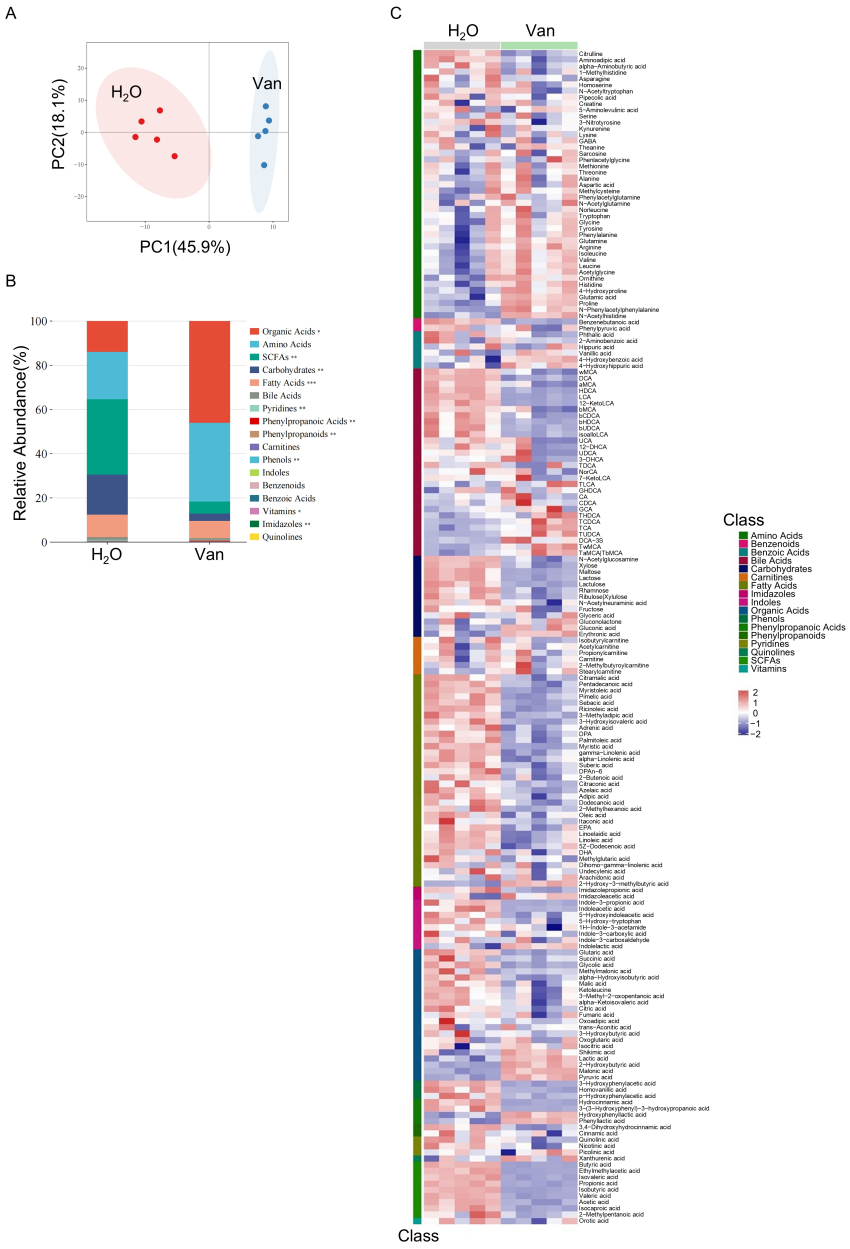
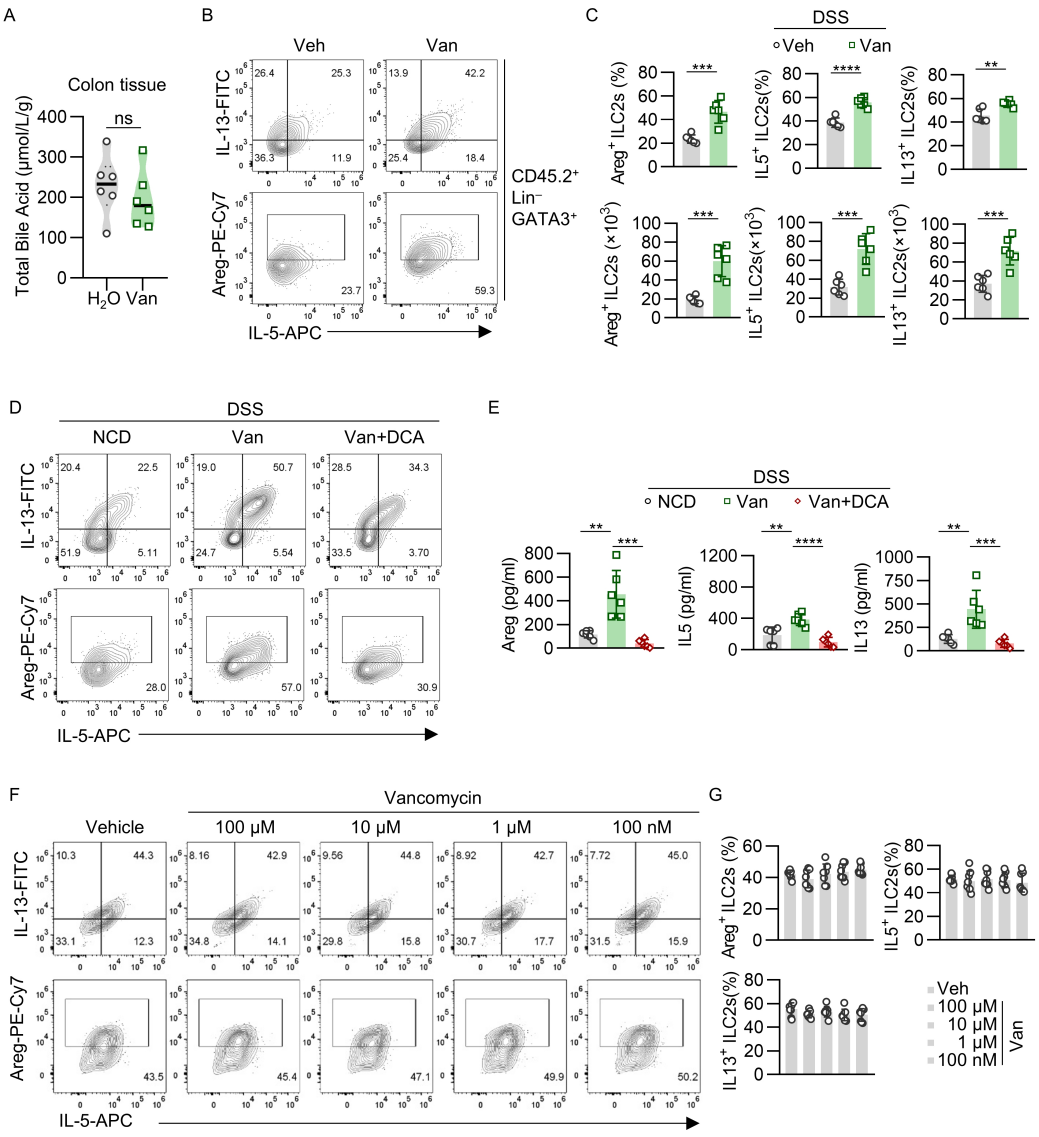
Figure S1




**Supplementary Figure S1. Metabolite profiles in Vancomycin treated mice in feces**

(**A–C**) WT Mice were gavaged a 5-day $H_2O$ or Vancomycin after the 2.5% DSS administration for 5 days. (A) Principal coordinate analysis (PCA) score plot of fecal metabolite in separately housed mice treated or untreated with vancomycin. (B) The relative abundance of each metabolite classes between the $H_2O$ group and vancomycin group. (C) Heat map of metabolite between the $H_2O$ group and vancomycin group.

Figure S2




**Supplementary Figure S2. Vancomycin promotes ILC2s indirectly**

(**A**) The contents of total bile acid in colon tissue after Vancomycin gavage. n = 6 mice per group. The experiment was repeated three times.

(**B** and **C**) (B) Representative flow cytometry plots. (C, top) Percentages of Areg$^+$, IL-5$^+$, and IL-13$^+$ ILC2s (CD45.2$^+$Lin$^-$GATA3$^+$) and (C, bottom) absolute numbers of Areg$^+$ ILC2s, IL-5$^+$ ILC2s, and IL-13$^+$ ILC2s in large intestine. n = 6 mice per group. The experiment was repeated three times.

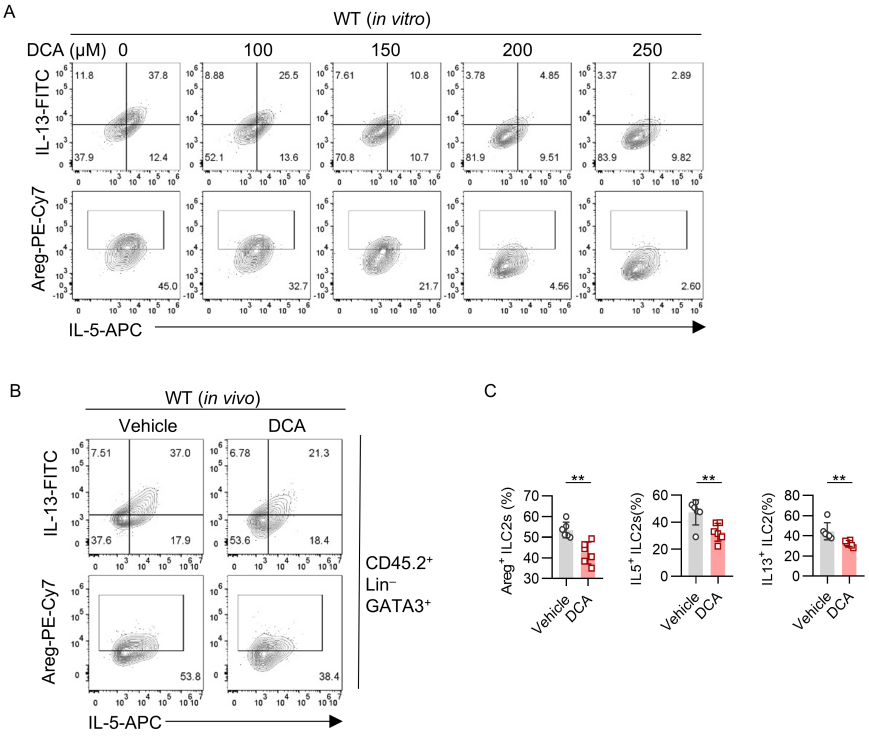
(**D** and **E**) WT mice were gavaged a 5-day $H_2O$ or Vancomycin after the 2.5% DSS administration for 5 days. One group of Vancomycin-gavaged mice simultaneously

were fed a 2% DCA diet on day 5 to day 10. (D) Representative flow cytometry plots. (E) The concentrations of Areg, IL-5 and IL-13 in colonic tissue lysates were detected by Cytometric Bead Array. n = 6 mice per group. The experiment was repeated three times.

(**F** and **G**) Large intestinal ILC2s were sorted from WT mice and cultured in the presence of IL-2, IL-7, IL-25, and IL-33 for 5 days. ILC2s were treated with Vancomycin at the indicated concentrations for 24 h. (F) Representative flow cytometry plots. (G) Percentages of $Areg^+$, $IL\text{-}5^+$, and $IL\text{-}13^+$ ILC2s ($CD45.2^+Lin^-GATA3^+$) in large intestine. n = 8 wells per group. The experiment was repeated three times.

Data are represented as mean ± SD. The two-sided unpaired t test or two-sided Mann–Whitney U test was used in panel **A** and **C**, depending on data normality. One-way ANOVA with Tukey's multiple-comparison test or the Kruskal–Wallis test with Dunn's multiple-comparison test was used in panels **E** and **G**, based on data normality. The statistical methods and exact P values are provided in the Supporting Data Values file. Significance reported as $^{**}p < 0.01$, $^{***}p < 0.001$, $^{****}p < 0.0001$.

Figure S3



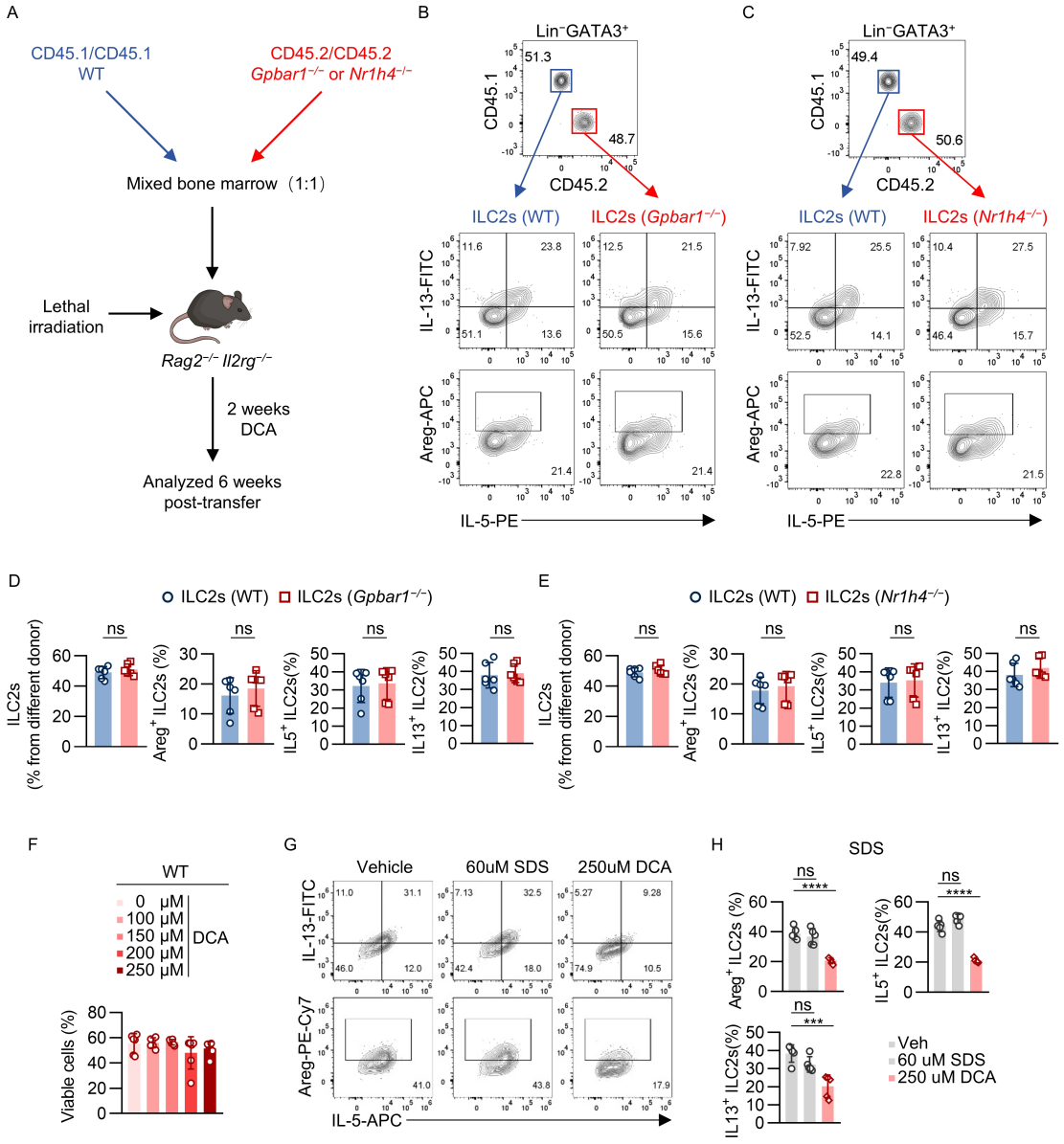

**Supplementary Figure S3. DCA inhibits ILC2 function**

(**A**) Representative flow cytometry plots. Large intestinal ILC2s were sorted from WT mice and cultured in the presence of IL-2, IL-7, IL-25, and IL-33 for 5 days. ILC2s were treated with DCA at the indicated concentrations for 24 h.

(**B** and **C**) WT mice were injected intraperitoneally (i.p.) with DCA or DMSO for 14 days. (B) Representative flow cytometry plots. (C) Percentages of $Areg^+$, $IL\text{-}5^+$, and $IL\text{-}13^+$ ILC2s ($CD45.2^+Lin^-GATA3^+$) in large intestine. n = 6 mice per group. The experiment was repeated three times.

Data are represented as mean ± SD. Statistical analysis was performed using unpaired two-tailed t test. Significance reported as $^{**}p < 0.01$.

Figure S4




**Supplementary Figure S4. DCA suppresses colonic ILC2 function independently of receptor signaling and without inducing cell death via detergent-like activity**

(**A–E**) The lethally irradiated *Rag2*$^{-/-}$*Il2rg*$^{-/-}$ recipient mice were transferred with an equal mixture (1:1) of bone marrow cells from WT (CD45.1/CD45.1) and either *Gpbar1*$^{-/-}$ (CD45.2/CD45.2) or *Nr1h4*$^{-/-}$ (CD45.2/CD45.2) donor mice. (A) Experimental strategy. (B) Flow cytometry analyses of CD45.1 (WT ILC2s) and CD45.2 (*Gpbar1*$^{-/-}$ ILC2s) expression (upper), Areg, IL-5 and IL-13 expression (bottom) after gating on indicated populations. (C) Flow cytometry analyses of CD45.1 (WT ILC2s) and CD45.2 (*Nr1h4*$^{-/-}$ ILC2s) expression (upper), Areg, IL-5

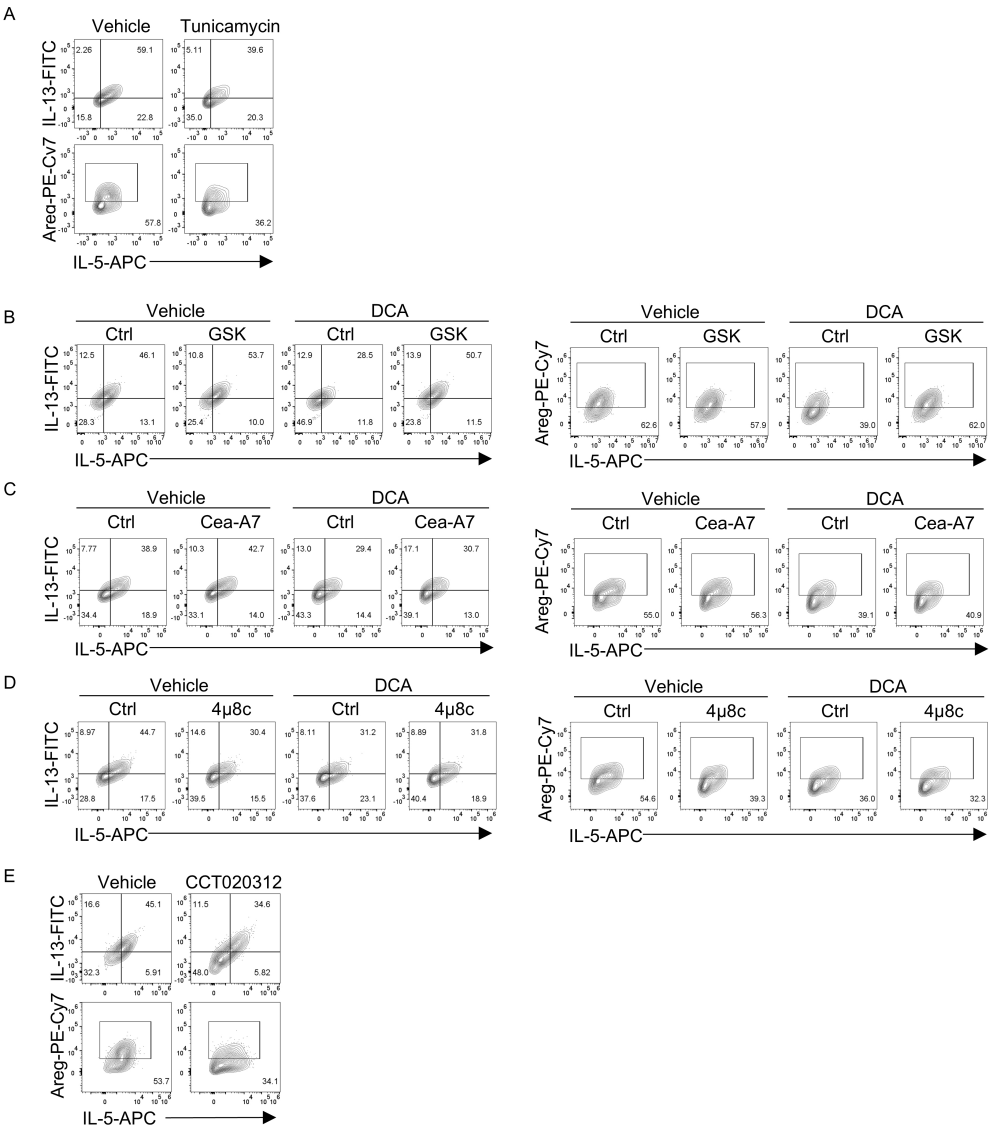
and IL-13 expression (bottom) after gating on indicated populations. (D) Proportion of ILC2s ($Lin^{-}GATA3^{+}$) from different donors, and percentages of $Areg^{+}$, $IL\text{-}5^{+}$, and $IL\text{-}13^{+}$ cells in recovered WT or *Gpbar1*$^{-/-}$ ILC2s. n = 6 mice per group. The experiment was repeated twice. (E) Proportion of ILC2s ($Lin^{-}GATA3^{+}$) from different donors, and percentages of $Areg^{+}$, $IL\text{-}5^{+}$, and $IL\text{-}13^{+}$ cells in recovered WT or *Nr1h4*$^{-/-}$ ILC2s. n = 6 mice per group. The experiment was repeated twice.

(**F**) Large intestinal ILC2s were sorted from WT mice and cultured in the presence of IL-2, IL-7, IL-25, and IL-33 for 5 days. ILC2s were treated with DCA at the indicated concentrations for 24 h. Flow cytometry analysis of viability in ILC2s. n = 6 mice per group. The experiment was repeated three times.

(**G** and **H**) Large intestinal ILC2s were sorted from WT mice and cultured in the presence of IL-2, IL-7, IL-25, and IL-33 for 5 days. ILC2s were treated with SDS (60 μM) or DCA (250 μM) for 24 h. (E) Representative flow cytometry plots. (F) Percentages of $Areg^{+}$, $IL\text{-}5^{+}$, and $IL\text{-}13^{+}$ ILC2s ($CD45.2^{+}Lin^{-}GATA3^{+}$). n = 5 wells per group. The experiment was repeated twice.

Data are represented as mean ± SD. The two-sided unpaired t test or two-sided Mann–Whitney U test was used in panel **D** and **E**, depending on data normality. One-way ANOVA with Tukey's multiple-comparison test or the Kruskal–Wallis test with Dunn's multiple-comparison test was used in panels **F** and **H**, based on data normality. The statistical methods and exact P values are provided in the Supporting Data Values file. Significance reported as ***$p < 0.001$, ****$p < 0.0001$.

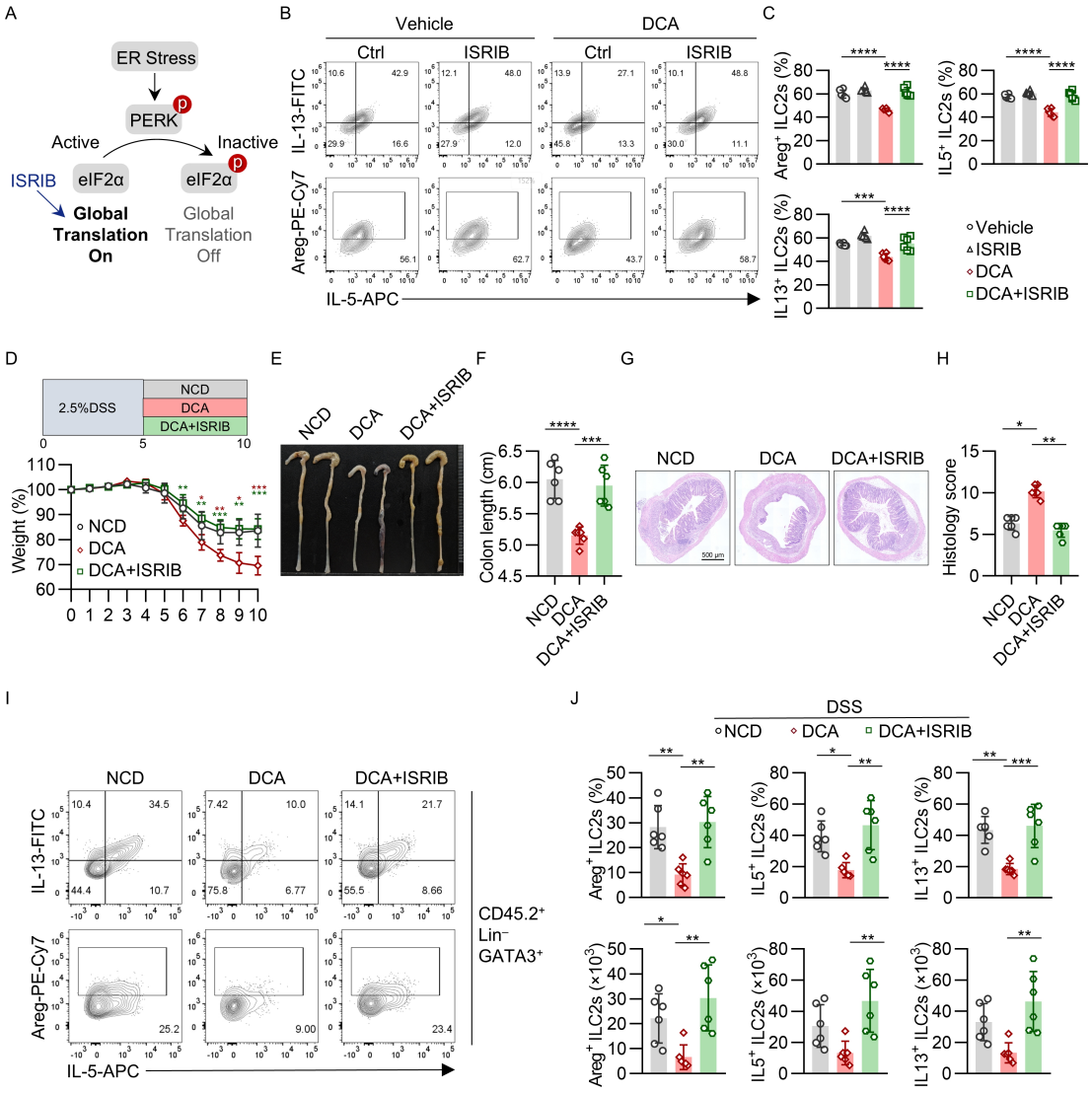
Figure S5




**Supplementary Figure S5. DCA enhances UPR in ILC2s**

(**A–E**) Representative flow cytometry plots. Large intestinal ILC2s were sorted from WT mice and cultured in the presence of IL-2, IL-7, IL-25, and IL-33 for 5 days. (A) ILC2s were treated with ER stress activator (tunicamycin, 0.3 μM) for 24 h. ILC2s were treated with DCA (100 μM) and ER stress inhibitors targeting (B) PERK phosphorylation (GSK, 10 μM), (C) ATF6 (Cea-A7, 10 μM), (D) IRE1α (4μ8c, 20 μM) and (E) PERK phosphorylation activator (CCT020312, 10 μM).

Figure S6




**Supplementary Figure S6. PERK-eIF2a branch of UPR mediates the inhibitory effects of DCA on ILC2 function and colitis recovery**

(**A–C**) Large intestinal ILC2s were sorted from WT mice and cultured in the presence of IL-2, IL-7, IL-25, and IL-33 for 5 days. ILC2s were treated with DCA (100 μM) and PERK phosphorylation inhibitor (ISRIB, 10 μM) for 24 h. (A) Schematic illustration of the PERK-eIF2α arm of the UPR. (B) Representative flow cytometry plots. (C) Percentages of Areg$^+$, IL-5$^+$, and IL-13$^+$ ILC2s (CD45.2$^+$Lin$^-$GATA3$^+$). n = 6 wells per group. The experiment was repeated three times.

(**D–J**) WT mice were fed a 5-day NCD or DCA after the 2.5% DSS administration for 5 days. One group of NCD-fed or DCA-fed mice simultaneously injected

intraperitoneally (i.p.) with ISRIB or DMSO for 5 days. (D, top) The experimental outline is shown. (D, bottom) Weight course. The red * represents the comparison between the NCD and DCA groups, the green * represents the comparison between the DCA and DCA+ISRIB groups. (E) Representative image of colons and (F) statistic data of colon length. (G) H&E-stained histological sections. Scale bar, 500 μm. (H) Histopathology scores. (I) Representative flow cytometry plots. (J, top) Percentages of $Areg^+$, IL-$5^+$, and IL-$13^+$ ILC2s ($CD45.2^+Lin^-GATA3^+$) and (J, bottom) absolute numbers of $Areg^+$ ILC2s, IL-$5^+$ ILC2s, and IL-$13^+$ ILC2s in large intestine. n = 6 mice per group. The experiment was repeated three times.

Data are represented as mean ± SD. One-way ANOVA with Tukey's multiple-comparison test or the Kruskal–Wallis test with Dunn's multiple-comparison test was used in panels **C**, **D**, **F**, **H**, and **J**, based on data normality. The statistical methods and exact P values are provided in the Supporting Data Values file. Significance reported as *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001.

Supplemental table 1. Metabolite profiles in Vancomycin-treated compared to $H_2O$-treated in feces.

| Class | Metabo | C1 | C2 | C3 | C4 | C5 | W1 | W2 | W3 | W4 | W5 | log2fc | p |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Phenyl | Hydroc | 100.8 | 21.8 | 38.0 | 109.2 | 49.6 | 0.2 | 0.2 | 0.5 | 0.4 | 0.3 | -7.65 | 0.0218 |
| Bile Ac | DCA | 165.0 | 130.1 | 238.6 | 244.3 | 127.4 | 0.1 | 1.9 | 1.4 | 4.0 | 0.9 | -6.78 | 0.0022 |
| Phenol | 3-Hydr | 77.5 | 29.8 | 31.3 | 61.9 | 28.4 | 0.4 | 0.7 | 0.1 | 0.6 | 0.6 | -6.55 | 0.0109 |
| Bile Ac | 12-Ket | 34.8 | 12.5 | 63.5 | 24.2 | 20.3 | 0.3 | 0.5 | 0.3 | 0.6 | 0.4 | -6.20 | 0.0259 |
| SCFAs | Butyric | 3317.4 | 1613.3 | 2226.9 | 2568.0 | 2755.3 | 36.1 | 33.0 | 41.4 | 41.8 | 39.0 | -6.03 | 0.0010 |
| Bile Ac | HDCA | 27.0 | 8.7 | 22.4 | 22.6 | 7.4 | 0.2 | 0.9 | 0.1 | 0.3 | 0.1 | -5.77 | 0.0123 |
| Bile Ac | LCA | 20.3 | 14.2 | 14.5 | 21.0 | 9.5 | 0.2 | 0.3 | 0.1 | 0.6 | 0.3 | -5.70 | 0.0019 |
| Bile Ac | wMCA | 287.4 | 89.9 | 256.8 | 295.4 | 108.4 | 9.2 | 23.1 | 0.4 | 1.6 | 0.1 | -4.92 | 0.0107 |
| SCFAs | Ethylm | 47.3 | 50.8 | 33.4 | 85.3 | 73.4 | 1.8 | 2.0 | 2.0 | 2.2 | 2.1 | -4.85 | 0.0039 |
| SCFAs | Propion | 7356.3 | 4547.1 | 5735.4 | 8901.6 | 4146.7 | 227.1 | 248.4 | 211.9 | 169.4 | 225.3 | -4.83 | 0.0026 |
| SCFAs | Isovale | 34.8 | 52.4 | 61.6 | 55.3 | 103.1 | 2.4 | 1.6 | 2.2 | 2.8 | 2.0 | -4.80 | 0.0064 |
| Phenyl | 3-(3-Hy | 3.1 | 2.1 | 1.0 | 4.6 | 1.9 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | -4.80 | 0.0164 |
| Carboh | N-Acet | 292.8 | 185.2 | 172.4 | 263.0 | 289.8 | 9.6 | 30.3 | 2.6 | 0.9 | 11.6 | -4.45 | 0.0007 |
| SCFAs | Isobuty | 123.4 | 160.6 | 182.2 | 166.6 | 201.2 | 8.5 | 7.9 | 7.9 | 9.0 | 10.0 | -4.27 | 0.0003 |
| Bile Ac | bHDCA | 8.4 | 1.7 | 5.8 | 4.6 | 2.1 | 0.2 | 0.6 | 0.2 | 0.1 | 0.3 | -4.00 | 0.0262 |
| Carboh | Maltose | 2461.8 | 1408.2 | 2290.1 | 2748.7 | 561.6 | 130.1 | 136.7 | 106.8 | 133.4 | 155.0 | -3.84 | 0.0118 |
| Carboh | Lactose | 2386.5 | 1358.4 | 2148.4 | 2634.1 | 571.1 | 135.8 | 144.1 | 98.2 | 137.1 | 167.1 | -3.74 | 0.0112 |
| Carboh | Xylose | 9004.9 | 5017.3 | 5054.5 | 9330.1 | 6229.6 | 552.8 | 1137.2 | 231.3 | 303.7 | 543.0 | -3.65 | 0.0021 |
| SCFAs | Valeric | 276.0 | 190.8 | 265.4 | 232.2 | 181.0 | 21.9 | 15.8 | 18.7 | 21.0 | 21.0 | -3.54 | 0.0004 |
| Indoles | Indole- | 5.9 | 1.6 | 2.5 | 3.1 | 2.5 | 0.3 | 0.3 | 0.2 | 0.4 | 0.2 | -3.52 | 0.0182 |
| Bile Ac | aMCA | 78.7 | 17.8 | 67.2 | 66.0 | 19.4 | 5.6 | 16.2 | 0.2 | 0.6 | 0.3 | -3.44 | 0.0230 |
| Bile Ac | isoallol | 8.6 | 2.0 | 8.9 | 3.9 | 2.2 | 0.4 | 0.5 | 0.3 | 0.8 | 0.5 | -3.36 | 0.0389 |
| Organi | Glutari | 54.4 | 47.9 | 19.4 | 25.9 | 23.7 | 3.0 | 4.0 | 2.4 | 4.6 | 4.4 | -3.21 | 0.0123 |
| Bile Ac | bCDCA | 9.7 | 2.4 | 10.7 | 6.6 | 2.7 | 0.6 | 2.4 | 0.0 | 0.3 | 0.3 | -3.16 | 0.0278 |
| Carboh | Lactulo | 51.2 | 41.8 | 21.4 | 40.4 | 17.8 | 5.7 | 4.8 | 5.1 | 4.1 | 5.1 | -2.80 | 0.0098 |
| Bile Ac | bUDCA | 1.3 | 0.5 | 1.2 | 1.2 | 0.4 | 0.1 | 0.2 | 0.1 | 0.2 | 0.1 | -2.78 | 0.0151 |
| Phenol | Homov | 9.7 | 7.1 | 2.4 | 8.1 | 4.3 | 1.0 | 1.0 | 1.0 | 0.8 | 0.7 | -2.78 | 0.0145 |
| Indoles | Indolea | 1.3 | 1.7 | 4.8 | 5.4 | 2.5 | 0.4 | 0.5 | 0.5 | 0.6 | 0.5 | -2.64 | 0.0329 |
| Fatty A | Pentade | 311.6 | 169.9 | 147.9 | 257.5 | 109.2 | 38.3 | 39.3 | 22.2 | 14.8 | 47.9 | -2.62 | 0.0102 |
| SCFAs | Acetic | 17621.7 | 10536.8 | 18773.1 | 18621.2 | 15480.6 | 3193.8 | 3272.7 | 2309.0 | 2289.5 | 3444.1 | -2.48 | 0.0008 |
| Amino | Citrulli | 1481.5 | 1523.8 | 1164.6 | 647.9 | 1196.6 | 155.3 | 228.9 | 148.5 | 276.6 | 342.1 | -2.38 | 0.0027 |
| SCFAs | Isocapr | 2.5 | 1.9 | 3.1 | 4.0 | 2.5 | 0.7 | 0.4 | 0.6 | 0.6 | 0.5 | -2.37 | 0.0029 |
| Carboh | Rhamn | 390.5 | 185.9 | 103.4 | 424.5 | 338.5 | 52.5 | 88.4 | 25.6 | 48.0 | 70.8 | -2.34 | 0.0189 |
| Fatty A | Citram | 8.5 | 8.0 | 8.5 | 3.2 | 6.4 | 1.8 | 1.6 | 0.4 | 1.8 | 1.4 | -2.30 | 0.0044 |
| Imidaz | Imidaz | 3.2 | 3.0 | 2.2 | 4.0 | 6.5 | 1.1 | 0.8 | 0.6 | 0.6 | 1.0 | -2.26 | 0.0141 |
| Fatty A | Myristo | 10.6 | 8.7 | 7.4 | 8.1 | 10.8 | 1.9 | 2.0 | 1.4 | 1.9 | 2.9 | -2.19 | 0.0002 |
| Fatty A | Pimelic | 6.4 | 4.3 | 2.9 | 7.3 | 4.0 | 0.9 | 0.7 | 0.8 | 1.4 | 1.7 | -2.18 | 0.0076 |
| Fatty A | Sebacic | 11.6 | 8.4 | 9.2 | 14.8 | 8.2 | 2.5 | 2.1 | 1.9 | 2.5 | 3.0 | -2.11 | 0.0028 |
| Benzen | Benzen | 1.9 | 1.7 | 1.2 | 1.5 | 1.3 | 0.3 | 0.4 | 0.4 | 0.3 | 0.4 | -2.07 | 0.0004 |
| Carboh | Ribulos | 691.1 | 368.3 | 292.5 | 569.1 | 355.6 | 131.0 | 151.2 | 76.9 | 110.1 | 155.9 | -1.86 | 0.0106 |
| Fatty A | 3-Meth | 1.7 | 1.2 | 0.8 | 1.1 | 0.9 | 0.2 | 0.4 | 0.4 | 0.4 | 0.3 | -1.80 | 0.0054 |
| Bile Ac | bMCA | 560.4 | 204.7 | 411.0 | 557.3 | 205.9 | 135.2 | 412.2 | 4.1 | 6.4 | 3.0 | -1.79 | 0.0393 |
| Organi | Glycoli | 65.5 | 42.1 | 68.9 | 58.5 | 45.3 | 14.4 | 17.2 | 14.6 | 18.0 | 17.3 | -1.78 | 0.0015 |
| Organi | Succini | 684.1 | 2384.3 | 293.8 | 780.6 | 199.9 | 249.7 | 269.1 | 165.9 | 306.0 | 294.2 | -1.76 | 0.1964 |
| Fatty A | Ricinol | 5.5 | 6.1 | 5.7 | 5.7 | 3.3 | 1.5 | 1.1 | 1.3 | 1.5 | 2.5 | -1.75 | 0.0008 |
| Fatty A | Adreni | 13.3 | 9.0 | 12.4 | 16.8 | 32.7 | 3.0 | 6.7 | 3.3 | 5.2 | 8.6 | -1.65 | 0.0487 |
| Fatty A | DPAn- | 9.3 | 9.8 | 8.4 | 16.0 | 24.8 | 3.9 | 6.1 | 2.3 | 3.7 | 5.7 | -1.65 | 0.0380 |
| Fatty A | Citraco | 0.3 | 0.1 | 0.3 | 0.1 | 0.2 | 0.1 | 0.1 | 0.1 | 0.0 | 0.1 | -1.62 | 0.0421 |
| Organi | Methyl | 768.1 | 2031.0 | 336.6 | 1121.3 | 203.8 | 273.7 | 307.2 | 271.3 | 321.6 | 304.4 | -1.59 | 0.1428 |
| Fatty A | Adipic | 7.5 | 9.2 | 4.4 | 7.4 | 5.4 | 2.8 | 2.8 | 0.7 | 2.1 | 3.6 | -1.50 | 0.0037 |
| Phenol | p-Hydr | 17.8 | 56.4 | 51.0 | 17.3 | 36.2 | 12.7 | 14.6 | 10.6 | 13.0 | 13.4 | -1.47 | 0.0480 |
| Fatty A | 3-Hydr | 1.0 | 0.7 | 0.8 | 1.2 | 0.8 | 0.4 | 0.3 | 0.3 | 0.3 | 0.4 | -1.47 | 0.0027 |
| Fatty A | DPA | 37.2 | 49.7 | 23.9 | 22.8 | 36.9 | 11.2 | 15.7 | 7.8 | 11.2 | 15.8 | -1.47 | 0.0094 |
| Fatty A | Palmito | 189.3 | 291.9 | 169.1 | 168.0 | 342.8 | 74.1 | 109.5 | 46.7 | 63.4 | 125.7 | -1.47 | 0.0110 |
| Amino | Aspara | 197.2 | 49.7 | 20.8 | 65.8 | 171.2 | 34.8 | 37.2 | 40.0 | 52.5 | 25.4 | -1.41 | 0.1466 |
| Fatty A | Myristi | 99.7 | 70.1 | 72.8 | 85.0 | 69.3 | 30.5 | 30.6 | 28.7 | 28.6 | 34.6 | -1.38 | 0.0009 |
| Organi | alpha-H | 2.9 | 2.3 | 3.9 | 2.7 | 2.4 | 1.3 | 0.9 | 0.8 | 1.0 | 1.5 | -1.37 | 0.0020 |
| Fatty A | alpha-L | 382.3 | 603.3 | 427.1 | 485.5 | 284.9 | 114.6 | 104.6 | 151.6 | 206.4 | 277.7 | -1.35 | 0.0042 |
| Fatty A | gamma | 30.9 | 51.1 | 36.6 | 41.3 | 36.9 | 11.0 | 15.0 | 11.7 | 16.8 | 22.9 | -1.35 | 0.0006 |
| Fatty A | Suberic | 15.7 | 12.2 | 10.1 | 18.7 | 9.5 | 5.6 | 5.8 | 2.9 | 5.0 | 6.7 | -1.34 | 0.0076 |
| Amino | Amino | 47.8 | 58.8 | 36.1 | 36.2 | 35.4 | 18.6 | 24.8 | 10.2 | 17.8 | 18.6 | -1.25 | 0.0031 |
| Carniti | Isobuty | 0.4 | 1.0 | 0.1 | 0.6 | 1.1 | 0.3 | 0.5 | 0.2 | 0.2 | 0.2 | -1.22 | 0.1092 |
| Fatty A | Azelaic | 74.6 | 52.9 | 39.0 | 49.3 | 32.8 | 25.6 | 22.7 | 17.6 | 18.4 | 22.7 | -1.22 | 0.0155 |
| Organi | Ketoleu | 566.8 | 563.2 | 662.0 | 299.9 | 409.1 | 208.2 | 347.2 | 101.2 | 122.7 | 355.8 | -1.14 | 0.0122 |
| Organi | 3-Meth | 474.5 | 379.7 | 465.7 | 221.0 | 244.4 | 146.6 | 291.7 | 60.6 | 83.6 | 232.0 | -1.13 | 0.0238 |
| Carboh | N-Acet | 371.5 | 337.7 | 144.8 | 285.8 | 470.1 | 166.6 | 211.4 | 99.4 | 36.8 | 231.5 | -1.11 | 0.0316 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Organi | Oxoadi | 0.6 | 2.0 | 0.6 | 0.5 | 0.6 | 0.3 | 0.5 | 0.3 | 0.3 | 0.5 | -1.11 | 0.1788 |
| Vitami | Orotic | 3.1 | 7.3 | 2.2 | 8.2 | 5.3 | 1.3 | 1.7 | 0.4 | 2.8 | 5.9 | -1.10 | 0.1029 |
| Phenyl | 3,4-Dih | 15.9 | 14.8 | 10.3 | 15.7 | 16.1 | 8.1 | 5.8 | 5.6 | 6.5 | 8.7 | -1.07 | 0.0007 |
| Amino | alpha-A | 50.9 | 29.3 | 70.1 | 34.9 | 49.5 | 19.3 | 25.7 | 15.0 | 24.9 | 27.8 | -1.06 | 0.0235 |
| Pyridin | Quinol | 4.3 | 4.7 | 1.9 | 4.1 | 2.3 | 2.7 | 1.8 | 0.8 | 1.6 | 1.5 | -1.03 | 0.0315 |
| Fatty A | 2-Meth | 0.3 | 0.4 | 0.2 | 0.5 | 0.5 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | -0.96 | 0.0213 |
| Organi | alpha-K | 211.7 | 224.4 | 265.7 | 108.1 | 125.1 | 94.1 | 158.5 | 33.8 | 57.7 | 147.0 | -0.93 | 0.0528 |
| Organi | Malic a | 905.4 | 1258.8 | 661.6 | 667.0 | 880.9 | 352.6 | 752.9 | 218.7 | 367.8 | 609.9 | -0.93 | 0.0219 |
| Fatty A | Dodeca | 50.3 | 29.8 | 34.3 | 65.9 | 50.6 | 34.0 | 25.6 | 19.4 | 18.4 | 26.3 | -0.90 | 0.0255 |
| Fatty A | Oleic a | 2517.8 | 3259.5 | 2620.6 | 1459.1 | 2273.8 | 844.9 | 1450.9 | 841.1 | 1614.0 | 1840.5 | -0.88 | 0.0165 |
| Fatty A | 2-Buter | 34.1 | 71.5 | 46.9 | 61.9 | 58.0 | 24.2 | 50.7 | 18.2 | 21.4 | 38.2 | -0.83 | 0.0272 |
| Fatty A | EPA | 54.6 | 102.5 | 60.1 | 80.5 | 79.1 | 33.1 | 45.5 | 30.5 | 36.6 | 70.8 | -0.80 | 0.0216 |
| Fatty A | Linolei | 2809.3 | 3866.2 | 3169.9 | 3343.4 | 2944.4 | 1499.8 | 1443.4 | 1773.2 | 2065.3 | 2713.1 | -0.76 | 0.0023 |
| Organi | Citric a | 1224.8 | 1416.7 | 750.2 | 864.9 | 935.1 | 681.7 | 697.2 | 440.4 | 598.2 | 638.8 | -0.76 | 0.0219 |
| Fatty A | 5Z-Doc | 0.7 | 0.8 | 0.7 | 0.8 | 0.5 | 0.2 | 0.3 | 0.4 | 0.5 | 0.7 | -0.75 | 0.0391 |
| Fatty A | Methyl | 1.1 | 0.8 | 0.6 | 0.6 | 0.4 | 0.3 | 0.5 | 0.4 | 0.5 | 0.3 | -0.75 | 0.0759 |
| Pyridin | Nicotin | 412.2 | 260.5 | 279.5 | 345.8 | 246.6 | 191.4 | 235.5 | 121.2 | 135.8 | 234.1 | -0.75 | 0.0136 |
| Fatty A | Linoela | 114.9 | 165.3 | 128.6 | 147.5 | 117.4 | 64.6 | 62.9 | 75.1 | 85.6 | 112.8 | -0.75 | 0.0033 |
| Bile Ac | UCA | 0.8 | 0.3 | 0.7 | 0.9 | 0.7 | 0.7 | 1.1 | 0.1 | 0.1 | 0.1 | -0.73 | 0.2449 |
| Indoles | 5-Hydr | 6.3 | 4.8 | 5.1 | 4.1 | 5.3 | 3.1 | 2.8 | 3.6 | 2.6 | 3.9 | -0.67 | 0.0030 |
| Benzoi | Phthali | 4.1 | 3.2 | 1.6 | 3.3 | 1.9 | 2.4 | 2.3 | 1.3 | 1.4 | 1.6 | -0.65 | 0.0954 |
| Bile Ac | 12-DH | 1.2 | 0.5 | 2.5 | 1.2 | 0.5 | 1.0 | 2.3 | 0.1 | 0.2 | 0.2 | -0.64 | 0.4753 |
| Organi | 3-Hydr | 58.8 | 36.9 | 108.0 | 33.3 | 39.6 | 40.4 | 38.8 | 29.4 | 35.0 | 35.1 | -0.63 | 0.2322 |
| Phenyl | Cinnan | 0.2 | 0.4 | 0.2 | 0.3 | 0.2 | 0.2 | 0.2 | 0.3 | 0.0 | 0.2 | -0.61 | 0.2154 |
| Fatty A | Itaconi | 2.0 | 3.1 | 1.5 | 1.5 | 1.7 | 1.4 | 1.3 | 1.1 | 1.4 | 1.3 | -0.60 | 0.0948 |
| SCFAs | 2-Meth | 0.5 | 0.5 | 0.4 | 0.8 | 0.7 | 0.4 | 0.3 | 0.3 | 0.4 | 0.4 | -0.59 | 0.0655 |
| Fatty A | DHA | 177.9 | 239.5 | 120.7 | 123.9 | 269.7 | 114.6 | 175.4 | 64.3 | 112.5 | 165.2 | -0.56 | 0.1415 |
| Indoles | 1H-Ind | 3.3 | 2.7 | 4.5 | 4.3 | 2.8 | 3.8 | 2.9 | 1.8 | 0.2 | 3.3 | -0.55 | 0.1822 |
| Indoles | 5-Hydr | 4.4 | 4.2 | 2.9 | 4.5 | 2.8 | 2.6 | 2.2 | 3.4 | 1.8 | 3.0 | -0.52 | 0.0440 |
| Indoles | Indole- | 2.2 | 1.0 | 1.1 | 1.1 | 1.5 | 0.6 | 1.3 | 1.0 | 1.1 | 0.8 | -0.52 | 0.1546 |
| Amino | 1-Meth | 1.7 | 2.4 | 1.3 | 1.9 | 2.6 | 1.0 | 2.4 | 0.7 | 1.2 | 1.9 | -0.47 | 0.1833 |
| Bile Ac | NorCA | 0.2 | 0.2 | 0.2 | 0.5 | 0.3 | 0.3 | 0.3 | 0.1 | 0.2 | 0.1 | -0.46 | 0.2727 |
| Fatty A | Undecy | 0.4 | 0.3 | 0.5 | 0.8 | 0.4 | 0.3 | 0.5 | 0.2 | 0.4 | 0.3 | -0.44 | 0.2503 |
| Amino | Homos | 105.9 | 47.4 | 31.3 | 48.3 | 110.5 | 47.3 | 91.3 | 24.8 | 31.5 | 58.0 | -0.44 | 0.3985 |
| Amino | N-Acet | 2.5 | 1.3 | 1.9 | 2.1 | 2.4 | 2.3 | 2.4 | 0.8 | 0.7 | 1.4 | -0.41 | 0.2685 |
| Amino | 3-Nitro | 1.3 | 1.5 | 1.6 | 1.9 | 1.5 | 1.2 | 1.4 | 0.7 | 1.2 | 1.4 | -0.40 | 0.0517 |
| Bile Ac | TDCA | 0.7 | 0.4 | 0.5 | 0.6 | 0.7 | 0.4 | 0.3 | 0.3 | 0.8 | 0.4 | -0.35 | 0.2800 |
| Fatty A | Dihom | 121.8 | 133.0 | 58.2 | 48.5 | 148.7 | 59.4 | 170.0 | 29.7 | 55.8 | 93.8 | -0.32 | 0.5403 |
| Amino | Kynure | 4.0 | 4.4 | 2.5 | 1.0 | 8.5 | 2.0 | 5.4 | 2.9 | 3.0 | 3.2 | -0.30 | 0.5982 |
| Organi | Fumari | 104.2 | 225.5 | 162.7 | 98.8 | 189.4 | 96.1 | 231.6 | 30.8 | 63.3 | 219.0 | -0.28 | 0.5777 |
| Amino | Pipecol | 7.3 | 5.6 | 5.9 | 2.9 | 6.1 | 4.7 | 4.8 | 2.9 | 5.0 | 5.4 | -0.28 | 0.2758 |
| Carboh | Fructos | 206.2 | 96.3 | 93.8 | 95.7 | 107.0 | 126.2 | 222.8 | 33.6 | 33.0 | 78.1 | -0.28 | 0.6285 |
| Indoles | Indole- | 1.7 | 1.3 | 2.1 | 1.0 | 1.0 | 1.0 | 2.1 | 0.5 | 0.8 | 1.5 | -0.25 | 0.5433 |
| Carniti | Acetylc | 35.2 | 54.2 | 10.5 | 19.7 | 55.6 | 31.3 | 37.3 | 16.4 | 29.9 | 33.3 | -0.24 | 0.5993 |
| Benzoi | 2-Amir | 3.3 | 2.8 | 1.9 | 1.6 | 2.7 | 2.5 | 2.0 | 2.0 | 2.0 | 1.9 | -0.23 | 0.3240 |
| Benzoi | Hippur | 0.2 | 0.3 | 0.2 | 0.4 | 0.6 | 0.2 | 0.1 | 0.2 | 0.6 | 0.4 | -0.22 | 0.6870 |
| Benzen | Phenyl | 32.4 | 35.3 | 41.1 | 16.1 | 20.2 | 23.3 | 46.2 | 11.9 | 11.6 | 33.2 | -0.20 | 0.6529 |
| Amino | Lysine | 2025.5 | 1665.1 | 1131.8 | 1480.4 | 2301.5 | 1296.5 | 1758.5 | 1226.5 | 1817.8 | 1405.1 | -0.20 | 0.3880 |
| Fatty A | Arachi | 183.6 | 209.5 | 153.1 | 122.8 | 437.1 | 142.1 | 294.9 | 85.6 | 172.1 | 292.9 | -0.16 | 0.7438 |
| Amino | Serine | 866.2 | 736.6 | 516.7 | 621.7 | 1123.1 | 607.8 | 1119.3 | 455.6 | 595.2 | 690.6 | -0.16 | 0.6217 |
| Amino | Creatin | 781.5 | 1772.7 | 84.4 | 586.3 | 1503.5 | 976.4 | 1792.9 | 228.8 | 490.4 | 784.1 | -0.15 | 0.8286 |
| Bile Ac | UDCA | 0.9 | 1.1 | 1.4 | 1.0 | 1.1 | 1.2 | 3.1 | 0.2 | 0.3 | 0.3 | -0.13 | 0.8683 |
| Carboh | Glyceri | 73.9 | 94.2 | 145.4 | 58.1 | 69.2 | 68.5 | 92.0 | 48.0 | 68.7 | 125.7 | -0.13 | 0.7202 |
| Carniti | Propion | 2.8 | 5.2 | 1.1 | 2.4 | 4.1 | 2.4 | 5.8 | 2.2 | 1.5 | 2.4 | -0.11 | 0.8308 |
| Carniti | Carniti | 45.0 | 53.3 | 15.7 | 32.9 | 57.4 | 41.7 | 63.6 | 20.6 | 29.9 | 39.7 | -0.06 | 0.8719 |
| Amino | 5-Amir | 20.8 | 20.7 | 29.3 | 13.4 | 15.0 | 11.2 | 18.5 | 24.0 | 22.1 | 20.6 | -0.04 | 0.8800 |
| Bile Ac | 7-Keto | 0.6 | 0.5 | 0.5 | 0.4 | 0.5 | 0.5 | 1.0 | 0.3 | 0.3 | 0.4 | -0.03 | 0.9438 |
| Organi | trans-A | 1.4 | 2.2 | 0.4 | 1.0 | 0.7 | 1.9 | 0.7 | 1.0 | 1.1 | 1.1 | 0.04 | 0.9275 |
| Amino | Methio | 438.8 | 329.2 | 202.7 | 276.5 | 553.0 | 297.4 | 552.0 | 230.0 | 391.7 | 416.7 | 0.07 | 0.8374 |
| Amino | Phenla | 0.2 | 0.2 | 0.1 | 0.2 | 0.2 | 0.2 | 0.1 | 0.2 | 0.3 | 0.2 | 0.08 | 0.6801 |
| Pyridin | Picolin | 7.6 | 8.5 | 10.3 | 7.4 | 8.0 | 3.9 | 8.0 | 9.5 | 13.2 | 9.9 | 0.08 | 0.7659 |
| Bile Ac | TLCA | 0.3 | 0.3 | 0.3 | 0.3 | 0.3 | 0.3 | 0.3 | 0.3 | 0.3 | 0.3 | 0.10 | 0.0732 |
| Amino | GABA | 29.5 | 35.9 | 17.9 | 18.1 | 18.5 | 27.0 | 35.8 | 14.4 | 22.4 | 30.5 | 0.12 | 0.7057 |
| Organi | Oxoglu | 150.6 | 171.9 | 341.6 | 54.4 | 70.4 | 187.9 | 287.1 | 61.0 | 62.9 | 259.6 | 0.12 | 0.8474 |
| Amino | Sarcosi | 38.3 | 30.7 | 26.9 | 28.9 | 43.9 | 34.6 | 51.6 | 21.9 | 34.4 | 42.3 | 0.13 | 0.5981 |
| Carboh | Glucon | 303.3 | 603.2 | 253.6 | 418.0 | 442.9 | 300.4 | 463.7 | 343.7 | 605.4 | 552.5 | 0.16 | 0.5781 |
| Amino | Phenyl | 0.3 | 0.2 | 0.3 | 0.4 | 0.4 | 0.5 | 0.3 | 0.3 | 0.3 | 0.4 | 0.17 | 0.4427 |
| Amino | Asparti | 1124.8 | 1294.1 | 909.6 | 930.1 | 1693.2 | 1338.5 | 1854.2 | 821.2 | 1045.9 | 1676.6 | 0.18 | 0.5321 |
| Amino | Threon | 402.2 | 297.7 | 122.0 | 247.8 | 556.7 | 338.8 | 618.8 | 208.0 | 316.4 | 367.7 | 0.19 | 0.6668 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bile Ac | GHDC | 0.2 | 0.4 | 0.6 | 0.6 | 0.3 | 0.8 | 0.4 | 0.3 | 0.6 | 0.5 | 0.19 | 0.5828 |
| Organi | Isocitri | 22.5 | 24.9 | 12.8 | 22.4 | 20.3 | 24.4 | 26.0 | 22.6 | 18.8 | 27.2 | 0.21 | 0.2420 |
| Amino | Alanine | 2116.2 | 1511.7 | 1441.6 | 1561.2 | 2588.7 | 1922.0 | 3234.0 | 1194.5 | 1864.3 | 2667.0 | 0.24 | 0.4517 |
| Amino | N-Acet | 3.5 | 2.1 | 4.0 | 2.4 | 3.4 | 4.3 | 3.5 | 2.8 | 3.0 | 4.9 | 0.25 | 0.3043 |
| Amino | Theani | 1.0 | 1.9 | 1.2 | 0.3 | 0.9 | 0.4 | 1.6 | 1.7 | 1.3 | 1.3 | 0.25 | 0.5938 |
| Amino | Tryptop | 89.3 | 91.4 | 56.3 | 74.8 | 124.1 | 94.1 | 149.8 | 64.8 | 100.6 | 111.8 | 0.26 | 0.3659 |
| Benzoi | Vanilli | 2.4 | 1.7 | 3.9 | 1.6 | 1.4 | 2.1 | 3.3 | 3.0 | 2.7 | 2.2 | 0.26 | 0.4396 |
| Bile Ac | GCA | 0.4 | 0.4 | 0.4 | 0.5 | 0.5 | 0.4 | 0.6 | 0.5 | 0.8 | 0.4 | 0.29 | 0.2867 |
| Amino | Norleuc | 1.2 | 0.8 | 0.3 | 1.0 | 1.7 | 1.0 | 2.4 | 0.7 | 0.8 | 1.3 | 0.33 | 0.5445 |
| Amino | Phenyla | 502.9 | 382.9 | 201.2 | 350.5 | 606.7 | 447.3 | 761.3 | 364.9 | 516.8 | 612.6 | 0.40 | 0.2126 |
| Amino | Tyrosin | 382.5 | 300.9 | 178.3 | 279.5 | 530.8 | 379.8 | 632.5 | 320.8 | 373.1 | 504.7 | 0.40 | 0.2228 |
| Carniti | 2-Meth | 0.2 | 0.4 | 0.1 | 0.2 | 0.4 | 0.3 | 0.7 | 0.1 | 0.2 | 0.3 | 0.40 | 0.4791 |
| Amino | Glycine | 975.3 | 1119.9 | 584.0 | 618.4 | 1583.8 | 1229.3 | 1732.2 | 917.4 | 1219.7 | 1481.2 | 0.43 | 0.1790 |
| Amino | Methyl | 0.6 | 0.3 | 0.2 | 0.3 | 0.9 | 0.6 | 0.9 | 0.5 | 0.5 | 0.7 | 0.44 | 0.3042 |
| Amino | Ornithi | 115.7 | 167.9 | 117.4 | 101.5 | 249.8 | 240.5 | 253.5 | 191.1 | 160.3 | 201.3 | 0.48 | 0.1111 |
| Amino | Glutam | 552.7 | 516.7 | 234.2 | 413.8 | 864.0 | 673.8 | 901.6 | 608.3 | 764.7 | 722.4 | 0.51 | 0.1073 |
| Amino | Arginin | 972.9 | 869.7 | 618.7 | 948.9 | 1235.0 | 1076.7 | 1534.4 | 1183.2 | 1626.6 | 1283.3 | 0.53 | 0.0210 |
| Imidaz | Imidaz | 1.2 | 1.2 | 1.5 | 0.8 | 0.8 | 2.0 | 1.3 | 1.4 | 1.7 | 1.7 | 0.53 | 0.0277 |
| Benzoi | 4-Hydr | 5.1 | 5.4 | 4.1 | 6.5 | 2.5 | 6.4 | 6.8 | 7.2 | 7.3 | 8.1 | 0.59 | 0.0183 |
| Quinol | Xanthu | 0.2 | 0.9 | 0.5 | 0.6 | 0.4 | 1.2 | 1.0 | 0.5 | 0.4 | 1.2 | 0.65 | 0.1757 |
| Amino | Isoleuc | 591.1 | 370.3 | 252.1 | 413.0 | 847.0 | 674.0 | 1111.0 | 544.1 | 729.7 | 857.3 | 0.66 | 0.0757 |
| Amino | Leucine | 947.3 | 627.0 | 357.4 | 677.8 | 1542.7 | 1160.3 | 1846.4 | 925.1 | 1297.0 | 1442.3 | 0.68 | 0.0843 |
| Bile Ac | THDC | 0.6 | 0.4 | 0.5 | 0.6 | 0.7 | 0.7 | 0.5 | 1.0 | 1.4 | 1.2 | 0.72 | 0.0804 |
| Amino | Valine | 602.9 | 419.2 | 288.4 | 397.8 | 934.7 | 778.7 | 1302.4 | 602.8 | 775.2 | 1035.3 | 0.77 | 0.0573 |
| Amino | Acetylg | 56.9 | 41.0 | 29.4 | 40.4 | 87.9 | 77.2 | 129.0 | 58.6 | 74.4 | 99.1 | 0.78 | 0.0514 |
| Benzoi | 4-Hydr | 4.0 | 3.0 | 5.6 | 6.2 | 2.4 | 9.5 | 6.7 | 5.1 | 8.3 | 7.2 | 0.79 | 0.0177 |
| Carniti | Stearyl | 0.3 | 0.6 | 0.4 | 0.3 | 0.7 | 0.8 | 1.5 | 0.3 | 0.6 | 1.0 | 0.86 | 0.1537 |
| Bile Ac | CDCA | 1.9 | 1.7 | 3.1 | 1.6 | 2.4 | 3.7 | 9.5 | 2.0 | 2.2 | 1.9 | 0.86 | 0.2997 |
| Organi | Shikim | 9.4 | 3.3 | 3.7 | 5.5 | 5.1 | 12.2 | 10.2 | 8.9 | 11.0 | 7.0 | 0.87 | 0.0139 |
| Carboh | Glucon | 19.8 | 32.7 | 14.3 | 20.7 | 18.2 | 41.8 | 43.1 | 21.1 | 55.5 | 37.0 | 0.91 | 0.0255 |
| Amino | Histidi | 279.4 | 277.8 | 137.3 | 211.4 | 408.2 | 443.9 | 670.3 | 320.3 | 480.9 | 597.7 | 0.94 | 0.0147 |
| Amino | Glutam | 639.8 | 586.5 | 621.5 | 245.7 | 881.1 | 1479.1 | 1593.6 | 1017.6 | 1195.7 | 1343.0 | 1.16 | 0.0010 |
| Bile Ac | 3-DHC | 4.6 | 2.6 | 3.3 | 3.8 | 2.8 | 16.8 | 21.6 | 0.9 | 1.3 | 1.3 | 1.30 | 0.3301 |
| Amino | N-Pher | 0.3 | 0.2 | 0.2 | 0.2 | 0.2 | 0.6 | 0.6 | 0.3 | 0.5 | 0.4 | 1.32 | 0.0038 |
| Amino | 4-Hydr | 7.2 | 10.1 | 7.1 | 3.8 | 8.1 | 23.8 | 25.6 | 10.4 | 14.0 | 20.7 | 1.37 | 0.0132 |
| Carboh | Erythro | 2.3 | 6.1 | 2.5 | 1.9 | 3.5 | 10.0 | 8.4 | 8.4 | 8.5 | 12.0 | 1.54 | 0.0003 |
| Amino | Proline | 488.2 | 395.3 | 281.1 | 333.1 | 657.1 | 1656.2 | 1863.9 | 1016.7 | 1263.5 | 1344.3 | 1.73 | 0.0012 |
| Indoles | Indolel | 7.4 | 11.1 | 28.7 | 4.9 | 1.4 | 49.7 | 38.1 | 23.6 | 30.8 | 40.1 | 1.77 | 0.0042 |
| Bile Ac | TCDC | 0.5 | 0.4 | 0.4 | 0.4 | 0.6 | 0.8 | 1.1 | 3.5 | 1.5 | 2.1 | 1.92 | 0.0498 |
| Phenyl | Hydrox | 12.0 | 8.2 | 17.9 | 23.3 | 9.5 | 97.1 | 113.0 | 50.6 | 79.8 | 75.9 | 2.56 | 0.0020 |
| Bile Ac | TCA | 9.7 | 4.0 | 8.2 | 11.6 | 14.9 | 21.8 | 18.5 | 146.3 | 71.1 | 72.4 | 2.77 | 0.0714 |
| Bile Ac | CA | 5.8 | 4.3 | 11.2 | 6.1 | 9.1 | 56.9 | 183.2 | 2.6 | 5.4 | 2.9 | 2.78 | 0.2858 |
| Amino | N-Acet | 1.3 | 1.5 | 5.1 | 2.7 | 1.5 | 22.3 | 24.1 | 13.4 | 14.7 | 25.1 | 3.04 | 0.0013 |
| Organi | Lactic a | 1152.5 | 3674.9 | 2268.4 | 693.0 | 3371.6 | 20858.9 | 15576.9 | 14066.0 | 29284.4 | 14117.0 | 3.07 | 0.0040 |
| Bile Ac | TaMCA | 9.6 | 4.8 | 6.4 | 12.1 | 17.8 | 23.5 | 37.7 | 227.3 | 69.8 | 89.7 | 3.14 | 0.0940 |
| Phenyl | Phenyl | 8.7 | 12.5 | 26.4 | 4.0 | 4.7 | 109.0 | 107.7 | 82.0 | 118.7 | 84.0 | 3.15 | 3.07E-05 |
| Bile Ac | TUDC | 0.2 | 0.1 | 0.1 | 0.2 | 0.3 | 0.8 | 0.6 | 3.2 | 1.1 | 2.2 | 3.22 | 0.0449 |
| Bile Ac | TwMC | 1.0 | 0.6 | 0.6 | 1.2 | 1.5 | 3.8 | 1.7 | 17.9 | 8.7 | 14.2 | 3.24 | 0.0531 |
| Organi | 2-Hydr | 19.1 | 12.2 | 14.7 | 12.2 | 11.8 | 180.4 | 146.0 | 77.7 | 170.1 | 98.0 | 3.26 | 0.0038 |
| Fatty A | 2-Hydr | 14.1 | 13.8 | 16.6 | 11.3 | 7.1 | 205.4 | 152.6 | 110.7 | 216.2 | 150.6 | 3.73 | 0.0013 |
| Organi | Maloni | 16.7 | 17.2 | 8.2 | 12.1 | 12.8 | 246.3 | 111.5 | 203.5 | 224.5 | 233.1 | 3.93 | 0.0013 |
| Organi | Pyruvic | 14.8 | 15.6 | 24.1 | 9.5 | 14.5 | 261.6 | 382.0 | 119.5 | 267.7 | 364.3 | 4.15 | 0.0048 |
| Bile Ac | DCA-3 | 0.3 | 0.9 | 0.5 | 0.2 | 0.1 | 71.6 | 112.3 | 1.8 | 2.0 | 7.0 | 6.67 | 0.1634 |

Supplemental table 2. Clinical characteristics and demographic information of UC participants.

| **Patients with UC** | **1** | | **2** | | **3** | | **4** | |
|---|---|---|---|---|---|---|---|---|
| **Age(years)** | 19 | | 63 | | 21 | | 72 | |
| **Gender** | Male | | Female | | Female | | Male | |
| **Weight(kg)** | 64 | | 72 | | 52 | | 55 | |
| **BMI(kg/m$^2$)** | 19.1 | | 24.9 | | 18.9 | | 19 | |
| **Vancomycin treatment** | Before | After | Before | After | Before | After | Before | After |
| **Truelove-Witts score** | Severe | Mild | Moderate | Mild | Severe | Mild | Severe | Moderate |
| **Bloody stools/d** | ≥10 | 0 | 6-8 | 0 | 6-10 | 0 | ≥10 | 0 |
| **Pulse (≥90 bmp)** | 95 | 73 | 84 | 64 | 100 | 68 | 95 | 75 |
| **Temperature(℃)** | 36.5 | 36.4 | 36.8 | 36.5 | 36.2 | 36 | 39 | 36.1 |
| **Hemoglobin(g/L)** | 82 | 83 | 143 | 129 | 111 | 135 | 115 | 108 |
| **ESR (≥30 mm/h)** | 109 | 56 | 31 | 3 | 47 | 6 | 2 | 72 |
| **CRP (0-10 mg/L)** | 41.72 | 1.19 | 14.33 | 0.64 | 163.91 | 0.2 | 10.22 | 7.81 |

**Supplemental table 3. Demographic information of healthy donors.**

| ID | Age (years) | Gender | Weight (kg) | BMI (kg/m$^2$) | Index |
|---|---|---|---|---|---|
| HC-1 | 55 | Male | 66.0 | 22.8 | Colonic LPMNCs, Flow cytometry, DMSO treatment |
| HC-2 | 64 | Female | 68.0 | 25.0 | Colonic LPMNCs, Flow cytometry, DMSO treatment |
| HC-3 | 55 | Female | 70.0 | 24.8 | Colonic LPMNCs, Flow cytometry, DMSO treatment |
| HC-4 | 53 | Male | 80.0 | 27.7 | Colonic LPMNCs, Flow cytometry, DMSO treatment |
| HC-5 | 60 | Male | 70.0 | 23.4 | Colonic LPMNCs, Flow cytometry, DMSO treatment |
| HC-6 | 57 | Male | 86.0 | 28.7 | Colonic LPMNCs, Flow cytometry, DMSO treatment |
| HC-7 | 20 | Female | 76.0 | 25.7 | Colonic LPMNCs, Flow cytometry, DMSO treatment |
| HC-8 | 62 | Female | 70.0 | 23.9 | Colonic LPMNCs, Flow cytometry, DMSO treatment |
| HC-9 | 56 | Female | 55.0 | 19.5 | Colonic LPMNCs, Flow cytometry, DMSO treatment |
| HC-10 | 35 | Male | 85.0 | 27.8 | Colonic LPMNCs, Flow cytometry, DMSO treatment |
| HC-11 | 36 | Female | 72.0 | 28.1 | Colonic LPMNCs, Flow cytometry, GSK2606414 treatment |
| HC-12 | 28 | Male | 87.5 | 29.9 | Colonic LPMNCs, Flow cytometry, GSK2606414 treatment |
| HC-13 | 68 | Female | 80.0 | 28.7 | Colonic LPMNCs, Flow cytometry, GSK2606414 treatment |
| HC-14 | 58 | Male | 77.0 | 26.6 | Colonic LPMNCs, Flow cytometry, GSK2606414 treatment |
| HC-15 | 63 | Male | 75.0 | 25.4 | Colonic LPMNCs, Flow cytometry, GSK2606414 treatment |
| HC-16 | 67 | Female | 64.0 | 23.5 | Colonic LPMNCs, Flow cytometry, GSK2606414 treatment |
| HC-17 | 61 | Male | 71.0 | 23.2 | Colonic LPMNCs, Flow cytometry, GSK2606414 treatment |
| HC-18 | 60 | Female | 67.7 | 24.9 | Colonic LPMNCs, Flow cytometry, GSK2606414 treatment |
| HC-19 | 68 | Male | 65.0 | 21.7 | Colonic LPMNCs, Flow cytometry, GSK2606414 treatment |
| HC-20 | 46 | Male | 75.0 | 26.6 | Colonic LPMNCs, Flow cytometry, GSK2606414 treatment |
| HC-21 | 36 | Female | 72.0 | 28.1 | Colonic LPMNCs, Flow cytometry, DCA treatment |
| HC-22 | 49 | Female | 61.0 | 23.0 | Colonic LPMNCs, Flow cytometry, DCA treatment |
| HC-23 | 50 | Male | 73.0 | 23.0 | Colonic LPMNCs, Flow cytometry, DCA treatment |
| HC-24 | 50 | Female | 64.0 | 24.4 | Colonic LPMNCs, Flow cytometry, DCA treatment |
| HC-25 | 63 | Female | 51.0 | 19.9 | Colonic LPMNCs, Flow cytometry, DCA treatment |
| HC-26 | 35 | Male | 79.0 | 25.5 | Colonic LPMNCs, Flow cytometry, DCA treatment |
| HC-27 | 43 | Female | 62.0 | 24.8 | Colonic LPMNCs, Flow cytometry, DCA treatment |
| HC-28 | 36 | Female | 65.0 | 26.0 | Colonic LPMNCs, Flow cytometry, DCA treatment |
| HC-29 | 38 | Female | 60.0 | 22.9 | Colonic LPMNCs, Flow cytometry, DCA treatment |
| HC-30 | 56 | Male | 80.0 | 26.4 | Colonic LPMNCs, Flow cytometry, DCA treatment |
| HC-31 | 63 | Female | 70.0 | 24.2 | Colonic LPMNCs, Flow cytometry, DCA + GSK2606414 treatment |
| HC-32 | 60 | Female | 65.0 | 25.1 | Colonic LPMNCs, Flow cytometry, DCA + GSK2606414 treatment |
| HC-33 | 65 | Female | 65.0 | 25.4 | Colonic LPMNCs, Flow cytometry, DCA + GSK2606414 treatment |
| HC-34 | 75 | Male | 76.5 | 23.6 | Colonic LPMNCs, Flow cytometry, DCA + GSK2606414 treatment |
| HC-35 | 56 | Male | 95.0 | 32.1 | Colonic LPMNCs, Flow cytometry, DCA + GSK2606414 treatment |
| HC-36 | 57 | Female | 48.0 | 19.2 | Colonic LPMNCs, Flow cytometry, DCA + GSK2606414 treatment |
| HC-37 | 75 | Male | 69.0 | 23.1 | Colonic LPMNCs, Flow cytometry, DCA + GSK2606414 treatment |
| HC-38 | 49 | Female | 55.5 | 21.1 | Colonic LPMNCs, Flow cytometry, DCA + GSK2606414 treatment |
| HC-39 | 55 | Male | 67.0 | 23.7 | Colonic LPMNCs, Flow cytometry, DCA + GSK2606414 treatment |
| HC-40 | 63 | Male | 61.5 | 21.5 | Colonic LPMNCs, Flow cytometry, DCA + GSK2606414 treatment |

**Supplemental table 4. Proteins Bound to DCA.**

| |
|---|
| Actg2 |
| Actc1 |
| Acta1 |
| Acta2 |
| Hbb-b2 |
| Hbbt2 |
| 3000002C10Rik |
| Rps9 |
| Pcx |
| Pc |
| Dars1 |
| Dars |
| Trappc11 |
| Nefh |
| Dop1b |
| Vps13a |
| Naa25 |
| Chd9 |
| Atl3 |
| Haus8 |
| Myo7b |
| Slfn1 |
| OTTMUSWSBG00059304 |
| Sltm |
| Cabin1 |
| Cracdl |
| Kif13b |
| Scn10a |
| H1-4 |
| Fbxl18 |
| Gm1141 |
| Phip |
| 2210010C04Rik |
| Dnah2 |
| RP23-56I20.8-001 |
| Ccdc25 |
| Arid5b |
| Taf1d |
| L3mbtl1 |
| Szt2 |
| mKIAA0467 |
| Shroom2 |
| Shroom3 |
| Ubr4 |
| Atp2c2 |
| Prr19 |
| H2az2 |
| H2az1 |
| H2ax |
| H2ac21 |
| Parp4 |
| Apob |
| Ell |
| Hyal2 |
| Gtf2h4 |
| Bard1 |

| |
|---|
| Clec11a |
| Mkln1 |
| Mos |
| Ucp1 |
| Npr1 |
| Npr-a |
| Hoxb9 |
| Hoxc10 |
| Hoxa10 |
| Hoxa11 |
| Hoxd9 |
| Hoxd11 |
| Hoxd10 |
| Hoxa9 |
| Hoxc9 |
| Wnt2 |
| Lmnb2 |
| Lmna |
| Zfp42 |
| Mboat4 |
| Rcc2 |
| Twist1 |
| Fbl |
| Rpl29 |
| Pkm |
| Osm |
| Atp5f1b |
| Kcnj3 |
| Kcnj1 |
| Renbp |
| Rpl19 |
| Smad4 |
| Rbbp6 |
| Col17a1 |
| Fbln1 |
| Ak8 |
| Igfn1 |
| Treml4 |
| Vrtn |
| Trim43a |
| Trim43c |
| Trim43b |
| Gm15737 |
| Ckap2 |
| Fbxo31 |
| Ogfod1 |
| Ccdc177 |
| Gpr35 |
| D5Ertd579e |
| Kiaa0232 |
| Dipk2a |
| Otol1 |
| Syce1l |
| Ermn |
| Cep44 |
| Heatr5a |
| Trpc6 |
| Adam12 |

| |
|---|
| Cnga2 |
| Pptc7 |
| Ift122 |
| Rrp12 |
| Osgepl1 |
| Jade2 |
| Hexim2 |
| Gimap8 |
| Scoc |
| Kif27 |
| Hook2 |
| Trpm4 |
| Lrrc75a |
| Cep120 |
| Dpp8 |
| Arhgap33 |
| Ankrd45 |
| Tmco3 |
| Gabra5 |
| Txlng |
| Cdkn2aip |
| Frmd4a |
| Zc2hc1a |
| Zcchc3 |
| Zdhhc14 |
| Cep55 |
| Lcmt2 |
| Ttc39b |
| Tiparp |
| Scara3 |
| Amer2 |
| Phf20l1 |
| Ccdc87 |
| Akr7a2 |
| Lonp1 |
| Pum1 |
| Mical3 |
| Asb2 |
| Tnfaip8l1 |
| Sdha |
| Shtn1 |
| Ahsa2 |
| Acat1 |
| Angptl8 |
| Stx19 |
| C1qtnf12 |
| Top1mt |
| Rttn |
| Abcc9 |
| Apbb1ip |
| Ndc1 |
| Ttc29 |
| Cant1 |
| Cdhr5 |
| Cox4i2 |
| Hpx |
| Cfap44 |
| Pip4k2c |

| |
|---|
| Uncharacterized protein C6orf132 homolog |
| Tspan2 |
| Tssk6 |
| Homer3 |
| Znhit2 |
| Mbip |
| Erc1 |
| Mrpl36 |
| Ankrd17 |
| Znf318 |
| Ndufa3 |
| Ddx28 |
| Prkrip1 |
| Narf |
| Mettl18 |
| Zbed3 |
| Chaf1b |
| Synj2 |
| Ttyh1 |
| Cers5 |
| Btbd17 |
| Mettl7b |
| Tsc1 |
| Pik3ap1 |
| Oga |
| Invs |
| Ddx24 |
| Cpb2 |
| Utp3 |
| Pard6g |
| Tnfrsf19 |
| Cdc42ep4 |
| Dnajb1 |
| Ppie |
| Cdyl |
| Cfap206 |
| Pole |
| Heph |
| Tulp1 |
| Elapor1 |
| Ddr2 |
| Pcdh9 |
| Bcar3 |
| Srrt |
| Spata1 |
| Crybg1 |
| Anapc5 |
| Scn8a |
| Golga1 |
| Cmas |
| Recql4 |
| Lingo4 |
| Gtf3c1 |
| Spink5 |
| Pigq |
| Fcer2a |
| Fcer2 |
| Jakmip1 |

| |
|---|
| Casc1 |
| Dnai7 |
| Fubp1 |
| Las1 |
| Sst |
| Gm10775 |
| Taldo1 |
| Rab11fip1 |
| Mast3 |
| Gm11639 |
| Ric8b |
| Pam16l |
| Spata19 |
| Cyp27a1 |
| Ccdc7a |
| Gtf3c6 |
| Slc16a10 |
| Tbc1d5 |
| Adam6a |
| Adam6b |
| Gpr19 |
| Pcnt |
| Gopc |
| Kidins220 |
| Zfp410 |
| Catsperb |
| Eml5 |
| Lrguk |
| Fam135b |
| ARHGAP28 |
| Lztr1 |
| Vmn2r111 |
| Vmn2r116 |
| Sil1 |
| Matr3 |
| Cspp1 |
| Faf2 |
| Prr33 |
| Dnah7b |
| Mpz |
| Pakap |
| Akap2 |
| 1810058I24Rik |
| Stmp1 |
| 4930433I11Rik |
| Ccdc50 |
| Gsdmc4 |
| Gsdmc |
| Braf |
| If1ia2 |
| Ifnl3 |
| Otud5 |
| Zfp937 |
| Zfp442 |
| 3300002I08Rik |
| Ndufaf7 |
| Tnrc6c |
| Pcdhga6 |

| |
|---|
| Arl6 |
| Epc1 |
| Ankrd35 |
| Hars |
| Hars1 |
| Carf |
| Gm49340 |
| Spata22 |
| Clspn |
| Wdpcp |
| Gale |
| Vwa5b1 |
| Lpcat2b |
| Asxl2 |
| Clec3a |
| Cfap77 |
| Hal |
| Ibtk |
| Kirrel2 |
| Cdr2l |
| Wfdc1 |
| Dlgap4 |
| Pde4dip |
| Sptan1 |
| Eprs |
| Eprs1 |
| Zfp174 |
| Herc2 |
| Cacna1c |
| Cnnm4 |
| Smtn |
| Stk16 |
| Ddx23 |
| Tmx2 |
| Stxbp5 |
| Ica1 |
| Pikfyve |
| Tbc1d14 |
| Il12rb2 |
| Rps15a |
| Fbxo22 |
| Selenbp1 |
| Selenbp2 |
| Gjb6 |
| Kctd18 |
| Etv1 |
| Etv5 |
| Etv4 |
| Kcnma1 |
| Myo18b |
| Krcc1 |
| Cftr |
| Myo9b |
| Fcf1 |
| Rnf25 |
| Dennd4c |
| Cep192 |
| Hk2 |

| |
|---|
| Col6a6 |
| Lrrc7 |
| Rgl1 |
| Pnpla8 |
| Arhgap17 |
| Tjp3 |
| Mdc1 |
| Nol8 |
| Hjurp |
| Cenpe |
| Mga |
| Taf12 |
| Trpm2 |
| Ndufa12 |
| Pla2g6 |
| Srsf11 |
| Npepl1 |
| Mtmr1 |
| Fgfr3 |
| Mlxip |
| Ppp1r35 |
| Bcl3 |
| Lipi |
| Fam98c |
| Mgat4b |
| Nrap |
| Mpdz |
| Pdia6 |
| Bdp1 |
| Bcorl1 |
| Pkn2 |
| Aoc2 |
| Scart2 |
| Xlr3c |
| Xlr3a |
| Scart1 |
| Slitrk2 |
| Themis2 |
| Xlr3b |
| Xlr3 |
| Slc43a1 |
| Cobl |
| Ermp1 |
| Lhx2 |
| Nptn |
| Ip6k1 |
| Senp6 |
| Acadl |
| Gbf1 |
| Wdr90 |
| Samd11 |
| Pfn1 |
| Ccdc180 |
| Usp13 |
| Wfikkn2 |
| Pramel45 |
| Gm17078 |
| Mta1 |

| |
|---|
| Mta3 |
| SKI |
| Skiv2l |
| Por |
| Necap1 |
| Snx21 |
| Ncf2 |
| Ccr8 |
| Crlf1 |
| Il1f10 |
| Vmn2r112 |
| Lmnb1 |
| F830208F22Rik |
| Arhgap6 |
| Appl2 |
| Mob3b |
| Emilin2 |
| Phyh |
| Hexa |
| Rps6ka1 |
| Phaf1 |
| Rad23b |
| Ptpn13 |
| B3gnt2 |
| Gm10642 |
| Pxk |
| Unc5b |
| Serpina3h |
| Serpina3g |
| Serpina3n |
| Zfp384 |
| Etv3 |
| Sidt2 |
| Snx13 |
| Hspa5 |
| Ccl9 |
| Arpc5 |
| Gbp2 |
| Etl4 |
| Skt |
| Morn1 |
| Nipsnap1 |
| Mill1 |
| Siglech |
| Reln |
| Acad8 |
| Clpp |
| Sf1 |
| Ldha |
| Hs3st6 |
| Ndufs1 |
| Maoa |
| Gart |
| Pcdhb6 |
| Kctd17 |
| B3gnt3 |
| Cyp2j13 |
| Alg8 |

| |
|---|
| Mef2d |
| Gm10629 |
| Nptx1 |
| A130057D12Rik |
| Gm10631 |
| Eftud2 |
| Gm906 |
| Gm8765 |
| Tcfl5 |
| 1700001L05Rik |
| Or6c69 |
| Chek1 |
| Huwe1 |
| Ets1 |
| Ets2 |
| Chek2 |
| Fgl2 |
| Otor |
| Uhrf1bp1 |
| N4bp1 |
| Spata33 |
| Rpl15 |
| Gm6525 |
| Gm12258 |
| Foxo6 |
| Haus4 |
| Ccdc92b |
| Hmgn2 |
| NMDA2C |
| mKIAA1769 |
| Helz2 |
| Exoc4 |
| Vps13d |
| Zfp975 |
| Zfp976 |
| Dhx37 |
| Stat2 |
| Kat2a |
| Kat2b |
| Hdac5 |
| Notch2 |
| Tha1 |
| Cpne1 |
| Gm28036 |
| Rbm12 |
| Rap250 |
| Ncoa6 |
| Arpc4 |
| Mast1 |
| Or52r1c |
| trypsinogen |
| Gm2663 |
| 1810009J06Rik |
| Mcm3ap |
| Tbc1d22b |
| Asz1 |
| Myh1 |
| Myh4 |

| |
|---|
| Ror1 |
| Cntnap4 |
| Copb1 |
| Penk |
| Rusc2 |
| Synm |
| 5730596B20Rik |
| Sox6 |
| Epb41l5 |
| 9530077C05Rik |
| Matcap2 |
| Incenp |
| Dpp6 |
| Cacnb3 |
| Vangl2 |
| Extl3 |
| Agap3 |
| Dsel |
| H1f0 |
| H1-0 |
| Epha3 |
| B230217C12Rik |
| Dnaaf6b |
| Nfib |
| Ptpn14 |
| Klhl1 |
| Thoc7 |
| Chchd2l |
| 1700084P21Rik |
| 1500015L24Rik |
| Map1b |
| Plekha5 |
| Aldh1l1 |
| Aldh1l2 |
| Nos1 |
| Psmc5 |
| Clcn1 |
| Oas1b |
| Oas1d |
| Oas1e |
| Oas1f |
| BC022960 |
| Slc25a24 |
| Vmn1r18 |
| Ighg2b |
| Ppp1r37 |
| Wdr74 |
| Ddx20 |
| Hmmr |
| Or1ab2 |
| Or8k41 |
| Olfr1285 |
| Or4k37 |
| Or4k38 |
| Or4k40 |
| Or4c127 |
| Or4c52 |
| Or4c126 |

| |
|---|
| pol |
| Itga9 |
| Gzmn |
| AY036118 |
| Slc38a10 |
| Mrps23 |
| Hmgb2 |
| Ccdc178 |
| Tubb4b |
| Tubb3 |
| Tubb5 |
| Tubb4a |
| Gramd3 |
| Slxl1 |
| Gm16405 |
| Gm14625 |
| 4922502B01Rik |
| Tab3 |
| Il17ra |
| Gpa33 |
| 1700063H04Rik |
| Rad51d |
| Rad5113 |
| TRAD/RAD51L3 |
| Elp1 |
| Klra21 |
| Klra8 |
| Zim1 |
| Ccdc154 |
| Atp13a4 |
| Rbm46 |
| Arhgef40 |
| Arfgap1 |
| Gsdma3 |
| Atad5 |
| Disc1 |

Supplemental table 5. Reagent or resource.

| REAGENT or RESOURCE | SOURCE | IDENTIFIER |
|---|---|---|
| Antibodies | | |
| Anti-mouse CD3e, APC-eFluor 780 | eBioscience | Cat# 47-0031-82 ; RRID: AB_11149861 |
| Anti-mouse CD5, APC-eFluor 780 | eBioscience | Cat# 47-0051-82; RRID: AB_2573940 |
| Anti-mouse CD19, APC-eFluor 780 | eBioscience | Cat# 47-0193-82; RRID: AB_10853189 |
| Anti-mouse/human CD45R/B220, APC/Cyanine7 | BioLegend | Cat# 103224; RRID: AB_313007 |
| Anti-mouse CD16/32, APC/Cyanine7 | BioLegend | Cat# 101328; RRID: AB_2104158 |
| Anti-mouse FcεRIα, APC/Cyanine7 | BioLegend | Cat# 134326; RRID: AB_2572064 |
| Anti-human/mouse CD11b, APC/Cyanine7 | Tonbo Biosciences | Cat# 25-0112-U100; RRID: AB_3094465 |
| Anti-mouse CD11c, APC/Cyanine7 | Tonbo Biosciences | Cat# 25-0114; RRID: AB_2621626 |
| Anti-mouse Ly-6G, APC/Cyanine7 | Tonbo Biosciences | Cat# 25-1276; RRID: AB_2621632 |
| Anti-mouse TER-119, APC-eFluor 780 | eBioscience | Cat# 47-5921-82; RRID: AB_1548786 |
| Streptavidin, PE-Cyanine7 | eBioscience | Cat# 25-4317-82; RRID: AB_10116480 |
| Anti-mouse CD45.2, Alexa Fluor 700 | eBioscience | Cat# 56-0454-82; RRID: AB_657752 |

| | | |
|---|---|---|
| Anti-mouse IL-13, Alexa Fluor 488 | eBioscience | Cat# 53-7133-82; RRID: AB_2016708 |
| Anti-mouse GATA3, BV421 | BD Biosciences | Cat# 563349; RRID: AB_2738152 |
| Anti-mouse/human IL-5, APC | BioLegend | Cat# 504306; RRID: AB_315330 |
| Anti-mouse Amphiregulin biotin | R&D Systems | Cat# BAF989; RRID: AB_2060662 |
| Anti-mouse CD16/CD32 | eBioscience | Cat# 14-0161-85; RRID: AB_467134 |
| Anti-mouse/human IL-5, PE | BD Biosciences | Cat# 554395; RRID: AB_395364 |
| Anti-mouse CD45.1, PE-Cyanine7 | eBioscience | Cat# 25-0453-82; RRID: AB_469629 |
| Streptavidin, APC | BioLegend | Cat# 405207 |
| Anti-mouse CD16/CD32 | eBioscience | Cat# 14-0161-85; RRID: AB_467134 |
| Anti-human CD303α, FITC | eBioscience | Cat# 11-9818-42; RRID: AB_11149122 |
| Anti-human CD94, FITC | eBioscience | Cat# 11-0949-42; RRID: AB_11149673 |
| Anti-human CD19, FITC | Tonbo Biosciences | Cat# 35-0198; RRID: AB_2621683 |
| Anti-human CD123, FITC | eBioscience | Cat# 11-1239-42; RRID: AB_10854578 |
| Anti-human CD3, FITC | eBioscience | Cat# 11-0036-42; RRID: AB_1272072 |

| | | |
|---|---|---|
| Anti-human CD16, FITC | eBioscience | Cat# 11-0168-42; RRID: AB_10805747 |
| Anti-human CD14, FITC | Tonbo Biosciences | Cat# 35-0149; RRID: AB_2621680 |
| Anti-human Amphiregulin biotin | R&D Systems | Cat# BAF262; RRID: AB_2060677 |
| Anti-human CD45, Alexa Fluor700 | BioLegend | Cat# 304024; RRID: AB_493761 |
| Anti-human CD127 (IL-7Ra), Brilliant Violet 421 | BioLegend | Cat# 351310; RRID: AB_10960140 |
| Anti-mouse CD3, FITC | BioLegend | Cat# 100204; RRID: AB_312661 |
| Anti-mouse CD5, FITC | eBioscience | Cat# 11-0051-82; RRID: AB_464908 |
| Anti-mouse CD16/32, FITC | BioLegend | Cat# 101306; RRID: AB_312805 |
| Anti-mouse/human CD11b, FITC | BioLegend | Cat# 101206; RRID: AB_312789 |
| Anti-mouse CD11c, FITC | BioLegend | Cat# 117306; RRID: AB_313775 |
| Anti-mouse CD19, FITC | Tonbo Biosciences | Cat# 35-0193; RRID: AB_2621682 |
| Anti-mouse/human CD45R/B220, FITC | BioLegend | Cat# 103206; RRID: AB_312991 |
| Anti-mouse TER-119/Erythroid Cells, FITC | BioLegend | Cat# 116206; RRID: AB_313707 |
| Anti-mouse Ly-6G, FITC | Tonbo | Cat# 35-1276; RRID: |

| | | |
|---|---|---|
| | Biosciences | AB_2621704 |
| Anti-mouse FcεRIα, FITC | BioLegend | Cat# 134306; RRID: AB_1626108 |
| Anti-mouse CD127 (IL-7Rα), PE | BioLegend | Cat# 135010; RRID: AB_1937251 |
| Anti-mouse CD127 (IL-7Rα), APC | BioLegend | Cat# 135012; RRID: AB_1937216 |
| Anti-mouse KLRG1, PerCP-eFluor 710 | eBioscience | Cat# 46-5893-82; RRID: AB_10670282 |
| Anti-mouse CD45.2, Pacific Blue | BioLegend | Cat# 109820; RRID: AB_492872 |
| Anti-IL13 Rabbit Polyclonal antibody | Affinity | Cat# DF2520; RRID: AB_2839726 |
| Anti-TMX2 Rabbit Polyclonal antibody | Proteintech | Cat# 19838-1-AP; RRID: AB_10642435 |
| HRP-conjugated Goat Anti-Mouse IgG (H+L) | Proteintech | Cat# SA00001-1; RRID: AB_2722565 |
| HRP-conjugated Affinipure Goat Anti-Rabbit IgG (H+L) | Proteintech | Cat# SA00001-2; RRID: AB_2722564 |
| Anti-PERK (C33E10) Rabbit mAb | Cell Signaling Technology | Cat# 3192; RRID:AB_2095847 |
| Anti-Phospho-PERK (Thr980) (16F8) Rabbit mAb | Cell Signaling Technology | Cat# 3179, RRID:AB_2095853 |
| Anti-Phospho-PERK-T982 Rabbit pAb | ABclonal | Cat# AP0886; RRID:AB_2771413 |
| Anti-eIF2α (D7D3) Rabbit mAb | Cell Signaling Technology | Cat# 5324; RRID:AB_10692650 |

| | | |
|---|---|---|
| Anti-Phospho-eIF2 α (Ser51) (D9G8) Rabbit mAb | Cell Signaling Technology | Cat# 3398; RRID:AB_2096481 |
| Anti-Xbp-1s (E9V3E) Rabbit mAb | Cell Signaling Technology | Cat# 40435; RRID: AB_2891025 |
| Anti-ATF6 (70B1413.1) Mouse mAb | Novus | Cat# NBP1-40256, RRID:AB_2058774 |
| Anti- β 3-Tubulin (TU-20) Mouse mAb | Cell Signaling Technology | Cat# 4466, RRID:AB_1904176 |
| **Chemicals, Peptides, and Recombinant Proteins** | | |
| 4μ8c | TOPSCIENCE | Cat# T6363 |
| Ceapin-A7 | TOPSCIENCE | Cat# T9110 |
| ISRIB | TOPSCIENCE | Cat# T2027 |
| Tunicamycin | TOPSCIENCE | Cat# T13229 |
| GSK2606414 | MedChemExpress | Cat# HY-18072 |
| CCT020312 | MedChemExpress | Cat# HY-119240 |
| Deoxycholic acid | Sigma | Cat# D2510 |
| Deoxycholic acid-iFluor 647 conjugate | AAT Bioquest | Cat# 36705 |
| Sodium dodecyl sulfate | Beyotime | Cat# ST2681 |
| Recombinant Human TMX2 (N-6His) | Novoprotein | Cat# CH30 |
| Recombinant Human Insulin | Solarbio | Cat# I8830 |
| RIPA lysis buffer | Servicebio | Cat# G2002 |
| Protein Phosphatase Inhibitor (All-in-one, 100×) | Solarbio | Cat# P1260 |
| Enhanced luminescent liquid | Biosharp | Cat# BL520B |
| Hybridization Nitrocellulose Filter | Merck Millipore | Cat# HATF00010 |
| Protease Inhibitor Cocktail (EDTA-Free, | MedChemExpress | Cat# HY-K0010 |

| | | |
|---|---|---|
| 100× in DMSO) | | |
| PMSF (100 mM) | Solarbio | Cat# P0100 |
| Penicillin-Streptomycin, 100× | MACGENE | Cat# CC004 |
| Recombinant Murine IL-2 | Peprotech | Cat# 212-12 |
| Recombinant Mouse IL-7 (carrier-free) | Biolegend | Cat# 577802 |
| Recombinant Murine IL-17E | Peprotech | Cat# 210-17E |
| Recombinant Murine IL-33 | Peprotech | Cat# 210-33 |
| Dextran Sulfate Sodium Salt | MP Biomedicals | Cat# 160110 |
| Phorbol 12-myristate 13-acetate (PMA) | BioGems | Cat# 1652981 |
| Ionomycin calcium salt | BioGems | Cat# 5608212 |
| Brefeldin A | BioGems | Cat# 2031560 |
| DNase I | Sigma | Cat# DN25 |
| Collagenase VIII | Sigma | Cat# C2139 |
| HEPES | Solarbio | Cat# H8090 |
| EDTA | Solarbio | Cat# E1170 |
| Phosphate Buffer Saline | Solarbio | Cat# P1010 |
| Dimethyl sulfoxide | Solarbio | Cat# D8317 |
| Isopropanol | FUYU CHEMICAL | CAS# 67-63-0 |
| Ethanol | FUYU CHEMICAL | CAS# 64-17-5 |
| Fetal Bovine Serum | GIBCO | Cat# 10099141C |
| RPMI 1640 | MACGENE | Cat# CM10041 |
| Vancomycin hydrochloride | MACKLIN | Cat# V820413 |
| Fixation/Permea-bilizationConcentrate | eBioscience | Cat# 00-5223-56 |
| IMDM | MACGENE | Cat# CM10016 |
| Methanol | Fisher Scientific | Cat# DN25 |

| | | |
|---|---|---|
| RNA isolater Total RNA Extraction Reagent | Vazyme | Cat# R401-01 |
| Percoll | Cytiva | Cat# 17089109 |
| **Biological samples** | | |
| Human: feces of patients with UC | Qilu hospital of Shandong University | See Table S2 |
| **Critical commercial assays** | | |
| SMART-Seq HT Kit | TaKaRa | Cat# 634437 |
| Nextera XT Library Prep Kit | Illumina | Cat# 15032350 |
| Nextera XT Index Kit | Illumina | Cat# 15052163 |
| AMPure XP Beads | Beckman Coulter | Cat# A63881 |
| TruePrep Index Kit V2 for Illumina | Vazyme | Cat# TD202 |
| Qubit ssDNA Assay Kit | Thermo Fisher Scientific | Cat# Q10212 |
| Zombie Aqua™ Fixable Viability Kit | BioLegend | Cat# 423102 |
| Hoechst Staining Kit | Beyotime | Cat# C0003 |
| Mito-Tracker Green | Beyotime | Cat# C1048 |
| ER-Tracker Green | Beyotime | Cat# C1042S |
| BCA Protein Assay Kit | Beyotime | Cat# P0011 |
| Multiplex Assay Kit for IL5, IL13, AREG, etc. by FLIA (Flow Luminescence Immunoassay) | Cloud-Clone Corp. | Cat# IS135-Mouse |
| TNT® T7 Quick Coupled Transcription/Translation System | Promega | Cat# L1170 |
| PROTEOSTAT® Aggresome detection kit | Enzo | Cat# ENZ-51035 |
| Total Bile Acid (TBA) Colorimetric Assay | Elabscience | Cat# E-BC-K181-M |

| Kit | | |
|---|---|---|
| Experimental Models: Organisms/Strains | | |
| Mouse: C57BL/6 | Gempharmatech | Cat# N000013 |
| Mouse: *IL5*$^{RFP\text{-}Cre}$ | Jackson Laboratories | Cat# R5/+ |
| Mouse: Rag2$^{-/-}$Il2rg$^{-/-}$ | Taconics Biosciences | Cat# 4111 |
| Mouse: Nr1h4$^{-/-}$ | Gempharmatech | Cat# T012640 |
| Mouse: Gpbar1$^{-/-}$ | Gempharmatech | Cat# T012754 |
| Deposited Data | | |
| RNA-seq data; ILC2s treated with DCA | This paper | GEO: GSE294014 |
| RNA-seq data; ILC2s treated with FK866 | Shen J et al. 2022 | GEO: GSE218368 |
| Software and Algorithms | | |
| Progenesis QI | Waters Corporation | N/A |
| Biacore T200 Evaluation Software | Cytiva | N/A |
| ImageJ 1.52v | NIH | https://fiji.sc/ |
| FlowJo version 10.4.2 | FlowJo | https://www.flowjo.com |
| Prism 8.0.1 | GraphPad Software | https://www.graphpad.com |
| Other | | |
| Normal control diet | Jiangsu Xietong Pharmaceutical Bio-engineering Co., Ltd | Cat# XT93G |
| BA-containing diets | This paper; Jiangsu Xietong | N/A |