

Table S1 List of primers used in this study

Gene	5'-3' sequence	Reference
<i>Tnfa</i>	F: TCGAGTGACAAGCCTGTAG R: GTTGGTTGTCTTTGAGATCC	
<i>Il6</i>	F: GTTGCCTTCTTGGGACTGATG R: GGGAGTGGTATCCTCTGTGAAGTCT	
<i>Il1β</i>	F: AAGATGAAGGGCTGCTTCCA R: GTGCTGCTGCGAGATTGAA	
<i>Saa1</i>	F: GACAAATACTGAGCGTCCTC R: ATTACCCTCTCCTCCTCAAG	
<i>Icam1</i>	F: CAGTCCGCTGTGCTTTGAGA R: CGGAAACGAATACACGGTGAT	
<i>Mcp1</i>	F: GCAGTTAACGCCCACTCA R: CCCAGCCTACTCATTGGGATCA	
<i>Ifnγ</i>	F: AGCTCTTCCTCATGGCTGTT R: TCCTTTTGCCAGTTCCTCCA	
<i>Pepck</i>	F: TGTCGGAAGAAGACTTTGAGAAA R: TGCTGAATGGGATGACATACATG	
<i>G6pase</i>	F: GGAGTCTTGTGAGGCATTGCT R: GCGCGAAACCAAACAAGAAG	
<i>α-Sma</i>	F: ACTGGTATTGTGCTGGACTC R: CATGAGGTAGTCGGTGAGAT	
<i>Timp1</i>	F: CCTGGTCATAAGGGCTAAATTCA R: TTAGTCATCTTGATCTTATAACGCTGC	
<i>Smpd3</i>	F: TCATGGACGTGGCCTATCACTGTT R: TGCAGGCGATGTACCCAACAATTC	
<i>Cd36</i>	F: AGGTCTATCTACGCTGTGTTGGA R: CAATGGTTGTCTGGATTCTGGAGGG	
<i>Cyp4a10</i>	F: TCCAGGTTTGCACCAGACTCT R: TCCTGGCTCCTCCTGAGAAG	
<i>Cyp4a14</i>	F: CAAGACCCTCCAGCATTTC R: GAGCTCCTTGTCTTCAGATGGT	
<i>Errα</i>	F: TCAAGGAGGGTGTGCGTCTG R: CTTGGCCCAGCTGATGGTGA	
<i>Srebp1c</i>	F: TGTGATCTACTTCTTGTGGCCCGT R: AGGCTGCTCAGGTCATGTTGAAA	
<i>Fasn</i>	F: GGTGTGGTGGGTTTGGTGAATTGT R: TGCTTTAGCACCTGCTGTAGCTCT	
<i>Fgf21</i>	F: CTGGGGTCTACCAAGCATA R: CACCCAGGATTTGAATGACC	
<i>Fxr</i>	F: TGCTCACAGCGATCGTCATC R: TCTCAGCGTGGTGTGGTTG	
<i>Fgf15</i>	F: TGAAGACGATTGCCATCAAG R: GAGTAGCGAATCAGCCCGTA	
<i>Tgr5</i>	F: CTGCCCAAAGGTGTCTACGA R: GCATTGGCTACTGGTGTGGT	
<i>Gcg</i>	F: TGAGATGAGCACCATTCTGGA R: TCCGCAGAGATGTTGTGAAGA	
<i>Pc1/3</i>	F: TCAACCAGAGCACATGAAGC R: ATTGCTGCTGCTGGAGTTTT	
Functional microbial gene		
<i>baiJ</i>	F: TCAGGACGTGGAGGCGATCCA R: TACRTGATACTGGTAGCTCCA	(52)
<i>bsh</i>	F: ATGGGCGGACTAGGATTACC R: TGCCACTCTGTCTGCATC	(53)
<i>bcoA</i>	F: GCIGAICATTTACITGGAAYWSITGGCAYATG R: CCTGCCTTTGCAATRTCIACRAANGC	(54)
<i>pduP</i>	F: GTGGATGARACIGGIATGGGNAAYGTNGG R: CAATAGCCYTCICCCRAAICCIADNGC	(55)
<i>mmdA</i>	F: AATGACTCGGGIGGICIMGNATHCARGA R: GATTGTTACYTTIGGIACNGTNGCYTC	(55)
<i>lcdA</i>	F: CTGGTGTGCTGGWSIGCIWSIGTIGCNCC R: CAGATAGGTCCAIAYIGCDATNCCYTCCTCA	(55)

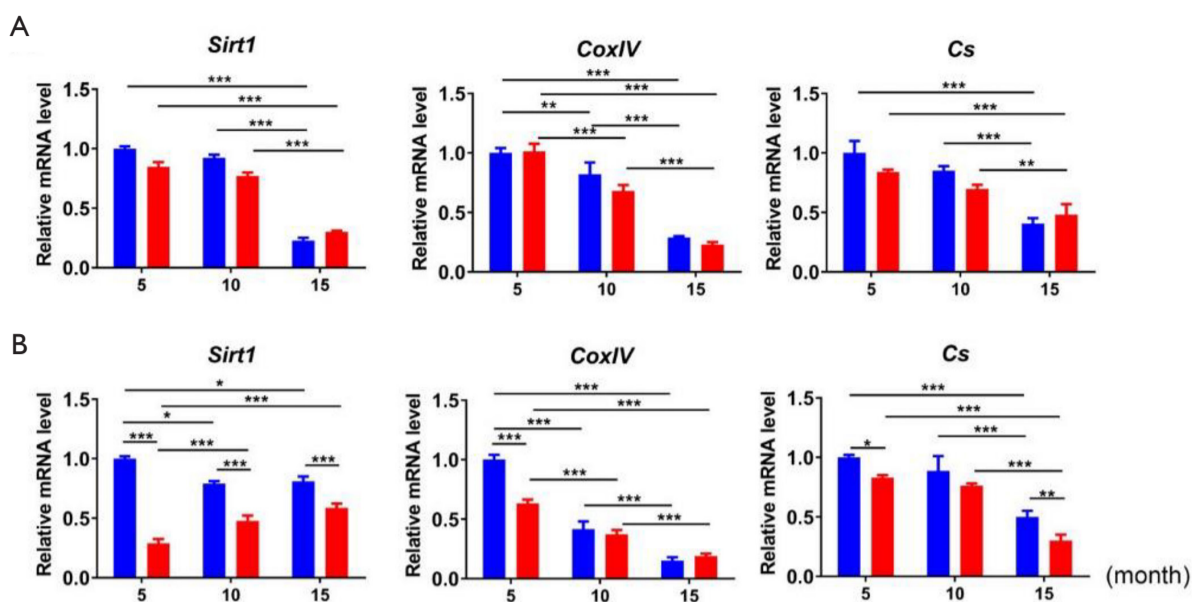


Figure S1 The expression of mitochondrial biogenesis related gene in liver (A) and adipose tissue (B). n=8 per group. Data are expressed as mean \pm SD. Two-way ANOVA with Tukey's correction. *, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$.

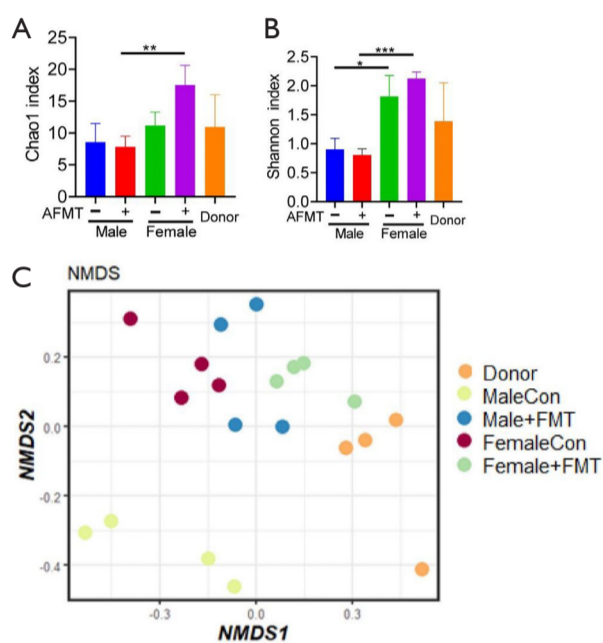


Figure S2 Alpha and beta diversity analysis of gut microbiota composition after aged male fecal microbiota transplantation (AFMT). (A) Chao1 index; (B) Shannon index; (C) Bray_curtis based NMDS analysis. *, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$.

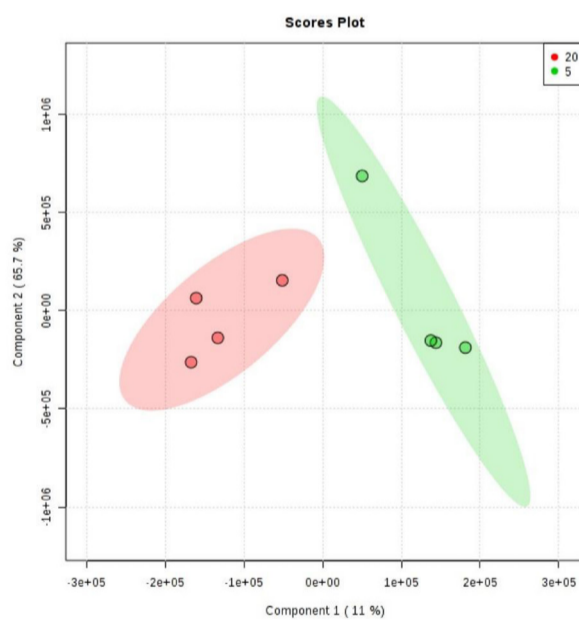


Figure S3 Partial least squares-discriminant analysis (PLS-DA) of metabolites detected by GC-TOFMS in 5- and 20-month-old male mice.

Table S2 Metabolic pathway and function analysis between 5- and 20-month-old male mice

Pathway name	Hits/total compounds	P	FDR	Function
Ubiquinone and other terpenoid-quinone biosynthesis	1/3	0.000243	0.004595	Metabolism of cofactors and vitamins
Tyrosine metabolism	3/44	0.000286	0.004595	Amino acid metabolism
Phenylalanine, tyrosine and tryptophan biosynthesis	2/4	0.000312	0.004595	Amino acid metabolism
Phenylalanine metabolism	4/11	0.000312	0.004595	Amino acid metabolism
Valine, leucine and isoleucine biosynthesis	4/11	0.001602	0.015756	Amino acid metabolism
Valine, leucine and isoleucine degradation	4/38	0.001602	0.015756	Amino acid metabolism
Pantothenate and CoA biosynthesis	4/15	0.003982	0.033561	Metabolism of cofactors and vitamins
Citrate cycle (TCA cycle)	5/20	0.036678	0.2705	Carbohydrate metabolism
Tryptophan metabolism	2/40	0.042778	0.28043	Amino acid metabolism
Riboflavin metabolism	1/11	0.049989	0.29494	Metabolism of cofactors and vitamins

Top 10 pathways are listed.

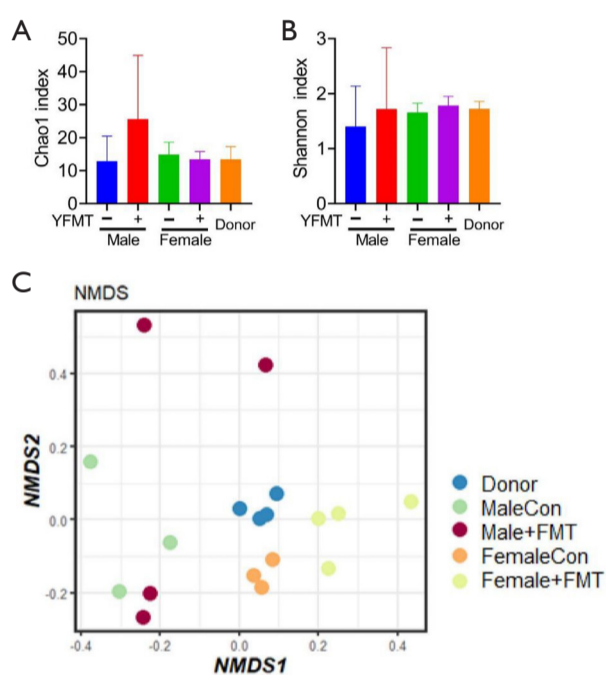


Figure S4 Alpha and beta diversity analysis of gut microbiota composition after young female fecal microbiota transplantation (YFMT). (A) Chao1 index; (B) Shannon index; (C) Bray_curtis based NMDS analysis.

References

- Yoshimoto S, Loo TM, Atarashi K, et al. Obesity-induced gut microbial metabolite promotes liver cancer through senescence secretome. *Nature* 2013;499:97-101. Erratum in: *Nature*. 2014 Feb 20;506(7488):396. Hattori, Masahisa [corrected to Hattori, Masahira].
- Li CY, Dempsey JL, Wang D, et al. PBDEs Altered Gut Microbiome and Bile Acid Homeostasis in Male C57BL/6 Mice. *Drug Metab Dispos* 2018;46:1226-40.
- Louis P, Flint HJ. Development of a semiquantitative degenerate real-time pcr-based assay for estimation of numbers of butyryl-coenzyme A (CoA) CoA transferase genes in complex bacterial samples. *Appl Environ Microbiol* 2007;73:2009-12.
- Reichardt N, Duncan SH, Young P, et al. Phylogenetic distribution of three pathways for propionate production within the human gut microbiota. *ISME J* 2014;8:1323-35. Erratum in: *ISME J*. 2014 Jun;8(6):1352.