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Siblings Of Crohn's Disease Patients Exhibit A Biologically Relevant Dysbiosis In The Mucosal Microbial Community: A 16S rRNA Gene Pyrosequencing Study

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Introduction Reduced mucosal *Faecalibacterium prausnitzii* predicts disease recurrence in Crohn's disease (CD) patients. Siblings (SIBS) of CD patients have elevated risk of developing CD and share aspects of CD phenotype including faecal dysbiosis. [1] No study has compared mucosal microbiota in CD SIBS to unrelated healthy controls (HC).

Methods Phenol/chloroform DNA extraction from rectal biopsies of 21 patients with quiescent CD, 17 of their healthy SIBS and 19 unrelated HC, and PCR amplification of the V1-V3 region of the bacterial 16S ribosomal RNA gene were performed. Microbiota composition was resolved by 454 pyrosequencing.

Results For each group, mucosal microbiota were classified into common/abundant (core) vs. infrequent/rare.² In terms of both microbial diversity (Shannon-Wiener and Simpson's indexes of diversity) and species richness, core microbiota of both SIBS and CD patients were significantly less diverse than HC. The rare microbiota diversity was lower in CD compared with HC, but was not different between SIBS and HC. Metacommunity profiling (Bray-Curtis (SBC) index of similarity with unweighted pair group averages) showed core microbial metacommunity of SIBS to be more similar to CD (SBC=0.70) than to HC, whereas the rare microbial metacommunity of SIBS was more similar to HC (SBC=0.42). As in CD patients, the species that contributed most to the dissimilarity of healthy SIBS vs. HC was *F. prausnitzii*, Table 1.

Conclusion This is the first in depth case-control study of the mucosal microbiota of SIBS of CD patients. Dysbiosis in SIBS was characterised by reduced diversity of core microbiota and lower abundance of *F. prausnitzii*. This dysbiosis in otherwise healthy, but at-risk people implicates microbiological processes in CD pathogenesis and risk.

References 1 Hedin C et al. Gut 2014 doi:10.1136/gutjnl-2013-306226. 2 van der Gast CJ et al. ISME J 5:780-791

Table 1 Similarity of Percentages analysis of bacterial community similarity (Bray-Curtis) between whole metacommunities. The 9 species with the greatest contribution to dissimilarity are shown.

	Siblings mean abundance (%)	Healthy mean abundance (%)	Average dissimilarity (%)	Contribution to dissimilarity (%)
<i>Faecalibacterium prausnitzii</i>	23.4	30.0	10.4	18.9
<i>Escherichia fergusonii</i>	9.6	3.9	5.8	10.6
<i>Sutterella wadsworthensis</i>	5.8	8.6	5.2	9.4
<i>Shigella flexneri</i>	6.9	3.5	4.6	8.4
<i>Bacteroides vulgatus</i>	7.3	7.9	4.6	8.4
<i>Eubacterium rectale</i>	6.1	9.5	3.9	7.0
<i>Oscillospira guilliermondii</i>	7.6	8.1	3.9	7.0
<i>Bacteroides dorei</i>	5.5	0.0	3.0	5.4
<i>Ruminococcus gnavus</i>	4.7	4.0	2.2	4.1