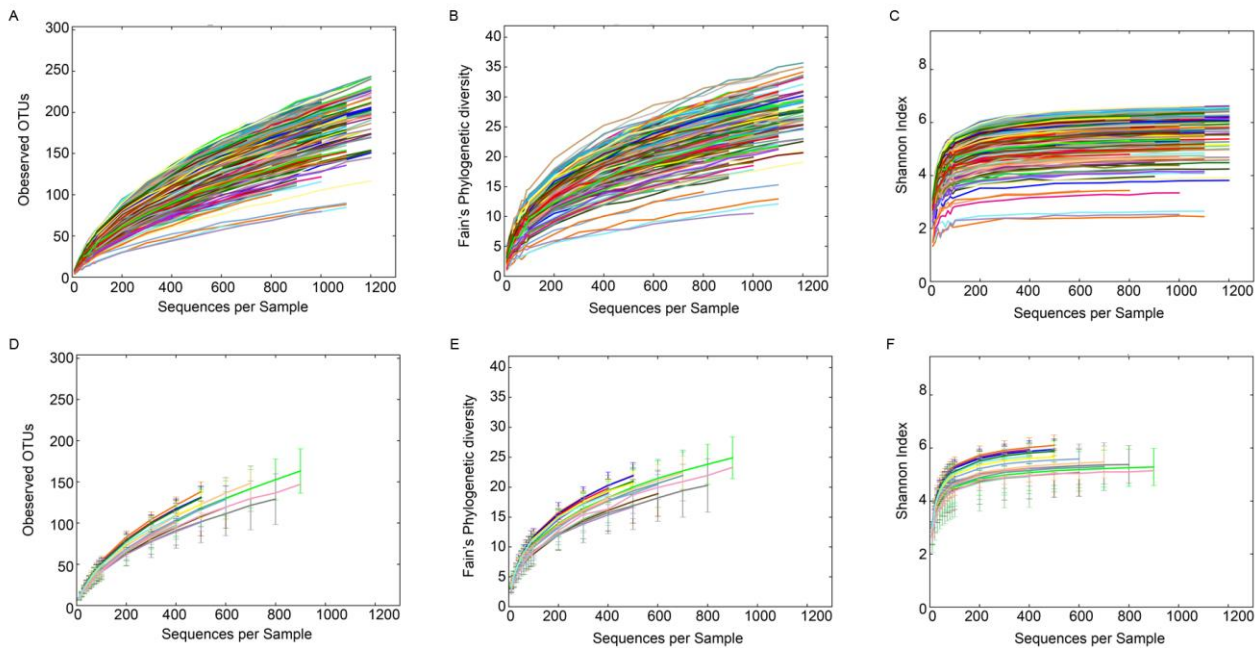
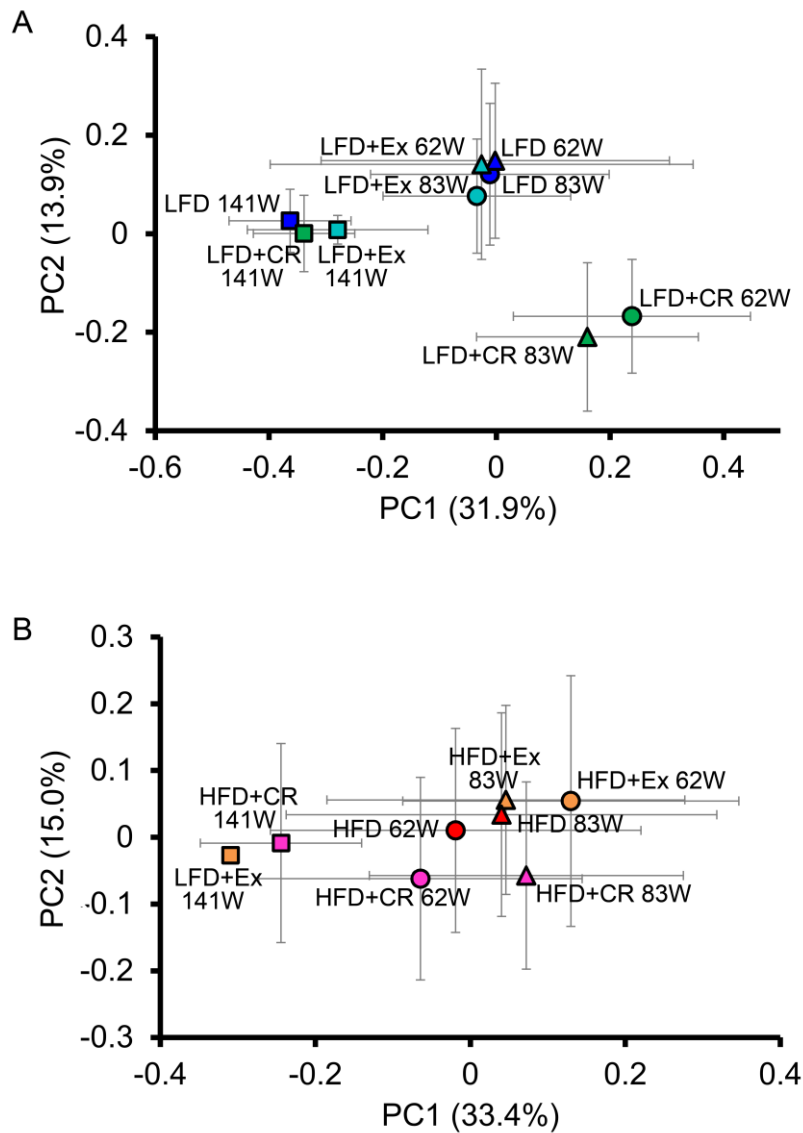


# Supplementary Information

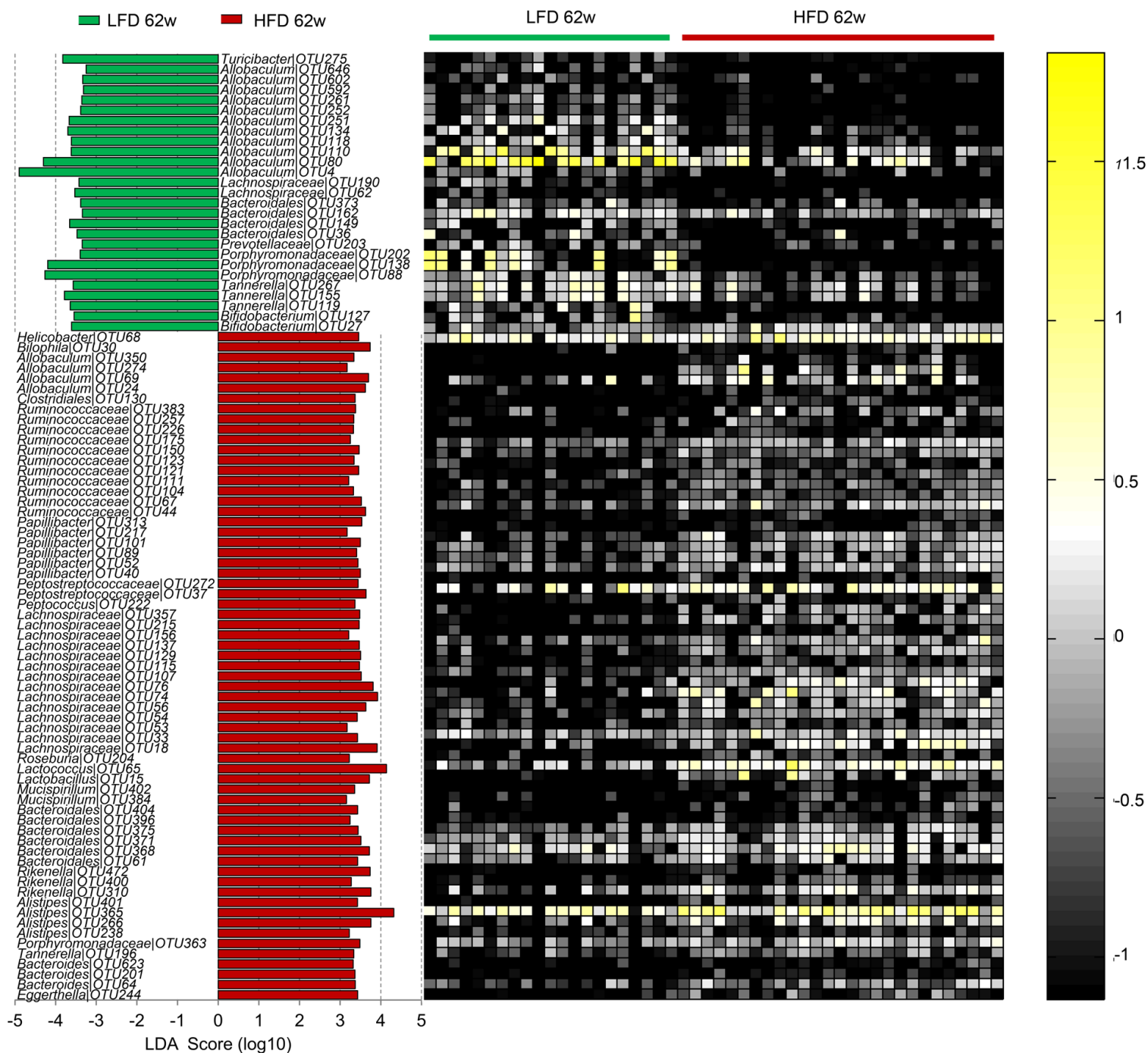
## Supplementary Figures



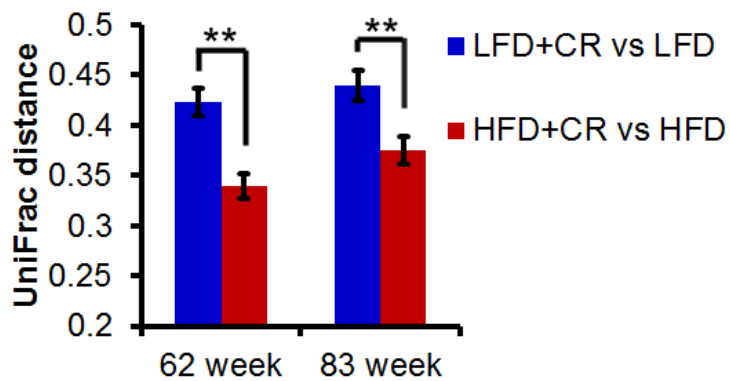
**Supplementary Figure S1. Diversity of the gut microbiota.** (A) Rarefaction analysis of sampling by observed OTU method. (B) Rarefaction analysis of sampling by PD whole tree method. (C) Shannon Diversity Index curves to estimate the diversity of taxa present in individual animals. (D) Rarefaction analysis of 6 groups by observed OTU method. (E) Rarefaction analysis of 6 groups by PD whole tree method. (F) Shannon Diversity Index curves to estimate the diversity of taxa present in 6 groups. Data in D, E and F are shown as mean  $\pm$  s.d.. For 62 weeks, LFD, n=21; LFD+CR, n=29; LFD+Ex, n=22; HFD, n=28; HFD+CR, n=29; and HFD+Ex, n=23. For 83 weeks, LFD, n=16; LFD+CR, n=22; LFD+Ex, n=19; HFD, n=12; HFD+CR, n=14; and HFD+Ex, n=15. For 141 weeks, LFD, n=6; LFD+CR, n=15; LFD+Ex, n=6; HFD, n=0; HFD+CR, n=10; and HFD+Ex, n=1.



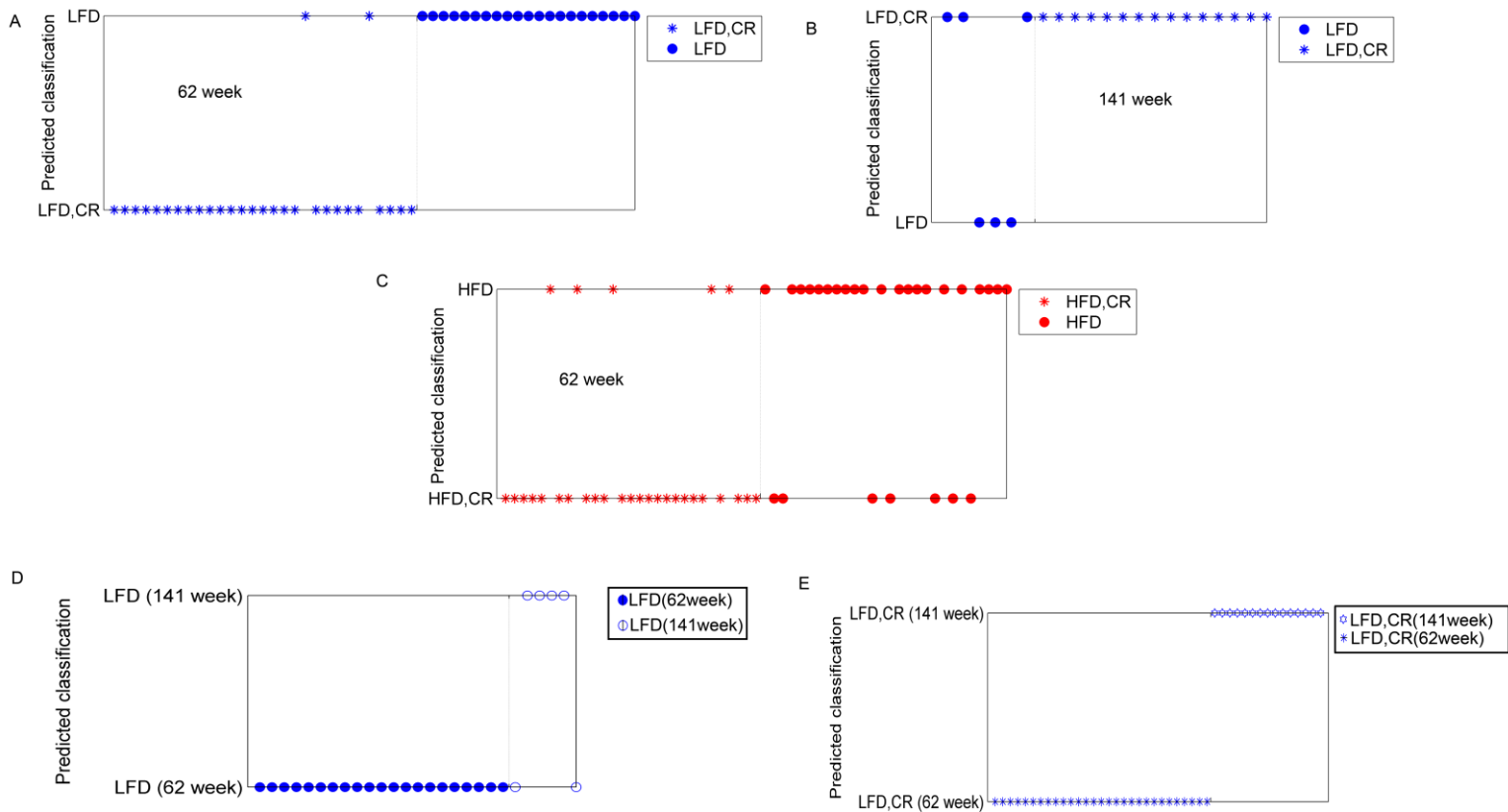
**Supplementary Figure S2** Trajectory analysis of the gut microbiota. (A) normal chow and (B) high fat diet. Weighted UniFrac PCoA of the gut microbiota between different treatment groups at 62, 83 and 141 weeks based on pyrosequencing OTU (97% identity) data. Each point represents the mean principal coordinate (PC) score from all of the mice in a group at one time point, and the error bar represents the s.d. Sample size was the same as Supplementary Figure S1.



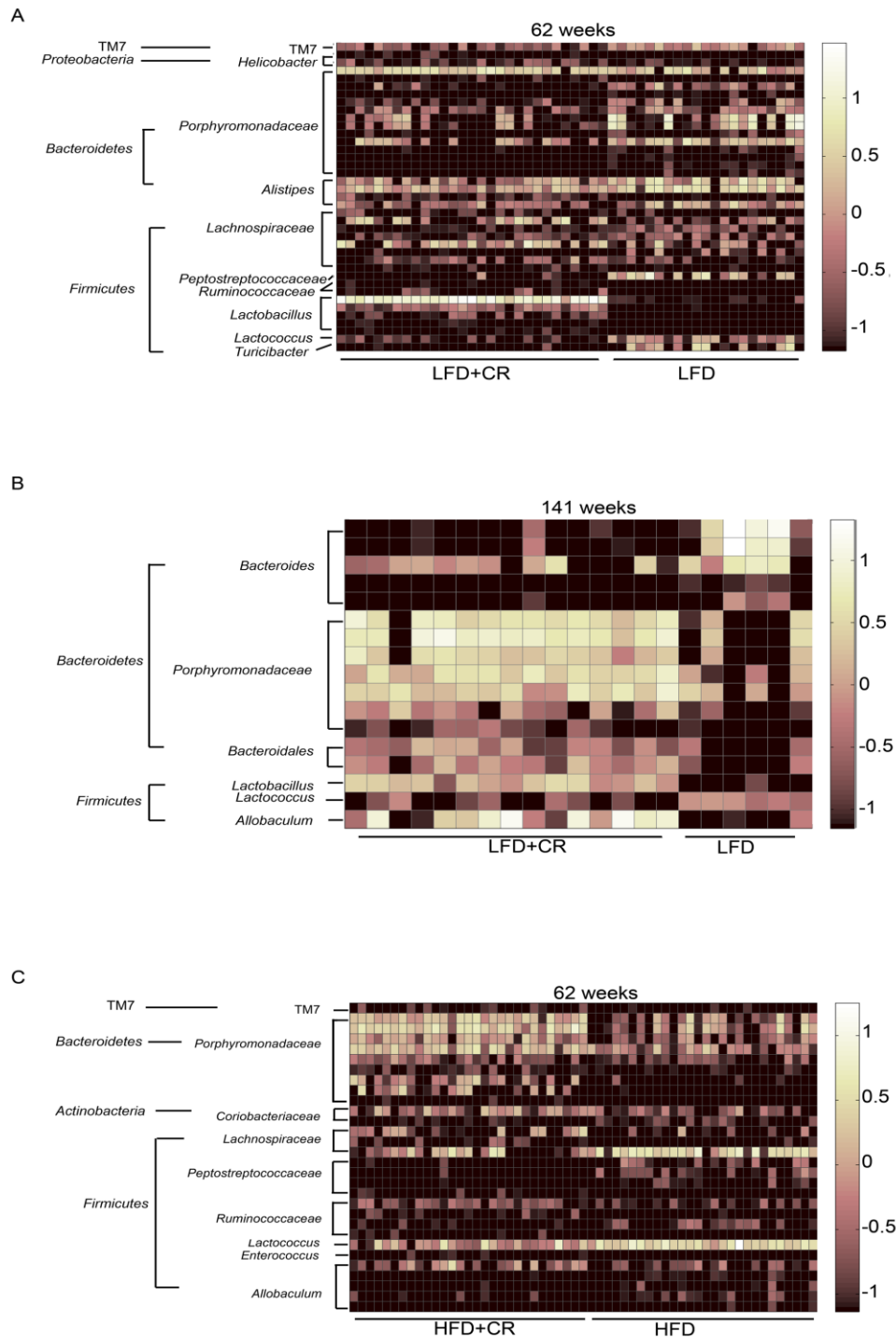
**Supplementary Figure S3. The key phylotypes of the gut microbiota responding to high-fat diet identified by LEfSE.** LFD (n=21) vs. HFD (n=28) at 62 weeks. The left histogram shows the LDA scores computed for features (on OTU level) differentially abundant between the *ab libitum* and CR mice. The right heat-map shows the relative abundance (log10 transformation) of OTUs.



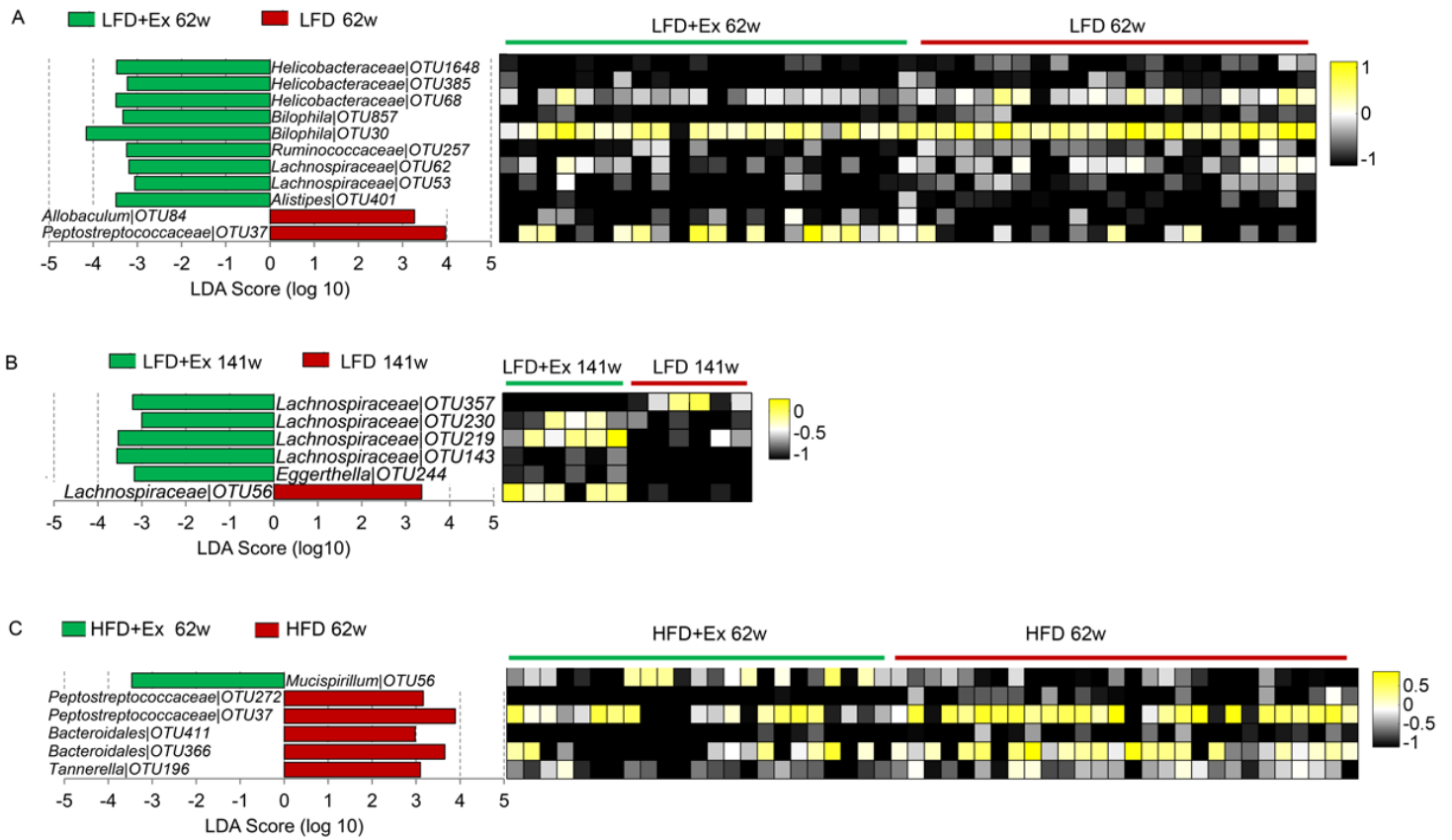
**Supplementary Figure S4. The variation of the gut microbiota induced by restriction of normal chow was larger than the variation of the gut microbiota induced by restriction of a high-fat diet.** The distance between two samples (one from the *ad libitum* group and the other from the CR group) was calculated using the UniFrac distance and is shown as the mean  $\pm$  SEM. \*\* $P < 0.01$  by one-way ANOVA. For 62 weeks, LFD,  $n=21$ ; LFD+CR,  $n=29$ ; HFD,  $n=28$ ; HFD+CR,  $n=29$ . For 83 weeks, LFD,  $n=16$ ; LFD+CR,  $n=22$ ; HFD,  $n=12$ ; HFD+CR,  $n=14$ .



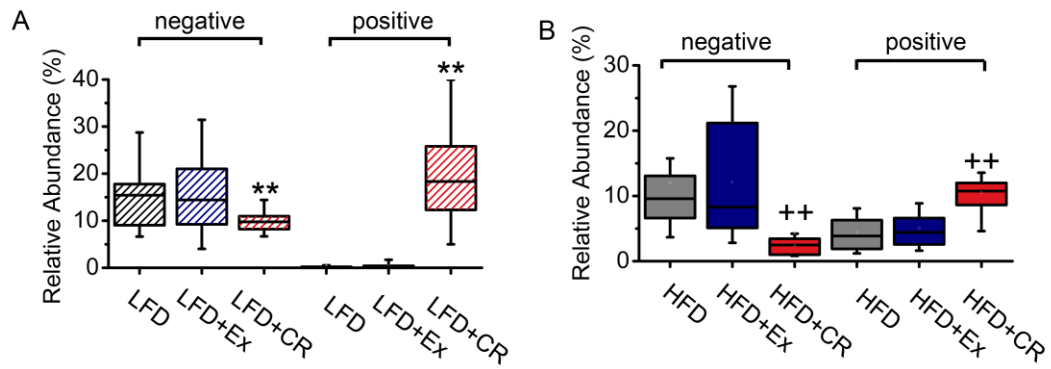
**Supplementary Figure S5. PLS-DA model plots.** (A) Plot based on the first two components of the gut microbiota data in LFD+CR and LFD at 62 weeks (LFD, n=21; LFD+CR, n=29). The correct classification rate of this PLD model is 96% by Leave-one-out cross validation. (B) Plot based on the first component of the gut microbiota data in LFD+CR and LFD at 141 weeks (LFD, n=6; LFD+CR, n=15). The correct classification rate of this PLD model is 85.7% by Leave-one-out cross validation. (C) Plot based on the first two components of the gut microbiota data in HFD+CR and HFD at 62 weeks (HFD, n=28; HFD+CR, n=29). The correct classification rate of this PLD model is 78.9% by Leave-one-out cross validation. (D) Plot based on the first two components of the gut microbiota data in LFD from between 62 weeks (n=21) and 141 weeks (n=6). The correct classification rate of this PLD model is 92.6% by Leave-one-out cross validation. (E) Plot based on the first two components of the gut microbiota data in LFD+CR from between 62 weeks (n=29) and 141 weeks (n=15). The correct classification rate of this PLD model is 100% by Leave-one-out cross validation.



**Supplementary Figure S6. Abundance distribution of the key phylotypes of gut microbiota responding to life-long CR based on PLS-DA. (A) LFD vs. LFD+CR at 62 weeks. (B) LFD vs. LFD+CR at 141 weeks. (C) HFD vs. HFD+CR at 62 weeks. The relative abundance of each OTU was shown after log transformation. The taxa of the OTUs were shown on the left of heat map. Sample size was the same as Supplementary Figure S5.**



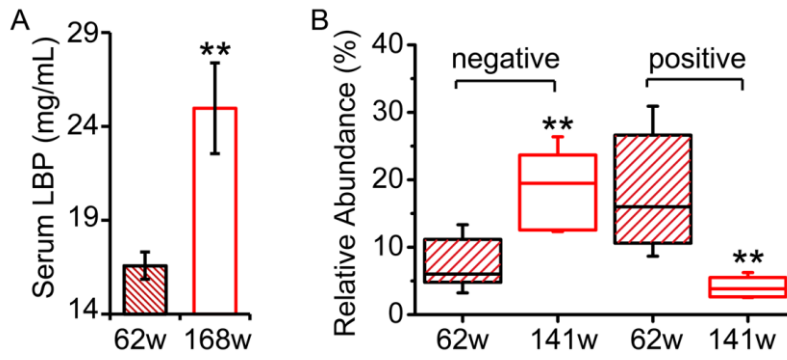
**Supplementary Figure S7 The key phylotypes of the gut microbiota responding to exercise identified by LEfSE.** (A) LFD (n=21) vs. LFD+Ex (n=22) at 62 weeks. (B) LFD (n=6) vs. LFD+Ex (n=6) at 141 weeks. (C) HFD (n=28) vs. HFD+Ex (n=23) at 62 weeks. The left histogram shows the LDA scores computed for features (on OTU level) differentially abundant between the ab libitum and CR mice. The right heat-map shows the relative abundance (log<sub>10</sub> transformation) of OTUs.



**Supplementary Figure S8. Gut microbiota-associated antigen load changes.**

Relative abundance of the phylotypes negative and positive correlated with lifespan of mice on (A) normal chow (LFD n=16, LFD+CR n=22 and LFD+Ex n=19) and (B) high fat diet (HFD n=12, HFD+CR n=14 and HFD+Ex n=15) at 83 weeks. \*P < 0.05 and \*\*P<0.01 vs. LFD, +P < 0.05 and ++P<0.01 by ANOVAs.





**Supplementary Figure S9. Gut microbiota-associated antigen load changes. (A)**

The serum level of LBP of LFD+CR mice at 62 (n=8) and 141 (n=5) weeks. (B)

Relative abundance of the phylotypes negative and positive correlated with lifespan of

LFD+CR mice at 62 (n=22) and 141 (n=12) weeks. \*\*P<0.01 vs. 62 weeks by

ANOVA.

## Supplementary Tables

**Supplementary Table S1. The phylotypes of gut microbiota differentially abundant between the LFD and LFD+ CR mice at 62 weeks using LEfSe.**

OTU id	Taxon					Riched group	LDA Score (log10)	p value
	Phylum	Class	Order	Family	Genus			
138	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>unclassified_Porphyromonadacea</i>	LFD	4.144615785	0.0320901
88	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>unclassified_Porphyromonadacea</i>	LFD	4.205998027	0.0156271
203	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Prevotellaceae</i>	<i>unclassified_Prevotellaceae</i>	LFD	3.487361873	0.0061756
197	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Rikenellaceae</i>	<i>Alistipes</i>	LFD	3.992423507	0.0050575
365	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Rikenellaceae</i>	<i>Alistipes</i>	LFD	4.04667192	0.0020967
162	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD	3.386314821	5.05E-05
36	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD	3.36646927	0.0426008
366	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD	3.863822126	4.60E-05
368	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD	3.589722551	0.021847
61	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD	3.221283311	0.0320297
65	<i>Firmicutes</i>	<i>Bacilli</i>	<i>Lactobacillales</i>	<i>Streptococcaceae</i>	<i>Lactococcus</i>	LFD	3.589825899	8.51E-06
109	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD	3.462251164	0.000515
137	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD	3.345797064	0.028643
158	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD	3.308857749	0.0481984
37	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Peptostreptococcaceae</i>	<i>unclassified_Peptostreptococcaceae</i>	LFD	4.055118466	3.22E-06
319	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Ruminococcaceae</i>	<i>unclassified_Ruminococcaceae</i>	LFD	3.300274656	0.0377343
275	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Turicibacter</i>	LFD	3.824262017	0.0001214
98	TM7	TM7	TM7	TM7	TM7	LFD	3.56002886	2.29E-05
127	<i>Actinobacteria</i>	<i>Actinobacteria</i>	<i>Bifidobacteriales</i>	<i>Bifidobacteriaceae</i>	<i>Bifidobacterium</i>	LFD+CR	3.188005229	0.0386341
119	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>Tannerella</i>	LFD+CR	3.534155124	0.0208986
155	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>Tannerella</i>	LFD+CR	3.820219305	0.005241
267	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>Tannerella</i>	LFD+CR	3.388663847	0.0183096
401	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Rikenellaceae</i>	<i>Alistipes</i>	LFD+CR	3.49557915	7.68E-05
2219	<i>Firmicutes</i>	<i>Bacilli</i>	<i>Lactobacillales</i>	<i>Lactobacillaceae</i>	<i>Lactobacillus</i>	LFD+CR	3.247744113	3.24E-05
171	<i>Firmicutes</i>	<i>Bacilli</i>	<i>Lactobacillales</i>	<i>Lactobacillaceae</i>	<i>Lactobacillus</i>	LFD+CR	4.233077538	5.82E-08
45	<i>Firmicutes</i>	<i>Bacilli</i>	<i>Lactobacillales</i>	<i>Lactobacillaceae</i>	<i>Lactobacillus</i>	LFD+CR	4.777967716	1.78E-09
94	<i>Firmicutes</i>	<i>Bacilli</i>	<i>Lactobacillales</i>	<i>Lactobacillaceae</i>	<i>Lactobacillus</i>	LFD+CR	3.477016185	2.04E-09
107	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD+CR	3.193247236	0.0242898
167	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD+CR	3.776316152	0.0059123
215	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD+CR	3.203140408	0.024161
429	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD+CR	3.235403134	0.0289817
56	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD+CR	3.176237582	0.0452262
1648	<i>Proteobacteria</i>	<i>Epsilonproteobacteria</i>	<i>Campylobacterales</i>	<i>Helicobacteraceae</i>	<i>Helicobacter</i>	LFD+CR	3.345237409	0.0151948
68	<i>Proteobacteria</i>	<i>Epsilonproteobacteria</i>	<i>Campylobacterales</i>	<i>Helicobacteraceae</i>	<i>Helicobacter</i>	LFD+CR	3.434951149	0.0220252

**Supplementary Table S2. The phylotypes of gut microbiota differentially abundant between the LFD and LFD+ CR mice at 141 weeks using LEfSe.**

OTU id	Taxon					Riched group	LDA Score (log 10)	p value
	Phylum	Class	Order	Family	Genus			
2	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Bacteroidaceae</i>	<i>Bacteroides</i>	LFD	4.664610955	0.0002907
32	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Bacteroidaceae</i>	<i>Bacteroides</i>	LFD	4.535055345	0.0029167
64	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Bacteroidaceae</i>	<i>Bacteroides</i>	LFD	4.049256617	0.0064179
359	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Bacteroidaceae</i>	<i>Bacteroides</i>	LFD	3.527444806	0.0006587
1814	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Bacteroidaceae</i>	<i>Bacteroides</i>	LFD	3.280757212	0.0171097
28	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>Parabacteroides</i>	LFD	3.350061712	0.0006587
161	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>Parabacteroides</i>	LFD	4.05917781	0.0310213
65	<i>Firmicutes</i>	<i>Bacilli</i>	<i>Lactobacillales</i>	<i>Streptococcaceae</i>	<i>Lactococcus</i>	LFD	3.470212939	0.0013621
8	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD	3.681947504	0.0223864
18	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD	3.74084249	0.0223864
109	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD	3.344854868	0.0006363
116	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD	3.470720525	0.0309853
146	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD	3.562016593	0.0409811
165	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD	4.260024928	0.009266
186	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD	3.032208863	0.0329084
205	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD	3.258480921	0.023159
211	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD	3.295629717	0.0040196
270	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD	3.252701305	0.0146974
279	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD	3.284036389	0.008506
300	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD	3.20455479	0.0426813
357	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD	3.314070833	0.030639
391	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD	3.334297353	0.0309853
418	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD	3.312117979	0.0139421
878	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD	3.295130868	0.0067571
113	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Ruminococcaceae</i>	<i>Anaerotruncus</i>	LFD	3.365899684	0.0309853
271	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Ruminococcaceae</i>	<i>unclassified_Ruminococcaceae</i>	LFD	3.751876841	0.0060952
469	<i>Proteobacteria</i>	<i>Deltaproteobacteria</i>	<i>Desulfobrivionales</i>	<i>Desulfobrivionaceae</i>	<i>Bilophila</i>	LFD	3.185494208	0.0222422
27	<i>Actinobacteria</i>	<i>Actinobacteria</i>	<i>Bifidobacteriales</i>	<i>Bifidobacteriaceae</i>	<i>Bifidobacterium</i>	LFD+CR	3.526214224	0.018182
127	<i>Actinobacteria</i>	<i>Actinobacteria</i>	<i>Bifidobacteriales</i>	<i>Bifidobacteriaceae</i>	<i>Bifidobacterium</i>	LFD+CR	3.494137948	0.0116483
119	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>Tannerella</i>	LFD+CR	4.254104153	0.0026384
155	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>Tannerella</i>	LFD+CR	4.438143404	0.0022427
267	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>Tannerella</i>	LFD+CR	4.038756992	0.0037396
77	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>unclassified_Porphyromonadaceae</i>	LFD+CR	3.207694391	0.0187177
95	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>unclassified_Porphyromonadaceae</i>	LFD+CR	3.603326918	0.0018205
133	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>unclassified_Porphyromonadaceae</i>	LFD+CR	4.165967787	0.0010726
169	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>unclassified_Porphyromonadaceae</i>	LFD+CR	3.361994083	0.041613
202	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>unclassified_Porphyromonadaceae</i>	LFD+CR	3.531989935	0.0121577
280	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>unclassified_Porphyromonadaceae</i>	LFD+CR	3.145360411	0.0325094
266	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Rikenellaceae</i>	<i>Alistipes</i>	LFD+CR	3.108725557	0.0198409
401	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Rikenellaceae</i>	<i>Alistipes</i>	LFD+CR	3.193451285	0.0325094
36	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD+CR	3.452216999	0.0290139
149	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD+CR	4.040868034	0.0194779
151	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD+CR	3.446905993	0.0154685
371	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD+CR	3.542915229	0.0077159
372	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD+CR	3.432205144	0.0325094
411	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD+CR	3.397278522	0.0232056
45	<i>Firmicutes</i>	<i>Bacilli</i>	<i>Lactobacillales</i>	<i>Lactobacillaceae</i>	<i>Lactobacillus</i>	LFD+CR	3.926391919	0.0004215
171	<i>Firmicutes</i>	<i>Bacilli</i>	<i>Lactobacillales</i>	<i>Lactobacillaceae</i>	<i>Lactobacillus</i>	LFD+CR	3.170648335	0.0325094
104	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Ruminococcaceae</i>	<i>unclassified_Ruminococcaceae</i>	LFD+CR	3.19605109	0.037373
130	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>unclassified_Clostridiales</i>	<i>unclassified_Clostridiales</i>	LFD+CR	3.179064242	0.0232056
4	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD+CR	4.395047933	0.0037396
80	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD+CR	3.509490951	0.009266
118	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD+CR	3.096987174	0.0198409
340	<i>Firmicutes</i>	<i>unclassified_Firmicutes</i>	<i>unclassified_Firmicutes</i>	<i>unclassified_Firmicutes</i>	<i>unclassified_Firmicutes</i>	LFD+CR	3.497072446	0.0065515

**Supplementary Table S3. The phylotypes of gut microbiota differentially abundant between the HFD and HFD+ CR mice at 62 weeks using LEfSe.**

OTU id	Taxon					Riched group	LDA Score (log10)	p value
	Phylum	Class	Order	Family	Genus			
201	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Bacteroidaceae</i>	<i>Bacteroides</i>	HFD 62w	3.176948567	0.0217163
197	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Rikenellaceae</i>	<i>Alistipes</i>	HFD 62w	3.604770481	0.0311649
603	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Rikenellaceae</i>	<i>Rikenella</i>	HFD 62w	3.285106054	0.01147
366	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>			HFD 62w	3.54638156	0.0167422
65	<i>Firmicutes</i>	<i>Bacilli</i>	<i>Lactobacillales</i>	<i>Streptococcaceae</i>	<i>Lactococcus</i>	HFD 62w	4.044902641	9.557E-07
56	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>		HFD 62w	3.407139746	0.0332791
37	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Peptostreptococcaceae</i>		HFD 62w	4.019781623	3.838E-05
272	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Peptostreptococcaceae</i>		HFD 62w	3.198120582	3.05E-05
67	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Ruminococcaceae</i>		HFD 62w	2.961705141	0.01699
111	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Ruminococcaceae</i>		HFD 62w	2.908277051	0.0037356
383	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Ruminococcaceae</i>		HFD 62w	3.29613159	0.0008372
274	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	HFD 62w	3.020033245	0.0148607
136	<i>Actinobacteria</i>	<i>Actinobacteria</i>	<i>Coriobacteriales</i>	<i>Coriobacteriaceae</i>		HFD+CR 62w	-3.297986153	0.0067829
119	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>Tannerella</i>	HFD+CR 62w	-3.679871117	1.091E-05
155	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>Tannerella</i>	HFD+CR 62w	-3.980043818	3.848E-06
267	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>Tannerella</i>	HFD+CR 62w	-3.536213343	3.276E-05
95	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>		HFD+CR 62w	-3.082032334	0.0496024
97	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>		HFD+CR 62w	-3.741273501	4.692E-05
105	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>		HFD+CR 62w	-3.041747706	0.0143589
133	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>		HFD+CR 62w	-3.504805533	0.0052153
302	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>		HFD+CR 62w	-3.035750534	0.0372928
317	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>		HFD+CR 62w	-3.238369838	0.0050136
203	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Prevotellaceae</i>		HFD+CR 62w	-2.867921832	0.037927
148	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>			HFD+CR 62w	-3.094052222	0.0123578
372	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>			HFD+CR 62w	-3.506072058	1.584E-06
388	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>			HFD+CR 62w	-3.403292555	0.0001101
224	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>		HFD+CR 62w	-3.27163541	0.010389
79	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Ruminococcaceae</i>		HFD+CR 62w	-3.083050938	0.0039614
118	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	HFD+CR 62w	-3.212688875	0.0243299
30	<i>Proteobacteria</i>	<i>Deltaproteobacteria</i>	<i>Desulfobivriales</i>	<i>Desulfobivriaceae</i>	<i>Bilophila</i>	HFD+CR 62w	-3.764877032	0.0159383

**Supplementary Table S4. The phylotypes of gut microbiota differentially abundant between 62 weeks and 141 weeks of LFD mice at using LEfSe.**

OTU id	Taxon					Riched group	LDA Score (log10)	p value
	Phylum	Class	Order	Family	Genus			
2	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Bacteroidaceae</i>	<i>Bacteroides</i>	LFD 141w	4.631740467	0.0155676
32	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Bacteroidaceae</i>	<i>Bacteroides</i>	LFD 141w	4.514991056	0.0073971
58	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Bacteroidaceae</i>	<i>Bacteroides</i>	LFD 141w	4.207613699	0.0415959
64	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Bacteroidaceae</i>	<i>Bacteroides</i>	LFD 141w	4.078467675	0.0104056
359	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Bacteroidaceae</i>	<i>Bacteroides</i>	LFD 141w	3.80021585	0.0222296
28	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>Parabacteroides</i>	LFD 141w	3.451031169	0.0495102
142	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>Parabacteroides</i>	LFD 141w	3.756452645	0.0055875
161	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>Parabacteroides</i>	LFD 141w	4.050020758	0.0495102
8	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD 141w	3.736077439	0.0249747
18	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD 141w	3.883117836	0.0078928
76	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD 141w	3.704765195	0.0239683
186	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD 141w	3.426317393	0.0222296
206	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD 141w	3.644114416	0.0210252
270	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD 141w	3.467560894	0.0222296
279	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD 141w	3.473310618	0.0415959
300	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD 141w	3.463392319	0.0210252
357	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD 141w	3.456000581	0.0078928
271	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Ruminococcaceae</i>	<i>unclassified_Ruminococcaceae</i>	LFD 141w	3.805031233	0.0055875
30	<i>Proteobacteria</i>	<i>Deltaproteobacteria</i>	<i>Desulfovibrionales</i>	<i>Desulfovibrionaceae</i>	<i>Bilophila</i>	LFD 141w	4.47346355	0.0163092
469	<i>Proteobacteria</i>	<i>Deltaproteobacteria</i>	<i>Desulfovibrionales</i>	<i>Desulfovibrionaceae</i>	<i>Bilophila</i>	LFD 141w	3.494964192	0.0073971
27	<i>Actinobacteria</i>	<i>Actinobacteria</i>	<i>Bifidobacteriales</i>	<i>Bifidobacteriaceae</i>	<i>Bifidobacterium</i>	LFD 62w	3.526175806	0.0308885
127	<i>Actinobacteria</i>	<i>Actinobacteria</i>	<i>Bifidobacteriales</i>	<i>Bifidobacteriaceae</i>	<i>Bifidobacterium</i>	LFD 62w	3.508570096	0.0222296
136	<i>Actinobacteria</i>	<i>Actinobacteria</i>	<i>Coriobacteriales</i>	<i>Coriobacteriaceae</i>	<i>unclassified_Coriobacteriaceae</i>	LFD 62w	3.47889475	0.0073971
78	<i>Actinobacteria</i>	<i>Actinobacteria</i>	<i>unclassified_Actinobacteria</i>	<i>unclassified_Actinobacteria</i>	<i>unclassified_Actinobacteria</i>	LFD 62w	3.529626712	0.0495102
61	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD 62w	3.481228079	0.0493362
151	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD 62w	3.610210014	0.0224867
362	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD 62w	3.852380231	0.0222296
371	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD 62w	3.750700751	0.0144833
190	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD 62w	3.571596873	0.0073971
4	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD 62w	4.928914395	0.0308885
50	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD 62w	4.348260668	0.0495102
80	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD 62w	4.220165781	0.0047627
83	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD 62w	3.456317931	0.0222296
110	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD 62w	3.734571074	0.0495102
134	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD 62w	3.670708642	0.0495102
251	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD 62w	3.548367455	0.0222296
252	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD 62w	3.419144203	0.0222296
261	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD 62w	3.433024354	0.0222296
592	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD 62w	3.714465991	0.0222296
602	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD 62w	3.50866848	0.0222296
646	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD 62w	3.574437836	0.0222296

**Supplementary Table S5. The phylotypes of gut microbiota differentially abundant between 62 weeks and 141 weeks of LFD+CR mice at using LefSe.**

OTU id	Taxon					Riched group	LDA Score (log10)	p value
	Phylum	Class	Order	Family	Genus			
1	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Bacteroidaceae</i>	<i>Bacteroides</i>	LFD+CR 141w	3.0969322	0.0070847
58	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Bacteroidaceae</i>	<i>Bacteroides</i>	LFD+CR 141w	3.625619109	0.0023601
64	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Bacteroidaceae</i>	<i>Bacteroides</i>	LFD+CR 141w	3.554851109	0.0009316
173	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Bacteroidaceae</i>	<i>Bacteroides</i>	LFD+CR 141w	4.15062865	0.0006218
243	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Bacteroidaceae</i>	<i>Bacteroides</i>	LFD+CR 141w	3.23311406	0.0413277
623	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Bacteroidaceae</i>	<i>Bacteroides</i>	LFD+CR 141w	3.546105153	0.0053026
1732	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Bacteroidaceae</i>	<i>Bacteroides</i>	LFD+CR 141w	3.443172744	0.0009332
142	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>Parabacteroides</i>	LFD+CR 141w	3.607881539	0.0013089
119	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>Tannerella</i>	LFD+CR 141w	4.004177601	0.0010487
155	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>Tannerella</i>	LFD+CR 141w	4.162701352	0.0036868
267	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>Tannerella</i>	LFD+CR 141w	3.735146654	0.0070099
963	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>Tannerella</i>	LFD+CR 141w	3.455146744	0.0141727
77	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>mclassified_Porphyromonadaceae</i>	LFD+CR 141w	3.143478576	0.0020629
88	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>mclassified_Porphyromonadaceae</i>	LFD+CR 141w	4.460082006	0.0053389
95	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>mclassified_Porphyromonadaceae</i>	LFD+CR 141w	3.370258468	0.0294359
97	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>mclassified_Porphyromonadaceae</i>	LFD+CR 141w	3.586071129	0.0065914
133	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>mclassified_Porphyromonadaceae</i>	LFD+CR 141w	4.156102649	1.21E-05
169	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>mclassified_Porphyromonadaceae</i>	LFD+CR 141w	3.585976841	7.53E-06
202	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>mclassified_Porphyromonadaceae</i>	LFD+CR 141w	3.389202775	0.0479373
280	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>mclassified_Porphyromonadaceae</i>	LFD+CR 141w	3.352335091	0.0084241
282	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>mclassified_Porphyromonadaceae</i>	LFD+CR 141w	3.30857375	0.0013891
302	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>mclassified_Porphyromonadaceae</i>	LFD+CR 141w	3.352776728	0.0237567
363	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>mclassified_Porphyromonadaceae</i>	LFD+CR 141w	3.44371154	0.0119975
395	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>mclassified_Porphyromonadaceae</i>	LFD+CR 141w	3.135311506	0.0060251
544	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Porphyromonadaceae</i>	<i>mclassified_Porphyromonadaceae</i>	LFD+CR 141w	3.541918594	0.0013891
197	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Rikenellaceae</i>	<i>Alistipes</i>	LFD+CR 141w	3.739282696	0.0029878
238	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Rikenellaceae</i>	<i>Alistipes</i>	LFD+CR 141w	3.212395647	0.0081218
365	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Rikenellaceae</i>	<i>Alistipes</i>	LFD+CR 141w	3.955909724	0.0009755
36	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD+CR 141w	3.402350695	0.0156895
148	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD+CR 141w	3.505935801	0.0027921
149	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD+CR 141w	3.933370923	0.0135891
162	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD+CR 141w	3.199768967	0.0180926
393	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD+CR 141w	3.14070003	0.0398618
411	<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	<i>unclassified_Bacteroidales</i>	LFD+CR 141w	3.244878014	0.0092355
76	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD+CR 141w	3.301916984	0.0027243
101	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Ruminococcaceae</i>	<i>Papillibacter</i>	LFD+CR 141w	3.252061789	0.0205306
271	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Ruminococcaceae</i>	<i>unclassified_Ruminococcaceae</i>	LFD+CR 141w	3.15859468	0.0138786
130	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>unclassified_Clostridiales</i>	<i>unclassified_Clostridiales</i>	LFD+CR 141w	3.201037496	0.0121571
340	<i>Firmicutes</i>	<i>unclassified_Firmicutes</i>	<i>unclassified_Firmicutes</i>	<i>unclassified_Firmicutes</i>	<i>unclassified_Firmicutes</i>	LFD+CR 141w	3.417317548	0.0218347
30	<i>Proteobacteria</i>	<i>Deltaproteobacteria</i>	<i>Desulfovibrionales</i>	<i>Desulfovibrionaceae</i>	<i>Bilophila</i>	LFD+CR 141w	3.98159411	0.0051139
98	<i>TM7</i>	<i>TM7</i>	<i>TM7</i>	<i>TM7</i>	<i>TM7</i>	LFD+CR 141w	3.315465909	0.0056213
127	<i>Actinobacteria</i>	<i>Actinobacteria</i>	<i>Bifidobacteriales</i>	<i>Bifidobacteriaceae</i>	<i>Bifidobacterium</i>	LFD+CR 62w	3.387708547	0.0210453
78	<i>Actinobacteria</i>	<i>Actinobacteria</i>	<i>unclassified_Actinobacteria</i>	<i>unclassified_Actinobacteria</i>	<i>unclassified_Actinobacteria</i>	LFD+CR 62w	3.712032344	0.0272958
250	<i>Actinobacteria</i>	<i>Actinobacteria</i>	<i>unclassified_Actinobacteria</i>	<i>unclassified_Actinobacteria</i>	<i>unclassified_Actinobacteria</i>	LFD+CR 62w	3.337765569	0.0053026
45	<i>Firmicutes</i>	<i>Bacilli</i>	<i>Lactobacillales</i>	<i>Lactobacillaceae</i>	<i>Lactobacillus</i>	LFD+CR 62w	4.842011044	1.76E-05
94	<i>Firmicutes</i>	<i>Bacilli</i>	<i>Lactobacillales</i>	<i>Lactobacillaceae</i>	<i>Lactobacillus</i>	LFD+CR 62w	3.674075708	1.77E-05
171	<i>Firmicutes</i>	<i>Bacilli</i>	<i>Lactobacillales</i>	<i>Lactobacillaceae</i>	<i>Lactobacillus</i>	LFD+CR 62w	4.293138907	0.0006114
2219	<i>Firmicutes</i>	<i>Bacilli</i>	<i>Lactobacillales</i>	<i>Lactobacillaceae</i>	<i>Lactobacillus</i>	LFD+CR 62w	3.484890578	0.0003401
109	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD+CR 62w	3.653813651	0.0052249
129	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD+CR 62w	3.559366431	0.0224266
165	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD+CR 62w	3.439447365	0.0050259
205	<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>unclassified_Lachnospiraceae</i>	LFD+CR 62w	3.414132006	0.0007124
4	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD+CR 62w	4.80509099	0.0011298
80	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD+CR 62w	4.406775797	0.0006617
83	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD+CR 62w	3.566830839	0.0013053
110	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD+CR 62w	3.567277401	0.00441
118	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD+CR 62w	3.591845857	0.0109715
134	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD+CR 62w	3.698486383	0.0057186
252	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD+CR 62w	3.237366726	0.0119192
261	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD+CR 62w	3.372001984	0.0287007
315	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD+CR 62w	3.438837753	0.0261741
592	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD+CR 62w	3.328625929	0.0023919
602	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD+CR 62w	3.046755607	0.0206314
646	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD+CR 62w	3.272986421	0.0177051
1821	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD+CR 62w	3.552567805	0.0044794
2231	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD+CR 62w	3.419542616	0.0231258
2563	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD+CR 62w	3.744610901	0.0023659
3793	<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	<i>Erysipelotrichaceae</i>	<i>Allobaculum</i>	LFD+CR 62w	3.428173621	0.0261229

**Supplementary Table S6 The phylotypes of midlife (62 weeks) gut microbiota of normal chow that significantly correlated with lifespan.**

OTU id	Phylum	Class	Order	Family	Genus	p value with lifespan	r with lifespan	r with food intake	r with body weight	r with fat content
273	Actinobacteria	Actinobacteria	Coriobacteriales	Coriobacteriaceae	Eggerthella	0.023616998	-0.242865374	0.148461967	0.076722918	0.314613891
173	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	0.018755583	-0.221211399	0.129946179	0.003496504	-0.058823529
142	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Parabacteroides	0.013116368	-0.254245454	0.137434574	-0.024308167	-0.115517213
963	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Tannerella	0.014079841	-0.257361405	0.049003528	-0.000914915	-0.082512295
97	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae		0.006868157	-0.255455487	0.020747537	-0.049209653	-0.102941176
133	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae		0.038047943	-0.195378343	0.243925427	0.043371811	-0.25
203	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae		0.008622378	-0.267992916	0.290822732	0.169385338	0.188648444
365	Bacteroidetes	Bacteroidia	Bacteroidales	Rikenellaceae	Alistipes	0.000137404	-0.35841847	0.373021973	0.2412588	0.029411765
510	Bacteroidetes	Bacteroidia	Bacteroidales	Rikenellaceae	Alistipes	0.004216812	-0.302549613	0.101408749	0.118597314	0.061494005
364	Bacteroidetes	Bacteroidia	Bacteroidales	Rikenellaceae	Alistipes	0.017907098	-0.248202636	0.161011593	0.15187589	0.102490008
197	Bacteroidetes	Bacteroidia	Bacteroidales	Rikenellaceae	Alistipes	0.010453381	-0.241658258	0.345183386	0.310878418	0.228783845
381	Bacteroidetes	Bacteroidia	Bacteroidales	Rikenellaceae	Rikenella	0.007685566	-0.274351631	-0.013955233	0.084261758	0.152812461
162	Bacteroidetes	Bacteroidia	Bacteroidales			5.75E-06	-0.447130625	0.403000458	0.293736408	0.300828419
366	Bacteroidetes	Bacteroidia	Bacteroidales			0.000219439	-0.351086435	0.33069749	0.230269204	0.287824838
1408	Bacteroidetes	Bacteroidia	Bacteroidales			0.017526742	-0.256045727	0.22226312	0.086685867	0.225188675
643	Bacteroidetes	Bacteroidia	Bacteroidales			0.018253231	-0.253244236	0.249325441	0.245720696	0.270226409
371	Bacteroidetes	Bacteroidia	Bacteroidales			0.00960476	-0.244124883	0.003063987	-0.016117745	-0.081789473
65	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Lactococcus	0.042369948	-0.195173649	0.363318941	0.392815108	0.541491154
137	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae		0.00597929	-0.271309769	0.008275163	0.064349471	-0.171498585
211	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae		0.02066821	-0.241508762	0.417622975	0.375783998	0.295358674
18	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae		0.044897634	-0.203062113	0.129342088	0.069226195	0.163984012
190	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae		0.043096949	-0.195623379	0.077819552	0.092986969	-0.085749293
37	Firmicutes	Clostridia	Clostridiales	Peptostreptococcaceae		0.011589197	-0.259867228	0.385164443	0.38471025	0.260680081
43	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Papillibacter	0.024355208	-0.223219672	0.119365776	0.145093135	-0.071965465
104	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae		0.006801408	-0.259895369	0.051097408	0.109314702	0.060165684
319	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae		0.021887844	-0.229084959	0.220365286	0.155676439	0.08795779
67	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae		0.030615391	-0.212735899	-0.00738739	-0.006758347	-0.038976951
108	Firmicutes	Clostridia	Clostridiales			0.01491153	-0.257550146	0.221635617	0.173113821	0.171498585
506	Proteobacteria	Alphaproteobacteria				0.018877857	-0.260449806	0.119012099	0.039592041	0.169411303
98	TM7					0.000228534	-0.349251557	0.236997601	0.229529447	0.275110046
372	Bacteroidetes	Bacteroidia	Bacteroidales			0.019010391	0.254002676	-0.290675363	-0.198335059	-0.472961743
4114	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.015696867	0.269272616	-0.318943918	-0.281147548	-0.214373231
171	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.005172567	0.28399147	-0.474949499	-0.491571858	-0.360147029
45	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.002179804	0.304764718	-0.482743447	-0.454740099	-0.488905865
534	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.005557949	0.308826785	-0.318943918	-0.31914046	-0.415827745
2386	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.001021483	0.363780435	-0.346217014	-0.320978336	-0.171498585
94	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.000265355	0.373396789	-0.627617887	-0.543161804	-0.617394907
2219	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.000283177	0.387121165	-0.528385757	-0.439082198	-0.337783012
63	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.000222729	0.401053693	-0.442955514	-0.423657348	-0.292619524
335	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae		0.014076118	0.264616296	-0.164942631	-0.114510961	-0.046203083
167	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae		0.002074515	0.298400162	-0.136561782	-0.103015281	-0.126401913
2105	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae		0.0035163	0.320662088	-0.135093405	-0.138723562	-0.128623939
634	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Papillibacter	0.023938024	0.250541389	-0.267390819	-0.192304201	-0.128623939
497	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Allobaculum	0.035325199	0.221754441	-0.156318213	-0.071036445	0.066693894
3941	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Allobaculum	0.019717367	0.249007624	-0.069350631	0.005035346	0.01278275

**Supplementary Table S7 The phylotypes of midlife (62 weeks) gut microbiota of high fat diet that significantly correlated with lifespan.**

OTU id	Phylum	Class	Order	Family	Genus	p value with lifespan	r with lifespan	r with food intake	r with body weight	r with fat content
2231	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Allobaculum	0.036604227	0.221066994	-0.175088658	-0.136455204	0.015401028
118	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Allobaculum	0.044435774	0.186218929	-0.113110914	0.02045617	0.168061391
80	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Allobaculum	0.047082932	0.177577253	-0.090436866	0.102143637	0.367647059
257	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae		0.000154637	0.345652514	-0.151337013	-0.234558335	-0.167919418
337	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae		0.011481343	0.260219537	-0.381690722	-0.335184529	-0.370699745
1044	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae		0.02052191	0.24062536	-0.053278498	0.042853072	0
372	Bacteroidetes	Bacteroidia	Bacteroidales			0.000852359	0.323933094	-0.397300923	-0.399406007	-0.390635666
388	Bacteroidetes	Bacteroidia	Bacteroidales			0.004892554	0.288366731	-0.452574816	-0.435158529	-0.447396243
193	Bacteroidetes	Bacteroidia	Bacteroidales			0.037545681	0.218018561	-0.2084053	-0.164406921	0.089479249
97	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae		0.002824444	0.266099558	-0.427171735	-0.37104497	-0.405906823
317	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae		0.006788124	0.265071518	-0.269895824	-0.191049904	-0.257247878
658	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae		0.033673716	0.223613261	-0.22051572	-0.043123368	0.022518867
105	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae		0.03637556	0.202622702	-0.186549078	-0.096405466	-0.085749293
963	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Tannerella	0.00427132	0.294038683	-0.331600076	-0.273541397	0.128623939
119	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Tannerella	0.001490164	0.290301004	-0.387447872	-0.274560532	-0.53474079
155	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Tannerella	0.004229091	0.258663404	-0.391239973	-0.323662119	-0.450187567
410	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Tannerella	0.040046777	0.217188626	-0.279866122	-0.24773906	-0.231015414
267	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Tannerella	0.018180463	0.216647519	-0.350341927	-0.279290466	-0.412514324
96	Actinobacteria	Actinobacteria				0.026704923	0.233231036	-0.271798446	-0.117049142	-0.089479249
1273	Actinobacteria	Actinobacteria				0.046393987	0.210724679	-0.19576842	-0.104659817	0.046203083
111	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae		0.015954199	-0.219810576	0.26816439	0.087304962	-0.226066317
249	Firmicutes	Clostridia	Clostridiales	Peptostreptococcaceae		0.021238538	-0.231320075	0.112817637	0.185743468	-0.225478017
272	Firmicutes	Clostridia	Clostridiales	Peptostreptococcaceae		0.008962554	-0.264517691	0.273242981	0.341759846	0.143486011
37	Firmicutes	Clostridia	Clostridiales	Peptostreptococcaceae		0.001603442	-0.283937355	0.191239092	0.354071596	0.199263349
156	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae		0.033191299	-0.203016349	0.140209398	-0.024761187	0.368547701
649	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae		0.044891199	-0.206672557	0.100181292	-0.009011212	-0.01278275
152	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae		0.035544509	-0.207677906	0.209814595	0.035026969	0.128623939
421	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae		0.047012555	-0.209186599	-0.005128273	-0.013553059	-0.169411303
323	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae		0.027521756	-0.224148632	0.213586944	0.116144079	0.34299717
2031	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae		0.031318753	-0.224669615	0.127781966	0.00231559	0.085749293
115	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae		0.005129296	-0.263709724	0.177685579	0.148759802	-0.026966905
65	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Lactococcus	0.000869514	-0.295898457	0.436823581	0.402688486	0.058823529
366	Bacteroidetes	Bacteroidia	Bacteroidales			0.006824323	-0.253917297	0.080770971	0.06114136	0.055973139
966	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae		0.02517116	-0.23563548	0.097437179	0.077622063	0.063913749
142	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Parabacteroides	0.033472705	-0.204260355	0.115939876	0.127235268	-0.450956034
201	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	0.028357514	-0.211398642	0.157878286	0.064501499	0.152812461
1	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	0.03027774	-0.2270556	0.087939809	0.038194983	-0.063913749
11	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	0.003095035	-0.304372311	0.135244744	-0.113654524	-0.300122524



## Supplementary Methods

As a supervised method, Partial Least Square Discriminate Analysis (PLS-DA) was used to establish classification models of phenotypes based on OTUs data<sup>61</sup>. The correct prediction rate of PLS-DA model was performed with leave-one-out cross valuation<sup>62</sup>. Martens' uncertainty test was used to select significant OTUs which can distinguish different treatment groups at the same age or the same group during aging<sup>63</sup>. One-way ANOVA was further performed to validate these differential variables. All statements of significance are at  $P < 0.05$ .

## Supplementary References

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