

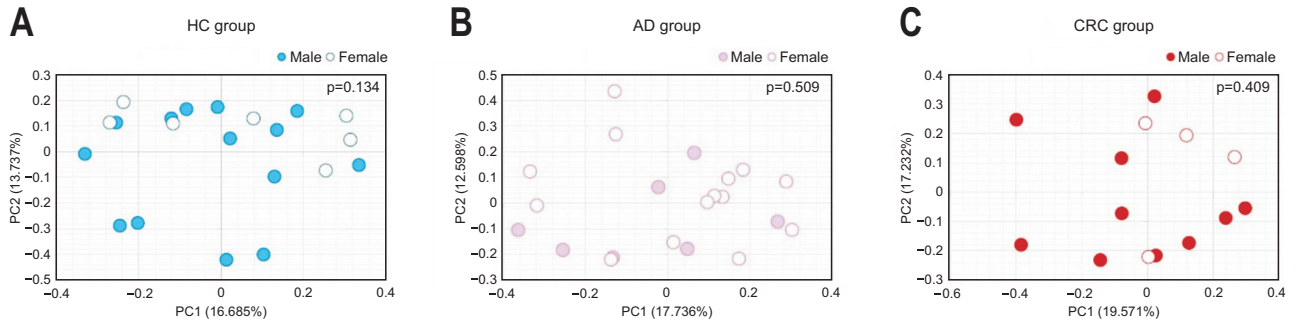
Supplementary Table 1. Alpha Diversity of Gut Microbiota from Fecal Contents

Variable	HC group			AD group			CRC group		
	Younger (n=16)	Older (n=5)	p-value	Younger (n=4)	Older (n=17)	p-value	Younger (n=3)	Older (n=11)	p-value
No. of OTUs	235.06	150.00	0.063	194.50	235.41	0.282	181.33	253.09	0.243
Good's library coverage, %	97.48	98.46	0.047*	97.68	97.36	0.347	98.14	97.33	0.311
Alpha diversity									
ACE	678.86	377.65	0.083	625.73	694.50	0.929	396.59	602.65	0.392
Chao1	445.64	295.93	0.058	390.43	466.44	0.282	320.97	460.28	0.312
Jackknife	552.32	330.52	0.039*	435.35	610.58	0.152	419.88	947.76	0.312
Shannon	3.22	2.51	0.069	2.37	2.93	0.152	2.54	3.16	0.186
Simpson	0.13	0.21	0.160	0.26	0.16	0.179	0.20	0.12	0.102

Data are presented as the median. Younger means age ≤ 55 years and older means age > 55 years.

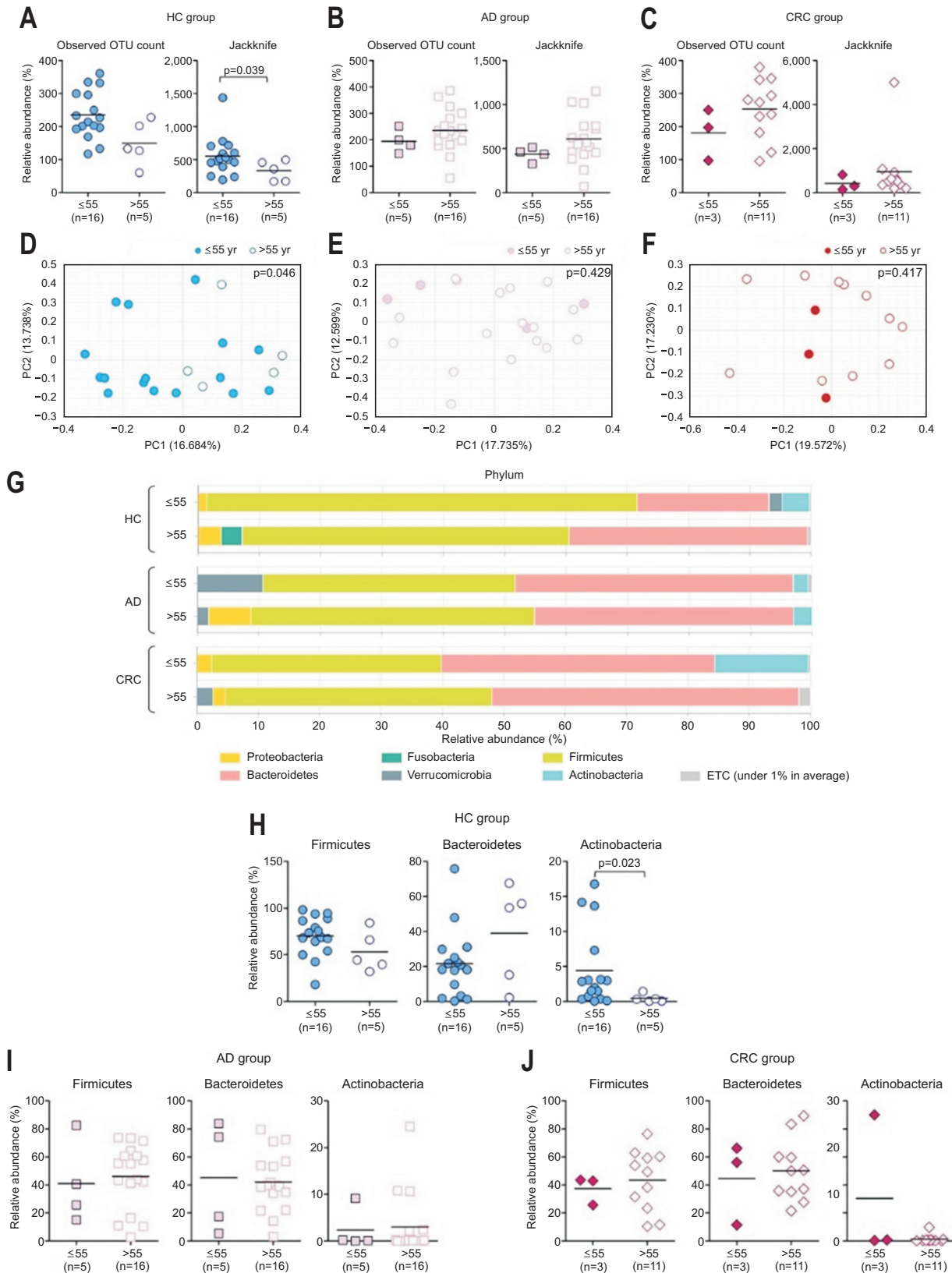
HC, healthy control; AD, colorectal adenoma; CRC, colorectal carcinoma; OTU, operational taxonomic unit.

Mann-Whitney U-test for comparison difference between independent two groups was performed. *p-value < 0.05 .



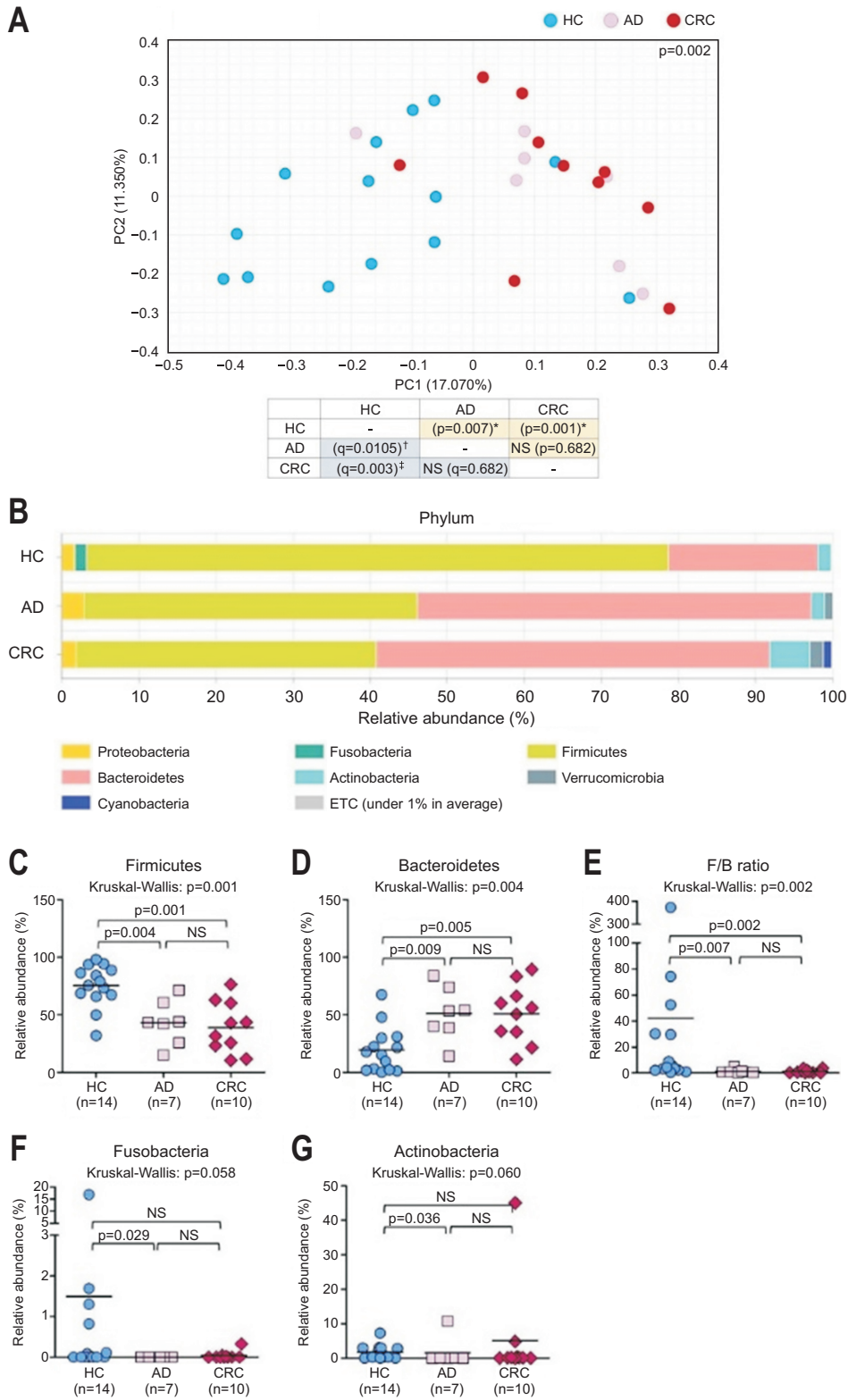
Supplementary Fig. 1. Beta diversity of gut microbiota according to sex in HC (A), AD (B), and CRC (C) groups. Samples were clustered by PCoA plot using the Generalized UniFrac method at the species level. Significance of similarity of bacterial population structure was analyzed using PERMANOVA.

HC, healthy control; AD, colorectal adenoma; CRC, colorectal adenocarcinoma; PCoA, principal coordinates analysis; PERMANOMA, permutational multivariate analysis of variance.

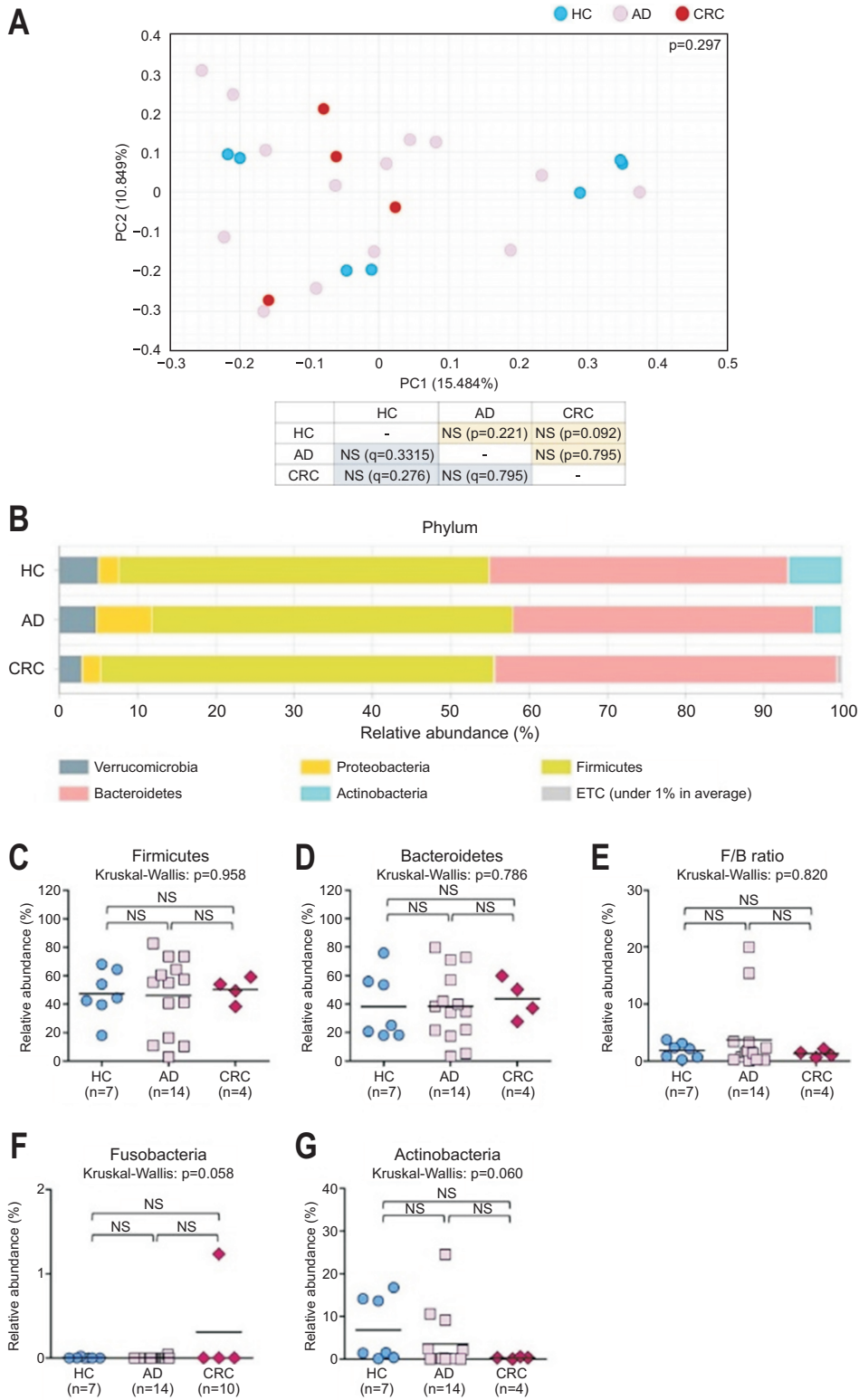


Supplementary Fig. 2. Gut microbial diversity according to age in the HC, AD, and CRC subjects. [A-C] Alpha diversity of gut microbiota. Scatter plots for relative abundance according to age in HC (A), AD (B), and CRC (C) groups. Data are expressed as the mean \pm SEM. [D-F] Beta diversity of gut microbiota in HC (D), AD (E), and CRC (F) group. (G) Bar graph for taxonomic composition. [H-J] Scatter plots for relative taxonomic abundance according to age in HC (H), AD (I), and CRC (J) group. Data are expressed as the mean \pm SEM.

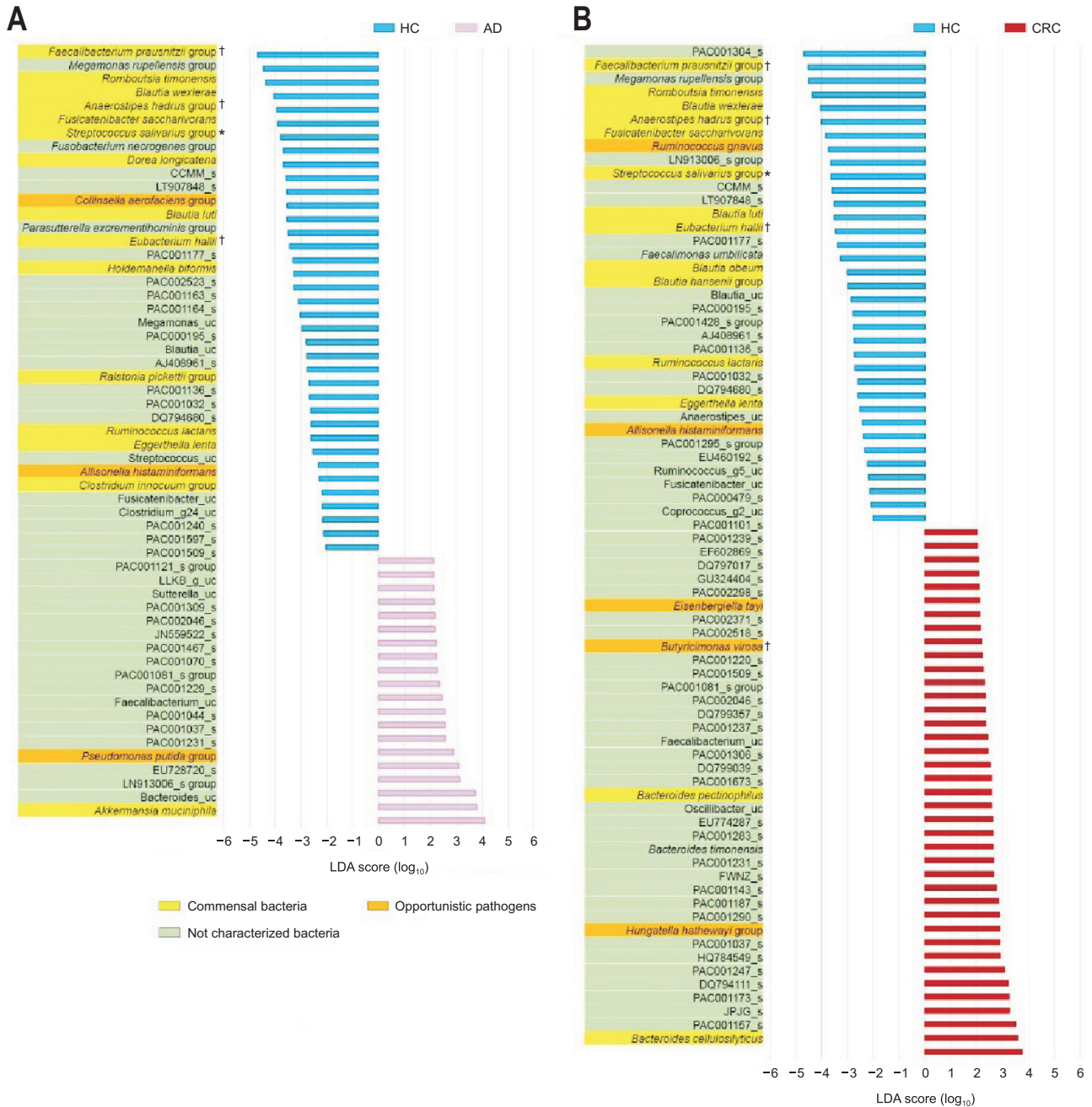
HC, healthy control; AD, colorectal adenoma; CRC, colorectal adenocarcinoma; OUT, operational taxonomic unit; SEM, standard error of the mean.



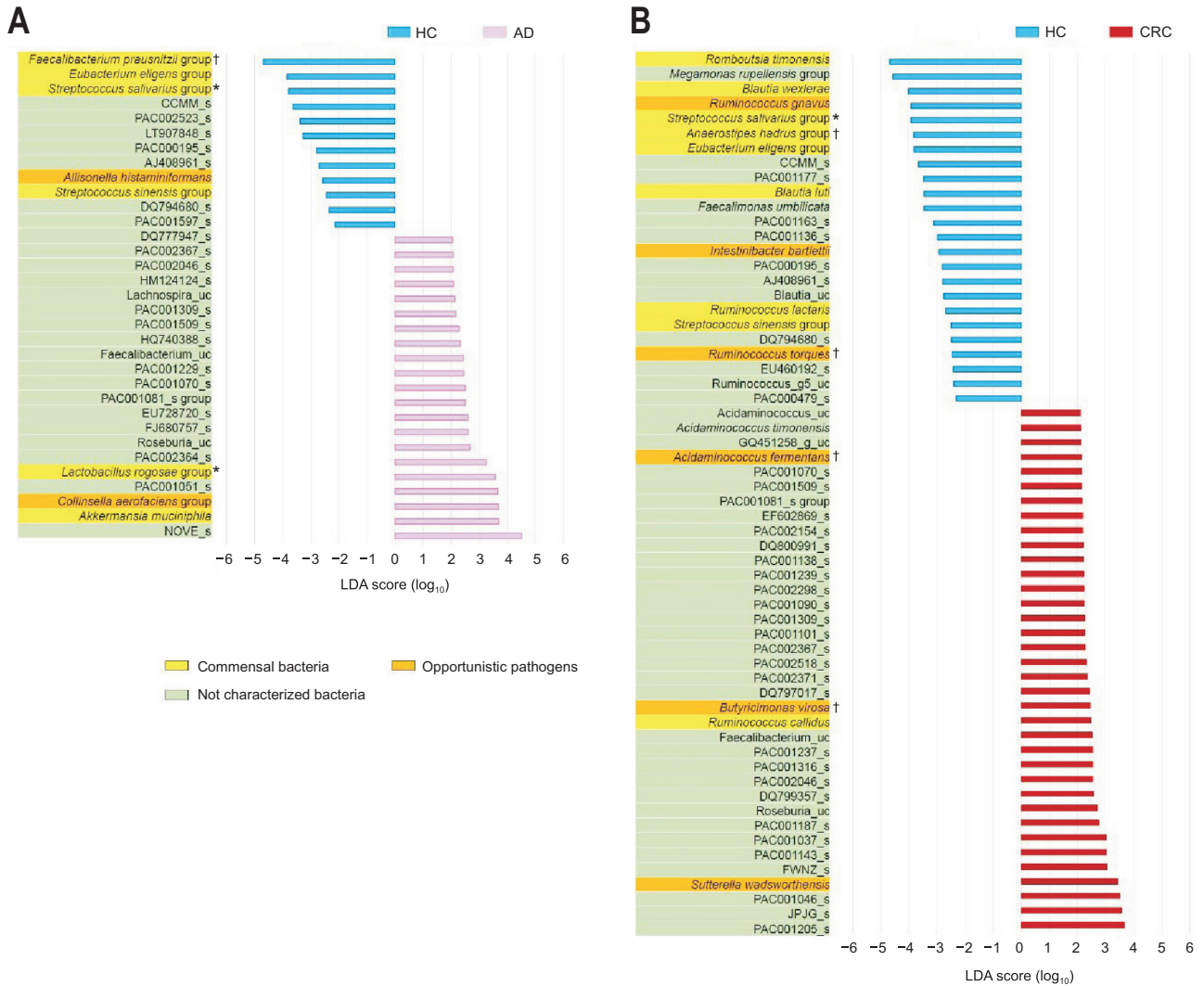
Supplementary Fig. 3. Distribution of gut microbiome according to the HC-AD-CRC sequence in male participants. (A) Beta diversity of gut microbiota. (B-G) Gut microbiota compositions at the phylum level. Bar graph for taxonomic composition (B) and scatter plots for relative taxonomic abundance [C-G]. Data are expressed as the mean±SEM. HC, healthy control; AD, colorectal adenoma; CRC, colorectal adenocarcinoma; SEM, standard error of the mean; NS, not significant. * $p < 0.01$, † $q < 0.05$, ‡ $q < 0.01$.



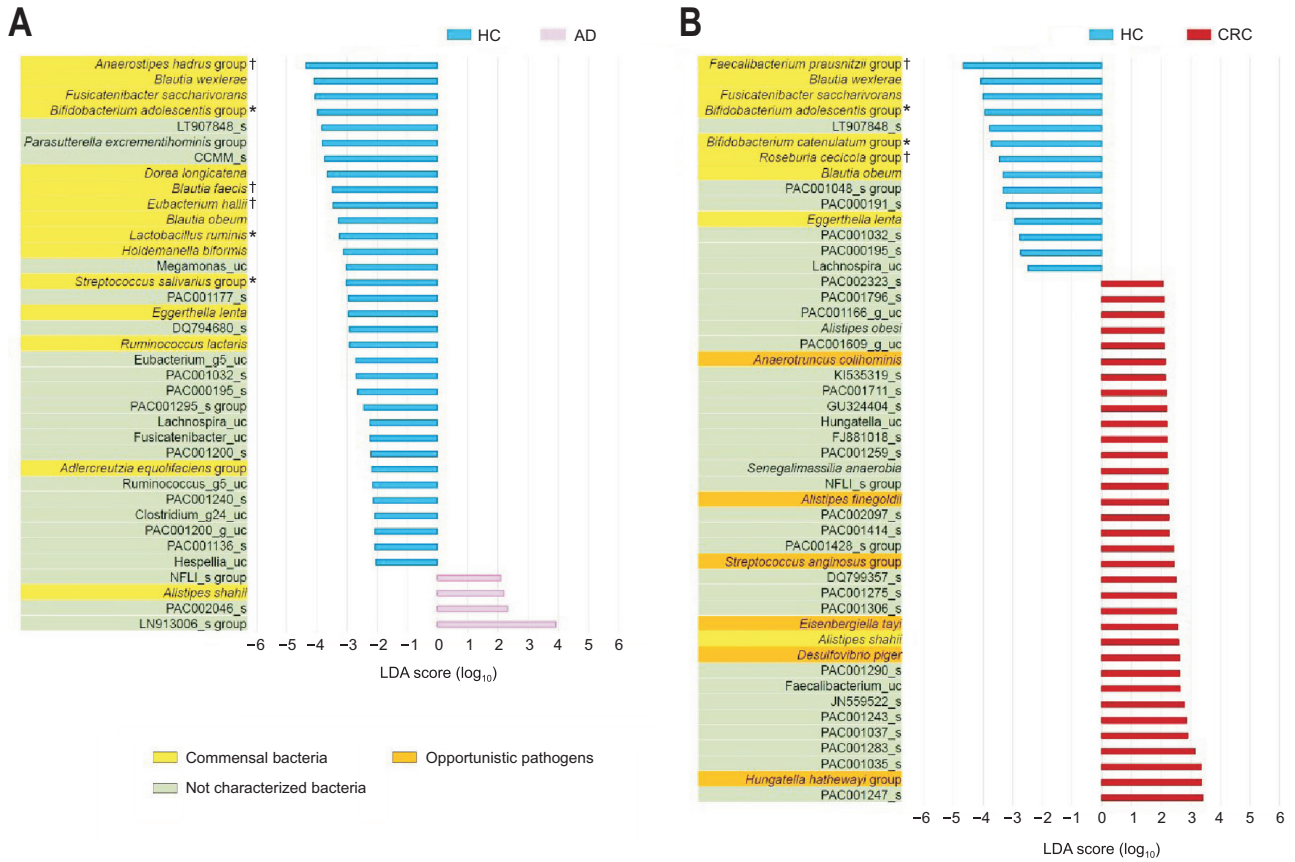
Supplementary Fig. 4. Distribution of gut microbiome according to the HC-AD-CRC sequence in female participants. (A) Beta diversity of gut microbiota. (B-G) Gut microbiota compositions at the phylum level. Bar graph for taxonomic composition (B) and scatter plots for relative taxonomic abundance [C-G]. Data are expressed as the mean±SEM. HC, healthy control; AD, colorectal adenoma; CRC, colorectal adenocarcinoma; SEM, standard error of the mean; NS, not significant; F/B, Firmicutes-to-Bacteroidetes.



Supplementary Fig. 5. Linear discriminant analysis (LDA) effect size (LEfSe) analysis according to the HC-AD-CRC sequence in all participants. The color bars show the LDA scores of species that enriched in indicated condition; (A, B) blue bar (HC group), (A) pink bar (AD group), (B) red bar (CRC group). The color and symbol on the species name indicate the characteristics of each species: yellow for commensal bacteria, orange for opportunistic pathogens, green color for not characterized bacteria. HC, healthy control; AD, colorectal adenoma; CRC, colorectal adenocarcinoma. *Lactate-producing bacteria; †Butyrate-producing bacteria.



Supplementary Fig. 6. Linear discriminant analysis (LDA) effect size (LEfSe) analysis according to the HC-AD-CRC sequence in male subjects. The color bars show the LDA scores of species that enriched in indicated condition; (A, B) blue bar (male HC group), (A) pink bar (male AD group), (B) red bar (male CRC group). The color and symbol on the species name indicate the characteristics of each species: yellow for commensal bacteria, orange for opportunistic pathogens, green color for not characterized bacteria. HC, healthy control; AD, colorectal adenoma; CRC, colorectal adenocarcinoma. *Lactate-producing bacteria; †Butyrate-producing bacteria.



Supplementary Fig. 7. Linear discriminant analysis (LDA) effect size (LEfSe) analysis according to the HC-AD-CRC sequence in female subjects. The color bars show the LDA scores of species that enriched in indicated condition; (A, B) blue bar (female HC group), (A) pink bar (female AD group), (B) red bar (female CRC group). The color and symbol on the species name indicate the characteristics of each species: yellow for commensal bacteria, orange for opportunistic pathogens, green color for not characterized bacteria. HC, healthy control; AD, colorectal adenoma; CRC, colorectal adenocarcinoma. *Lactate-producing bacteria; †Butyrate-producing bacteria.