

Supplemental Materials

Table S1. Disease activity index scoring system

| Score | Weight loss (%) | Fecal consistency | Blood in feces |
|-------|-----------------|----------------------|-----------------------------|
| 0 | None | Normal | Negative (no bleeding) |
| 1 | 1%-5% | Fecal fluffiness | Negative |
| 2 | 6%-10% | Loose stools | Hemoccult positive (slight) |
| 3 | 11%-18% | Loose and damp stool | Hemoccult positive |
| 4 | >18% | Diarrhea | Gross bleeding |

Table S2. Murine endoscopic index of colitis severity (MEICS) scores.

| | Murine endoscopic index of colitis severity (MEICS) | | | | |
|------------------------------------|---|--------------|----------|---------------|--------------|
| | 0 | 1 | 2 | 3 | Total |
| Thickening of the colon | transparent | moderate | marked | untransparent | 0-3 |
| Changes of the vascular pattern | Normal | moderate | marked | bleeding | 0-3 |
| Fibrin visible | None | little | marked | extreme | 0-3 |
| Granularity of the mucosal surface | None | moderate | marked | extreme | 0-3 |
| Stool consistence | normal +solid | still shaped | unshaped | spread | 0-3 |
| | | | | Overall: | 0-15 |

Table S3. Histopathological scores

| Score | Inflammation severity | Crypt Damage | Inflammation extent | Extent of disease |
|--------------|------------------------------|--|----------------------------|--------------------------|
| 0 | None | None | None | None |
| 1 | Mild | Basal 1/3 damage | Mucosa | 1%-25% |
| 2 | Moderate | Basal 2/3 damage | Submucosa | 26%-50% |
| 3 | Severe | Crypt lost, surface epithelium present | Transmural | 51%-75% |
| 4 | – | Crypt lost, surface epithelium lost | – | 76%-100% |

Table S4. Primer sequences

| Genes | Primer sequences (5' to 3') |
|----------------|-----------------------------|
| IL-6 | F: CTCCCAACAGACCTGTCTATAC |
| | R: CCATTGCACAACCTTTTCTCA |
| TNF- α | F: CTCCCAACAGACCTGTCTATAC |
| | R: CCACAAGCAGGAATGAGAAGAGG |
| IL-1 β | F: TCGCAGCAGCACATCAACAAGAG |
| | R: TGCTCATGTCCTCATCCTGGAAGG |
| IL-2 | F: GTGCTCCTTGCAACAGCG |
| | R: GGGGAGTTTCAGGTCCTGTA |
| IL-17A | F: TTAACTCCCTGGCGCAAAA |
| | R: CTTTCCCTCCGCATTGACAC |
| iNOS | F: ACTCAGCCAAGCCCTCACCTAC |
| | R: TCCAATCTCTGCCTATCCGTCTCG |
| Muc2 | F: ATGCCACCTCCTCAAAGAC |
| | R: GTAGTTCCGTTGGAACAGTGAA |
| β -actin | F: CTACCTCATGAAGATCCTGACC |
| | R: CACAGCTTCTTTGATGTCAC |

Table S5. The all metabolites information in MSS.

| No. | RT [min] | m/z | Metabolites name | Ontology |
|-----|----------|---------|--|--|
| 1 | 4.060 | 131.072 | 2-Hydroxy-4-methylpentanoic acid | Hydroxy fatty acids |
| 2 | 4.444 | 165.056 | 3-Phenyllactic acid | Phenylpropanoic acids |
| 3 | 7.864 | 415.212 | Niranthin | Dibenzylbutane lignans |
| 4 | 1.382 | 121.065 | Phenylacetaldehyde | Phenylacetaldehydes |
| 5 | 1.430 | 132.102 | Norleucine | L-alpha-amino acids |
| 6 | 1.429 | 132.102 | D-Alloisoleucine | Isoleucine and derivatives |
| 7 | 1.431 | 132.102 | Isoleucine | Isoleucine and derivatives |
| 8 | 1.506 | 130.086 | Leucine | Leucine and derivatives |
| 9 | 9.905 | 149.023 | 4-Methylthio-2-oxobutanoic acid | Thia fatty acids |
| 10 | 7.104 | 274.274 | Lauryldiethanolamine | 1,2-aminoalcohols |
| 11 | 1.682 | 164.072 | Phenylalanine | Phenylalanine and derivatives |
| 12 | 1.980 | 181.051 | 3-(4-Hydroxyphenyl)lactic acid | Phenylpropanoic acids |
| 13 | 4.445 | 147.045 | Cinnamic acid | Cinnamic acids |
| 14 | 1.161 | 116.071 | Proline | Proline and derivatives |
| 15 | 4.445 | 119.050 | 4-Vinylphenol | Styrenes |
| 16 | 1.201 | 118.086 | Valine | Valine and derivatives |
| 17 | 7.161 | 318.299 | Phytosphingosine | 1,3-aminoalcohols |
| 18 | 1.166 | 151.026 | Oxypurinol | Xanthines |
| 19 | 1.166 | 151.026 | Xanthine | Xanthines |
| 20 | 2.045 | 117.056 | 3-Hydroxyvaleric acid | Hydroxy fatty acids |
| 21 | 1.980 | 203.082 | Tryptophan | Indolyl carboxylic acids and derivatives |
| 22 | 4.655 | 204.066 | Indolelactic acid | Indolyl carboxylic acids and derivatives |
| 23 | 9.902 | 279.159 | Di-n-butyl phthalate | Benzoic acid esters |
| 24 | 1.371 | 129.019 | Itaconic acid | Organic acids |
| 25 | 16.180 | 118.086 | Betaine | Alpha amino acids |
| 26 | 8.131 | 302.305 | Tetradecyldiethanolamine | 1,2-aminoalcohols |
| 27 | 7.161 | 230.247 | N,N-Dimethyldodecylamine N-oxide | Long-chain alkyl amine oxides |
| 28 | 5.969 | 163.039 | 4-Methylphthalic anhydride | Phthalic anhydrides |
| 29 | 5.971 | 163.039 | Umbelliferone | 7-hydroxycoumarins |
| 30 | 7.396 | 593.129 | [6-[2-(3,4-dihydroxyphenyl)-8-hydroxy-4-oxochromen-7-yl]oxy-3,4,5-trihydroxyoxan-2-yl]methyl (E)-3-(4-hydroxyphenyl)prop-2-enoate | NA |
| 31 | 1.424 | 86.096 | Piperidine | Piperidines |
| 32 | 4.018 | 955.484 | (3R,4R,6aR,6bS,8aS,14bR)-8a-[6-[[3,4-dihydroxy-6-(hydroxymethyl)-5-[(2S,3R,4R,5R,6S)-3,4,5-trihydroxy-6-methylloxan-2-yl]oxyoxan-2-yl]oxymethyl]-3,4,5-trihydroxyoxan-2-yl]oxycarbonyl-3-hydroxy-4,6a,6b,11,11,14b-hexamethyl-1,2,3,4a,5,6,7,8,9,10,12,12a,14,14a- | Triterpene saponins |

| | | | | |
|----|--------|---------|---|--|
| | | | tetradecahydricene-4-carboxylic acid | |
| 33 | 12.296 | 338.341 | Erucamide | Fatty amides |
| 34 | 4.915 | 187.097 | Azelaic acid | Organic acids |
| 35 | 1.093 | 104.107 | Choline | Cholines |
| 36 | 1.974 | 135.045 | Phenylacetic acid | Benzene and substituted derivatives |
| 37 | 1.980 | 163.040 | Phenylpyruvic acid | Phenylpyruvic acid derivatives |
| 38 | 8.503 | 265.148 | Lauryl sulfate | Sulfuric acid monoesters |
| 39 | 10.052 | 250.144 | 2,6-Di-tert-butyl-4-nitrophenol | Nitrophenols |
| 40 | 6.584 | 149.023 | Phthalic anhydride | Phthalic anhydrides |
| 41 | 6.142 | 329.233 | FA 18:1+3O | Oxidized fatty acids |
| 42 | 6.142 | 329.233 | (Z)-5,8,11-trihydroxyoctadec-9-enoic acid | Long-chain fatty acids |
| 43 | 1.438 | 117.020 | Succinic acid | Organic acids |
| 44 | 5.927 | 139.111 | Isophorone | Cyclohexenones |
| 45 | 1.121 | 116.072 | 5-Aminovaleric acid | Delta amino acids and derivatives |
| 46 | 1.387 | 138.091 | Tyramine | Phenethylamines |
| 47 | 1.205 | 130.049 | L-5-Oxoproline | Alpha amino acids and derivatives |
| 48 | 8.198 | 258.279 | Myristamine oxide | Long-chain alkyl amine oxides |
| 49 | 7.866 | 453.168 | 5-O-methylvisammioside | Furanochromones |
| 50 | 4.340 | 862.429 | N-[3-[5,17-bis[3-[acetyl(hydroxy)amino]propyl]-14-benzyl-8-(hydroxymethyl)-11-(2-methylpropyl)-3,6,9,12,15,18-hexaoxo-1,4,7,10,13,16-hexazacyclooctadec-2-yl]propyl]-N-hydroxyacetamide | NA |
| 51 | 7.610 | 429.118 | 6,7-dimethoxy-1-phenyl-8H-benzo[c]indolo[3,2,1-ij][1,5]naphthyridin-8-one | Indolonaphthyridine alkaloids |
| 52 | 8.016 | 313.238 | Octadecanedioic acid | Long-chain fatty acids |
| 53 | 9.106 | 233.154 | (4S,5Z,6S)-4-(2-methoxy-2-oxoethyl)-5-[2-[(E)-3-phenylprop-2-enoyl]oxyethylidene]-6-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy-4H-pyran-3-carboxylic acid | Eremophilane, 8,9-secoeremophilane and furoeremophilane sesquiterpenoids |
| 54 | 9.106 | 233.154 | (E)-5-(2,3-dimethyl-4,5,6,7-tetrahydro-1H-tricyclo[2.2.1.0 ^{2,6}]heptan-3-yl)-2-methylpent-2-enoic acid | Sesquiterpenoids |
| 55 | 8.014 | 313.237 | 9,10-DiHOME | Long-chain fatty acids |
| 56 | 9.877 | 325.183 | Dodecylbenzenesulfonic acid | Benzenesulfonic acids and derivatives |
| 57 | 10.677 | 339.199 | Canrenone | Steroid lactones |
| 58 | 12.058 | 391.283 | Diocetyl Phthalate | Benzoic acid esters |
| 59 | 7.531 | 460.269 | Bullatine B | Aconitane-type diterpenoid alkaloids |
| 60 | 4.648 | 351.250 | 1,4-dihydroxyheptadec-16-en-2-yl acetate | Long-chain fatty alcohols |
| 61 | 4.362 | 195.066 | Hydroferulic acid | Phenylpropanoic acids |
| 62 | 1.205 | 147.030 | Citramalic acid | Hydroxy fatty acids |

| | | | | |
|-----|--------|---------|------------------------------------|-------------------------------------|
| 63 | 1.099 | 146.046 | Glutamic acid | Glutamic acid and derivatives |
| 64 | 12.037 | 413.266 | 2-acetoxy-4-pentadecylbenzoic acid | Acylsalicylic acids |
| 65 | 1.223 | 133.014 | Malate | Beta hydroxy acids and derivatives |
| 66 | 1.144 | 247.140 | Octopine | Arginine and derivatives |
| 67 | 1.192 | 129.019 | Mesaconic acid | Methyl-branched fatty acids |
| 68 | 1.192 | 129.019 | Citraconic acid | Methyl-branched fatty acids |
| 69 | 4.479 | 206.082 | N-acetylphenylalanine | Phenylalanine and derivatives |
| 70 | 1.433 | 73.030 | Propionic acid | Carboxylic acids |
| 71 | 1.077 | 181.072 | Mannitol | Sugar alcohols |
| 72 | 1.077 | 181.072 | Sorbitol | Sugar alcohols |
| 73 | 8.000 | 279.232 | Linolenic acid | Lineolic acids and derivatives |
| 74 | 11.132 | 427.302 | Leupeptin | Dipeptides |
| 75 | 1.101 | 154.062 | Histidine | Histidine and derivatives |
| 76 | 1.200 | 191.020 | Citric acid | Organic acids |
| 77 | 9.366 | 540.330 | LPC 16:0 | Lipids |
| 78 | 7.855 | 313.237 | FA 18:1+2O | Long-chain fatty acids |
| 79 | 6.562 | 329.136 | Decursinol angelate | Linear pyranocoumarins |
| 80 | 1.702 | 218.103 | Pantothenate | Secondary alcohols |
| 81 | 1.360 | 182.081 | Tyrosine | Tyrosine and derivatives |
| 82 | 8.009 | 337.235 | 8-Hydroxy-9,10-epoxystearic acid | Lineolic acids and derivatives |
| 83 | 10.386 | 299.259 | 12-Hydroxyoctadecanoic acid | Long-chain fatty acids |
| 84 | 10.387 | 299.258 | (R)-2-hydroxystearic acid | Long-chain fatty acids |
| 85 | 8.534 | 311.222 | FA 18:2+2O | Oxidized fatty acids |
| 86 | 1.161 | 258.110 | sn-Glycero-3-phosphocholine | Glycerophosphocholines |
| 87 | 1.204 | 421.073 | Mangiferin | Xanthenes |
| 88 | 1.415 | 175.024 | Ascorbic acid | Butenolides |
| 89 | 1.360 | 111.008 | Pyruvic acid | Alpha-keto acids and derivatives |
| 90 | 1.205 | 259.022 | D-Glucose-6-phosphate | Hexose phosphates |
| 91 | 9.504 | 297.242 | FA 18:1+1O | Oxidized fatty acids |
| 92 | 2.129 | 178.054 | Cyclamate | Cyclamates |
| 93 | 10.372 | 283.263 | Elaidic acid | Long-chain fatty acids |
| 94 | 8.808 | 302.305 | Dihydrosphingosine | 1,2-aminoalcohols |
| 95 | 8.157 | 318.299 | D-ribo-Phytosphingosine | 1,3-aminoalcohols |
| 96 | 8.858 | 564.330 | LPC 18:2 | Lipids |
| 97 | 9.641 | 522.354 | 1_18_1_lyso phosphatidylcholine | 1-acyl-sn-glycero-3-phosphocholines |
| 98 | 1.075 | 75.009 | Glycolic acid | Alpha hydroxy acids and derivatives |
| 99 | 4.716 | 197.117 | Loliolide | Benzofurans |
| 100 | 7.630 | 355.222 | 10-Shogaol | Shogaols |
| 101 | 5.858 | 327.217 | FA 18:2+3O | Oxidized fatty acids |

| | | | | |
|-----|--------|---------|--|--|
| 102 | 5.858 | 327.217 | (10E,15Z)-9,12,13-trihydroxyoctadeca-10,15-dienoic acid | Lineolic acids and derivatives |
| 103 | 1.204 | 611.143 | Glutathione | Peptides |
| 104 | 1.198 | 259.022 | Glucose-1-phosphate | Monosaccharide phosphates |
| 105 | 9.106 | 496.339 | (6aR,8aS)-11-(3-acetamido-2-methylpropyl)-6a,8a,9-trimethyl-10-oxo-1,3,4,5,6,6a,6b,7,8,8a,8b,9,10,12,12a,12b-hexadecahydropentaleno[2,1-a]phenanthren-4-yl acetate | Steroid esters |
| 106 | 10.107 | 295.226 | 9-HODE | Lineolic acids and derivatives |
| 107 | 9.614 | 478.292 | LPE 18:1 | Lipids |
| 108 | 1.196 | 173.009 | trans-Aconitic acid | Tricarboxylic acids and derivatives |
| 109 | 9.591 | 281.247 | Linoleic acid | Lineolic acids and derivatives |
| 110 | 9.081 | 452.276 | LPE 16:0 | Lipids |
| 111 | 4.470 | 359.167 | Vindoline | Carbazoles |
| 112 | 8.817 | 476.277 | LPE 18:2 | Lipids |
| 113 | 5.531 | 269.136 | 4-benzyl-7-hydroxy-1-hydroxymethyl-3,5,6,7-tetrahydro-8h-pyrrolizinium | Alkaloids and derivatives |
| 114 | 10.690 | 321.239 | 6-Oxocatic acid | Isoprene diterpenes |
| 115 | 1.559 | 229.032 | 5-(1,2-dithiolan-3-yl)pentanoic acid | Lipoic acids and derivatives |
| 116 | 9.623 | 357.299 | monoolein | Monoradylglycerols |
| 117 | 8.267 | 562.314 | LPC 18:3 | Lipids |
| 118 | 8.630 | 476.277 | 1-Hydroxy-2-(9Z,12Z-octadecadienoyl)-sn-glycero-3-phosphoethanolamine | 2-acyl-sn-glycero-3-phosphoethanolamines |
| 119 | 9.321 | 293.211 | FA 18:2+O | Long-chain fatty acids |
| 120 | 9.437 | 566.344 | LPC 18:1 | Lipids |
| 121 | 6.377 | 345.087 | Lysionotin | 8-O-methylated flavonoids |
| 122 | 9.588 | 355.177 | Dehydroandrographolide | Butenolides |
| 123 | 1.077 | 105.019 | D-Glyceric acid | Sugar acids and derivatives |

Table S6. The information of metabolites with significant difference between DSS group and MSS group.

| No. | RT [min] | m/z | Metabolites name | Ontology |
|-----|----------|---------|---|---|
| 1 | 0.575 | 140.068 | Betaine | Alpha amino acids |
| 2 | 0.589 | 104.107 | Choline | Cholines |
| 3 | 1.082 | 218.102 | Pantothenic acid | Secondary alcohols |
| 4 | 2.921 | 261.139 | gamma-Glutamylleucine | Dipeptides |
| 5 | 3.222 | 321.130 | Pseudo-anisatin | Lactones |
| 6 | 3.247 | 212.002 | Indoxyl sulfate | Arylsulfates |
| 7 | 3.252 | 321.130 | Mycophenolic acid | Phthalides |
| 8 | 3.252 | 283.175 | Hexaethylene glycol | Polyethylene glycols |
| 9 | 3.662 | 365.157 | MMV659004 | Pyridinylpyrimidines |
| 10 | 3.962 | 393.209 | Octaethylene glycol | Polyethylene glycols |
| 11 | 4.085 | 347.168 | Quinidine | Cinchona alkaloids |
| 12 | 4.345 | 467.247 | Bufotalin | Bufanolides and derivatives |
| 13 | 5.103 | 717.367 | Subsessiline | Aspidospermatan-type alkaloids |
| 14 | 5.149 | 517.308 | Ganoderic acid A | Triterpenoids |
| 15 | 5.201 | 761.392 | Polyphyllin VI | Steroidal saponins |
| 16 | 5.206 | 745.419 | Prosapogenin A | Steroidal saponins |
| 17 | 5.299 | 789.445 | Scabioside C | Triterpenoids |
| 18 | 5.931 | 539.281 | Oleaside A | O-glycosyl compounds |
| 19 | 6.994 | 516.299 | Taurocholic acid | Trihydroxy bile acids, alcohols and derivatives |
| 20 | 9.994 | 357.279 | Deoxycholate | Dihydroxy bile acids, alcohols and derivatives |
| 21 | 5.039 | 144.045 | 4-Hydroxyquinoline | Hydroquinolones |
| 22 | 5.039 | 144.045 | 2-hydroxyquinoline | Hydroquinolones |
| 23 | 5.197 | 261.133 | 9-(2,3-dihydroxypropoxy)-9-oxononanoic acid | Medium-chain fatty acids |
| 24 | 5.44 | 187.097 | Azelaic acid | Medium-chain fatty acids |
| 25 | 9.805 | 391.284 | Hyodeoxycholic acid | Dihydroxy bile acids, alcohols and derivatives |
| 26 | 9.805 | 391.284 | Chenodiol | Dihydroxy bile acids, alcohols and derivatives |
| 27 | 10.789 | 317.210 | 12-HEPE | Hydroxyeicosapentaenoic acids |
| 28 | 10.863 | 295.228 | 9-hydroxy-10,12-octadecadienoic acid | Lineolic acids and derivatives |
| 29 | 10.863 | 295.228 | 12,13-EODE | Long-chain fatty acids |
| 30 | 10.868 | 277.216 | gamma-Linolenic acid | Lineolic acids and derivatives |
| 31 | 10.934 | 297.241 | FA 18:1+10 | Oxidized fatty acids |
| 32 | 10.969 | 452.278 | LPE 16:0 | Lipids |
| 33 | 11.01 | 319.228 | 9-HETE | Hydroxyeicosatetraenoic acids |
| 34 | 11.379 | 327.233 | Docosahexanoic acid | Very long-chain fatty acids |
| 35 | 11.647 | 293.177 | Tetradecylsulfate | Sulfuric acid monoesters |
| 36 | 11.379 | 327.233 | Docosahexaenoic acid | Very long-chain fatty acids |

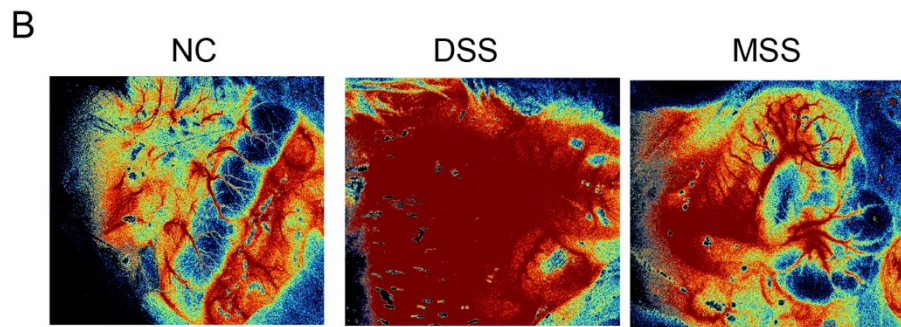
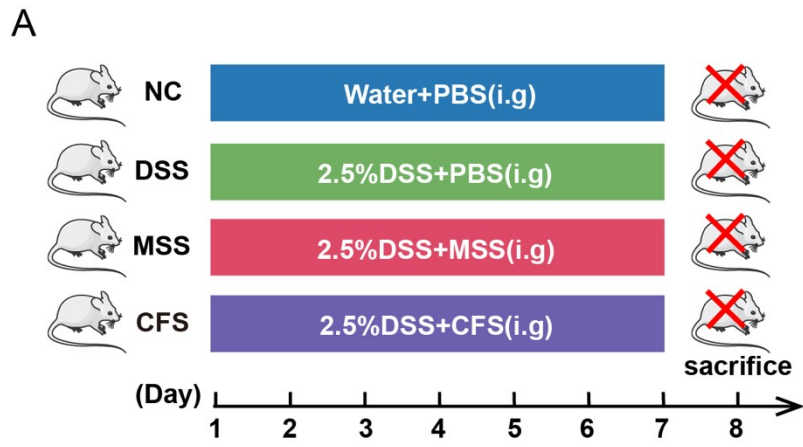
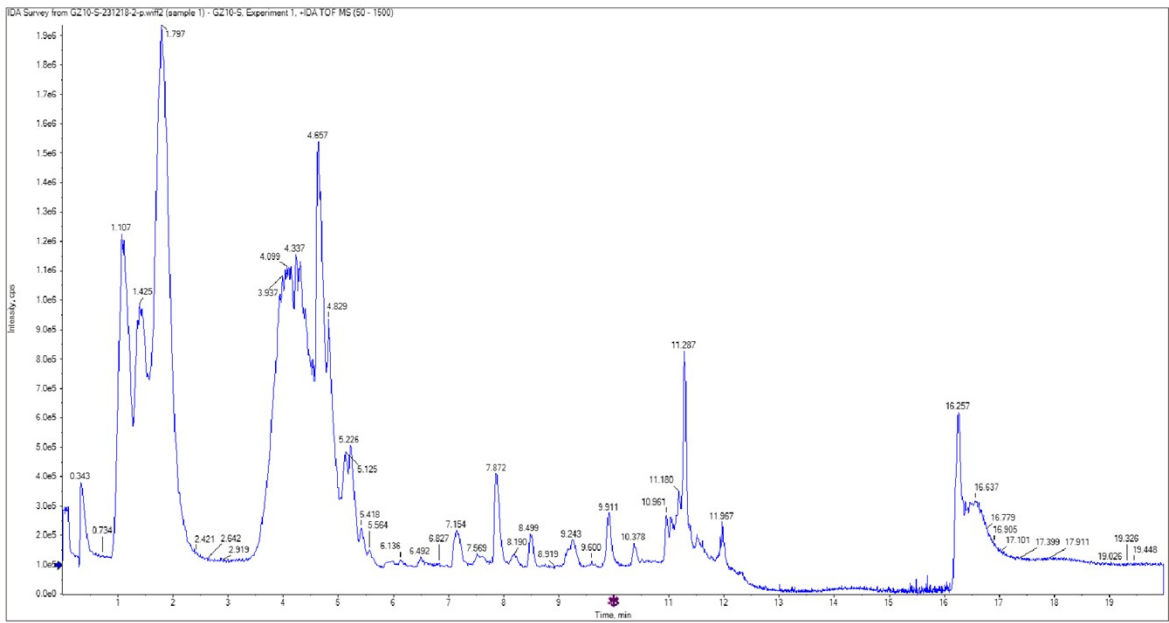
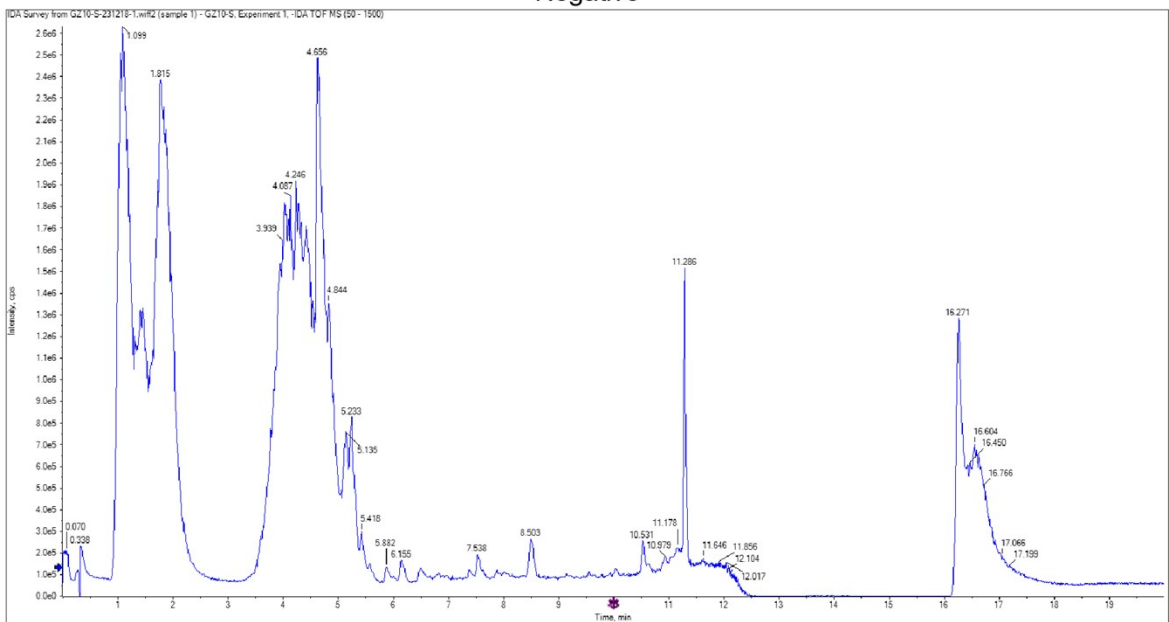


Fig S1. (A) Animals experimental protocol. (B) Representative images of mesenteric vascular microcirculation.

A**Positive****B****Negative****Fig S2.** Total ion chromatograms of MSS in positive(A) and negative(B) ion modes.

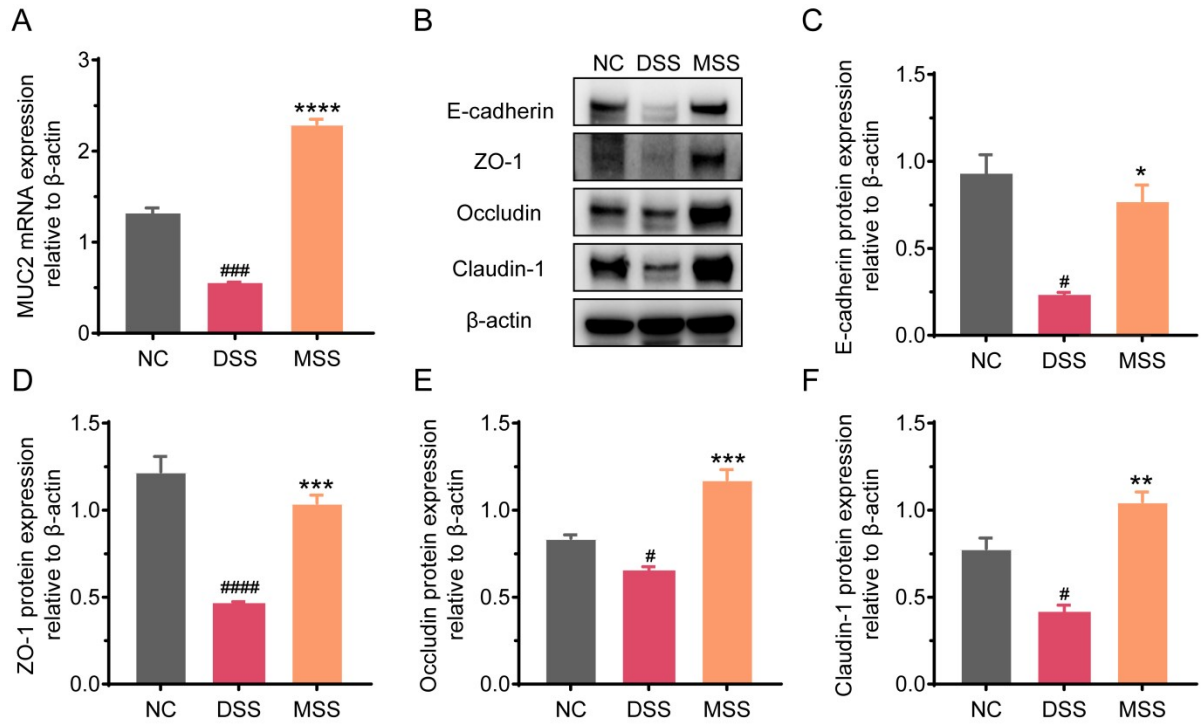


Fig S3. MSS repaired the gut barrier in DSS-induced colitis mice. (A) The mRNA level of MUC2. (B) Representative images of western blotting. Protein expression levels of E-cadherin (C), ZO-1 (D), Occludin (E), and Claudin-1 (F). Significant differences compared to NC group are denoted by #: $p < 0.05$, ###: $p < 0.001$; significant differences compared to DSS group are denoted by *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$, ****: $p < 0.0001$.

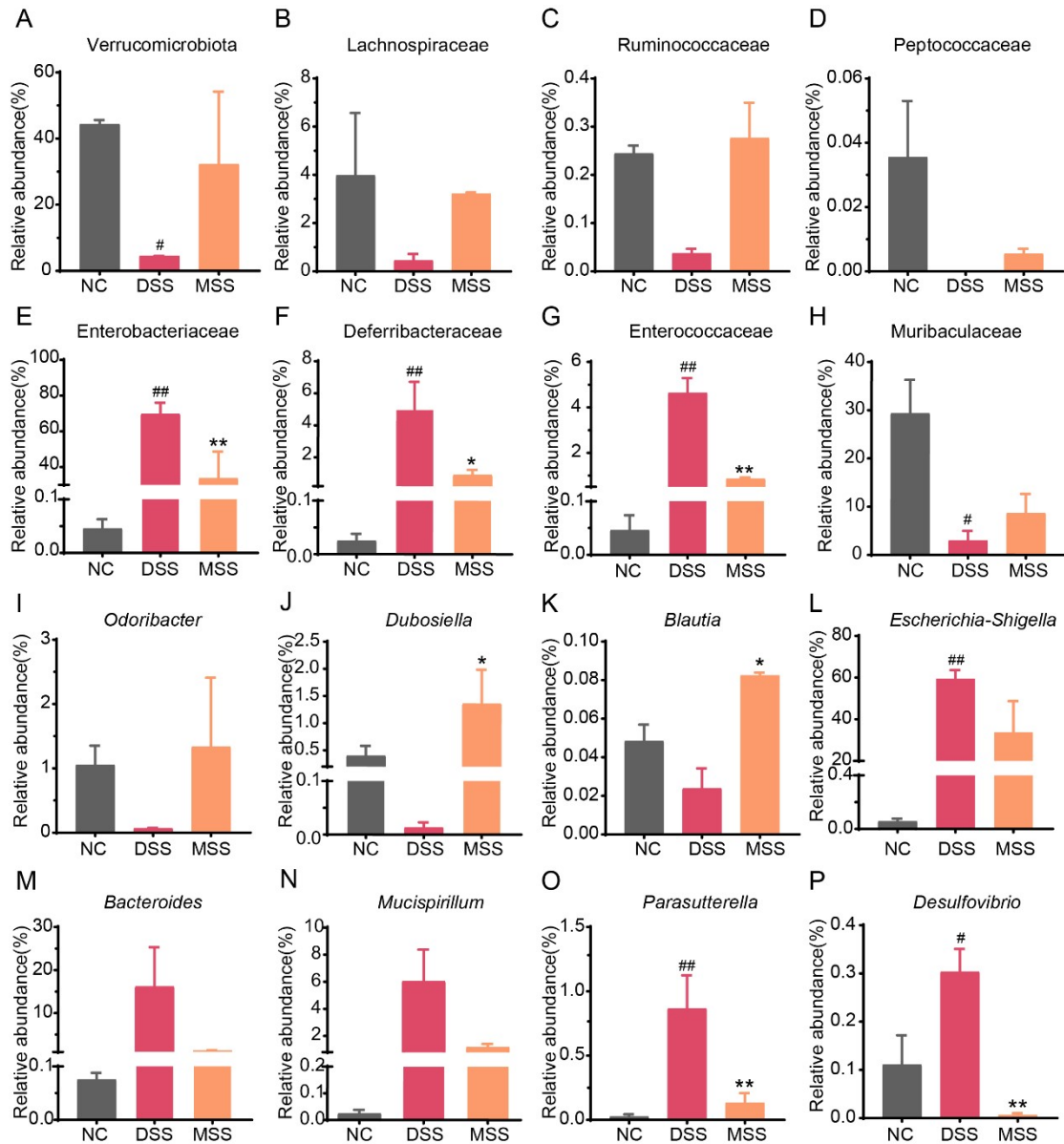


Fig S4. MSS modulated gut microbiota composition in DSS-induced colitis mice. (A-P) Relative abundance of Verrucomicrobiota, Lachnospiraceae, Ruminococcaceae, Peptococcaceae, Enterobacteriaceae, Deferribacteraceae, Enterococcaceae, Muribaculaceae, *Odoribacter*, *Dubosiella*, *Blautia*, *Escherichia-Shigella*, *Bacteroides*, *Mucispirillum*, *Parasutterella*, and *Desulfovibrio*. Data are shown as mean \pm SEM. Significant differences compared to NC group are denoted by #: $p < 0.05$, ##: $p < 0.01$; significant differences compared to DSS group are denoted by *: $p < 0.05$, **: $p < 0.01$.

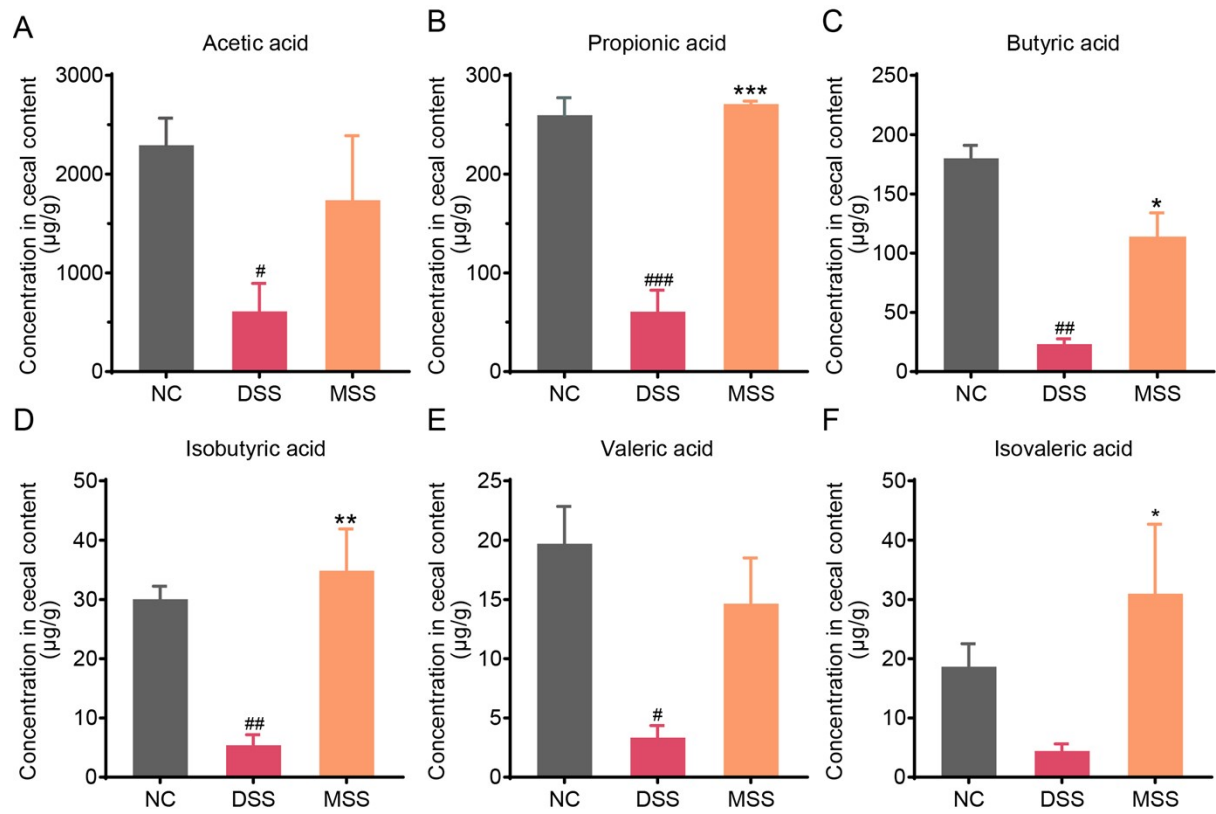


Fig S5. MSS increased the Concentration of short-chain fatty acids in cecum of mice with DSS induced colitis. (A–F) Concentration of Acetic acid, Propionic acid, Butyric acid, Isobutyric acid, Valeric acid, and Isovaleric acid in the cecal content. Data are shown as mean \pm SEM. Significant differences compared to NC group are denoted by #: $p < 0.05$, ##: $p < 0.01$, ###: $p < 0.001$; significant differences compared to DSS group are denoted by *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$.

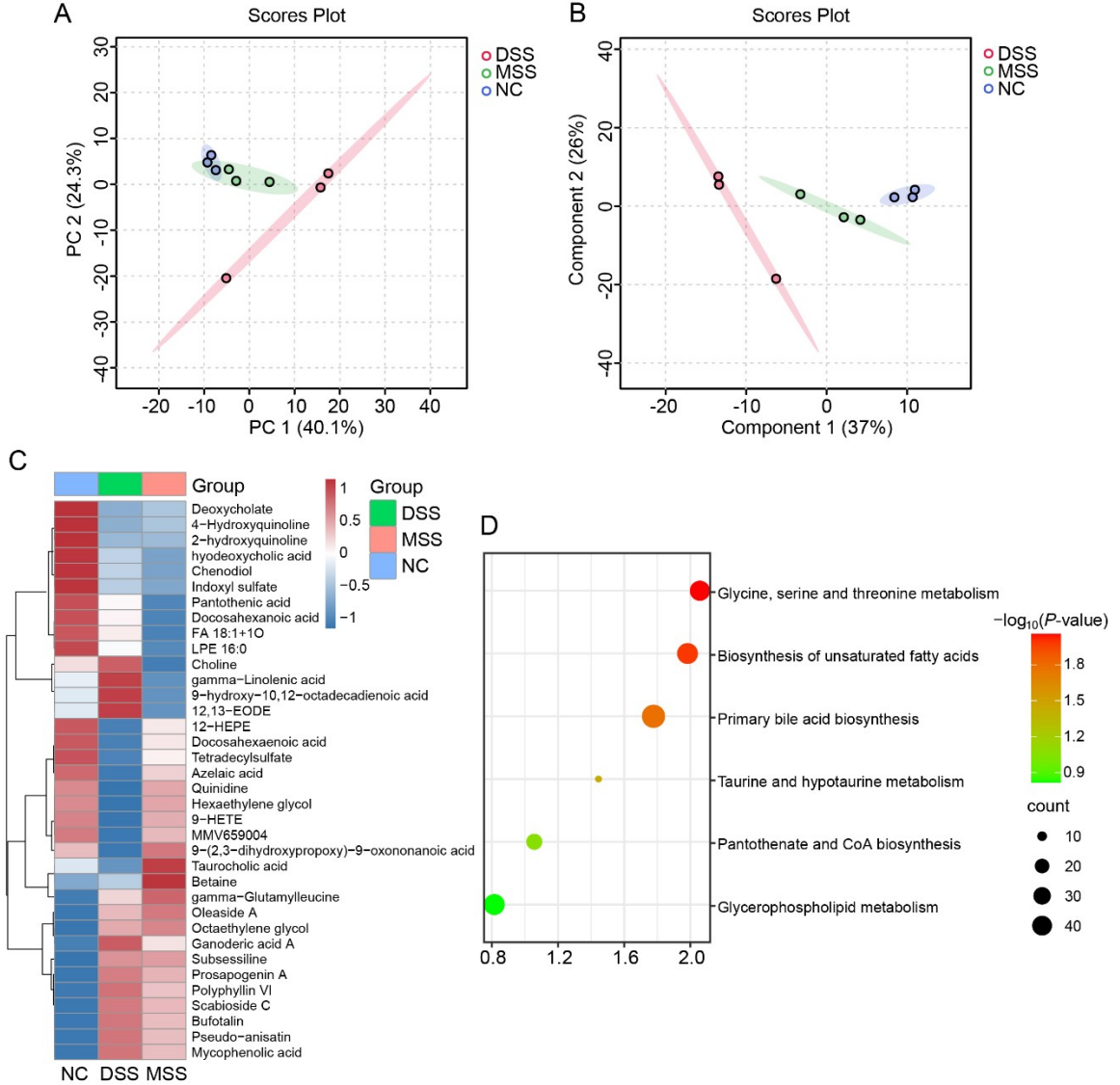


Fig S6. MSS changed the serum metabolic profiles of DSS-induced colitis mice. PCA (A) and PLS-DA (B) scores plot of serum metabolite profiles among the three groups. (C) Heatmap of metabolites with significant differences between the DSS group and the MSS group. (D) KEGG pathway enrichment analysis of metabolites with significant differences between the DSS group and the MSS group.