Therapeutic Potential of the Gut Microbiota in the Management of Ulcerative colitis

Theme: Shaping the Future of Therapeutics

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1. Overview

Purpose

- To study gut microbiota composition in healthy and diseased state.
- Application of NGS in gut microbiome studies.
- To explore the therapeutic potential of gut microbiome.

Method

- Stool samples from healthy and ulcerative colitis patients were collected after consent.
- Fecal meta-DNA was extracted, quantified and sequenced
- The whole Genome Sequence reads were analysed to define diversity and richness of bacterial species.

Results

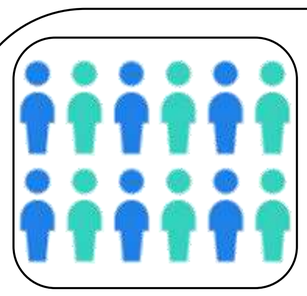
- Gut microbiome profiling and its association with ulcerative colitis pathogenesis.
- Healthy gut are relatively less diverse with high species richness individually, compared to diseased gut.
- Higher abundance of pathobionts like *Escherichia, Ralstonia* and lower abundance of commensals *Lactobacillus, Alistipes* and *Dorea* in diseased gut.

2. Introduction

Background: **Each human has a unique gut microbial composition which is dynamic and shaped by lifestyle, age, and host genetic composition. Gut microbial composition is closely related to host health and disease. The ulcerative colitis, an autoimmune inflammatory disorder of the colon has been associated with the gut microbiota composition. Metagenomics give good taxonomic coverage of gut microbes.**

Objective: **The objective of the current study was to examine the gut microbiome composition via whole genome sequence analysis of meta-DNA extracted from human fecal samples.**

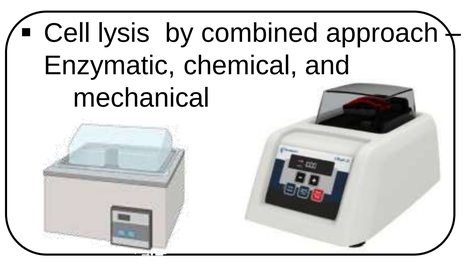
3. Experimental Approach



Sample population

Stool collection

- Homogenized using glass beads
- Microbial recovery by centrifugation



- Cell lysis by combined approach – Enzymatic, chemical, and mechanical

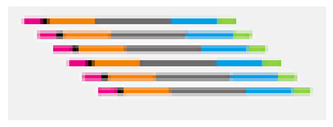
Sample processing

DNA quantification

- Qubit dsDNA High Sensitivity Assay
- DNA purity – QIAxpert
- DNA integrity - 0.8% agarose gel

Library preparation

- Prepared with KAPA Hyper prep kit for Illumina



WGS sequencing

- NovaSeq 6000 System
- Generate 60 million reads per sample

Whole genome Sequencing

Microbiome analysis

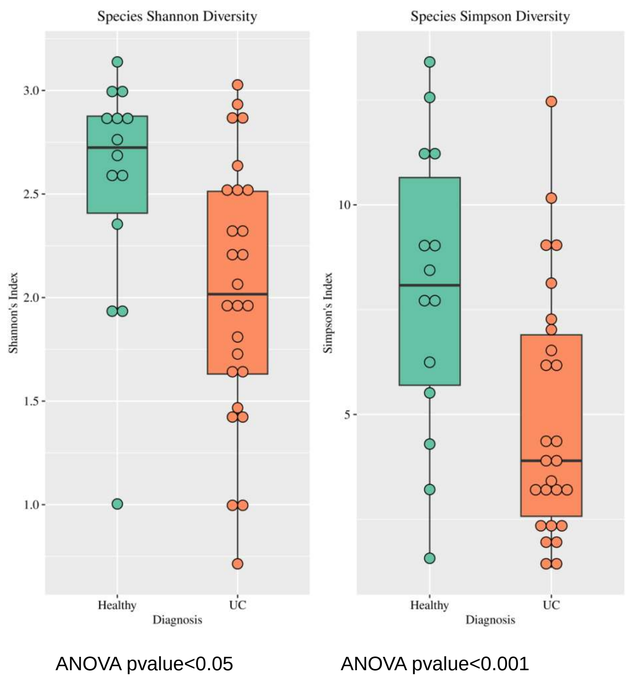
- bioBakery pipeline
- KneadData
- HUMAnN3
- Python (pandas, numpy)
- R (dplyr, Vegan, ggplot2, gplots, etc)

- **Bacterial alpha Diversity**
- **Bacterial Beta Diversity**
- **Species relative abundance**

Bioinformatics analysis

4. RESULTS

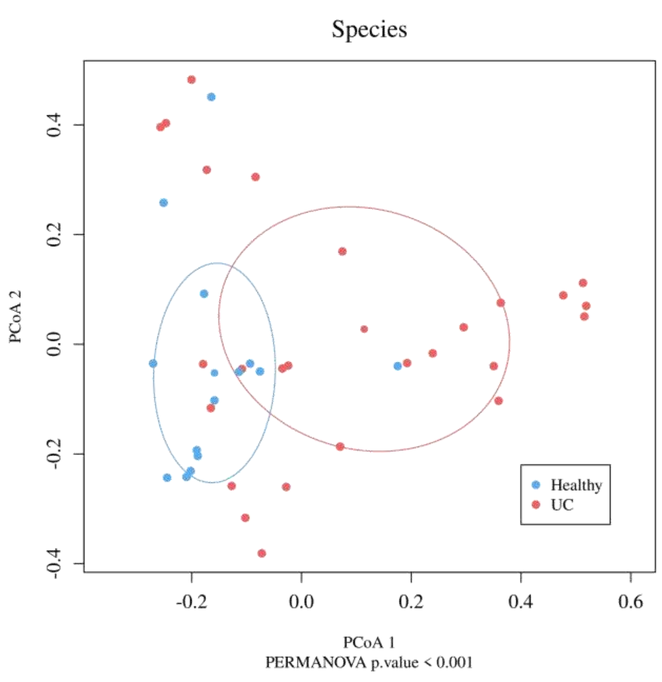
Bacterial alpha Diversity



ANOVA pvalue<0.05 ANOVA pvalue<0.001

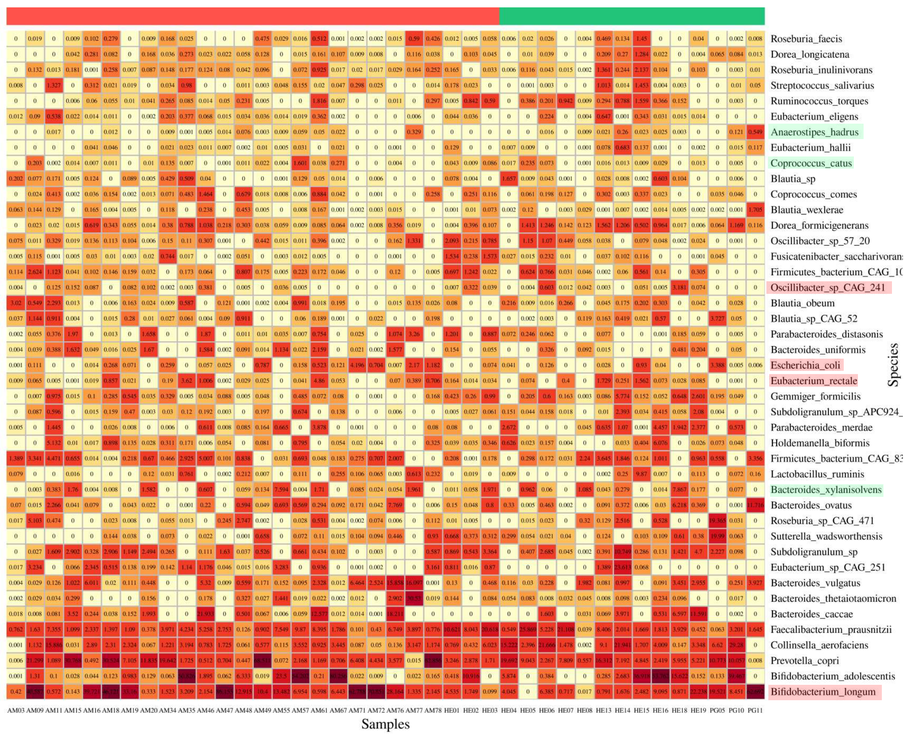
Graphical representation of alpha diversity calculated using Shannon and inverse Simpson index.

Beta diversity



Graphical representation of beta diversity using Bray Curtis diversity index.

Species relative abundance



Heatmap representing relative abundance of bacterial species of UC patients and healthy controls. The red bar above the heat map indicates UC samples and green bar indicates healthy samples.

Ethical statement: The study was ethically approved by the Institutional Ethical Committee (number IHEC/19/75).

5. Conclusion

The diversity index analysis revealed that bacterial communities in the healthy gut are relatively less diverse with high species richness individually, compared to diseased gut. The relative abundance analysis at bacterial species level indicated higher abundance of pathobionts like *Escherichia, Ralstonia* and lower abundance of beneficial gut commensal *Lactobacillus, Alistipes* and *Dorea*. There was a higher abundance of members of family *Lachnospiraceae* in diseased gut, which favours the growth of facultative anaerobes and pathobionts, like Adherent-Invasive *Escherichia coli* (AIEC), aggravating the disease severity. It was observed that dysbiotic gut was dominated by opportunistic pathogens like *Ralstonia mannitolilytic, Cutibacterium acnes, Bacteroides caccae*, and *Alistipes shahii*.

Here, we present metagenomic profiling to confirm the association between gut microbiome with UC pathogenesis. The ongoing study has potential to integrate clinical factors and next generation sequencing techniques in a larger cohort to validate the current findings. This will serve to design more effective diagnostic tools and provide new insights for future treatment regime targeted towards gut microbiota.

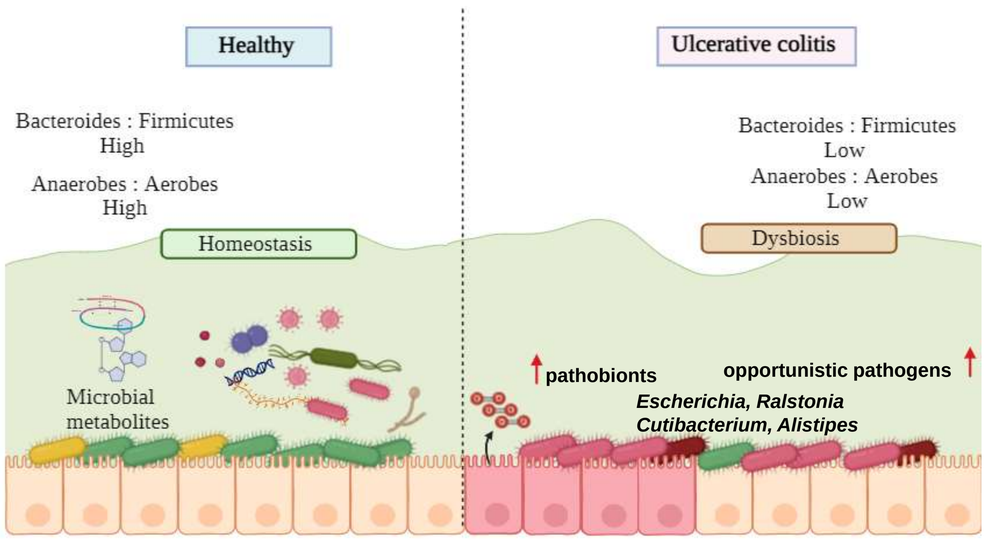


Fig : Comparative gut microbiome status in healthy and ulcerative colitis condition

6. ACKNOWLEDGEMENT

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