

## Supplementary table captions

**Supplementary Table S1.** Clinicopathological factors of the study cohort including CRC patients and H volunteers.

**Supplementary Table S2.** Bacterial libraries after taxonomic assignment of OTUs at the 97% minimum similarity level. V, H group; C, CRC group.

**Supplementary Table S3.** Heat map analysis for the 76 discriminatory OTUs by Wilcoxon rank-sum test.

**Supplementary Table S4.** Processed, imputed, normalized, log transformed, and scaled GC-MS-based metabolite abundance data for the H (H volunteers, n = 42) and CRC (colorectal cancer patients, n = 46) group fecal samples. Twelve outlier samples (samples # 1, 2, 7, 9, 11, 28, 32, 49, 53, 62, 75, 109) were discarded. H, H participants group; CRC, CRC patient group.

**Supplementary Table S5.** Fold changes (FC) for GC-MS-based metabolomics datasets for the H and CRC groups. Highlighted in yellow are the significantly ( $\alpha = 0.05$ , p values obtained from t-test, t-test adjusted and false discovery rates (FDRs)) different metabolites, and FC values highlighted in red and green represent increased and decreased metabolites in CRC, respectively.

**Supplementary Table S6.** List of metabolites showing higher and lower abundances in CRC patients than in H subjects.

**Supplementary Table S7.** List of unique metabolites quantified in samples from the H and CRC groups.

**Supplementary Table S8.** The KEGG and HMDB metabolite IDs for the identified/quantified metabolites in the entire metabolomics study.

**Supplementary Table S9.** Pearson's correlation (r) values for metabolites and microbes in the CRC group. Pearson correlation r values, p values and p values (adjusted) are provided.

**Supplementary Table S10.** Pearson's correlation (r) values for metabolites and microbes in the H group. Pearson correlation r values, p values and p values (adjusted) are provided.

**Supplementary Table S11.** Pearson correlation (r) values for metabolites and 76 discriminatory microbes. Pearson correlation r values, p values and p values (adjusted) are provided.

## **Supplementary figures**

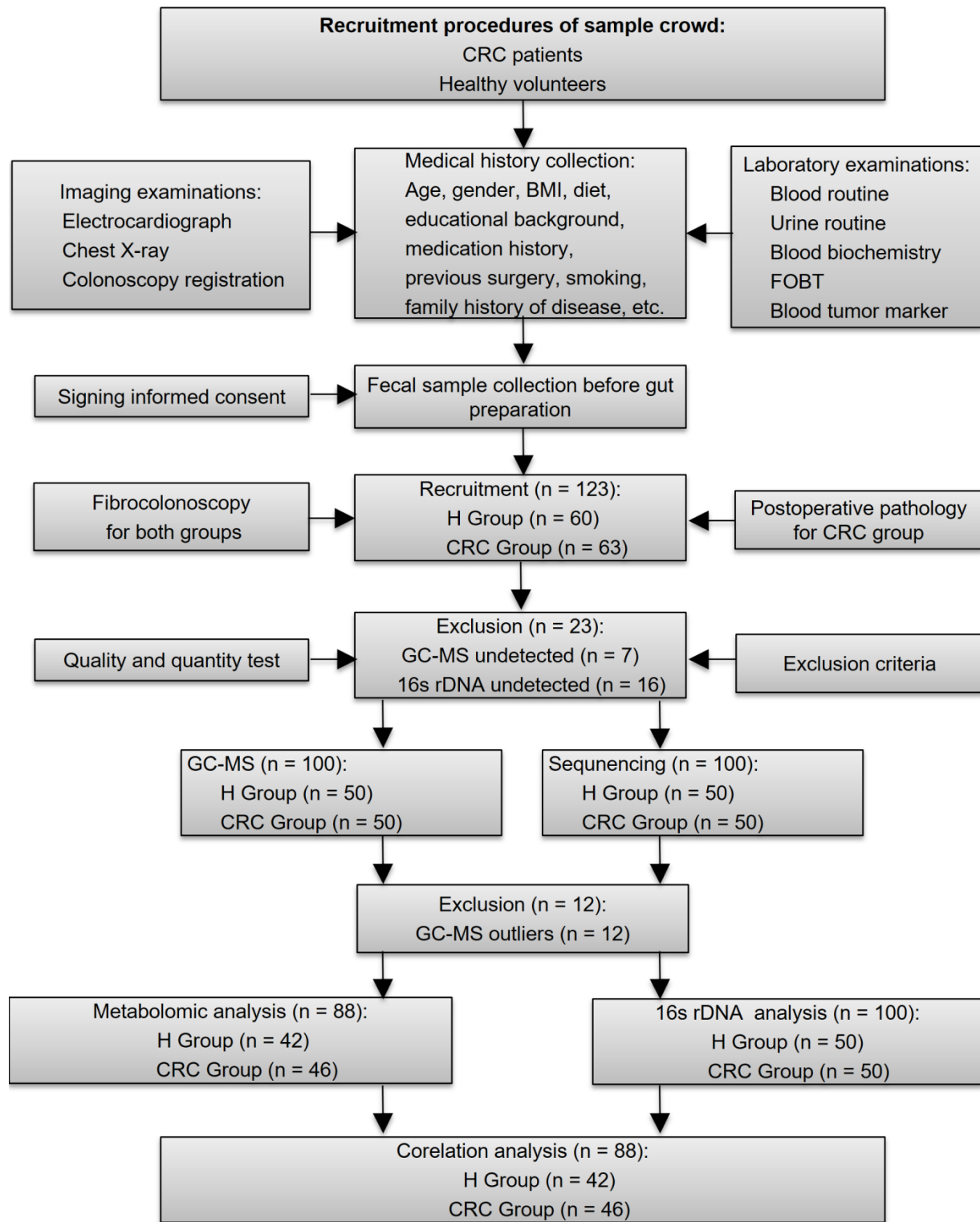
**Supplementary Figure S1.** Flow diagram of the enrollment and analysis process of the CRC patients and H volunteers.

**Supplementary Figure S2.** Relative bacterial richness and evenness analyses. **(A)** Species accumulation curves assessing the number sequences likely required to detect additional OTUs. CRC, CRC patient group; H, H volunteer group. **(B)** Rarefaction curve evaluating the relative bacterial richness to determine whether further sequencing would identify additional OTUs. CRC, CRC patients (red); H, H volunteers (blue). **(C)** Rank abundance distribution curve to visualize species evenness and species richness. The horizontal axis of the graph shows the OTU rank, and the vertical axis shows the relative abundance. CRC, CRC volunteers (blue); H, H volunteers (red). **(D)** *Firmicutes/Bacteroidetes* ratio. NS, not significant.

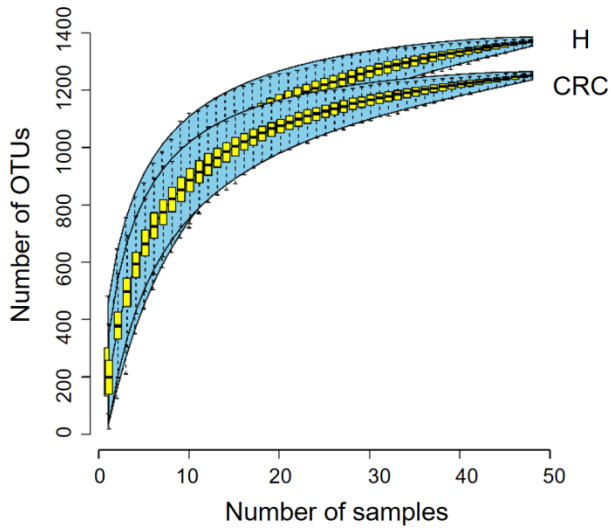
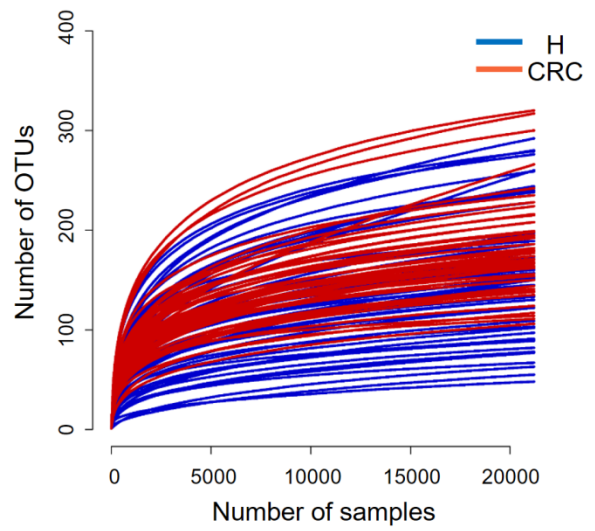
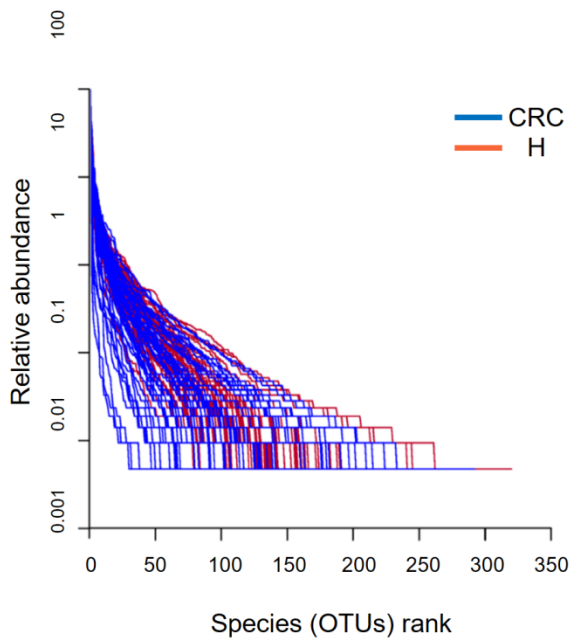
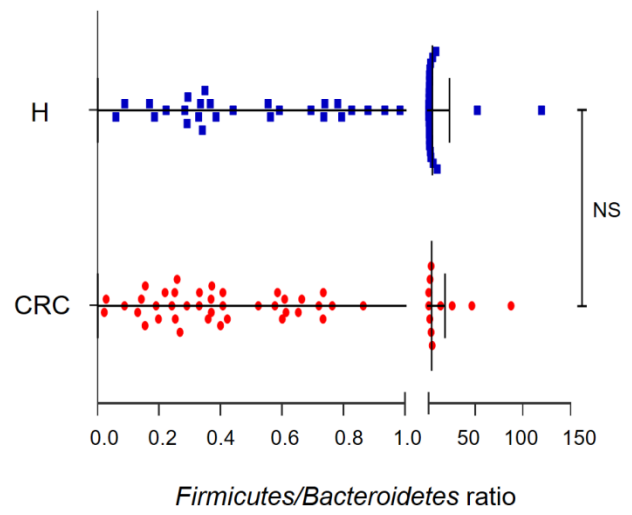
**Supplementary Figure S3.** Alterations in the composition of fecal microflora associated with CRC. **(A)** Welch's t-test results for evaluating the relative abundance of significantly different microbiota at the phylum level. CRC (blue) and H (yellow) groups for bars and dots. **(B)** Welch's t-test results for evaluating the relative abundance of significantly different microbiota at the genus level. CRC (blue) and H (yellow) groups for bars and dots.

**Supplementary Figure S4.** Gut metabolism in the fecal metabolome of the CRC and H groups. **(A)** Pathway enrichment and the significance for the total metabolites identified using a GC-MS-based metabolomics platform in both groups. **(B)** Metabolite-metabolite (Pearson's  $r$ ) correlations showing the correlation between various groups of metabolites for the combined H and CRC metabolomics datasets. High (1, red) and low (0, green) correlations are shown. Four discernible highly correlated groups of metabolites were (i) polyamines and amino acids, (ii) xenobiotics, sugars, sugar alcohols, fatty acids, (iii) amino acids, and (iv) sugars.

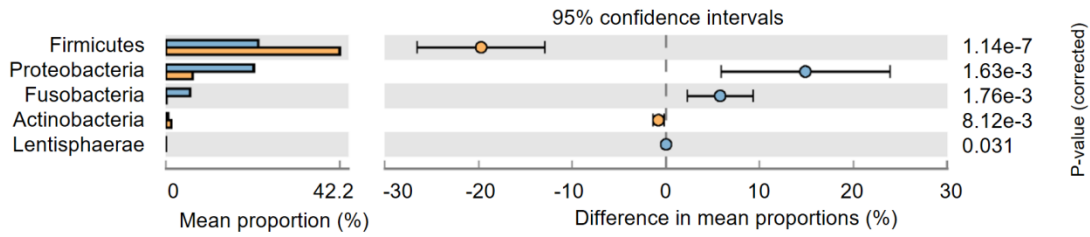
**Supplementary Figure S1**



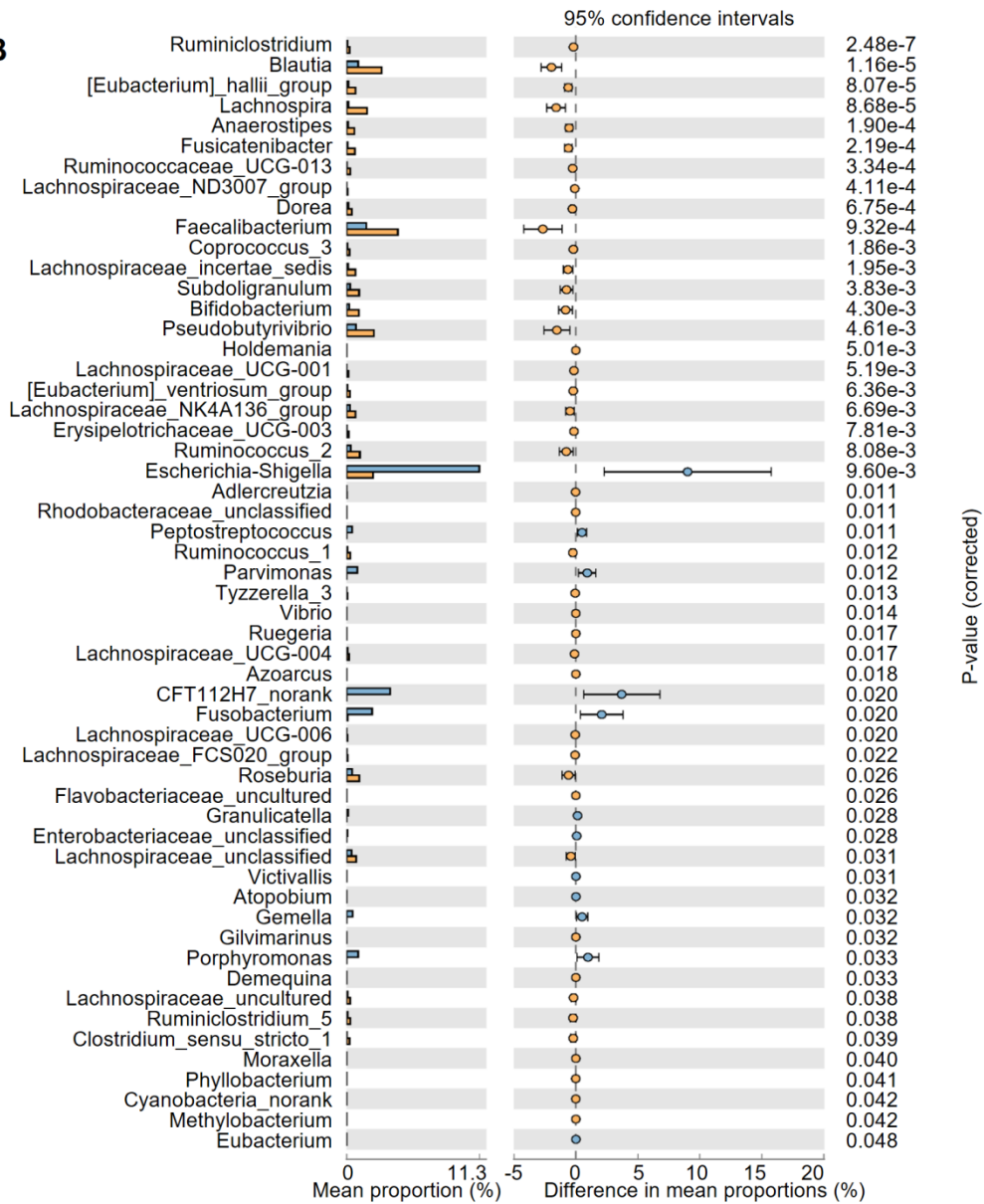
**Supplementary Figure S2**

**A****B****C****D****Supplementary Figure S3**

**A**



**B**



# Supplementary Figure S4

