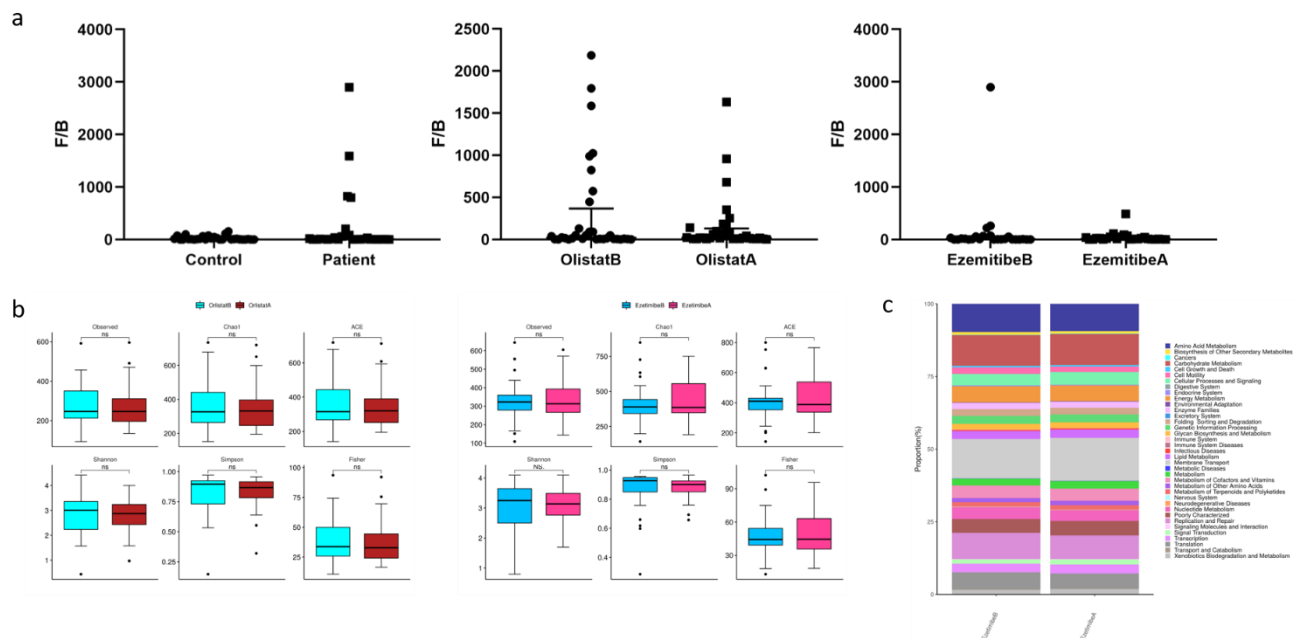


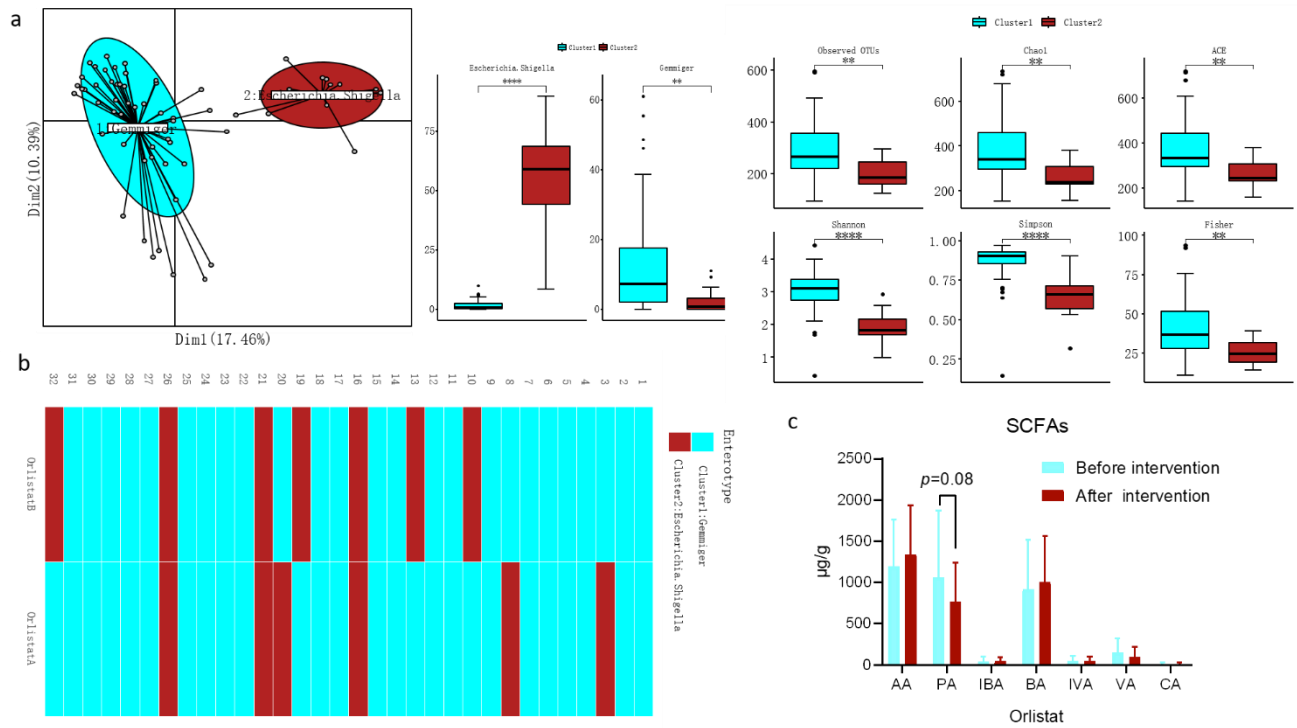
Supplementary Material

1 Supplementary Figures and Tables

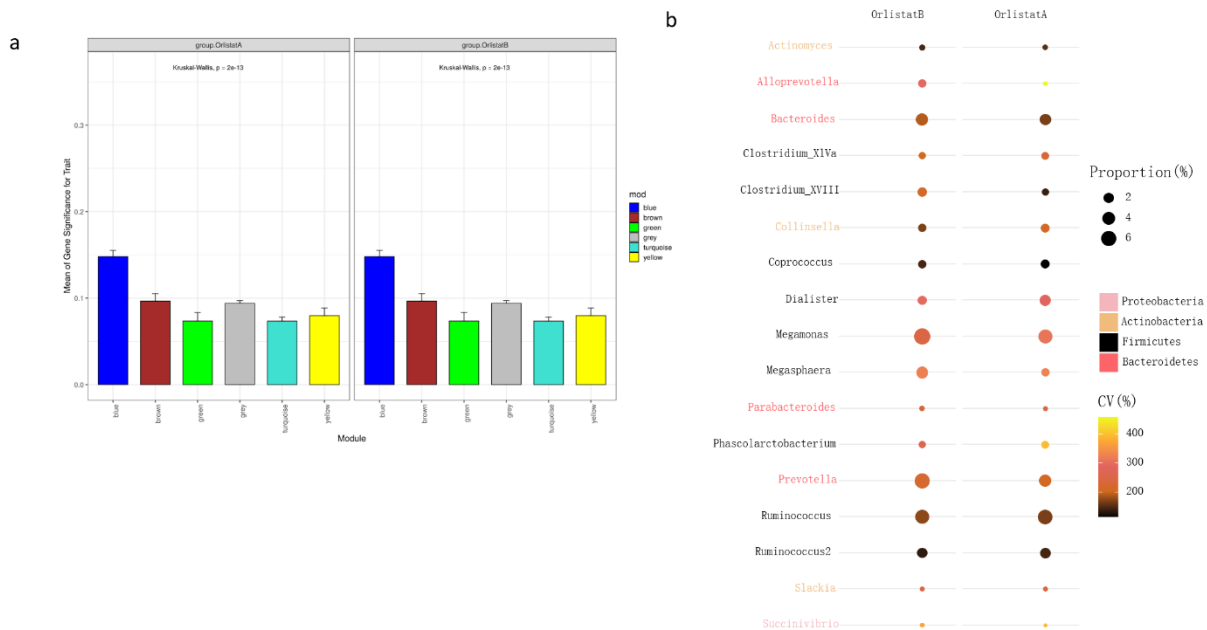
1.1 Supplementary Figures



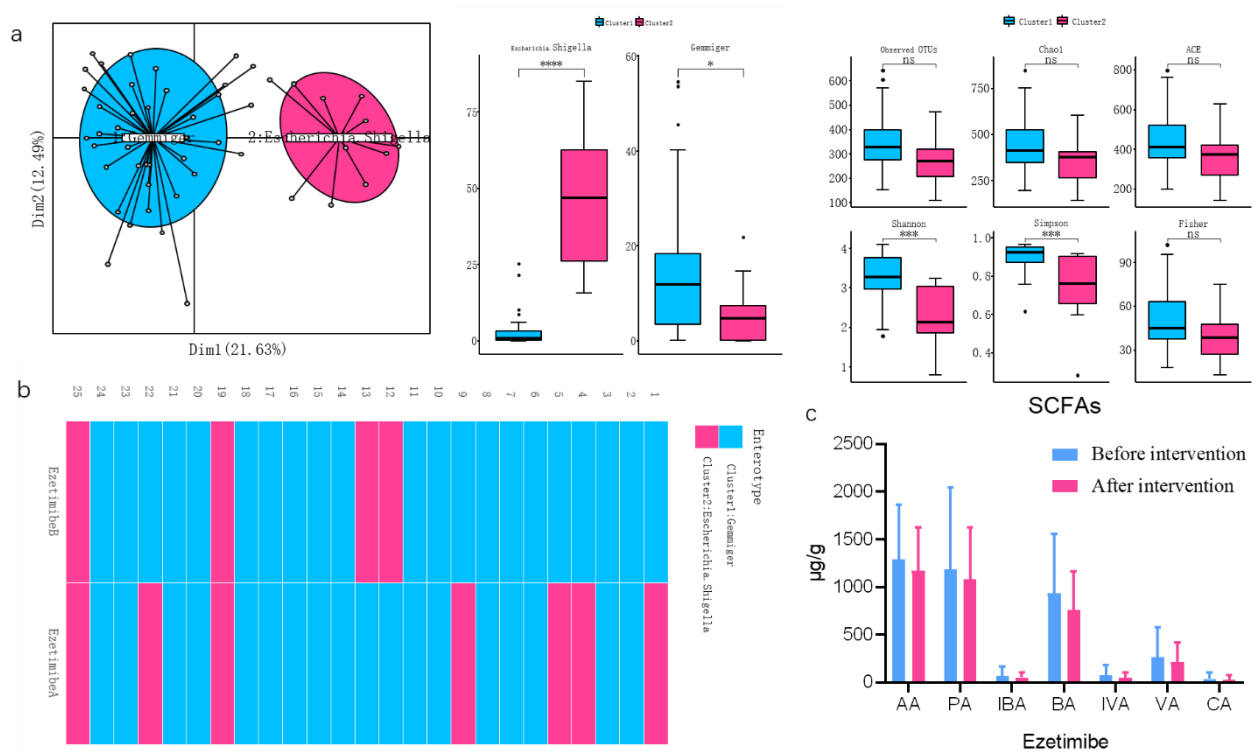
Supplementary Figure 1. Gut microbiota diversity and F/B. a) alpha diversity index before and after orlistat/ezetimibe intervention. b) *Firmicutes/Bacteroidetes* ratio. c) Proportions of KEGG pathways at level 2 encoded in the microbiome in two groups. No significant differences were found in these comparisons between groups. ns: not significant.



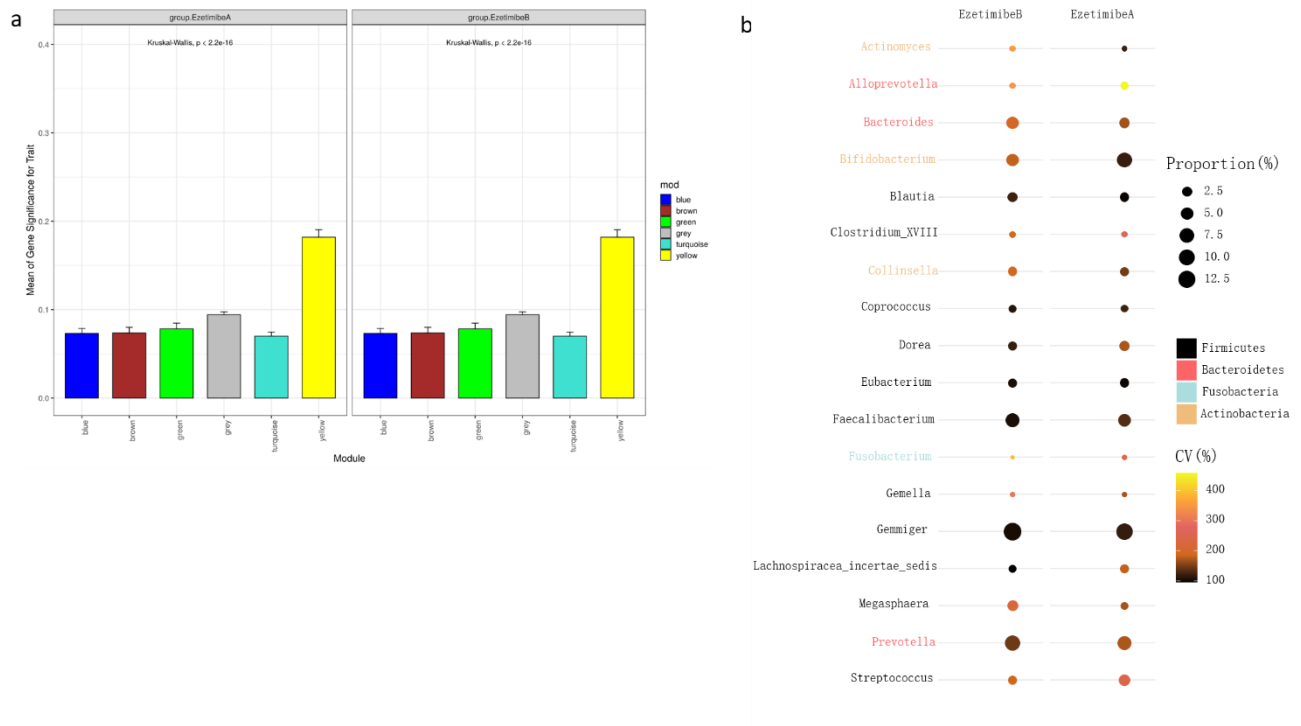
Supplementary Figure 2. Differences of Enterotypes and SCFAs before and after orlistat intervention. a) Determinations of enterotypes between groups. b) Heatmap of individual's enterotype. c) Fecal SCFAs level presented as mean \pm SD.



Supplementary Figure 3. Core taxa responded to orlistat by WGCNA. a) Modules which were significantly related to orlistat. b) Mean relative abundance of core taxa in blue module before and after intervention.



Supplementary Figure 4. Differences of Enterotypes and SCFAs before and after ezetimibe intervention. a) Determinations of enterotypes between groups. b) Heatmap of individual's enterotype. C) Fecal SCFAs level were presented as mean \pm SD.



Supplementary Figure 5. Core taxa responded to ezetimibe by WGCNA. a) Modules which were significantly related to ezetimibe. b) Mean relative abundance of core taxa in yellow module before and after intervention.

1.2 Supplementary Tables

Table S1 Mean relative abundance of core microbes responded to orlistat

Genus	mean. OrlistatB.	variance. OrlistatB.	stderr. OrlistatB.	mean. OrlistatA	variance. OrlistatA	stderr. OrlistatA	p-value	q-value	change
<i>Actinomyces</i>	0.240325762	1.20607E-05	0.000613918	0.180754423	7.35274E-06	0.000479346	0.790297874	1	down
<i>Alloprevotella</i>	0.956975051	0.000774411	0.004919385	0.081624493	1.39167E-05	0.000659468	7.21563E-07	9.71E-05	down
<i>Bacteroides</i>	3.347874589	0.003990421	0.011166944	2.752561823	0.002057618	0.008018764	0.705294705	1	down
<i>Clostridium_XIVa</i>	0.640695275	0.000166197	0.002278961	0.813617878	0.000328752	0.003205233	0.558608306	1	up
<i>Clostridium_XVIII</i>	1.717257995	0.001303505	0.006382361	0.693491377	8.89328E-05	0.001667078	0.133866134	1	down
<i>Collinsella</i>	1.027259084	0.000292369	0.003022671	1.316996106	0.000750828	0.004843901	0.633366633	1	up
<i>Coprococcus</i>	1.011989239	0.000205985	0.002537129	1.328121729	0.000227957	0.002669018	0.410589411	1	up
<i>Dialister</i>	1.400717999	0.001675593	0.007236178	2.537457014	0.005112468	0.012639803	0.456543457	1	up
<i>Megamonas</i>	7.418658632	0.033551229	0.032380177	5.036436819	0.023675471	0.027200339	0.579420579	1	down
<i>Megasphaera</i>	3.303173669	0.011243199	0.018744331	1.159465845	0.001399895	0.00661413	0.323676324	1	down
<i>Parabacteroides</i>	0.210408684	2.272E-05	0.000842615	0.12177018	8.61504E-06	0.000518864	0.548475261	1	down
<i>Phascolarctobacterium</i>	0.607129873	0.000242568	0.002753228	0.841726384	0.001092563	0.005843167	0.300246211	1	up
<i>Prevotella</i>	6.103416406	0.018040311	0.023743625	3.481826397	0.004998668	0.012498334	0.323676324	1	down
<i>Ruminococcus</i>	4.864406958	0.007063878	0.01485753	5.501673284	0.008242883	0.016049614	0.797202797	1	up
<i>Ruminococcus2</i>	2.002285506	0.000697672	0.004669288	2.153480207	0.000927798	0.00538458	0.848151848	1	up
<i>Slackia</i>	0.118082723	7.85739E-06	0.000495523	0.084408315	3.65109E-06	0.000337782	1	1	down
<i>Succinivibrio</i>	0.089797372	1.09762E-05	0.000585667	0.049981999	3.85808E-06	0.000347225	1	1	down

Metastat analysis was used to compare the differences of the relative abundance of species between groups, and $p < 0.05$ was considered statistically significant.

Table S2 Mean relative abundance of core microbes responded to ezetimibe

Genus	mean. OrlistatB.	variance. OrlistatB.	stderr. OrlistatB.	mean. OrlistatA	variance. OrlistatA	stderr. OrlistatA	p-value	q-value	change
<i>Actinomyces</i>	0.399985254	0.00019747	0.002810481	0.245611873	8.33872E-06	0.000577537	0.453764	1	down
<i>Alloprevotella</i>	0.315046258	0.000116233	0.002156225	1.132985865	0.002661345	0.010317646	0.749251	1	up
<i>Bacteroides</i>	5.113960135	0.009854705	0.019854173	3.295887367	0.002940735	0.010845709	0.461538	1	down
<i>Bifidobacterium</i>	4.9527519	0.007783812	0.017645183	8.21440652	0.00911012	0.01908939	0.242757	1	up
<i>Blautia</i>	2.488799716	0.00088149	0.005937981	2.152549283	0.000425435	0.004125216	0.661339	1	down
<i>Clostridium_XVIII</i>	0.402710317	5.45029E-05	0.001476521	0.3727711	9.25865E-05	0.001924437	1	1	down
<i>Collinsella</i>	2.015685547	0.001417033	0.0075287	1.771627421	0.000654658	0.005117256	0.789211	1	down
<i>Coprococcus</i>	1.130068017	0.000146092	0.002417369	0.814224744	9.35041E-05	0.00193395	0.328671	1	down
<i>Dorea</i>	1.608749454	0.000345609	0.003718113	2.792800196	0.002201144	0.009383269	0.27972	1	up
<i>Eubacterium</i>	1.920586909	0.00038411	0.003919746	2.047126974	0.000389529	0.0039473	0.821179	1	up
<i>Faecalibacterium</i>	6.81544584	0.004827889	0.013896602	5.726696996	0.005559265	0.014912096	0.573427	1	down
<i>Fusobacterium</i>	0.010405639	1.59765E-07	7.99412E-05	0.205095371	2.39868E-05	0.000979527	0.062375	1	up
<i>Gemella</i>	0.069442586	4.25531E-06	0.000412568	0.085225258	2.02087E-06	0.000284314	1	1	up
<i>Gemmiger</i>	13.37164956	0.01796322	0.026805388	11.62223634	0.017686009	0.026597751	0.633367	1	down
<i>Lachnospiracea_incertae_sedis</i>	0.938258993	7.68574E-05	0.001753368	1.812262804	0.001034363	0.006432302	0.23976	1	up
<i>Megasphaera</i>	3.297380245	0.005363717	0.01464748	1.008915721	0.000281546	0.003355868	0.142857	1	down
<i>Prevotella</i>	9.544610636	0.018405155	0.02713312	7.720814146	0.016918383	0.026014137	0.639361	1	down
<i>Streptococcus</i>	2.128972592	0.001515052	0.007784733	3.455576312	0.006787768	0.016477582	0.58042	1	up

Metastat analysis was used to compare the differences of the relative abundance of species between groups, and $p < 0.05$ was considered statistically significant.