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Molecular characterization of mucosal adherent bacteria and associations with colorectal adenomas

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Abbreviations: FISH, florescence in situ hybridization; CRC, colorectal cancer; T-RFLP terminal restriction fragment length polymorphism; T-RF, terminal restriction fragment

The human large bowel is colonized by complex and diverse bacterial communities. However, the relationship between commensal bowel bacteria and adenomas (colorectal cancer precursors) is unclear. This study aimed to characterize adherent bacteria in normal colon and evaluate differences in community composition associated with colorectal adenomas. We evaluated adherent bacteria in normal colonic mucosa of 21 adenoma and 23 non-adenoma subjects enrolled in a cross sectional study. Terminal restriction fragment length polymorphism, clone sequencing and fluorescent in-situ hybridization analysis of the 16S rRNA genes were used to characterize adherent bacteria. A total of 335 clones were sequenced and processed for phylogenetic and taxonomic analysis. Differences in bacterial composition between cases and controls were evaluated by UniFrac and analysis of similarity matrix. Overall, Firmicutes (62%), Bacteroidetes (26%) and Proteobacteria (11%) were the most dominant phyla. The bacterial composition differed significantly between cases and controls (UniFrac $p < 0.001$). We observed significantly higher abundance of Proteobacteria ($p < 0.05$) and lower abundance of Bacteroidetes ($p < 0.05$) in cases compared to controls. At the genus level, case subjects showed increased abundance of *Dorea spp.* ($p < 0.005$), *Faecalibacterium spp.* ($p < 0.05$) and lower proportions of *Bacteroides spp.* ($p < 0.03$) and *Coprococcus spp.* ($p < 0.05$) than controls. Cases had higher bacterial diversity and richness than controls. These findings reveal that alterations in bacterial community composition associated with adenomas may contribute to the etiology of colorectal cancer. Extension of these findings could lead to strategies to manipulate the microbiota to prevent colorectal adenomas and cancer as well as to identify individuals at high risk.

Supplementary Material

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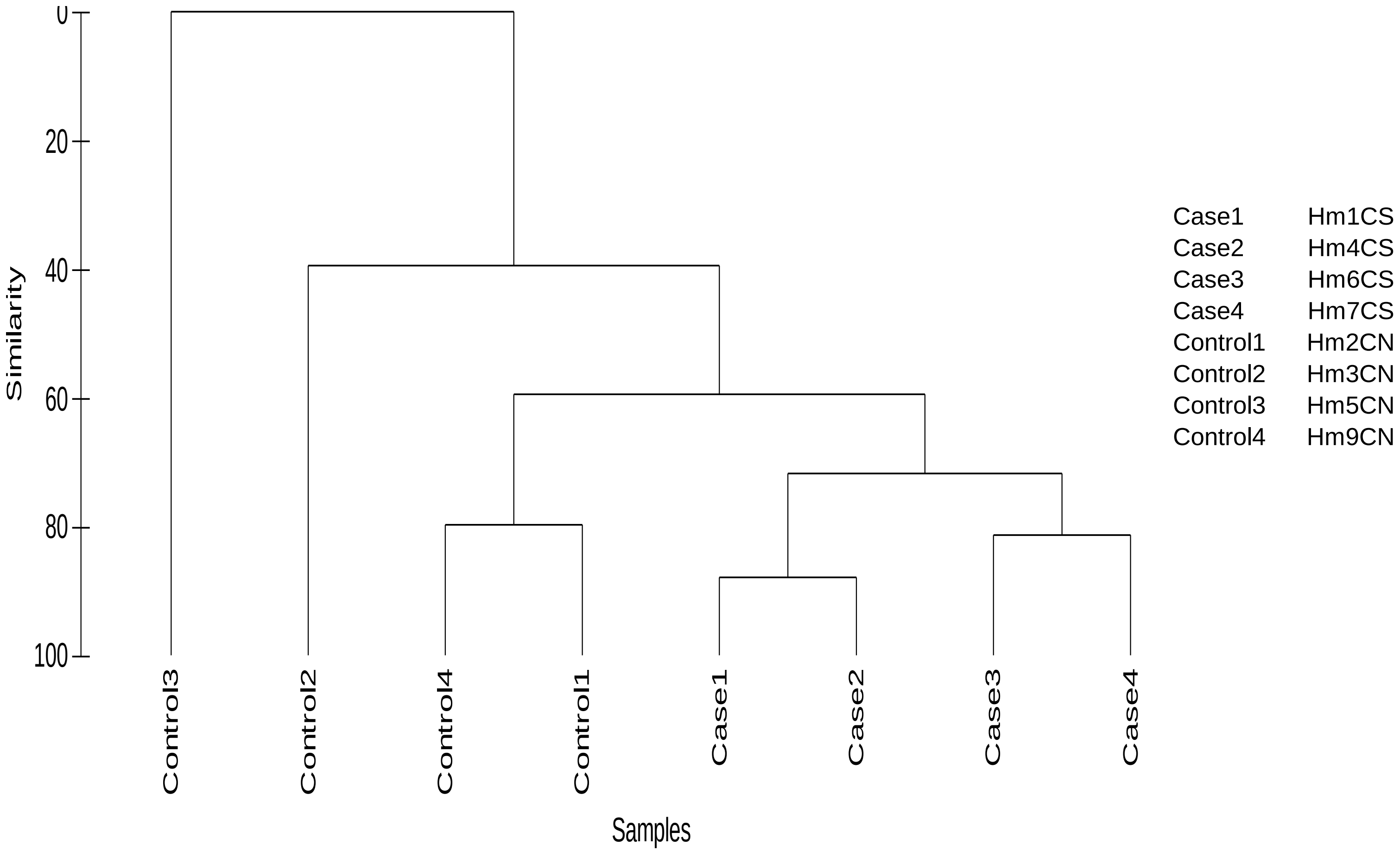
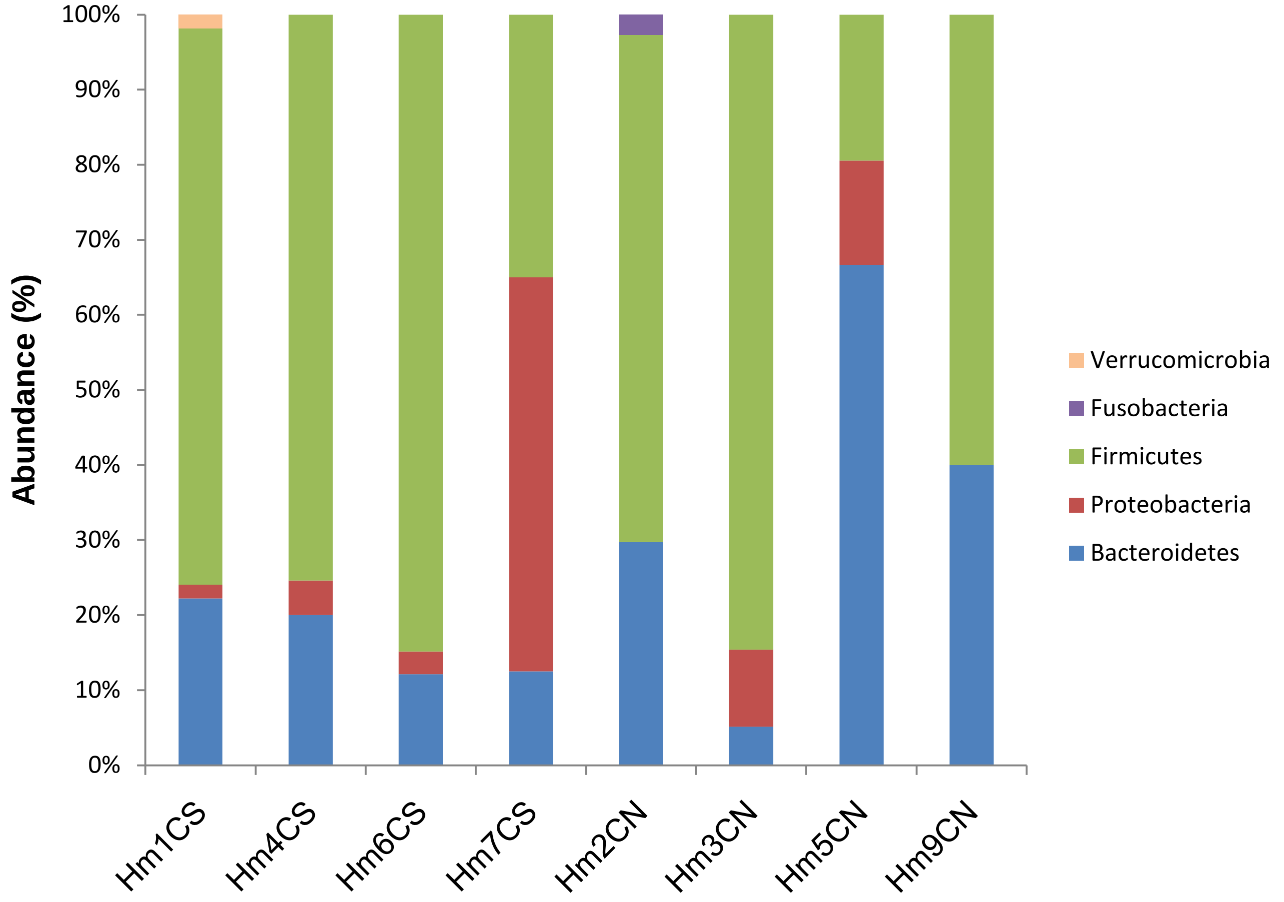


Supplemental Figure 1S Cluster Analysis of Unifrac distances among adenoma cases and controls. Cluster Analysis of UNIFRAC distances among cases and controls based on the 16S rRNA sequence similarities of the adherent bacterial communities.



Supplemental Figure 2S Phylum level composition of bacterial phylotypes by individual subjects. Relative abundance of phylum-level bacterial phylotypes identified in each subject based on clone library sequences.