	3853.0	1000.0	4748.5	1000.0	4748.5

Table S2. RT-qPCR primer sequences.

Primer	Sequences (5'-3')
PPAR γ	F: AGGACTACCAAAGTGCCATCAAA
	R: GAGGCTTTATCCCCACAGACAC
FABP4	F: GAGCACCATTAACCTTAGATGGA
	R: AAATTCTGGTAGCCGTGACA
C/EBP α	F: CGATGCTCTTAGCTGAGTGT
	R: GGTTCAAGAATTTACCTCT
C/EBP β	F: CACCACGACTTCCTCTCCGA
	R: ATCCACGGTCTTCTTGGTCTTA
HSL	F: CACTGACTGCTGACCCCAAG
	R: TCCTCACTGTCCTGTCCTTCAC
TNF- α	F: AGGCACTCCCCCAAAGATG
	R: CCACTTGGTGGTTTGTGAGTG
IL-6	F: CTCTGCAAGAGACTTCCATCCA
	R: GACAGGTCTGTTGGGAGTGG
IL-1 β	F: TGCCACCTTTTGACAGTGATG
	R: AAGGTCCACGGGAAAGACAC
Claudin-1	F: ACTGTGGATGTCCTGCGTTT
	R: ACTAATGTCGCCAGACCTGAA
Occludin	F: CAGGTGAATGGGTCACCGAG
	R: CCAAGATAAGCGAACCTGCC
ZO-1	F: CTTCCCGGACTTTTGTCCCA
	R: CATTGCTGTGCTCTTAGCGG
MUC-2	F: CCTGAAGACTGTCGTGCTGT
	R: GGGTAGGGTCACCTCCATCT
MUC-3	F: AGTGCTGTTGGTGATCCTCG
	R: AGAGTCCAGGGGCATGTAGT

Table S3. The results of Multi Response Permutation Procedure (MRPP) analysis.

Group	A	observed-delta	expected-delta	Significance
ND+LA-HFD	0.1511	0.5086	0.5992	0.013
ND+LA-HFD+LA	0.1193	0.4853	0.5510	0.025
ND-HFD	0.2005	0.4311	0.5392	0.005
HFD+LA-HFD	0.0335	0.4859	0.5027	0.103
ND-HFD+LA	0.1732	0.3992	0.4828	0.008
ND+LA-ND	0.0181	0.4306	0.4385	0.245

Annotation: the value of observe-delta reflects within-group differences; the value of expect-delta reflects between-group differences. $A > 0$, the difference between groups is greater than the difference within the group. Significance < 0.05 , the difference of result is significant.

Table S4. Significant difference lipid information in serum

Metabolite ID	Lipid Description	Class	P-value	Fold Change
M203T450	Caryophyllene epoxide	PL	4.75E-04	2.54
M129T588	Sulcatol	FA	6.45E-04	2.58
M604T610_1	1,2-Dioleoyl-sn-glycerol	Gly	8.03E-04	0.25
M273T653	alpha-Camphorene	PL	2.53E-03	4.40
M330T658	1-Hexadecyl-2-O-methyl-glycerol	Gly	3.64E-03	7.64
M125T147	Caprylic acid	FA	6.18E-03	0.54
M402T818	2-Methyl-6-phytylhydroquinone	PL	9.35E-03	1.53
M384T737	1-Arachidonoyl Glycerol-d5	Gly	1.14E-02	5.34
M824T619_3	Propionyl-CoA	FA	1.68E-02	0.44
M341T68	MG(18_0_0_0_0_0)	GL	1.88E-02	2.23
M844T972_2	Coenzyme Q10	PL	2.21E-02	1.53
M285T869	9-cis-Retinal	PL	2.32E-02	0.49
M804T938	1-Stearoyl-2-Docosahexaenoyl-sn-Glycero-3-[Phospho-rac-(1-glycerol)]	Gly	2.39E-02	2.10
M353T694	Prostaglandin F2a	FA	2.40E-02	0.24
M207T476	Genipin	PL	2.68E-02	0.48
M406T607	LysoPE(14_1(9Z)_0_0)	GP	2.78E-02	14.49
M115T503	Caproic acid	FA	2.85E-02	1.68
M159T469	3-Hydroxyvalproic acid	FA	2.86E-02	0.60
M173T144	Glycerol 3-phosphate	GP	3.07E-02	0.55
M305T858	11,14,17-Eicosatrienoic acid	FA	3.11E-02	2.12
M241T802	Pentadecanoic acid	FA	3.15E-02	1.75
M407T90	Ginkgolide B	PL	3.16E-02	0.24
M309T942	11Z-Eicosenoic acid	FA	3.35E-02	2.31
M195T689	Tridecanoic acid	FA	3.42E-02	3.27
M387T547	Dihydoroseoside	FA	3.49E-02	0.28
M338T977_1	Tricosanoic acid	FA	3.60E-02	0.47
M303T869	8-HETE	FA	3.61E-02	0.56
M835T475_2	L-3-Aminobutyryl-CoA	FA	3.67E-02	2.71
M319T439_1	Menthyl pyrrolidone carboxylate	PL	3.79E-02	1.55
M288T625	L-Octanoylcarnitine	FA	4.35E-02	1.62
M455T743	Boswellic acid	PL	4.37E-02	4.84
M386T802	2-Arachidonoyl Glycerol-d8	Gly	4.41E-02	2.85
M804T958_1	NBD-Stearoyl-2-Arachidonoyl-sn-glycerol	Gly	4.42E-02	1.57
M279T797	Bovinic acid	FA	4.83E-02	3.57
M130T399	Heptanoic acid	FA	6.40E-02	0.79
M103T951	Valeric acid	FA	6.41E-02	0.07

Abbreviations: GL, glycerolipids; ST, sterol lipids; GP, glycerophospholipids; SP, sphingolipids;

FA, fatty acids. Fold Change, the lipid content that HFD+LA group vs HFD group.

Table S5. Significant difference lipid information in adipose tissue

Lipid ID	Lipid Description	Lipid Category	Fold Change	P-value
Com_45_pos	TG (13:0/13:0/18:3(9Z,12Z,15Z))	GL	5.4	1.62E-06
Com_661_pos	MG (0:0/24:0/0:0)	GL	10.68	2.92E-05
Com_67_pos	TG (13:0/14:1(9Z)/15:0)	GL	6.34	3.45E-05
Com_541_pos	TG (12:0/12:0/18:2(9Z,12Z))	GL	4.72	3.49E-05
Com_539_pos	6-Deoxohomodolichosterone	ST	25.01	4.76E-05
Com_64_pos	TG (16:0/14:1(9Z)/14:1(9Z))	GL	2.3	2.74E-04
Com_553_pos	TG (12:0/12:0/16:0)	GL	11.54	2.12E-03
Com_635_pos	TG (17:1(9Z)/18:1(9Z)/18:2(9Z,12Z))	GL	0.5	4.61E-03
Com_1397_neg	PS (17:0/20:3(8Z,11Z,14Z))	GP	0.22	4.91E-03
Com_546_pos	SM(d16:1/24:1(15Z))	SP	2.19	6.46E-03
Com_940_pos	5-Ethyl-4-methyl-2-octylthiazole	Other	0.55	6.80E-03
Com_672_pos	TG(15:1(9Z)/16:0/18:3(6Z,9Z,12Z))	GL	2.24	7.22E-03
Com_44_pos	TG(12:0/12:0/18:3(6Z,9Z,12Z))	GL	2.73	7.58E-03
Com_1045_pos	Oleyl alcohol	FA	0.58	9.06E-03
Com_600_pos	Myristoylcarnitine	FA	8.47	9.89E-03
Com_537_pos	Aplidiasphingosine	SP	6.72	1.01E-02
Com_1486_neg	PC(18:4(6Z,9Z,12Z,15Z)/P-16:0)	GP	0.34	1.19E-02
Com_1498_neg	PS(22:1(11Z)/22:4(7Z,10Z,13Z,16Z))	GP	0.57	1.31E-02
Com_783_pos	1-Hexadecylamine	Other	1.86	1.42E-02
Com_1472_neg	Emopamil	ST	0.33	1.60E-02
Com_82_neg	Erythrodiol 3-palmitate	GL	0.59	1.72E-02
Com_1267_neg	17-phenyl-trinor-PGF2alpha isopropyl ester	FA	2.03	1.77E-02
Com_1295_pos	trans-4-(Aminomethyl)cyclohexanecarboxylic acid	FA	5.83	2.13E-02
Com_591_pos	TG(12:0/14:1(9Z)/18:3(9Z,12Z,15Z))	GL	8.7	2.42E-02
Com_1277_pos	Zymosterol	ST	0.19	2.42E-02
Com_784_pos	(22E)-1alpha-hydroxy-22,23-didehydrovitamin D3 /didehydrocholecalciferol	ST	2.85	2.71E-02
Com_354_neg	PE-NMe2(O-14:0/O-14:0)	GP	0.64	2.91E-02
Com_1151_neg	(S1)-Methoxy-3-heptanethiol	ST	1.51	3.00E-02
Com_1004_pos	1-[1,4-Dihydro-4-nonyl-5-(1-oxodecyl)-3-pyridinyl]- 1-dodecanone	Other	0.57	3.09E-02
Com_1391_neg	Milnacipran	Other	0.61	3.30E-02
Com_289_pos	Menthyl ethylene glycol carbonate	Other	0.33	3.33E-02
Com_1506_neg	15-Ketobimatoprost	Other	0.61	3.36E-02
Com_544_pos	5beta-Cholestane-3alpha,6beta,7alpha,26-tetrol	ST	2.03	3.53E-02
Com_49_neg	Ethanol, 2-(2-ethoxyethoxy)-	Other	2.07	3.54E-02
Com_562_pos	TG (12:0/14:1(9Z)/17:1(9Z))	GL	2.9	3.73E-02
Com_862_neg	Disperse Orange 1	Other	1.57	3.77E-02
Com_125_pos	Glycerol 1-(9Z-octadecenoate) 2-octanoate 3- tetradecanoate	GL	1.76	3.82E-02

Com_683_pos	Glycerol trimyristate	GL	1.82	4.35E-02
Com_1004_neg	Stanozolol-d3	Other	5.14	4.40E-02
Com_1264_neg	17-HDoHE	Other	0.62	4.47E-02
Com_1017_neg	2-Pentadecylfuran	FA	0.35	4.68E-02
Com_1307_pos	Vitamin D2 3-glucuronide	ST	1.92	4.69E-02
Com_191_pos	Aquifoliunine EI	ST	1.95	4.87E-02
Com_31_neg	Nonapropylene glycol monobutyl ether	Other	0.42	4.87E-02
Com_797_neg	5-Aminolevulinic acid	FA	1.66	4.99E-02

Abbreviations: GL, glycerolipids; ST, sterol lipids; GP, glycerophospholipids; SP, sphingolipids;

FA, fatty acids. Fold Change, the lipid content that HFD+LA group vs HFD group.

Table S6. Information of gut microbiome used for correlation analysis

Taxonomy	Re.HFD	Re.LA	Fold Change	P-Value
Helicobacter	3.85%	18.11%	4.70	0.056535
Intestinimonas	0.04%	0.11%	2.92	0.043674
Faecalibaculum	3.89%	8.90%	2.29	0.013938
Lachnospiraceae	1.67%	2.81%	1.69	0.682326
Roseburia	1.13%	0.74%	0.65	0.820938
Enterorhabdus	0.44%	0.28%	0.63	0.00186
Desulfovibrio	0.86%	0.50%	0.58	0.034729
Oscillibacter	0.12%	0.07%	0.53	0.675093
Alistipes	0.13%	0.07%	0.52	0.141341
Bifidobacterium	0.35%	0.16%	0.46	0.152527
Anaerotruncus	0.26%	0.08%	0.31	0.085775
Bacteroides	0.10%	0.03%	0.29	0.063171
Erysipelatoclostridium	2.25%	0.64%	0.28	0.043209
Acetatifactor	0.08%	0.02%	0.21	0.238372
Streptococcus	1.21%	0.25%	0.21	0.158558
Streptococcus	1.21%	0.25%	0.21	0.021
Enterococcus	0.09%	0.02%	0.18	0.016628
Lactococcus	0.60%	0.07%	0.11	0.029736
Allobaculum	3.59%	0.36%	0.10	0.048814
Akkermansia	1.97%	0.08%	0.04	0.074504

Abbreviations: Re.HFD, the relative abundance of microorganisms of the HFD group; Re.LA, the relative abundance of microorganisms of the HFD+LA group. Fold Change, Re.LA vs Re.HFD.

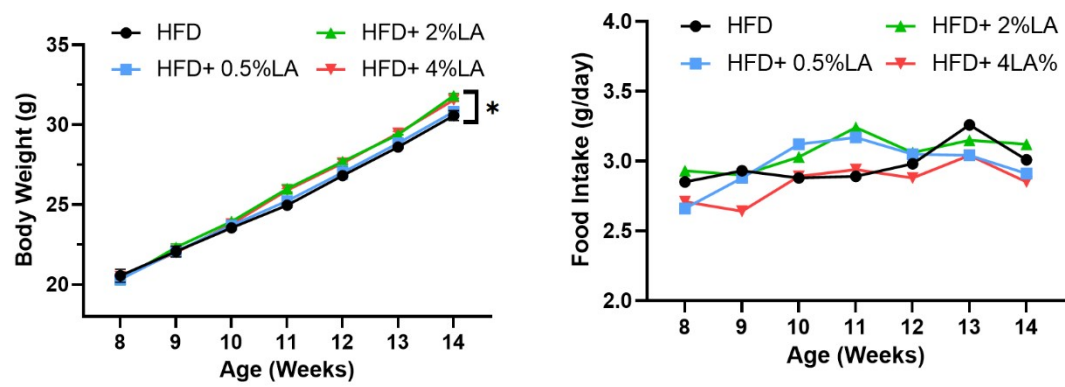


Figure S1. Results of the pre-experiments of body weight and food intake of mice. * represents the significant difference between the HFD+ 2%LA, HFD+ 4%LA group and the HFD group.

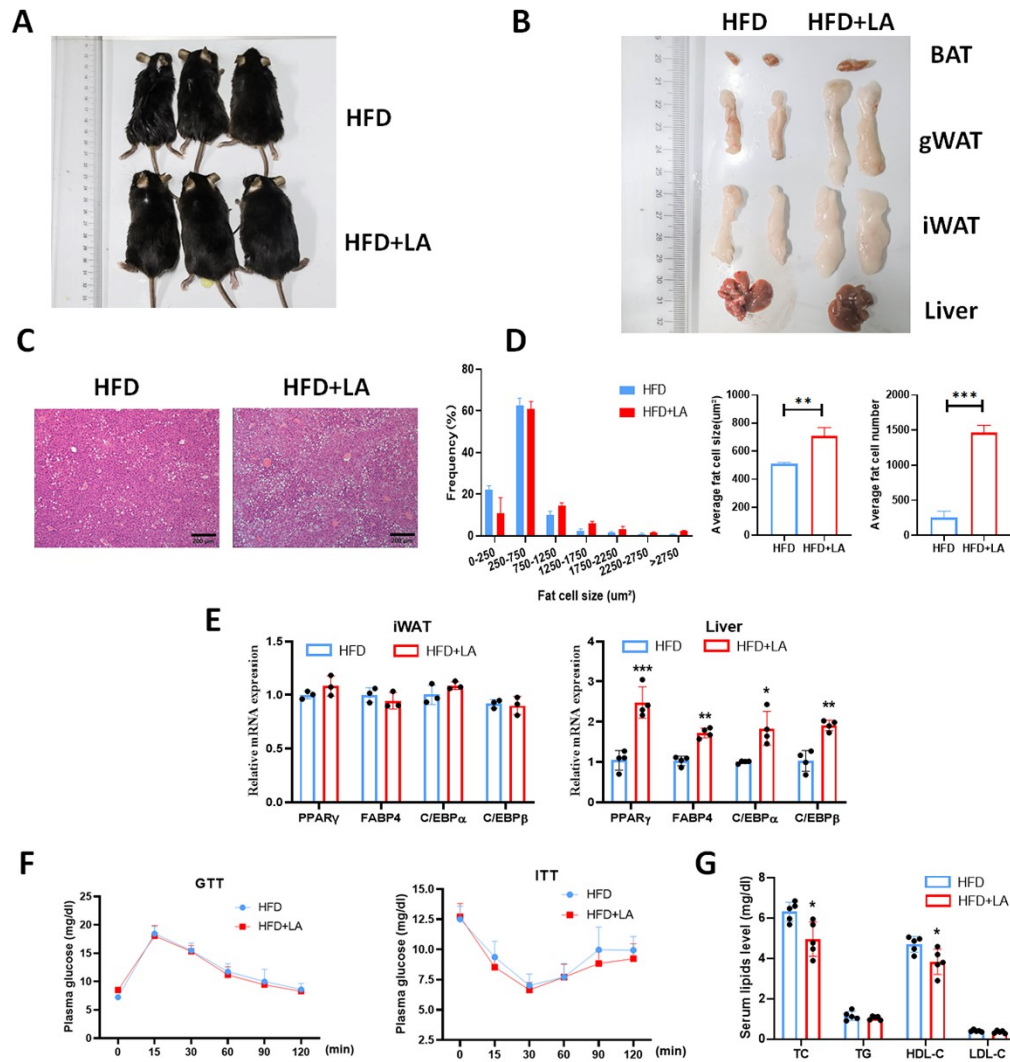


Figure S2. (A) Body size of mice fed a normal diet and high-fat diet. (B) The phenotypes of BAT, gWAT, iWAT and Liver of mice. (C-D) H&E staining and quantitative results of size and number of adipocytes for Liver, n=5. (E) RT-qPCR analysis of adipogenic genes in iWAT and Liver of mice. (F) glucose tolerance of mice on 18th week (Left panel), Insulin sensitivity of mice on 19th week (Right panel). (G) serum TG, TC, HDL-C and LDL-C levels. The results were representative of means $\pm$ SD.

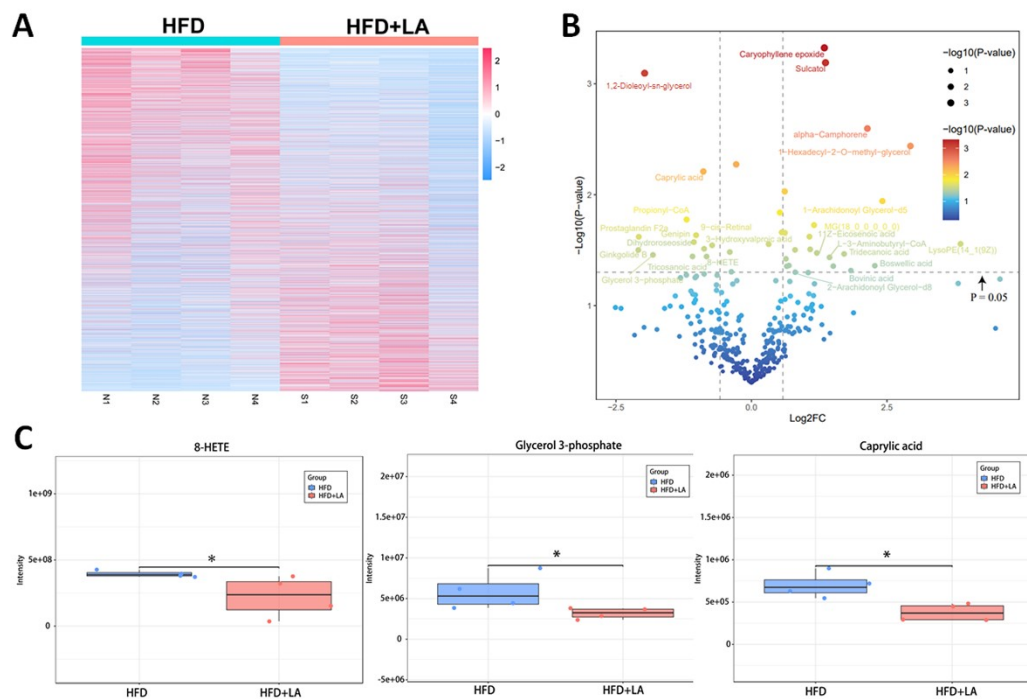


Figure S3. Supplementation Results of Serum and Lipid Metabolome Based on LC-MS. (A) Heatmap of relative expression of all mouse serum metabolites. (B) Volcano plot of the difference in lipid content of mouse serum. (C) Relative quantification results of lipid metabolites.

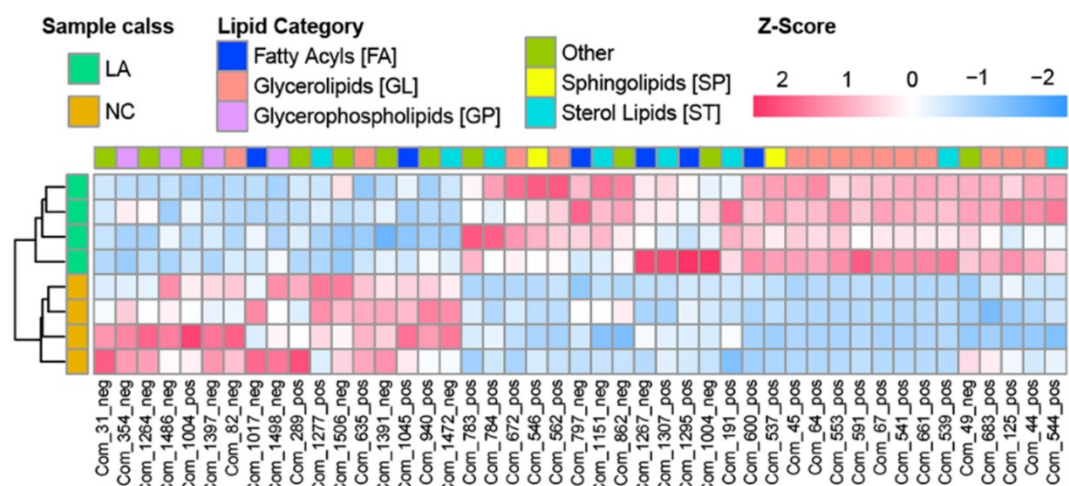


Figure S4. Cluster heat map and lipid classification of differential lipids in mouse gWAT (The details of the lipids in the figure are presented in Table S5).

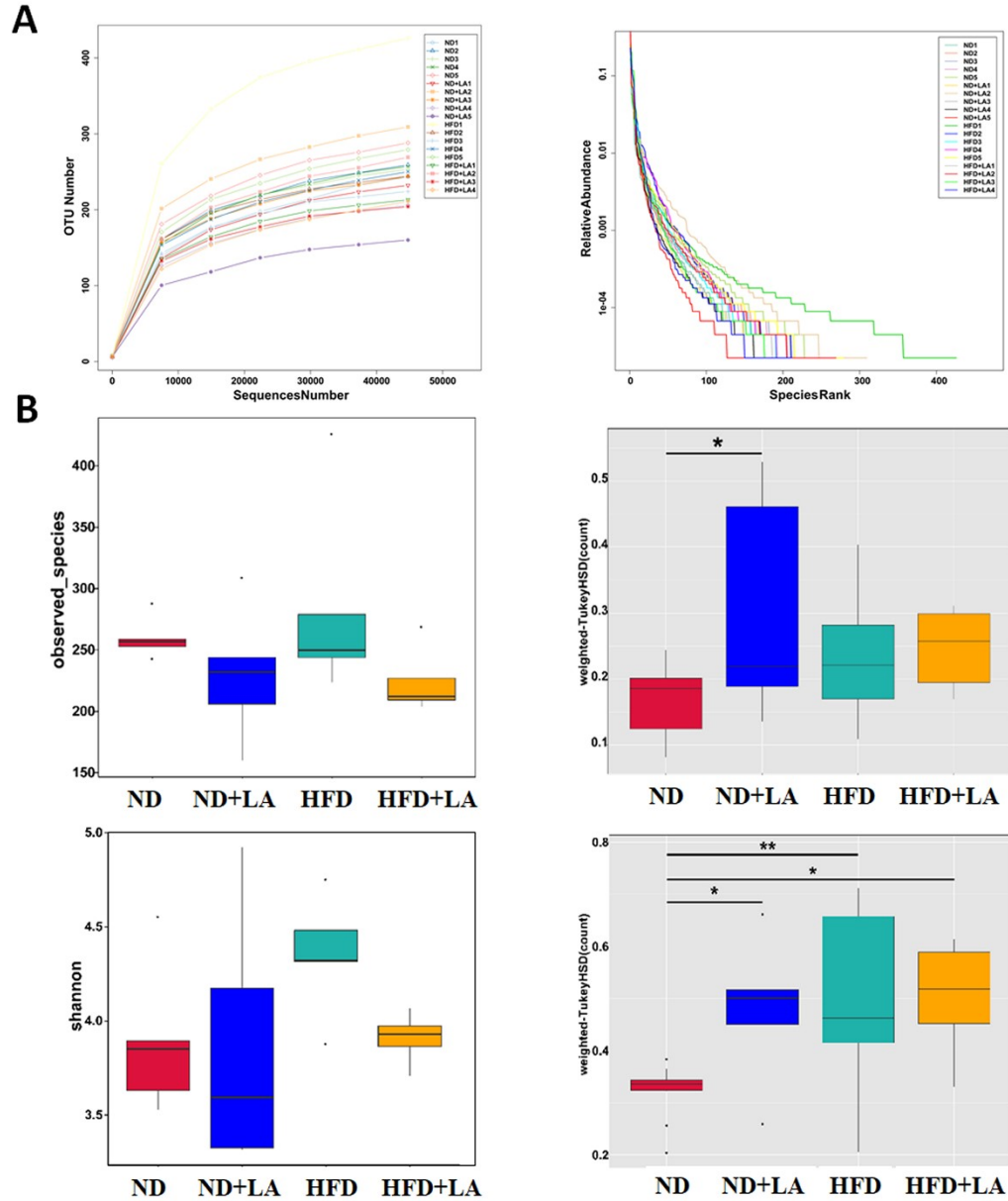
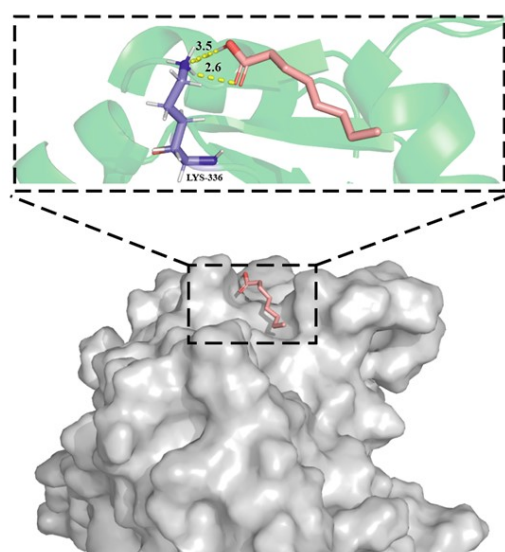
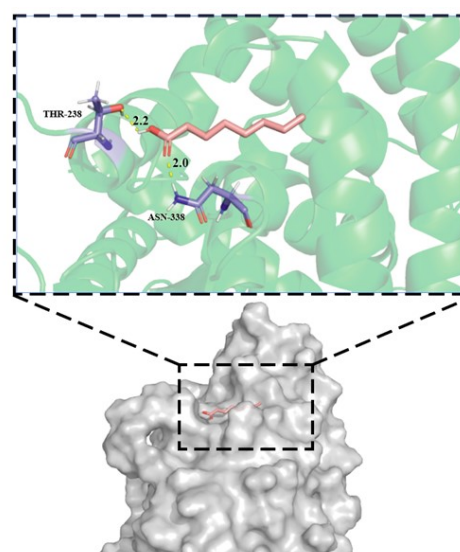


Figure S5. (A) Number of OTUs and species accumulation curve for each 16s rDNA sequencing sample. (B) Analysis of gut microbiota Alpha and Beta diversity differences between groups based on observed species index (upper left panel) and weighted-TukeyHSD (upper right panel). Lower left panel: Alpha diversity (Shannon index), Lower right panel: Beta diversity (unweighted-TukeyHSD) analysis.



Binding Domain 2 Binding Energy = -1.78 kcal/mol
Ligand Efficiency = -0.18 kcal/ (mol * Atom)



Binding Domain 3 Binding Energy = -1.35 kcal/mol
Ligand Efficiency = -0.14 kcal/ (mol * Atom)

Figure S6. Prediction of molecular docking domains between octanoic acid and PPAR γ proteins.