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The keystone bacterium Christensenella minuta improves colitis in in vivo preclinical Inflammatory Bowel Disease models

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Background: There is increasing evidence that microbiome-based therapies can correct dysbiosis and reduce inflammation associated with Inflammatory Bowel Diseases (IBD). In particular, the human commensal family of *Christensenellaceae* bacteria has been reported as missing in several cohorts of Crohn's disease patients, indicating that it may have a role in maintaining microbial symbiosis in this population. To assess its potential for IBD management, we used the reference type species *Christensenella minuta* DSM 22607 to examine its anti-inflammatory properties.
Methods: We first performed two distinct independent preclinical colitis models: i) a moderate DNBS-induced colitis model in mice and ii) a severe TNBS-induced colitis model in rats. To decipher the mechanisms of action of *C. minuta* underlying the observed effects, we determined its ability to produce short chain fatty acids (SCFA) at different growth phases and we assessed its capacity to modulate the inflammatory response of human colonic cells.
Results: Our results showed that in both rodent models, *C. minuta* prevented intestinal damages by decreasing macroscopic scores, reduced colonic inflammation by limiting neutrophils infiltration in the colon and stimulated mucosal healing. We also confirmed that *C. minuta* is a high acetate and moderate butyrate producer. Finally, we showed that *C. minuta* displayed potent anti-inflammatory properties by decreasing the secretion of the pro-inflammatory cytokine IL-8 through NF-kB inhibition in HT-29 cells.
Conclusion: Together, these results revealed for the first time the strong anti-inflammatory properties of *C. minuta* and confirm its high potential as an innovative microbiome-based biotherapy for IBD.

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Similar gut bacterial composition between patients with ulcerative colitis and healthy controls in a high prevalence population: a cross-sectional study of the Faroe Islands IBD cohort

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Background: The Faroe Islands, a genetically and geographically isolated population in the North Atlantic, has the world's highest prevalence of inflammatory bowel disease (IBD). Epidemiological studies have characterized this unique cohort, which consists predominately of an ulcerative colitis phenotype, and a decreased risk of developing IBD with emigration. Therefore, the well-characterized Faroese IBD cohort gives the opportunity to better understand the interplay between genetic predisposition and environmental triggers for this complex disease. This study represents the first investigation into the composition of the gut microbiome for the cohort.
Methods: This cross-sectional study consisted of 41 patients with established ulcerative colitis (UC) and 144 age-and sex matched healthy controls (HC) recruited through the Faroese Genome project (FarGen). Participants donated a one-time fecal sample and completed questionnaires on food-frequency, background health and lifestyle. DNA extractions were completed and 16S rRNA amplicon sequencing of the V3-V4 region was performed followed by bioinformatic analysis of taxonomy and diversity metrics.
Results: The overall composition of the sequenced fecal bacteria was dominated by Firmicutes (64,5% of total amplicon sequence variants) and Bacteroidetes (20,95% of total amplicon sequence variants). *Akkermansia muciniphila* was absent from 30% of the study samples. Discriminatory analysis for indicator taxa identified that *Coprococcus* and *Prevotella_9* characterized healthy controls while genus *Ruminiclostridium* characterizes UC patients. However, no statistically significant differences were found between UC and HC based on metrics of alpha or beta diversity. Food frequency questionnaires revealed no differences in dietary patterns of the two groups.

	UC	Healthy
Sex		
Male	18 [44]	57 [39.6]
Female	23 [56]	87 [60.4]
Age		
Age at inclusion (SD; years)	48	55
Body mass index (SD; kg/m^2)	26.4	25.4
Age at diagnosis (SD; years)	27	-
Disease duration (IQR; years)	17	-
UC extent		-
E1, proctitis	22 [53.7]	
E2, left-sided	9 [22]	
E3, extensive	10 [24.4]	
Disease activity		-
Active	17 [41.5]	
Remission	24 [58.5]	
Medical treatment		-
None	3 [7.3]	
5-ASA	38 [90.2]	
Immunosuppressants	22 [53.7]	
Biological	9 [22]	
Combination therapy	22 [53.7]	

Table 1 Data is expressed as number [%], median [IQR] or mean [SD]. The study cohort included 185 participants with 41 patients diagnosed with ulcerative colitis and 144 healthy controls.
Conclusion: The similarity between the microbiome of Faroese UC and HC samples within this study and the absence of the beneficial taxa *Akkermansia muciniphila* in both groups, raises further questions concerning the underlying susceptibility toward inflammatory and metabolic disorders within this population. This study represents the first 16s rRNA amplicon sequencing data and insights into the Faroese UC and background population. The results highlight the importance of having regionally tuned reference ranges for microbial data.