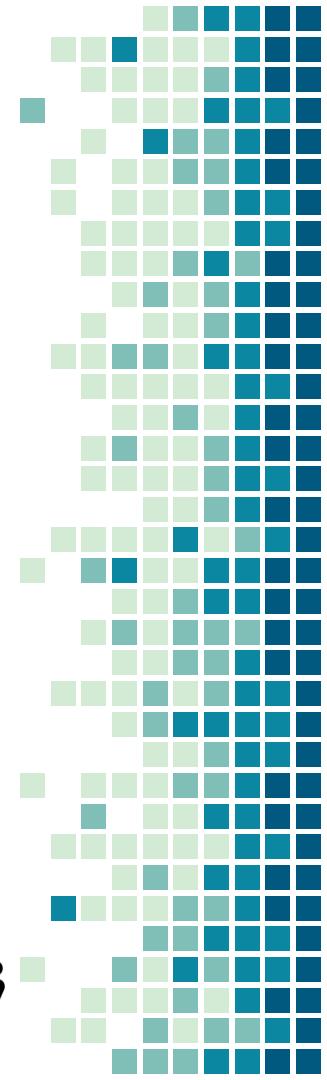


Profils métagénomiques et métabolomiques dans les MICI : comprendre les changements microbiens et métaboliques à partir d'une vaste cohorte profondément phénotypée

Marius Bredon

marius.bredon@sorbonne-universite.fr

CRSA, APHP, Sorbonne Université



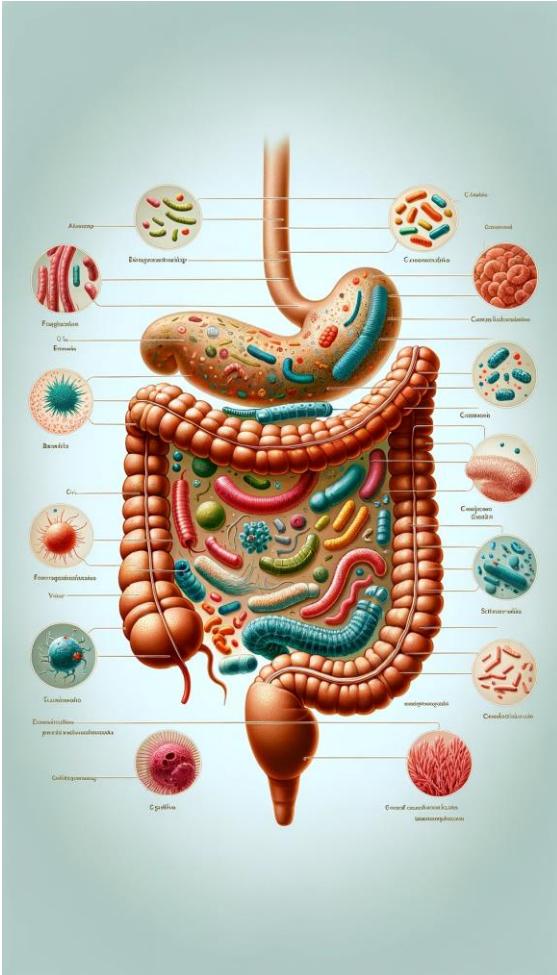
IBD

Inflammatory Bowel Disease

Principal types:

- Crohn's Disease (CD):
May affect any segment of the gastrointestinal tract

- Ulcerative Colitis (UC):
Colon and rectum



IBD

Inflammatory Bowel Disease

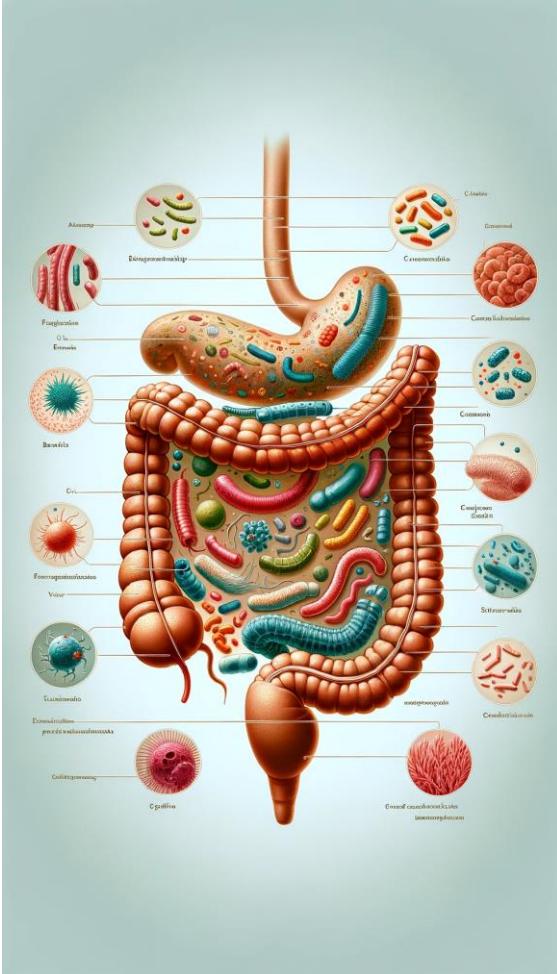
Principal types:

- Crohn's Disease (CD):
May affect any segment of the gastrointestinal tract
- Ulcerative Colitis (UC):
Colon and rectum



Alterations in gut microbiota composition and functionality

- ↳ microbial diversity
- ↳ tryptophan & butyrate-producing bacteria
 - ↗ pathobionts



IBD

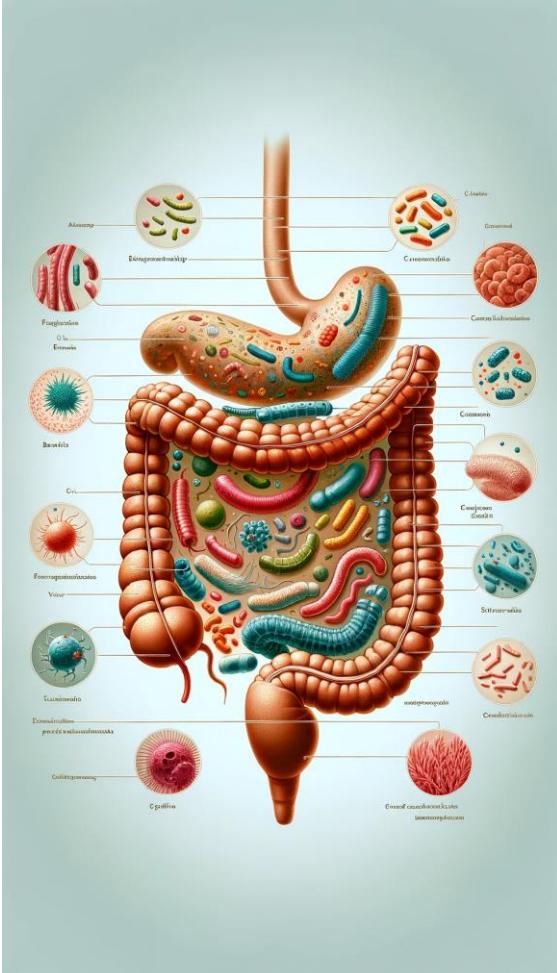
Inflammatory Bowel Disease

Principal types:

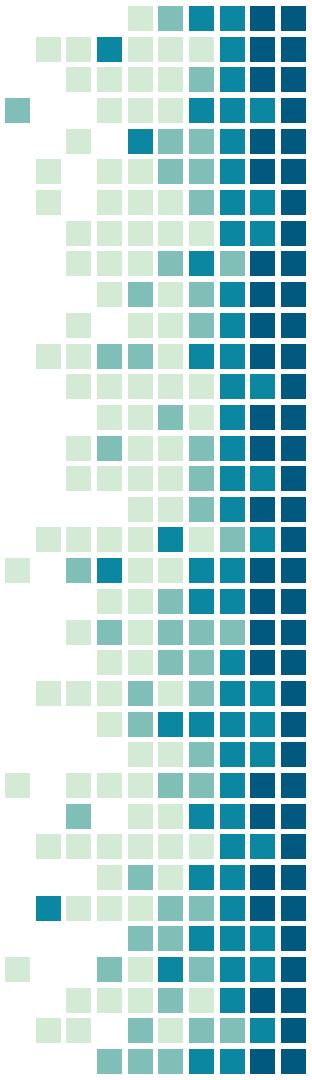
- Crohn's Disease (CD):
May affect any segment of the gastrointestinal tract
- Ulcerative Colitis (UC):
Colon and rectum



Large studies analyzing both gut microbiota and metabolomics data are scarce



Metagenomic and metabolomic profiles in IBD: understanding microbial and metabolic shifts from a large deeply phenotyped cohort

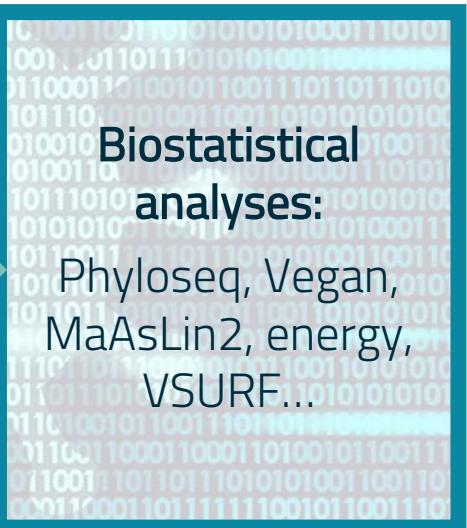
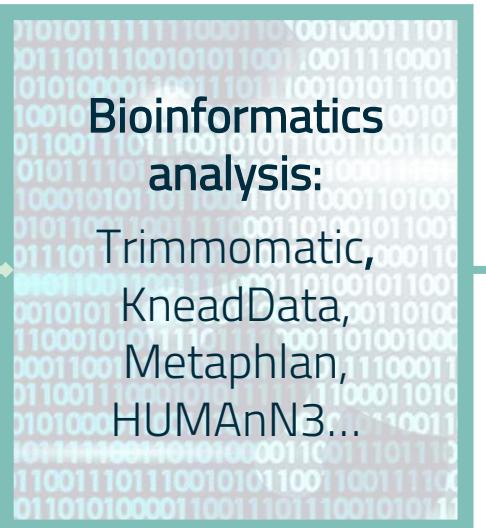
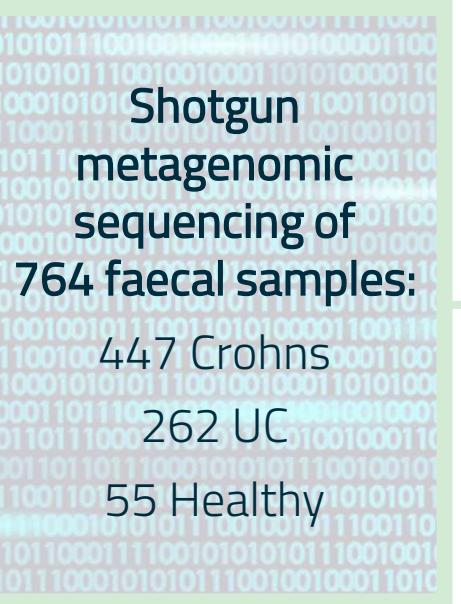
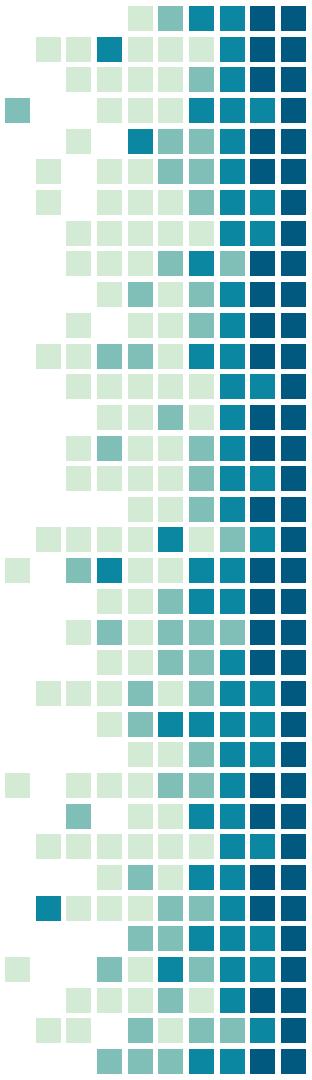


Shotgun metagenomic sequencing of 764 faecal samples:
447 Crohns
262 UC
55 Healthy

Bioinformatics analysis:
Trimmomatic,
KneadData,
Metaphlan,
HUMAnN3...

Biostatistical analyses:
Phyloseq, Vegan,
MaAsLin2, energy,
VSURF...

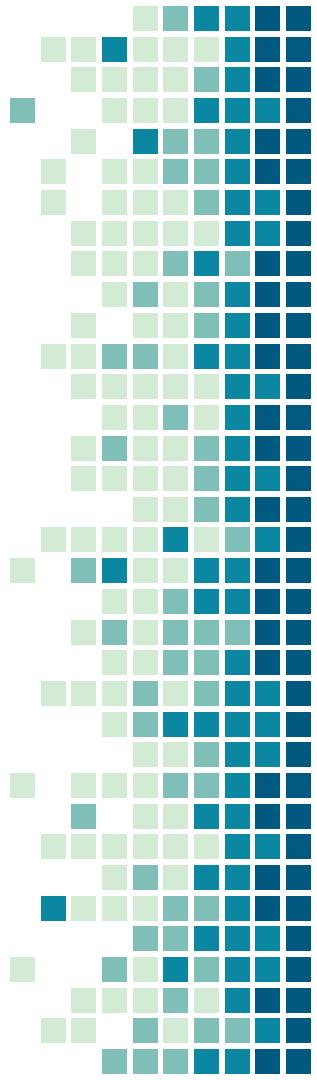
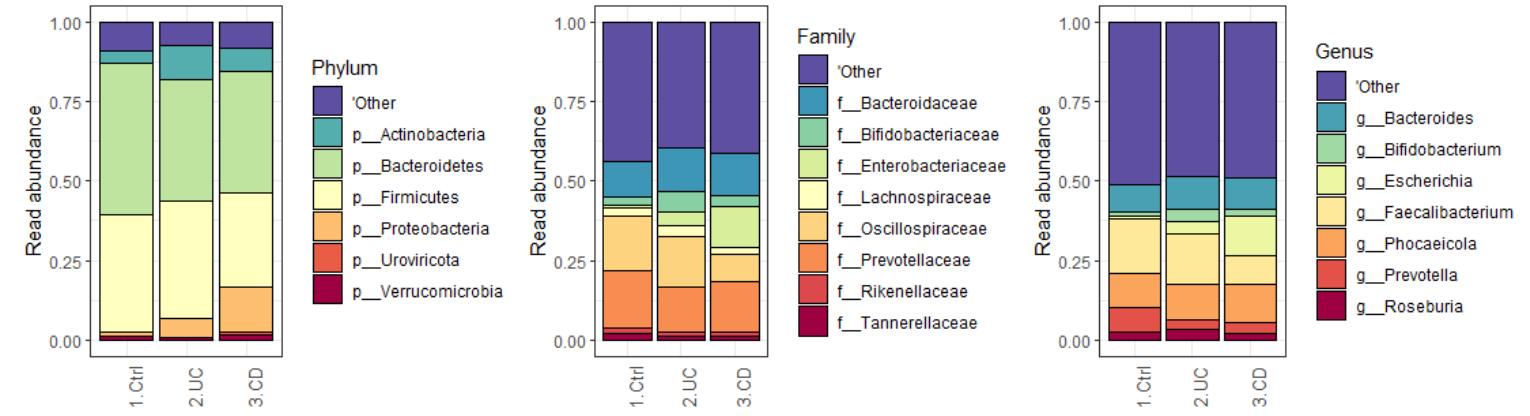
Metagenomic and metabolomic profiles in IBD: understanding microbial and metabolic shifts from a large deeply phenotyped cohort



+ Metabolomics data encompassing 294 different molecules

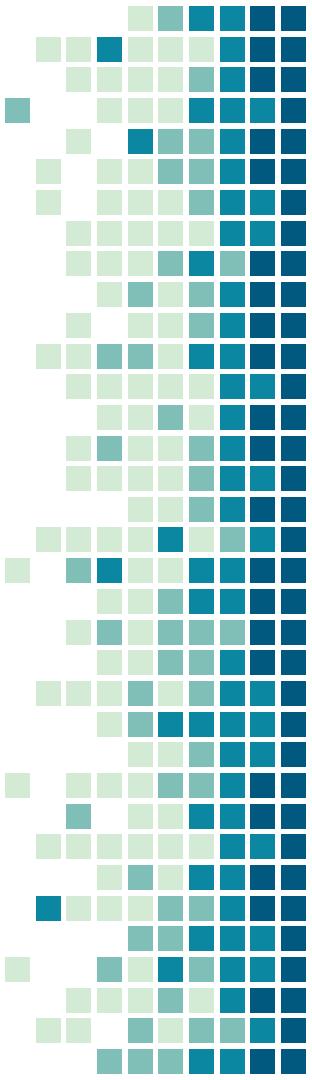
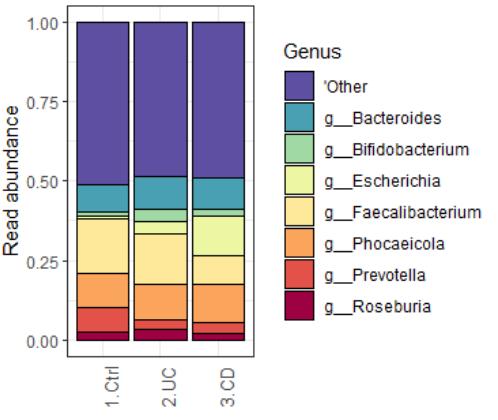
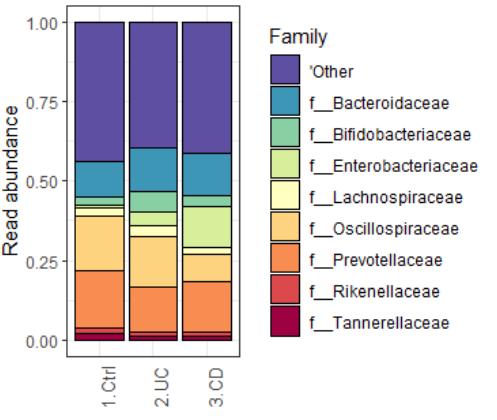
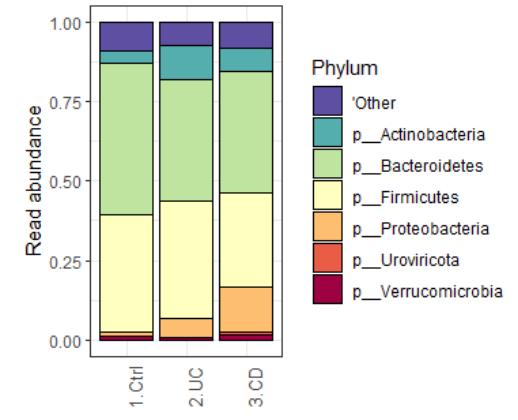
Generalities

Taxonomic profiles



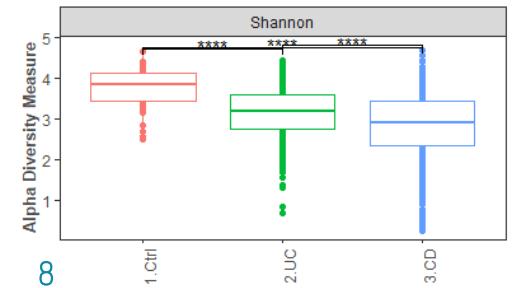
Generalities

Taxonomic profiles

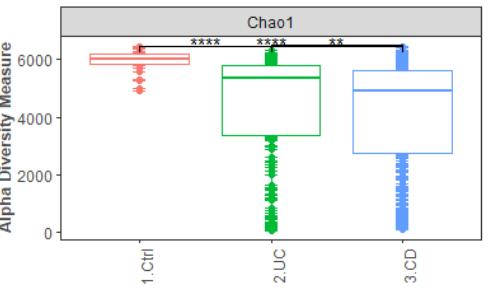


Alpha diversity

Kruskal-Wallis, $\chi^2(2) = 77.9, p = <0.0001, n = 733$

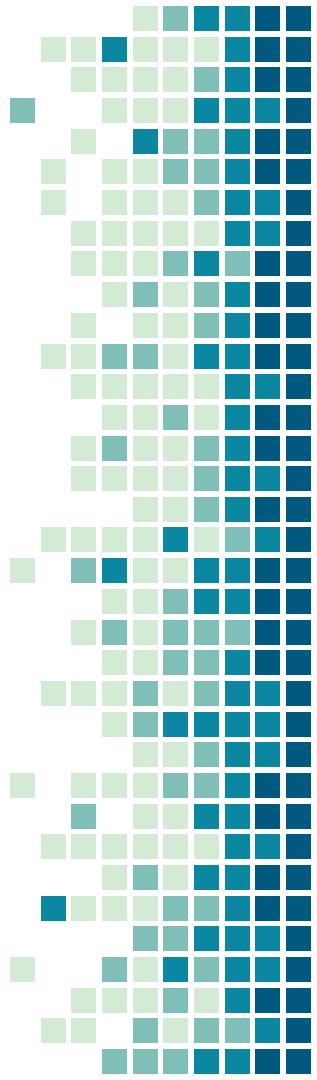
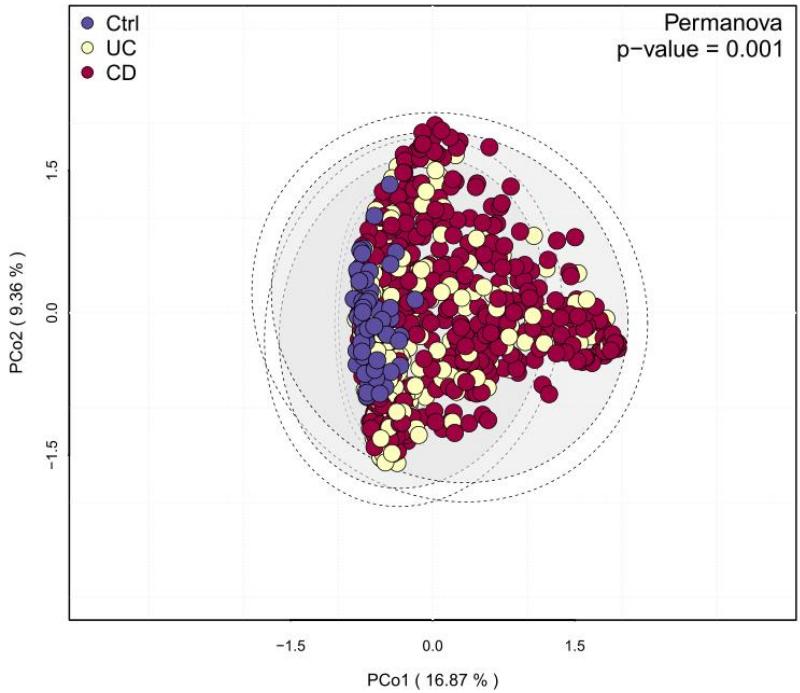


Kruskal-Wallis, $\chi^2(2) = 92.49, p = <0.0001, n = 733$



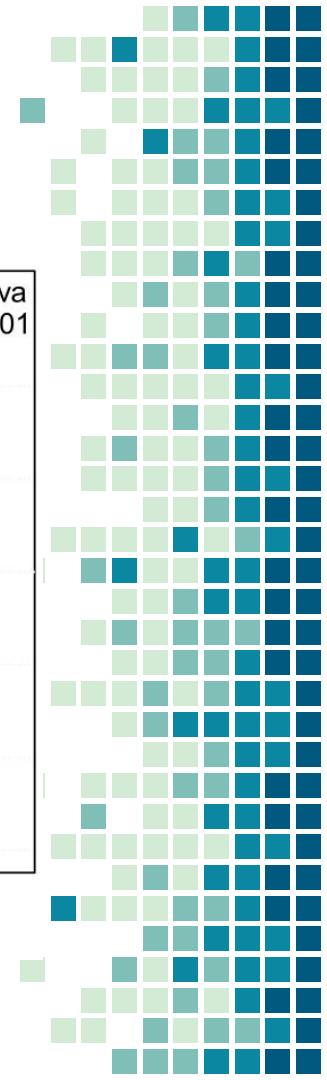
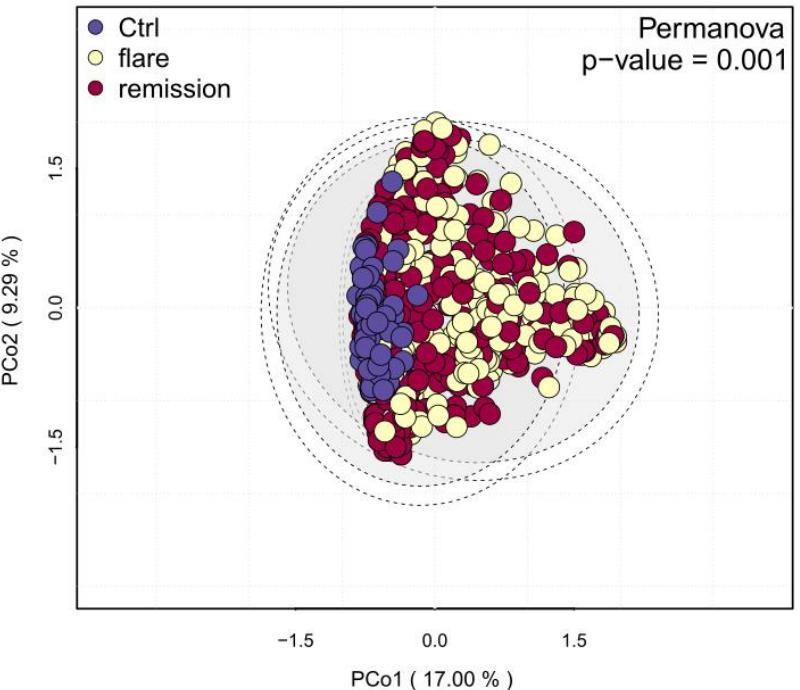
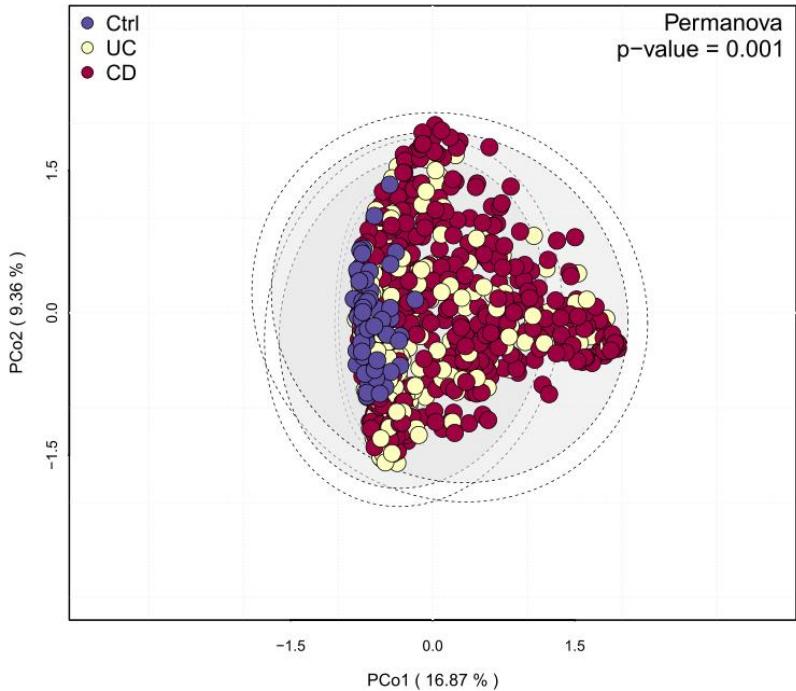
Beta Diversity

Taxonomy



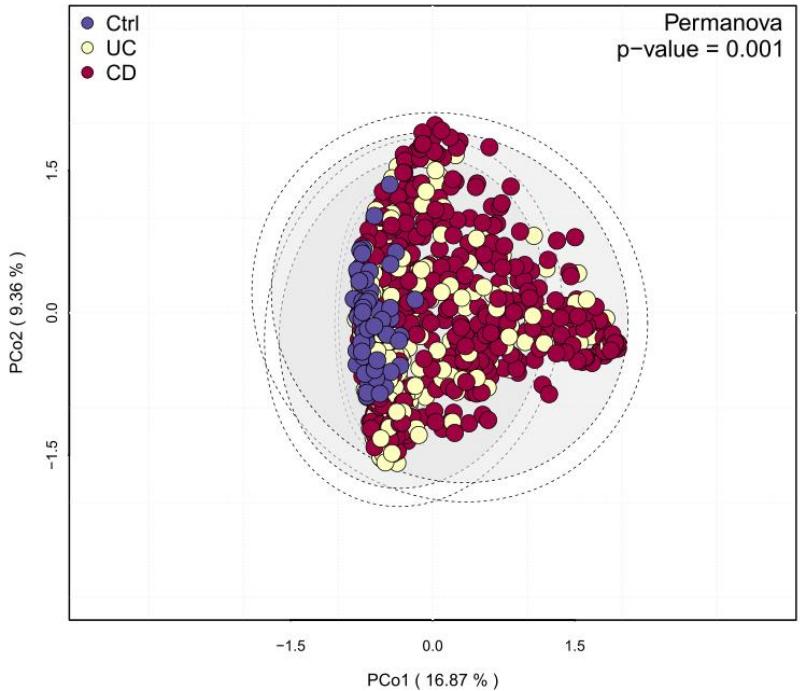
Beta Diversity

Taxonomy

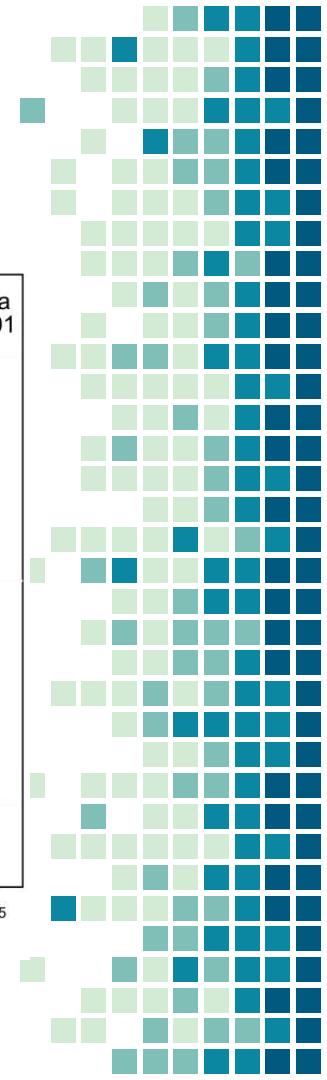
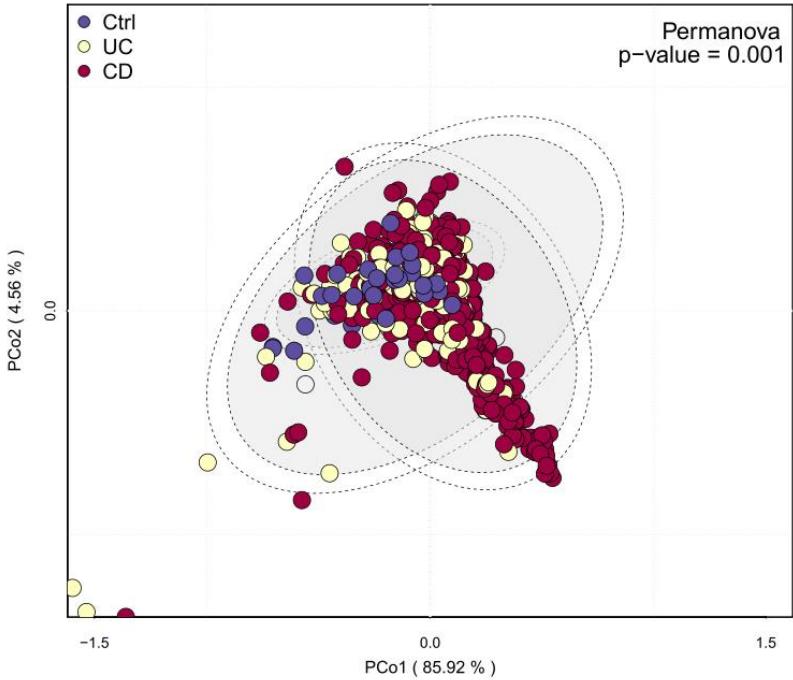


Beta Diversity

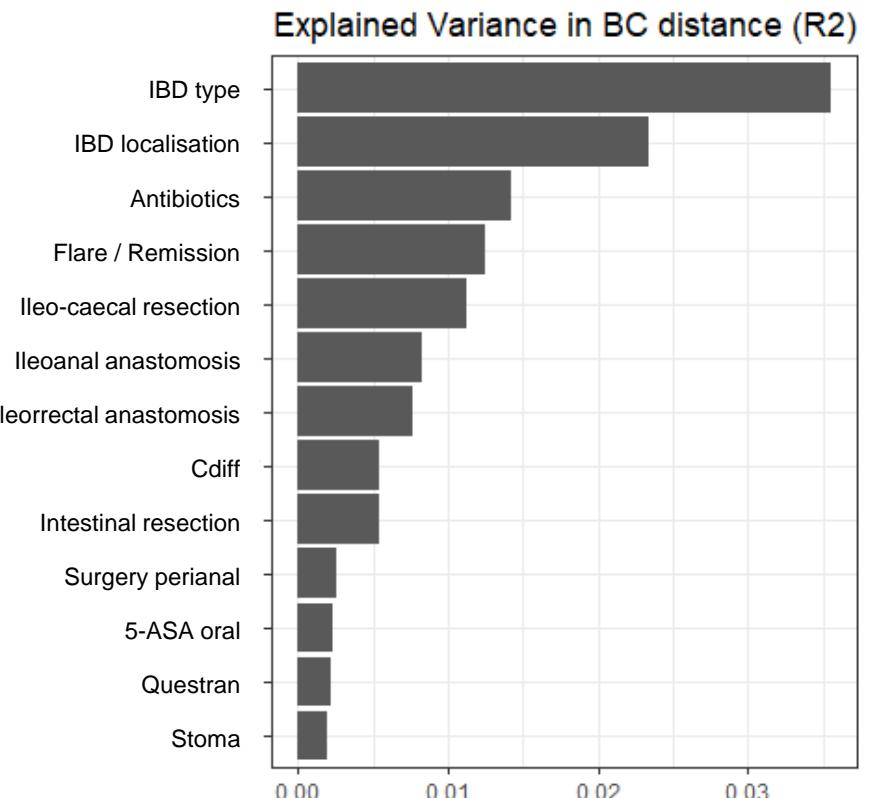
Taxonomy



Pathways

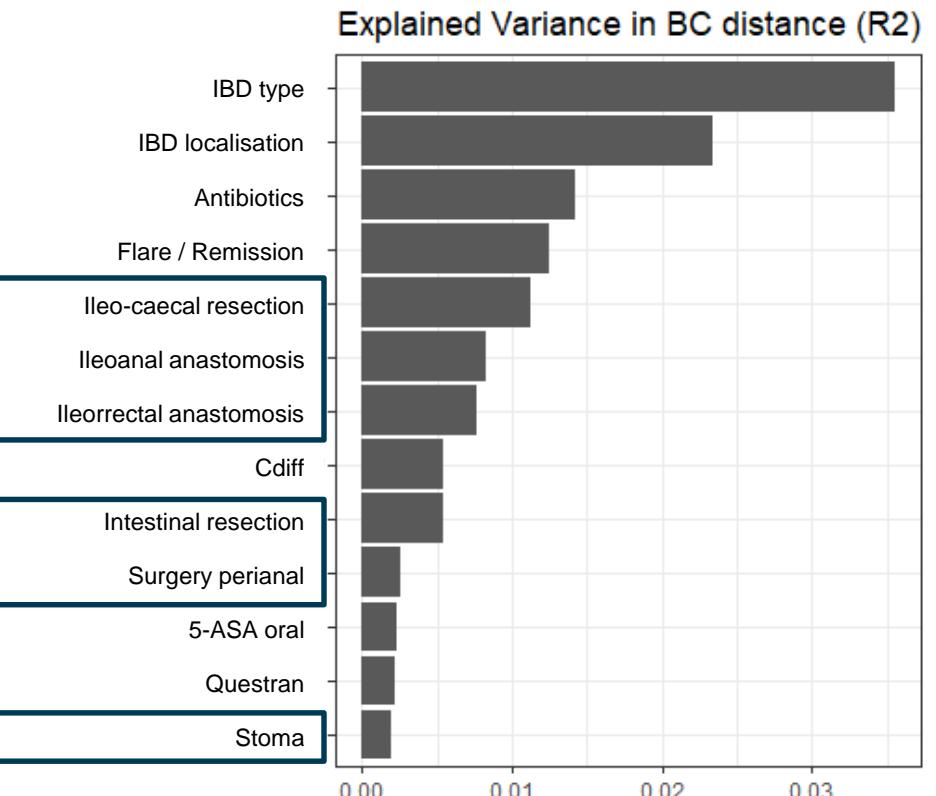


Explained Variance



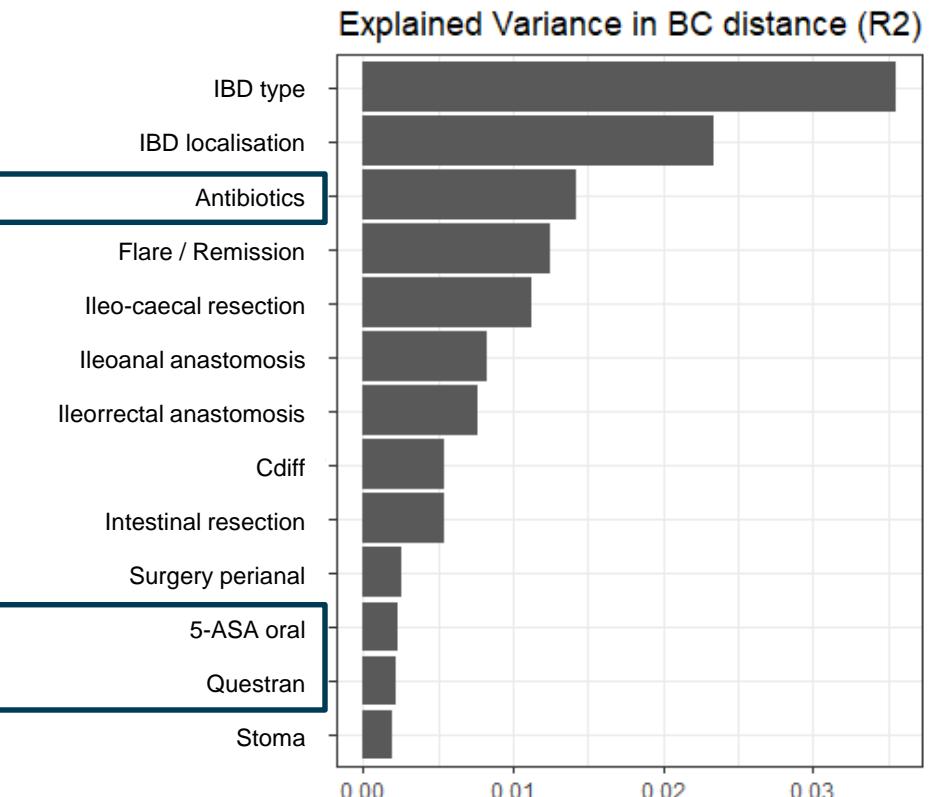
Explained Variance

Surgery

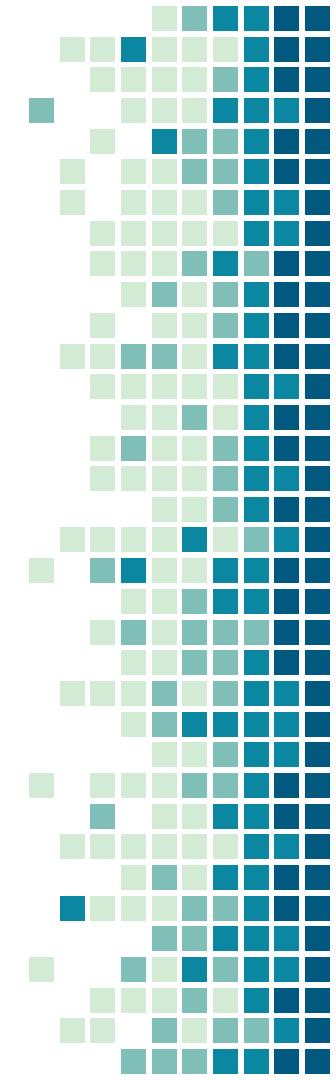
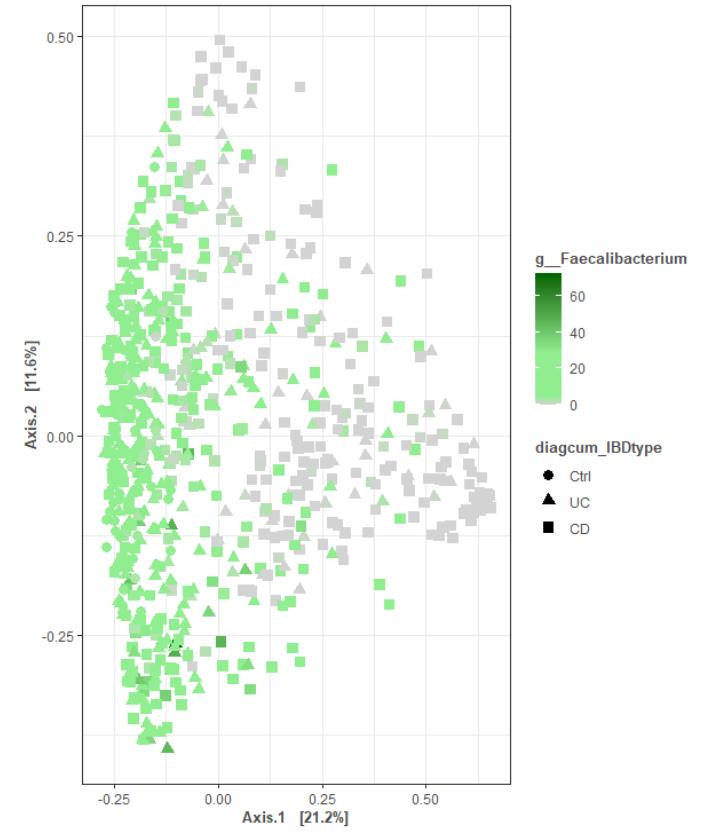


Explained Variance

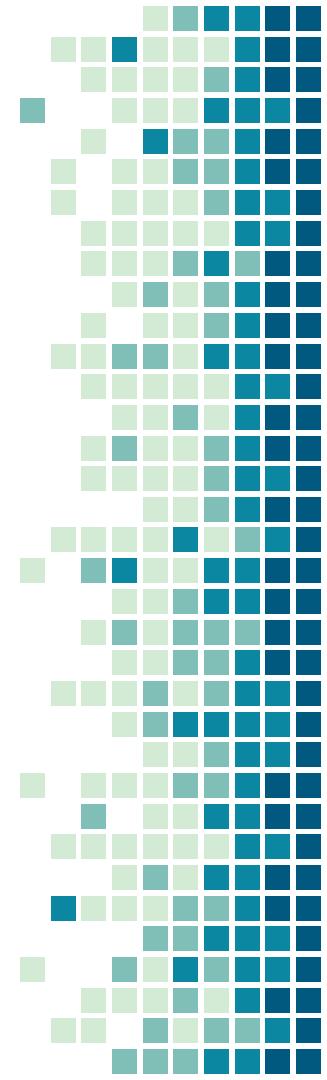
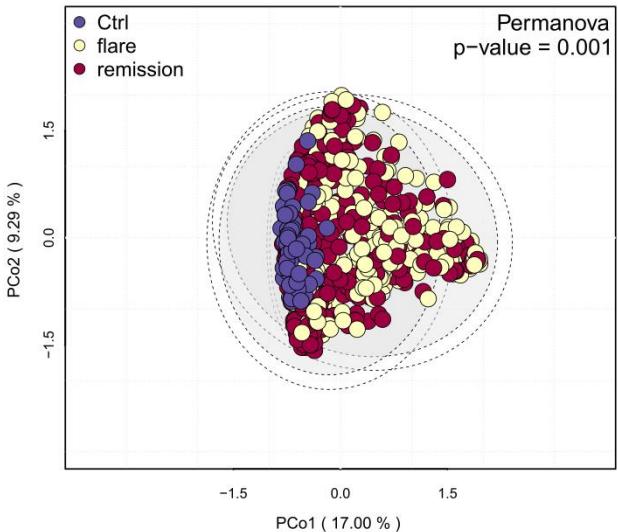
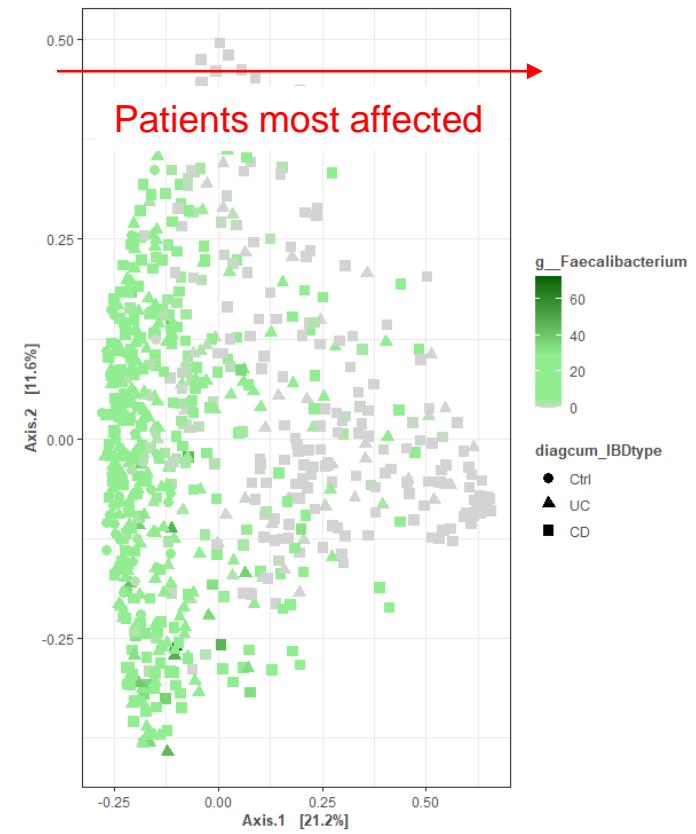
Treatment



Faecalibacterium prausnitzii



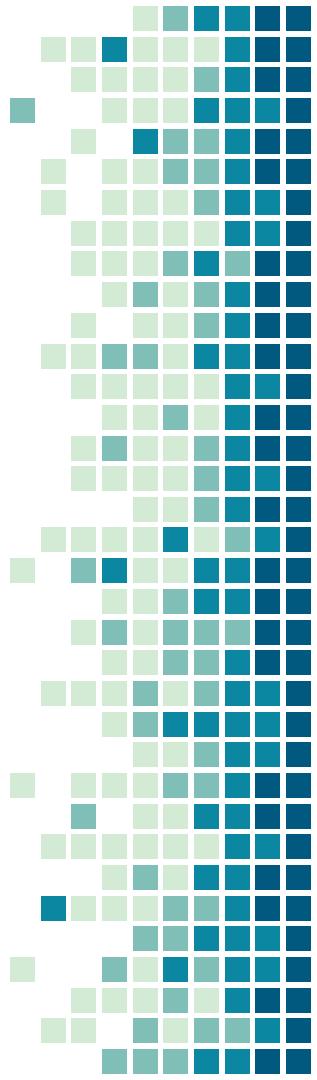
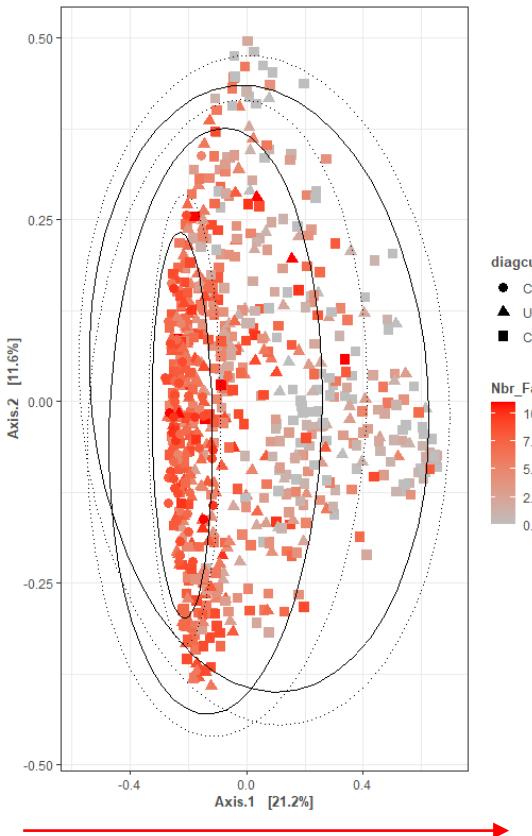
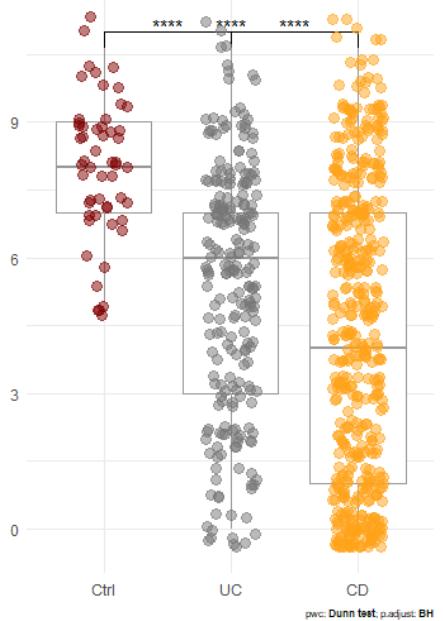
Faecalibacterium prausnitzii



Faecalibacterium strains

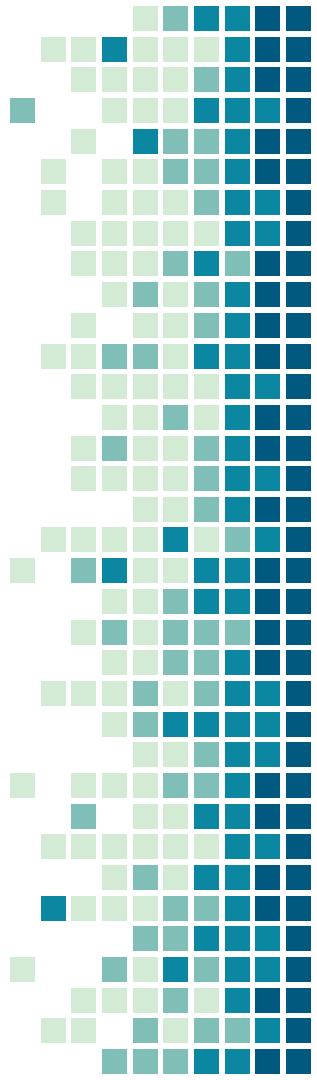
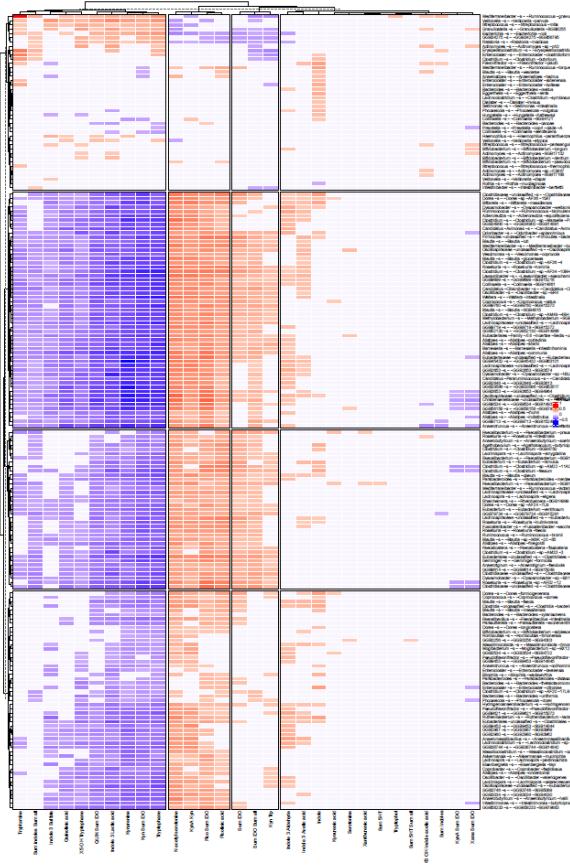
#*Faecalibacterium*

Kruskal-Wallis, $\chi^2(2) = 73.72$, $p = <0.0001$, $n = 741$



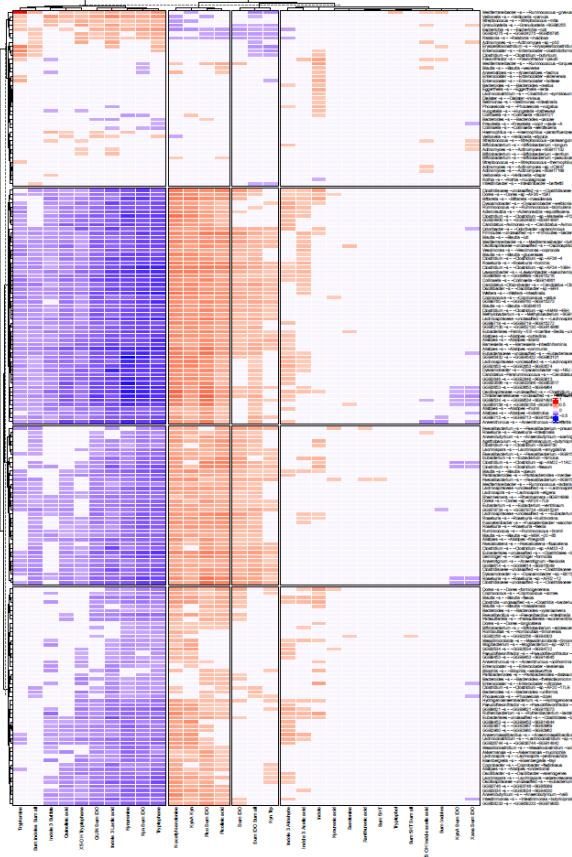
Metabolite correlations

Feces $FDR = 0,001$

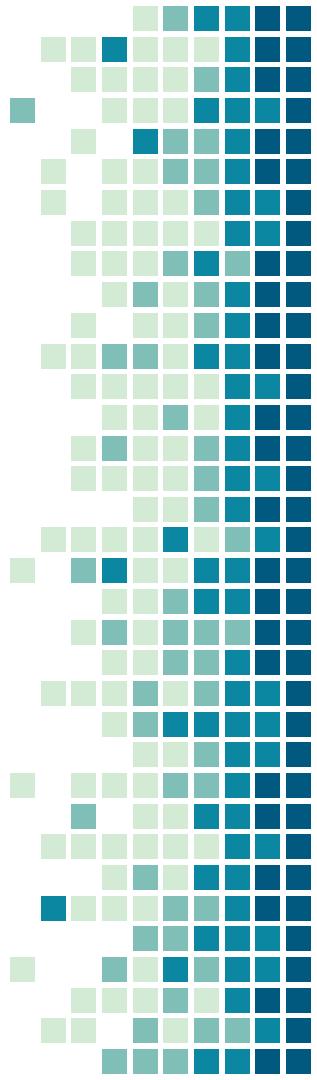
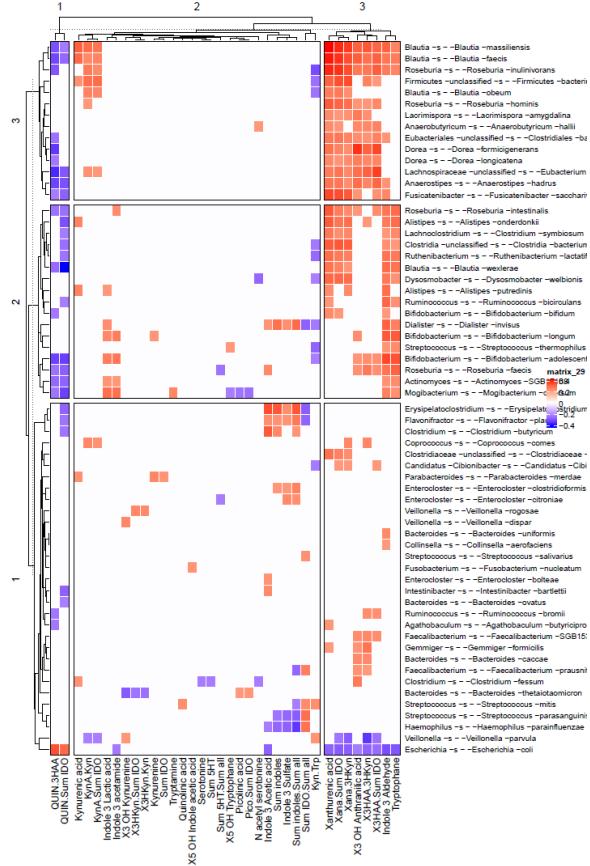


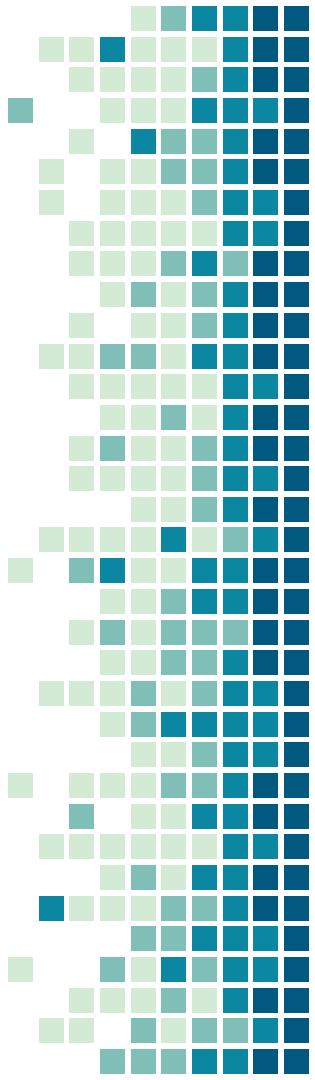
Metabolite correlations

Feces $FDR = 0,001$

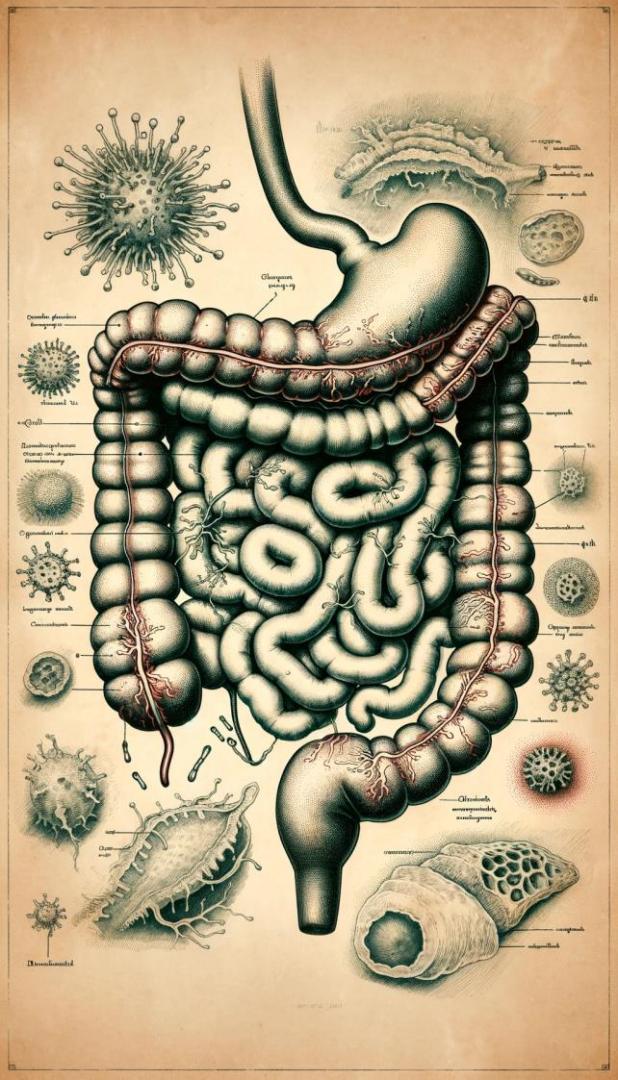


Serum $FDR = 0,25$





Conclusion:



- The most important drivers of microbiota composition were the disease location, treatment, disease activity (flare vs remission) and history of surgery
- The decrease in microbiota diversity was stronger in CD than in UC
- In parallel to a decreased amount of *Faecalibacterium* in IBD, there is also a decrease in the diversity of *Faecalibacterium* strains
- There are many correlations between metabolites and microbial abundance

Thank you for your attention!

Acknowledgements:

Harry Sokol

Nathalie Rolhion

Laura Creusot

Antoine Lefevre

Iria Alonso

Loïc Brot

Camille Danne

Anne Bourrier

Laurene Parrot

Mélanie Draullette

Nicolas Benech

Isabelle Nion-Larmurier

Paul Mclellan

Cecilia Landman

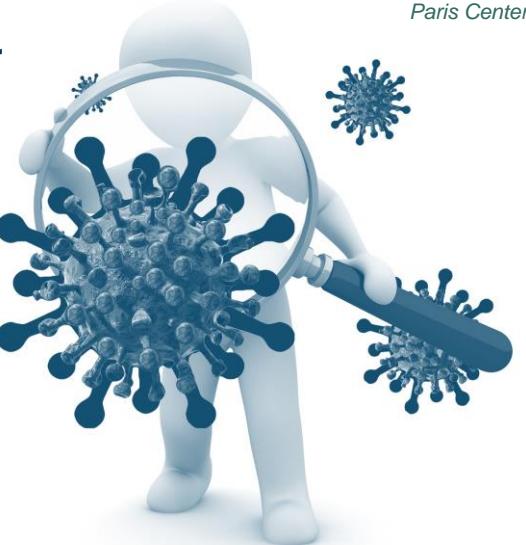
Laurent Beaugerie

Philippe Seksik

Patrick Emond

Julien Kirchgesner

And the **Sokol's lab!**



FHU PaCeMM

Fédération Hospitalo-Universitaire
Paris Center for Microbiome Medicine

