Supplementary Figures

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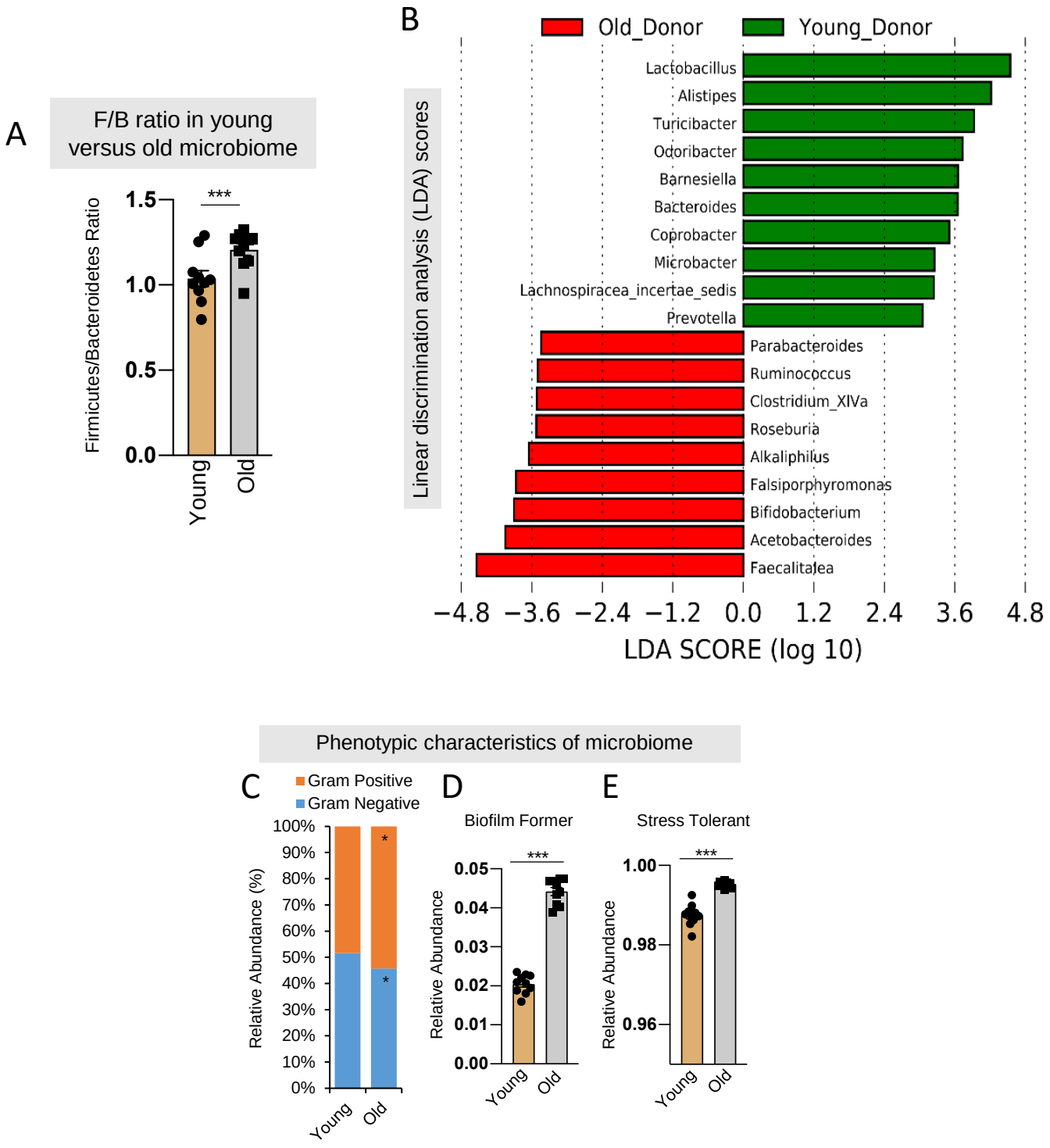
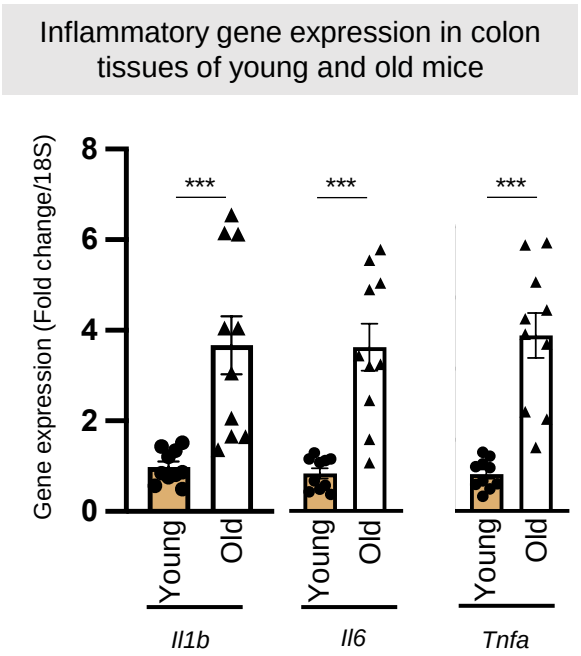


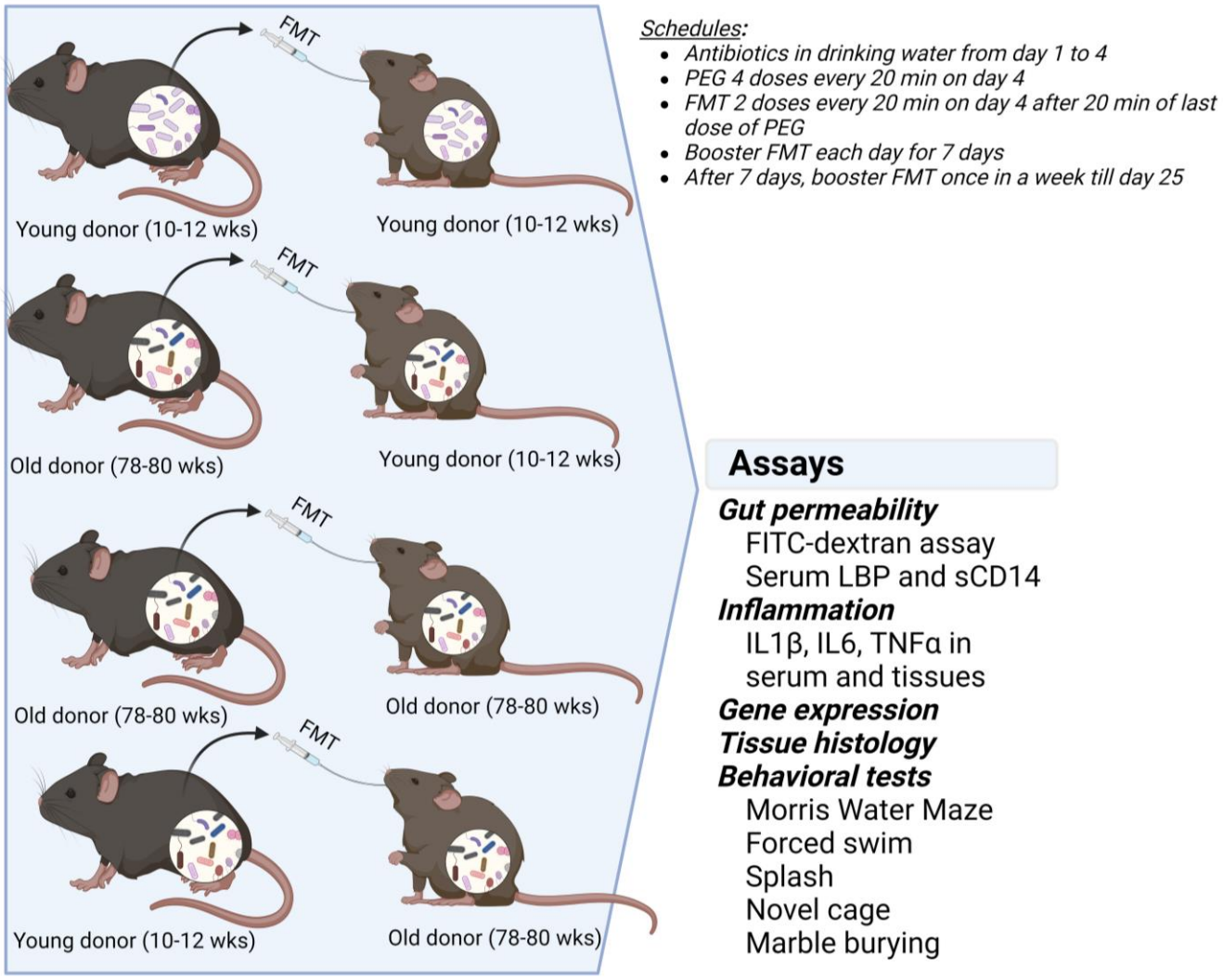
Supplementary Figure S1. (**A**) The Firmicutes versus Bacteroidetes (F/B) ratio was significantly increased in old mice compared to young mice. (**B**) The LDA score of microbes that abundant in young (green) compared to old (red) and represent a biomarker ability. (**C-E**) The relative abundance of Gram positive and Gram negative (C) as well as biofilm former (D) and stress tolerant (E) microbes in young and old gut. All values represent the mean of 5-10 animals in each group, and error bars represent the standard error of means. Statistical significance was determined using a t-test, and the p-value ***p<0.001 is statistically significant.

Mishra et al Supplementary Figure S2

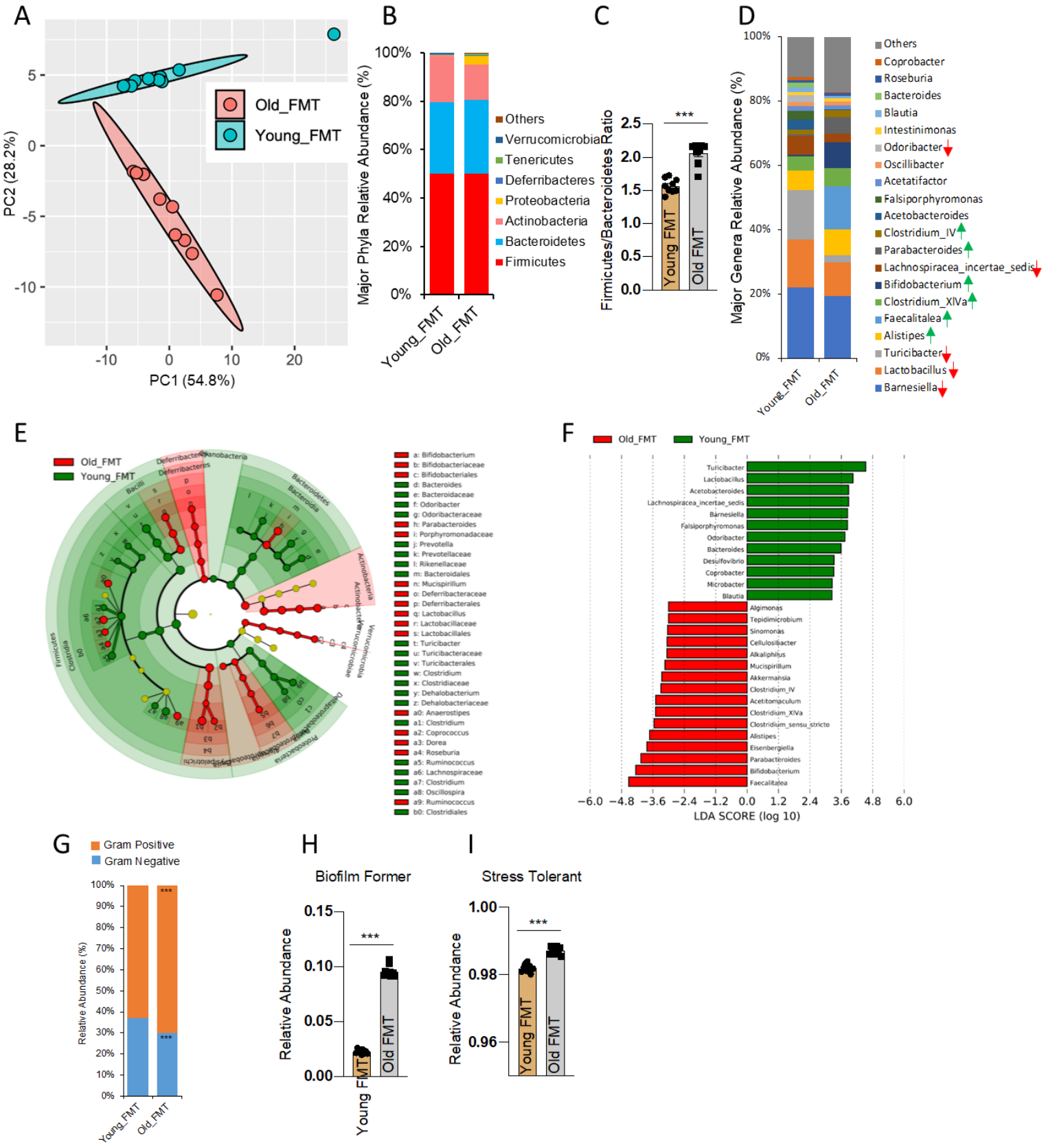


Supplementary Figure S2. The expression of inflammatory genes (*Il1b, Il6*, and *Tnfa*) significantly increased in the colon of old mice compared to young mice. All values represent the mean of 5-10 animals in each group, and error bars represent the standard error of means. Statistical significance was determined using a t-test, and the p-value ***p<0.001 is statistically significant.

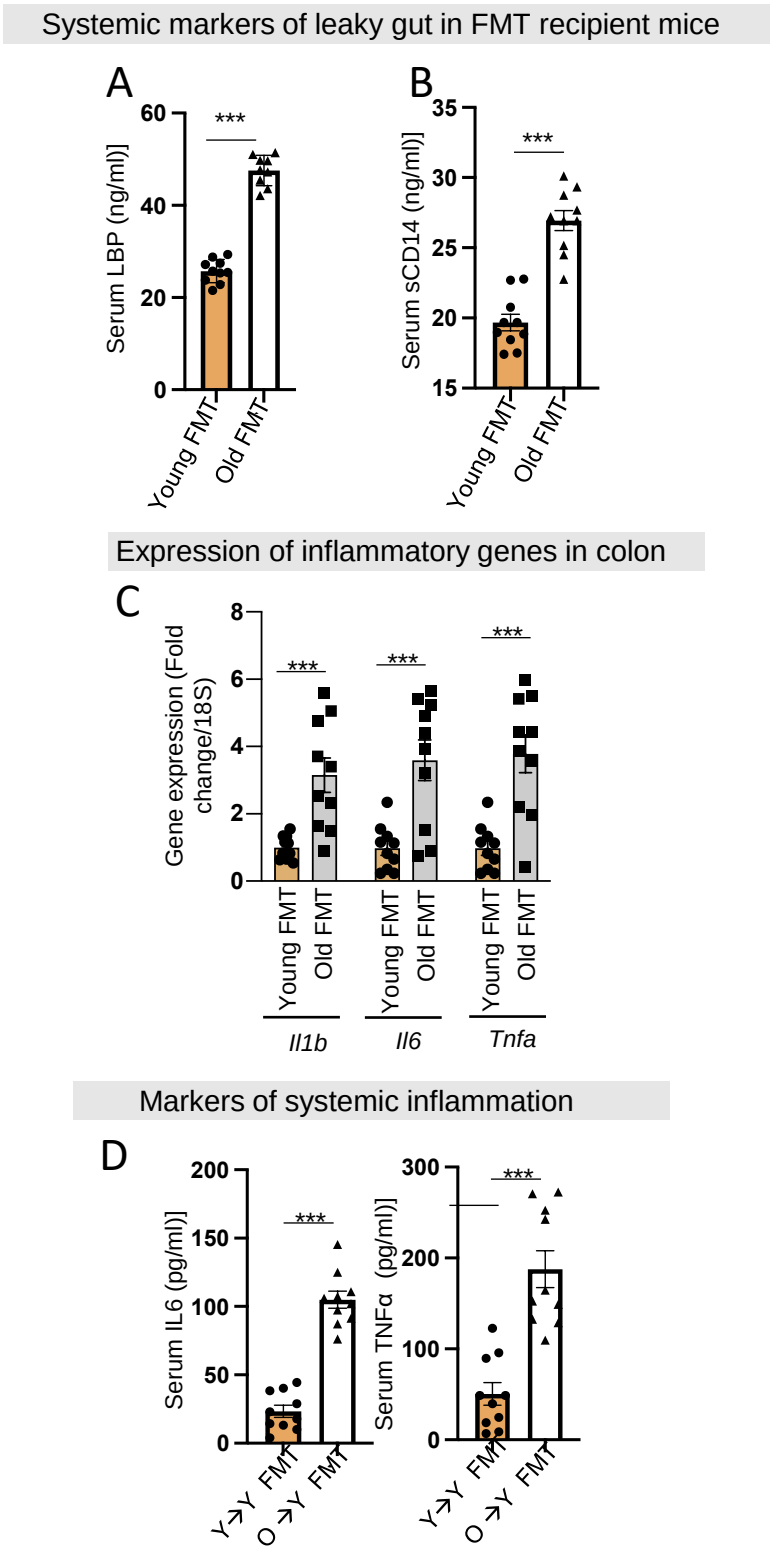
Mishra et al Supplementary Figure S3



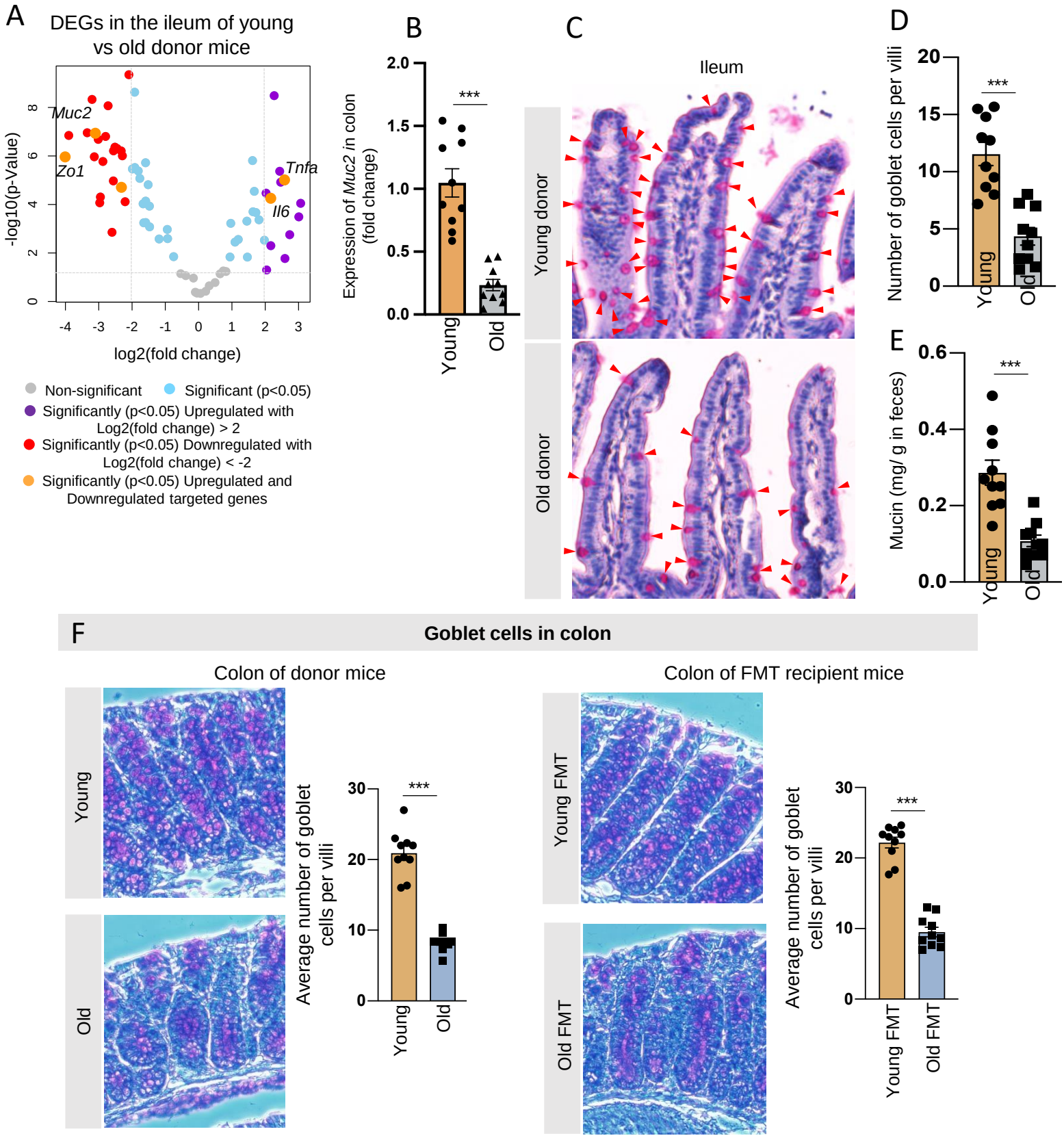
Supplementary Figure S3. Schematic presentation of the fecal microbiome transplantation (FMT) experiment and the schedules for young to young, old to young, old to old, and young to old, along with the assays performed.



Supplementary Figure S4. (**A**) The microbiome's β-diversity was significantly different between old and young FMT recipient mice and was similar to that of their respective donors. (**B,C**) The abundance of major phyla (B), specifically the Firmicutes/Bacteroidetes ratio (C), was significantly distinct in older FMT recipients compared to younger recipients. D) The abundance of major genera differed significantly between old and young FMT recipient feces. (**E,F**) Similarly, the cladogram (E) and LDA scores (F). (**G-I**) Abundance of higher gram-negative bacteria (G), biofilm former (H) and stress tolerant (I) in old FMT mice as compared to Young FMT mice. All values represent the mean of 5-10 animals in each group, and error bars represent the standard error of the means. Statistical significance was determined using a t-test and/or ANOVA, with a p-value of ***p<0.001, indicating statistical significance.

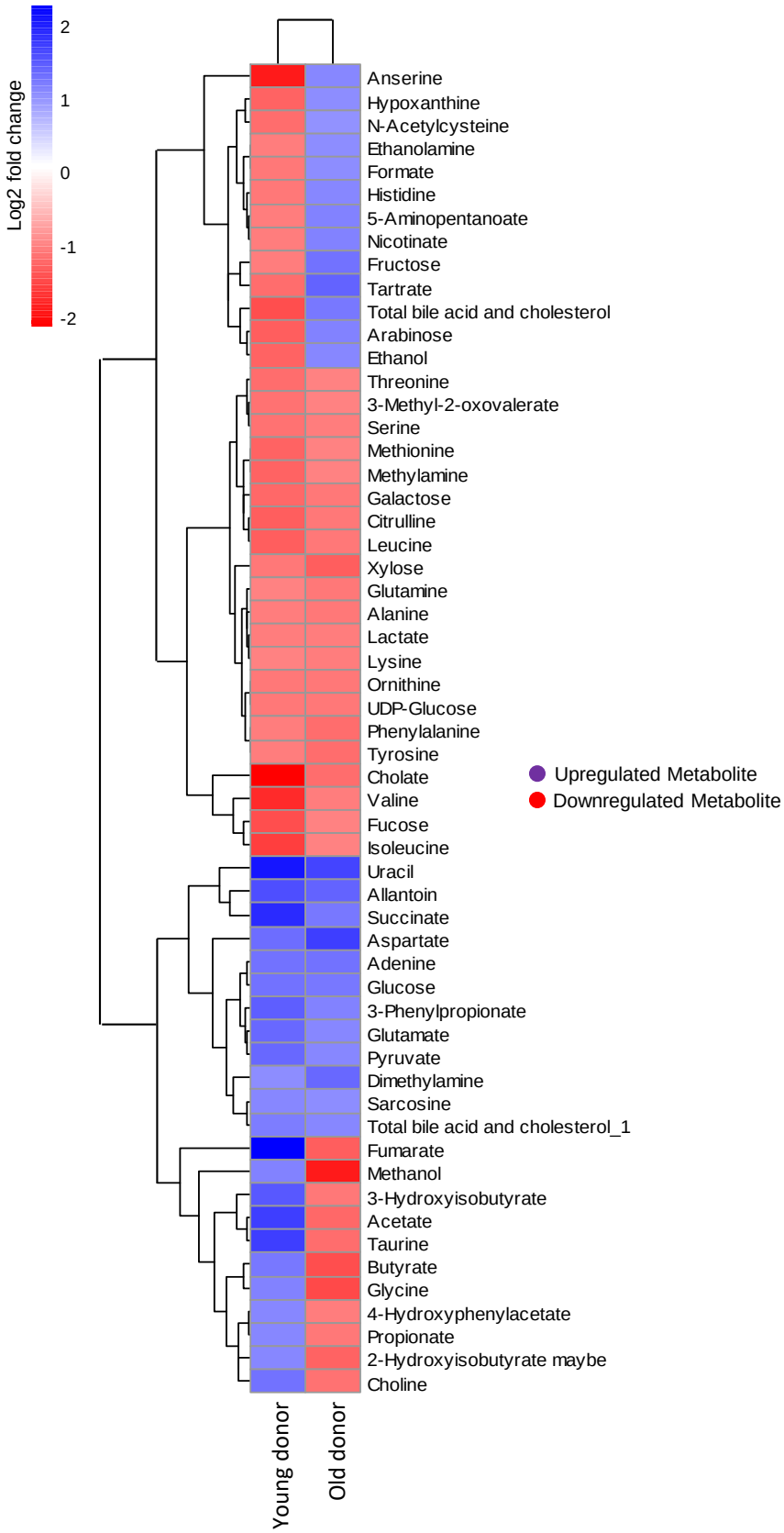


Supplementary Figure S5. (**A,B**) The levels of systemic markers of leaky gut (LBP and sCD14) significantly increased in 10-12 weeks old mice who received old FMT compared to those who received young FMT. (**C**) The expression of inflammatory genes (*Il1b*, *Il6*, and *Tnfa*) significantly increased in old FMT recipients compared to young FMT recipients. (**D**) Similarly, the old FMT recipient mice showed higher systemic inflammatory markers like IL6 and TNFα compared to the levels in young FMT recipients. All values represent the mean of 5-10 animals in each group, and error bars represent the standard error of the means. Statistical significance was determined using a t-test and/or ANOVA, with a p-value of ***p<0.001, indicating statistical significance.



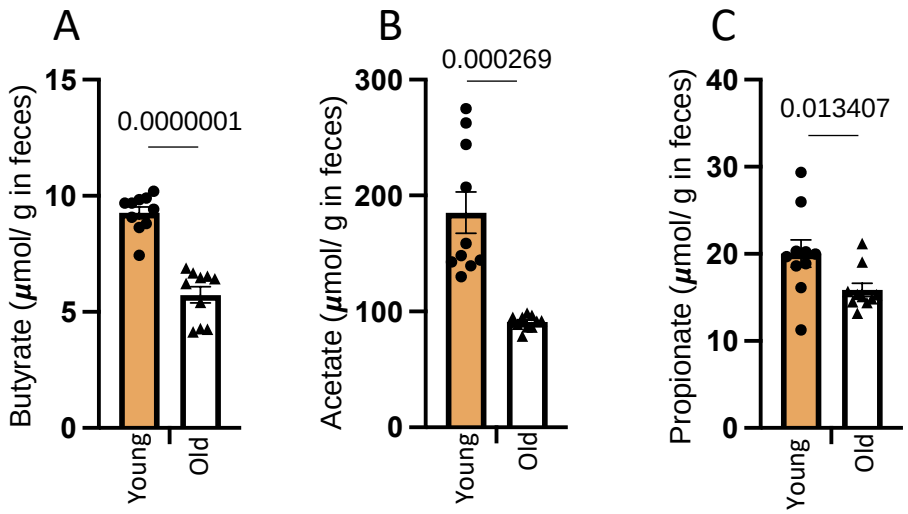
Supplementary Figure S6. (**A**) Volcano graph of differentially expressed genes in the intestines of old and young mice. (**B**) Muc2 expression in the ileum of old and young donor mice. (**C,D**) Small intestine histology (H&E staining) shows fewer goblet cells (white bubble-like structures indicated by red arrows) in old mice than in young mice. (**E**) Fecal mucin content in older mice decreased compared to young mice. (**F**) The goblet cell population in the colon was found to be lower in older mice than in younger mice, and old FMT recipients also showed decreased goblet cells compared to young FMT recipients. Number of goblet cells per villi was measured by FIJI. All values represent the mean of 5-10 animals in each group, and the pictures are representative of 5-10 animals. Five pictures were taken of each animal's tissue sections. Statistical significance was determined using a t-test, and the p-value ***p<0.001 is statistically significant.

Mishra et al Supplementary Figure S7



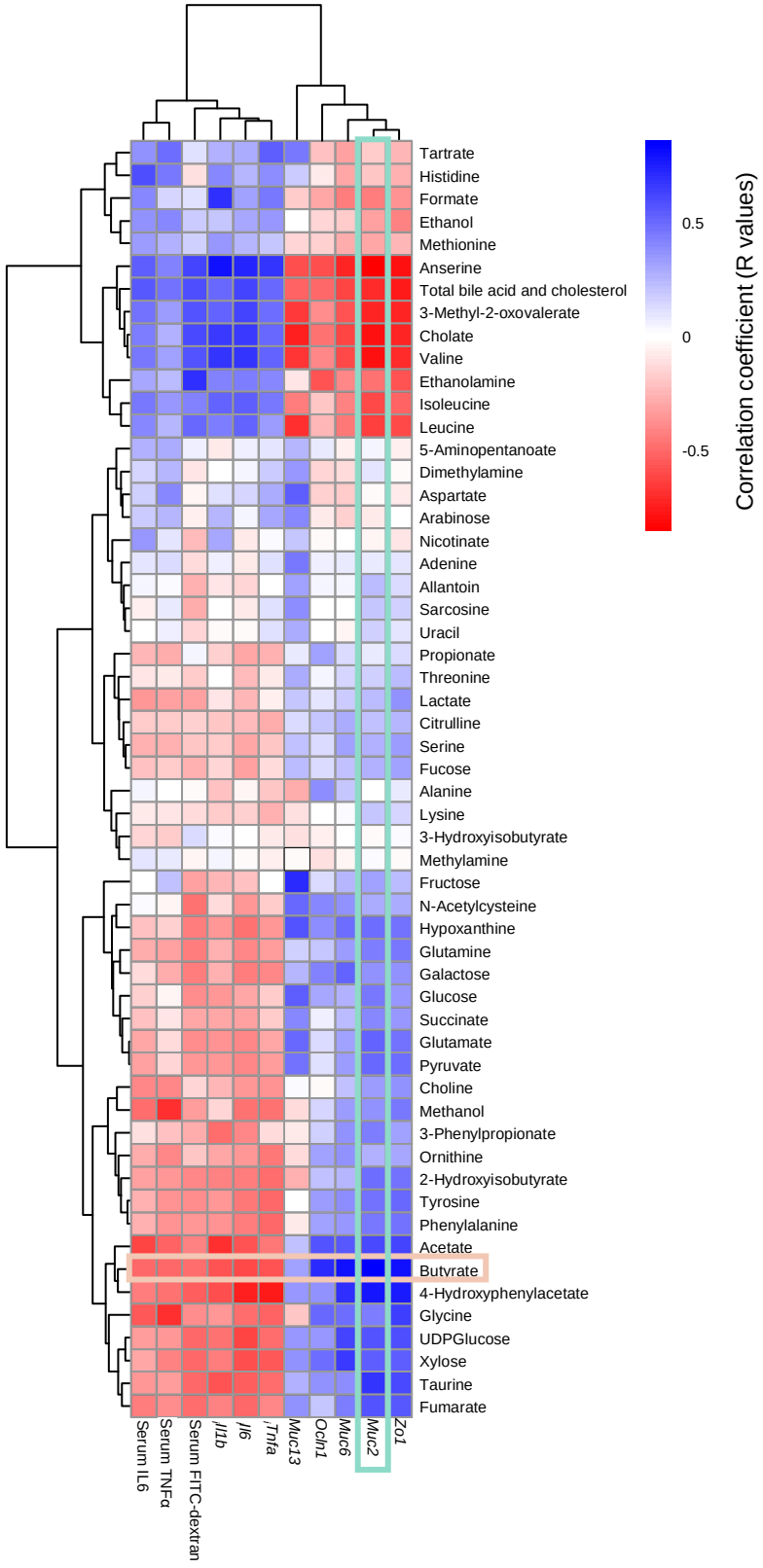
Supplementary Figure S7. Hierarchical differential clustering analyses reveal significant differences in metabolites between old and young gut (ileum). All the values represent the mean of 5-10 animals in each group, and error bars represent the standard error of means. Statistical significance was determined using t-test.

Mishra et al Supplementary Figure S8

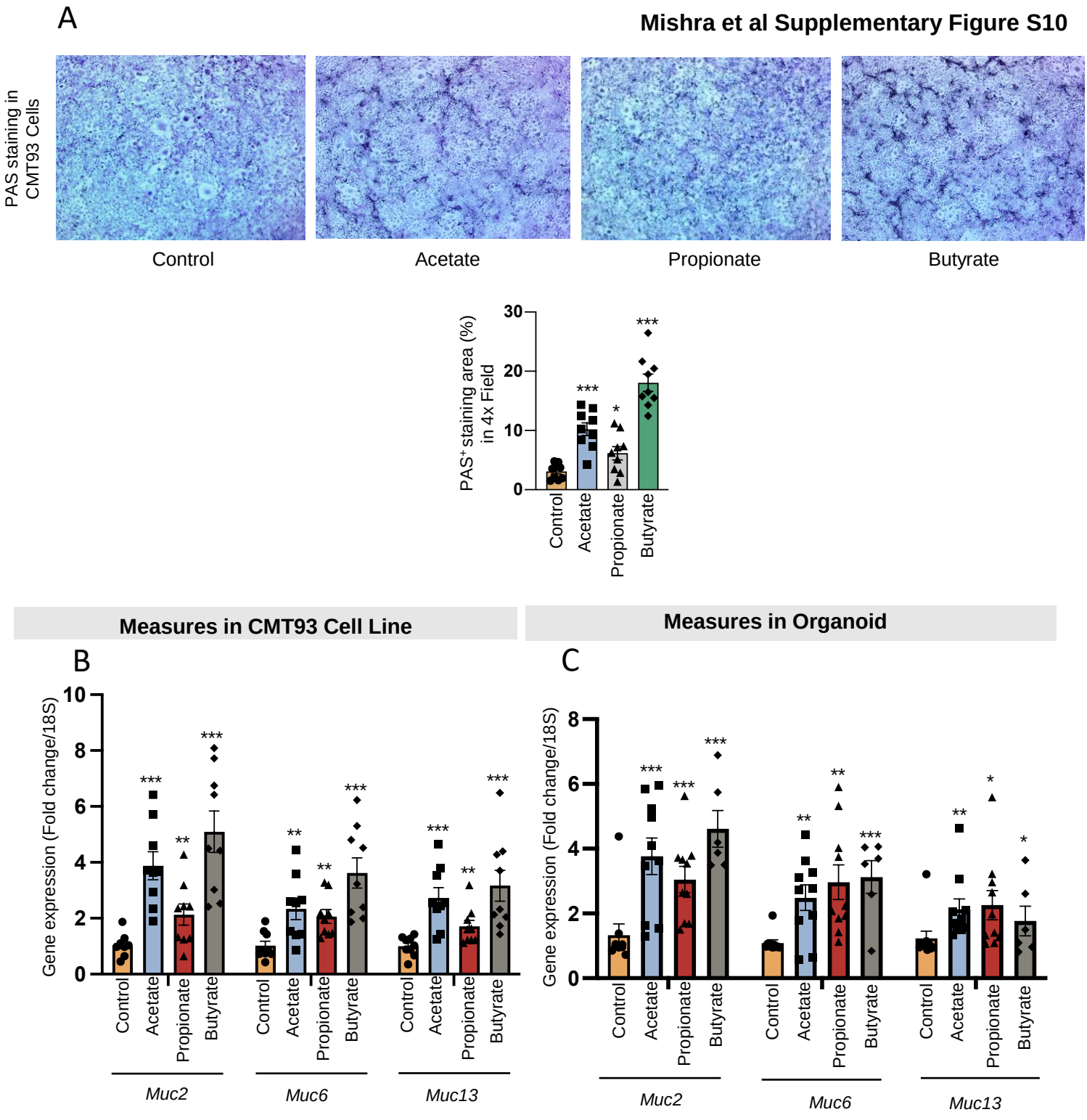


Supplementary Figure S8. Comparing the abundance of three SCFAs—(**A**) Butyrate, (**B**) Acetate, and (**C**) Propionate —in old to young feces shows the greatest decrease (based on p-values) in butyrate. Values represent the mean of 5-10 animals in each group, and error bars represent the standard error of means. Statistical significance was determined using t-test, and the actual p-values are presented in the graphs.

Mishra et al Supplementary Figure S9

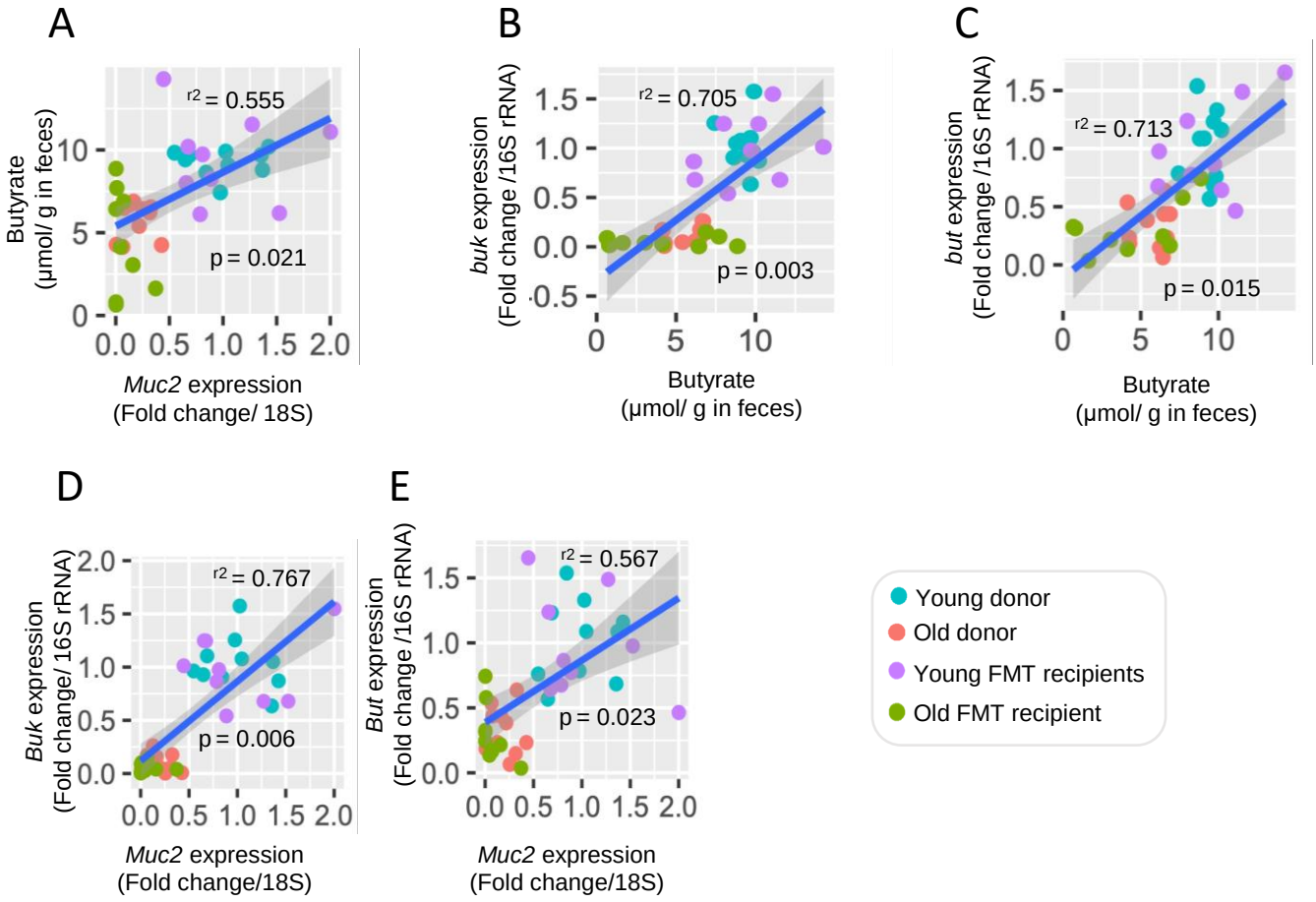


Supplementary Figure S9. Heatmap of Pearson correlation values among fecal metabolites with mucin genes (*Muc2, Muc6, Muc13*), tight junction protein genes (*Zo1, Ocln1*), leaky-gut markers (FITC-dextran permeability [indicated as "FITC"], and inflammation (both intestinal [indicated by "i"] and systemic [serum IL6 and TNFα]) revealed unique clustering. The highest correlation was between butyrate and *Muc2* gene expression.



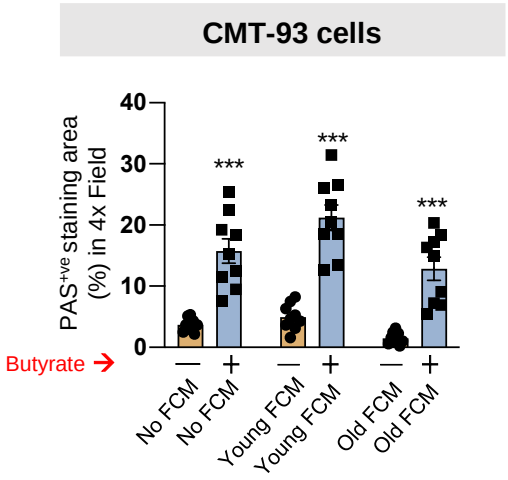
Supplementary Figure S10. Acetate (10μM), propionate (6μM), and butyrate (6μM) treatment enhances mucin production (indicated by increased blue of Periodic Acid–Schiff [PAS] staining) and increased PAS positive (PAS^+) area percentage (%) quantification measured by FIJI (A) and *Muc2*, *Muc6,* and *Muc13* gene expression in both CMT93 cells (B) and enteroids (C). All the values represent the mean of 3-4 independent replicates in cells and organoid cultures for each group, and error bars represent the standard error of means. Statistical analyses were performed using one- and/or two-way ANOVAs, and p-values *p<0.05, **p<0.01, and ***p<0.001 are statistically significant.

Mishra et al Supplementary Figure S11



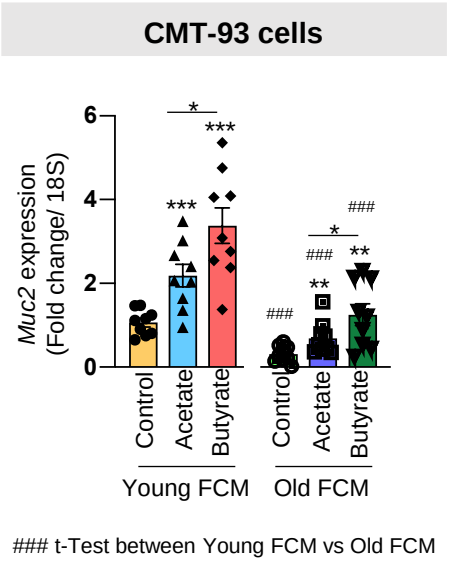
Supplementary Figure S11. (**A-E**) Multivariate analyses correlating butyrate with *Muc2* (A), *buk* (B), and *but (C)* genes as well as *Muc2* expression with *buk* and *but* genes (D,E) in young donors, old donors, young FMT recipients, and old FMT recipients. Analyses are done using Pearson correlation analysis and r^2 values plotted using r-scripts. Values represent the mean of 3-4 independent replicates in cells cultures for each group, and error bars represent the standard error of means. Statistical analyses were performed using t-test and/or ANOVA, as applicable, and the actual p-values are presented in the graphs.

Mishra et al Supplementary Figure S12



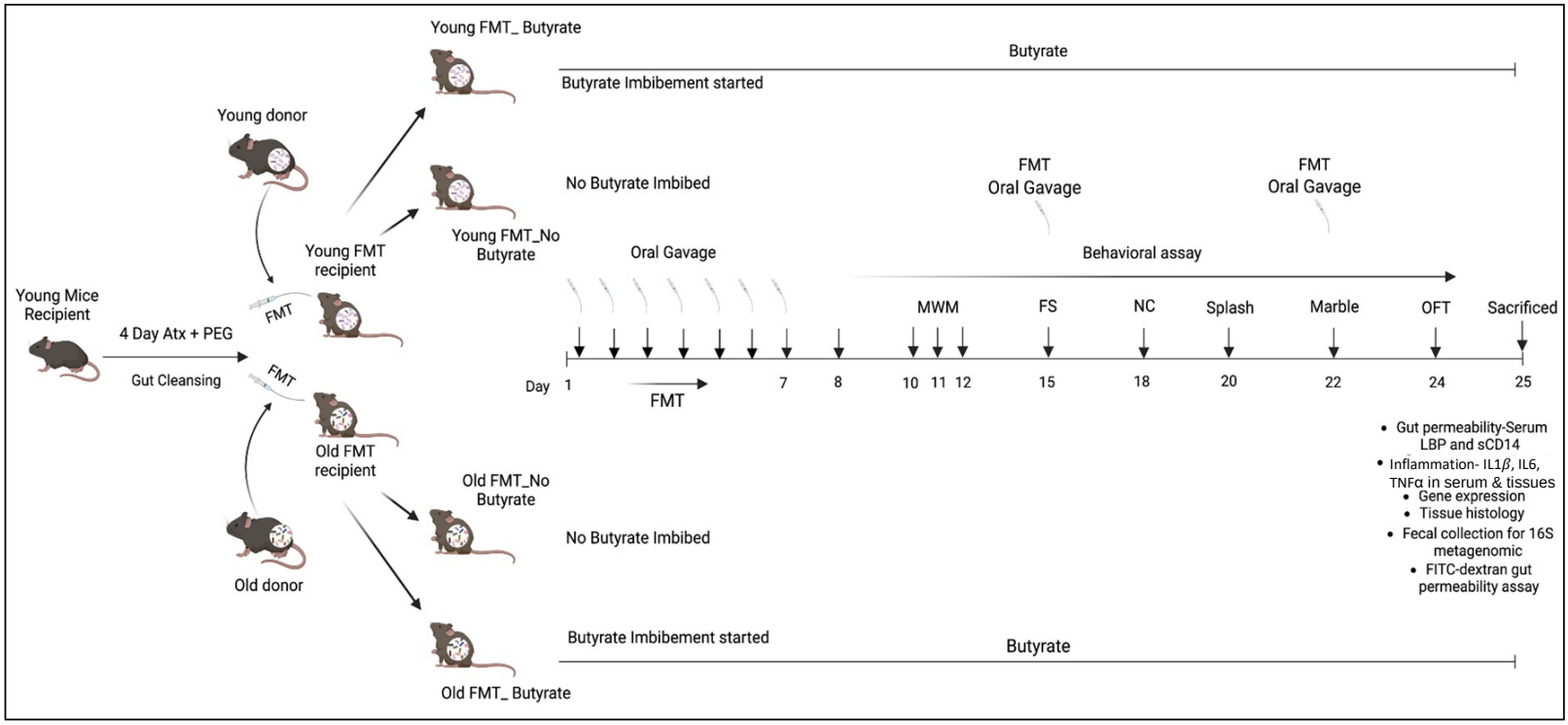
Supplementary Figure S12. Butyrate treatment increased PAS positive (PAS^+) area percentage (%) quantification in CMT93 cells dampened by old FCM treatment measured by FIJI. Values represent the mean of 3-4 independent replicates in cells cultures for each group, and error bars represent the standard error of means. Statistical analyses were performed using t-test and p-values ***$p<0.001$ are statistically significant.

Mishra et al Supplementary Figure S13



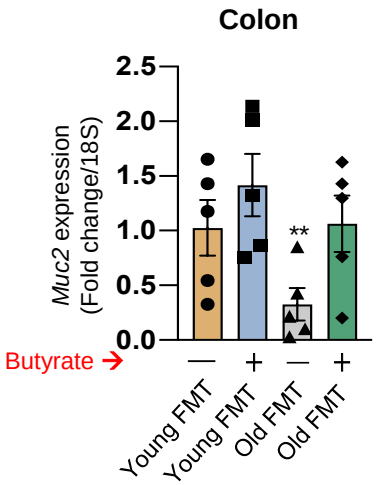
Supplementary Figure S13. Both acetate and butyrate significantly increased the expression of *Muc2* expression in CMT93 cells treated with young and old FCMs, however, butyrate effects were significantly higher than acetate in both young and old FCM treated cells. Values represent the mean of 3-4 independent replicates in cells cultures for each group, and error bars represent the standard error of means. Statistical analyses were performed using t-test and p-values *p<0.05, **p<0.01, and ***p<0.001 are statistically significant.

Mishra et al Supplementary Figure S14



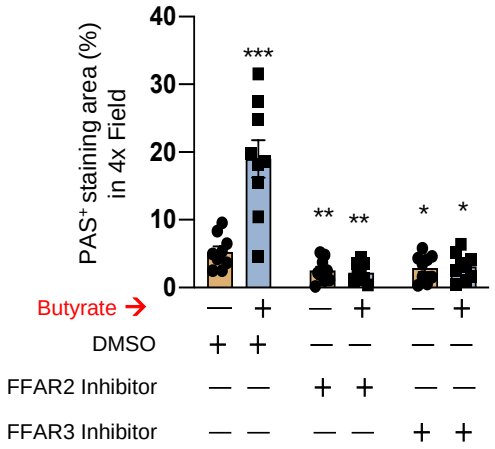
Supplementary Figure S14. Schematic of group randomization, gut cleansing, FMTs, treatments, and assays conducted to test the effects of butyrate in old FMT recipient mice compared to young FMT recipients, as data presented in main Figure 5D-M.

Mishra et al Supplementary Figure S15



Supplementary Figure S15. Expression of *Muc2* in the colon of mice received old and young FMTs and treated with and without butyrate. All the values represent the mean of 5-8 animals for each group, and error bars represent the standard error of means. Statistical significance was determined using t-Test, and p-values **p<0.01 is statistically significant.

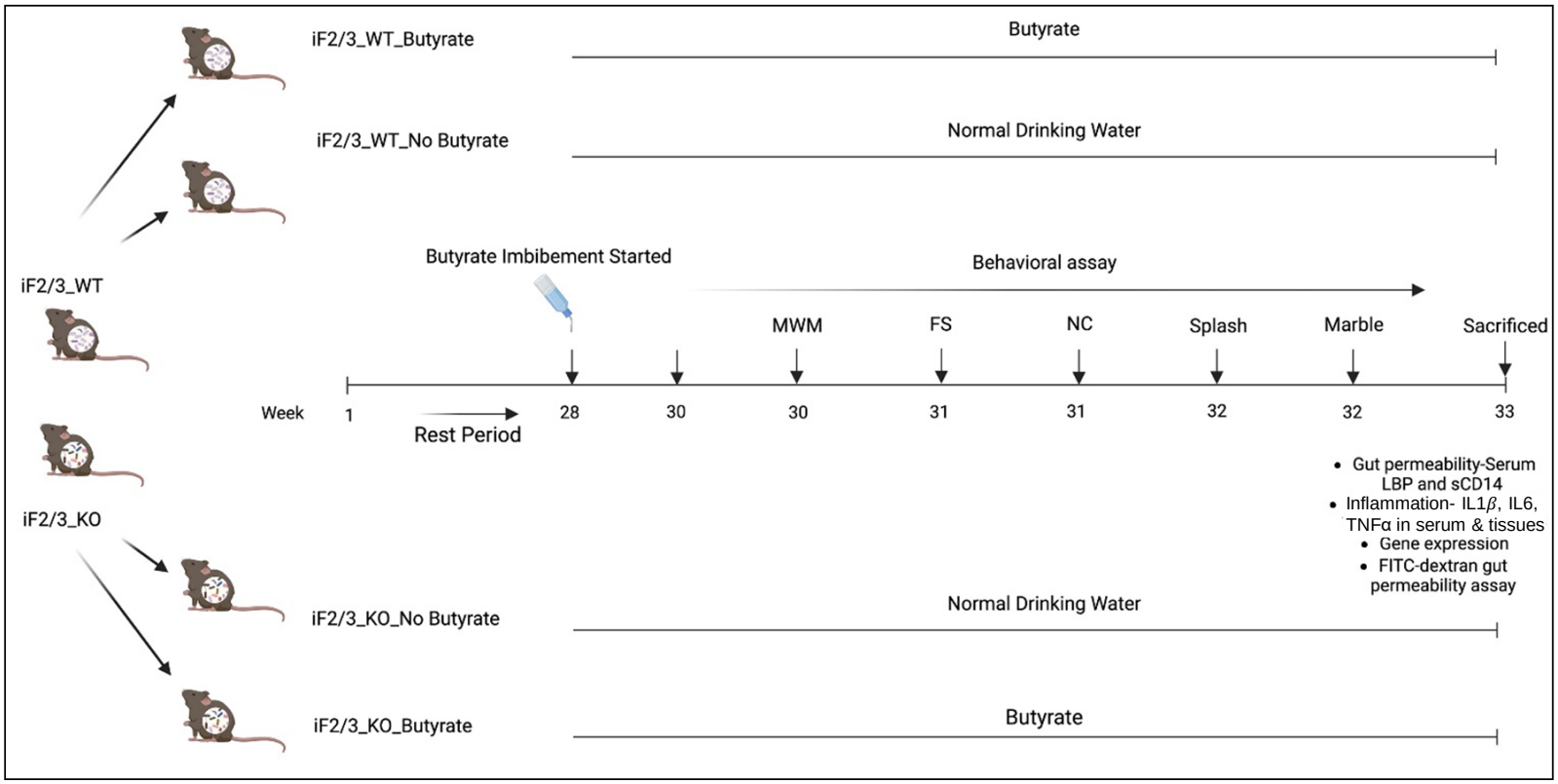
Mishra et al Supplementary Figure S16



Supplementary Figure S16. Positive effect of butyrate increased in PAS positive (PAS^+) area percentage (%) quantification in CMT93 cells reduced by challenging with FFAR2 inhibitor and FFAR3 inhibitor measured by FIJI. Values represent the mean of 3-4 independent replicates in cells cultures for each group, and error bars represent the standard error of means. Statistical analyses were performed using t-test and/or ANOVA, as applicable, and p-values *p<0.05, **p<0.01, and ***p<0.001 are statistically significant.

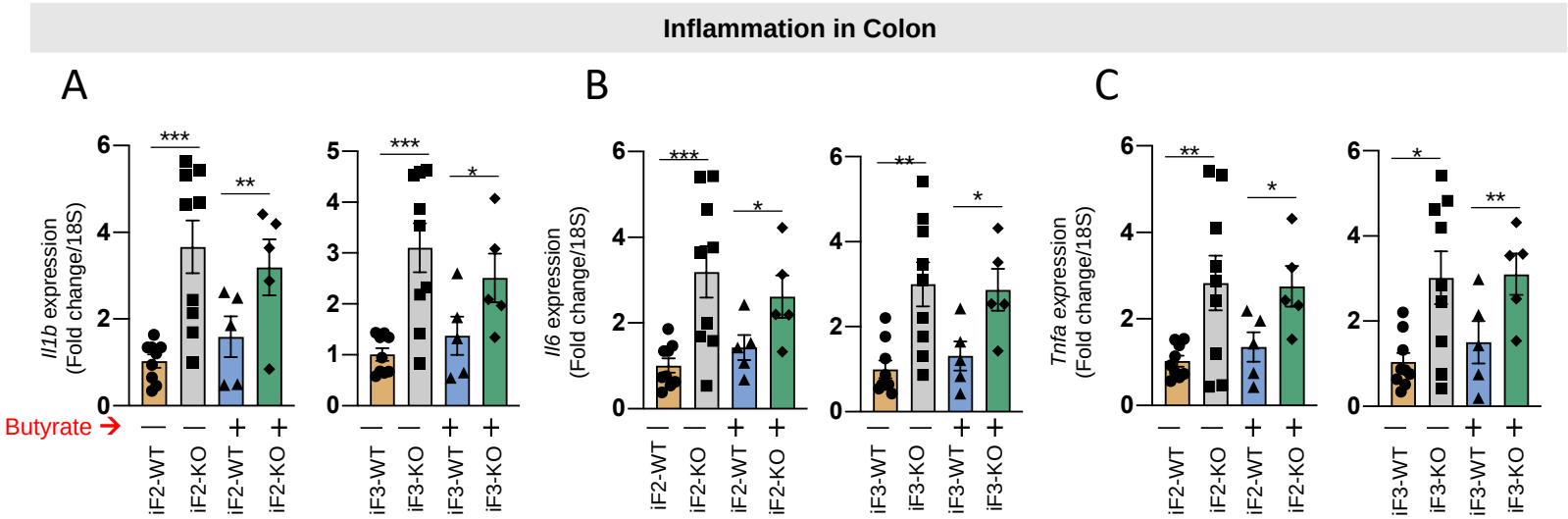
Mishra et al Supplementary Figure S17

Ffar2/3 Mice study Design



Supplementary Figure S17. Schematic of group randomization, gut cleansing, FMTs, treatments, and assays conducted to test the effects of butyrate in Villin-Cre driven intestine specific *Ffar2* (iF2) and *Ffar3* (iF3) knockout (KO) mice compared to their wildtypes (WT), as data presented in main Figure 7A-M.

Mishra et al Supplementary Figure S18



Supplementary Figure S18. The expression of inflammatory markers (*Il1b*, *Il6*, *Tnfa*) (A-C) significantly increased in the colon of 7-months old intestine-specific *Ffar2* (iF2) and *Ffar3* (iF3) knockout (KO) mice compared to their age- and sex-matched wildtype (WT) controls. All values represent the mean of 5-10 animals in each group, and error bars represent the standard error of the means. Statistical significance was determined using a t-test, as applicable, and p-values of *p<0.05, **p<0.01, and ***p<0.001 are statistically significant.

Supplementary Table S1. Mouse key intestinal epithelial, neuronal, tight junction protein and inflammatory markers primer sequence

Sl. No.	Gene	Gene sequence (5`-3`)	GenBank Accession number/Ref.
1	***Notch1***	F: GATGGCCTCAATGGGTACAAG	NM_008714*
		R: TCGTTGTTGTTGATGTCACAGT	
2	***Wnt3***	F: CTCGCTGGCTACCCAATTTG	NM_009521*
		R: CTTCACACCTTCTGCTACGCT	
3	***Ocln***	F: TTGAAAGTCCACCTCCTTACAGA	NM_008756*
		R: CCGGATAAAAAGAGTACGCTGG	
4	***Zo1***	F: GCCGCTAAGAGCACAGCAA	NM_001163574*
		R: GCCCTCCTTTTAACACATCAGA	
5	***Pcna***	F: TTTGAGGCACGCCTGATCC	NM_011045*
		R: GGAGACGTGAGACGAGTCCAT	
6	***Ccnd1***	F: GCGTACCCTGACACCAATCTC	NM_007631*
		R: CTCCTCTTCGCACTTCTGCTC	
7	***Kir67***	F: ATCATTGACCGCTCCTTTAGGT	NM_001081117*
		R: GCTCGCCTTGATGGTTCCT	
8	***Lyz1***	F: GAGACCGAAGCACCGACTATG	PMID: 26159695#
		R: CGGTTTTGACATTGTGTTCGC	
9	***Gp2***	F: ACAGTGTCAACCATCTTGCTC	NM_025989*
		R: CCCGATTATAGTCAATGGCTGG	
10	***Tff3***	F: TTGCTGGGTCCTCTGGGATAG	PMID: 19185845#
		R: TACACTGCTCCGATGTGACAG	
11	***Elf3***	F: GCTGCCACCTGTGAGATCAG	NM_001163131*
		R: GTGCCAAAGGTAGTCGGAGG	
12	***Spdef***	F: AAGGCAGCATCAGGAGCAATG	NM_013891*
		R: CTGTCAATGACGGGACACTG	
13	***Gfi***	F: AGAAGGCGCACAGCTATCAC	NM_010278*
		R: GGCTCCATTTTCGACTCGC	
14	***Math1***	F: GAGTGGGCTGAGGTAAAAGAGT	NM_007500*
		R: GGTCGGTGCTATCCAGGAG	
15	***Muc2***	F: TTCGGCACGAGCAACTTTG	PMID: 32916121#
		R: GGCAGGACACCTTGTCATTG	
16	***Muc6***	F: CGGCTGCGTCTGTCCTAAG	NM_181729*
		R: GCATAGTCACATGGGCATTCCT	
17	***Muc13***	F: GATCTCTGCAACCCTAACCCC	NM_010739*
		R: TCCTTTCACACATGACGACAG	
18	***Il10***	F: GCTCTTACTGACTGGCATGAG	PMID: 32302292#
		R: CGCAGCTCTAGGAGCATGTG	
19	***Tgfβ1***	F: CTCCCGTGGCTTCTAGTGC	NM_011577*
		R: GCCTTAGTTTGGACAGGATCTG	
20	***Il1β***	F: GCAACTGTTCCTGAACTCAACT	NM_008361*
		R: ATCTTTTGGGGTCCGTCAACT	

Sl. No.	Gene	Gene sequence (5`-3`)	GenBank Accession number/Ref.
21	***Il6***	F: CCAAGAGGTGAGTGCTTCCC	PMID: 32302292#
		R: CTGTTGTTCAGACTCTCTCCCT	
22	***Tnfα***	F: CCCTCACACTCAGATCATCTTCT	NM_013693*
		R: GCTACGACGTGGGCTACAG	
23	***Sis***	F: GCTATCGCTCTTGTTGTGGTT	NM_001081137*
		R: TTCCAGGACTAGGGGTTGAAG	
24	***CaII***	F: TCCCACCACTGGGGATACAG	NM_009801*
		R: CTCTTGGACGCAGCTTTATCATA	
25	***Hes1***	F: CCAGCCAGTGTCAACACGA	NM_008235*
		R: AATGCCGGGAGCTATCTTTCT	
26	***Casp3***	F: ATGGAGAACAACAAAACCTCAGT	NM_009810*
		R: TTGCTCCCATGTATGGTCTTTAC	
27	***Casp8***	F: TGCTTGGACTACATCCCACAC	NM_009812*
		R: TGCAGTCTAGGAAGTTGACCA	
28	***Bad***	F: GAGGAGGAGCTTAGCCCTTT	PMID: 32294437#
		R: AGGAACCCTCAAACTCATCG	
29	***Myc***	F: GCTGTTTGAAGGCTGGATTTC	PMID: 32550000#
		R: GATGAAATAGGGCTGTACGGAG	
30	***Bax***	F: TAGCAAACTGGTGCTCAAGG	PMID: 25288756#
		R: TCTTGGATCCAGACAAGCAG	
31	***Bcl2l2***	F: GCGGAGTTCACAGCTCTATAC	NM_007537*
		R: AAAAGGCCCCTACAGTTACCA	
32	***Bcl2***	F: GATGACTGAGTACCTGAACCG	PMID: 25830089#
		R: CAGAGACAGCCAGGAGAAATC	
33	***Villin1***	F: TCAAAGGCTCTCTCAACATCAC	NM_009509*
		R: AGCAGTCACCATCGAAGAAGC	
34	***Epcam***	F: GCGGCTCAGAGAGACTGTG	NM_008532*
		R: CCAAGCATTTAGACGCCAGTTT	
35	***Vimentin***	F: CGTCCACACGCACCTACAG	NM_011701*
		R: GGGGGATGAGGAATAGAGGCT	
36	***Lgr5***	F: CCTACTCGAAGACTTACCCAGT	NM_010195*
		R: GCATTGGGGTGAATGATAGCA	
37	***Olfm4***	F: AAACAATGTCCTTAGCATTCGCC	NM_001030294*
		R: GCTTCCAAGGGCCAATGAAAC	
38	***Sox9***	F: AGTACCCGCATCTGCACAAC	NM_011448*
		R: ACGAAGGGTCTCTTCTCGCT	
39	***Sox4***	F: GACCTGCTCGACCTGAACC	NM_009238*
		R: ACTCCAGCCAATCTCCCGA	
40	***Ngn3***	F: CCAAGAGCGAGTTGGCACT	NM_009719*
		R: CGGGCCATAGAAGCTGTGG	
41	***Chga***	F: ATCCTCTCTATCCTGCGACAC	NM_007693*
		R: GGGCTCTGGTTCTCAAACACT	
42	***Cck***	F: AAGAGCGGCGTATGTCTGTG	NM_031161*
		R: CATCCAGCCCATGTAGTCCC	

Sl. No.	Gene	Gene sequence (5`-3`)	GenBank Accession number/Ref.
43	***Ffar2***	F: CTTGATCCTCACGGCCTACAT	NM_146187*
		R: CCAGGGTCAGATTAAGCAGGAG	
44	***Ffar3***	F: CTAAACCTGACCATTTCGGACC	NM_001033316*
		R: GATAGGCCACGCTCAGAAAAC	
45	***Mct2***	F: GCTGGGTCGTAGTCTGTGC	NM_011391*
		R: ATCCAAGCGATCTGACTGGAG	
46	***Mct1***	F: TGTTAGTCGGAGCCTTCATTTC	NM_009196*
		R: CACTGGTCGTTGCACTGAATA	
47	***Glp1r***	F: ACGGTGTCCCTCTCAGAGAC	NM_021332*
		R: ATCAAAGGTCCGGTTGCAGAA	
48	***Neurog2***	F: AACTCCACGTCCCCATACAG	NM_009718*
		R: GAGGCGCATAACGATGCTTCT	
49	***Gcg***	F: TTACTTTGTGGCTGGATTGCTT	NM_008100*
		R: AGTGGCGTTTGTCTTCATTCA	
50	***Pcsk1***	F: AGTTGGAGGCATAAGAATGCTG	NM_013628*
		R: GCCTTCTGGGCTAGTCTGC	
51	***Pcsk2***	F: AGAGAGACCCCAGGATAAAGATG	NM_008792*
		R: CTTGCCCAGTGTTGAACAGGT	
52	***Slc5a1***	F: AATGCGGCTGACATCTCAGTC	NM_019810*
		R: ACCAAGGCGTTCCATTCAAAG	
53	***Bdnf***	F: TCATACTTCGGTTGCATGAAGG	NM_007540*
		R: AGACCTCTCGAACCTGCCC	
54	***Calb***	F: TCTGGCTTCATTTCGACGCTG	NM_009788*
		R: ACAAAGGATTTCATTTCCGGTGA	
55	***Bmi1***	F: ATCCCCACTTAATGTGTGTCCT	NM_007552*
		R: CTTGCTGGTCTCCAAGTAACG	
56	***Chat***	F: CCATTGTGAAGCGGTTTGGG	NM_009891*
		R: GCCAGGCGGTTGTTTAGATACA	
57	***Dbh***	F: GAGGCGGCTTCCATGTACG	NM_138942*
		R: TCCAGGGGGATGTGGTAGG	
58	***Drd3***	F: CCTCTGAGCCAGATAAGCAGC	NM_007877*
		R: AGACCGTTGCCAAAGATGATG	
59	***Elavl3***	F: ATGGTCACTCAGATACTGGGG	NM_010487*
		R: TTCTGGGGTAGGTAGTTGACG	
60	***Fabp7***	F: GGACACAATGCACATTCAAGAAC	NM_021272*
		R: CCGAACCACAGACTTACAGTTT	
61	***Gfap***	F: GGGGCAAAAGCACCAAAGAAG	NM_001131020*
		R: GGGACAACTTGTATTGTGAGCC	
62	***Mef2c***	F: GTCAGTTGGGAGCTTGCACTA	NM_001170537*
		R: CGGTCTCTAGGAGGAGAAACA	
63	***Myogenin***	F: GAGACATCCCCCTATTTCTACCA	NM_031189*
		R: GCTCAGTCCGCTCATAGCC	

Sl. No.	Gene	Gene sequence (5`-3`)	GenBank Accession number/Ref.
64	***Ngfr***	F: CTAGGGGTGTCCTTTGGAGGT	NM_033217*
		R: CAGGGTTCACACACGGTCT	
65	***Nos1***	F: CTGGTGAAGGAACGGGTCAG	NM_008712*
		R: CCGATCATTGACGGCGAGAAT	
66	***Phox2b***	F: TACGCCGCAGTTCCATACAAACTC	PMID: 30626698#
		R: TCTTTGAGCTGCGCGCTTGTGAAG	
67	***Ret***	F: GCATGTCAGACCCGAACTGG	PMID: 25986924#
		R: CGCTGAGGGTGAAACCATCC	
68	***S100b***	F: TGGTTGCCCTCATTGATGTCT	PMID: 31043739#
		R: CCCATCCCCATCTTCGTCC	
69	***Sox10***	F: GAAGCCCCACATCGACTTCG	NM_011437*
		R: GGCAGGTATTGGTCCAGCTC	
70	***Tac1***	F: ATTCCTTTGTTGGACTAATGGGC	NM_145123*
		R: ACGTCTTCTTTCGTAGTTCTGC	
71	***Tert***	F: GCACTTTGGTTGCCCAATG	NM_009354*
		R: GCACGTTTCTCTCGTTGCG	
72	***Htr1a***	F: GACAGGCGGCAACGATACT	NM_008308*
		R: CCAAGGAGCCGATGAGATAGTT	
73	***Tubb3***	F: TAGACCCCAGCGGCAACTAT	NM_001080971*
		R: GTTCCAGGTTCCAAGTCCACC	
74	***Vip***	F: AGTGTGCTGTTCTCTCAGTCG	NM_011702*
		R: GCCATTTTCTGCTAAGGGATTCT	
75	***Uchl1***	F: AGGGACAGGAAGTTAGCCCTA	NM_011670*
		R: AGCTTCTCCGTTTCAGACAGA	
76	***Mcp1***	F: TTAAAAACCTGGATCGGAACCAA	NM_011333*
		R: GCATTAGCTTCAGATTTACGGGT	
77	***18s***	F: GCAATTATTCCCCATGAACG	PMID: 32302292#
		R: GGCCTCACTAAACCATCCAA	

* The accession number and primer sequences are optained from Harvard primer bank

The primer sequence optained from the published article that mentioned herewith PMID

Supplementary Table S2. RFA (Randon forest analysis) of intestinal specific marker gene expression in mice administration with Young vs Old FMT (fecal microbiome transplant)

FMT administration to Mice				
Sl. No.	**Gene**	**Young FMT**	**Old FMT**	**p-Value**
				Young vs Old FMT
1	*Muc2*	0.950	0.074	0.000
2	*Mct1*	1.026	0.264	0.000
3	*Myogenin*	1.015	0.118	0.000
4	*Drd3*	1.000	0.287	0.000
5	*Math1*	1.035	0.085	0.000
6	*Gfi*	0.960	0.047	0.000
7	*Sox9*	0.988	4.215	0.000
8	*Bcl2*	1.009	0.186	0.000
9	*Zo1*	0.991	0.110	0.001
10	*Elavl3*	0.951	0.137	0.000
11	*Gfap*	0.977	3.117	0.000
12	*Tnfα*	0.987	9.307	0.000
13	*Casp8*	1.000	2.101	0.010
14	*Muc13*	0.988	2.150	0.008
15	*Bcl2l2*	0.990	0.162	0.000
16	*Muc6*	1.007	0.126	0.000
17	*Mef2c*	0.979	4.701	0.000
18	*Bdnf*	1.030	0.249	0.000
19	*Ffar2*	0.943	0.060	0.000
20	*Il10*	1.015	0.246	0.013
21	*Bad*	0.995	10.926	0.001
22	*Epcam*	0.926	5.458	0.000
23	*Villin*	0.931	3.490	0.003
24	*Hes1*	0.963	3.609	0.001
25	*Tgfβ1*	1.031	0.228	0.000
26	*Lyz1*	1.005	5.326	0.002
27	*Ffar3*	0.982	0.091	0.000
28	*Calb*	0.995	0.202	0.006
29	*Il6*	0.980	4.825	0.000
30	*Tert*	0.943	0.164	0.000

Supplementary Table S3. Fold change and p-Value of metabolite abundance in Young vs Old Donor Mice according to RFA (Randon forest analysis)

Sl. No.	Metabolite	Young	Old	p-Value
				Young vs Old
1	Butyrate	1.275	0.789	0.000
2	Taurine	1.485	0.639	0.002
3	Propionate	1.136	0.861	0.003
4	Cholate	0.432	1.579	0.000
5	Acetate	1.402	0.764	0.000
6	Anserine	0.681	1.331	0.000
7	Methanol	0.989	0.713	0.008
8	Valine	0.711	1.291	0.000
9	3-Phenylpropionate	1.415	0.806	0.065
10	Glycine	1.161	0.900	0.005
11	3-Hydroxyisobutyrate	1.053	0.966	0.322
12	Total bile acid & cholesterol	0.579	1.259	0.000
13	3-Methyl-2-oxovalerate	0.796	1.132	0.002
14	Xylose	1.642	0.756	0.003
15	Choline	1.070	0.925	0.045
16	Isoleucine	0.850	1.126	0.005
17	4-Hydroxyisophenylacetate	1.172	0.957	0.000
18	Tartrate	0.868	1.100	0.050
19	Arabinose	0.929	1.030	0.181
20	Ethanolamine	0.850	1.061	0.025
21	2-Hydroxyisobutyrate	1.087	0.891	0.023
22	Leucine	0.815	1.093	0.006
23	Pyruvate	1.148	0.929	0.035
24	Glutamine	1.104	0.956	0.037
25	Hypoxanthine	1.145	0.873	0.034
26	Formate	0.889	1.120	0.014
27	Dimethylamine	0.973	1.059	0.319
28	Furmate	1.555	0.591	0.002
29	Ethanol	0.920	1.038	0.066
30	Alanine	0.976	0.957	0.334

Supplementary Table S4. Details of chemicals and reagents used in this study.

S. No.	Name	Cat. Number	Vendor
Chemicals and Reagents			
1	Ampicillin	A0166	Sigma
2	Metronidazole	M1547	Sigma
3	Neomycin	N6386	Sigma
4	Vancomycin	195540	MP Biochemicals
5	polyethylene glycol	25322-68-3	Millipore Sigma
6	Resazurin	R7017	Sigma Aldrich
7	L-cysteine-HCl	2430	Calbiochem, EMD Millipore Corp.
8	Butyrate	B5887	Sigma
9	Acetate	S5636	Sigma
10	Proionate	P5436	Sigma
9	4-kD-FITC (Fluroescein isothiocyanate)-dextran	FD4	Sigma Aldrich
10	LBP ELISA kit	HK205-01	Hycult Biotech Inc.
11	sCD14 ELISA kit	MC140	R&D Systems
12	IL6 ELISA kit	KMC0061	Invitrogen
13	TNFα ELISA kit	BMS607-3	Invitrogen
14	Fecal Mucin ELISA kit	FFA-MU-KO1	Cosmo BioCo. Ltd
15	Hematoxylin and Eosin	3530-16	Ricca
16	Alcian Blue/PAS staining kit	395B-1KT	Sigma Aldrich
17	QiaAmp PowerFecal Pro kit (50)	2830-50	Qiagen
18	Miseq reagent kit v3	MS-102-3003	Illumina
19	Agencourt AMPure XP 60ml kit	A63881	Beckman Coulter Genomics
20	0.45 µm pore nylon membrane sterile filter	431225	Corning Incorporated
21	0.22 µm nylon membrane sterile syringe filter	379-2215-OEM	EZFlow, Foxx, Life Sciences
22	Dulbecco`s phosphate buffered saline (DPBS)	17-512F	BioWhittaker
23	Trypsin	25300-054	Gibco, Life technologies
24	Bovine serum albumin (BSA)	BP1600-100	Fisher Scientific
25	70µm cell strainer	352350	Falcon, Corning Incorporation
26	Dulbecco's Modified Eagle Medium: Nutrient Mixture F-12 (DMEM/F12)	11330-032	Gibco, Life technologies
27	IntestiCult Organoid Growth Medium	#06005	Stemcell
28	Gentamicin	15710-064	Gibco, Life technologies
29	Matrigel Matrix	354230	Corning
30	CATBP	5903	Tocris
31	Pertussis Toxin	PHZ1174	Invitrogen
32	4.5 g/L D-Glucose with L-Glutamine DMEM	11995-065	Gibco
33	Fetal bovine serum (FBS)	26140-079	Gibco
34	100 U/mL penicillin, 100 U/mL streptomycin	15140-122	Gibco
35	0.4 µm pore size of 12-well transwell plates	3460	Costar, Corning
36	Trimethylsilylpropanoic acid (TSP)	AC432120010	ThermoFisher Scientific
37	HT-29 cells	HTB-38	ATCC
38	CMT-93	CCL-223	ATCC
39	RNeasy Mini Kit	74106	Qiagen
40	High-Capacity cDNA reverse transcription kit	4368814	Applied Biosystems
41	PowerUp SYBR Green master mix	100029284	Applied Biosystem

Supplementary Table S4. Details of instruments used in this study.

Instruments			
1	Fluorescence 96-well plate reader		PolarStar Omega, BMG Labtech
2	AmScope microscope		Nikon Corporation
3	MiSeq Sequencer		Illumina
4	Qubit-3 Fluorimeter		Invitrogen
5	Bruker Ascend 400 MHz high-resolution NMR		Bruker Biospin
6	Refrigerated Centrifuge machine		Eppendroff
7	EVOM2 Epithelial Voltohmmeter		WPI
8	NMR		Bruker BioSpin
9	7500 qRTPCR machine	4351106	Applied Biosystem

Supplementary Table S5. The human gene primer sequence

Sl. No.	Gene	Seuence	Asseccion No.
1	h*Ffar2*	F: CCGTGCAGTACAAGCTCTCC	NM_005306*
		R: CTGCTCAGTCGTGTTCAAGTATT	
2	h*Ffar3*	F: TTCACCACCATCTATCTCACCG	NM_005304*
		R: GGAACTCCAGGTAGCAGGTC	

* The accession number and primer sequences are optained from Harvard primer bank

Supplementary Table S6. The buk and but gene primer sequence

Sl. No.	Gene	Seuence	Asseccion No.
1	*But*	F: GCIGAICATTTCACITGGAAYWSITGGCAYATG	PMID: 30212649
		R: CCTGCCTTTGCAATRTCIACRAANGC	
2	*Buk*	5F1: CCATGCATTAAATCAAAAAGC	PMID: 23836895
		5F2: CCATGCGTTAAACCAAAAAGC	
		6R1: AGTACCTCCACCCATGTG	
		6R2: AATACCTCCGCCCATATG	
		6R3: AATACCGCCRCCCATATG	
3	Total Bacteria	F: GCAGGCCTAACACATGCAAGTC	PMID: 23836895
		R: CTGCTGCCTCCCGTAGGAGT	