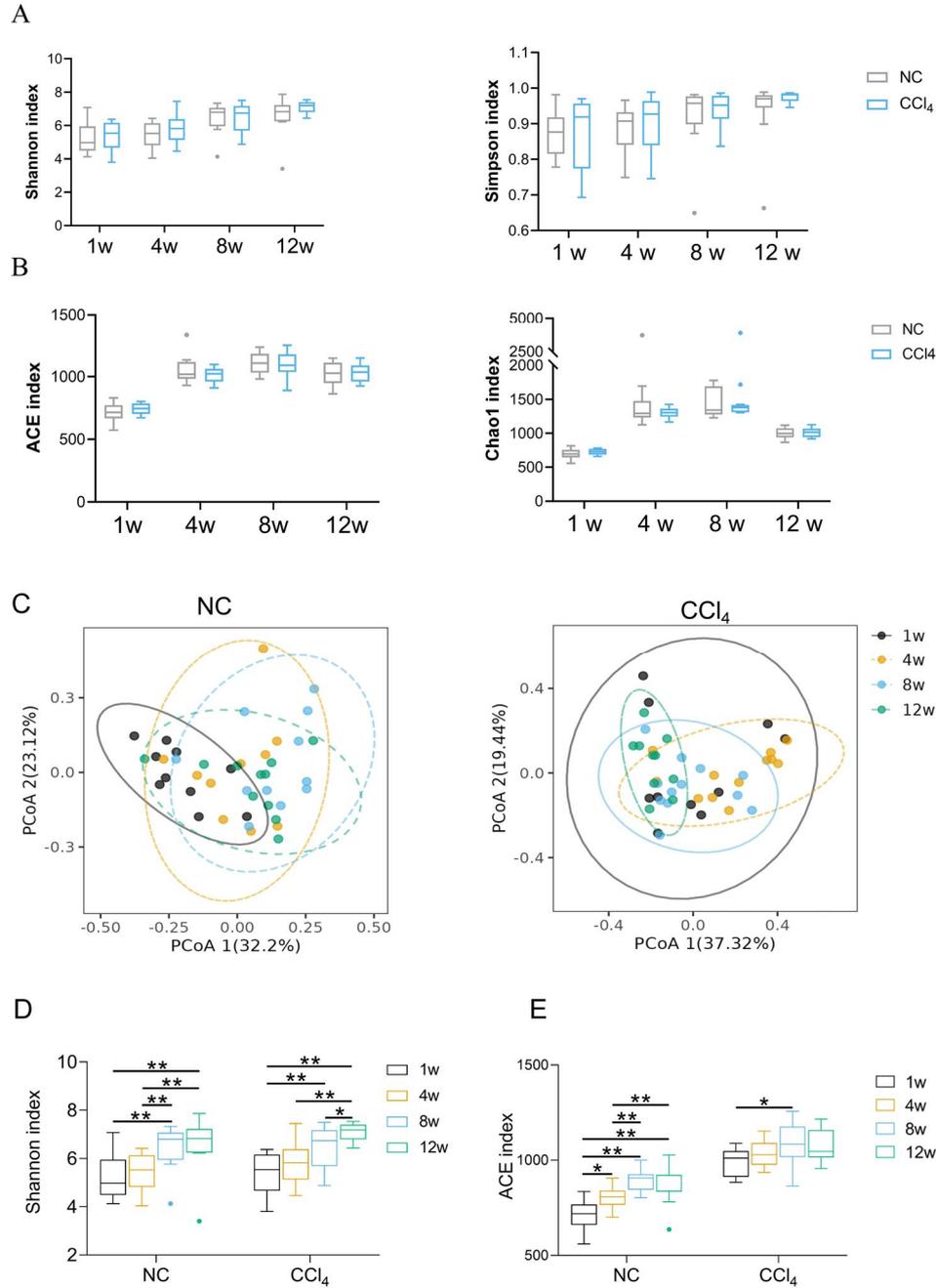
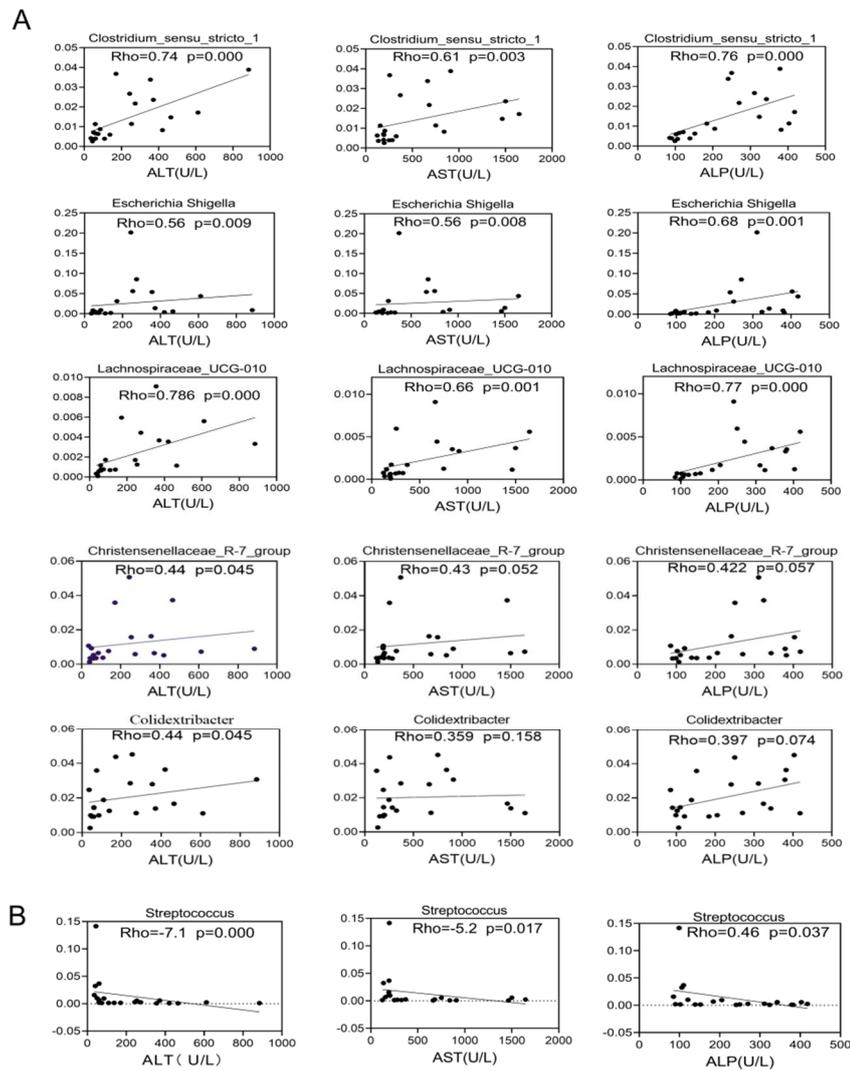


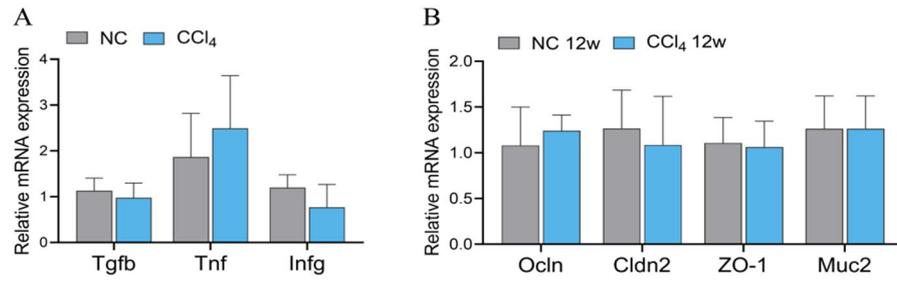
**Figure S1. Liver injury and fibrosis were induced successfully by CCl<sub>4</sub>.** (A) Body weight of rats over the whole experimental period (n=12 per group). (B) Liver mass/ body weight (n=12 per group). (C) Serum ALT, AST, ALP, TBa , DBili, TBili, and ALB levels (8w n=10,12w n=12). Each value is expressed as the mean  $\pm$  SEM. NC, normal control group; CCl<sub>4</sub>, CCl<sub>4</sub>-treated group; ALT, alanine transaminase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; TBa, total bile acid; DBili, direct bilirubin; TBili, total bilirubin; ALB, albumin. \*p<0.05, \*\*p<0.01.



**Figure S2. Comparison of  $\alpha$  diversity and  $\beta$  diversity.** (A) Microbial diversity (Shannon index and Simpson index) and (B) microbial richness (ACE index and Chao1 index) between NC groups and CCl<sub>4</sub> groups. Box plots show the median  $\pm$  interquartile range (IQR) and 1.5 IQR ranges (whiskers), with outliers denoted by dots. (C) PCoA plots of microbial communities based on weighted\_UniFrac distance. (D) Microbial diversity (Shannon index) and (E) microbial richness (ACE index) at different time points (n=10-12). \*p<0.05, \*\*P<0.01.



**Figure S3. Correlation between distinctive gut microbiota and serum ALT, AST and ALP levels at the advanced fibrosis stage. (A) Positive correlation between distinctive gut microbiota and serum ALT, AST and ALP levels. (B) Negative correlation between distinctive gut microbiota and serum ALT, AST and ALP levels (n=21).**



**Figure S4. Assessment of the mRNA levels of inflammatory factors and barrier proteins in the advanced fibrosis stage in the colon (n=3-5).** Gene expression of inflammatory factors (A) and barrier proteins (B) in the colon. Each value is expressed as the mean  $\pm$  SEM.

| gene name      | direction | 5' to 3'                  |
|----------------|-----------|---------------------------|
| <i>Acta2</i>   | Forward   | AATGACCCAGATTATGTTTGAGACC |
|                | Reverse   | ATCTCCAGAGTCCAGCACAATACC  |
| <i>Colla1</i>  | Forward   | GTCAGACCTGTGTGTTCCCC      |
|                | Reverse   | GATCGGAACCTTCGCTTCCA      |
| <i>Ifng</i>    | Forward   | ACAACCCACAGATCCAGCAC      |
|                | Reverse   | CCAGAATCAGCACCGACTCC      |
| <i>Tnf</i>     | Forward   | CATCCGTTCTCTACCCAGCC      |
|                | Reverse   | AATTCTGAGCCCGGAGTTGG      |
| <i>Tgfb</i>    | Forward   | CTGCTGACCCCACTGATAC       |
|                | Reverse   | TCGACGTTTGGGACTGATCC      |
| <i>Il10</i>    | Forward   | TTGAACCACCCGGCATCTAC      |
|                | Reverse   | CCAAGGAGTTGCTCCCGTTA      |
| <i>Il1b</i>    | Forward   | GACTTCACCATGGAACCCGT      |
|                | Reverse   | CAGGGAGGGAAACACACGTT      |
| <i>Il6</i>     | Forward   | TCTGGTCTTCTGGAGTCCG       |
|                | Reverse   | AGCATTGGAAGTTGGGGTAGG     |
| <i>Muc2</i>    | Forward   | TCTGCATTGACTGGCGGAAT      |
|                | Reverse   | GTCATAGCCAGGGGCAAAC       |
| <i>ZO-1</i>    | Forward   | AGATGAGCGGGCTACCTTAT      |
|                | Reverse   | TCATGGGAGCGAACTGAATG      |
| <i>Ocln</i>    | Forward   | CCCTTCTTTCCTTAGGCGACC     |
|                | Reverse   | GTGCATCTCTCCGCCATACA      |
| <i>Cldn2</i>   | Forward   | GACTGTGGATGTCCTGCGTT      |
|                | Reverse   | CATCAAGGCTCTGGTTGCCT      |
| <i>Cyp7a1</i>  | Forward   | GAATTGCCGTGTTGGTGAGC      |
|                | Reverse   | CCCAGGTACGGAATCAACCC      |
| <i>Cyp8b1</i>  | Forward   | CAGTACACATGGACCCCGAC      |
|                | Reverse   | AGGGCATGTTGTAGTGGTGG      |
| <i>Cyp27a1</i> | Forward   | GTGATTAAGGAGACCCTGCG      |
|                | Reverse   | CCGGAGTTATCGTCCTCTCT      |
| <i>Cyp7b1</i>  | Forward   | TTTCTGGGCATTTCAGCATCCA    |
|                | Reverse   | TGTGCAGCCTTATTCCGCTA      |
| <i>Bsep</i>    | Forward   | TGGGGCTCGTCAGATAAGGA      |
|                | Reverse   | ACATGCGCTGGAGGAAATGA      |
| <i>Mrp2</i>    | Forward   | TGCCATTATCCGTGCCTTT       |
|                | Reverse   | GAACAAAGCCCACAACGTCC      |
| <i>Asbt</i>    | Forward   | CAAATGGCCCCAAAAGCGA       |
|                | Reverse   | CTGTACCAGGGTTGACCAGC      |
| <i>Oatp1</i>   | Forward   | TTGCGGGCTGTAAGAAGTTT      |

|              |         |                           |
|--------------|---------|---------------------------|
|              | Reverse | ACCCAGGTATGGCTGTAAGT      |
| <i>Osta</i>  | Forward | TCCATCTTGGCTAACAGCGG      |
|              | Reverse | TTGAGCGTTGAGTCCAGGTC      |
| <i>Ostβ</i>  | Forward | TGGTGATGGTGATAGGCGTG      |
|              | Reverse | GCGTCTCTCTTAGGATGCCC      |
| <i>Ntcp</i>  | Forward | AAGGGGGACATGAACCTCAG      |
|              | Reverse | TTGGACTTGAGGACGATCCC      |
| <i>Mrp3</i>  | Forward | AACACTCCAGACCTCACACC      |
|              | Reverse | GGACTATGTAGCCAAGCCGA      |
| <i>Mrp4</i>  | Forward | TGCAAGCCACATCCTCATAC      |
|              | Reverse | AGGGTCTGGATGACTGTTGA      |
| <i>Fxr</i>   | Forward | GGGAGCTGAAAATGACCCA       |
|              | Reverse | AAATGCTGAGGGTTCTCGGG      |
| <i>Shp</i>   | Forward | GCTAGAGGAACCCAACAGTG      |
|              | Reverse | AGTGCCTTTCAGGTATGCGT      |
| <i>Ibabp</i> | Forward | GTCTTACTCTGGGGGCAACA      |
|              | Reverse | CACCCTCCATCTTCACGGTT      |
| <i>Fgf15</i> | Forward | AGGAGGACCAGAACGAACGA      |
|              | Reverse | GAGTAGCGAATCAGCCCGTA      |
| <i>Gapdh</i> | Forward | AAGAGAGAGGCCCTCAGTTGCCTGA |
|              | Reverse | CCCAGGCCCTCCTGTTGTTAT     |

**Supplementary Table S1. Primer sequences for RT-PCR.**

| p value of AMOVA analysis at the same time point of different groups |                              |                              |                                |
|--|------------------------------|------------------------------|--------------------------------|
| NC 1w vs CCl <sub>4</sub> 1w   | NC 4w vs CCl <sub>4</sub> 4w | NC 8w vs CCl <sub>4</sub> 8w | NC 12w vs CCl <sub>4</sub> 12w |
| 0.001  | 0.002                        | 0.23                         | 0.02                           |
| p value of AMOVA analysis between different time points              |                              |                              |                                |
| p <sup>a</sup>   | NC group                     |                              |                                |
|  | 1w                           | 4w                           | 8w                             |
| 4w   | 0.004                        |                              |                                |
| 8w   | 0.003                        | 0.048                        |                                |
| 12w  | 0.003                        | 0.006                        | 0.048                          |
| p <sup>a</sup>   | CCl <sub>4</sub> group       |                              |                                |
|  | 1w                           | 4w                           | 8w                             |
| 4w   | 0.028                        |                              |                                |
| 8w   | 0.016                        | 0.008                        |                                |
| 12w  | 0.016                        | 0.003                        | 0.003                          |

**Supplementary Table S2. Difference analysis of  $\beta$  diversity by AMOVA method.** a, P values were corrected by the method of Benjamini-Hochberg.

| CCl <sub>4</sub> 1w vs NC 1w |                  |                    |                     |                              |                               |
|------------------------------|------------------|--------------------|---------------------|------------------------------|-------------------------------|
| phylum                       | class            | order              | family              | genus                        | species                       |
| Actinobacteriota             | Actinobacteria   | Corynebacteriales  | Corynebacteriaceae  | Corynebacterium              | Corynebacterium_urealyticum   |
|                              |                  |                    | Dietziaceae         | Dietzia                      |                               |
|                              | Coriobacteriia   | Coriobacteriales   | Eggerthellaceae     | Adlercreutzia                |                               |
|                              |                  |                    | Coriobacteriaceae   | Collinsella                  | Collinsella_provencensis      |
| Bacteroidota                 | Bacteroidia      | Bacteroidales      | Bacteroidaceae      | Bacteroides                  |                               |
|                              |                  |                    | F082                |                              |                               |
|                              |                  |                    | Marinifilaceae      | Odoribacter                  |                               |
|                              |                  |                    | Prevotellaceae      | Prevotella                   |                               |
|                              |                  |                    | Rikenellaceae       | Rikenellaceae_R_C9_gut_group |                               |
|                              |                  |                    | Tannerellaceae      | Parabacteroides              |                               |
| Campilobacterota             | Campylobacteriia | Campylobacterales  | Helicobacteraceae   | Helicobacter                 | Helicobacter_bilis            |
| Desulfobacterota             | Desulfovibrionia | Desulfovibrionales | Desulfovibrionaceae | Desulfovibrio                | Desulfovibrio_sp_UNSW3caefatS |
| Firmicutes                   | Bacilli          | Lactobacillales    | Lactobacillaceae    | Lactobacillus                | Lactobacillus_intestinalis    |
|                              |                  |                    |                     |                              | Lactobacillus_johnsonii       |
|                              |                  |                    |                     |                              | Lactobacillus_murinus         |
|                              |                  |                    |                     |                              | Lactobacillus_reuteri         |
|                              |                  |                    |                     |                              | Lactobacillus_sp_KC38         |
|                              |                  |                    | Streptococcaceae    | Streptococcus                | Streptococcus_respiraculi     |
|                              |                  |                    | Vagococcaceae       | Vagococcus                   |                               |
|                              |                  | Bacillales         | Bacillaceae         | Oceanobacillus               |                               |
|                              |                  | Erysipelotrichales | Erysipelotrichaceae | Dubosiella                   |                               |
| Izemoplasmales               |                  |                    |                     |                              |                               |

|                |                      |                                |                     |                                      |  |
|----------------|----------------------|--------------------------------|---------------------|--------------------------------------|--|
|                |                      | Staphylococcales               | Gemellaceae         | Gemella                              |  |
|                | Clostridia           | Christensenellales             | Christensenellaceae | unidentified_Christensenellaceae     | Christensenella_sp_Marseille_P2437.              |
|                |                      | Clostridia_UCG_014             |                     |                                      |  |
|                |                      | Clostridiales                  | Clostridiaceae      | Candidatus_Arthromitus               |  |
|                |                      | Lachnospirales                 | Lachnospiraceae     | Blautia                              | Lachnospiraceae_bacterium_28_4                   |
|                |                      |                                |                     |                                      | Lachnospiraceae_bacterium_615                    |
|                |                      |                                |                     |                                      | Lachnospiraceae_bacterium_DW59                   |
|                |                      |                                |                     | Lachnospira                          |  |
|                |                      |                                |                     | Lachnospiraceae_UCG_001              |  |
|                |                      | Oscillospirales                | Oscillospiraceae    | Colidextribacter                     |  |
|                |                      |                                |                     | _Eubacterium_coprostanoligenes_group | unidentified_Eubacterium_coprostanoligenes_group |
|                |                      |                                |                     | Candidatus_Soleaferrea               | Ruminococcaceae_bacterium_GD6                    |
|                | Negativicutes        | Veillonellales_Selenomonadales | Selenomonadaaceae   | Quinella                             |  |
|                |                      |                                | Veillonellaceae     | Veillonella.                         |  |
| Proteobacteria | Gamma proteobacteria | Burkholderiales                | Alcaligenaceae      | Oligella                             |  |
|                |                      |                                | Neisseriaceae       | Neisseria                            | Neisseria_sp_10022                               |
|                |                      | Oceanospirillales              | Alcanivoracaceae1   | Alcanivorax                          |  |
|                |                      | Pseudomonadales                | Moraxellaceae       | Acinetobacter                        | Acinetobacter_lwoffii                            |
| Spirochaetota  | Spirochaetia         | Spirochaetales                 | Spirochaetaceae     | Treponema                            |  |

| unidentified_Bacteria              | Clostridia              | Oscillospirales    | Butyricicoccaeae          |                               |  |
|------------------------------------|-------------------------|--------------------|---------------------------|-------------------------------|--|
|                                    |                         |                    | Oscillospiraceae          |                               |  |
|                                    | Saccharimonadia         | Saccharimonadales  | Saccharimonadaeae         | Candidatus_Saccharimonas      |  |
| <b>CCl<sub>4</sub> 4w vs NC 4w</b> |                         |                    |                           |                               |  |
| phylum                             | class                   | order              | family                    | genus                         | species  |
| Actinobacteriota                   | Actinobacteria          | Corynebacteriales  | Corynebacteriaceae        | Corynebacterium               | Corynebacterium glutamicum.<br>Corynebacterium urealyticum |
|                                    |                         |                    | Atopobiaceae              | Coriobacteriaceae_UCG_002     |  |
|                                    |                         |                    | Coriobacteriaceae         | Collinsella                   | Collinsella provencensis                                   |
|                                    |                         |                    | Eggerthellaceae           | DNF00809                      |  |
| Bacteroidota                       | Bacteroidia             | Bacteroidales      | Rikenellaceae             | Alistipes                     | Alistipes indistinctus                                     |
| Desulfobacterota                   | Desulfovibrionia        | Desulfovibrionales | Desulfovibrionaceae       | Desulfovibrio                 | Desulfovibrio sp_UNSW3caefatS                              |
| Fibrobacterota                     | Fibrobacteria           | Fibrobacterales    | Fibrobacteraceae          | Fibrobacter                   | Fibrobacter intestinalis                                   |
| Firmicutes                         | Bacilli                 | Lactobacillales    | Lactobacillaceae          | Lactobacillus                 | Lactobacillus murinus                                      |
|                                    |                         | Erysipelotrichales | Erysipelatoclostridiaceae | Erysipelatoclostridium        | Clostridiales_bacterium_CHK CI006                          |
|                                    | Clostridia              | Christensenellales | Christensenellaceae       | Christensenellaceae_R_7_group | Christensenella sp_Marseille_P3954                         |
|                                    |                         | Clostridiales      | Clostridiaceae            | Clostridium_sensu_stricto_1   | Clostridium_sp_ND2   |
|                                    |                         | Lachnospirales     | Lachnospiraceae           | Roseburia                     |  |
|                                    |                         |                    |                           | Lachnospiraceae_ND3007_group  |  |
|                                    | Lachnospiraceae_UCG_010 |                    |                           |                               |  |
|                                    | Coprococcus             |                    |                           |                               |  |

|                                    |                                     | Oscillospirales    | Ruminococcaeae            | Ruminococcus                 | Ruminococcus_sp_N15_MGS_57     |
|------------------------------------|-------------------------------------|--------------------|---------------------------|------------------------------|--------------------------------|
|                                    |                                     |                    |                           | Caproiciproducens            |                                |
|                                    |                                     |                    |                           | Anaerotruncus                |                                |
|                                    |                                     | Oscillospiraceae   | Colidextribacter          |                              |                                |
|                                    | Peptostreptococcales_Tissierellales | Anaerovoracaeae    | Eubacterium_nodatum_group |                              |                                |
| Negativicutes                      | Veillonellales_Selenomonadales      | Veillonellaceae    |                           |                              |                                |
| unidentified_Firmicutes            | DTU014                              |                    |                           |                              |                                |
| Proteobacteria                     | Gamma proteobacteria                | Burkholderiales    | Neisseriaceae             | Neisseria                    | Neisseria_sp_10022             |
|                                    |                                     |                    | Sutterellaceae            | Parasutterella               | Burkholderiales_bacterium_YL45 |
| Spirochaetota                      | Spirochaetia                        | Spirochaetales     | Spirochaetaceae           | Treponema                    |                                |
| Verrucomicrobiota                  | Verrucomicrobiae                    | Verrucomicrobiales | Akkermansiaceae           | Akkermansia                  | Akkermansia_muciniphila        |
| <b>CCl<sub>4</sub> 8w vs NC 8w</b> |                                     |                    |                           |                              |                                |
| phylum                             | class                               | order              | family                    | genus                        | species                        |
| Bacteroidota                       | Bacteroidia                         | Bacteroidales      | Rikenellaceae             | Rikenellaceae_R_C9_gut_group |                                |
|                                    |                                     |                    | Bacteroidaceae            | Bacteroides                  | Bacteroides_caecigallinarum    |
| Firmicutes                         | Bacilli                             | Lactobacillales    | Enterococcaceae           | Enterococcus                 |                                |
|                                    |                                     |                    | Streptococcaceae          | Streptococcus                | Streptococcus_hyointestinalis  |
|                                    |                                     |                    | Lactobacillaceae          | Lactobacillus                | Lactobacillus_murinus          |

|                       |                 |                   |                    |                             |  |
|-----------------------|-----------------|-------------------|--------------------|-----------------------------|--|
|                       | Clostridia      | Clostridiales     | Clostridiaceae     | Clostridium_sensu_stricto_1 |  |
|                       |                 | Lachnospirales    | Lachnospiraceae    | Lachnospiraceae_UCG_010     |  |
|                       |                 | Oscillospirales   | Ruminococcaceae    | Ruminococcus                | Ruminococcaceae_bacterium_Marseille_3738 |
| unidentified_Bacteria | Saccharimonadia | Saccharimonadales | Saccharimonadaceae | Candidatus_Saccharimonas    |  |

### CCl<sub>4</sub> 12w vs NC 12w

| phylum           | class            | order              | family              | genus                         | species                       |
|------------------|------------------|--------------------|---------------------|-------------------------------|-------------------------------|
| Actinobacteriota | Coriobacteriia   | Coriobacteriales   | Eggerthellaceae     | Adlercreutzia                 |                               |
|                  |                  |                    |                     | Parvibacter                   |                               |
| Bacteroidota     | Bacteroidia      | Bacteroidales      | Bacteroidaceae      | Bacteroides                   | Bacteroides_sartorii          |
|                  |                  |                    | Barnesiellaceae     | Barnesiella                   |                               |
|                  |                  |                    | Prevotellaceae      | Prevotellaceae_UCG_003        |                               |
|                  |                  |                    |                     | Prevotellaceae_UCG_004        |                               |
|                  |                  |                    | Rikenellaceae       | Rikenellaceae_R_C9_gut_group  |                               |
| Desulfobacterota | Desulfovibrionia | Desulfovibrionales | Desulfovibrionaceae | Bilophila                     |                               |
|                  |                  |                    |                     | Desulfovibrio                 | Desulfovibrio_fairfieldensi   |
| Firmicutes       | Bacilli          | Bacillales         | Planococcaceae      | Kurthia                       | Kurthia_sp_11kri321           |
|                  |                  | Erysipelotrichales | Erysipelotrichaceae | Turicibacter                  |                               |
|                  |                  | Lactobacillales    | Enterococcaceae     | Enterococcus                  |                               |
|                  |                  |                    | Lactobacillaceae    | Lactobacillus                 | Lactobacillus_murinus         |
|                  |                  |                    | Streptococcaceae    | Streptococcus                 | Streptococcus_hyointestinalis |
|                  | Clostridia       | Christensenellales | Christensenellaceae | Christensenella               |                               |
|                  |                  |                    |                     | Christensenellaceae_R_7_group |                               |

|                       |                      |                    |                                      |  |                     |
|-----------------------|----------------------|--------------------|--------------------------------------|--|---------------------|
|                       |                      | Clostridiales      | Clostridiaceae                       | Clostridium_sensu_stricto_1                      |                     |
|                       |                      | Lachnospirales     | Lachnospiraceae                      | Anaerostipes                                     |                     |
|                       |                      |                    |                                      | A2   |                     |
|                       |                      |                    |                                      | Lachnospiraceae_UCG_010                          |                     |
|                       |                      | Oscillospirales    | Oscillospiraceae                     | Colidextribacter                                 |                     |
|                       |                      |                    | _Clostridium_methylpentosum_group    |  |                     |
|                       |                      |                    | _Eubacterium_coprostanoligenes_group | unidentified_Eubacterium_coprostanoligenes_group |                     |
|                       |                      |                    | Ruminococcaceae                      | Paludicola                                       |                     |
|                       | Negativicutes        | Acidaminococcales  | Acidaminococcaceae                   | Phascolarctobacterium                            |                     |
|                       |                      |                    | Veillonellales_Selenomonadales       | Selenomonadaceae                                 |                     |
| Proteobacteria        | Gamma proteobacteria | Enterobacterales   | Enterobacteriaceae                   | Escherichia_Shigella                             | Escherichia_coli    |
|                       |                      | Burkholderiales    | Sutterellaceae                       |  |                     |
| unidentified_Bacteria | Clostridia           | Oscillospirales    | Ruminococcaceae                      | unidentified_Ruminococcaceae                     | _Clostridium_leptum |
| Verrucomicrobiota     | Verrucomicrobiae     | Verrucomicrobiales | Akkermansiaceae                      | Akkermansia                                      |                     |

**Supplementary Table 3. Differences in the gut microbiota at different fibrosis stages.**

LDA>3, red color represents taxa increased in CCl<sub>4</sub> group, green color represents taxa decreased in CCl<sub>4</sub> group, and black color represents no difference between the two groups.

| Phylum                | NC group               |                   |                     |                   |                     |                   |                     |                   |
|-----------------------|------------------------|-------------------|---------------------|-------------------|---------------------|-------------------|---------------------|-------------------|
|                       | Week 1                 |                   | Week 4              |                   | Week 8              |                   | Week 12             |                   |
|                       | mean <sup>a</sup> %    | SD <sup>b</sup> % | mean <sup>a</sup> % | SD <sup>b</sup> % | mean <sup>a</sup> % | SD <sup>b</sup> % | mean <sup>a</sup> % | SD <sup>b</sup> % |
| Firmicutes            | 57.43                  | 12.87             | 54.23               | 15.56             | 45.05               | 13.04             | 52.93               | 15.38             |
| Bacteroidota          | 27.56                  | 13.80             | 30.16               | 15.73             | 28.69               | 10.32             | 29.56               | 12.69             |
| Spirochaetota         | 1.01                   | 1.77              | 8.82                | 14.25             | 11.90               | 11.86             | 4.00                | 5.55              |
| Proteobacteria        | 10.15                  | 14.40             | 0.79                | 0.49              | 1.05                | 0.60              | 1.93                | 1.51              |
| Actinobacteriota      | 0.63                   | 0.22              | 0.43                | 0.11              | 1.48                | 3.39              | 0.76                | 0.60              |
| Verrucomicrobiota     | 0.09                   | 0.05              | 0.07                | 0.04              | 1.84                | 3.12              | 1.82                | 3.41              |
| unidentified_Bacteria | 1.27                   | 0.71              | 2.71                | 2.17              | 4.06                | 1.58              | 4.16                | 1.75              |
| Fibrobacterota        | 0.19                   | 0.55              | 0.24                | 0.27              | 0.82                | 0.69              | 0.28                | 0.14              |
| Campilobacterota      | 0.35                   | 0.36              | 0.24                | 0.09              | 0.56                | 0.46              | 0.32                | 0.52              |
| Desulfobacterota      | 0.16                   | 0.12              | 0.15                | 0.17              | 0.12                | 0.09              | 0.38                | 0.33              |
| Cyanobacteria         | 0.04                   | 0.05              | 0.02                | 0.01              | 0.16                | 0.31              | 0.04                | 0.03              |
| Deferribacteres       | 0.04                   | 0.06              | 0.03                | 0.02              | 0.04                | 0.04              | 0.01                | 0.01              |
| Fusobacteriota        | <0.01                  | <0.01             | <0.01               | <0.01             | 0.03                | 0.03              | 0.01                | 0.02              |
| Phylum                | CCl <sub>4</sub> group |                   |                     |                   |                     |                   |                     |                   |
|                       | Week 1                 |                   | Week 4              |                   | Week 8              |                   | Week 12             |                   |
|                       | mean <sup>a</sup> %    | SD <sup>b</sup> % | mean <sup>a</sup> % | SD <sup>b</sup> % | mean <sup>a</sup> % | SD <sup>b</sup> % | mean <sup>a</sup> % | SD <sup>b</sup> % |
| Firmicutes            | 28.04                  | 6.83              | 31.56               | 13.64             | 36.53               | 13.19             | 47.39               | 9.85              |
| Bacteroidota          | 38.54                  | 19.09             | 30.27               | 9.02              | 30.28               | 9.53              | 30.12               | 12.10             |
| Proteobacteria        | 12.18                  | 19.62             | 1.71                | 1.23              | 1.45                | 0.94              | 8.12                | 7.12              |
| Spirochaetota         | 14.22                  | 16.25             | 25.07               | 16.58             | 10.83               | 10.01             | 3.50                | 3.50              |
| Verrucomicrobiota     | 0.01                   | 0.01              | 3.81                | 5.95              | 5.41                | 6.80              | 0.05                | 0.03              |
| Fibrobacterota        | 0.02                   | 0.01              | 0.04                | 0.03              | 1.43                | 2.74              | 0.48                | 0.43              |
| unidentified_Bacteria | 4.15                   | 2.42              | 2.36                | 0.69              | 2.82                | 1.21              | 3.51                | 1.02              |
| Actinobacteriota      | 0.70                   | 0.36              | 0.35                | 0.19              | 0.91                | 1.59              | 1.33                | 0.75              |
| Fusobacteriota        | 0.04                   | 0.04              | 0.00                | 0.00              | 0.37                | 1.15              | 0.03                | 0.04              |
| Desulfobacterota      | 0.46                   | 0.46              | 0.23                | 0.15              | 0.10                | 0.03              | 0.27                | 0.16              |
| Campilobacterota      | 0.43                   | 0.32              | 0.37                | 0.22              | 0.46                | 0.34              | 0.38                | 0.34              |
| Deferribacteres       | 0.11                   | 0.12              | 0.03                | 0.02              | 0.03                | 0.03              | 0.07                | 0.10              |
| Cyanobacteria         | 0.05                   | 0.04              | 0.03                | 0.03              | 0.06                | 0.05              | 0.01                | 0.01              |
| Elusimicrobia         | <0.01                  | <0.01             | <0.01               | <0.01             | 0.01                | 0.02              | <0.01               | <0.01             |

**Supplementary Table S4. The relative abundance of major phyla at different ages (average**

relative abundance > 0.01 %). mean<sup>a</sup>, average relative abundance; SD<sup>b</sup>, standard deviation.

| genus  | NC group               |                      |                        |                      |                        |                      |                        |                      |
|--|------------------------|----------------------|------------------------|----------------------|------------------------|----------------------|------------------------|----------------------|
|  | Week 1                 |                      | Week 4                 |                      | Week 8                 |                      | Week 12                |                      |
|  | mean <sup>a</sup><br>% | SD <sup>b</sup><br>% |
| Lactobacillus  | 38.92                  | 18.16                | 24.30                  | 15.48                | 15.42                  | 17.64                | 16.50                  | 21.02                |
| Treponema  | 1.00                   | 1.77                 | 8.80                   | 14.25                | 11.88                  | 11.87                | 3.99                   | 5.54                 |
| Prevotellaceae_UCG-003                                 | 2.60                   | 2.33                 | 10.22                  | 13.34                | 2.54                   | 2.58                 | 4.58                   | 6.41                 |
| Ruminococcus   | 1.09                   | 0.78                 | 12.53                  | 6.42                 | 3.59                   | 1.16                 | 2.13                   | 1.77                 |
| Escherichia-Shigella                                   | 9.55                   | 14.48                | 0.37                   | 0.36                 | 0.20                   | 0.10                 | 0.36                   | 0.28                 |
| Bacteroides  | 1.57                   | 1.11                 | 2.45                   | 1.64                 | 3.27                   | 1.55                 | 1.96                   | 1.19                 |
| Romboutsia   | 3.05                   | 4.32                 | 0.96                   | 0.31                 | 0.79                   | 0.34                 | 1.75                   | 0.99                 |
| Lachnospiraceae_NK4A136_group                          | 0.47                   | 0.47                 | 0.85                   | 0.64                 | 3.08                   | 3.70                 | 1.92                   | 1.75                 |
| Rikenellaceae_RC9_gut_group                            | 1.30                   | 0.52                 | 2.26                   | 1.67                 | 1.48                   | 0.48                 | 0.83                   | 0.41                 |
| Candidatus_Saccharimonas                               | 0.52                   | 0.44                 | 1.57                   | 1.81                 | 1.89                   | 1.13                 | 1.73                   | 1.49                 |
| Prevotella   | 0.35                   | 0.65                 | 0.46                   | 0.33                 | 2.53                   | 2.47                 | 1.46                   | 2.51                 |
| Prevotellaceae_UCG-001                                 | 0.68                   | 0.59                 | 1.64                   | 0.98                 | 1.88                   | 3.32                 | 0.25                   | 0.22                 |
| NK4A214_group  | 0.24                   | 0.10                 | 1.11                   | 0.87                 | 1.05                   | 0.48                 | 1.53                   | 1.09                 |
| unidentified_[Eubacterium]_coprostano<br>ligenes_group | 2.30                   | 6.14                 | 0.97                   | 1.19                 | 0.43                   | 0.39                 | 0.17                   | 0.15                 |
| Akkermansia  | 0.09                   | 0.05                 | 0.07                   | 0.04                 | 1.84                   | 3.12                 | 1.82                   | 3.41                 |
| Streptococcus  | 0.17                   | 0.39                 | 0.26                   | 0.19                 | 0.84                   | 1.39                 | 2.36                   | 4.10                 |
| Colidextribacter                                       | 0.26                   | 0.12                 | 0.43                   | 0.19                 | 1.15                   | 0.48                 | 1.47                   | 0.91                 |
| Turicibacter   | 1.31                   | 1.43                 | 0.39                   | 0.15                 | 0.40                   | 0.25                 | 0.56                   | 0.37                 |
| Parabacteroides  | 0.42                   | 0.19                 | 0.67                   | 0.39                 | 0.72                   | 0.25                 | 0.64                   | 0.29                 |
| [Eubacterium]_xylanophilum_group                       | 0.34                   | 0.55                 | 0.30                   | 0.21                 | 0.74                   | 0.57                 | 0.96                   | 0.64                 |
| Monoglobus   | 0.21                   | 0.11                 | 0.32                   | 0.15                 | 0.79                   | 0.69                 | 0.96                   | 0.53                 |
| Dubosiella   | 0.70                   | 0.48                 | 0.19                   | 0.15                 | 0.63                   | 1.05                 | 0.51                   | 0.69                 |
| Christensenellaceae_R-7_group                          | 0.30                   | 0.28                 | 0.66                   | 0.52                 | 0.52                   | 0.48                 | 0.54                   | 0.29                 |
| Alistipes  | 0.58                   | 0.54                 | 0.36                   | 0.27                 | 0.21                   | 0.10                 | 0.75                   | 1.29                 |
| Parasutterella   | 0.50                   | 0.32                 | 0.22                   | 0.07                 | 0.59                   | 0.57                 | 0.37                   | 0.48                 |
| Alloprevotella   | 0.25                   | 0.19                 | 0.42                   | 0.22                 | 0.82                   | 0.75                 | 0.11                   | 0.09                 |
| UCG-005  | 0.17                   | 0.12                 | 0.50                   | 0.27                 | 0.47                   | 0.23                 | 0.42                   | 0.39                 |
| Fibrobacter  | 0.19                   | 0.55                 | 0.24                   | 0.27                 | 0.82                   | 0.69                 | 0.28                   | 0.14                 |
| Allobaculum  | 0.10                   | 0.05                 | 0.08                   | 0.03                 | 0.52                   | 1.01                 | 0.83                   | 1.71                 |
| Clostridium_sensu_stricto_1                            | 0.27                   | 0.13                 | 0.35                   | 0.13                 | 0.28                   | 0.10                 | 0.58                   | 0.26                 |



|   |       |       |       |       |       |       |       |       |
|---|-------|-------|-------|-------|-------|-------|-------|-------|
| Prevotellaceae_UCG-004                  | <0.01 | <0.01 | 0.01  | <0.01 | 0.06  | 0.08  | 0.02  | 0.02  |
| Eubacterium                             | 0.03  | 0.06  | 0.02  | 0.02  | 0.02  | 0.01  | 0.02  | 0.02  |
| Tuzzerella                              | 0.02  | 0.02  | 0.02  | 0.01  | 0.03  | 0.02  | 0.03  | 0.02  |
| GCA-900066575                           | 0.02  | 0.02  | 0.03  | 0.02  | 0.02  | 0.02  | 0.02  | <0.01 |
| Negativibacillus                        | 0.01  | 0.01  | 0.03  | 0.04  | 0.03  | 0.02  | 0.02  | 0.03  |
| Marvinbryantia                          | 0.02  | 0.02  | 0.03  | 0.01  | 0.02  | <0.01 | 0.02  | 0.02  |
| unidentified_Clostridia_vadinBB60_group | 0.01  | <0.01 | 0.03  | 0.02  | 0.02  | 0.02  | 0.02  | 0.01  |
| Anaeroplasma                            | 0.06  | 0.17  | <0.01 | 0.01  | 0.01  | 0.01  | <0.01 | <0.01 |
| Faecalibaculum                          | <0.01 | <0.01 | <0.01 | <0.01 | 0.05  | 0.08  | 0.02  | 0.03  |
| Lachnospiraceae_NK4B4_group             | <0.01 | <0.01 | <0.01 | <0.01 | 0.04  | 0.03  | 0.03  | 0.02  |
| Erysipelatoclostridium                  | 0.04  | 0.07  | 0.01  | 0.01  | 0.02  | 0.01  | <0.01 | <0.01 |
| Mycoplasma                              | 0.03  | 0.04  | 0.02  | 0.02  | 0.02  | 0.03  | <0.01 | <0.01 |
| Rikenella                               | 0.02  | 0.02  | 0.02  | 0.05  | 0.02  | 0.05  | <0.01 | 0.01  |
| unidentified_Christensenellaceae        | 0.01  | <0.01 | 0.02  | 0.01  | 0.01  | <0.01 | 0.03  | 0.01  |
| dgA-11_gut_group                        | 0.02  | 0.01  | 0.05  | 0.08  | <0.01 | <0.01 | <0.01 | <0.01 |
| Staphylococcus                          | 0.02  | 0.02  | <0.01 | <0.01 | 0.01  | <0.01 | 0.03  | 0.03  |
| unidentified_Ruminococcaceae            | <0.01 | 0.01  | 0.02  | 0.01  | 0.03  | 0.02  | 0.01  | 0.01  |
| Veillonella                             | <0.01 | <0.01 | <0.01 | <0.01 | 0.01  | <0.01 | 0.04  | 0.04  |
| Defluviitaleaceae_UCG-011               | 0.01  | <0.01 | 0.02  | 0.02  | 0.01  | <0.01 | 0.01  | 0.01  |
| Coprococcus                             | <0.01 | <0.01 | <0.01 | <0.01 | 0.03  | 0.02  | 0.03  | 0.02  |
| Sporosarcina                            | 0.01  | 0.01  | <0.01 | <0.01 | 0.01  | 0.01  | 0.04  | 0.05  |
| Collinsella                             | 0.01  | 0.02  | 0.02  | 0.02  | 0.01  | <0.01 | 0.01  | <0.01 |
| Paenacaligenes                          | <0.01 | <0.01 | <0.01 | <0.01 | 0.01  | <0.01 | 0.04  | 0.06  |
| Pygmaibacter                            | <0.01 | <0.01 | <0.01 | <0.01 | 0.01  | <0.01 | 0.03  | 0.03  |
| Erysipelotrichaceae_UCG-003             | <0.01 | 0.02  | 0.01  | 0.02  | <0.01 | <0.01 | 0.02  | 0.04  |
| [Eubacterium]_nodatum_group             | <0.01 | <0.01 | <0.01 | 0.01  | 0.02  | 0.01  | 0.02  | <0.01 |
| DNF00809                                | <0.01 | <0.01 | 0.02  | 0.01  | <0.01 | <0.01 | 0.01  | 0.01  |
| Coriobacteriaceae_UCG-002               | <0.01 | <0.01 | <0.01 | <0.01 | 0.03  | 0.07  | <0.01 | 0.01  |
| [Clostridium]_innocuum_group            | 0.02  | 0.06  | <0.01 | <0.01 | 0.02  | 0.02  | <0.01 | 0.01  |
| UBA1819                                 | 0.01  | 0.01  | <0.01 | <0.01 | 0.01  | <0.01 | 0.02  | 0.01  |
| Atopostipes                             | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.04  | 0.06  |
| Fusobacterium                           | <0.01 | <0.01 | <0.01 | <0.01 | 0.03  | 0.03  | 0.01  | 0.02  |
| unidentified_Xanthomonadaceae           | <0.01 | <0.01 | 0.01  | 0.01  | <0.01 | <0.01 | 0.02  | 0.04  |
| Facklamia                               | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.03  | 0.03  |
| Oligella                                | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.02  | 0.03  |
| Ileibacterium                           | <0.01 | <0.01 | <0.01 | <0.01 | 0.04  | 0.09  | <0.01 | <0.01 |
| UCG-004                                 | <0.01 | 0.01  | 0.02  | 0.03  | <0.01 | <0.01 | 0.01  | 0.03  |
| Granulicatella                          | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.04  | 0.07  |
| Butyrivicoccus                          | <0.01 | <0.01 | <0.01 | <0.01 | 0.01  | <0.01 | 0.01  | <0.01 |
| Globicatella                            | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.03  | 0.05  |
| Pseudomonas                             | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.02  | 0.02  |
| Harryflintia                            | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.01  | 0.01  | 0.01  |

|  |                              |                   |                     |                   |                     |                   |                     |                   |
|--|------------------------------|-------------------|---------------------|-------------------|---------------------|-------------------|---------------------|-------------------|
| Brachy bacterium                                   | <0.01                        | <0.01             | <0.01               | <0.01             | <0.01               | <0.01             | 0.02                | 0.04              |
| Psychrobacter                                      | <0.01                        | <0.01             | <0.01               | <0.01             | <0.01               | <0.01             | 0.02                | 0.02              |
| Epulopiscium                                       | <0.01                        | <0.01             | <0.01               | <0.01             | <0.01               | <0.01             | 0.03                | 0.02              |
| Pseudogracilibacillus                              | <0.01                        | <0.01             | <0.01               | <0.01             | <0.01               | <0.01             | 0.03                | 0.06              |
| Gemella  | <0.01                        | <0.01             | <0.01               | <0.01             | <0.01               | <0.01             | 0.03                | 0.06              |
| Acetatifactor                                      | 0.01                         | 0.03              | <0.01               | <0.01             | 0.01                | 0.01              | <0.01               | <0.01             |
| [Eubacterium]_brachy_group                         | <0.01                        | <0.01             | <0.01               | <0.01             | <0.01               | <0.01             | 0.01                | <0.01             |
| Anaerofilum  | <0.01                        | <0.01             | <0.01               | <0.01             | <0.01               | <0.01             | 0.01                | 0.01              |
| Aerococcus   | 0.01                         | <0.01             | <0.01               | <0.01             | <0.01               | <0.01             | <0.01               | <0.01             |
| Dietzia  | <0.01                        | <0.01             | <0.01               | <0.01             | <0.01               | 0.01              | 0.01                | 0.01              |
| Ruminiclostridium                                  | <0.01                        | <0.01             | <0.01               | <0.01             | 0.01                | 0.01              | <0.01               | <0.01             |
| Muribaculum  | <0.01                        | <0.01             | <0.01               | <0.01             | 0.02                | 0.02              | <0.01               | <0.01             |
| Paraprevotella                                     | <0.01                        | <0.01             | <0.01               | <0.01             | 0.02                | 0.02              | <0.01               | <0.01             |
| Brevibacterium                                     | <0.01                        | <0.01             | <0.01               | <0.01             | <0.01               | <0.01             | 0.01                | 0.02              |
| Coprobacillus                                      | <0.01                        | 0.01              | <0.01               | <0.01             | 0.01                | 0.01              | <0.01               | <0.01             |
| Clostridium_sensu_stricto_13                       | <0.01                        | <0.01             | <0.01               | <0.01             | <0.01               | <0.01             | 0.01                | 0.01              |
| Citrobacter  | <0.01                        | <0.01             | <0.01               | <0.01             | <0.01               | <0.01             | 0.01                | 0.03              |
| Actinomyces  | <0.01                        | <0.01             | <0.01               | <0.01             | <0.01               | <0.01             | 0.01                | 0.03              |
| Lautropia  | <0.01                        | <0.01             | <0.01               | <0.01             | <0.01               | <0.01             | 0.01                | 0.02              |
| <b>genus</b>                                       | <b>CCl<sub>4</sub> group</b> |                   |                     |                   |                     |                   |                     |                   |
|  | <b>Week 1</b>                |                   | <b>Week 4</b>       |                   | <b>Week 8</b>       |                   | <b>Week 12</b>      |                   |
|  | mean <sup>a</sup> %          | SD <sup>b</sup> % | mean <sup>a</sup> % | SD <sup>b</sup> % | mean <sup>a</sup> % | SD <sup>b</sup> % | mean <sup>a</sup> % | SD <sup>b</sup> % |
| Treponema  | 14.22                        | 17.12             | 25.05               | 16.58             | 10.81               | 10.02             | 3.48                | 3.50              |
| Lactobacillus                                      | 4.76                         | 4.46              | 4.39                | 4.15              | 8.47                | 11.38             | 8.25                | 4.87              |
| Escherichia-Shigella                               | 11.59                        | 20.52             | 0.81                | 0.96              | 0.32                | 0.37              | 5.04                | 5.94              |
| Rikenellaceae_RC9_gut_group                        | 3.28                         | 2.08              | 3.40                | 1.62              | 3.09                | 2.05              | 3.62                | 2.59              |
| Bacteroides  | 4.20                         | 2.56              | 2.28                | 1.15              | 3.41                | 3.65              | 1.39                | 0.74              |
| Prevotellaceae_UCG-003                             | 3.75                         | 3.57              | 4.73                | 2.93              | 1.43                | 0.55              | 1.25                | 1.97              |
| Akkermansia  | <0.01                        | 0.01              | 3.81                | 5.95              | 5.40                | 6.81              | 0.03                | 0.03              |
| Ruminococcus                                       | 1.01                         | 0.77              | 3.64                | 3.28              | 2.45                | 1.07              | 1.89                | 1.44              |
| Lachnospiraceae_NK4A136_group                      | 0.57                         | 0.49              | 1.25                | 0.71              | 2.46                | 1.53              | 2.00                | 1.21              |
| Colidextribacter                                   | 0.88                         | 0.57              | 1.05                | 0.66              | 1.35                | 0.39              | 2.64                | 1.29              |
| Prevotellaceae_UCG-001                             | 0.70                         | 0.73              | 3.29                | 2.96              | 1.56                | 1.17              | 0.09                | 0.09              |
| Romboutsia   | 2.65                         | 1.95              | 1.11                | 0.35              | 0.63                | 0.24              | 1.03                | 0.44              |
| Candidatus_Saccharimonas                           | 2.27                         | 2.45              | 0.99                | 0.45              | 1.00                | 0.81              | 0.78                | 0.55              |
| Christensenellaceae_R-7_group                      | 0.53                         | 0.43              | 1.51                | 0.99              | 0.62                | 0.21              | 1.90                | 1.63              |
| Alloprevotella                                     | 3.22                         | 8.69              | 0.71                | 0.98              | 0.43                | 0.45              | 0.18                | 0.19              |
| unidentified_[Eubacterium]_coprostanoligenes_group | 0.75                         | 0.49              | 0.93                | 0.83              | 0.95                | 0.88              | 1.62                | 1.83              |
| Clostridium_sensu_stricto_1                        | 0.25                         | 0.23              | 0.54                | 0.33              | 0.77                | 0.78              | 2.33                | 1.07              |
| NK4A214_group                                      | 0.31                         | 0.20              | 0.88                | 0.41              | 1.00                | 0.53              | 1.63                | 1.03              |
| Parabacteroides                                    | 1.39                         | 1.31              | 0.73                | 0.26              | 0.75                | 0.41              | 0.66                | 0.38              |
| Parasutterella                                     | 0.38                         | 0.33              | 0.72                | 0.71              | 0.86                | 0.64              | 1.42                | 2.10              |

|                                  |       |       |       |       |       |       |       |       |
|----------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|
| Turicibacter                     | 2.38  | 3.24  | 0.36  | 0.09  | 0.22  | 0.11  | 0.18  | 0.09  |
| Dubosiella                       | 0.25  | 0.28  | 0.29  | 0.32  | 0.62  | 0.68  | 1.82  | 2.80  |
| Barnesiella                      | 0.87  | 1.93  | 0.73  | 0.98  | 0.27  | 0.27  | 1.02  | 1.41  |
| Monoglobus                       | 0.27  | 0.07  | 0.44  | 0.25  | 0.61  | 0.27  | 0.83  | 0.42  |
| [Eubacterium]_xylanophilum_group | 0.12  | 0.09  | 0.51  | 0.39  | 0.85  | 0.50  | 0.65  | 0.49  |
| Enterococcus                     | 0.09  | 0.06  | 0.07  | 0.05  | 0.31  | 0.29  | 1.49  | 1.72  |
| Fibrobacter                      | 0.02  | 0.01  | 0.04  | 0.03  | 1.43  | 2.74  | 0.47  | 0.43  |
| UCG-005                          | 0.33  | 0.34  | 0.45  | 0.14  | 0.60  | 0.36  | 0.55  | 0.27  |
| Prevotella                       | 0.10  | 0.03  | 0.27  | 0.21  | 0.85  | 0.70  | 0.41  | 0.35  |
| Helicobacter                     | 0.43  | 0.33  | 0.37  | 0.22  | 0.46  | 0.34  | 0.38  | 0.34  |
| Roseburia                        | 0.16  | 0.15  | 0.42  | 0.31  | 0.32  | 0.22  | 0.49  | 0.58  |
| Alistipes                        | 0.33  | 0.14  | 0.24  | 0.07  | 0.25  | 0.08  | 0.49  | 0.37  |
| Lachnospiraceae_UCG-010          | 0.06  | 0.03  | 0.40  | 0.29  | 0.33  | 0.42  | 0.40  | 0.25  |
| Desulfovibrio                    | 0.46  | 0.48  | 0.23  | 0.14  | 0.09  | 0.03  | 0.26  | 0.16  |
| Allobaculum                      | 0.08  | 0.07  | 0.12  | 0.19  | 0.47  | 0.70  | 0.19  | 0.19  |
| Bifidobacterium                  | 0.02  | 0.03  | 0.07  | 0.10  | 0.57  | 1.57  | 0.18  | 0.20  |
| Adlercreutzia                    | 0.28  | 0.30  | 0.09  | 0.04  | 0.08  | 0.03  | 0.37  | 0.19  |
| Papillibacter                    | 0.22  | 0.34  | 0.12  | 0.05  | 0.11  | 0.05  | 0.34  | 0.24  |
| Quinella                         | 0.24  | 0.40  | 0.06  | 0.05  | 0.09  | 0.04  | 0.26  | 0.46  |
| Oscillibacter                    | 0.03  | 0.02  | 0.08  | 0.10  | 0.18  | 0.11  | 0.25  | 0.13  |
| [Ruminococcus]_torques_group     | 0.04  | 0.02  | 0.19  | 0.32  | 0.13  | 0.06  | 0.16  | 0.08  |
| Enterorhabdus                    | 0.19  | 0.10  | 0.08  | 0.04  | 0.07  | 0.03  | 0.17  | 0.11  |
| Corynebacterium                  | 0.11  | 0.06  | 0.05  | 0.03  | 0.07  | 0.04  | 0.28  | 0.26  |
| Streptococcus                    | 0.04  | 0.04  | 0.07  | 0.04  | 0.15  | 0.09  | 0.24  | 0.19  |
| Intestinimonas                   | 0.12  | 0.07  | 0.13  | 0.10  | 0.10  | 0.04  | 0.13  | 0.09  |
| Rodentibacter                    | 0.05  | 0.04  | 0.01  | <0.01 | 0.04  | 0.02  | 0.37  | 0.32  |
| Phascolarctobacterium            | 0.06  | 0.10  | 0.04  | 0.03  | 0.07  | 0.04  | 0.29  | 0.40  |
| Frasingicoccus                   | 0.07  | 0.09  | 0.17  | 0.14  | 0.07  | 0.03  | 0.14  | 0.07  |
| Fusobacterium                    | 0.04  | 0.04  | <0.01 | <0.01 | 0.37  | 1.15  | 0.03  | 0.04  |
| Sutterella                       | 0.01  | 0.01  | 0.07  | 0.09  | 0.10  | 0.12  | 0.22  | 0.24  |
| unidentified_Muribaculaceae      | 0.01  | <0.01 | 0.03  | 0.02  | 0.04  | 0.03  | 0.28  | 0.51  |
| [Eubacterium]_ruminantium_group  | <0.01 | <0.01 | 0.04  | 0.04  | 0.24  | 0.18  | 0.06  | 0.06  |
| Anaerovibrio                     | 0.29  | 0.66  | 0.02  | 0.02  | 0.01  | 0.03  | <0.01 | <0.01 |
| Prevotellaceae_NK3B31_group      | 0.05  | 0.03  | 0.05  | 0.04  | 0.17  | 0.11  | 0.03  | 0.03  |
| Blautia                          | 0.11  | 0.08  | 0.05  | 0.05  | 0.07  | 0.08  | 0.08  | 0.04  |
| Odoribacter                      | 0.16  | 0.21  | 0.05  | 0.04  | 0.05  | 0.03  | 0.03  | 0.03  |
| Anaerostipes                     | <0.01 | <0.01 | <0.01 | <0.01 | 0.01  | 0.01  | 0.26  | 0.30  |
| dgA-11_gut_group                 | 0.08  | 0.15  | 0.17  | 0.15  | <0.01 | <0.01 | <0.01 | 0.02  |
| Anaerobiospirillum               | 0.09  | 0.14  | 0.03  | 0.02  | 0.03  | 0.02  | 0.12  | 0.18  |
| Mucispirillum                    | 0.11  | 0.12  | 0.03  | 0.02  | 0.03  | 0.03  | 0.08  | 0.10  |
| Lachnospira                      | <0.01 | <0.01 | 0.03  | 0.03  | 0.11  | 0.14  | 0.11  | 0.20  |
| Family_XIII_AD3011_group         | <0.01 | <0.01 | 0.04  | 0.03  | 0.12  | 0.19  | 0.08  | 0.08  |
| UCG-009                          | 0.02  | 0.01  | 0.06  | 0.05  | 0.06  | 0.03  | 0.10  | 0.06  |

|   |       |       |       |       |       |       |       |       |
|---|-------|-------|-------|-------|-------|-------|-------|-------|
| Vagococcus                              | 0.03  | 0.02  | 0.03  | 0.03  | 0.04  | 0.05  | 0.14  | 0.14  |
| Coprococcus                             | <0.01 | <0.01 | <0.01 | <0.01 | 0.06  | 0.03  | 0.17  | 0.12  |
| Butyricimonas                           | 0.09  | 0.05  | 0.04  | 0.03  | 0.06  | 0.07  | 0.04  | 0.04  |
| Dorea                                   | 0.05  | 0.06  | 0.08  | 0.08  | 0.06  | 0.04  | 0.03  | 0.02  |
| [Eubacterium]_siraeum_group             | 0.13  | 0.22  | 0.04  | 0.05  | 0.05  | 0.03  | 0.01  | 0.02  |
| Acinetobacter                           | <0.01 | <0.01 | 0.02  | 0.03  | <0.01 | <0.01 | 0.16  | 0.17  |
| Neisseria                               | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.17  | 0.20  |
| Staphylococcus                          | 0.02  | 0.01  | 0.01  | <0.01 | 0.01  | <0.01 | 0.12  | 0.12  |
| Lachnoclostridium                       | 0.02  | 0.02  | 0.02  | 0.01  | 0.05  | 0.06  | 0.05  | 0.04  |
| Jeotgalicoccus                          | 0.03  | 0.03  | 0.02  | <0.01 | 0.02  | 0.02  | 0.07  | 0.05  |
| Eubacterium                             | 0.02  | <0.01 | 0.03  | 0.03  | 0.02  | 0.03  | 0.06  | 0.04  |
| Negativibacillus                        | 0.02  | 0.02  | 0.05  | 0.07  | 0.02  | 0.01  | 0.03  | 0.04  |
| Defluviitaleaceae_UCG-011               | 0.02  | 0.02  | 0.05  | 0.04  | 0.03  | 0.02  | 0.02  | 0.02  |
| Epulopiscium                            | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.12  | 0.11  |
| Lachnospiraceae_NK4B4_group             | <0.01 | 0.01  | 0.03  | 0.02  | 0.06  | 0.06  | 0.02  | <0.01 |
| Marvinbryantia                          | 0.02  | 0.02  | 0.05  | 0.10  | 0.02  | 0.02  | 0.03  | 0.03  |
| Prevotellaceae_Ga6A1_group              | <0.01 | <0.01 | 0.01  | 0.01  | 0.03  | 0.03  | 0.07  | 0.09  |
| unidentified_Christensenellaceae        | 0.05  | 0.07  | 0.03  | 0.02  | <0.01 | <0.01 | 0.02  | 0.02  |
| Oligella                                | <0.01 | <0.01 | 0.01  | 0.01  | 0.04  | 0.05  | 0.05  | 0.05  |
| Dietzia                                 | <0.01 | <0.01 | <0.01 | <0.01 | 0.02  | 0.03  | 0.08  | 0.11  |
| Anaerovorax                             | <0.01 | <0.01 | 0.03  | 0.02  | 0.03  | 0.02  | 0.03  | 0.02  |
| Erysipelatoclostridium                  | 0.03  | 0.07  | <0.01 | 0.01  | 0.05  | 0.08  | 0.01  | 0.01  |
| GCA-900066575                           | 0.03  | 0.03  | 0.02  | 0.02  | 0.04  | 0.02  | 0.02  | 0.01  |
| [Clostridium]_innocuum_group            | <0.01 | <0.01 | <0.01 | <0.01 | 0.04  | 0.07  | 0.05  | 0.13  |
| Sporosarcina                            | 0.02  | 0.01  | <0.01 | <0.01 | 0.02  | 0.01  | 0.07  | 0.07  |
| Collinsella                             | 0.03  | 0.04  | <0.01 | <0.01 | 0.02  | 0.02  | 0.04  | 0.06  |
| Paenacaligenes                          | <0.01 | <0.01 | 0.01  | <0.01 | 0.02  | 0.03  | 0.05  | 0.05  |
| Rothia                                  | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.07  | 0.12  |
| Psychrobacter                           | <0.01 | <0.01 | <0.01 | <0.01 | 0.02  | 0.04  | 0.05  | 0.04  |
| [Eubacterium]_hallii_group              | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.07  | 0.10  |
| [Eubacterium]_nodatum_group             | <0.01 | <0.01 | 0.02  | <0.01 | 0.03  | 0.03  | 0.02  | 0.02  |
| Veillonella                             | 0.02  | 0.01  | <0.01 | <0.01 | 0.02  | 0.02  | 0.02  | 0.02  |
| Butyricicoccus                          | <0.01 | <0.01 | <0.01 | <0.01 | 0.02  | 0.02  | 0.04  | 0.02  |
| Coprobacillus                           | <0.01 | <0.01 | <0.01 | <0.01 | 0.06  | 0.18  | <0.01 | <0.01 |
| Prevotellaceae_UCG-004                  | 0.01  | 0.02  | 0.01  | <0.01 | 0.03  | 0.03  | <0.01 | 0.01  |
| Lachnospiraceae_UCG-006                 | <0.01 | <0.01 | <0.01 | <0.01 | 0.03  | 0.03  | 0.02  | 0.01  |
| Tuzzerella                              | <0.01 | <0.01 | 0.02  | 0.01  | 0.02  | 0.02  | 0.02  | 0.01  |
| Faecalibaculum                          | <0.01 | <0.01 | <0.01 | <0.01 | 0.03  | 0.04  | 0.03  | 0.03  |
| unidentified_Clostridia_vadinBB60_group | <0.01 | <0.01 | 0.02  | 0.01  | 0.02  | <0.01 | 0.01  | 0.01  |
| Mycoplasma                              | 0.03  | 0.03  | 0.02  | 0.02  | 0.01  | 0.02  | <0.01 | <0.01 |
| Coriobacteriaceae_UCG-002               | <0.01 | 0.01  | <0.01 | <0.01 | 0.04  | 0.08  | <0.01 | 0.01  |
| unidentified_Xanthomonadaceae           | <0.01 | <0.01 | 0.02  | 0.03  | 0.01  | 0.03  | 0.01  | 0.02  |

|                              |       |       |       |       |       |       |       |       |
|------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|
| Erysipelotrichaceae_UCG-003  | 0.01  | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.03  | 0.03  |
| Candidatus_Arthromitus       | 0.04  | 0.05  | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 |
| unidentified_Ruminococcaceae | 0.01  | 0.01  | 0.01  | 0.01  | 0.02  | 0.02  | <0.01 | 0.01  |
| Ruminiclostridium            | <0.01 | <0.01 | <0.01 | <0.01 | 0.01  | <0.01 | 0.03  | 0.01  |
| Ileibacterium                | <0.01 | <0.01 | <0.01 | <0.01 | 0.04  | 0.11  | <0.01 | <0.01 |
| UBA1819                      | 0.02  | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.01  | 0.02  |
| Paludicola                   | <0.01 | <0.01 | 0.01  | <0.01 | <0.01 | <0.01 | 0.02  | <0.01 |
| Facklamia                    | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.02  | 0.01  |
| DNF00809                     | <0.01 | <0.01 | <0.01 | 0.01  | <0.01 | <0.01 | 0.01  | 0.01  |
| Sphaerochaeta                | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.01  | 0.01  | 0.02  |
| Gemella                      | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.03  | 0.05  |
| Granulicatella               | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.03  | 0.06  |
| Pygmaibacter                 | <0.01 | <0.01 | 0.01  | 0.01  | <0.01 | <0.01 | 0.01  | 0.01  |
| Rikenella                    | <0.01 | <0.01 | 0.01  | <0.01 | 0.01  | 0.01  | <0.01 | <0.01 |
| Pseudomonas                  | <0.01 | <0.01 | <0.01 | 0.01  | 0.01  | 0.02  | <0.01 | 0.01  |
| Citrobacter                  | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.03  | 0.06  |
| UCG-004                      | <0.01 | <0.01 | 0.01  | 0.02  | <0.01 | <0.01 | 0.01  | 0.02  |
| Atopostipes                  | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.02  | 0.02  |
| Brachybacterium              | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.02  | 0.05  |
| Muribaculum                  | <0.01 | <0.01 | <0.01 | <0.01 | 0.03  | 0.03  | <0.01 | <0.01 |
| Globicatella                 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.02  | 0.03  |
| Holdemania                   | <0.01 | <0.01 | <0.01 | 0.01  | 0.01  | 0.01  | <0.01 | <0.01 |
| Mogibacterium                | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.02  | 0.01  |
| Oceanobacillus               | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.01  | 0.01  |
| Paraprevotella               | <0.01 | <0.01 | <0.01 | <0.01 | 0.03  | 0.04  | <0.01 | <0.01 |
| Elusimicrobium               | <0.01 | <0.01 | <0.01 | <0.01 | 0.01  | 0.02  | <0.01 | <0.01 |
| Enteractinococcus            | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.01  | 0.01  |
| Proteus                      | <0.01 | 0.01  | <0.01 | <0.01 | <0.01 | <0.01 | 0.01  | 0.01  |
| Brevibacterium               | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.01  | 0.01  |
| Lautropia                    | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.02  | 0.03  |
| Actinomyces                  | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.01  | 0.03  |
| Clostridium_sensu_stricto_13 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.01  | 0.02  |
| Clostridium_sensu_stricto_11 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.01  | 0.02  |
| Morganella                   | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.01  | 0.01  |

**Supplementary Table S5. The relative abundance of major genera at different ages (average relative abundance > 0.01 %).** mean<sup>a</sup>, average relative abundance; SD<sup>b</sup>, standard deviation.