Conclusion: These data suggest that CD with ileal involvement (Montreal L1+L3) is a major determinant of the tissue-associated microbial composition in both ileal and colonic mucosa irrespective of variables such as endoscopic activity and GRS. The reduction of several beneficial microbes in CD with ileal involvement might partially explain the more progressive phenotype in such patients.

P709

Distinct Pattern of Gut Microbial Dysbiosis in Crohn’s Disease and Intestinal Tuberculosis - A Machine Learning-based classification model

M. Markandey*1, A. Bajaj1, S.K. Vuyyuru1, S. Mohra1, M. Singh1, M. Verma1, S. Kumar1, B. Kante1, P. Kumar1, G. Makharia1, S. Kedia1, V. Ahuja1

1All India Institute of Medical Sciences, Department of Gastroenterology and Human Nutrition, New Delhi, India

Background: Crohn’s disease (CD) and intestinal tuberculosis (ITB) are chronic granulomatous inflammatory disorders characterized by a compromised mucosal immunity. Even with diverging etiologies, CD and ITB presents an uncanny resemblance in clinical manifestation resulting in diagnostic dilemma. The gut microbiota regulates myriad of gut mucosal immunological processes. Present study aims to decipher gut microbial dysbiosis in the two disorders and utilize the CD and ITB-specific gut dysbiosis to construct a machine learning (ML)-based predictive model, which can aid in their differential diagnosis.

Methods: Fecal samples from healthy controls (n=12) and from patients with CD (n=23) and ITB (n=25) were subjected to 16S (V3-V4) amplicon sequencing. Processing of raw reads, construction of ASV feature tables, diversity, core microbiome analysis and ML classifier construction was done using QIIME2-2021.4. Differential abundance analysis (DAA) between the groups was carried out using Deseq2, after adjusting for the subject-specific confounders.

Results: The α and β diversity indices in CD and ITB groups were significantly reduced than HC group (p = 0.011 and 0.012 resp.), with no significant differences between the two diseases (Fig.1A, 1B). On comparison with HC, CD and ITB groups showed reduction in members of Firmicutes and Bacteroidetes, with enhancement of Actinobacteria and Proteobacteria (Fig.1C and 1D). DAA (FDR q <0.1, FC >2.5)

Fig.1. Diversity indices and differential taxa in HC, CD, and ITB groups (A) Comparisons of Shannon diversity (A1) and Pielou’s evenness index across the three groups, assessed by Wilcoxon rank-sum test. B) Ordination centroids dispersion for the three groups; the counts are centred-log ratio (CLR) normalised. (C and D) Deseq2 based DAA between the three groups. (FDR p <0.05)

Poster presentations

Downloaded from https://academic.oup.com/ecco-jcc/article/16/Supplement_1/i606/6513310 by guest on 03 February 2022
between CD and ITB groups revealed expansion of *Succinivibrio dextrinisolvens*, *Odoribacter splanchnicus*, *Megasphaera massiliensis*, *Bacteroides uniformis* and *B. xylanisolvens* in CD group, while *Clostridium sp.*, *Haemophilus parainfluenzae* and *Bifidobacterium* sp. were elevated in ITB (Fig.2A). Random Forest-based ML model constructed on the basis of raw microbiome reads and using 80% of the samples to train the model, showed predictive accuracy of 0.78 (AUC=93%); (Fig.2B).

**Conclusion:** Our study shows that CD and ITB witnesses significant changes in gut microbial structure. With no significant differences in microbial diversity between two diseases, the signature of gut dysbiosis is distinct between CD and ITB. Exploitation of these differences to construct ML models can potentiate differential diagnosis of CD and ITB.

**Background:** With the increasing complexity of inflammatory bowel disease (IBD) new therapies are clearly required. Recent evidence is coming to light demonstrating beneficial effects of helminth proteins. We aim to assess the prophylactic and therapeutic effects of extracellular vesicles (EVs) from the nematode *N. brasiliensis*, which serves as a model organism for human hookworm infections, in an acute and chronic model of colitis.

**Methods:** Prophylactic and therapeutic effects of EVs were assessed in an acute model of colitis by the administration of 20 µg intraperitoneally (i.p) of Nb EVs or grape EVs. Mice were sacrificed after 5 days. The therapeutic effects of Nb EVs were also assessed in a chronic model of colitis. Here, Rag1 knockout mice were treated twice weekly for three weeks with 20µg of either Nb EV, grape EV or aIL-12. Outcomes assessed for both experiments included weight loss, clinical disease, as well as macroscopic and histologic disease scores. Groups were statistically compared for significant differences.

**Results:** The prophylactic administration of Nb EVs significantly reduced weight loss, clinical disease, as well as macroscopic and histologic disease scores. Groups were statistically compared for significant differences.

**Conclusion:** The current study provides important evidence that the anti-inflammatory effects of helminth EVs can be harnessed to prevent and reverse inflammation in an acute and chronic mouse model.