Gut Microbiome Dynamics and Immune Responses in People With HIV Receiving N-803

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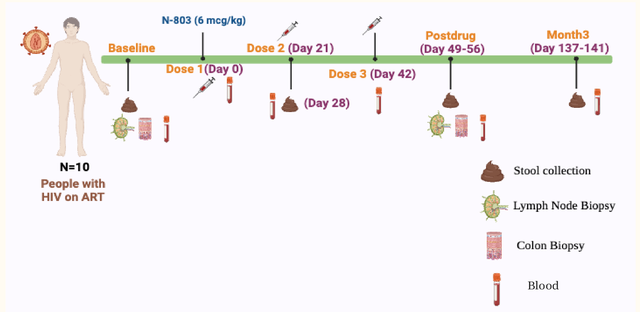
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BACKGROUND

- The gut microbiota is crucial in maintaining immune responses.
- Originally developed for cancer therapy, N-803, an IL-15 superagonist, is now being researched for its potential to boost immune responses in people with HIV (PWH).
- Current understanding of how gut microbiota interacts with immune-modulating agents like N-803 in PWH is limited.
- This pilot study investigated the relationship between gut microbiota and immune responses in PWH.
- We defined Virus responders and Virus Non-responders based on decrease and increase in viral RNA levels in lymph nodes from Baseline to Postdrug, respectively.

METHODS



Shotgun metagenomics on fecal samples	• Fastqc • Trimmomatic • Bowtie2 & Samtools
Taxonomic and Functional profiling	• Kraken2 • Bracken • Humann3
Biopsy of lymph node(LN) and colon	• In situ hybridization for vRNA levels • Immunohistochemistry for NKG2A counts
Immune markers from LN	• Helios Mass Cytometer • CyTOF • FlowJo

RESULTS

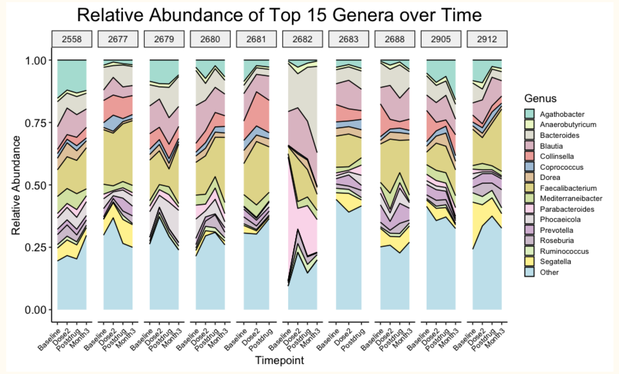


Figure 1 : Relative abundance of bacterial genera across timepoints

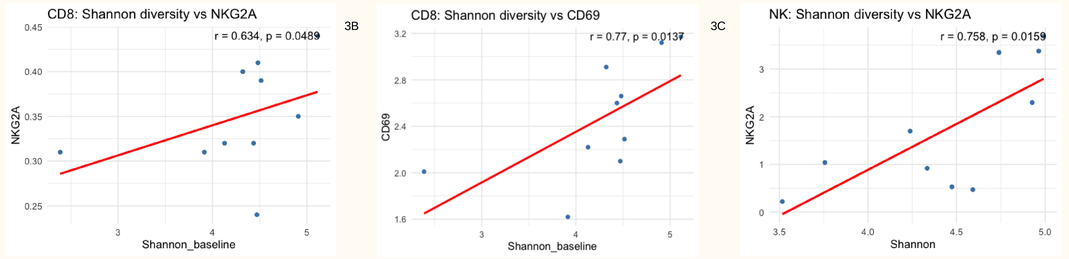


Figure 3 : Spearman correlation matrix between microbial diversity and immune markers after N-803. *3 A-B* :The baseline alpha diversity of microbiota is significantly correlated with elevated NK cell activation biomarkers post N-803 3C: A higher alpha diversity significantly correlates with elevated levels of NKG2A after N-803

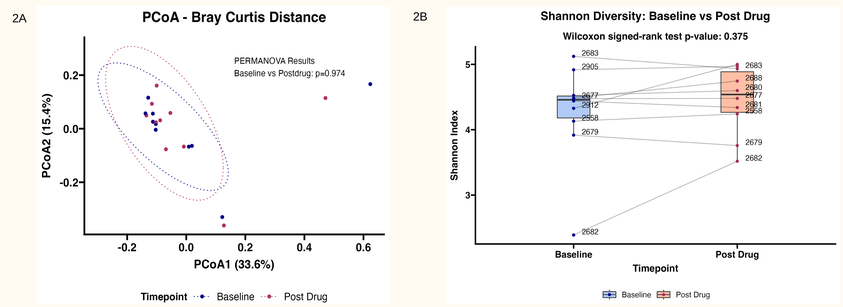


Figure 2: Gut microbiome remains stable during the treatment A) Beta diversity before and after N-803 b) Alpha diversity of participants before and after N-803

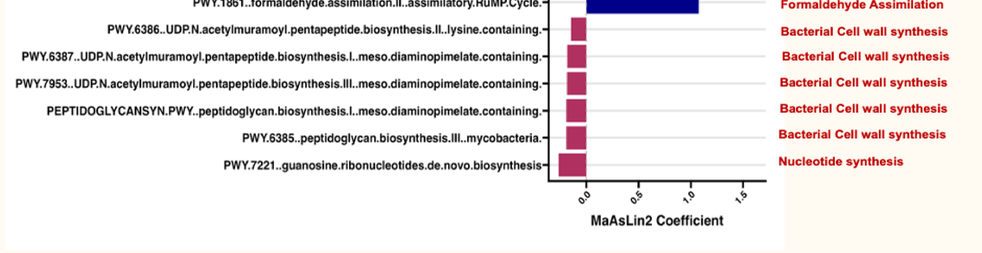


Figure 4: Microbial pathways that were differentially abundant between Virus responders and Virus non responders

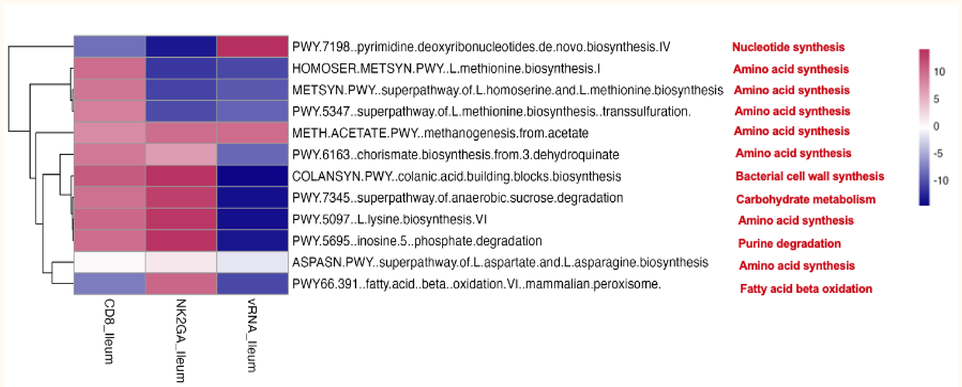


Figure 5: Heatmap of metabolic pathways of microbiota-immune marker associations in the ileum. Microbial pathways that correlated positively with CD8 and NKG2A counts in Ileum often showed inverse correlations with vRNA levels in ileum, particularly in pathways related to lysine, colanic acid, and chorismate biosynthesis.

CONCLUSIONS

- This pilot study shows that gut microbiota composition remains stable during N-803 treatment in people with HIV.
- The immunostimulatory effects of N-803 are potentially influenced by the gut microbiome of PWH at the baseline.
- Higher gut microbiome diversity at baseline tend to exhibit a more favorable NK cell activation profile following N-803 treatment, which could translate into better therapeutic outcomes.
- The findings from this study suggest specific microbial metabolic functions may influence activity of immune biomarkers after N-803.

Acknowledgements

• Funding from NIH grant 5UM1AI126611

• We would like to thank all the participants enrolled in this study.