Table S1. Significantly different genus between groups as revealed by taxon-based comparisons

Taxon	C5 %	B5 %	M5 %	C5 vs M5 p value	B5 vs M5 p value
S24-7_norank	41.63	48.02	57.5	0.175	0.251
Lachnospiraceae_uncultured	32.37	25.97	19.14	0.117	0.251
Ruminococcaceae_uncultured	7.28	4.29	7.41	0.754	0.117
*Ruminococcaceae_incertae_sedis	4.6	3.72	2.1	0.175	0.016
Lachnospiraceae_unclassified	3.65	4.61	4.35	0.917	0.602
*Desulfovibrio	1.68	3.8	0.77	0.602	0.028
Roseburia	1.47	1.38	0.89	0.917	0.116
Ruminococcaceae_unclassified	1.54	1.47	2	0.917	0.917
Anaerotruncus	1.02	1.07	0.97	0.754	0.602
#*Akkermansia	0.11	0.2	1.12	0.028	0.047
Oscillibacter	1.12	0.82	0.87	0.602	0.834
*Alistipes	0.33	1.02	0.29	0.402	0.047
#*Lachnospiraceae_incertae_sedis	0.5	0.42	0	0.005	0.005
Ruminococcus	0.92	0.39	0.32	0.175	0.53
Odoribacter	0.32	0.35	0.15	0.249	0.175
#Bacteroides	0.00	0.44	0.18	0.008	0.173
#Prevotellaceae_uncultured	0.00	0.34	0.15	0.007	0.834
Escherichia-Shigella	0	0	0.08	0.419	0.572

[#] p<0.05: Control vs.Model; [*]p<0.05: BBR vs.Model

Table S2. Significantly different phylum between groups as revealed by taxon-based comparisons

Taxon	C5(%)	B5(%)	M5(%)	C5 vs M5 p value	B5 vs M5 p value
Bacteroidetes	42.28	50.17	58.27	0.251	0.251
Firmicutes	55.7	45.37	39.48	0.251	0.465
*Proteobacteria	**1.69**	**4.17**	**1.01**	**0.602**	**0.028**
#*Verrucomicrobia	**0.11**	**0.2**	**1.12**	**0.028**	**0.047**

# p<0.05: Control vs.Model; *p<0.05: BBR vs.Model
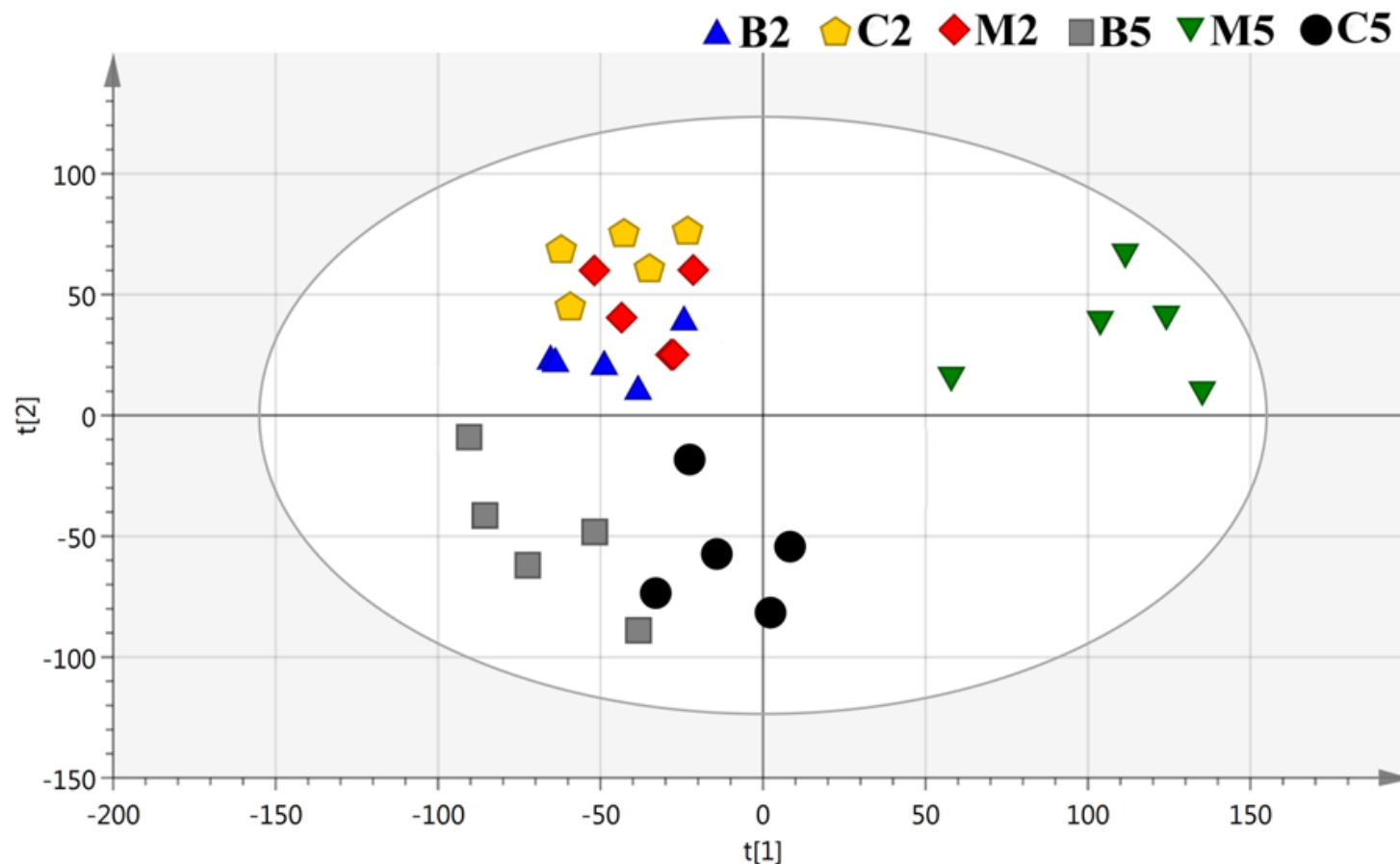
Figure S1. PCA score plot for both 0-week collected and 12-week collected samples. C5: samples from wild type mice fed with standard diet after 12 weeks; M5: samples from $Apc^{min/+}$ mice fed with high fat diet after 12 weeks; B5: samples from $Apc^{min/+}$ mice fed with high fat diet and BBR supplemented after 12 weeks. C2: samples from wild type mice fed with standard diet after 0 weeks; M2: samples from $Apc^{min/+}$ mice fed with high fat diet after 0 weeks; B2: samples from $Apc^{min/+}$ mice fed with high fat diet and BBR supplemented after 0 weeks.
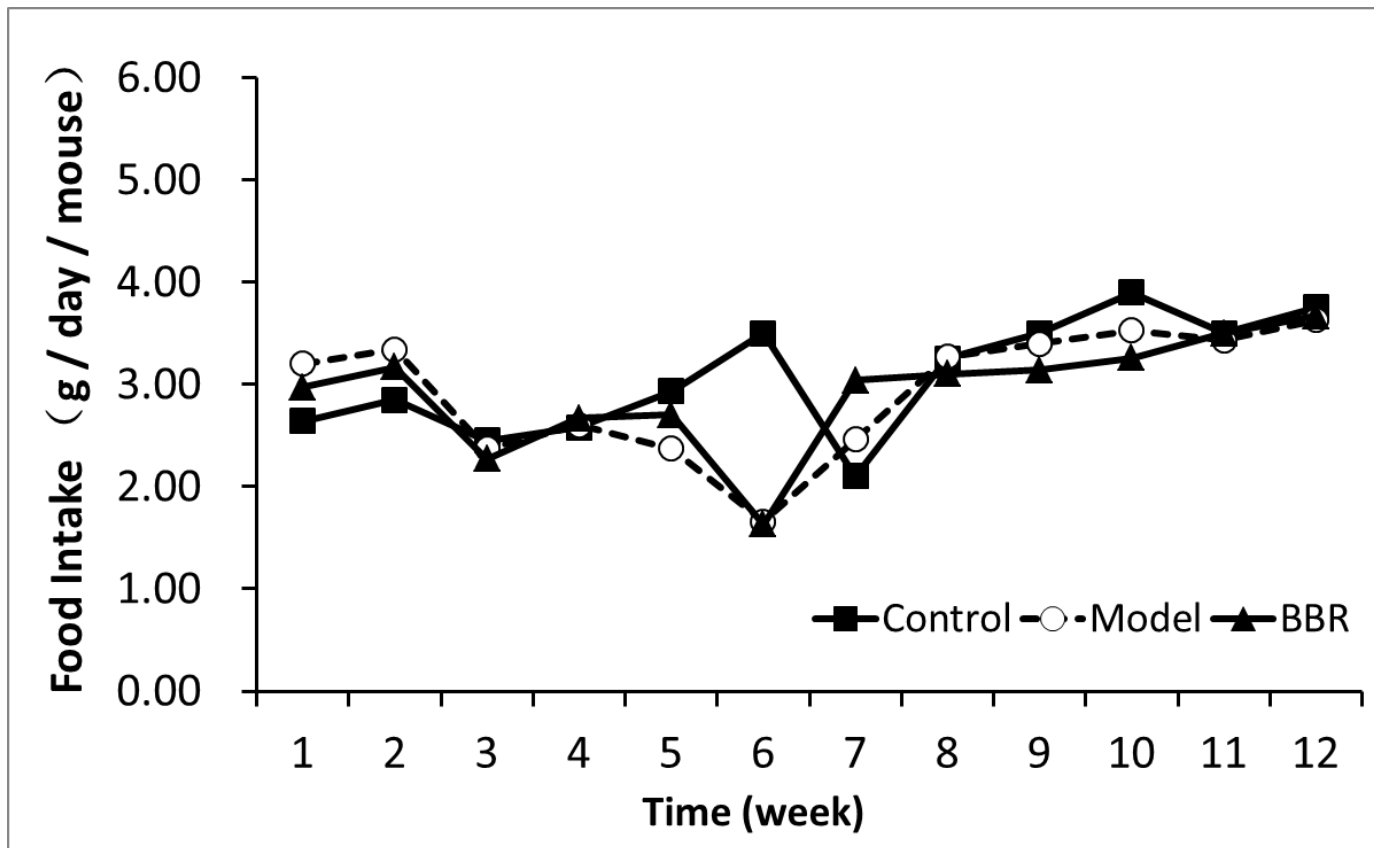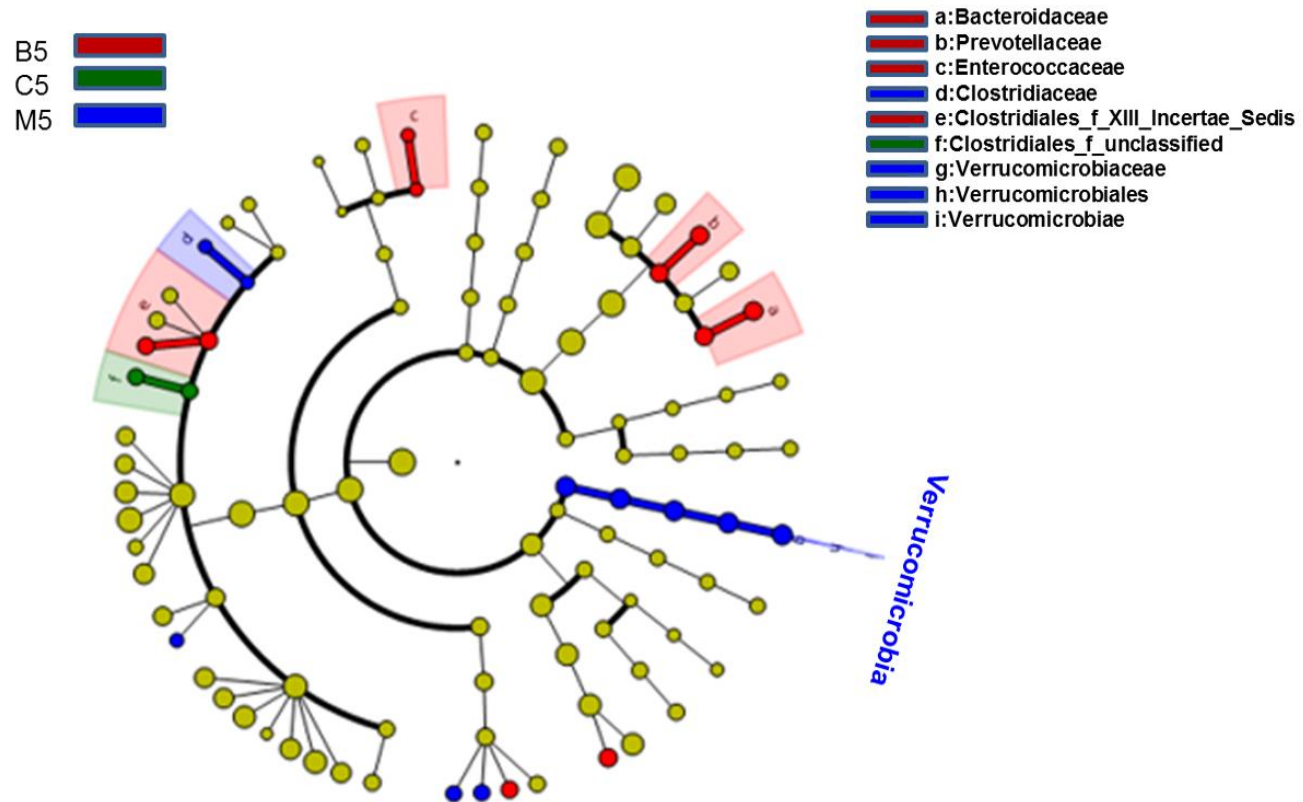
**Figure S2. Food intake per mouse per day in the experimental period.**

Figure S3. Taxonomic representation of statistically and biologically consistent differences in three groups.
Differences are represented by the color of the most abundant class (red indicating berberine group, green for control group, blue indicating model group and yellow for non-significant). The diameter of each circle is proportional to the taxon's abundance.

Berberine (BBR)

Model

Model+BBR
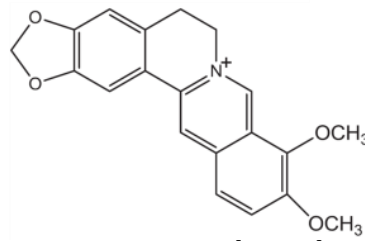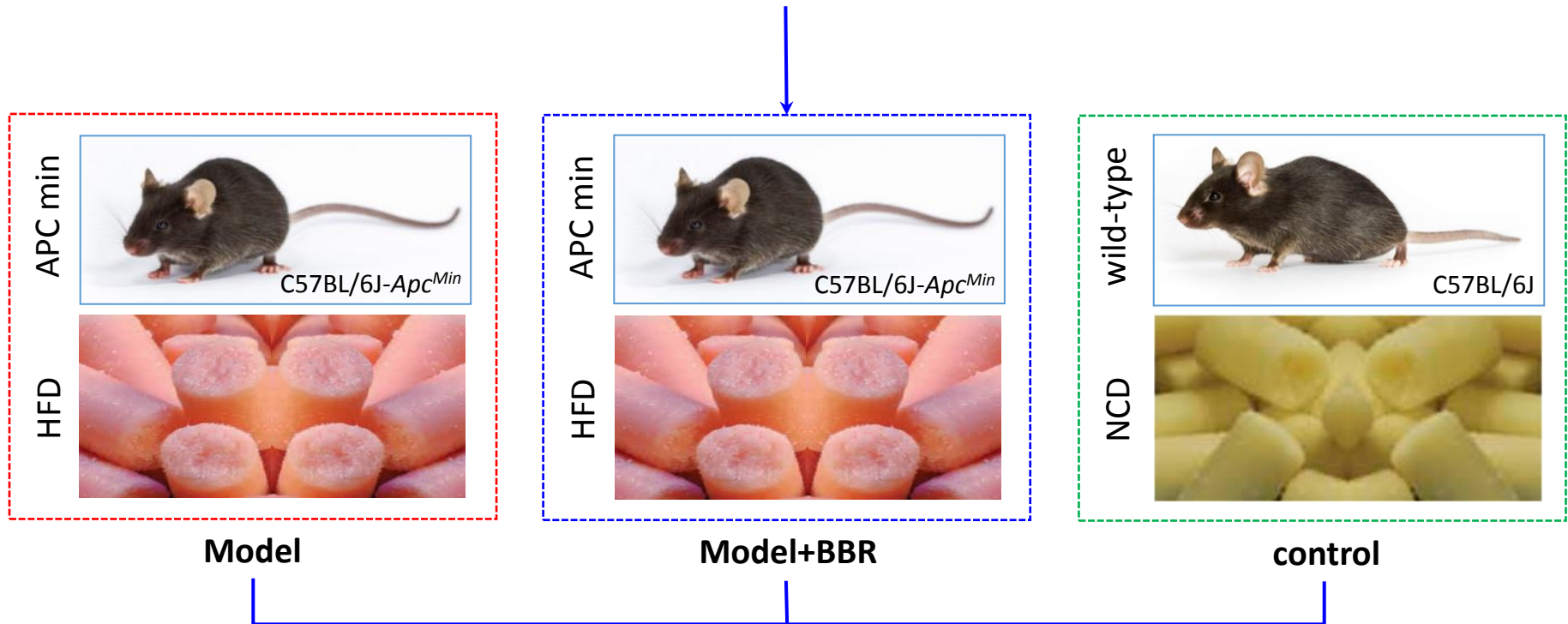
control

➢ **Gut microbiota structural changes**
BBR supplementary restored the changes of microbiota structure in model group almost nearly to control group

➢ **Anti-tumor activity**

Figure S4 Animal groups in this study