



Beyond HOMINGS

**Forsyth Oral Microbiome Core**

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- *New 16S rRNA analyses*
- *Big data genomic analysis*
- *Collaborations*

# Final Data Analysis Report

Project Number **FOMC-17924/300101 FRODO**

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# I. Overall Summary

A total of 408 clinical oral samples were collected for two types of next generation sequencing (NGS) – 1) 16S rRNA V1V3 gene amplicon sequencing and 2) Shot-gun meta-transcriptomic RNA sequencing. The 16S rRNA sequencing can help answer the question regarding what bacterial species are in the samples and comparing the species profiles of different sample group can help answer whether a product or a treatment impact the microbial composition. The meta-transcriptomic sequencing determines the RNA levels for the genes expressed in the samples and helps to answer the functional related question and compare different levels of microbial activities in different sample groups.

The 16S rRNA V1V3 NGS sequences were assigned to species level taxonomy using the FOMC reference set (<https://microbiome.forsyth.org/ftp/refseq/>) and provides the best specie-level taxonomy assignment. Based on the species-level sequence abundance results, overall, the microbiomes were modified more with treatment Product B. In general, with the exception of subgingival microbiomes, there appeared to be a microbiological benefit with this treatment.

The metagenomic shotgun sequences were processed with CosmosID-Hub's Host-Agnostic Functional Profiling Pipeline for functional/activity inferencing. Alpha and beta diversities of functional profiles (Gene Ontology, Enzyme Commission and MetaCyc Pathways) were affected by Product A for samples from individual sites - saliva and tongue samples. No significant differences were detected for combined sites, supra- and sub-gingiva sites. For Product B, functional diversities were affected when samples of 4 sites were combined, as well as tongue and supragingival samples. No significant effects were observed for saliva and subgingival samples. When Product A and B were directly compared for effect of treatment, significant differences between these two products were observed for combined and subgingival samples, but not for individual saliva, tongue and subgingival samples. This is also true for bacterial composition analysis. Finally, bacterial compositions and functional profiles for the baseline group differ between the saliva/tongue and supragingival/subgingival grouping. There were only two significant differences in functional diversity between Product A and B at baseline.



## II. Data Download Links

### 1. Raw Sequence Data

#### 16S rRNA V1V3 amplicon sequences

Raw sequence reads can be downloaded from a link in the FOMC 16S report:

[https://microbiome.forsyth.org/ftp/fomc/FOMC\\_project/haleon/ef8268d4-4bde-4eb7-94c8-09aabee1e8bf](https://microbiome.forsyth.org/ftp/fomc/FOMC_project/haleon/ef8268d4-4bde-4eb7-94c8-09aabee1e8bf)

#### Meta-transcriptome shot-gun sequences

Meta-transcriptome shotgun sequencing reads can be downloaded from this link:

[https://microbiome.forsyth.org/ftp/fomc/FOMC\\_project/haleon/b0eb797b-ac3d-43d5-9958-7d86868ad149](https://microbiome.forsyth.org/ftp/fomc/FOMC_project/haleon/b0eb797b-ac3d-43d5-9958-7d86868ad149)

### 2. Analysis Results

#### 16S rRNA V1V3 Bioinformatics Analyses (FOMC Pipeline)

[https://microbiome.forsyth.org/ftp/fomc/FOMC\\_project/haleon/ef8268d4-4bde-4eb7-94c8-09aabee1e8bf](https://microbiome.forsyth.org/ftp/fomc/FOMC_project/haleon/ef8268d4-4bde-4eb7-94c8-09aabee1e8bf)

#### Meta-transcriptomic Analyses (CosmosID Pipeline)

[https://microbiome.forsyth.org/ftp/fomc/FOMC\\_project/haleon/48b41065-dd02-49db-9ebe-da0e7d463cdf](https://microbiome.forsyth.org/ftp/fomc/FOMC_project/haleon/48b41065-dd02-49db-9ebe-da0e7d463cdf)

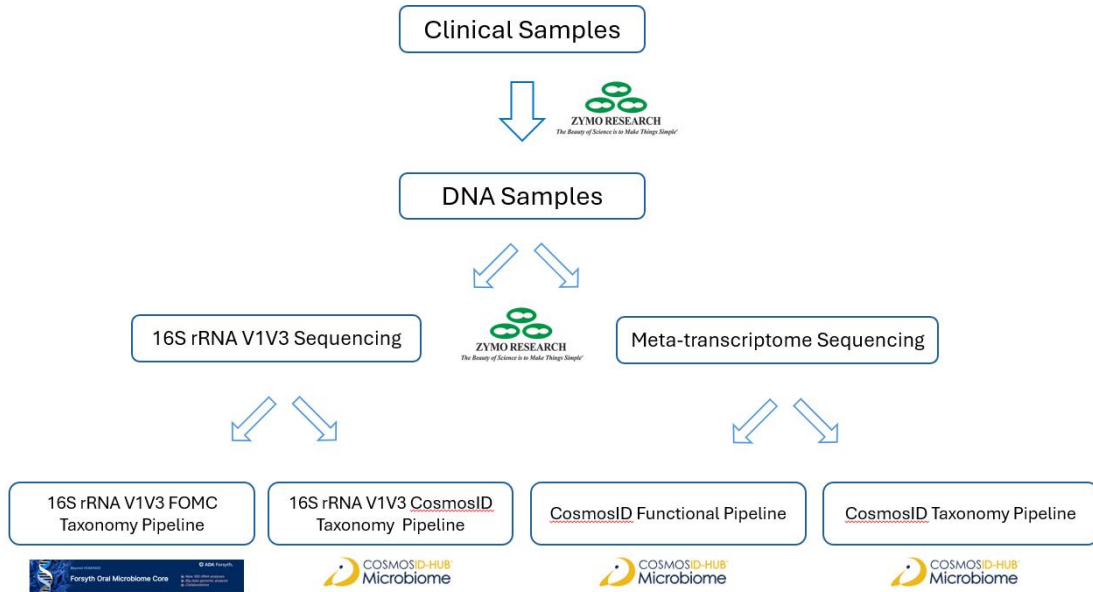
### 3. Final Report – this document

This report can also be downloaded (and shared) online from this link:

[https://microbiome.forsyth.org/ftp/fomc/FOMC\\_project/haleon/d6e5a990-c912-4a4b-8573-b877c3072f37](https://microbiome.forsyth.org/ftp/fomc/FOMC_project/haleon/d6e5a990-c912-4a4b-8573-b877c3072f37)

# III. Project Workflow

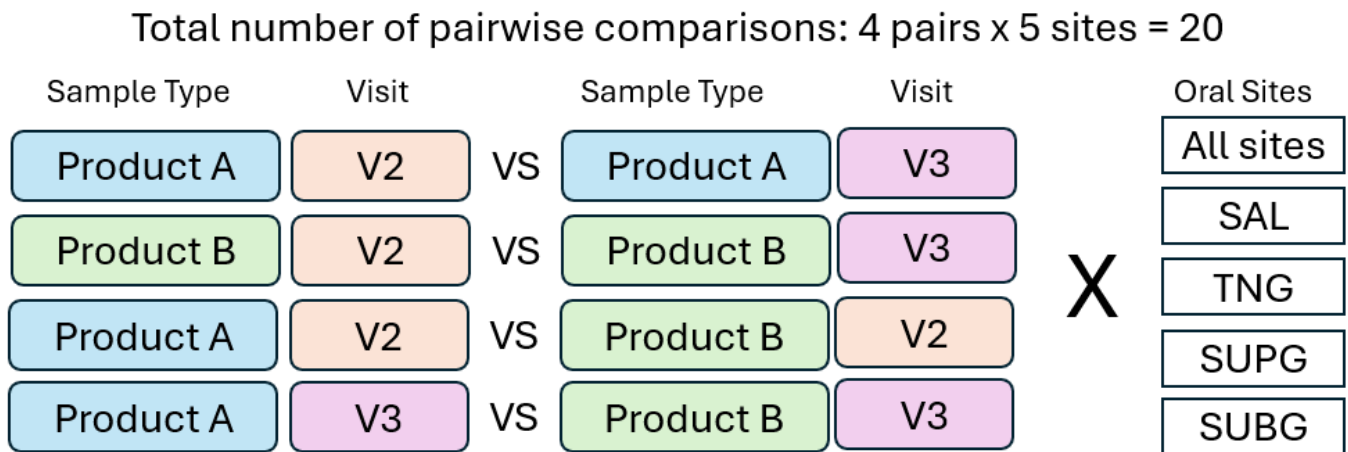
Figure 1 shows the overall project workflow that was performed by FOMC starting from the clinical samples.



**Figure 1. Overall experimental and analytic workflow**

# IV. Analyses Overview

Figure 2 depicts the number of combinations of sample types, visits and oral sites of all samples. A total of 20 comparisons were performed and the comparison IDs and labeling are listed in Table 1. The VII. Results section focuses on the 4 major questions described in the section V. Objectives and Endpoints. The figures and tables for all the comparison are shown in the Appendix section.



**Figure 2. Comparative analyses performed in this study.**

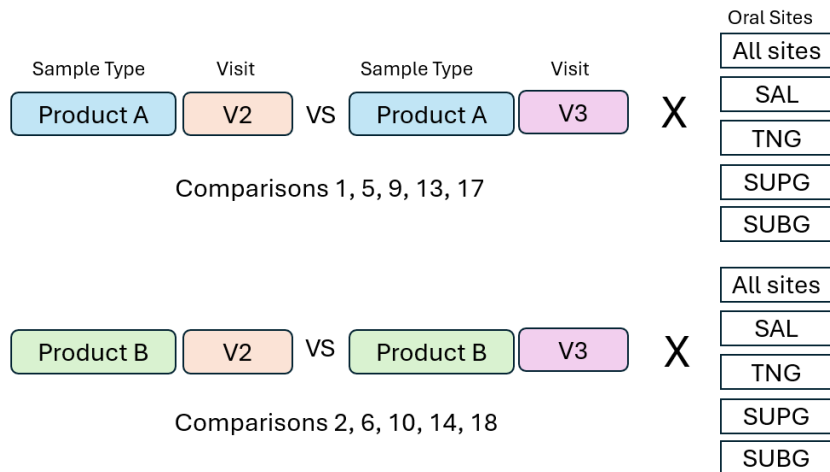
**Table 1. List of all comparative analyses**

Comparison List		
1. A V2 vs A V3 ALL	9. A V2 TNG vs A V3 TNG	17. A V2 SUBG vs A V3 SUBG
2. B V2 vs B V3 ALL	10. B V2 TNG vs B V3 TNG	18. B V2 SUBG vs B V3 SUBG
3. A V2 vs B V2 ALL	11. A V2 TNG vs B V2 TNG	19. A V2 SUBG vs B V2 SUBG
4. A V3 vs B V3 ALL	12. A V3 TNG vs B V3 TNG	20. A V3 SUBG vs B V3 SUBG
5. A V2 SAL vs A V3 SAL	13. A V2 SUPG vs A V3 SUPG	<i>A: Product A</i> All: All sites <i>B: Product B</i> SAL: Saliva <i>V2: Baseline</i> TNG: Tongue <i>V3: 6 Weeks</i> SUPG: Supragingival SUB: Subgingival
6. B V2 SAL vs B V3 SAL	14. B V2 SUPG vs B V3 SUPG	
7. A V2 SAL vs B V2 SAL	15. A V2 SUPG vs B V2 SUPG	
8. A V3 SAL vs B V3 SAL	16. A V3 SUPG vs B V3 SUPG	

# V. Objectives and Endpoints

## 1. Describe and compare the bacterial **composition** by different areas of the mouth at week 6 compared to baseline by treatment.

Results related to this objective are depicted in the illustration below and described in section 7. [Week 6 vs Baseline Comparisons – Bacterial Composition](#).

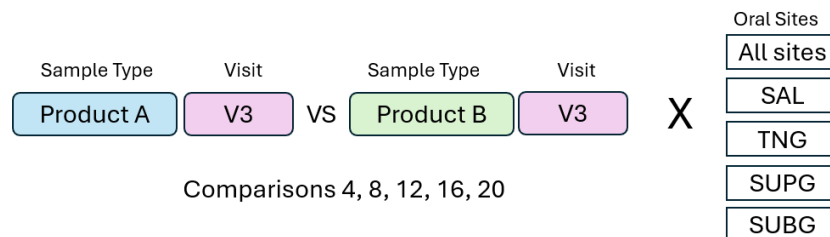


## 2. Describe and compare the bacterial **activity** by different areas of the mouth at week 6 compared to baseline by treatment.

Results related to this objective are depicted in the illustration [above](#) and described in section 8. [Week 6 vs Baseline Comparisons – Activities](#).

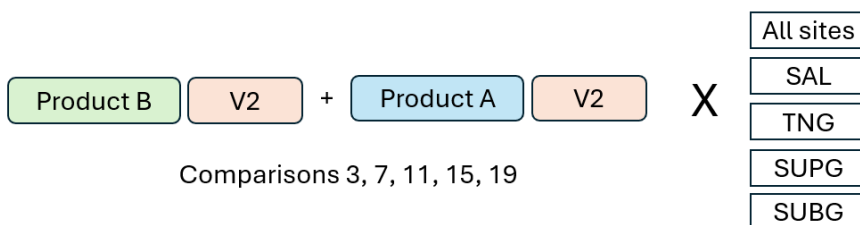
## 3. Compare the bacterial **composition** and **activity** by different areas of the mouth at week 6 between treatment A.

Results related to this objective are depicted in the illustration below and are described in sections 9. [Products A vs B at Week 6 vs– Bacterial Composition](#) and 10. [Products A vs B at Week 6 vs– Activities](#).



## 4. Describe the bacterial **composition** of the different areas of the mouth at baseline.

Results related to this objective are depicted in the illustration below and are described in section 11. [Bacterial Compositions of Oral Sites at Baseline](#).



# VI. Methods

## 4. FOMC 16S rRNA V1V3 Amplicon Analysis Pipeline

### Sequence Data Processing

Raw 16S V1V3 amplicon sequences obtained from Zymo Research were quality-filtered, denoised, pair-end merged, and chimera removed with the DADA2 tool [1].

### Taxonomy Assignment

Amplicon sequence variants (ASVs) generated by DADA2 were subjected to species level taxonomy assignment based on the approach developed by Al-Hebshi et. al. (2015) [2] against the FOMC Reference Sequence Set (<https://microbiome.forsyth.org/ftp/refseq>) that consists of 1,015 full-length 16S rRNA sequences from HOMD V15.22, 356 from MOMD V5.1, and 22,126 from NCBI, a total of 23,497 sequences. Altogether these sequences represent a total of 17,035 oral and non-oral microbial species.

### Taxonomy bar plots

Graphically displays differences between groups—a good visual aid. Only shown for the first comparison for illustrative purposes. If desired, taxonomy plots can be provided for all comparisons. Dynamic taxonomy bar plot is available in the original analysis report ([https://microbiome.forsyth.org/ftp/fomc/FOMC17924\\_haleon\\_16S\\_full/qiime/data\\_mc100/qiime2/barplot/index.html](https://microbiome.forsyth.org/ftp/fomc/FOMC17924_haleon_16S_full/qiime/data_mc100/qiime2/barplot/index.html)) using QIIME2 package [3].

### Alpha diversity

Alpha diversity ( $\alpha$ -diversity) is the mean species diversity in sites or habitats. Data are presented in 3 measurements: 1) number of species (observed), 2) Shannon index, and 3) Simpson index.  $p$  values were calculated for these metrics. Alpha diversity was calculated with QIIME2 package [3] and R [4] “phyloseq” package [5]. Alpha diversity significance tests were evaluated with QIIME2’ “alpha-group-significance” function [3].

### Beta diversity

Compares the similarity (or dissimilarity) of entire microbial profiles between different groups of samples. Presently in dot graphs and  $p$ -values are calculated. Best diversity significance tests were evaluated with QIIME2’ “beta-group-significance” function [3].

### Differential abundance

ANCOMB-BC2 was used to test the significance of differential abundance between two test groups [6]. ANCOM-BC2 (Analysis of Compositions of Microbiomes with Bias Correction) provides the following: (a) statistically valid test with appropriate  $p$ -values, (b) provides confidence intervals for differential abundance of each taxon, (c) controls the False Discovery Rate (FDR), (d)

maintains adequate power, and (e) is computationally simple to implement. Key here is that p-values are calculated for specific taxa.

## LEfSe

Linear discriminant analysis LDA Effect Size (LEfSe), a 2-stage statistical analysis [7]. It uses the non-parametric factorial Kruskal-Wallis (KW) sum-rank test to detect features with significant differential abundance with respect to the class of interest and then biological significance is determined using a set of pairwise tests among subclasses using the (unpaired) Wilcoxon rank-sum test. For the output, LEfSe uses Linear Discriminant Analysis to estimate the effect size of each differentially abundant feature. These data clearly illustrate key microbiological differences among groups. P-values cannot be calculated for Lefse, but I use the p-values as determined from the differential abundance data.

## Heat map

Graphically displays differences between groups - a visual aid. Heat maps were done using R's "gplots" function [4].

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## 5. CosmosID-HUB Meta-transcriptomics Analysis Pipeline

### Host-Agnostic Functional Profiling

Initial QC, adapter trimming and preprocessing of metagenomic sequencing reads are done using BBduk [1]. The quality controlled reads are then subjected to a translated search against a comprehensive and non-redundant protein sequence database, UniRef 90. The UniRef90 database, provided by UniProt [2], represents a clustering of all non-redundant protein sequences in UniProt, such that each sequence in a cluster aligns with 90% identity and 80% coverage of the longest sequence in the cluster. The mapping of metagenomic reads to gene sequences are weighted by mapping quality, coverage and gene sequence length to estimate community wide weighted gene family abundances as described by Franzosa et al [3]. Gene families are then annotated to MetaCyc [4] reactions (Metabolic Enzymes) to reconstruct and quantify MetaCyc [4] metabolic pathways in the community as described by Franzosa et al [3]. Furthermore, the UniRef\_90 gene families are also regrouped to Enzyme Commission Enzymes and GO Terms in order to get an exhaustive overview of gene functions in the community. Lastly, to facilitate comparisons across multiple samples with different sequencing depths, the abundance values are normalized using Total-sum scaling (TSS) normalization to produce "Copies per million" (analogous to TPMs in RNA-Seq) units.

## RelativeAbundance Stacked Bars

Stacked Bar figures were generated using phylum, genus, species, and strain-level filtered matrices for bacteria from CosmosID-HUB. Stacked bar figures for each group were generated using the R package ggpubr [5,6].

## Heatmaps

Heatmaps were created using the pheatmap R package [7] generated using the phylum, genus, species, and strain matrices for bacteria from CosmosID-HUB. Hierarchical clustering and dendrograms are generated using the hclust and dist functions from the R stats package [8,9], with default parameters using euclidean distance and complete linkage.

## Alpha Diversity Boxplots (with Wilcoxon Rank-Sum)

Alpha diversity boxplots were calculated from the phylum, genus, species, and strain level abundance score matrices from CosmosID-HUB analysis. Species or Chao1, Simpson, and Shannon alpha diversity metrics were calculated in R using the R package Vegan [9,10]. Wilcoxon Rank-Sum tests were performed between groups using the R package *ggsignif* [11]. Boxplots with overlaid significance in *p* value format were generated using the R package ggpubr [6].

## Beta Diversity PCoA (with PERMANOVA)

Beta Diversity Principal Coordinate Analyses were calculated from phylum, genus, species, and strain-level matrices for bacteria from CosmosID-HUB. Bray-Curtis dissimilarity was calculated in R using the vegan package with the function vegdist, and PCoA tables were generated using ape's function pcoa [12]. PERMANOVA tests for each distance matrix were generated using vegan's [10] function adonis2, and beta dispersion was calculated and compared using the ANOVA method for the betadisper function from vegan [10]. Plots were visualized using the R package ggpubr [6].

## LEfSe

Linear Discriminant Analysis Effect Size figures were generated using the LEfSe tool [13] from the Huttenhower lab implemented in the R package lefser [14], based on phylum, genus, species, and strain matrices for bacteria from CosmosID-HUB. LEfSe is calculated with a Kruskal-Wallis alpha value of 0.05, a Wilcoxon alpha value of 0.05, and a logarithmic LDA score threshold of 2.0. In the LEfSe figures, red bars to the left convey that the feature in that group is more associated with the “red” group than the other. Blue bars to the right convey that the organism is more associated with the “blue” group.

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- 14) Asya Khleborodova (2020). lefser: R implementation of the LEfSE method for microbiome biomarker discovery. R package version 1.0.0. <https://github.com/waldronlab/lefser>



# VII. Results

## 6. Summary Statistics

The impact of the treatments/products on microbiome composition and functional profiles can be evaluated in two ways: 1) diversity measures, including both alpha and beta diversities and 2) by the number and significance of the features (i.e., species for composition and GO/EC/pathways for metatranscriptomic functional profiles).

We performed a wide range of statistical tests evaluating the significance of differences between the two groups in each of the 20 comparisons listed in Table 1.  $p$  values of all the tests were listed in Table 2 to indicate whether there are significant differences between two groups measured by the diversity indices listed in the column “Measurement” of Table 2. When  $p$  values are  $\leq 0.05$  they are highlighted in green - the smaller  $p$  values the darker green shading is used. Gray shading (from white to dark gray) was used for when  $p$  values are  $> 0.05$ , the larger the darker gray. Thus Table 2 shows where the most significant results are for various types of comparisons.

When many statistical tests were performed (620 in Table 2), naturally some results can be false positive, depending on the confidence level chosen. We did not perform the FDR adjustment because Microbiome studies such as this project, are exploratory in nature. So original  $p$  values were presented to allow more flexible interpretation of the significance.

However, we did observe that, unlike simulations of randomly generated data, which result in uniform distributions of  $p$  values, the  $p$  values in Table 2 do not follow a uniform distribution. The significant results are twice as numerous as would be expected by chance, which indicates a lower likelihood that these results are false positives (Figure 3).

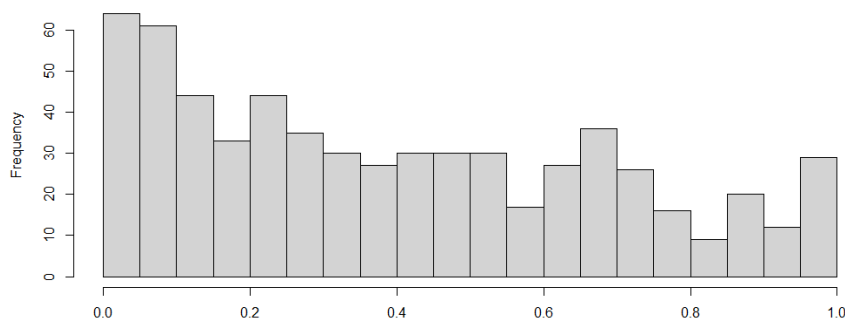


Figure 3. Distribution of all 620  $p$  values for various type of comparisons.

With the exploratory purpose in mind, we can begin to examine the table for the most significant results. Notably comparison 5 (Product A V2 vs V3 saliva) and 6 (Product B V2 vs V3 saliva) show significant differences in alpha and beta diversity between V2 and V3 in MetaCyc Pathway profiles. This indicates that both products impacted metabolic pathways after treatment in the saliva samples.

Sections 7 to 11 are focused result presentation addressing the 4 objectives listed in Section V. Not all comparisons in Table 2 were described in this report.



# 7. Week 6 vs Baseline Comparison – Bacterial Compositions

## Section summary

Based on the species-level sequence abundance results, overall, the microbiomes were modified more with treatment Product B. In general, with the exception of subgingival microbiomes, there appeared to be a microbiological benefit with this treatment.

## Product A V2 vs Product A V3:

### Comparison 1: All sites

- a. No significant differences were detected in Alpha diversity and Beta diversity analyses
- b. There was little or no change in Differential abundance and LefSe analyses
- c. Additional species composition and abundance charts are provided in Appendix A Comparison 1.

### Comparison 5: Saliva

- a. Only a slight change was seen in all analyses. No trends were observed with Differential abundance and LefSe analyses
- b. Treatment did not affect the microbiome.
- c. Additional species composition and abundance charts are provided in Appendix A Comparison 5.

### Comparison 9: Tongue

- a. No significant differences were detected in Alpha diversity and Beta diversity analyses
- b. Minimal trends were observed with Differential abundance. No change in LefSe analyses
- c. Treatment A had little or no effect on tongue microbiomes
- d. Additional species composition and abundance charts are provided in Appendix A Comparison 9.

### Comparison 13: Supragingival

- a. No significant differences were noted in Alpha diversity and Beta diversity analyses
- b. No or few trends were observed with Differential abundance and LefSe analyses
- c. Treatment did not appreciably affect the supragingival microbiome
- d. Additional species composition and abundance charts are provided in Appendix A Comparison 13.

### Comparison 17: Subgingival

- a. No significant differences were detected in Alpha diversity and Beta diversity analyses
- b. Subgingival microbiomes were significantly altered with treatment A. Higher levels of putative pathogens (e.g., *Fusobacterium*, *Treponema*, *Selenomonas* and *Prevotella*) were observed. Conversely, *Streptococcus* species were reduced after treatment.

- c. Additional species composition and abundance charts are provided in Appendix A Comparison 17.

## Product B V2 vs Product B V3:

### Comparison 2: All sites

- a. No significant differences were noted in Alpha diversity and Beta diversity analyses.
- b. Many differences were detected in Differential abundance and Lefse analyses. Some health associated species were prevalent after treatment, e.g., *Streptococcus gordonii*, *Slackia spp*, *Abiotrophia defectiva*. However, a few putative pathogens were also prevalent after treatment, e.g., *Dialister invisus* and species of *Aggregatibacter*.
- c. Treatment B modified the microbiome as compared to Treatment B baseline.
- d. Additional species composition and abundance charts are provided in Appendix A Comparison 2.

### Comparison 6: Saliva

- a. No significant differences were found in Alpha diversity. However, there was a significant difference in Beta diversity with a p value of 0.027.
- b. Trends were observed with a few species using differential abundance, but significance was lost after multiple comparisons.
- c. Lefse indicated reduced levels of a putative pathogen, *Aggregatibacter* and increased levels of the health-associated *Streptococcus gordonii*.
- d. Treatment B modified salivary microbiome with an apparent health associated profile
- e. Additional species composition and abundance charts are provided in Appendix A Comparison 6.

### Comparison 10: Tongue

- a. No significant differences were noted in Alpha diversity and Beta diversity analyses.
- b. Minimal trends (not statistically significant) were observed with Differential abundance analysis.
- c. Similar to salivary microbiome analyses, Lefse showed a reduction in *Aggregatibacter*, a putative pathogen.
- d. Although it was not as effective as compared to salivary microbiomes, Product B was also effective on tongue microbiome.
- e. Additional species composition and abundance charts are provided in Appendix A Comparison 10.

### Comparison 14: Supragingival

- a. No significant differences were noted in Alpha diversity and Beta diversity. However, statistical differences approached significance at 0.09 in each.
- b. Differential abundance indicated several differences, although not significantly different.

- c. Many differences were indicated using Lefse. The health-associated *Streptococcus gordonii* again was more prevalent after treatment. Similarly, *Aggregatibacter* sp were reduced after treatment with Product B.
- d. Modulations of other species are difficult to interpret. However, it is clear that treatment B modified the supragingival microbiome.
- e. Additional species composition and abundance charts are provided in Appendix A Comparison 14.

### Comparison 18: Subgingival

- a. No significant differences were noted in Alpha diversity and Beta diversity.
- b. Differential abundance indicated several differences, such as the reduction in *Aggregatibacter* as seen with other microbiomes, although the differences were not significantly different and it was difficult to assess biological significance. These results conflict with data from other sampling sites.
- c. Additional species composition and abundance charts are provided in Appendix A Comparison 18.

## 8. Week 6 vs Baseline Comparison – Activities

Product A V2 vs Product A V3:

### Comparison 1: All sites

**Summary:** No significant difference was noted after Product A treatment based on diversity assessment (all p values > 0.05). Based on differential abundance analysis (LEfSe), there are 6 Gene Ontology terms, 22 enzymes (Enzyme Commission) and 27 metabolic pathways (Metacyc Pathways) that are significantly affected (p value < 0.05).

The top-most (based on LDA scores) increased functions by Product A are:

- hydrolase activity
- Pyridoxal 5'-phosphate synthase
- fatty acid biosynthesis initiation (mitochondria)

The top-most reduced functions by Product A are:

- NADPH:quinone reductase activity
- 1,4-alpha-glucan branching enzyme
- glycogen biosynthesis I (from ADP-D-Glucose)

Detailed analysis results are shown in Appendix B. Comparison 1.

### Comparison 5: Saliva

**Summary:** In saliva samples, Product A significantly affected the bacterial pathways listed in MetaCyc, when measured by alpha diversity Chao1 (p = 0.003), Shannon (p = 0.034) but not Simpson. This indicates that functions with lower read abundance (low expression level) were impacted. Enzyme activities were also affected when measured with alpha index Chao1 (p = 0.039).

A total of 5 GO terms, 4 enzymes, and 20 pathways were impacted based on LEfSe differential abundance analysis.

The top-most (based on LDA scores) increased functions by Product A are:

- DNA replication
- Alanine--tRNA ligase
- fatty acid  $\beta$ -oxidation I (generic)

The top-most reduced functions by Product A are:

- NADPH:quinone reductase activity
- Glutamine synthetase
- superpathway of anaerobic sucrose degradation

Detailed analysis results are shown in Appendix B. Comparison 5.

### Comparison 9: Tongue

**Summary:** On tongue, alpha diversity was significantly affected by Product A based on Chao1 measurement ( $p = 0.013$ ) of GO terms. Alpha diversity of enzyme profile was also impacted when measured with Shannon and Simpson indexes ( $p=0.008$  and  $0.042$  respectively). This means medium to higher abundant enzymatic gene expression were affected by Product A. Beta diversity of enzyme activities was affected with marginal significance by Product A ( $p=0.053$ ). Alpha diversity of pathways was also affected when measured with Chao1 ( $p=0.026$ ).

A total of 11 GO terms, 52 enzymes, and 28 pathways were impacted based on LEfSe differential abundance analysis.

The top-most (based on LDA scores) increased functions by Product A are:

- metal ion binding
- Formate C-acetyltransferase
- gondoate biosynthesis (anaerobic)

The top-most reduced functions by Product A are:

- hydrolase activity
- Glutamine synthetase

Detailed analysis results are shown in Appendix B. Comparison 9.

### Comparison 13: Supragingival

**Summary:** Alpha and Beta diversity of bacterial activities of supragingival samples **were not significantly** affected by the treatment of Product A.

A total of 17 GO terms, 5 enzymes, and 3 pathways were impacted based on LEfSe differential abundance analysis.

The top-most (based on LDA scores) increased functions by Product A are:

- mitochondrion
- Pyridoxal 5'-phosphate synthase
- UMP biosynthesis

Only one function was significantly reduced by Product A:

- Formimidoyltetrahydrofolate cyclodeaminase

Detailed analysis results are shown in Appendix B. Comparison 13.

### Comparison 17: Subgingival

**Summary:** Alpha and Beta diversity of bacterial activities of subgingival samples **were not significantly** affected by the treatment of Product A.

A total of 17 GO terms, 28 enzymes, and 18 pathways were impacted based on LEfSe differential abundance analysis.

The top-most (based on LDA scores) increased functions by Product A are:

- periplasmic flagellum

- 3-hydroxybutyryl-CoA dehydrogenase
- fatty acid biosynthesis initiation (mitochondria)

The top-most reduced functions by Product A are:

- phosphoenolpyruvate-dependent sugar phosphotransferase system
- 1,4-alpha-glucan branching enzyme

Detailed analysis results are shown in Appendix B. Comparison xxx.

## Product B V2 vs Product B V3:

### Comparison 2: All sites

**Summary:** Beta diversity of MetaCyc pathway profile was significantly affected by Product B ( $p = 0.007$ ). Alpha Simpson diversity of Gene Ontology has significant difference ( $p=0.049$ ) after Product B treatment.

A total of 4 GO terms, 21 enzymes, and 38 pathways were impacted based on LEfSe differential abundance analysis.

The top-most (based on LDA scores) increased functions by Product B are:

- extracellular region
- Galactose-6-phosphate isomerase
- glycolysis IV

The top-most reduced functions by Product B are:

- cell outer membrane
- Bacterial non-heme ferritin
- Calvin-Benson-Bassham cycle

Detailed analysis results are shown in Appendix B. Comparison 2.

### Comparison 6: Saliva

**Summary:** Alpha and Beta diversity of bacterial activities of saliva samples were not significantly affected by the treatment of Product A.

A total of 3 GO terms, 0 enzymes, and 48 pathways were impacted based on LEfSe differential abundance analysis.

The top-most (based on LDA scores) increased functions by Product B are:

- glyceraldehyde-3-phosphate dehydrogenase (NAD<sup>+</sup>) (phosphorylating) activity

The top-most reduced functions by Product B are:

- riboflavin biosynthetic process
- superpathway of glucose and xylose degradation
- glycolysis IV

Detailed analysis results are shown in Appendix B. Comparison 6.



## Comparison 10: Tongue

**Summary:** On Tongue, Alpha diversity of both GO and Enzymes profiles were significantly affected by Product B, measured by Chao1 index ( $p=0.031$  and  $0.045$ , respectively). Beta diversity was not significantly affected.

A total of 6 GO terms, 14 enzymes, and 4 pathways were impacted based on LEfSe differential abundance analysis.

The top-most (based on LDA scores) increased functions by Product B are:

- 6-phosphofructokinase
- Rubisco shunt

The top-most reduced functions by Product B are:

- porin activity
- Nitrite reductase (NO-forming)
- phosphatidylglycerol biosynthesis I (plastidic)

Detailed analysis results are shown in Appendix B. Comparison 10.

## Comparison 14: Supragingival

**Summary:** Alpha diversity of GO profiles was affected significantly by Product B, measured with Chao1 ( $p=0.037$ ), Shannon ( $p=0.011$ ) and Simpson ( $p=0.008$ ). Beta diversity of GO and MetaCyc profiles were significantly affected by Product B ( $p=0.031$ , and  $0.044$ , respectively).

A total of 25 GO terms, 41 enzymes, and 28 pathways were impacted based on LEfSe differential abundance analysis.

The top-most (based on LDA scores) increased functions by Product B are:

- cytoplasm
- Triose-phosphate isomerase
- UMP biosynthesis II

The top-most reduced functions by Product B are:

- integral component of membrane
- Transaldolase
- Calvin-Benson-Bassham cycle

Detailed analysis results are shown in Appendix B. Comparison 14.

## Comparison 18: Subgingival

**Summary:** Alpha and Beta diversity of bacterial activities of subgingival samples were not significantly affected by the treatment of Product B.

A total of 17 GO terms, 28 enzymes, and 18 pathways were impacted based on LEfSe differential abundance analysis.

The top-most (based on LDA scores) increased functions by Product B are:

- periplasmic flagellum

- 3-hydroxybutyryl-CoA dehydrogenase
- fatty acid biosynthesis initiation (mitochondria)

The top-most reduced functions by Product B are:

- phosphoenolpyruvate-dependent sugar phosphotransferase system
- 1,4-alpha-glucan branching enzyme
- glucose and glucose-1-phosphate degradation

Detailed analysis results are shown in Appendix B. Comparison 18.

## 9. Product A vs B at Week 6 – Bacterial Composition

### Comparison 4: All sites

- a. Data indicated that the microbiomes of the subject populations were not similar. Many differences were observed.
- b. Longitudinal data should be used to evaluate, as in Comparison 2
- c. Additional species composition and abundance charts are provided in Appendix A Comparison 4

### Comparison 8: Saliva

- a. **No significant differences** were noted in Alpha diversity and Beta diversity
- b. Differential abundance indicated many differences, but statistical significance was lost after multiple comparisons.
- c. Lefse also indicated many differences. Many health associated species had increased levels in B, e.g. *S. gordonii*, *Gemella hemolysans*, *Abiotrophia defectiva*, *Granulicatella elegans*. In contrast, species of *Campylobacter*, putative pathogens, were reduced in B.
- d. Treatment B appeared to be beneficial for salivary microbiome composition.
- e. Additional species composition and abundance charts are provided in Appendix A Comparison 8.

### Comparison 12: Tongue

- a. **No significant differences** were detected in Alpha diversity and Beta diversity.
- b. Differential abundance indicated several differences, although not significantly different between the subject populations.
- c. Very few differences were detected with Lefse analysis. *Campylobacter* sp (putative pathogens), were again reduced with Treatment B.
- d. Additional species composition and abundance charts are provided in Appendix A Comparison 12.

### Comparison 16: Supragingival

- a. No significant differences were noted in Alpha diversity. However, there was a significant difference in Beta diversity with a p value of 0.023.
- b. As expected, many differences observed with both differential abundance and Lefse analyses. Compared to cross-sectional study design as used in this study, longitudinal data should be more useful to detect differences between two treatments.
- c. Additional species composition and abundance charts are provided in Appendix A Comparison 16.

### Comparison 20: Subgingival

- a. **No significant differences** were noted in Alpha diversity and Beta diversity.
- b. Many differences were detected in Differential abundance and Lefse analyses, as expected.
- c. Longitudinal analyses would be a better assessment.

d. Additional species composition and abundance charts are provided in Appendix A Comparison 20.

## 10. Product A vs B at Week 6 – Activities

### Comparison 4: All sites

**Summary:** When all sites combined, alpha and beta diversities of MetaCyc pathway profiles are significantly different after 2 weeks of treatment between Product A and Product B. Alpha diversities measured with Shannon and Simpson indexes have p values of 0.033 and 0.004 respectively. Beta diversities of MetaCyc pathway profiles differed at a significant level with  $p=0.005$ .

A total of 12 GO terms, 45 enzymes, and 41 pathways were impacted based on LEfSe differential abundance analysis.

The top-most (based on LDA scores) increased functions by Product A are:

- cytolysis
- DNA-directed RNA polymerase
- gondoate biosynthesis (anaerobic)

The top-most increased functions by Product B are:

- glutamine biosynthetic process
- 6-phospho-beta-galactosidase
- glycogen biosynthesis I (from ADP-D-Glucose)

Detailed analysis results are shown in Appendix B. Comparison 4.

### Comparison 8: Saliva

**Summary:** For saliva samples, alpha and beta diversity of bacterial activities **were not** significantly different between the treatment of Product A and B at week 6.

A total of 14 GO terms, 2 enzymes, and 4 pathways were impacted based on LEfSe differential abundance analysis.

The top-most (based on LDA scores) increased functions by Product A are:

- metal ion transport
- Bacterial non-heme ferritin
- gondoate biosynthesis (anaerobic)

The top-most increased functions by Product B are:

- nucleus
- sucrose biosynthesis II

Detailed analysis results are shown in Appendix B. Comparison 8.

### Comparison 16: Supragingival

**Summary:** For supragingival samples, alpha and beta diversity of bacterial activities **were not** significantly different between the treatment of Product A and B at week 6.

A total of 14 GO terms, 7 enzymes, and 5 pathways were impacted based on LEfSe differential abundance analysis.

The top-most (based on LDA scores) increased functions by Product A are:

- cytolysis
- [Formate-C-acetyltransferase]-activating enzyme
- palmitate biosynthesis (type II fatty acid synthase)

The top-most increased functions by Product B are:

- integral component of membrane
- glucose and glucose-1-phosphate degradation

Detailed analysis results are shown in Appendix B. Comparison 16.

### Comparison 16: Supragingival

**Summary:** In supragingival samples, alpha diversity of the MetaCyc Pathways profiles differ between the treatment of Product A and B at week 6 for the most abundant features. The Simpson index differed with a p value of 0.009 and the beta diversity differed at p = 0.003.

A total of 16 GO terms, 23 enzymes, and 34 pathways were impacted based on LEfSe differential abundance analysis.

The top-most (based on LDA scores) increased functions by Product A are:

- integral component of membrane
- tRNA (guanine(37)-N(1))-methyltransferase
- Calvin-Benson-Bassham cycle

The top-most increased functions by Product B are:

- oxidoreductase activity, acting on the aldehyde or oxo group of donors, NAD or NADP as acceptor
- Glucose-1-phosphate adenylyltransferase
- glycogen biosynthesis I (from ADP-D-Glucose)

Detailed analysis results are shown in Appendix B. Comparison 16.

### Comparison 20: Subgingival

**Summary:** for subgingival samples, alpha and beta diversity of bacterial activities were not significantly affected between the treatment of Product A and B at week 6.

However, numerous functional features had differential abundance between the treatment of Product A and B in week 6. A total of 40 GO terms, 72 enzymes, and 32 pathways were impacted based on LEfSe differential abundance analysis. Product A triggered higher expression for 72 enzymes and 23 pathway related genes. This suggests that Product B affected the bacterial activities more than Product A did.

The top-most (based on LDA scores) increased functions by Product A are:

- translation
- DNA-directed RNA polymerase

- fatty acid biosynthesis initiation (mitochondria)

The top-most reduced functions by Product B are:

- extracellular exosome
- glycolysis III (from glucose)

Detailed analysis results are shown in Appendix B. Comparison 20.

# 11. Bacterial Compositions of Oral Sites at Baseline (V2)

**Summary.** Bacterial compositions differ most significantly by sites. Saliva and tongue samples have similar compositions and supra- and sub-gingival samples are similar to each other. At baseline (V2), the difference in compositions was driven by sample source (sites) instead of the two product groups. As Figure 4 shows, the saliva and tongues samples have marked differences than supra- and sub-gingival ones, as measured by both alpha (data not shown) and beta diversity analysis (Figure 4). The microbiome profiles between saliva/tongue and supra-/sub-gingival samples are distinct at any stage of the samples, both at baseline and after the treatment of products. This distinction between saliva/tongue and supra-/sub-gingival samples was also observed in the meta-transcriptomic data for all the samples (Figure 5, all p values are significant for pairwise and group comparisons). This is expected and the distinct microbiome profile separation by sites indicates that the sequence quality was adequate to show this distinction.

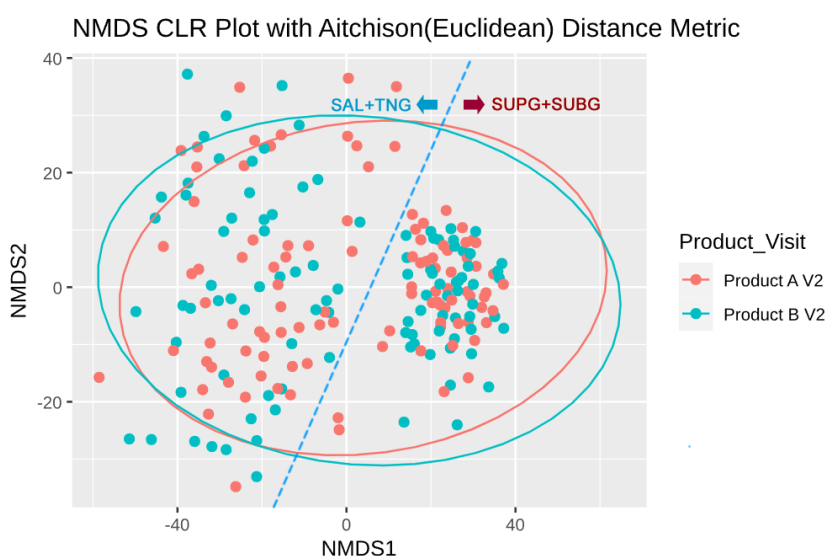


Figure 4. Beta diversity ordinate plots of samples at baseline (V2).

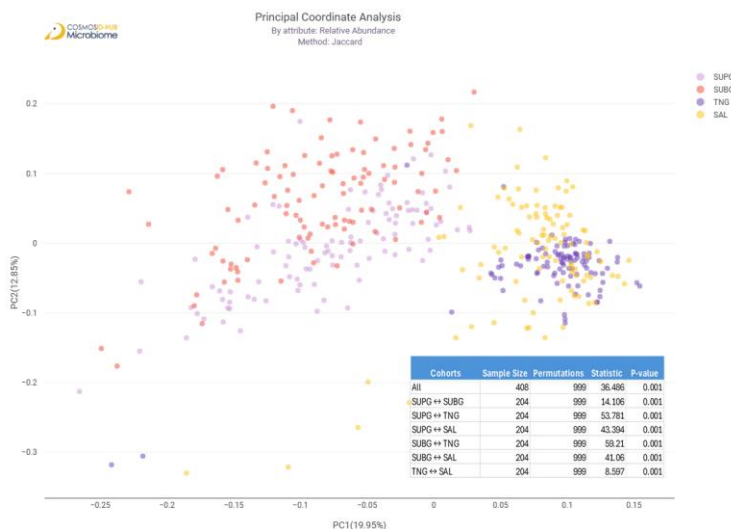


Figure 5. Beta diversity ordinate plots of all samples.



### Comparison 3: Product A V2 vs Product B V2 (All Sites)

- a. Data indicated that the microbiomes of the subject populations were not similar. Many differences were observed.
- b. Longitudinal data should be used to evaluate, as in Comparison 1.
- c. Additional compositional and abundance charts are available in Appendix A Comparison 3.

### Comparison 7: Product A V2 SAL vs Product B V2 SAL (Saliva)

No significant differences were noted in Alpha diversity and Beta diversity and only minor differences were detected in Differential abundance and Lefse analyses.

- a. Data indicates that the salivary microbiomes of subjects in A were similar to those in subjects in B. A good control.
- b. Additional compositional and abundance charts are available in Appendix A Comparison 7.

### Comparison 11: Product A V2 TNG vs Product B V2 TNG (Tongue)

- a. No significant differences were noted in Alpha diversity and Beta diversity
- b. Differential abundance indicated many differences, although not significantly different between the subject populations. Many differences observed using Lefse analysis.
- c. Longitudinal analysis would be the preferential comparison (5 and 6 above).
- d. Additional compositional and abundance charts are available in Appendix A Comparison 11.

### Comparison 15: Product A V2 SUPG vs Product B V2 SUPG (Supragingival)

- a. No significant differences were detected in Alpha diversity and Beta diversity.
- b. Differential abundance indicated several differences, although not significantly different
- c. Many differences were observed with Lefse. Several pathogens were observed, e.g., *Treponema* spp., TM7, and *Prevotella*.
- d. These data indicate that there were differences in the 2 groups (populations)—longitudinal data should be used to determine the effectiveness of treatment
- e. Additional compositional and abundance charts are available in Appendix A Comparison 15.

### Comparison 19: Product A V2 SUBG vs Product B V2 SUBG (Subgingival)

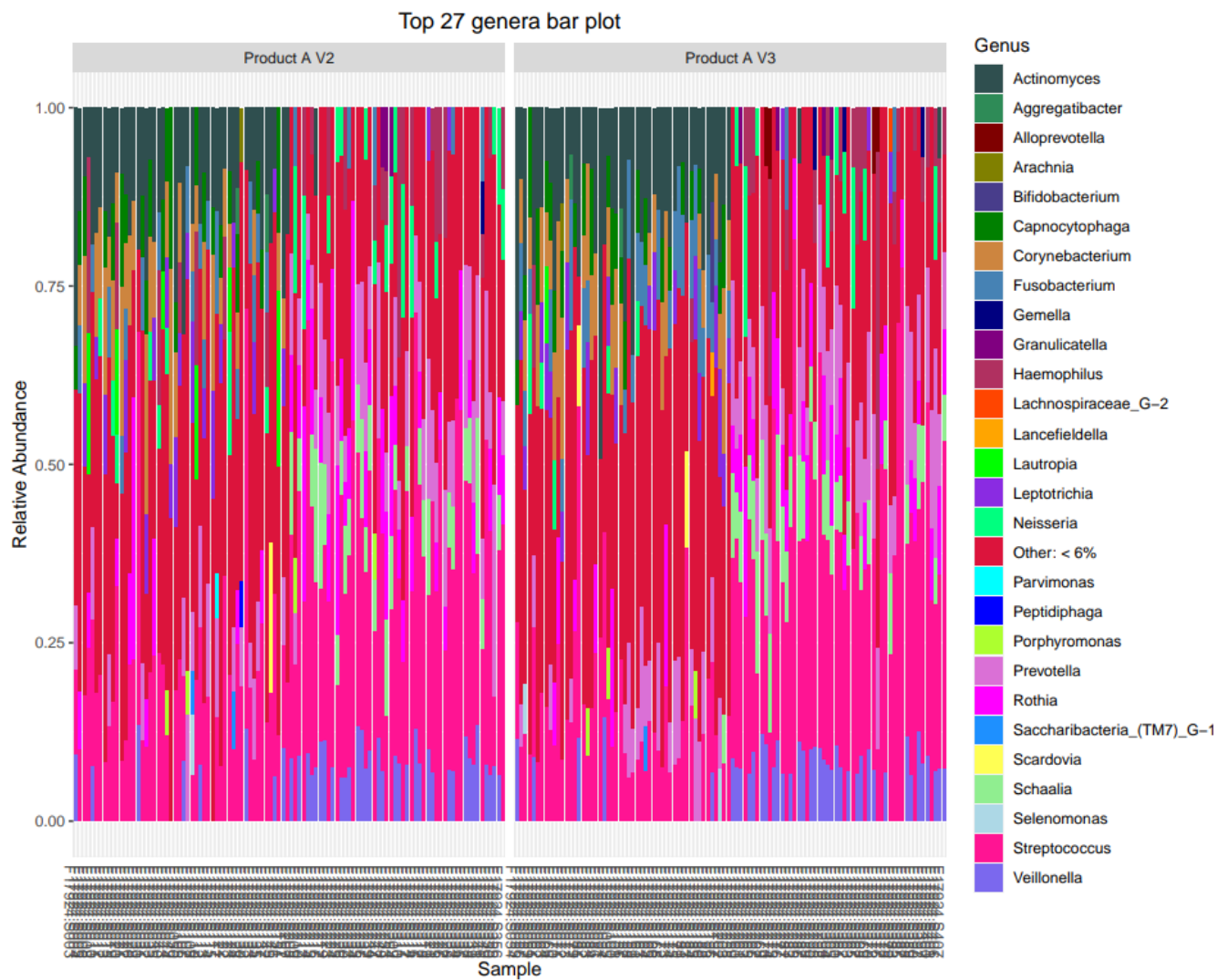
- a. No significant differences were detected in Alpha diversity and Beta diversity.
- b. Differential abundance indicated several differences, although not significantly different.
- c. Microbiomes are reasonably similar and serve as an adequate control.
- d. Additional compositional and abundance charts are available in Appendix A Comparison 19.

# VIII. Appendix

## Appendix A – 16S rRNA V1V3 Analysis Figures and Charts

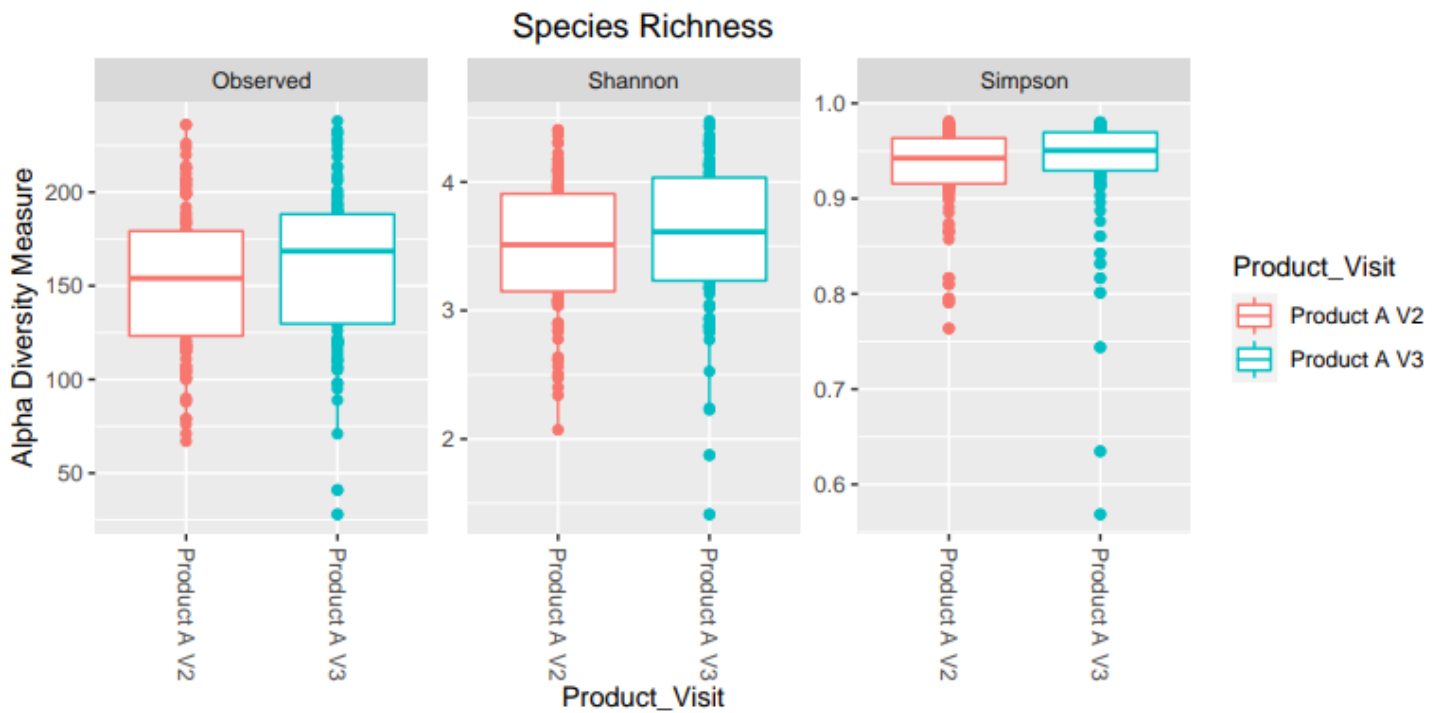
### Comparison 1: Product A V2 vs Product A V3

#### 1) Taxonomy bar graph



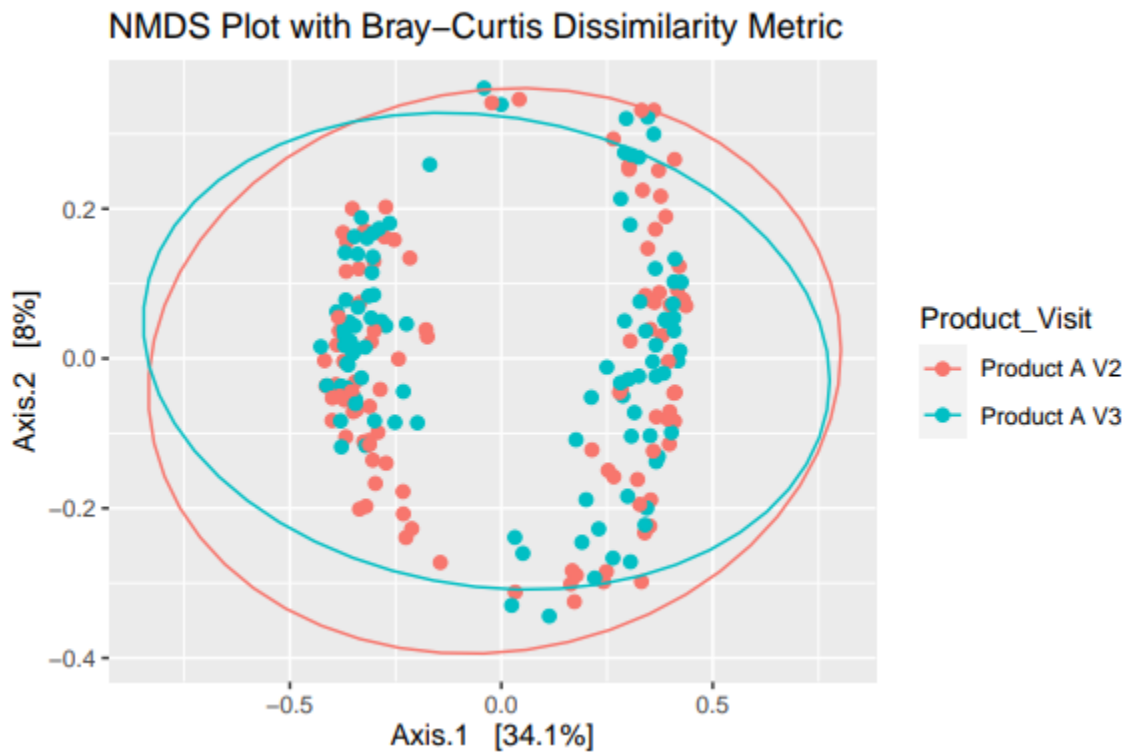
Note: Too crowded to visualize, but can detect the differences in the different sites

## 2) Alpha diversity



Note: No statistical differences. Simpson is  $p=0.09$

### 3) Beta diversity



Note: We can detect the differences, but not significantly different.

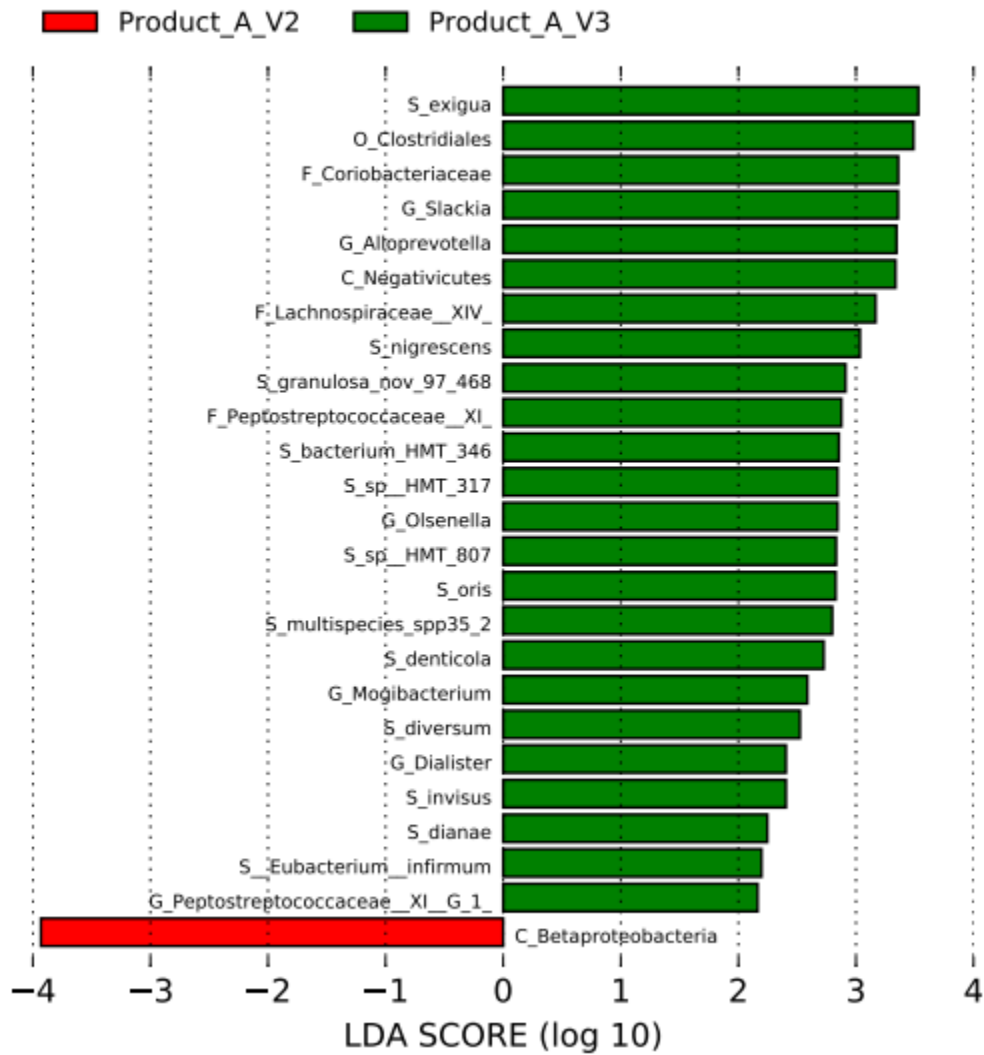
#### 4) Differential abundance

taxon	lfc_(Interc	lfc_Product	se_(Interc	se_Product	W_(Interc	W_Product	p_(Interc	p_Product	q_(Interc	q_Product	diff_(Interc	diff_Product
Abiotrophia defectiva (SP206)	0.38908	-0.77816	0.295257	0.417556	1.317768	-1.8636	0.187581	0.062378	1	1	FALSE	FALSE
Saccharibacteria_(TM7)_[G-1] bacterium_HMT_346 (SP293)	-0.40966	0.819312	0.312126	0.441412	-1.31247	1.856115	0.189362	0.063437	1	1	FALSE	FALSE
Olsenella sp._HMT_807 (SP81)	-0.37103	0.742059	0.289497	0.409411	-1.28163	1.812504	0.199972	0.069908	1	1	FALSE	FALSE
Fusobacterium nucleatum_nucleatum_subsp._animalis (SPP)	-0.36275	0.725497	0.292774	0.414044	-1.23901	1.752222	0.215343	0.079736	1	1	FALSE	FALSE
Bergeyella sp._HMT_322 (SP67)	0.229577	-0.45915	0.19425	0.274711	1.181863	-1.6714	0.23726	0.094642	1	1	FALSE	FALSE
Peptostreptococcaceae_[XII][G-1][Eubacterium]_infirmum (SP)	-0.2648	0.529594	0.224869	0.318012	-1.17756	1.665324	0.238972	0.095848	1	1	FALSE	FALSE
Prevotella sp._HMT_317 (SP111)	-0.37734	0.754675	0.331954	0.469454	-1.13672	1.607561	0.255657	0.107931	1	1	FALSE	FALSE
Bacteroidales_[G-2] bacterium_HMT_274 (SP21)	-0.32801	0.656014	0.289524	0.409449	-1.13292	1.602189	0.257249	0.109114	1	1	FALSE	FALSE
Actinomyces sp._HMT_175_nov_97.951% (SPN405)	0.287502	-0.575	0.254998	0.360622	1.127466	-1.59447	0.259546	0.11083	1	1	FALSE	FALSE
Slackia exigua (SP147)	-0.23843	0.476852	0.217091	0.307014	-1.09827	1.553194	0.272086	0.120377	1	1	FALSE	FALSE
Granulicatella adiacens (SP134)	0.213839	-0.42768	0.196476	0.277858	1.088375	-1.53919	0.27643	0.123758	1	1	FALSE	FALSE
Prevotella oris (SP65)	-0.30248	0.604954	0.27809	0.393279	-1.08769	1.53823	0.276732	0.123992	1	1	FALSE	FALSE
Streptococcus sp._HMT_064 (SP305)	0.327807	-0.65561	0.308876	0.436817	1.061289	-1.50089	0.288558	0.133385	1	1	FALSE	FALSE
Schaalia odontolyticus (SP28)	0.372968	-0.74594	0.361548	0.511306	1.031587	-1.45888	0.302265	0.144598	1	1	FALSE	FALSE
Mogibacterium diversum (SP365)	-0.24519	0.490377	0.239267	0.338375	-1.02475	1.449213	0.305483	0.147278	1	1	FALSE	FALSE
Prevotella denticola (SP30)	-0.29611	0.592222	0.289957	0.410061	-1.02122	1.44423	0.307149	0.148674	1	1	FALSE	FALSE
Absconditabacteria_(SR1)_[G-1] bacterium_HMT_875 (SP235)	0.177854	-0.35571	0.174606	0.24693	1.018602	-1.44052	0.308392	0.149722	1	1	FALSE	FALSE
Prevotella nigrescens (SP259)	-0.28534	0.57069	0.283397	0.400784	-1.00687	1.423935	0.313996	0.154465	1	1	FALSE	FALSE
Streptococcus chosunense (SP133)	0.312705	-0.62541	0.313337	0.443126	0.997982	-1.41136	0.318288	0.158139	1	1	FALSE	FALSE

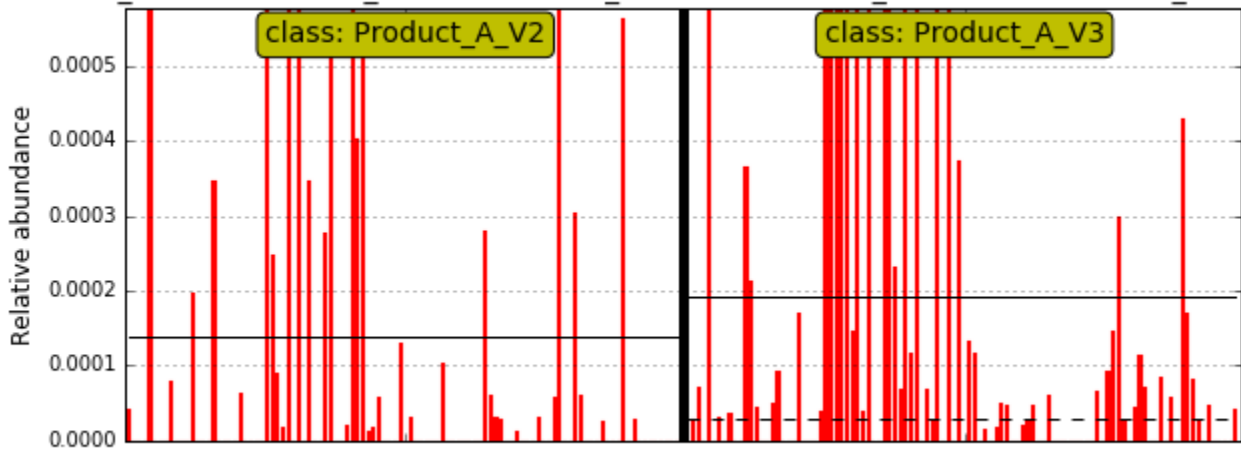
Note: Little or no difference after treatment

5) Lefse

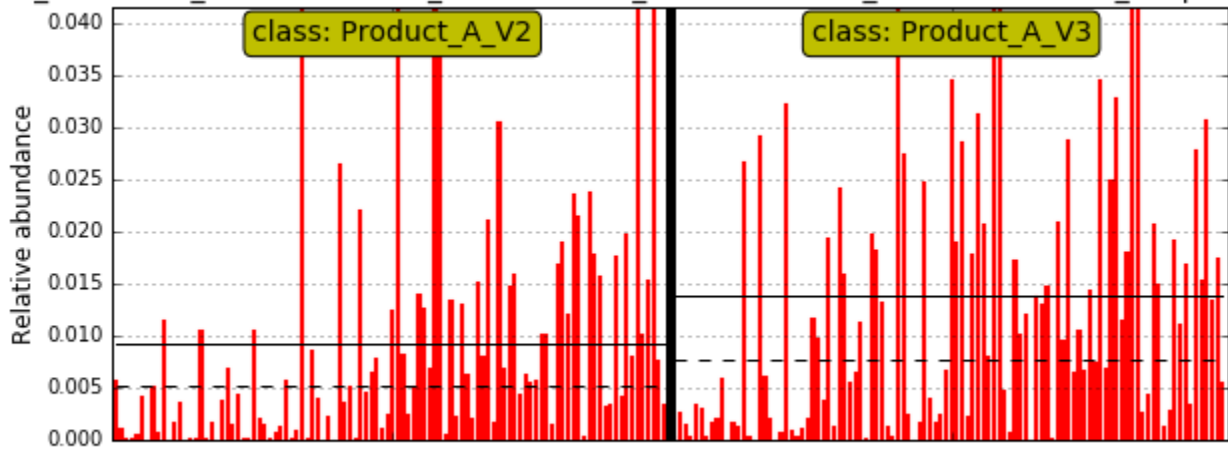
Significantly Represented Taxa



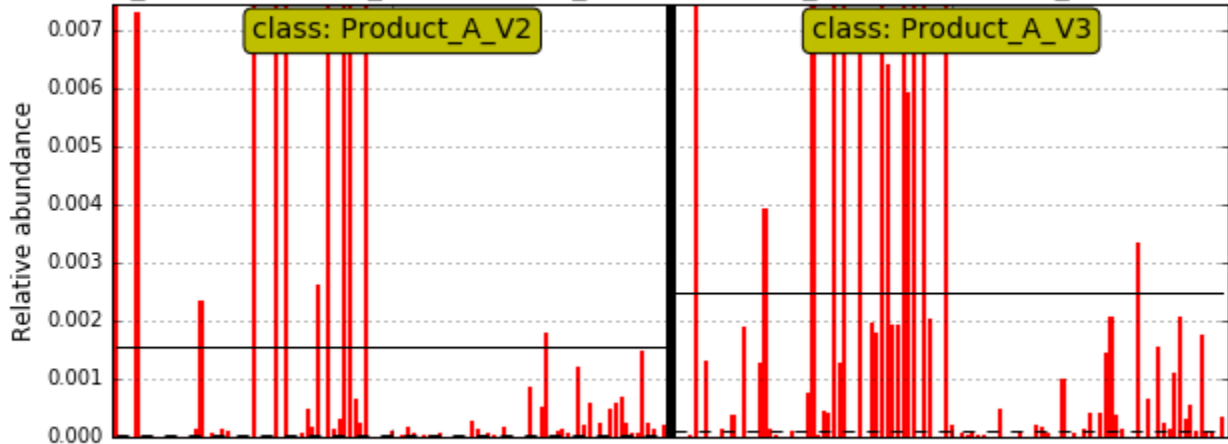
K\_Bacteria.P\_Actinobacteria.C\_Coriobacteriia.O\_Coriobacteriales.F\_Coriobacteriaceae.G\_Slackia.S\_exig



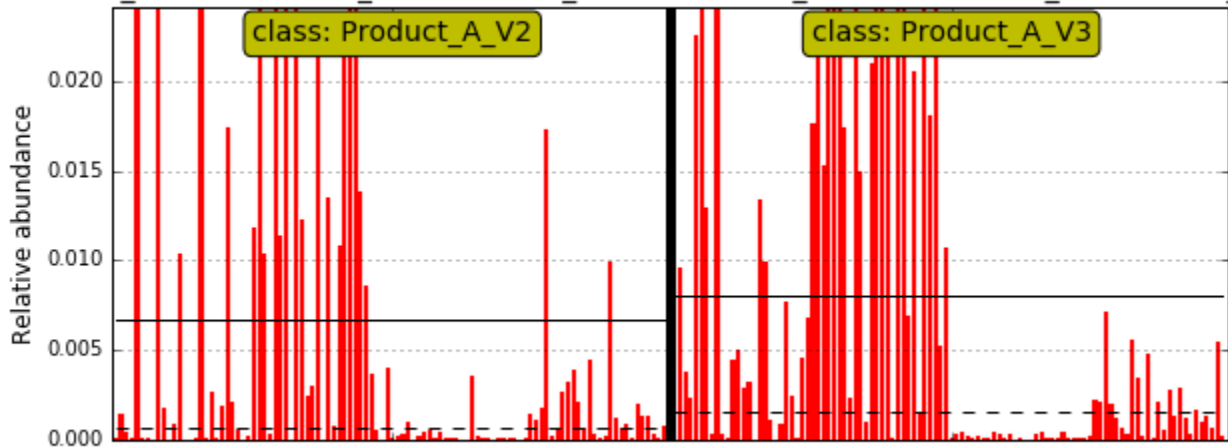
K\_Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Alloprevotella



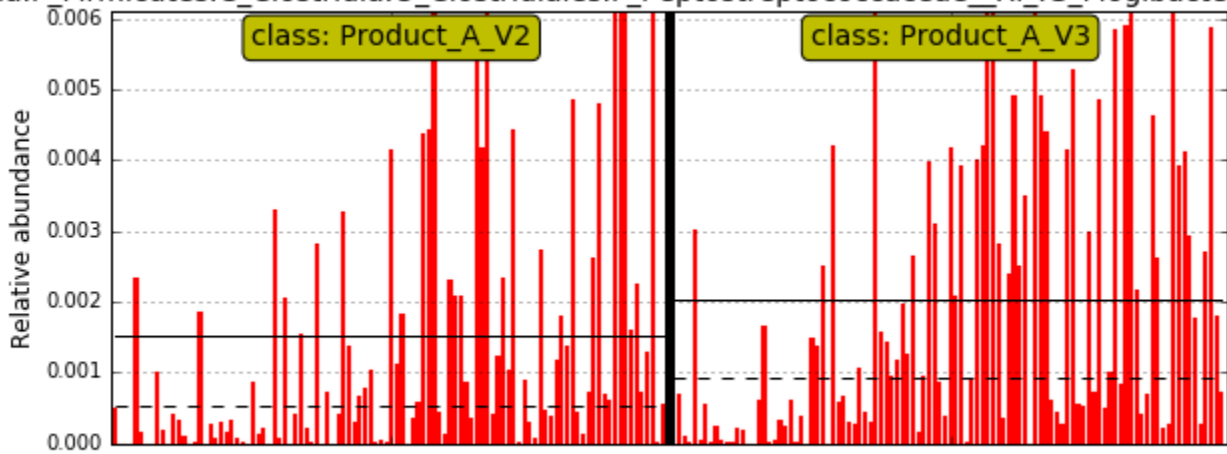
K\_Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Prevotella.S\_denticola



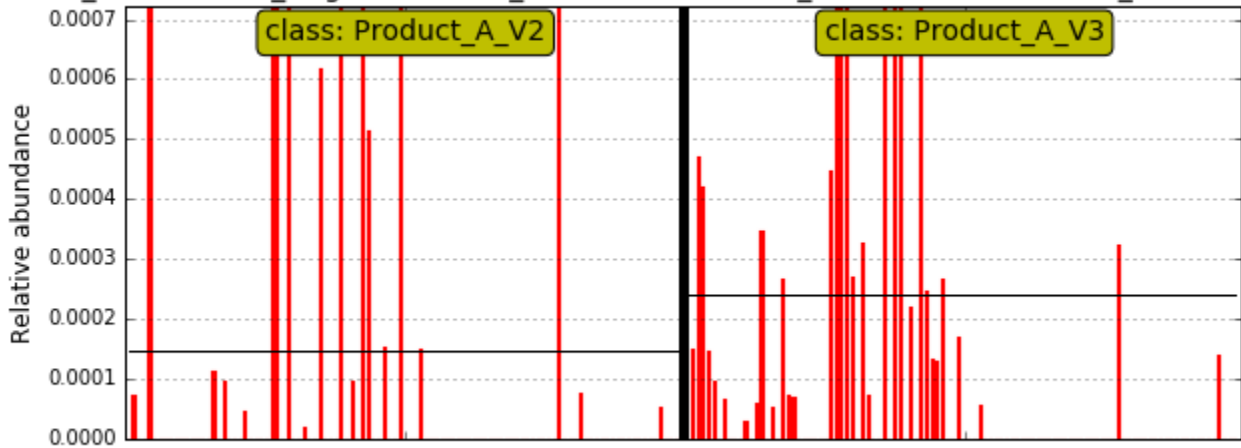
K\_Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Prevotella.S\_nigrescer



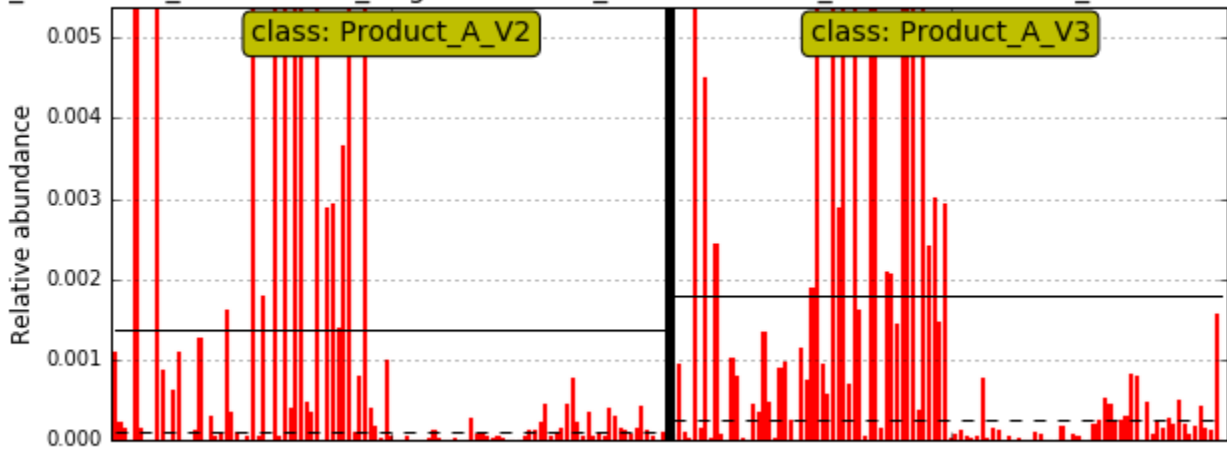
acteria.P\_Firmicutes.C\_Clostridia.O\_Clostridiales.F\_Peptostreptococcaceae\_XI\_G\_Mogibacterium.S\_div



Bacteria.P\_Firmicutes.C\_Negativicutes.O\_Selenomonadales.F\_Selenomonadaceae.G\_Selenomonas.S\_di

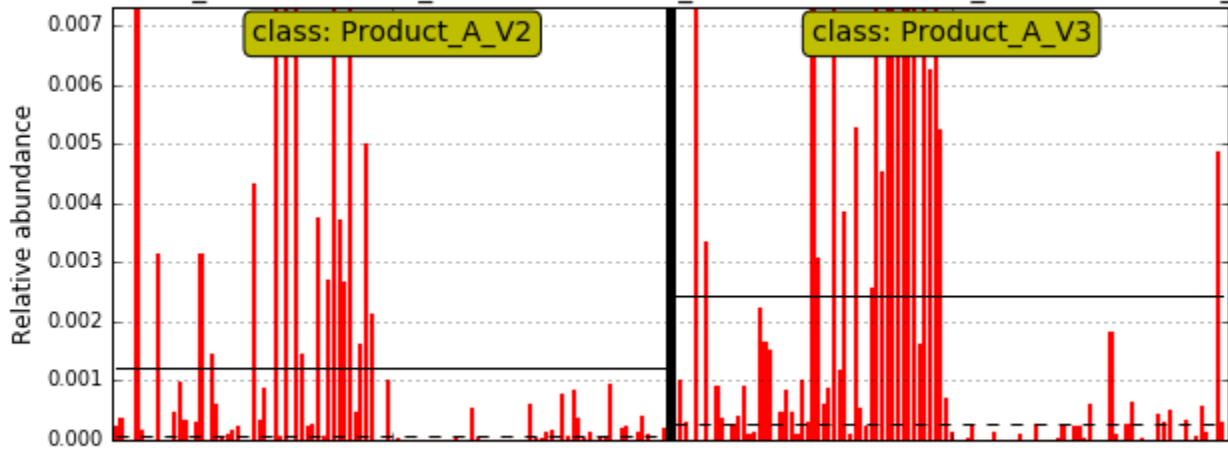


K\_Bacteria.P\_Firmicutes.C\_Negativicutes.O\_Veillonellales.F\_Veillonellaceae.G\_Dialister.S\_invisus

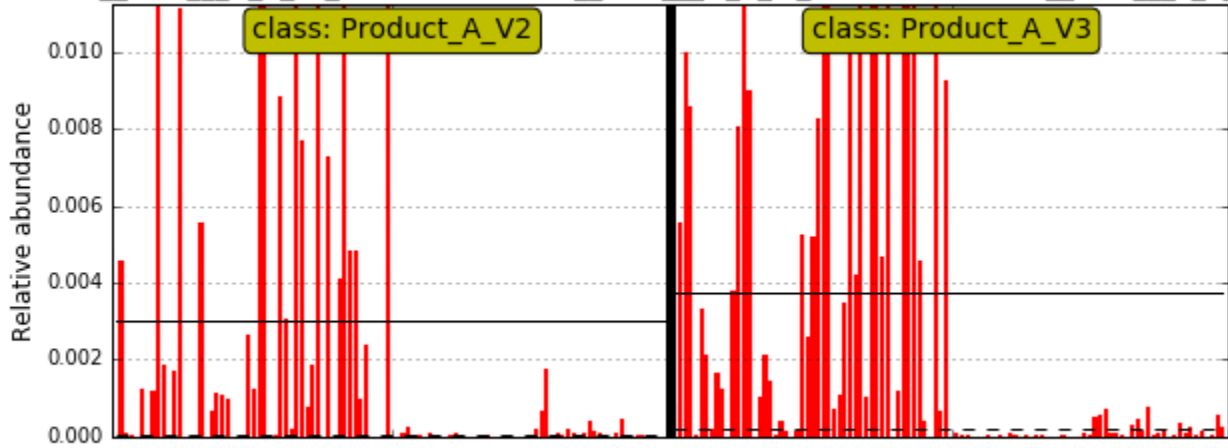




a.P\_Fusobacteria.C\_Fusobacteria.O\_Fusobacteriales.F\_Fusobacteriaceae.G\_Fusobacterium.S\_multispec

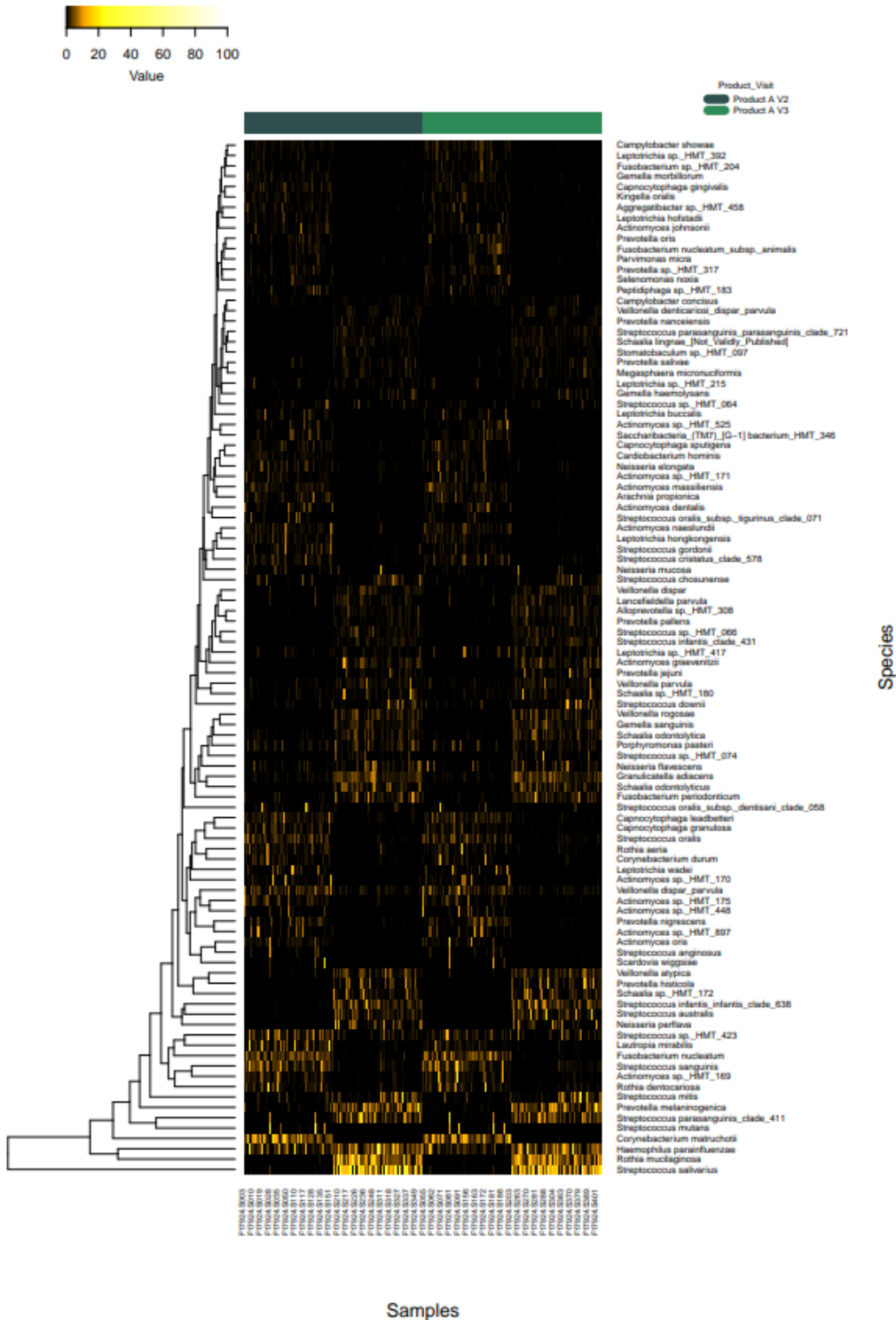


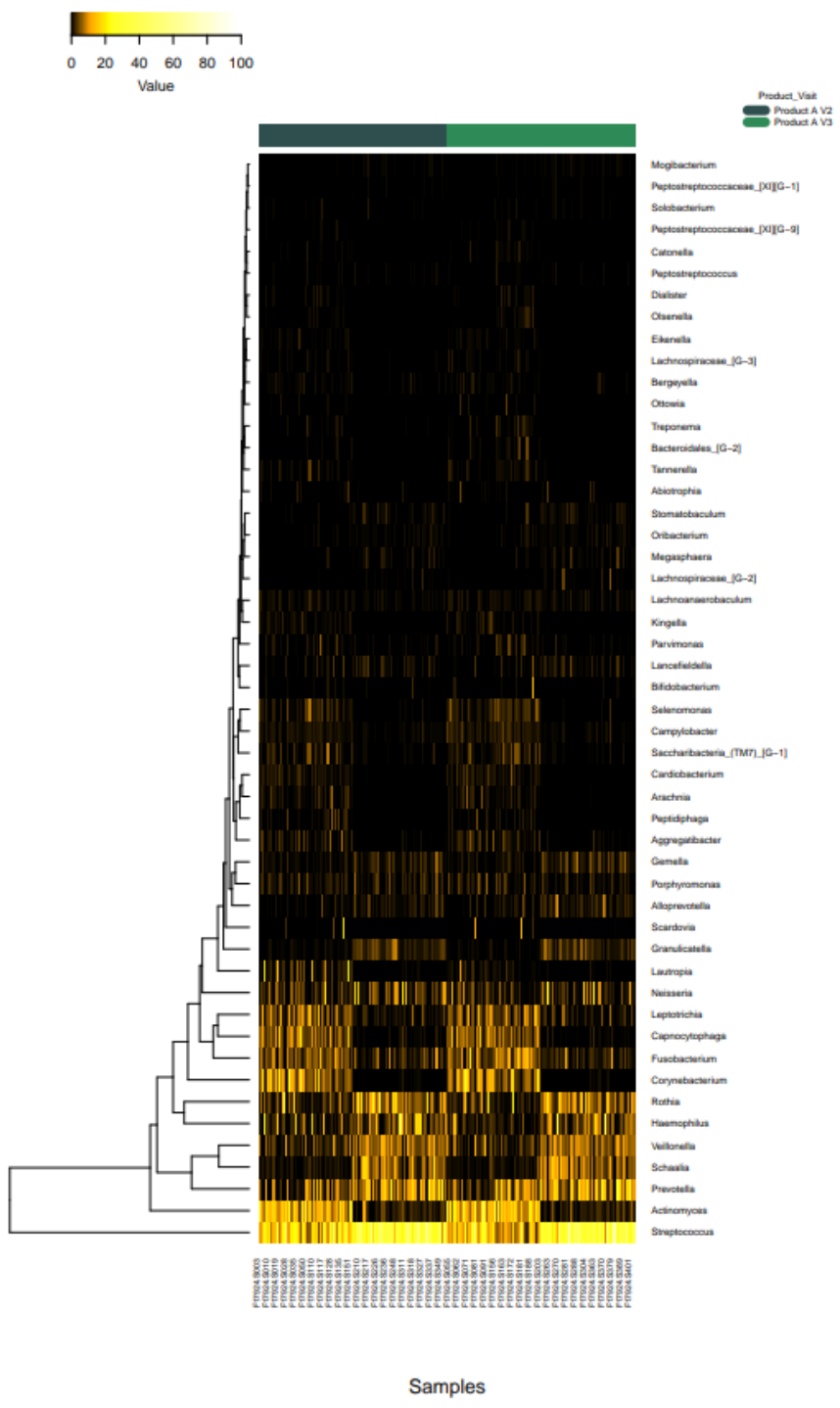
haribacteria\_TM7\_C\_1\_O\_Saccharibacteria\_TM7\_O\_1\_F\_Saccharibacteria\_TM7\_F\_1\_G\_Saccha



## 6) Heat maps

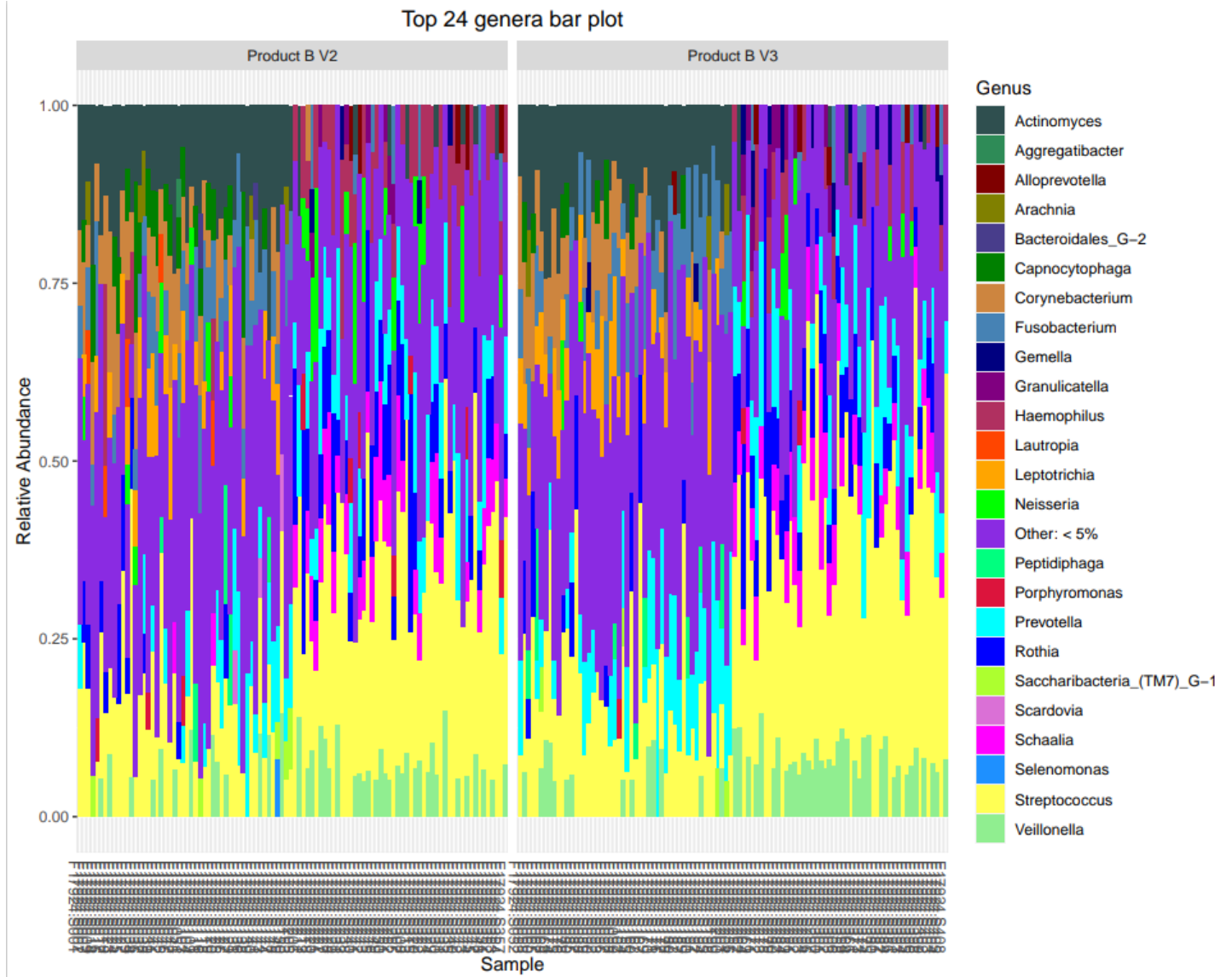
Note: Differences are clearly seen.



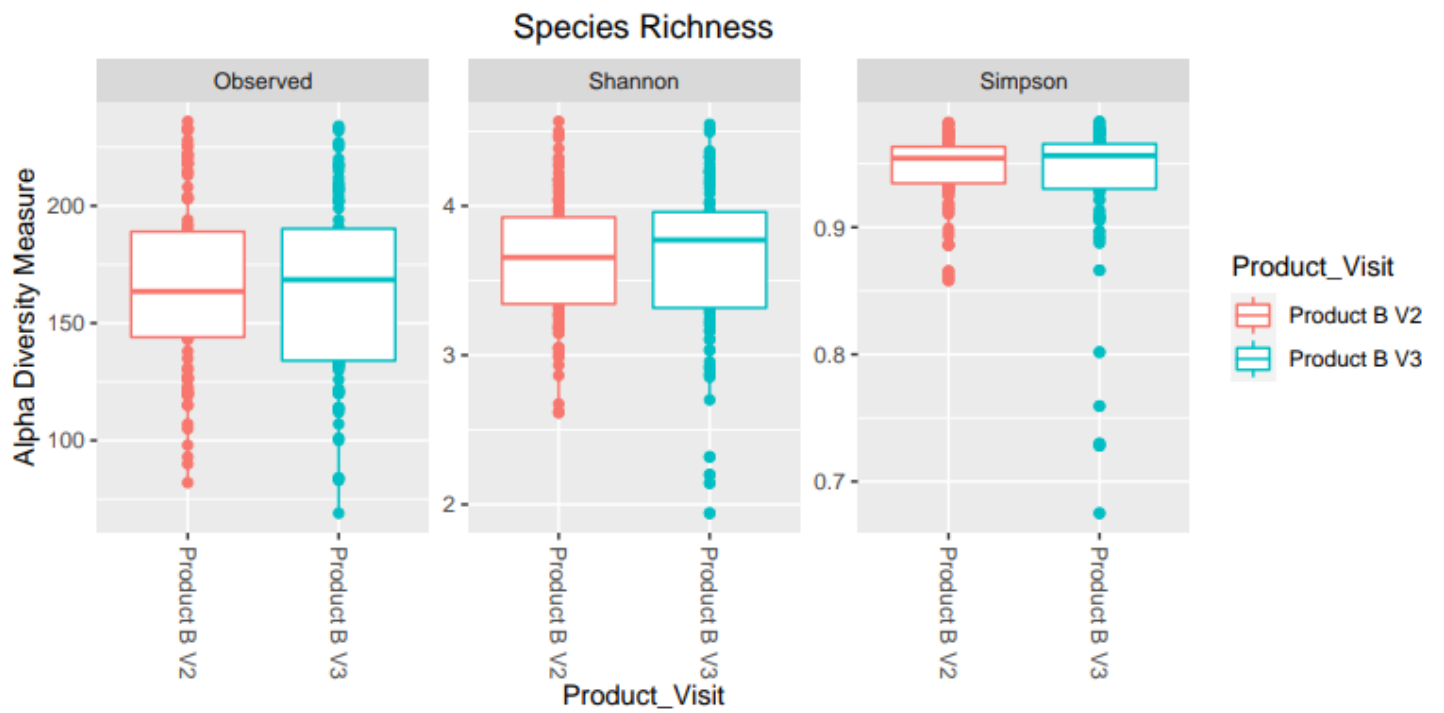


# Comparison 2. Product B V2 vs Product B V3

## 1) Taxonomy bar graphs

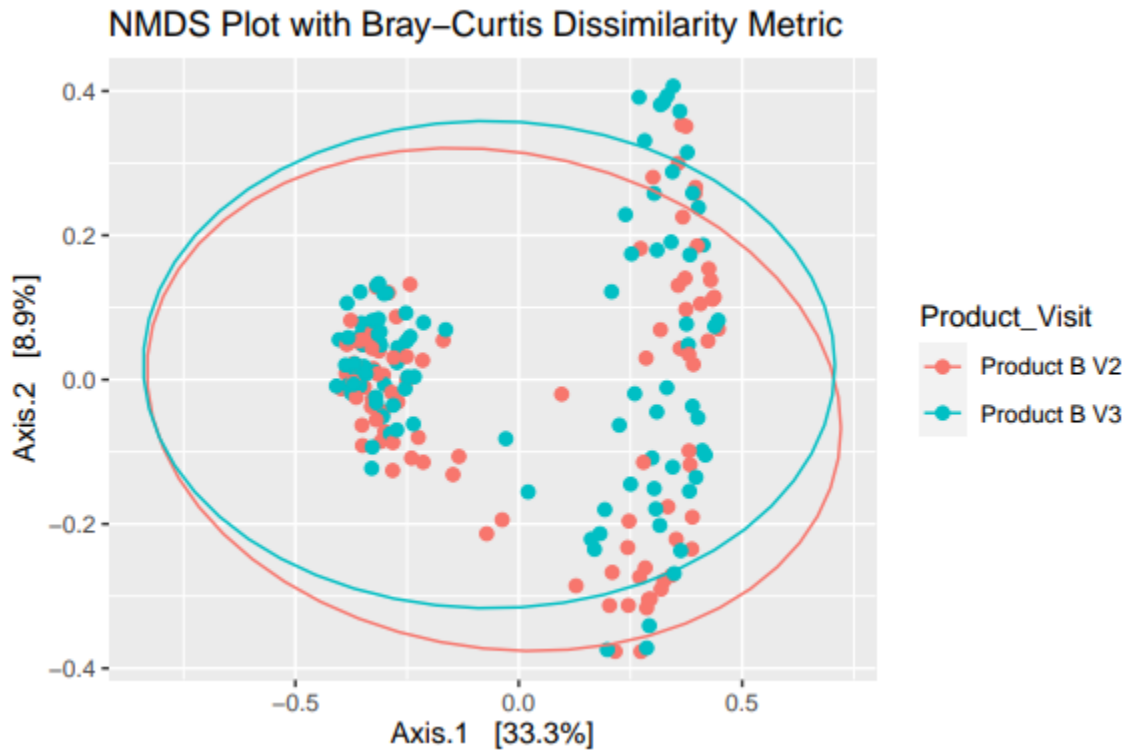


## 2) Alpha diversity



Note: No significant differences

### 3) Beta diversity



Note: Not significant, but p-value = 0.092

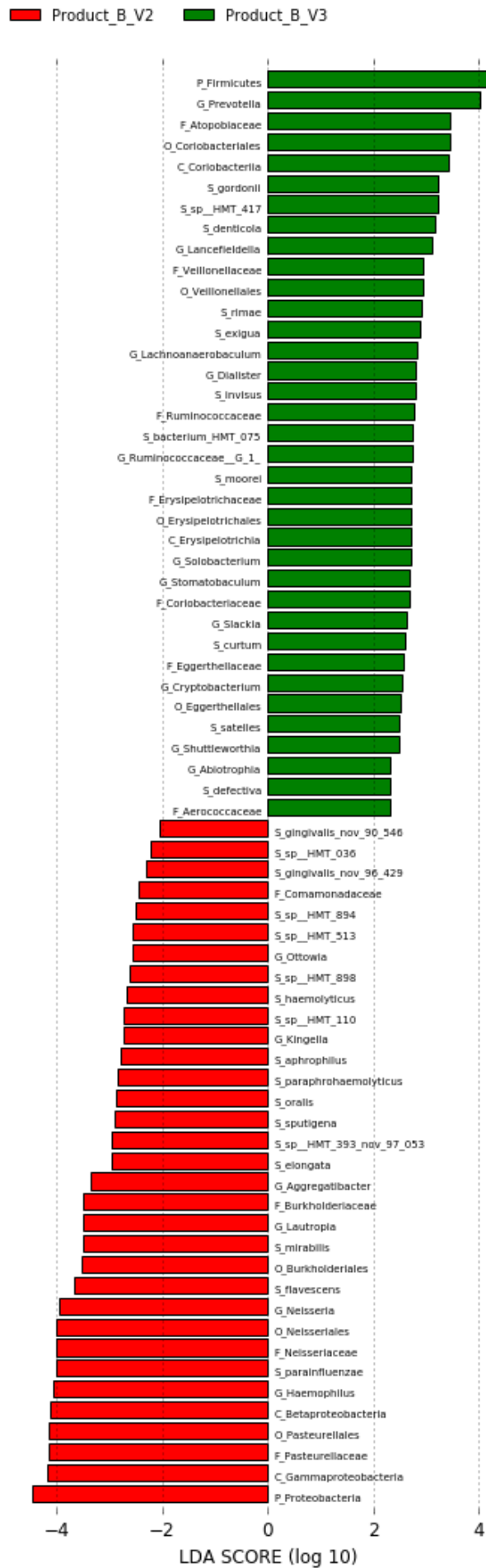
#### 4) Differential abundance

taxon	lfc_(Inter	lfc_Product	se_(Inter	se_Product	W_(Inter	W_Product	p_(Inter	p_Product	q_(Inter	q_Product	diff_(Inter	diff_Produ
Haemophilus parainfluenzae (SP19)	0.690595	-1.44299	0.24132	0.341277	2.861746	-4.2282	0.004213	2.36E-05	1	0.007915	FALSE	TRUE
Neisseria elongata (SP219)	0.544445	-1.15069	0.277129	0.391919	1.964594	-2.93604	0.049461	0.0033243	1	1	FALSE	FALSE
Aggregatibacter sp._HMT_898 (SP119)	0.469888	-1.00158	0.252307	0.356817	1.862362	-2.80698	0.062552	0.00500088	1	1	FALSE	FALSE
Parvimonas sp._HMT_110 (SP129)	0.493371	-1.04854	0.273437	0.386699	1.80433	-2.71152	0.07118	0.0066975	1	1	FALSE	FALSE
Aggregatibacter aphrophilus (SP218)	0.46591	-0.99362	0.260993	0.3691	1.785144	-2.69201	0.074238	0.00710228	1	1	FALSE	FALSE
Kingella oralis (SP198)	0.516574	-1.09495	0.289279	0.409102	1.785732	-2.67647	0.074143	0.00744022	1	1	FALSE	FALSE
Haemophilus sp._HMT_036 (SP93)	0.415446	-0.89269	0.257789	0.364569	1.611572	-2.44862	0.107055	0.01434037	1	1	FALSE	FALSE
Haemophilus haemolyticus (SP104)	0.439591	-0.94098	0.28498	0.403023	1.542532	-2.33481	0.122944	0.01955327	1	1	FALSE	FALSE
Neisseria mucosa (SP300)	0.357056	-0.77591	0.235753	0.333405	1.514534	-2.32723	0.129891	0.01995277	1	1	FALSE	FALSE
Parvimonas sp._HMT_393_nov_97.053% (SPN5)	0.444123	-0.95005	0.290673	0.411073	1.527915	-2.31114	0.126534	0.02082528	1	1	FALSE	FALSE
Ottowia sp._HMT_894 (SP249)	0.342879	-0.74756	0.230588	0.3261	1.486978	-2.29242	0.137021	0.02188156	1	1	FALSE	FALSE
Cryptobacterium curtum (SP465)	-0.41083	0.75985	0.236711	0.334759	-1.73556	2.269839	0.082642	0.02321733	1	1	FALSE	FALSE
Lautropia mirabilis (SP126)	0.429881	-0.92156	0.288663	0.408231	1.489213	-2.25745	0.136431	0.02397996	1	1	FALSE	FALSE
Haemophilus paraphrohaemolyticus (SP388)	0.313912	-0.68962	0.217696	0.307868	1.441977	-2.24	0.149309	0.02509094	1	1	FALSE	FALSE
Capnocytophaga sp._HMT_332 (SP49)	0.309673	-0.68115	0.217057	0.306965	1.426692	-2.21897	0.153669	0.02648847	1	1	FALSE	FALSE
Neisseria flavescens (SP195)	0.527393	-1.11659	0.359985	0.509096	1.465042	-2.19327	0.14291	0.02828764	1	1	FALSE	FALSE
Capnocytophaga gingivalis_nov_96.429% (SP1)	0.330918	-0.72364	0.242085	0.34236	1.366947	-2.11367	0.171642	0.03454372	1	1	FALSE	FALSE
Capnocytophaga sputigena (SP145)	0.385056	-0.83191	0.282738	0.399852	1.361882	-2.08055	0.173235	0.03747507	1	1	FALSE	FALSE
Haemophilus sputorum (SP115)	0.374405	-0.81061	0.275911	0.390197	1.356976	-2.07744	0.174789	0.03776136	1	1	FALSE	FALSE
Capnocytophaga gingivalis_nov_90.546% (SP1)	0.293909	-0.64962	0.221999	0.313955	1.323919	-2.06915	0.18553	0.03853215	1	1	FALSE	FALSE
Prevotella denticola (SP30)	-0.48534	0.908887	0.324308	0.458641	-1.49655	1.981698	0.13451	0.04751303	1	1	FALSE	FALSE
Aggregatibacter sp._HMT_513 (SP184)	0.375687	-0.81317	0.295795	0.418317	1.270094	-1.94392	0.204051	0.05190512	1	1	FALSE	FALSE
Veillonella sp._HMT_780 (SP10)	0.279737	-0.62127	0.229001	0.323856	1.221554	-1.91837	0.221876	0.0550647	1	1	FALSE	FALSE
Neisseria perflava (SP429)	0.460455	-0.98271	0.367454	0.519658	1.253097	-1.89107	0.210171	0.05861488	1	1	FALSE	FALSE
Slackia exigua (SP147)	-0.33619	0.61058	0.235951	0.333686	-1.42483	1.829804	0.154207	0.06727926	1	1	FALSE	FALSE
Shuttleworthia satelles (SP268)	-0.33842	0.615042	0.240466	0.34007	-1.40736	1.808575	0.159321	0.07051698	1	1	FALSE	FALSE
Aggregatibacter sp._HMT_458 (SP102)	0.347493	-0.75679	0.299604	0.423703	1.159843	-1.78612	0.246113	0.0740793	1	1	FALSE	FALSE
Ruminococcaceae_[G-1]_bacterium_HMT_075	-0.40739	0.752979	0.298292	0.421849	-1.36574	1.784948	0.172021	0.07426973	1	1	FALSE	FALSE
Campylobacter showae (SP204)	0.356605	-0.77501	0.311259	0.440186	1.145688	-1.76064	0.251924	0.07829888	1	1	FALSE	FALSE
Streptococcus sp._HMT_056 (SP276)	0.282766	-0.62733	0.257239	0.36379	1.099238	-1.72444	0.271664	0.08462924	1	1	FALSE	FALSE

Note: Red denotes more prevalent in baseline (V2), Green denotes more prevalent after treatment (V3)

5) Lefse

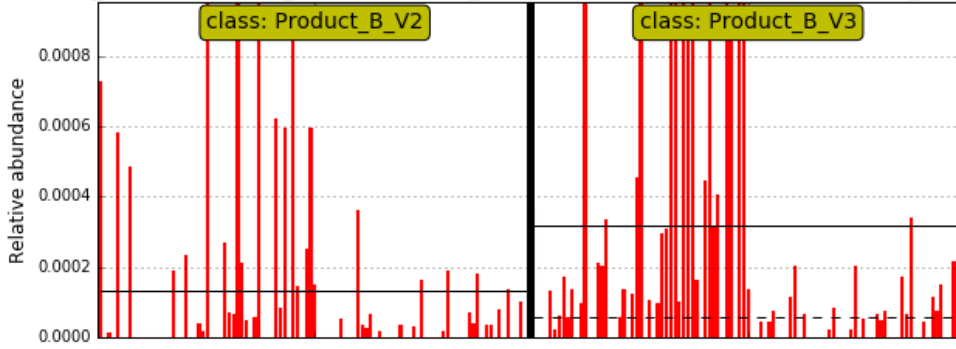
Significantly Represented Taxa





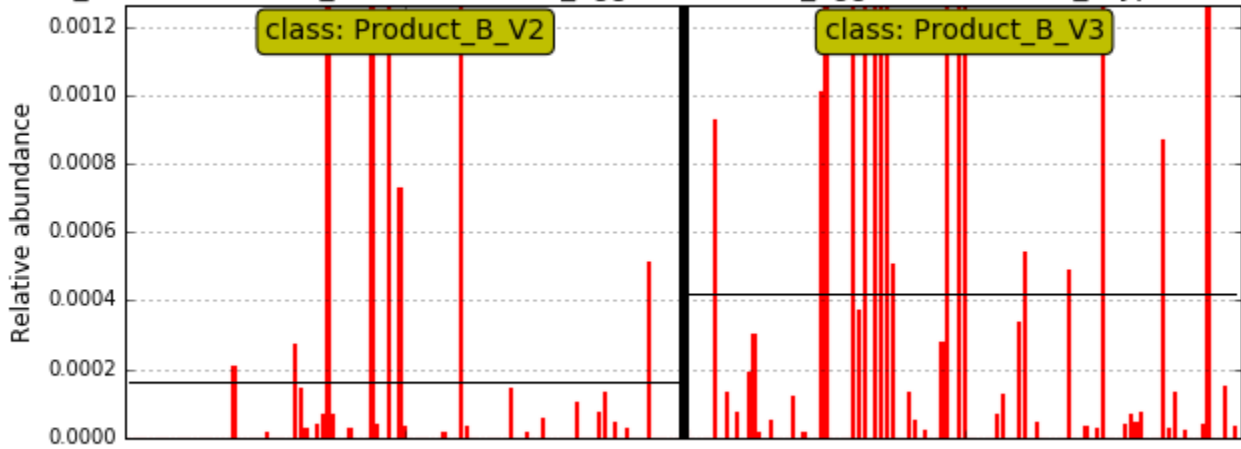
15)

K\_Bacteria.P\_Actinobacteria.C\_Coriobacteriia.O\_Coriobacteriales.F\_Coriobacteriaceae.G\_Slackia.S\_exig

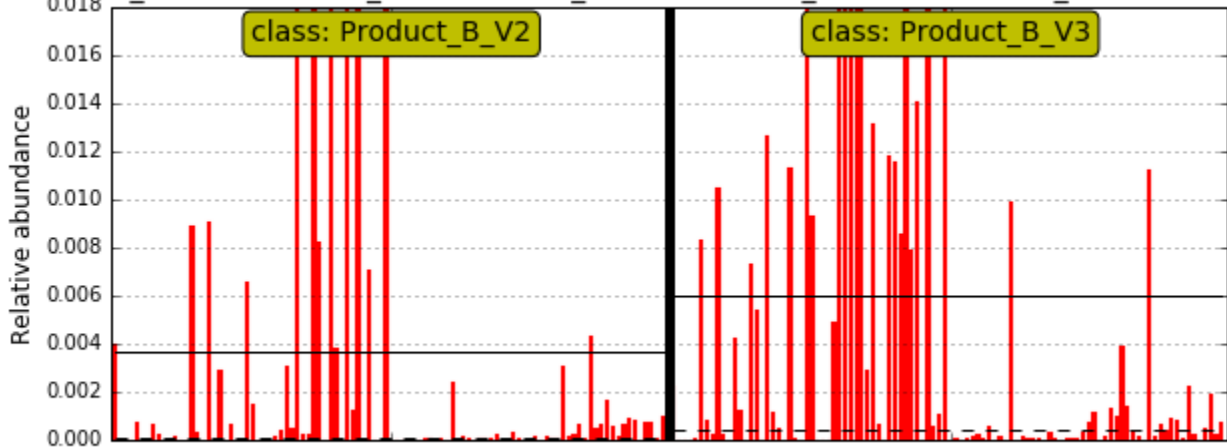


Health associated

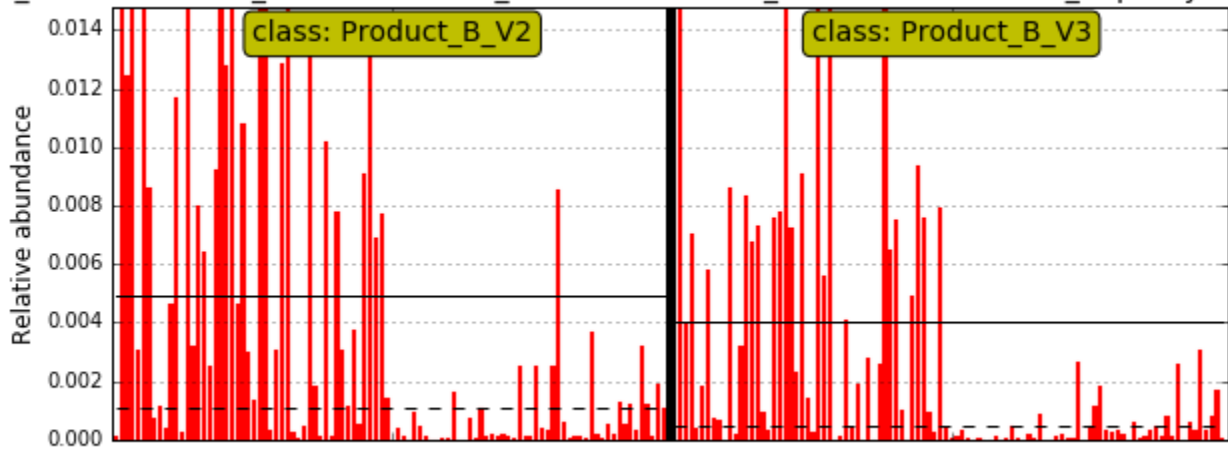
K\_Bacteria.P\_Actinobacteria.C\_Coriobacteriia.O\_Eggerthellales.F\_Eggerthellaceae.G\_Cryptobacterium.S\_c



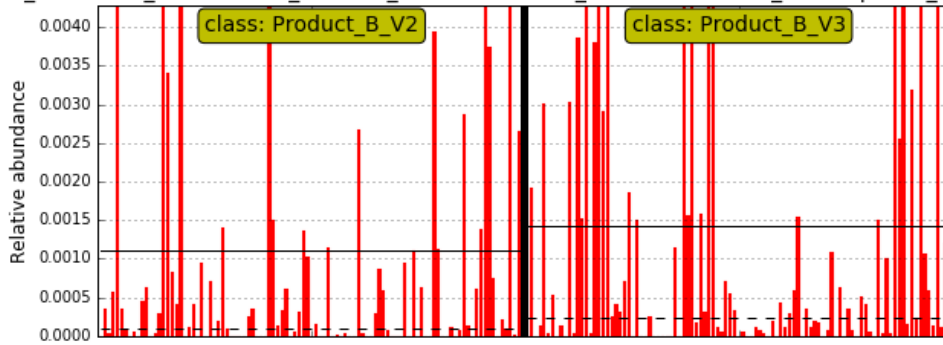
K\_Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Prevotella.S\_denticola



eria.P\_Bacteroidetes.C\_Flavobacteriia.O\_Flavobacteriales.F\_Flavobacteriaceae.G\_Capnocytophaga.S\_s

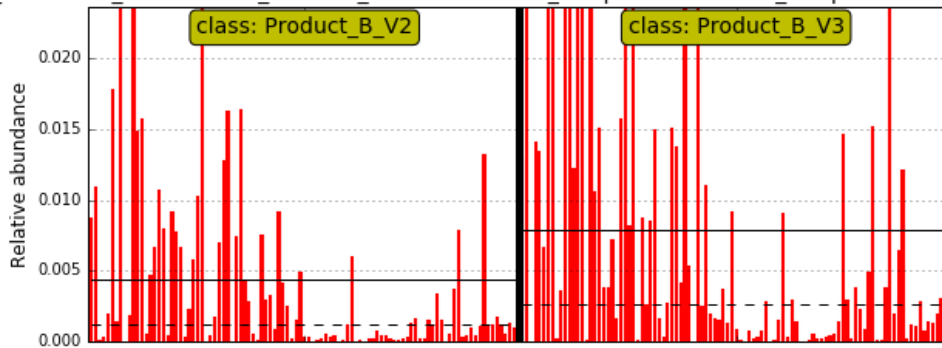


K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Aerococcaceae.G\_Abiotrophia.S\_defectiva



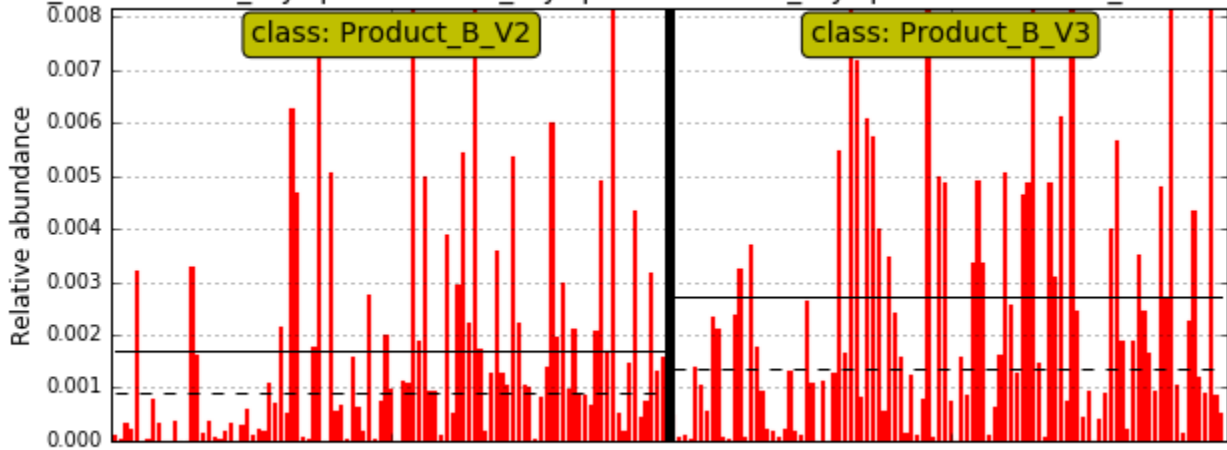
Health associated

K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Streptococcaceae.G\_Streptococcus.S\_gordonii

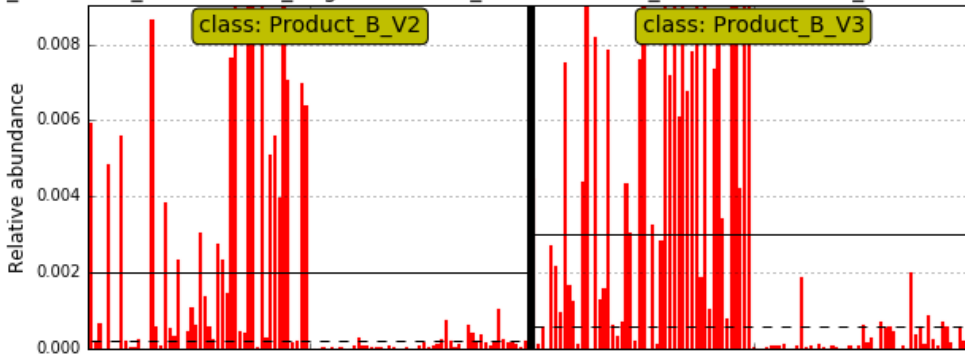


health-associated

acteria.P\_Firmicutes.C\_Erysipelotrichia.O\_Erysipelotrichales.F\_Erysipelotrichaceae.G\_Solobacterium.S\_I

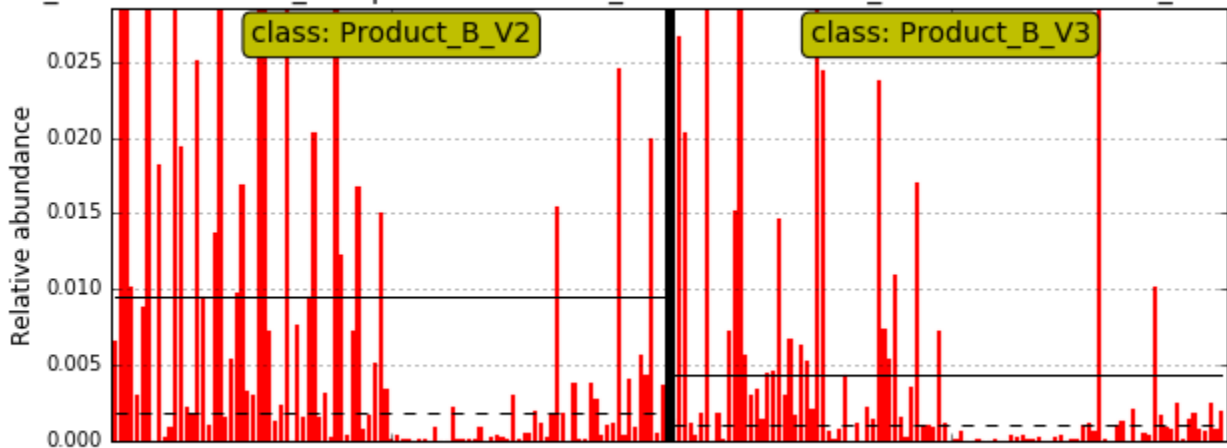


K\_Bacteria.P\_Firmicutes.C\_Negativicutes.O\_Veillonellales.F\_Veillonellaceae.G\_Dialister.S\_invisus

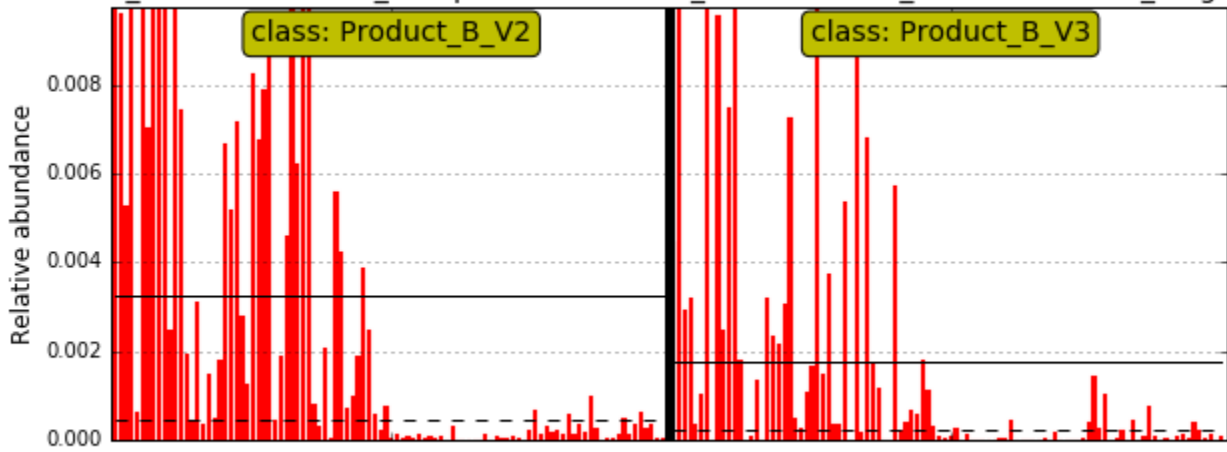


Note: This is considered as a periodontal pathogen

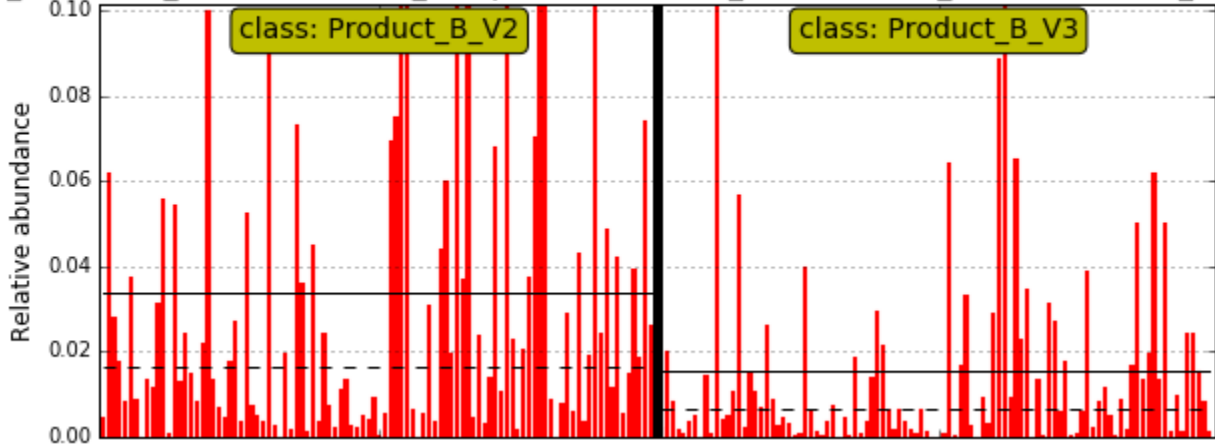
acteria.P\_Proteobacteria.C\_Betaproteobacteria.O\_Burkholderiales.F\_Burkholderiaceae.G\_Lautropia.S\_m



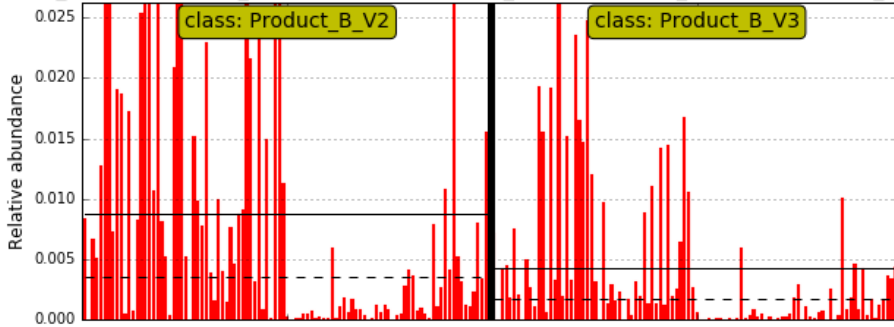
K\_Bacteria.P\_Proteobacteria.C\_Betaproteobacteria.O\_Neisseriales.F\_Neisseriaceae.G\_Kingella.S\_orali



K\_Bacteria.P\_Proteobacteria.C\_Betaproteobacteria.O\_Neisseriales.F\_Neisseriaceae.G\_Neis

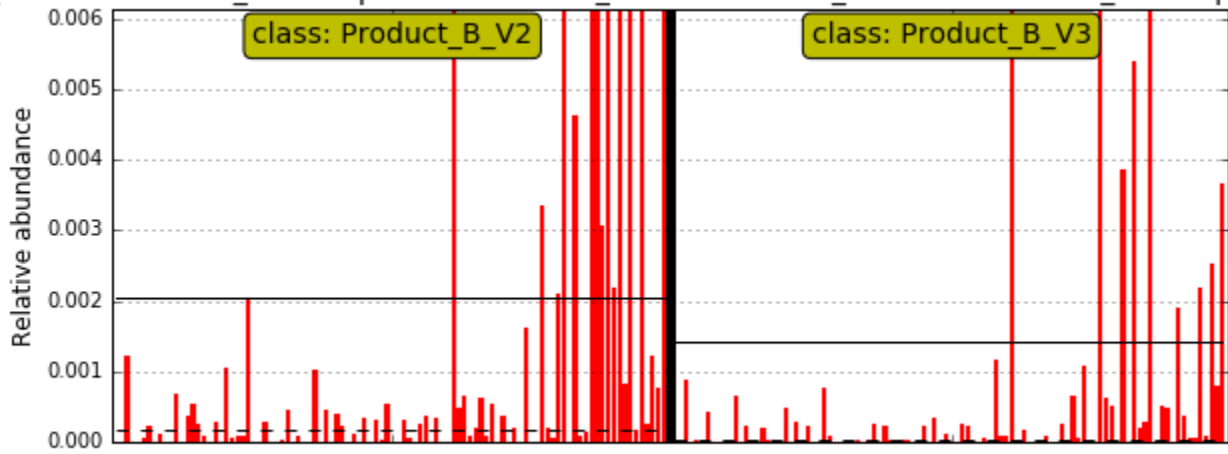


Bacteria.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Aggregatibacter

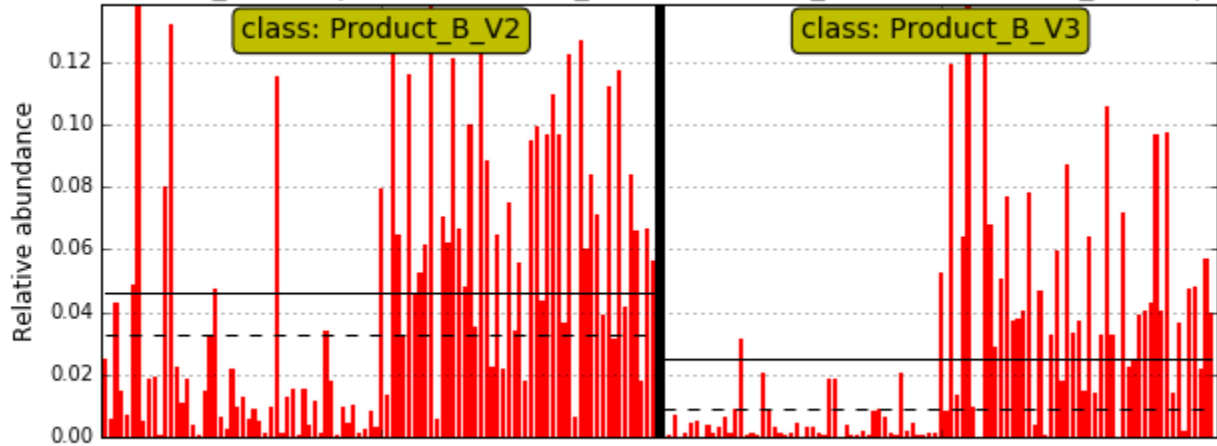


Note: Considered as a putative pathogen.

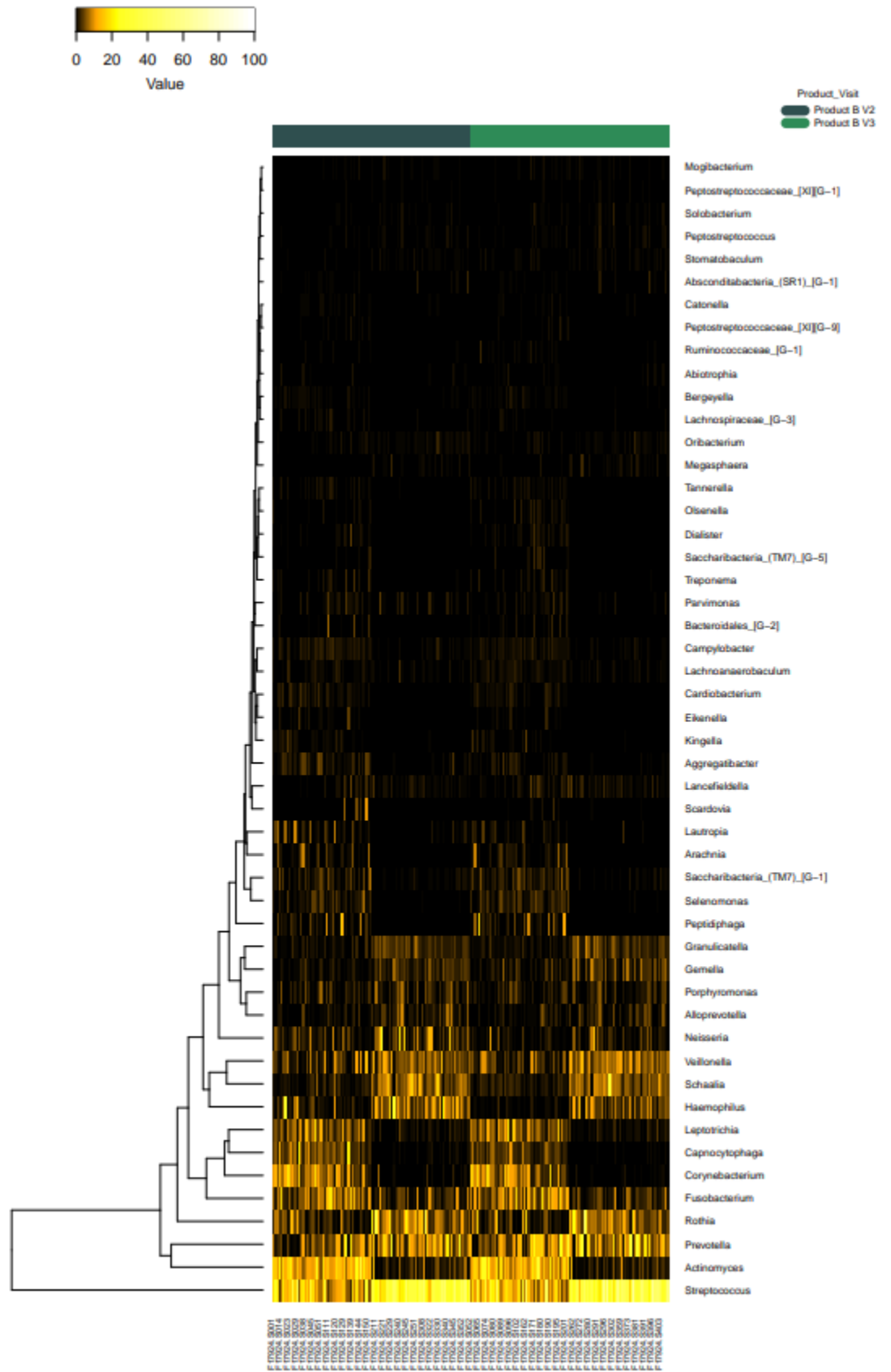
ia.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Haemophilus.S\_ha

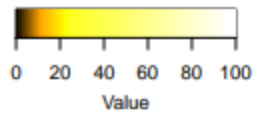


a.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Haemophilus.S\_par



## 6) Heat maps





Product\_Visit  
 Product B V2  
 Product B V3

- Cardiobacterium hominis*
- Campylobacter showae*
- Leptotrichia* sp.\_HMT\_212
- Selenomonas roxia*
- Schaalia* sp.\_HMT\_178
- Leptotrichia* sp.\_HMT\_215
- Kingella oralis*
- Aggregatibacter* sp.\_HMT\_458
- Leptotrichia hofstadii*
- Streptococcus cristatus*\_clade\_578
- Lancefieldella rimae*
- Dialister invisus*
- Fusobacterium nucleatum\_nucleatum\_subsp\_animalis*
- Fusobacterium nucleatum\_subsp\_animalis*
- Actinomyces* sp.\_HMT\_525
- Saccharibacteria* (TM7)\_JG-1 bacterium\_HMT\_348
- Prevotella* sp.\_HMT\_317
- Leptotrichia buccalis*
- Streptococcus gordonii*
- Gemella morbillorum*
- Capnocytophaga sputigena*
- Actinomyces* sp.\_HMT\_170
- Leptotrichia hongkongensis*
- Streptococcus mutans*
- Prevotella nanosensis*
- Prevotella pallens*
- Alloprevotella* sp.\_HMT\_308
- Streptococcus infantis*\_clade\_431
- Alloprevotella* sp.\_HMT\_473
- Streptococcus* sp.\_HMT\_074
- Veillonella denticariosi*\_dispar\_parvula
- Streptococcus parasanguinis*\_parasanguinis\_clade\_721
- Lancefieldella parvula*
- Prevotella salivae*
- Schaalia linguae* [Not\_Validly\_Published]
- Veillonella dispar*
- Veillonella parvula*
- Streptococcus oralis\_subsp\_dentisarii*\_clade\_058
- Leptotrichia* sp.\_HMT\_417
- Capnocytophaga granulosa*
- Neisseria elongata*
- Capnocytophaga gingivalis*
- Capnocytophaga leadbetteri*
- Leptotrichia* sp.\_HMT\_392
- Actinomyces oris*
- Leptotrichia* sp.\_HMT\_225
- Prevotella oris*
- Prevotella denticola*
- Actinomyces israelii*
- Peptidiphaga gingivicola*
- Leptotrichia vesicola*
- Actinomyces* sp.\_HMT\_448
- Prevotella nigrescens*
- Actinomyces dentalis*
- Schaalia odontolyticus*
- Streptococcus* sp.\_HMT\_066
- Streptococcus chosunensis*
- Gemella haemolyticus*
- Prevotella intermedia*
- Actinomyces* sp.\_HMT\_169
- Actinomyces* sp.\_HMT\_175
- Actinomyces naeslundii*
- Lautropia mirabilis*
- Rothia aerea*
- Corynebacterium durum*
- Actinomyces massiliensis*
- Anaerobaculum propionicum*
- Streptococcus oralis*
- Rothia dentocariosa*
- Streptococcus* sp.\_HMT\_064
- Actinomyces* sp.\_HMT\_171
- Streptococcus oralis\_subsp\_figurinus*\_clade\_071
- Peptidiphaga* sp.\_HMT\_183
- Veillonella dispar*\_parvula
- Gemella sanguinis*
- Veillonella rogosae*
- Streptococcus australis*
- Schaalia odontolyticus*
- Fusobacterium periodonticum*
- Porphyromonas pasteri*
- Granulicatella adiacens*
- Streptococcus infantis*\_infantis\_clade\_638
- Streptococcus downii*
- Neisseria perflava*
- Schaalia* sp.\_HMT\_180
- Neisseria flavescens*
- Streptococcus sanguinis*
- Streptococcus* sp.\_HMT\_423
- Prevotella histicola*
- Veillonella atypica*
- Actinomyces graevenitzii*
- Schaalia* sp.\_HMT\_172
- Streptococcus parasanguinis*\_clade\_411
- Prevotella melaninogenica*
- Haemophilus parainfluenzae*
- Streptococcus mitis*
- Corynebacterium matruchoti*
- Fusobacterium nucleatum*
- Rothia mucilaginosa*
- Streptococcus salivarius*

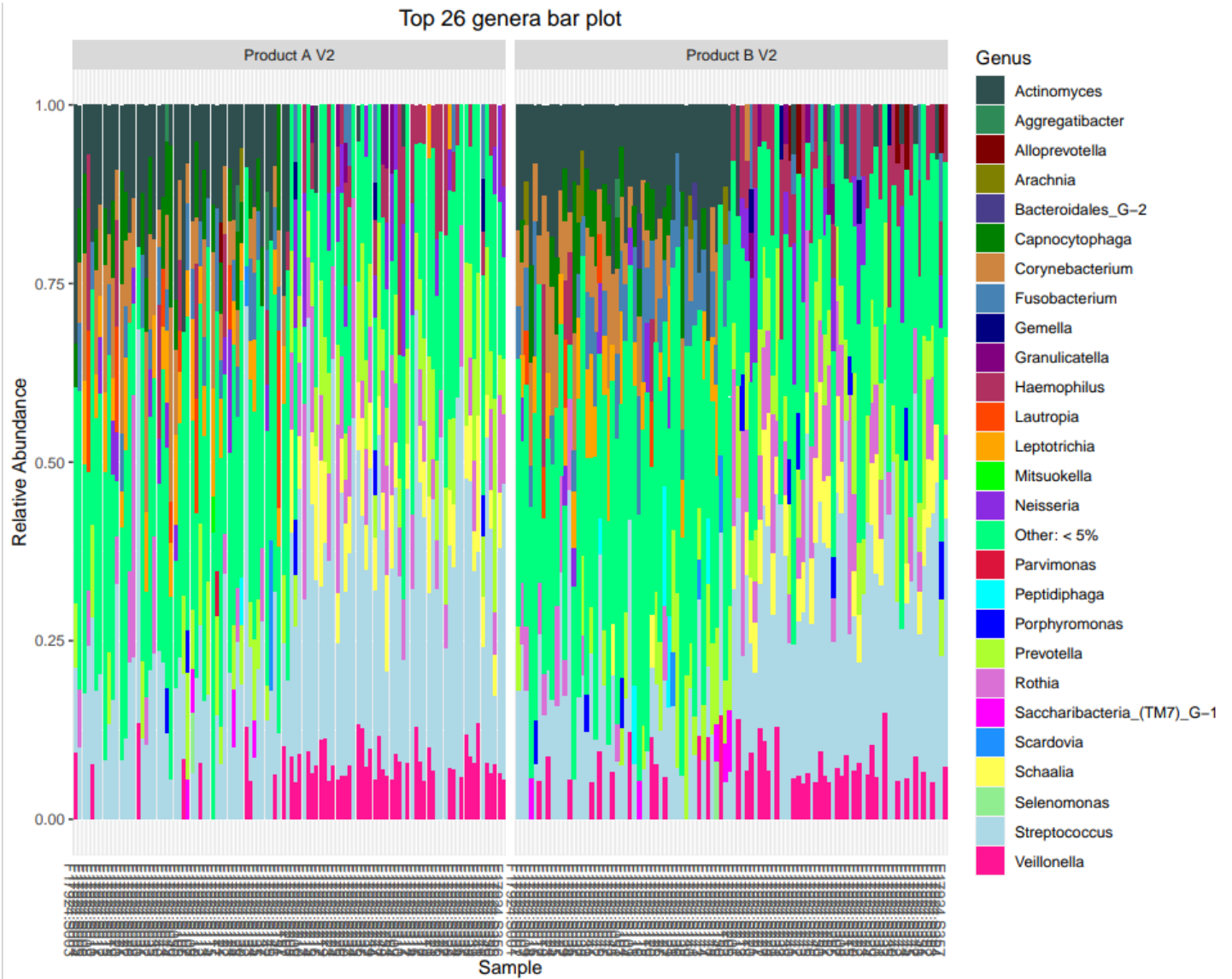
Species

- F\_17026\_02014
- F\_17026\_02023
- F\_17026\_02029
- F\_17026\_02040
- F\_17026\_02049
- F\_17026\_02111
- F\_17026\_02120
- F\_17026\_02139
- F\_17026\_02146
- F\_17026\_02171
- F\_17026\_02240
- F\_17026\_02254
- F\_17026\_02261
- F\_17026\_02270
- F\_17026\_02300
- F\_17026\_02345
- F\_17026\_02352
- F\_17026\_02365
- F\_17026\_02394
- F\_17026\_02402
- F\_17026\_02412
- F\_17026\_02471
- F\_17026\_02475
- F\_17026\_02485
- F\_17026\_02501
- F\_17026\_02509
- F\_17026\_02511
- F\_17026\_02541

Samples

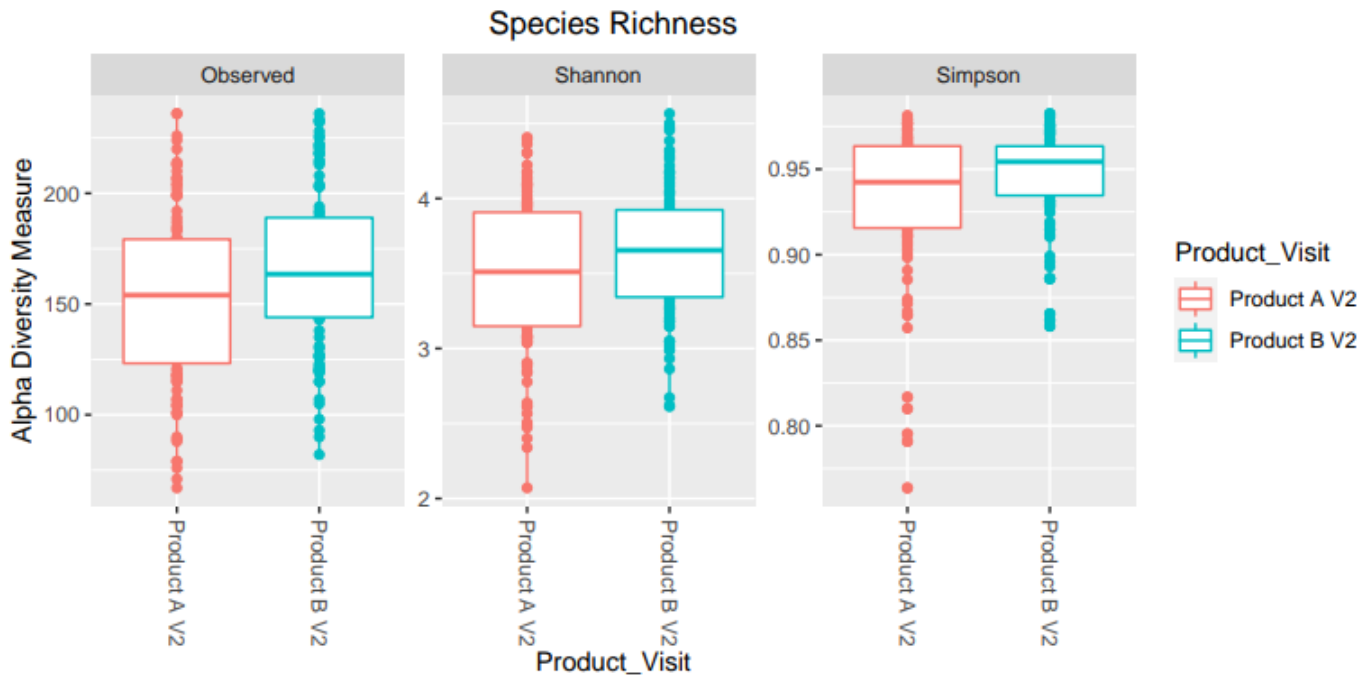
# Comparison 3 Product A V2 vs Product B V2

## 1) Taxonomy barplots



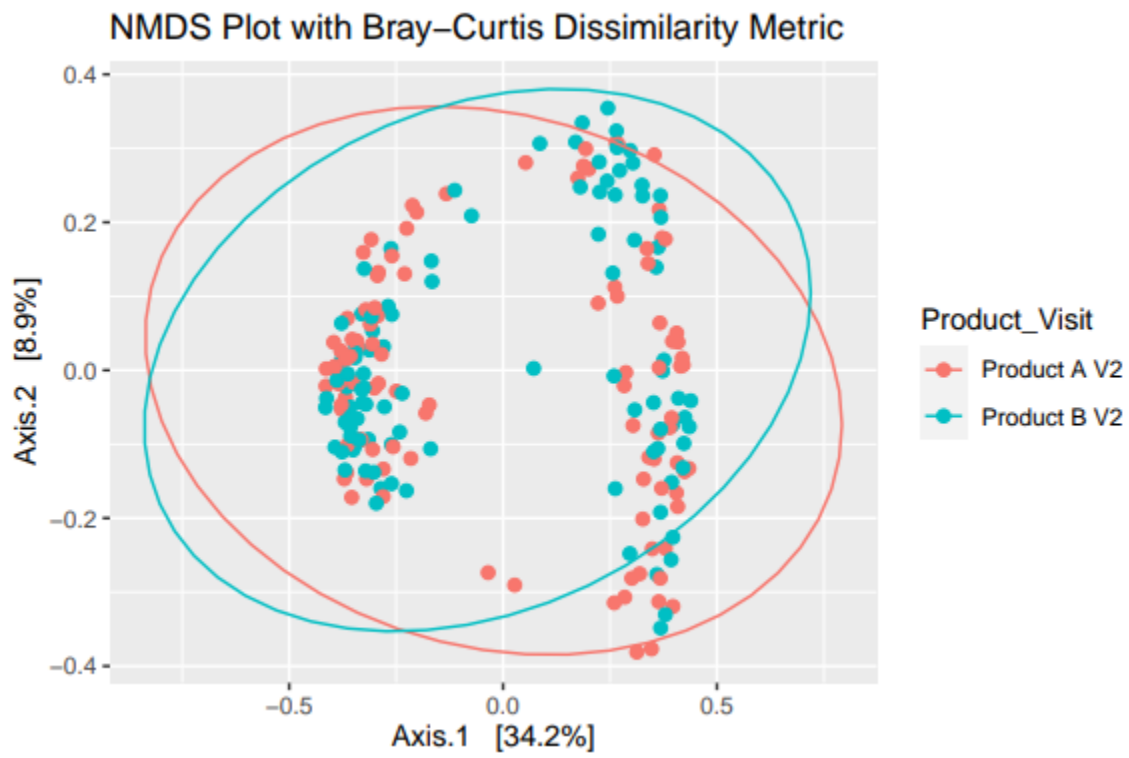


## 2) Alpha diversity



Note: Significant differences—indicates that the populations were different microbiologically at baseline. Observed  $p= 0.027$ ; Shannon  $p= 0.049$ ; Simpson  $p= 0.034$

### 3) Beta diversity



Note: No significant differences

#### 4) Differential abundance

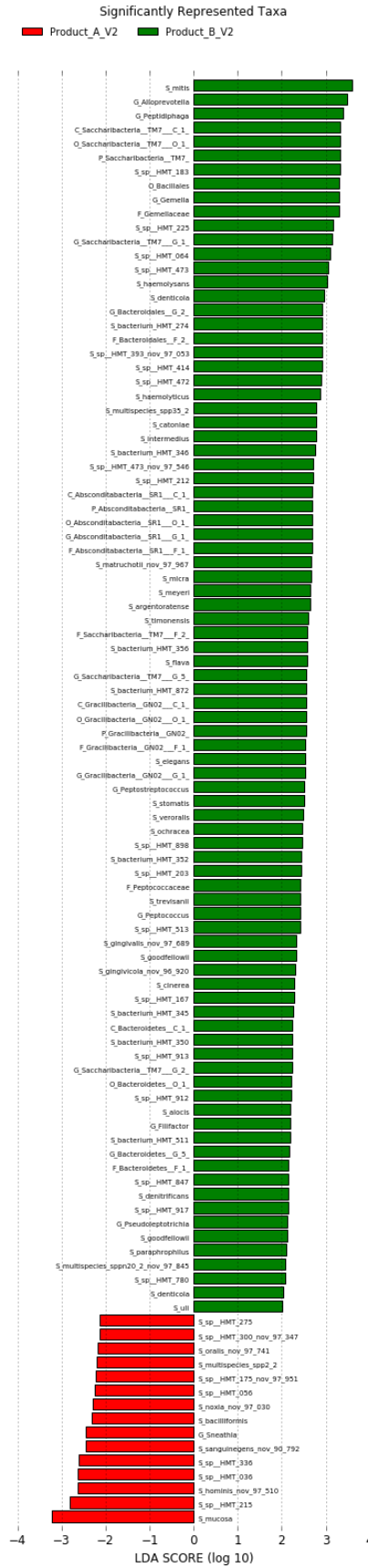
taxon	lfc_(Interco	lfc_Product	se_(Interco	se_Product	W_(Interco	W_Product	p_(Interco	p_Product	q_(Interco	q_Product	diff_(Inter	diff_Produ
Kingella oralis_nov_97.741% (SPN664)	0.542611	-1.07661	0.19976	0.285941	2.71632	-3.76516	0.006601	0.000166	1	0.056424	FALSE	FALSE
Prevotella veroralis (SP110)	-0.59947	1.253221	0.236726	0.338729	-2.53232	3.699773	0.011331	0.000216	1	0.072938	FALSE	FALSE
Absconditabacteria_(SR1)_[G-1] bacterium	-0.46492	0.978755	0.231752	0.331627	-2.00612	2.951374	0.044843	0.003164	1	1	FALSE	FALSE
Neisseria bacilliformis (SP447)	0.449633	-0.88694	0.211734	0.303041	2.123578	-2.92679	0.033705	0.003425	1	1	FALSE	FALSE
Veillonella sp._HMT_780 (SP10)	-0.39729	0.84078	0.203799	0.29171	-1.94941	2.882246	0.051246	0.003949	1	1	FALSE	FALSE
Fusobacterium nucleatum_nucleatum_sub	-0.56237	1.177541	0.287566	0.411326	-1.95561	2.862792	0.050511	0.004199	1	1	FALSE	FALSE
Porphyromonas sp._HMT_275 (SP363)	0.430805	-0.84853	0.208508	0.298434	2.066134	-2.84327	0.038816	0.004465	1	1	FALSE	FALSE
Granulicatella elegans (SP138)	-0.48394	1.017559	0.255445	0.365459	-1.89452	2.784332	0.058156	0.005364	1	1	FALSE	FALSE
Neisseria mucosa (SP300)	0.582621	-1.15823	0.294049	0.420584	1.981372	-2.75387	0.04755	0.005889	1	1	FALSE	FALSE
Selenomonas noxia_nov_97.030% (SPN548)	0.398997	-0.78364	0.200775	0.287392	1.987278	-2.72673	0.046892	0.006396	1	1	FALSE	FALSE
Actinomyces sp._HMT_175_nov_97.951% (S	0.481454	-0.95185	0.244789	0.350243	1.966813	-2.71769	0.049205	0.006574	1	1	FALSE	FALSE
Alloprevotella sp._HMT_473 (SP132)	-0.54015	1.13221	0.295684	0.422918	-1.82677	2.677137	0.067735	0.007425	1	1	FALSE	FALSE
Selenomonas sp._HMT_892_nov_97.041% (S	0.33624	-0.65562	0.173692	0.248707	1.935841	-2.6361	0.052887	0.008386	1	1	FALSE	FALSE
Haemophilus haemolyticus (SP104)	-0.48295	1.015524	0.269626	0.385709	-1.79117	2.632872	0.073266	0.008467	1	1	FALSE	FALSE
Capnocytophaga sp._HMT_336 (SP51)	0.545218	-1.08193	0.288865	0.413181	1.887449	-2.61854	0.0591	0.008831	1	1	FALSE	FALSE
Gemella haemolysans (SP8)	-0.45978	0.968266	0.260379	0.372506	-1.76581	2.599334	0.077427	0.00934	1	1	FALSE	FALSE
Aggregatibacter sp._HMT_512 (SP314)	0.356836	-0.69763	0.193331	0.27676	1.84572	-2.52071	0.064933	0.011712	1	1	FALSE	FALSE
Leptotrichia sp._HMT_212 (SP146)	-0.48752	1.024854	0.296804	0.424517	-1.64257	2.414165	0.100472	0.015771	1	1	FALSE	FALSE
Prevotella sp._HMT_300_nov_97.347% (SPN	0.399038	-0.78373	0.227028	0.324881	1.757662	-2.41235	0.078805	0.01585	1	1	FALSE	FALSE
Streptococcus sp._HMT_056 (SP276)	0.452148	-0.89207	0.263962	0.377622	1.712928	-2.36234	0.086726	0.01816	1	1	FALSE	FALSE
Cardiobacterium hominis_nov_97.510% (S	0.43643	-0.86001	0.255163	0.365057	1.710398	-2.35581	0.087192	0.018482	1	1	FALSE	FALSE
Leptotrichia sp._HMT_215 (SP11)	0.451204	-0.89014	0.276998	0.396236	1.628906	-2.2465	0.103333	0.024672	1	1	FALSE	FALSE
Capnocytophaga sp._HMT_863 (SP275)	0.309173	-0.6004	0.188866	0.270383	1.636992	-2.22055	0.101632	0.026381	1	1	FALSE	FALSE
Leptotrichia sp._HMT_225 (SP285)	-0.44445	0.936999	0.295794	0.423075	-1.50258	2.214736	0.132947	0.026778	1	1	FALSE	FALSE
Aggregatibacter sp._HMT_513 (SP184)	-0.44072	0.929381	0.294385	0.421064	-1.49709	2.207223	0.134371	0.027299	1	1	FALSE	FALSE
Peptidiphaga sp._HMT_183 (SP149)	-0.4801	1.009718	0.329107	0.470645	-1.4588	2.145392	0.14462	0.031922	1	1	FALSE	FALSE
Actinomyces sp._HMT_169 (SP239)	0.407664	-0.80132	0.268832	0.384575	1.516426	-2.08366	0.129412	0.037192	1	1	FALSE	FALSE
Bacteroidales_[G-2] bacterium_HMT_274 (S	-0.38878	0.823415	0.279391	0.399654	-1.39151	2.060322	0.164071	0.039368	1	1	FALSE	FALSE
Streptococcus sp._HMT_064 (SP305)	-0.38335	0.812346	0.288381	0.41249	-1.32932	1.969373	0.183743	0.04891	1	1	FALSE	FALSE
Peptostreptococcus stomatis (SP92)	-0.38397	0.813613	0.293946	0.420436	-1.30626	1.935164	0.191463	0.05297	1	1	FALSE	FALSE
Streptococcus constellatus (SP139)	0.346316	-0.67617	0.24788	0.354657	1.397112	-1.90655	0.16238	0.056579	1	1	FALSE	FALSE
Streptococcus salivarius (SP135)	0.496296	-0.98213	0.360868	0.516	1.375285	-1.90336	0.169043	0.056994	1	1	FALSE	FALSE
Streptococcus mitis (SP86)	-0.32216	0.687511	0.253455	0.362617	-1.27106	1.895969	0.203707	0.057964	1	1	FALSE	FALSE
Fusobacterium sp._HMT_204 (SP392)	0.391589	-0.76853	0.298122	0.426399	1.31352	-1.80237	0.189008	0.071487	1	1	FALSE	FALSE

Note: Many differences. It indicates that the 2 subject populations were not similar at baseline.

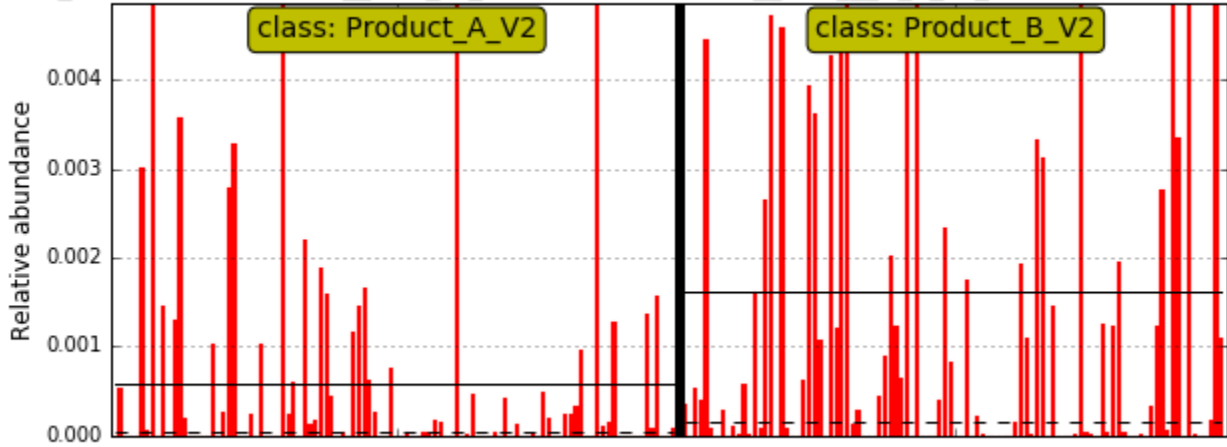
Red, more prevalent in B at baseline

Green, more prevalent in A at baseline

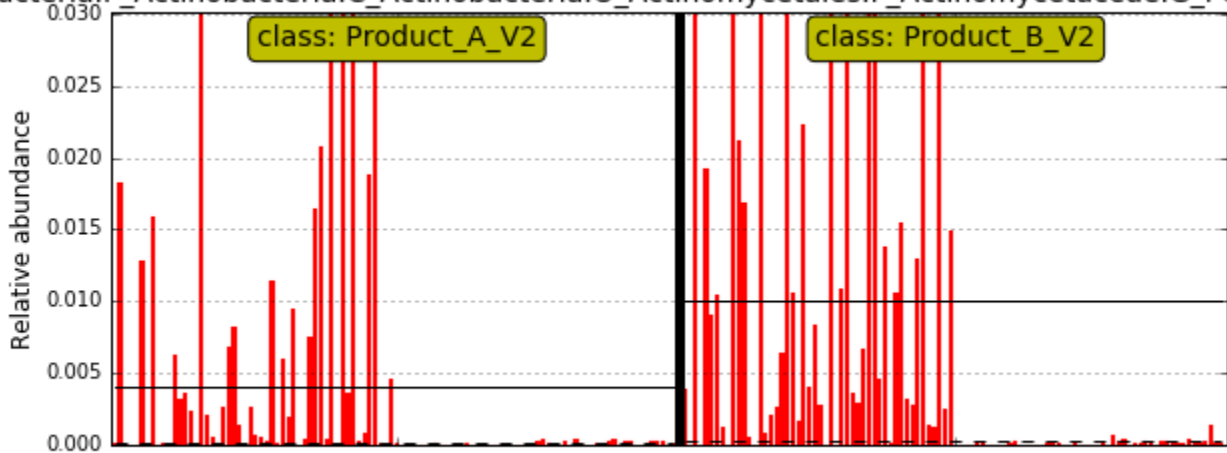
### 5) Lefse—Many differences



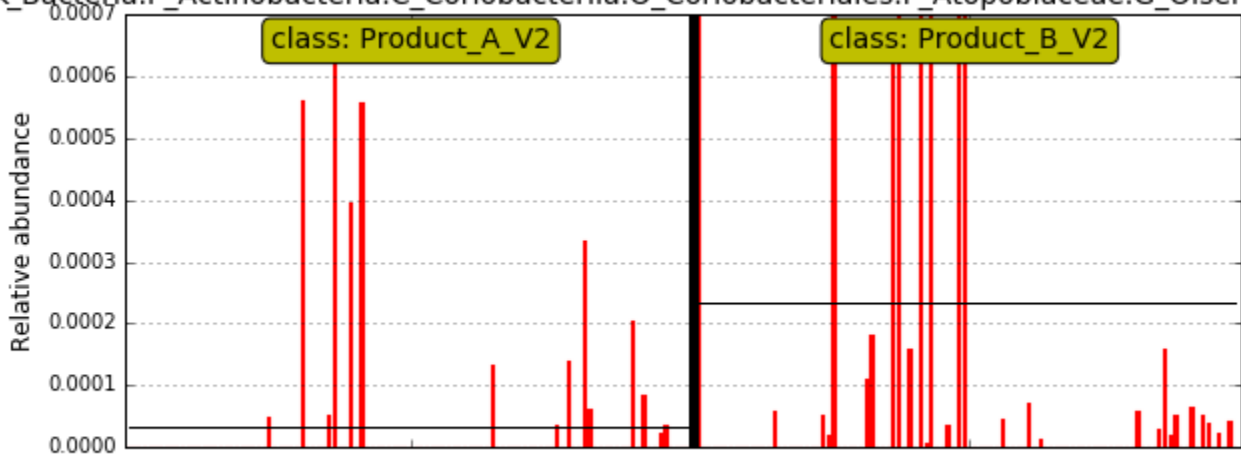
acteria.P\_Absconditabacteria\_SR1\_C\_Absconditabacteria\_SR1\_C\_1\_O\_Absconditabacteria\_SR1\_



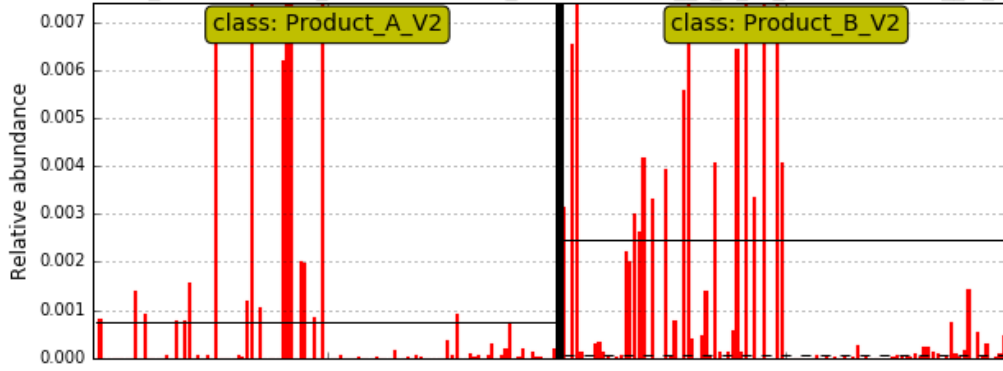
K\_Bacteria.P\_Actinobacteria.C\_Actinobacteria.O\_Actinomycetales.F\_Actinomycetaceae.G\_Peptidiphag



K\_Bacteria.P\_Actinobacteria.C\_Coriobacteriia.O\_Coriobacteriales.F\_Atopobiaceae.G\_Olsenella.S\_uli

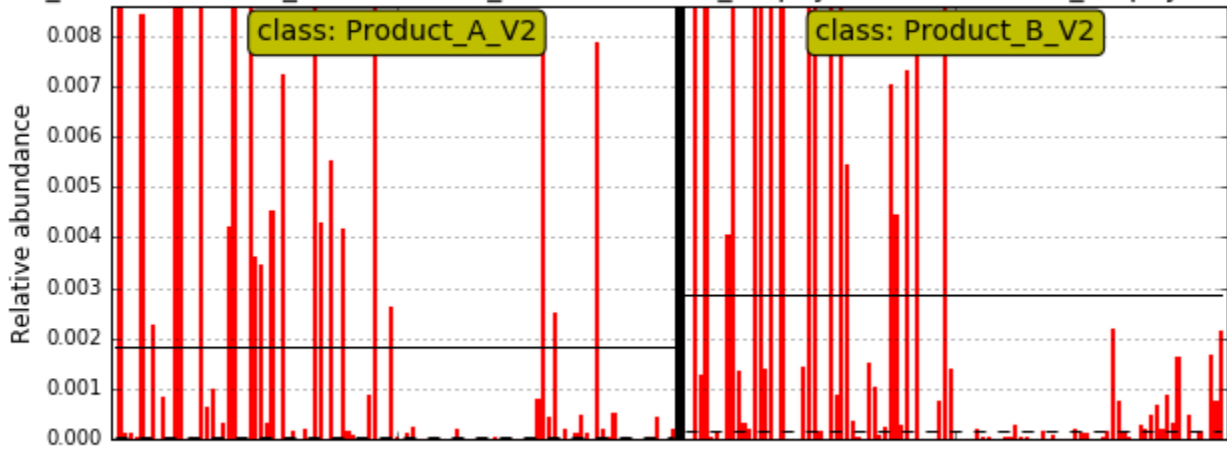


D\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Bacteroidales\_F\_2\_G\_Bacteroidales\_G\_2\_S\_bacter

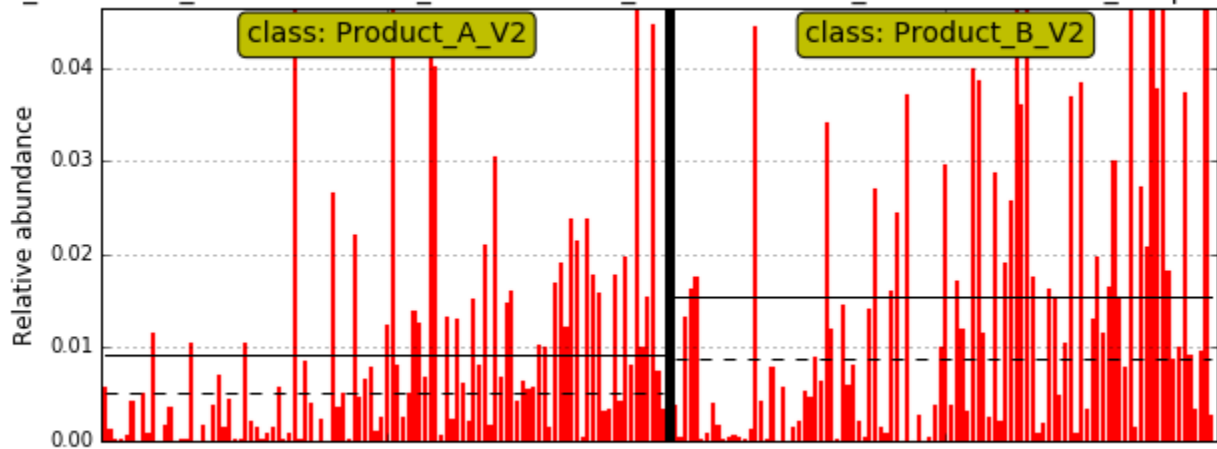


HMT274

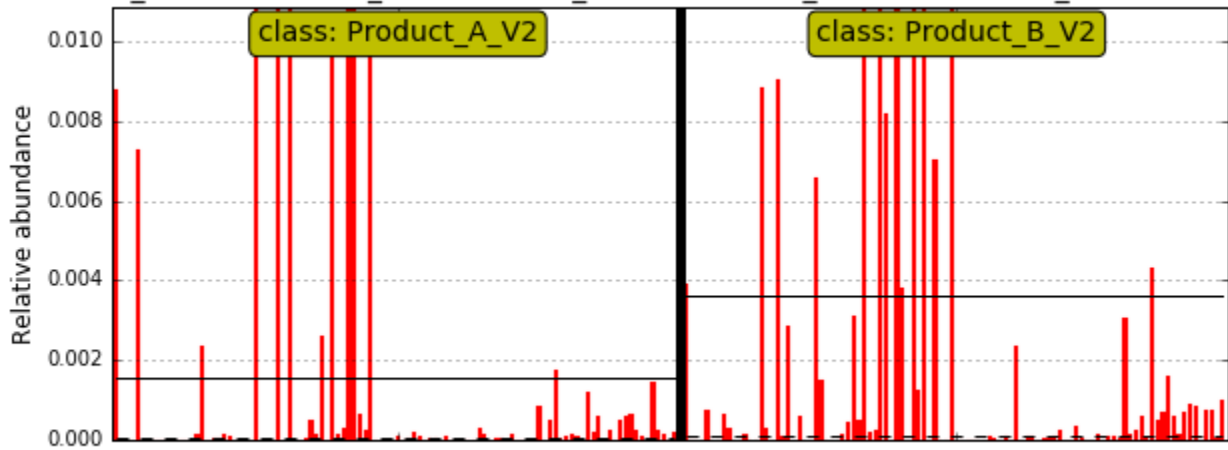
acteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Porphyrmonadaceae.G\_Porphyrmonas.S\_ca



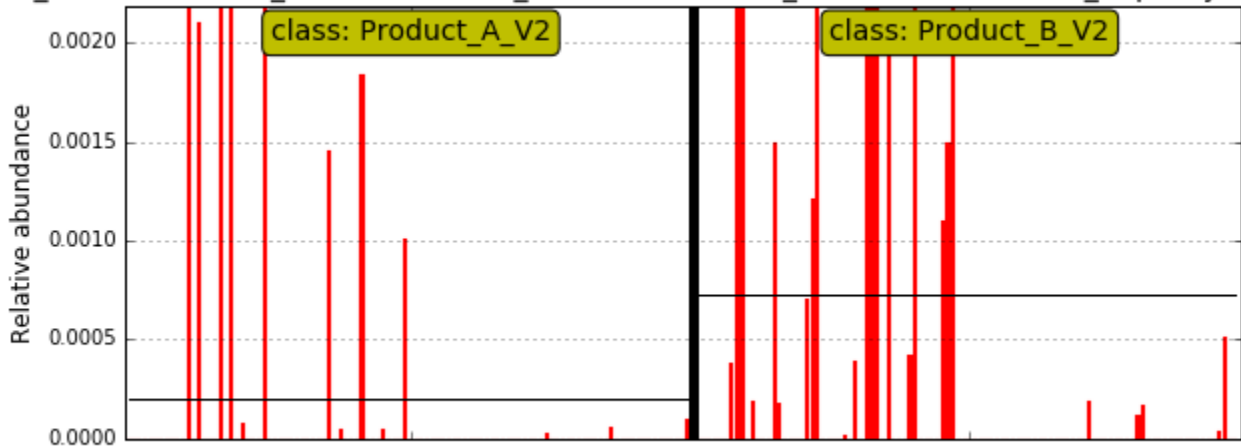
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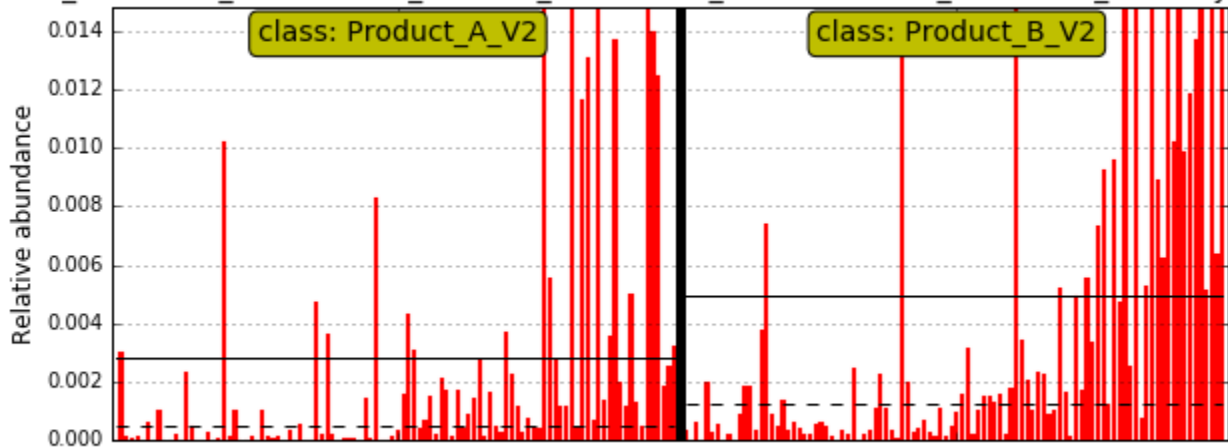
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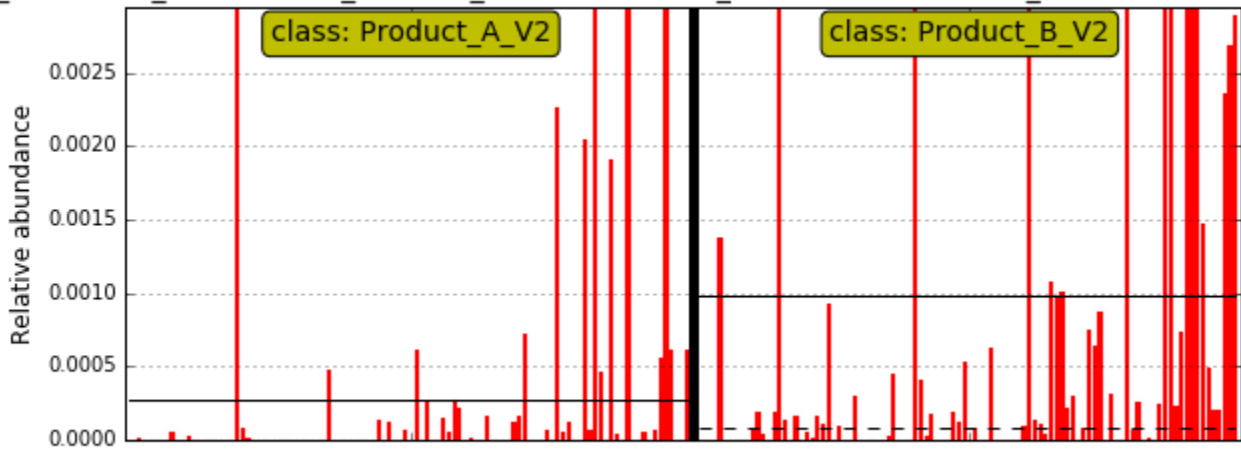
teria.P\_Bacteroidetes.C\_Flavobacteriia.O\_Flavobacteriales.F\_Flavobacteriaceae.G\_Capnocytophaga.S\_c



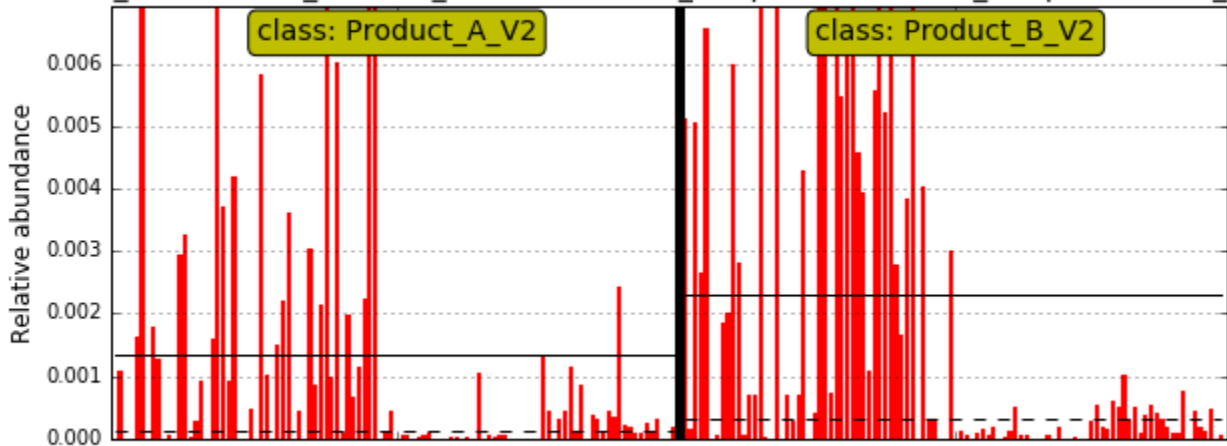
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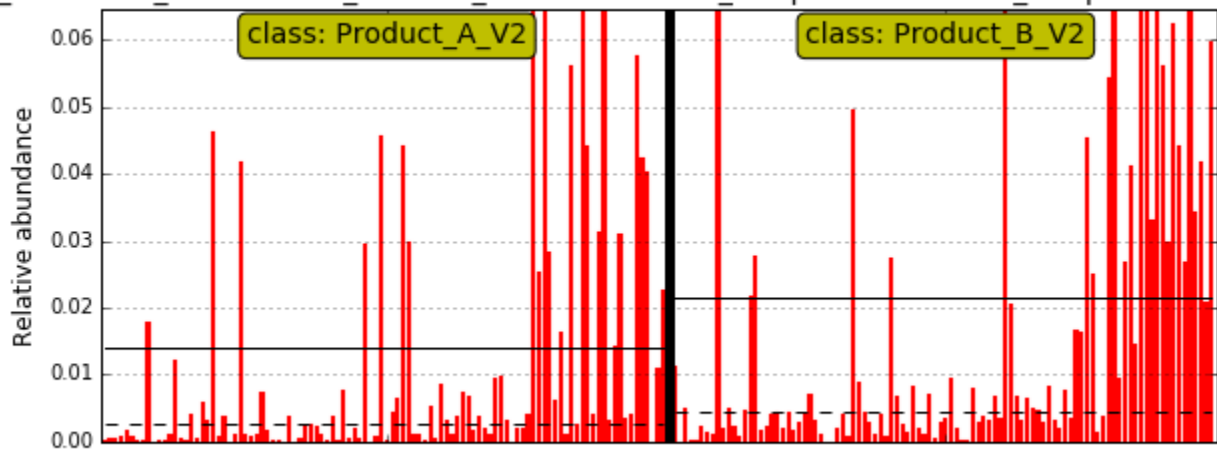
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Carnobacteriaceae.G\_Granulicatella.S\_elegans



K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Streptococcaceae.G\_Streptococcus.S\_intermedi

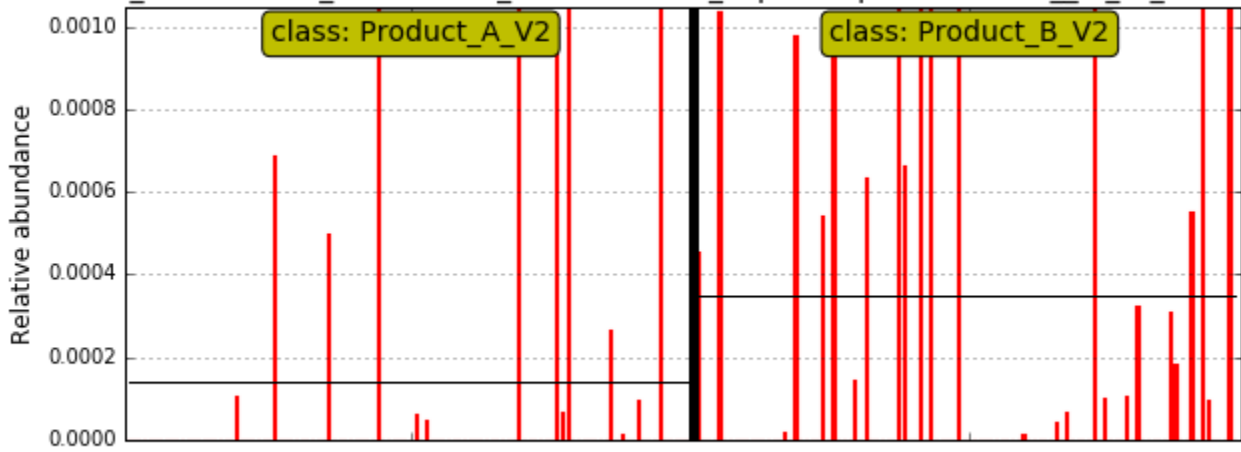


K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Streptococcaceae.G\_Streptococcus.S\_mitis

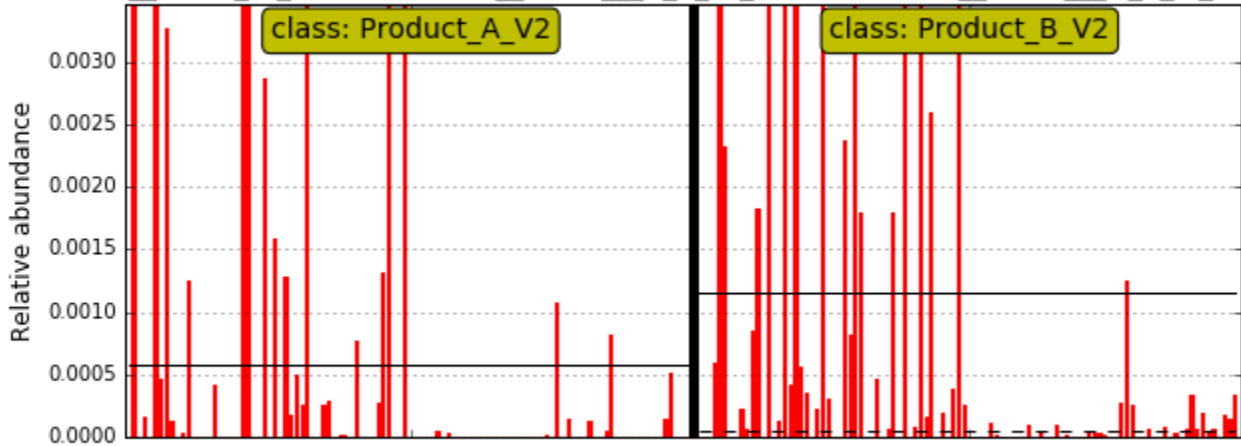




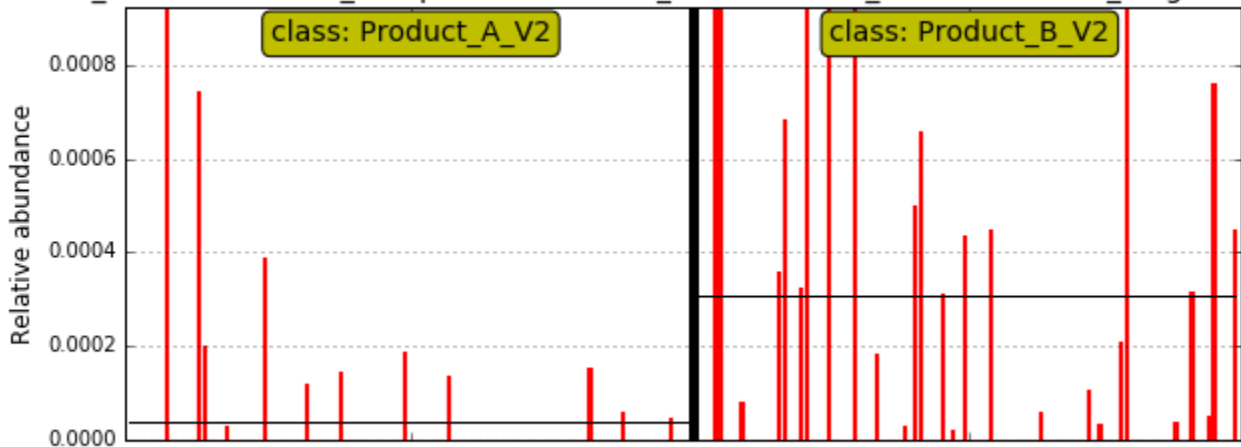
K\_Bacteria.P\_Firmicutes.C\_Clostridia.O\_Clostridiales.F\_Peptostreptococcaceae\_XI.G\_Filifactor.S\_aloc



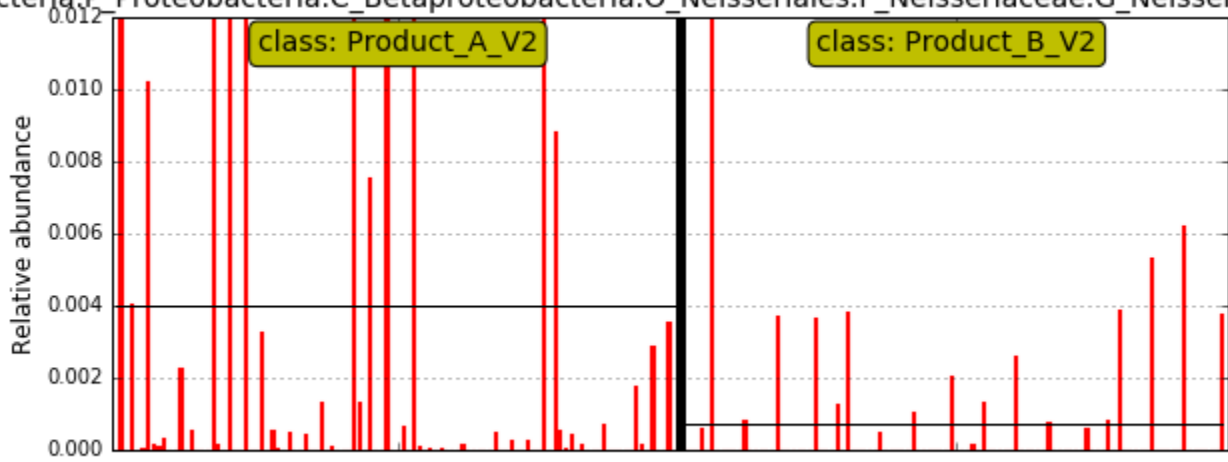
racilibacteria\_GN02.C\_Gracilibacteria\_GN02\_C\_1.O\_Gracilibacteria\_GN02\_O\_1.F\_Gracilibacteri



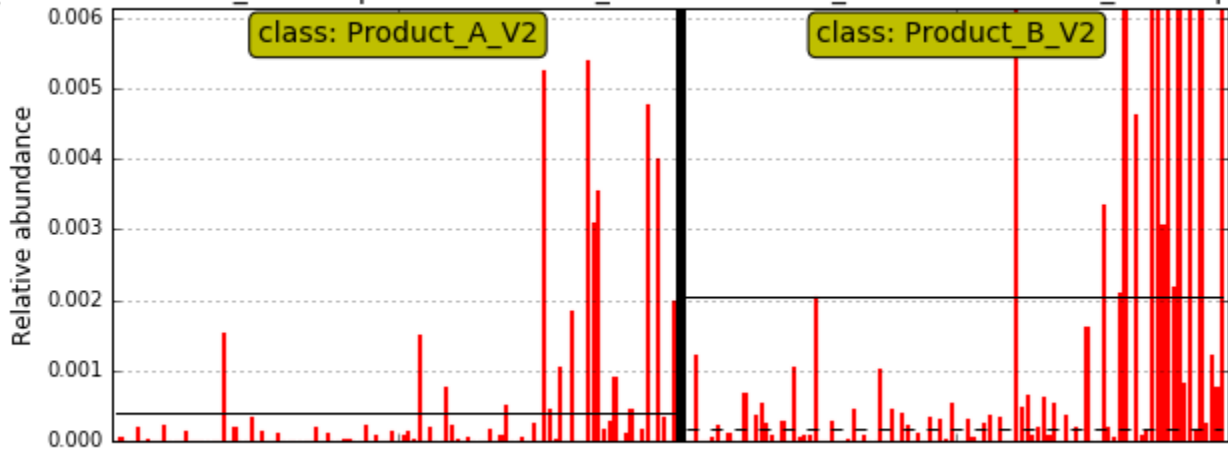
Bacteria.P\_Proteobacteria.C\_Betaproteobacteria.O\_Neisseriales.F\_Neisseriaceae.G\_Kingella.S\_denitrifi



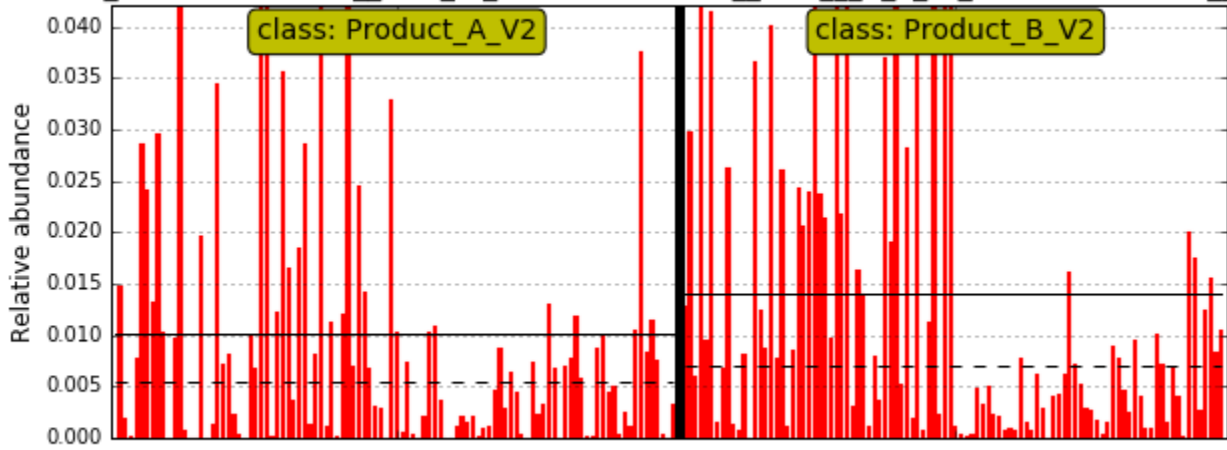
K\_Bacteria.P\_Proteobacteria.C\_Betaproteobacteria.O\_Neisseriales.F\_Neisseriaceae.G\_Neisseria.S\_mucc



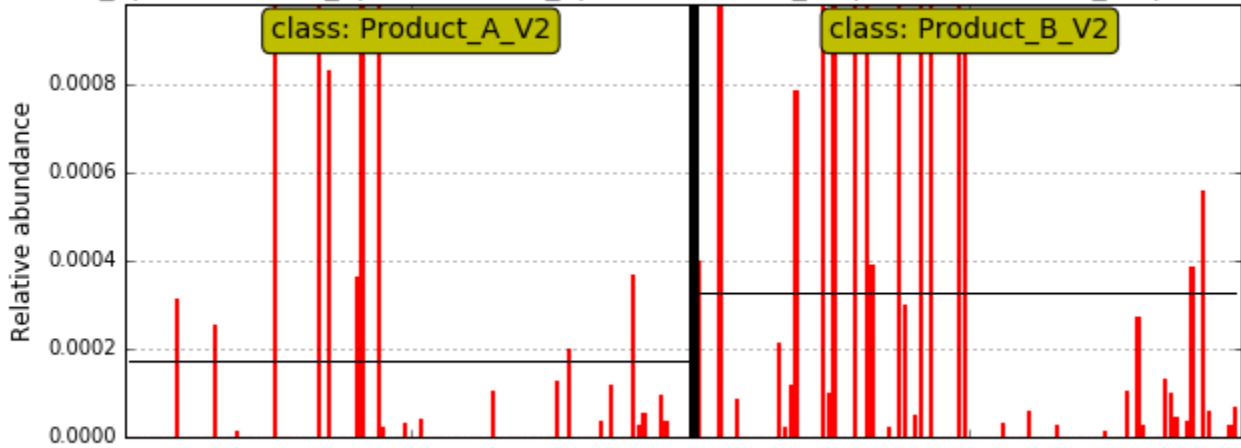
ia.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Haemophilus.S\_ha



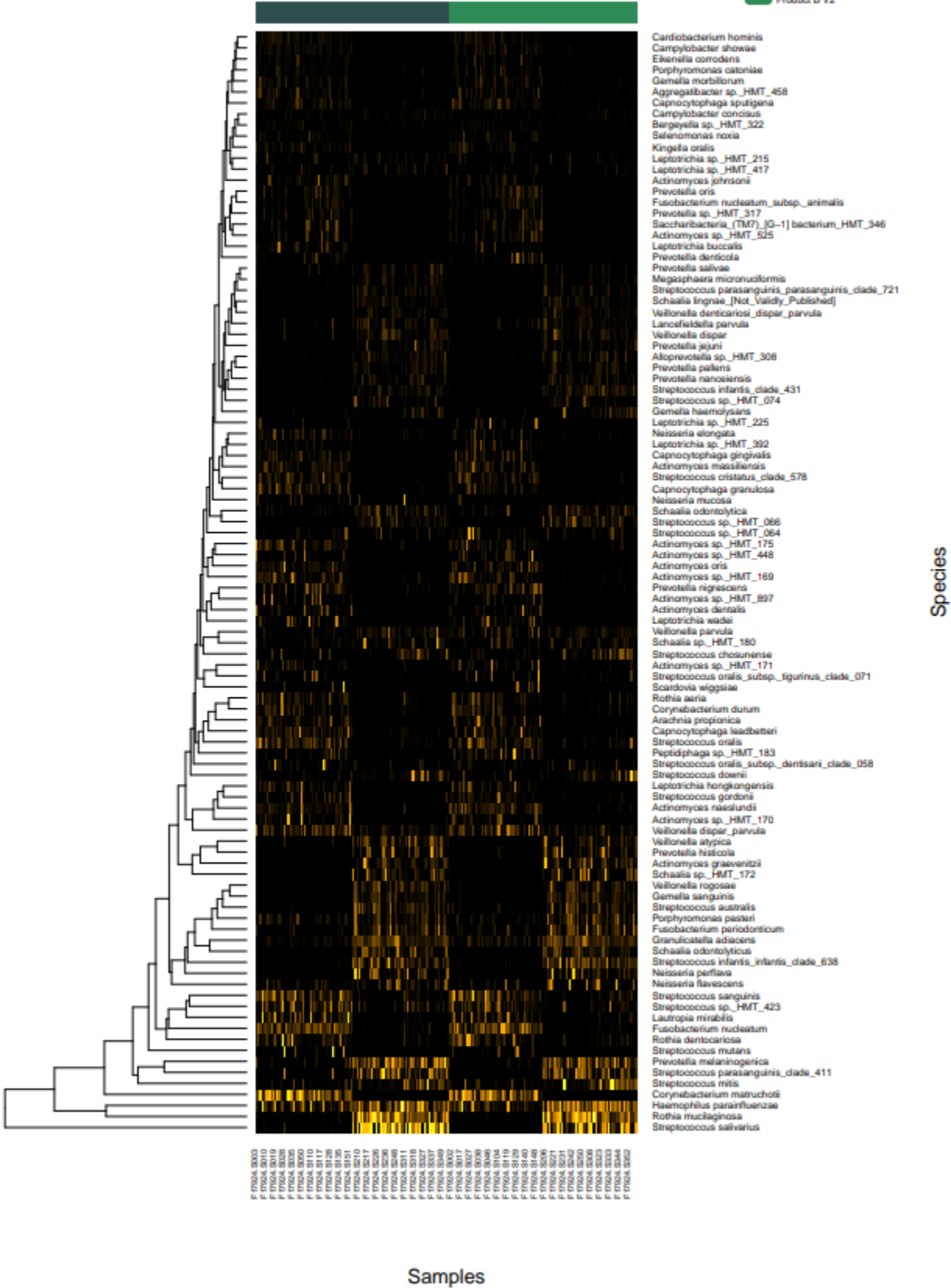
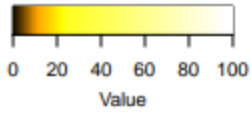
K\_Bacteria.P\_Saccharibacteria\_TM7\_C\_Saccharibacteria\_TM7\_C\_1\_O\_Saccharibacteria\_TM7\_O



\_Bacteria.P\_Spirochaetes.C\_Spirochaetia.O\_Spirochaetales.F\_Treponemataceae.G\_Treponema.S\_denti

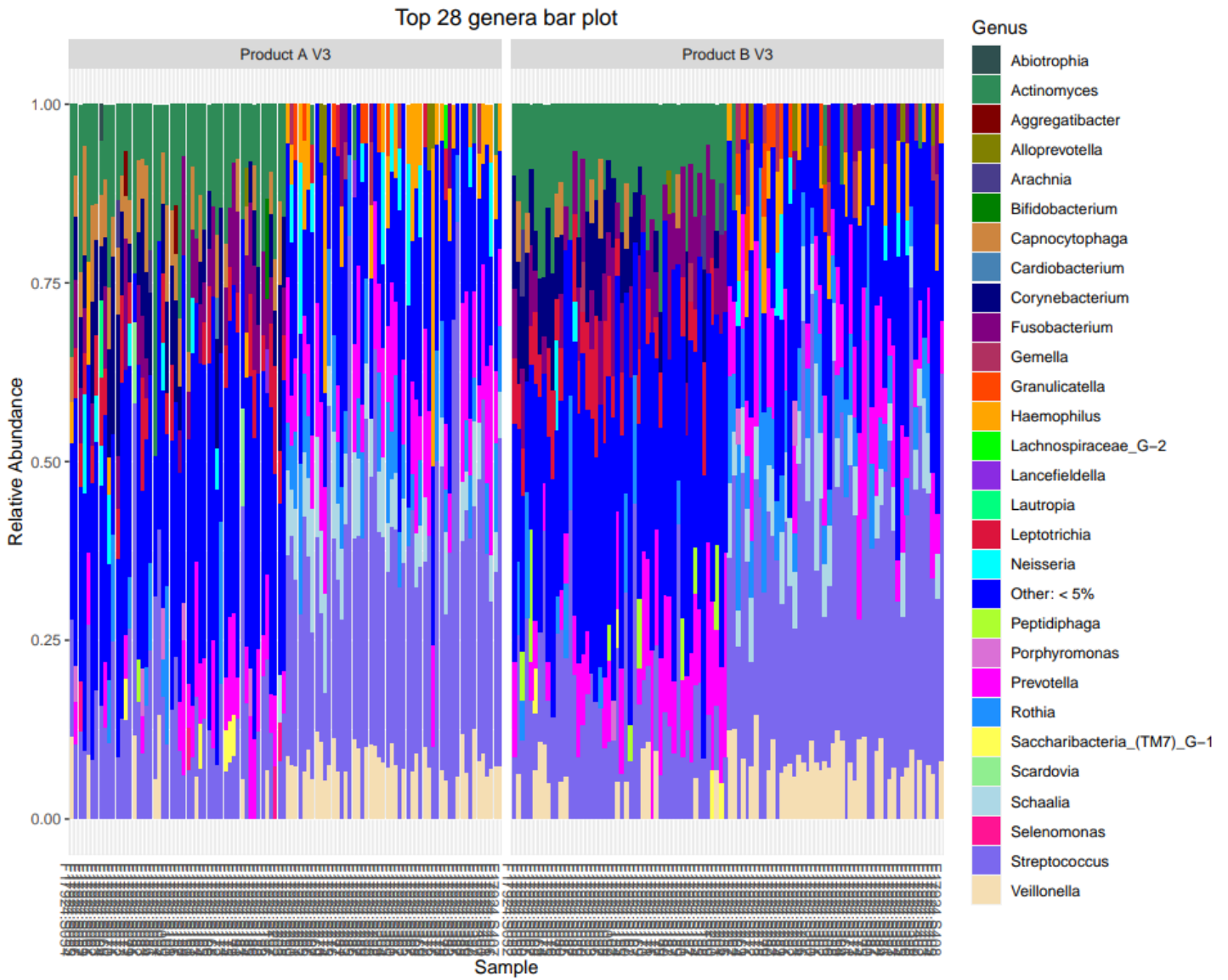




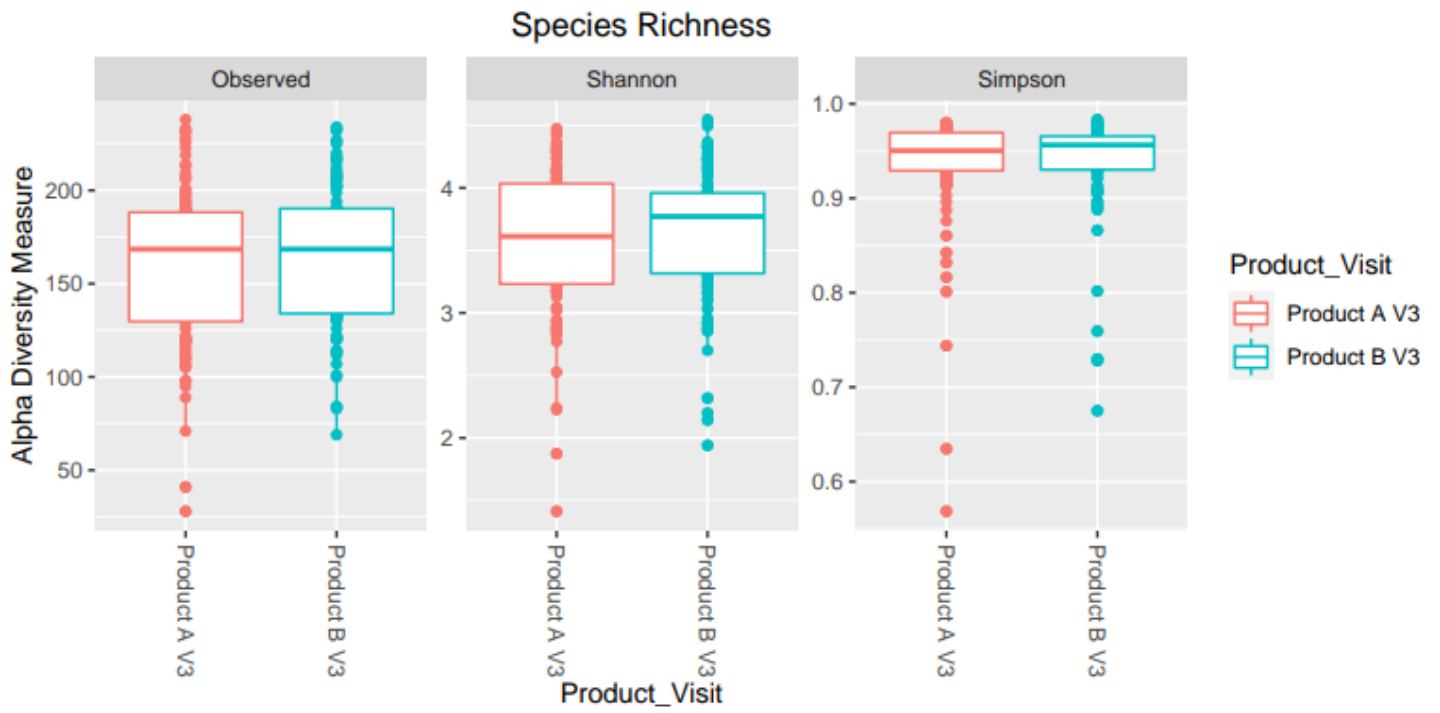


# Comparison 4. Product A V3 vs Product B V3

## 1) Taxonomy barplots

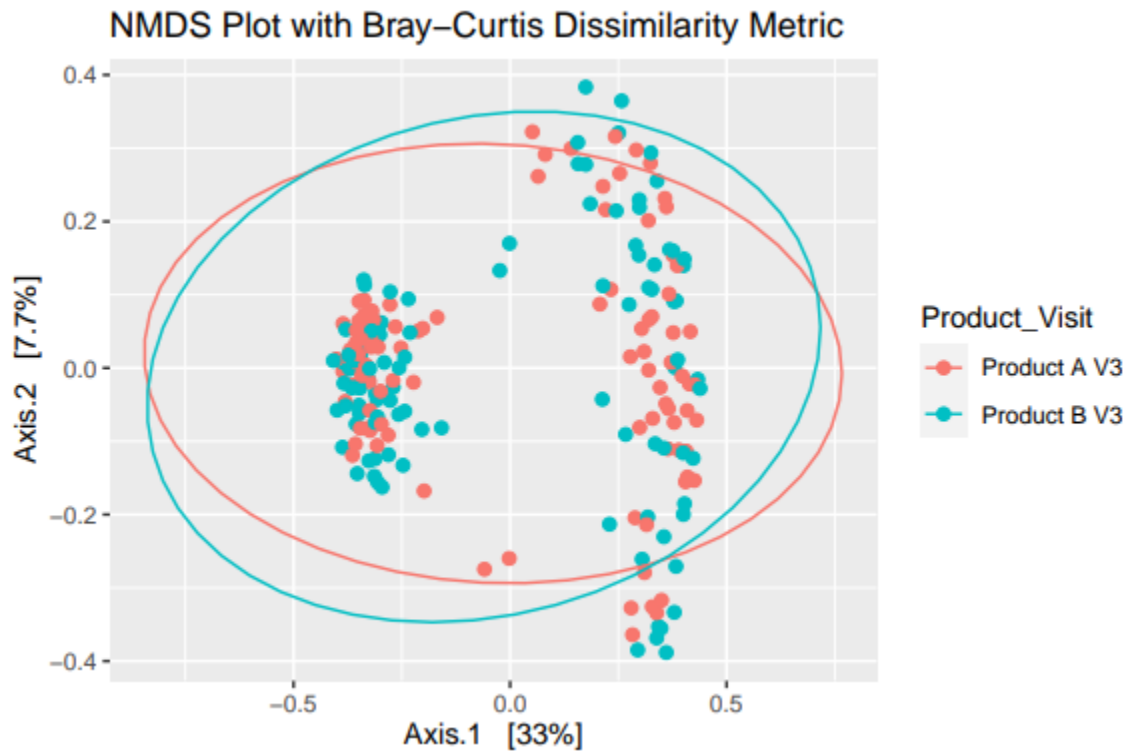


## 2) Alpha diversity



Note: No significant difference

### 3) Beta diversity



Note: P= 0.11

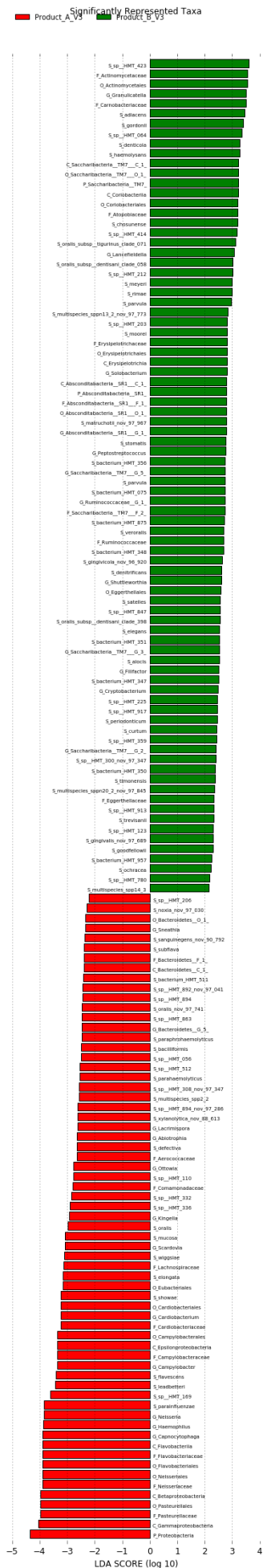


#### 4) Differential abundance

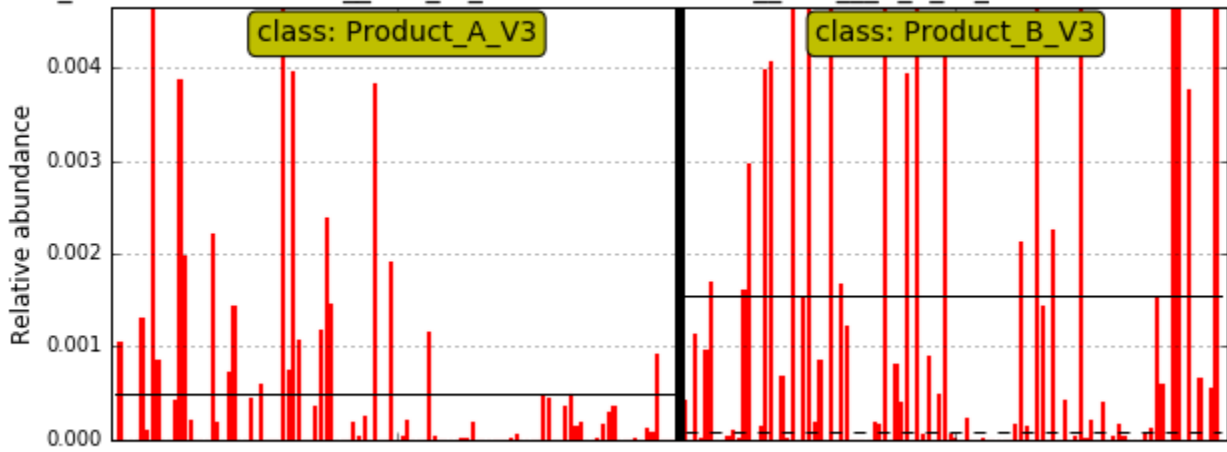
taxon	lfc_(Interce	lfc_Product	se_(Interce	se_Product	W_(Interce	W_Product	p_(Interce	p_Product	q_(Interce	q_Product	diff_(Interce	diff_Produ
Neisseria mucosa (SP300)	0.8524	-1.79377	0.258251	0.373941	3.300665	-4.79695	0.000965	1.61E-06	0.326986	0.000546	FALSE	TRUE
Gemella haemolysans (SP8)	-0.73784	1.450322	0.258162	0.373813	-2.85807	3.879803	0.004262	0.000105	1	0.035335	FALSE	TRUE
Streptococcus sp._HMT_064 (SP305)	-0.83645	1.651487	0.299899	0.43331	-2.78912	3.811325	0.005285	0.000138	1	0.046581	FALSE	TRUE
Streptococcus sp._HMT_056 (SP276)	0.661929	-1.40521	0.256675	0.371694	2.57886	-3.78056	0.009913	0.000156	1	0.052575	FALSE	FALSE
Aggregatibacter sp._HMT_512 (SP314)	0.546932	-1.17062	0.213626	0.310313	2.560227	-3.77238	0.01046	0.000162	1	0.054168	FALSE	FALSE
Prevotella veroralis (SP110)	-0.63488	1.240281	0.232903	0.337804	-2.72595	3.671597	0.006412	0.000241	1	0.080507	FALSE	FALSE
Capnocytophaga sp._HMT_336 (SP51)	0.690103	-1.46269	0.277025	0.400703	2.491121	-3.65031	0.012734	0.000262	1	0.087221	FALSE	FALSE
Capnocytophaga sp._HMT_332 (SP49)	0.58185	-1.24185	0.237862	0.344874	2.446166	-3.60088	0.014438	0.000317	1	0.10529	FALSE	FALSE
Haemophilus paraphrohaemolyticus (SP388)	0.491763	-1.05808	0.216376	0.314235	2.272731	-3.36715	0.023042	0.000759	1	0.251392	FALSE	FALSE
Granulicatella elegans (SP138)	-0.57213	1.112257	0.24032	0.348379	-2.38068	3.192668	0.017281	0.00141	1	0.465184	FALSE	FALSE
Kingella oralis (SP198)	0.592413	-1.2634	0.280336	0.405422	2.113227	-3.11626	0.034581	0.001832	1	0.602598	FALSE	FALSE
Streptococcus gordonii (SP171)	-0.61008	1.189686	0.264207	0.38243	-2.3091	3.110858	0.020938	0.001865	1	0.611866	FALSE	FALSE
Lacrimispora xylanolytica_nov_88.613% (SPN382)	0.501504	-1.07795	0.242196	0.351053	2.070659	-3.07061	0.038391	0.002136	1	0.698536	FALSE	FALSE
Haemophilus parahemolyticus (SP148)	0.492814	-1.06022	0.244403	0.354199	2.016398	-2.99328	0.043758	0.00276	1	0.899751	FALSE	FALSE
Campylobacter showae (SP204)	0.609373	-1.298	0.301924	0.436197	2.018297	-2.97571	0.04356	0.002923	1	0.949996	FALSE	FALSE
Parvimonas sp._HMT_110 (SP129)	0.543055	-1.16271	0.271114	0.392276	2.003053	-2.96401	0.045172	0.003037	1	0.983853	FALSE	FALSE
Haemophilus parainfluenzae (SP19)	0.495263	-1.06521	0.253322	0.366914	1.955074	-2.90317	0.050574	0.003694	1	1	FALSE	FALSE
Neisseria bacilliformis (SP447)	0.436659	-0.94566	0.232987	0.337924	1.874179	-2.79845	0.060906	0.005135	1	1	FALSE	FALSE
Neisseria flavescens (SP195)	0.640224	-1.36093	0.34189	0.493177	1.872604	-2.75953	0.061123	0.005789	1	1	FALSE	FALSE
Kingella oralis_nov_97.741% (SPN664)	0.339275	-0.747	0.191879	0.27927	1.768176	-2.67484	0.077031	0.007477	1	1	FALSE	FALSE
Capnocytophaga leadbetteri (SP89)	0.516558	-1.10866	0.289929	0.419098	1.781667	-2.64534	0.074804	0.008161	1	1	FALSE	FALSE
Ottowia sp._HMT_894 (SP249)	0.401186	-0.8733	0.234806	0.340518	1.708581	-2.56461	0.087529	0.010329	1	1	FALSE	FALSE
Streptococcus chosunense (SP133)	-0.55628	1.079936	0.294413	0.425489	-1.88946	2.538104	0.05883	0.011145	1	1	FALSE	FALSE
Prevotella sp._HMT_300_nov_97.347% (SPN392)	0.403614	-0.87825	0.245975	0.356441	1.640872	-2.46394	0.100824	0.013742	1	1	FALSE	FALSE
Selenomonas noxia_nov_97.030% (SPN548)	0.32993	-0.72794	0.207026	0.300895	1.593668	-2.41923	0.111011	0.015553	1	1	FALSE	FALSE
Neisseria subflava (SP450)	0.351267	-0.77146	0.22952	0.33298	1.53044	-2.31684	0.125908	0.020512	1	1	FALSE	FALSE
Actinomyces sp._HMT_169 (SP239)	0.38915	-0.84874	0.253298	0.36688	1.536334	-2.31341	0.124457	0.0207	1	1	FALSE	FALSE
Absconditabacteria_(SR1)_[G-1] bacterium_HMT_875 (SP225)	-0.38478	0.730067	0.219606	0.318842	-1.75212	2.289741	0.079753	0.022036	1	1	FALSE	FALSE
Aggregatibacter aphrophilus (SP218)	0.384092	-0.83843	0.254734	0.368928	1.507814	-2.2726	0.131602	0.02305	1	1	FALSE	FALSE
Neisseria elongata (SP219)	0.425472	-0.92284	0.287241	0.415266	1.481237	-2.22229	0.138543	0.026264	1	1	FALSE	FALSE
Capnocytophaga sp._HMT_863 (SP275)	0.260237	-0.58576	0.182321	0.265607	1.427358	-2.20538	0.153477	0.027428	1	1	FALSE	FALSE
Bergeyella sp._HMT_206 (SP2)	0.260818	-0.58695	0.187615	0.273176	1.390178	-2.1486	0.164475	0.031666	1	1	FALSE	FALSE
Neisseria oralis (SP399)	0.367065	-0.80369	0.259111	0.375167	1.416632	-2.14222	0.156591	0.032175	1	1	FALSE	FALSE
Saccharibacteria_(TM7)_[G-3] bacterium_HMT_351 (SP225)	-0.39894	0.758958	0.249568	0.361563	-1.59852	2.099103	0.109928	0.035808	1	1	FALSE	FALSE
Abiotrophia defectiva (SP206)	-0.44843	0.85991	0.290719	0.420224	-1.54247	2.046314	0.12296	0.040726	1	1	FALSE	FALSE
Leptotrichia sp._HMT_212 (SP146)	-0.45744	0.87829	0.298502	0.431319	-1.53243	2.036287	0.125415	0.041722	1	1	FALSE	FALSE
Actinomyces sp._HMT_414 (SP61)	-0.36019	0.679917	0.230975	0.335056	-1.55945	2.029267	0.118891	0.042431	1	1	FALSE	FALSE
Peptostreptococcus stomatis (SP92)	-0.4379	0.838438	0.28619	0.413767	-1.53011	2.026354	0.125991	0.042728	1	1	FALSE	FALSE
Actinomyces sp._HMT_175_nov_97.951% (SPN405)	0.298435	-0.66369	0.228177	0.331065	1.307911	-2.0047	0.190903	0.044995	1	1	FALSE	FALSE
Ruminococcaceae_[G-1] bacterium_HMT_075 (SP225)	-0.43022	0.822777	0.286707	0.414504	-1.50057	1.98497	0.133467	0.047148	1	1	FALSE	FALSE

Note: Green, more abundant in B after treatment; Red, more abundant in A after treatment

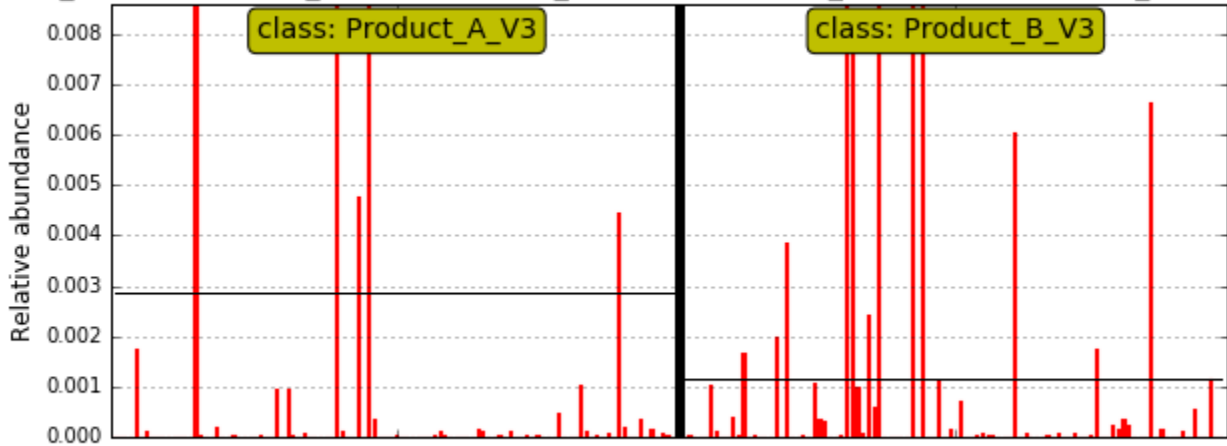
5) Lefse—as expected, many differences



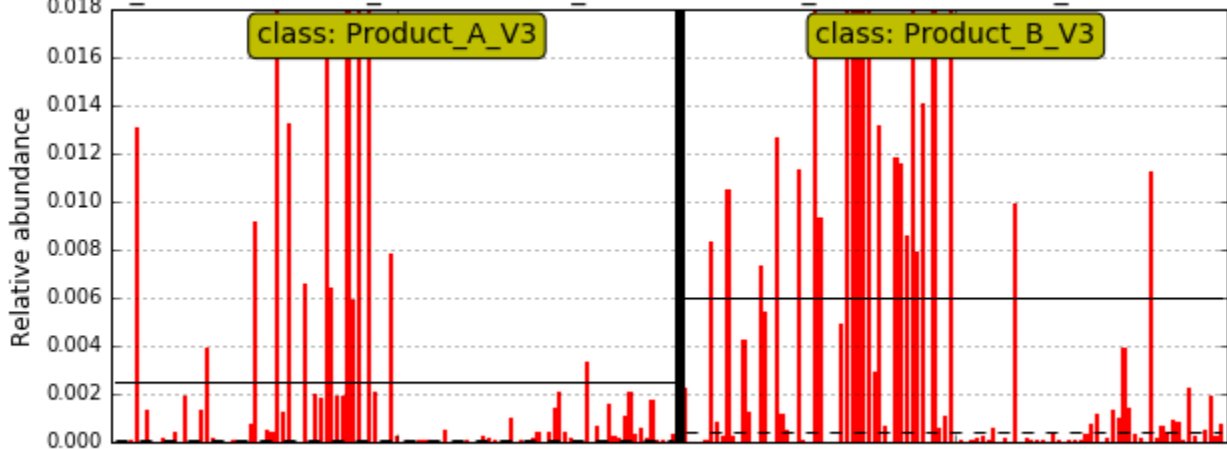
acteria.P\_Absconditabacteria\_SR1\_C\_Absconditabacteria\_SR1\_C\_1\_O\_Absconditabacteria\_SR1\_C



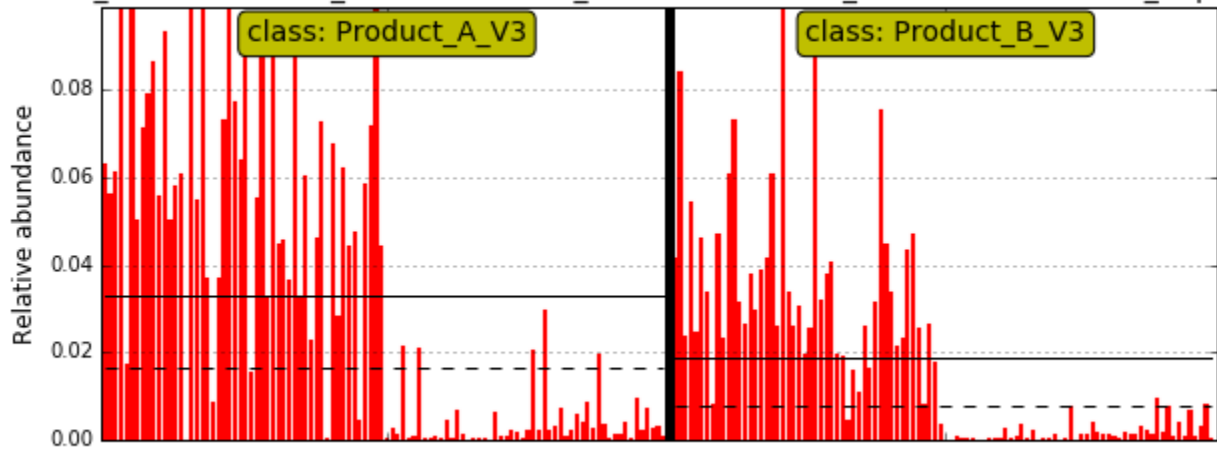
acteria.P\_Actinobacteria.C\_Actinobacteria.O\_Bifidobacteriales.F\_Bifidobacteriaceae.G\_Scardovia.S\_wig



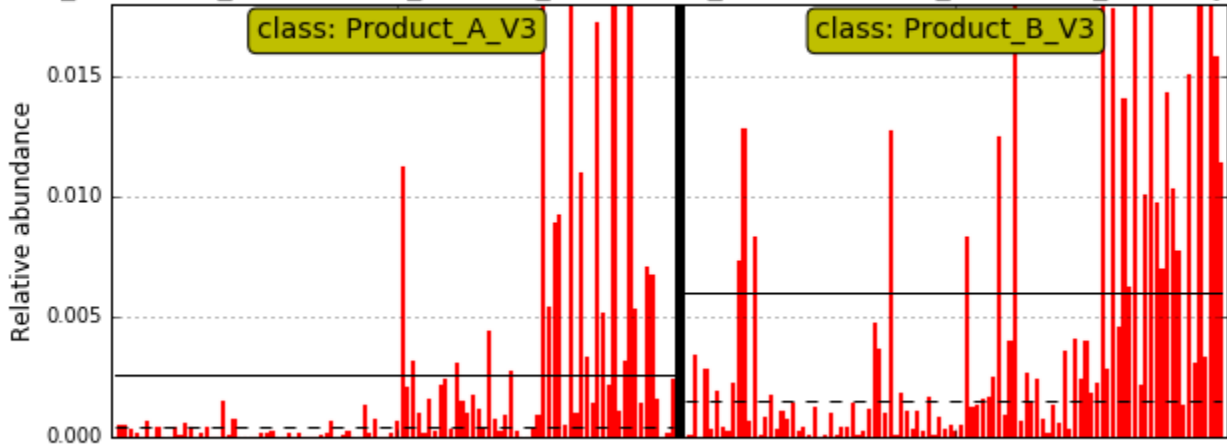
K\_Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Prevotella.S\_denticola



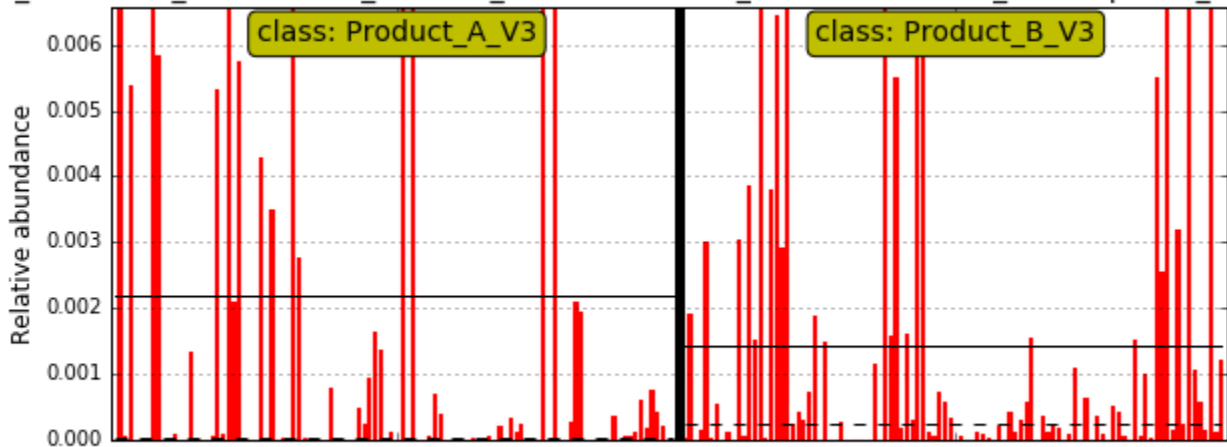
K\_Bacteria.P\_Bacteroidetes.C\_Flavobacteriia.O\_Flavobacteriales.F\_Flavobacteriaceae.G\_Capnocytopha



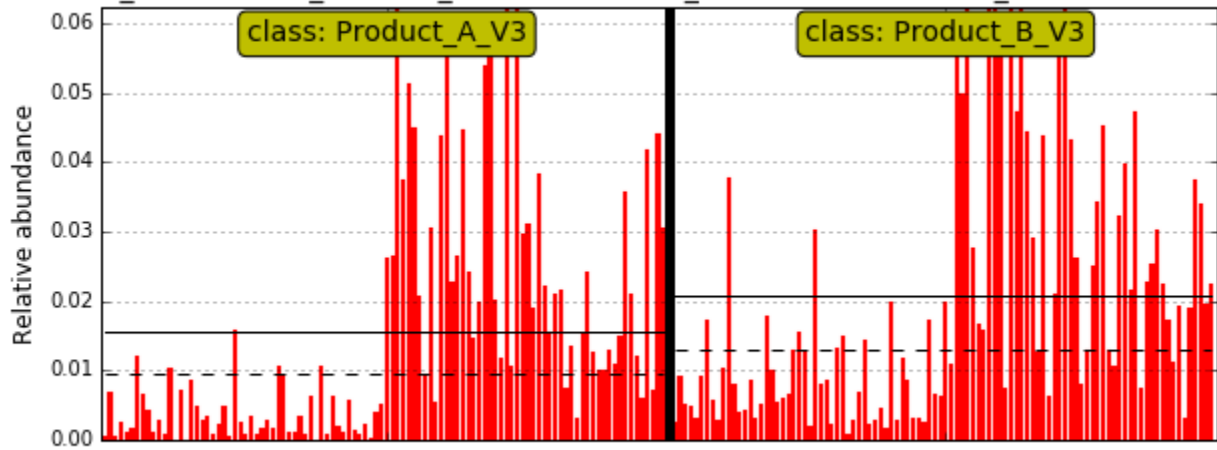
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Bacillales.F\_Gemellaceae.G\_Gemella.S\_haemolysans



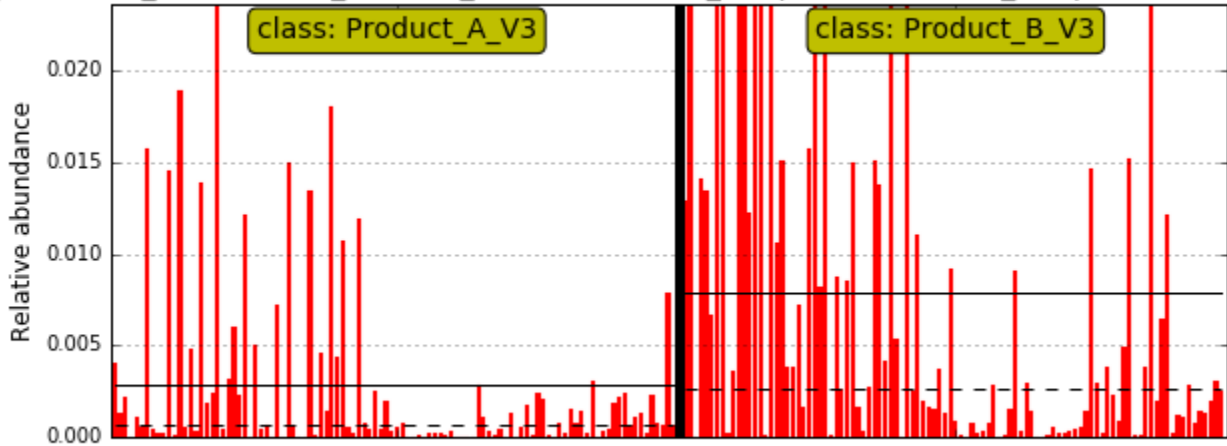
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Aerococcaceae.G\_Abiotrophia.S\_defectiva



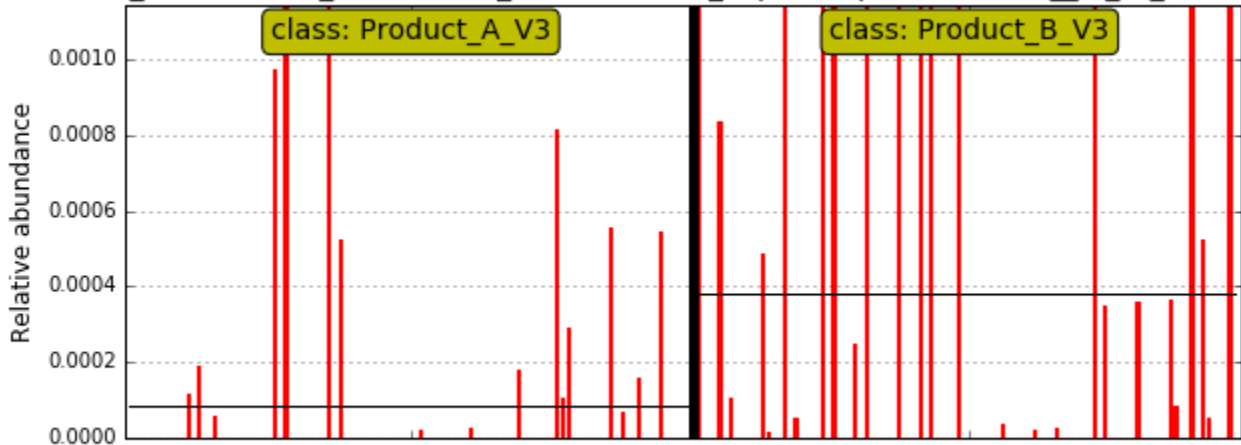
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Carnobacteriaceae.G\_Granulicatella.S\_adiacen:



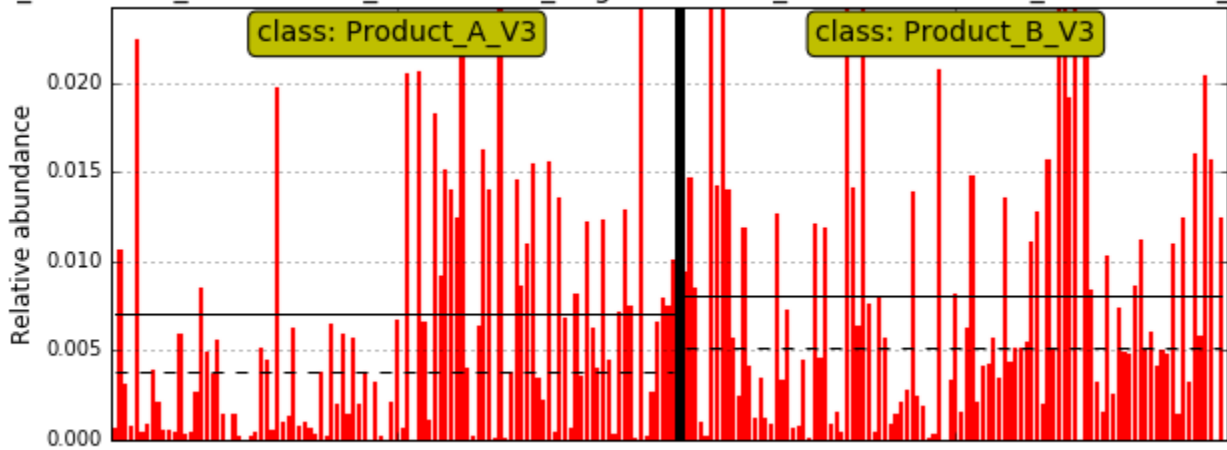
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Streptococcaceae.G\_Streptococcus.S\_gordonii



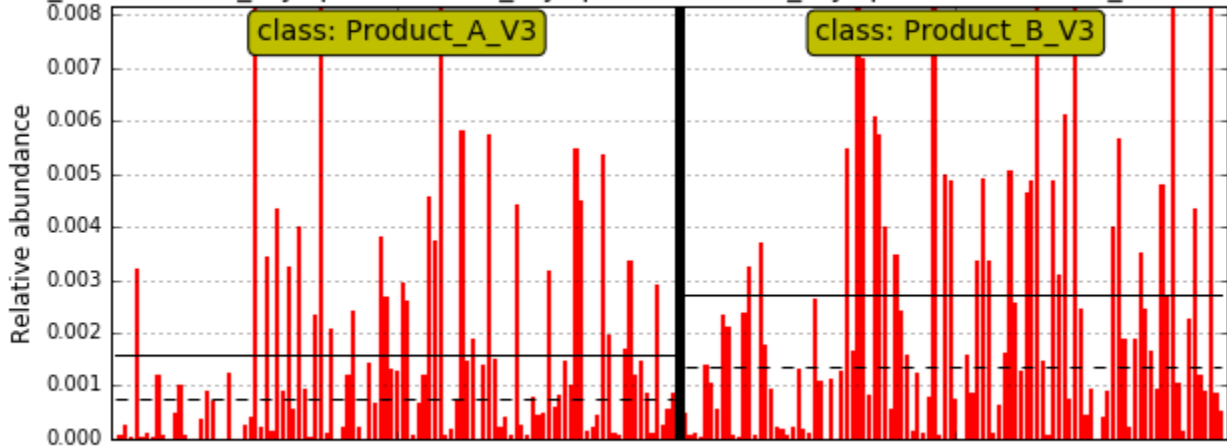
K\_Bacteria.P\_Firmicutes.C\_Clostridia.O\_Clostridiales.F\_Peptostreptococcaceae\_XI\_G\_Filifactor.S\_aloc



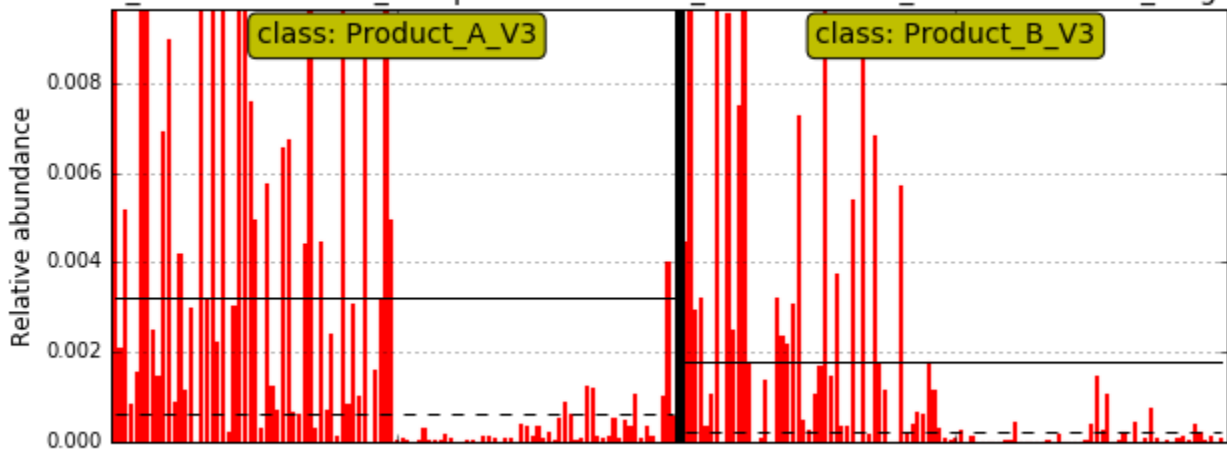
K\_Bacteria.P\_Firmicutes.C\_Clostridia.O\_Negativicutes.F\_Veillonellaceae.G\_Veillonella.S\_parvula



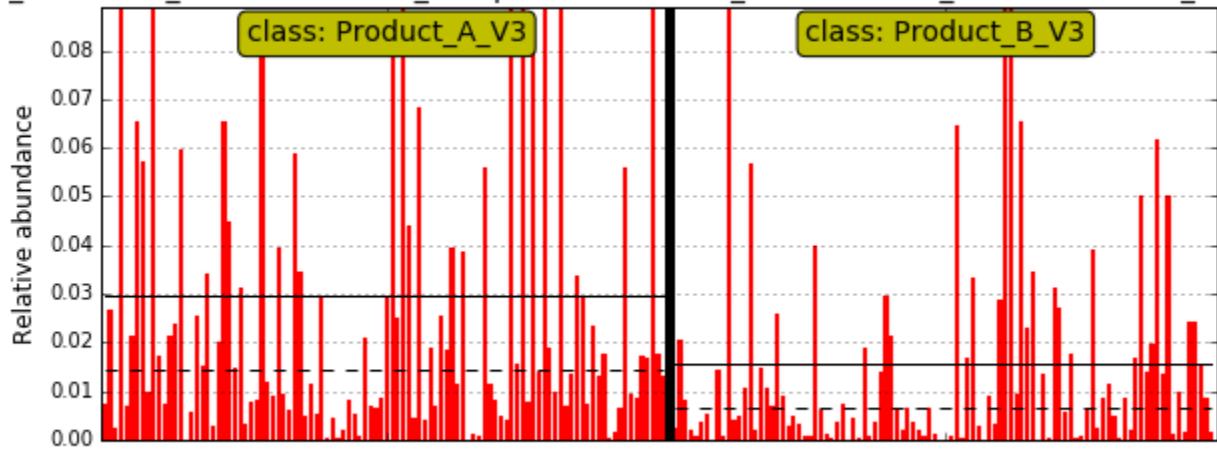
Bacteria.P\_Firmicutes.C\_Erysipelotrichia.O\_Erysipelotrichales.F\_Erysipelotrichaceae.G\_Solobacterium.S\_1



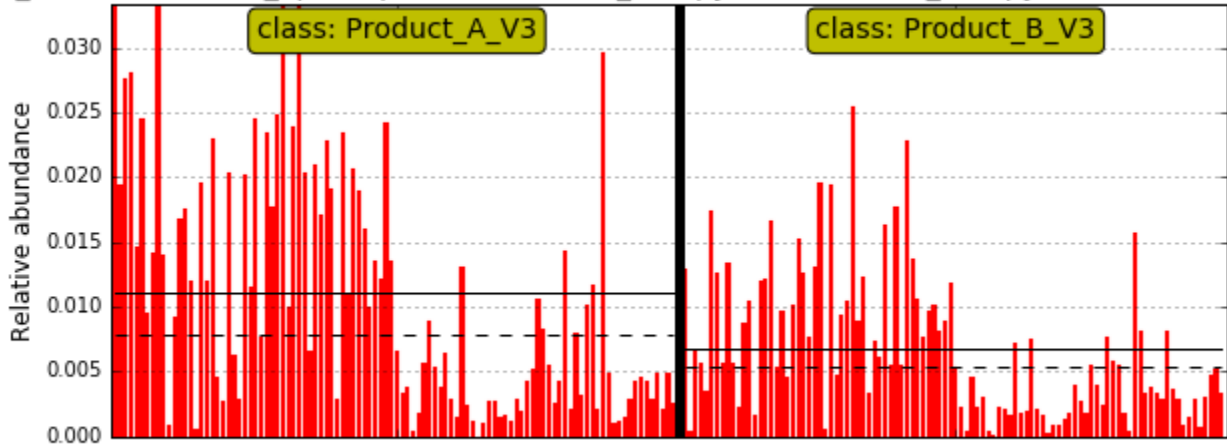
K\_Bacteria.P\_Proteobacteria.C\_Betaproteobacteria.O\_Neisseriales.F\_Neisseriaceae.G\_Kingella.S\_orali



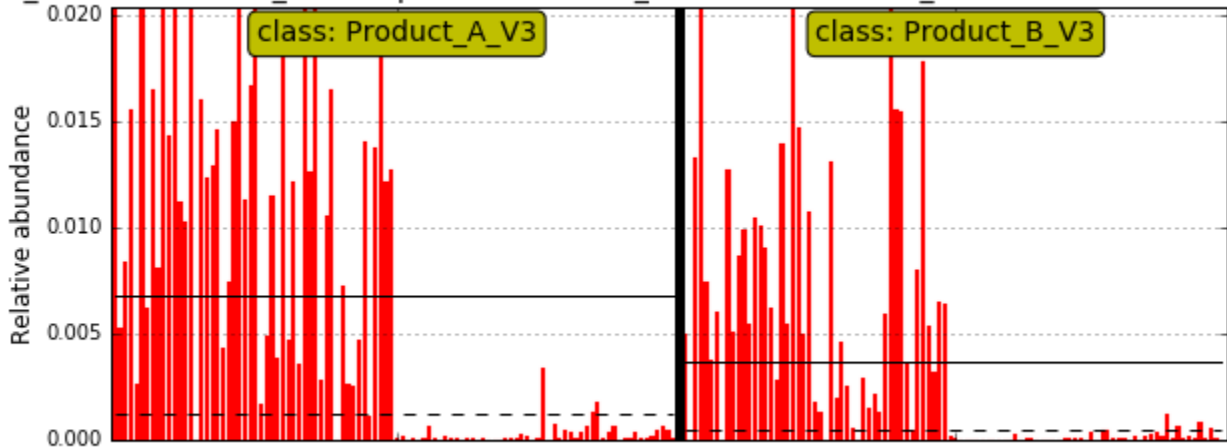
K\_Bacteria.P\_Proteobacteria.C\_Betaproteobacteria.O\_Neisseriales.F\_Neisseriaceae.G\_Neisseria



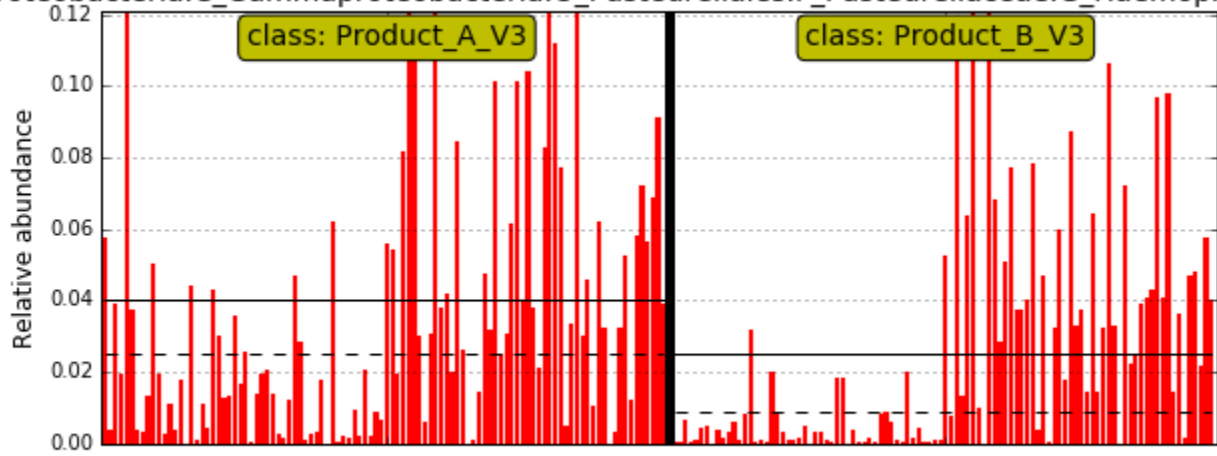
eria.P\_Proteobacteria.C\_Epsilonproteobacteria.O\_Campylobacteriales.F\_Campylobacteraceae.G\_Campy



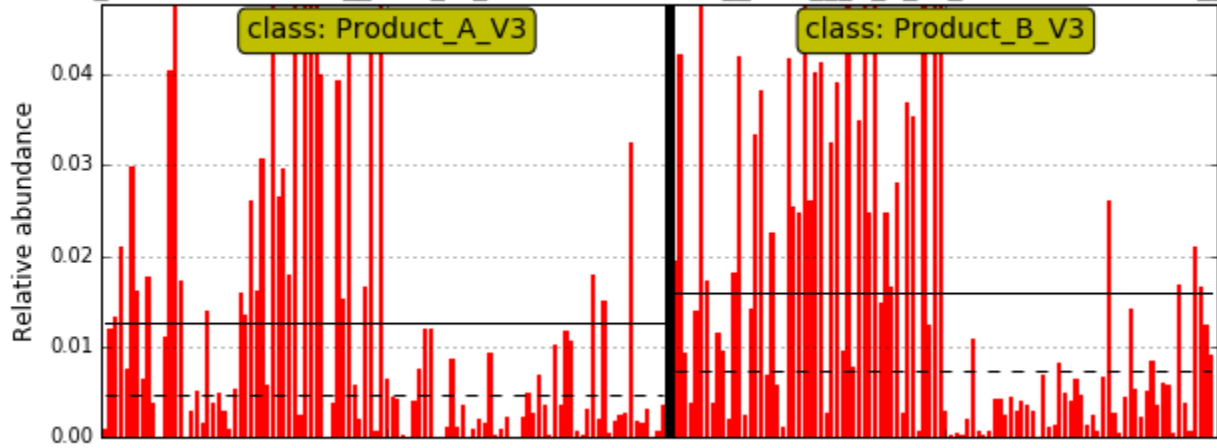
teria.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Cardiobacteriales.F\_Cardiobacteriaceae.G\_Cardioba



a.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Haemophilus.S\_par

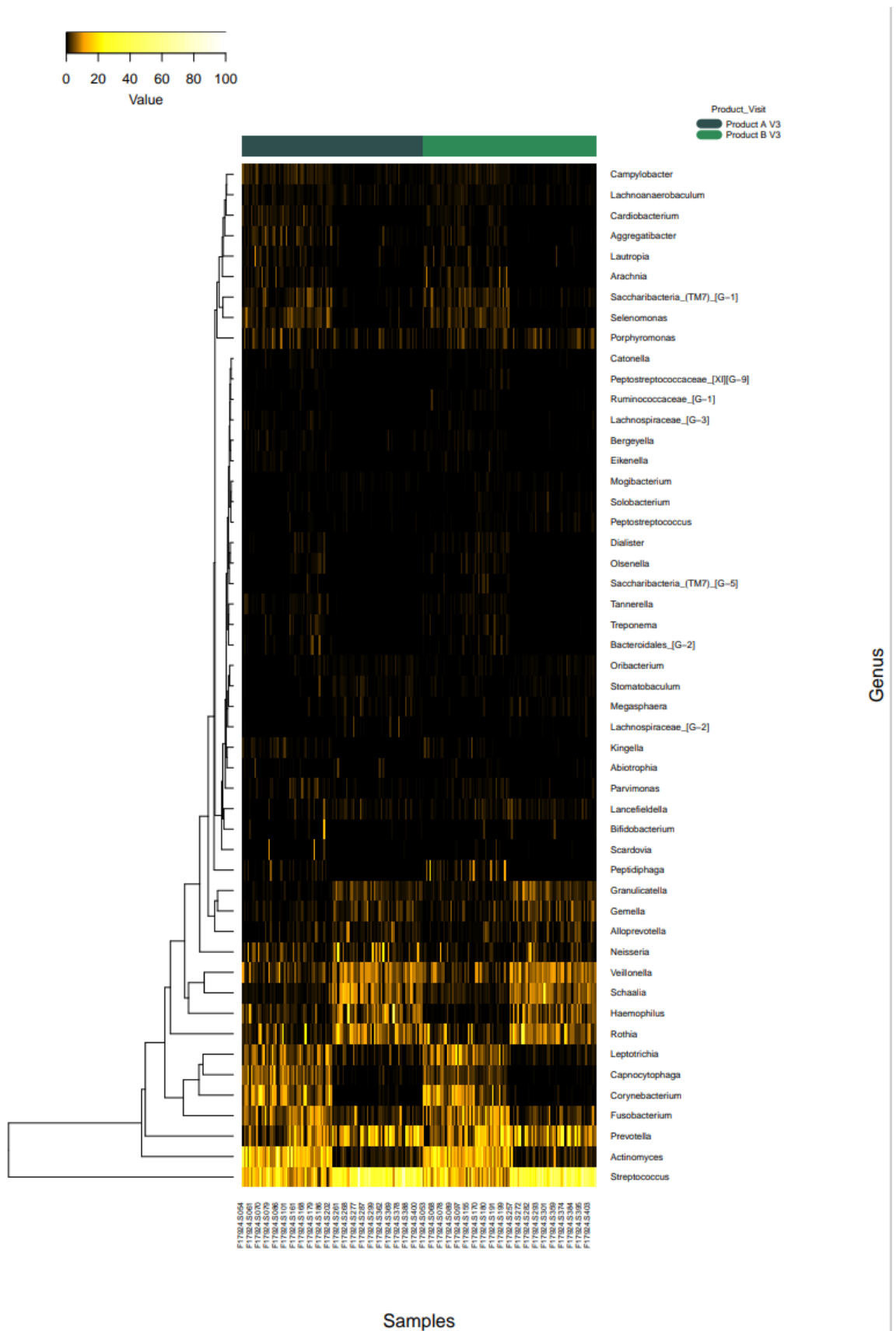


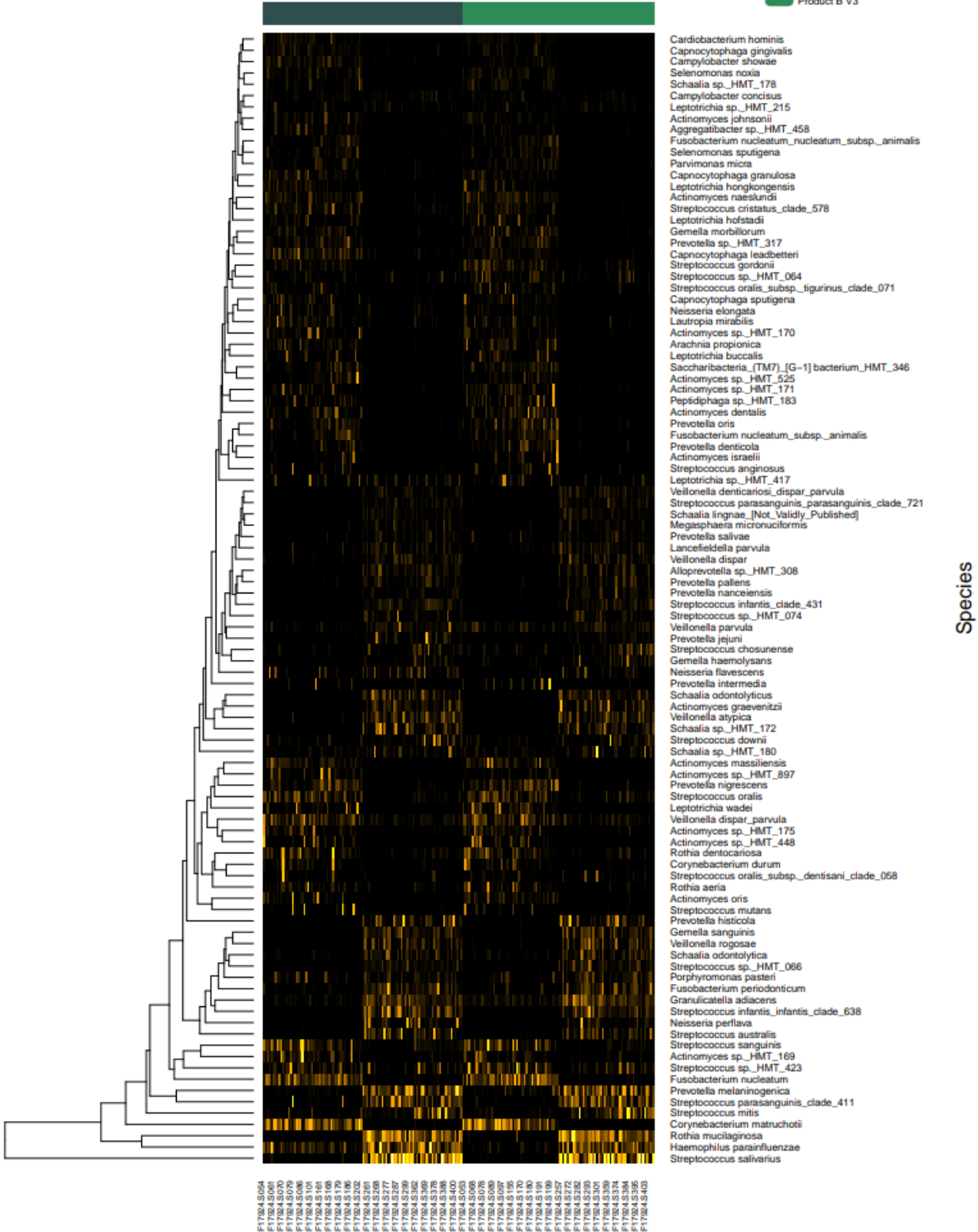
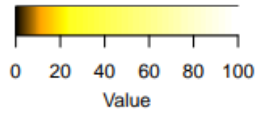
K\_Bacteria.P\_Saccharibacteria\_TM7\_C\_Saccharibacteria\_TM7\_C\_1\_O\_Saccharibacteria\_TM7\_O\_





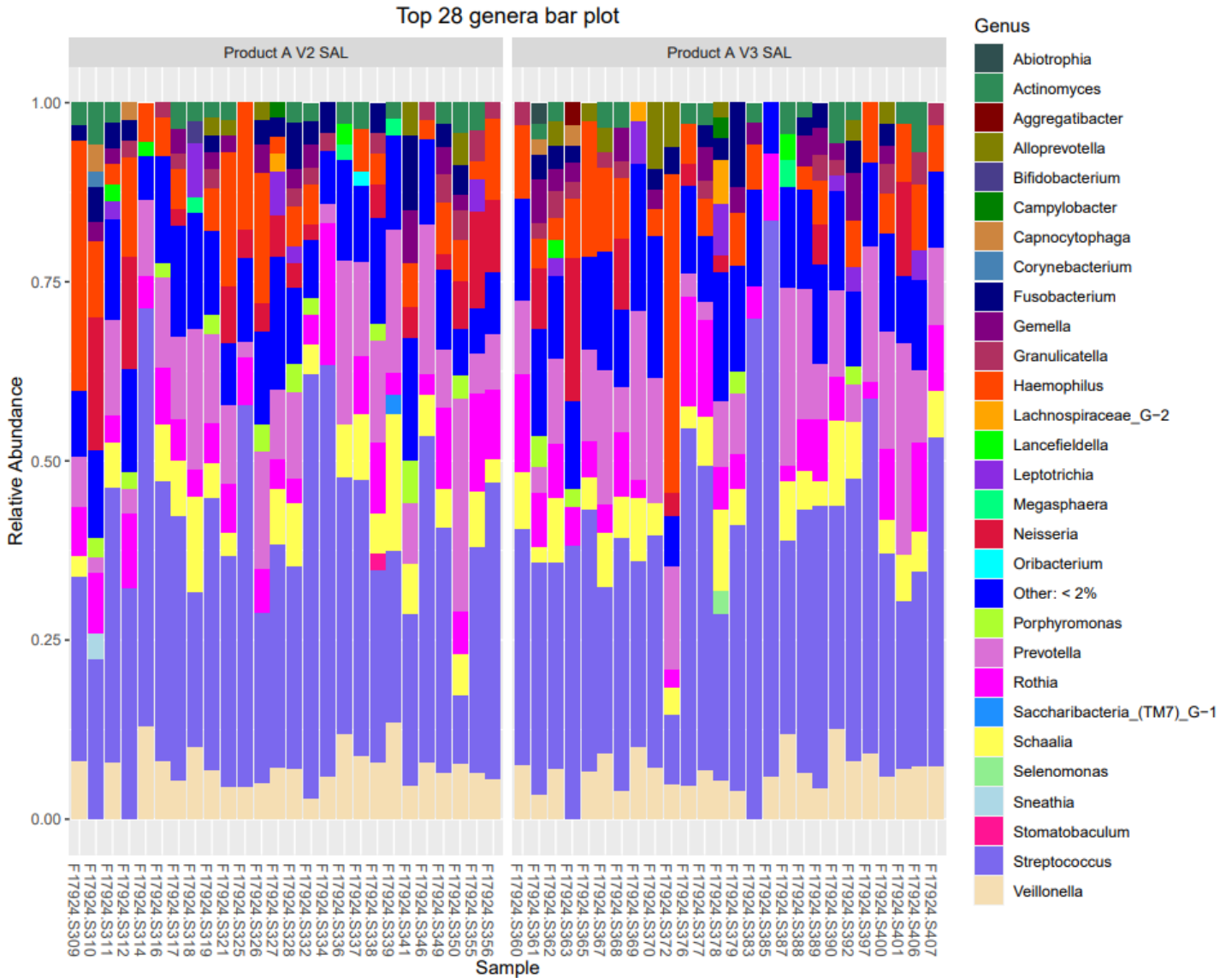
## 6) Heat maps





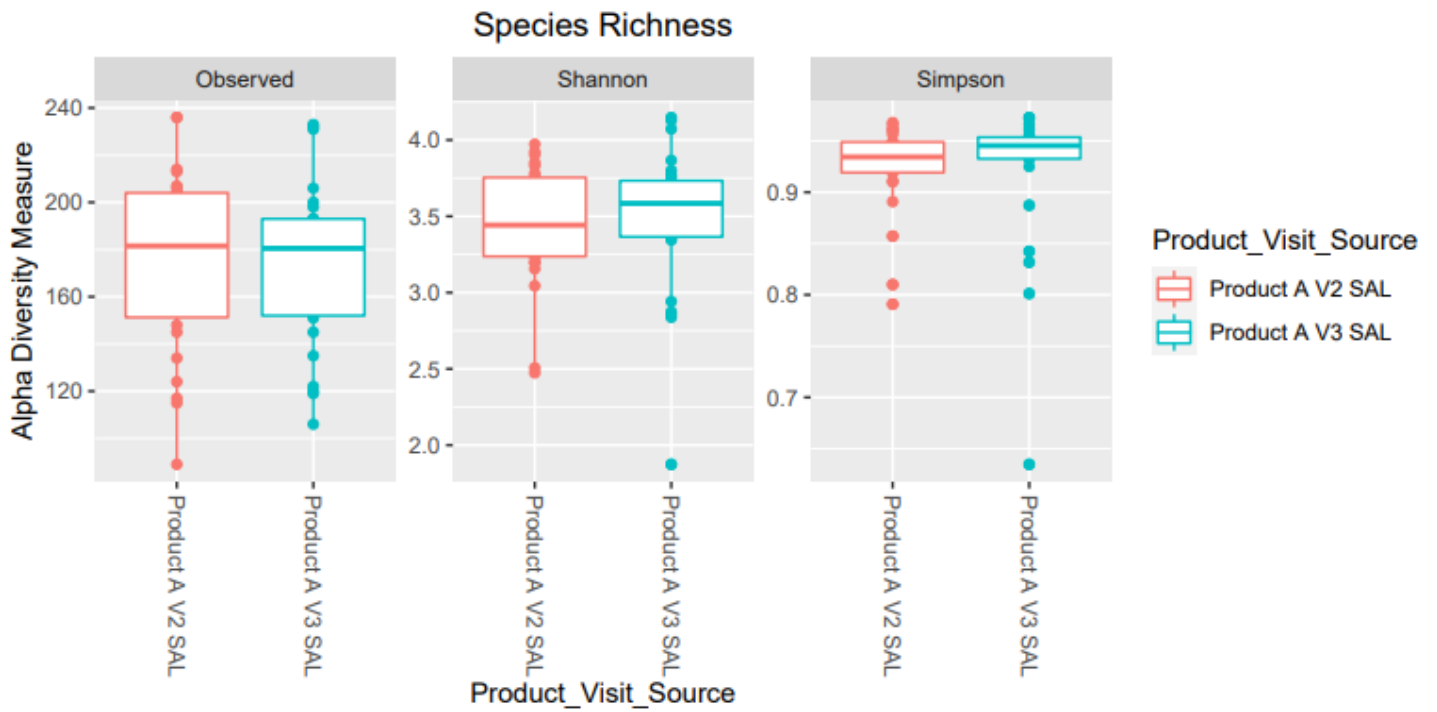
## Comparison 5. Product A V2 SAL vs Product A V3 SAL

### 1) Taxonomy bar plots



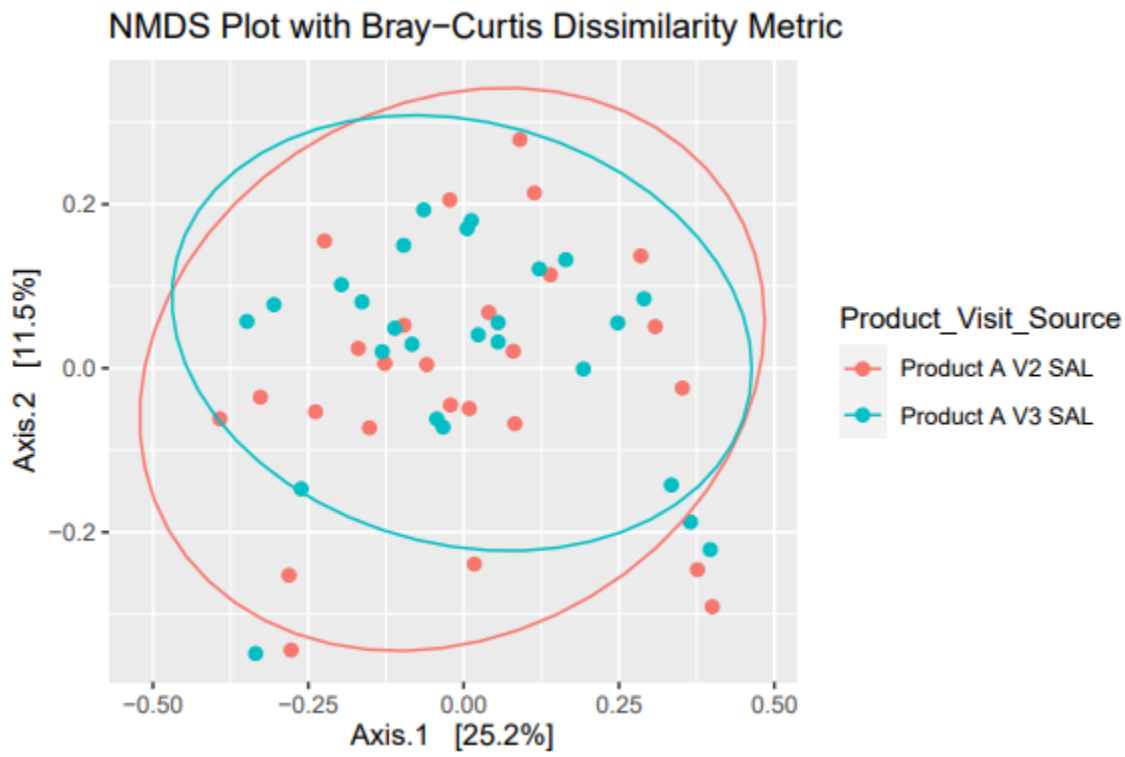
Note: Difficult to see any major differences. However, expected taxa are present. Specific taxa will be evaluated in subsequent analyses.

## 2) Alpha diversity



Note: Not Statistically significant

### 3) Beta diversity



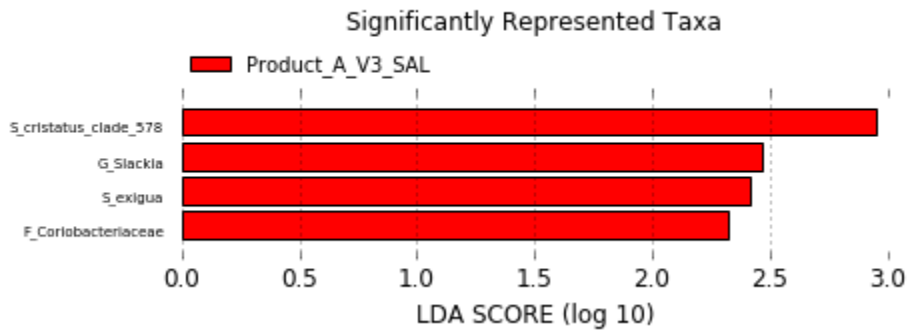
Note: Not Statistically significant;  $p=0.259$

#### 4) Differential abundance

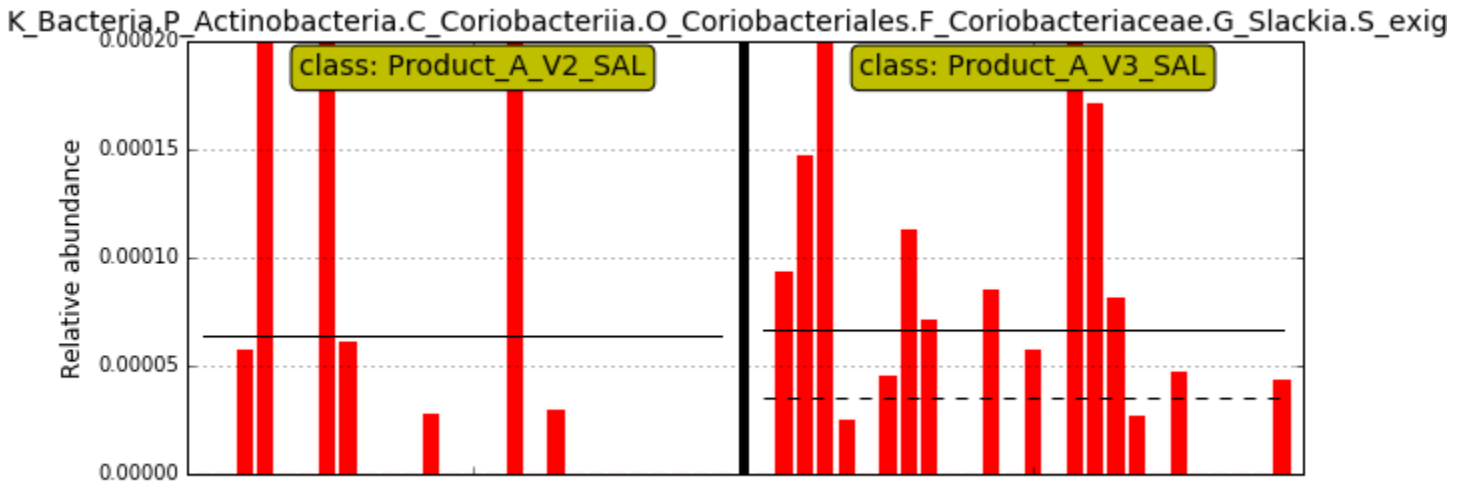
taxon	lfc_(Inter	lfc_Produc	se_(Inter	se_Produc	W_(Inter	W_Produc	p_(Inter	p_Produc	V	q_(Inter	q_Produc	diff_(Inte	diff_Prod
Tannerella serpentiformis_sp._HMT_286 (SPP54)	-0.37029	0.740582	0.287009	0.405892	-1.29017	1.824579	0.196993	0.068064591		1	1	FALSE	FALSE
Peptostreptococcaceae_[XI][G-1][Eubacterium]_inf	-0.30308	0.606167	0.309597	0.437836	-0.97896	1.38446	0.327601	0.166217735		1	1	FALSE	FALSE
Capnocytophaga sputigena (SP145)	0.405538	-0.81107	0.422161	0.597025	0.960626	-1.35853	0.33674	0.174296936		1	1	FALSE	FALSE
Ruminococcaceae_[G-1] bacterium_HMT_075 (SP225)	0.431125	-0.86225	0.461986	0.653346	0.933201	-1.31974	0.350716	0.186921437		1	1	FALSE	FALSE
Selenomonas flueggei (SP26)	-0.23404	0.468077	0.251554	0.355751	-0.93037	1.315743	0.352182	0.188260373		1	1	FALSE	FALSE
Slackia exigua (SP147)	-0.29153	0.583065	0.313657	0.443578	-0.92946	1.31446	0.352651	0.188691581		1	1	FALSE	FALSE
Tannerella sp._HMT_286 (SP45)	-0.30721	0.614419	0.340475	0.481505	-0.90229	1.276039	0.366902	0.201941865		1	1	FALSE	FALSE
Saccharibacteria_(TM7)[G-3] bacterium_HMT_351(	0.37569	-0.75138	0.419662	0.593492	0.89522	-1.26603	0.370669	0.205503103		1	1	FALSE	FALSE
Leptotrichia sp._HMT_215 (SP11)	0.37534	-0.75068	0.431806	0.610666	0.869233	-1.22928	0.38472	0.218968217		1	1	FALSE	FALSE
Olsenella sp._HMT_807 (SP81)	-0.27918	0.558356	0.323235	0.457123	-0.8637	1.221457	0.387755	0.221912878		1	1	FALSE	FALSE

Note: No statistically significant differences

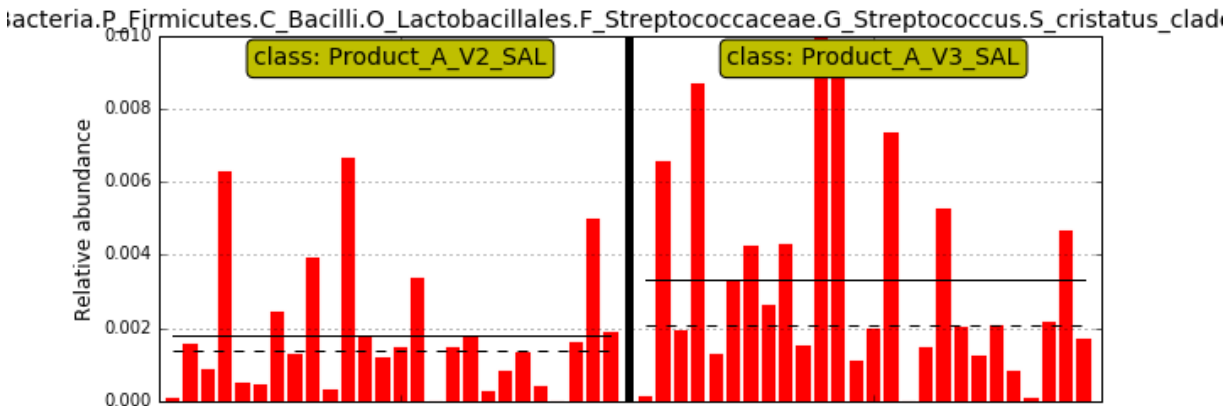
5) Lefse—only 2 species that differentiated—no clear differences—product A had little or no effect



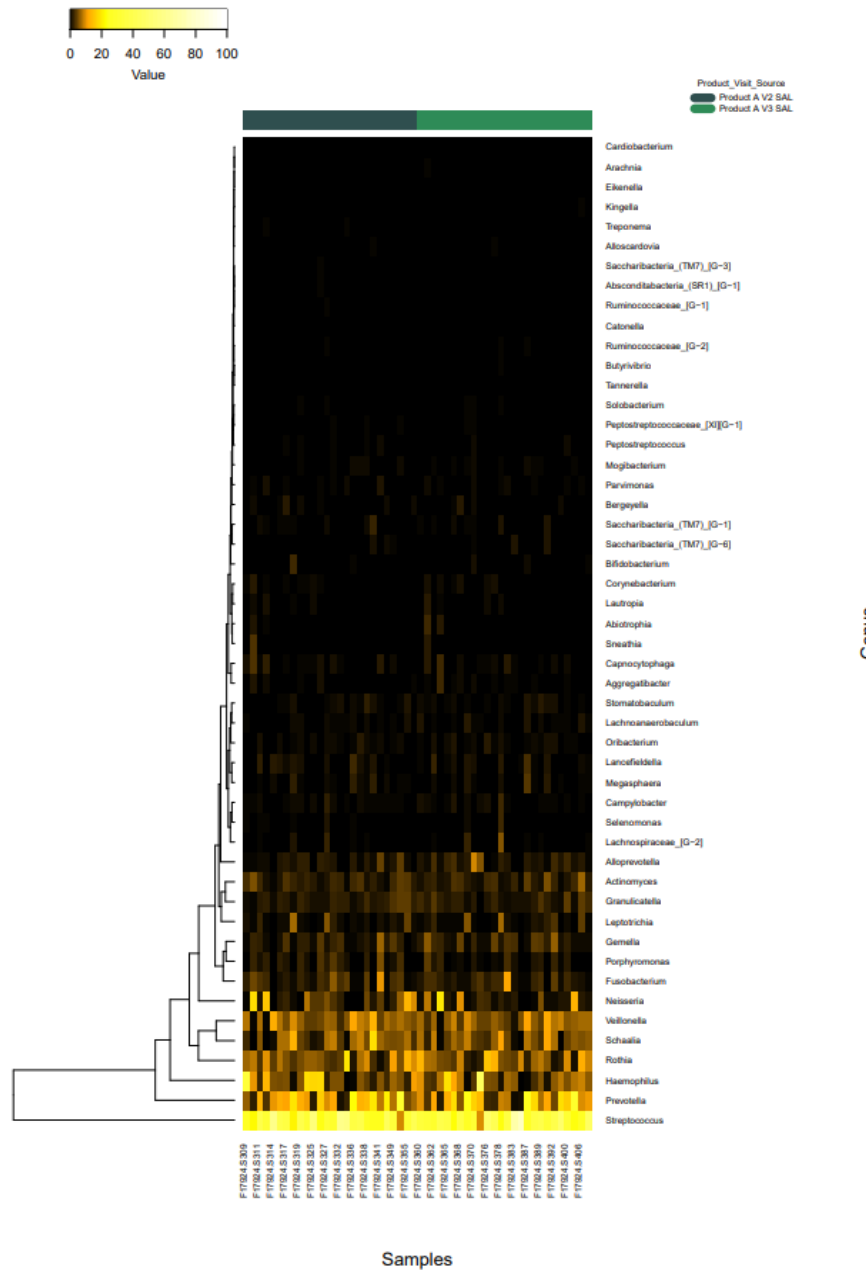
Note: Differences can be better seen in the following graphs for individual taxa



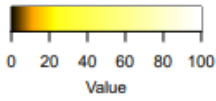
Note: Very low levels. Likely not biologically significant.



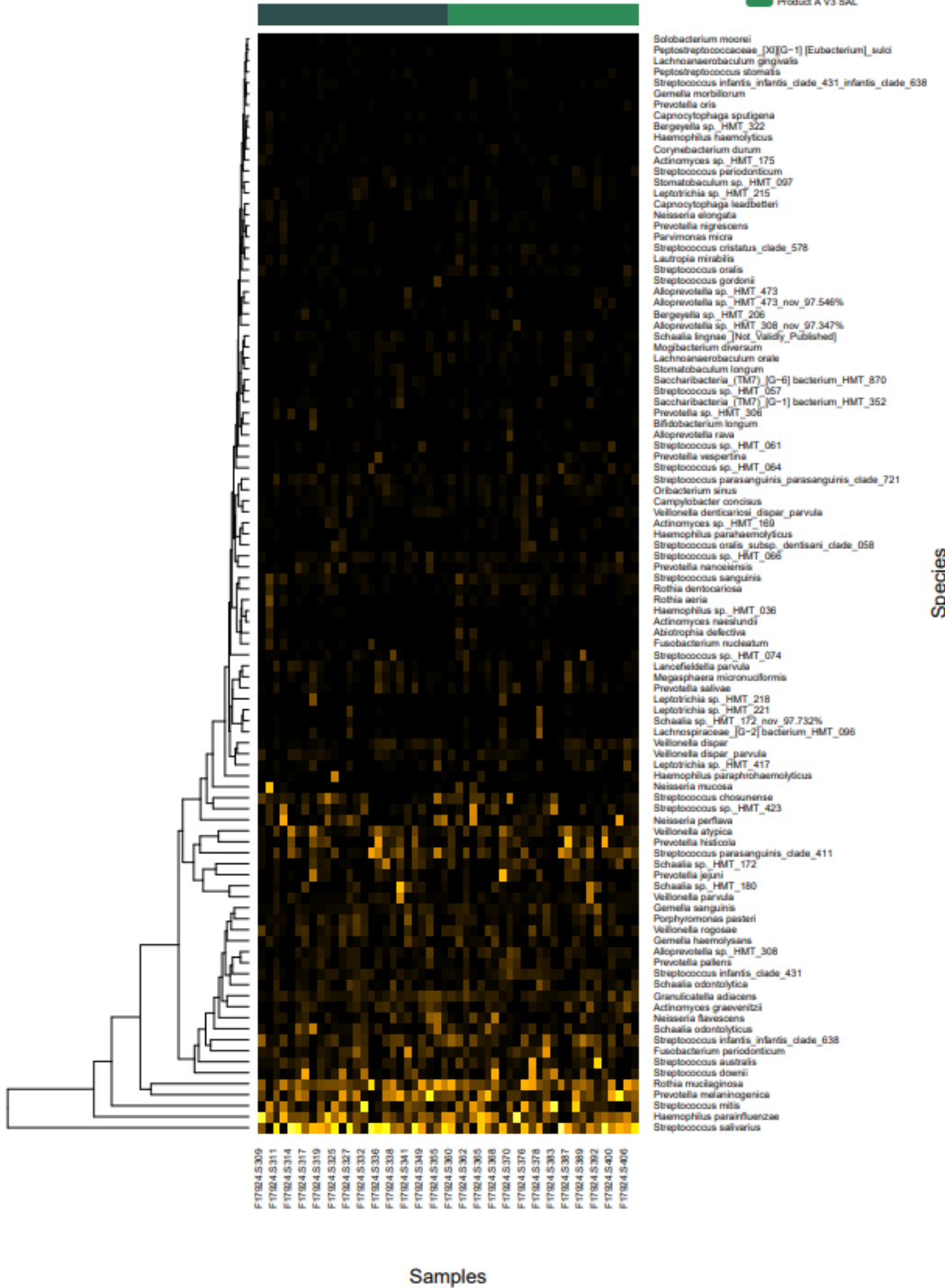
6. Heat maps—difficult to see, visualization of the differences at the species and genus levels is shown below.





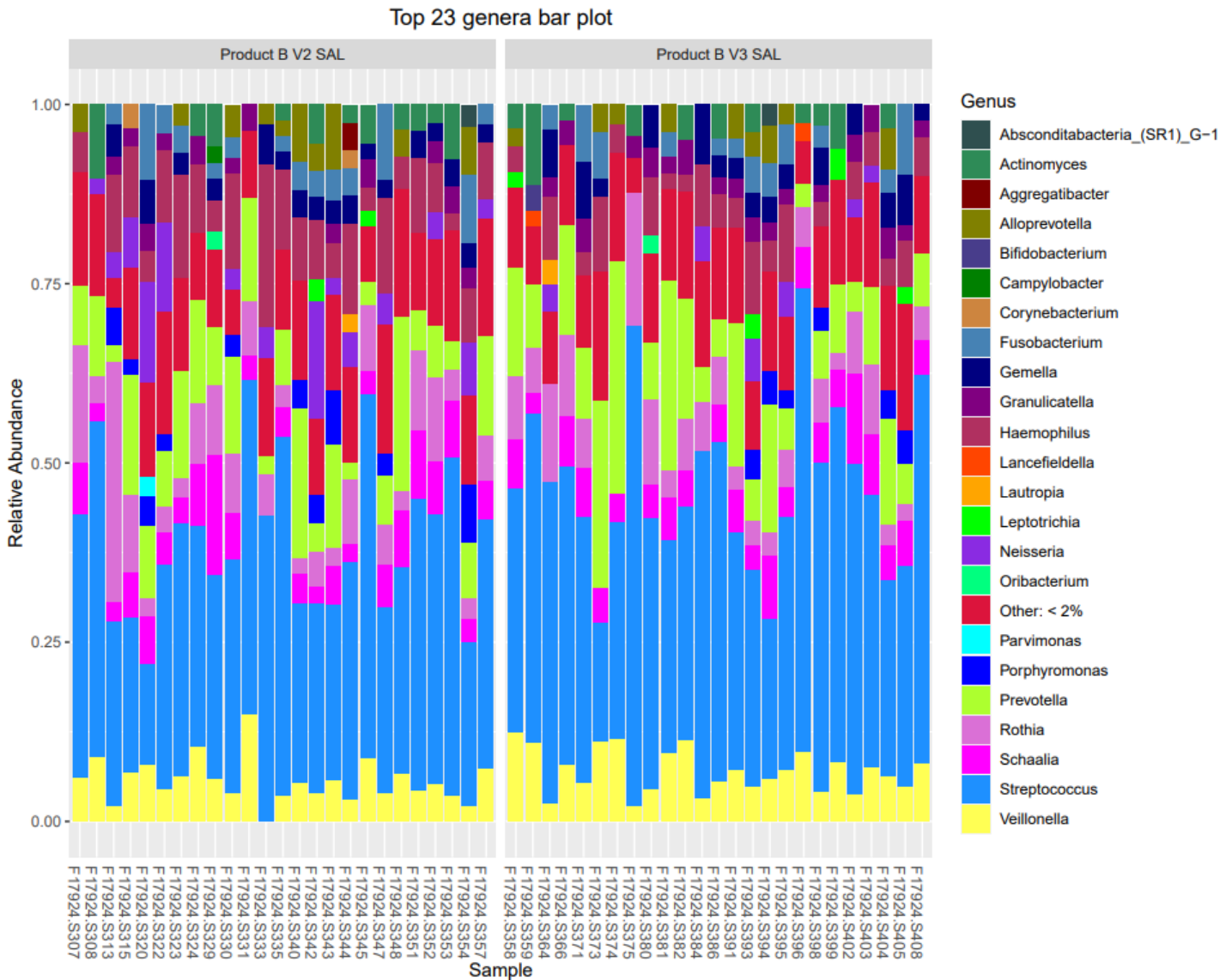


Product\_Visit\_Source  
 Product A V2 SAL  
 Product A V3 SAL

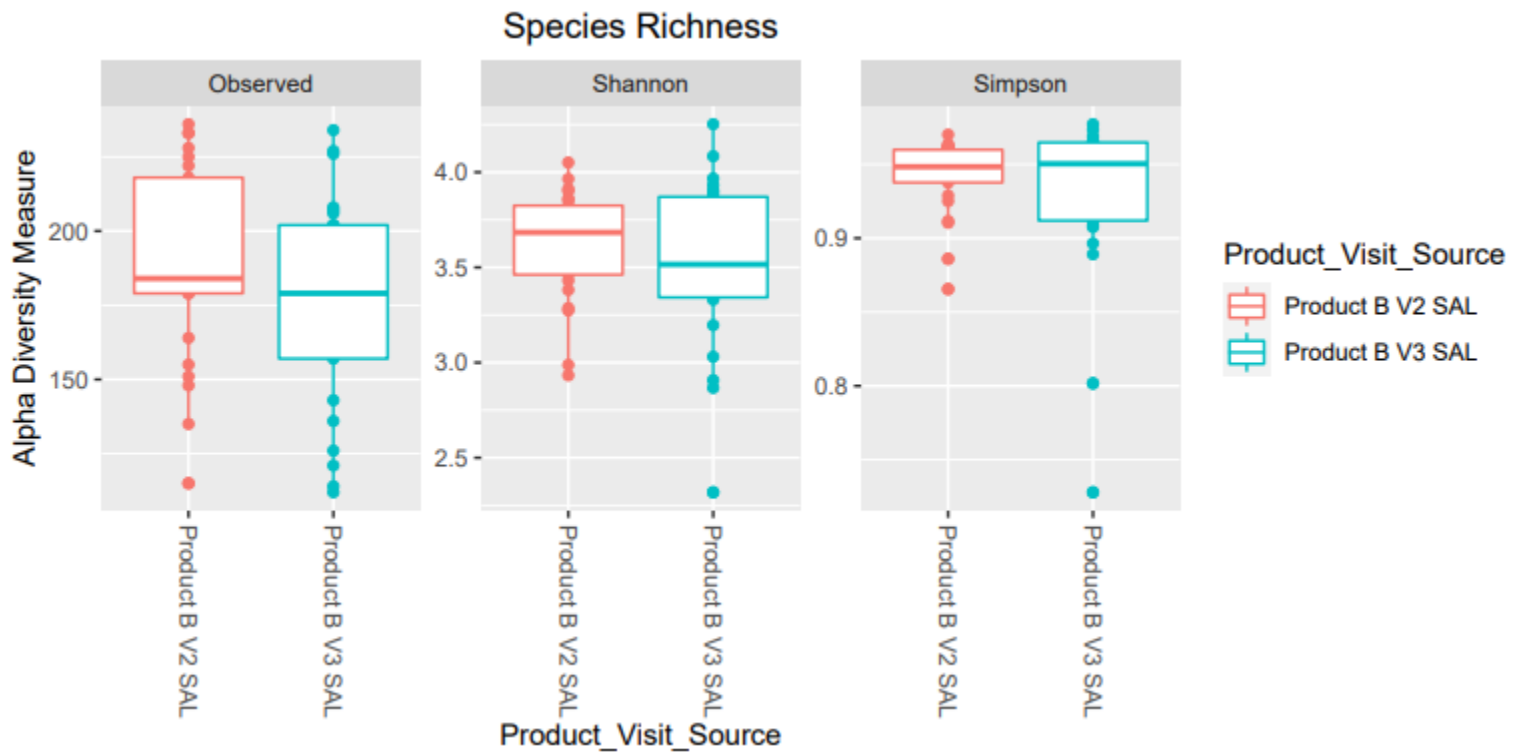


# Comparison 6. Product B V2 vs Product B V3

## 1) Taxonomy barplots

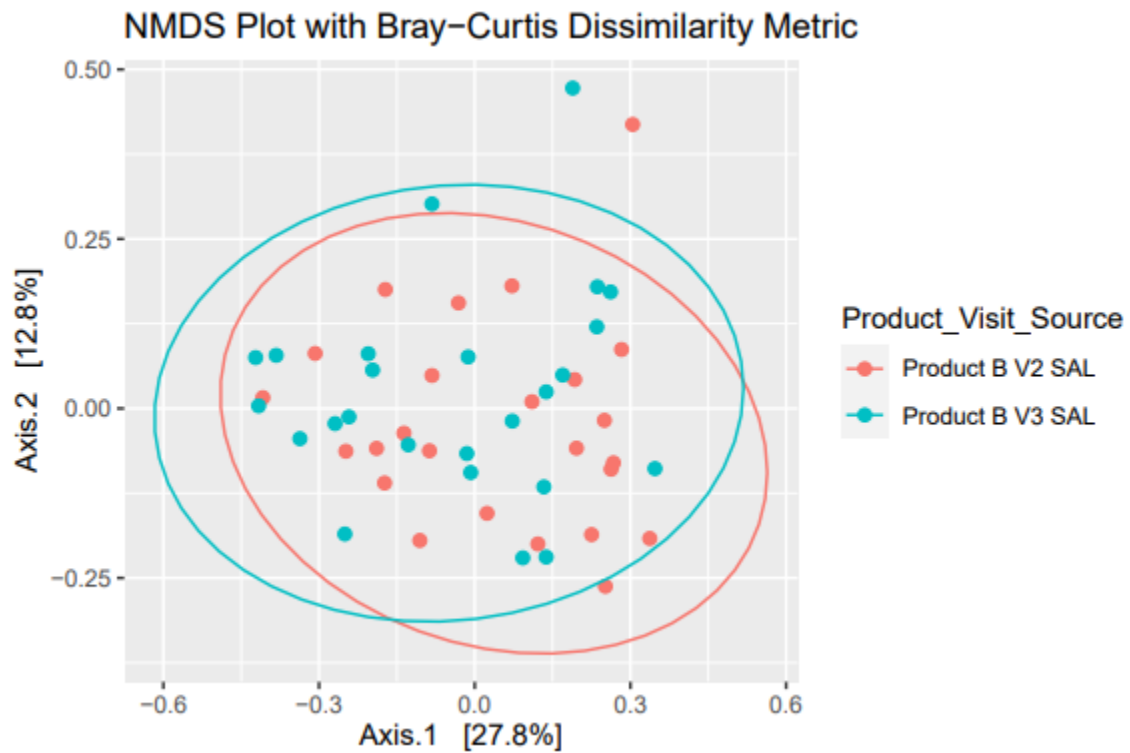


## 2) Alpha diversity



Note: No significant differences

### 3) Beta diversity



Note: Significant difference

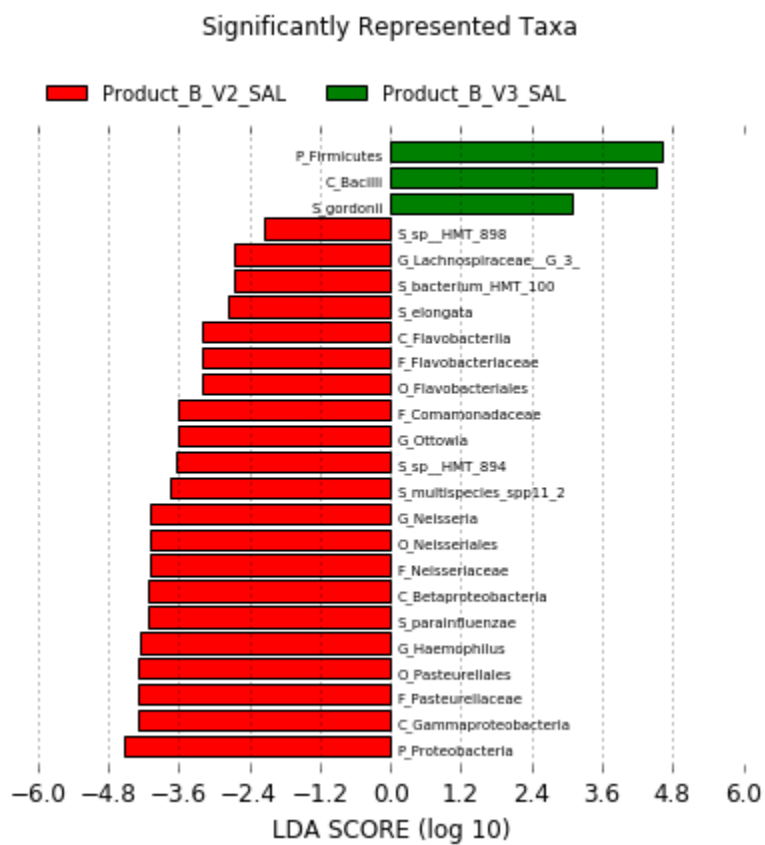
Group 1	Group 2	Sample size	Permutations	pseudo-F	p-value
Product B V2 SAL	Product B V3 SAL	50	999	2.081426	0.027

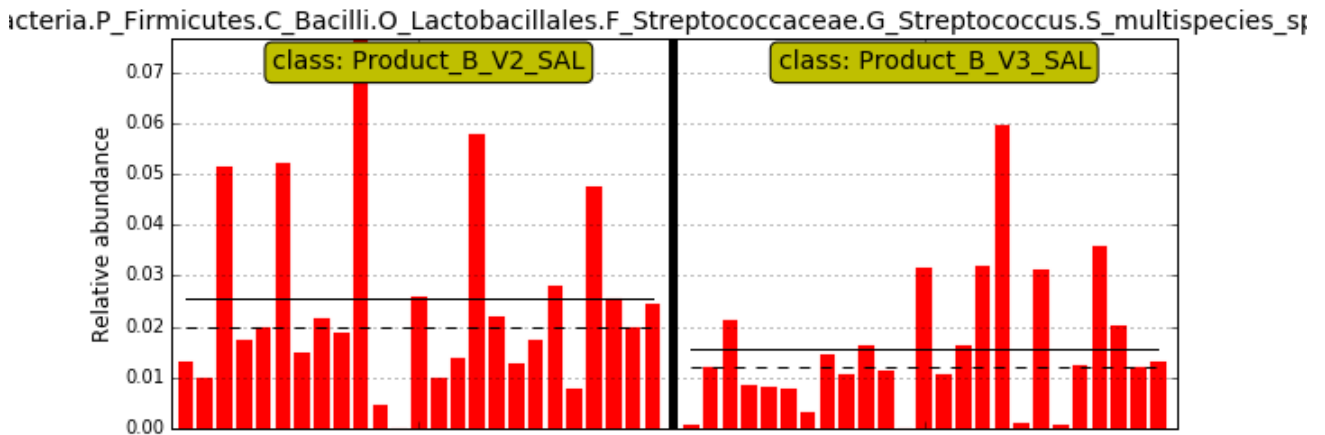
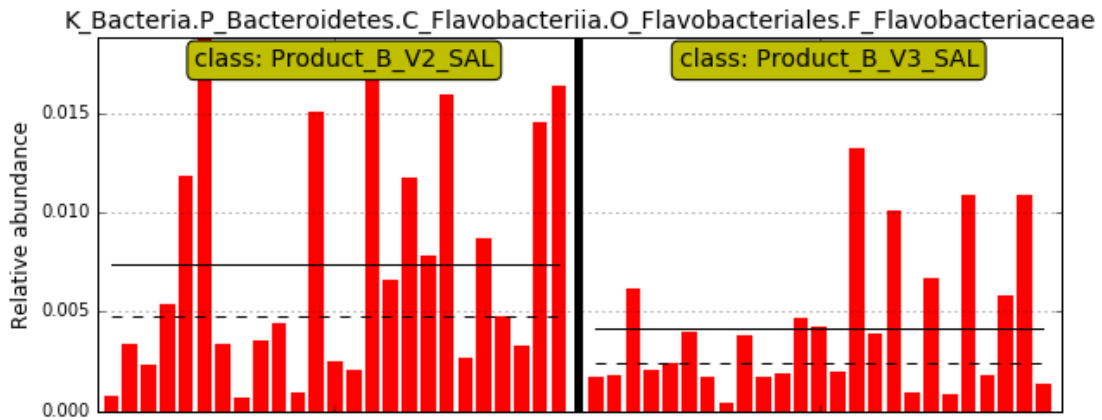
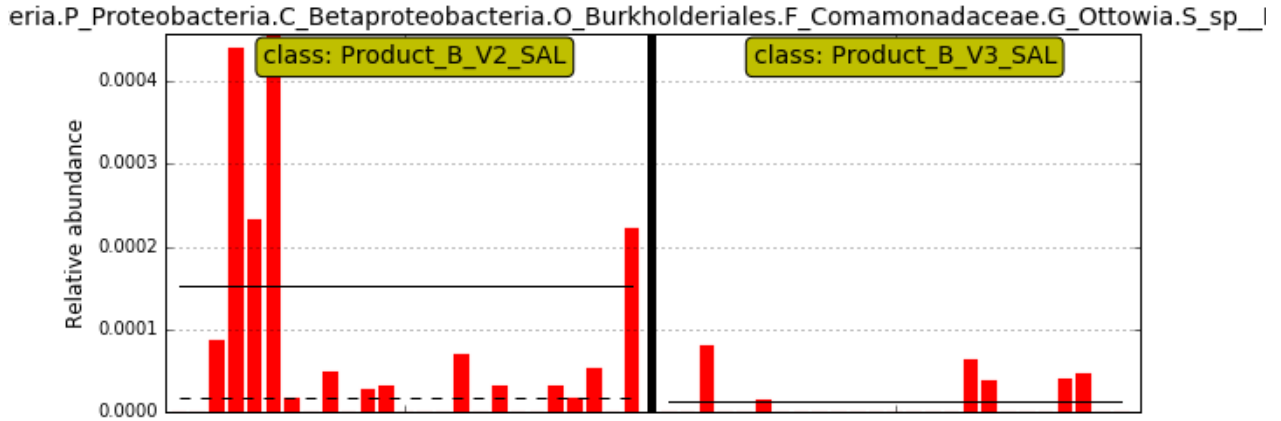
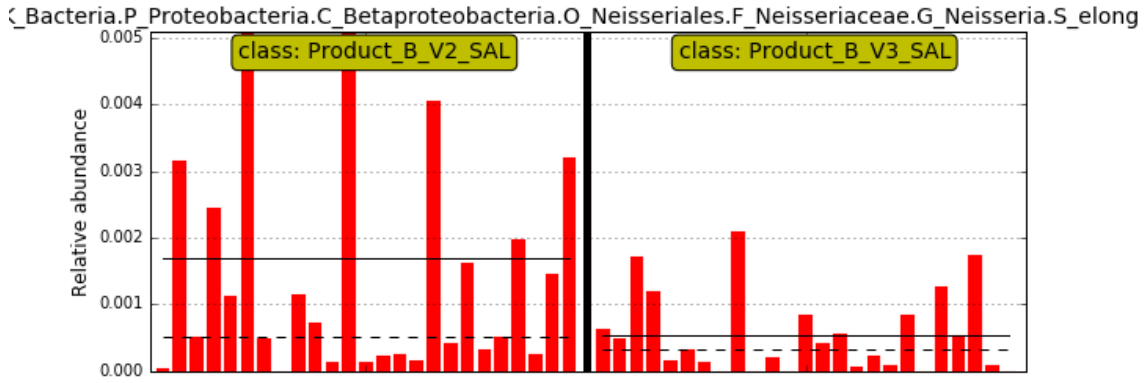
#### 4) Differential abundance

taxon	lfc_(Inter	lfc_Produc	se_(Inter	se_Produc	W_(Inter	W_Produc	p_(Inter	p_Product	q_(Inter	q_Product	diff_(Inte	diff_Prod
Neisseria elongata (SP219)	0.642883	-1.28577	0.397879	0.562686	1.615774	-2.28505	0.106143	0.02231	1	1	FALSE	FALSE
Haemophilus parainfluenzae (SP19)	0.501821	-1.00364	0.317301	0.448732	1.581527	-2.23662	0.113758	0.025311	1	1	FALSE	FALSE
Prevotella nanceiensis (SP203)	0.600703	-1.20141	0.446665	0.63168	1.344861	-1.90192	0.17867	0.057181	1	1	FALSE	FALSE
Ottowia sp._HMT_894 (SP249)	0.373347	-0.74669	0.30124	0.426018	1.239365	-1.75273	0.21521	0.079649	1	1	FALSE	FALSE
Prevotella buccae (SP9)	-0.3709	0.741802	0.299814	0.424001	-1.2371	1.749528	0.216048	0.0802	1	1	FALSE	FALSE
Aggregatibacter sp._HMT_898 (SP119)	0.480565	-0.96113	0.391906	0.554239	1.226225	-1.73415	0.220114	0.082892	1	1	FALSE	FALSE
Kingella oralis (SP198)	0.391588	-0.78318	0.31946	0.451784	1.225782	-1.73352	0.220281	0.083004	1	1	FALSE	FALSE
Shuttleworthia satellites (SP268)	-0.38679	0.773589	0.316075	0.446998	-1.22374	1.730633	0.221049	0.083517	1	1	FALSE	FALSE
Haemophilus haemolyticus (SP104)	0.656975	-1.31395	0.555752	0.785952	1.182137	-1.67179	0.237151	0.094565	1	1	FALSE	FALSE
Treponema maltophilum (SP47)	-0.23761	0.475213	0.206802	0.292462	-1.14896	1.62487	0.250573	0.10419	1	1	FALSE	FALSE
Streptococcus infantis_infantis_clade_638	0.427432	-0.85486	0.372246	0.526435	1.14825	-1.62387	0.250865	0.104403	1	1	FALSE	FALSE
Cryptobacterium curtum (SP465)	-0.38123	0.762453	0.334649	0.473265	-1.13918	1.611048	0.254626	0.107169	1	1	FALSE	FALSE
Lachnospiraceae_[G-3]_bacterium_HMT_10	0.478948	-0.9579	0.424491	0.60032	1.128288	-1.59564	0.259198	0.110569	1	1	FALSE	FALSE
Actinomyces israelii_nov_97.410% (SPN64)	-0.31901	0.638014	0.283879	0.401466	-1.12374	1.589211	0.261122	0.112013	1	1	FALSE	FALSE
Parvimonas sp._HMT_393_nov_97.053% (SF	0.664223	-1.32845	0.598395	0.846259	1.110007	-1.56979	0.266996	0.116464	1	1	FALSE	FALSE

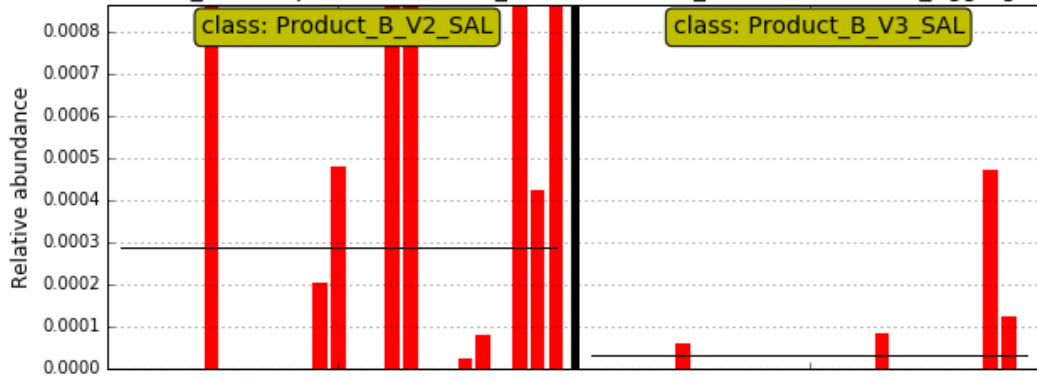
Note: Not significantly different, but a trend can be seen. P value is no longer significant after multiple comparisons.

## 5) LefSe

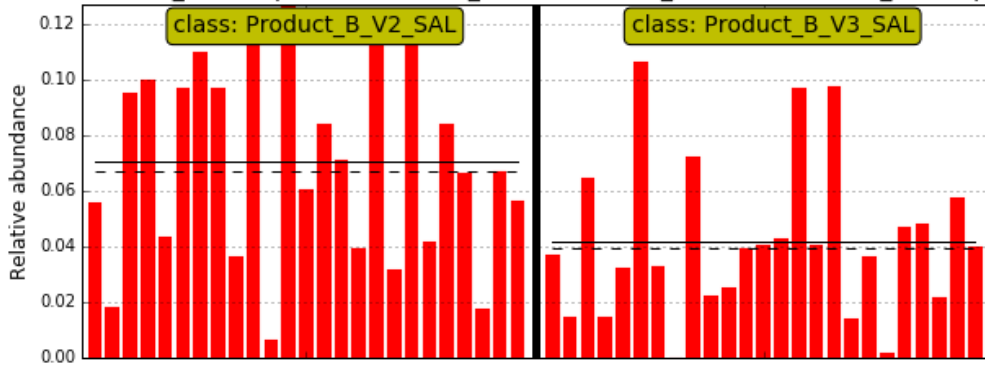




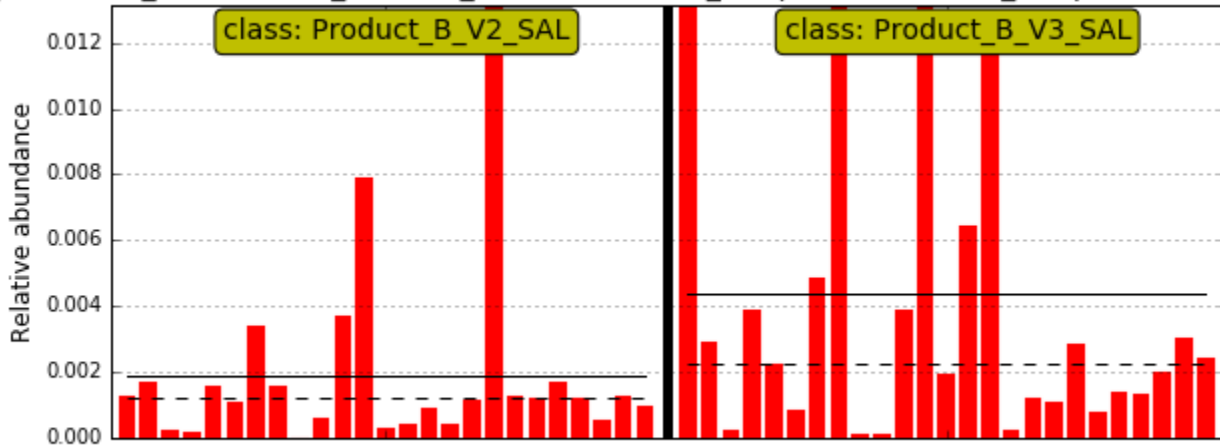
i.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Aggregatibacter.S\_s



a.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Haemophilus.S\_par

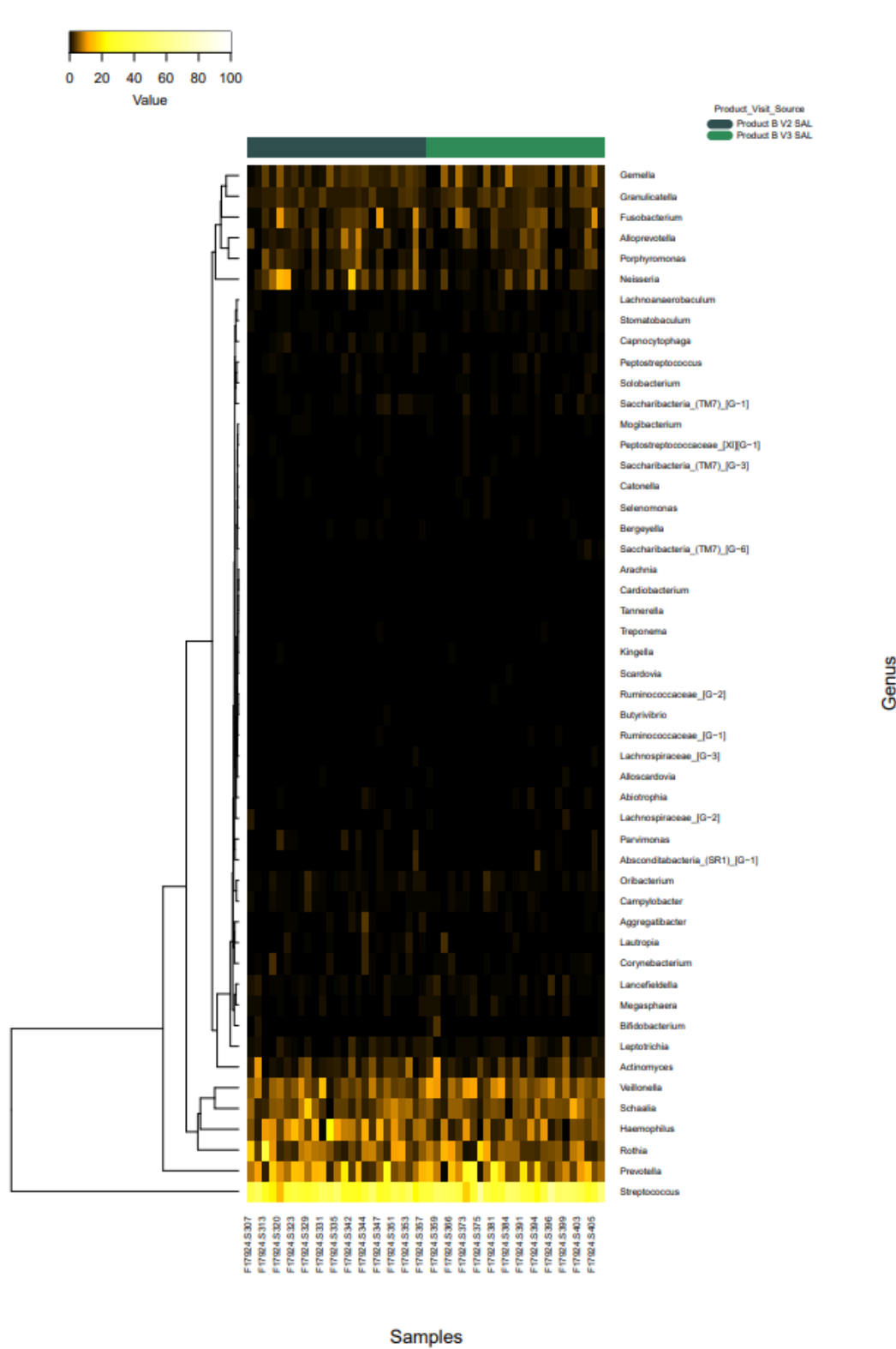


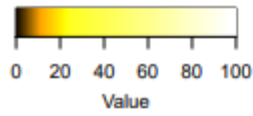
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Streptococcaceae.G\_Streptococcus.S\_gordonii



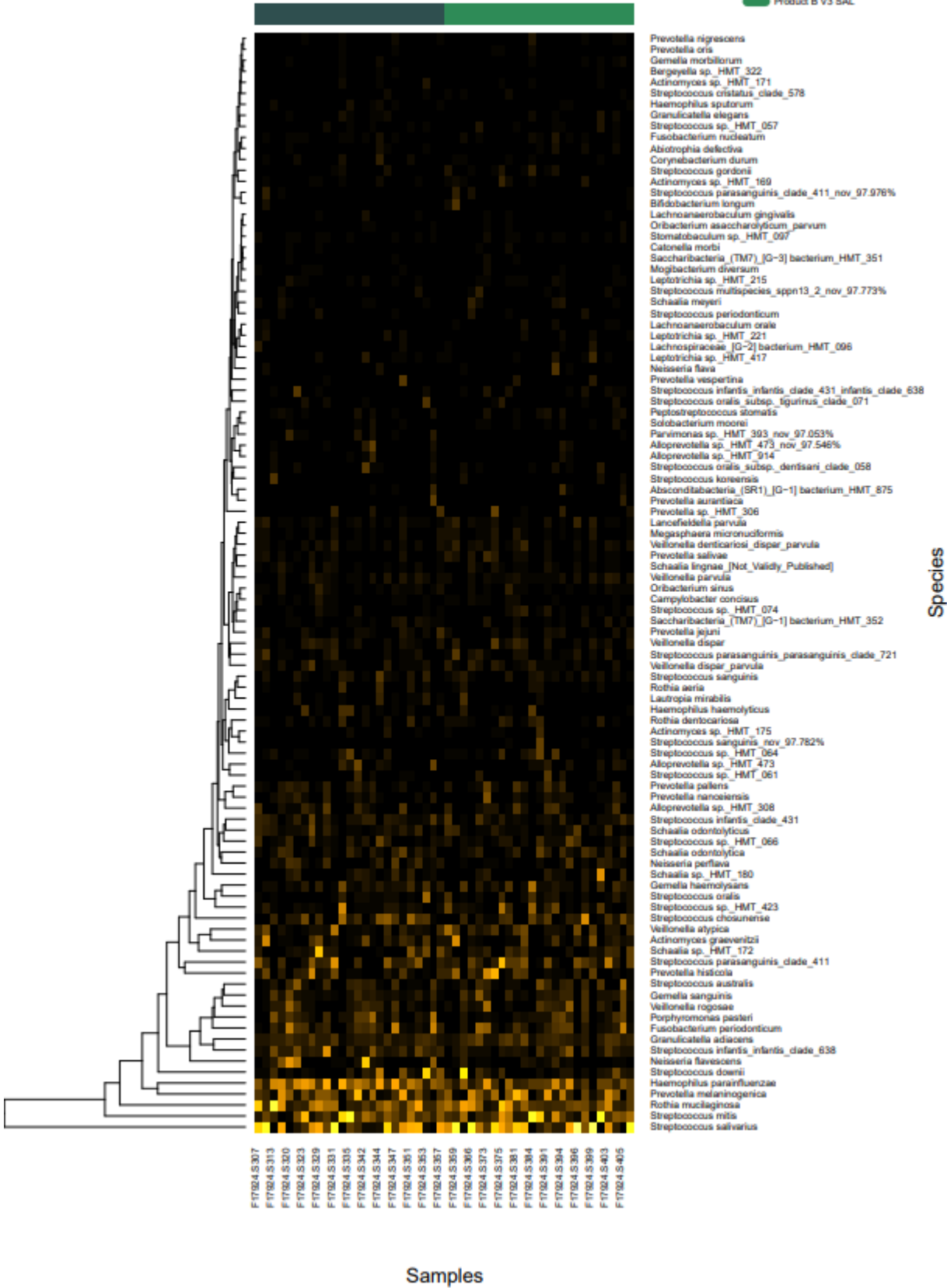


## 6) Heat maps



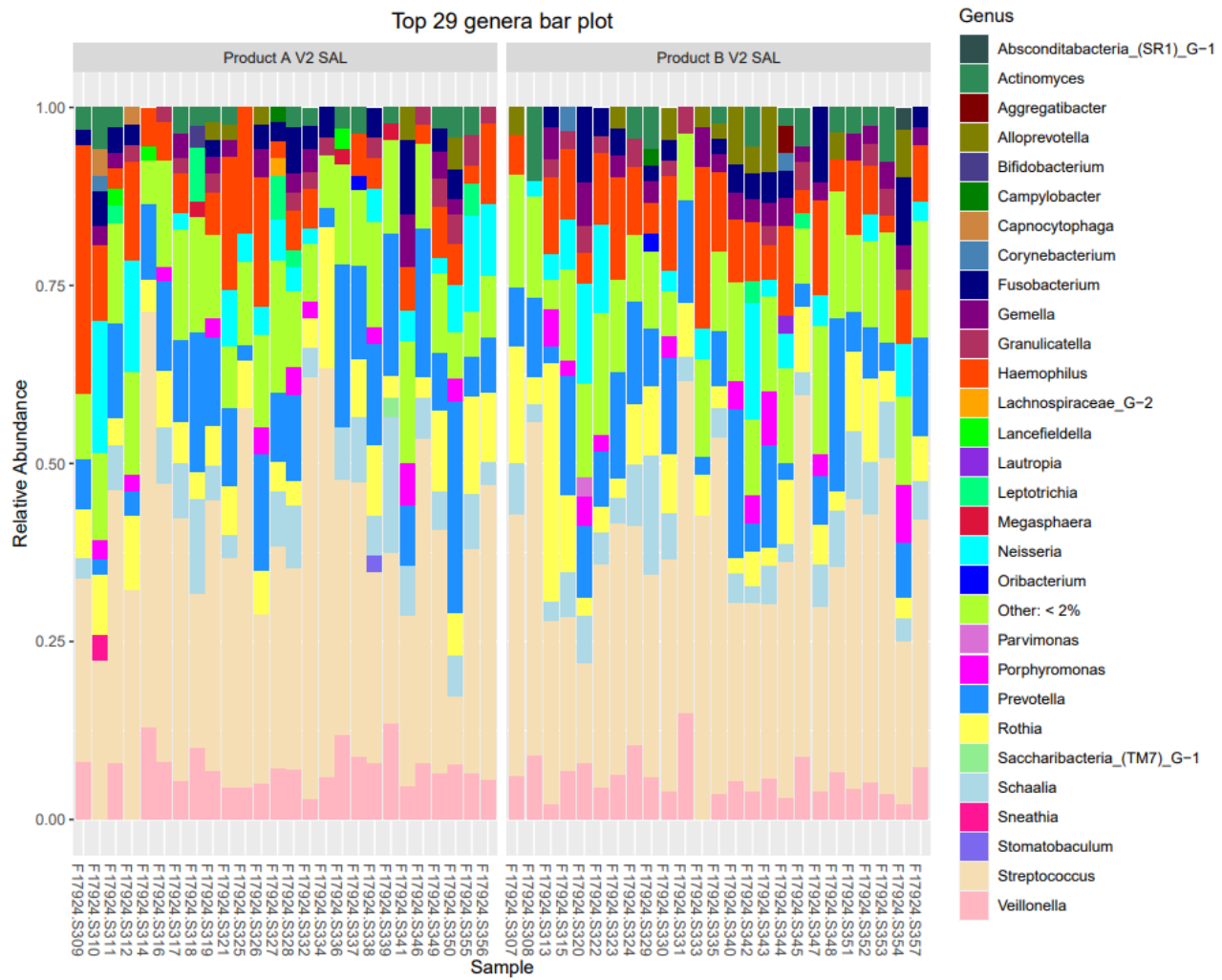


Product\_Visit\_Source  
 Product B V2 SAL  
 Product B V3 SAL

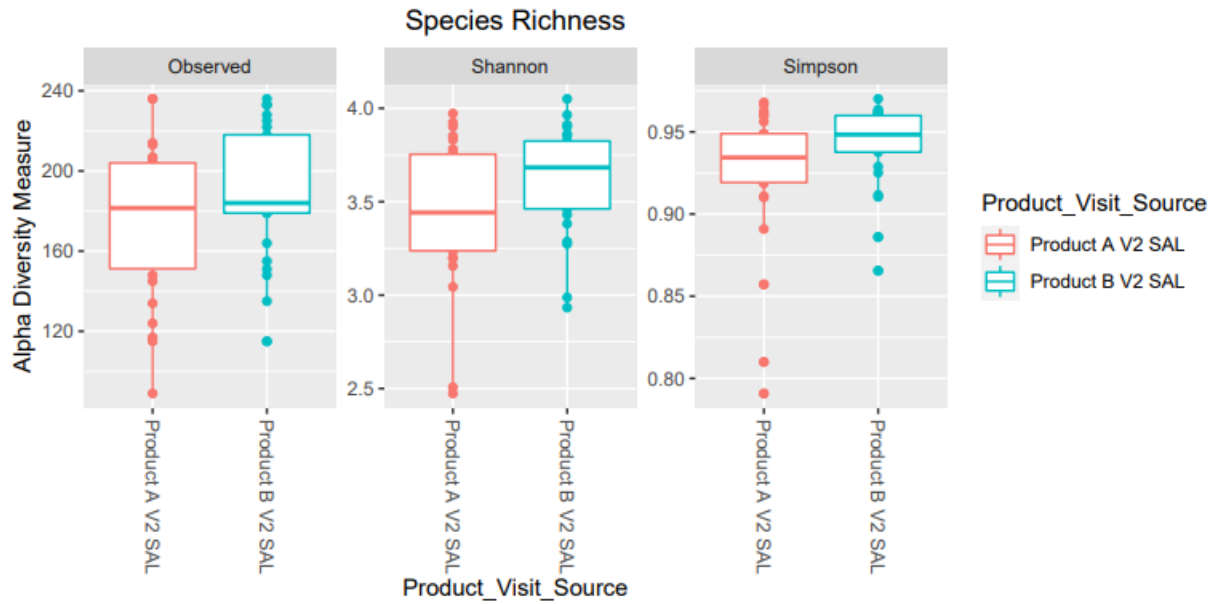


# Comparison 7. Product A V2 SAL vs Product B V2 SAL

## 1) Taxonomy Barplots



## 2) Alpha diversity



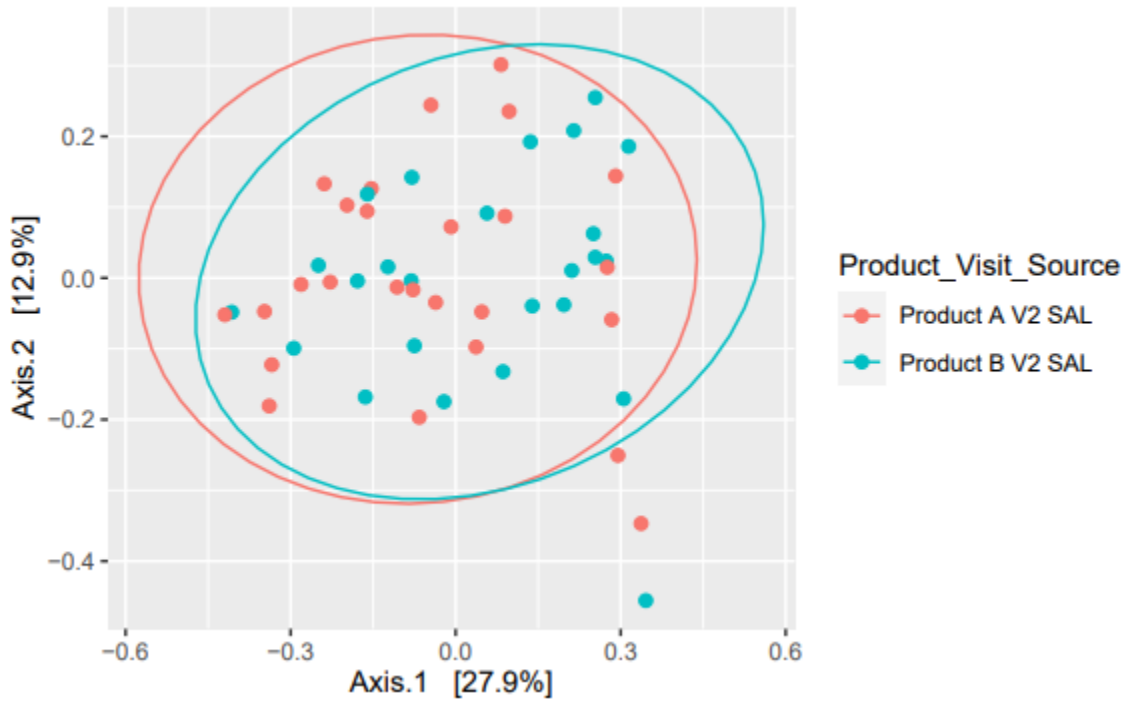
Note: No significant differences in observed with Shannon

No Significant difference but close to significance with Simpson

Group 1	Group 2	H	p-value	q-value
Product A V2 SAL (n=26)	Product B V2 SAL (n=25)	3.479645	0.062128	0.062128

### 3) Beta diversity

#### NMDS Plot with Bray-Curtis Dissimilarity Metric



Note: No Statistically significant differences

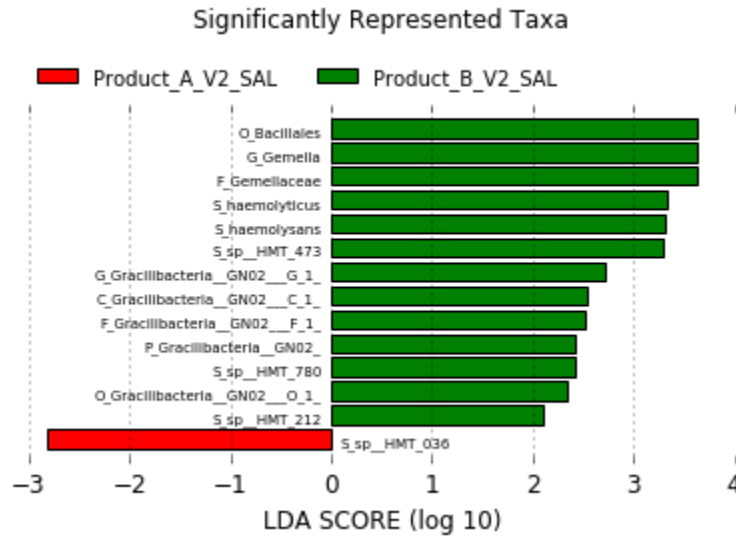
#### 4) Differential abundance

taxon	lfc_(Interc	lfc_Product	use_(Interc	se_Product	W_(Interc	W_Product	p_(Interc	p_Product	q_(Interc	q_Product	diff_(Inte	diff_Produ
Veillonella sp._HMT_780 (SP10)	-0.68859	1.404731	0.45337	0.647542	-1.51882	2.169328	0.128807	0.030058	1	1	FALSE	FALSE
Leptotrichia sp._HMT_212 (SP146)	-0.52622	1.073502	0.364752	0.52097	-1.44269	2.060584	0.149109	0.039343	1	1	FALSE	FALSE
Alloprevotella sp._HMT_473 (SP132)	-0.81471	1.662014	0.595538	0.850598	-1.36802	1.953935	0.171305	0.050709	1	1	FALSE	FALSE
Prevotella sp._HMT_300_nov_97.347% (SPN392)	0.419086	-0.85493	0.311201	0.444483	1.346676	-1.92342	0.178085	0.054427	1	1	FALSE	FALSE
Haemophilus haemolyticus (SP104)	-0.74779	1.525504	0.557227	0.79588	-1.34199	1.916752	0.1796	0.05527	1	1	FALSE	FALSE
Gemella haemolysans (SP8)	-0.39622	0.808294	0.296928	0.424098	-1.33439	1.905915	0.182075	0.056661	1	1	FALSE	FALSE
Prevotella veroralis (SP110)	-0.55766	1.137627	0.426491	0.60915	-1.30755	1.867563	0.191027	0.061823	1	1	FALSE	FALSE
Lachnoanaerobaculum umeaense (SP232)	0.546731	-1.11532	0.43214	0.617219	1.265172	-1.80701	0.20581	0.07076	1	1	FALSE	FALSE
Aggregatibacter sp._HMT_512 (SP314)	0.411936	-0.84034	0.325985	0.465599	1.263668	-1.80486	0.206349	0.071096	1	1	FALSE	FALSE
Streptococcus sp._HMT_064 (SP305)	-0.60957	1.243525	0.485277	0.693114	-1.25612	1.794113	0.209072	0.072795	1	1	FALSE	FALSE
Streptococcus salivarius (SP135)	0.515443	-1.0515	0.417819	0.596765	1.233653	-1.76199	0.217332	0.07807	1	1	FALSE	FALSE
Prevotella baroniae (SP288)	0.371826	-0.75852	0.329704	0.470912	1.127758	-1.61074	0.259422	0.107236	1	1	FALSE	FALSE
Streptococcus mitis (SP86)	-0.41284	0.842198	0.376772	0.538138	-1.09572	1.565022	0.2732	0.117578	1	1	FALSE	FALSE
Granulicatella elegans (SP138)	-0.5826	1.188503	0.533518	0.762017	-1.09199	1.559681	0.274839	0.118835	1	1	FALSE	FALSE

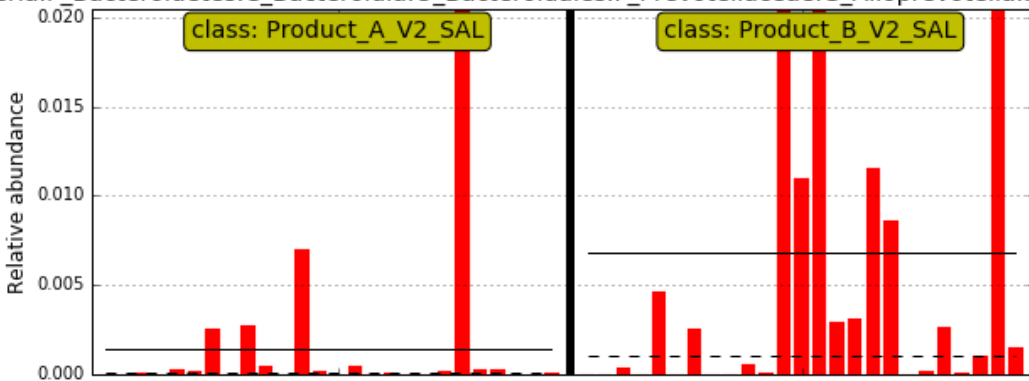
Note: No statistically significant differences. Similar results with Lefse.

5) LefSe -Individual plots will show better

Note: Overall, only minor differences

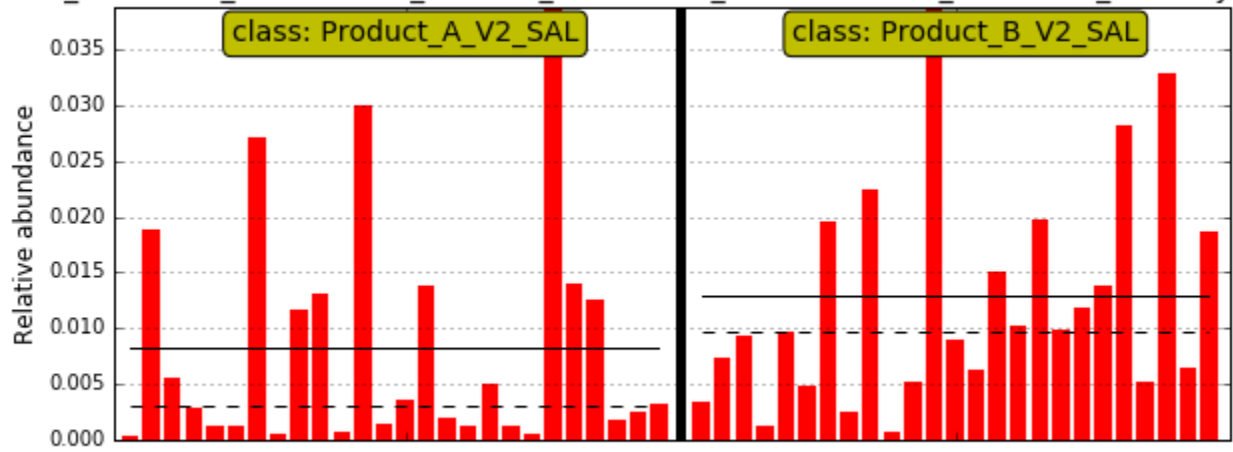


Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Alloprevotella.S\_sp\_HMT

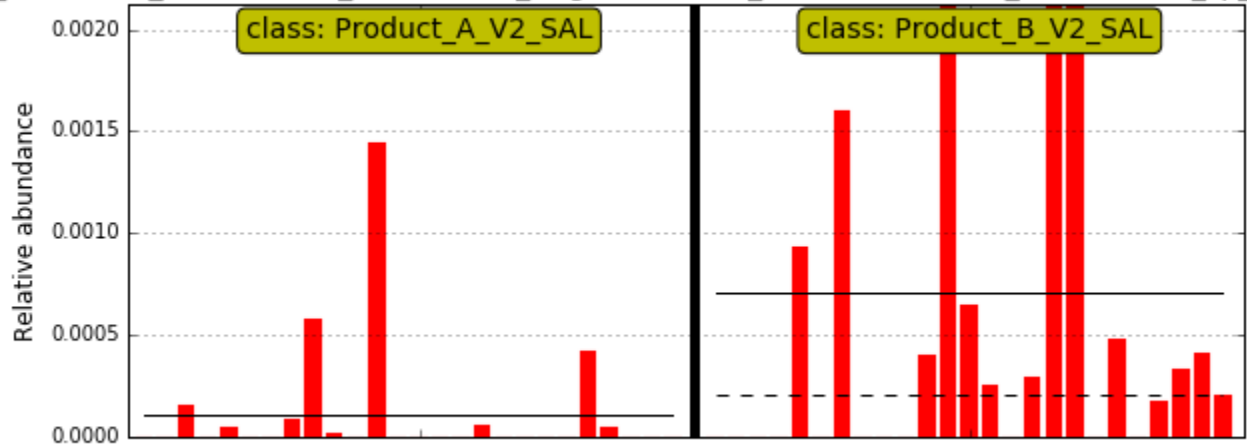


HMT473

K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Bacillales.F\_Gemellaceae.G\_Gemella.S\_haemolysans

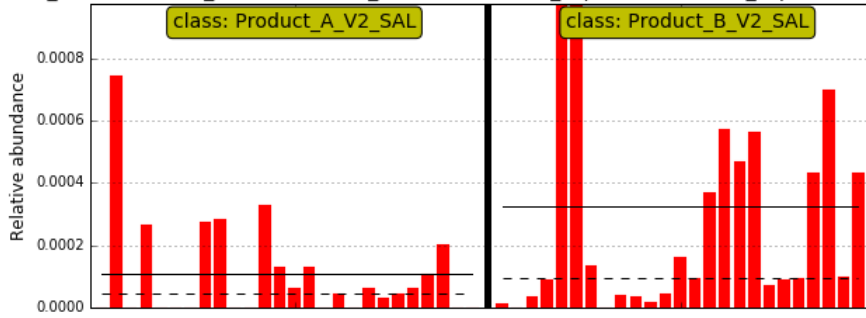


K\_Bacteria.P\_Firmicutes.C\_Clostridia.O\_Negativicutes.F\_Veillonellaceae.G\_Veillonella.S\_sp\_HMT\_780



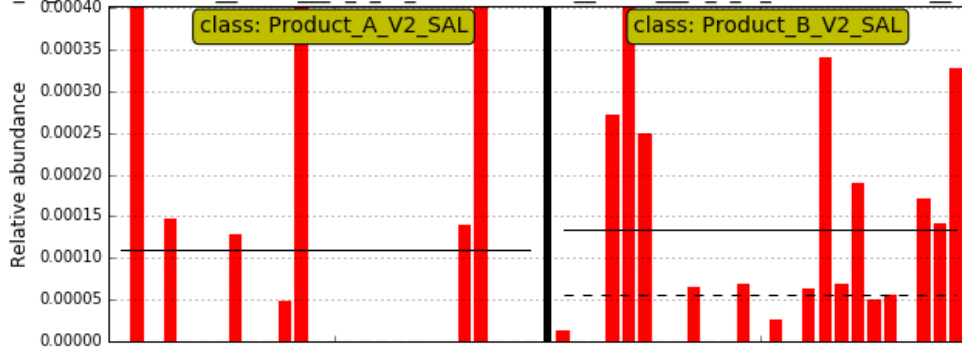


acteria.P\_Fusobacteria.C\_Fusobacteriia.O\_Fusobacteriales.F\_Leptotrichiaceae.G\_Leptotrichia.S\_sp\_HM

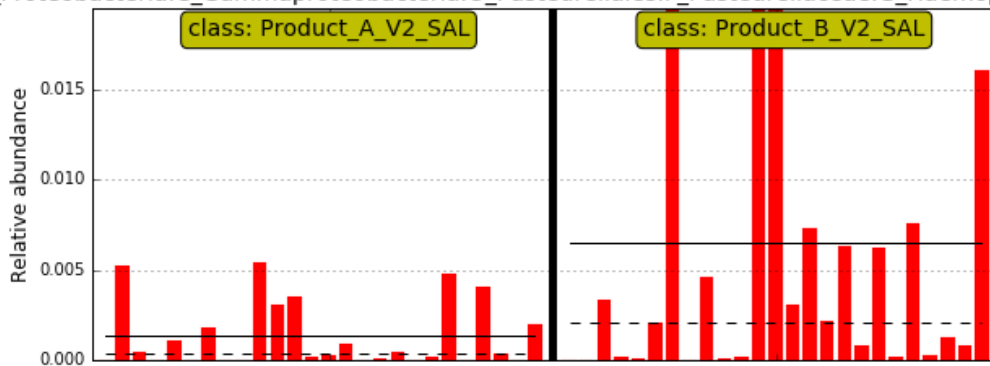


HMT212 very low levels

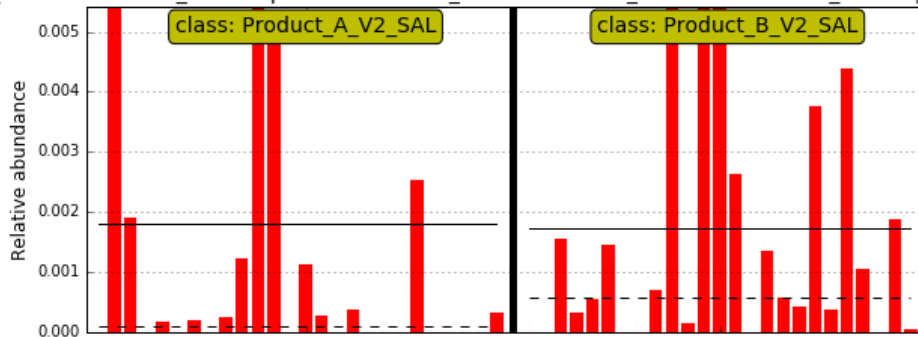
N02\_C\_Gracilibacteria\_GN02\_C\_1\_O\_Gracilibacteria\_GN02\_O\_1\_F\_Gracilibacteria\_GN02\_F\_1



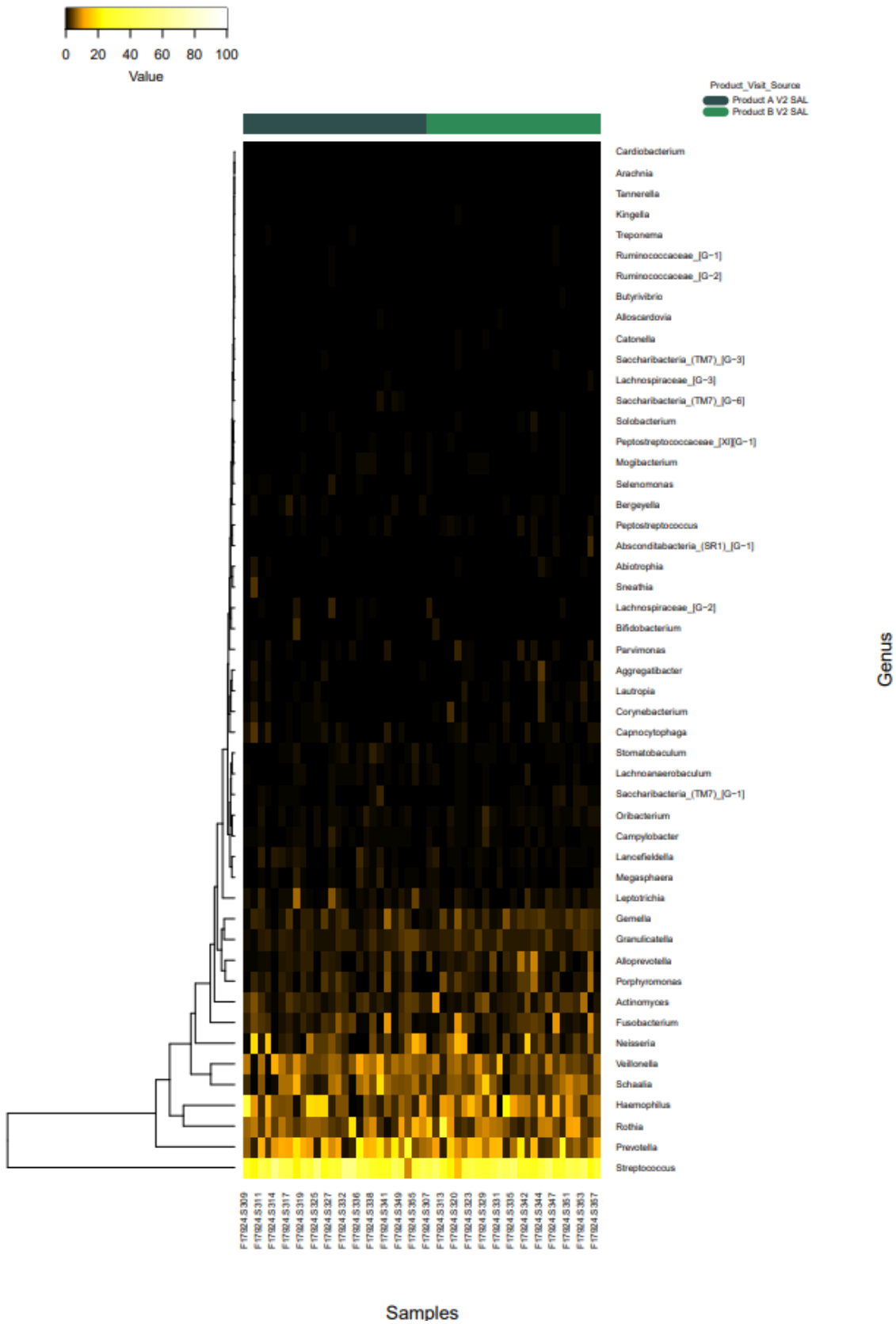
ia.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Haemophilus.S\_ha

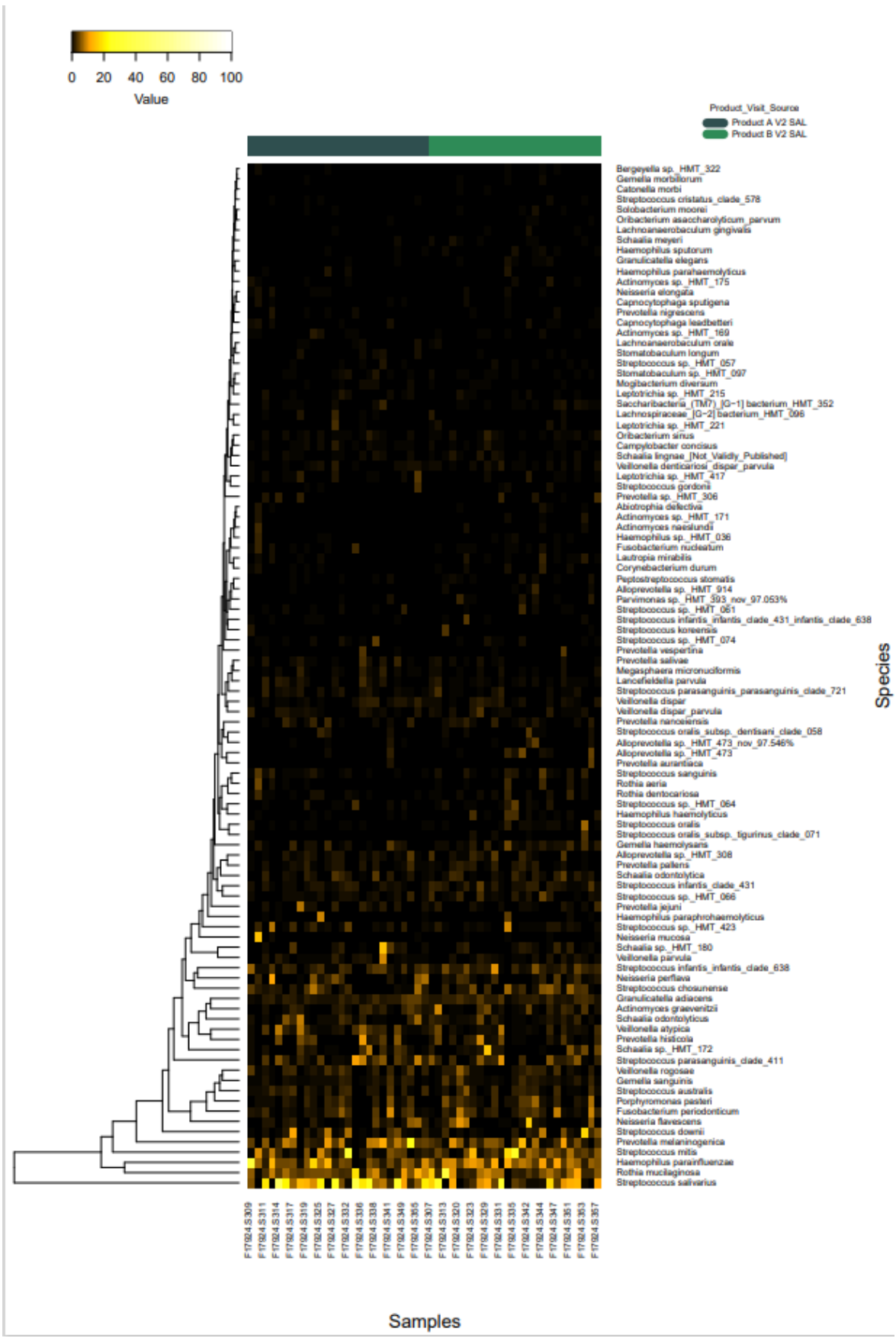


ia.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Haemophilus.S\_sp



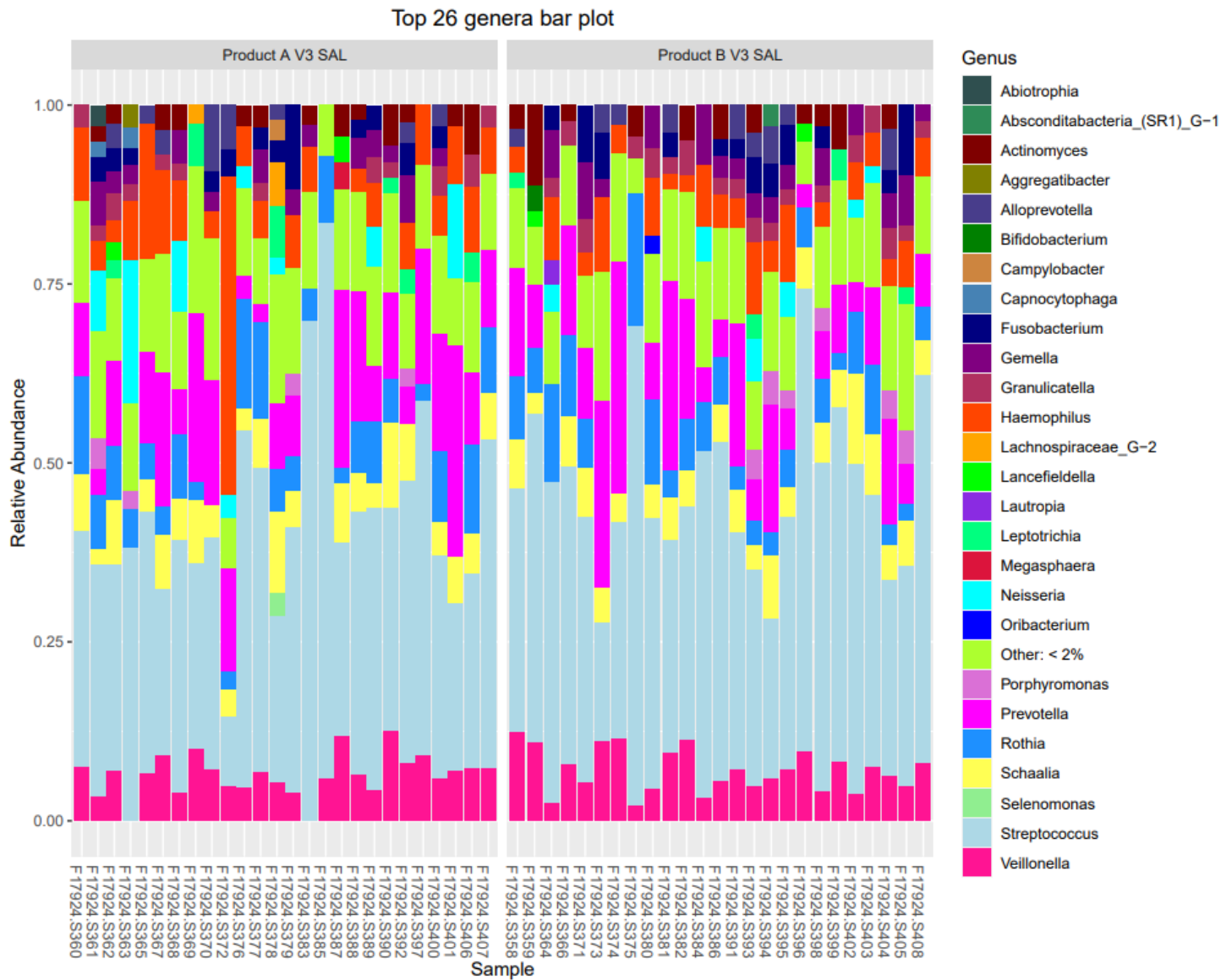
## 6) Heat maps





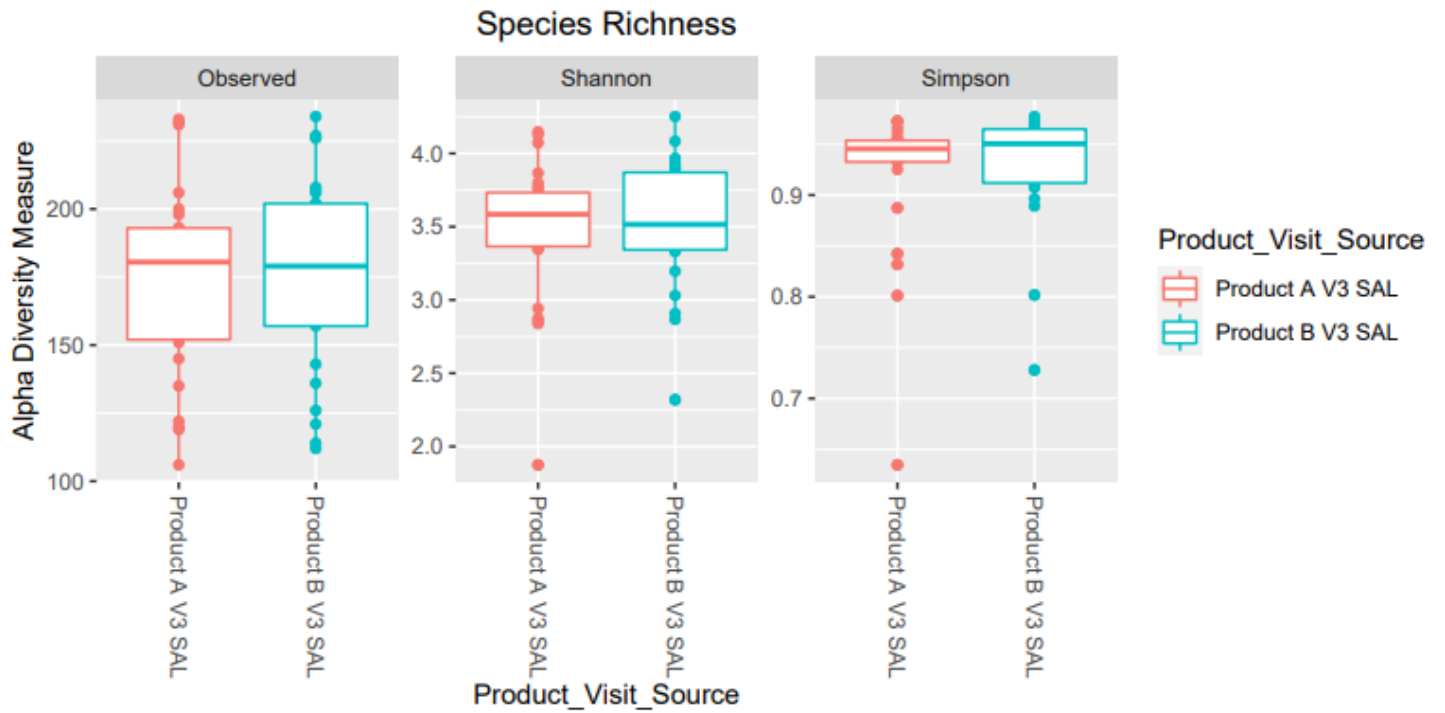
# Comparison 8. Product A V3 SAL vs Product B V3 SAL

## 1) Taxonomy bar graphs



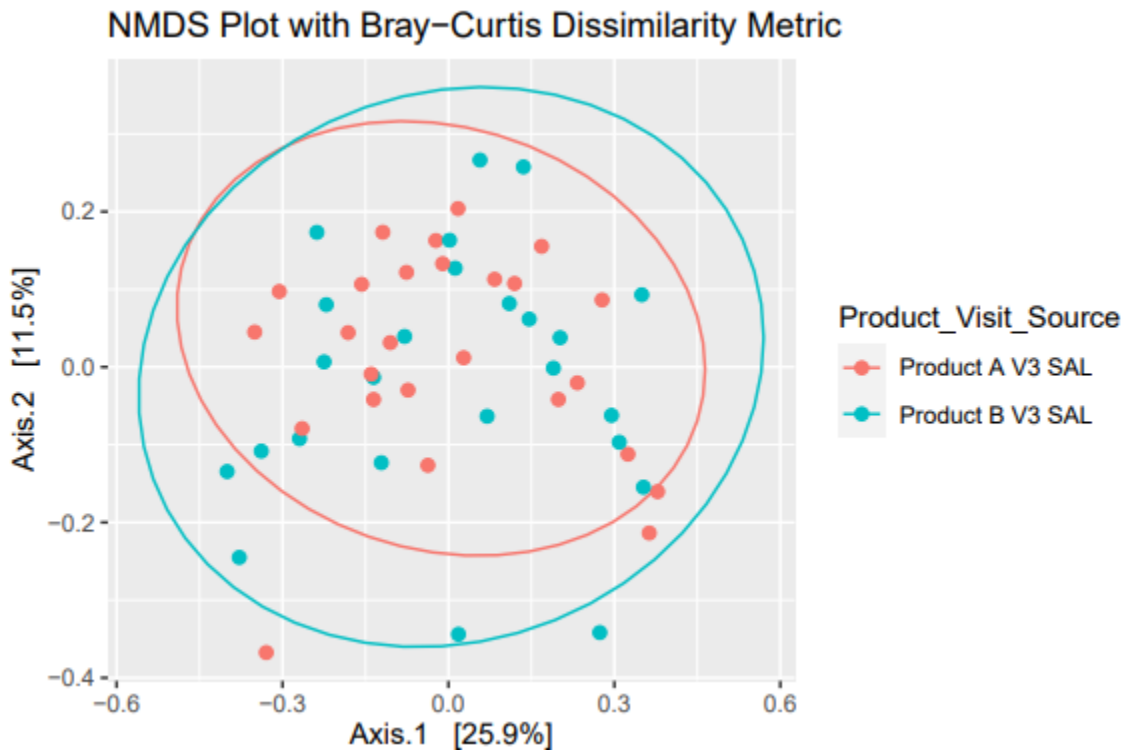
Note: Difficult to see major differences. These will be identified in subsequent analyses.

## 2) Alpha diversity



Note: No significant differences

### 3) Beta diversity



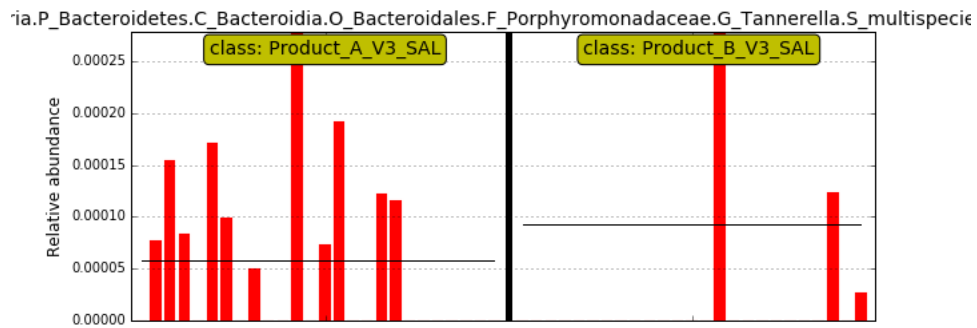
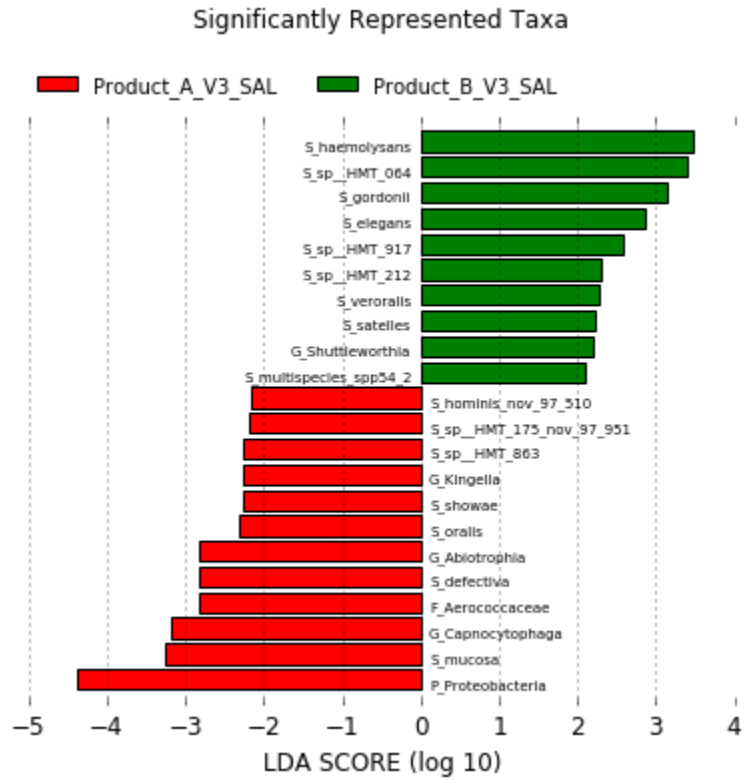
Note: No Significant differences.

#### 4) Differential abundance

taxon	lfc_(Interc	lfc_Produc	use_(Interc	se_Produc	W_(Interc	W_Produc	p_(Interc	p_Product	q_(Interc	q_Product	diff_(Inte	diff_Produ
<i>Neisseria mucosa</i> (SP300)	0.808885	-1.64839	0.4741	0.67715	1.706149	-2.43431	0.08798	0.01492	1	1	FALSE	FALSE
<i>Streptococcus gordonii</i> (SP171)	-0.51714	1.056691	0.308379	0.440453	-1.67695	2.399101	0.093553	0.016435	1	1	FALSE	FALSE
<i>Kingella oralis</i> (SP198)	0.493251	-1.0045	0.324129	0.462948	1.521776	-2.16978	0.128065	0.030023	1	1	FALSE	FALSE
<i>Gemella haemolysans</i> (SP8)	-0.48118	0.983333	0.340775	0.486724	-1.412	2.020307	0.15795	0.043352	1	1	FALSE	FALSE
<i>Streptococcus</i> sp._HMT_064 (SP305)	-0.70931	1.448722	0.504528	0.72061	-1.40588	2.010411	0.159759	0.044388	1	1	FALSE	FALSE
<i>Prevotella veroralis</i> (SP110)	-0.51486	1.052052	0.368871	0.526854	-1.39577	1.996858	0.162783	0.045841	1	1	FALSE	FALSE
<i>Abiotrophia defectiva</i> (SP206)	-0.68767	1.404583	0.501311	0.716015	-1.37174	1.961668	0.170143	0.049801	1	1	FALSE	FALSE
<i>Granulicatella elegans</i> (SP138)	-0.64512	1.317776	0.483061	0.689949	-1.33548	1.909962	0.181719	0.056138	1	1	FALSE	FALSE
<i>Shuttleworthia satelles</i> (SP268)	-0.37622	0.769218	0.284265	0.406011	-1.32347	1.894574	0.185678	0.058149	1	1	FALSE	FALSE
<i>Capnocytophaga</i> sp._HMT_332 (SP49)	0.417666	-0.8503	0.320686	0.458031	1.302417	-1.85643	0.192774	0.063392	1	1	FALSE	FALSE
<i>Prevotella</i> sp._HMT_300_nov_97.347% (SPN	0.375051	-0.76337	0.290806	0.415354	1.289695	-1.83787	0.197157	0.066081	1	1	FALSE	FALSE
<i>Actinomyces</i> sp._HMT_175_nov_97.951% (S	0.456653	-0.92984	0.35769	0.510883	1.276672	-1.82006	0.201718	0.068751	1	1	FALSE	FALSE
<i>Aggregatibacter</i> sp._HMT_512 (SP314)	0.432343	-0.88024	0.340192	0.485891	1.27088	-1.81161	0.203771	0.070047	1	1	FALSE	FALSE
<i>Streptococcus</i> sp._HMT_056 (SP276)	0.488199	-0.99419	0.384377	0.549	1.270104	-1.81091	0.204048	0.070155	1	1	FALSE	FALSE

Note: No significant differences, but lost after multiple comparisons. Similar results in Lefse

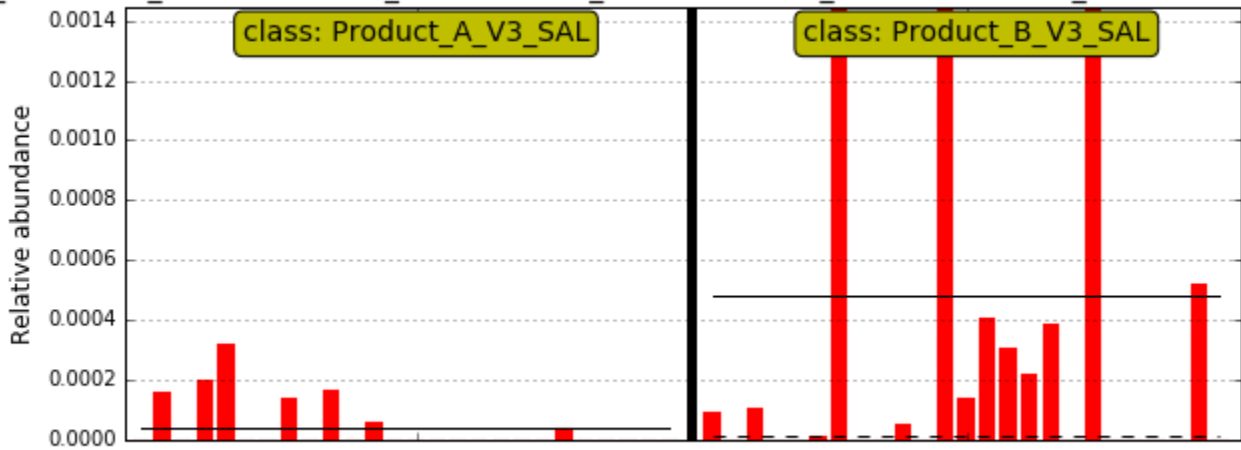
5) Lefse



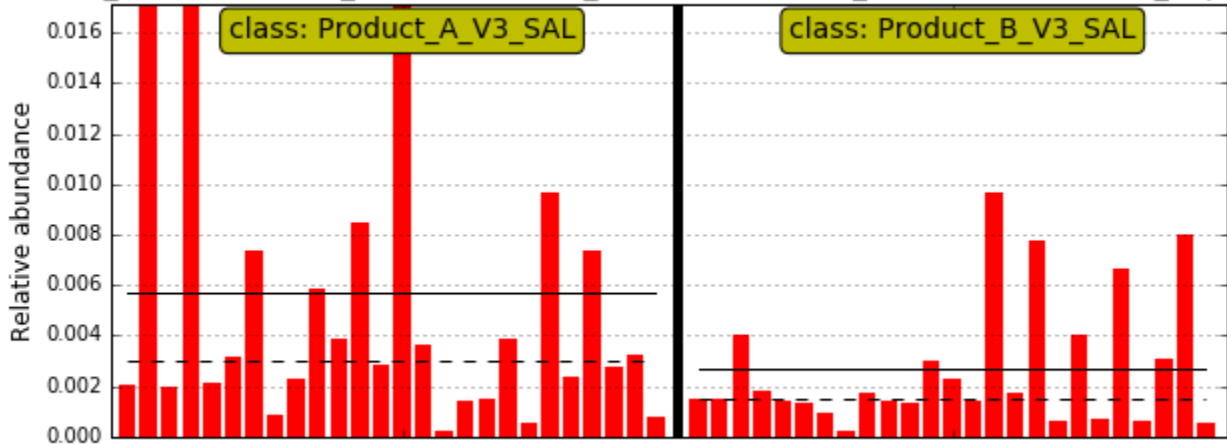
Note: very low levels



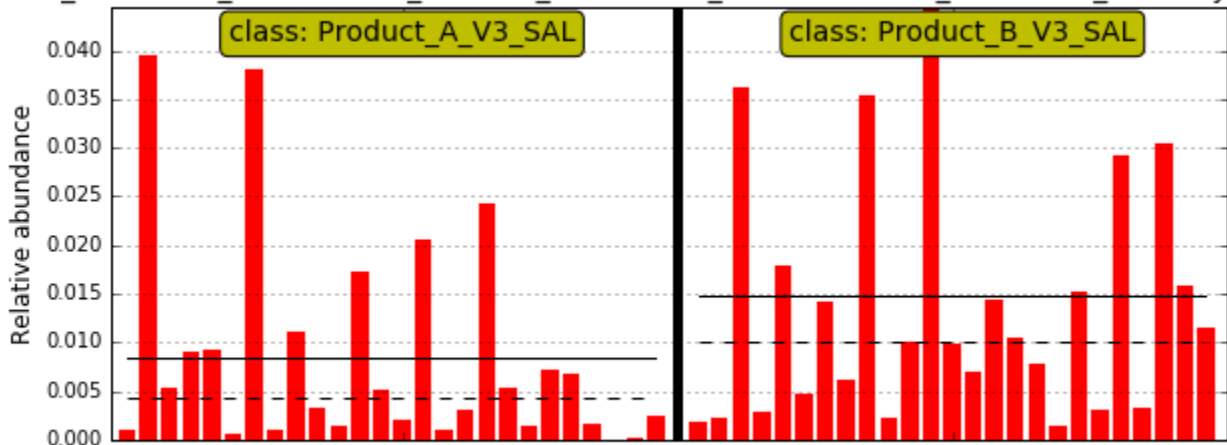
K\_Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Prevotella.S\_veroralis



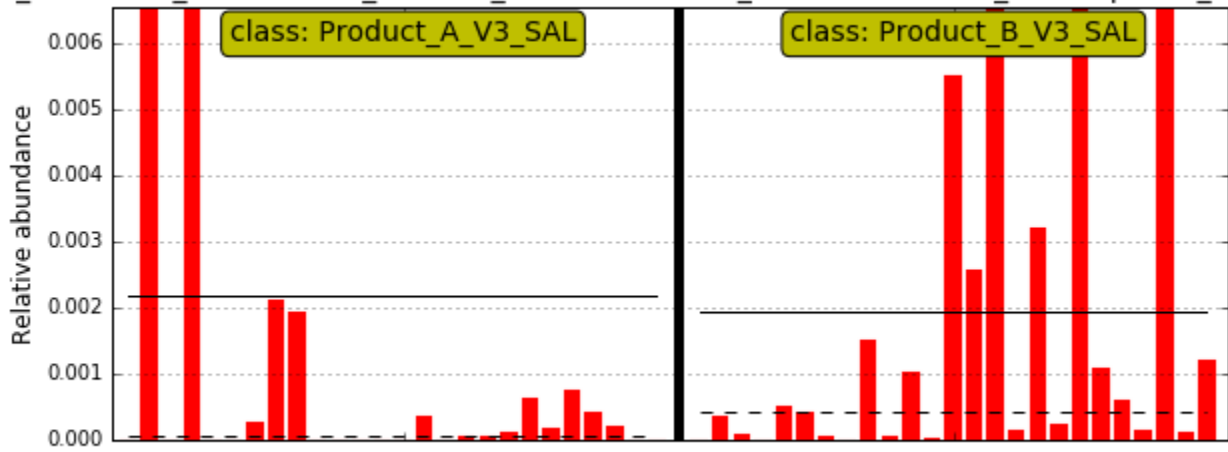
K\_Bacteria.P\_Bacteroidetes.C\_Flavobacteriia.O\_Flavobacteriales.F\_Flavobacteriaceae.G\_Capnocytopha



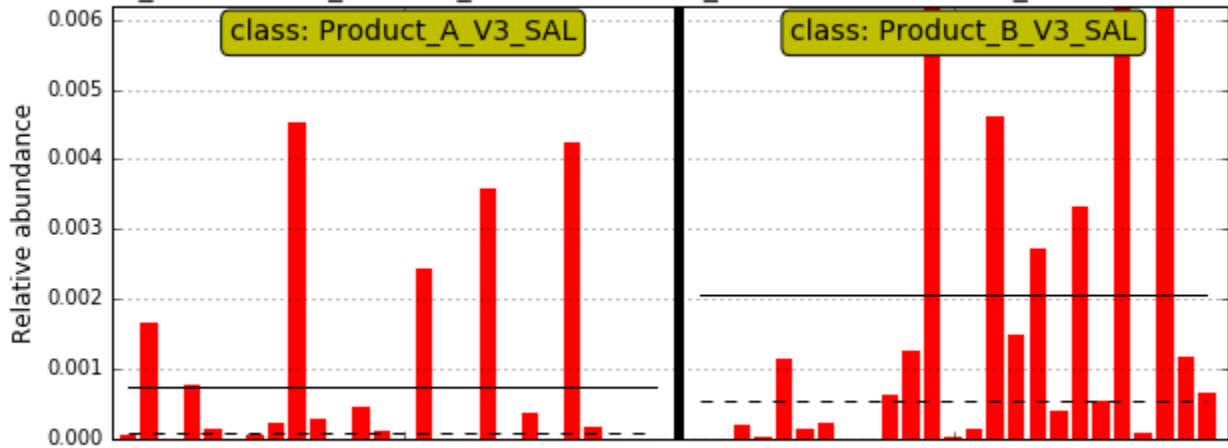
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Bacillales.F\_Gemellaceae.G\_Gemella.S\_haemolysans



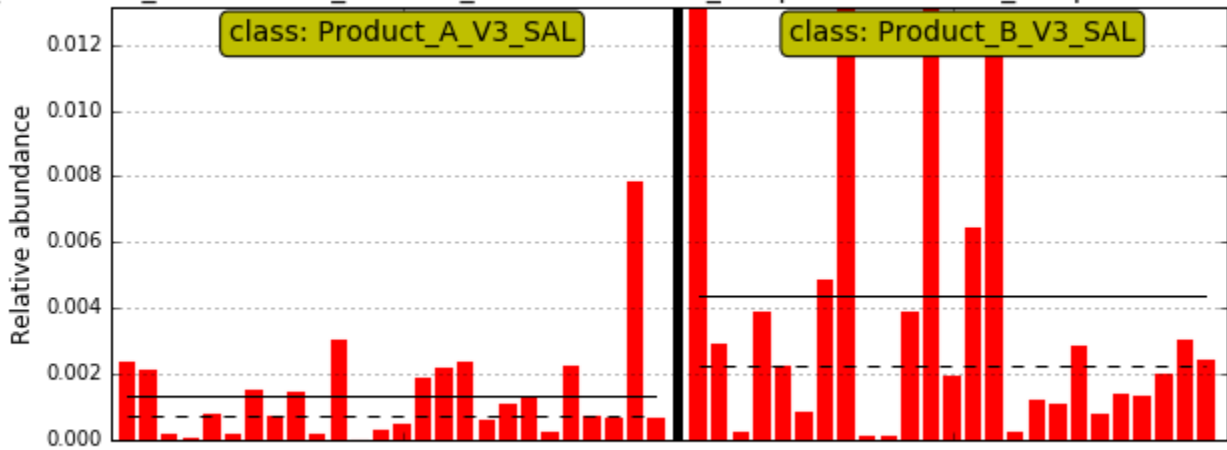
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Aerococcaceae.G\_Abiotrophia.S\_defectiva



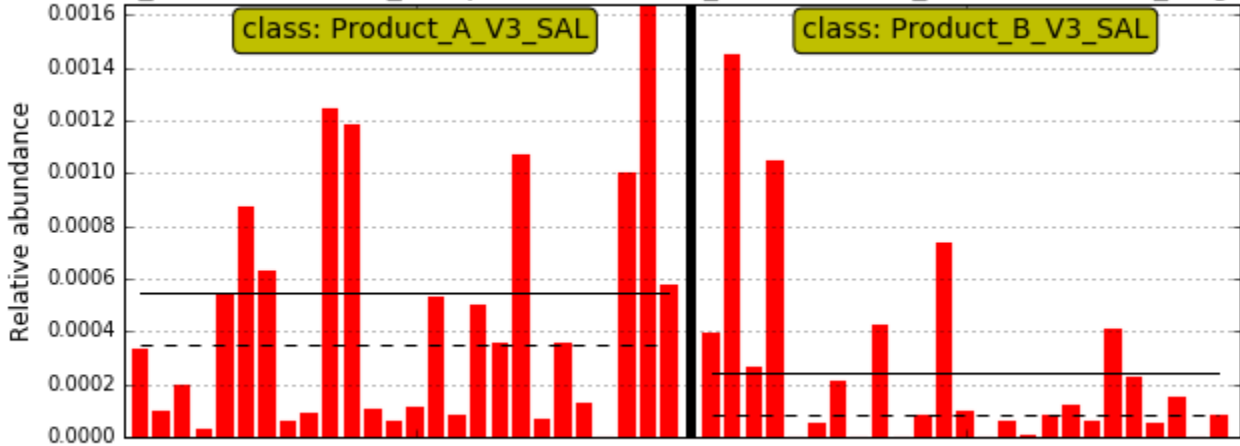
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Carnobacteriaceae.G\_Granulicatella.S\_elegans



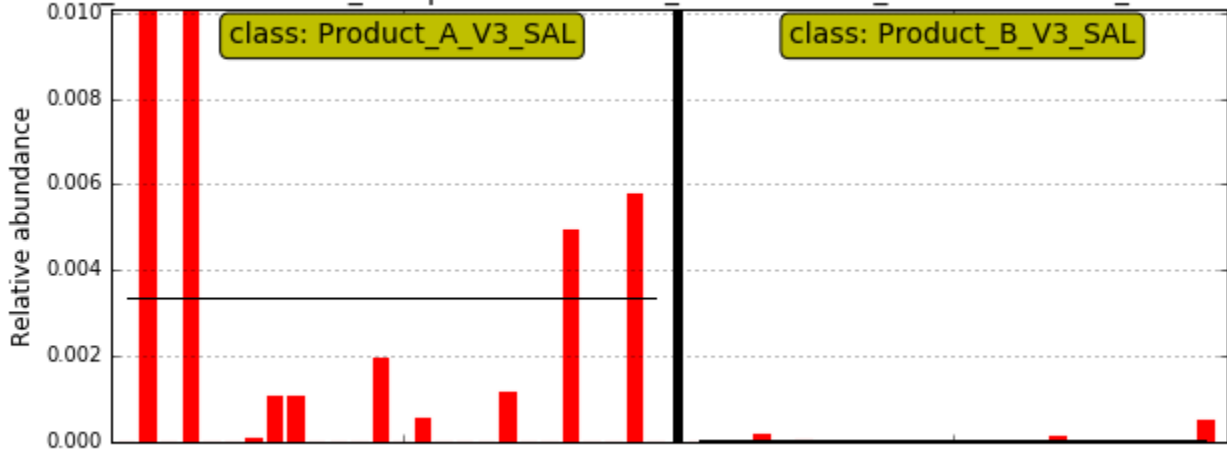
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Streptococcaceae.G\_Streptococcus.S\_gordonii



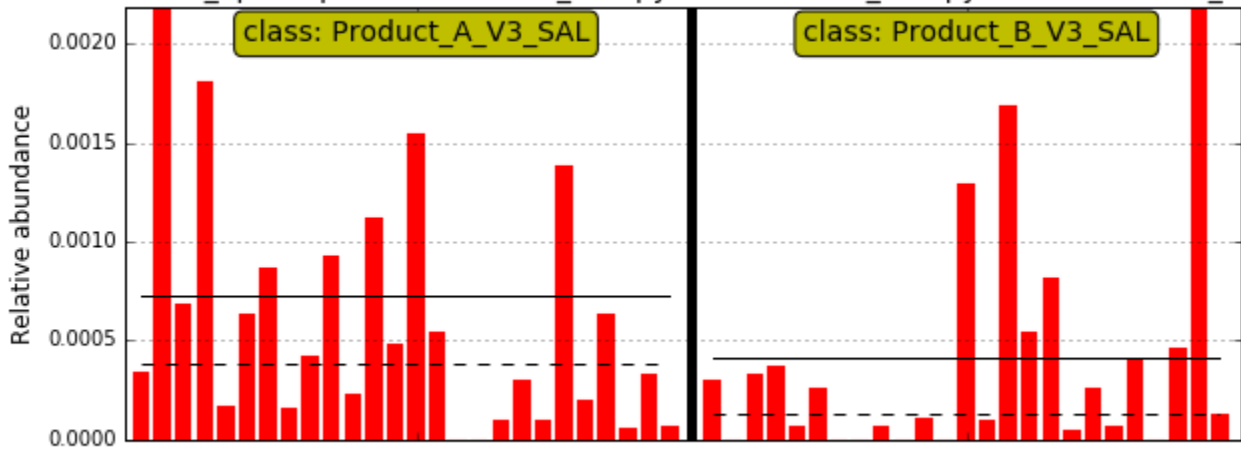
K\_Bacteria.P\_Proteobacteria.C\_Betaproteobacteria.O\_Neisseriales.F\_Neisseriaceae.G\_Kingella.S\_orali



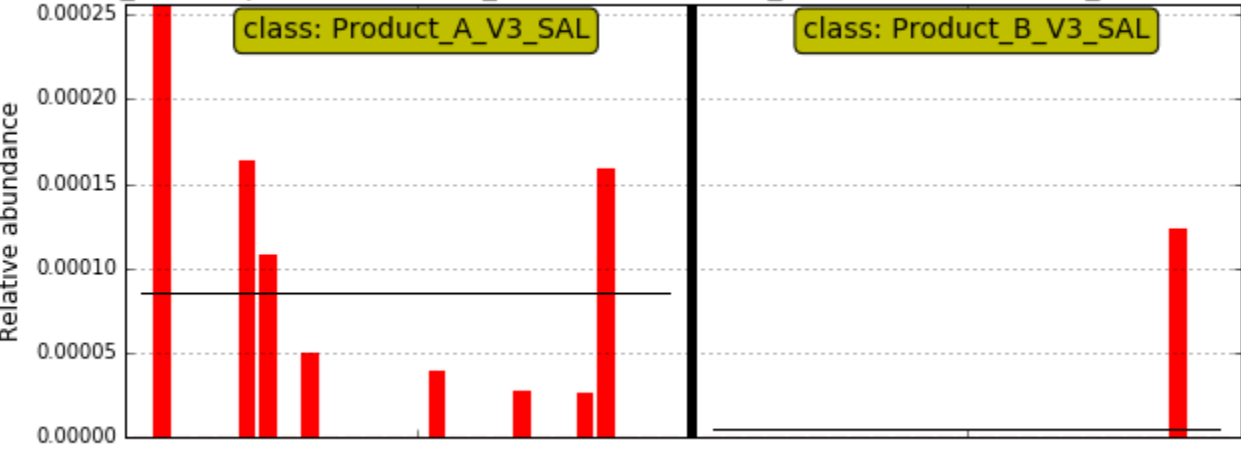
K\_Bacteria.P\_Proteobacteria.C\_Betaproteobacteria.O\_Neisseriales.F\_Neisseriaceae.G\_Neisseria.S\_mucc



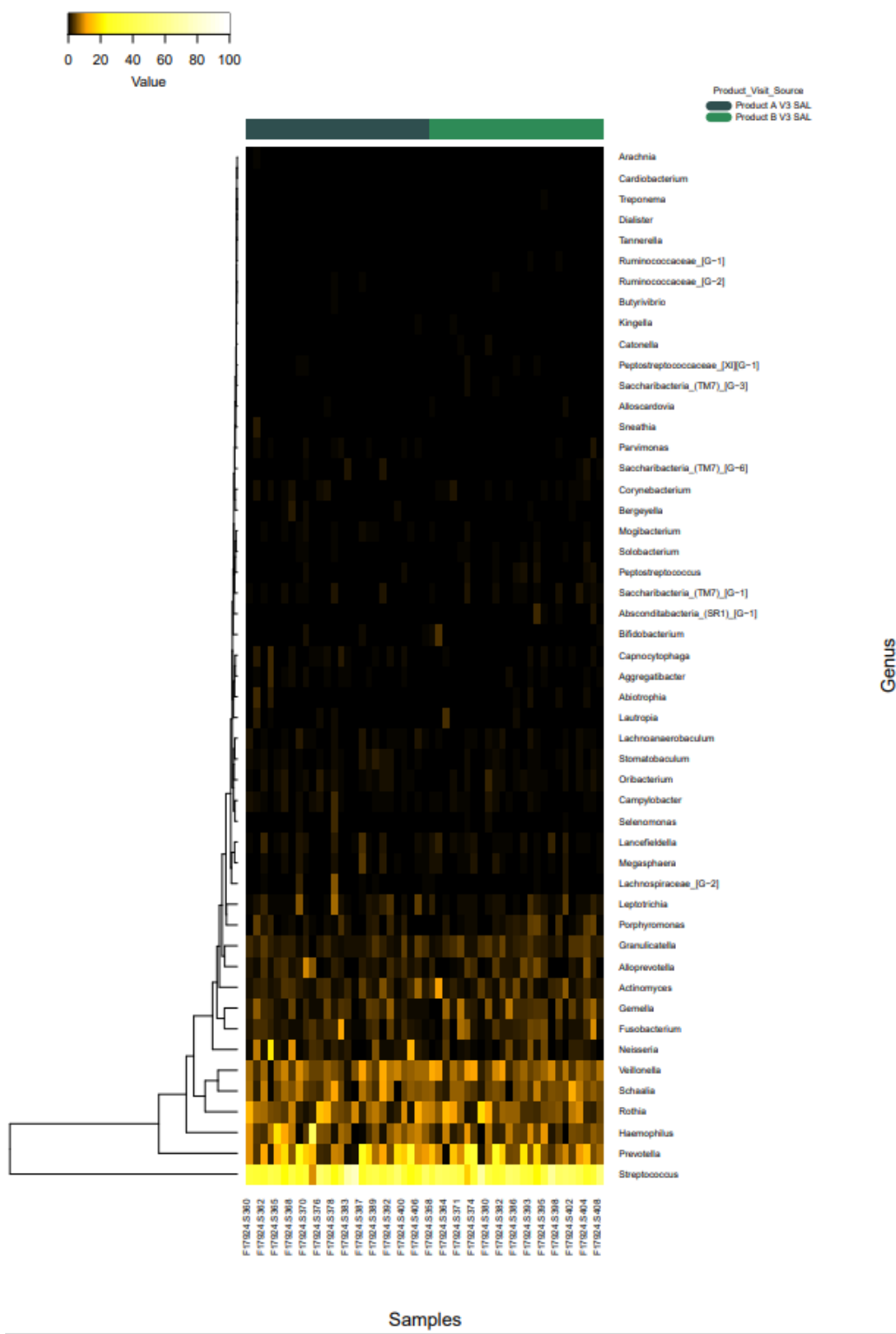
Proteobacteria.C\_Epsilonproteobacteria.O\_Campylobacterales.F\_Campylobacteraceae.G\_Campyloba

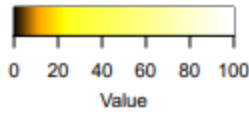


Gamma. C\_Gammaproteobacteria.O\_Cardiobacteriales.F\_Cardiobacteriaceae.G\_Cardiobacterium.S\_f

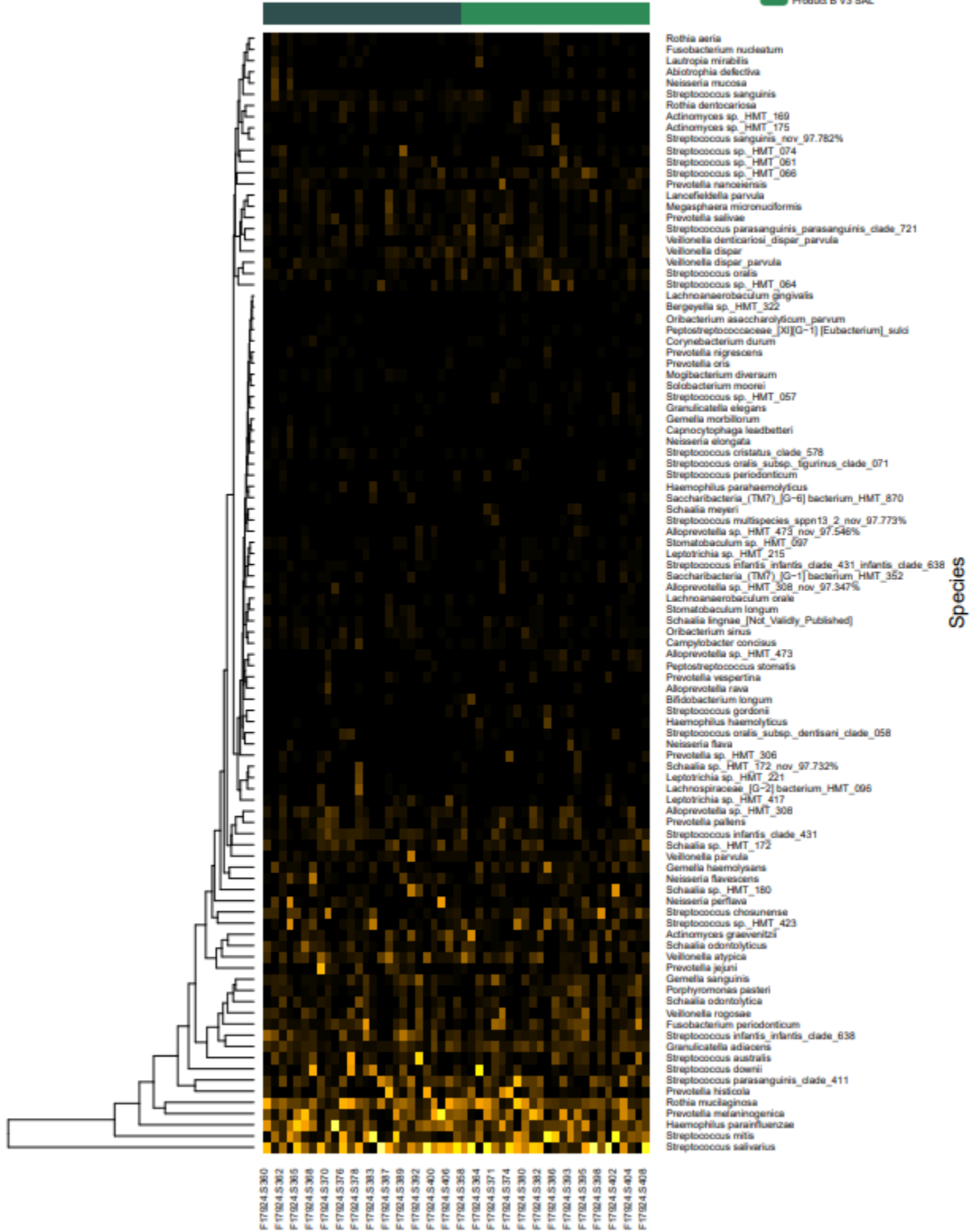


6) heat maps –difficult to see consistent differences



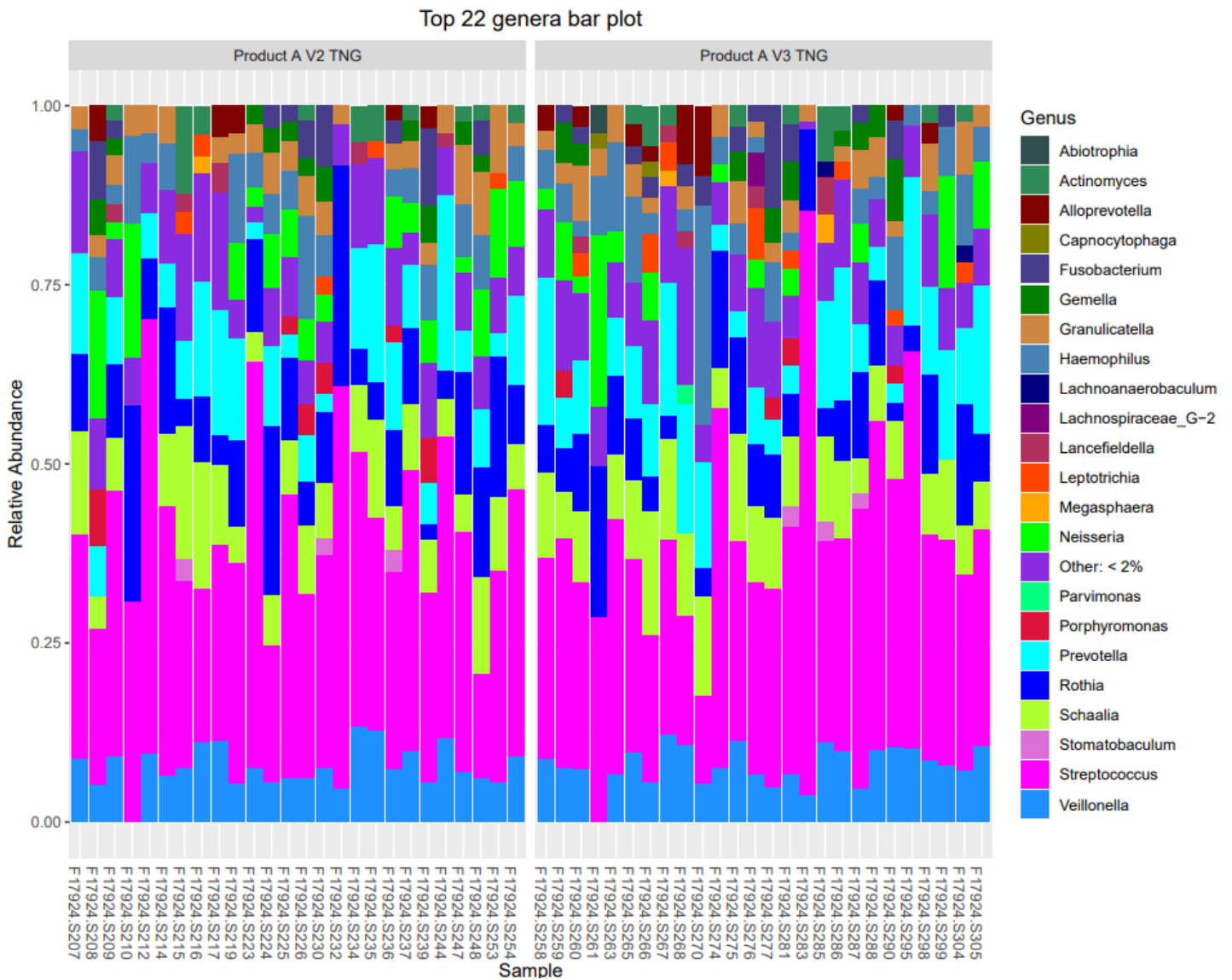


Product\_Visit\_Source  
 Product A V3 SAL  
 Product B V3 SAL



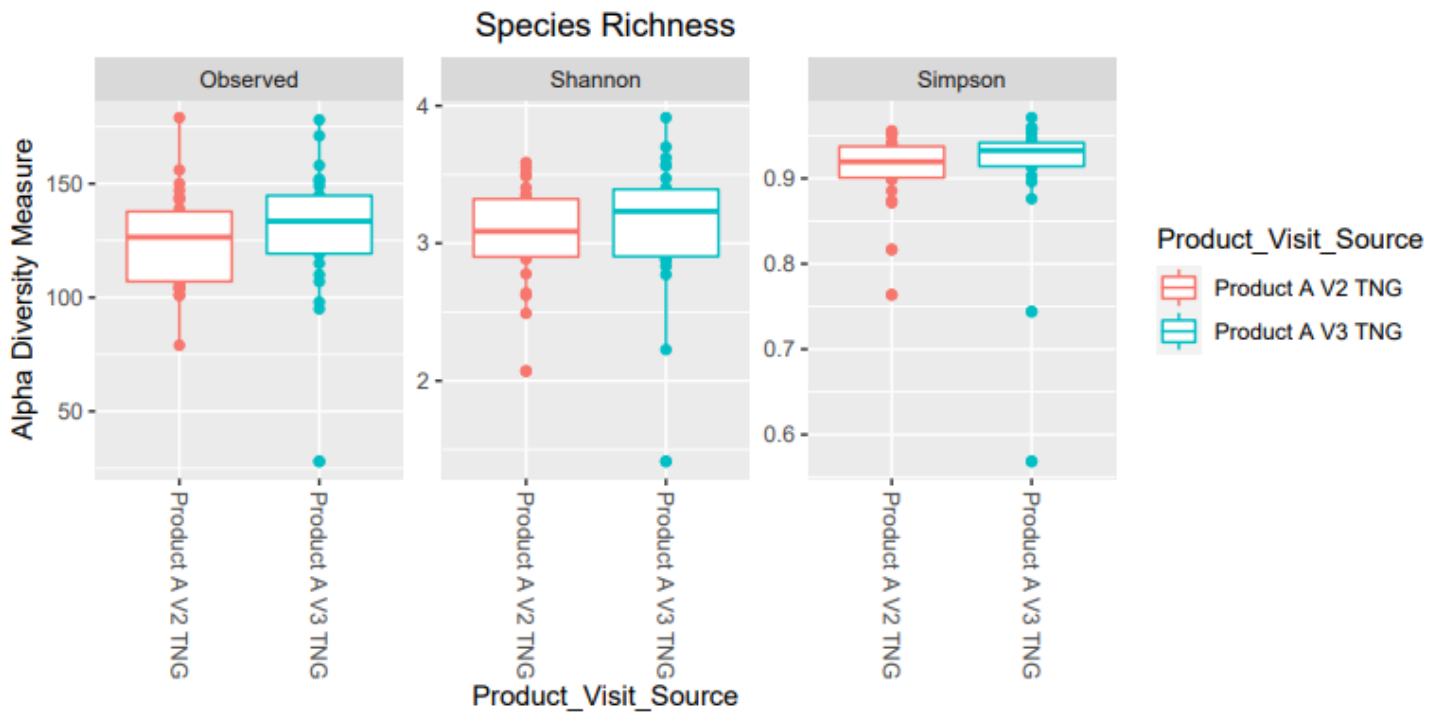
# Comparison 9. Product A V2 TNG vs Product A V3 TNG

## 1) Taxonomy bar graphs



Note: Some differences can be seen, but analyses below will be more informative.

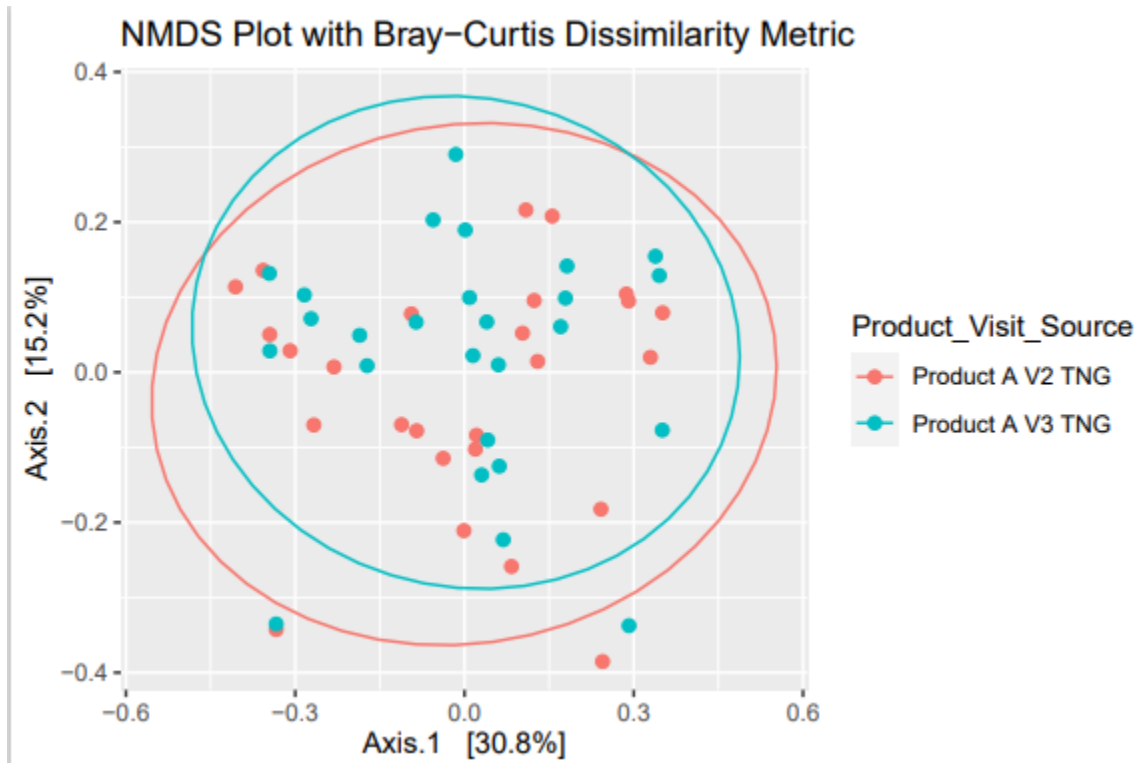
## 2) Alpha



Note: No significant differences



### 3) Beta



Note: No significant differences

#### 4) Differential abundance

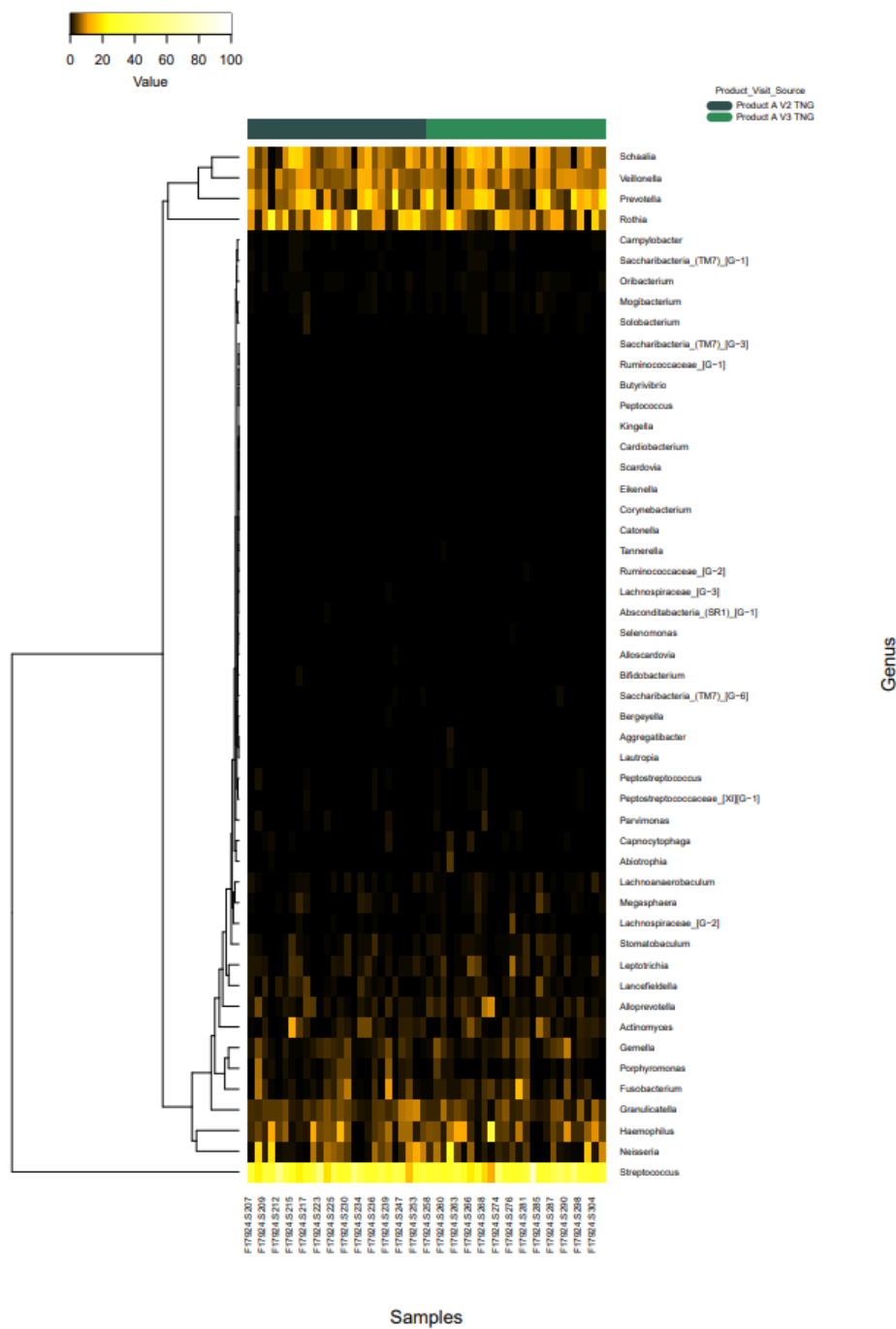
taxon	lfc_(Interce	lfc_Produc	se_(Interce	se_Produc	W_(Interce	W_Produc	p_(Interce	p_Product	q_(Interce	q_Product	diff_(Inter	diff_Produ
Fusobacterium nucleatum_nucleatum_	-0.38265	0.765304	0.266605	0.377037	-1.43528	2.029784	0.151207	0.042379	1	1	FALSE	FALSE
Anaeroglobus geminatus (SP72)	0.236366	-0.47274	0.189333	0.267757	1.248418	-1.76555	0.211878	0.077472	1	1	FALSE	FALSE
Actinomyces massiliensis (SP278)	-0.30577	0.611526	0.258506	0.365583	-1.18282	1.672742	0.236882	0.094378	1	1	FALSE	FALSE
Granulicatella adiacens (SP134)	0.151725	-0.30345	0.137469	0.194411	1.103703	-1.56089	0.269722	0.118549	1	1	FALSE	FALSE
Ottowia sp._HMT_894 (SP249)	0.135758	-0.27152	0.125773	0.17787	1.079388	-1.52651	0.280415	0.126883	1	1	FALSE	FALSE
Rothia mucilaginosa (SP304)	0.198886	-0.39778	0.184384	0.260758	1.078654	-1.52546	0.280742	0.127143	1	1	FALSE	FALSE
Parvimonas sp._HMT_110 (SP129)	-0.20412	0.408234	0.191836	0.271297	-1.06403	1.504751	0.287315	0.132388	1	1	FALSE	FALSE
Actinomyces johnsonii (SP290)	-0.2502	0.500391	0.244574	0.34588	-1.02299	1.446719	0.306311	0.147976	1	1	FALSE	FALSE
Peptidiphaga sp._HMT_183 (SP149)	-0.17696	0.353917	0.178846	0.252926	-0.98946	1.399288	0.322439	0.161727	1	1	FALSE	FALSE
Absconditabacteria_(SR1)_[G-1] bacteri	0.27863	-0.55726	0.291096	0.411672	0.957175	-1.35366	0.338479	0.175845	1	1	FALSE	FALSE
Prevotella pleuritidis (SP294)	0.220064	-0.44013	0.252248	0.356732	0.872412	-1.23379	0.382984	0.217281	1	1	FALSE	FALSE
Actinomyces dentalis (SP83)	-0.16628	0.33256	0.202016	0.285693	-0.82311	1.164045	0.410443	0.244406	1	1	FALSE	FALSE
Porphyromonas sp._HMT_275 (SP363)	0.131517	-0.26304	0.164884	0.233181	0.797633	-1.12804	0.425084	0.259302	1	1	FALSE	FALSE
Gemella morbillorum (SP153)	-0.26461	0.529215	0.336128	0.475356	-0.78723	1.113302	0.431147	0.265579	1	1	FALSE	FALSE

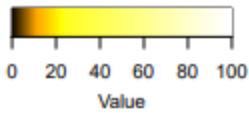
Note: No differences

5) Lefse

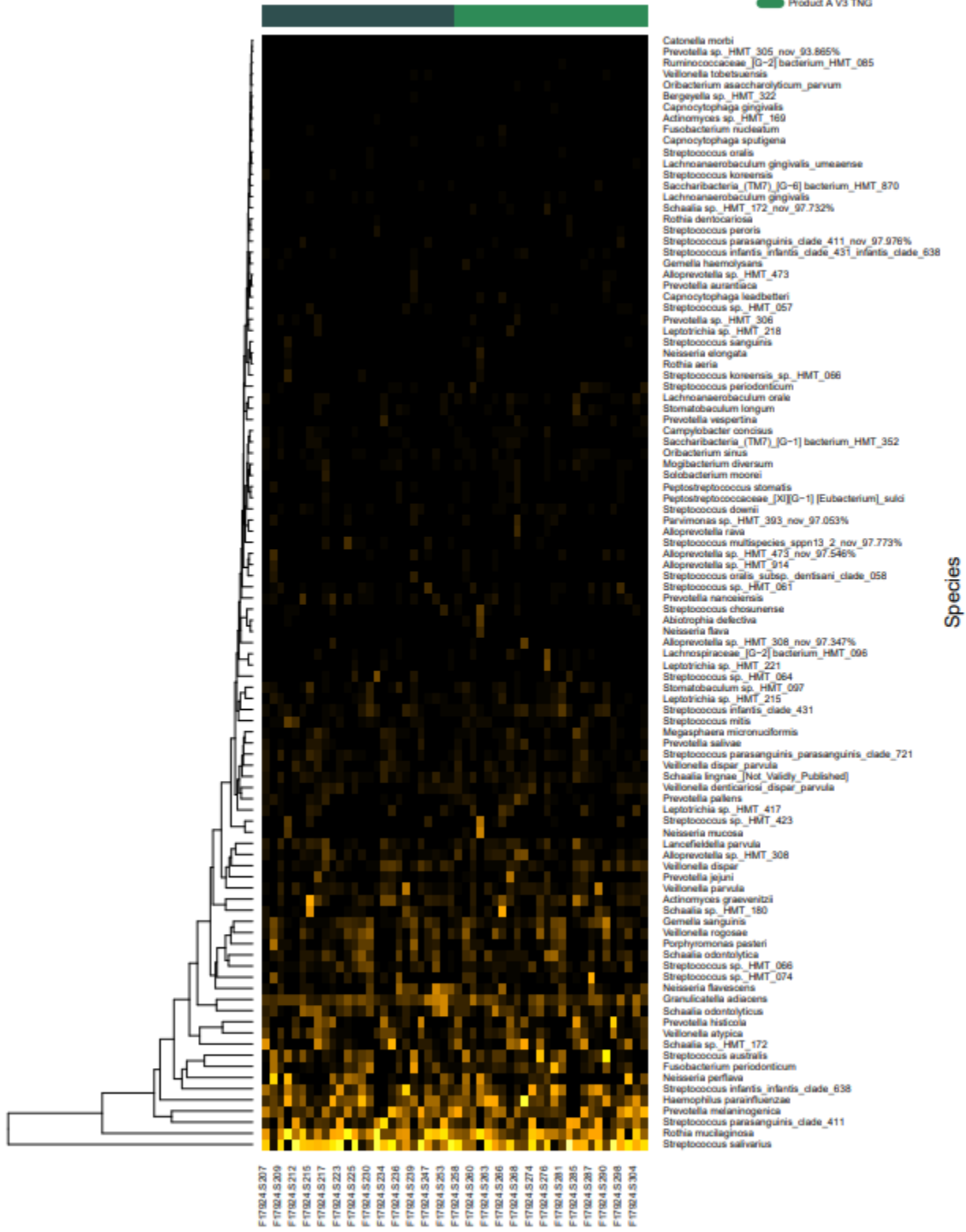
Not: NO differences –graph was not produced

## 6) Heat maps



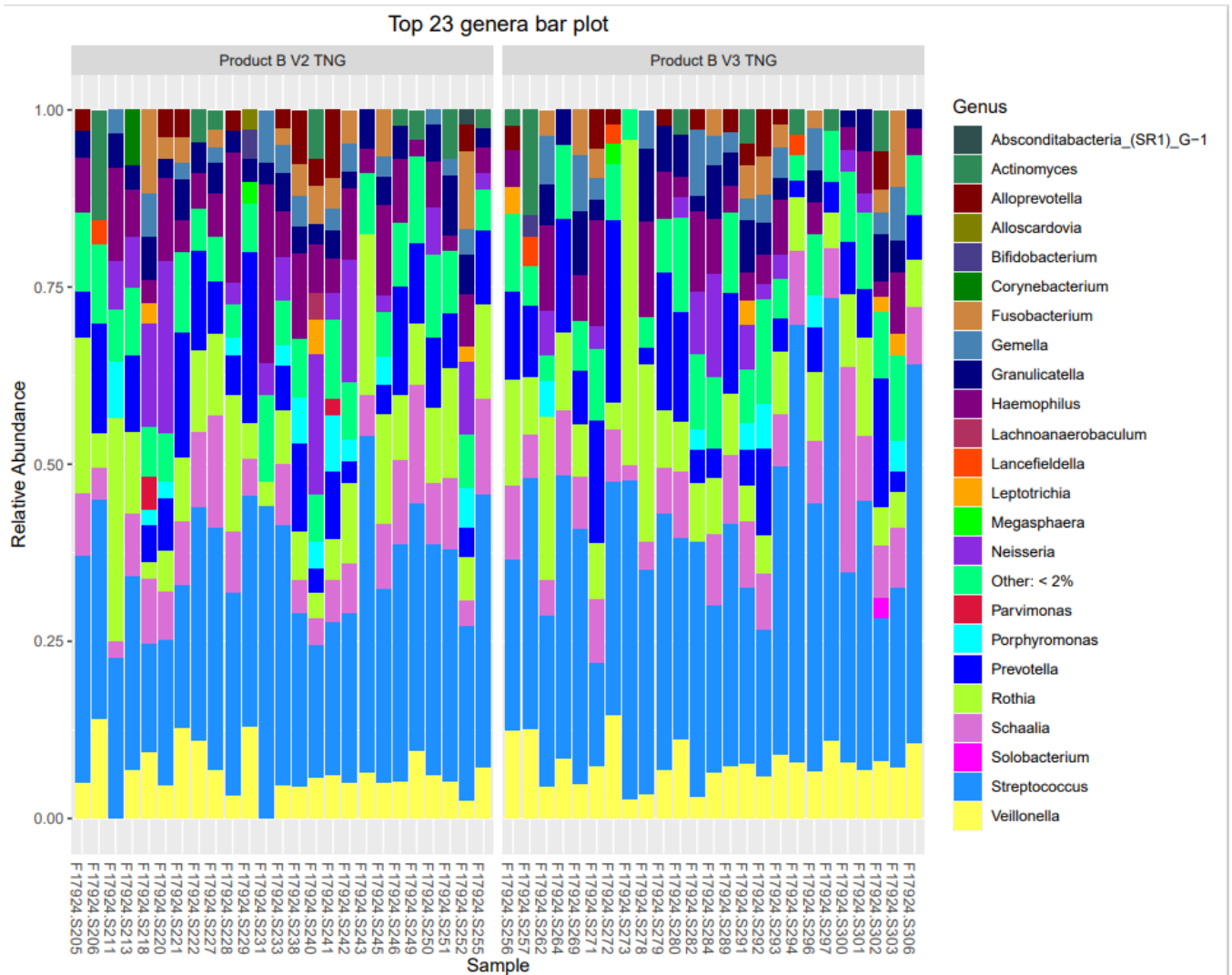


Product\_Visit\_Source  
 Product A V2 TNG  
 Product A V3 TNG

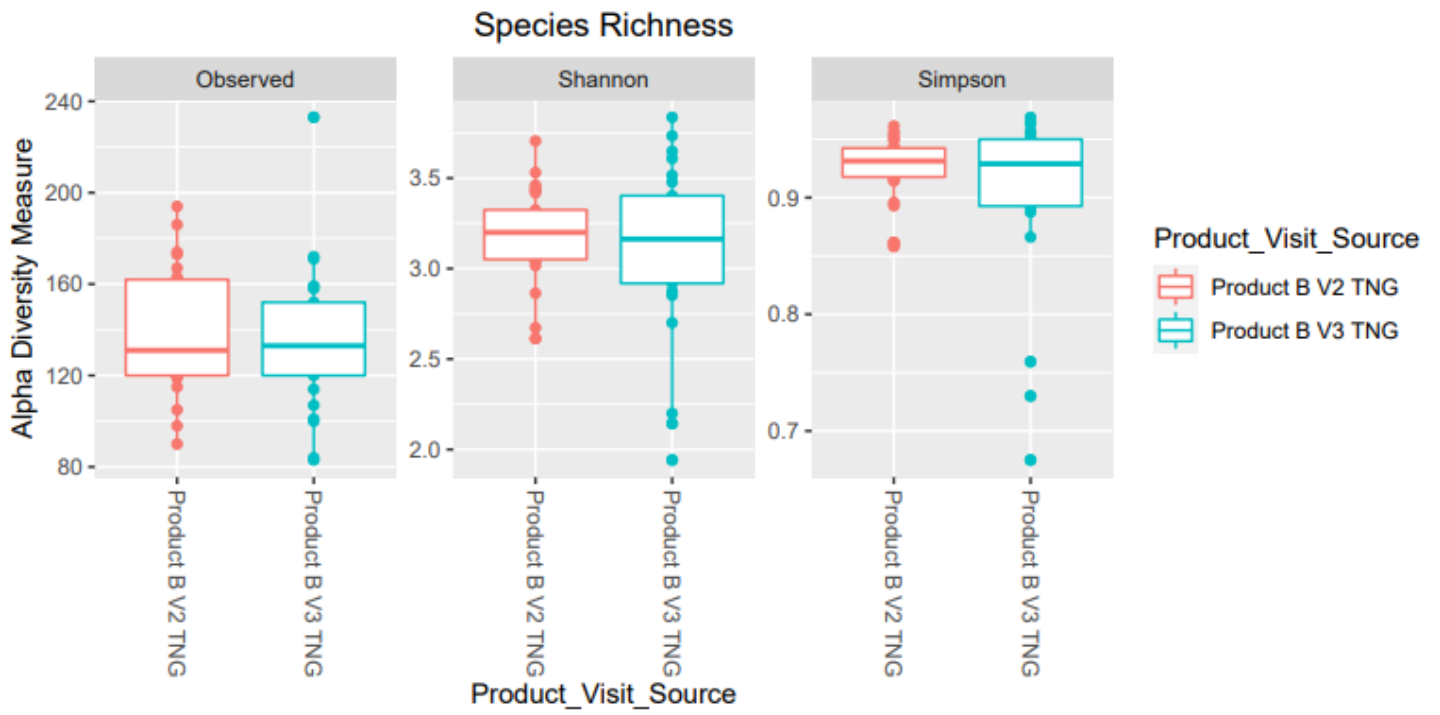


# Comparison 10. Product B V2 TNG vs Product B V3 TNG

## 1) Taxonomy bar graphs

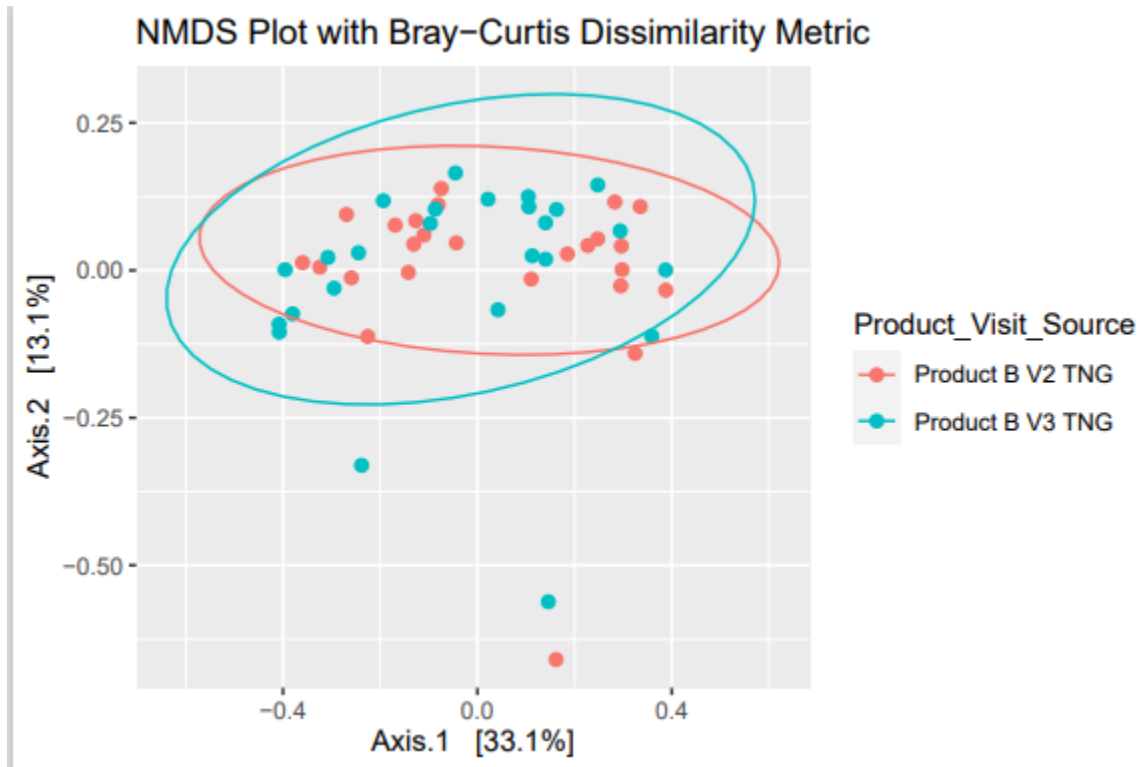


## 2) Alpha



Note: No significance

### 3) Beta diversity



Note: Not significant

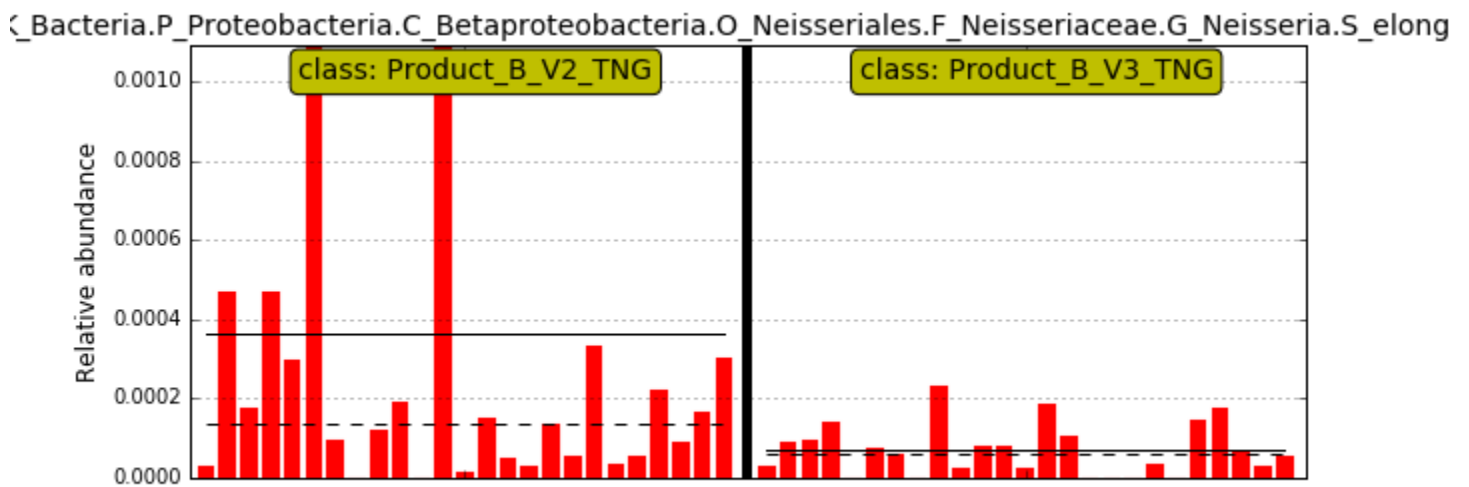
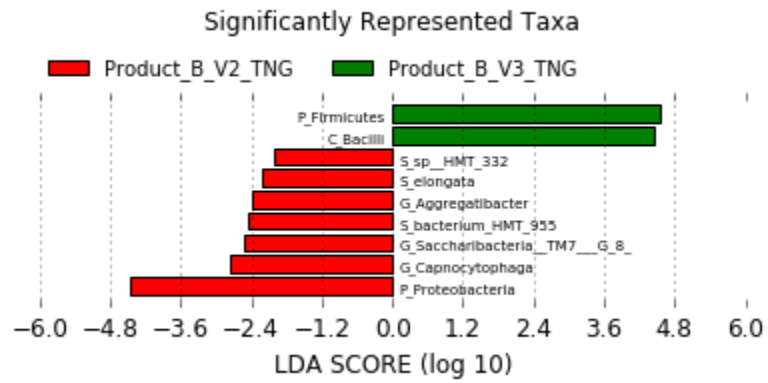


#### 4) Differential abundance

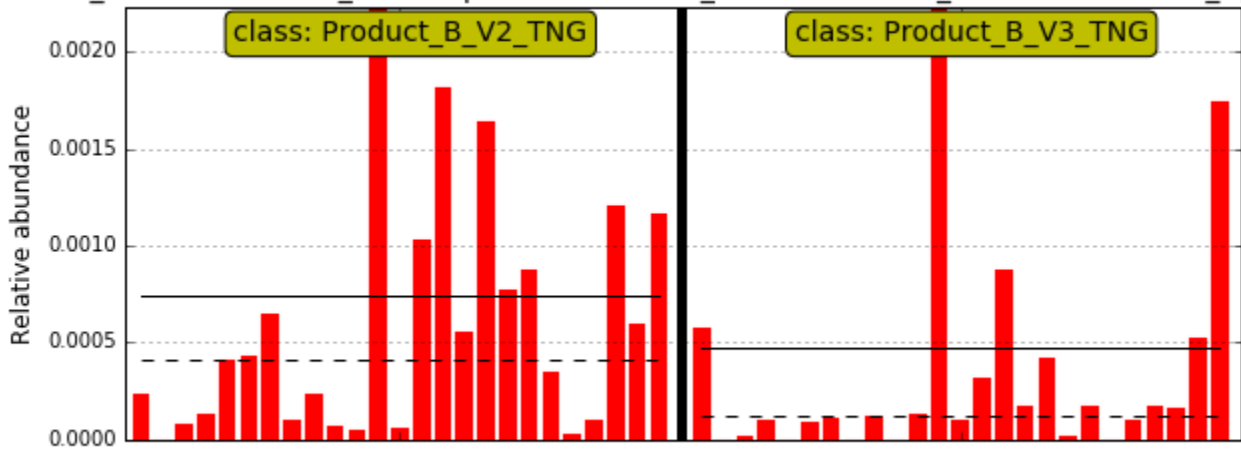
taxon	lfc_(Interce	lfc_Produc	se_(Interc	se_Produc	W_(Interc	W_Produc	p_(Interce	p_Product	q_(Interce	q_Product	diff_(Inte	diff_Produ
<i>Neisseria elongata</i> (SP219)	0.526296	-1.05915	0.305637	0.432249	1.721966	-2.45032	0.085076	0.014273	1	1	FALSE	FALSE
<i>Aggregatibacter</i> sp._HMT_898 (SP119)	0.390147	-0.78685	0.229033	0.323915	1.703455	-2.42918	0.088483	0.015133	1	1	FALSE	FALSE
<i>Capnocytophaga gingivalis</i> _nov_96.429% (S	0.317533	-0.64162	0.226896	0.320894	1.399465	-1.99949	0.161674	0.045556	1	1	FALSE	FALSE
<i>Neisseria mucosa</i> (SP300)	0.390951	-0.78846	0.321324	0.454435	1.216687	-1.73503	0.223723	0.082735	1	1	FALSE	FALSE
<i>Capnocytophaga granulosa</i> (SP99)	0.368392	-0.74334	0.304395	0.430493	1.210245	-1.72672	0.226185	0.084218	1	1	FALSE	FALSE
<i>Haemophilus parainfluenzae</i> (SP19)	0.418408	-0.84337	0.349195	0.493849	1.198209	-1.70775	0.230836	0.087682	1	1	FALSE	FALSE
<i>Lautropia mirabilis</i> (SP126)	0.406494	-0.81954	0.356784	0.504582	1.139328	-1.62421	0.254566	0.104332	1	1	FALSE	FALSE
<i>Aggregatibacter aphrophilus</i> (SP218)	0.285096	-0.57675	0.251144	0.355185	1.135188	-1.62379	0.256296	0.10442	1	1	FALSE	FALSE
<i>Actinomyces</i> sp._HMT_171 (SP29)	-0.45539	0.904226	0.408504	0.577725	-1.11478	1.565149	0.264946	0.117548	1	1	FALSE	FALSE
<i>Parvimonas</i> sp._HMT_110 (SP129)	0.281924	-0.5704	0.262151	0.370752	1.075425	-1.53851	0.282185	0.123925	1	1	FALSE	FALSE
<i>Streptococcus infantis</i> _infantis_clade_638 (	0.352025	-0.71061	0.33649	0.475882	1.046168	-1.49324	0.295484	0.135374	1	1	FALSE	FALSE
<i>Actinomyces</i> sp._HMT_896 (SP355)	-0.21151	0.41646	0.199121	0.281615	-1.06221	1.47883	0.288141	0.139186	1	1	FALSE	FALSE
<i>Prevotella nanceiensis</i> (SP203)	0.496414	-0.99938	0.488501	0.690858	1.016197	-1.44658	0.309536	0.148014	1	1	FALSE	FALSE
<i>Bergeyella</i> sp._HMT_206 (SP2)	0.231243	-0.46904	0.229322	0.324325	1.008374	-1.44621	0.313275	0.148119	1	1	FALSE	FALSE
<i>Kingella oralis</i> (SP198)	0.290735	-0.58803	0.290031	0.41018	1.002427	-1.43358	0.316137	0.151691	1	1	FALSE	FALSE
<i>Actinomyces dentalis</i> (SP83)	-0.28178	0.556999	0.280347	0.396485	-1.0051	1.404843	0.314848	0.160068	1	1	FALSE	FALSE
<i>Haemophilus sputorum</i> (SP115)	0.517062	-1.04068	0.52824	0.747057	0.978839	-1.39304	0.327659	0.163607	1	1	FALSE	FALSE

Not: Nothing significant but some trends as also shown in Lefse

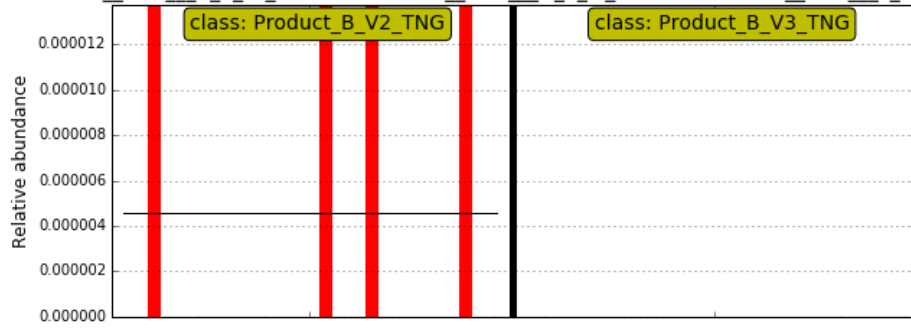
5) Lefse



Bacteria.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Aggregatibacter

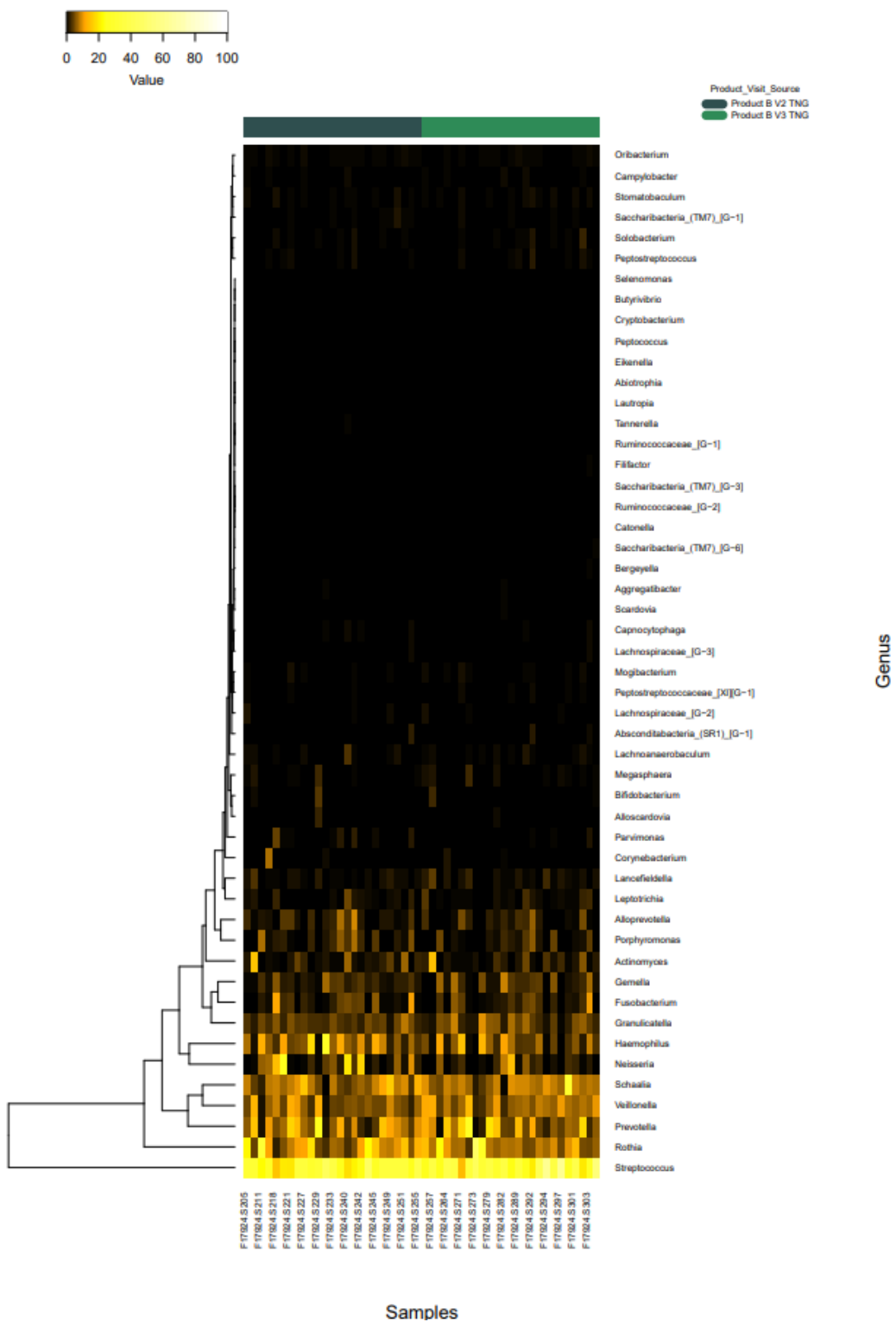


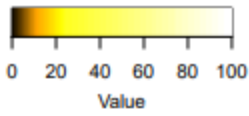
haribacteria\_TM7\_C\_1\_O\_Saccharibacteria\_TM7\_O\_1\_F\_Saccharibacteria\_TM7\_F\_1\_G\_Sacchi



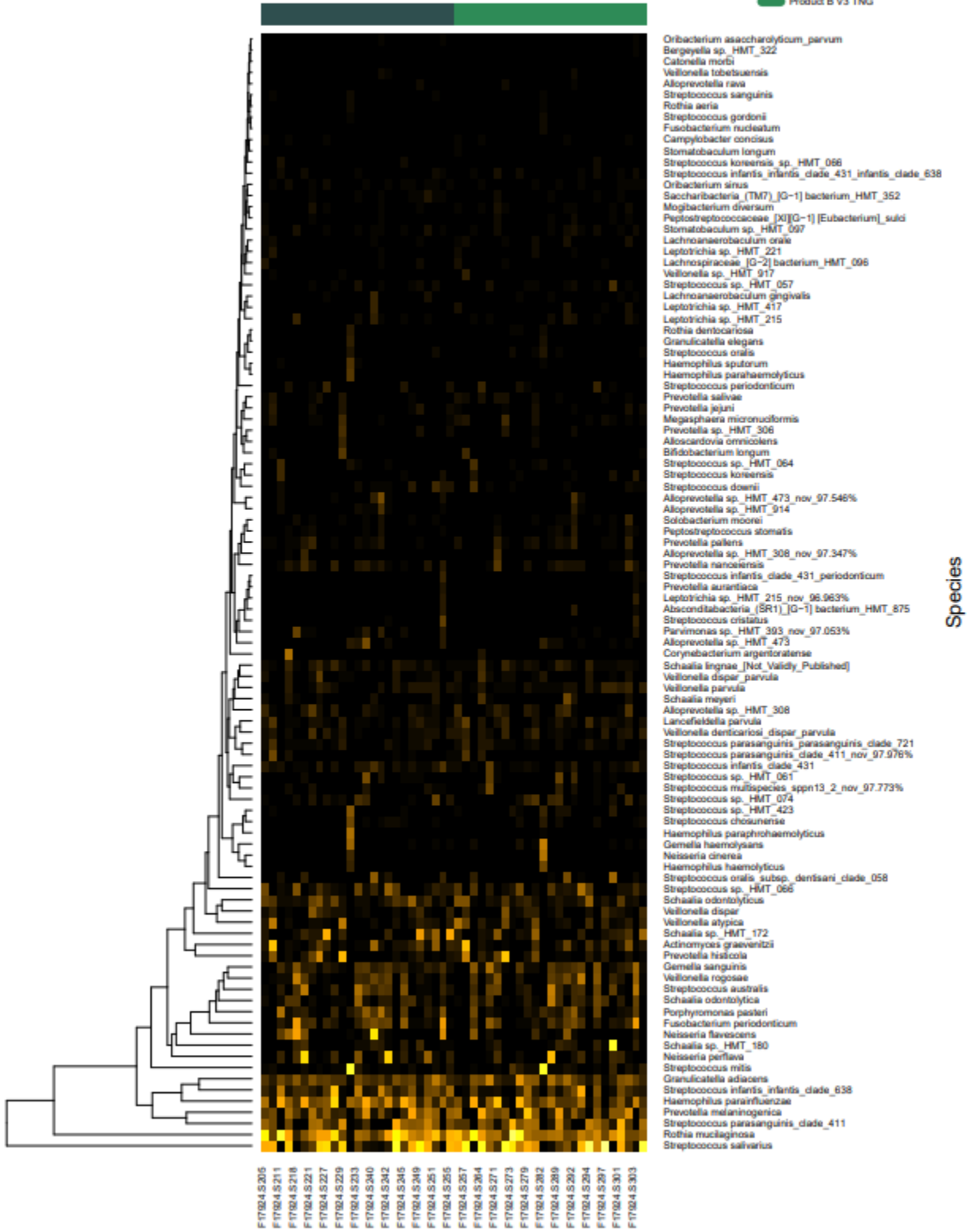
very low levels

6) Heat map. Difficult to see differences



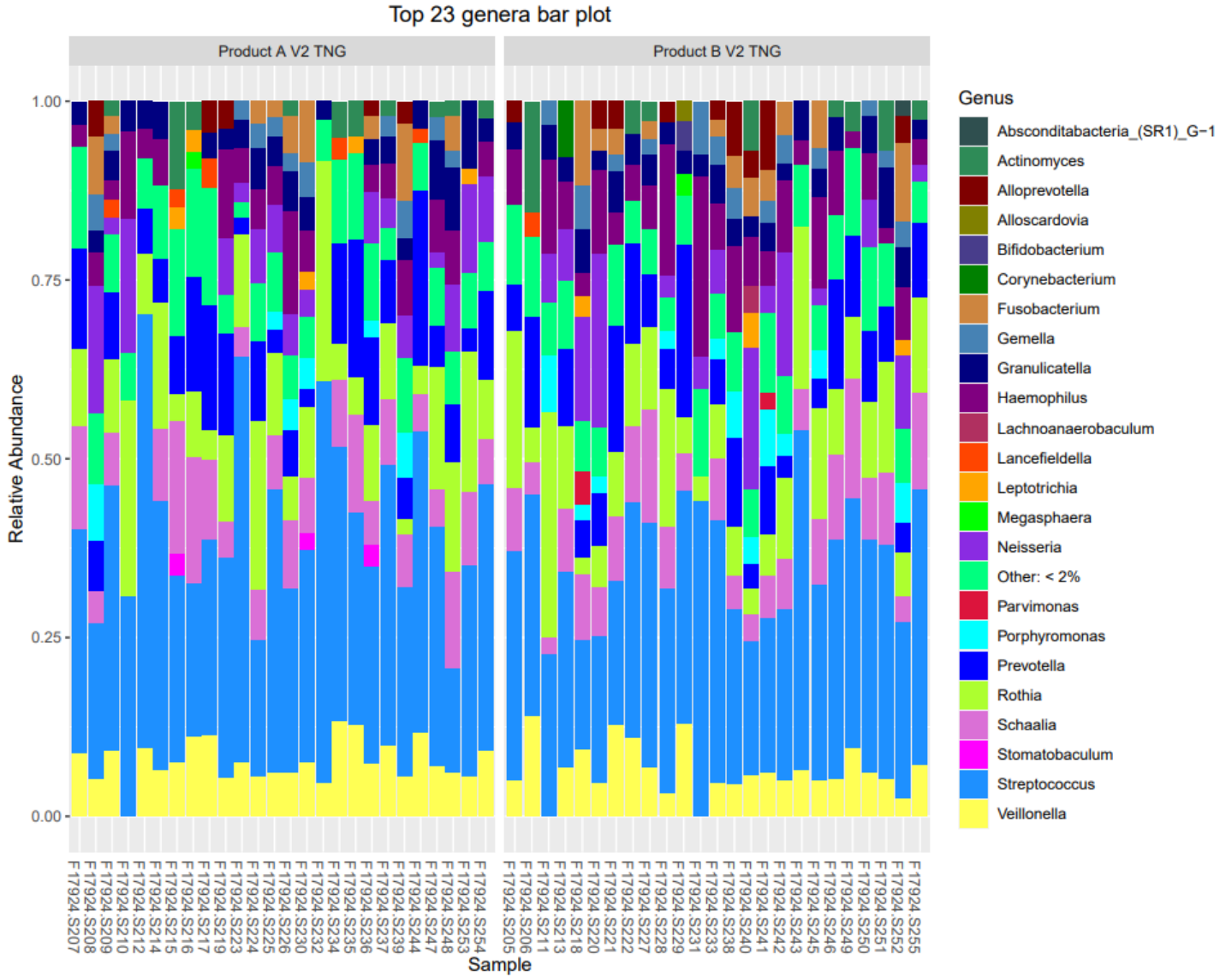


Product\_Visit\_Source  
 Product B V2 TNG  
 Product B V3 TNG

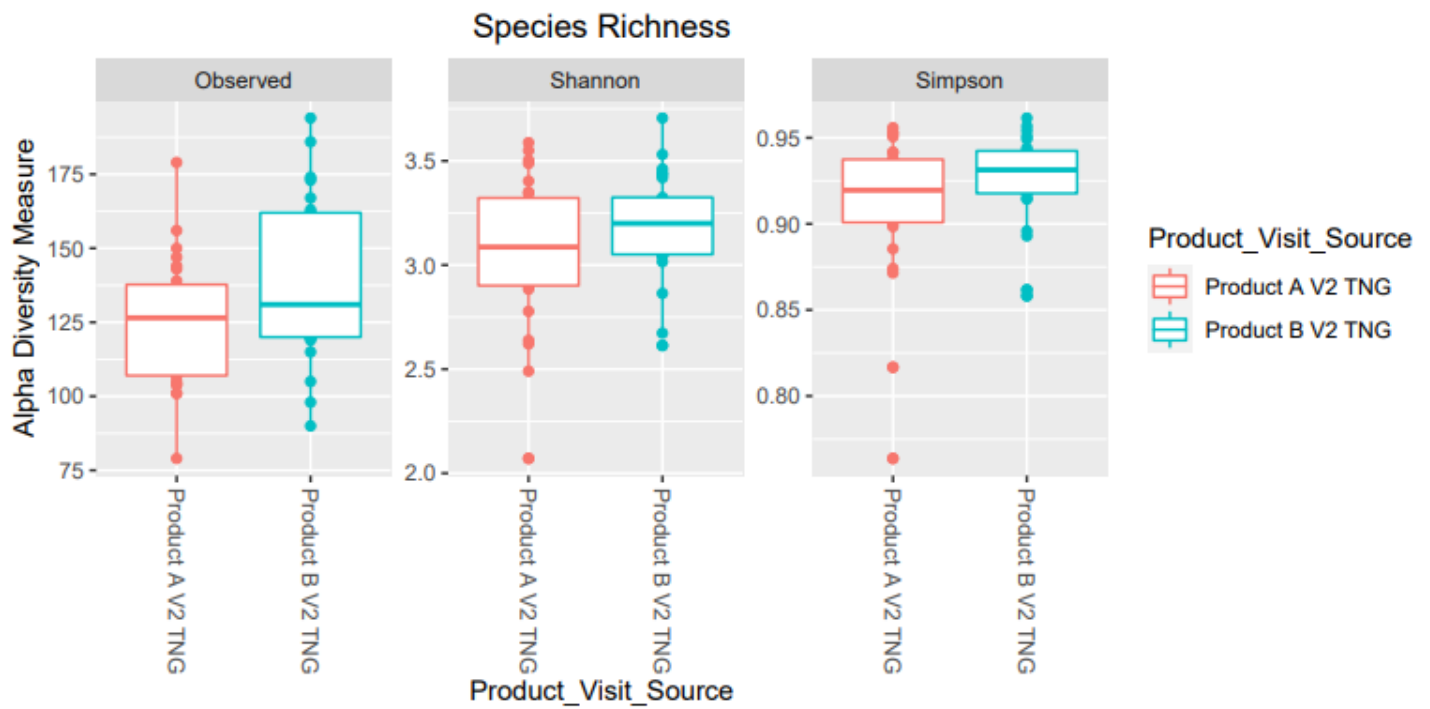


# Comparison 11. Product A V2 TNG vs Product B V2 TNG

## 1) Taxonomy bar graphs

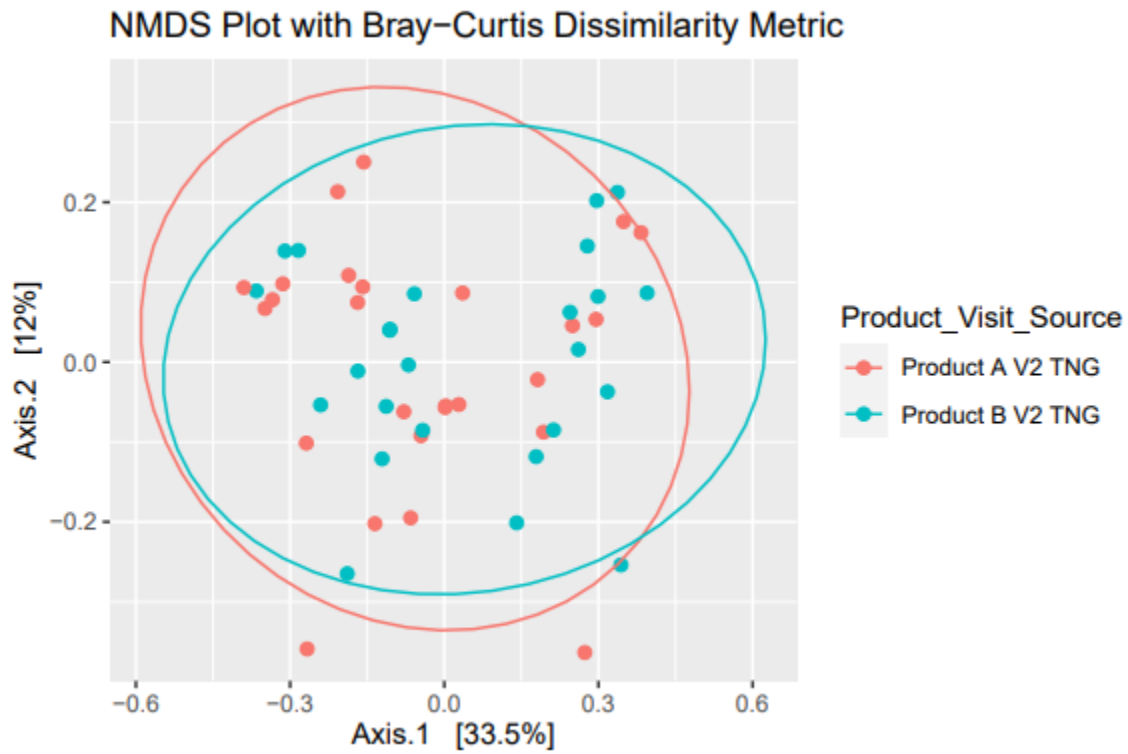


## 2) Alpha



Note: No significant differences

### 3) Beta diversity



Note: No significant differences

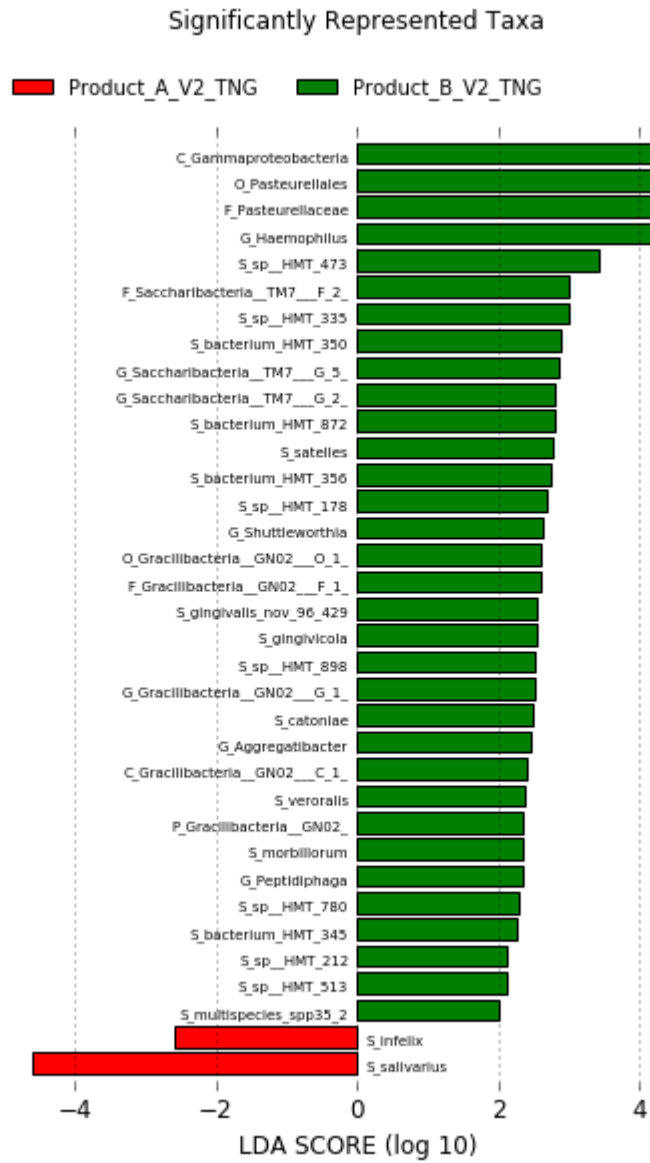


#### 4) Differential abundance

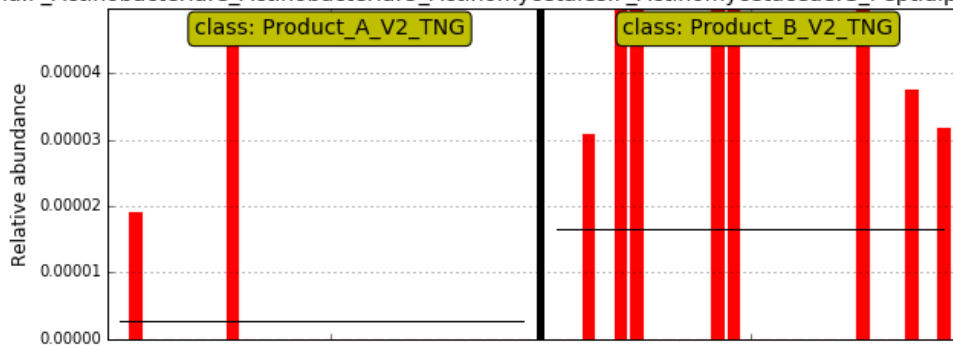
taxon	lfc_(Inter	lfc_Produc	se_(Inter	se_Produc	W_(Inter	W_Produc	p_(Inter	p_Product	q_(Inter	q_Product	diff_(Inte	diff_Prod
Fusobacterium nucleatum_nucleatum_subsp._	-0.54457	1.11764	0.294473	0.420602	-1.84931	2.657241	0.064413	0.007878	1	1	FALSE	FALSE
Actinomyces sp._HMT_175_nov_97.951% (SPN4	0.366631	-0.74122	0.222664	0.318039	1.646565	-2.33058	0.099647	0.019776	1	1	FALSE	FALSE
Streptococcus salivarius (SP135)	0.627931	-1.27427	0.388722	0.555216	1.615372	-2.29508	0.10623	0.021728	1	1	FALSE	FALSE
Gemella morbillorum (SP153)	-0.54627	1.1211	0.360599	0.515049	-1.51489	2.176687	0.1298	0.029504	1	1	FALSE	FALSE
Porphyromonas sp._HMT_275 (SP363)	0.237937	-0.47868	0.169669	0.242346	1.402361	-1.97518	0.160808	0.048248	1	1	FALSE	FALSE
Fusobacterium sp._HMT_204 (SP392)	0.421221	-0.85258	0.305997	0.437062	1.376553	-1.9507	0.168651	0.051092	1	1	FALSE	FALSE
Actinomyces sp._HMT_169 (SP239)	0.558224	-1.13206	0.409449	0.584821	1.363352	-1.93574	0.172772	0.052899	1	1	FALSE	FALSE
Aggregatibacter sp._HMT_513 (SP184)	-0.48723	1.000657	0.367637	0.525101	-1.32529	1.905648	0.185074	0.056696	1	1	FALSE	FALSE
Alloprevotella sp._HMT_473 (SP132)	-0.71793	1.471299	0.543439	0.776196	-1.32109	1.895525	0.18647	0.058023	1	1	FALSE	FALSE
Leptotrichia sp._HMT_212 (SP146)	-0.34313	0.706693	0.273555	0.390725	-1.25433	1.80867	0.209723	0.070502	1	1	FALSE	FALSE
Streptococcus gordonii (SP171)	-0.51685	1.061087	0.413637	0.590802	-1.24952	1.796012	0.211473	0.072493	1	1	FALSE	FALSE
Prevotella sp._HMT_313 (SP486)	0.395708	-0.80053	0.315299	0.450347	1.255025	-1.77759	0.20947	0.075472	1	1	FALSE	FALSE
Corynebacterium durum (SP177)	-0.35642	0.733812	0.301053	0.43	-1.18391	1.706539	0.236447	0.087908	1	1	FALSE	FALSE
Veillonella sp._HMT_780 (SP10)	-0.37564	0.773018	0.318147	0.454415	-1.18071	1.701126	0.237718	0.088919	1	1	FALSE	FALSE
Absconditabacteria_(SR1)_[G-1] bacterium_HM	-0.3308	0.681535	0.282601	0.403645	-1.17054	1.688452	0.241784	0.091325	1	1	FALSE	FALSE
Anaeroglobus geminatus (SP72)	0.247605	-0.4984	0.208819	0.298264	1.185738	-1.671	0.235726	0.094721	1	1	FALSE	FALSE

Note: No statistical differences. Data indicates that baseline subjects differ a little bit.

5) Lefse

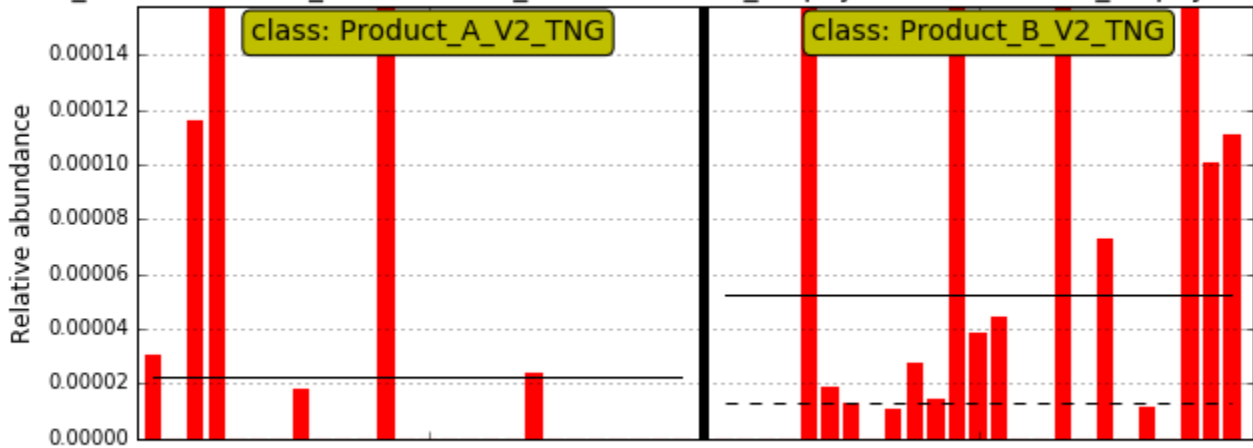


teria.P\_Actinobacteria.C\_Actinobacteria.O\_Actinomycetales.F\_Actinomycetaceae.G\_Peptidiphaga.S\_gir

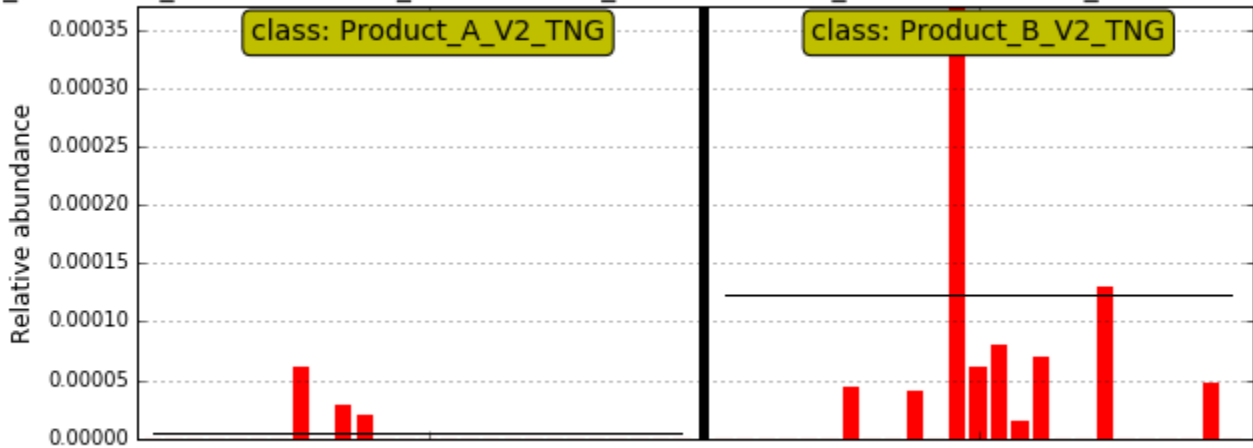


Note: very low levels

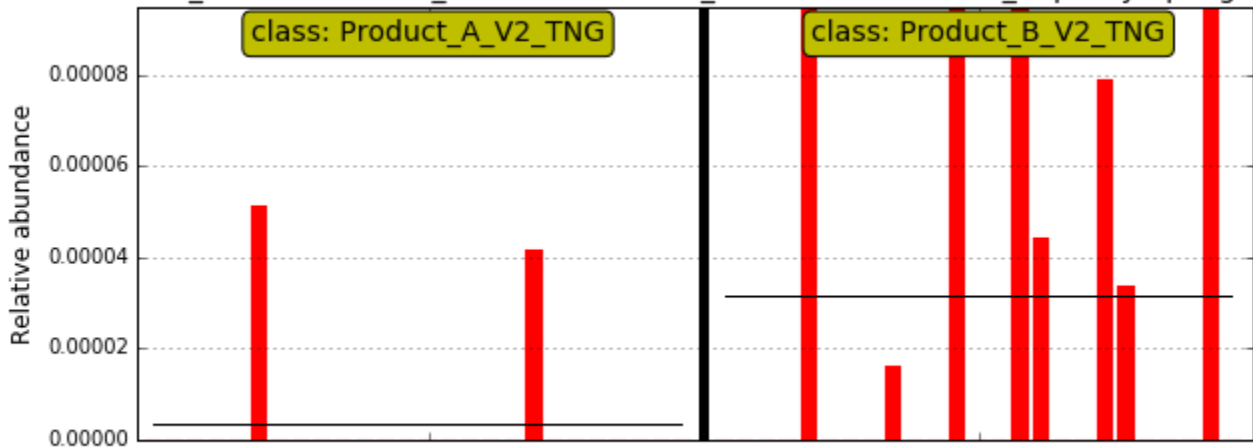
acteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Porphyrimonadaceae.G\_Porphyrimonas.S\_ca



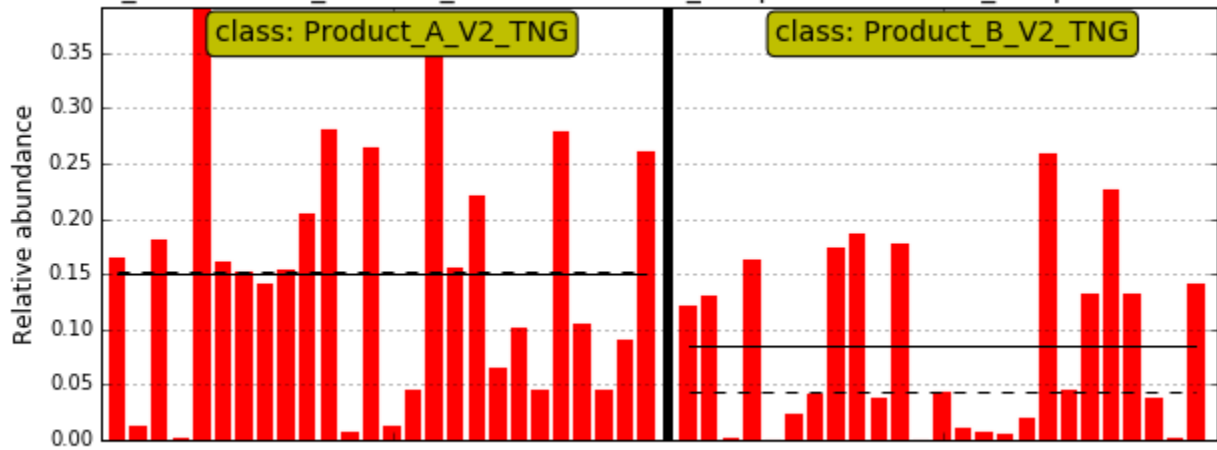
K\_Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Prevotella.S\_veroralis



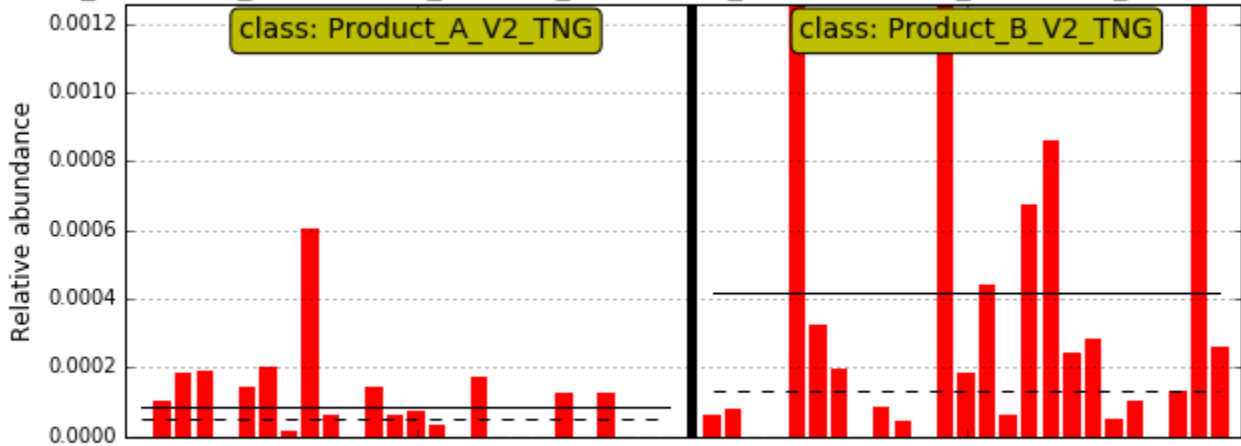
\_Bacteroidetes.C\_Flavobacteriia.O\_Flavobacteriales.F\_Flavobacteriaceae.G\_Capnocytophaga.S\_gingiva



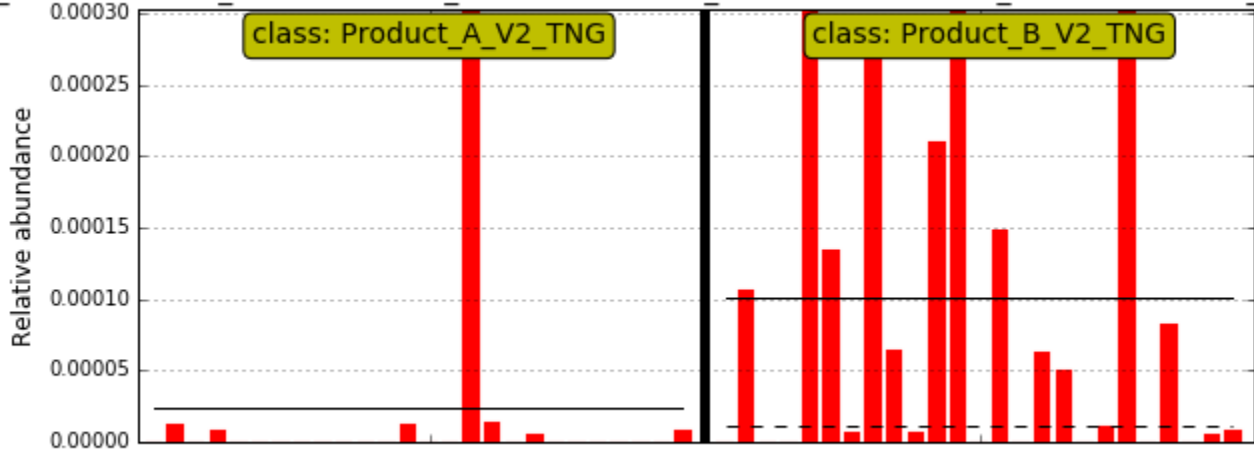
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Streptococcaceae.G\_Streptococcus.S\_salivarius



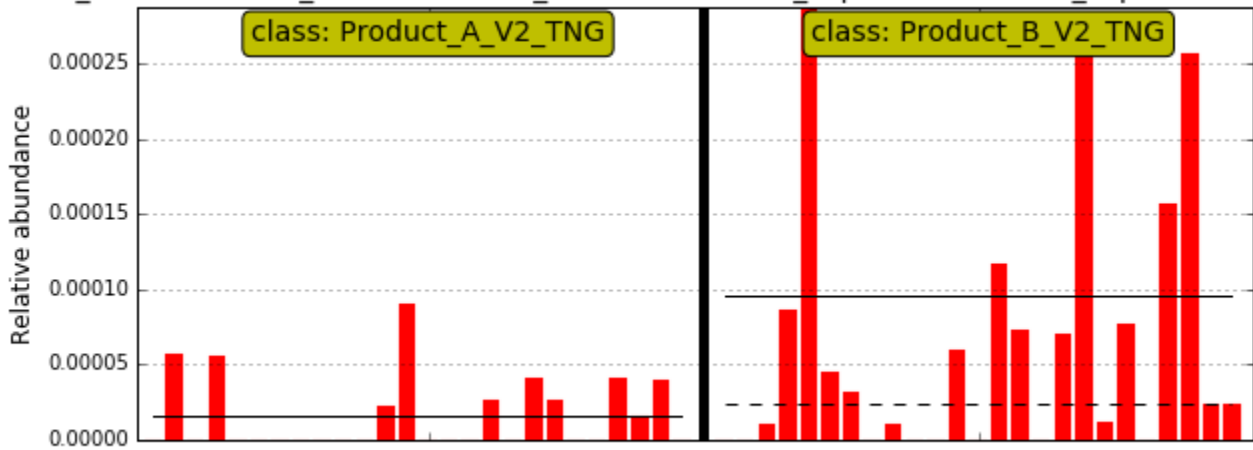
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Bacillales.F\_Gemellaceae.G\_Gemella.S\_morbilloorum



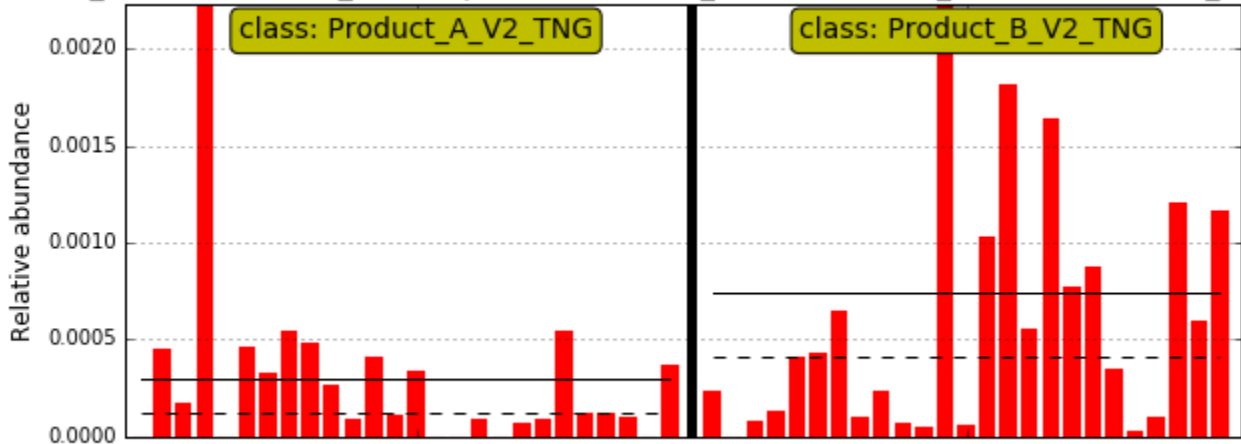
a.P\_Fusobacteria.C\_Fusobacteria.O\_Fusobacteriales.F\_Fusobacteriaceae.G\_Fusobacterium.S\_multispec



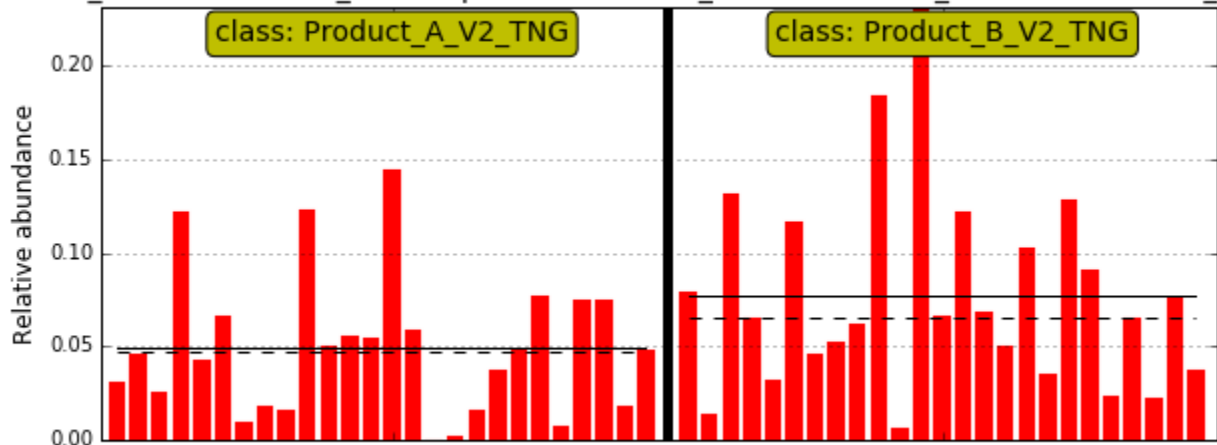
acteria.P\_Fusobacteria.C\_Fusobacteriia.O\_Fusobacteriales.F\_Leptotrichiaceae.G\_Leptotrichia.S\_sp\_HM



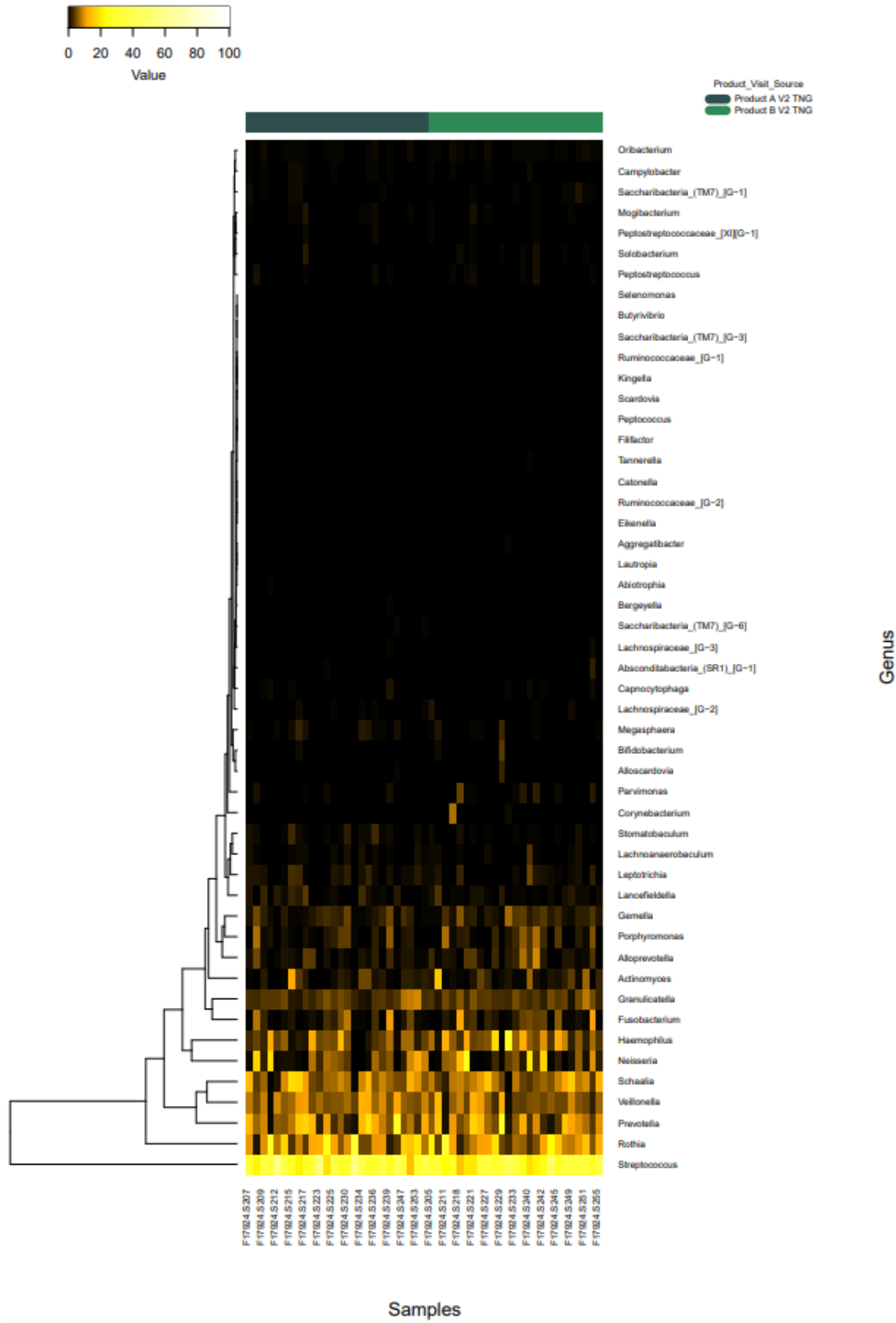
Bacteria.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Aggregatibacter

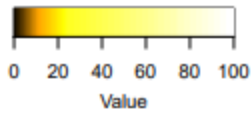


< Bacteria.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Haemophilus

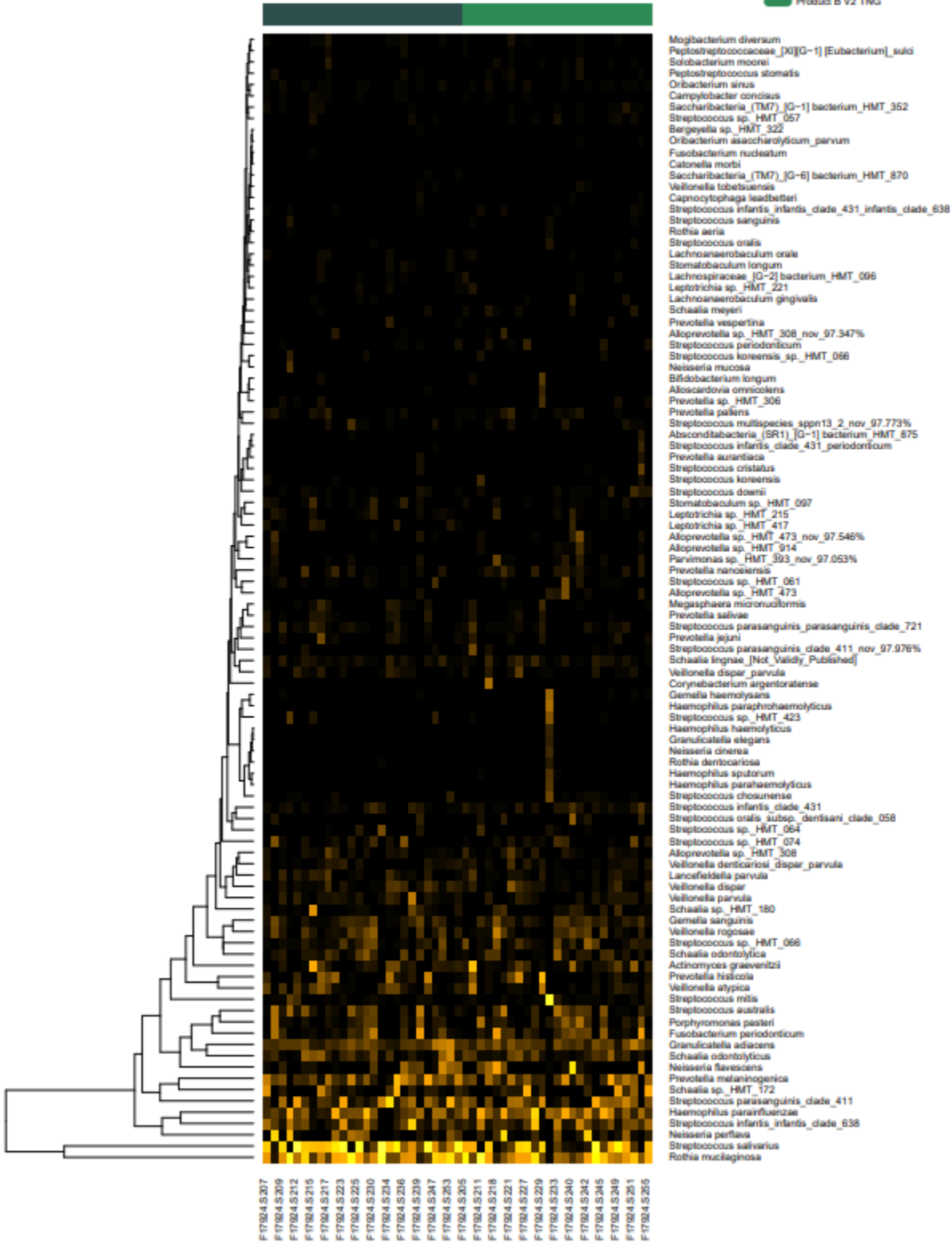


6) Heat map.





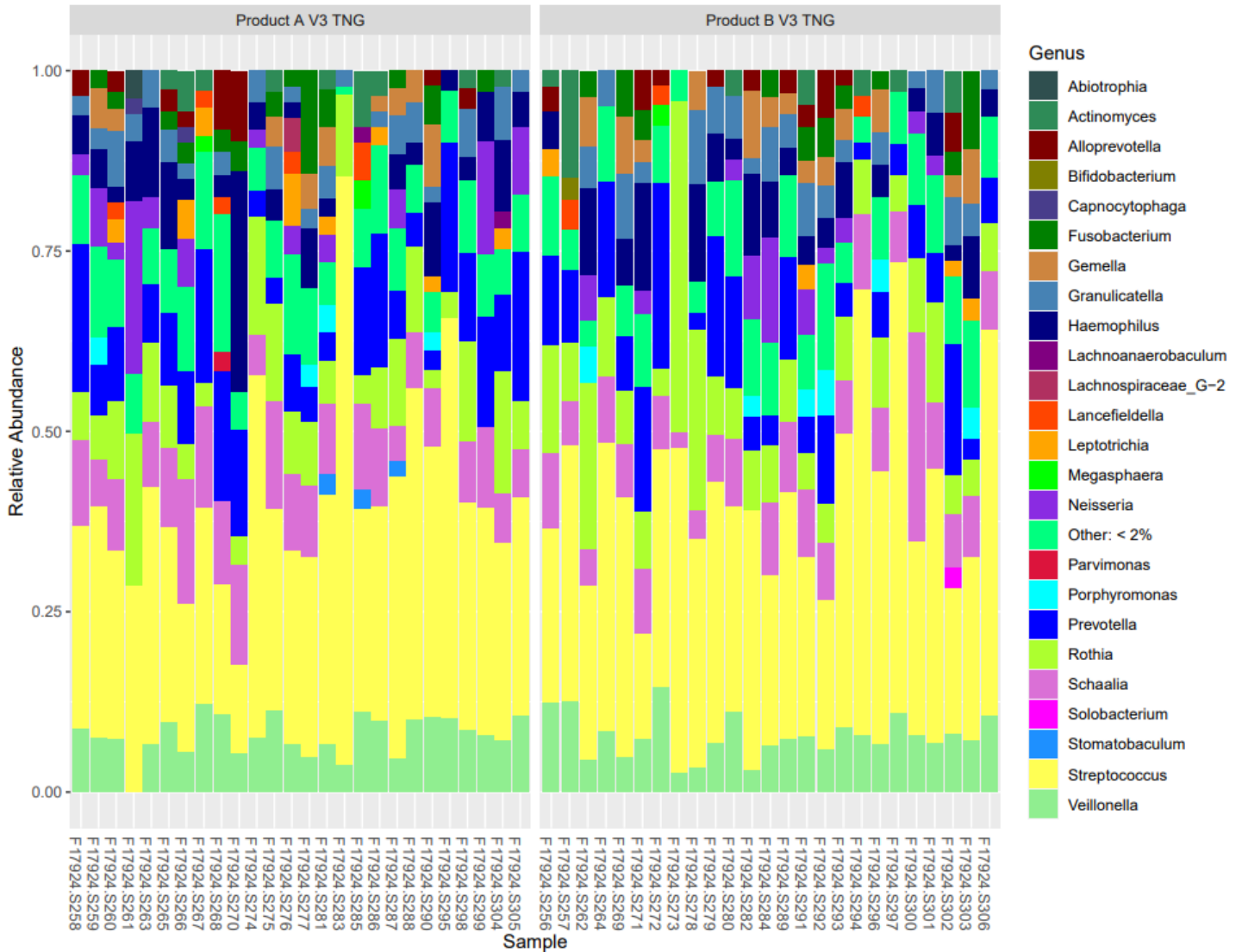
Product\_Visit\_Source  
 Product A V2 TNG  
 Product B V2 TNG



# Comparison 12. Product A V3 TNG vs Product B V3 TNG

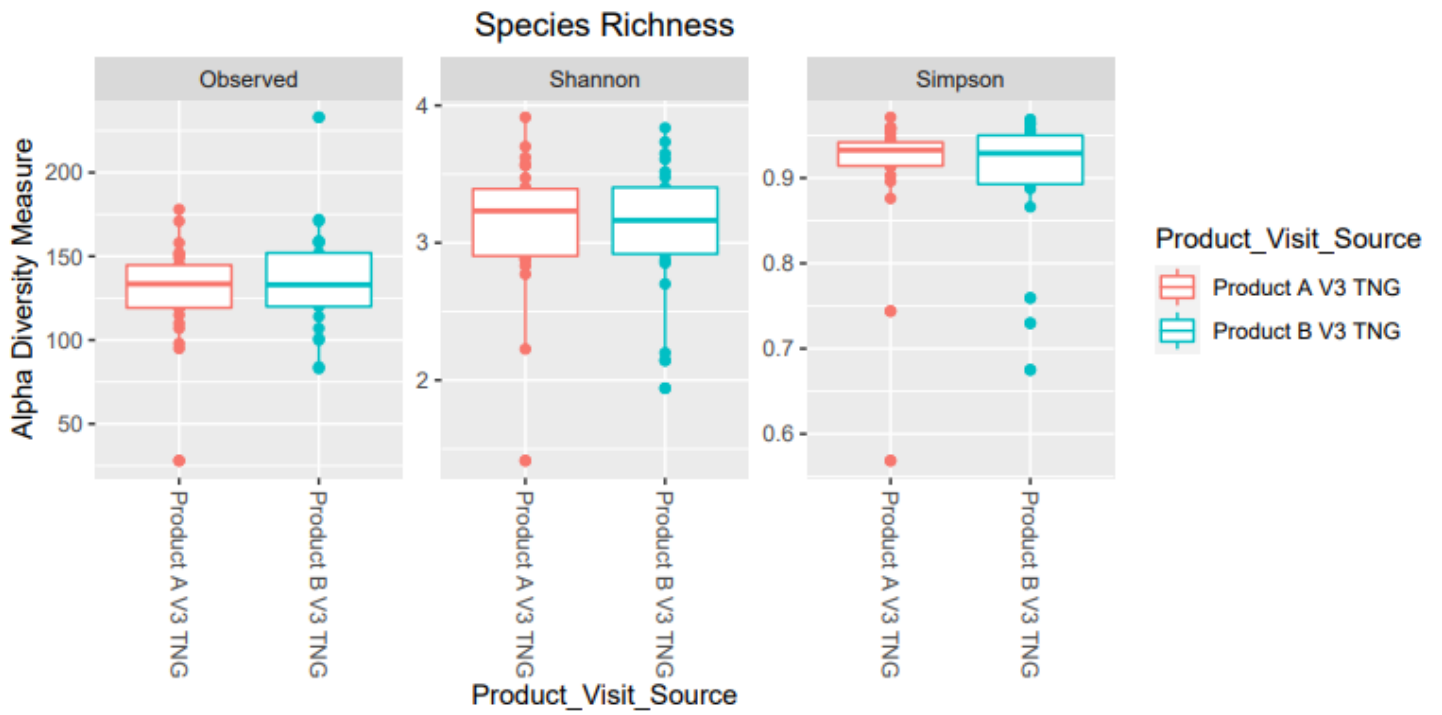
## 1) Taxonomy bar graphs

Top 24 genera bar plot



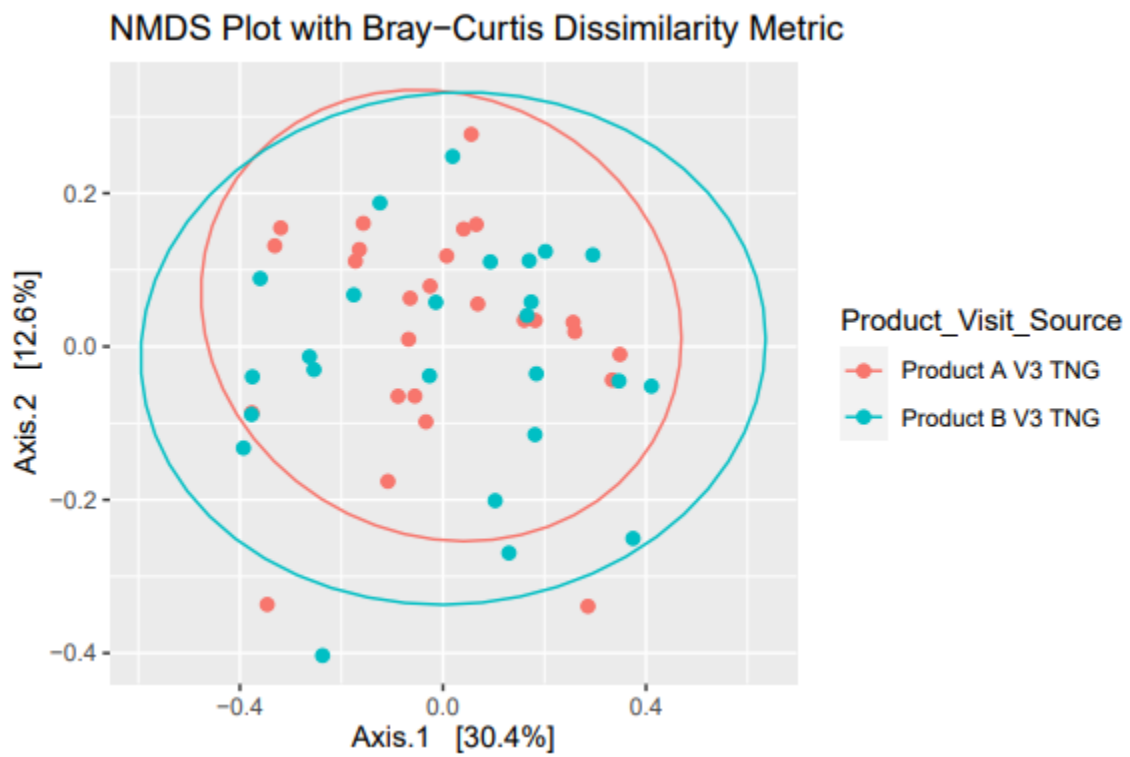


## 2) Alpha



Note: No significant differences

### 3) Beta diversity

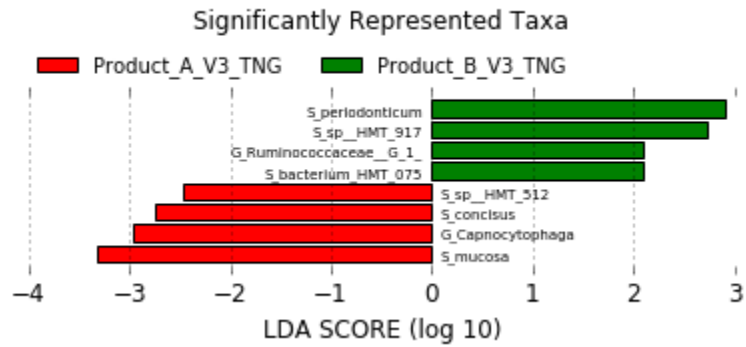


Note: No significant differences

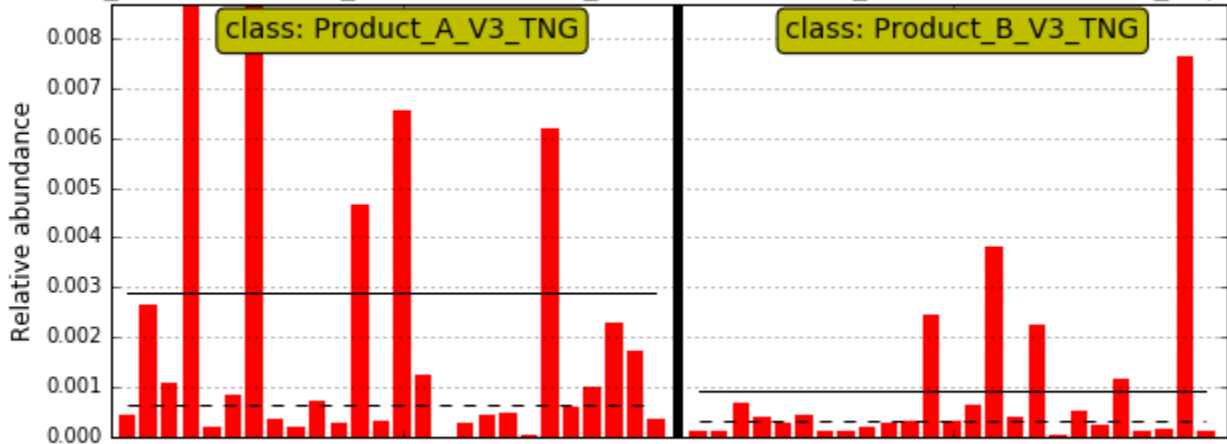
#### 4) Differential abundance

taxon	lfc_(Interc	lfc_Product	se_(Interc	se_Product	W_(Interc	W_Product	p_(Interc	p_Product	q_(Interc	q_Product	diff_(Inte	diff_Prod
Kingella oralis (SP198)	0.530104	-1.10588	0.282167	0.403014	1.878691	-2.74402	0.060287	0.006069	1	1	FALSE	FALSE
Neisseria mucosa (SP300)	0.728845	-1.51131	0.402708	0.575182	1.809859	-2.62753	0.070318	0.008601	1	1	FALSE	FALSE
Capnocytophaga sp._HMT_336 (SP51)	0.282605	-0.60098	0.193331	0.276131	1.461768	-2.17643	0.143805	0.029523	1	1	FALSE	FALSE
Cardiobacterium valvarum (SP159)	0.293395	-0.62299	0.212457	0.30345	1.380957	-2.05303	0.167292	0.04007	1	1	FALSE	FALSE
Absconditabacteria_(SR1)_[G-1] bacte	-0.59385	1.186988	0.41492	0.592625	-1.43124	2.002934	0.152362	0.045184	1	1	FALSE	FALSE
Neisseria elongata (SP219)	0.461786	-0.96651	0.344453	0.491977	1.340637	-1.96454	0.180038	0.049467	1	1	FALSE	FALSE
Bergeyella sp._HMT_206 (SP2)	0.334706	-0.70727	0.257609	0.367939	1.299282	-1.92224	0.193847	0.054575	1	1	FALSE	FALSE
Parvimonas sp._HMT_110 (SP129)	0.292335	-0.62083	0.228088	0.325775	1.281673	-1.9057	0.199957	0.05669	1	1	FALSE	FALSE
Streptococcus periodonticum (SP246)	-0.78556	1.578077	0.615279	0.878794	-1.27675	1.79573	0.201689	0.072537	1	1	FALSE	FALSE
Actinomyces johnsonii (SP290)	0.283173	-0.60214	0.239825	0.342538	1.180752	-1.75788	0.237701	0.078769	1	1	FALSE	FALSE
Prevotella veroralis (SP110)	-0.32927	0.647249	0.258063	0.368588	-1.27594	1.756022	0.201978	0.079085	1	1	FALSE	FALSE
Eikenella corrodens (SP174)	0.424123	-0.88968	0.355495	0.507748	1.193049	-1.7522	0.23285	0.079739	1	1	FALSE	FALSE
Streptococcus gordonii (SP171)	-0.50869	1.013269	0.420318	0.600334	-1.21026	1.687841	0.22618	0.091442	1	1	FALSE	FALSE
Gemella haemolysans (SP8)	-0.40442	0.800542	0.334017	0.477071	-1.21076	1.678034	0.225986	0.093341	1	1	FALSE	FALSE
Capnocytophaga granulosa (SP99)	0.427172	-0.8959	0.381688	0.545159	1.119166	-1.64337	0.263069	0.100307	1	1	FALSE	FALSE
Capnocytophaga leadbetteri (SP89)	0.453093	-0.94878	0.407426	0.58192	1.112087	-1.63042	0.266101	0.103012	1	1	FALSE	FALSE
Campylobacter showae (SP204)	0.409743	-0.86034	0.38656	0.552117	1.059973	-1.55826	0.289157	0.119172	1	1	FALSE	FALSE

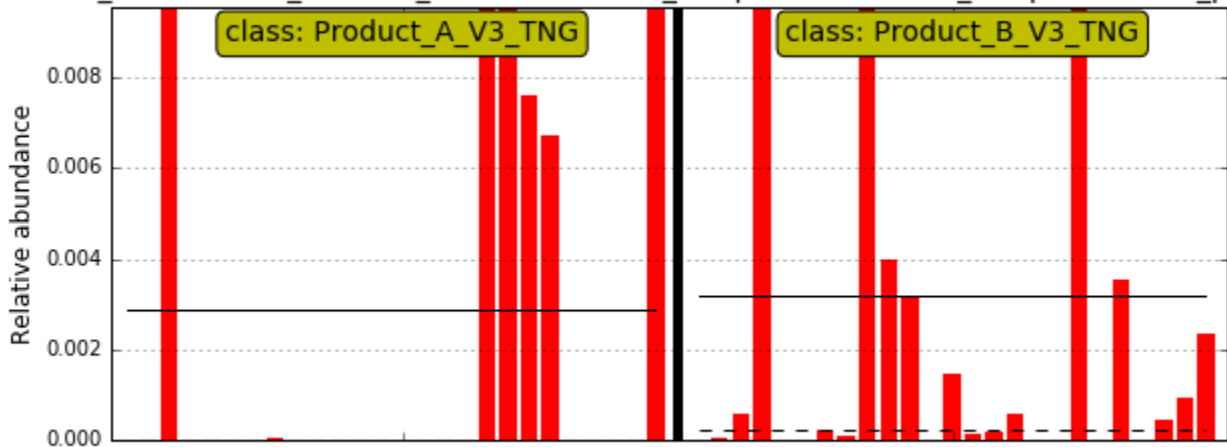
5) Lefse



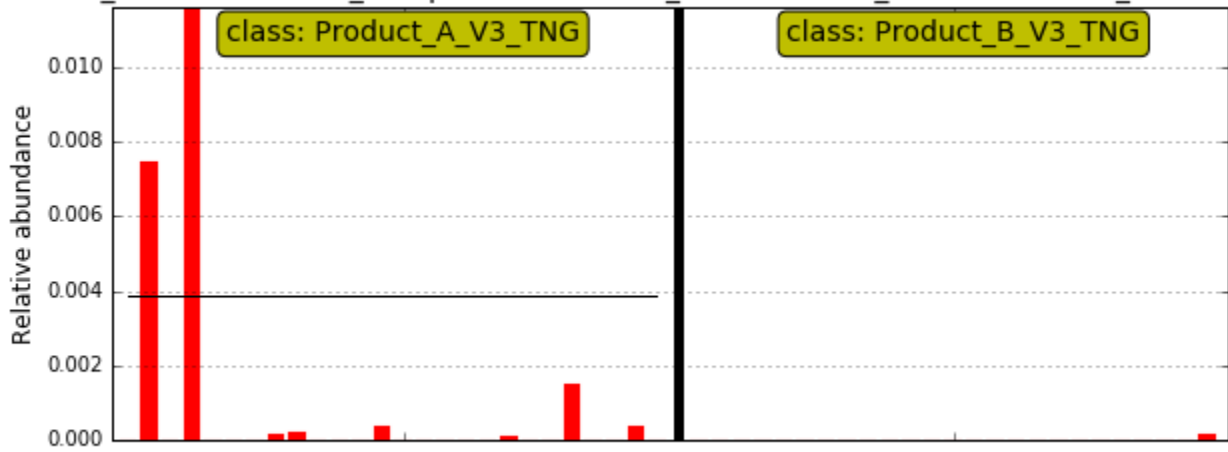
K\_Bacteria.P\_Bacteroidetes.C\_Flavobacteriia.O\_Flavobacteriales.F\_Flavobacteriaceae.G\_Capnocytophaga



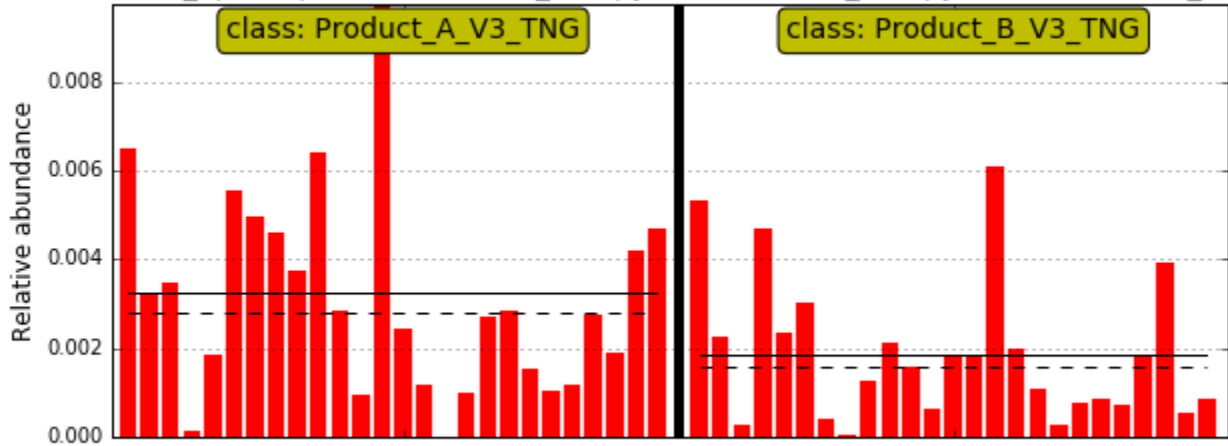
<\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Streptococcaceae.G\_Streptococcus.S\_periodontic



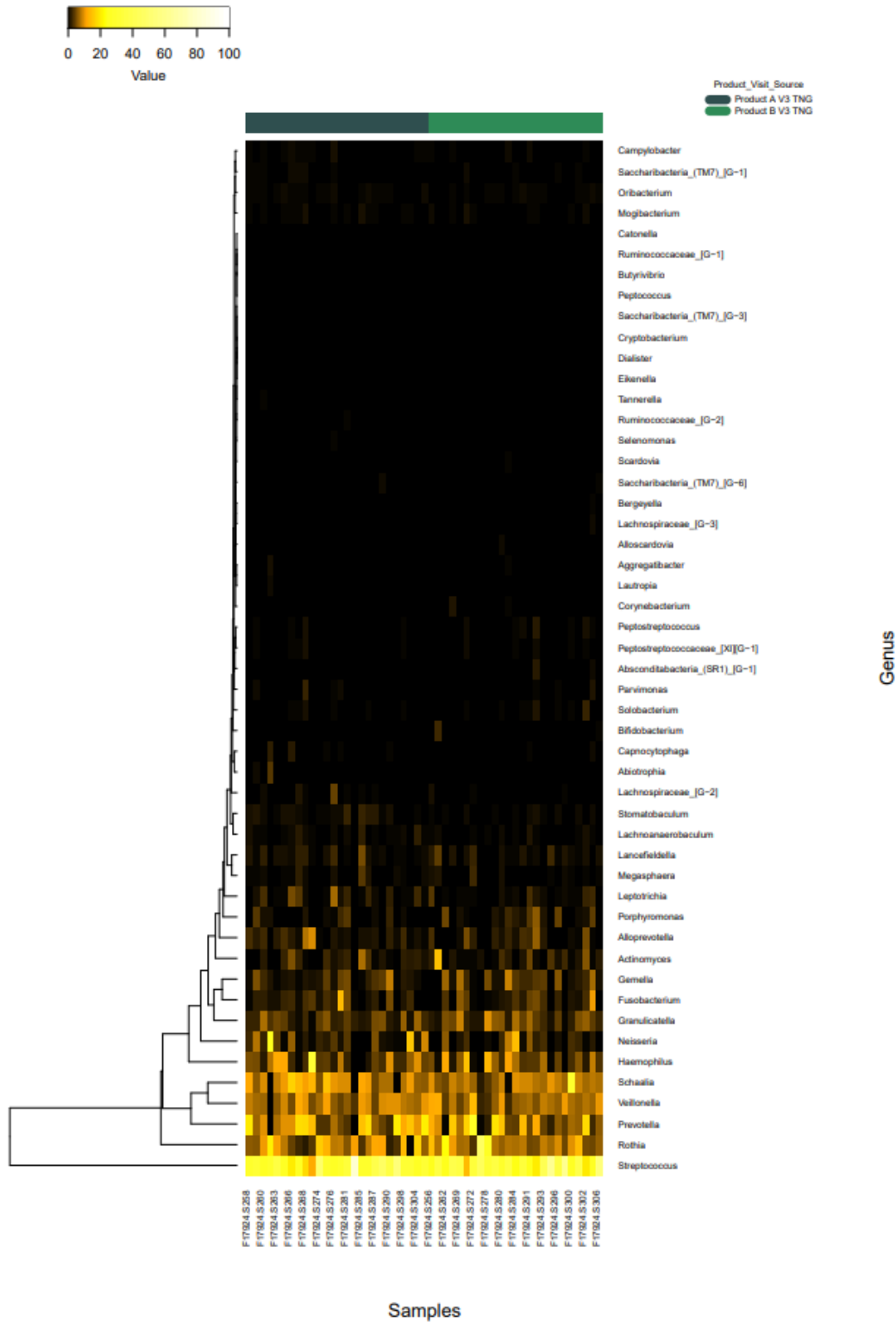
K\_Bacteria.P\_Proteobacteria.C\_Betaproteobacteria.O\_Neisseriales.F\_Neisseriaceae.G\_Neisseria.S\_mucc

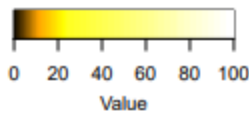


'\_Proteobacteria.C\_Epsilonproteobacteria.O\_Campylobacterales.F\_Campylobacteraceae.G\_Campylobac

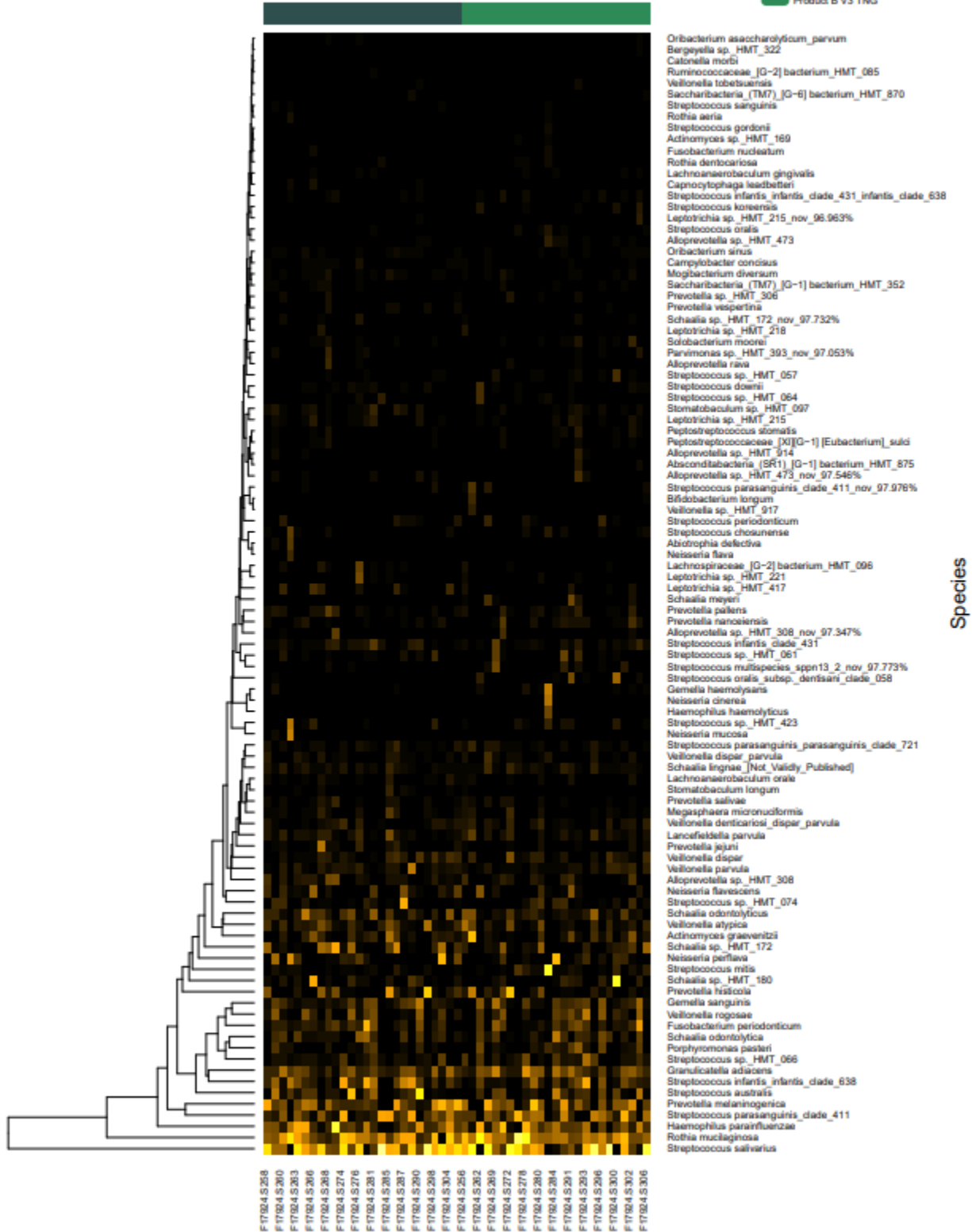


# 6) Heat Map



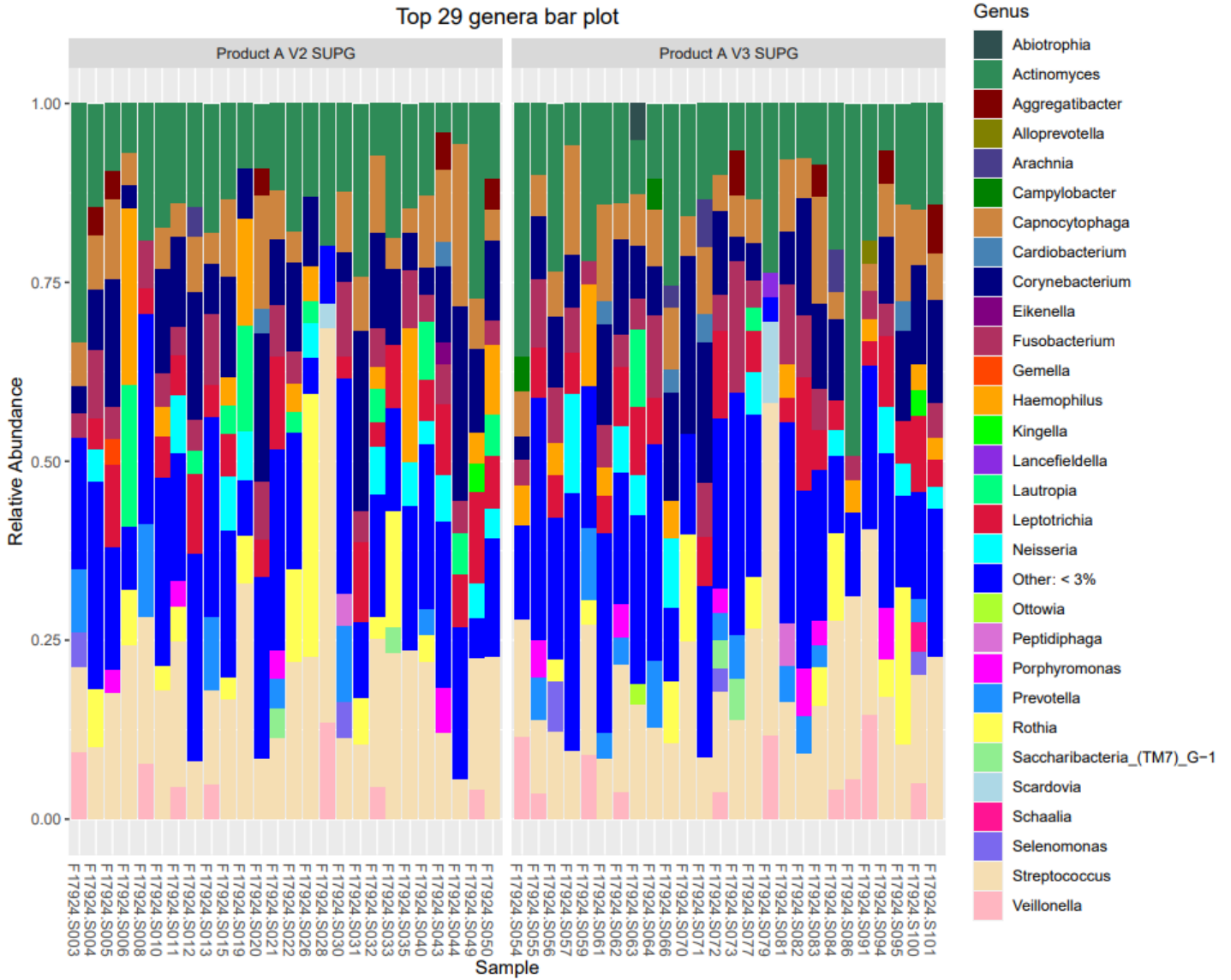


Product\_Visit\_Source  
 Product A V3 TNG  
 Product B V3 TNG



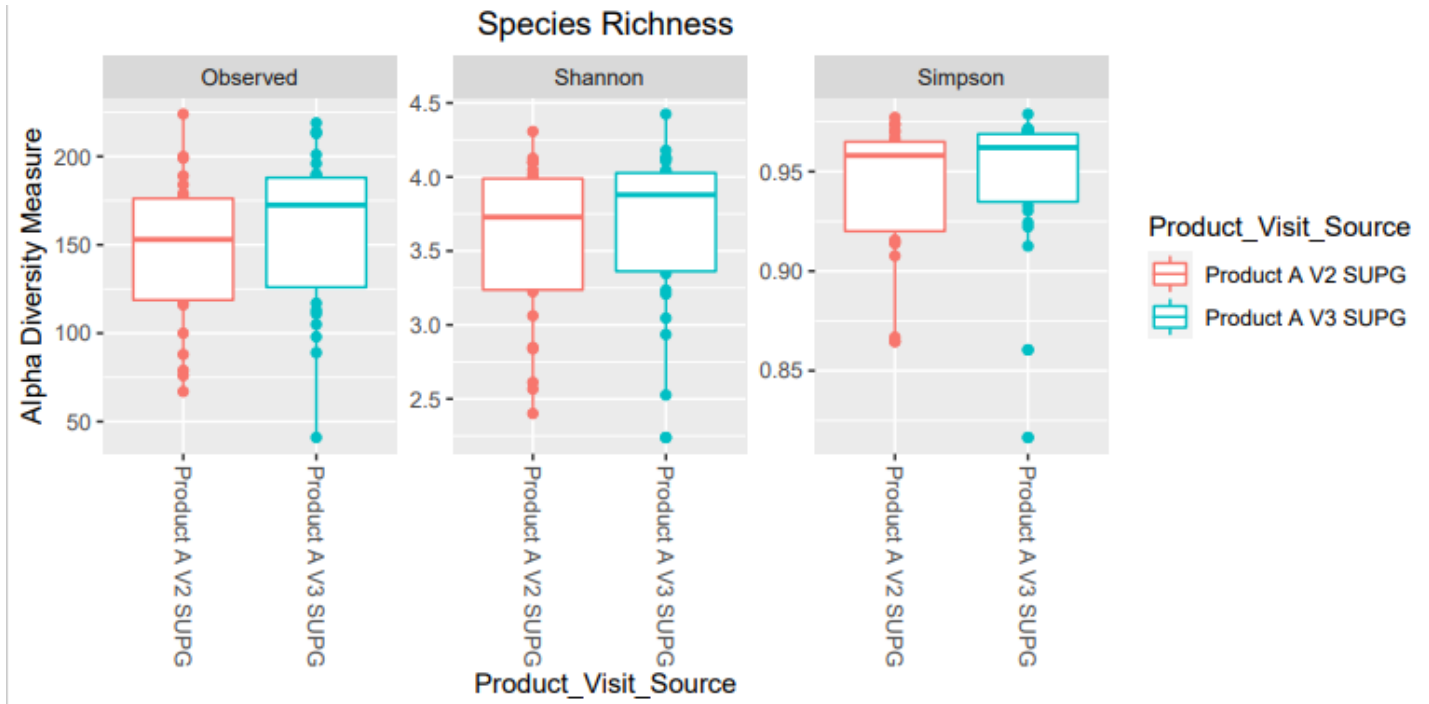
# Comparison 13. Product A V2 SUPG vs Product A V3 SUPG

## 1) Taxonomy bar graphs



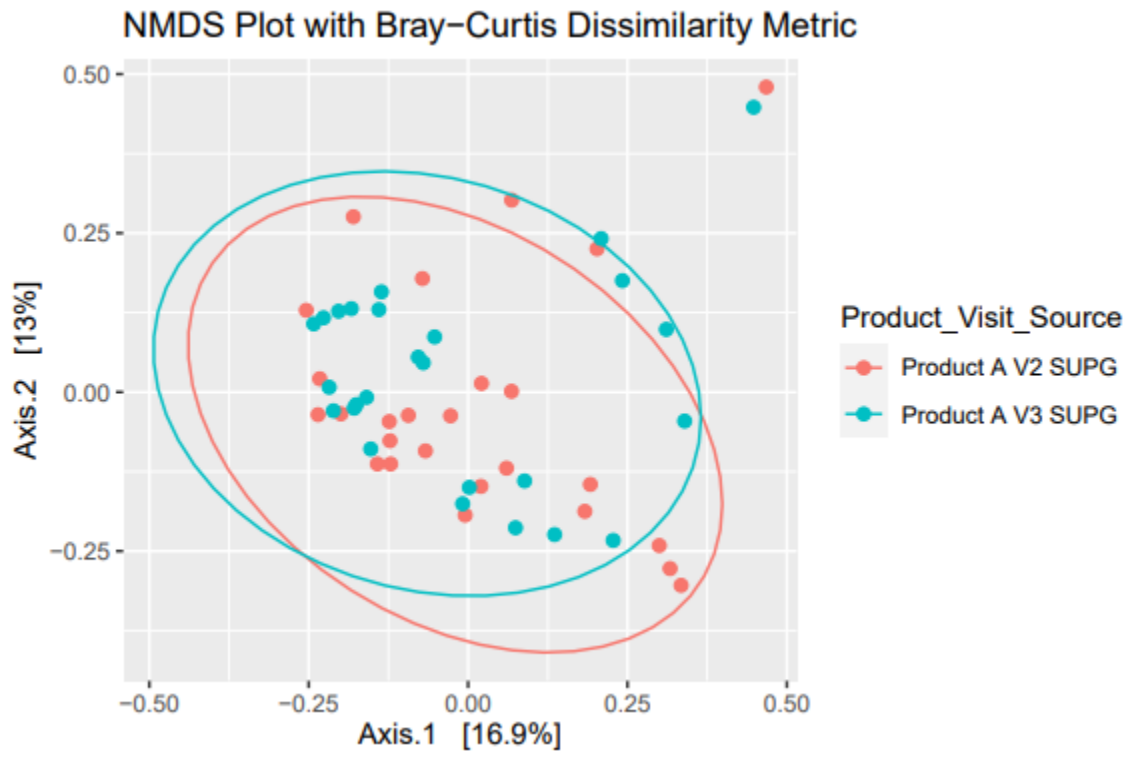


## 2) Alpha



Note: No significant differences

### 3) Beta diversity



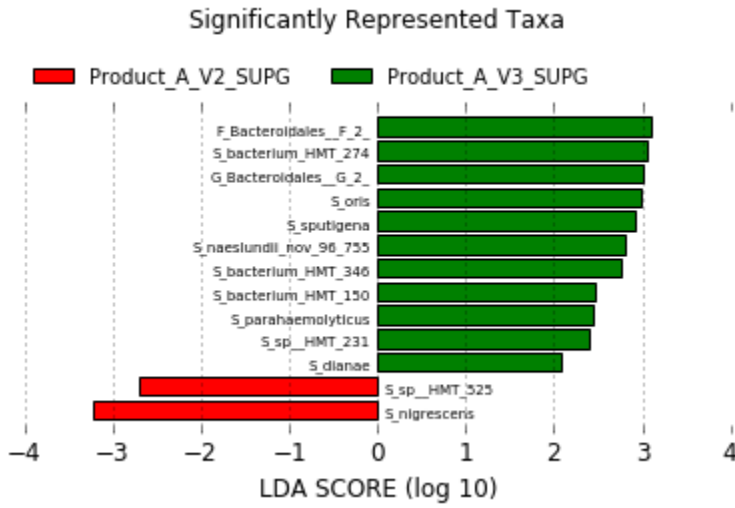
Note: No significant differences

#### 4) Differential abundance

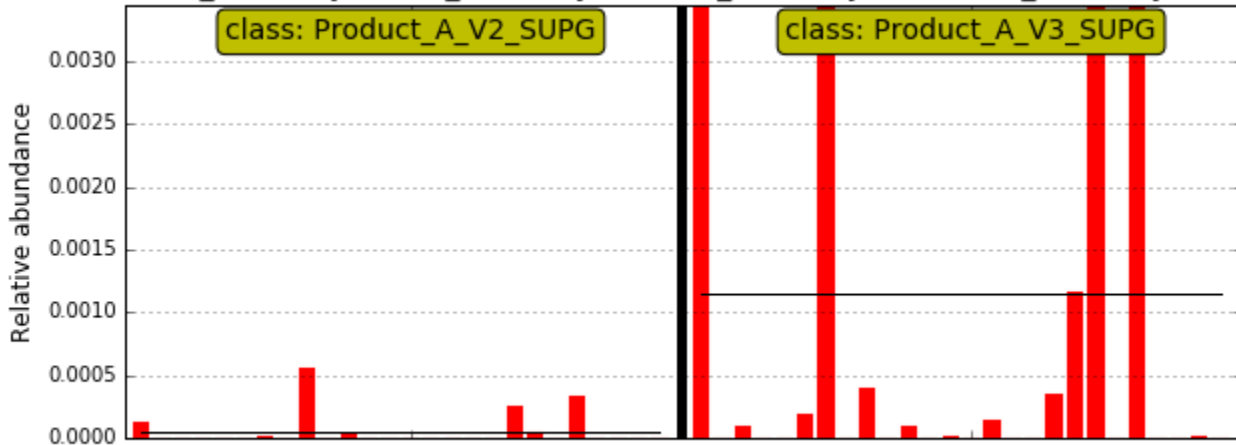
taxon	lfc_(Interc	lfc_Product	use_(Interc	se_Product	W_(Interc	W_Product	p_(Interc	p_Product	q_(Interc	q_Product	diff_(Inte	diff_Produ
Bacteroidales_[G-2] bacterium_HMT_274 (S	-0.73858	1.477154	0.559473	0.791214	-1.32013	1.866945	0.186792	0.061909	1	1	FALSE	FALSE
Prevotella nigrescens (SP259)	-0.72947	1.458935	0.564964	0.79898	-1.29118	1.825998	0.196643	0.067851	1	1	FALSE	FALSE
Prevotella oris (SP65)	-0.66337	1.326736	0.52408	0.741161	-1.26577	1.790077	0.205594	0.073442	1	1	FALSE	FALSE
Saccharibacteria_(TM7)[G-1] bacterium_H	-0.729	1.457994	0.581074	0.821763	-1.25457	1.774228	0.209636	0.076026	1	1	FALSE	FALSE
Actinomyces naeslundii_nov_96.755% (SPN	-0.57854	1.157073	0.47512	0.671921	-1.21766	1.722038	0.223352	0.085063	1	1	FALSE	FALSE
Haemophilus parahaemolyticus (SP148)	-0.51912	1.038244	0.442303	0.625511	-1.17368	1.659835	0.240523	0.096948	1	1	FALSE	FALSE
Treponema sp._HMT_231 (SP87)	-0.56311	1.126215	0.487301	0.689148	-1.15556	1.634214	0.24786	0.102214	1	1	FALSE	FALSE
Actinomyces sp._HMT_525 (SP24)	-0.63155	1.263109	0.547402	0.774144	-1.15373	1.631621	0.248611	0.102759	1	1	FALSE	FALSE
Abiotrophia defectiva (SP206)	0.705528	-1.41106	0.632528	0.89453	1.11541	-1.57743	0.264675	0.114697	1	1	FALSE	FALSE
Selenomonas sputigena (SP66)	-0.53065	1.061308	0.504071	0.712864	-1.05274	1.488794	0.292462	0.136542	1	1	FALSE	FALSE
Prevotella sp._HMT_317 (SP111)	-0.71738	1.43477	0.683653	0.966831	-1.04934	1.483992	0.294022	0.137811	1	1	FALSE	FALSE
Streptococcus gordonii (SP171)	0.473769	-0.94754	0.452083	0.639342	1.047968	-1.48205	0.294653	0.138327	1	1	FALSE	FALSE
Actinomyces sp._HMT_175_nov_97.951% (S	0.566662	-1.13332	0.555585	0.785716	1.019937	-1.44241	0.307758	0.149187	1	1	FALSE	FALSE
Alloprevotella sp._HMT_473_nov_97.546%	0.388176	-0.77635	0.380976	0.538781	1.0189	-1.44094	0.30825	0.149601	1	1	FALSE	FALSE

Note: No significant differences

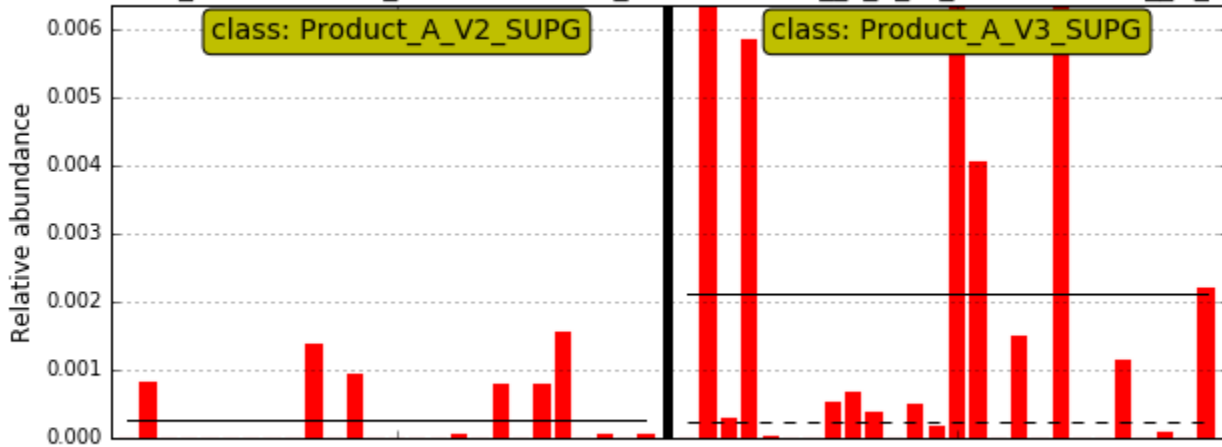
5) Lefse



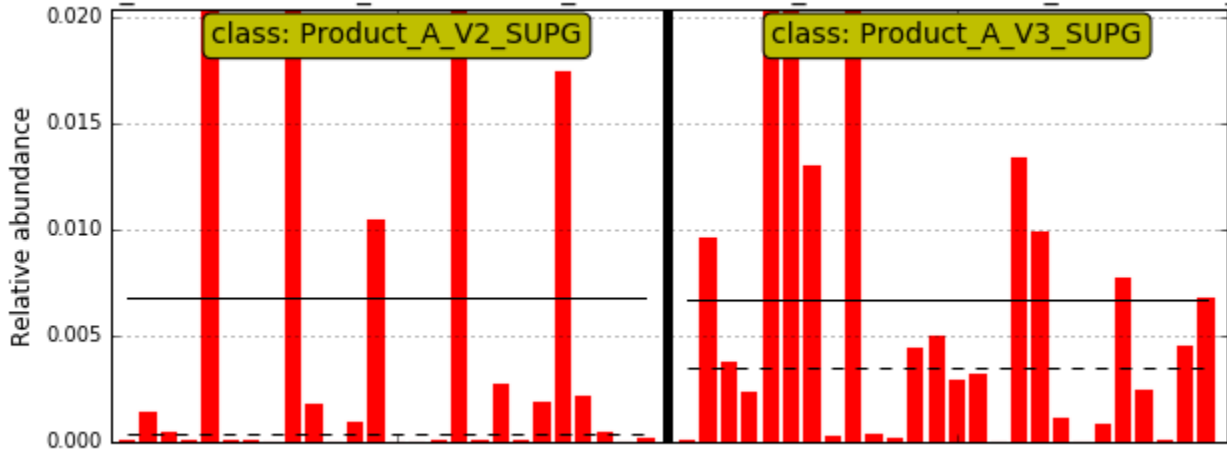
$\beta$  \_Actinobacteria.C\_Actinomycetia.O\_Actinomycetales.F\_Actinomycetaceae.G\_Actinomyces.S\_naeslund



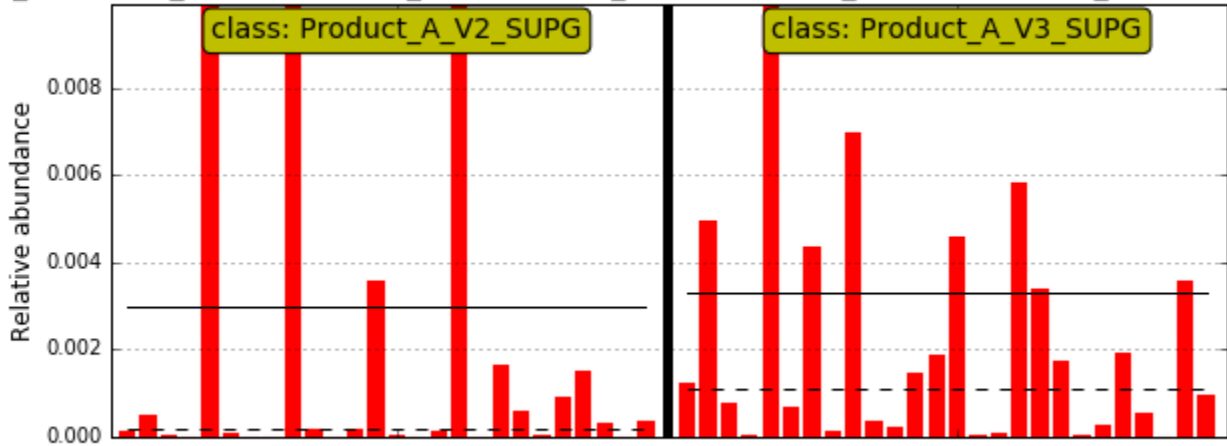
$\beta$  \_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Bacteroidales\_F\_2.G\_Bacteroidales\_G\_2.S\_bacter



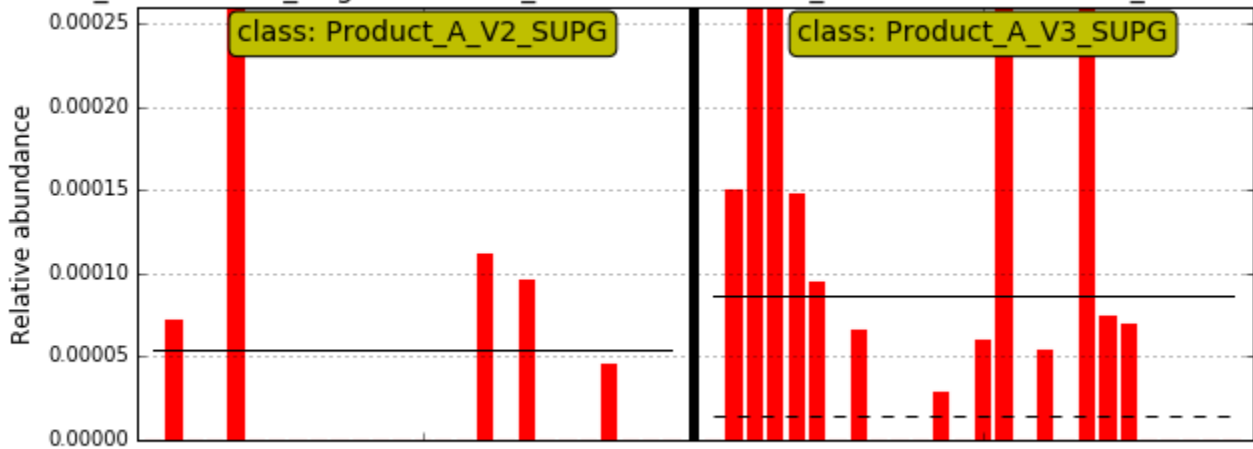
K\_Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Prevotella.S\_nigrescer



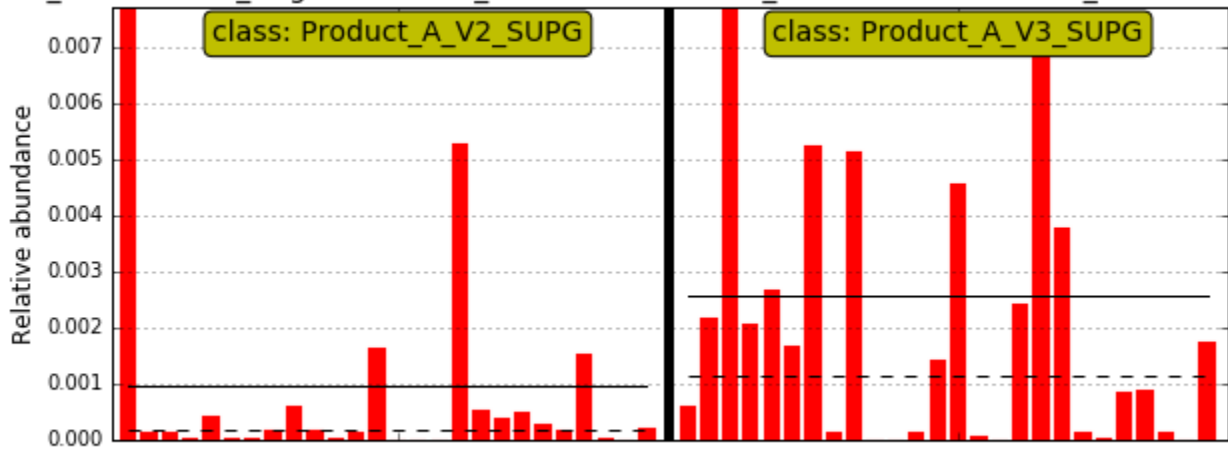
K\_Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Prevotella.S\_oris



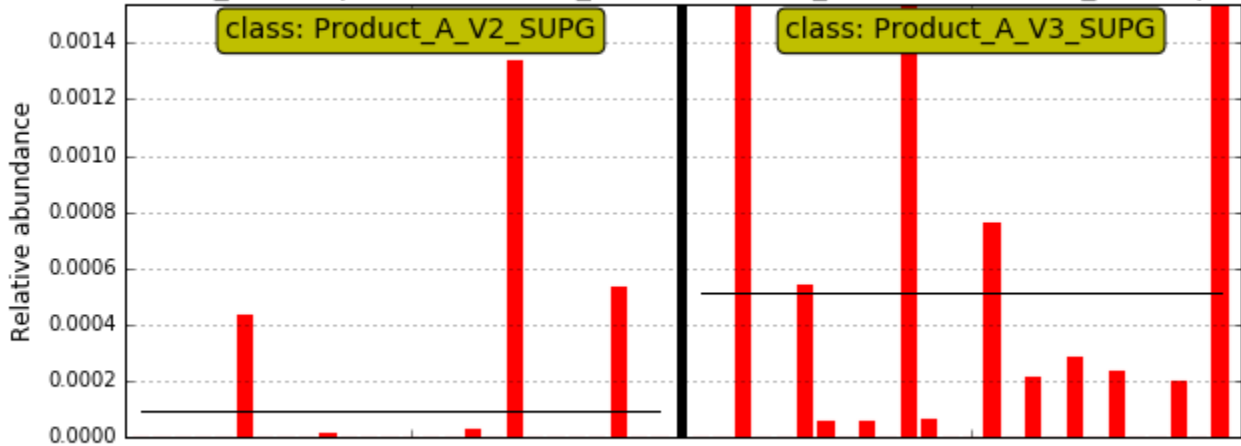
Bacteria.P\_Firmicutes.C\_Negativicutes.O\_Selenomonadales.F\_Selenomonadaceae.G\_Selenomonas.S\_di



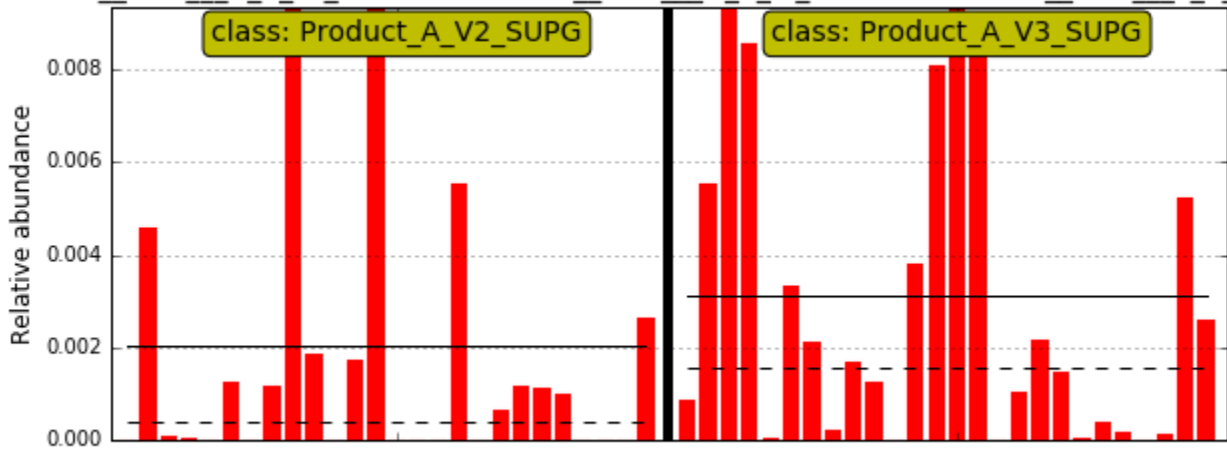
acteria.P\_Firmicutes.C\_Negativicutes.O\_Selenomonadales.F\_Selenomonadaceae.G\_Selenomonas.S\_spu



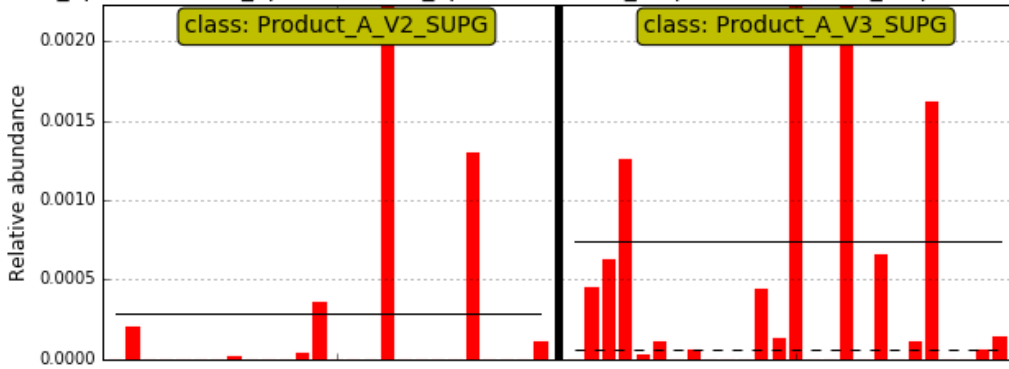
.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Haemophilus.S\_para



haribacteria\_TM7\_C\_1\_O\_Saccharibacteria\_TM7\_O\_1\_F\_Saccharibacteria\_TM7\_F\_1\_G\_Saccha

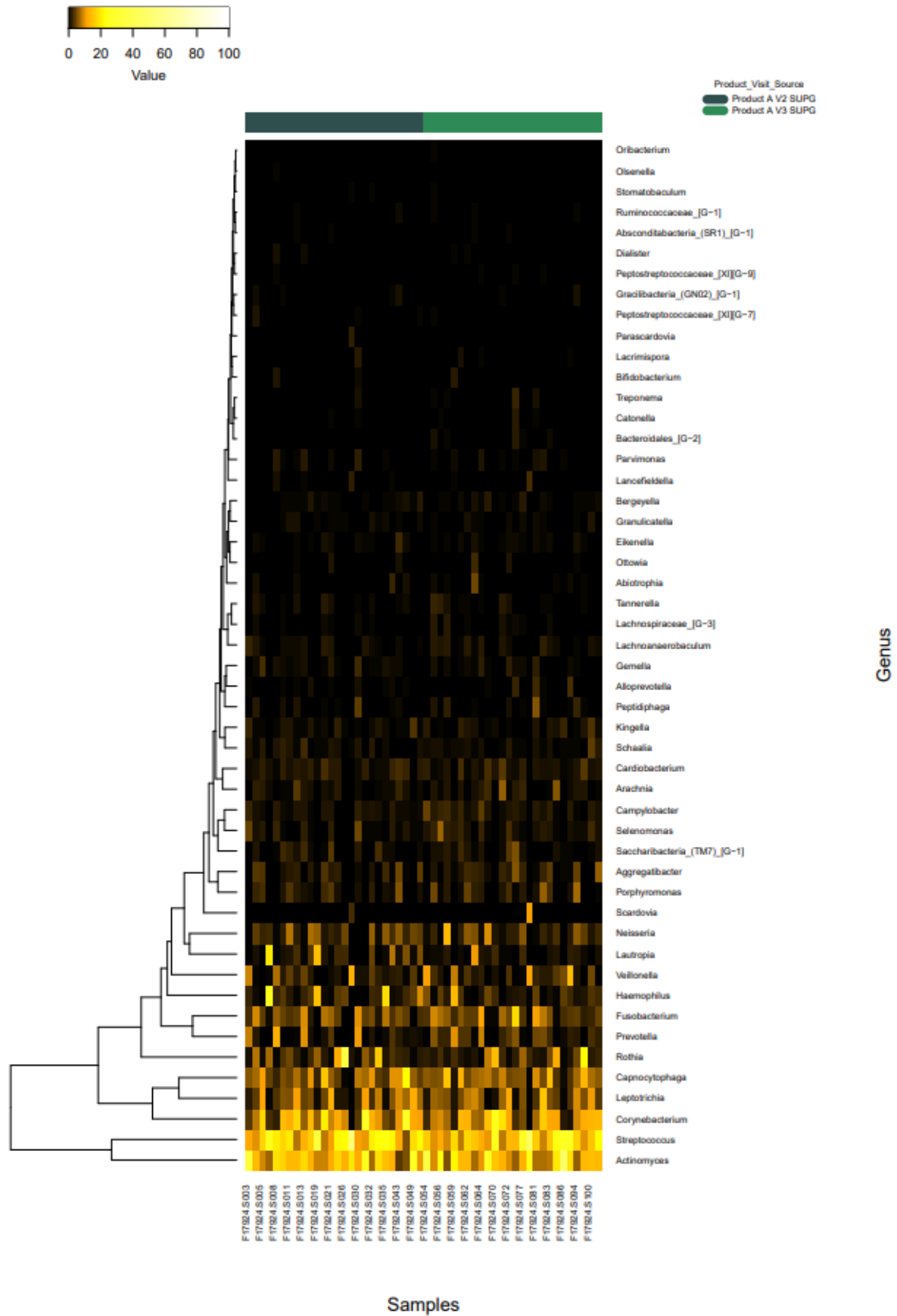


acteria.P\_Spirochaetes.C\_Spirochaetia.O\_Spirochaetales.F\_Treponemataceae.G\_Treponema.S\_sp\_HM

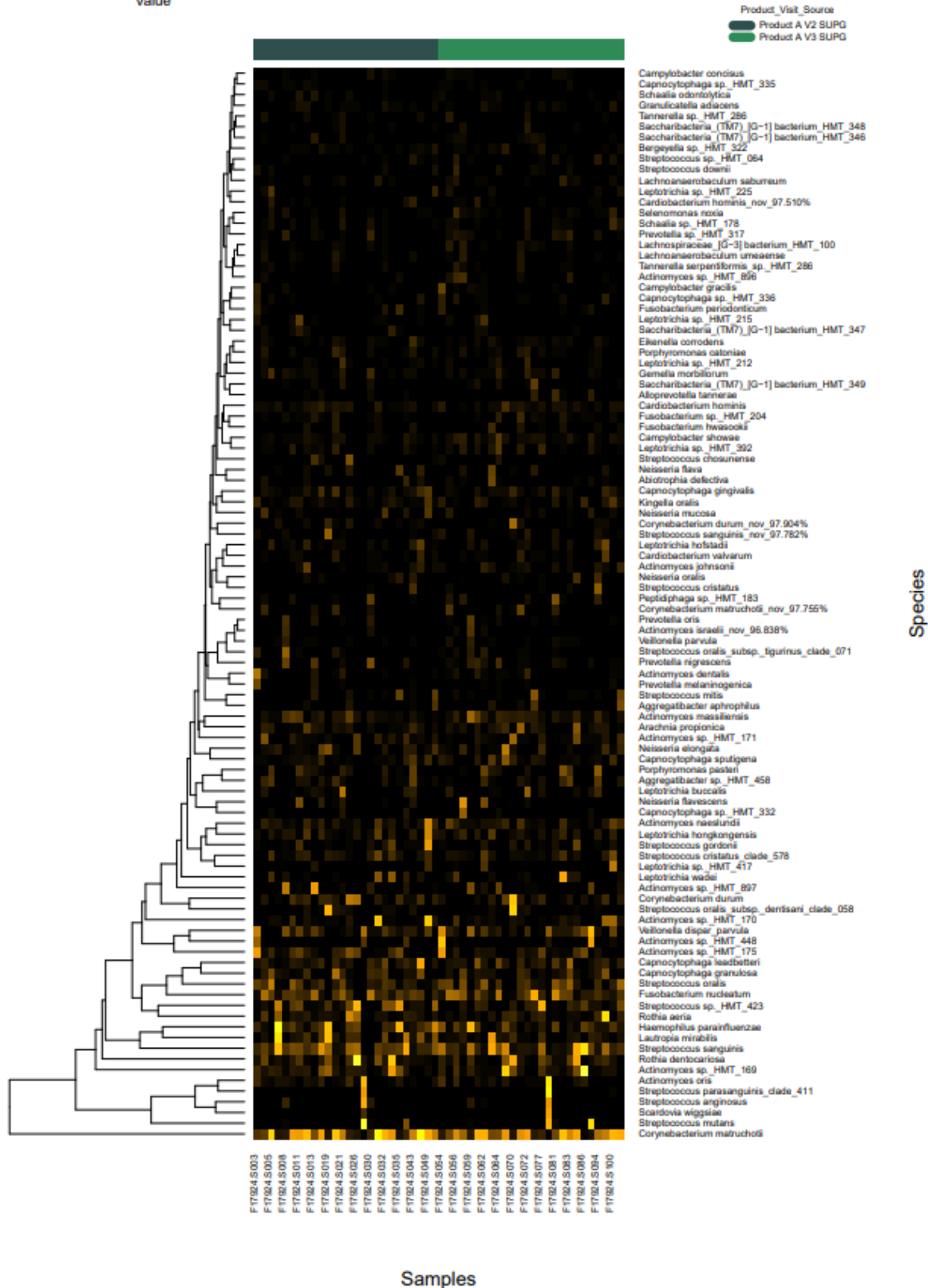
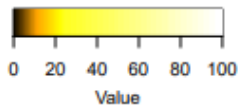


*Treponema sp. HMT-231*

6) Heat map.

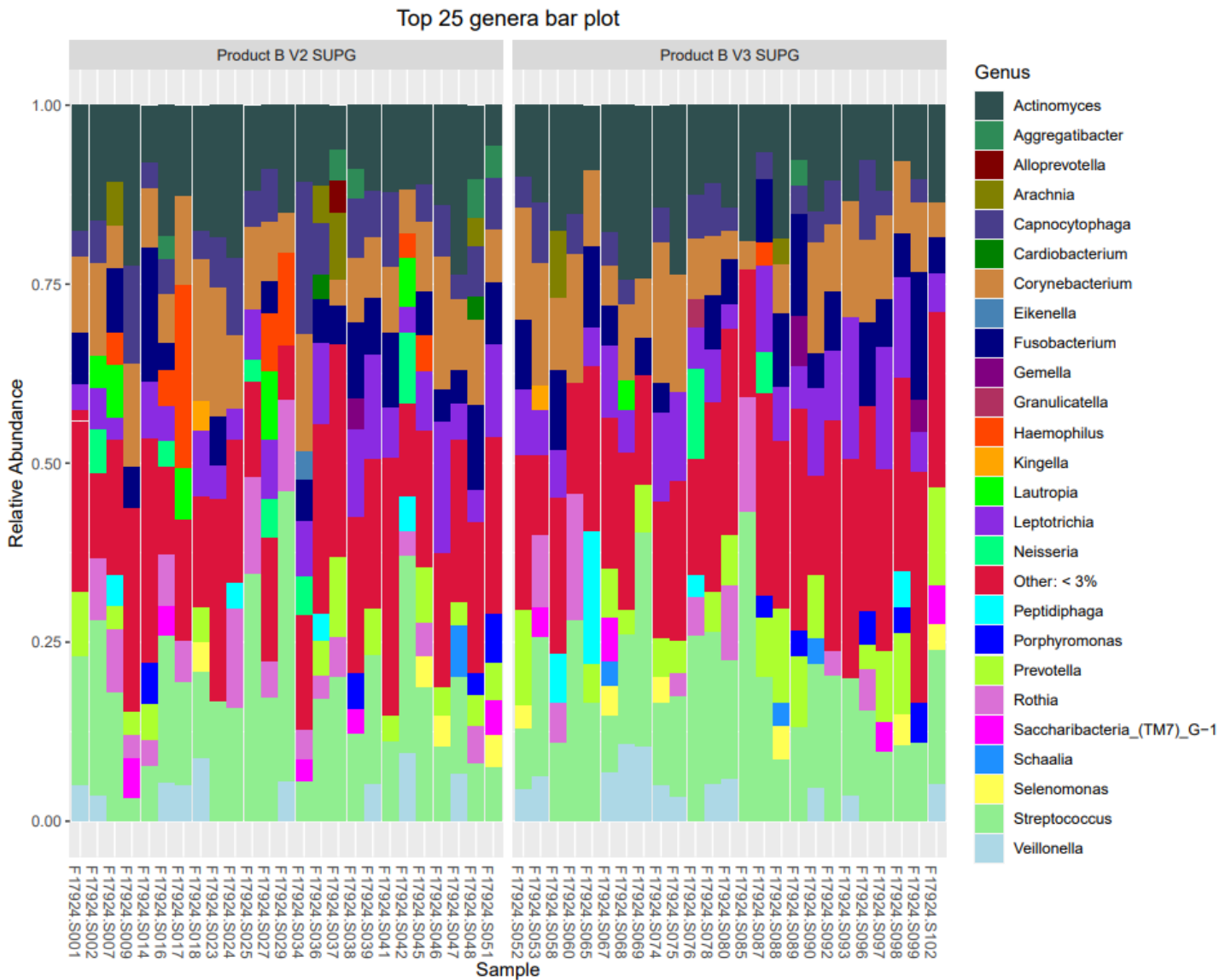




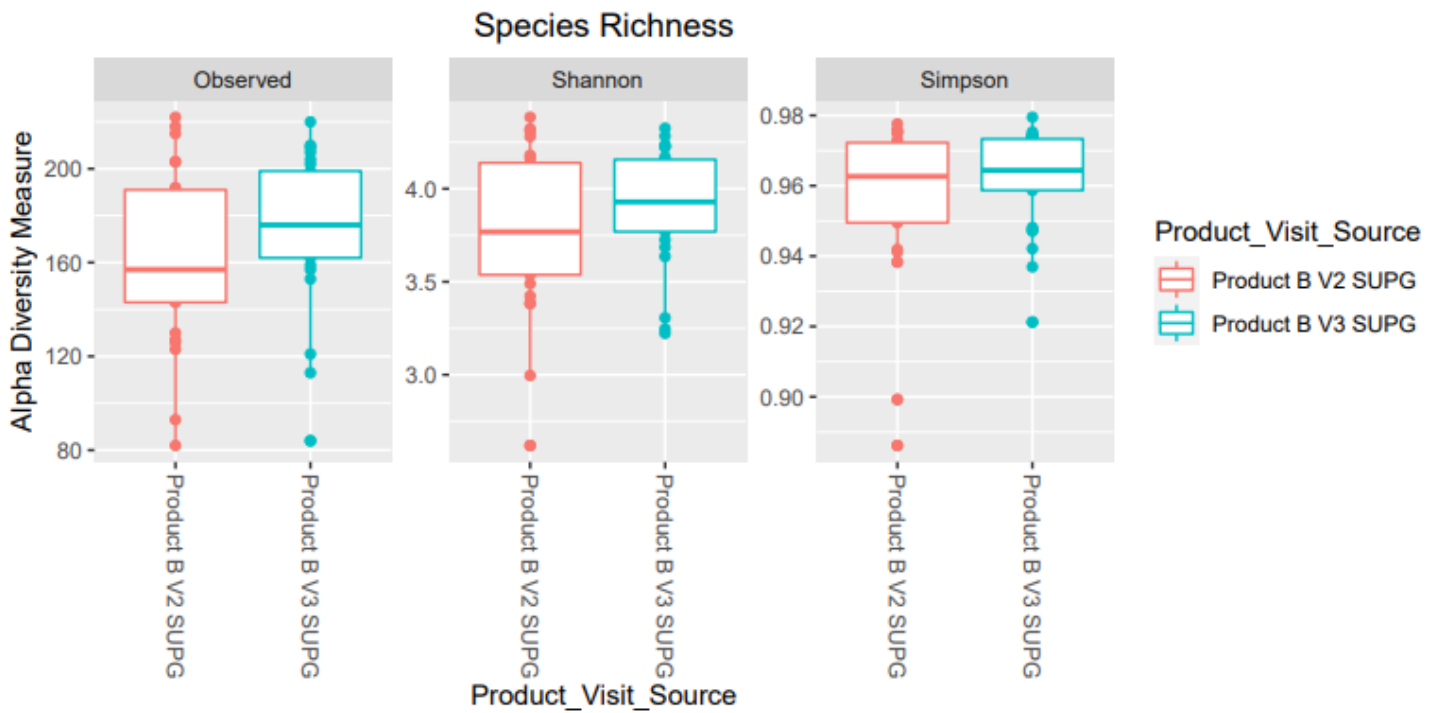


# Comparison 14. Product B V2 SUPG vs Product B V3 SUPG

## 1) Taxonomy bar graphs



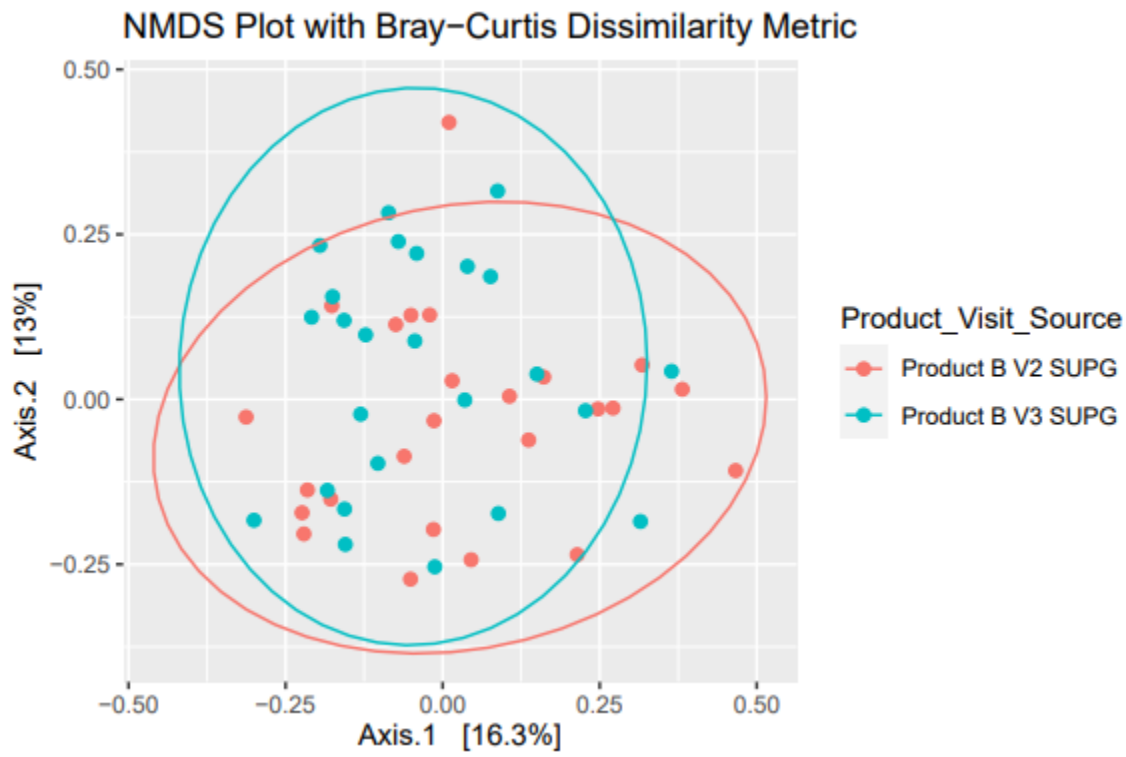
## 2) Alpha



Note: No significant differences

P value for Observed is 0.099

### 3) Beta diversity



Note: No significant differences but  $P = 0.09$

#### 4) Differential abundance

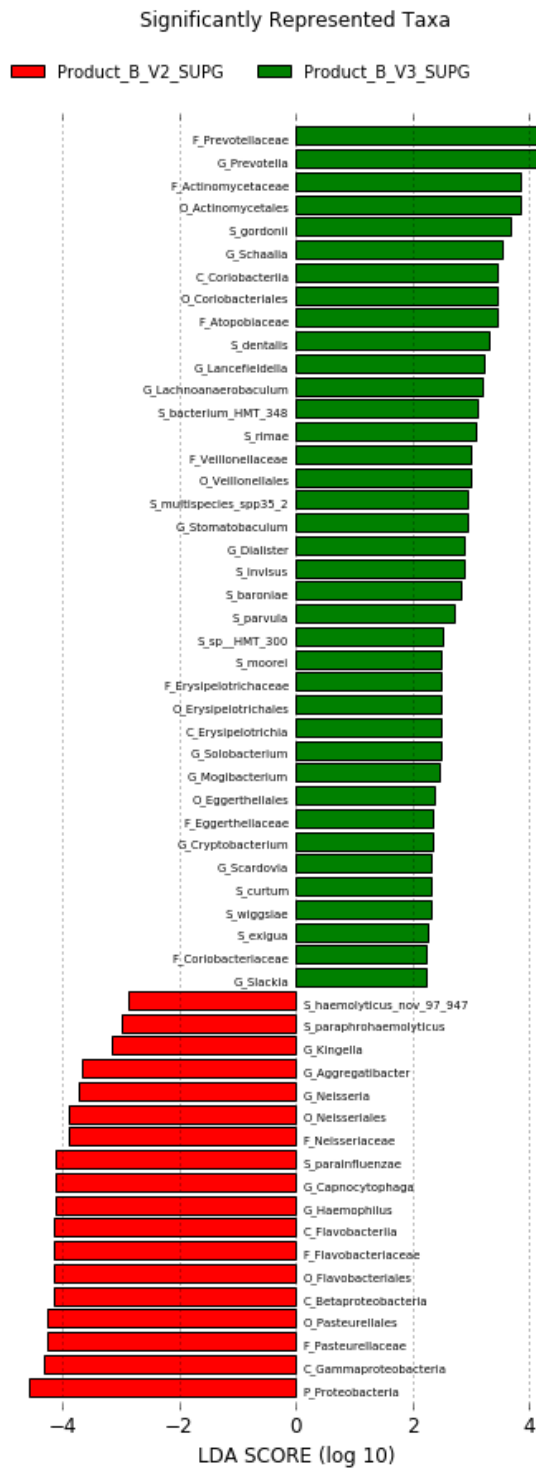
taxon	lfc_(Interc	lfc_Product	se_(Interc	se_Product	W_(Interc	W_Product	p_(Interc	p_Product	q_(Interc	q_Product	diff_(Inte	diff_Produ
Haemophilus parainfluenzae (SP19)	1.095638	-2.17965	0.387319	0.547752	2.828773	-3.97926	0.004673	6.91E-05	1	0.022605	FALSE	TRUE
Lancefieldella parvula (SP315)	-0.85883	1.729289	0.458738	0.648753	-1.87216	2.665558	0.061184	0.007686	1	1	FALSE	FALSE
Lancefieldella rimae (SP173)	-0.84209	1.695802	0.551558	0.780021	-1.52674	2.174046	0.126825	0.029702	1	1	FALSE	FALSE
Kingella oralis (SP198)	0.675897	-1.34017	0.439528	0.621587	1.537778	-2.15604	0.124103	0.03108	1	1	FALSE	FALSE
Dialister invisus (SP128)	-0.72534	1.462305	0.507517	0.717737	-1.42919	2.037383	0.152949	0.041612	1	1	FALSE	FALSE
Haemophilus sputorum (SP115)	0.429112	-0.8466	0.29523	0.417518	1.453484	-2.02769	0.146089	0.042592	1	1	FALSE	FALSE
Cryptobacterium curtum (SP465)	-0.47143	0.954489	0.334961	0.473706	-1.40742	2.01494	0.159302	0.043911	1	1	FALSE	FALSE
Mogibacterium diversum (SP365)	-0.62739	1.266402	0.464394	0.656752	-1.35098	1.928279	0.176701	0.05382	1	1	FALSE	FALSE
Solobacterium moorei (SP96)	-0.57312	1.157875	0.427488	0.604559	-1.34068	1.915239	0.180024	0.055462	1	1	FALSE	FALSE
Neisseria elongata (SP219)	0.634283	-1.25694	0.47763	0.675471	1.327979	-1.86083	0.184185	0.062768	1	1	FALSE	FALSE
Neisseria perflava (SP429)	0.541426	-1.07122	0.407831	0.57676	1.327573	-1.85731	0.184319	0.063267	1	1	FALSE	FALSE
Stomatobaculum longum (SP228)	-0.67582	1.363271	0.527157	0.745513	-1.28201	1.828634	0.199838	0.067454	1	1	FALSE	FALSE
Fusobacterium nucleatum_subsp._animalis	-0.64165	1.294927	0.509816	0.720988	-1.25859	1.796045	0.208177	0.072487	1	1	FALSE	FALSE
Saccharibacteria_(TM7)_[G-1] bacterium_HM	-0.73879	1.489209	0.60684	0.858202	-1.21744	1.735268	0.223437	0.082693	1	1	FALSE	FALSE
Saccharibacteria_(TM7)_[G-1] bacterium_HM	-0.71039	1.432403	0.593749	0.839687	-1.19645	1.705877	0.231522	0.088031	1	1	FALSE	FALSE
Capnocytophaga sp._HMT_332 (SP49)	0.60461	-1.19759	0.497303	0.703293	1.215778	-1.70284	0.224069	0.088598	1	1	FALSE	FALSE
Prevotella sp._HMT_300 (SP69)	-0.56406	1.13974	0.47378	0.670026	-1.19055	1.701039	0.233832	0.088936	1	1	FALSE	FALSE
Neisseria flavescens (SP195)	0.715319	-1.41901	0.592878	0.838456	1.206521	-1.69241	0.227617	0.090568	1	1	FALSE	FALSE

Note: *H. influenzae* is statistically different

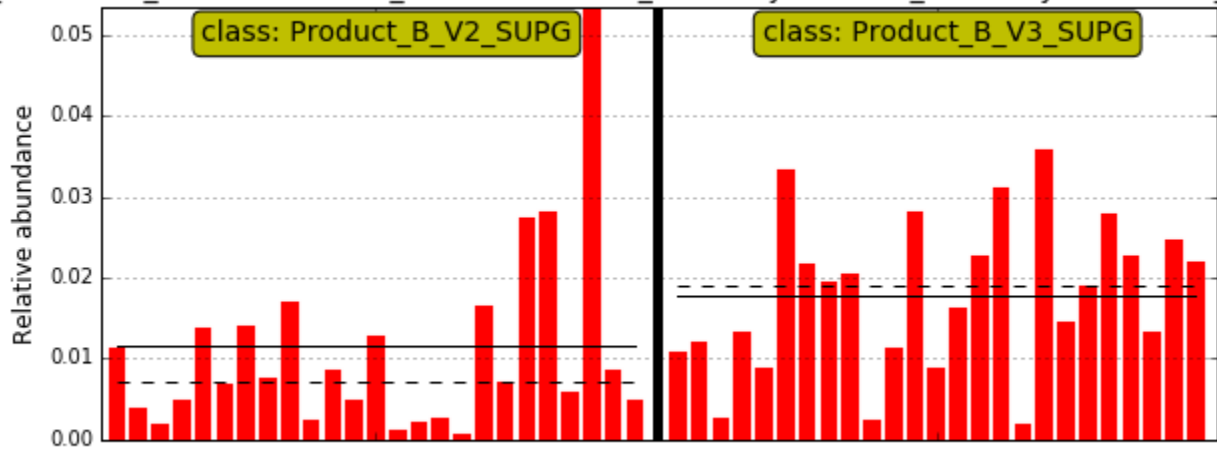
Green, more prevalent in V3

Red, more prevalent in V2

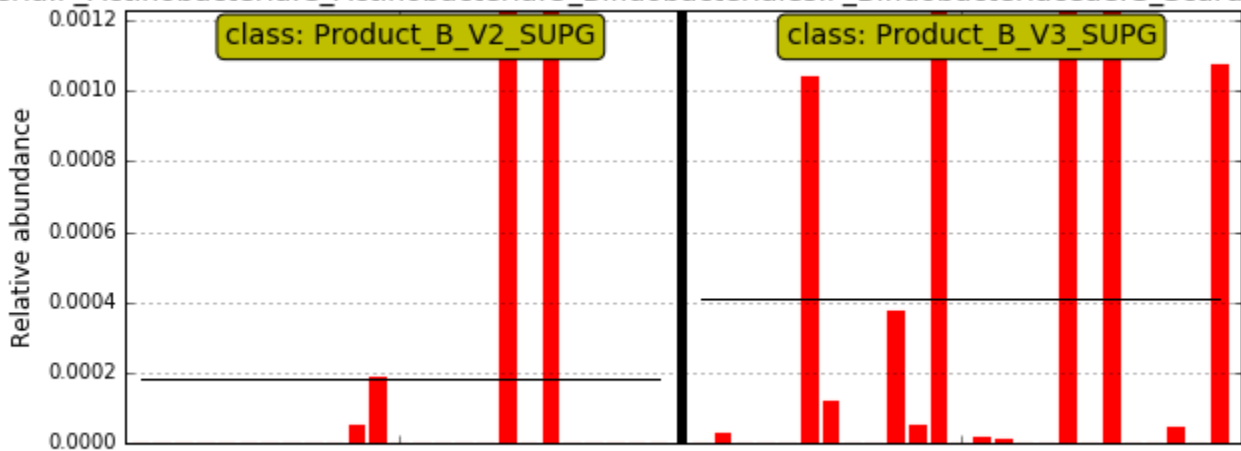
5) Lefse Many differences



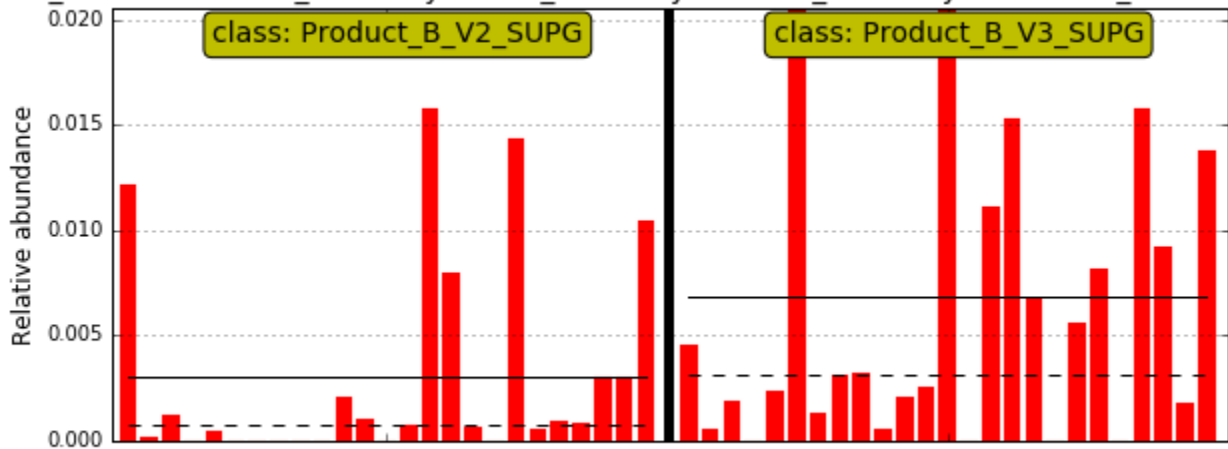
K\_Bacteria.P\_Actinobacteria.C\_Actinobacteria.O\_Actinomycetales.F\_Actinomycetaceae.G\_Schaalia



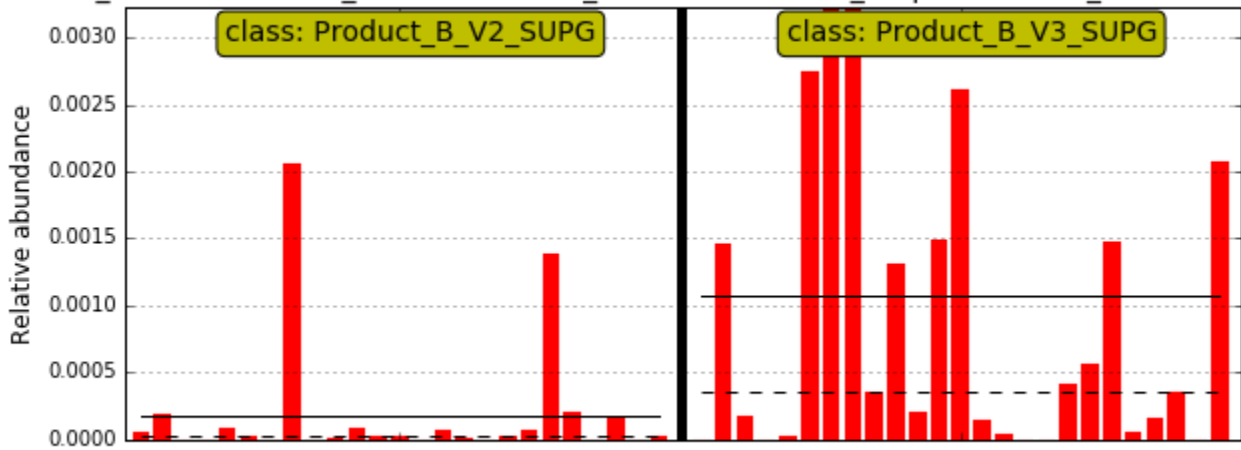
Bacteria.P\_Actinobacteria.C\_Actinobacteria.O\_Bifidobacteriales.F\_Bifidobacteriaceae.G\_Scardovia.S\_wig



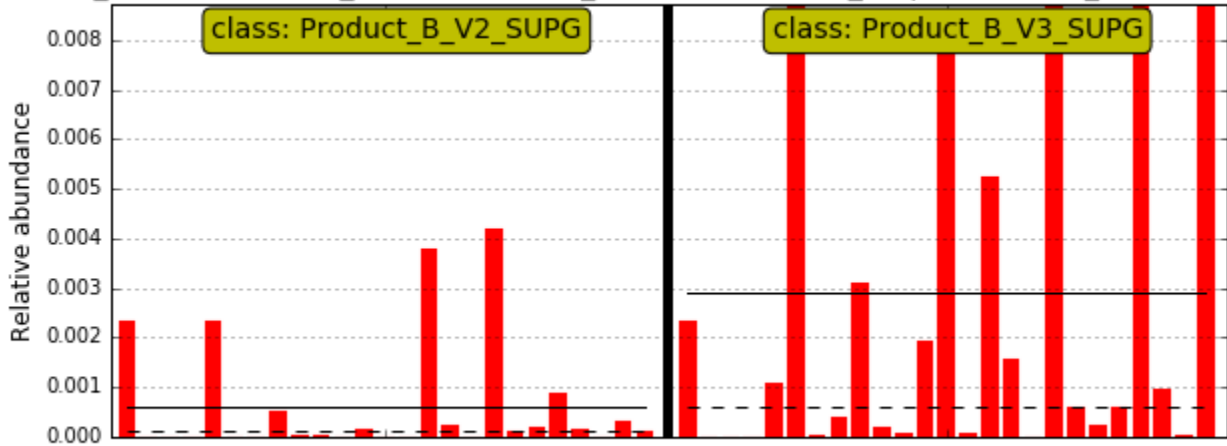
Bacteria.P\_Actinobacteria.C\_Actinomycetia.O\_Actinomycetales.F\_Actinomycetaceae.G\_Actinomyces.S\_d



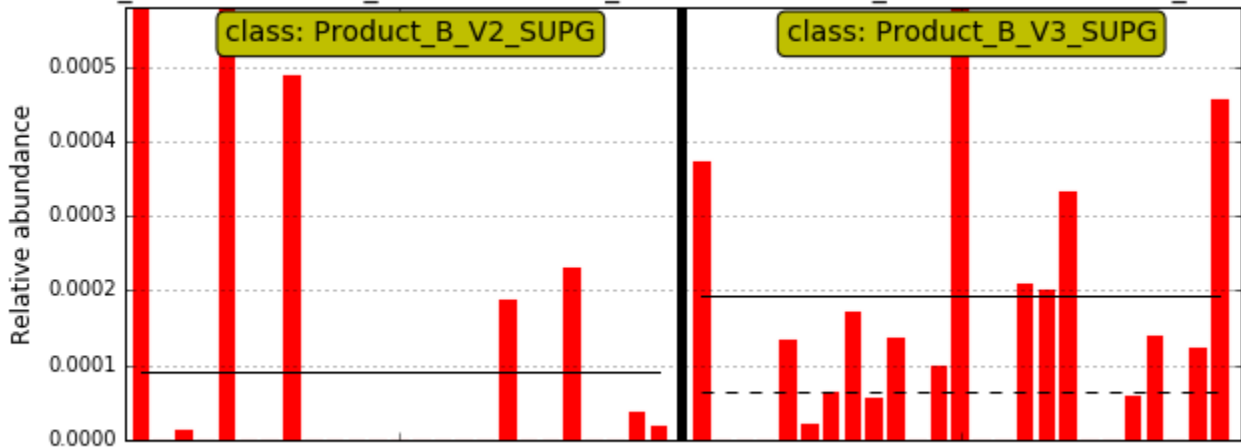
\_Bacteria.P\_Actinobacteria.C\_Coriobacteriia.O\_Coriobacteriales.F\_Atopobiaceae.G\_Lancefieldella.S\_par



∠\_Bacteria.P\_Actinobacteria.C\_Coriobacteriia.O\_Coriobacteriales.F\_Atopobiaceae.G\_Lancefieldella.S\_rin

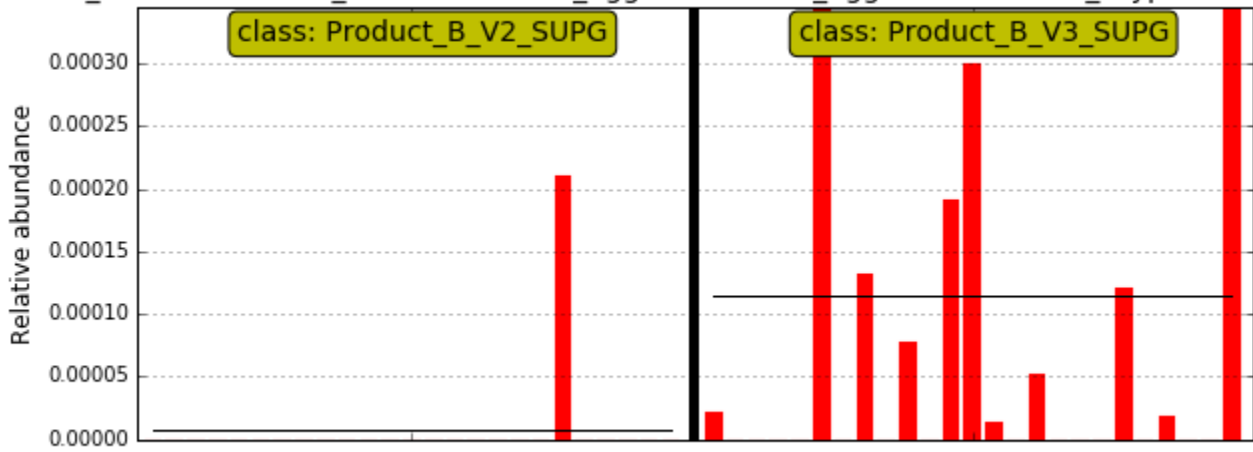


K\_Bacteria.P\_Actinobacteria.C\_Coriobacteriia.O\_Coriobacteriales.F\_Coriobacteriaceae.G\_Slackia.S\_exig

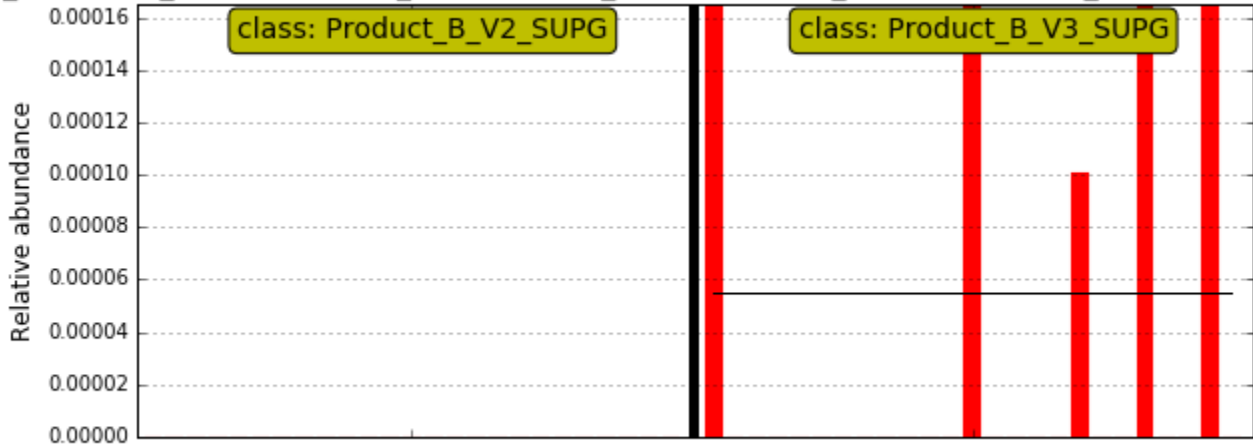




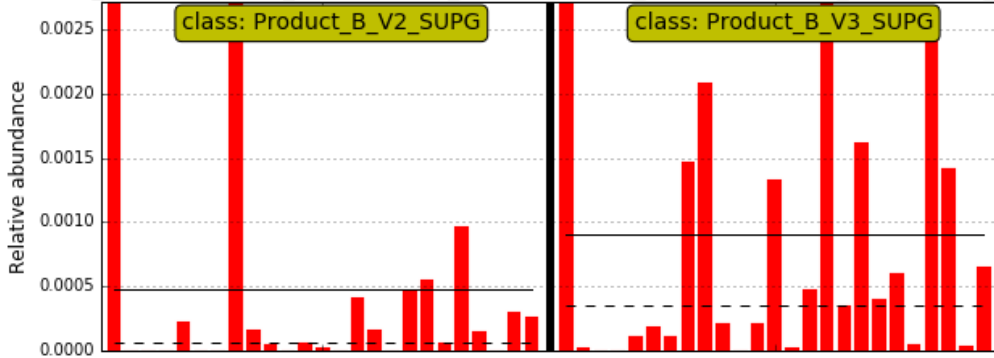
acteria.P\_Actinobacteria.C\_Coriobacteriia.O\_Eggerthellales.F\_Eggerthellaceae.G\_Cryptobacterium.S\_ci



K\_Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Prevotella.S\_baroniae

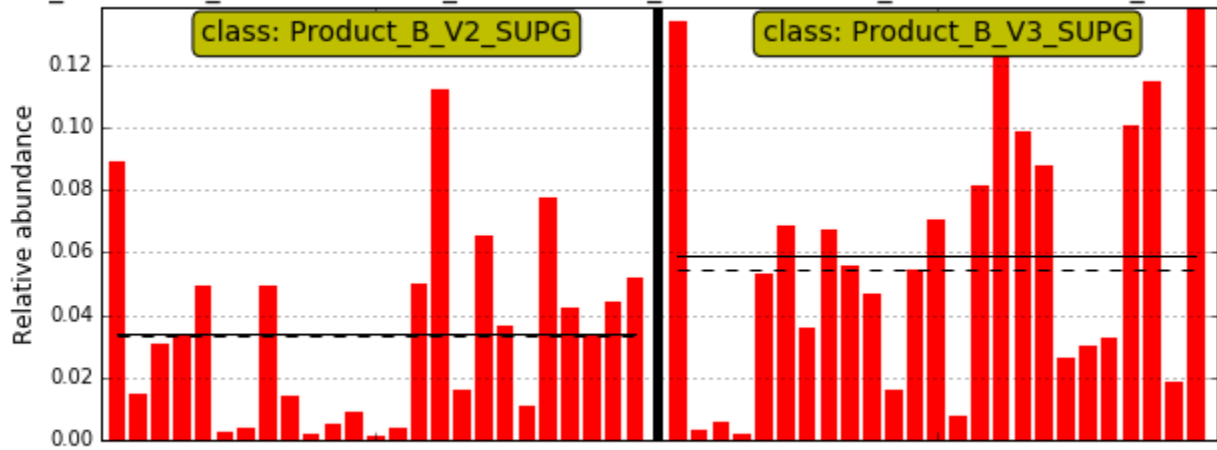


K\_Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Prevotella.S\_sp\_HMT\_3

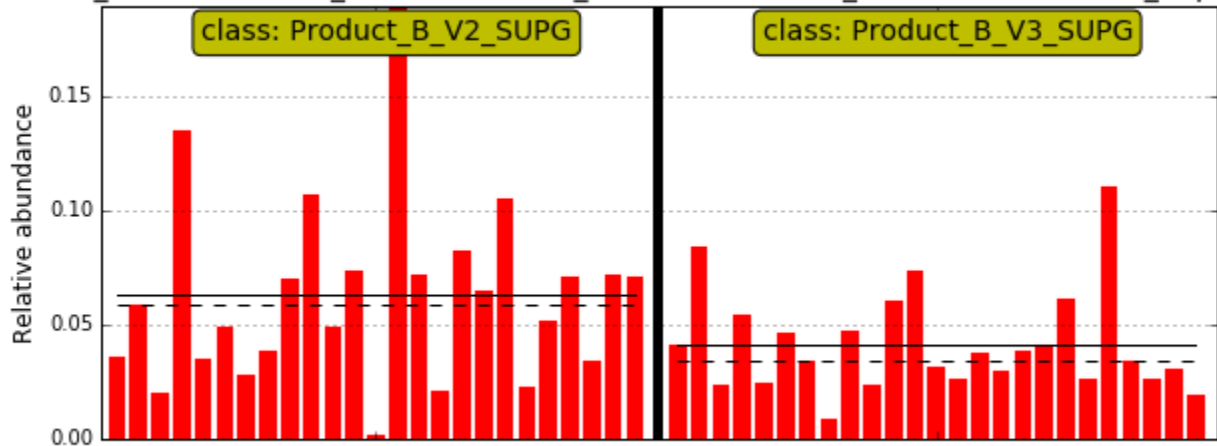


HMT300

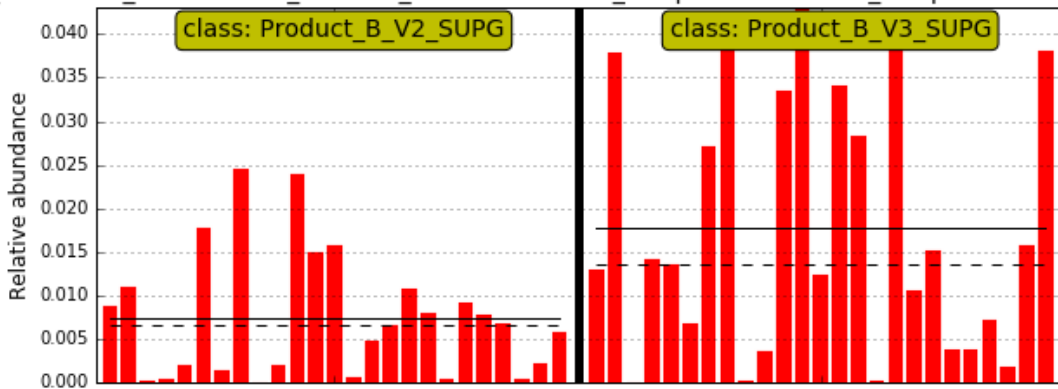
K\_Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Prevotella



K\_Bacteria.P\_Bacteroidetes.C\_Flavobacteriia.O\_Flavobacteriales.F\_Flavobacteriaceae.G\_Capnocytopha

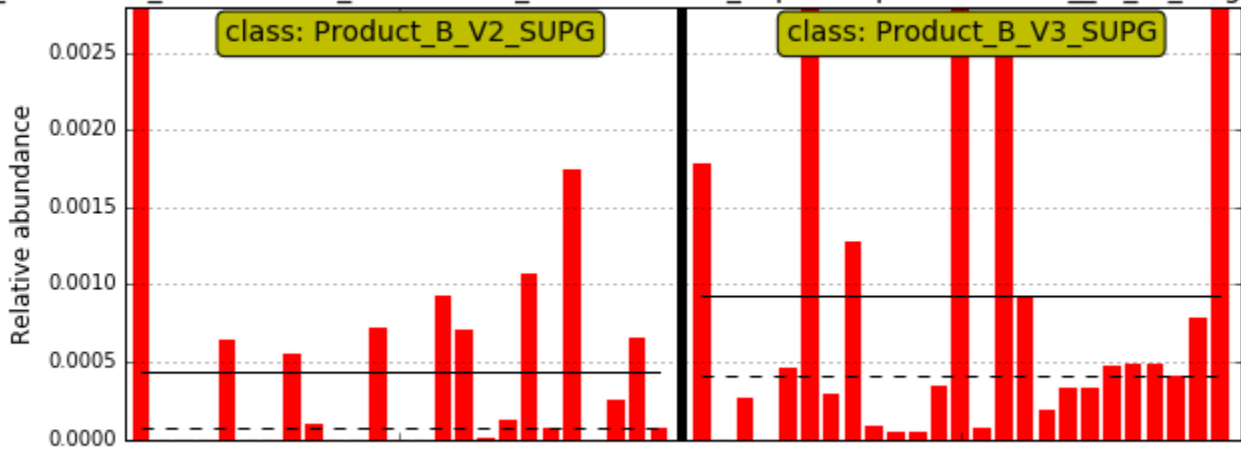


K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Streptococcaceae.G\_Streptococcus.S\_gordonii

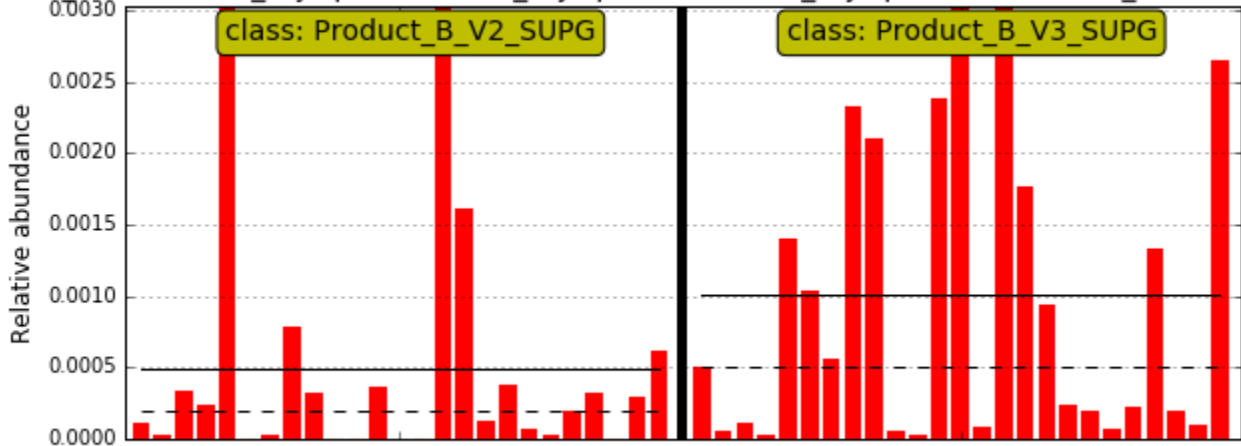


#####

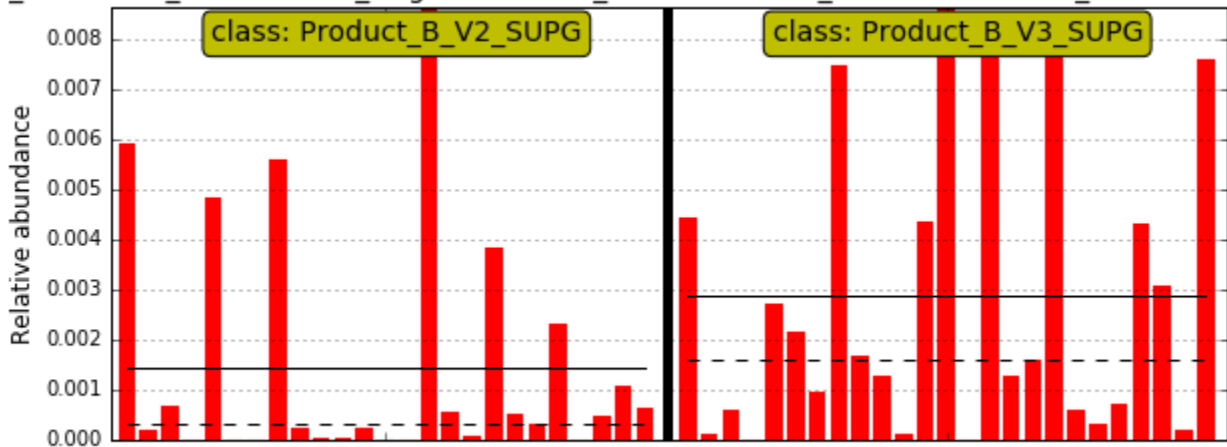
K\_Bacteria.P\_Firmicutes.C\_Clostridia.O\_Clostridiales.F\_Peptostreptococcaceae\_XI\_G\_Mogibacterium



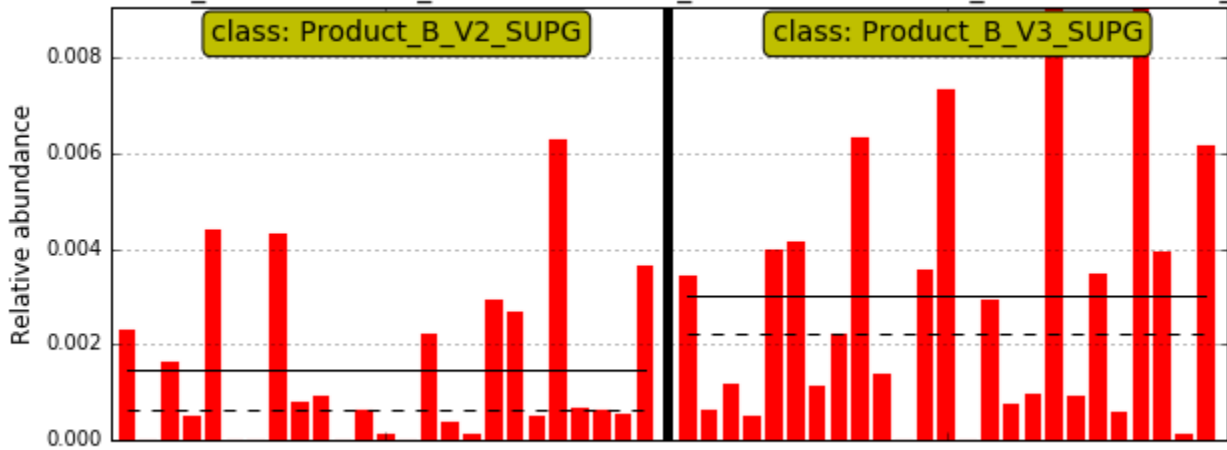
acteria.P\_Firmicutes.C\_Erysipelotrichia.O\_Erysipelotrichales.F\_Erysipelotrichaceae.G\_Solobacterium.S\_I



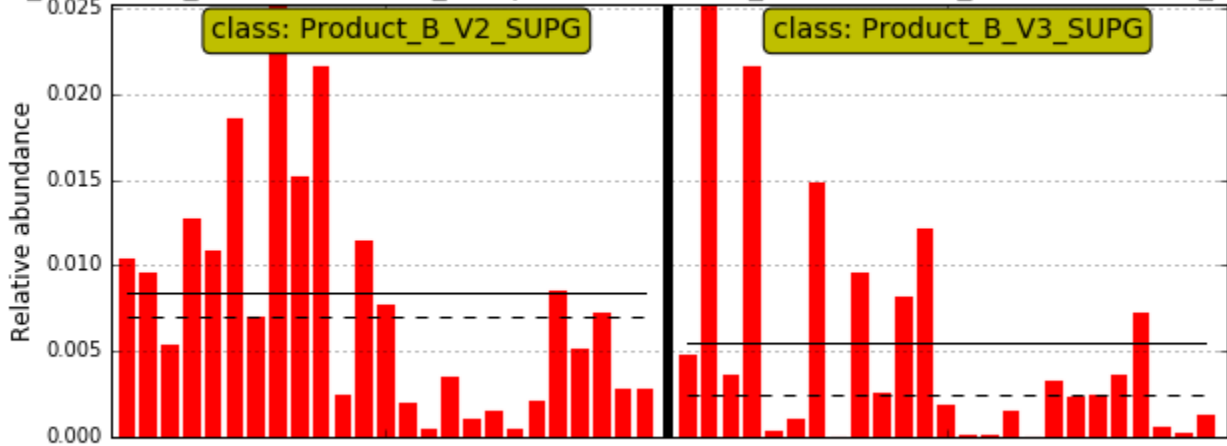
K\_Bacteria.P\_Firmicutes.C\_Negativicutes.O\_Veillonellales.F\_Veillonellaceae.G\_Dialister.S\_invisus



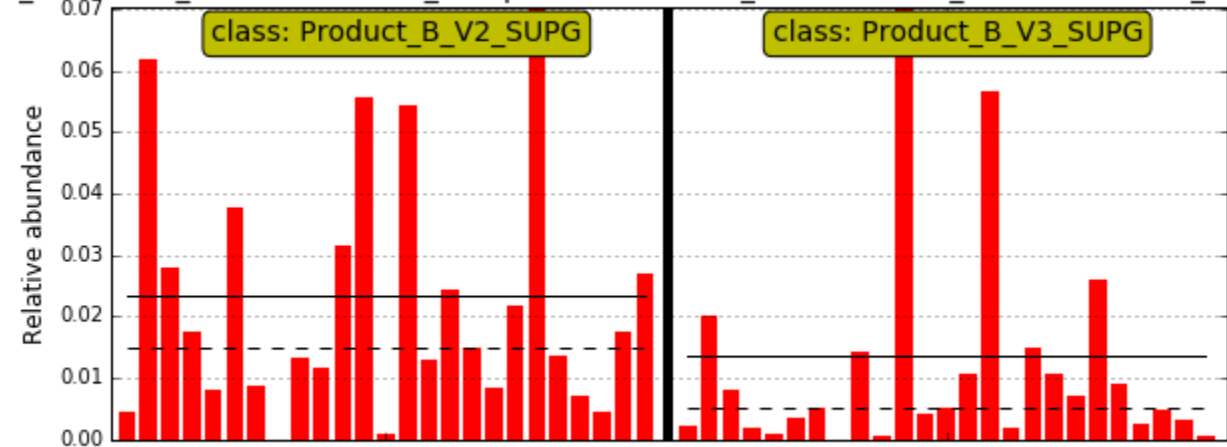
a.P\_Fusobacteria.C\_Fusobacteria.O\_Fusobacteriales.F\_Fusobacteriaceae.G\_Fusobacterium.S\_multispec



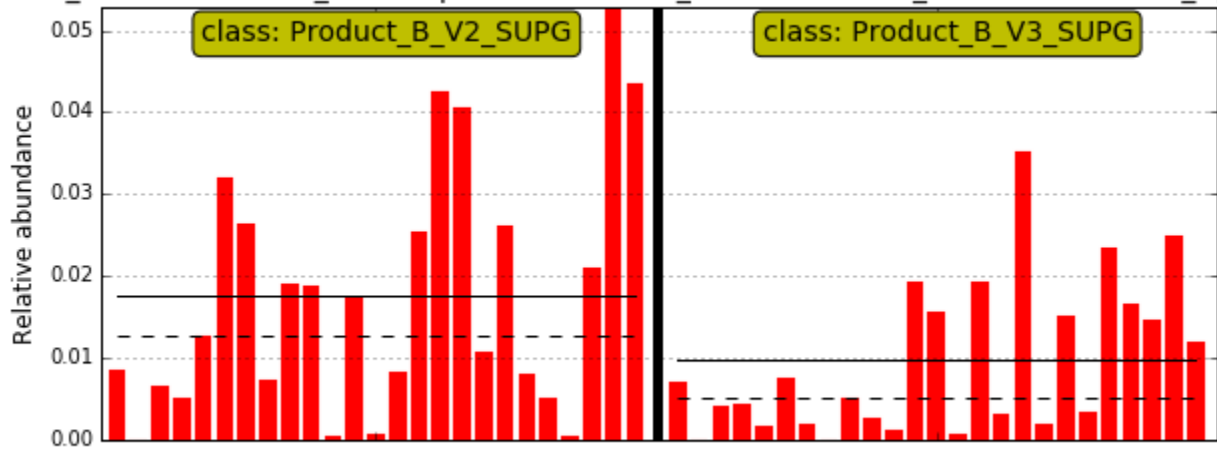
K\_Bacteria.P\_Proteobacteria.C\_Betaproteobacteria.O\_Neisseriales.F\_Neisseriaceae.G\_Kingella



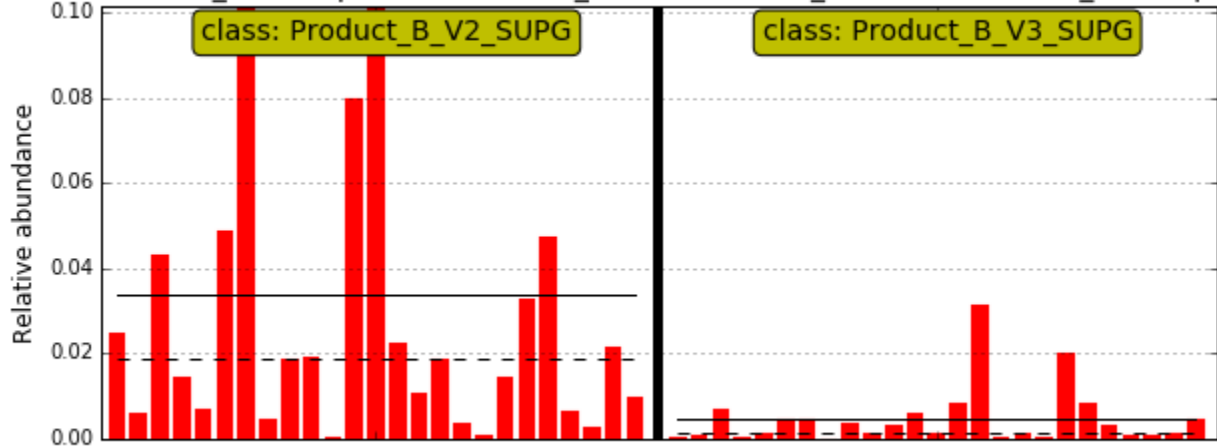
K\_Bacteria.P\_Proteobacteria.C\_Betaproteobacteria.O\_Neisseriales.F\_Neisseriaceae.G\_Neisseria



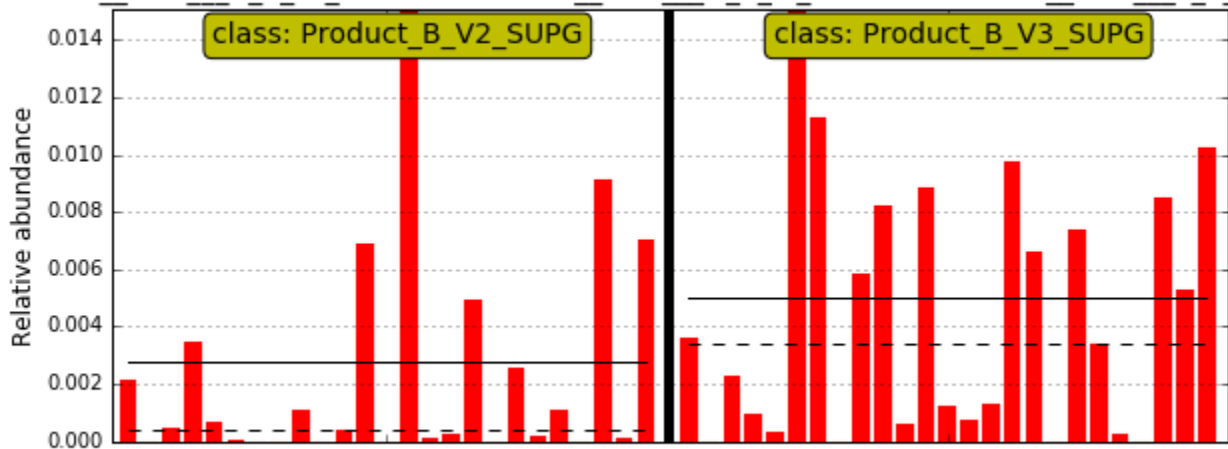
Bacteria.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Aggregatibacter



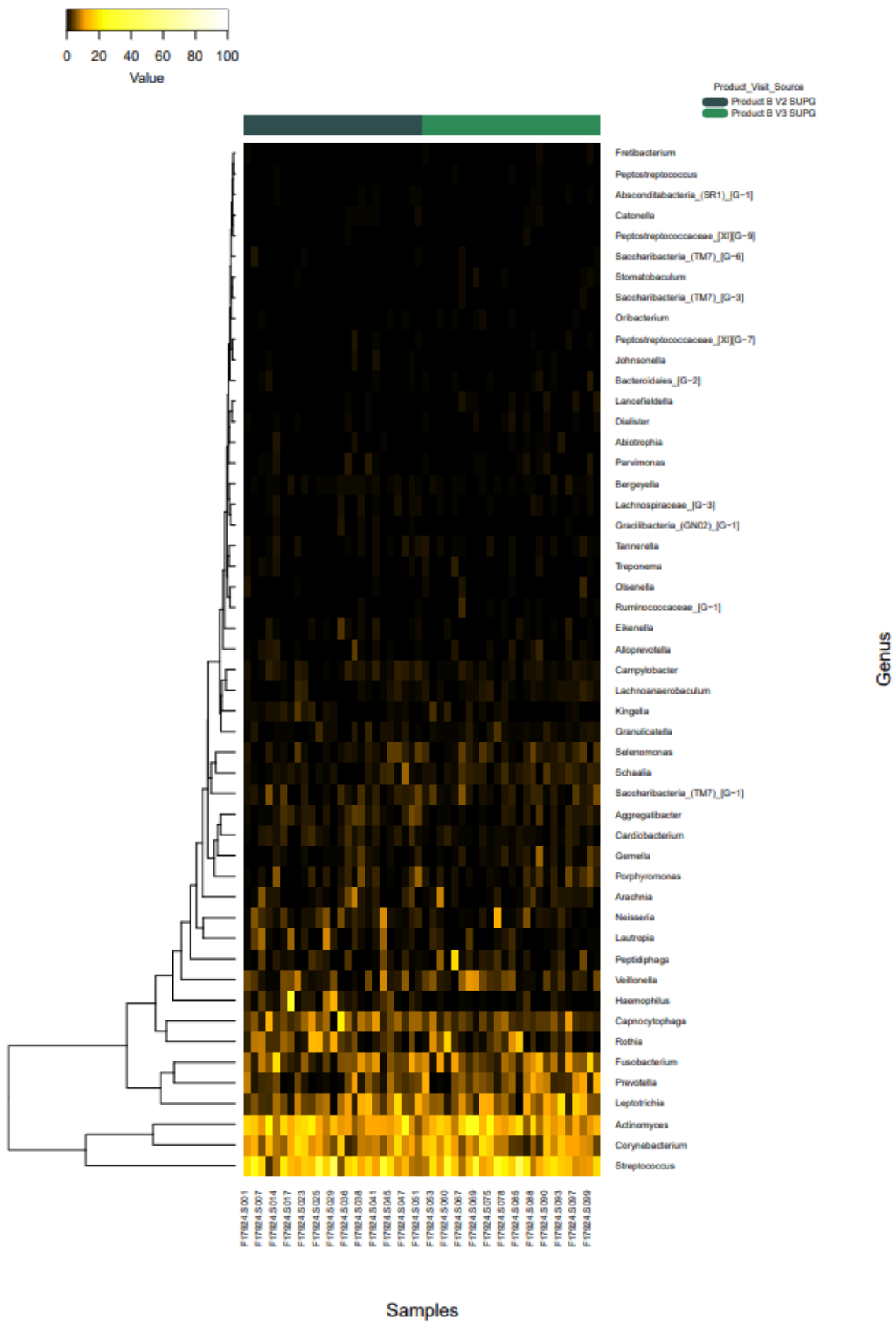
a.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Haemophilus.S\_p

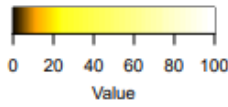


haribacteria\_TM7\_C\_1\_O\_Saccharibacteria\_TM7\_O\_1\_F\_Saccharibacteria\_TM7\_F\_1\_G\_Saccha

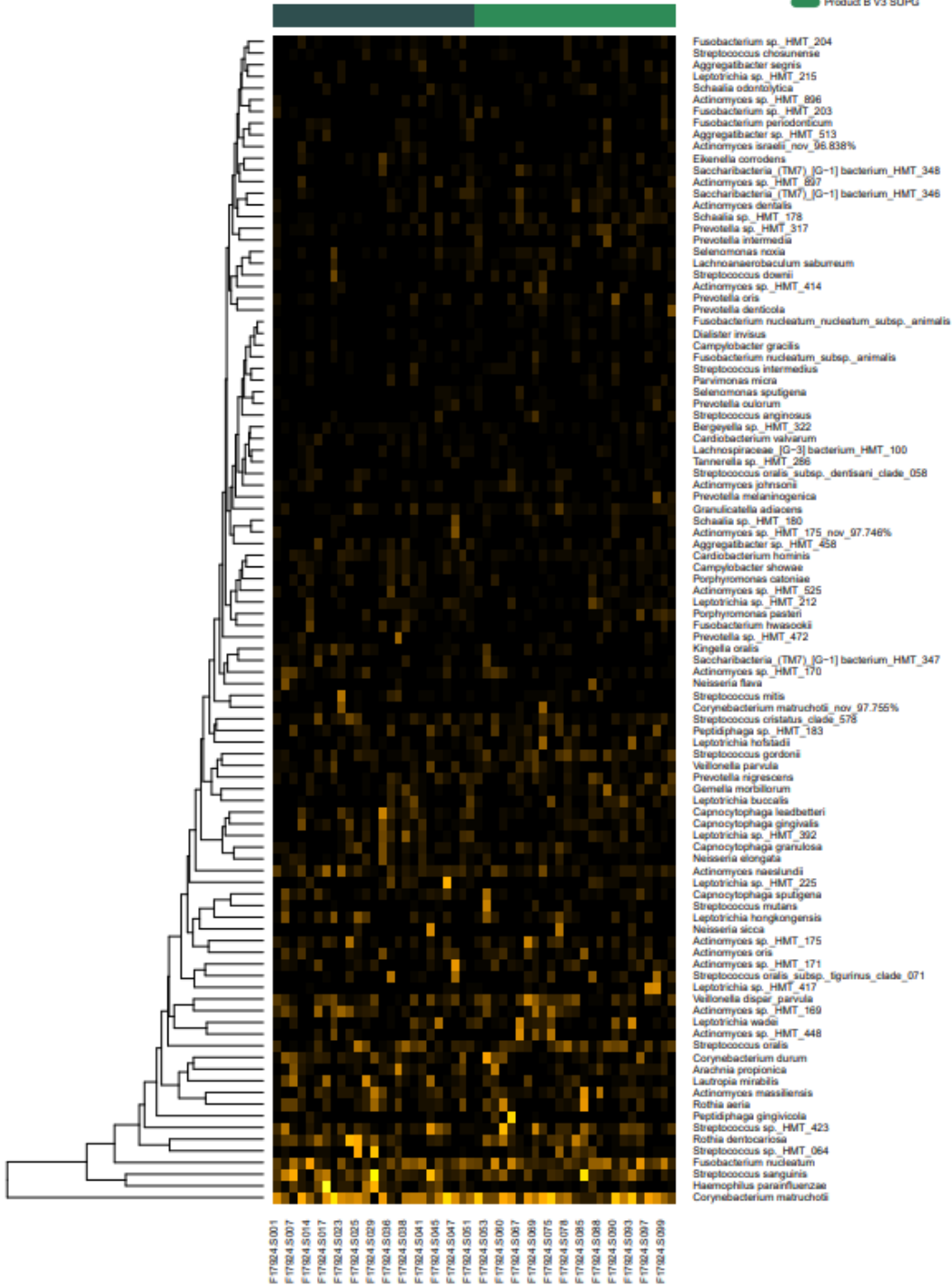


6) Heat map.





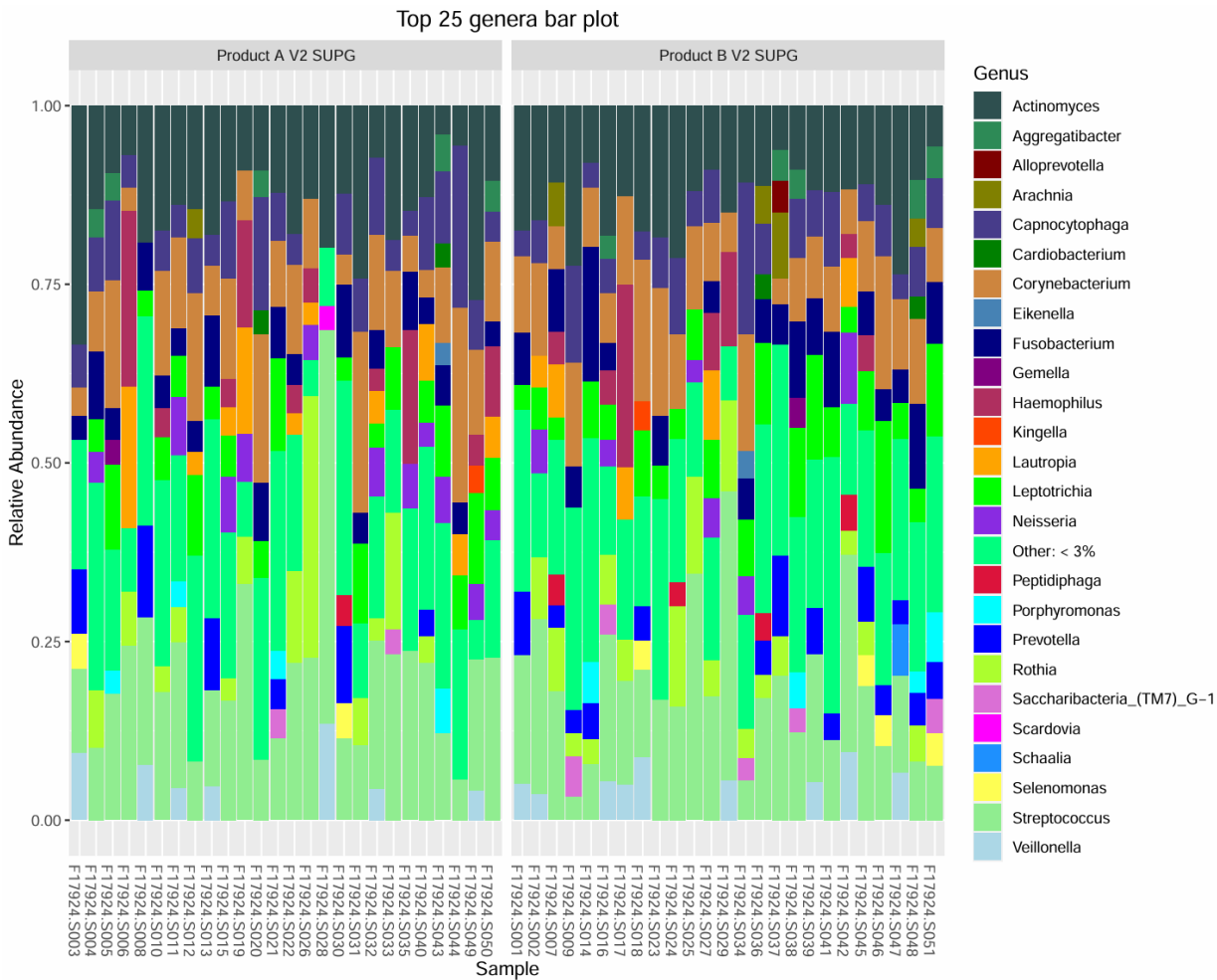
Product\_Visit\_Source  
 Product B V2 SUPG  
 Product B V3 SUPG



Samples

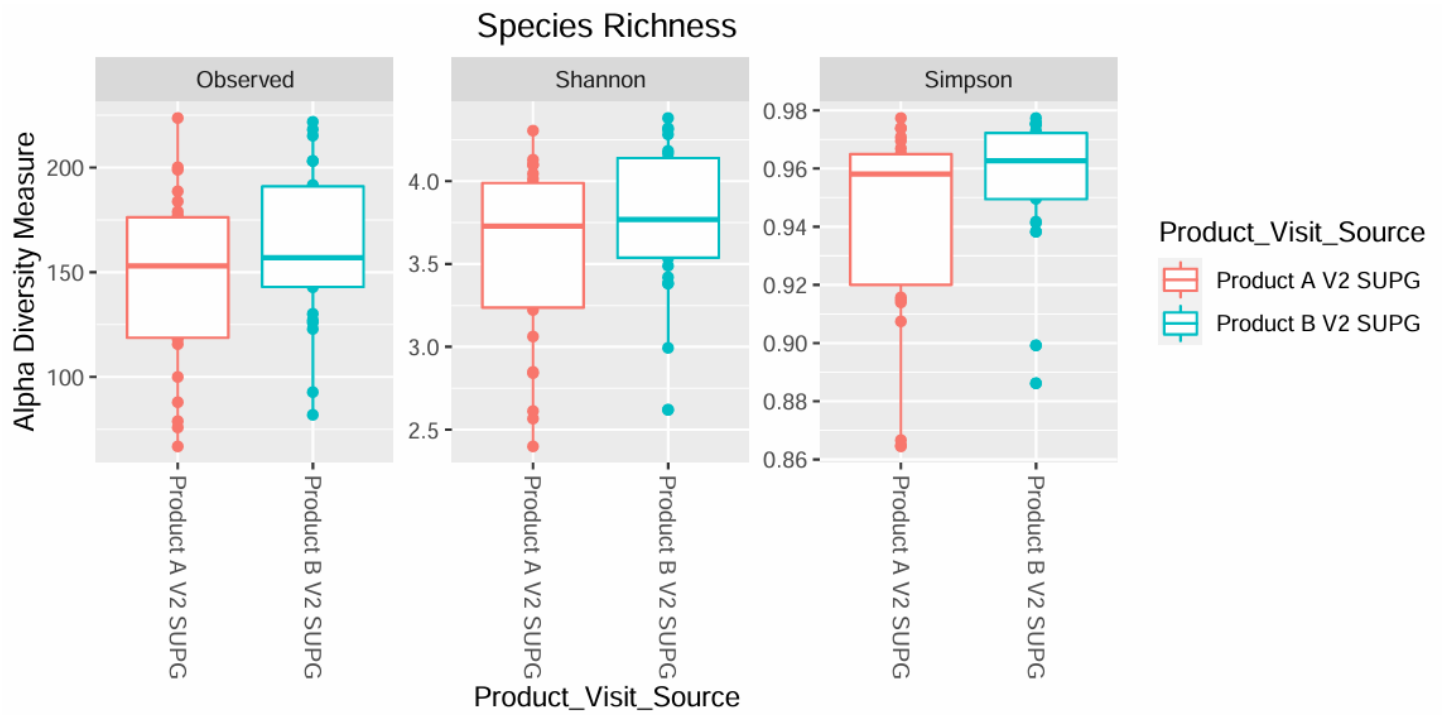
# Comparison 15. Product A V2 SUPG vs Product B V2 SUPG

## 1) Taxonomy bar graphs



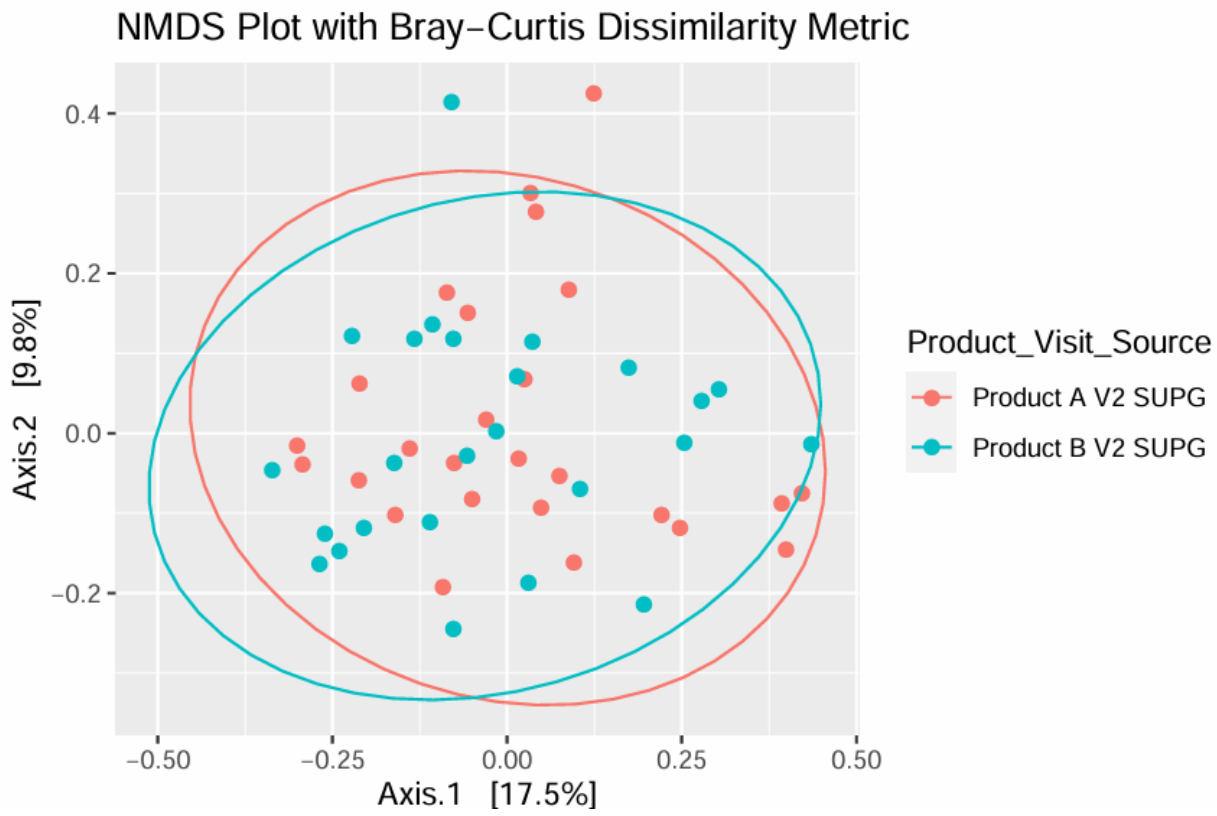


## 2) Alpha



Note: No significant differences

### 3) Beta diversity



Note: No significant differences

#### 4) Differential abundance

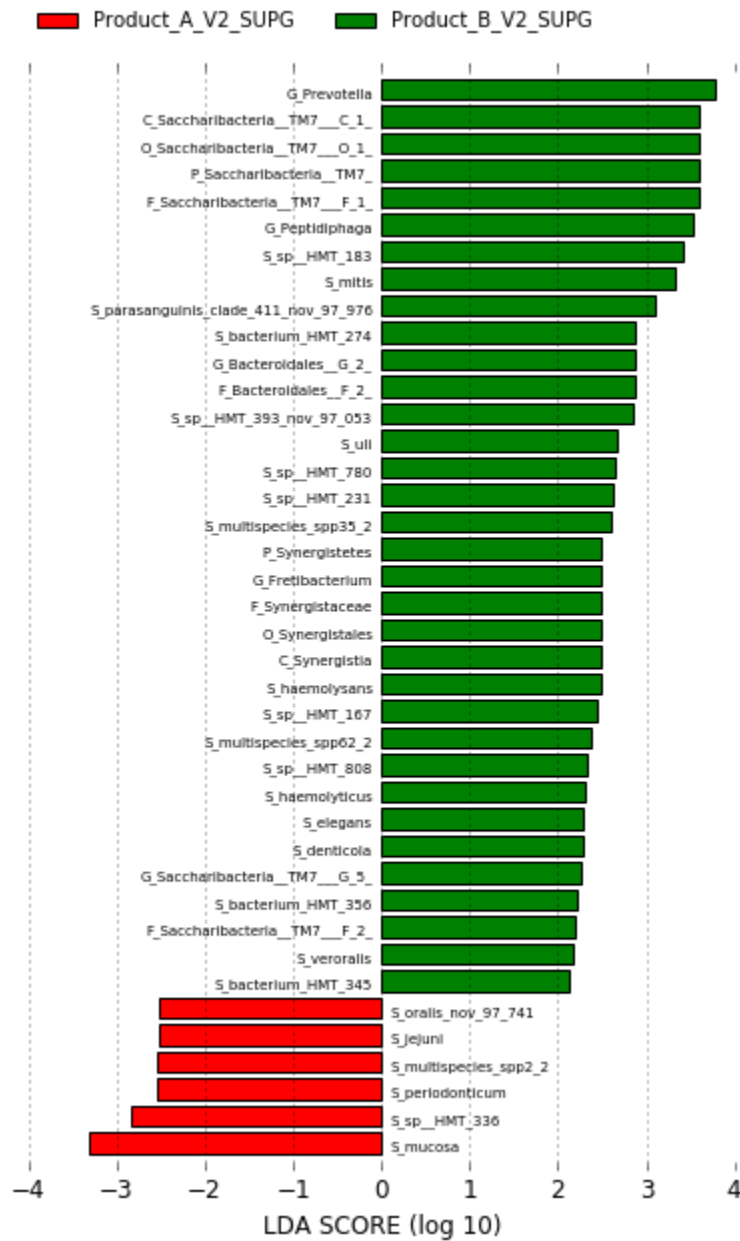
taxon	lfc_(Interc	lfc_Product	se_(Interc	se_Product	W_(Interc	W_Product	p_(Interc	p_Product	q_(Interc	q_Product	diff_(Interc	diff_Product
Kingella oralis_nov_97.741% (SPN664)	0.87804	-1.76861	0.444691	0.635145	1.974497	-2.78457	0.048325	0.00536	1	1	FALSE	FALSE
Bacteroidales_[G-2] bacterium_HMT_274 (SP21)	-0.84476	1.745912	0.53439	0.763261	-1.5808	2.287437	0.113924	0.02217	1	1	FALSE	FALSE
Neisseria bacilliformis (SP447)	0.775156	-1.55872	0.482523	0.68918	1.606466	-2.26171	0.108172	0.023716	1	1	FALSE	FALSE
Selenomonas noxia_nov_97.030% (SPN548)	0.61946	-1.2411	0.413822	0.591055	1.496925	-2.09981	0.134413	0.035746	1	1	FALSE	FALSE
Neisseria mucosa (SP300)	0.908978	-1.83172	0.633832	0.905294	1.434099	-2.02334	0.151544	0.043038	1	1	FALSE	FALSE
Capnocytophaga sp._HMT_336 (SP51)	0.854898	-1.7214	0.601827	0.859581	1.420503	-2.0026	0.155461	0.045221	1	1	FALSE	FALSE
Treponema sp._HMT_231 (SP87)	-0.70998	1.470959	0.514966	0.735518	-1.3787	1.999894	0.167988	0.045512	1	1	FALSE	FALSE
Lachnoanaerobaculum orale (SP74)	0.533618	-1.06599	0.380785	0.54387	1.401364	-1.96	0.161105	0.049996	1	1	FALSE	FALSE
Actinomyces sp._HMT_175_nov_97.951% (SPN40)	0.737834	-1.48259	0.531203	0.75871	1.388987	-1.95409	0.164837	0.050691	1	1	FALSE	FALSE
Selenomonas sp._HMT_892_nov_97.041% (SPN67)	0.498679	-0.99471	0.358704	0.512332	1.390225	-1.94153	0.164461	0.052193	1	1	FALSE	FALSE
Peptidiphaga sp._HMT_183 (SP149)	-0.81756	1.690426	0.639447	0.913313	-1.27855	1.850873	0.201056	0.064188	1	1	FALSE	FALSE
Actinomyces sp._HMT_169 (SP239)	0.52958	-1.05775	0.408287	0.583151	1.297077	-1.81385	0.194605	0.069701	1	1	FALSE	FALSE
Aggregatibacter sp._HMT_512 (SP314)	0.522574	-1.04345	0.405412	0.579044	1.288994	-1.80203	0.1974	0.071541	1	1	FALSE	FALSE
Tannerella sp._HMT_808 (SP63)	-0.51283	1.06877	0.419111	0.59861	-1.22361	1.785418	0.221098	0.074194	1	1	FALSE	FALSE
Gemella haemolysans (SP8)	-0.57831	1.20234	0.483557	0.690658	-1.19594	1.740862	0.23172	0.081708	1	1	FALSE	FALSE

Note: Red, more prevalent in A; Green, more prevalent in B

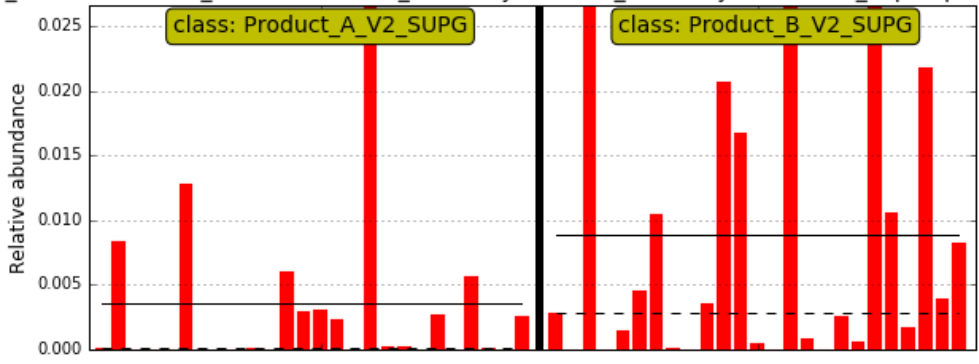
No statistical significance, lost after multiple comparisons.

5) Lefse

Significantly Represented Taxa

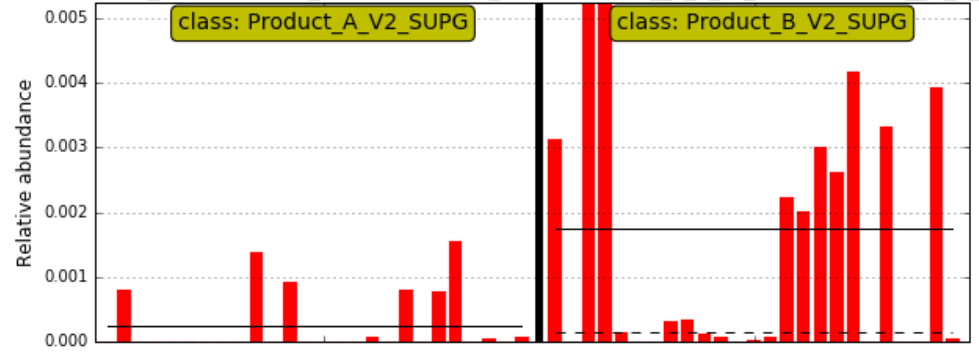


eria.P\_Actinobacteria.C\_Actinobacteria.O\_Actinomycetales.F\_Actinomycetaceae.G\_Peptidiphaga.S\_sp\_



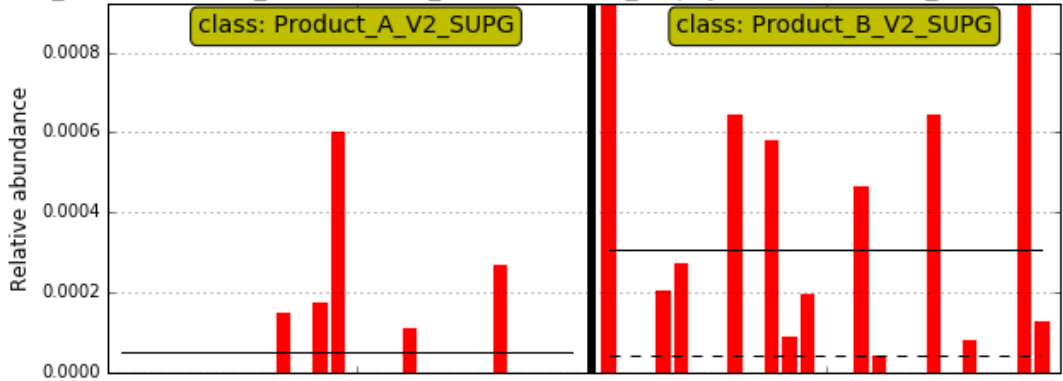
HMT183

2\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Bacteroidales\_F\_2\_G\_Bacteroidales\_G\_2\_S\_bacter



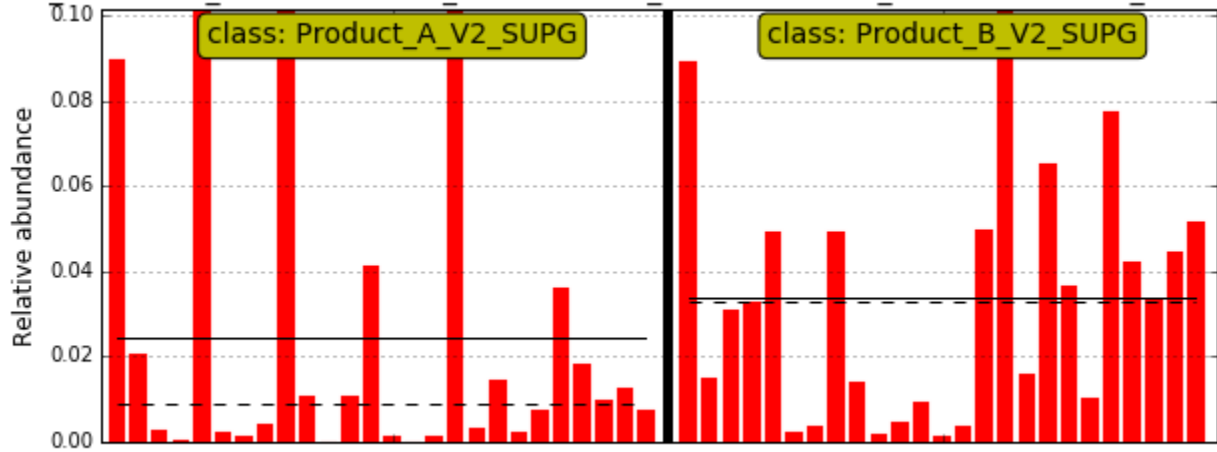
HMT274

acteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Porphyrimonadaceae.G\_Tannerella.S\_sp\_HM

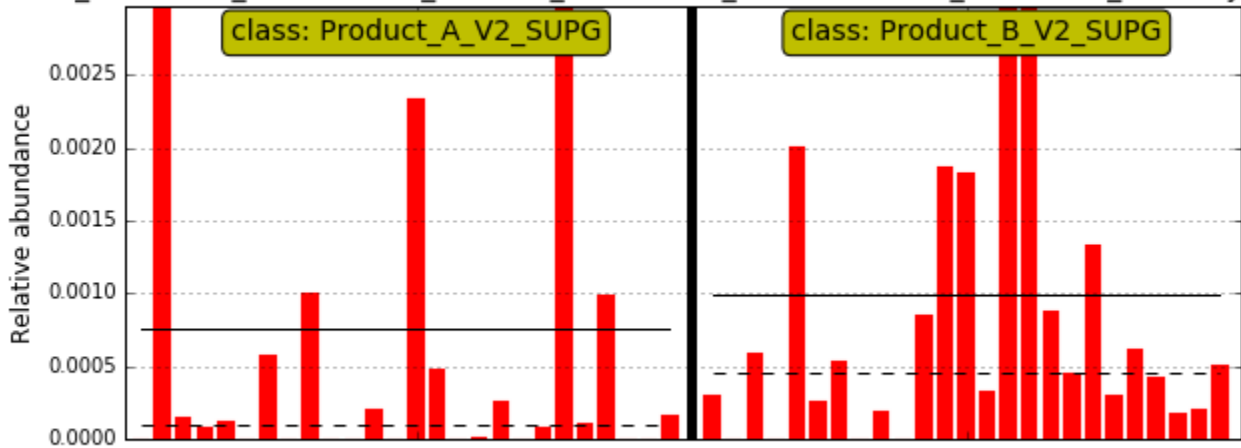


HMT808

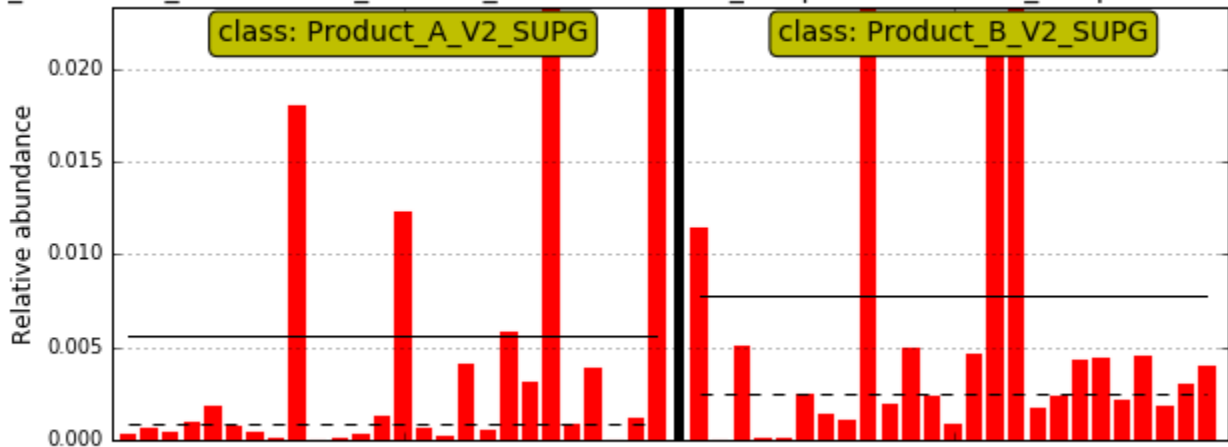
K\_Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Prevotella



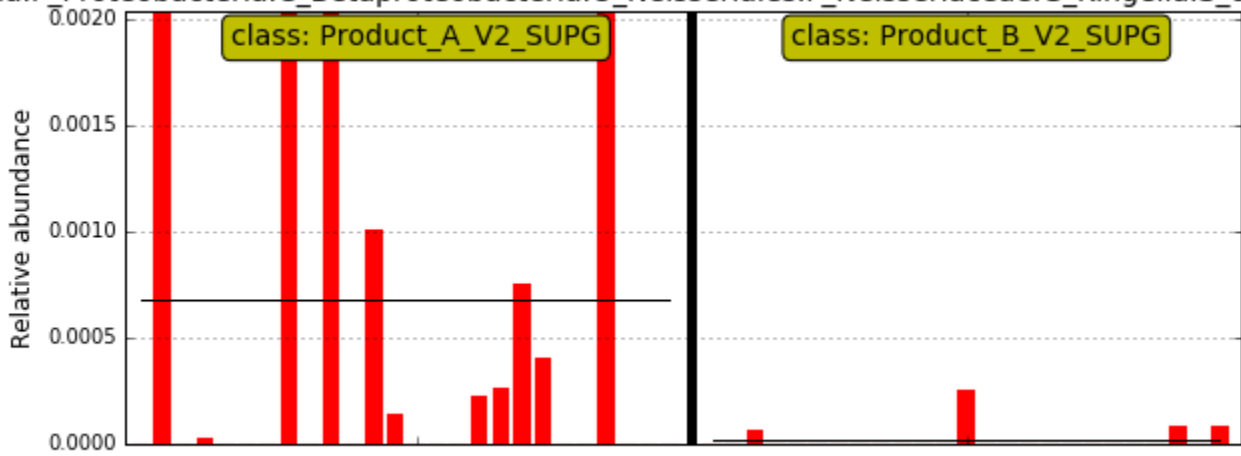
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Bacillales.F\_Gemellaceae.G\_Gemella.S\_haemolysans



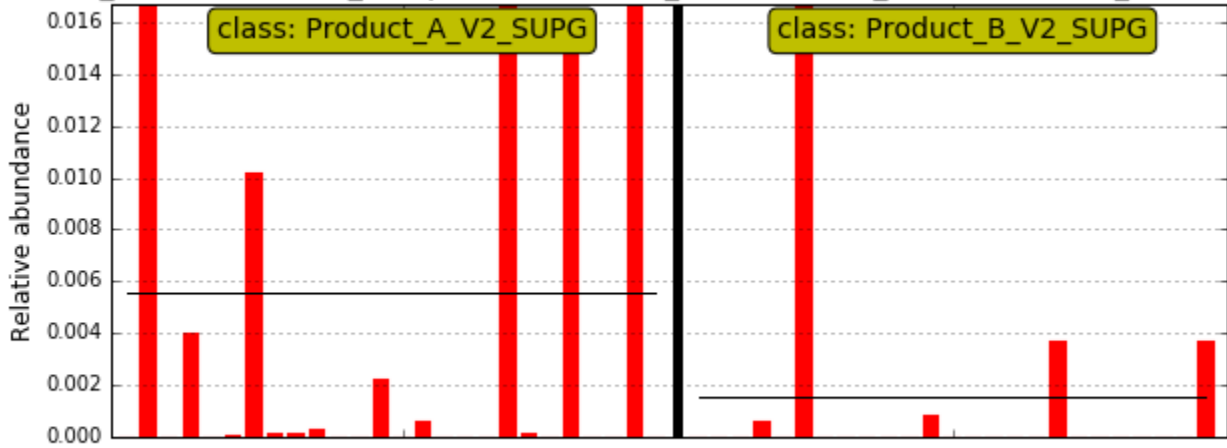
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Streptococcaceae.G\_Streptococcus.S\_mitis



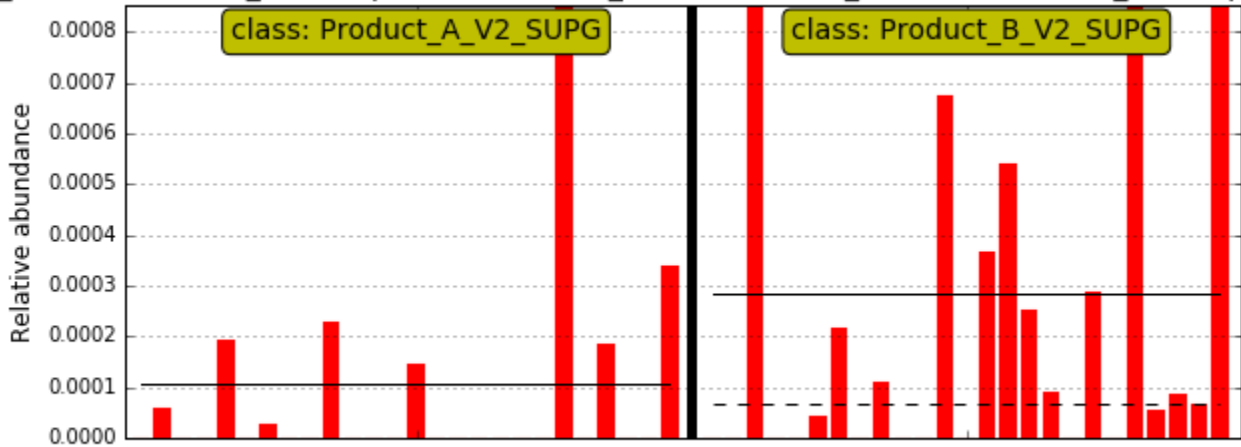
cteria.P\_Proteobacteria.C\_Betaproteobacteria.O\_Neisseriales.F\_Neisseriaceae.G\_Kingella.S\_oralis\_nov\_

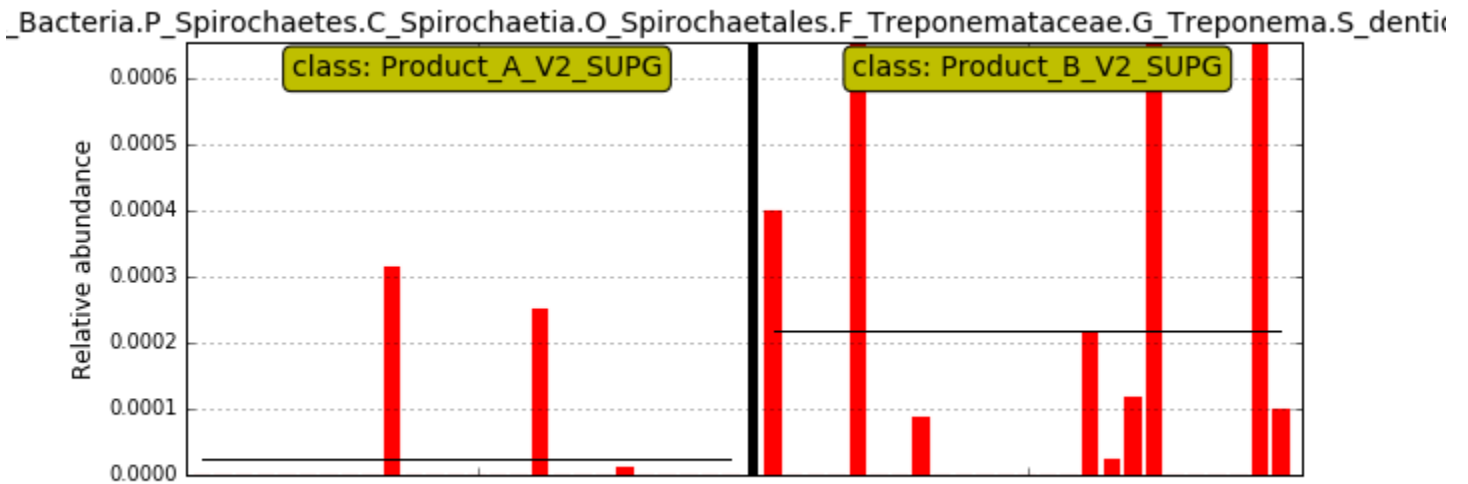
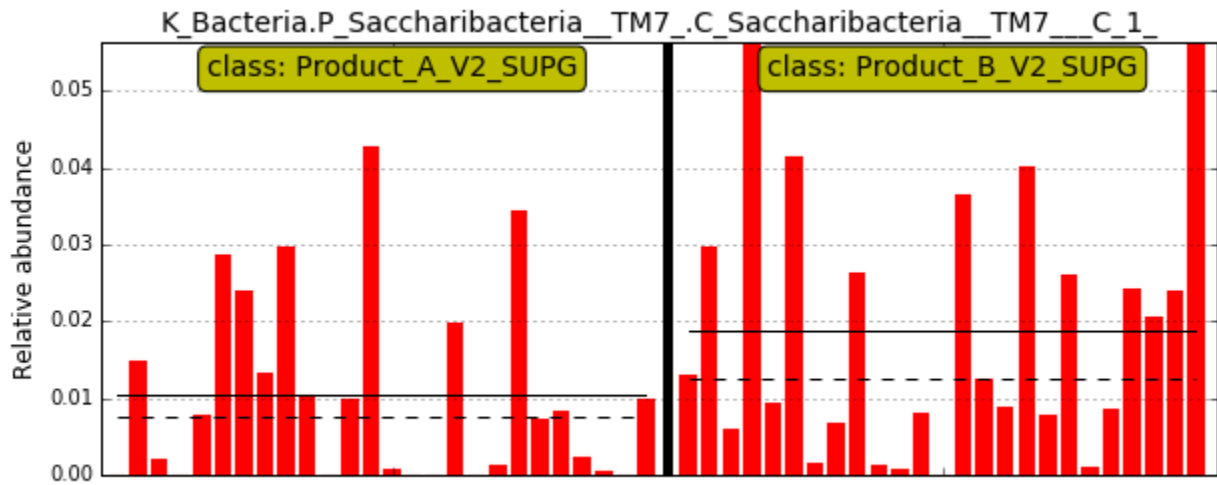


K\_Bacteria.P\_Proteobacteria.C\_Betaproteobacteria.O\_Neisseriales.F\_Neisseriaceae.G\_Neisseria.S\_mucc



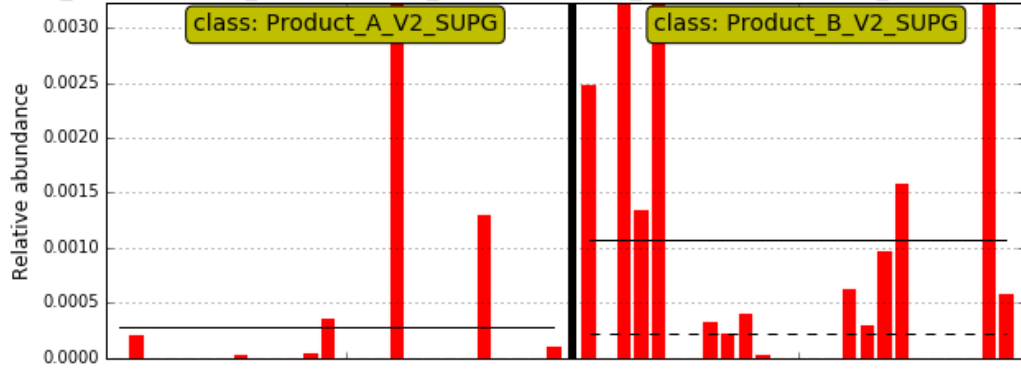
ia.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Haemophilus.S\_ha





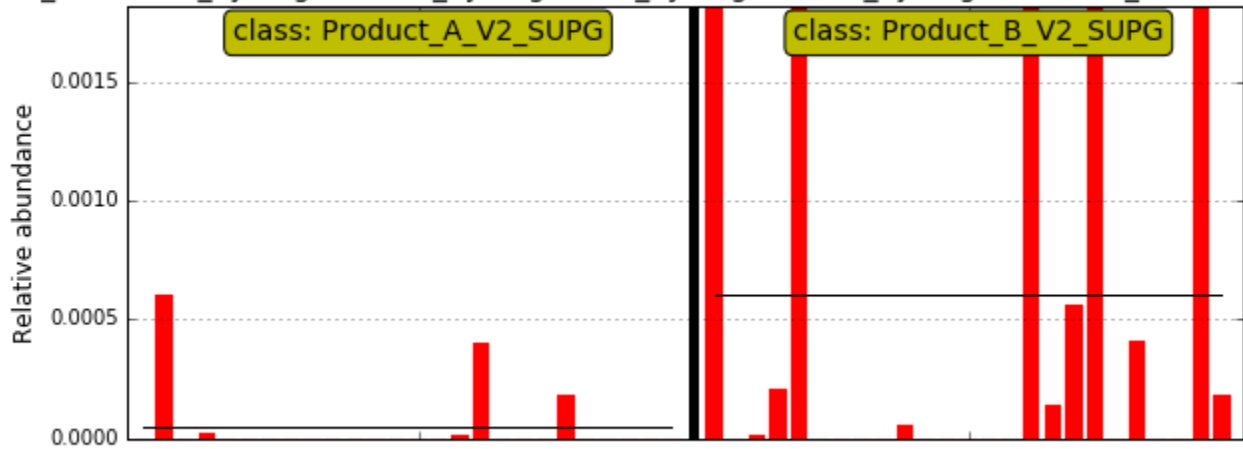


acteria.P\_Spirochaetes.C\_Spirochaetia.O\_Spirochaetales.F\_Treponemataceae.G\_Treponema.S\_sp\_HM

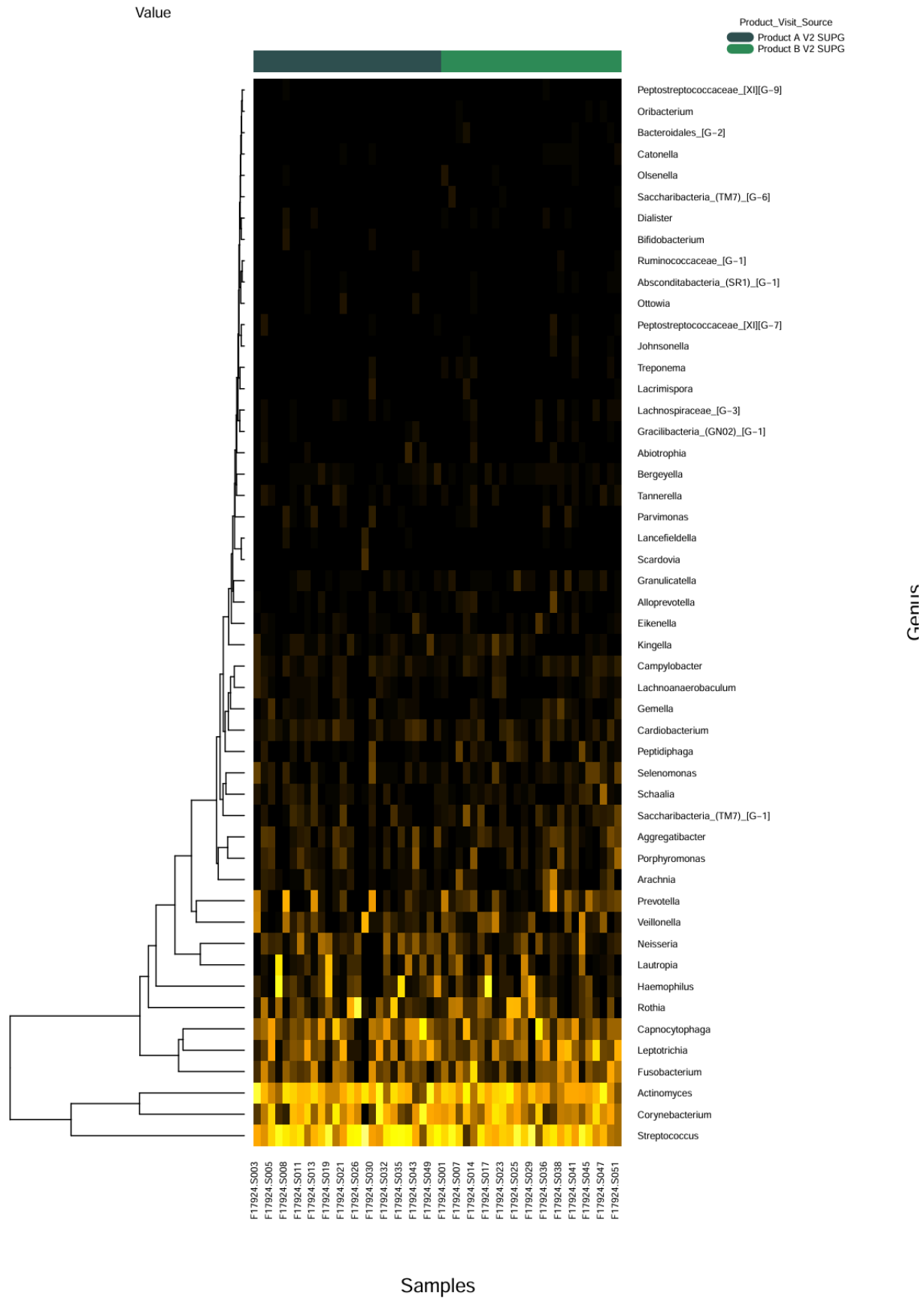


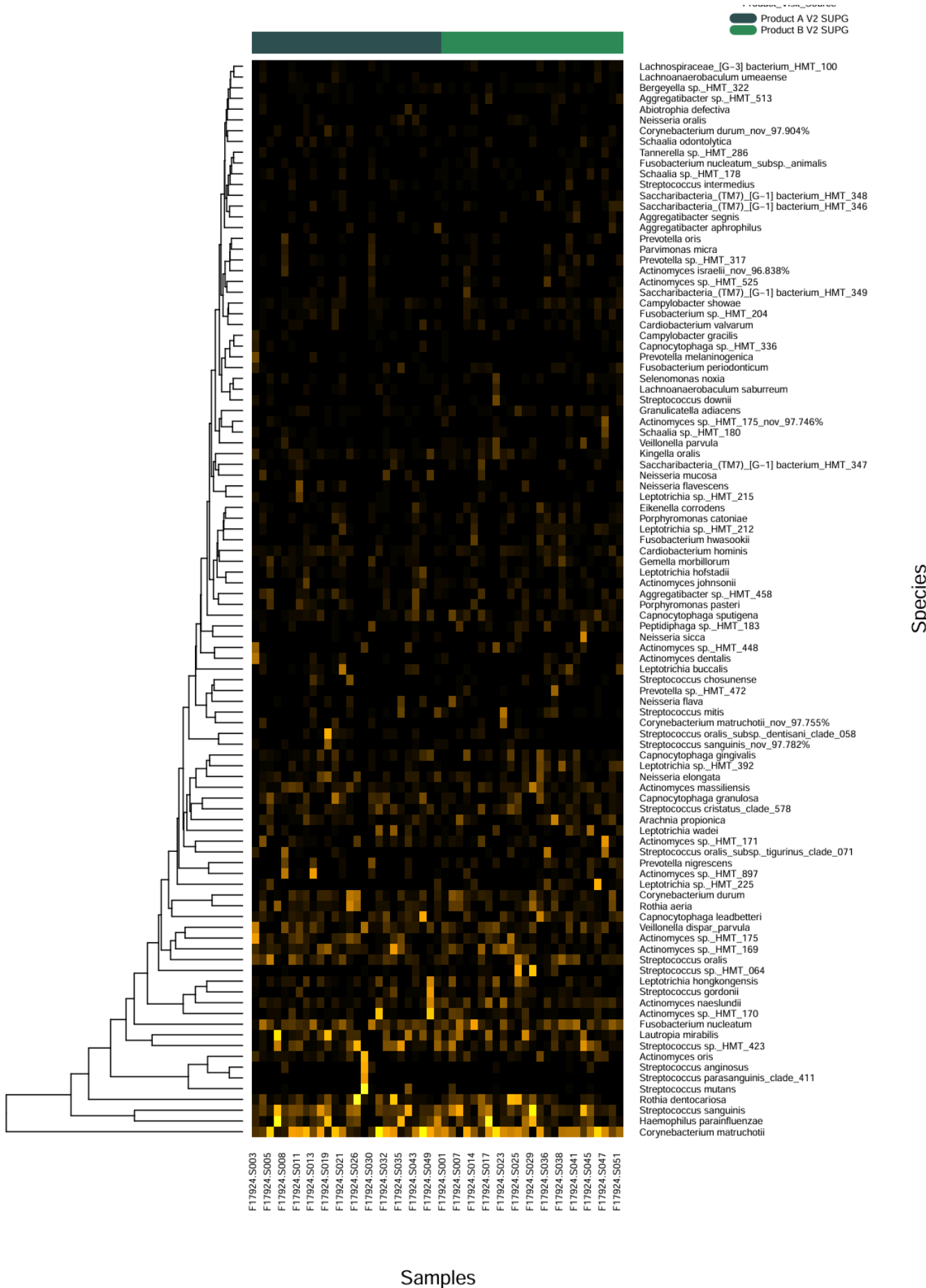
HMT231

K\_Bacteria.P\_Synergistetes.C\_Synergistia.O\_Synergistales.F\_Synergistaceae.G\_Fretibacterium



## 6) Heat map.

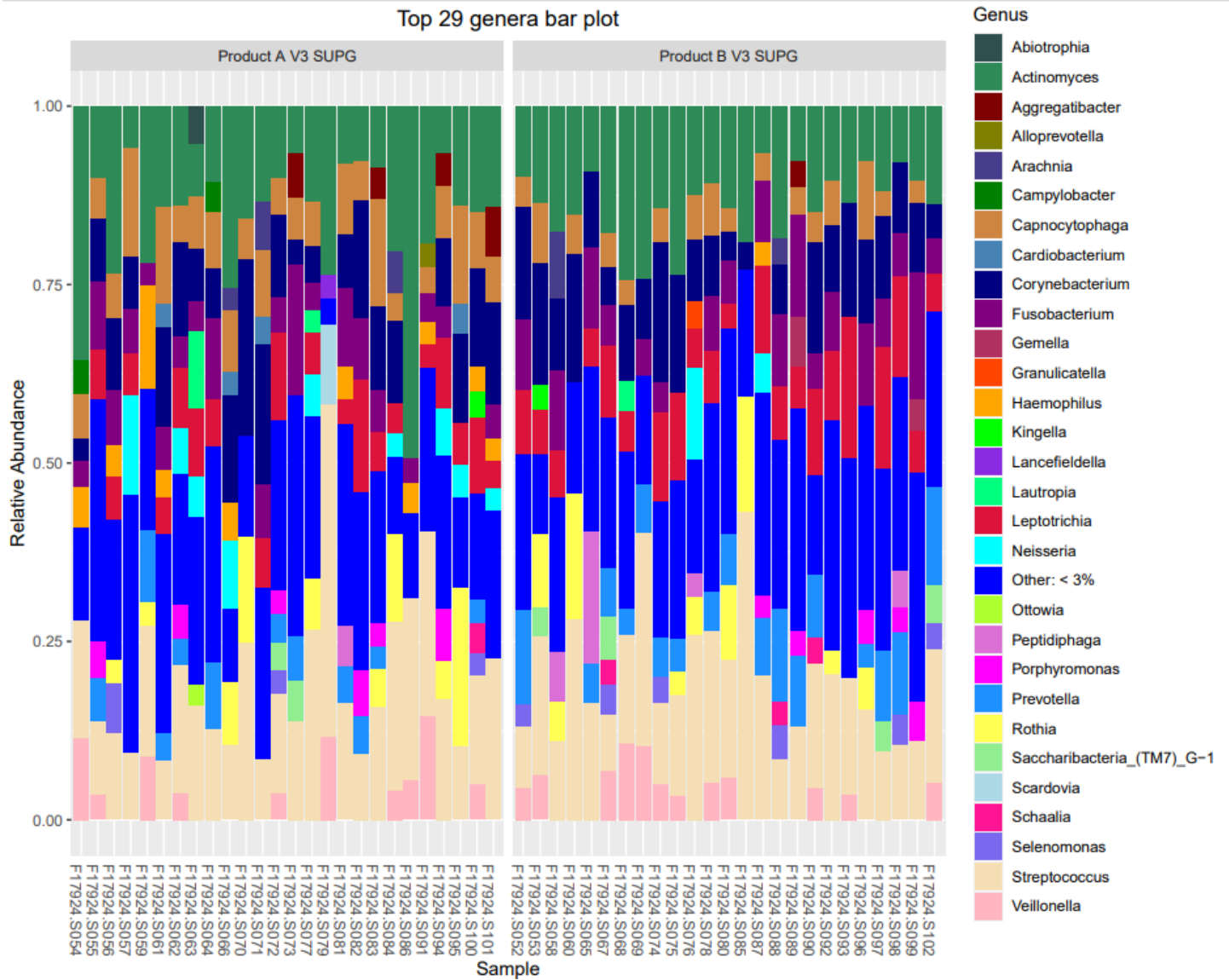




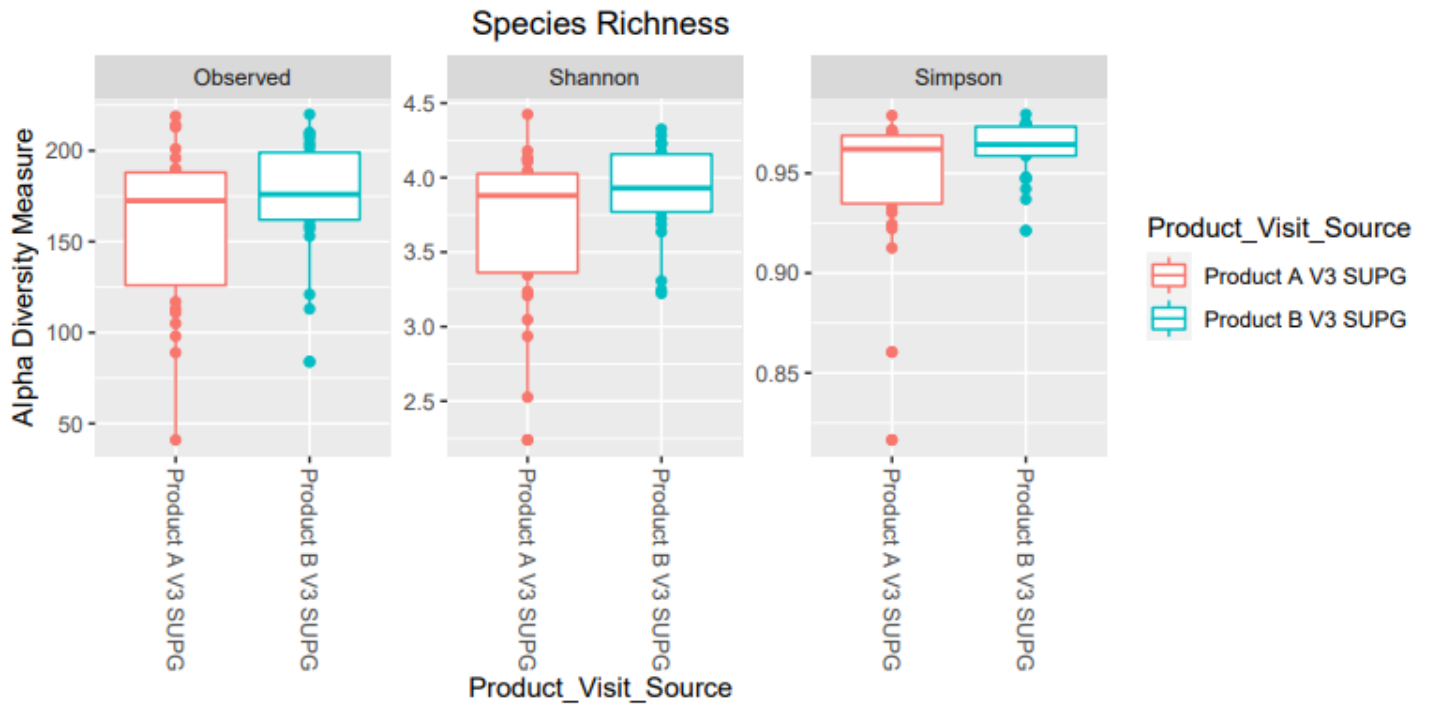


# Comparison 16. Product A V3 SUPG vs Product B V3 SUPG

## 1) Taxonomy bar graphs

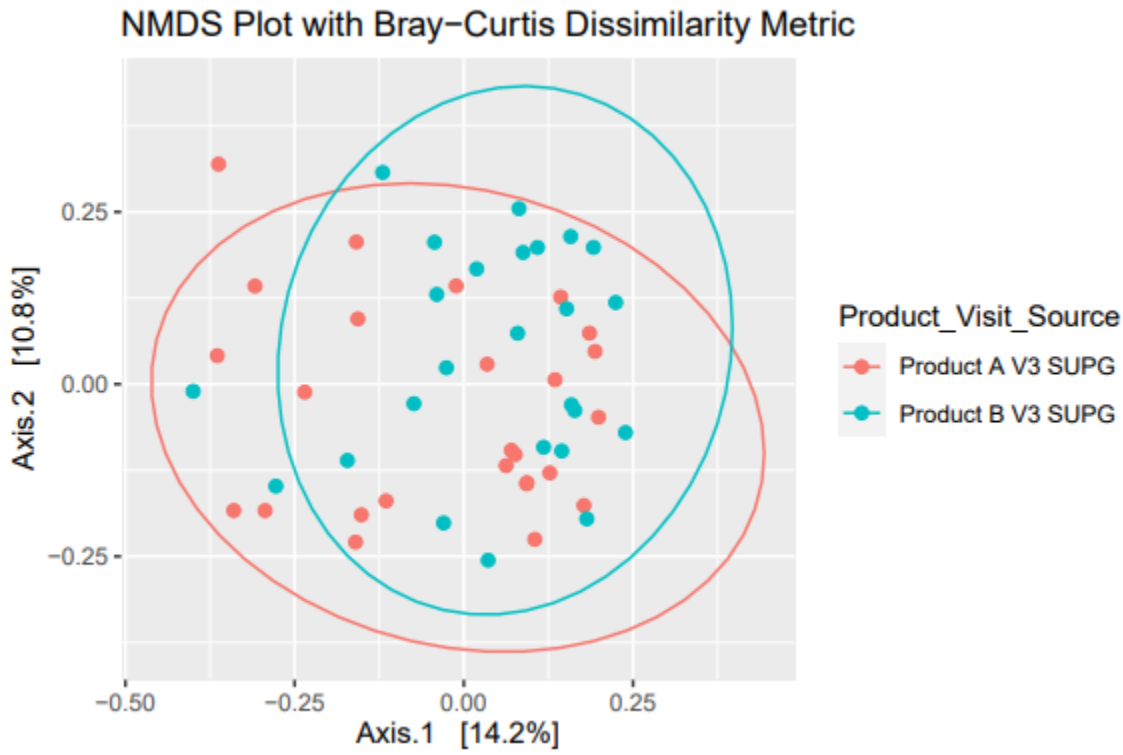


## 2) Alpha



Note: No significant differences

3) Beta diversity



Group 1	Group 2	Sample size	Permutati	pseudo-F	p-value
Product A V3 SUPG	Product B V3 SUPG	51	999	1.669907	0.023

Note: significant difference

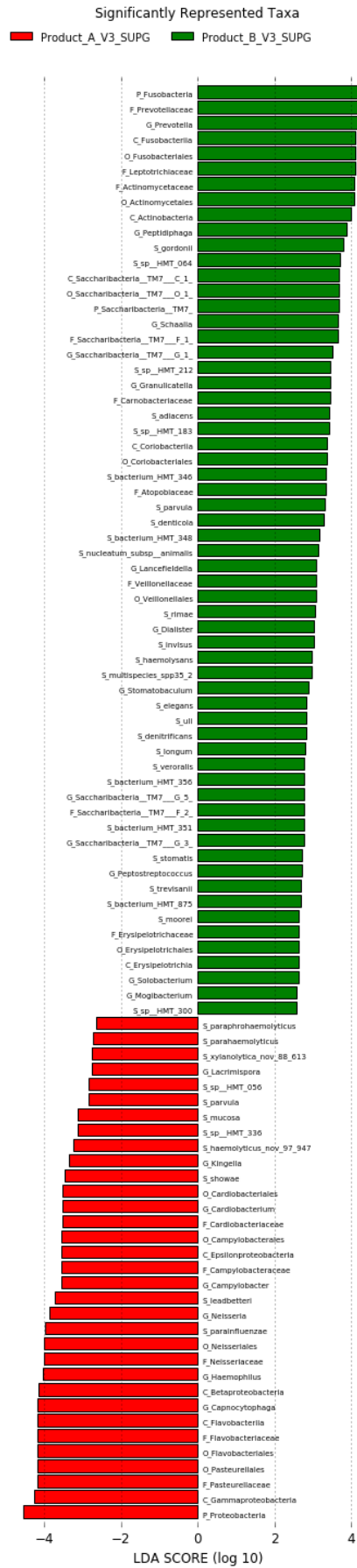
#### 4) Differential abundance

taxon	lfc_(Inter	lfc_Product	se_(Inter	se_Product	W_(Inter	W_Product	p_(Inter	p_Product	q_(Inter	q_Product	diff_(Inter	diff_Product
Haemophilus parainfluenzae (SP19)	0.999219	-2.02096	0.429882	0.614177	2.324402	-3.29051	0.020104	0.001	1	0.320019	FALSE	FALSE
Haemophilus parahaemolyticus (SP148)	0.911082	-1.84115	0.411774	0.588315	2.212575	-3.12954	0.026927	0.001751	1	0.558505	FALSE	FALSE
Gemella haemolysans (SP8)	-0.98991	2.036872	0.463494	0.662183	-2.13576	3.075997	0.032699	0.002098	1	0.667163	FALSE	FALSE
Granulicatella elegans (SP138)	-0.74812	1.54361	0.393969	0.562884	-1.89893	2.742325	0.057574	0.006101	1	1	FALSE	FALSE
Neisseria mucosa (SP300)	1.064796	-2.15473	0.573187	0.818849	1.857676	-2.63142	0.063215	0.008503	1	1	FALSE	FALSE
Fusobacterium nucleatum_subsp._animalis	-0.9586	1.972986	0.5289	0.755596	-1.81243	2.611164	0.069919	0.009023	1	1	FALSE	FALSE
Streptococcus sp._HMT_056 (SP276)	1.016608	-2.05643	0.583093	0.832997	1.743475	-2.46871	0.081251	0.01356	1	1	FALSE	FALSE
Streptococcus sp._HMT_064 (SP305)	-1.03487	2.128586	0.62131	0.887581	-1.66562	2.398189	0.095788	0.016476	1	1	FALSE	FALSE
Prevotella veroralis (SP110)	-0.67302	1.390414	0.416048	0.594419	-1.61765	2.339115	0.105738	0.019329	1	1	FALSE	FALSE
Lacrimispora xylanolytica_nov_88.613% (SP10)	0.841064	-1.69832	0.521338	0.744797	1.61328	-2.28025	0.106684	0.022593	1	1	FALSE	FALSE
Granulicatella adiacens (SP134)	-0.52825	1.095089	0.342067	0.488755	-1.5443	2.24057	0.122516	0.025054	1	1	FALSE	FALSE
Lancefieldella rimae (SP173)	-0.83586	1.722604	0.542665	0.775256	-1.54029	2.22198	0.123491	0.026285	1	1	FALSE	FALSE
Streptococcus gordonii (SP171)	-0.75582	1.559317	0.496484	0.709299	-1.52234	2.198391	0.127924	0.027921	1	1	FALSE	FALSE
Capnocytophaga sp._HMT_336 (SP51)	0.956185	-1.93317	0.618178	0.883106	1.546781	-2.18905	0.121916	0.028593	1	1	FALSE	FALSE
Prevotella sp._HMT_300 (SP69)	-0.7273	1.501134	0.48494	0.692813	-1.49976	2.166724	0.133676	0.030256	1	1	FALSE	FALSE
Campylobacter showae (SP204)	0.735197	-1.48235	0.479614	0.685206	1.532891	-2.16336	0.125303	0.030513	1	1	FALSE	FALSE
Solobacterium moorei (SP96)	-0.66791	1.379983	0.446876	0.638449	-1.49461	2.161463	0.135015	0.03066	1	1	FALSE	FALSE
Capnocytophaga sp._HMT_332 (SP49)	0.830966	-1.67772	0.549798	0.785444	1.511401	-2.13601	0.130686	0.032678	1	1	FALSE	FALSE
Kingella oralis_nov_97.741% (SPN664)	0.687063	-1.38416	0.460555	0.657984	1.491815	-2.10363	0.135748	0.035411	1	1	FALSE	FALSE
Haemophilus sputorum (SP115)	0.53114	-1.06607	0.35553	0.507985	1.493936	-2.09863	0.135192	0.035849	1	1	FALSE	FALSE
Fusobacterium nucleatum_nucleatum_subsp._nucleatum	-0.67809	1.400764	0.474704	0.678193	-1.42846	2.065437	0.15316	0.038882	1	1	FALSE	FALSE
Aggregatibacter sp._HMT_512 (SP314)	0.666551	-1.34231	0.46587	0.665575	1.430767	-2.01677	0.152497	0.04372	1	1	FALSE	FALSE
Actinomyces sp._HMT_169 (SP239)	0.5227	-1.04886	0.367031	0.52441	1.424131	-2.00007	0.154408	0.045493	1	1	FALSE	FALSE
Dialister invisus (SP128)	-0.65303	1.349636	0.472804	0.67548	-1.38119	1.998041	0.167221	0.045712	1	1	FALSE	FALSE
Prevotella denticola (SP30)	-0.82949	1.709602	0.622161	0.888796	-1.33323	1.923503	0.182456	0.054417	1	1	FALSE	FALSE
Capnocytophaga gingivalis_granulosa (SPP2)	0.607715	-1.22229	0.444966	0.63572	1.365755	-1.92268	0.172016	0.05452	1	1	FALSE	FALSE
Stomatobaculum longum (SP228)	-0.70518	1.456026	0.532248	0.760379	-1.32491	1.914869	0.185199	0.055509	1	1	FALSE	FALSE
Saccharibacteria_(TM7)_[G-3] bacterium_HM	-0.66657	1.37726	0.504228	0.72036	-1.32197	1.911907	0.186179	0.055888	1	1	FALSE	FALSE
Kingella oralis (SP198)	0.650189	-1.30893	0.48016	0.685986	1.354109	-1.90811	0.175702	0.056377	1	1	FALSE	FALSE
Neisseria bacilliformis (SP447)	0.711887	-1.4348	0.545011	0.778607	1.306188	-1.84277	0.191489	0.065362	1	1	FALSE	FALSE

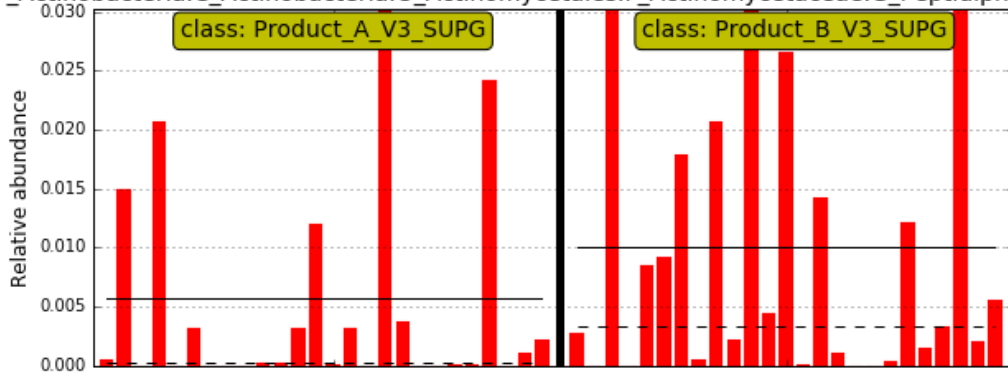
Note: Red, more prevalent in A; Green, more prevalent in B



## 5) Lefse

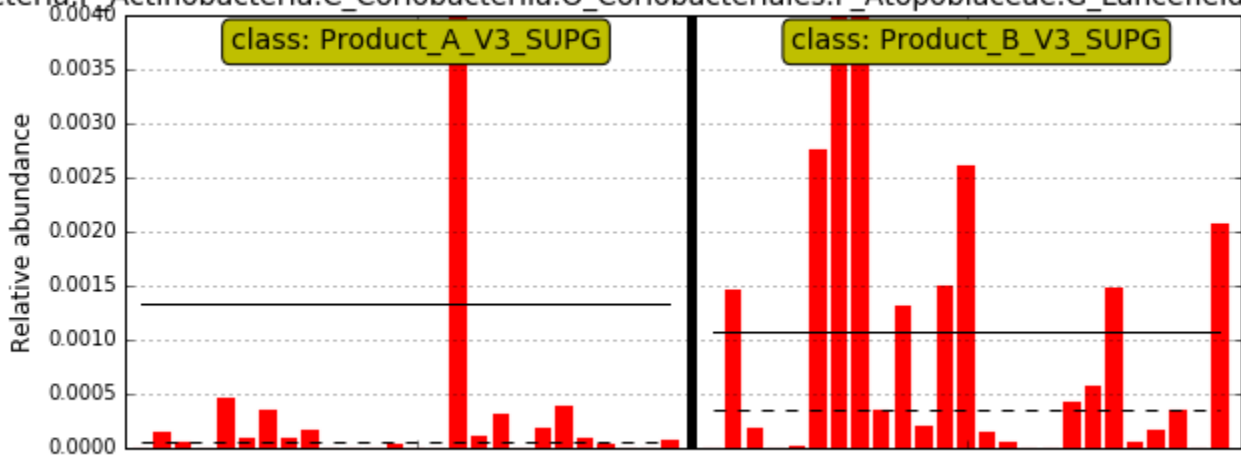


eria.P\_Actinobacteria.C\_Actinobacteria.O\_Actinomycetales.F\_Actinomycetaceae.G\_Peptidiphaga.S\_sp\_

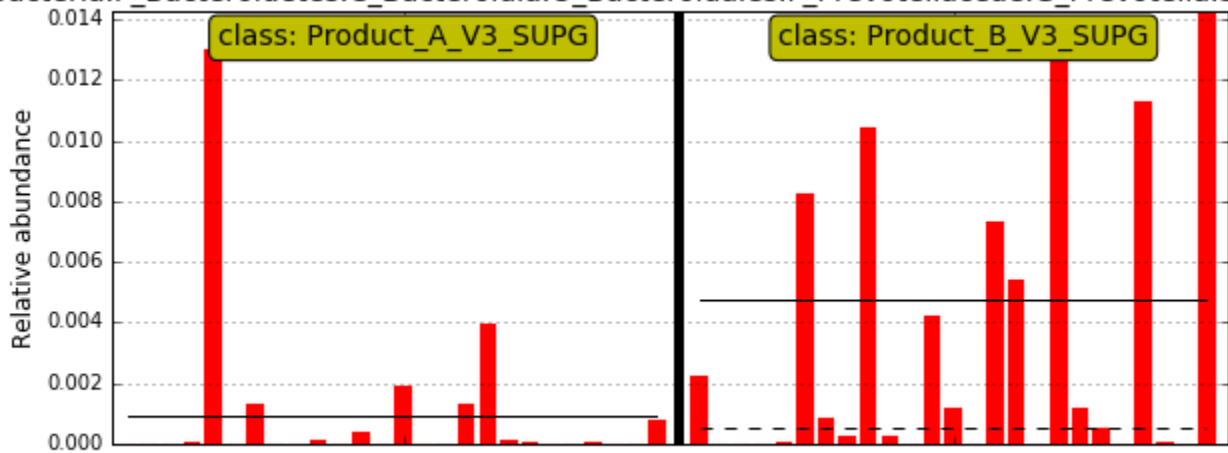


HMT183

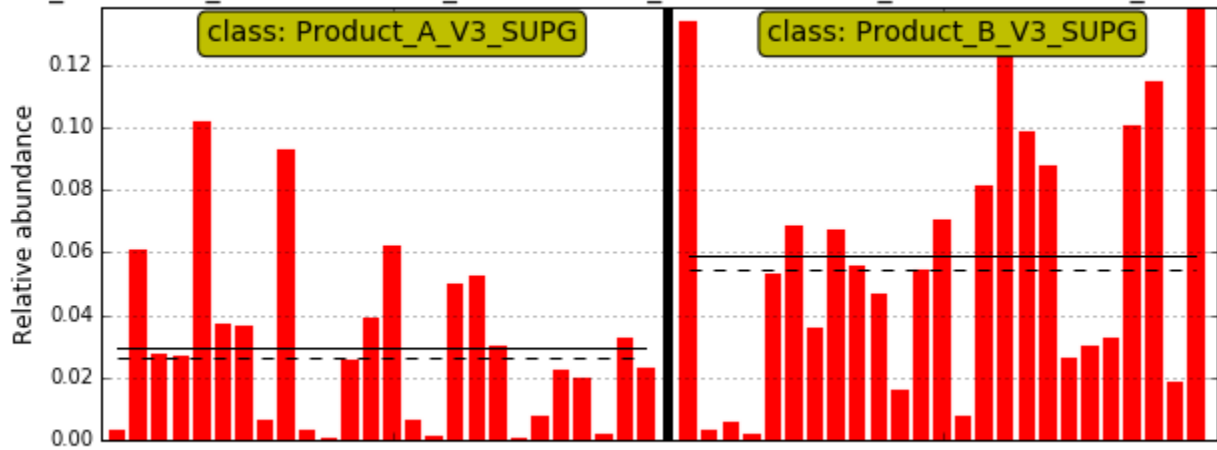
\_Bacteria.P\_Actinobacteria.C\_Coriobacteriia.O\_Coriobacteriales.F\_Atopobiaceae.G\_Lancefieldella.S\_par



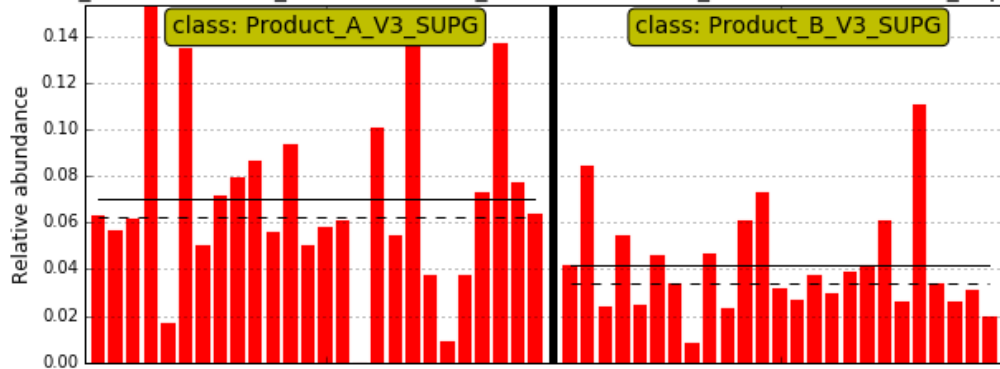
K\_Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Prevotella.S\_denticola



K\_Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Prevotella

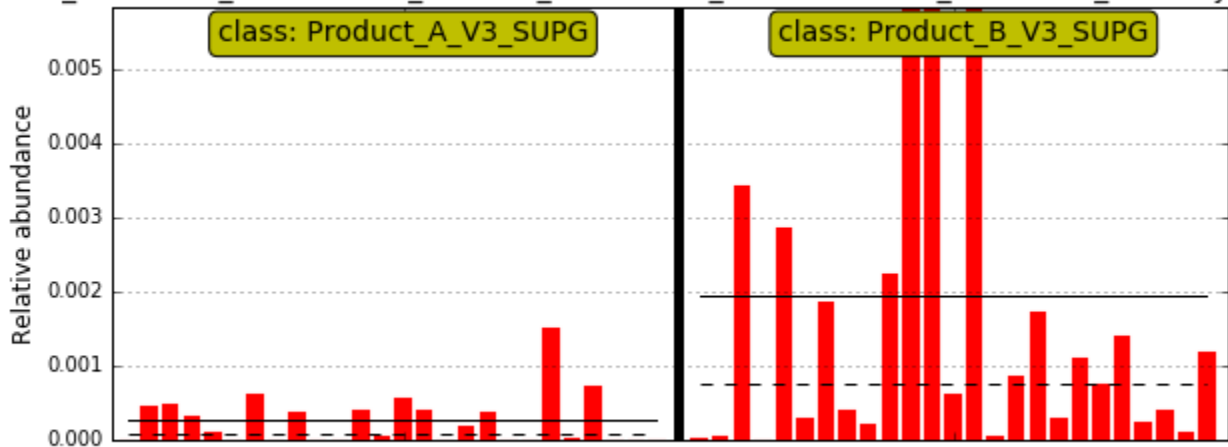


K\_Bacteria.P\_Bacteroidetes.C\_Flavobacteriia.O\_Flavobacteriales.F\_Flavobacteriaceae.G\_Capnocytopha

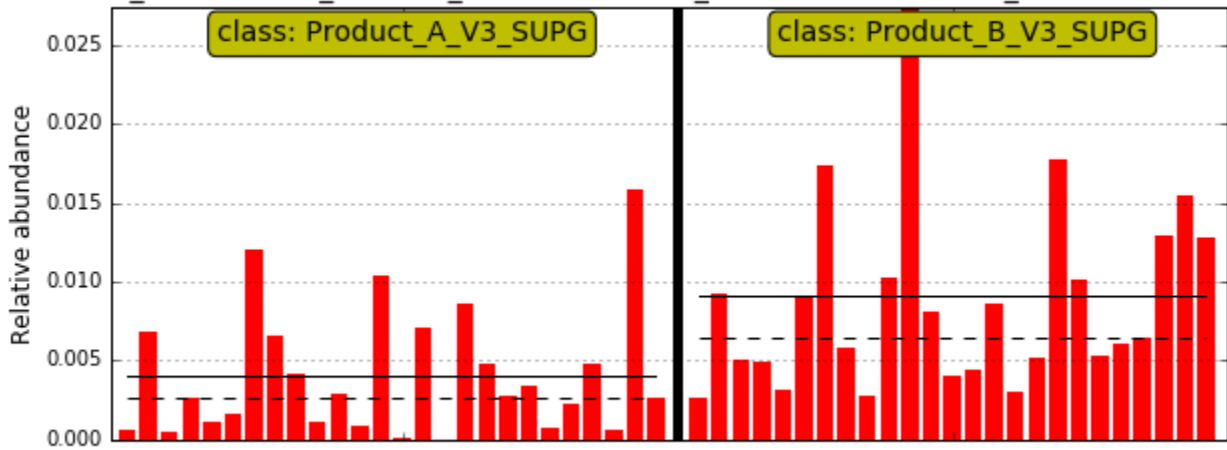


High levels

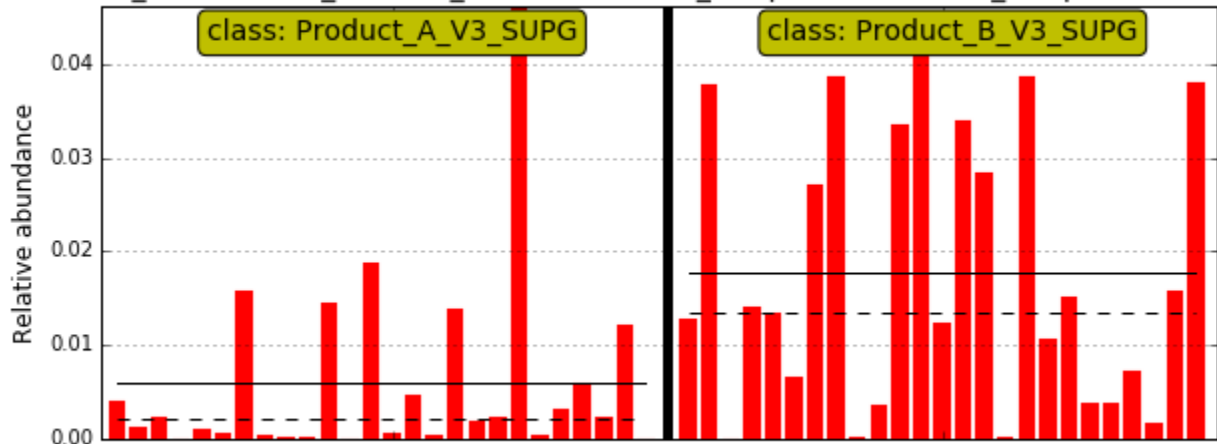
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Bacillales.F\_Gemellaceae.G\_Gemella.S\_haemolysans



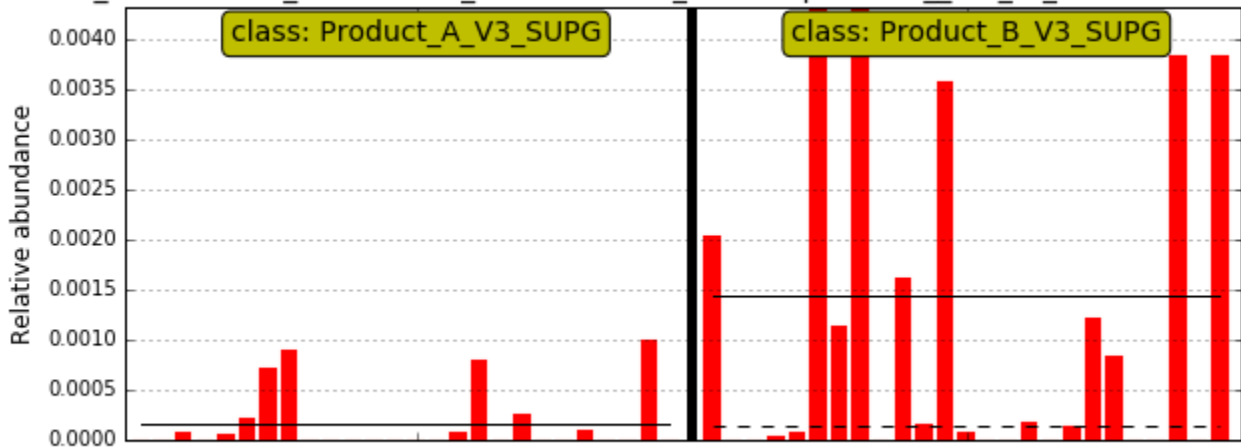
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Carnobacteriaceae.G\_Granulicatella.S\_adiacen:



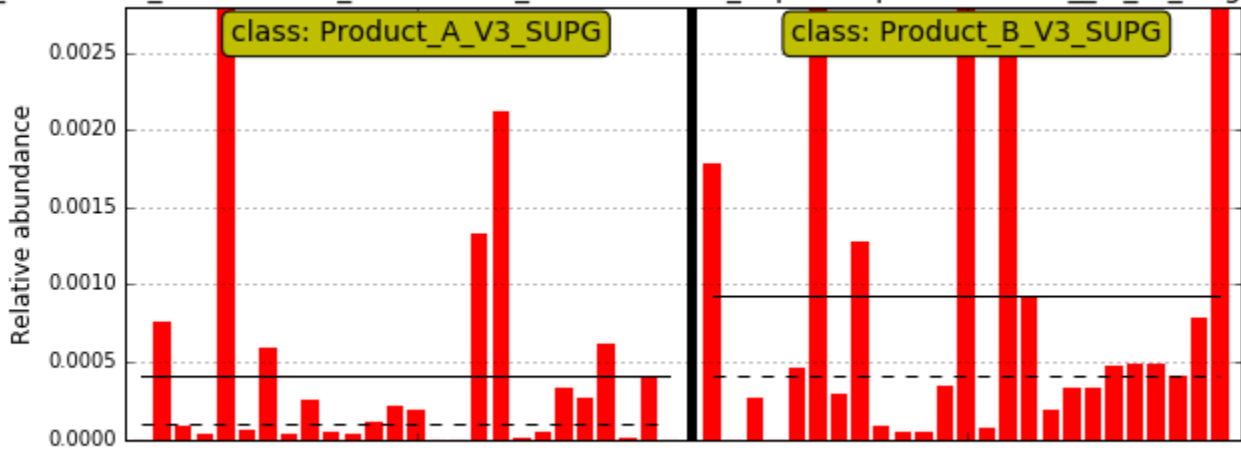
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Streptococcaceae.G\_Streptococcus.S\_gordonii



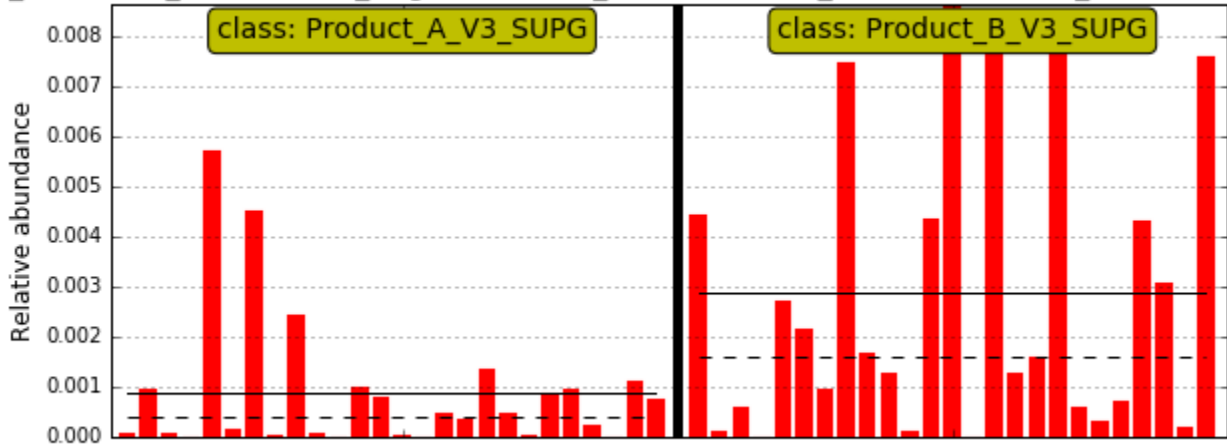
\_Bacteria.P\_Firmicutes.C\_Clostridia.O\_Clostridiales.F\_Lachnospiraceae\_XIV\_G\_Stomatobaculum.S\_loni



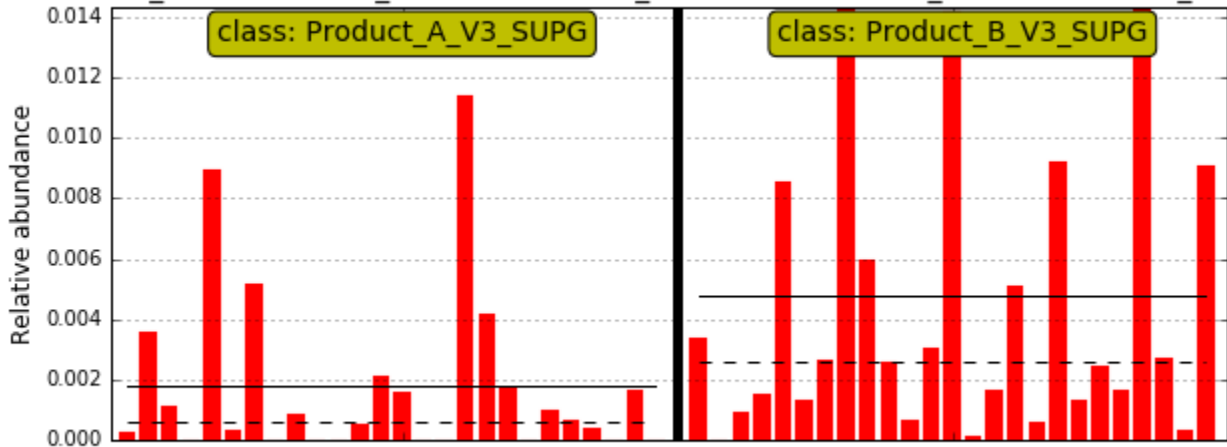
K\_Bacteria.P\_Firmicutes.C\_Clostridia.O\_Clostridiales.F\_Peptostreptococcaceae\_XI\_G\_Mogibacterium



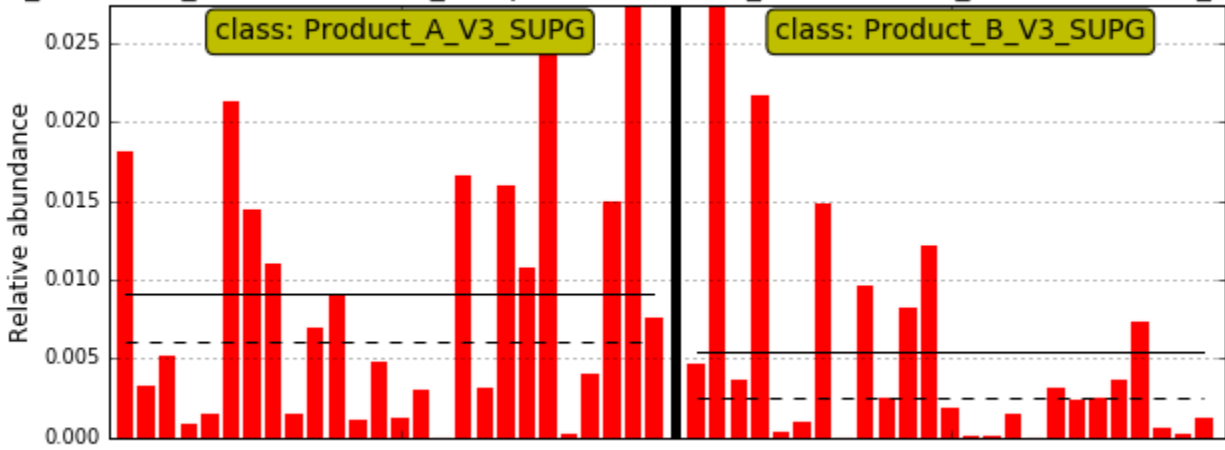
K\_Bacteria.P\_Firmicutes.C\_Negativicutes.O\_Veillonellales.F\_Veillonellaceae.G\_Dialister.S\_invisus



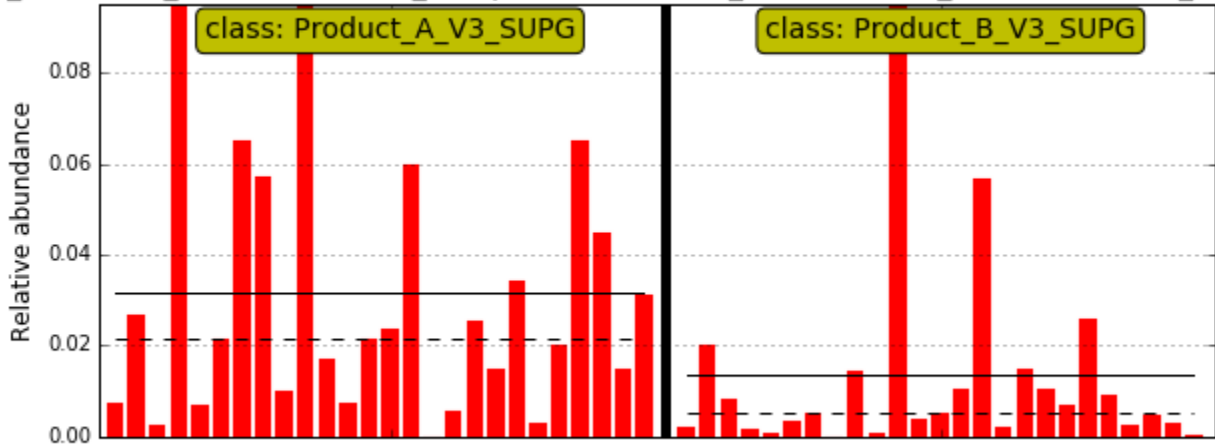
\_Fusobacteria.C\_Fusobacteria.O\_Fusobacteriales.F\_Fusobacteriaceae.G\_Fusobacterium.S\_nucleatum\_s



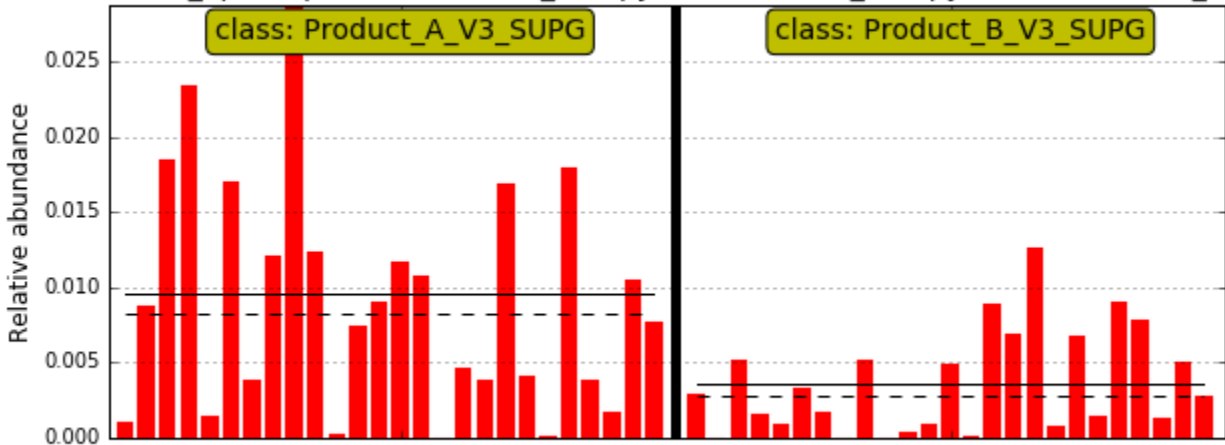
K\_Bacteria.P\_Proteobacteria.C\_Betaproteobacteria.O\_Neisseriales.F\_Neisseriaceae.G\_Kingella



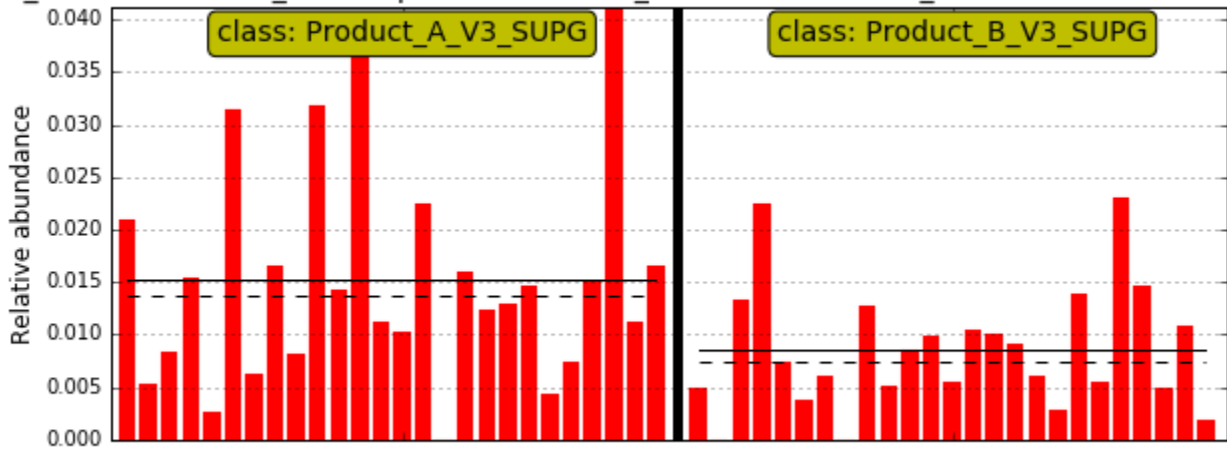
K\_Bacteria.P\_Proteobacteria.C\_Betaproteobacteria.O\_Neisseriales.F\_Neisseriaceae.G\_Neisseria



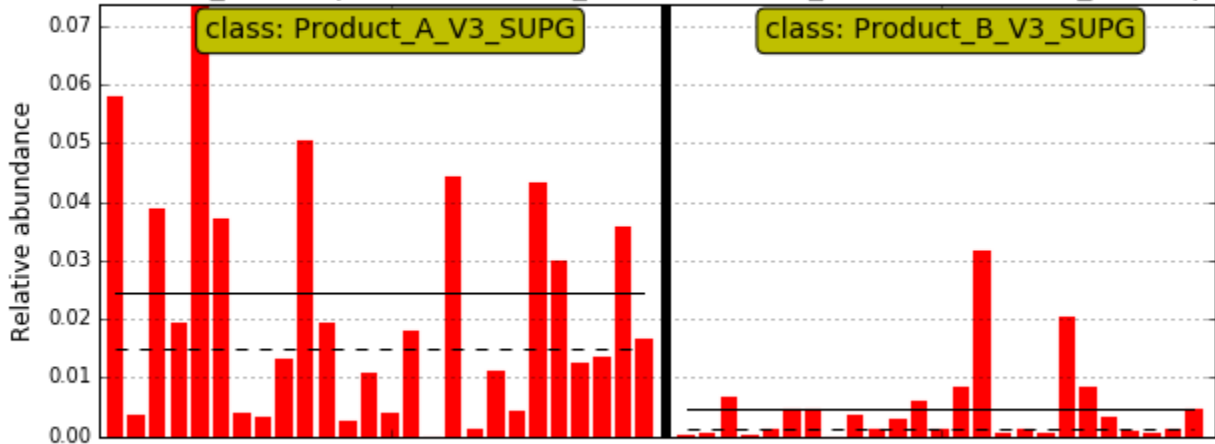
D\_Proteobacteria.C\_Epsilonproteobacteria.O\_Campylobacteriales.F\_Campylobacteraceae.G\_Campylobacter



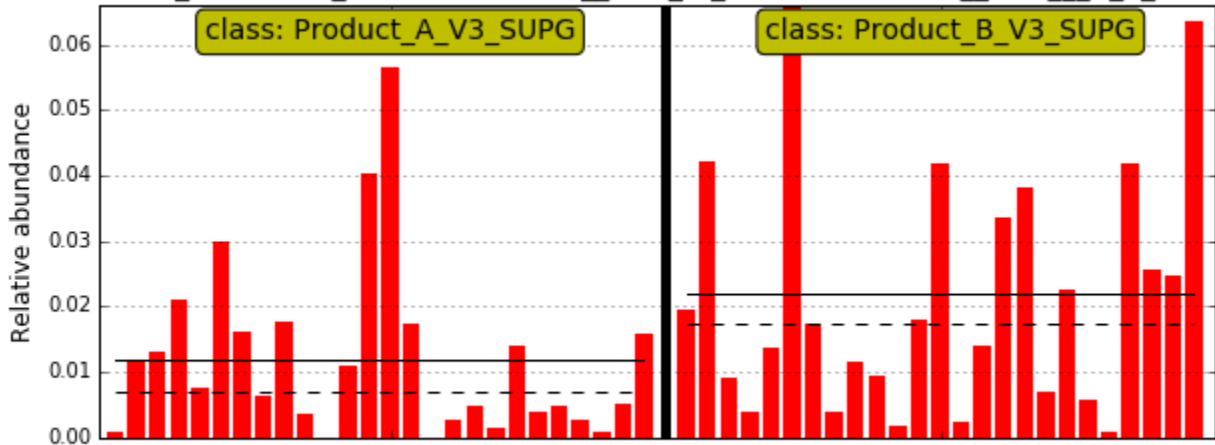
teria.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Cardiobacteriales.F\_Cardiobacteriaceae.G\_Cardioba



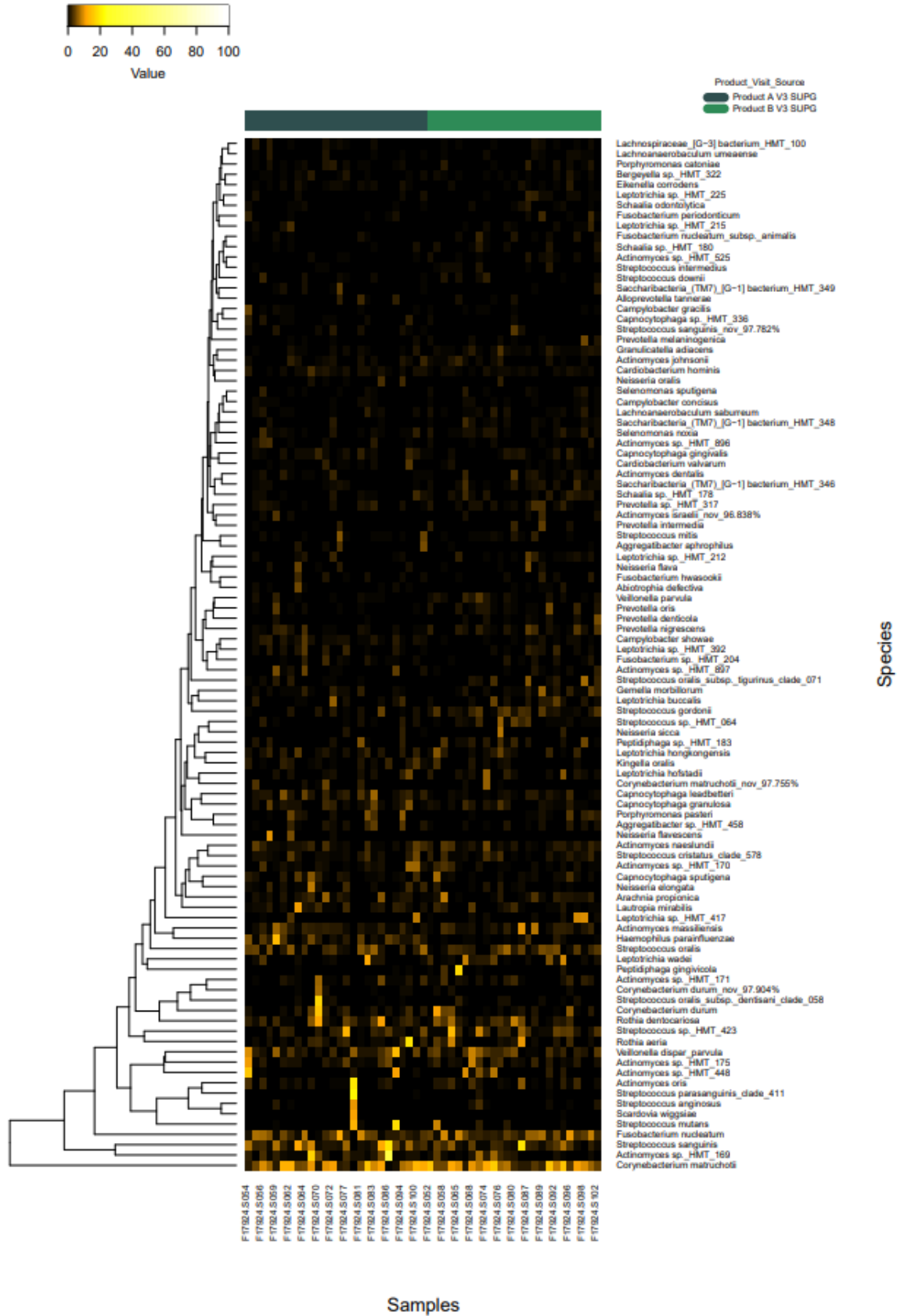
a.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Haemophilus.S\_par



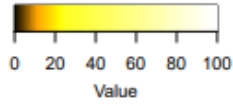
K\_Bacteria.P\_Saccharibacteria\_TM7\_C\_Saccharibacteria\_TM7\_C\_1



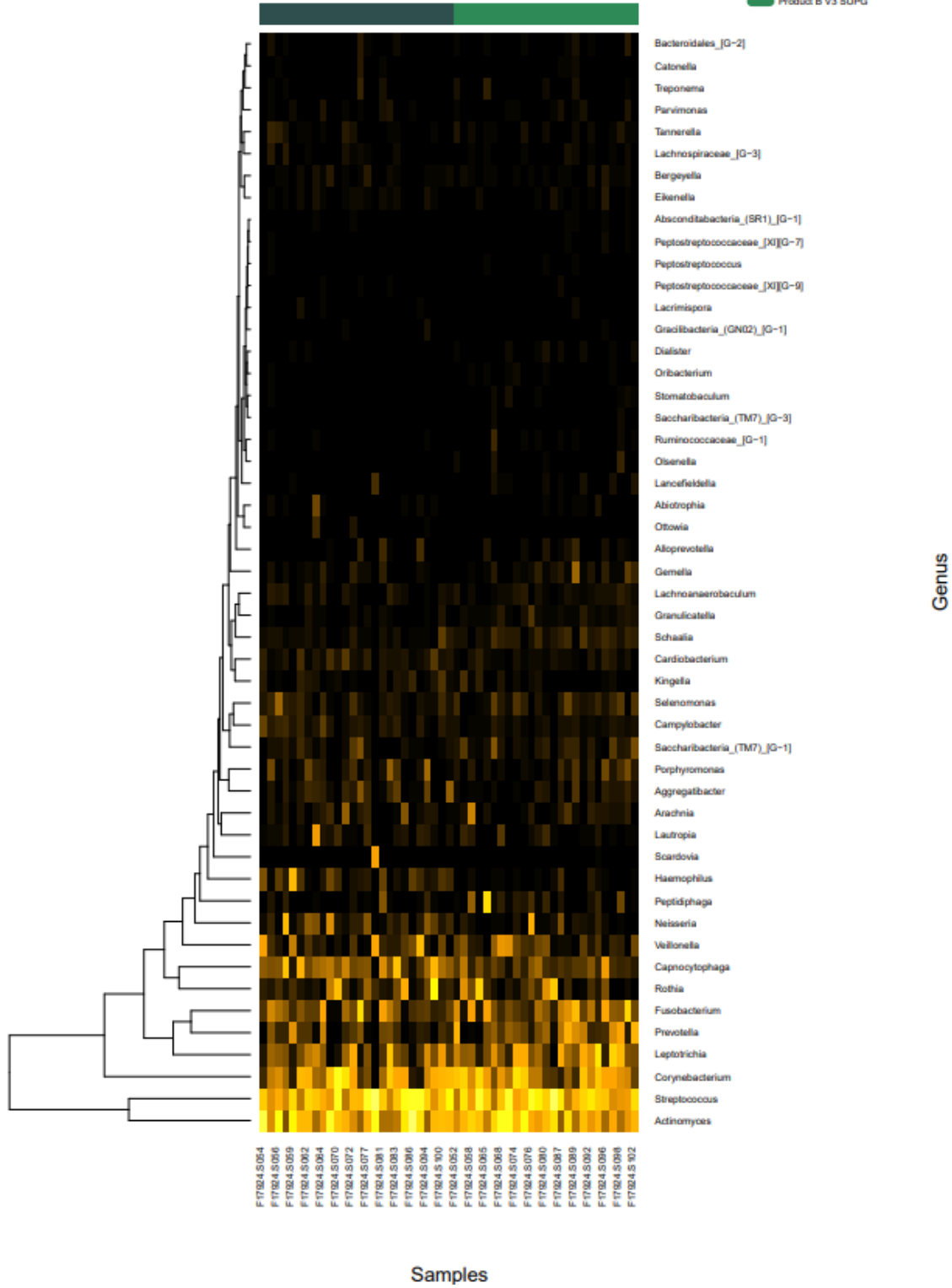
6) Heat map.





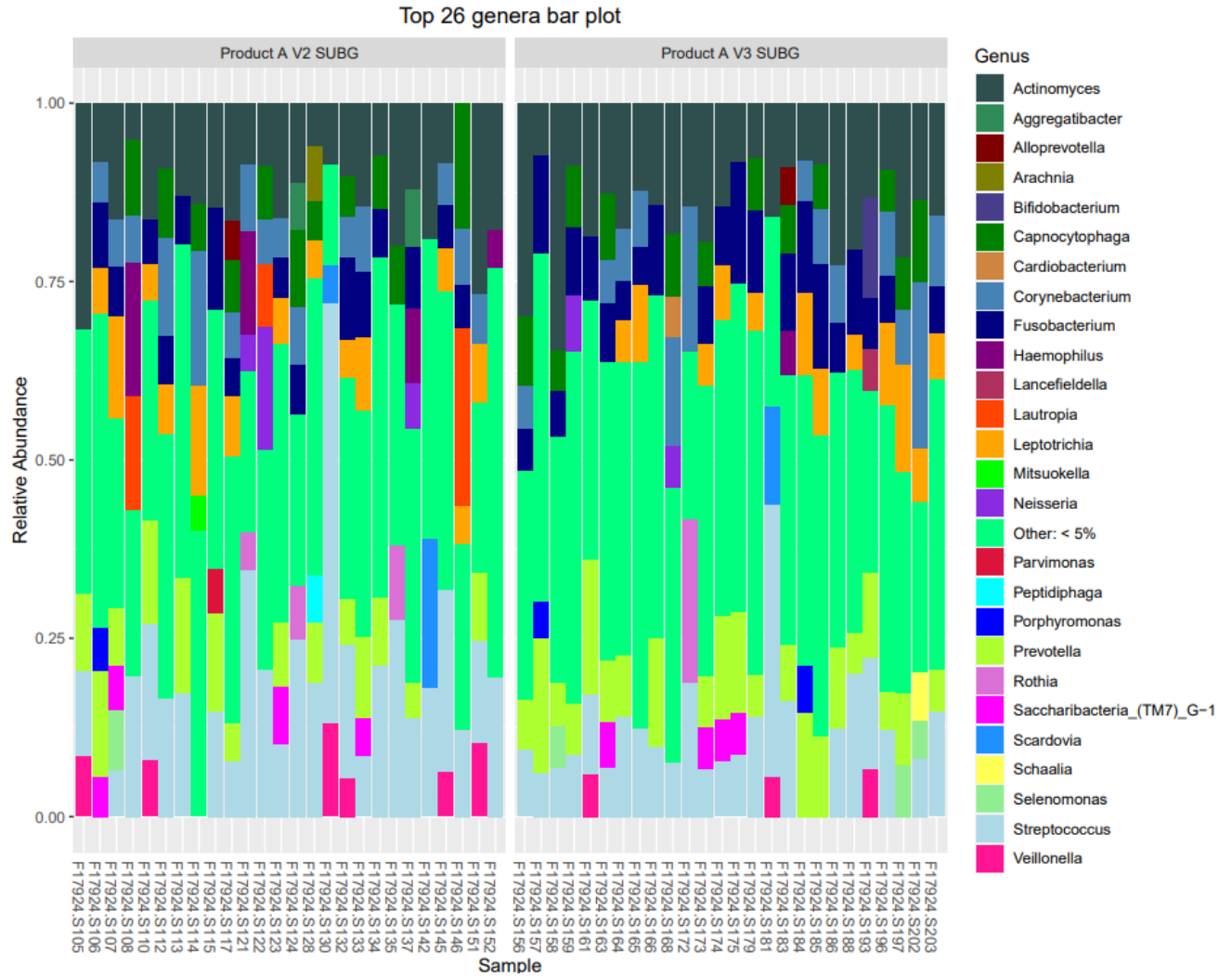


Product\_Visit\_Source  
 Product A V3 SUPG  
 Product B V3 SUPG

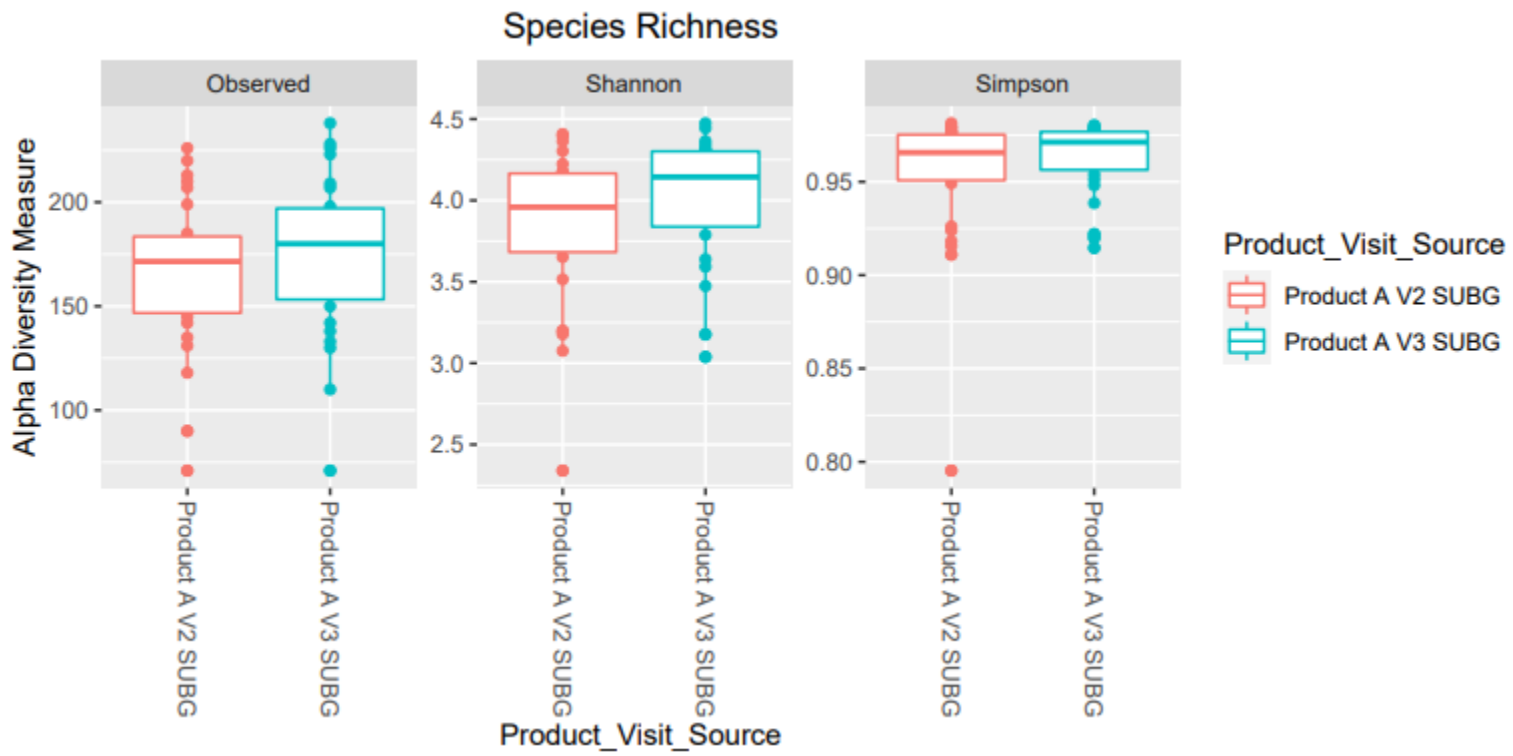


# Comparison 17. Product A V2 SUBG vs Product A V3 SUBG

## 1) Taxonomy bar graphs

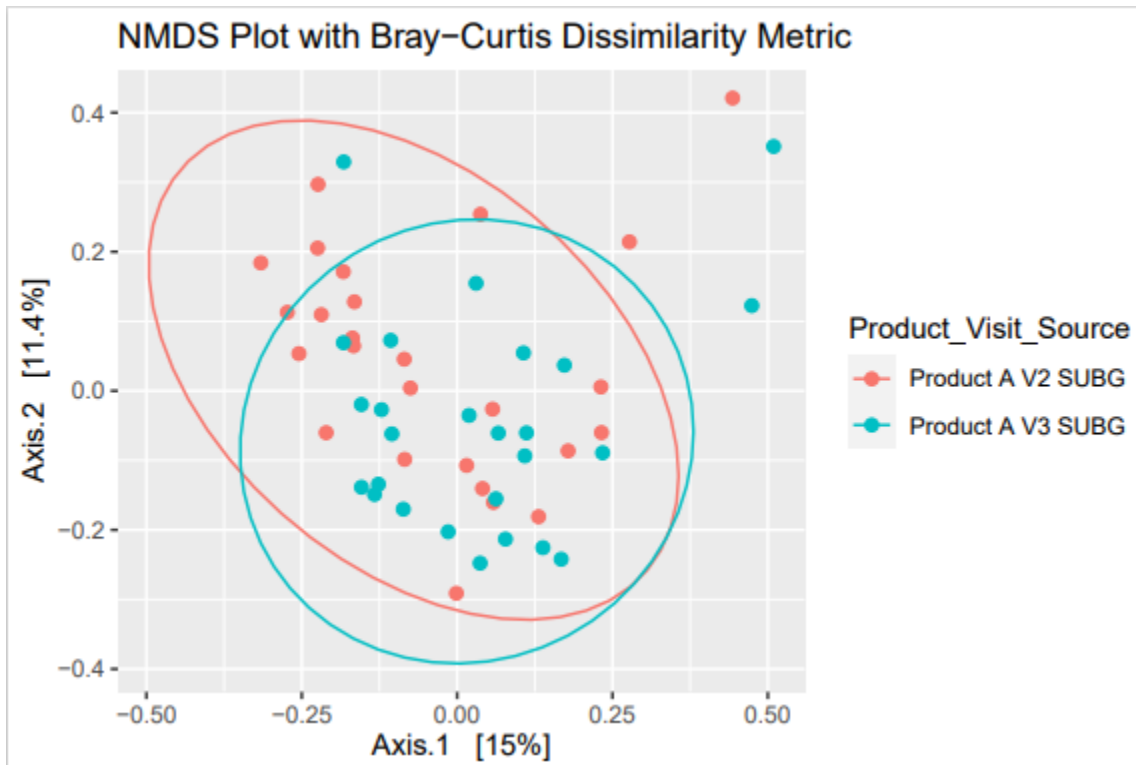


## 2) Alpha



Note: No significant differences

### 3) Beta diversity



Note: No significant differences

#### 4) Differential abundance

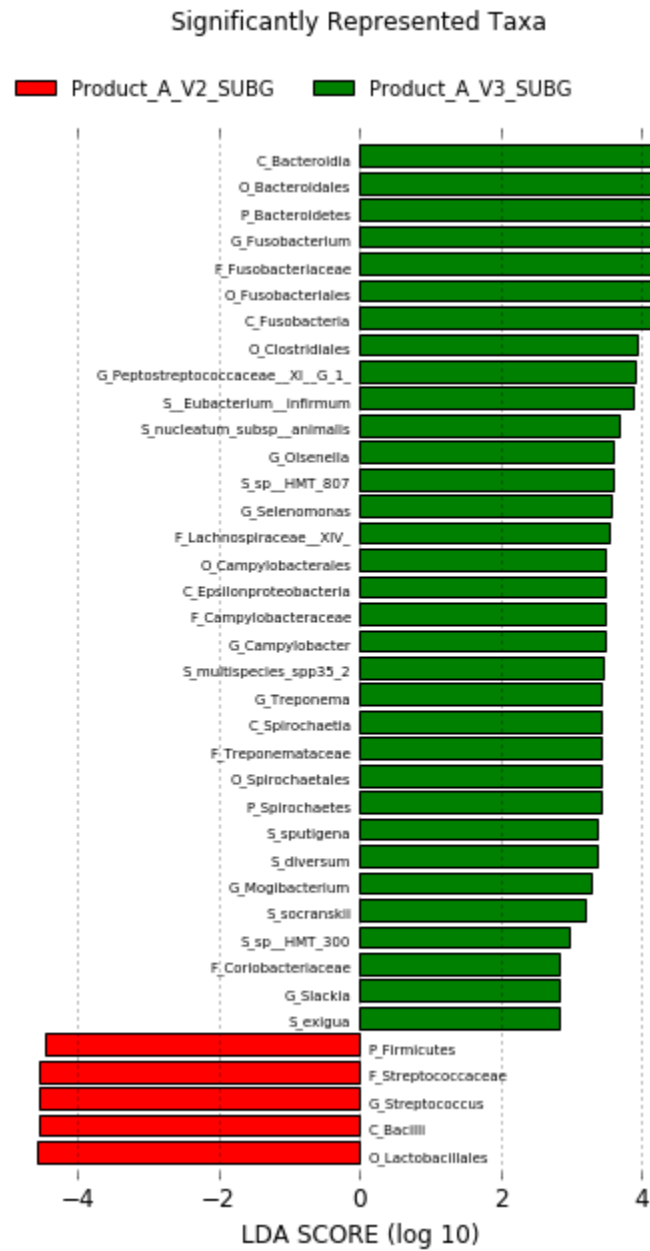
taxon	lfc_(Interc	lfc_Produc	se_(Interc	se_Produc	W_(Interc	W_Produc	p_(Interc	p_Produc	q_(Interc	q_Produc	diff_(Inte	diff_Prod
Fusobacterium nucleatum_nucleatum_subsp_ani	-0.76106	1.536331	0.488276	0.690526	-1.55867	2.224871	0.119075	0.02609	1	1	FALSE	FALSE
Mogibacterium diversum (SP365)	-0.65099	1.316188	0.432902	0.612216	-1.50378	2.149874	0.132639	0.031565	1	1	FALSE	FALSE
Olsenella sp._HMT_807 (SP81)	-0.82587	1.665948	0.582967	0.82444	-1.41666	2.020704	0.156581	0.04331	1	1	FALSE	FALSE
Prevotella sp._HMT_300 (SP69)	-0.72051	1.455226	0.521232	0.737134	-1.38232	1.974169	0.166875	0.048363	1	1	FALSE	FALSE
Treponema socranskii (SP84)	-0.50719	1.028597	0.391347	0.553449	-1.29602	1.858522	0.19497	0.063095	1	1	FALSE	FALSE
Peptostreptococcaceae_[X1][G-1] [Eubacterium]_i	-0.6256	1.265406	0.49541	0.700615	-1.26279	1.806134	0.206666	0.070897	1	1	FALSE	FALSE
Schaalia odontolyticus (SP28)	0.55245	-1.09069	0.427307	0.604304	1.292864	-1.80487	0.196058	0.071095	1	1	FALSE	FALSE
Streptococcus gordonii (SP171)	0.721476	-1.42874	0.572687	0.809902	1.259809	-1.76409	0.207738	0.077717	1	1	FALSE	FALSE
Fusobacterium nucleatum_subsp._animalis (SP23)	-0.63792	1.290051	0.530169	0.749772	-1.20324	1.720591	0.228884	0.085325	1	1	FALSE	FALSE
Streptococcus sp._HMT_064 (SP305)	0.763143	-1.51207	0.636075	0.899546	1.199769	-1.68093	0.230229	0.092776	1	1	FALSE	FALSE
Lacrimispora xylanolytica_nov_88.613% (SPN382)	-0.69089	1.395988	0.590013	0.834404	-1.17097	1.673035	0.24161	0.09432	1	1	FALSE	FALSE
Prevotella oris (SP65)	-0.53901	1.092241	0.471815	0.667247	-1.14243	1.636936	0.253276	0.101644	1	1	FALSE	FALSE
Ruminococcaceae_[G-2] bacterium_HMT_085 (SP1	-0.58881	1.191822	0.518027	0.732601	-1.13663	1.626837	0.255693	0.103772	1	1	FALSE	FALSE

Note: Green, more prevalent in V3

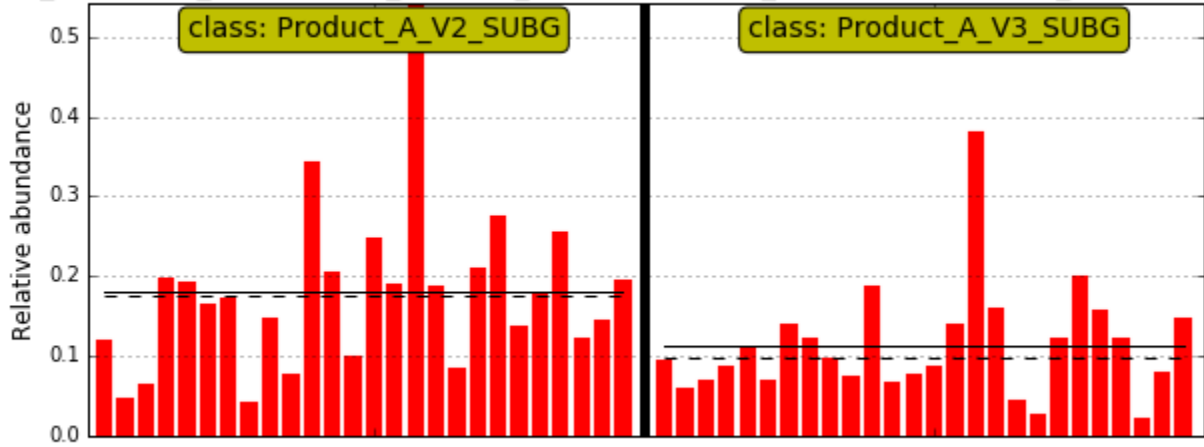
Red more prevalent in V2

Not much difference from baseline as compared to visit 3. No statistical difference.

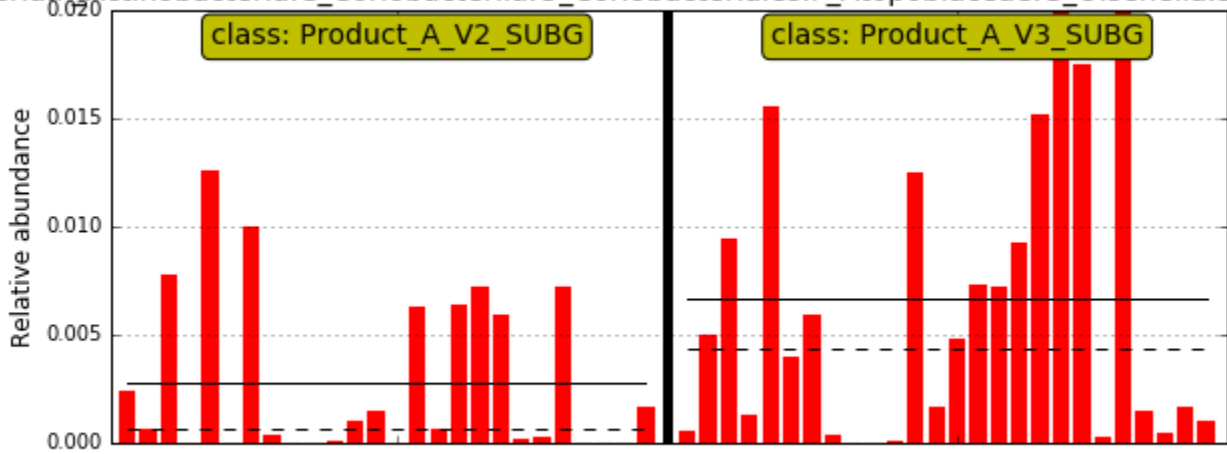
5) Lefse



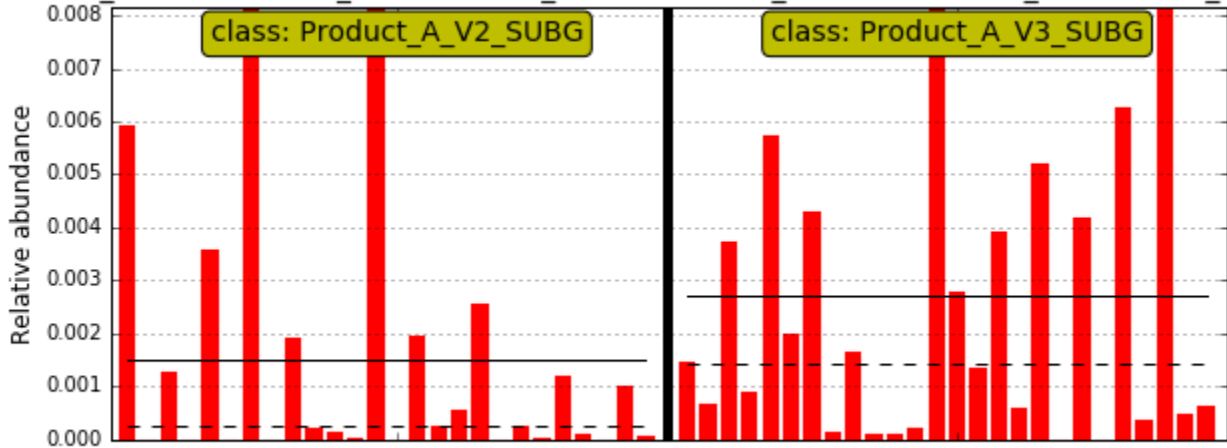
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Streptococcaceae.G\_Streptococcus



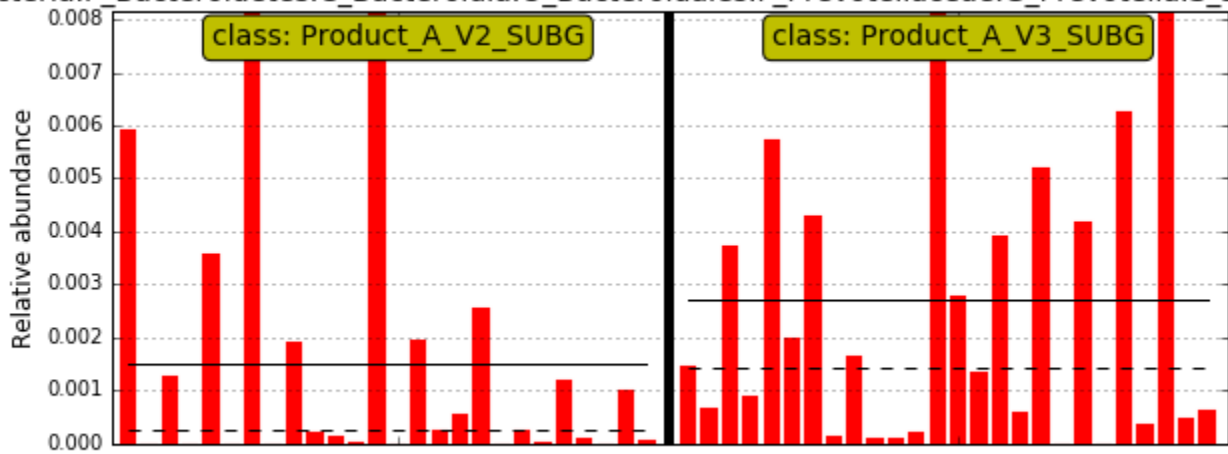
Bacteria.P\_Actinobacteria.C\_Coriobacteriia.O\_Coriobacteriales.F\_Atopobiaceae.G\_Olsenella.S\_sp\_HMT



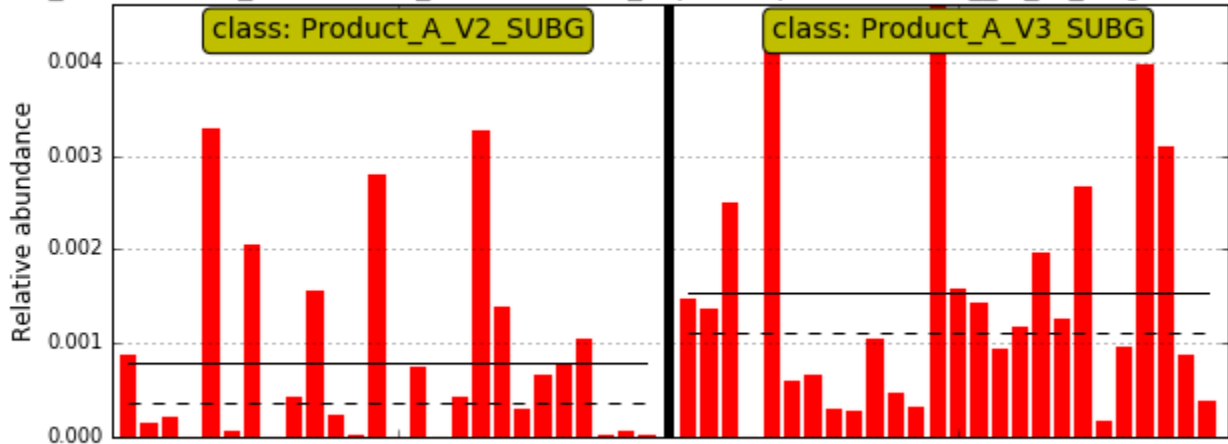
K\_Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Prevotella.S\_sp\_HMT\_3



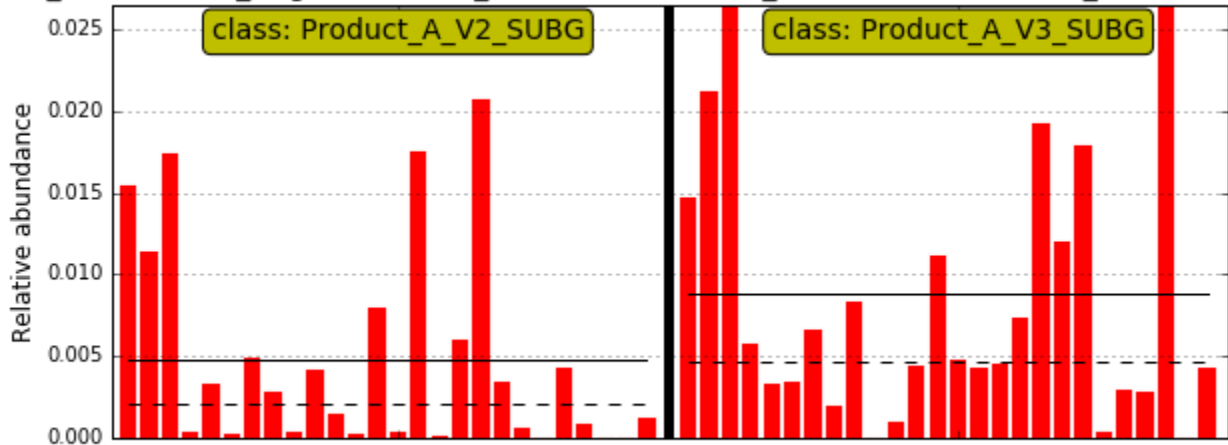
K\_Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Prevotella.S\_sp\_HMT\_3



acteria.P\_Firmicutes.C\_Clostridia.O\_Clostridiales.F\_Peptostreptococcaceae\_XI\_G\_Mogibacterium.S\_div

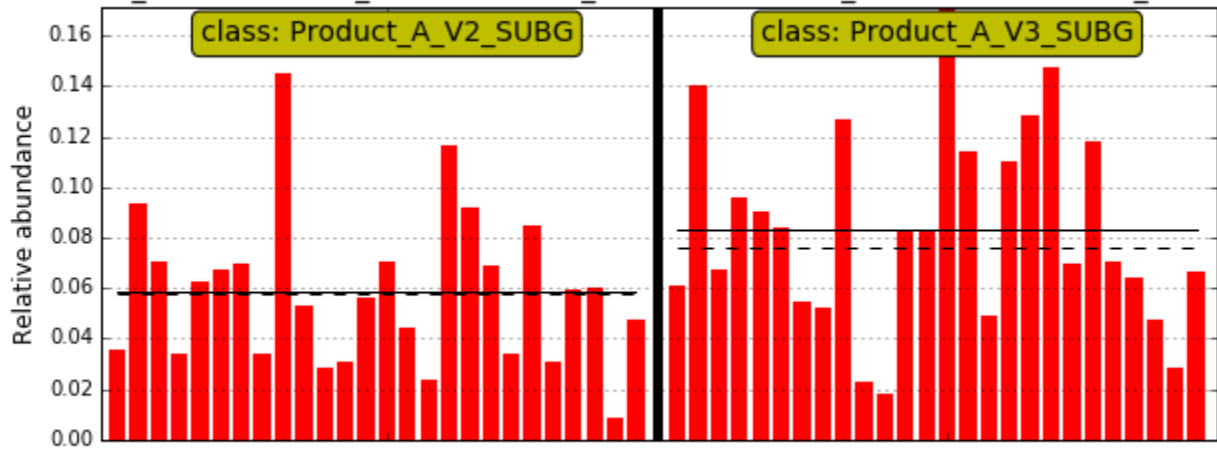


acteria.P\_Firmicutes.C\_Negativicutes.O\_Selenomonadales.F\_Selenomonadaceae.G\_Selenomonas.S\_spu

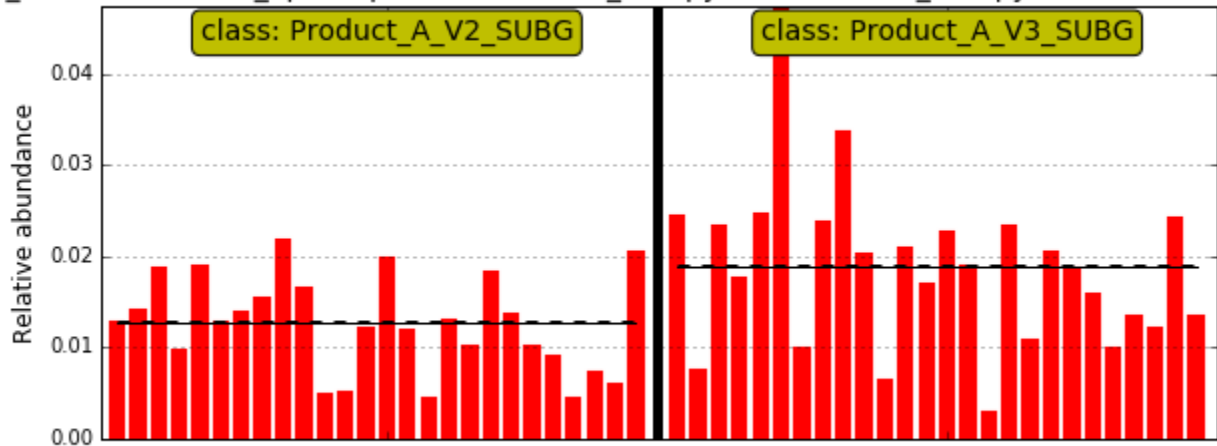




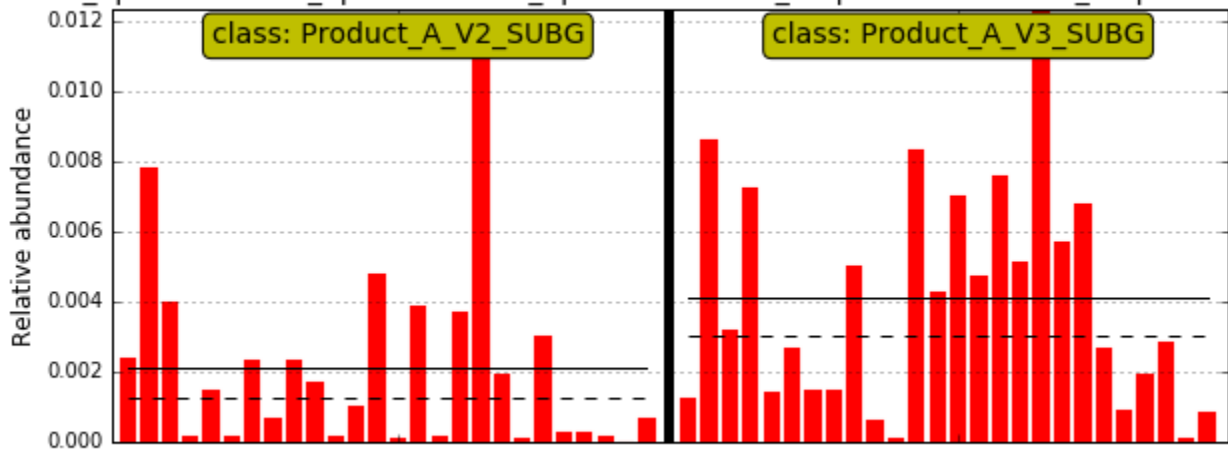
K\_Bacteria.P\_Fusobacteria.C\_Fusobacteria.O\_Fusobacteriales.F\_Fusobacteriaceae.G\_Fusobacterium



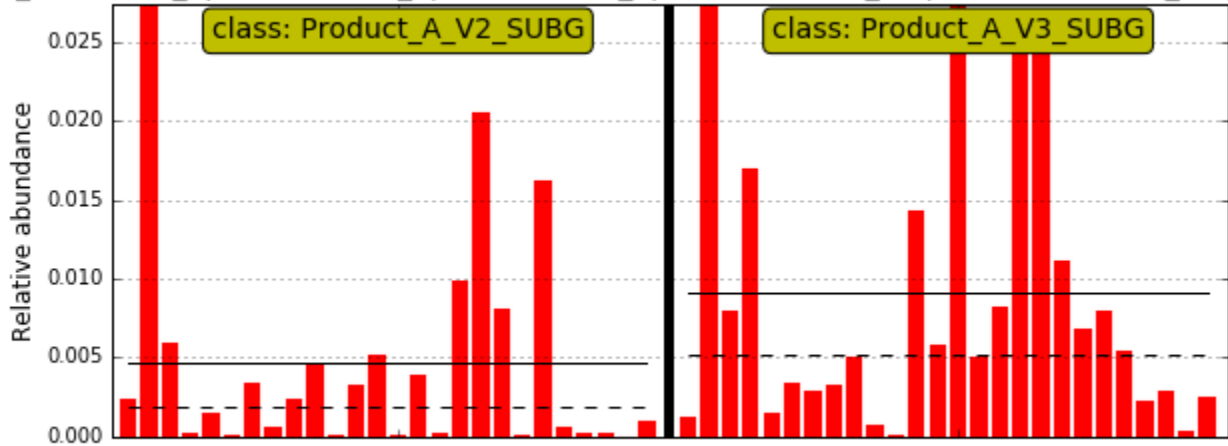
eria.P\_Proteobacteria.C\_Epsilonproteobacteria.O\_Campylobacteriales.F\_Campylobacteraceae.G\_Campylobacter



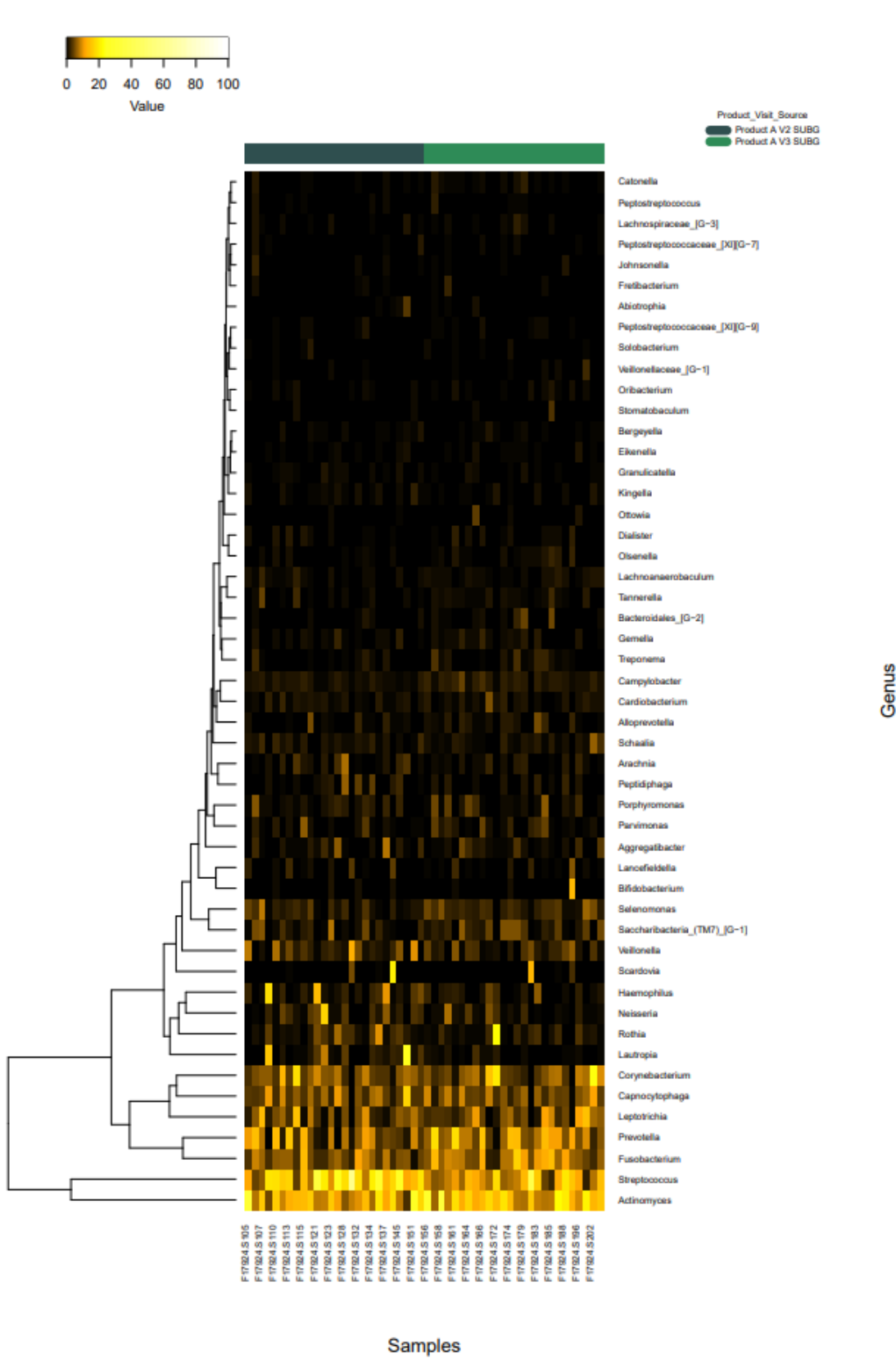
\_Bacteria.P\_Spirochaetes.C\_Spirochaetia.O\_Spirochaetales.F\_Treponemataceae.G\_Treponema.S\_socra

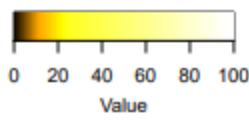


K\_Bacteria.P\_Spirochaetes.C\_Spirochaetia.O\_Spirochaetales.F\_Treponemataceae.G\_Treponema

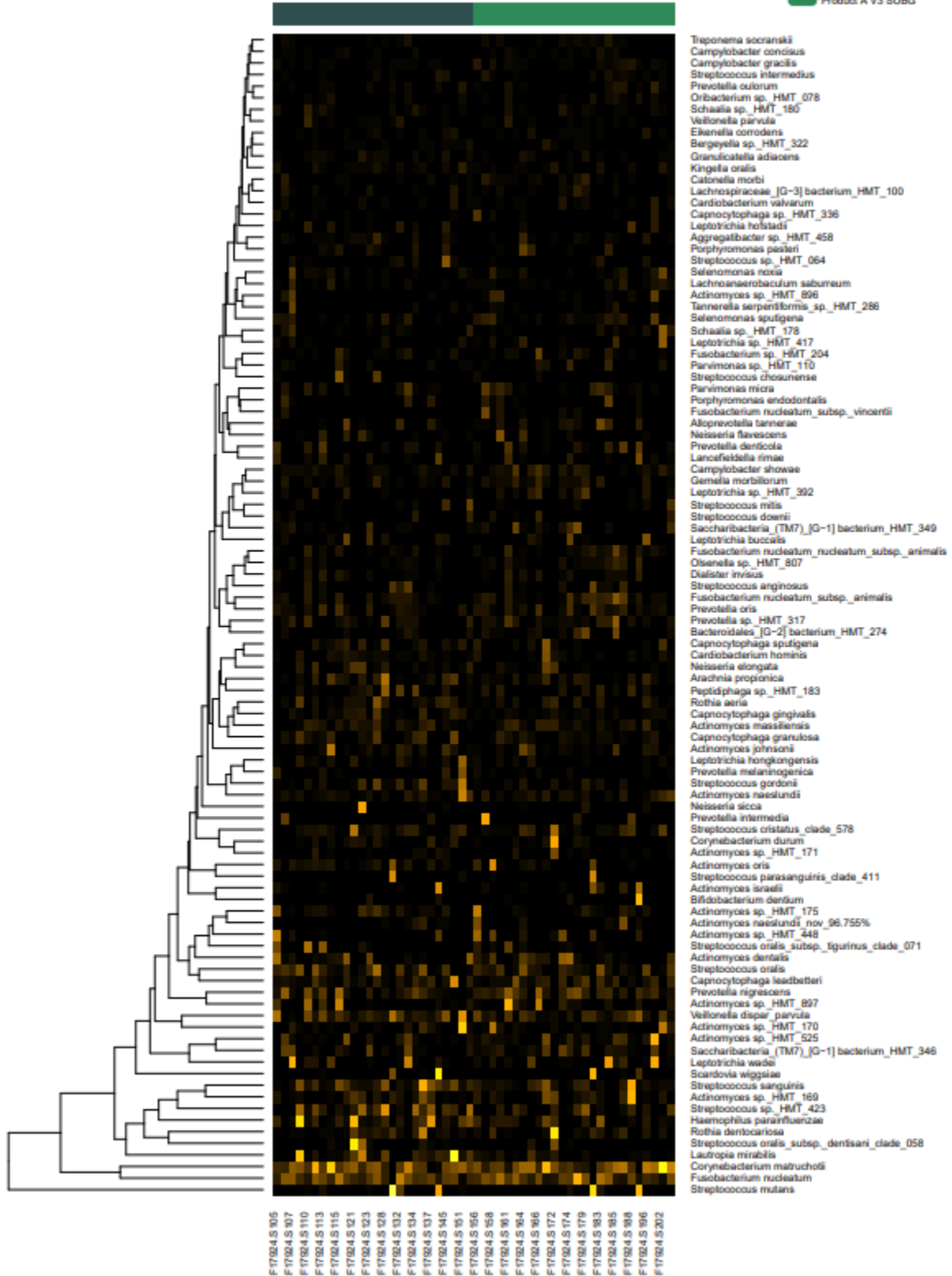


6) Heat map.



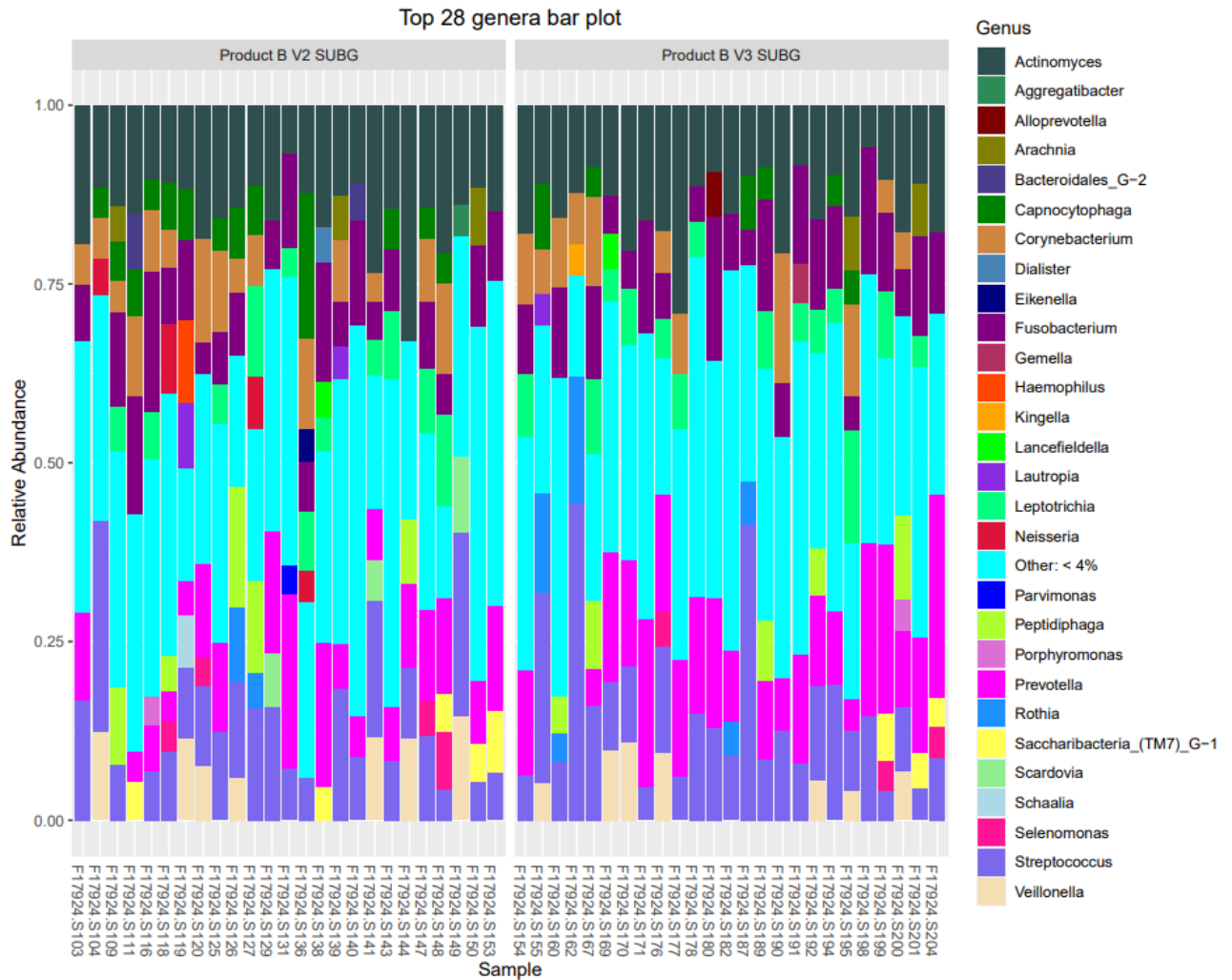


Product\_Visit\_Source  
 ■ Product A V2 SUBG  
 ■ Product A V3 SUBG

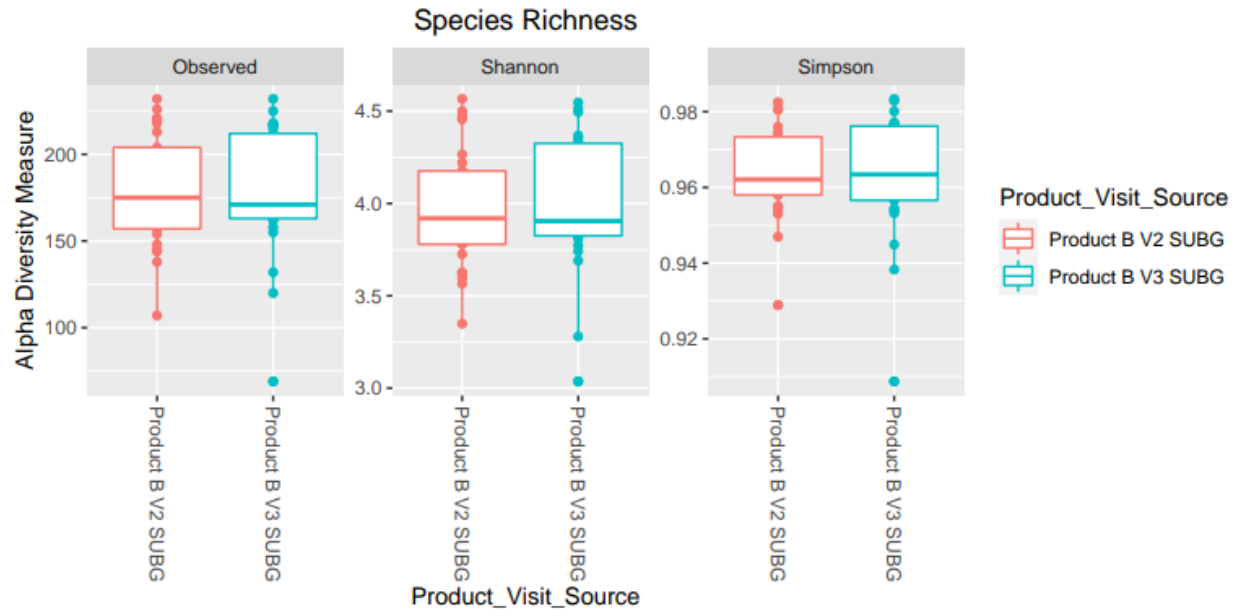


# Comparison 18. Product B V2 SUBG vs Product B V3 SUBG

## 1) Taxonomy bar graphs

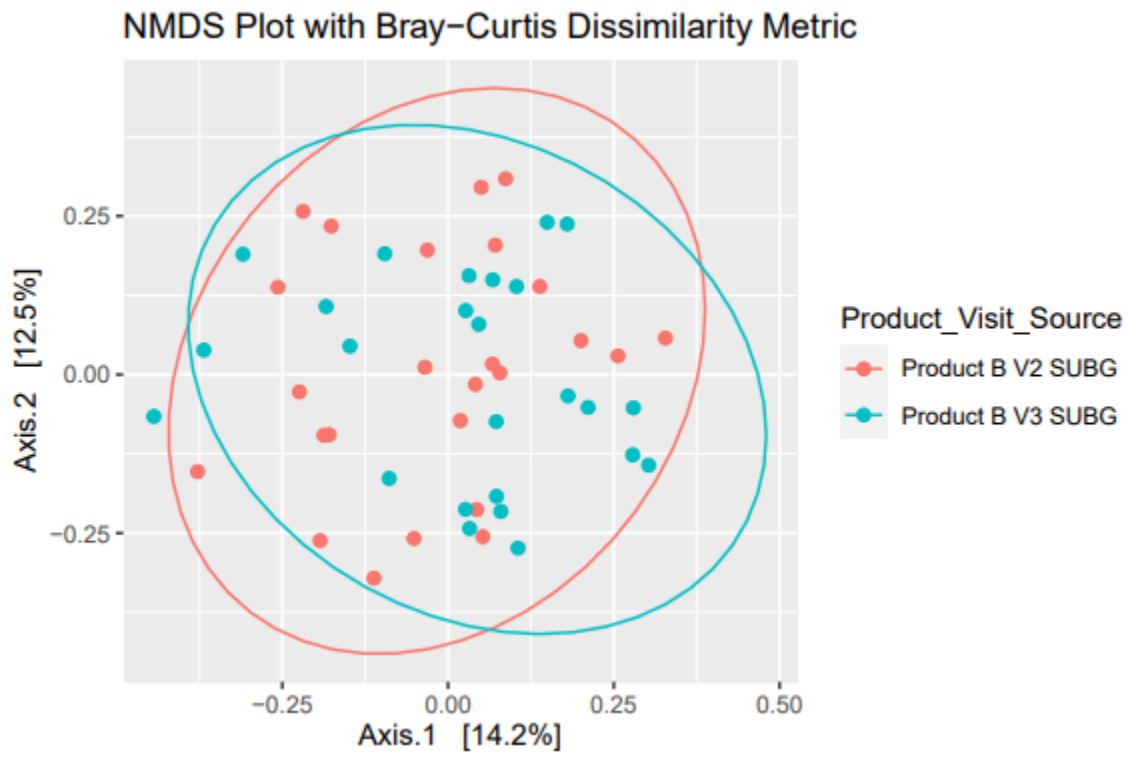


## 2) Alpha



Note: No significant differences

### 3) Beta diversity



Note: No significant differences

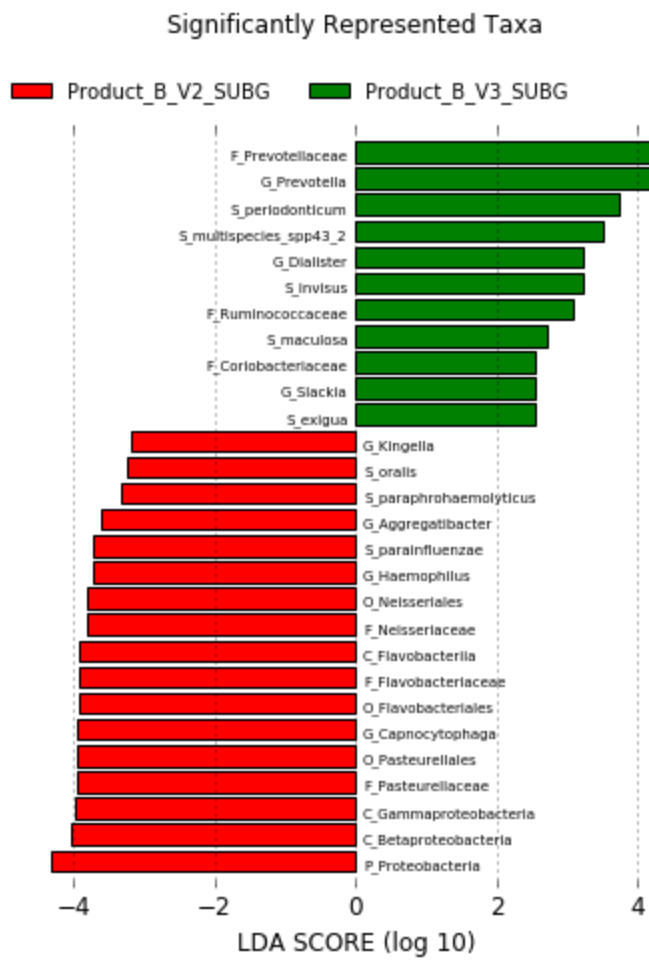
#### 4) Differential abundance

taxon	lfc_(Inter	lfc_Product	se_(Inter	se_Product	W_(Inter	W_Product	p_(Inter	p_Product	q_(Inter	q_Product	diff_(Inte	diff_Prod
Haemophilus parainfluenzae (SP19)	0.731639	-1.46328	0.38845	0.549351	1.883484	-2.66365	0.059635	0.00773	1	1	FALSE	FALSE
Kingella oralis (SP198)	0.6932	-1.3864	0.435041	0.615241	1.593414	-2.25343	0.111067	0.024232	1	1	FALSE	FALSE
Slackia exigua (SP147)	-0.61695	1.233908	0.485739	0.686939	-1.27013	1.796241	0.204037	0.072456	1	1	FALSE	FALSE
Parvimonas sp._HMT_110 (SP129)	0.765143	-1.53029	0.63243	0.894391	1.209846	-1.71098	0.226338	0.087085	1	1	FALSE	FALSE
Aggregatibacter aphrophilus (SP218)	0.602535	-1.20507	0.519036	0.734027	1.160874	-1.64172	0.245693	0.100647	1	1	FALSE	FALSE
Oribacterium asaccharolyticum_parvum	-0.3304	0.660807	0.288407	0.407869	-1.14562	1.620147	0.251954	0.105201	1	1	FALSE	FALSE
Prevotella denticola (SP30)	-0.77218	1.544359	0.727032	1.028179	-1.0621	1.502034	0.288191	0.133088	1	1	FALSE	FALSE
Shuttleworthia satellites (SP268)	-0.5922	1.18441	0.577976	0.817382	-1.02462	1.449029	0.305544	0.14733	1	1	FALSE	FALSE
Ruminococcaceae_[G-1] bacterium_HM	-0.62106	1.242111	0.606253	0.857371	-1.02442	1.448743	0.305639	0.147409	1	1	FALSE	FALSE
Lautropia mirabilis (SP126)	0.488557	-0.97711	0.478416	0.676583	1.021197	-1.44419	0.307161	0.148686	1	1	FALSE	FALSE
Peptostreptococcus stomatis (SP92)	-0.63041	1.260822	0.618029	0.874025	-1.02003	1.442547	0.307712	0.149148	1	1	FALSE	FALSE
Streptococcus sp._HMT_056 (SP276)	0.499236	-0.99847	0.522035	0.738268	0.956327	-1.35245	0.338907	0.176232	1	1	FALSE	FALSE
Ruminococcaceae_[G-2] bacterium_HM	-0.46555	0.931105	0.489111	0.691707	-0.95183	1.346097	0.341182	0.178271	1	1	FALSE	FALSE

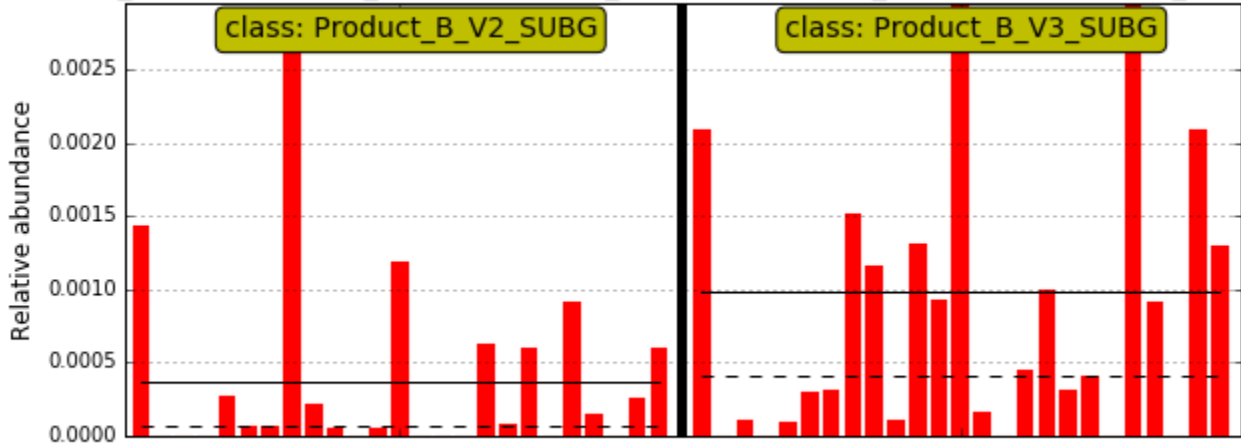
Note: Red, more prevalent in baseline (V2); Green, more prevalent in visit 3, after treatment.



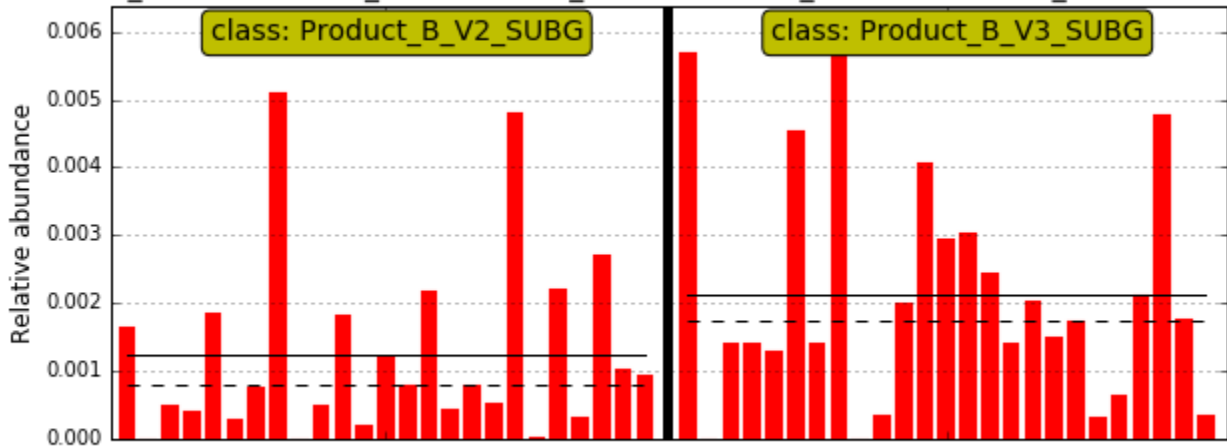
5) Lefse



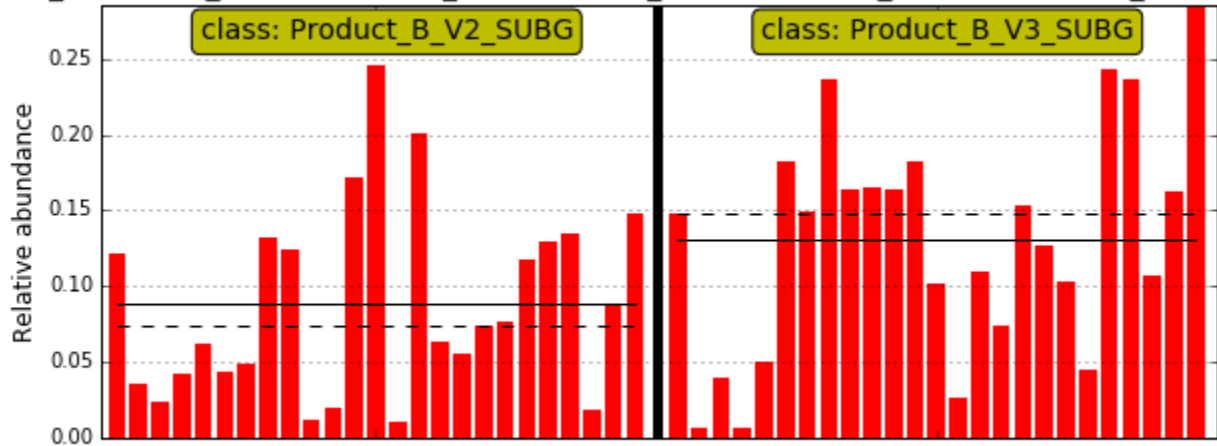
K\_Bacteria.P\_Actinobacteria.C\_Coriobacteriia.O\_Coriobacteriales.F\_Coriobacteriaceae.G\_Slackia.S\_exig



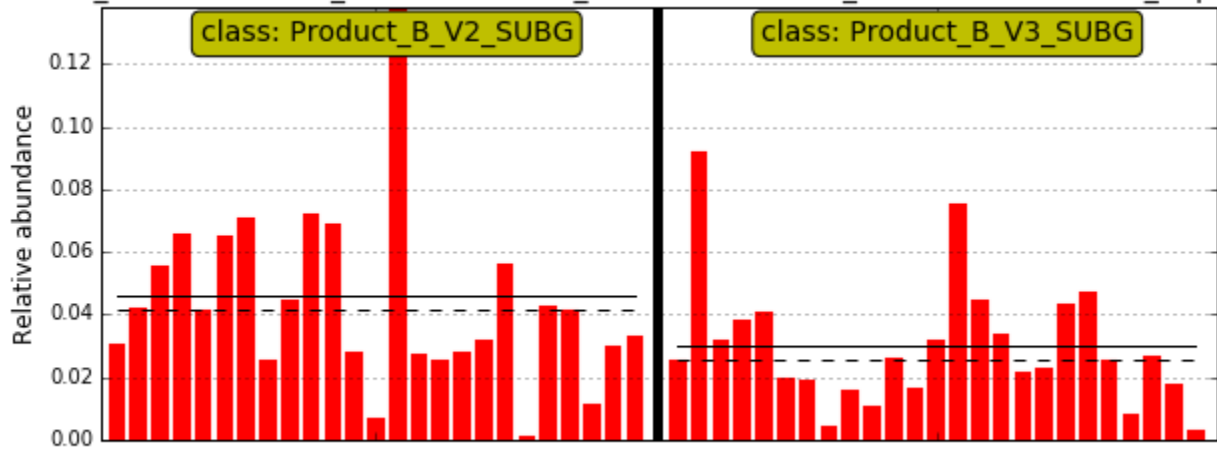
K\_Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Prevotella.S\_maculosi



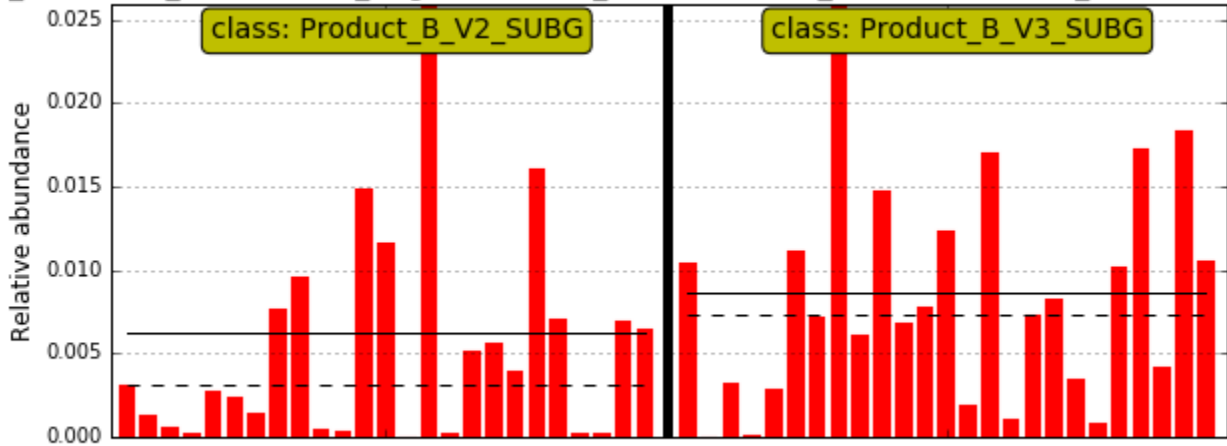
K\_Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Prevotella



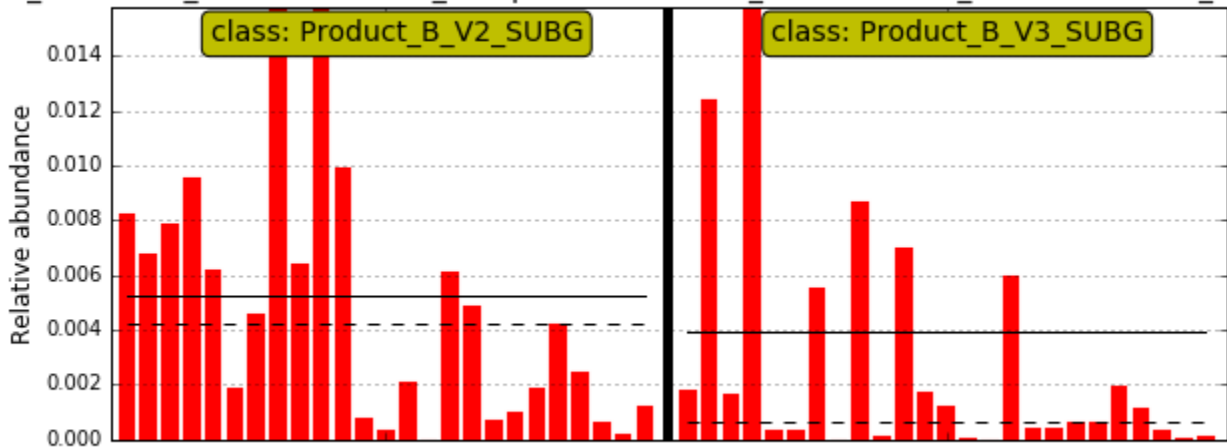
K\_Bacteria.P\_Bacteroidetes.C\_Flavobacteriia.O\_Flavobacteriales.F\_Flavobacteriaceae.G\_Capnocytopha



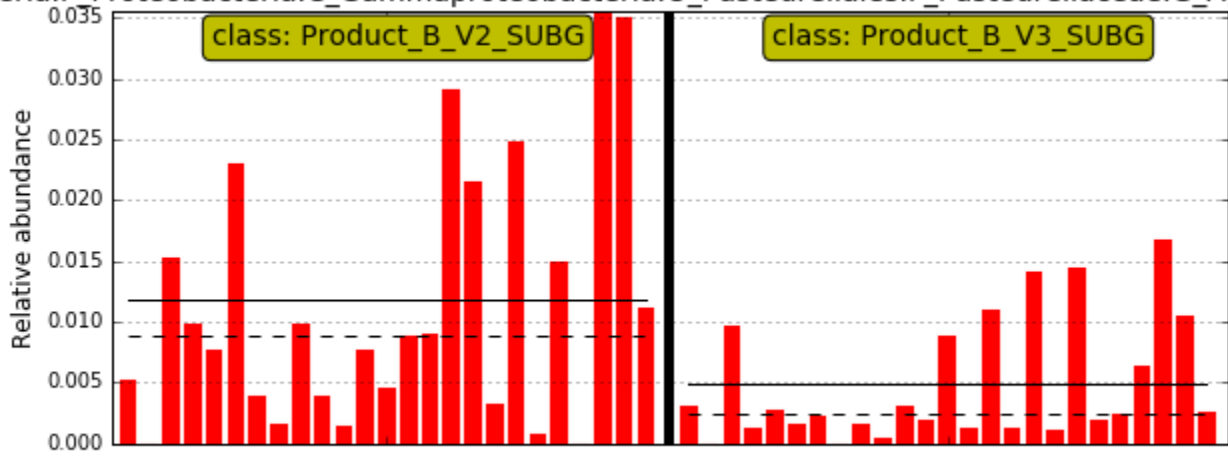
K\_Bacteria.P\_Firmicutes.C\_Negativicutes.O\_Veillonellales.F\_Veillonellaceae.G\_Dialister.S\_invisus



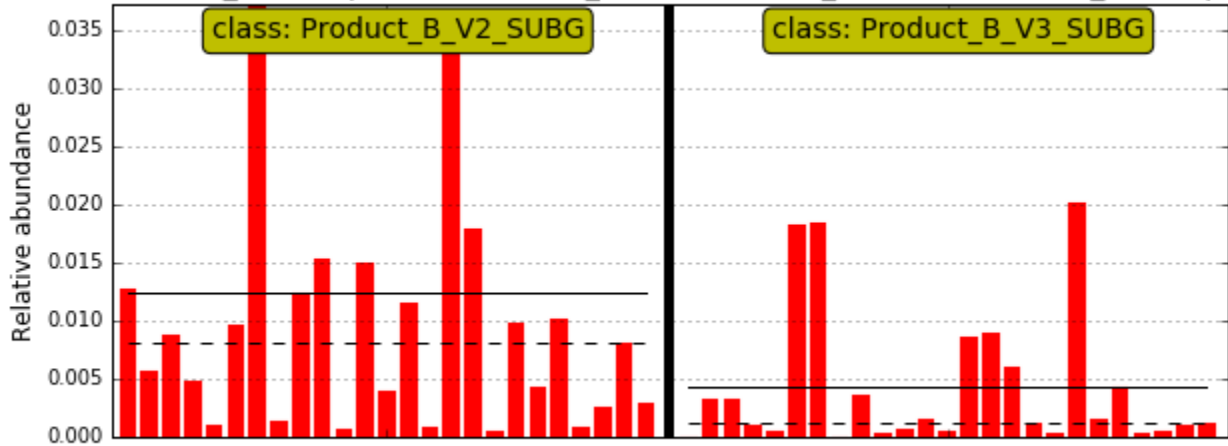
K\_Bacteria.P\_Proteobacteria.C\_Betaproteobacteria.O\_Neisseriales.F\_Neisseriaceae.G\_Kingella



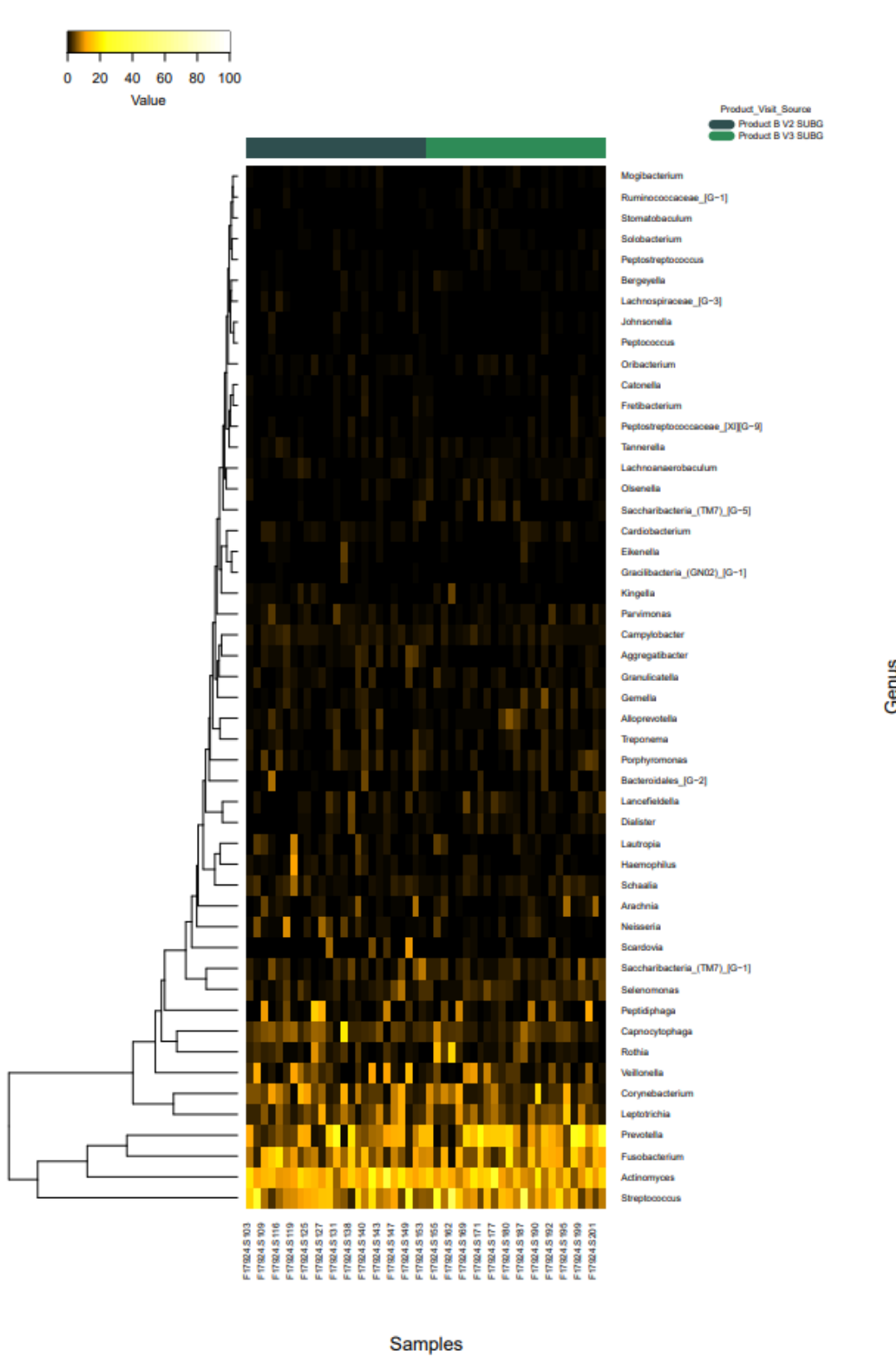
Bacteria.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Aggregatibacter

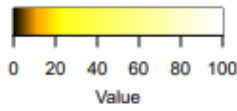


a.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Haemophilus.S\_p

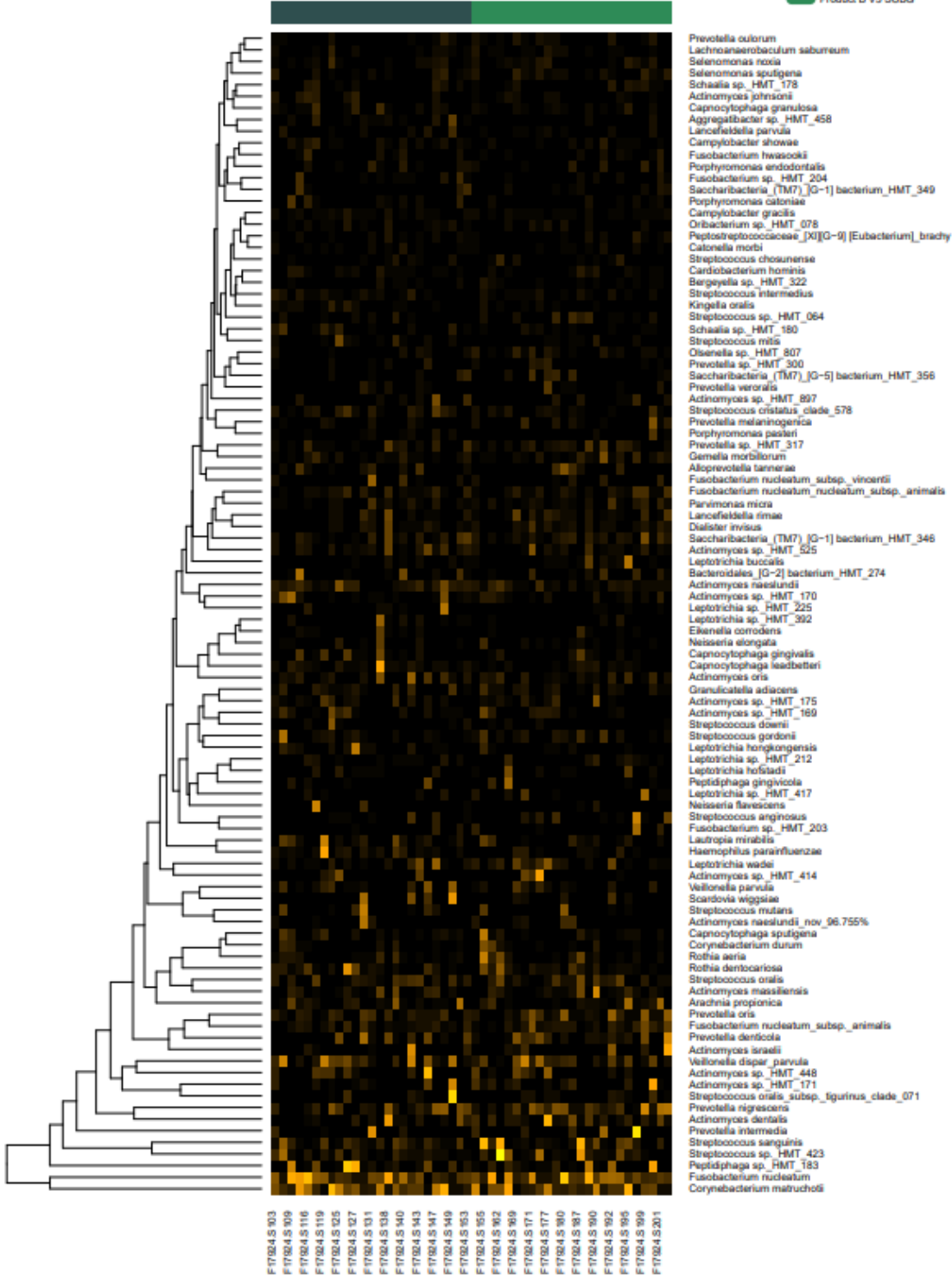


6) Heat map.



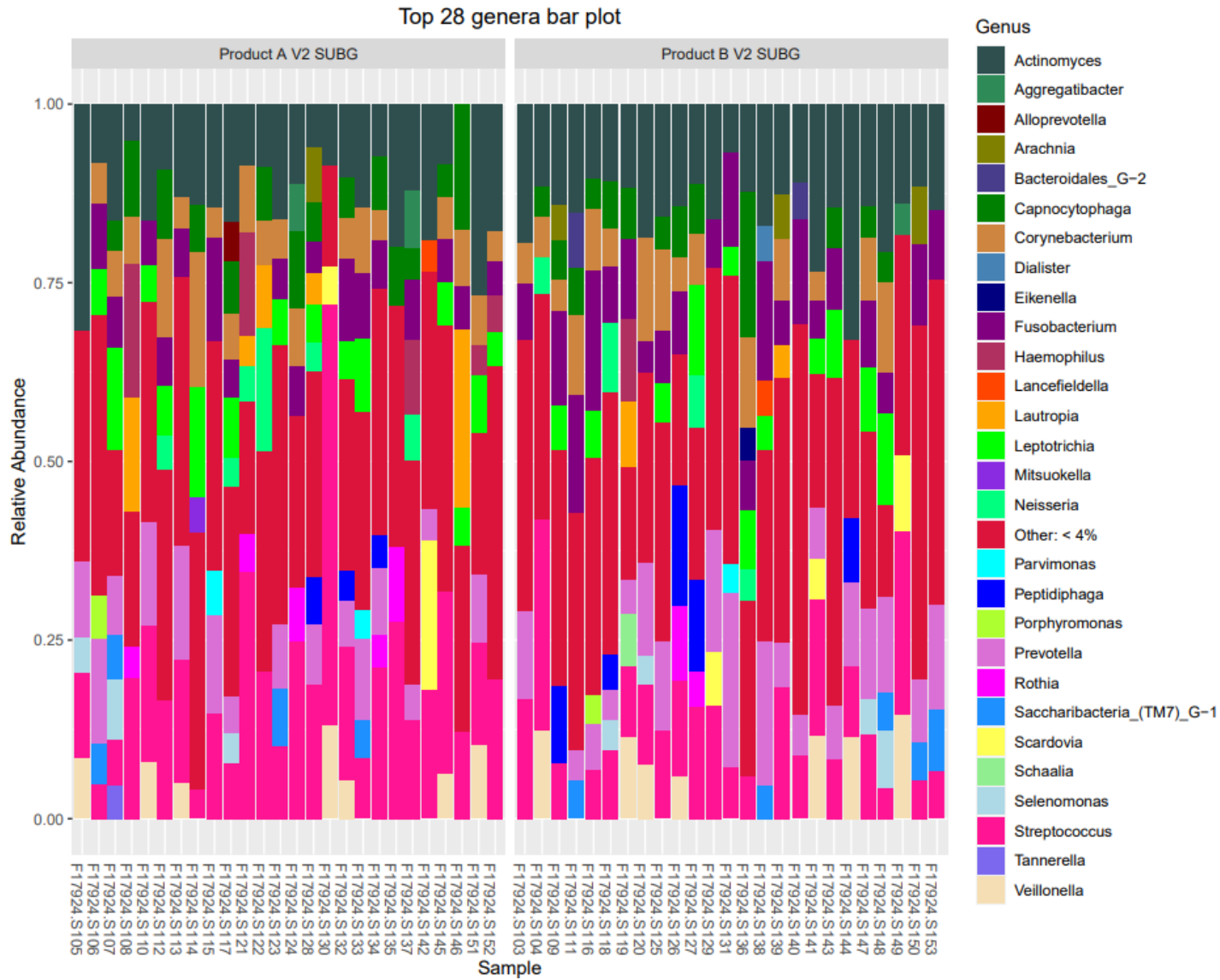


Product\_Visit\_Source  
 Product B V2 SUBG  
 Product B V3 SUBG

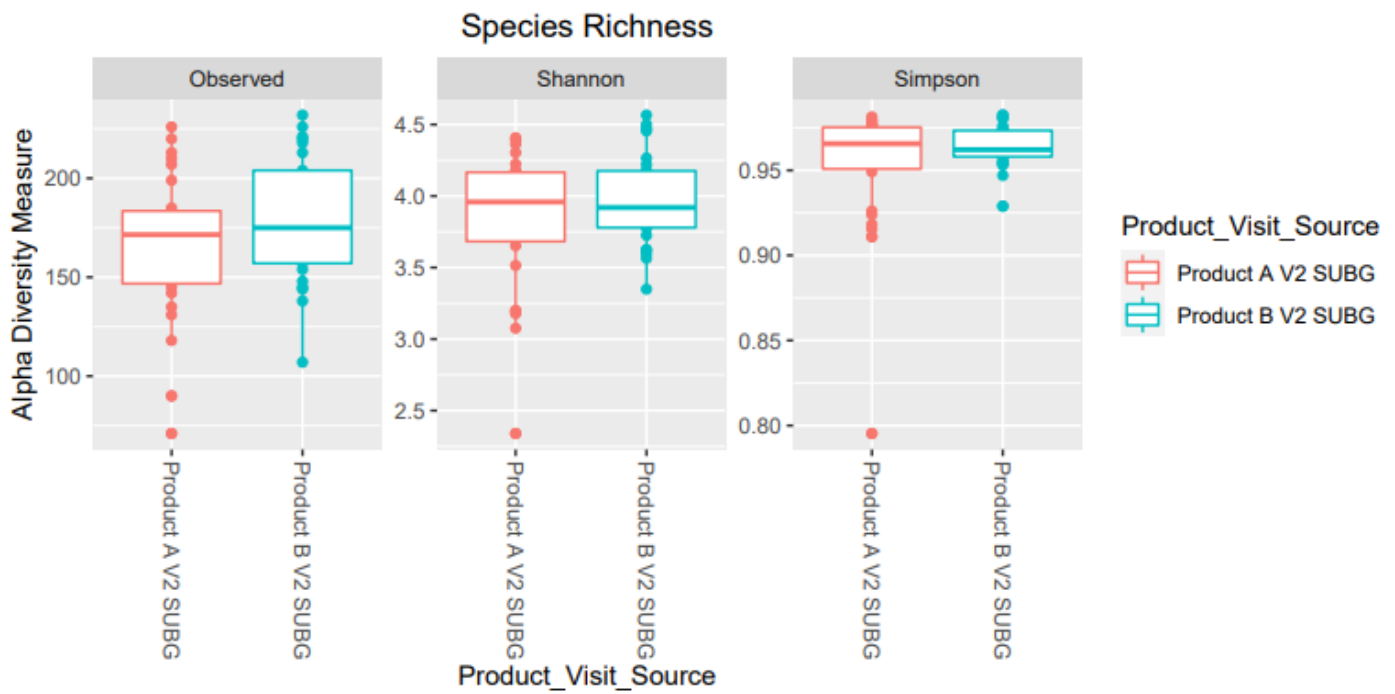


# Comparison 19. Product A V2 SUBG vs Product B V2 SUBG

## 1) Taxonomy bar graphs



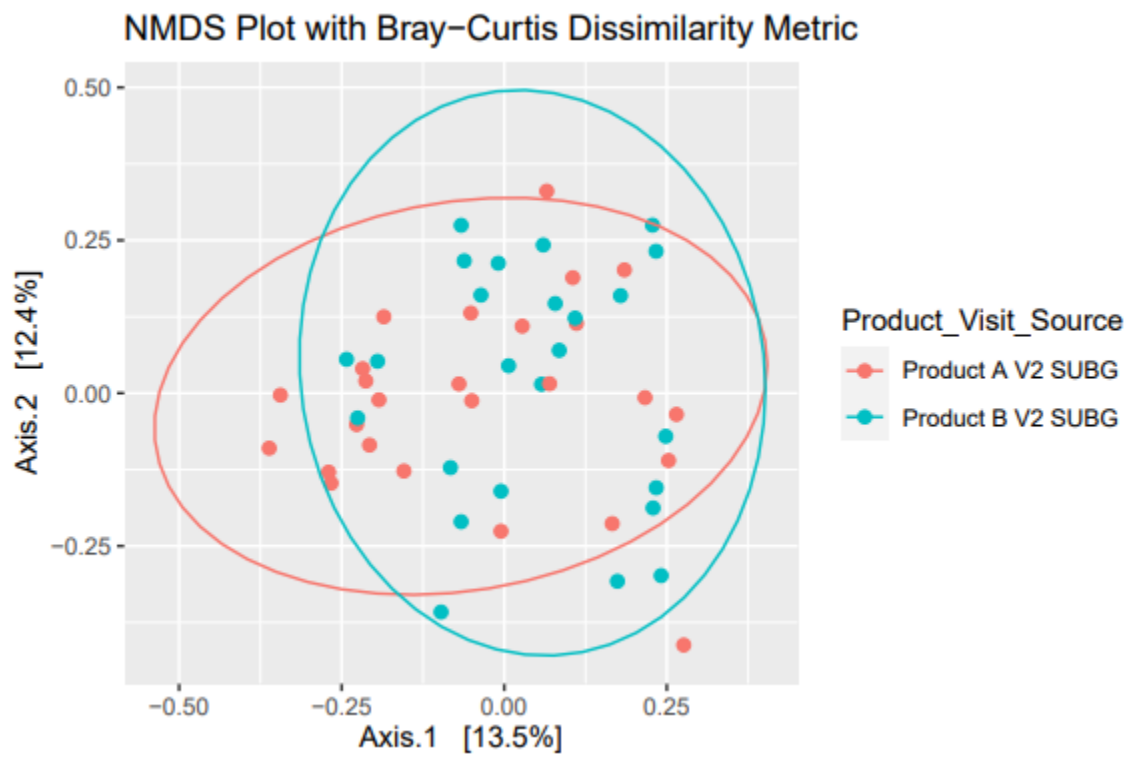
## 2) Alpha



Note: No significant differences



### 3) Beta diversity



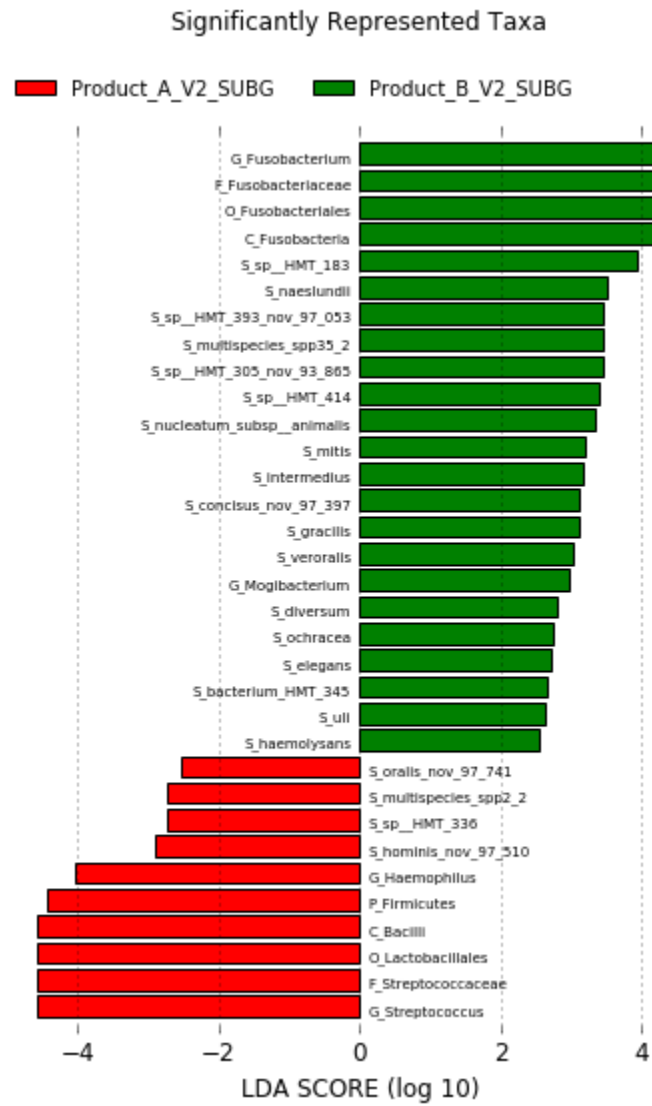
Note: No significant differences

#### 4) Differential abundance

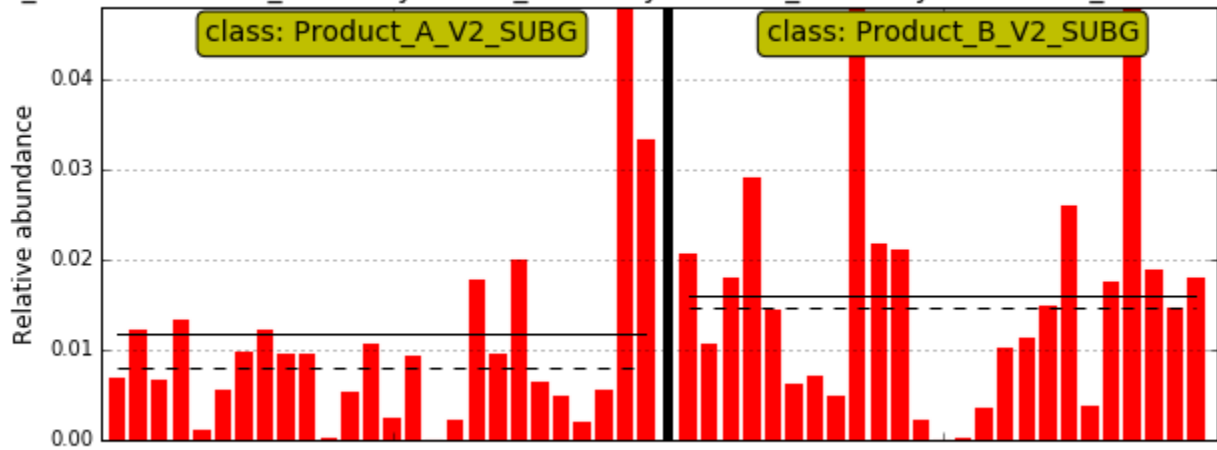
taxon	lfc_Interc	lfc_Product	se_Interc	se_Product	W_Interc	W_Product	p_Interc	p_Product	q_Interc	q_Product	diff_Interc	diff_Product
Kingella oralis nov_97.741% (SPN664)	0.946101	-1.92674	0.398236	0.569438	2.375728	-3.38358	0.017514	0.000715	1	0.232528	FALSE	FALSE
Prevotella veroralis (SP110)	-1.15068	2.350703	0.545667	0.77998	-2.10877	3.0138	0.034965	0.00258	1	0.835914	FALSE	FALSE
Fusobacterium nucleatum_nucleatum_subsp._animalis (SPP35)	-0.7945	1.624086	0.474767	0.678728	-1.67345	2.392836	0.094238	0.016719	1	1	FALSE	FALSE
Capnocytophaga sp._HMT_336 (SP51)	0.928023	-1.88986	0.592279	0.846547	1.566867	-2.23243	0.117146	0.025586	1	1	FALSE	FALSE
Fusobacterium nucleatum_subsp._animalis (SP23)	-0.67035	1.370818	0.472634	0.675682	-1.41833	2.02879	0.156096	0.04248	1	1	FALSE	FALSE
Absconditabacteria_(SR1)_[G-1]_bacterium_HMT_345 (SP291)	-0.71341	1.458663	0.510119	0.729214	-1.39852	2.000322	0.161958	0.045466	1	1	FALSE	FALSE
Porphyromonas sp._HMT_275 (SP363)	0.663004	-1.34922	0.472345	0.67527	1.403643	-1.99805	0.160425	0.045712	1	1	FALSE	FALSE
Selenomonas sp._HMT_892_nov_97.041% (SPN676)	0.521341	-1.06023	0.383287	0.54809	1.360184	-1.93441	0.173772	0.053063	1	1	FALSE	FALSE
Peptidiphaga sp._HMT_183 (SP149)	-0.83687	1.710517	0.625708	0.894288	-1.33747	1.912714	0.181069	0.055785	1	1	FALSE	FALSE
Gemella haemolysans (SP8)	-0.6196	1.267293	0.463803	0.663071	-1.33592	1.911248	0.181577	0.055973	1	1	FALSE	FALSE

Note: Red more prevalent in A; Green, more prevalent in B

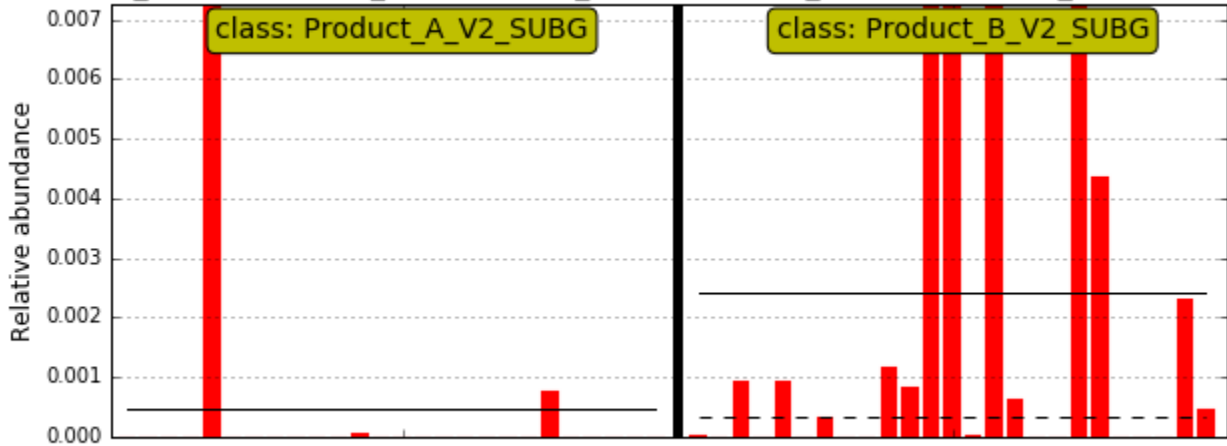
5) Lefse



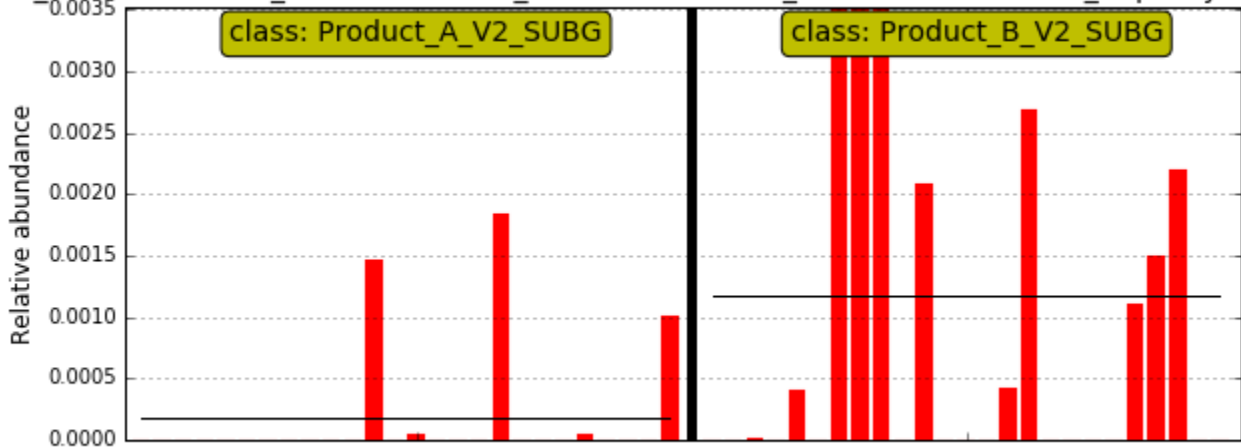
cteria.P\_Actinobacteria.C\_Actinomycetia.O\_Actinomycetales.F\_Actinomycetaceae.G\_Actinomyces.S\_na



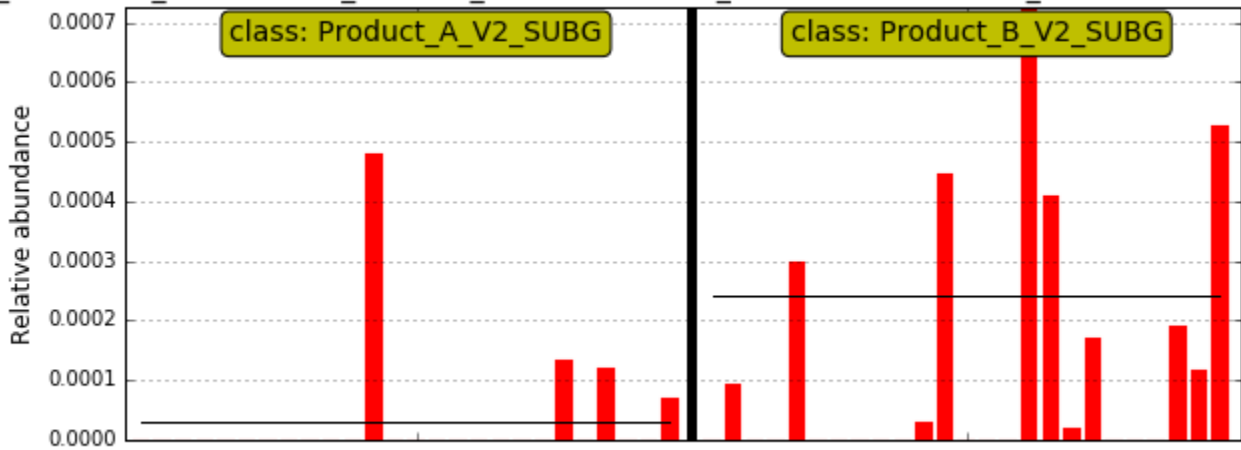
K\_Bacteria.P\_Bacteroidetes.C\_Bacteroidia.O\_Bacteroidales.F\_Prevotellaceae.G\_Prevotella.S\_veroralis



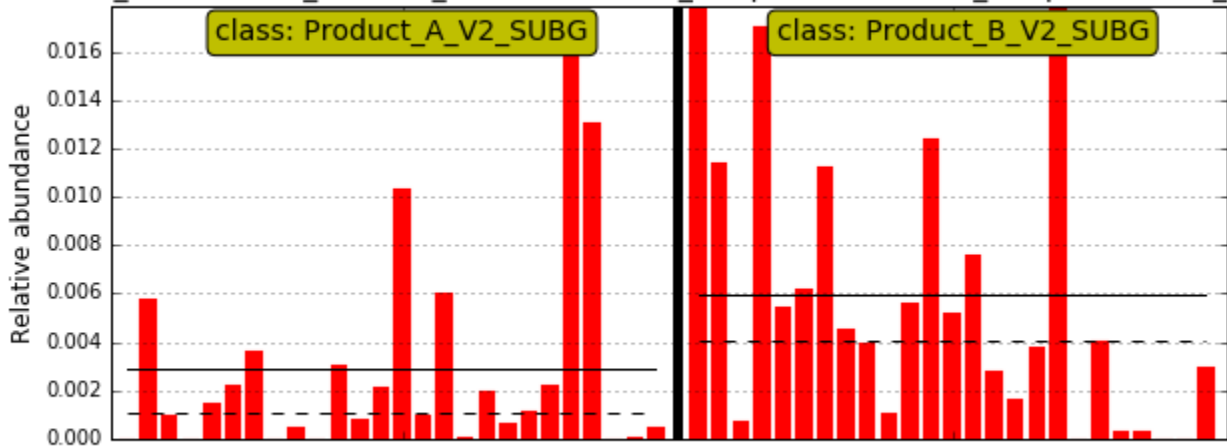
teria.P\_Bacteroidetes.C\_Flavobacteriia.O\_Flavobacteriales.F\_Flavobacteriaceae.G\_Capnocytophaga.S\_c



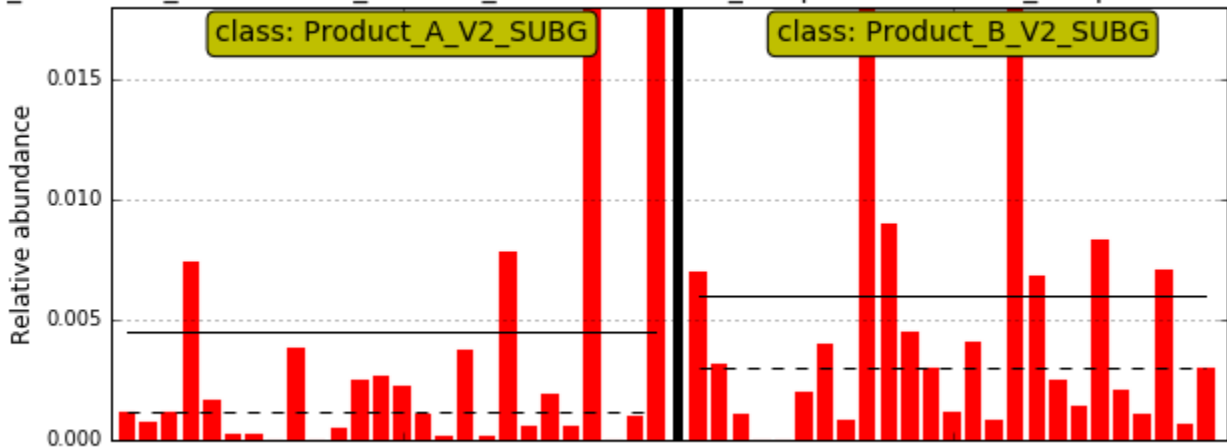
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Carnobacteriaceae.G\_Granulicatella.S\_elegans



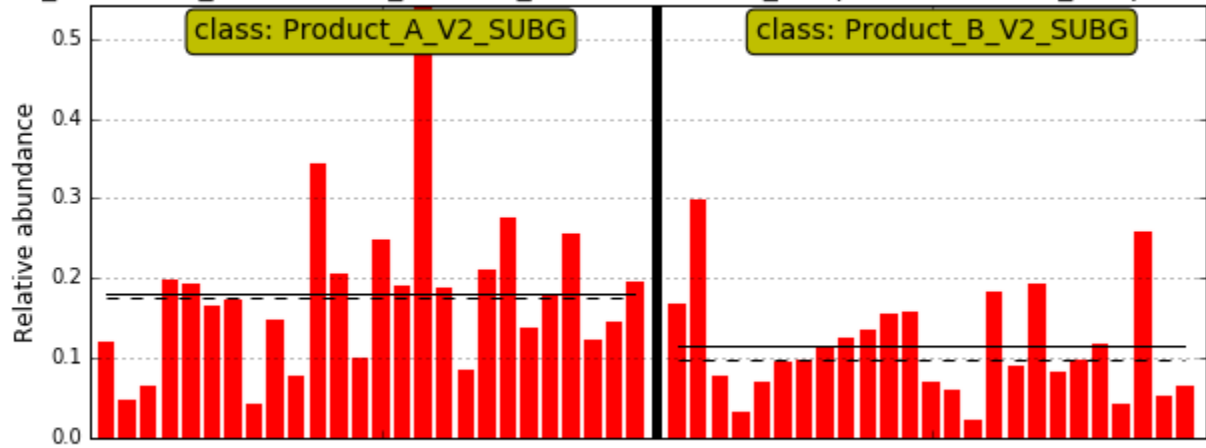
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Streptococcaceae.G\_Streptococcus.S\_intermedi



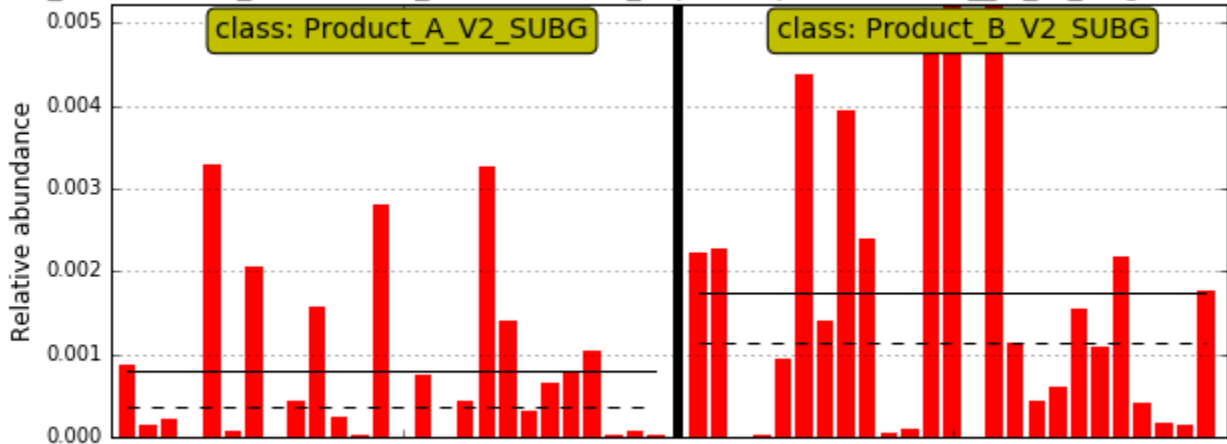
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Streptococcaceae.G\_Streptococcus.S\_mitis



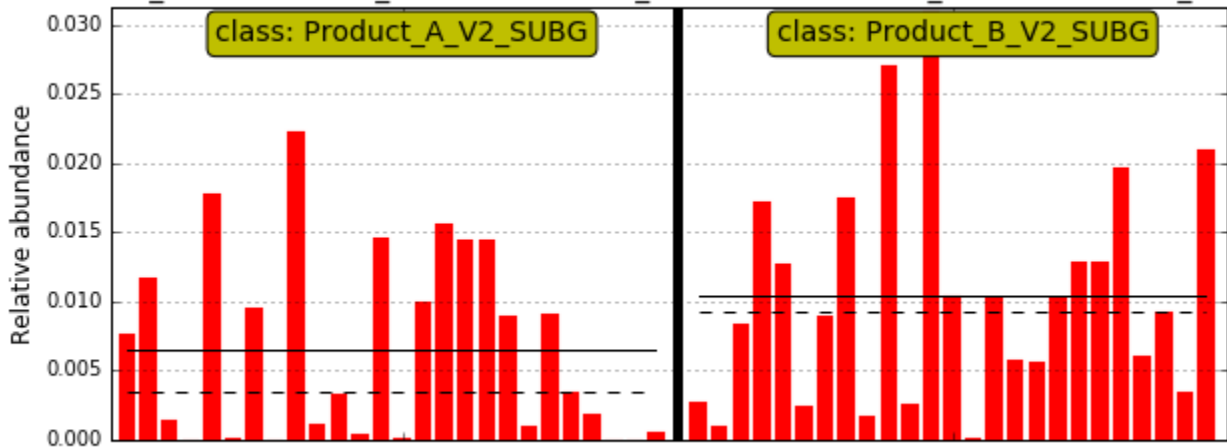
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Streptococcaceae.G\_Streptococcus



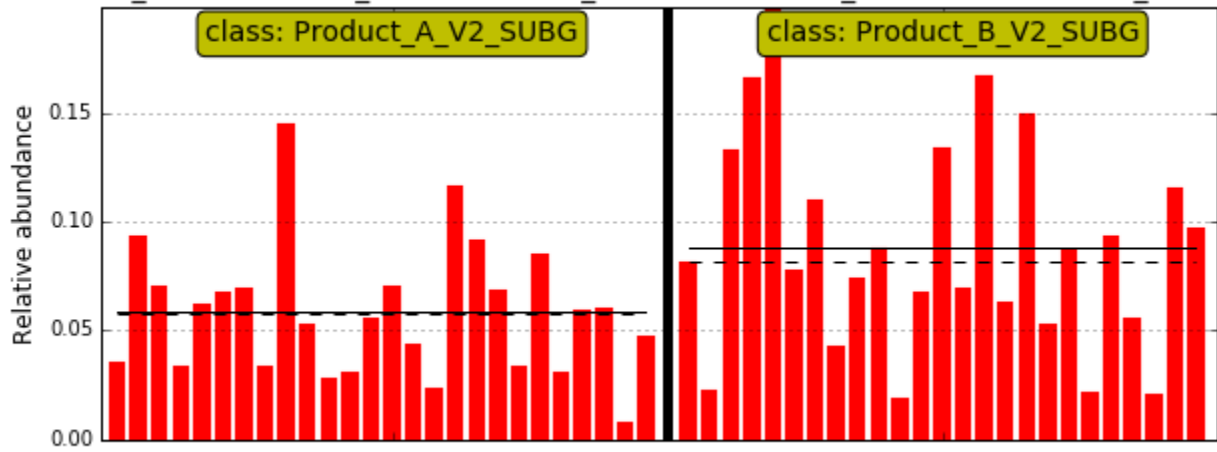
acteria.P\_Firmicutes.C\_Clostridia.O\_Clostridiales.F\_Peptostreptococcaceae\_XI\_G\_Mogibacterium.S\_div



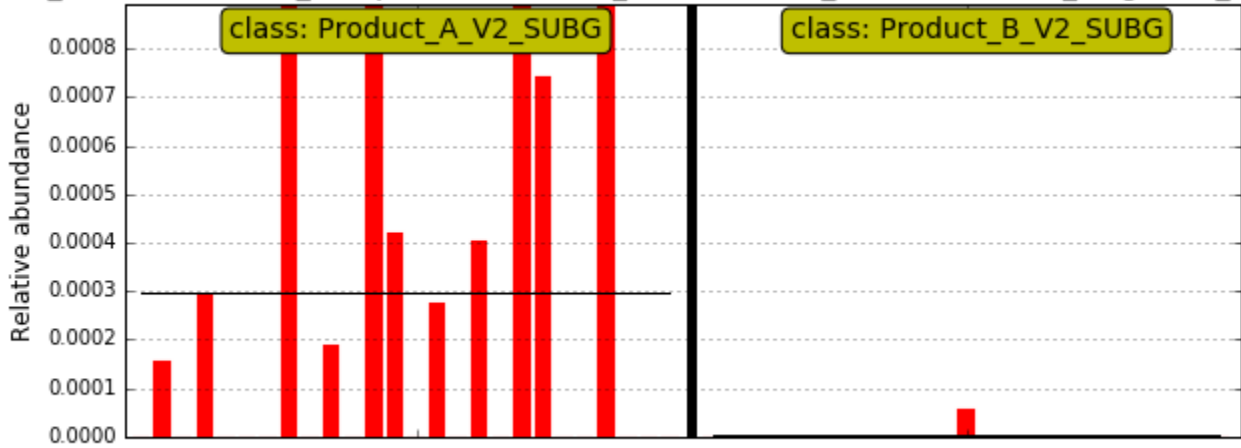
\_Fusobacteria.C\_Fusobacteria.O\_Fusobacteriales.F\_Fusobacteriaceae.G\_Fusobacterium.S\_nucleatum\_s



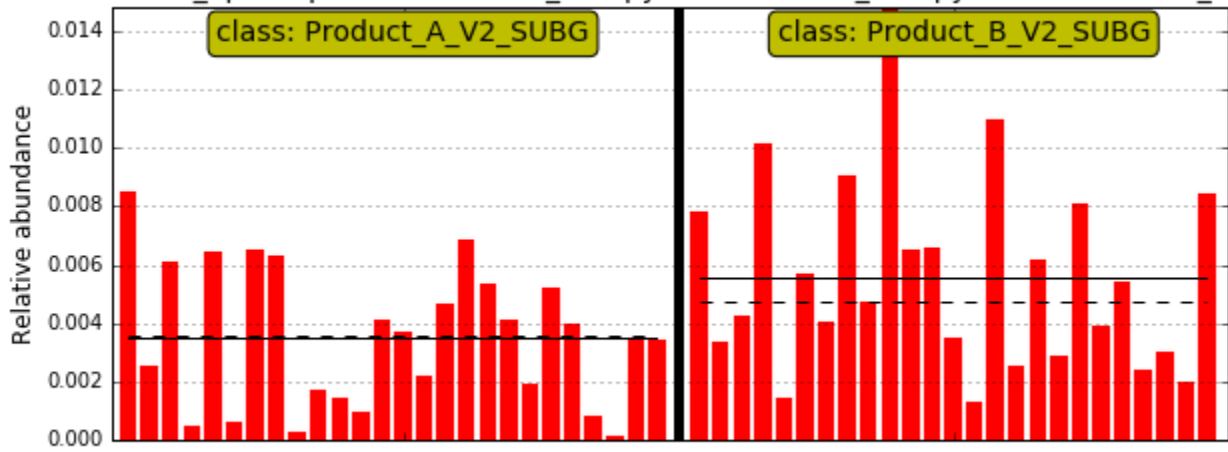
K\_Bacteria.P\_Fusobacteria.C\_Fusobacteria.O\_Fusobacteriales.F\_Fusobacteriaceae.G\_Fusobacterium



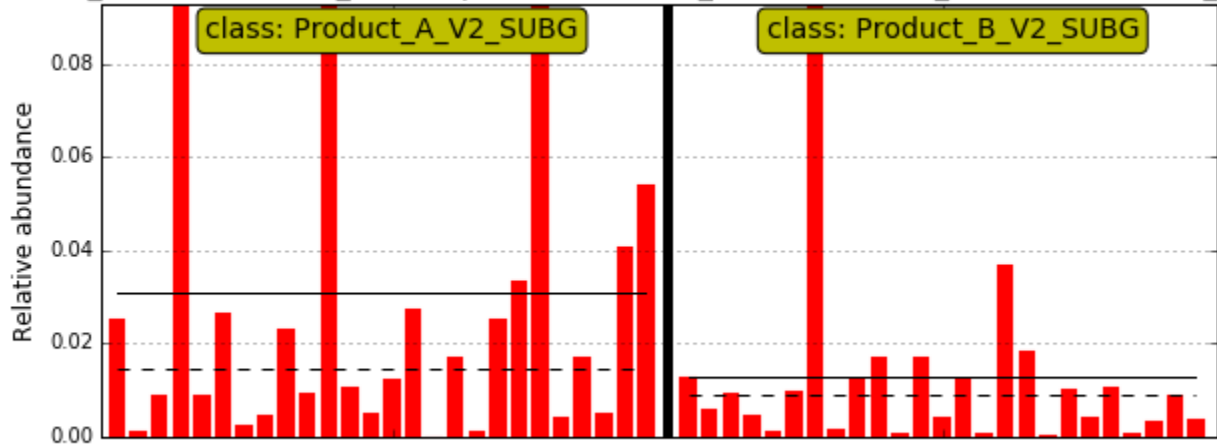
cteria.P\_Proteobacteria.C\_Betaproteobacteria.O\_Neisseriales.F\_Neisseriaceae.G\_Kingella.S\_oralis\_nov\_



P\_Proteobacteria.C\_Epsilonproteobacteria.O\_Campylobacteriales.F\_Campylobacteraceae.G\_Campyloba

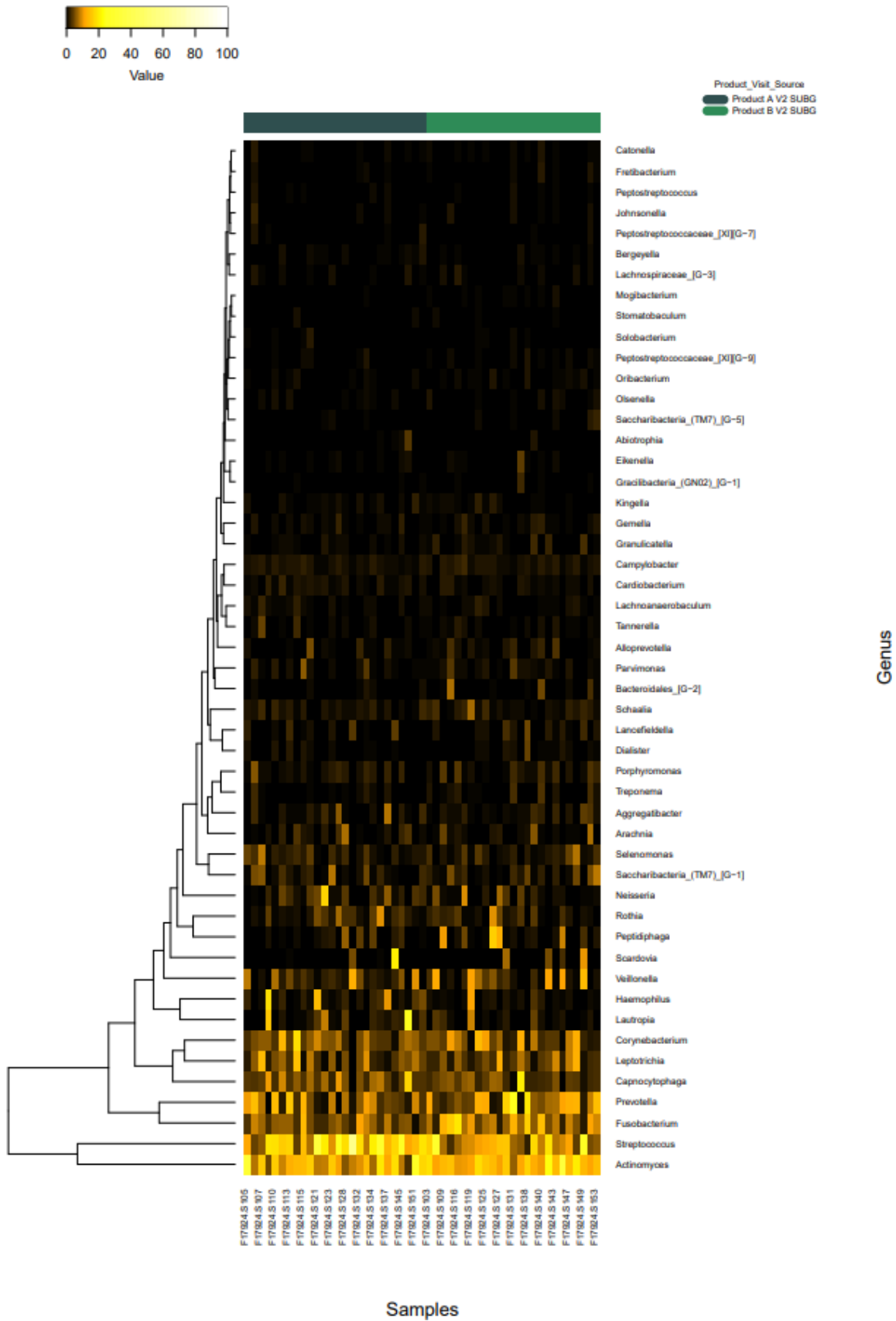


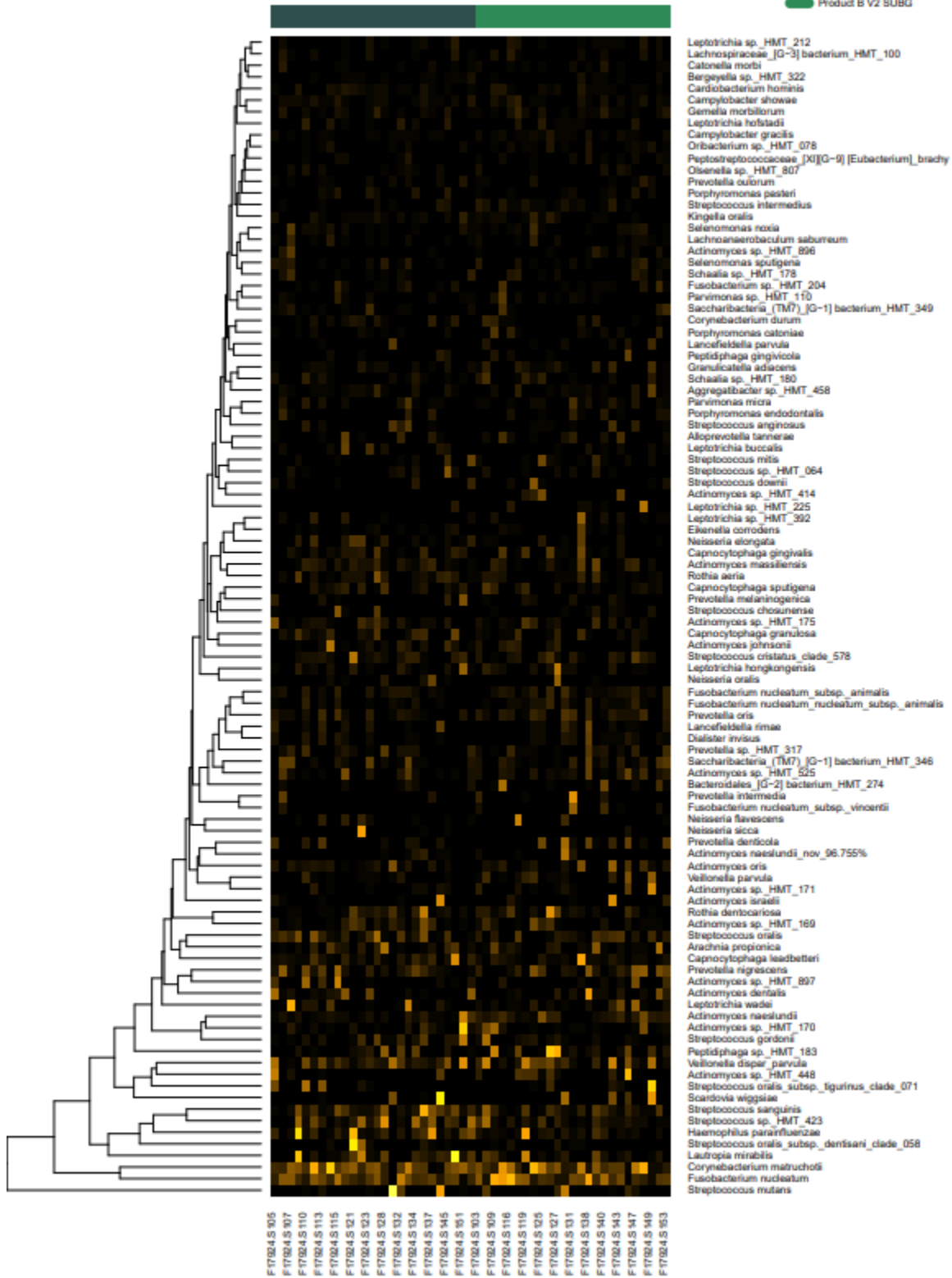
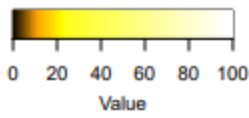
<\_Bacteria.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Haemophi





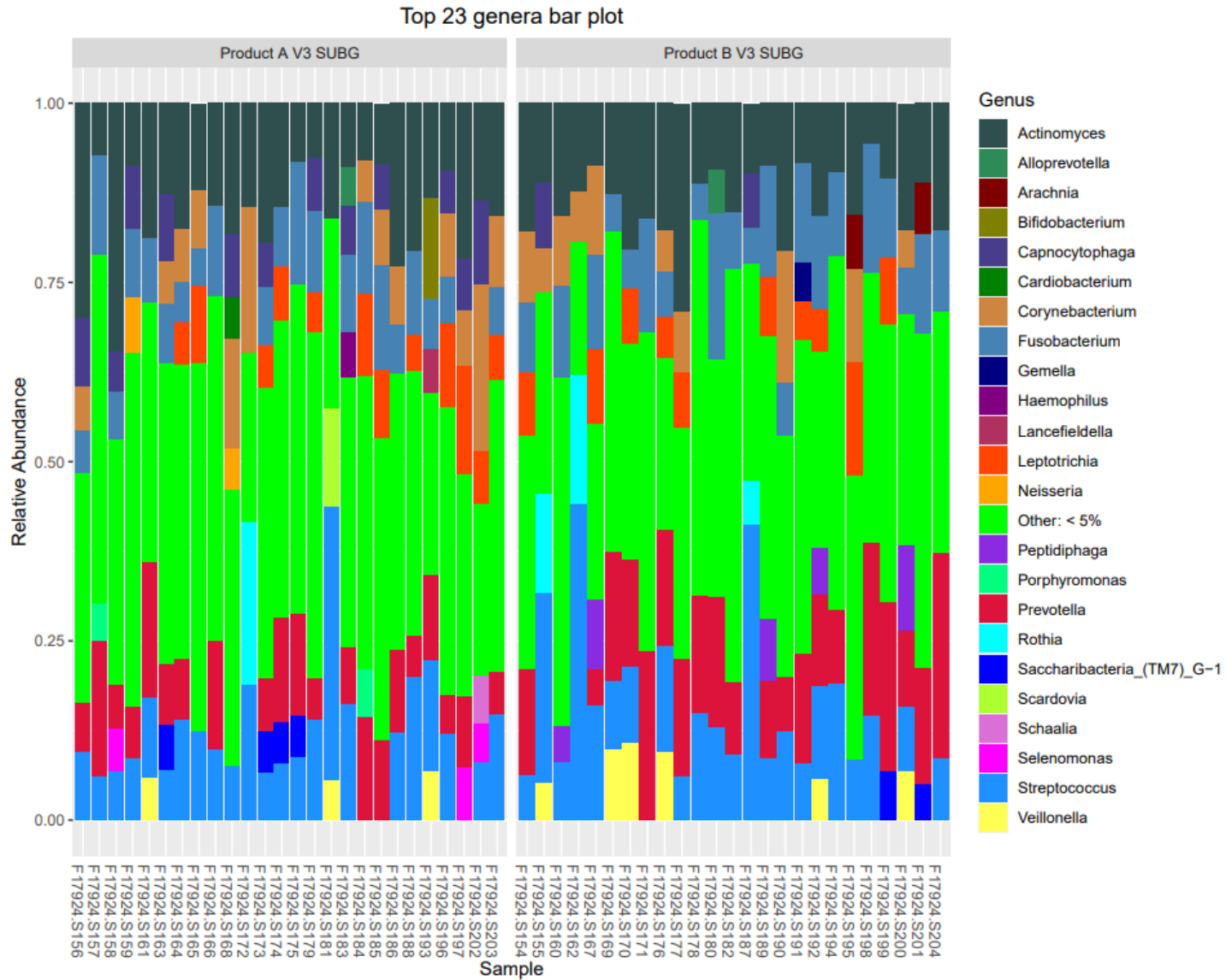
6) Heat map.



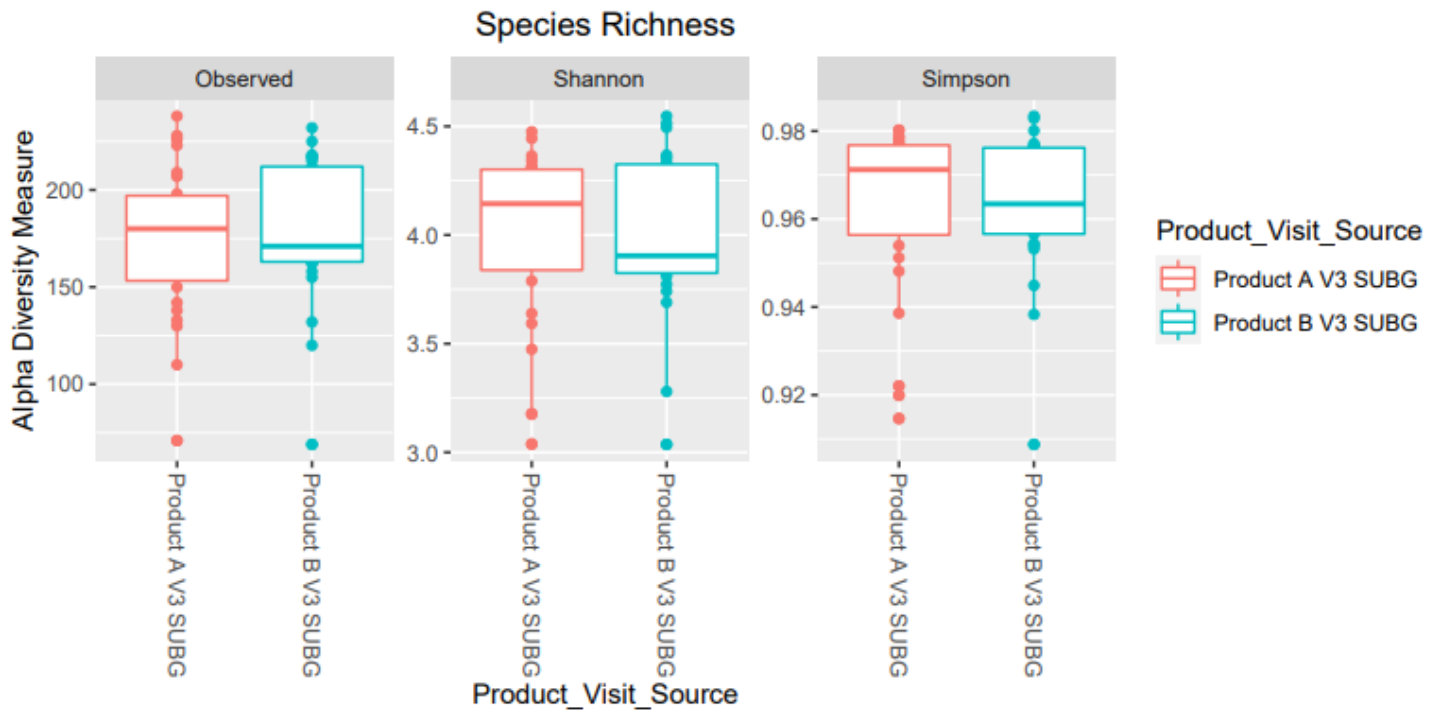


# Comparison 20. Product A V3 SUBG vs Product B V3 SUBG

## 1) Taxonomy bar graphs

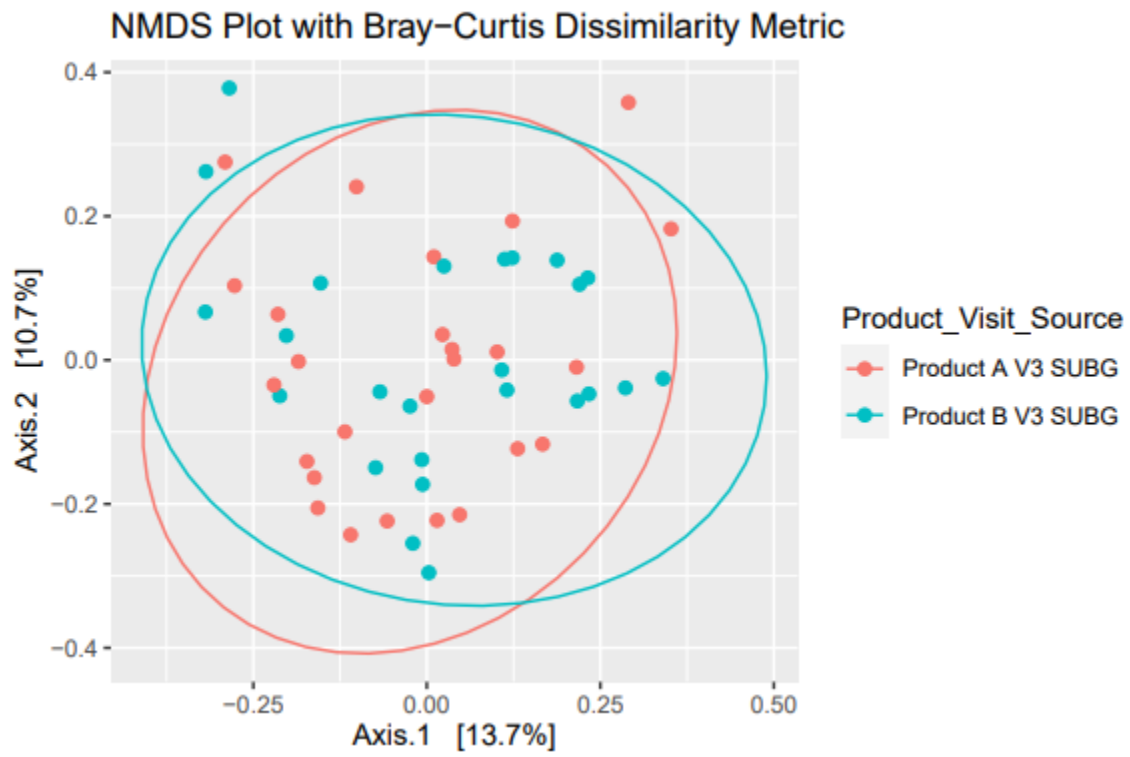


## 2) Alpha



Note: No significant differences

### 3) Beta diversity



Note: No significant differences

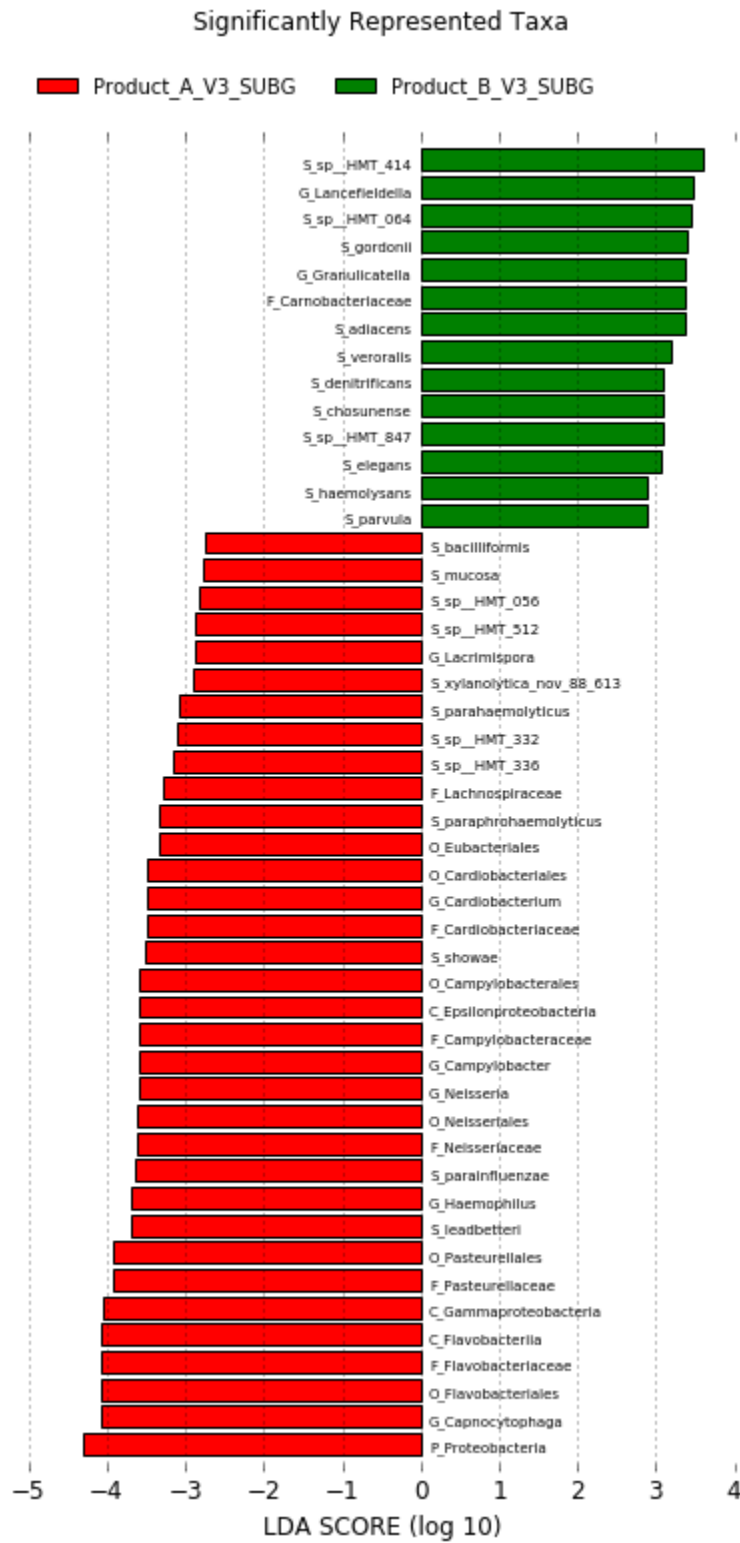
#### 4) Differential abundance

taxon	lfc_(Interc	lfc_Produ	se_(Interc	se_Produ	W_(Interc	W_Produ	p_(Interc	p_Produ	q_(Interc	q_Produ	diff_(Inte	diff_Produ
Gemella haemolysans (SP8)	-1.16912	2.320376	0.435045	0.621436	-2.68736	3.733896	0.007202	0.000189	1	0.060898	FALSE	FALSE
Streptococcus sp._HMT_064 (SP305)	-1.22476	2.433874	0.58359	0.833598	-2.09867	2.919722	0.035846	0.003503	1	1	FALSE	FALSE
Capnocytophaga sp._HMT_336 (SP51)	1.074172	-2.25595	0.5603	0.800334	1.917136	-2.81876	0.055221	0.004821	1	1	FALSE	FALSE
Prevotella veroralis (SP110)	-1.11563	2.211242	0.556744	0.795254	-2.00384	2.78055	0.045087	0.005427	1	1	FALSE	FALSE
Streptococcus sp._HMT_056 (SP276)	0.905471	-1.9118	0.545506	0.779203	1.659875	-2.45353	0.09694	0.014146	1	1	FALSE	FALSE
Campylobacter showae (SP204)	0.749363	-1.59334	0.464472	0.663465	1.613365	-2.40154	0.106665	0.016326	1	1	FALSE	FALSE
Neisseria mucosa (SP300)	0.713819	-1.52083	0.470119	0.671531	1.51838	-2.26472	0.128919	0.02353	1	1	FALSE	FALSE
Lacrimispora xylanolytica_nov_88.613% (SPN382)	0.87696	-1.85364	0.591319	0.844637	1.483057	-2.1946	0.138059	0.028193	1	1	FALSE	FALSE
Capnocytophaga sp._HMT_332 (SP49)	0.805904	-1.70868	0.54691	0.781208	1.47356	-2.18723	0.1406	0.028726	1	1	FALSE	FALSE
Haemophilus parainfluenzae (SP19)	0.65456	-1.39994	0.455255	0.6503	1.437789	-2.15276	0.150494	0.031338	1	1	FALSE	FALSE
Aggregatibacter sp._HMT_512 (SP314)	0.606327	-1.30154	0.436958	0.624168	1.387607	-2.08525	0.165257	0.037047	1	1	FALSE	FALSE
Granulicatella adiacens (SP134)	-0.5003	0.955968	0.322265	0.460354	-1.55244	2.076595	0.120556	0.037839	1	1	FALSE	FALSE
Haemophilus parahaemolyticus (SP148)	0.49774	-1.08003	0.365924	0.522712	1.36023	-2.0662	0.173757	0.038809	1	1	FALSE	FALSE
Treponema socranskii (SP84)	0.617351	-1.32403	0.455332	0.650411	1.355827	-2.03569	0.175154	0.041782	1	1	FALSE	FALSE
Streptococcus gordonii (SP171)	-0.75193	1.469303	0.51473	0.735247	-1.46083	1.998381	0.144063	0.045675	1	1	FALSE	FALSE
Neisseria bacilliformis (SP447)	0.691647	-1.4756	0.520528	0.743528	1.328741	-1.98459	0.183933	0.04719	1	1	FALSE	FALSE
Actinomyces sp._HMT_414 (SP61)	-0.78336	1.533411	0.541176	0.773019	-1.44751	1.983665	0.147755	0.047293	1	1	FALSE	FALSE
Kingella oralis (SP198)	0.602854	-1.29446	0.458878	0.655475	1.313758	-1.97484	0.188928	0.048286	1	1	FALSE	FALSE
Streptococcus chosunense (SP133)	-0.80719	1.582029	0.563007	0.8042	-1.43371	1.967209	0.151655	0.049159	1	1	FALSE	FALSE
Capnocytophaga leadbetteri (SP89)	0.615632	-1.32053	0.474118	0.677243	1.298478	-1.94986	0.194123	0.051193	1	1	FALSE	FALSE
Ottowia sp._HMT_894 (SP249)	0.699172	-1.49095	0.542139	0.774395	1.289654	-1.92531	0.197171	0.054191	1	1	FALSE	FALSE

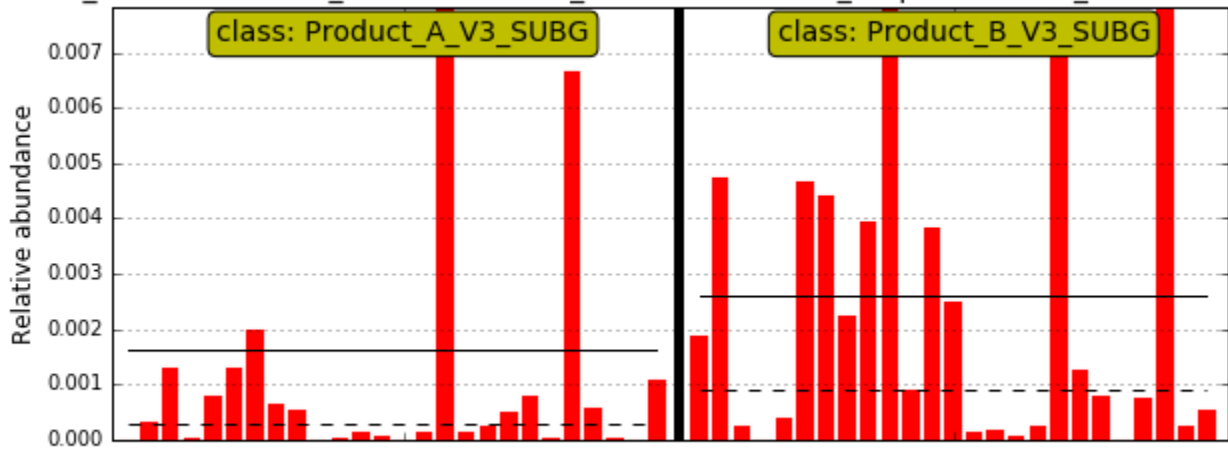
Green, more abundant in B

Red, more abundant in A

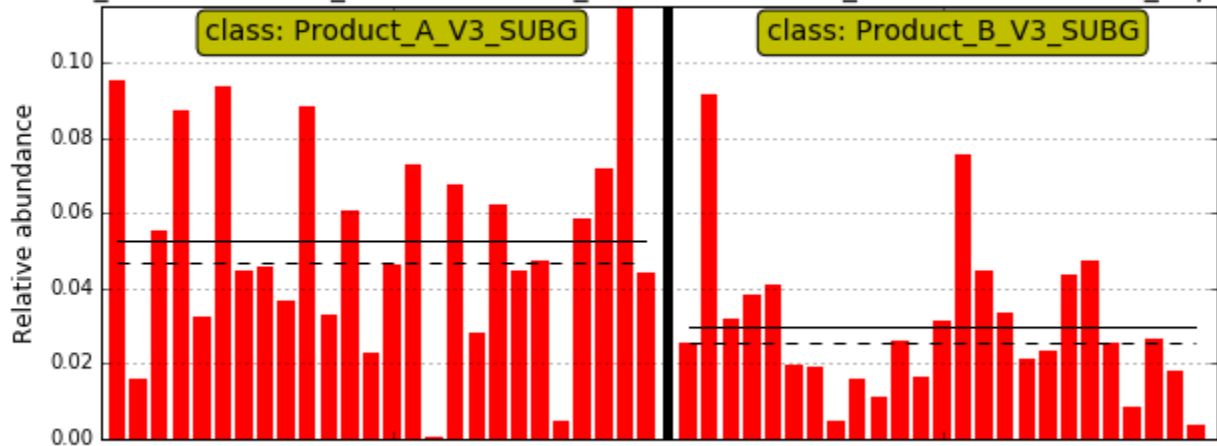
5) Lefse



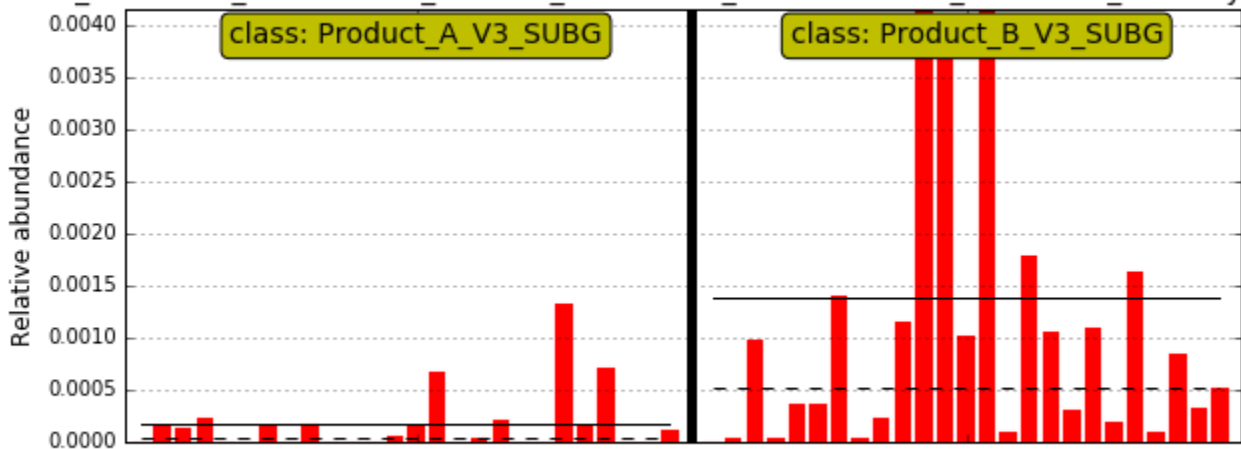
\_Bacteria.P\_Actinobacteria.C\_Coriobacteriia.O\_Coriobacteriales.F\_Atopobiaceae.G\_Lancefieldella.S\_par



K\_Bacteria.P\_Bacteroidetes.C\_Flavobacteriia.O\_Flavobacteriales.F\_Flavobacteriaceae.G\_Capnocytopha

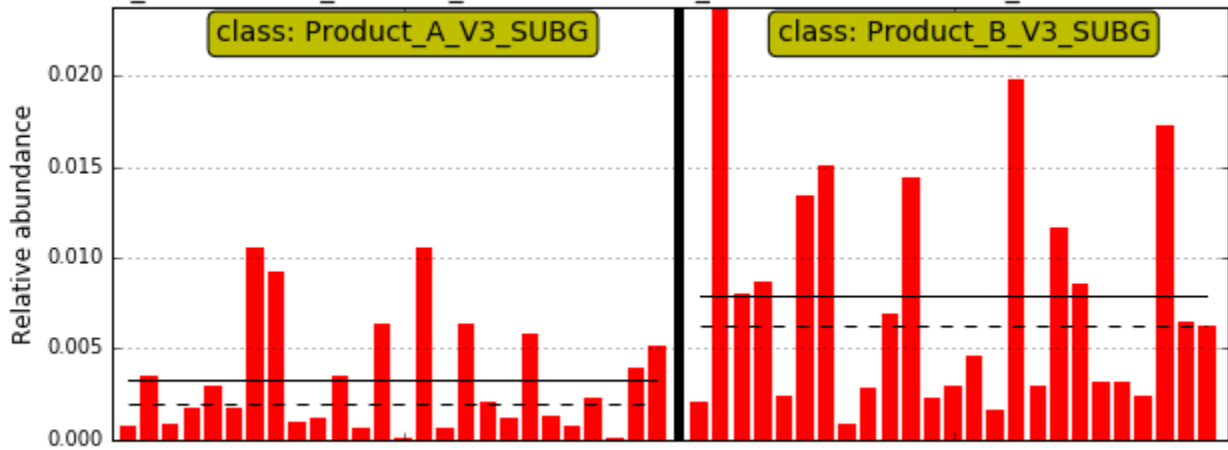


K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Bacillales.F\_Gemellaceae.G\_Gemella.S\_haemolysans

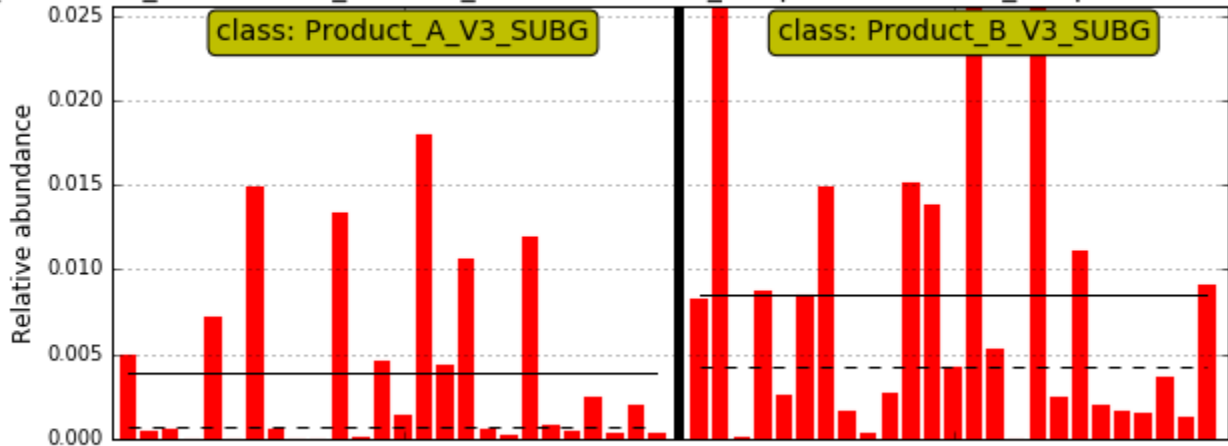




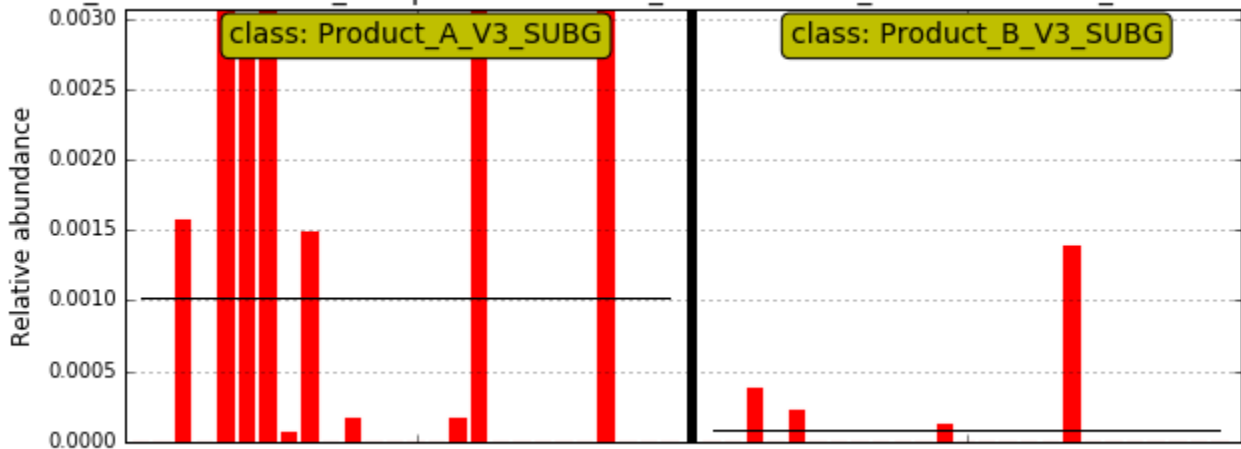
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Carnobacteriaceae.G\_Granulicatella.S\_adiacen:



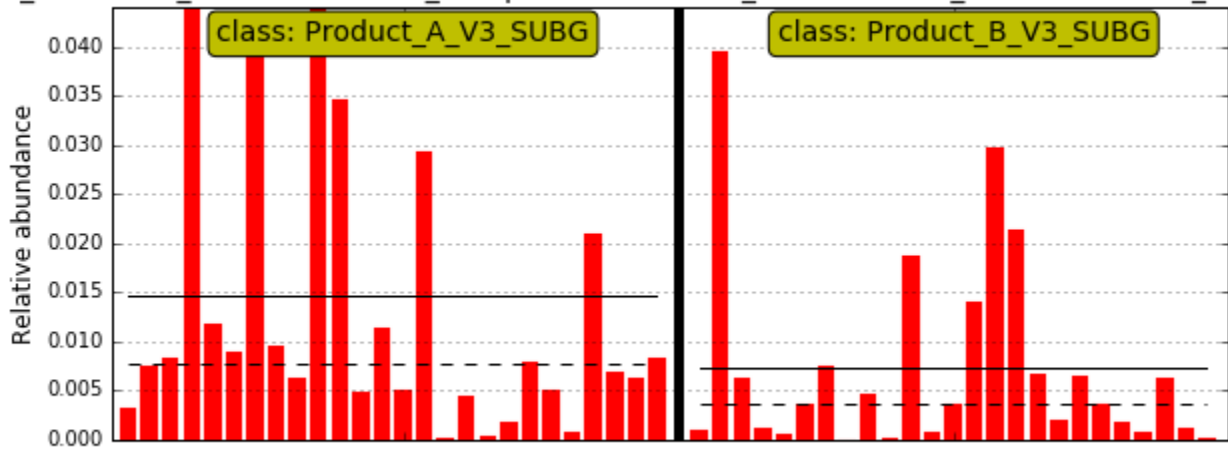
K\_Bacteria.P\_Firmicutes.C\_Bacilli.O\_Lactobacillales.F\_Streptococcaceae.G\_Streptococcus.S\_gordonii



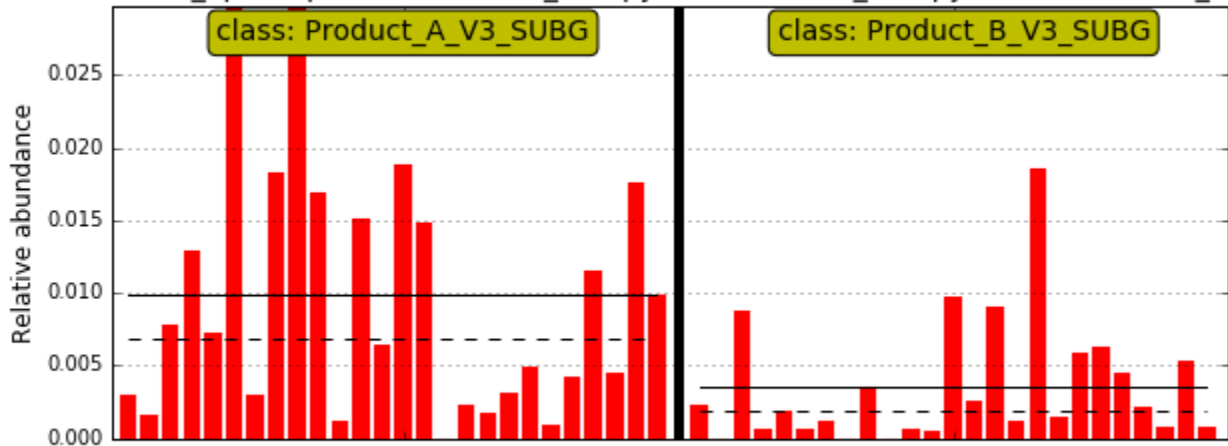
Bacteria.P\_Proteobacteria.C\_Betaproteobacteria.O\_Neisseriales.F\_Neisseriaceae.G\_Neisseria.S\_bacillif



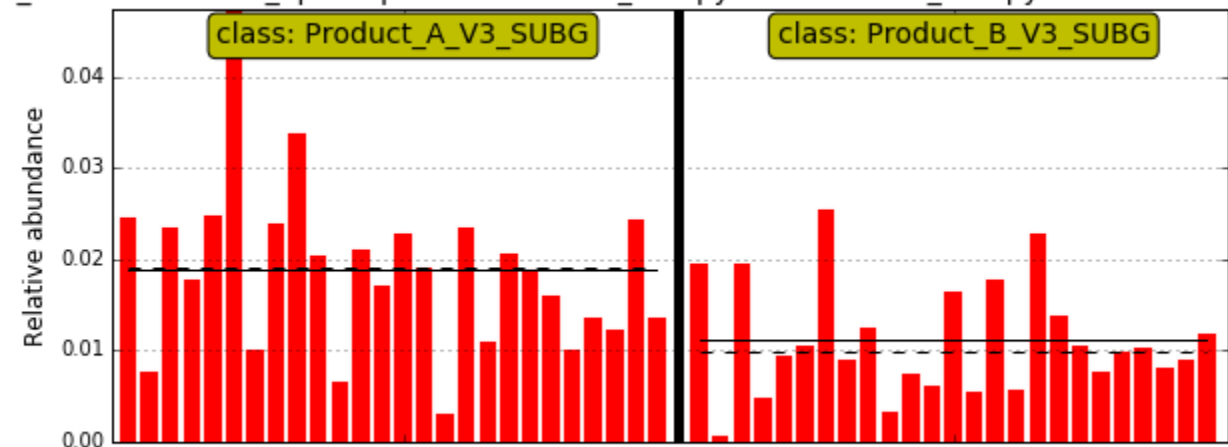
K\_Bacteria.P\_Proteobacteria.C\_Betaproteobacteria.O\_Neisseriales.F\_Neisseriaceae.G\_Neisseria



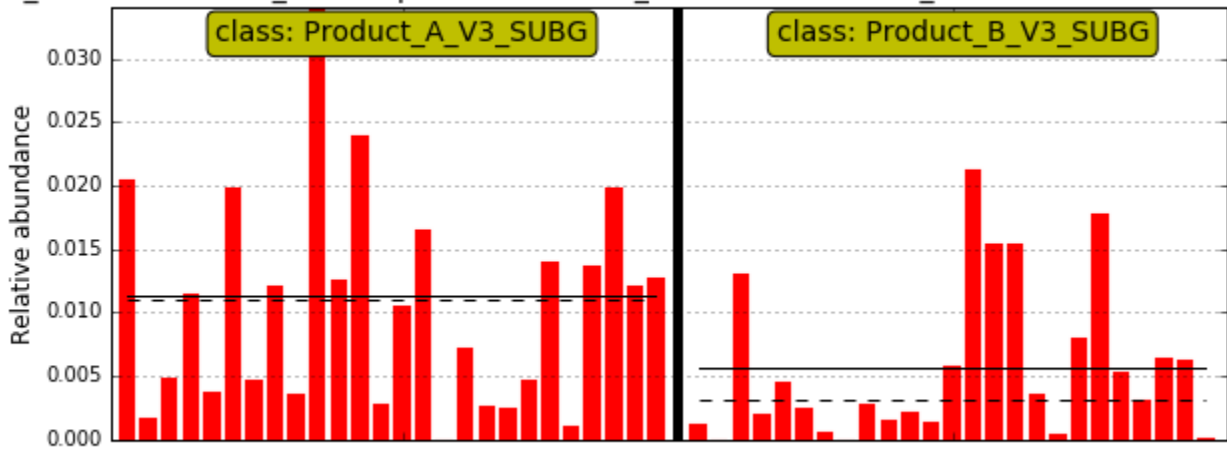
γ\_Proteobacteria.C\_Epsilonproteobacteria.O\_Campylobacterales.F\_Campylobacteraceae.G\_Campylobacter



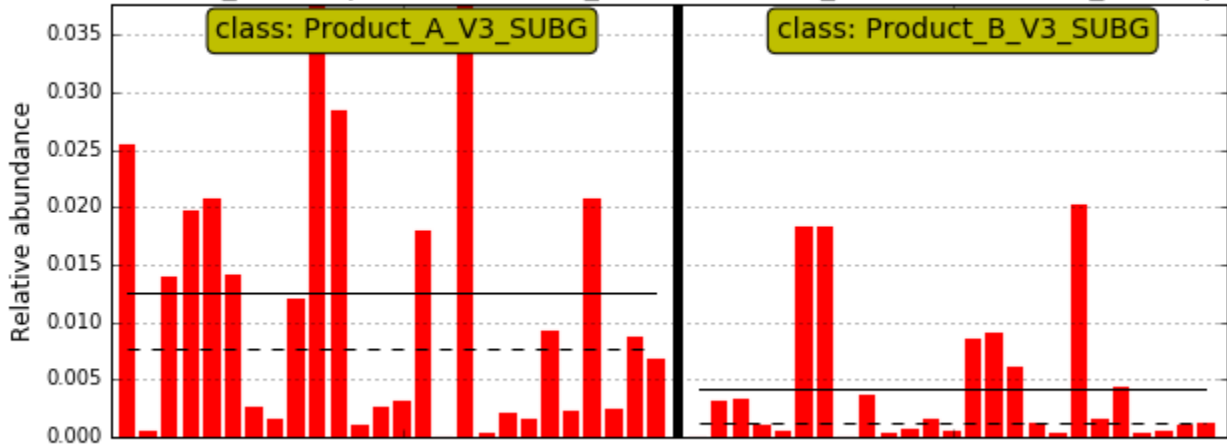
γ\_Proteobacteria.C\_Epsilonproteobacteria.O\_Campylobacterales.F\_Campylobacteraceae.G\_Campylobacter



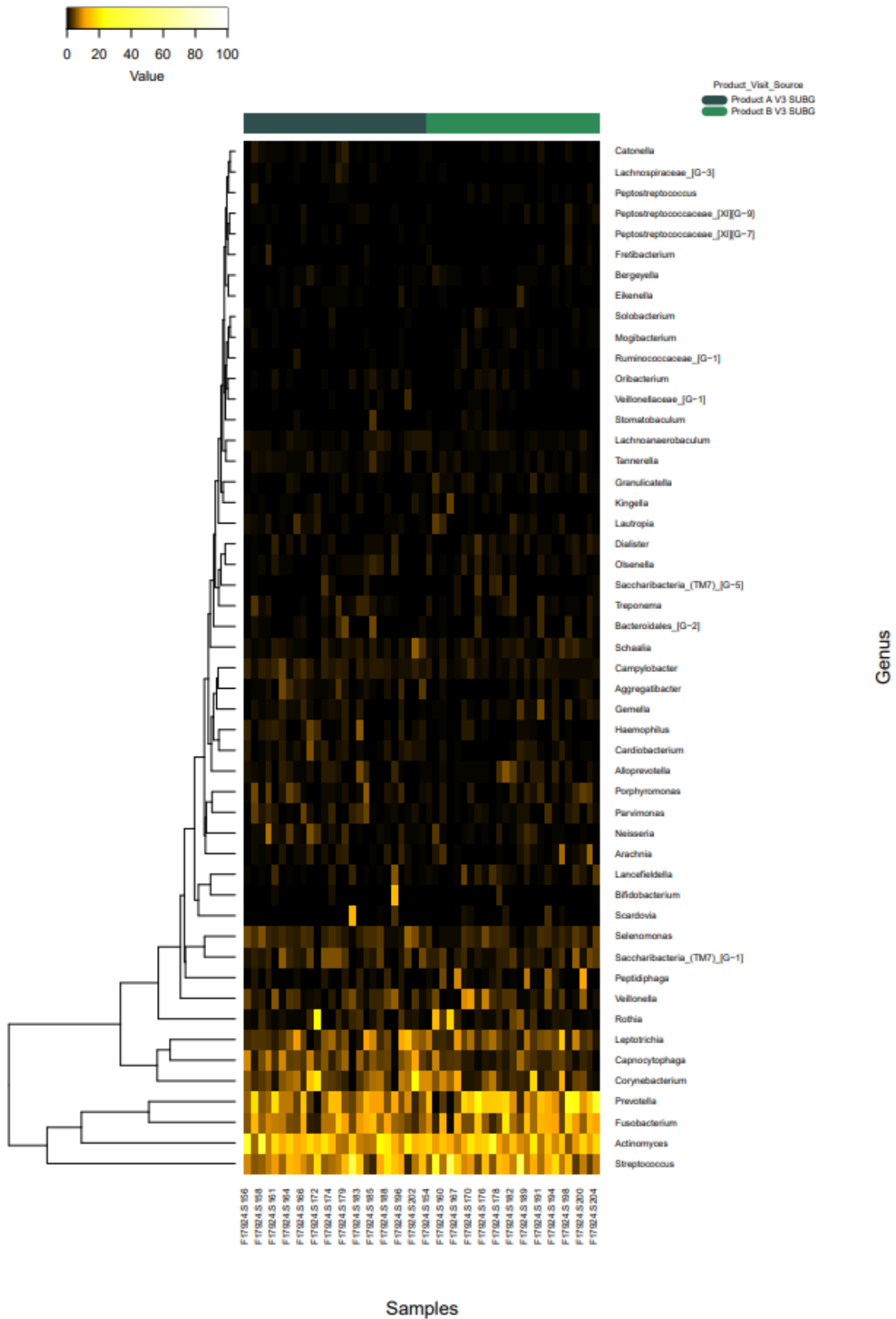
teria.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Cardiobacteriales.F\_Cardiobacteriaceae.G\_Cardioba

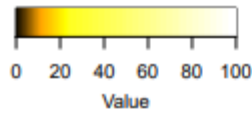


a.P\_Proteobacteria.C\_Gammaproteobacteria.O\_Pasteurellales.F\_Pasteurellaceae.G\_Haemophilus.S\_par

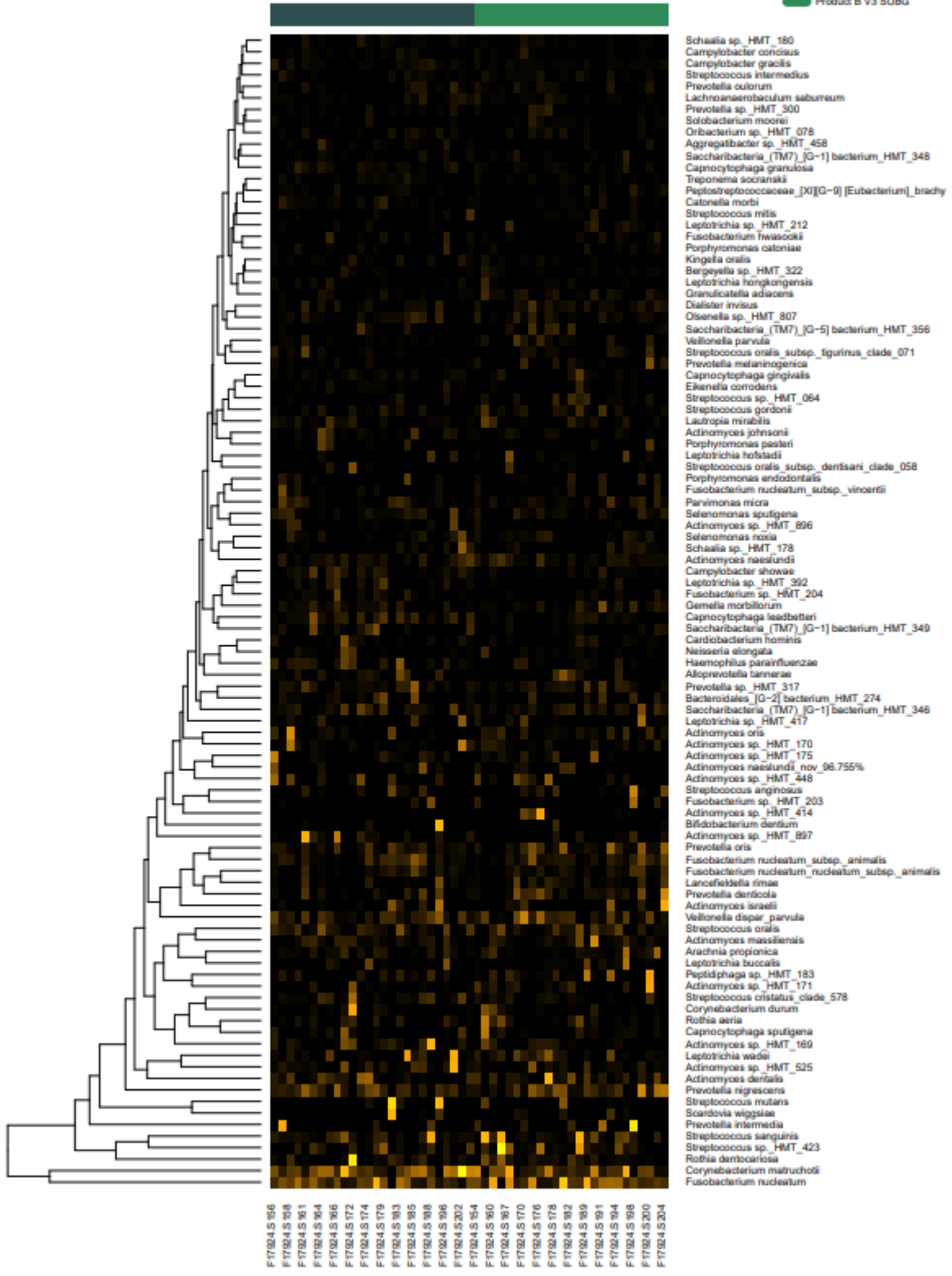


## 6) Heat map





Product\_Visit\_Source  
 Product A V3 SUBG  
 Product B V3 SUBG



# Appendix B. CosmosID-HUB Metatranscriptomic Analysis

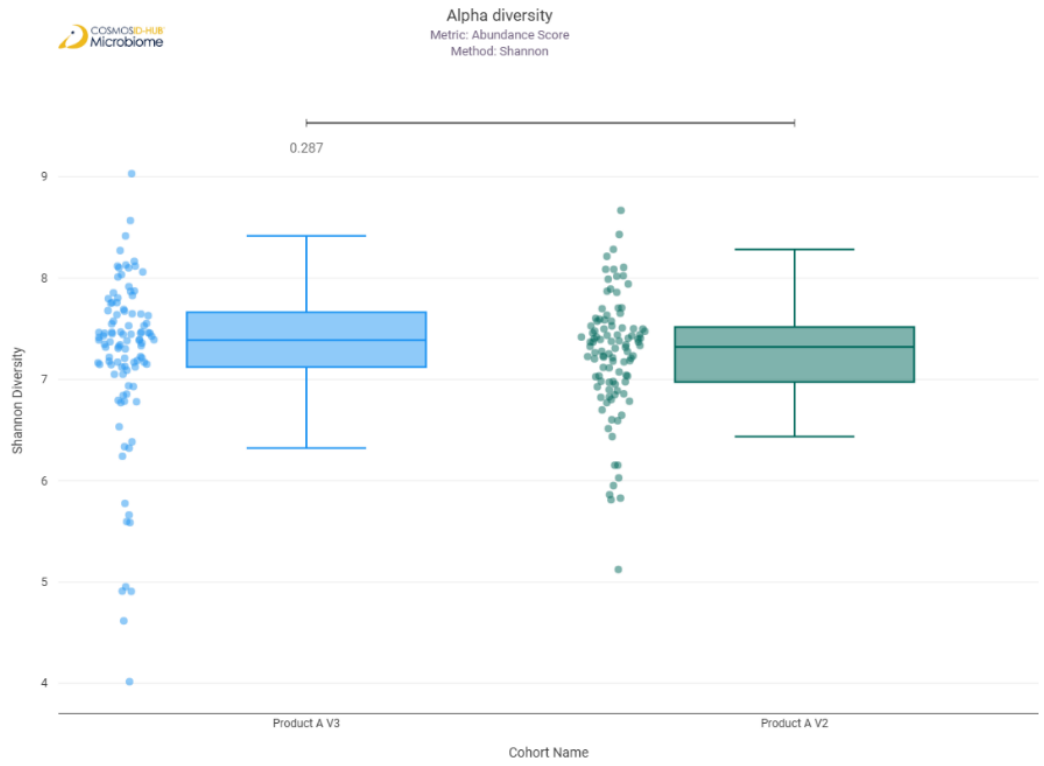
## Comparison 1: Product A V2 vs Product A V3

### Gene Ontology

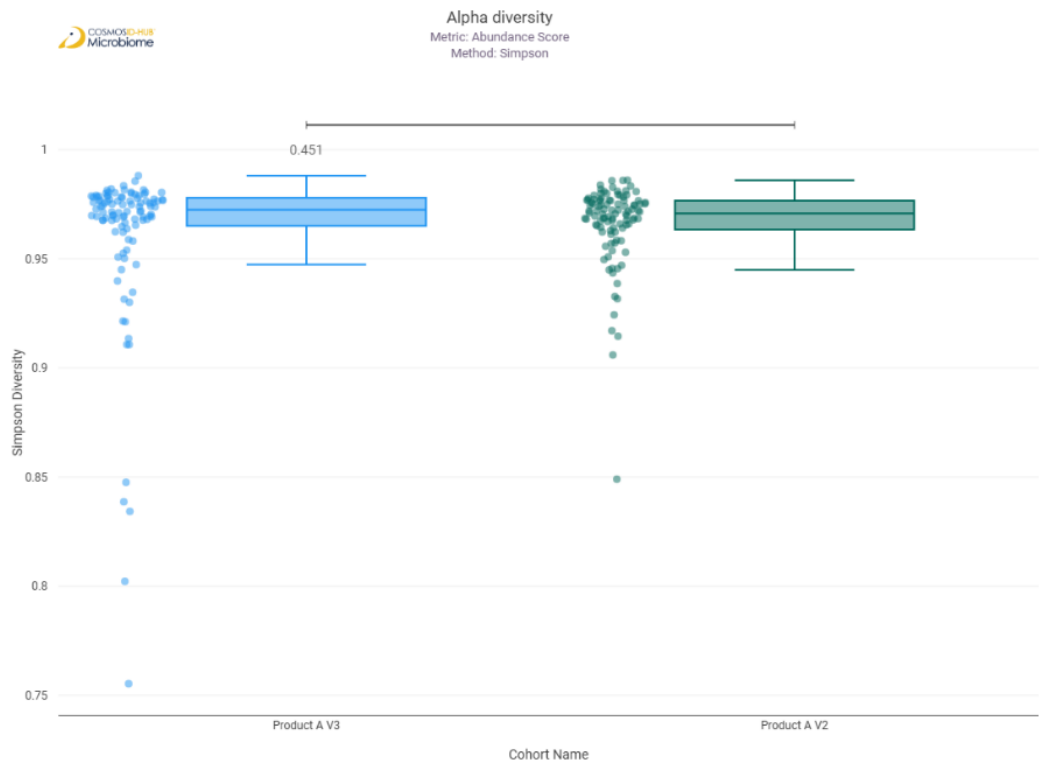
#### Alpha Diversity



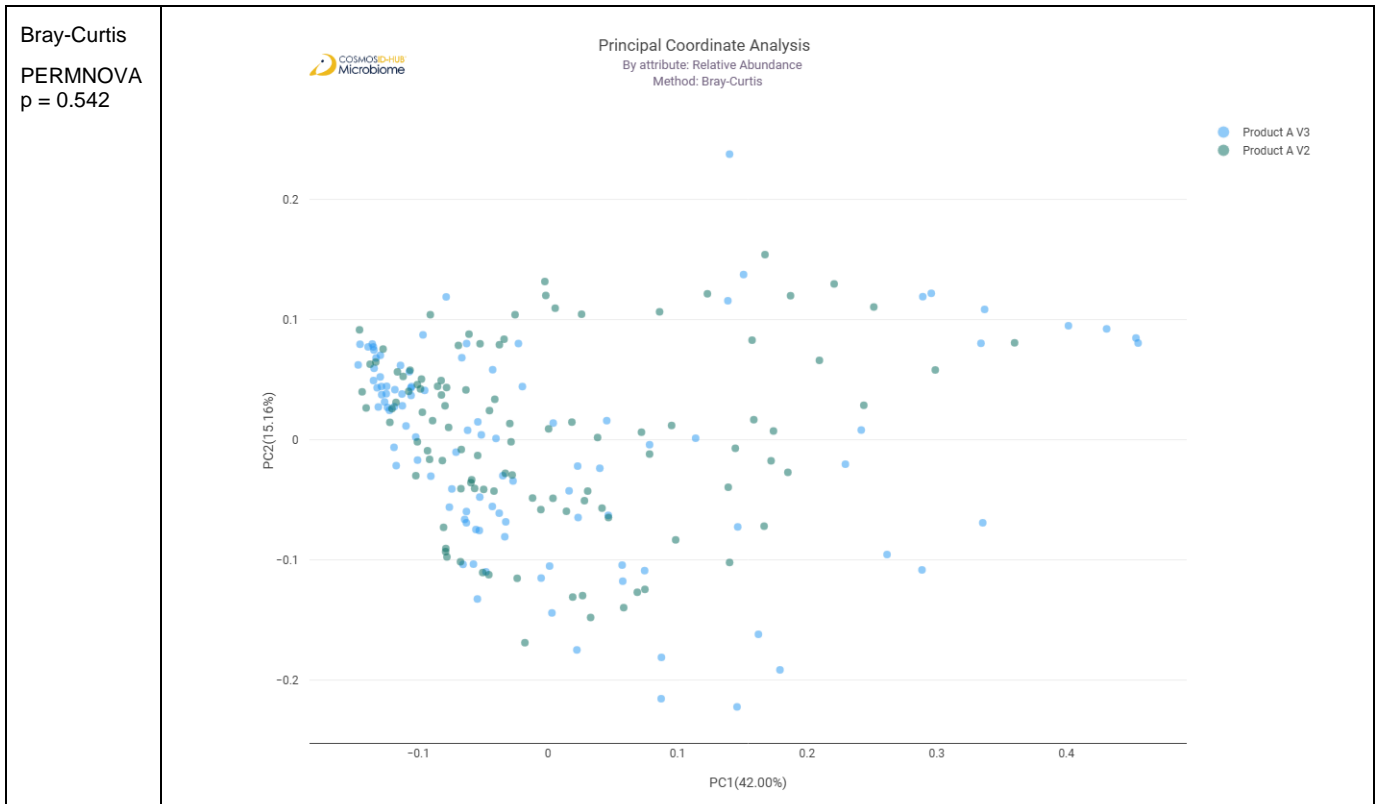
# Shannon



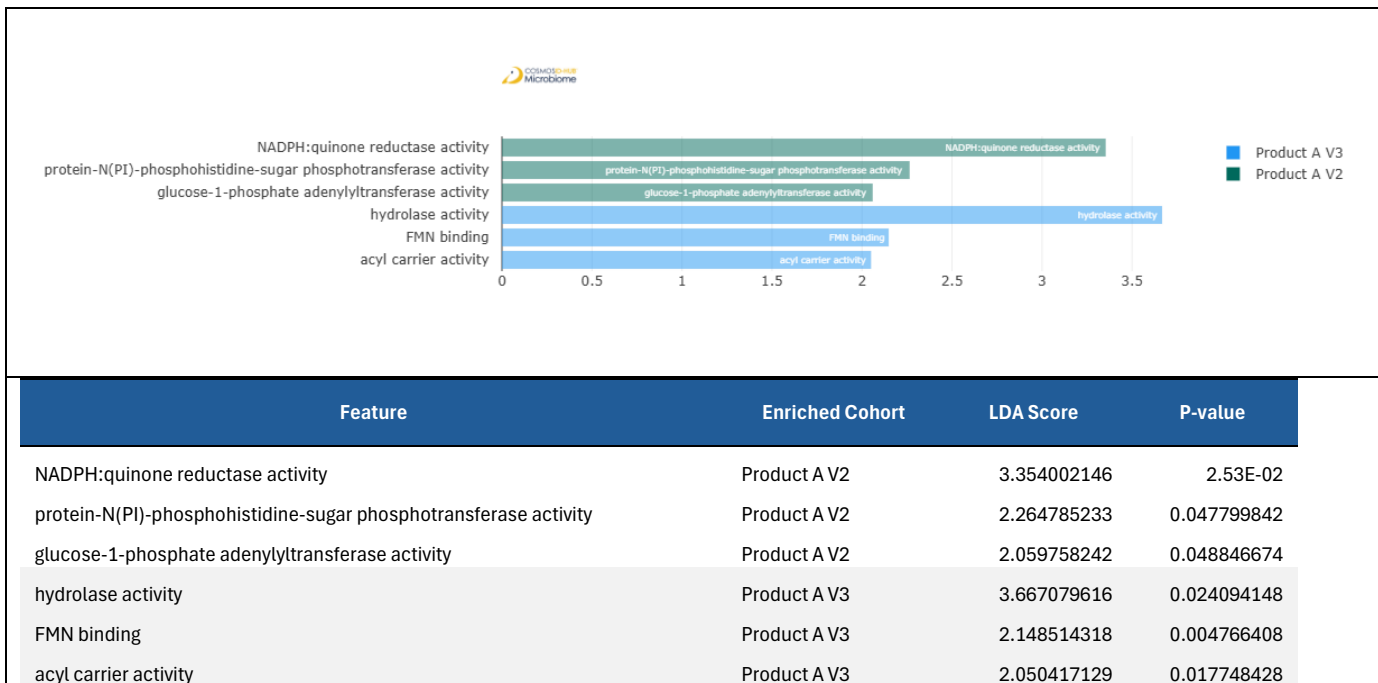
# Simpson



## Beta Diversity



## Differential Abundance (LEfSe)

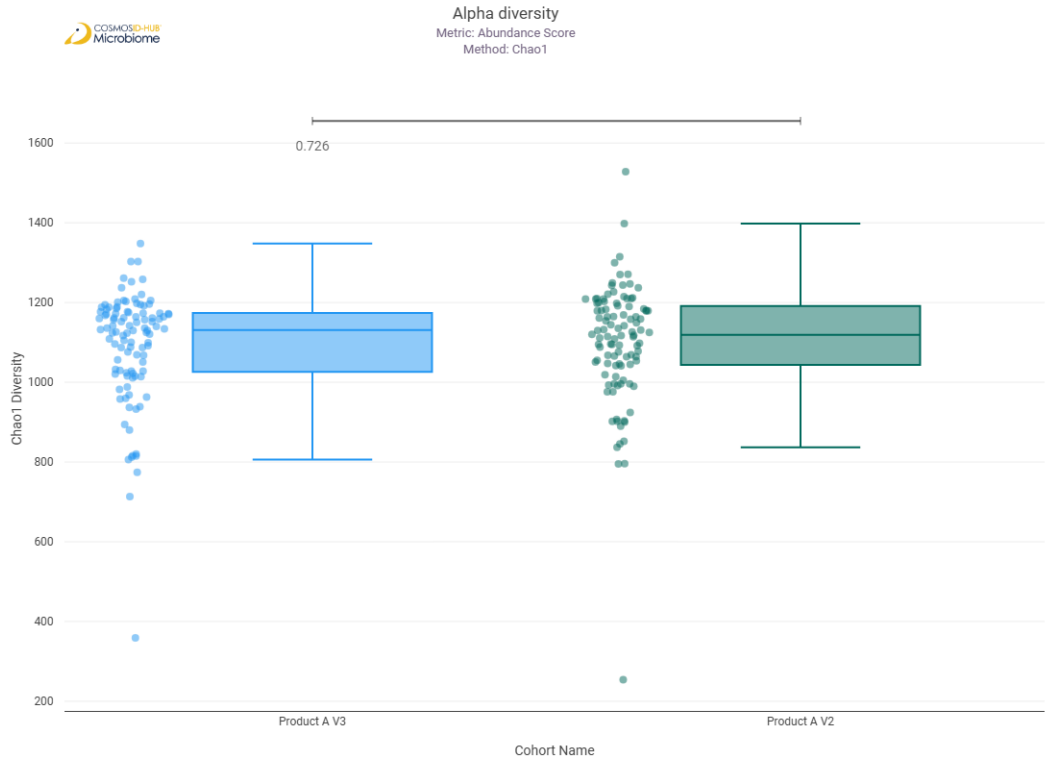


## Enzyme Commission

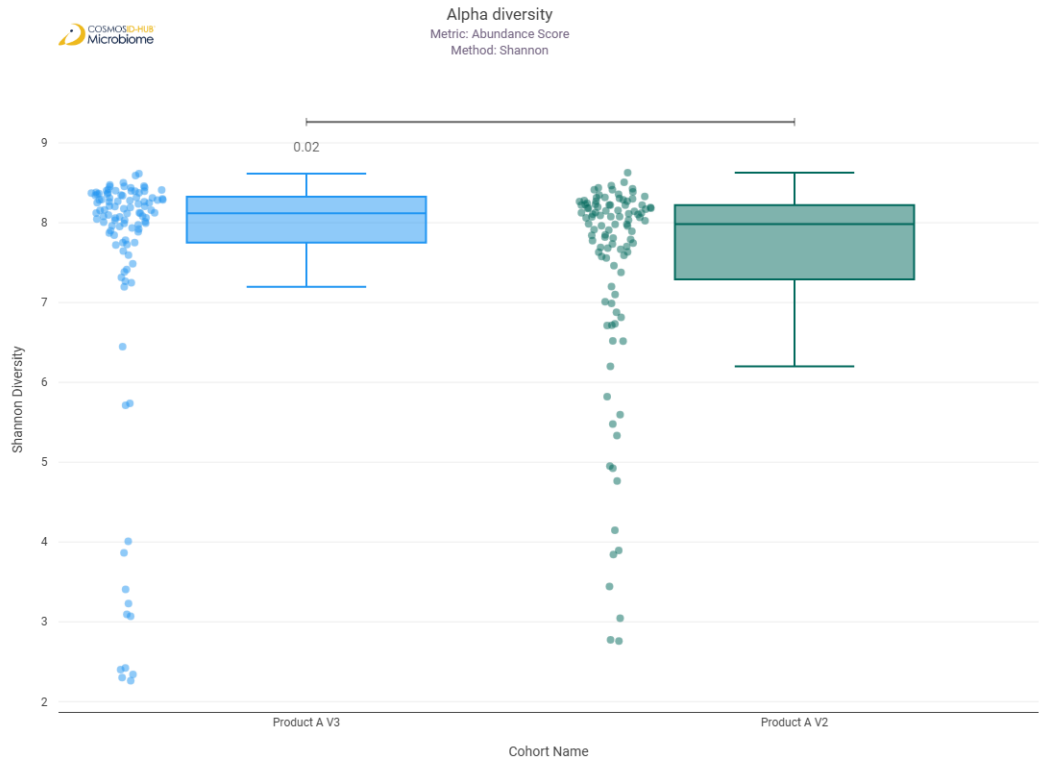


# Alpha Diversity (EC)

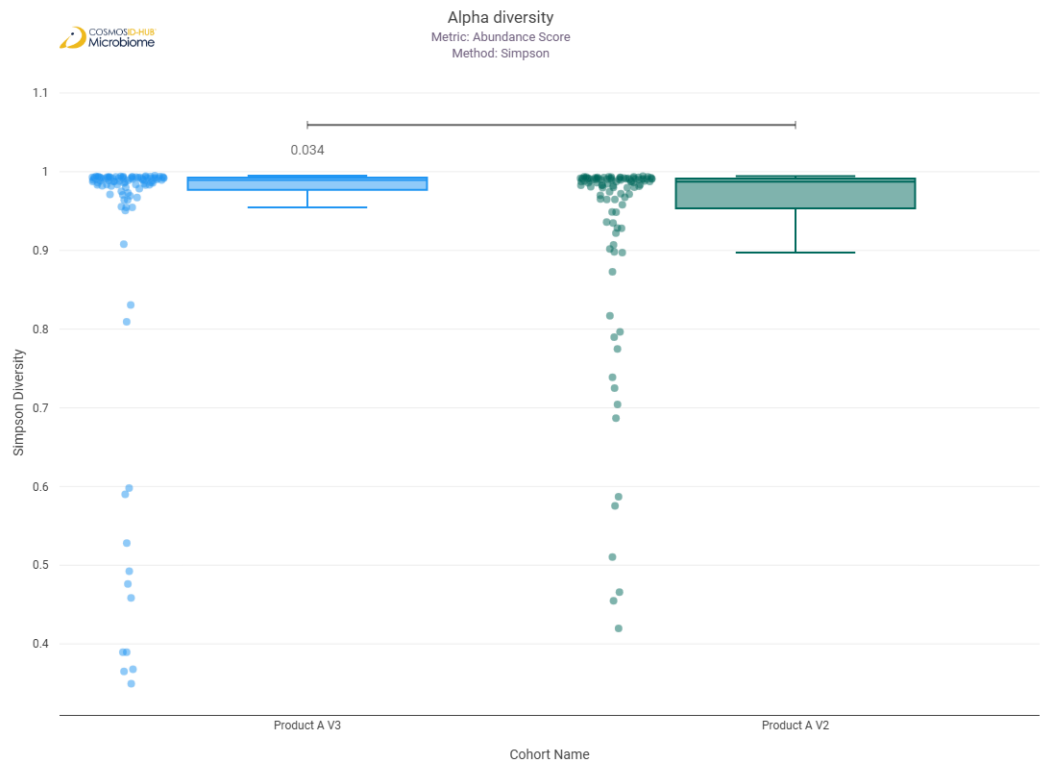
Chao1



Shannon

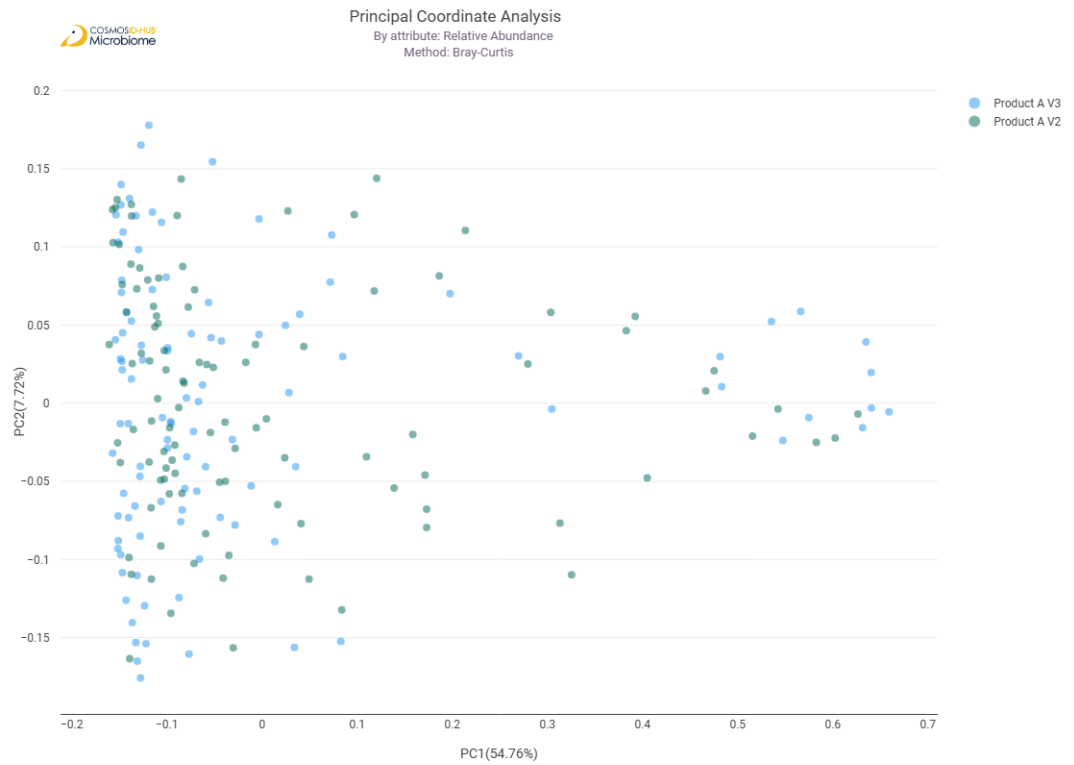


# Simpson

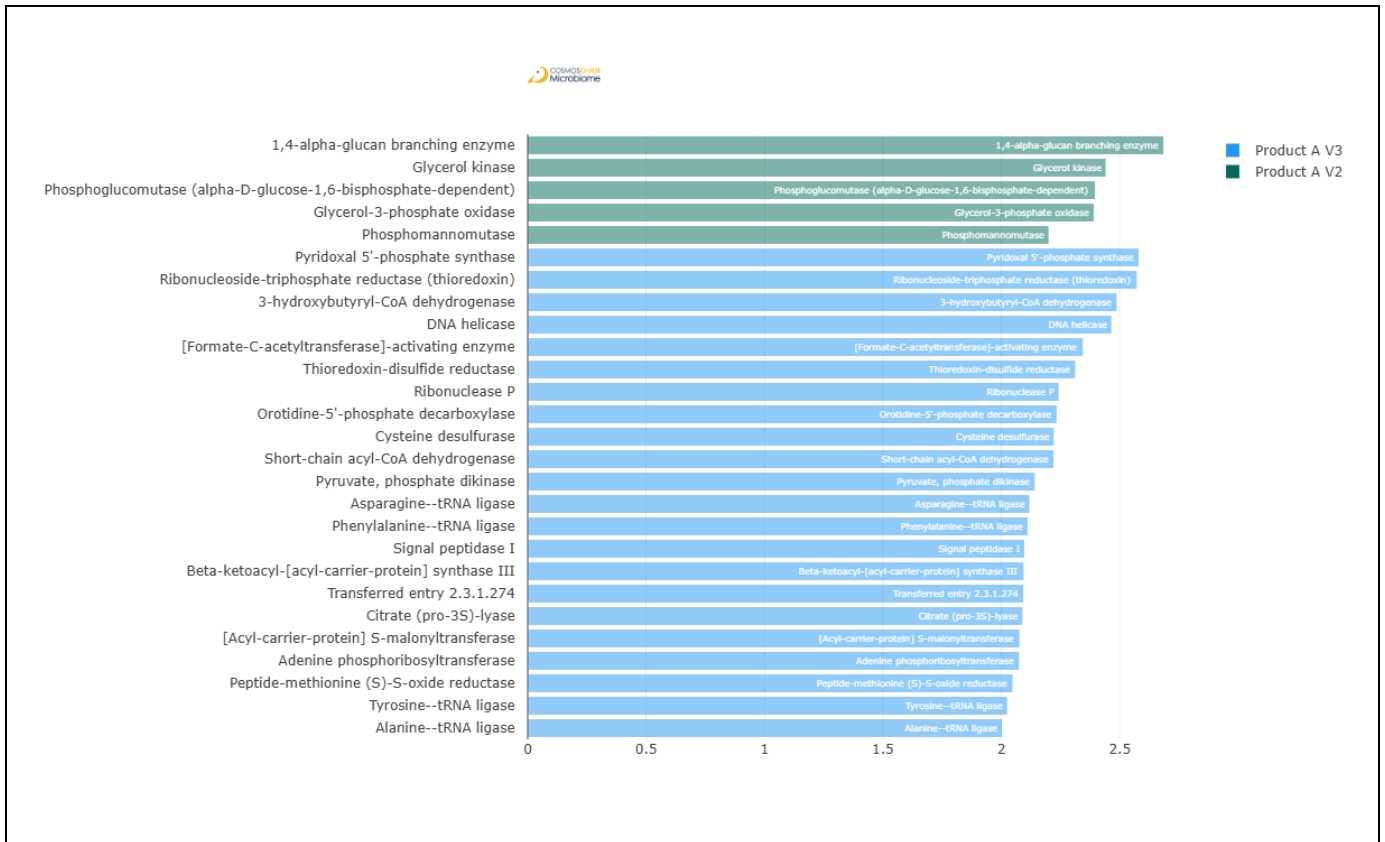


## Beta Diversity (EC)

Bray-Curtis  
PERMNOVA  
p = 0.280



## Differential Abundance (LEfSe) (EC)

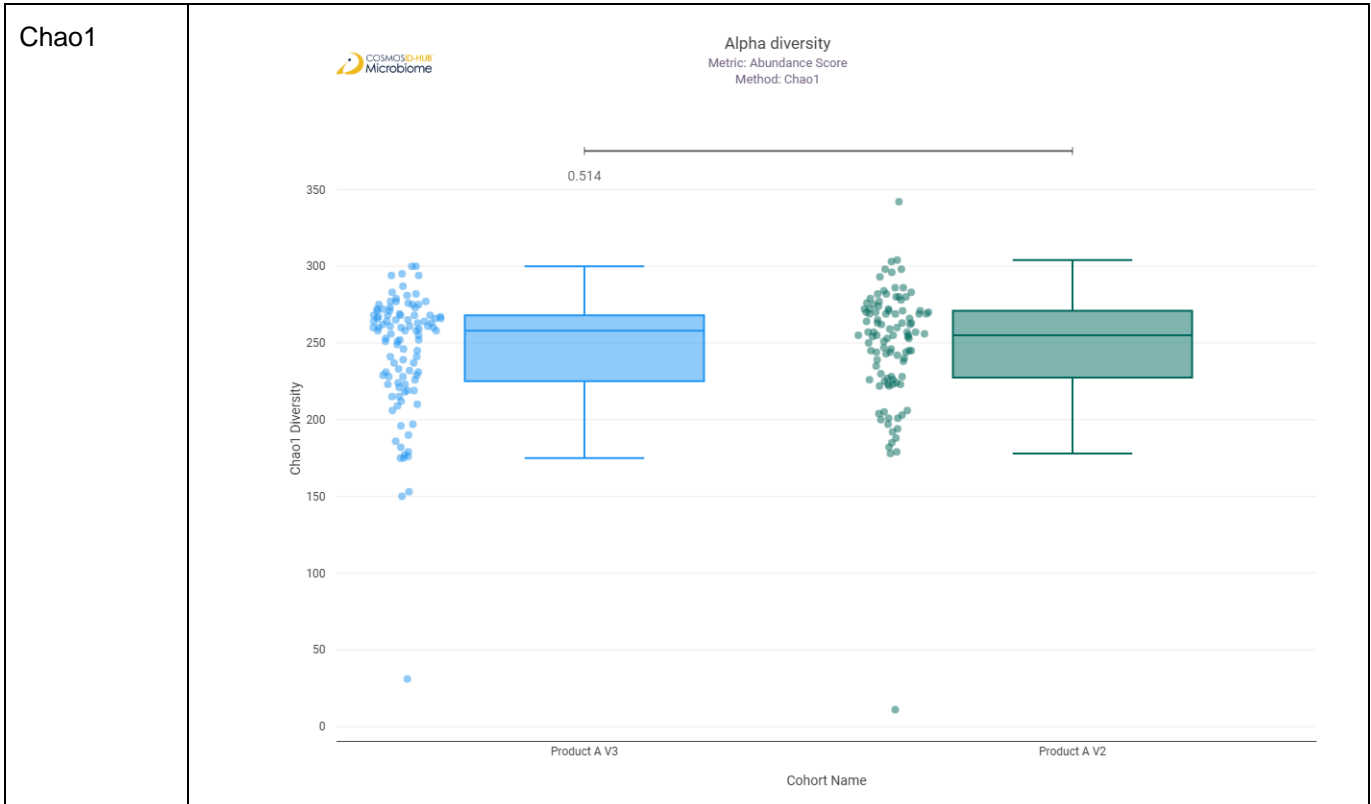


Feature	Enriched Cohort	LDA Score	P-value
1,4-alpha-glucan branching enzyme	Product A V2	2.684260612	2.44E-02
Glycerol kinase	Product A V2	2.440527929	0.013515178
Phosphoglucomutase (alpha-D-glucose-1,6-bisphosphate-dependent)	Product A V2	2.39543707	0.00904253
Glycerol-3-phosphate oxidase	Product A V2	2.390435287	0.031040567
Phosphomannomutase	Product A V2	2.199521301	0.007681948
Pyridoxal 5'-phosphate synthase	Product A V3	2.579541329	0.002826568
Ribonucleoside-triphosphate reductase (thioredoxin)	Product A V3	2.571583891	0.013256264
3-hydroxybutyryl-CoA dehydrogenase	Product A V3	2.486837375	0.029804167
DNA helicase	Product A V3	2.464351655	0.002198431
[Formate-C-acetyltransferase]-activating enzyme	Product A V3	2.343710979	0.036849101
Thioredoxin-disulfide reductase	Product A V3	2.311700333	0.037902094
Ribonuclease P	Product A V3	2.241667448	0.0029349
Orotidine-5'-phosphate decarboxylase	Product A V3	2.23363033	0.001957618
Cysteine desulfurase	Product A V3	2.221119485	0.042608467
Short-chain acyl-CoA dehydrogenase	Product A V3	2.220517395	0.011677397
Pyruvate, phosphate dikinase	Product A V3	2.140426457	0.019839554
Asparagine--tRNA ligase	Product A V3	2.118204505	0.007122062
Phenylalanine--tRNA ligase	Product A V3	2.110783168	0.00345801
Signal peptidase I	Product A V3	2.096427343	0.005695585
Beta-ketoacyl-[acyl-carrier-protein] synthase III	Product A V3	2.09399442	0.036849101
Transferred entry 2.3.1.274	Product A V3	2.092424107	0.000331128
Citrate (pro-3S)-lyase	Product A V3	2.08887282	0.000953333

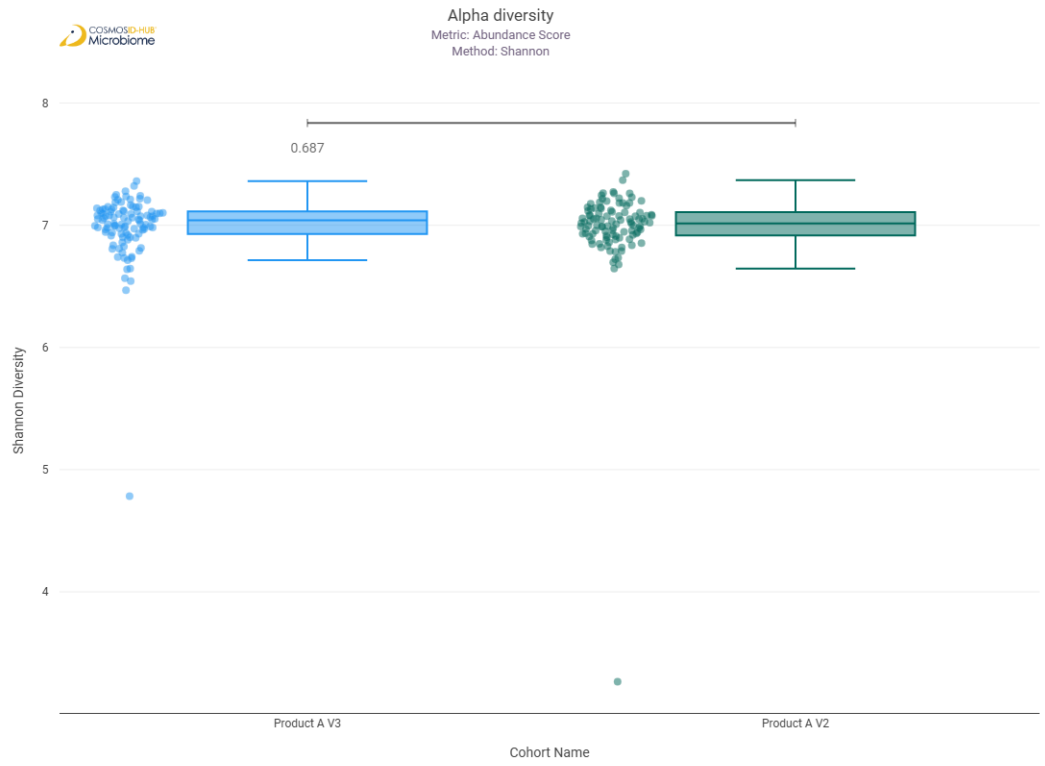
[Acyl-carrier-protein] S-malonyltransferase	Product A V3	2.076345774	0.023241053
Adenine phosphoribosyltransferase	Product A V3	2.074820233	0.011715972
Peptide-methionine (S)-S-oxide reductase	Product A V3	2.047296647	0.027783601
Tyrosine--tRNA ligase	Product A V3	2.024258503	0.034817712
Alanine--tRNA ligase	Product A V3	2.00263877	0.01535833

## MetaCyc Pathways

### Alpha Diversity (MetaCyc)



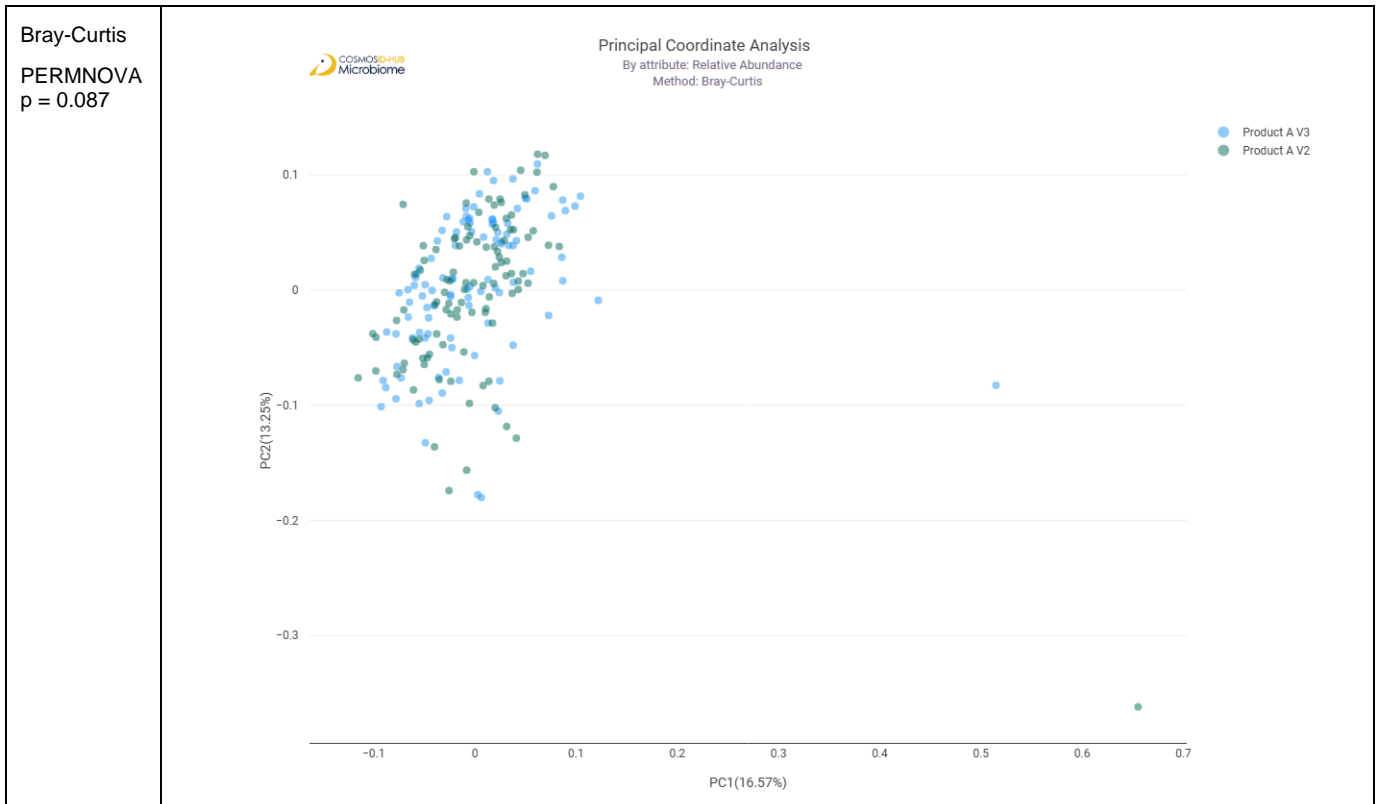
# Shannon



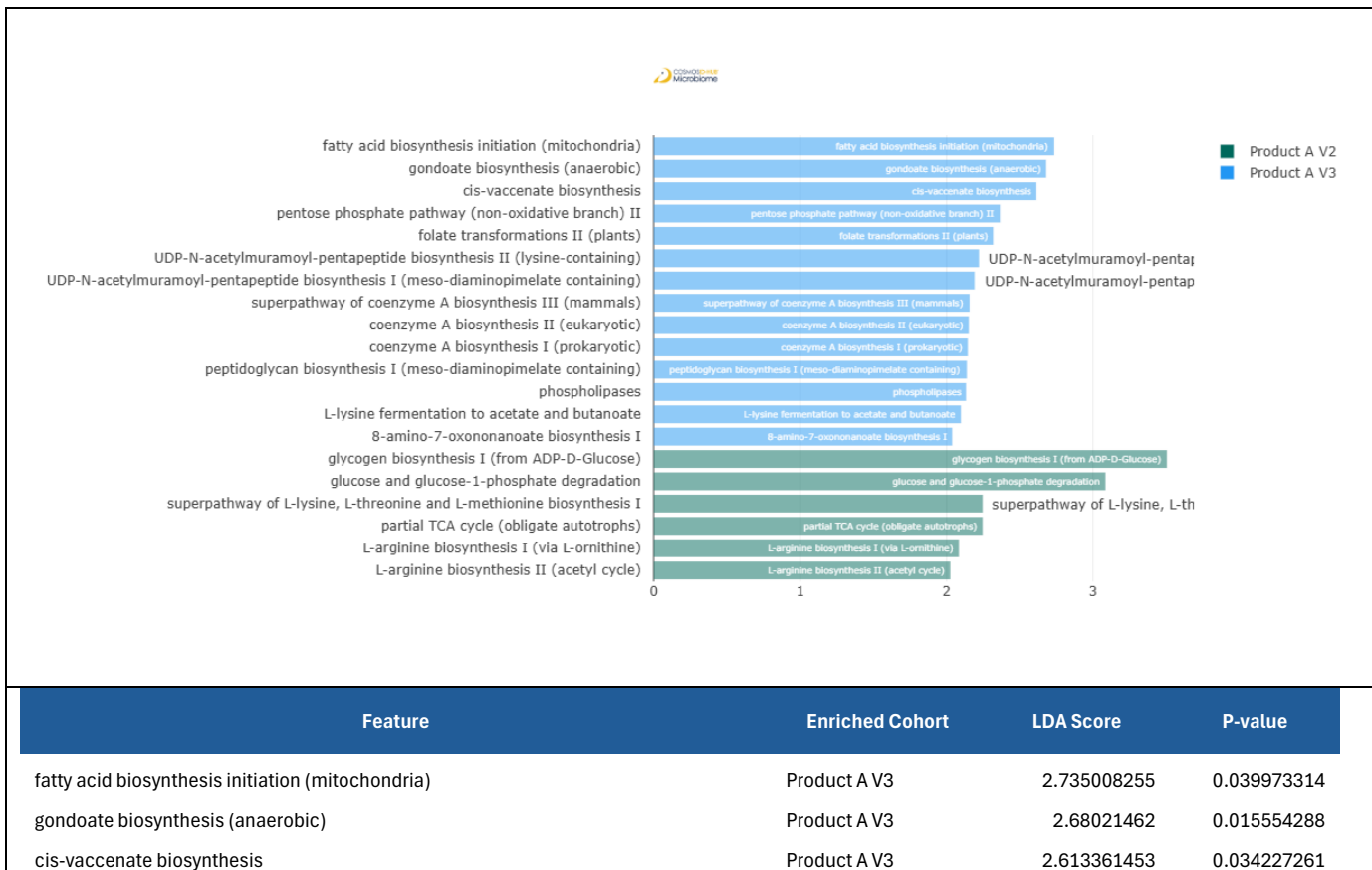
# Simpson



## Beta Diversity (MetaCyc)



## Differential Abundance (LEfSe) (MetaCyc)



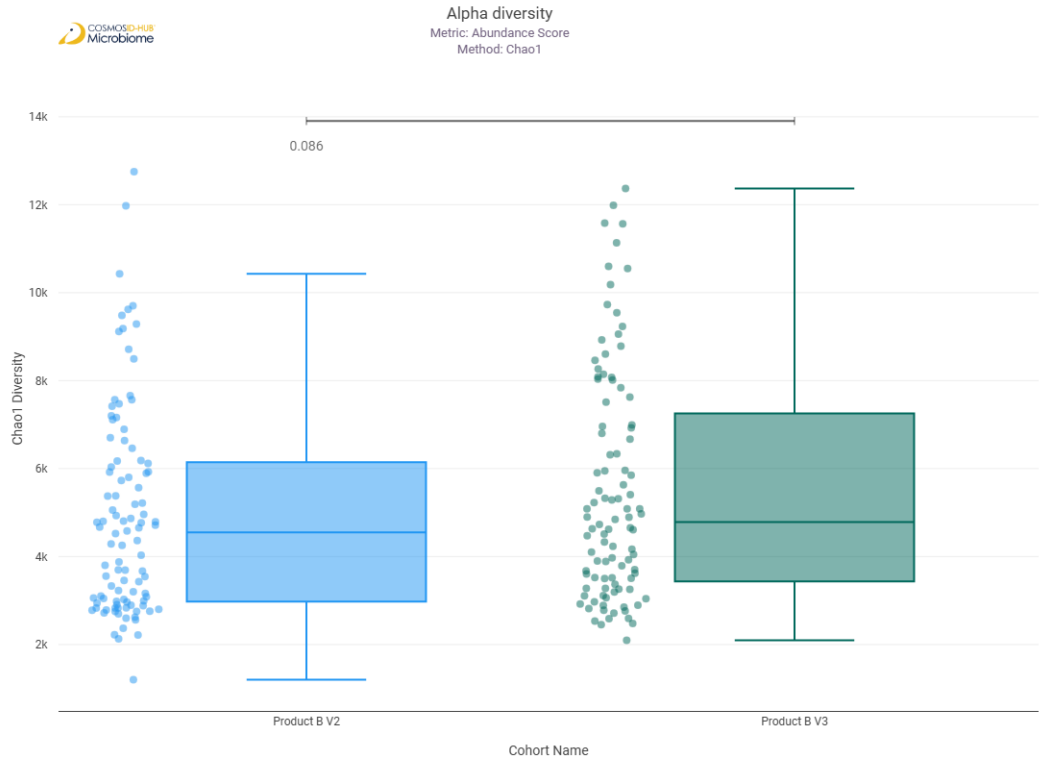
pentose phosphate pathway (non-oxidative branch) II	Product A V3	2.364544919	0.01871087
folate transformations II (plants)	Product A V3	2.31833131	0.038762815
UDP-N-acetylmuramoyl-pentapeptide biosynthesis II (lysine-containing)	Product A V3	2.221900027	0.024021987
UDP-N-acetylmuramoyl-pentapeptide biosynthesis I (meso-diaminopimelate containing)	Product A V3	2.191038313	0.020773626
superpathway of coenzyme A biosynthesis III (mammals)	Product A V3	2.157245055	0.001492812
coenzyme A biosynthesis II (eukaryotic)	Product A V3	2.151990248	0.001980554
coenzyme A biosynthesis I (prokaryotic)	Product A V3	2.145034758	0.006262567
peptidoglycan biosynthesis I (meso-diaminopimelate containing)	Product A V3	2.138440512	0.045141198
phospholipases	Product A V3	2.132849146	0.014251091
L-lysine fermentation to acetate and butanoate	Product A V3	2.098199076	0.02972225
Transferred entry 2.3.1.274	Product A V3	2.092424107	0.000331128
Citrate (pro-3S)-lyase	Product A V3	2.08887282	0.000953333
[Acyl-carrier-protein] S-malonyltransferase	Product A V3	2.076345774	0.023241053
Adenine phosphoribosyltransferase	Product A V3	2.074820233	0.011715972
Peptide-methionine (S)-S-oxide reductase	Product A V3	2.047296647	0.027783601
8-amino-7-oxononanoate biosynthesis I	Product A V3	2.03838881	0.023770185
Tyrosine--tRNA ligase	Product A V3	2.024258503	0.034817712
Alanine--tRNA ligase	Product A V3	2.00263877	0.01535833
glycogen biosynthesis I (from ADP-D-Glucose)	Product A V2	3.504241049	7.47E-03
glucose and glucose-1-phosphate degradation	Product A V2	3.085696443	0.001014125
superpathway of L-lysine, L-threonine and L-methionine biosynthesis I	Product A V2	2.246128695	0.000192166
partial TCA cycle (obligate autotrophs)	Product A V2	2.245865551	0.012144606
L-arginine biosynthesis I (via L-ornithine)	Product A V2	2.084419907	0.008864648
L-arginine biosynthesis II (acetyl cycle)	Product A V2	2.025666773	0.007998331

## Comparison 2: Product B V2 vs Product B V3

### Gene Ontology

# Alpha Diversity (GO)

Chao1

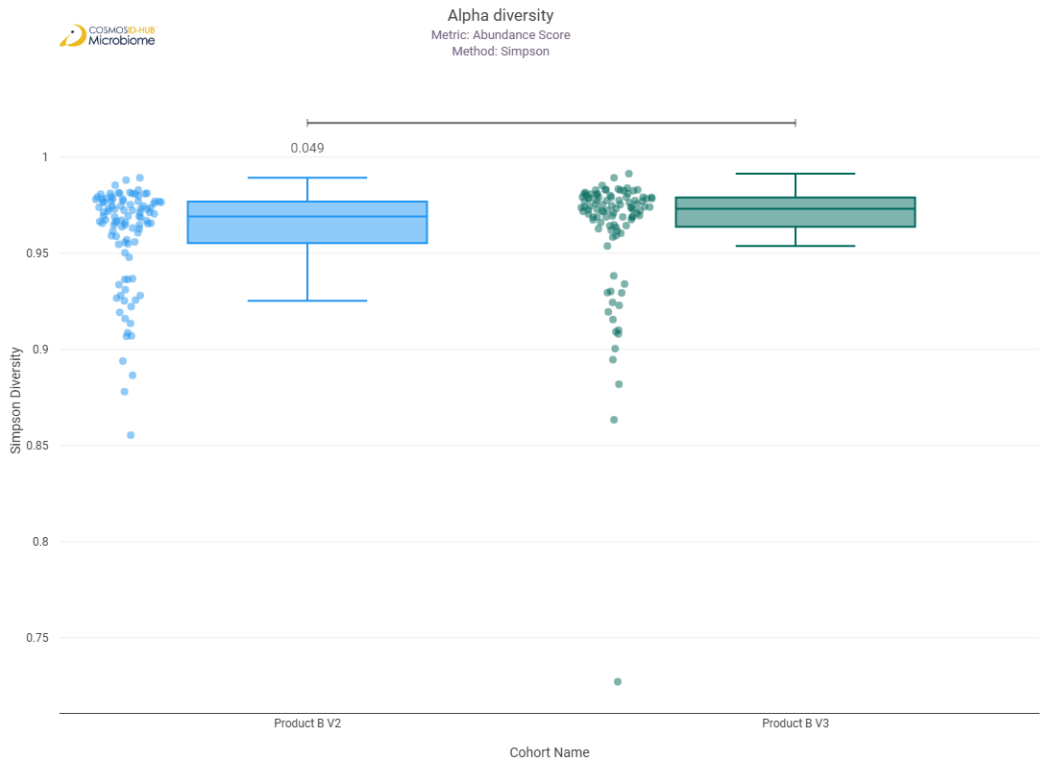


Shannon



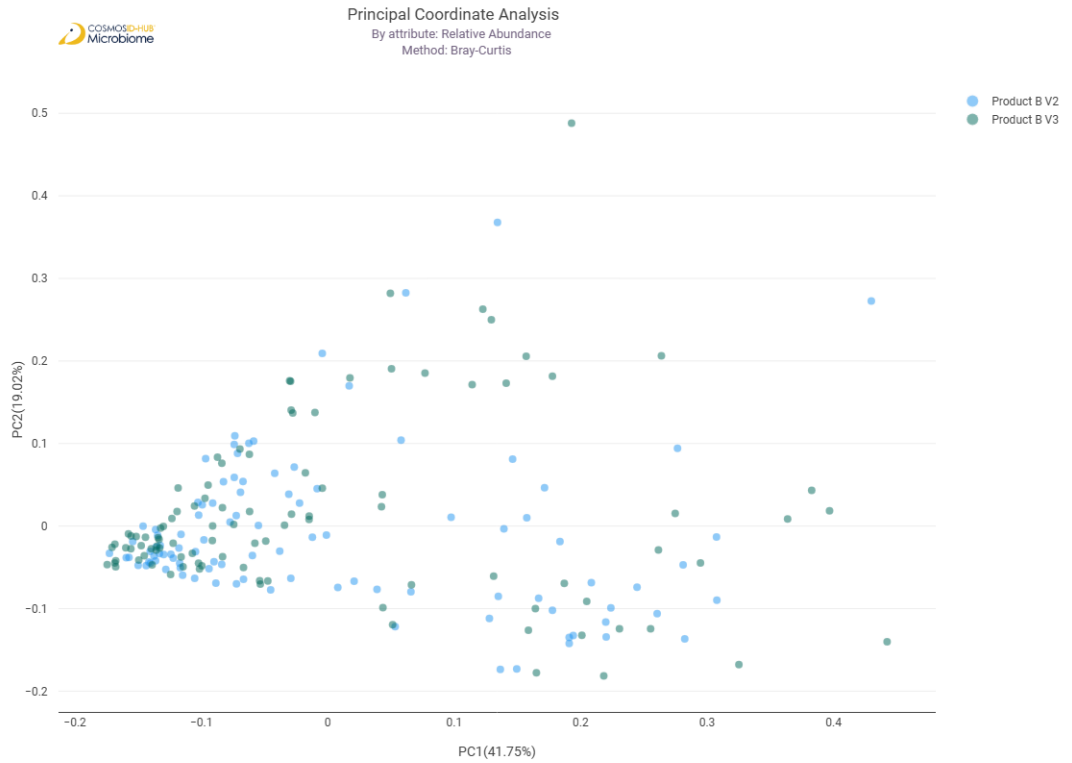


# Simpson

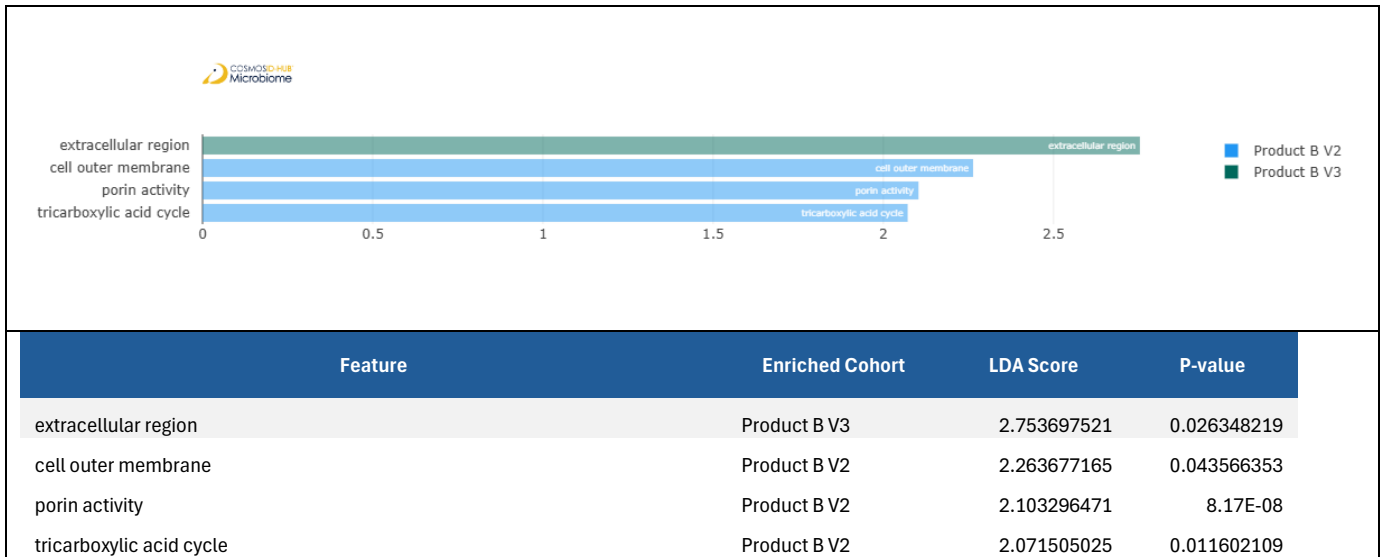


## Beta Diversity (GO)

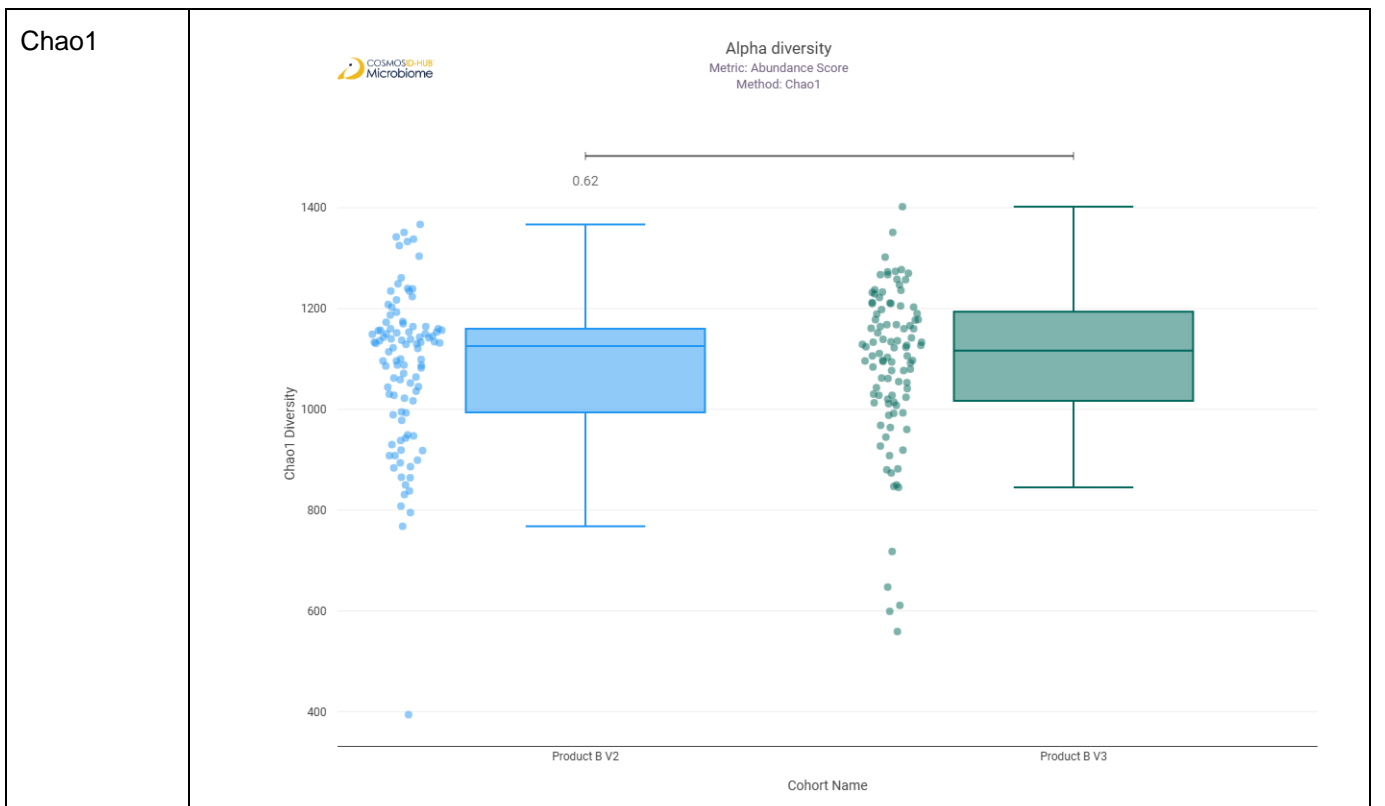
Bray-Curtis  
PERMNOVA  
 $p = 0.271$



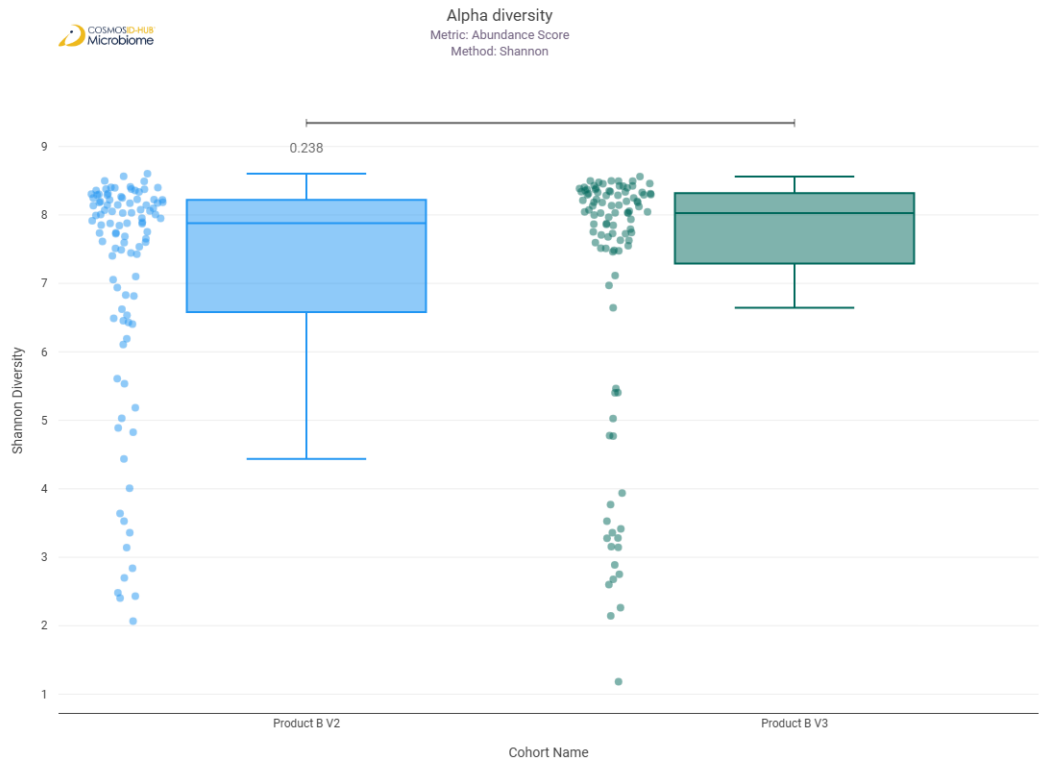
## Differential Abundance (LEfSe) (GO)



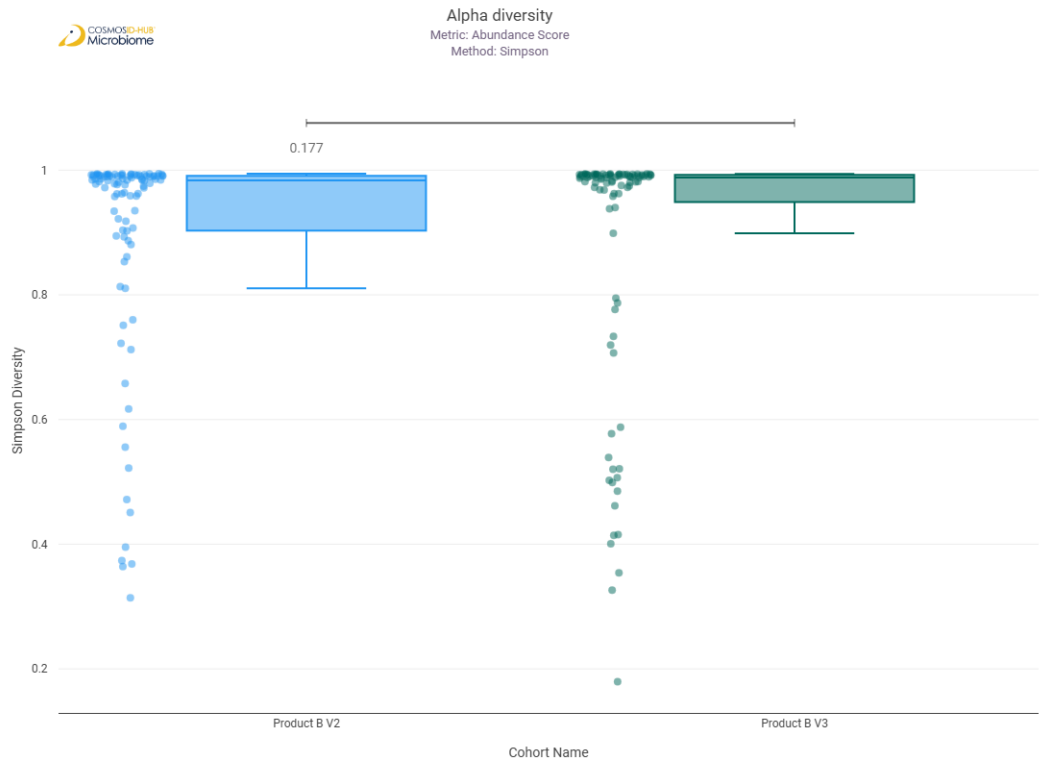
## Enzyme Commission Alpha Diversity (EC)



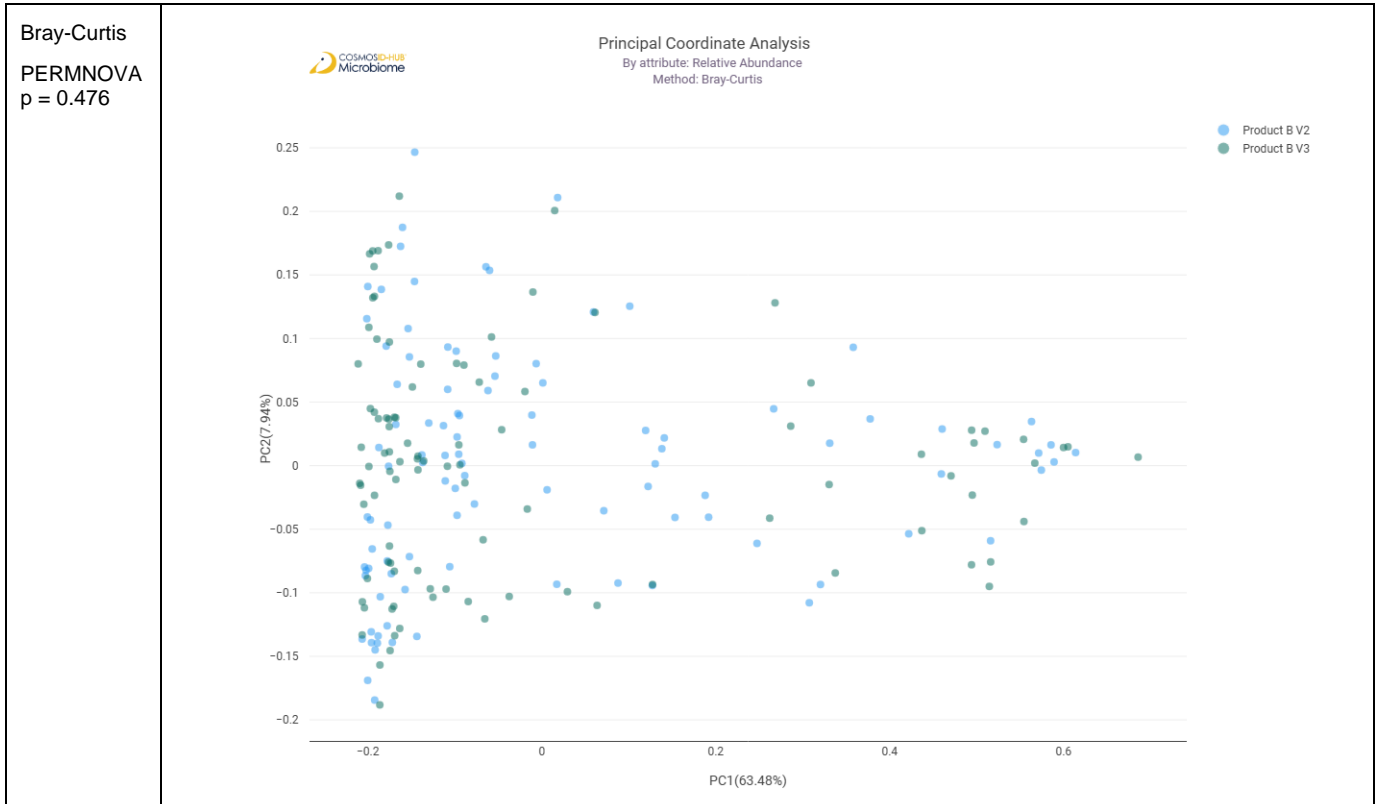
# Shannon



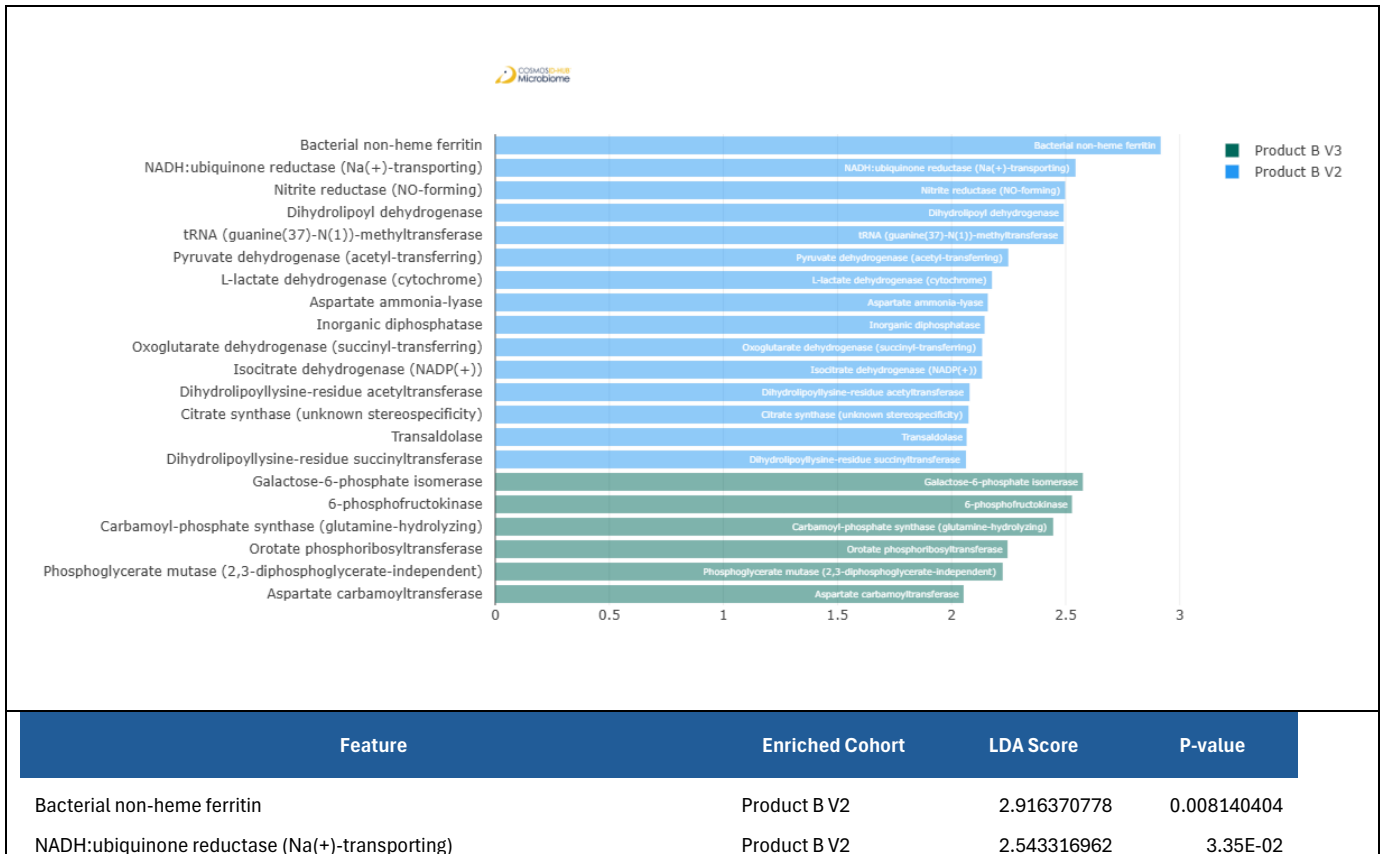
# Simpson



## Beta Diversity (EC)



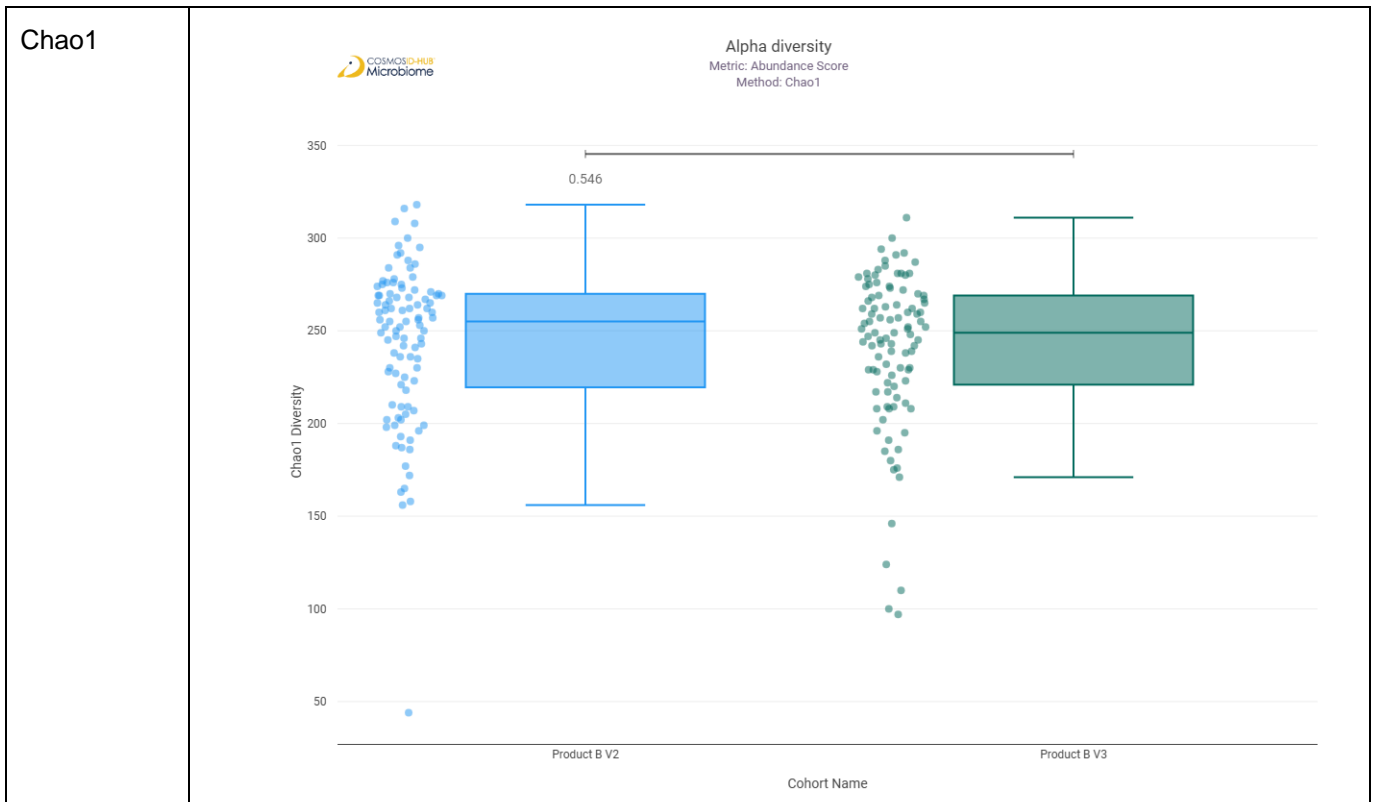
## Differential Abundance (LEfSe) (EC)



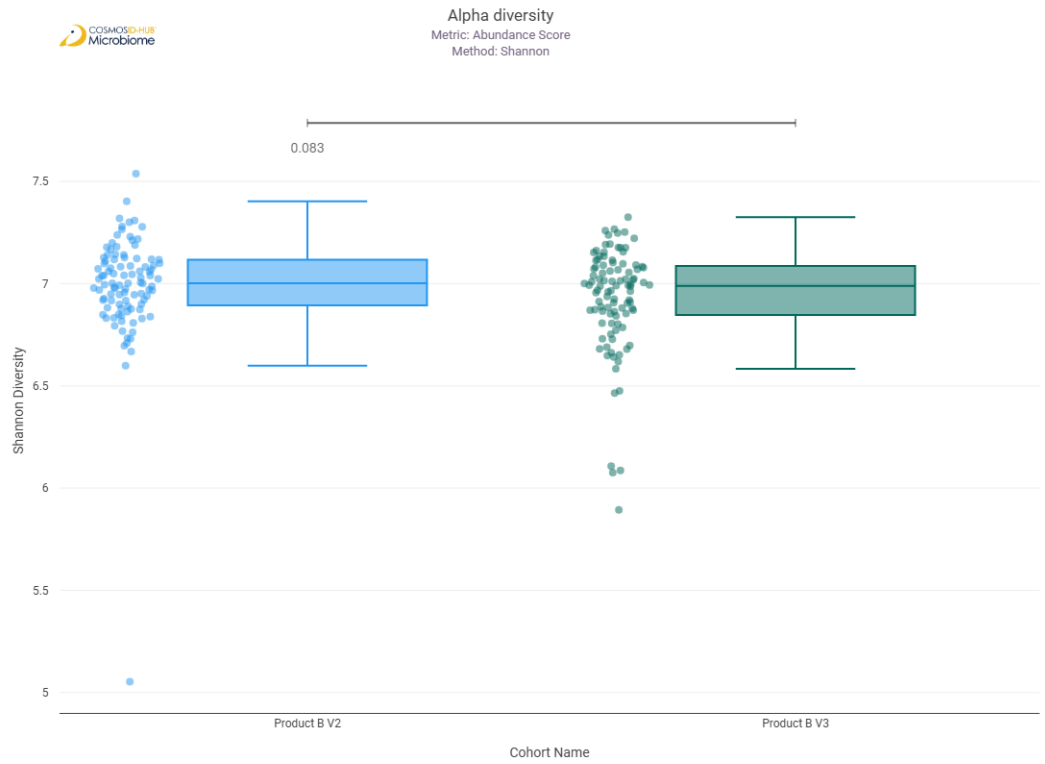
Nitrite reductase (NO-forming)	Product B V2	2.497728264	0.000588206
Dihydrolipoyl dehydrogenase	Product B V2	2.491221448	0.007299969
tRNA (guanine(37)-N(1))-methyltransferase	Product B V2	2.491026824	0.001868126
Pyruvate dehydrogenase (acetyl-transferring)	Product B V2	2.248619249	0.023812891
L-lactate dehydrogenase (cytochrome)	Product B V2	2.176913806	3.15038E-05
Aspartate ammonia-lyase	Product B V2	2.158608668	0.006538231
Inorganic diphosphatase	Product B V2	2.144704717	0.047525328
Oxoglutarate dehydrogenase (succinyl-transferring)	Product B V2	2.133982099	0.000116559
Isocitrate dehydrogenase (NADP(+))	Product B V2	2.13357857	0.007737888
Dihydrolipoyllysine-residue acetyltransferase	Product B V2	2.078756294	1.59585E-05
Citrate synthase (unknown stereospecificity)	Product B V2	2.074165128	0.014096561
Transaldolase	Product B V2	2.065814207	0.013686825
Dihydrolipoyllysine-residue succinyltransferase	Product B V2	2.063232884	0.001962993
Galactose-6-phosphate isomerase	Product B V3	2.575276965	0.040843374
6-phosphofructokinase	Product B V3	2.527683882	0.011764389
Carbamoyl-phosphate synthase (glutamine-hydrolyzing)	Product B V3	2.445328101	0.035613373
Orotate phosphoribosyltransferase	Product B V3	2.24538852	0.004285808
Phosphoglycerate mutase (2,3-diphosphoglycerate-independent)	Product B V3	2.224097039	0.038266022
Aspartate carbamoyltransferase	Product B V3	2.052876435	0.006116265

## MetaCyc Pathways

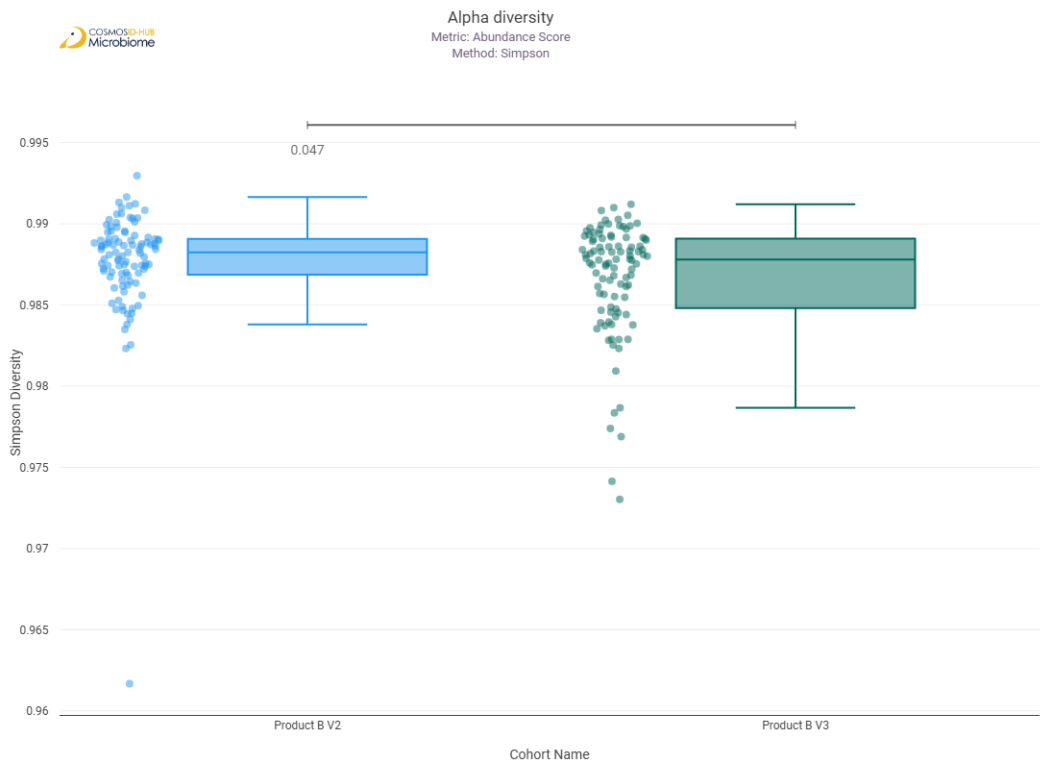
### Alpha Diversity (MetaCyc)



# Shannon

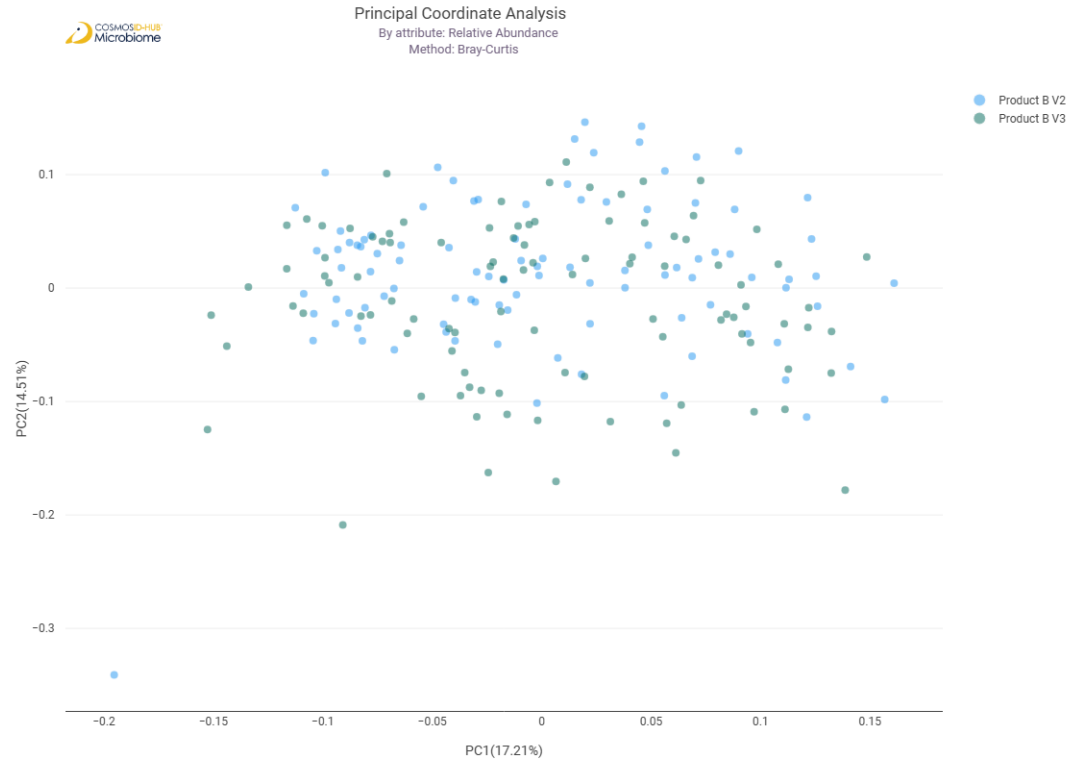


# Simpson

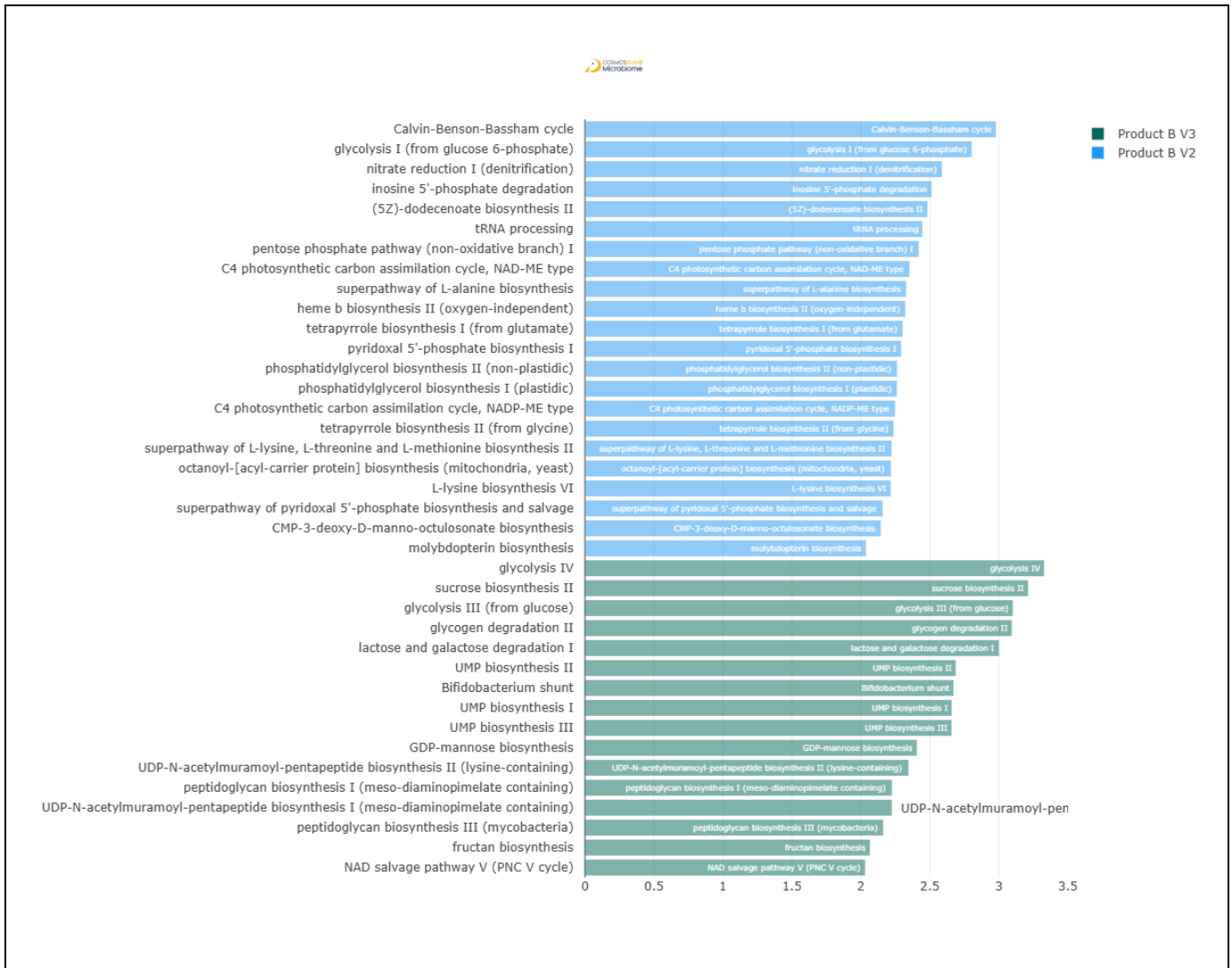


# Beta Diversity (MetaCyc)

Bray-Curtis  
PERMNOVA  
p = 0.007



## Differential Abundance (LEfSe) (MetaCyc)



Feature	Enriched Cohort	LDA Score	P-value
Calvin-Benson-Bassham cycle	Product B V2	2.980017469	0.002293376
glycolysis I (from glucose 6-phosphate)	Product B V2	2.803147252	0.049050725
nitrate reduction I (denitrification)	Product B V2	2.588156927	0.00033841
inosine 5'-phosphate degradation	Product B V2	2.512470778	0.040843374
(5Z)-dodecenoate biosynthesis II	Product B V2	2.482703129	0.002215853
tRNA processing	Product B V2	2.446113576	0.000101039
pentose phosphate pathway (non-oxidative branch) I	Product B V2	2.420285883	0.014160637
C4 photosynthetic carbon assimilation cycle, NAD-ME type	Product B V2	2.352117478	0.002962847
superpathway of L-alanine biosynthesis	Product B V2	2.328429283	0.001134473
heme b biosynthesis II (oxygen-independent)	Product B V2	2.32188526	5.35921E-06
tetrapyrrole biosynthesis I (from glutamate)	Product B V2	2.302670791	2.31E-02
pyridoxal 5'-phosphate biosynthesis I	Product B V2	2.292538957	0.019224991
phosphatidylglycerol biosynthesis II (non-plastidic)	Product B V2	2.262213821	0.012475606
phosphatidylglycerol biosynthesis I (plastidic)	Product B V2	2.261336783	0.011763758
C4 photosynthetic carbon assimilation cycle, NADP-ME type	Product B V2	2.248031239	0.036917997
tetrapyrrole biosynthesis II (from glycine)	Product B V2	2.236665884	0.014840025



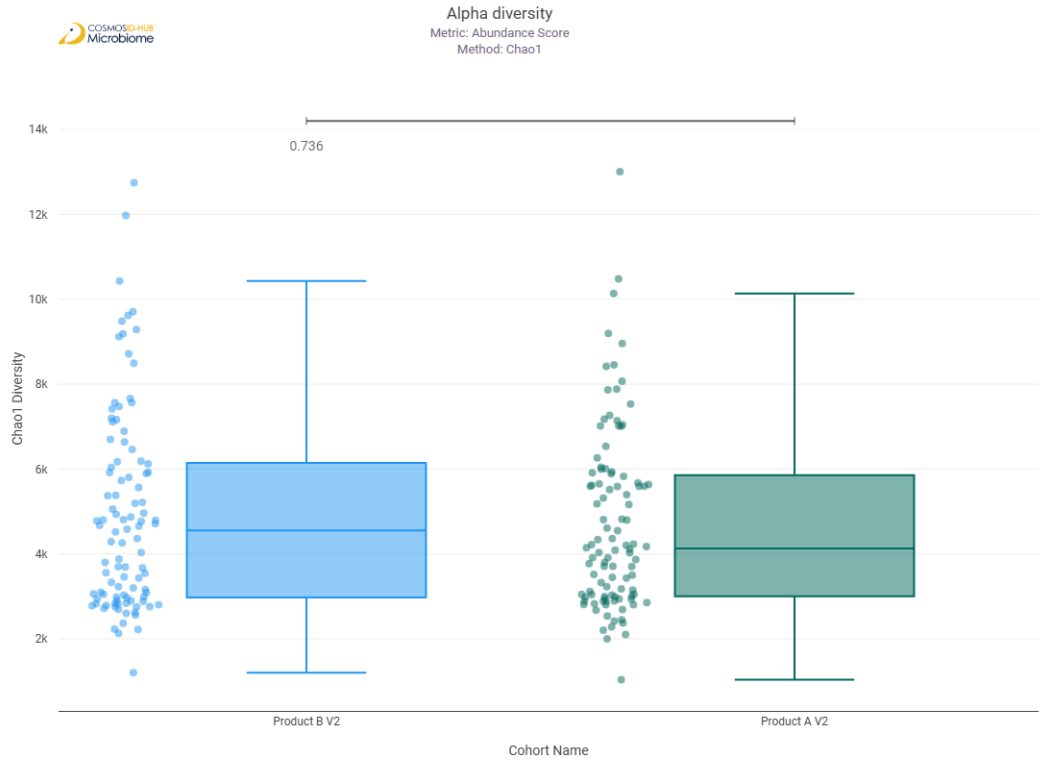
superpathway of L-lysine, L-threonine and L-methionine biosynthesis II	Product B V2	2.222294134	0.010593229
octanoyl-[acyl-carrier protein] biosynthesis (mitochondria, yeast)	Product B V2	2.218678927	0.02610799
L-lysine biosynthesis VI	Product B V2	2.215637736	0.011047972
superpathway of pyridoxal 5'-phosphate biosynthesis and salvage	Product B V2	2.157495637	0.01350269
CMP-3-deoxy-D-manno-octulosonate biosynthesis	Product B V2	2.144607845	0.004222717
molybdopterin biosynthesis	Product B V2	2.036690834	0.003881927
glycolysis IV	Product B V3	3.327911078	0.007851099
sucrose biosynthesis II	Product B V3	3.212667295	3.12E-02
glycolysis III (from glucose)	Product B V3	3.101708701	0.02351136
glycogen degradation II	Product B V3	3.09417983	0.035613373
lactose and galactose degradation I	Product B V3	3.001224899	0.038038729
UMP biosynthesis II	Product B V3	2.687935173	0.000363989
Bifidobacterium shunt	Product B V3	2.671196279	0.038942744
UMP biosynthesis I	Product B V3	2.658158059	0.000570683
UMP biosynthesis III	Product B V3	2.657607009	0.000565546
GDP-mannose biosynthesis	Product B V3	2.406080835	0.030213058
UDP-N-acetylmuramoyl-pentapeptide biosynthesis II (lysine-containing)	Product B V3	2.345372582	0.014748123
peptidoglycan biosynthesis I (meso-diaminopimelate containing)	Product B V3	2.224909222	0.031156435
UDP-N-acetylmuramoyl-pentapeptide biosynthesis I (meso-diaminopimelate containing)	Product B V3	2.224695184	0.040603143
peptidoglycan biosynthesis III (mycobacteria)	Product B V3	2.161540068	0.046039851
fructan biosynthesis	Product B V3	2.065573749	0.031928973
NAD salvage pathway V (PNC V cycle)	Product B V3	2.031437871	0.002049925

## Comparison 3: Product A V2 vs Product B V2

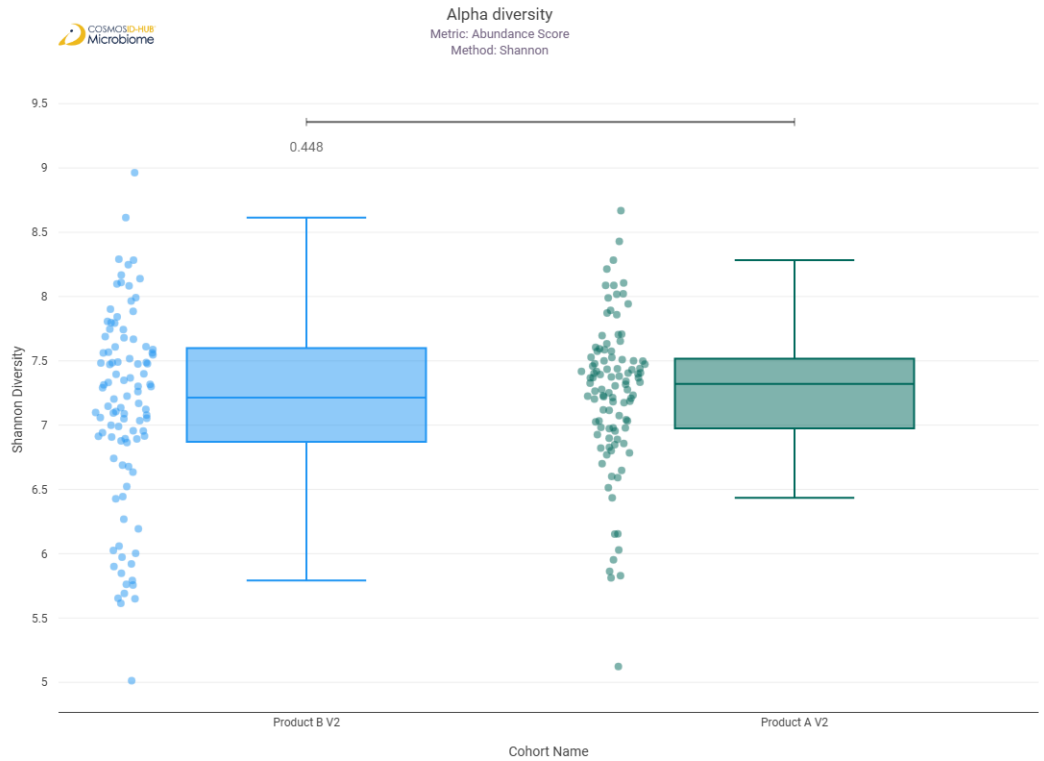
### Gene Ontology

# Alpha Diversity (GO)

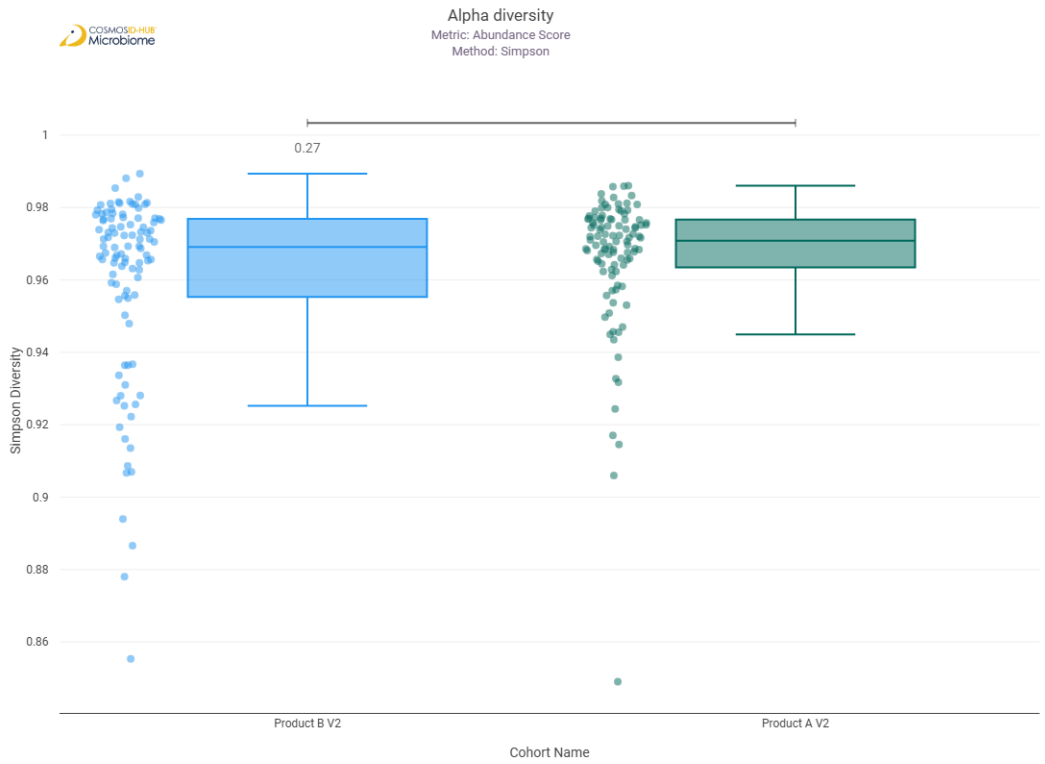
Chao1



Shannon

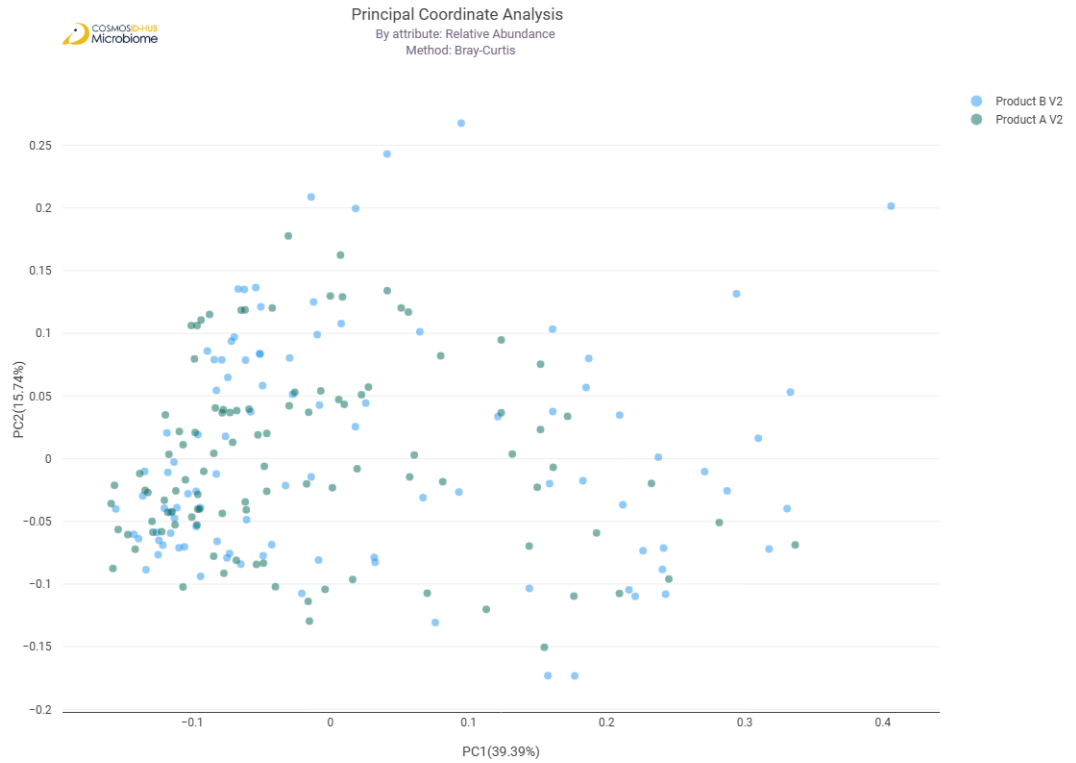


Simpson

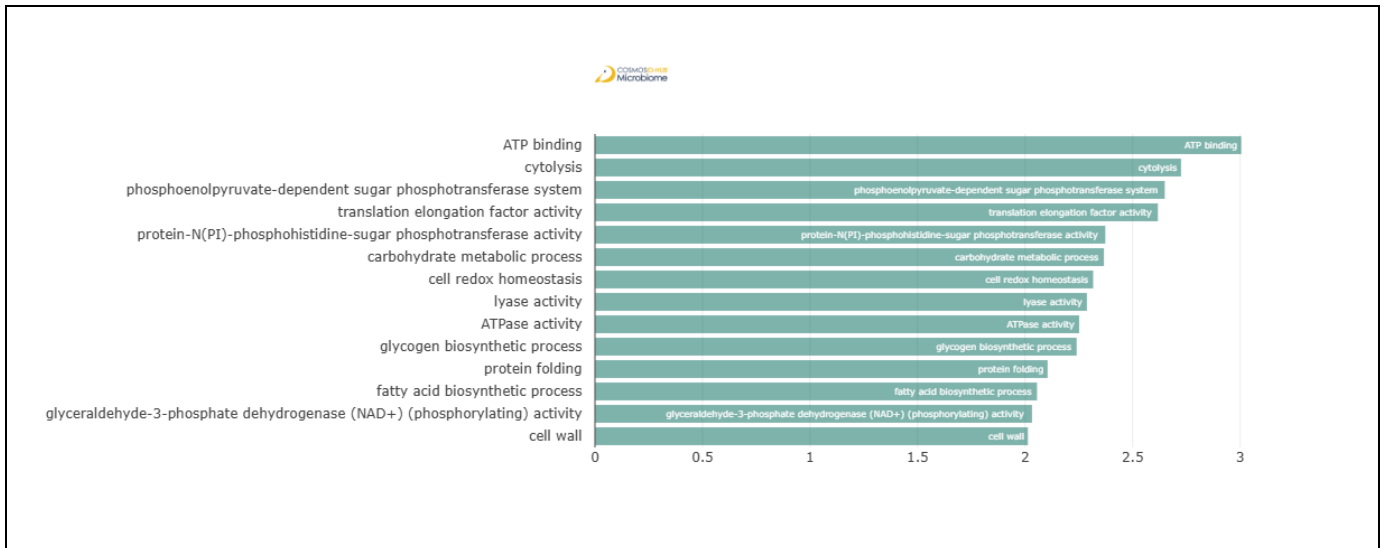


Beta Diversity (GO)

Bray-Curtis  
PERMNOVA  
p = 0.044



## Differential Abundance (LEfSe) (GO)

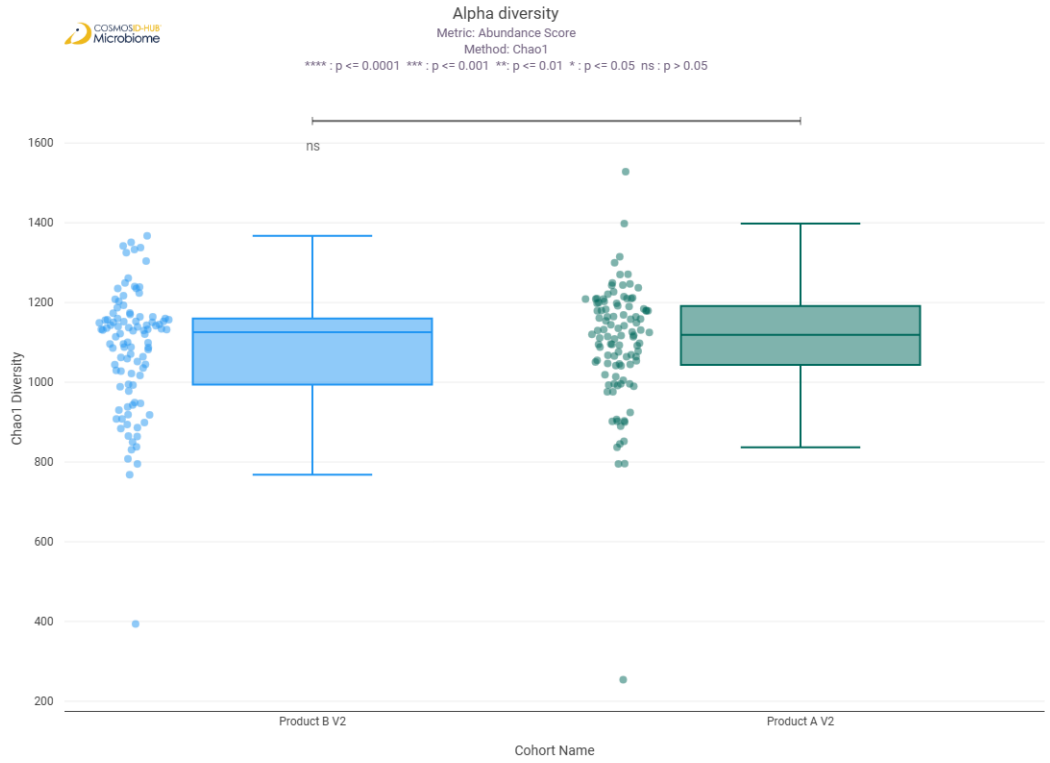


Feature	Enriched Cohort	LDA Score	P-value
ATP binding	Product A V2	3.005226801	0.031977275
cytolysis	Product A V2	2.725138877	0.000880468
phosphoenolpyruvate-dependent sugar phosphotransferase system	Product A V2	2.649451853	0.042757398
translation elongation factor activity	Product A V2	2.617507076	0.043739123
protein-N(Pi)-phosphohistidine-sugar phosphotransferase activity	Product A V2	2.372987284	0.047591773
carbohydrate metabolic process	Product A V2	2.366604496	0.047858458
cell redox homeostasis	Product A V2	2.316574729	0.048395595
lyase activity	Product A V2	2.287508955	0.008162299
ATPase activity	Product A V2	2.251478935	0.040616459
glycogen biosynthetic process	Product A V2	2.2397374	0.035346801
protein folding	Product A V2	2.104787498	1.88E-02
fatty acid biosynthetic process	Product A V2	2.055382736	0.002140946
glyceraldehyde-3-phosphate dehydrogenase (NAD+) (phosphorylating) activity	Product A V2	2.032207372	0.010614864
cell wall	Product A V2	2.013176421	0.042273563

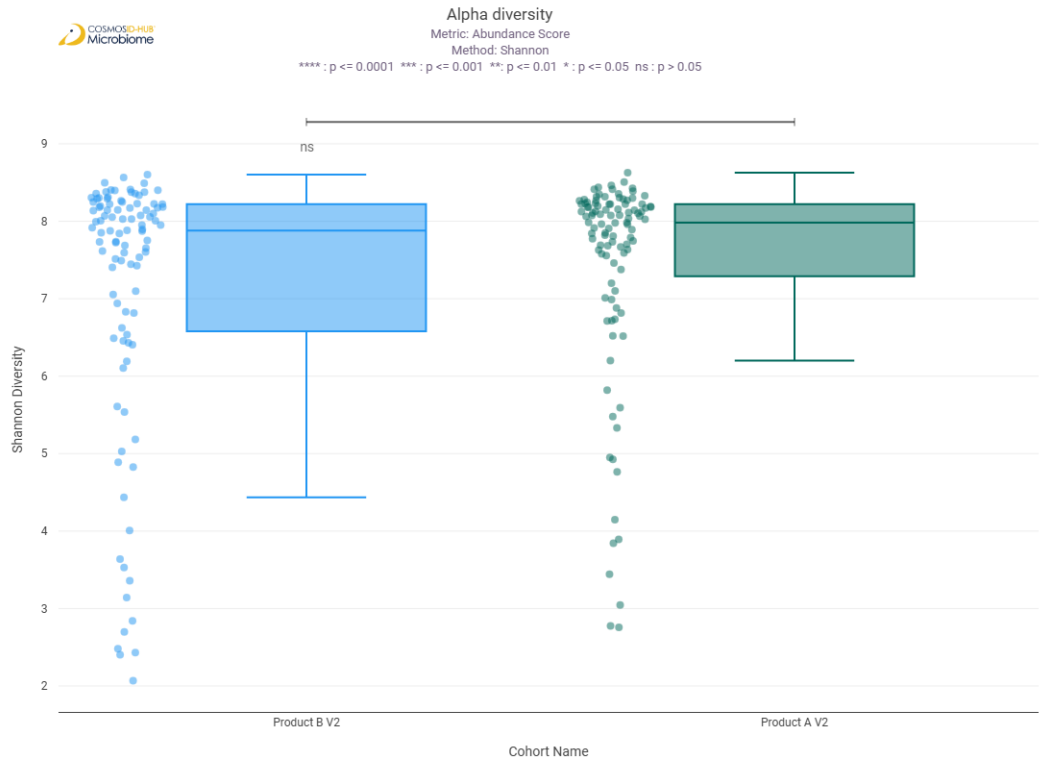
## Enzyme Commission

# Alpha Diversity (EC)

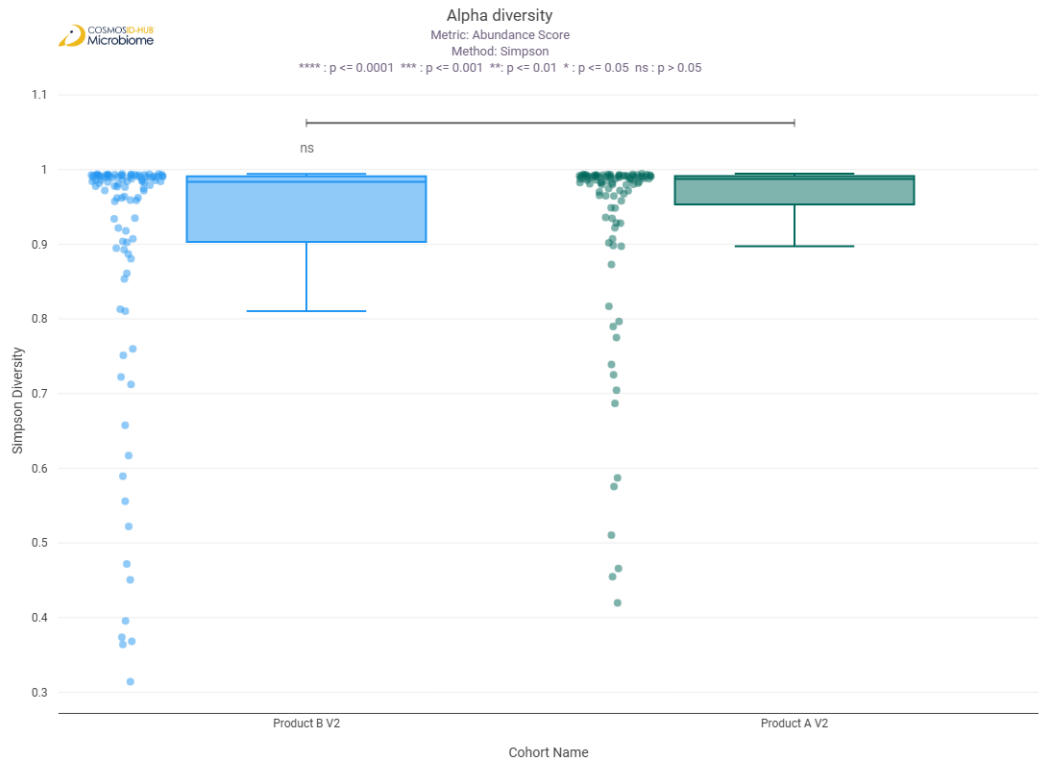
Chao1



Shannon

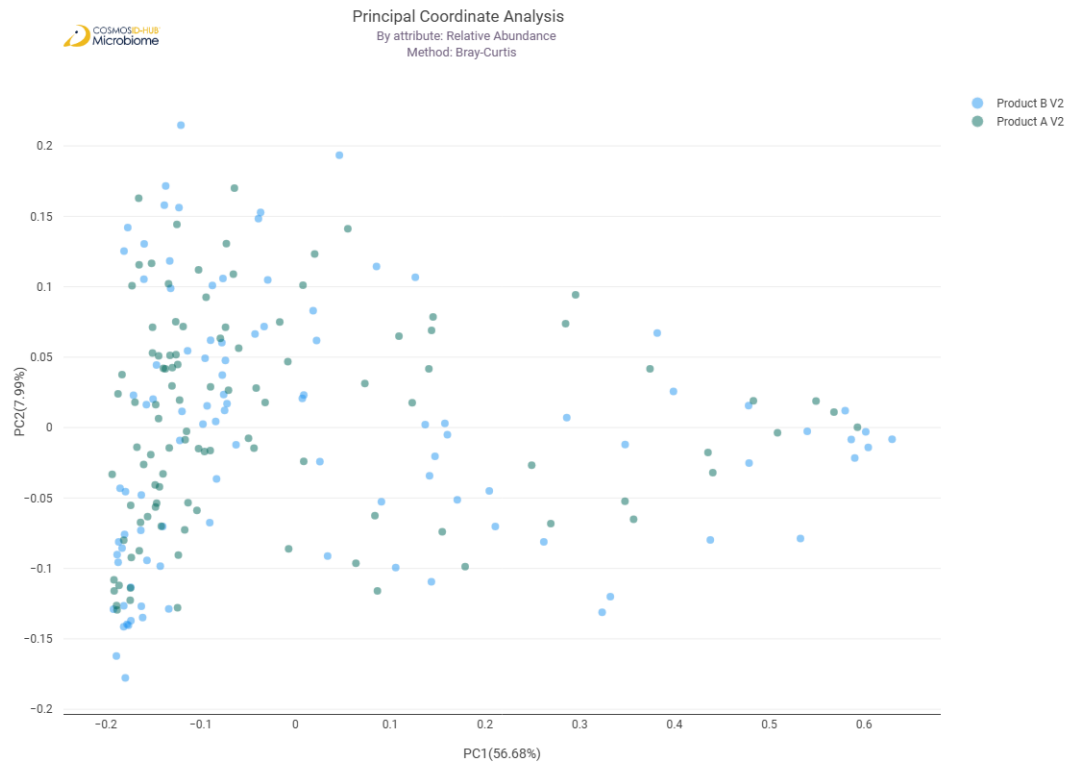


Simpson

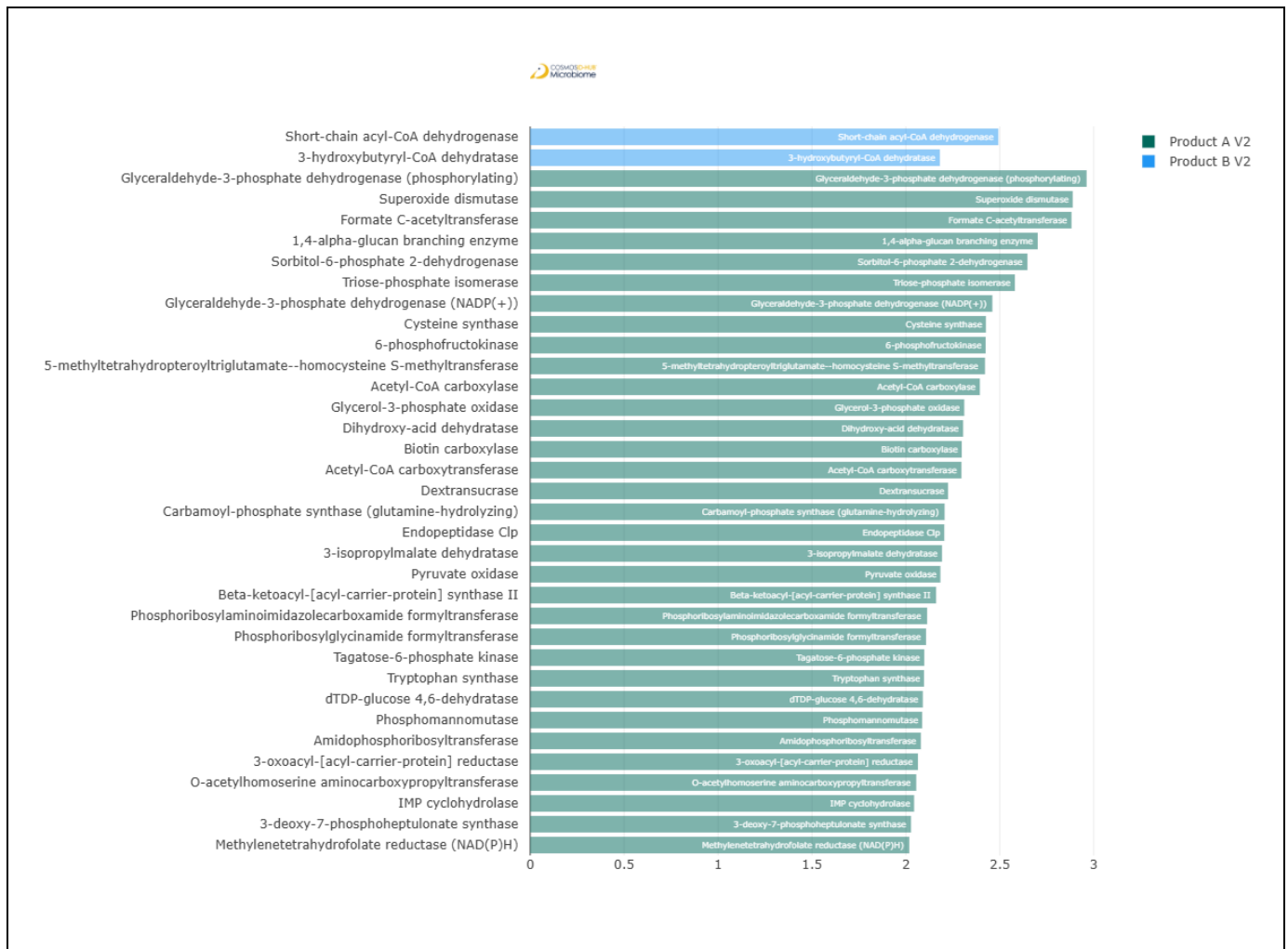


Beta Diversity (EC)

Bray-Curtis  
PERMNOVA  
 $p = 0.091$



## Differential Abundance (LEfSe) (EC)

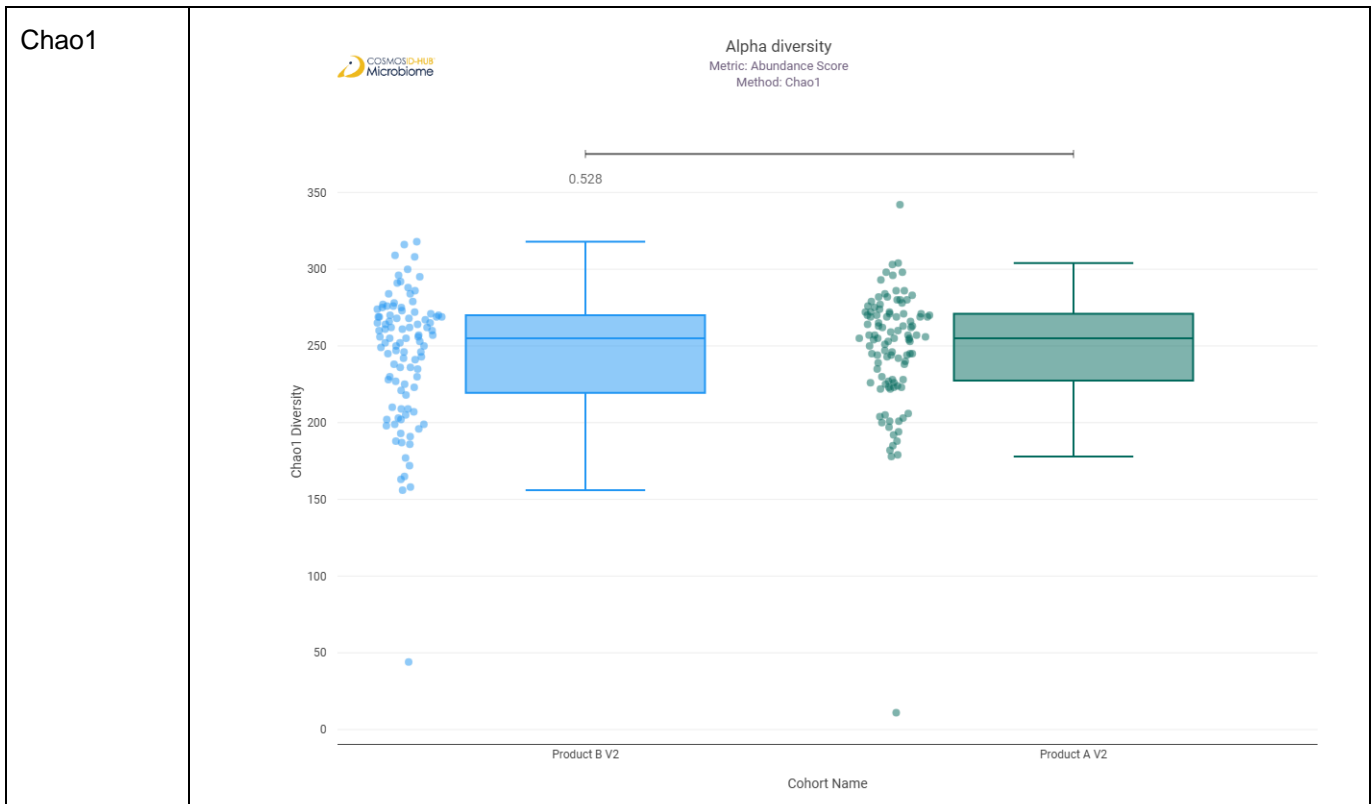


Feature	Enriched Cohort	LDA Score	P-value
Short-chain acyl-CoA dehydrogenase	Product B V2	2.49235307	0.047858458
3-hydroxybutyryl-CoA dehydratase	Product B V2	2.181214019	0.007008368
Glyceraldehyde-3-phosphate dehydrogenase (phosphorylating)	Product A V2	2.96240361	0.023181239
Superoxide dismutase	Product A V2	2.888470105	0.008512232
Formate C-acetyltransferase	Product A V2	2.882169725	0.049210789
1,4-alpha-glucan branching enzyme	Product A V2	2.702278422	0.01532342
Sorbitol-6-phosphate 2-dehydrogenase	Product A V2	2.674440049	0.009739743
Triose-phosphate isomerase	Product A V2	2.580449029	0.019446308
Glyceraldehyde-3-phosphate dehydrogenase (NADP(+))	Product A V2	2.460621406	0.000147279
Cysteine synthase	Product A V2	2.426220942	0.000177076
6-phosphofructokinase	Product A V2	2.42502775	0.046277021
5-methyltetrahydropteroyltriglutamate--homocysteine S-methyltransferase	Product A V2	2.421501802	5.84E-03
Acetyl-CoA carboxylase	Product A V2	2.393966755	0.001383544
Glycerol-3-phosphate oxidase	Product A V2	2.311155395	0.047591773
Dihydroxy-acid dehydratase	Product A V2	2.305025521	0.004189269
Biotin carboxylase	Product A V2	2.297534048	0.006551378
Acetyl-CoA carboxyltransferase	Product A V2	2.295974089	0.012071344

Dextranucrase	Product A V2	2.224701535	0.001199349
Carbamoyl-phosphate synthase (glutamine-hydrolyzing)	Product A V2	2.206170018	0.010399771
Endopeptidase Clp	Product A V2	2.204536759	0.026538437
3-isopropylmalate dehydratase	Product A V2	2.192743488	0.037794131
Pyruvate oxidase	Product A V2	2.184095944	0.041794368
Beta-ketoacyl-[acyl-carrier-protein] synthase II	Product A V2	2.161147246	0.032744287
Phosphoribosylaminoimidazolecarboxamide formyltransferase	Product A V2	2.11335053	3.97E-03
Phosphoribosylglycinamide formyltransferase	Product A V2	2.107677905	0.014829928
Tagatose-6-phosphate kinase	Product A V2	2.098303951	0.00984503
Tryptophan synthase	Product A V2	2.096956912	0.003188504
dTDP-glucose 4,6-dehydratase	Product A V2	2.090506399	0.010833904
Phosphomannomutase	Product A V2	2.086978462	0.027859375
Amidophosphoribosyltransferase	Product A V2	2.079994467	0.01522358
3-oxoacyl-[acyl-carrier-protein] reductase	Product A V2	2.064298956	0.010471034
O-acetylhomoserine aminocarboxypropyltransferase	Product A V2	2.055559479	0.000623736
IMP cyclohydrolase	Product A V2	2.044081157	0.009381425
3-deoxy-7-phosphoheptulonate synthase	Product A V2	2.027555519	0.044992985
Methylenetetrahydrofolate reductase (NAD(P)H)	Product A V2	2.018412166	0.040616459

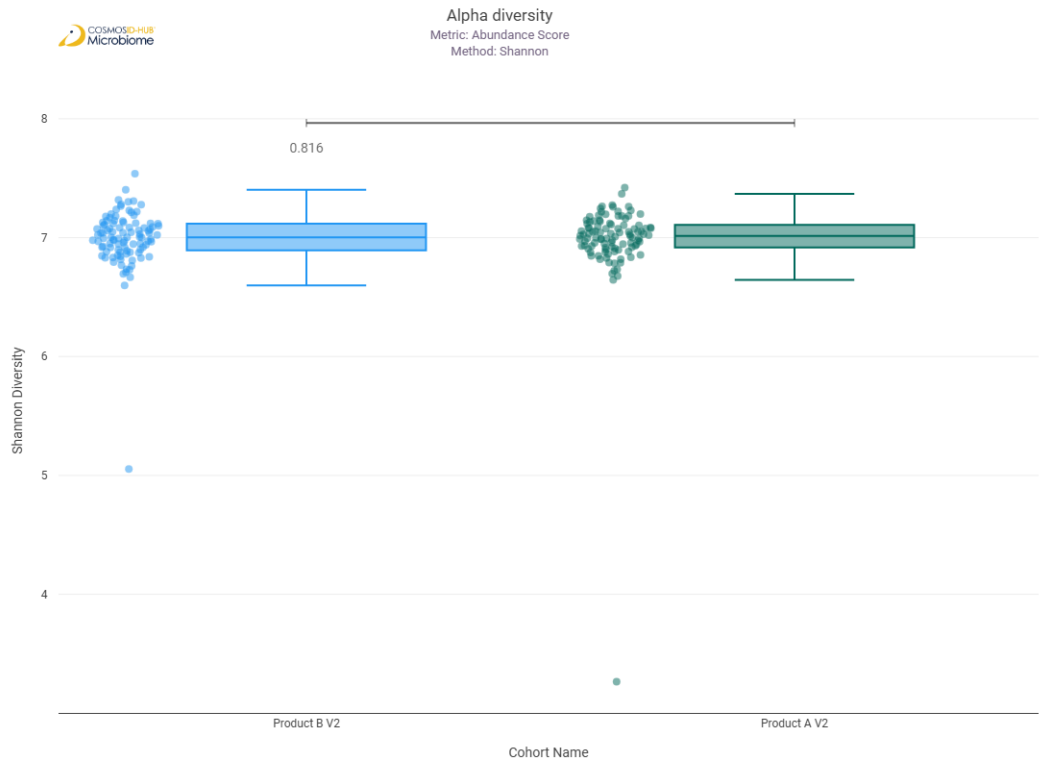
## MetaCyc Pathways

### Alpha Diversity (MetaCyc)





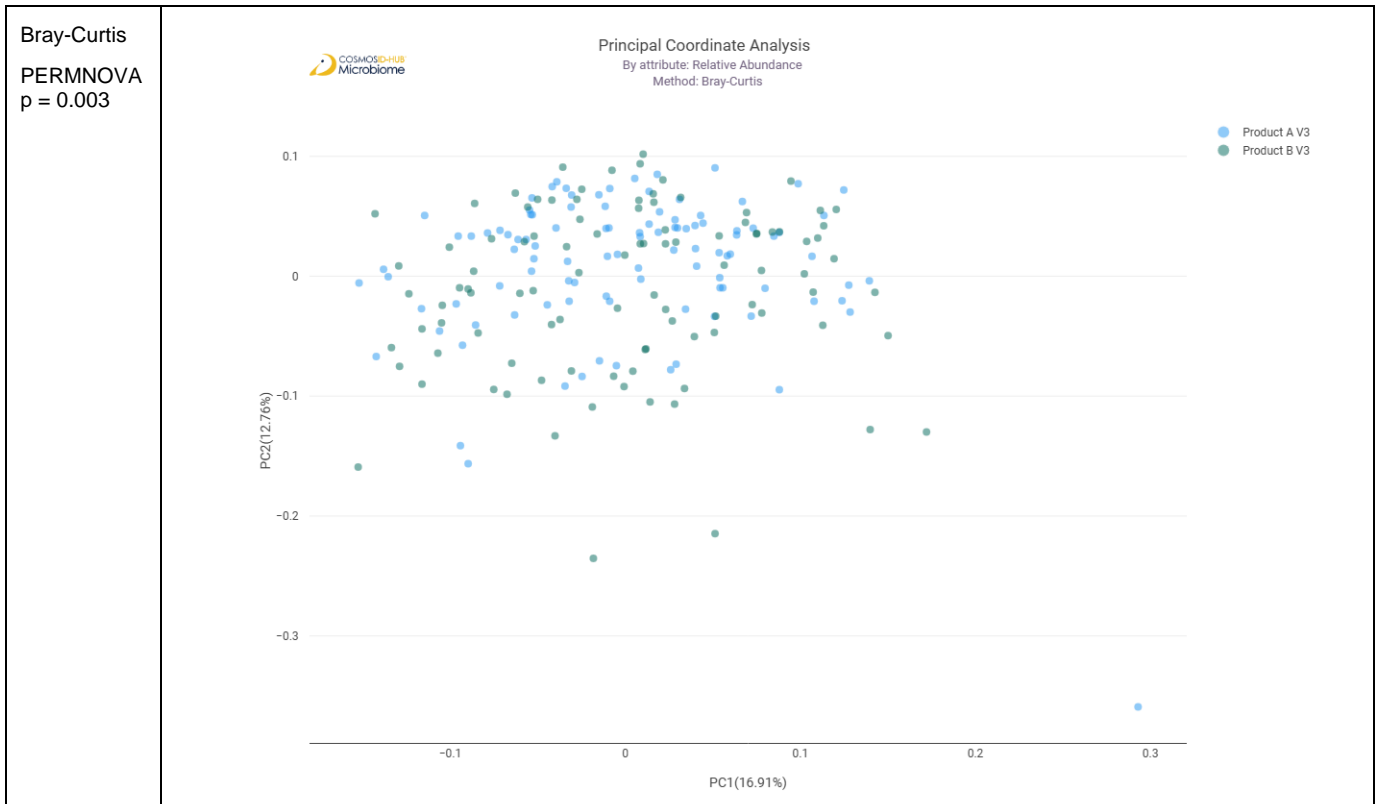
# Shannon



# Simpson



## Beta Diversity (MetaCyc)



## Differential Abundance (LEfSe) (MetaCyc)



superpathway of purine nucleotides de novo biosynthesis I	Product A V2	2.430450703	0.037903528
inosine-5'-phosphate biosynthesis III	Product A V2	2.406751294	0.014349805
fructan biosynthesis	Product A V2	2.401680055	0.021736476
C4 photosynthetic carbon assimilation cycle, PEPCk type	Product A V2	2.324662591	0.029148795
L-lysine biosynthesis III	Product A V2	2.213631989	4.16E-02

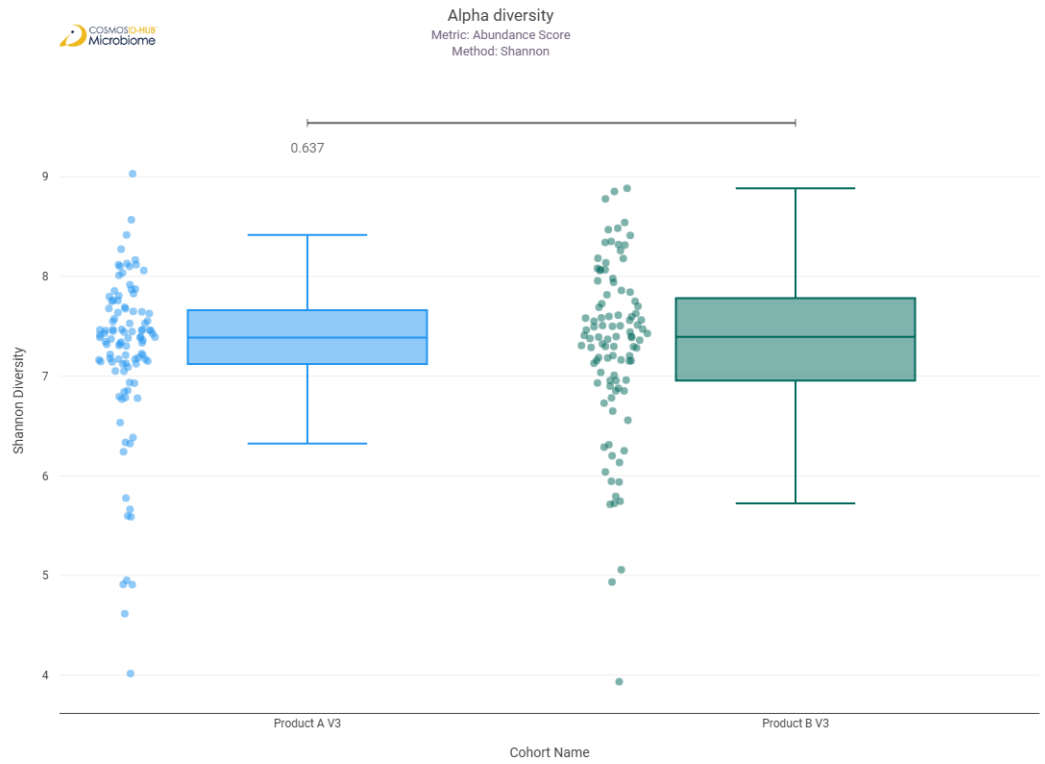
## Comparison 4: Product A V2 SAL vs Product A V3 SAL

### Gene Ontology

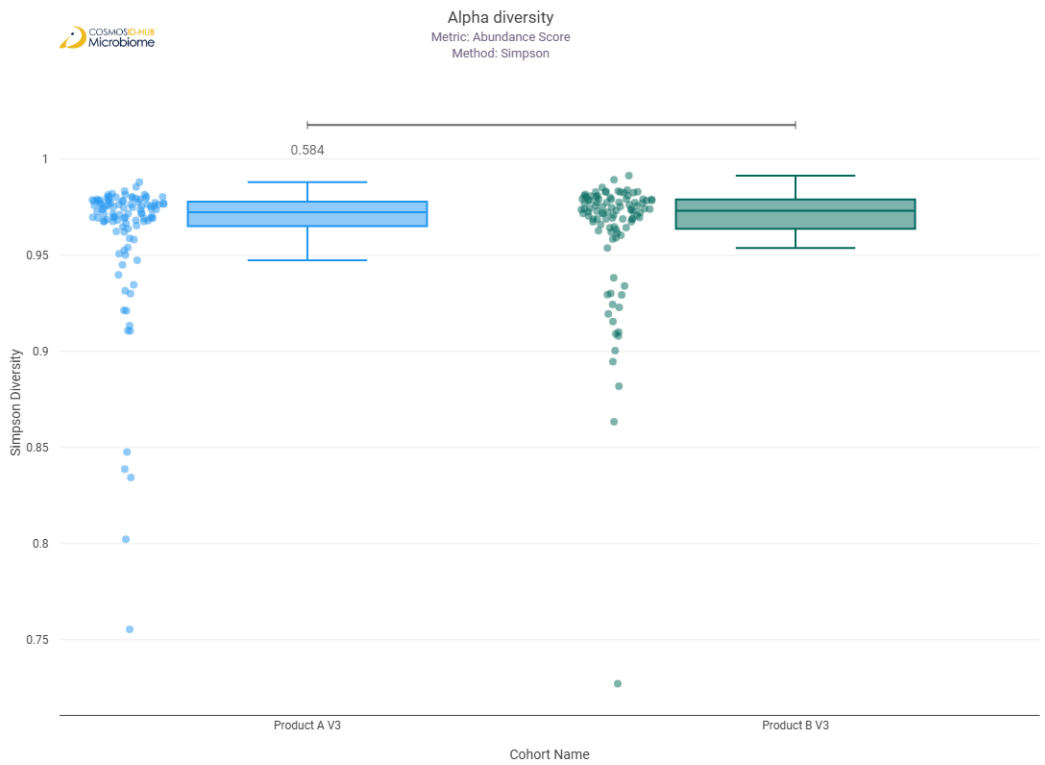
#### Alpha Diversity (GO)



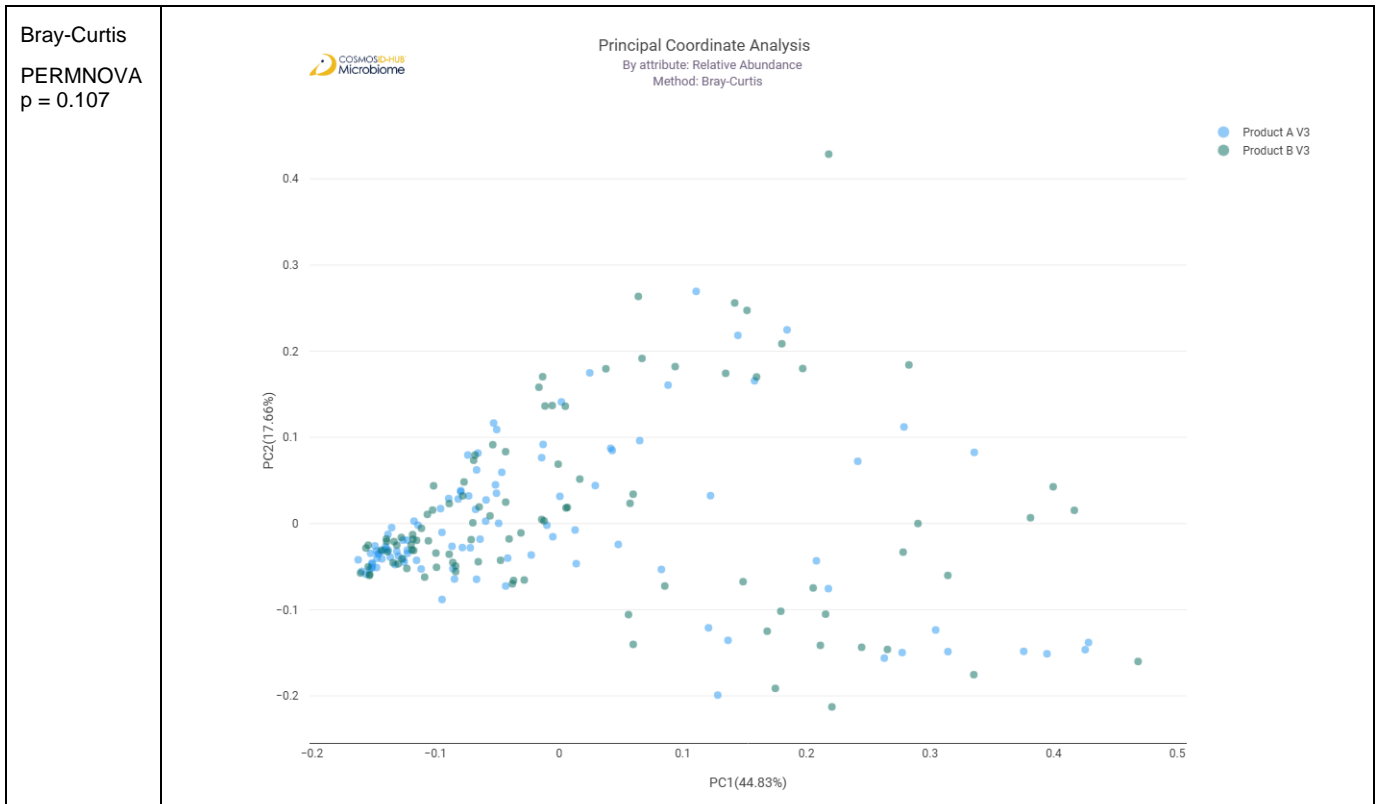
# Shannon



# Simpson



## Beta Diversity (GO)



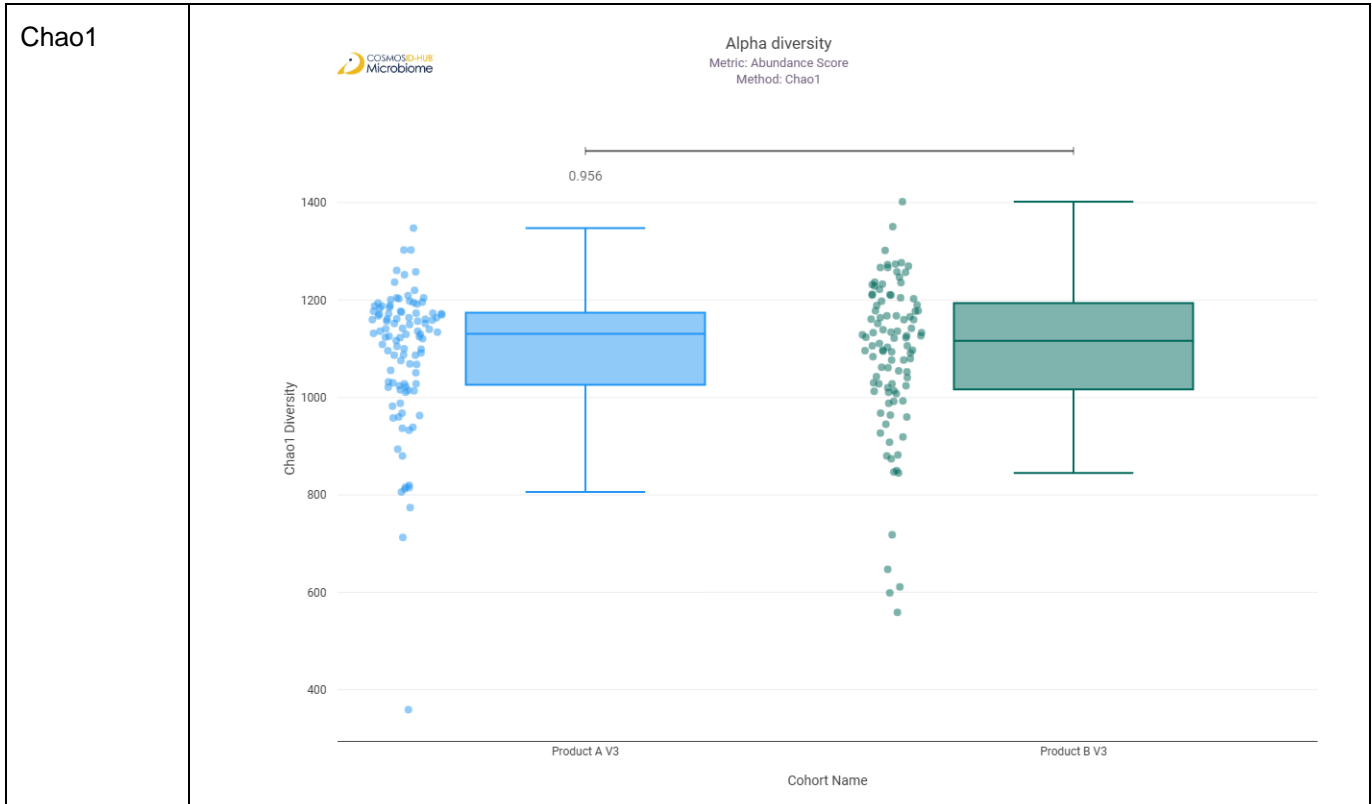
## Differential Abundance (LEfSe) (GO)



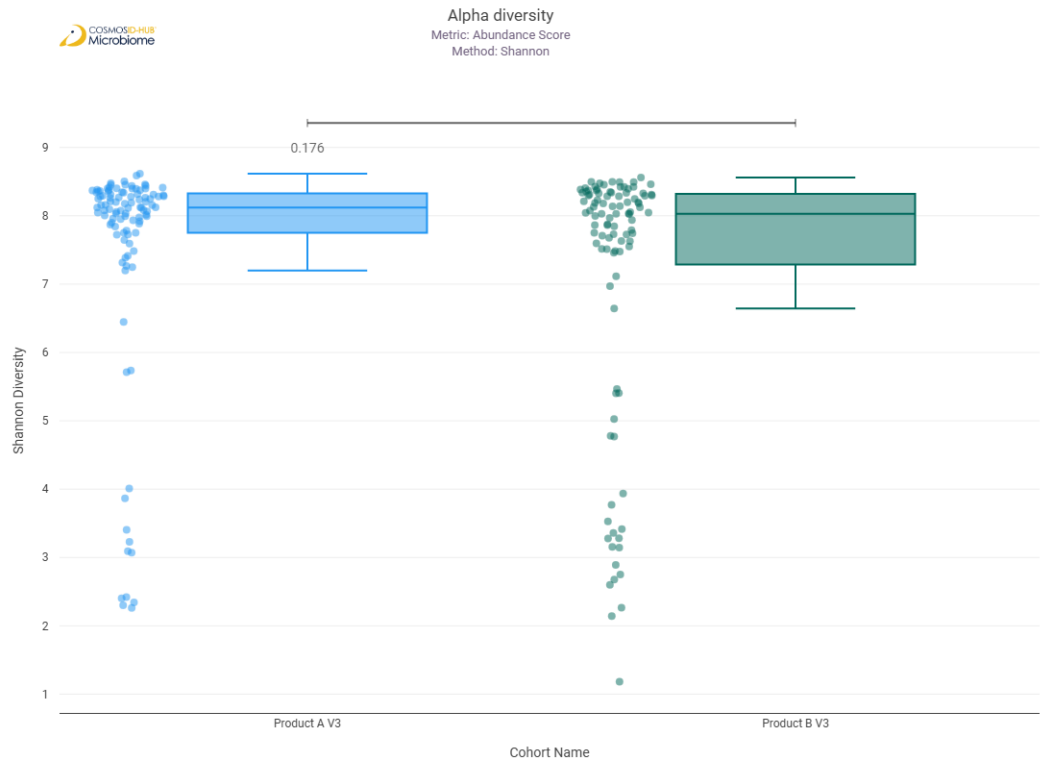
ATPase-coupled transmembrane transporter activity	Product A V3	2.072667654	0.004581458
protein transport	Product A V3	2.046545024	0.008571841
integral component of plasma membrane	Product A V3	2.032254996	0.008105245
glutamine biosynthetic process	Product B V3	2.004671978	2.19E-02
glutamate-ammonia ligase activity	Product B V3	2.00334107	0.025271957

## Enzyme Commission

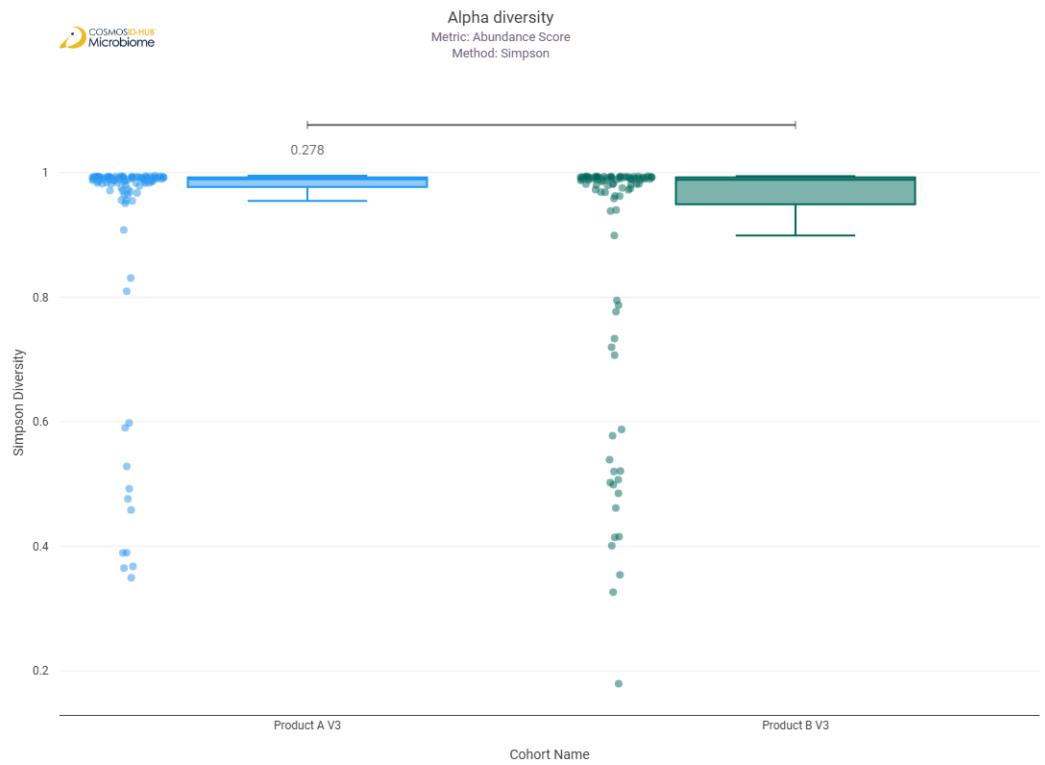
### Alpha Diversity (EC)



# Shannon

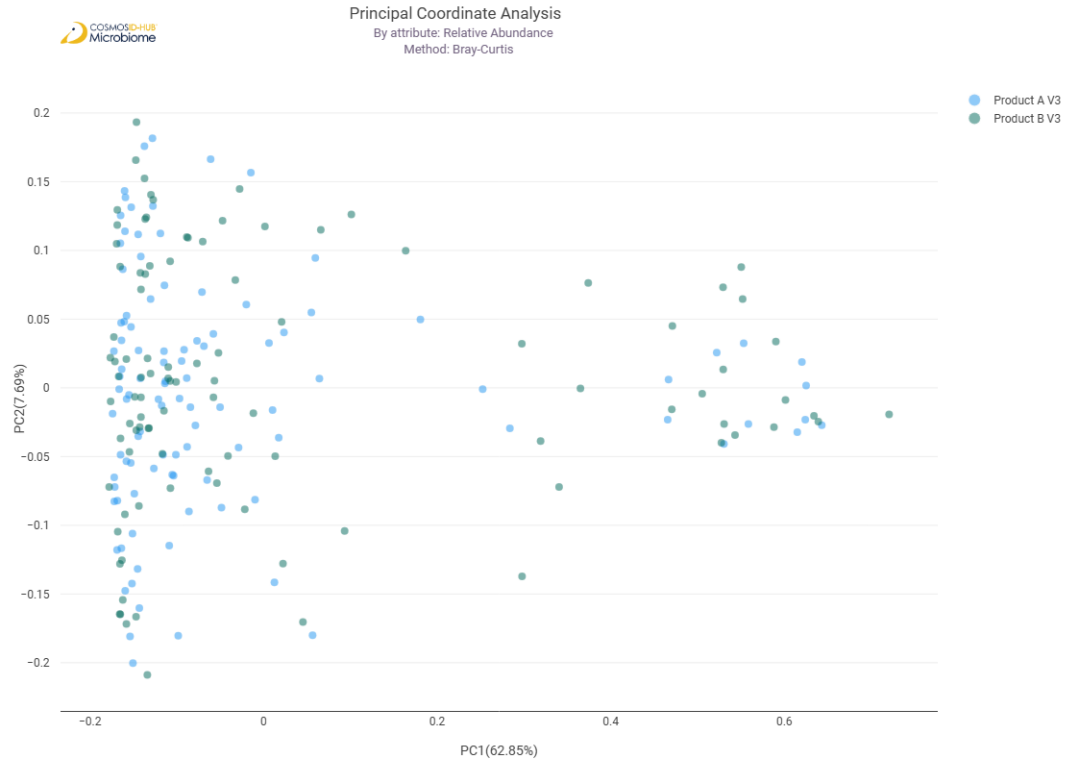


# Simpson



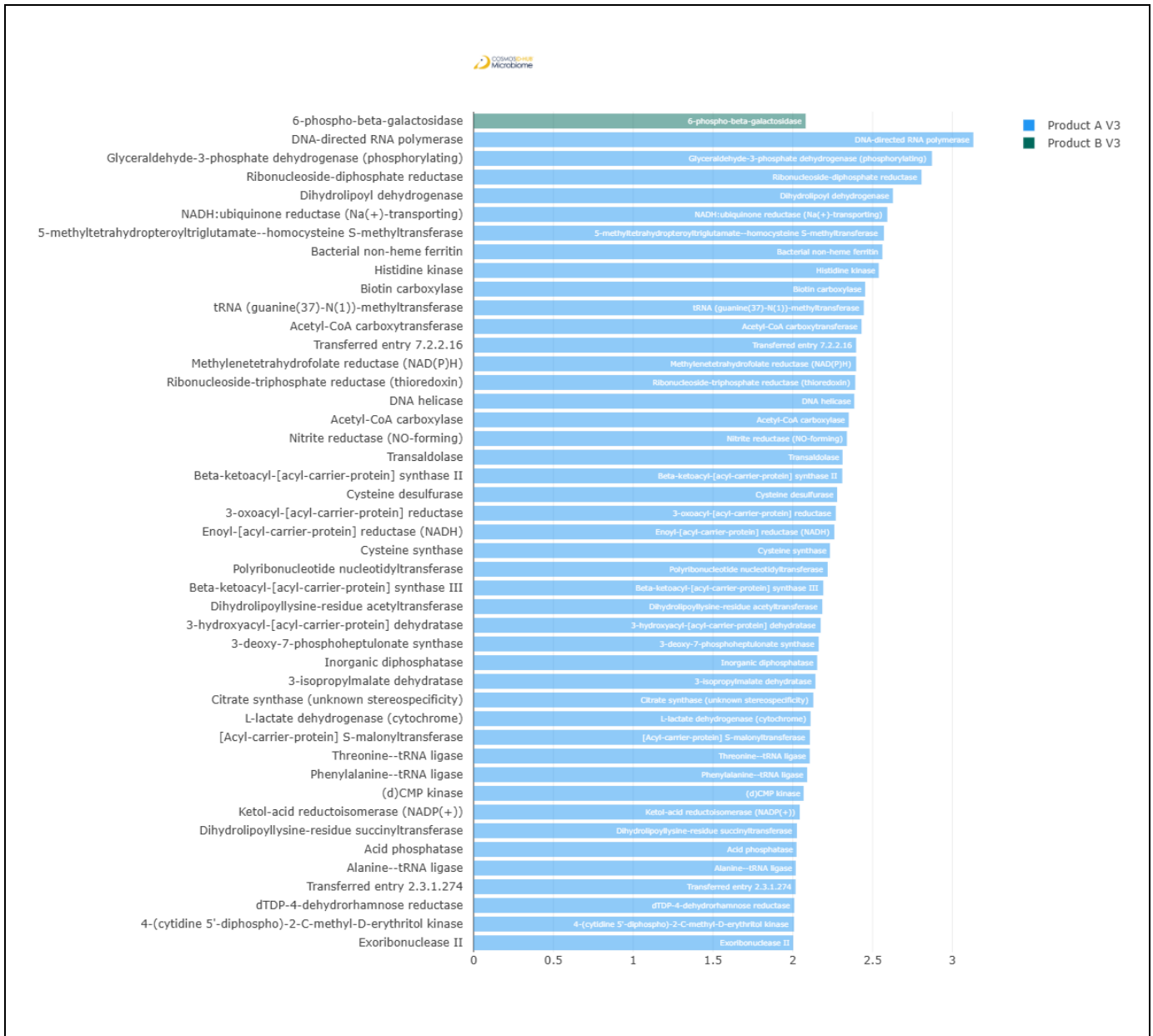
# Beta Diversity (EC)

Bray-Curtis  
PERMNOVA  
p = 0.072





## Differential Abundance (LEfSe) (EC)



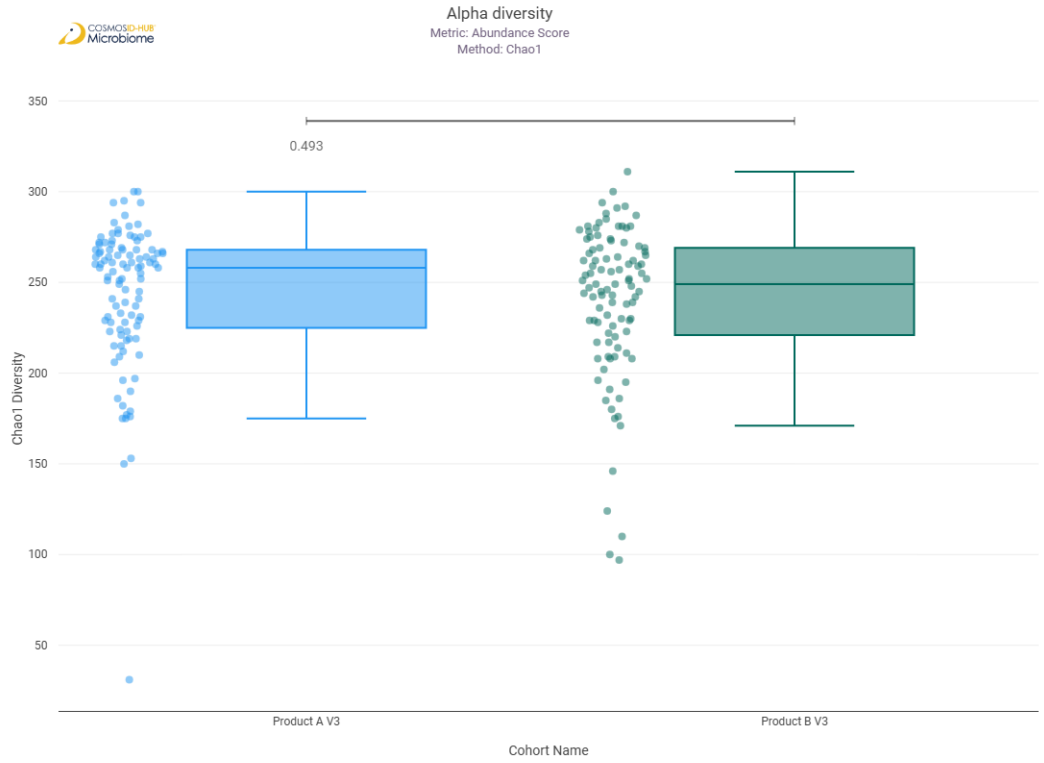
Feature	Enriched Cohort	LDA Score	P-value
6-phospho-beta-galactosidase	Product B V3	2.080727545	0.046385006
DNA-directed RNA polymerase	Product A V3	3.131684191	0.026538437
Glyceraldehyde-3-phosphate dehydrogenase (phosphorylating)	Product A V3	2.872341567	0.028198334
Ribonucleoside-diphosphate reductase	Product A V3	2.806603682	0.007770359
Dihydrolipoyl dehydrogenase	Product A V3	2.627544199	0.008937395
NADH:ubiquinone reductase (Na(+)-transporting)	Product A V3	2.59253101	0.013431321
5-methyltetrahydropteroyltriglutamate--homocysteine S-methyltransferase	Product A V3	2.571096295	0.012993227
Bacterial non-heme ferritin	Product A V3	2.561732858	0.022612184
Histidine kinase	Product A V3	2.53874264	0.017670566
Biotin carboxylase	Product A V3	2.453594887	0.002648014
tRNA (guanine(37)-N(1))-methyltransferase	Product A V3	2.445456033	0.000781151
Acetyl-CoA carboxyltransferase	Product A V3	2.430837617	1.91E-03

Transferred entry 7.2.2.16	Product A V3	2.397074415	0.03216757
Methylenetetrahydrofolate reductase (NAD(P)H)	Product A V3	2.397041877	0.027691217
Ribonucleoside-triphosphate reductase (thioredoxin)	Product A V3	2.391476364	0.009252593
DNA helicase	Product A V3	2.385246652	0.040384285
Acetyl-CoA carboxylase	Product A V3	2.350690765	0.014069443
Nitrite reductase (NO-forming)	Product A V3	2.339275293	0.006125811
Transaldolase	Product A V3	2.312003861	0.000815362
Beta-ketoacyl-[acyl-carrier-protein] synthase II	Product A V3	2.310457827	0.017001077
Cysteine desulfurase	Product A V3	2.277719109	0.003091956
3-oxoacyl-[acyl-carrier-protein] reductase	Product A V3	2.269677866	7.19E-03
Enoyl-[acyl-carrier-protein] reductase (NADH)	Product A V3	2.260621834	5.44775E-05
Cysteine synthase	Product A V3	2.232785492	0.011056954
Polyribonucleotide nucleotidyltransferase	Product A V3	2.218940509	0.00760761
Beta-ketoacyl-[acyl-carrier-protein] synthase III	Product A V3	2.191178527	0.016782914
Dihydrolipoyllysine-residue acetyltransferase	Product A V3	2.184992934	2.21596E-05
3-hydroxyacyl-[acyl-carrier-protein] dehydratase	Product A V3	2.174872472	0.006645961
3-deoxy-7-phosphoheptulonate synthase	Product A V3	2.162273672	0.000597086
Inorganic diphosphatase	Product A V3	2.152950641	0.028369142
3-isopropylmalate dehydratase	Product A V3	2.142110454	0.006693711
Citrate synthase (unknown stereospecificity)	Product A V3	2.128832033	0.047502293
L-lactate dehydrogenase (cytochrome)	Product A V3	2.111713408	0.000198287
[Acyl-carrier-protein] S-malonyltransferase	Product A V3	2.107247626	0.033133665
Threonine--tRNA ligase	Product A V3	2.106387094	0.01004989
Phenylalanine--tRNA ligase	Product A V3	2.090165423	0.01744488
(d)CMP kinase	Product A V3	2.068001372	0.007661517
Ketol-acid reductoisomerase (NADP(+))	Product A V3	2.043610854	0.047858458
Dihydrolipoyllysine-residue succinyltransferase	Product A V3	2.026340003	0.028886698
Acid phosphatase	Product A V3	2.023639908	0.002648014
Alanine--tRNA ligase	Product A V3	2.018798405	0.02332543
Transferred entry 2.3.1.274	Product A V3	2.017852023	0.003915394
dTDP-4-dehydrorhamnose reductase	Product A V3	2.009516698	0.005965544
4-(cytidine 5'-diphospho)-2-C-methyl-D-erythritol kinase	Product A V3	2.007683828	0.000111216
Exoribonuclease II	Product A V3	2.002632022	0.000131097

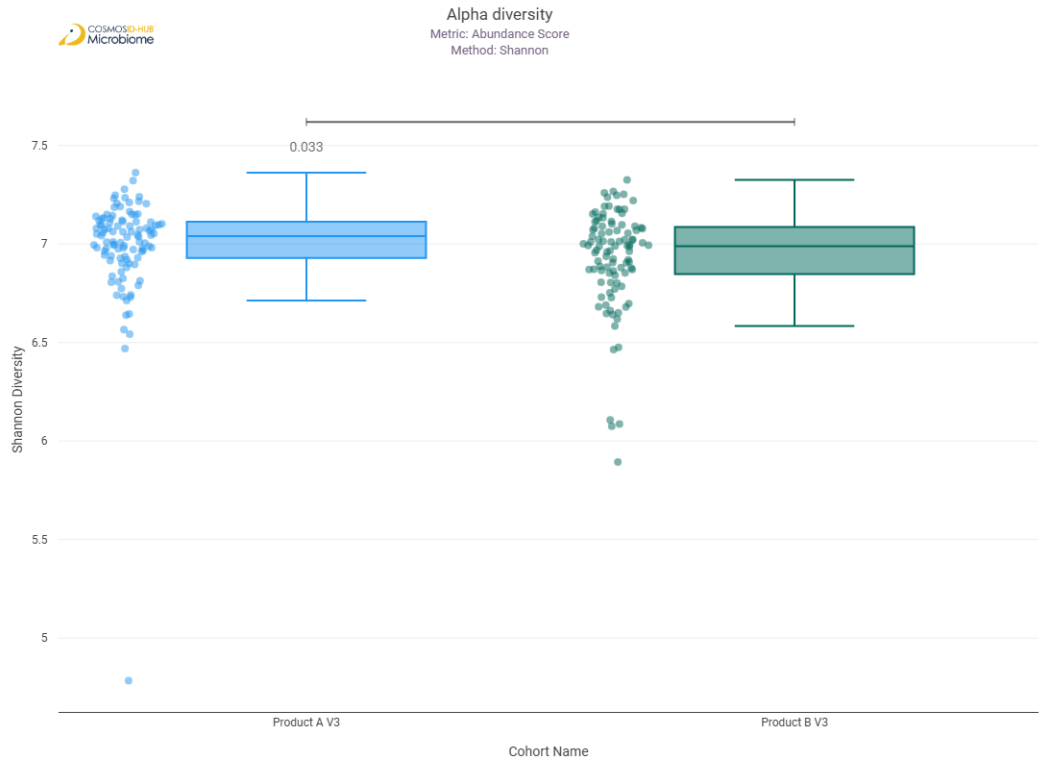
## MetaCyc Pathways

# Alpha Diversity (MetaCyc)

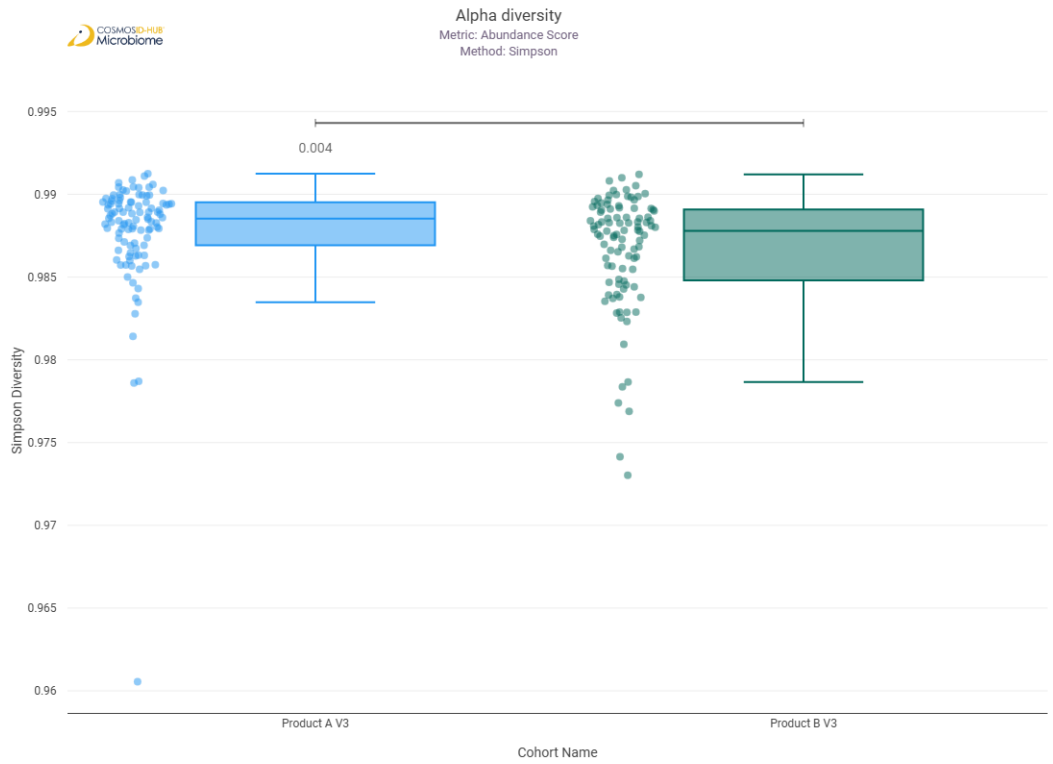
Chao1



Shannon

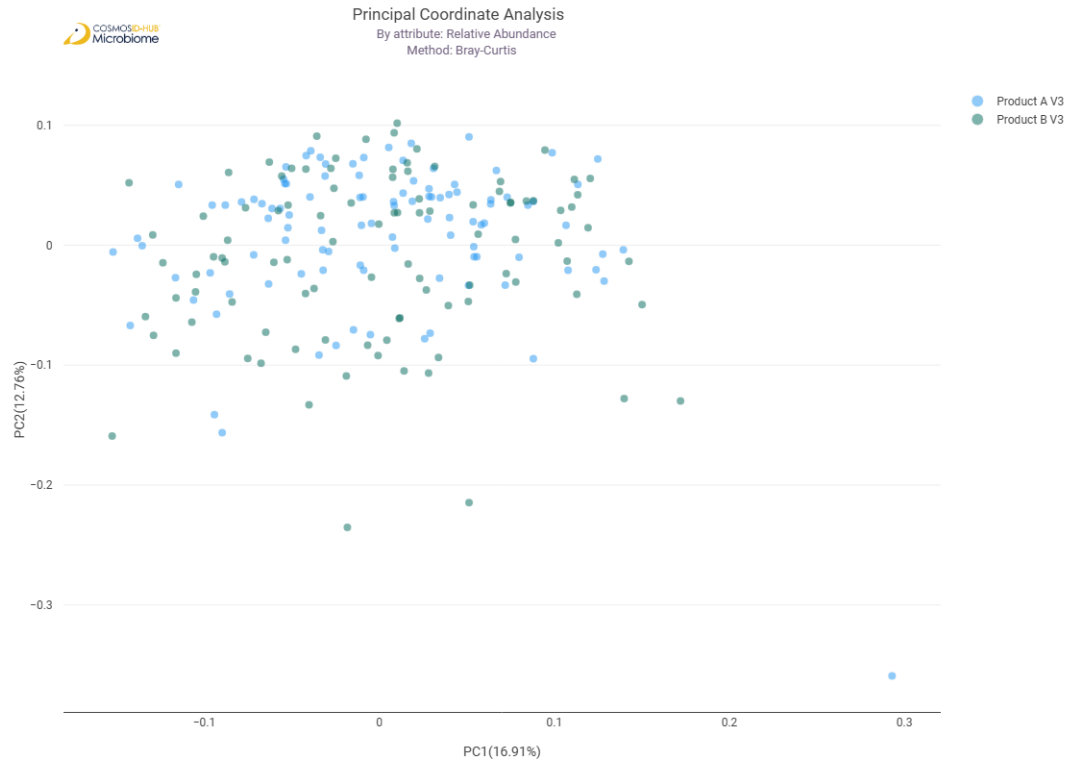


Simpson

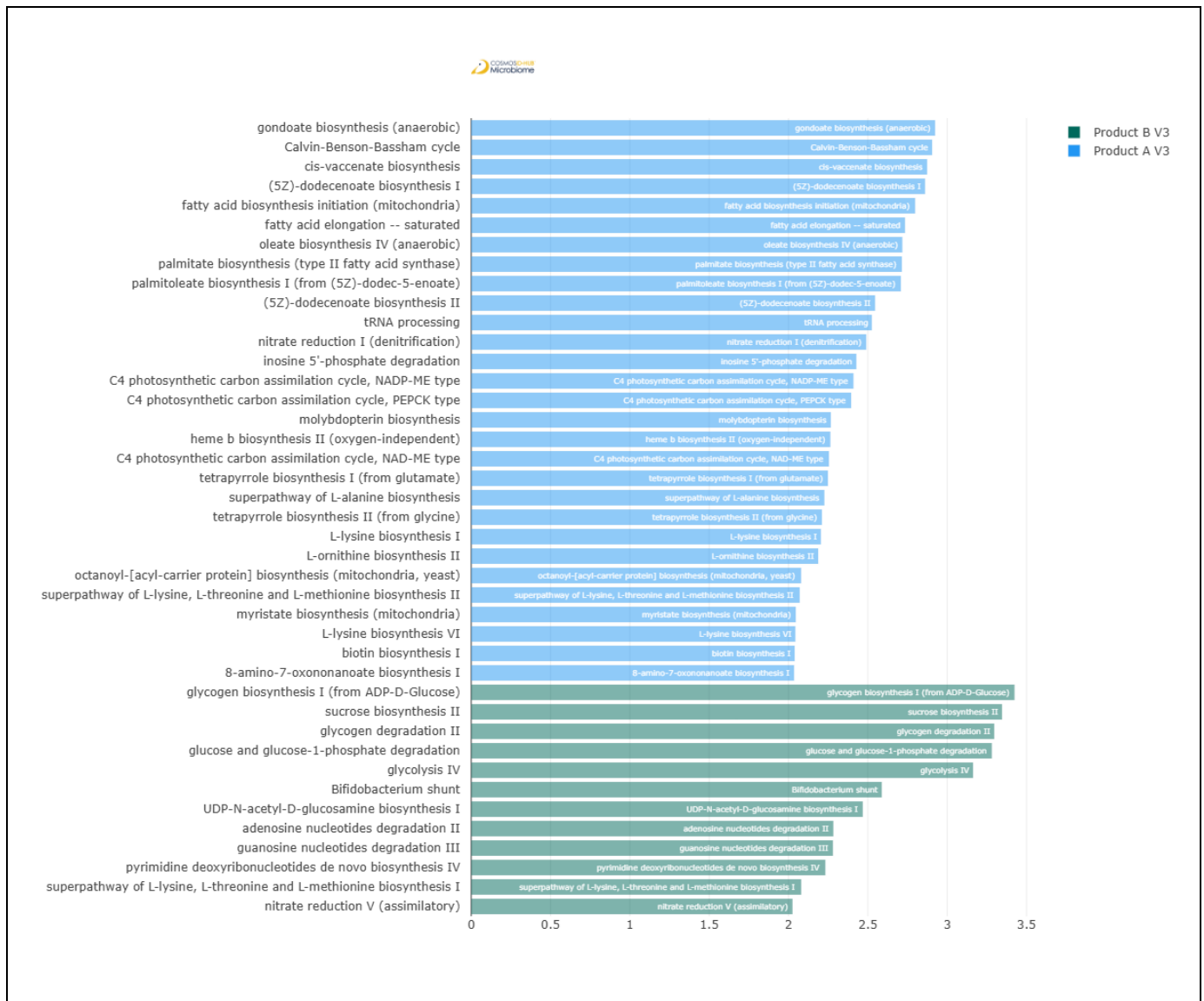


Beta Diversity (MetaCyc)

Bray-Curtis  
PERMNOVA  
p = 0.003



## Differential Abundance (LEfSe) (MetaCyc)



Feature	Enriched Cohort	LDA Score	P-value
gondoate biosynthesis (anaerobic)	Product A V3	2.924054289	1.71664E-05
Calvin-Benson-Bassham cycle	Product A V3	2.90518626	0.037034519
cis-vaccenate biosynthesis	Product A V3	2.873686051	0.000100888
(5Z)-dodecenoate biosynthesis I	Product A V3	2.860646941	0.000168085
fatty acid biosynthesis initiation (mitochondria)	Product A V3	2.798040194	0.014350494
fatty acid elongation -- saturated	Product A V3	2.734390918	0.000250374
oleate biosynthesis IV (anaerobic)	Product A V3	2.717536982	0.000364402
palmitate biosynthesis (type II fatty acid synthase)	Product A V3	2.714526789	0.007301725
palmitoleate biosynthesis I (from (5Z)-dodec-5-enoate)	Product A V3	2.708135225	0.000464298
(5Z)-dodecenoate biosynthesis II	Product A V3	2.545755648	0.000414729
tRNA processing	Product A V3	2.525229504	0.0003883
nitrate reduction I (denitrification)	Product A V3	2.489917921	0.001492854
inosine 5'-phosphate degradation	Product A V3	2.427780228	0.008219712
C4 photosynthetic carbon assimilation cycle, NADP-ME type	Product A V3	2.409347733	0.000732058
glycogen biosynthesis I (from ADP-D-Glucose)	Product B V3	2.924054289	1.71664E-05
sucrose biosynthesis II	Product B V3	2.90518626	0.037034519
glycogen degradation II	Product B V3	2.873686051	0.000100888
glucose and glucose-1-phosphate degradation	Product B V3	2.860646941	0.000168085
glycolysis IV	Product B V3	2.798040194	0.014350494
Bifidobacterium shunt	Product B V3	2.734390918	0.000250374
UDP-N-acetyl-D-glucosamine biosynthesis I	Product B V3	2.717536982	0.000364402
adenosine nucleotides degradation II	Product B V3	2.714526789	0.007301725
guanosine nucleotides degradation III	Product B V3	2.708135225	0.000464298
pyrimidine deoxyribonucleotides de novo biosynthesis IV	Product B V3	2.545755648	0.000414729
superpathway of L-lysine, L-threonine and L-methionine biosynthesis I	Product B V3	2.525229504	0.0003883
nitrate reduction V (assimilatory)	Product B V3	2.489917921	0.001492854

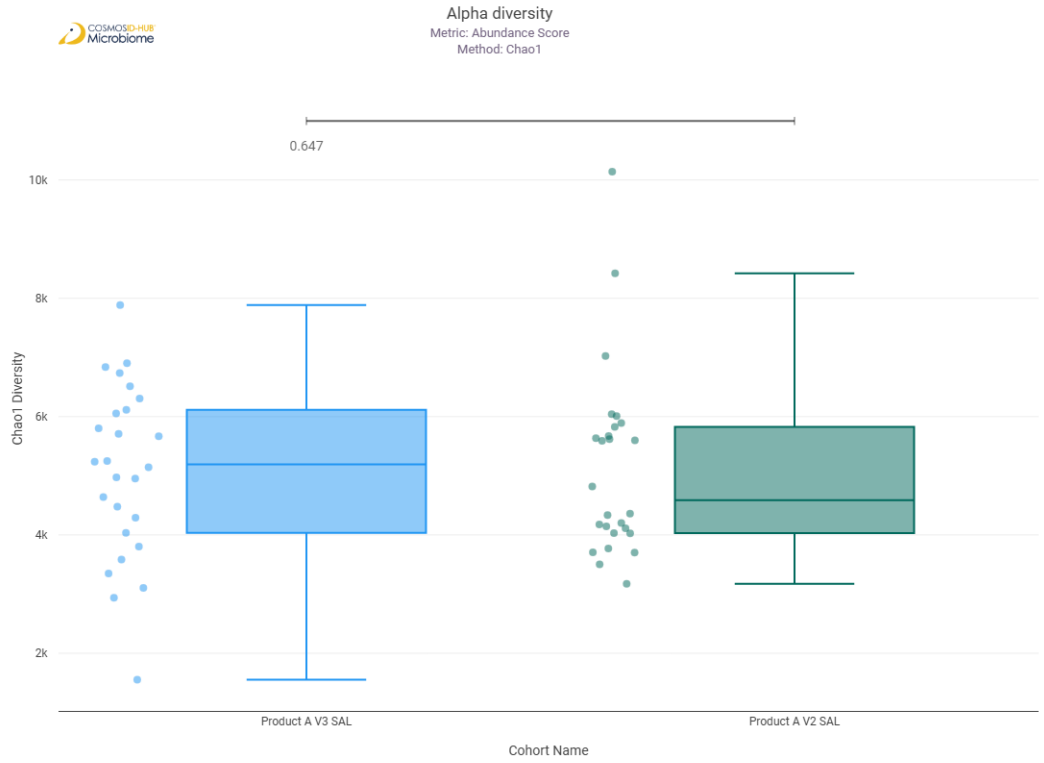
C4 photosynthetic carbon assimilation cycle, PEPC type	Product A V3	2.394946465	0.012152566
molybdopterin biosynthesis	Product A V3	2.266745981	7.60264E-06
heme b biosynthesis II (oxygen-independent)	Product A V3	2.264050701	1.53555E-06
C4 photosynthetic carbon assimilation cycle, NAD-ME type	Product A V3	2.254910685	1.72E-03
tetrapyrrole biosynthesis I (from glutamate)	Product A V3	2.248434275	0.003468115
superpathway of L-alanine biosynthesis	Product A V3	2.226385681	0.004459743
tetrapyrrole biosynthesis II (from glycine)	Product A V3	2.210751712	0.011432973
L-lysine biosynthesis I	Product A V3	2.204168356	0.006050982
L-ornithine biosynthesis II	Product A V3	2.187087921	9.90522E-05
octanoyl-[acyl-carrier protein] biosynthesis (mitochondria, yeast)	Product A V3	2.079495823	0.004954342
superpathway of L-lysine, L-threonine and L-methionine biosynthesis II	Product A V3	2.070683632	0.014539384
myristate biosynthesis (mitochondria)	Product A V3	2.045732729	0.007144376
L-lysine biosynthesis VI	Product A V3	2.04325135	0.017109717
biotin biosynthesis I	Product A V3	2.038724205	0.00151055
8-amino-7-oxononanoate biosynthesis I	Product A V3	2.034984754	0.0141078
glycogen biosynthesis I (from ADP-D-Glucose)	Product B V3	3.424674828	0.041084202
sucrose biosynthesis II	Product B V3	3.34606056	0.011750774
glycogen degradation II	Product B V3	3.296799534	0.00049628
glucose and glucose-1-phosphate degradation	Product B V3	3.28145505	0.000621487
glycolysis IV	Product B V3	3.163269183	0.041319779
Bifidobacterium shunt	Product B V3	2.587848076	0.031218555
UDP-N-acetyl-D-glucosamine biosynthesis I	Product B V3	2.468183133	1.29E-02
adenosine nucleotides degradation II	Product B V3	2.282555947	0.031371437
guanosine nucleotides degradation III	Product B V3	2.280018501	0.0383138
pyrimidine deoxyribonucleotides de novo biosynthesis IV	Product B V3	2.232203919	0.020694587
superpathway of L-lysine, L-threonine and L-methionine biosynthesis I	Product B V3	2.079988259	0.003202322
nitrate reduction V (assimilatory)	Product B V3	2.025191349	0.026585987

## Comparison 5: Product A V3 vs Product B V3

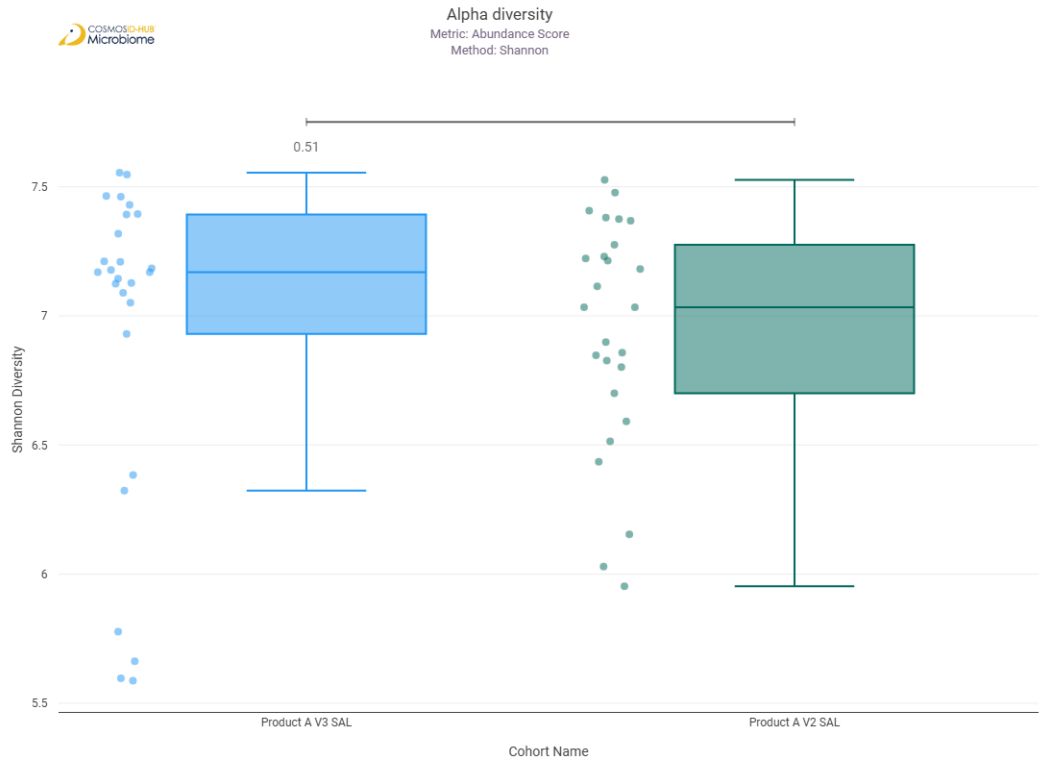
### Gene Ontology

# Alpha Diversity (GO)

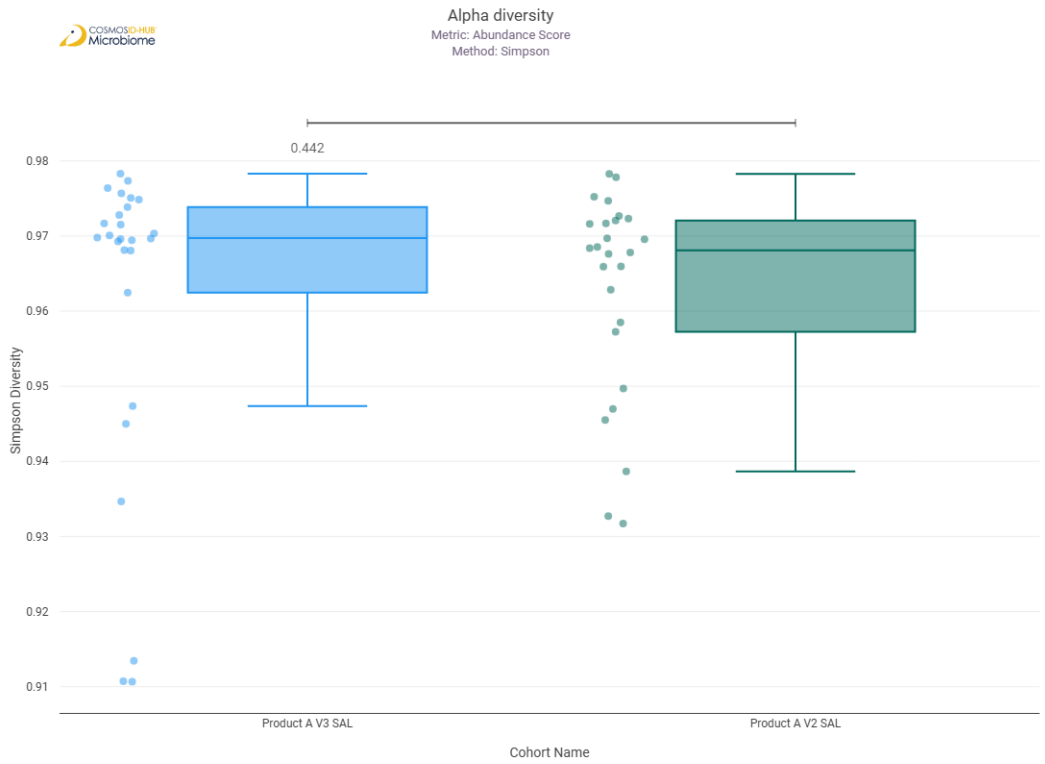
Chao1



Shannon

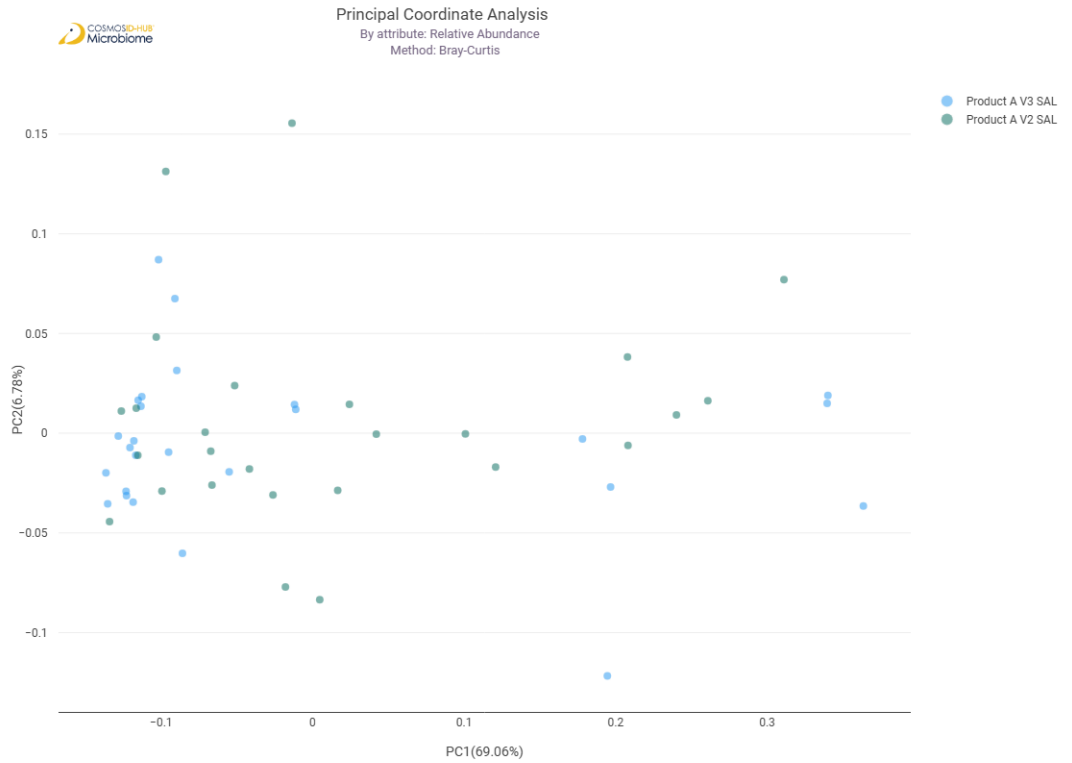


Simpson



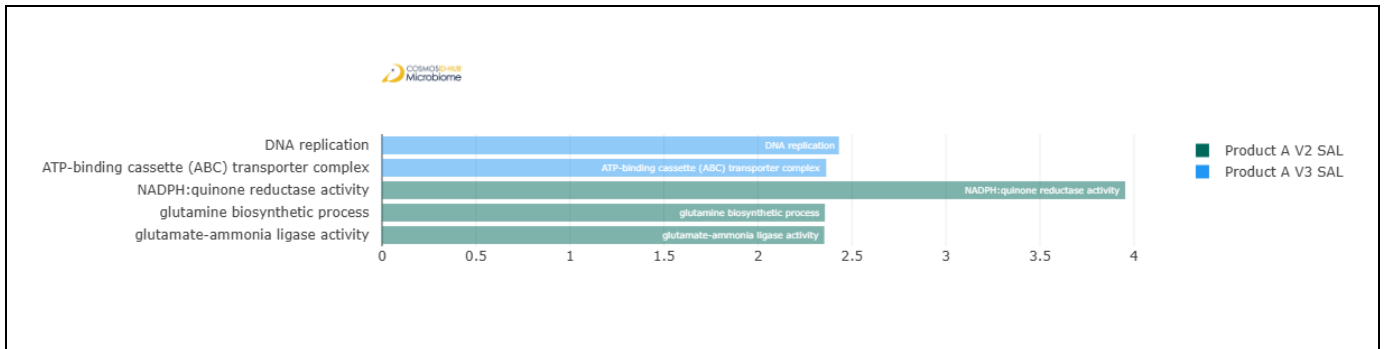
Beta Diversity (GO)

Bray-Curtis  
PERMNOVA  
p = 0.473



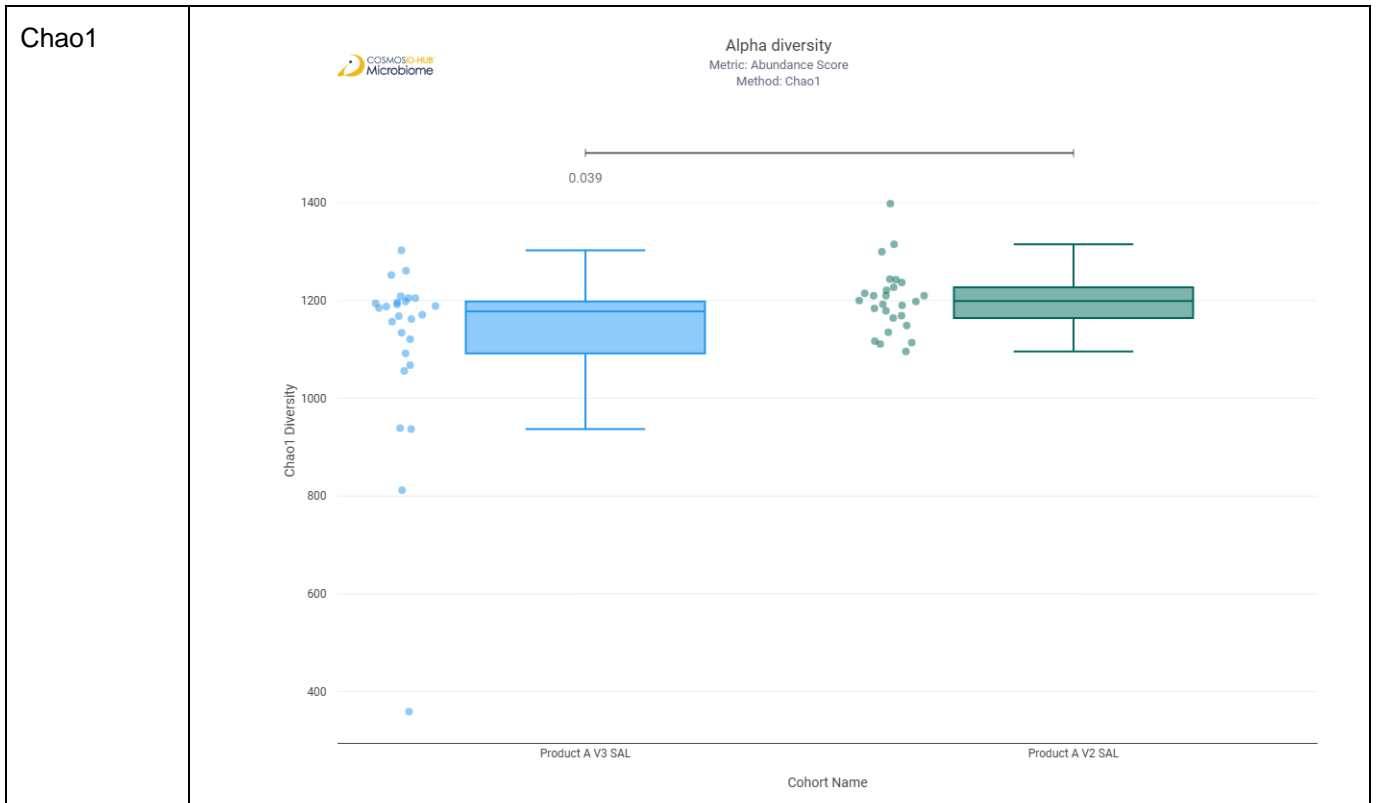


## Differential Abundance (LEfSe) (GO)

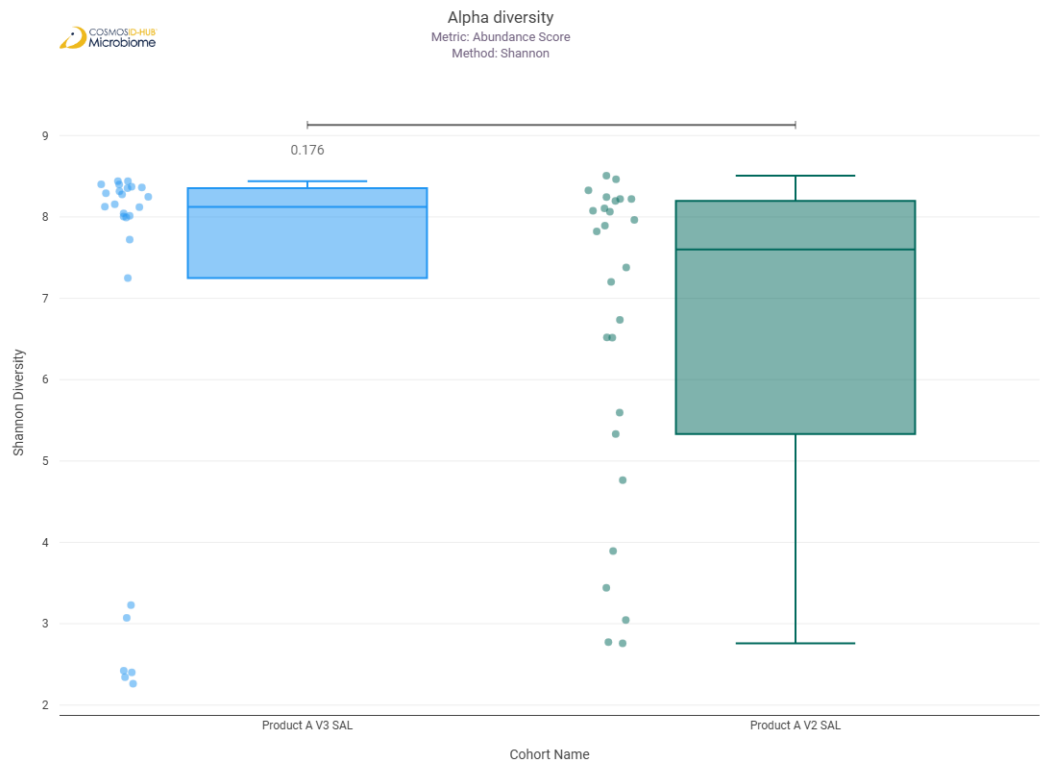


Feature	Enriched Cohort	LDA Score	P-value
DNA replication	Product A V3 SAL	2.430760658	0.035322927
ATP-binding cassette (ABC) transporter complex	Product A V3 SAL	2.362960966	0.032254747
NADPH:quinone reductase activity	Product A V2 SAL	3.953508756	0.040390461
glutamine biosynthetic process	Product A V2 SAL	2.355947932	0.007139316
glutamate-ammonia ligase activity	Product A V2 SAL	2.353037259	0.02556575

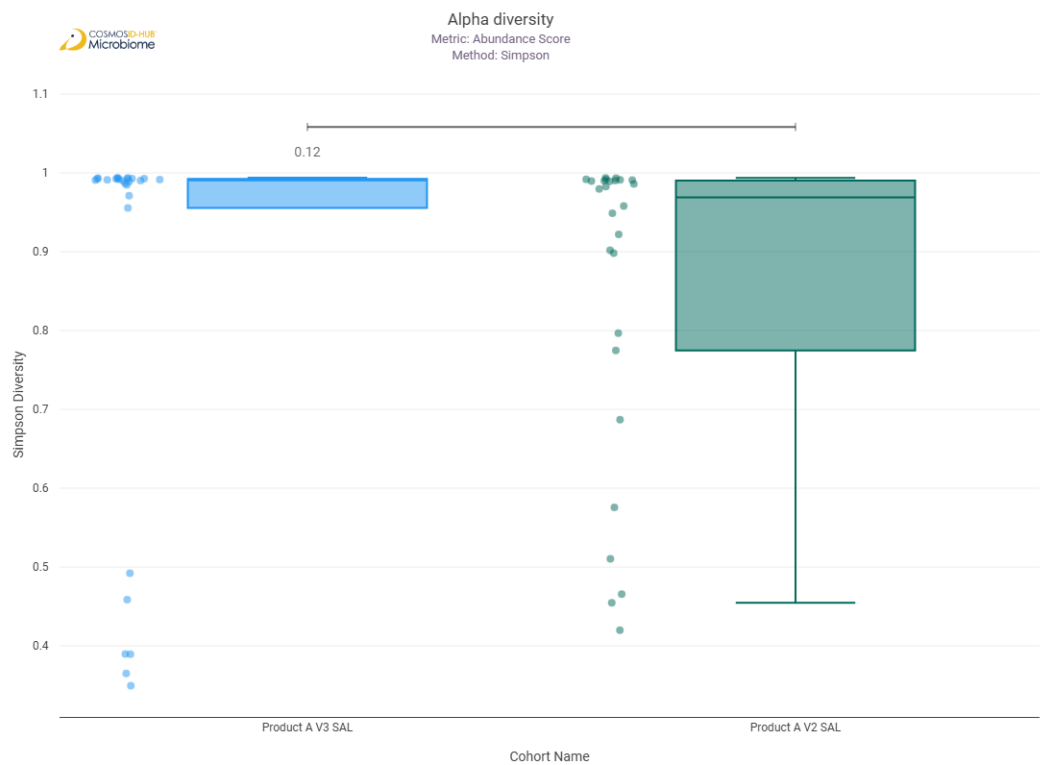
## Enzyme Commission Alpha Diversity (EC)



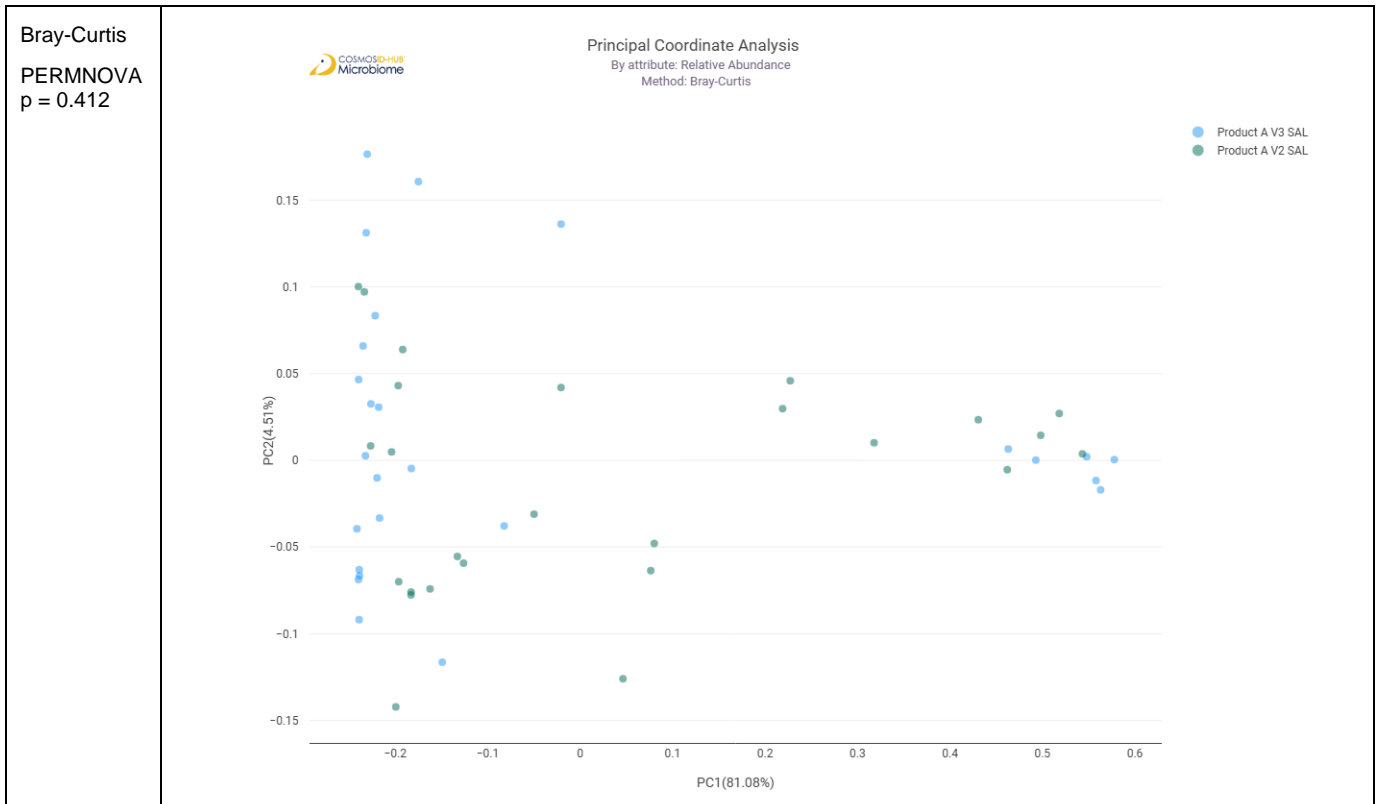
# Shannon



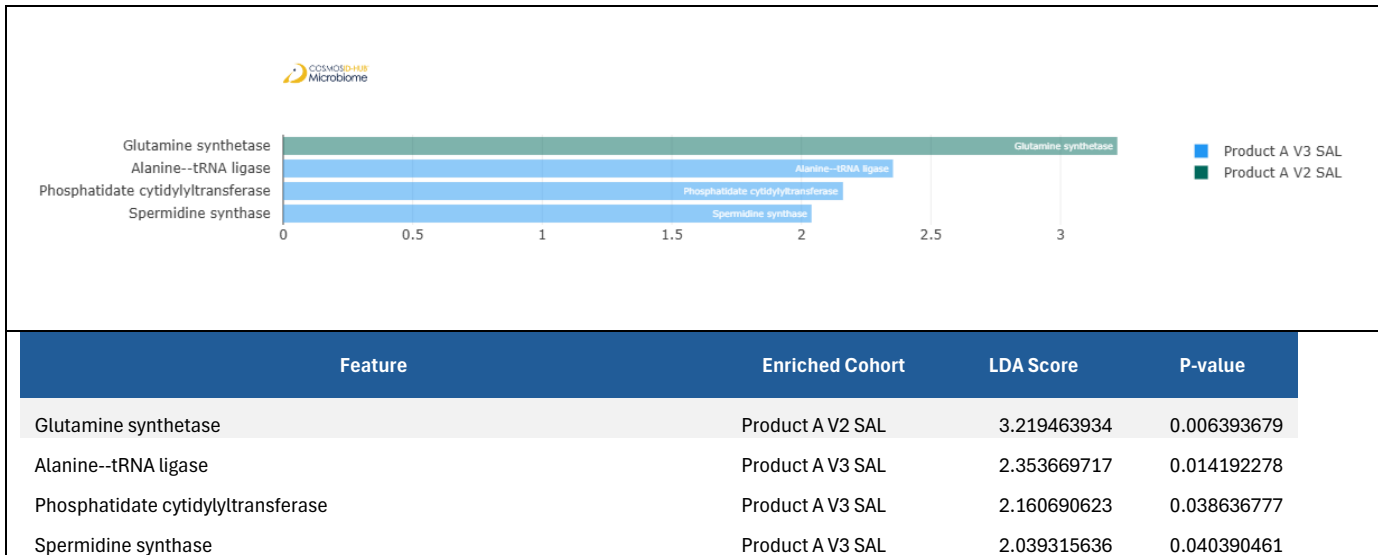
# Simpson



## Beta Diversity (EC)



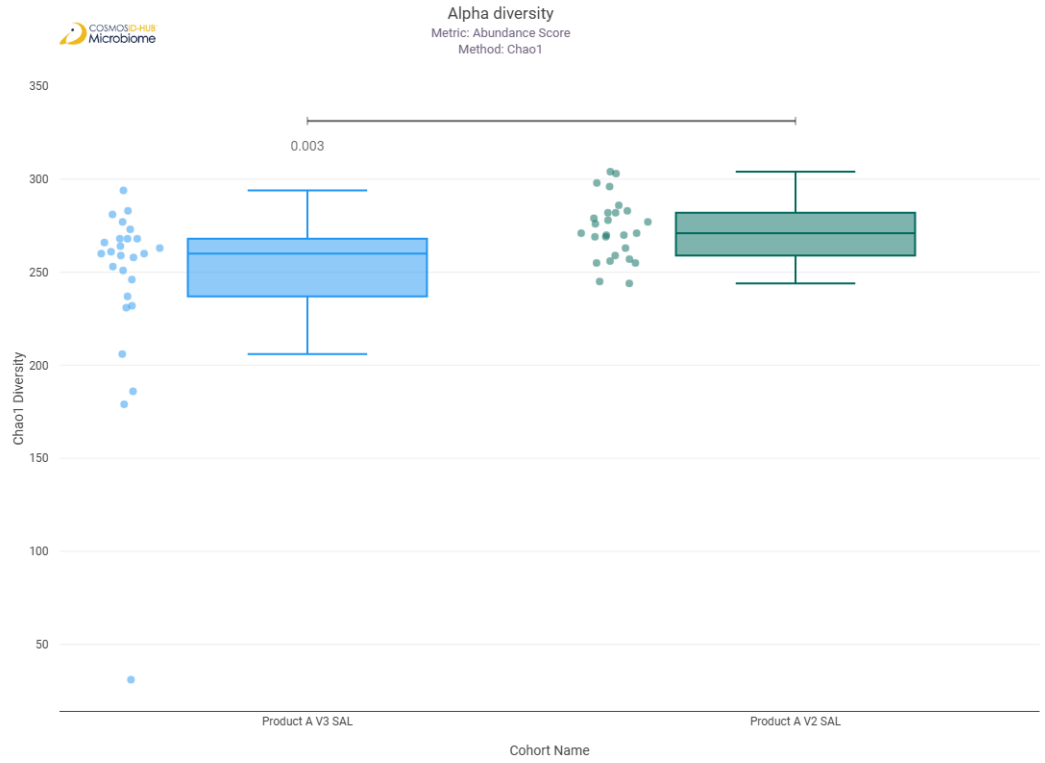
## Differential Abundance (LEfSe) (EC)



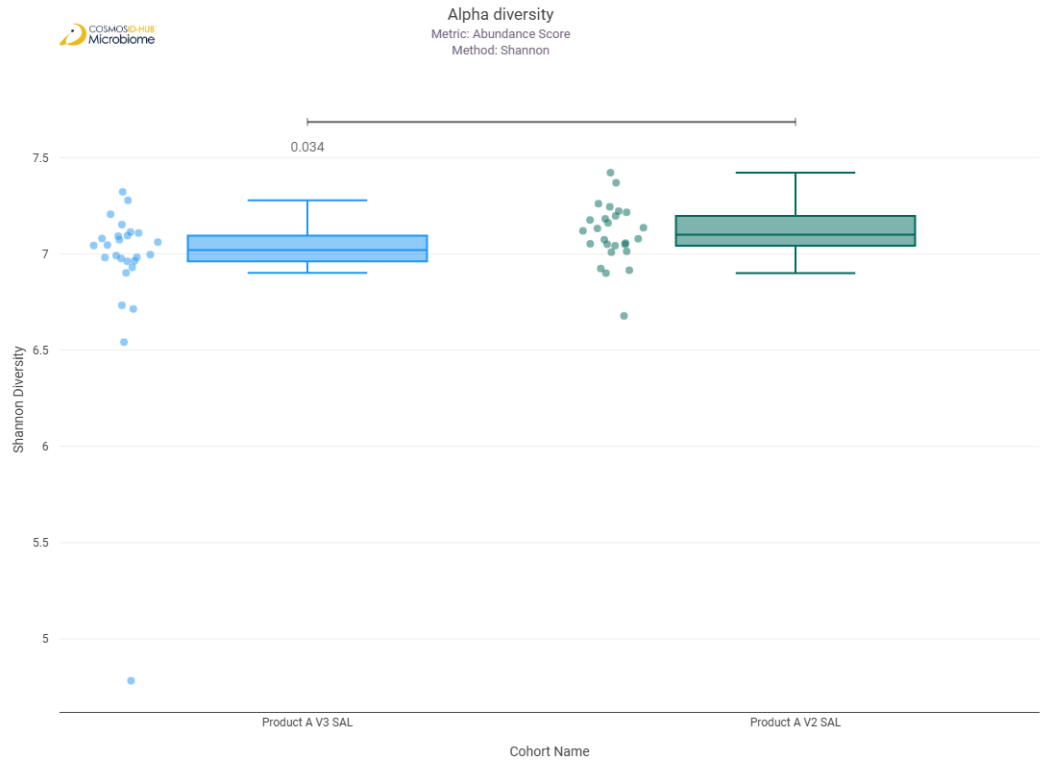
## MetaCyc Pathways

# Alpha Diversity (MetaCyc)

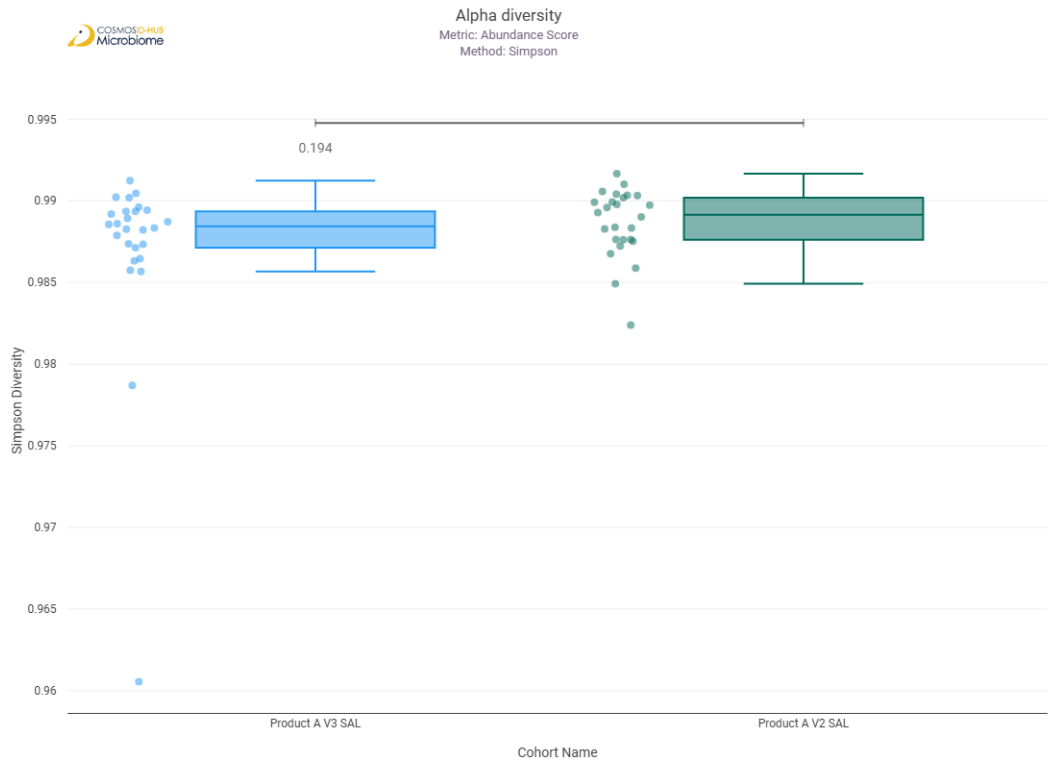
Chao1



Shannon

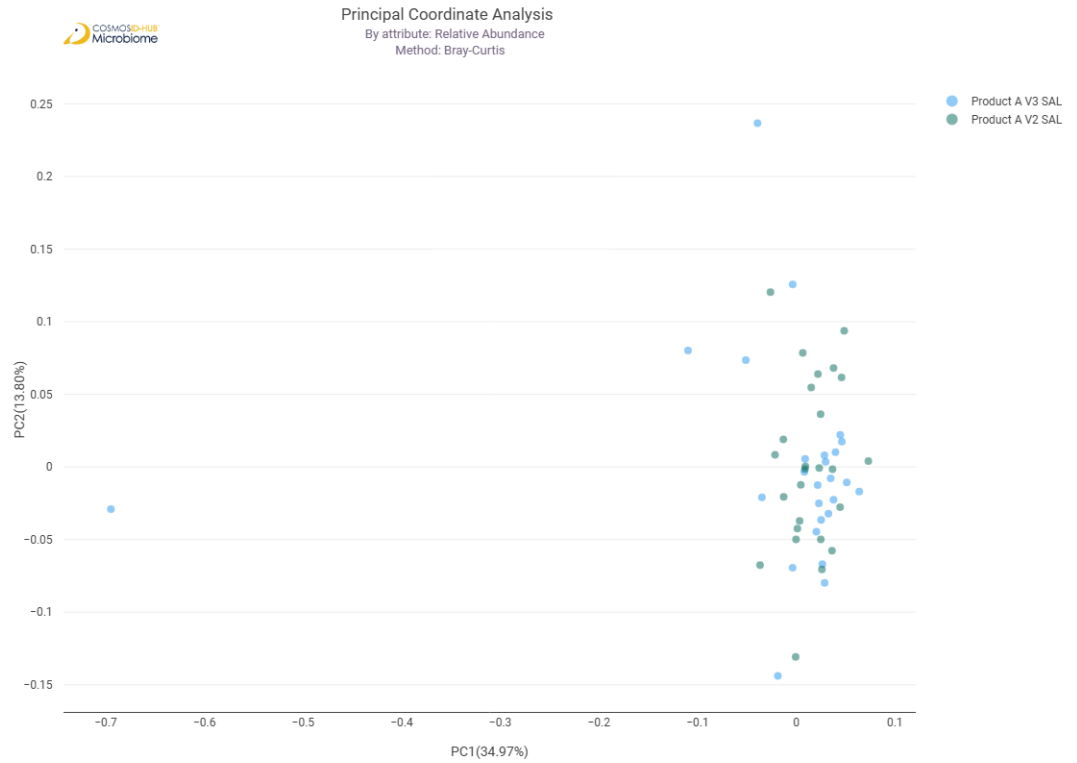


Simpson

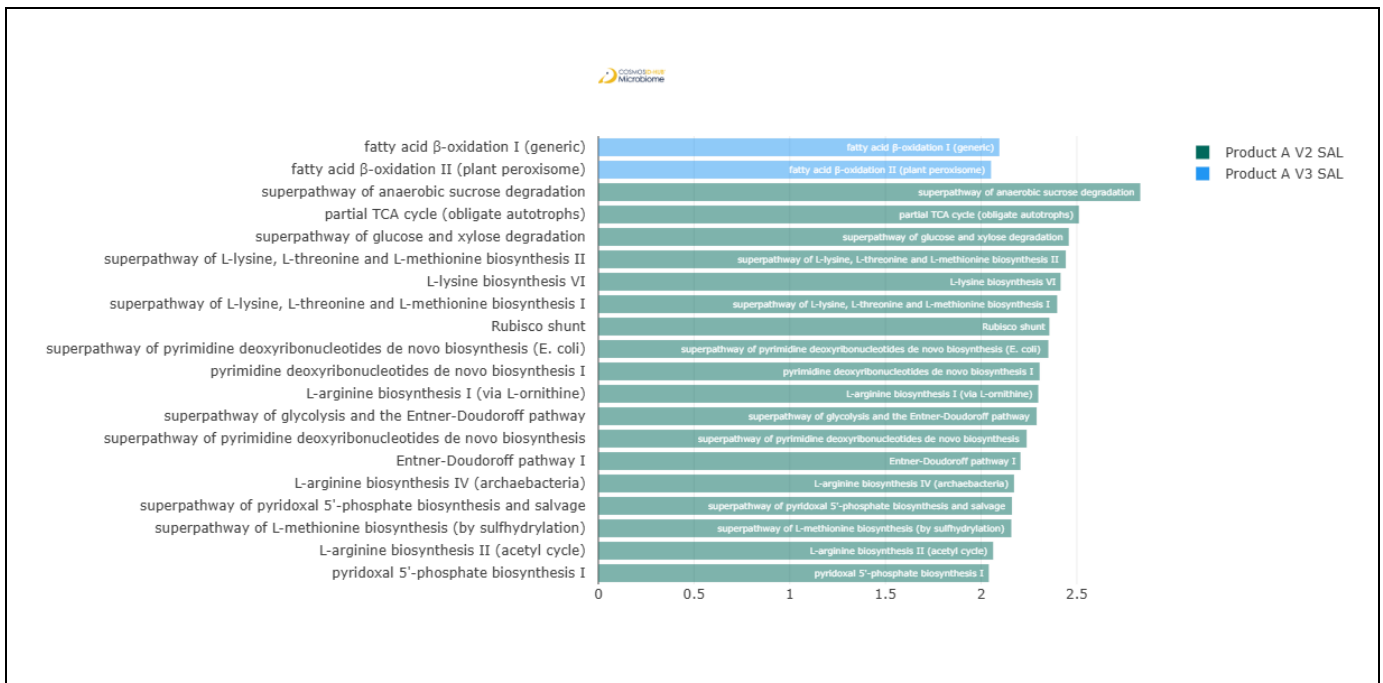


Beta Diversity (MetaCyc)

Bray-Curtis  
PERMNOVA  
p = 0.401



## Differential Abundance (LEfSe) (MetaCyc)



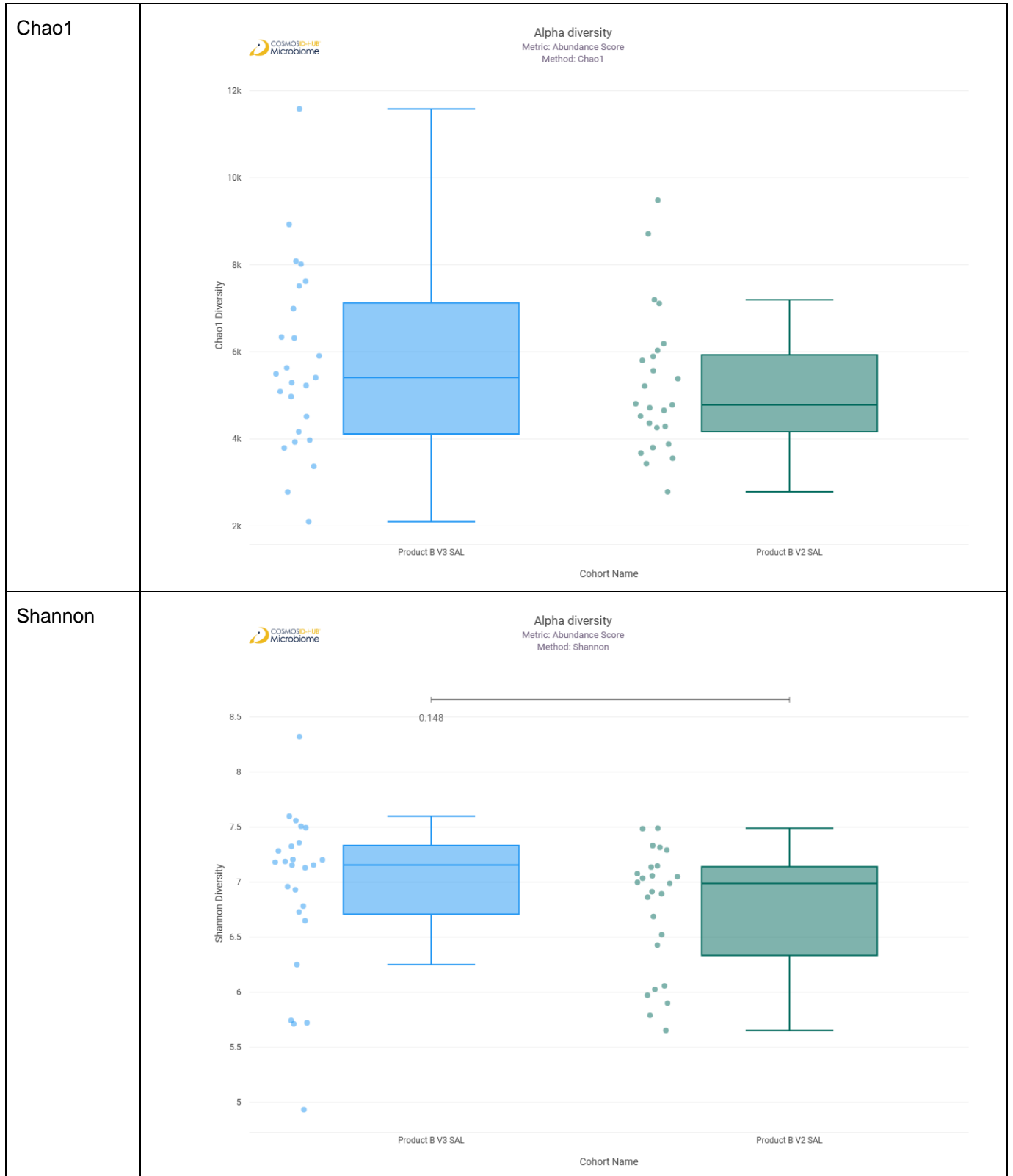
Feature	Enriched Cohort	LDA Score	P-value
fatty acid $\beta$ -oxidation I (generic)	Product A V3 SAL	2.095429545	0.022553634
fatty acid $\beta$ -oxidation II (plant peroxisome)	Product A V3 SAL	2.051853376	0.033983438
superpathway of anaerobic sucrose degradation	Product A V2 SAL	2.831636712	0.046061451
partial TCA cycle (obligate autotrophs)	Product A V2 SAL	2.510981802	0.014192278
superpathway of glucose and xylose degradation	Product A V2 SAL	2.458074599	0.001825689
superpathway of L-lysine, L-threonine and L-methionine biosynthesis II	Product A V2 SAL	2.442438549	0.02808172
L-lysine biosynthesis VI	Product A V2 SAL	2.415101559	0.030808261
superpathway of L-lysine, L-threonine and L-methionine biosynthesis I	Product A V2 SAL	2.397506712	0.002163783
Rubisco shunt	Product A V2 SAL	2.356421973	0.030608442
superpathway of pyrimidine deoxyribonucleotides de novo biosynthesis (E. coli)	Product A V2 SAL	2.351444885	0.004756827
pyrimidine deoxyribonucleotides de novo biosynthesis I	Product A V2 SAL	2.305719888	0.013266719
L-arginine biosynthesis I (via L-ornithine)	Product A V2 SAL	2.29886903	0.000911585
superpathway of glycolysis and the Entner-Doudoroff pathway	Product A V2 SAL	2.290181726	0.004455412
superpathway of pyrimidine deoxyribonucleotides de novo biosynthesis	Product A V2 SAL	2.237994675	2.09E-02
Entner-Doudoroff pathway I	Product A V2 SAL	2.205795946	0.004718777
L-arginine biosynthesis IV (archaeobacteria)	Product A V2 SAL	2.17211688	0.004825811
superpathway of pyridoxal 5'-phosphate biosynthesis and salvage	Product A V2 SAL	2.161332919	0.033683115
superpathway of L-methionine biosynthesis (by sulfhydrylation)	Product A V2 SAL	2.158067819	0.002046016
L-arginine biosynthesis II (acetyl cycle)	Product A V2 SAL	2.062786375	0.007905304
pyridoxal 5'-phosphate biosynthesis I	Product A V2 SAL	2.040191452	0.013446627



# Comparison 6: Product B V2 SAL vs Product B V3 SAL

## Gene Ontology

### Alpha Diversity (GO)

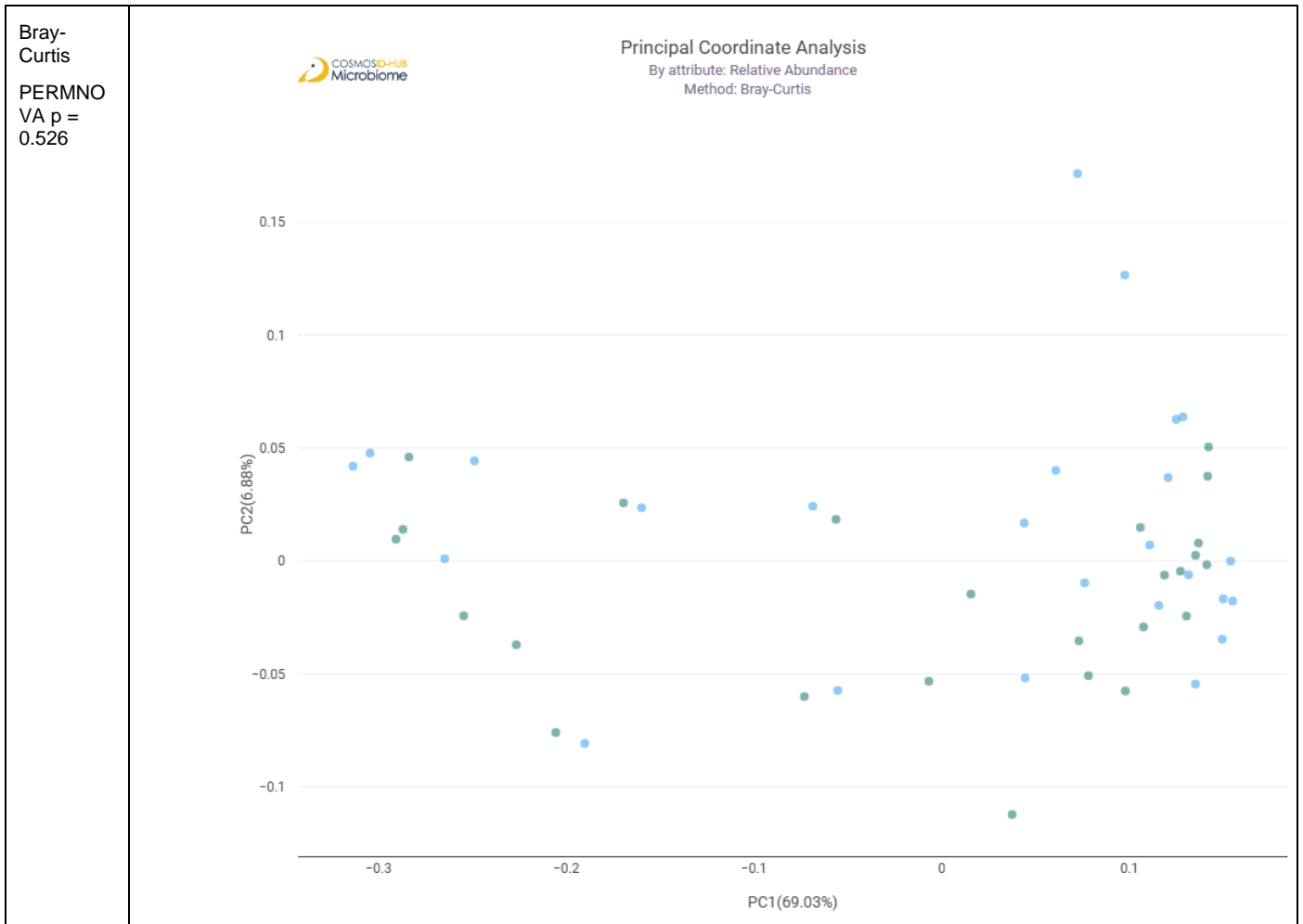




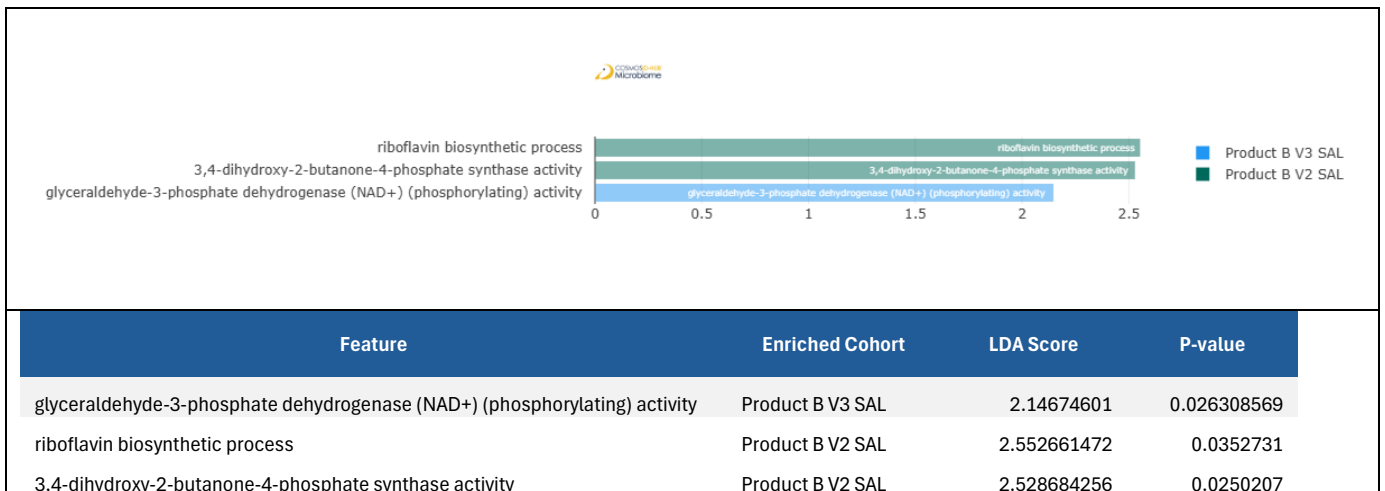
# Simpson



## Beta Diversity (GO)



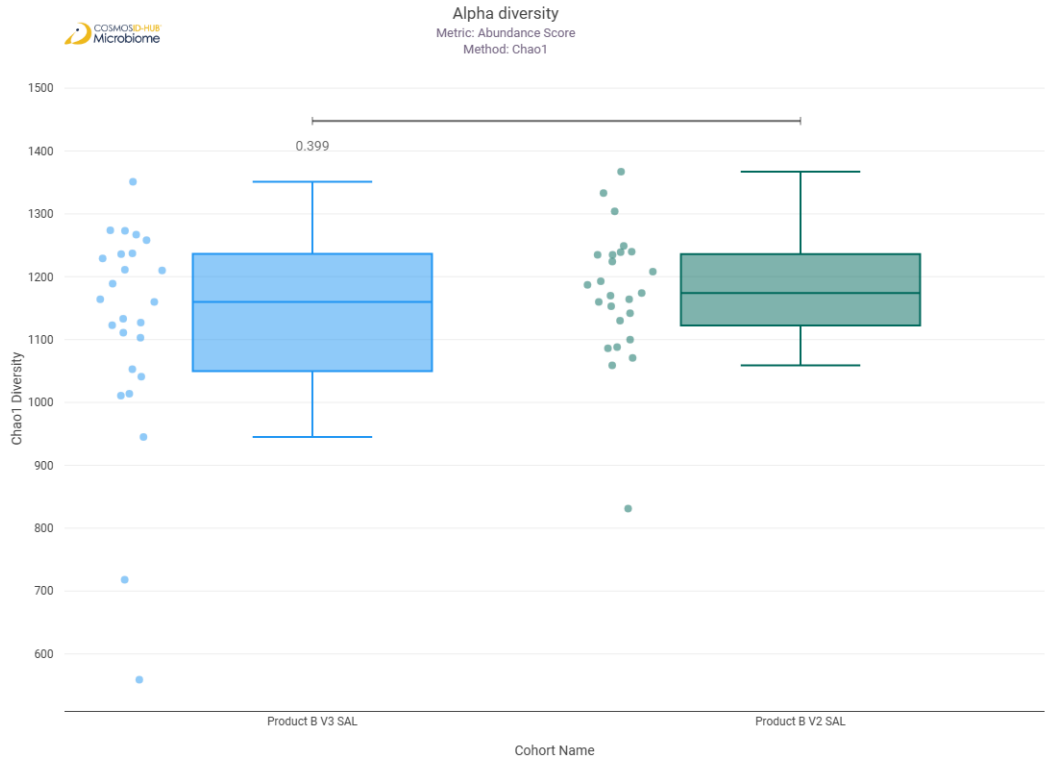
## Differential Abundance (LEfSe) (GO)



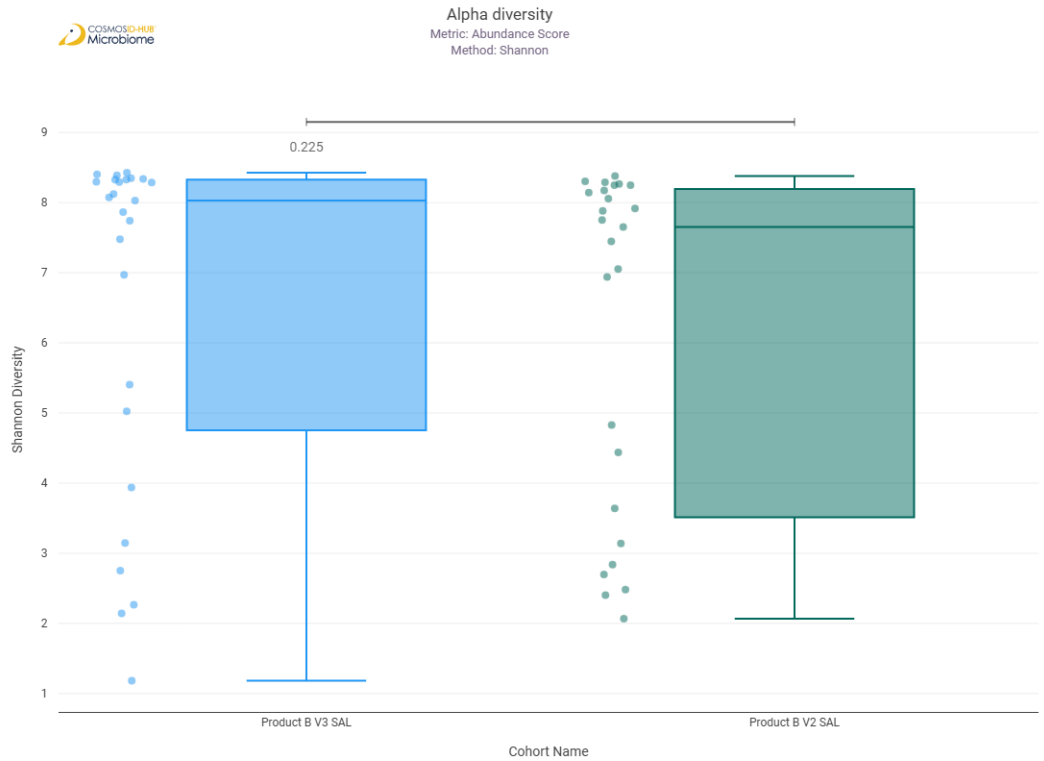
## Enzyme Commission

# Alpha Diversity (EC)

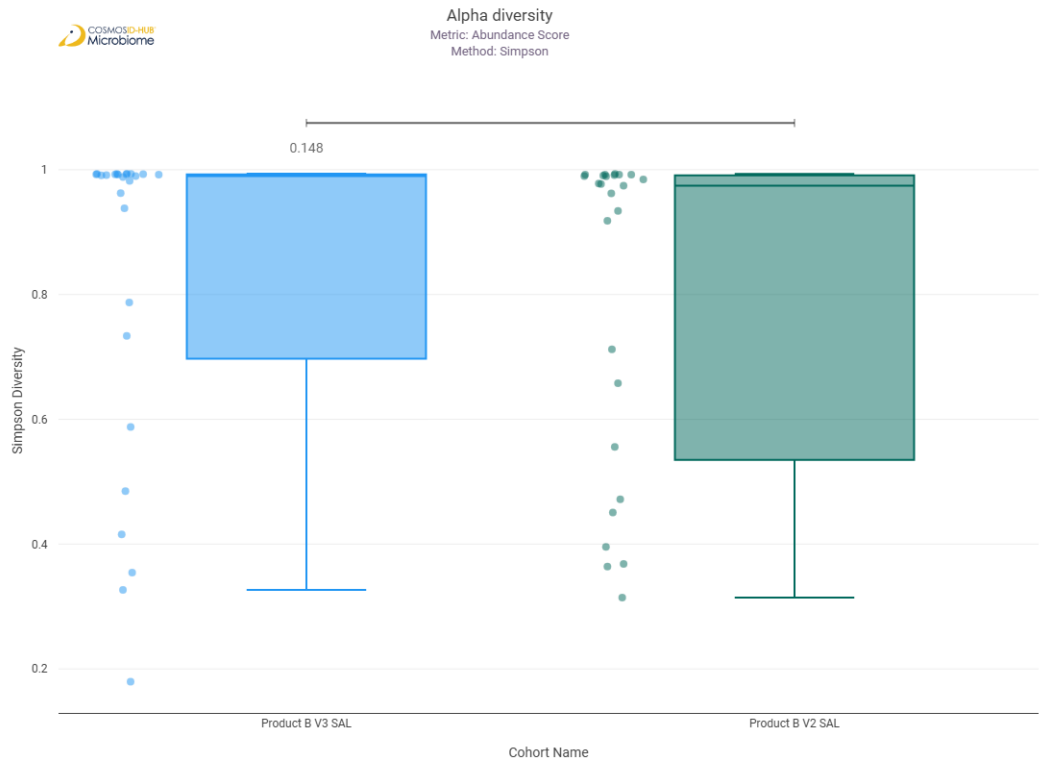
Chao1



Shannon

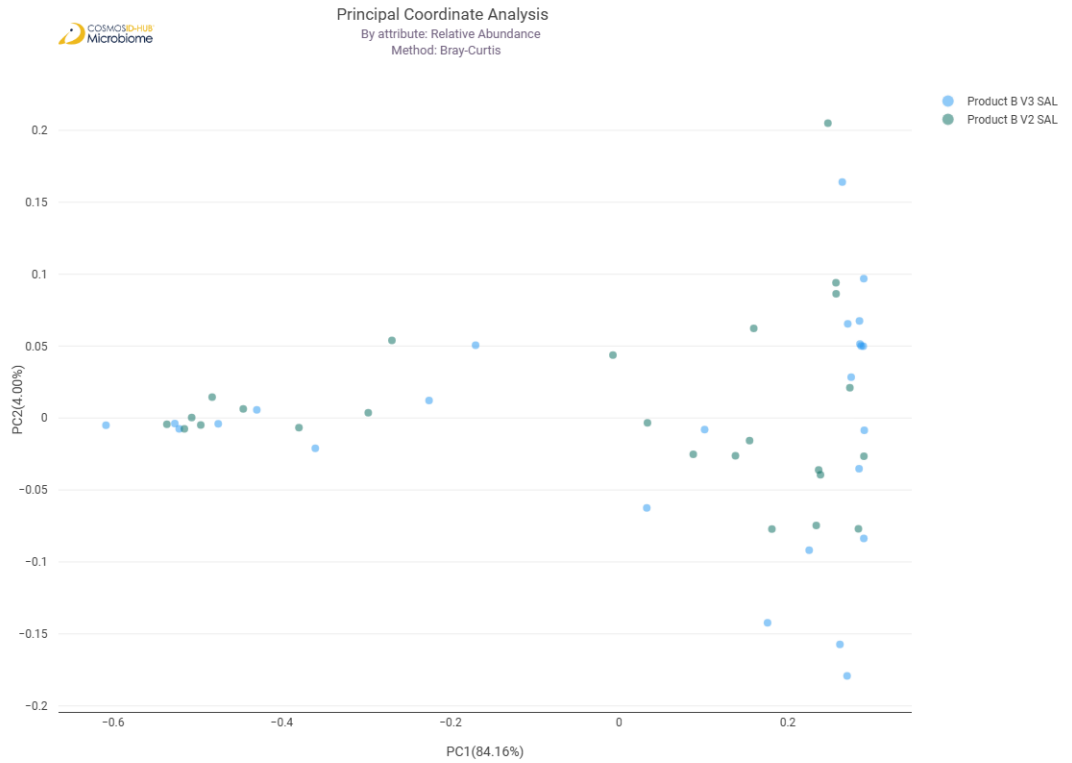


# Simpson



## Beta Diversity (EC)

Bray-Curtis  
PERMNOVA  
 $p = 0.440$



## Differential Abundance (LEfSe) (EC)

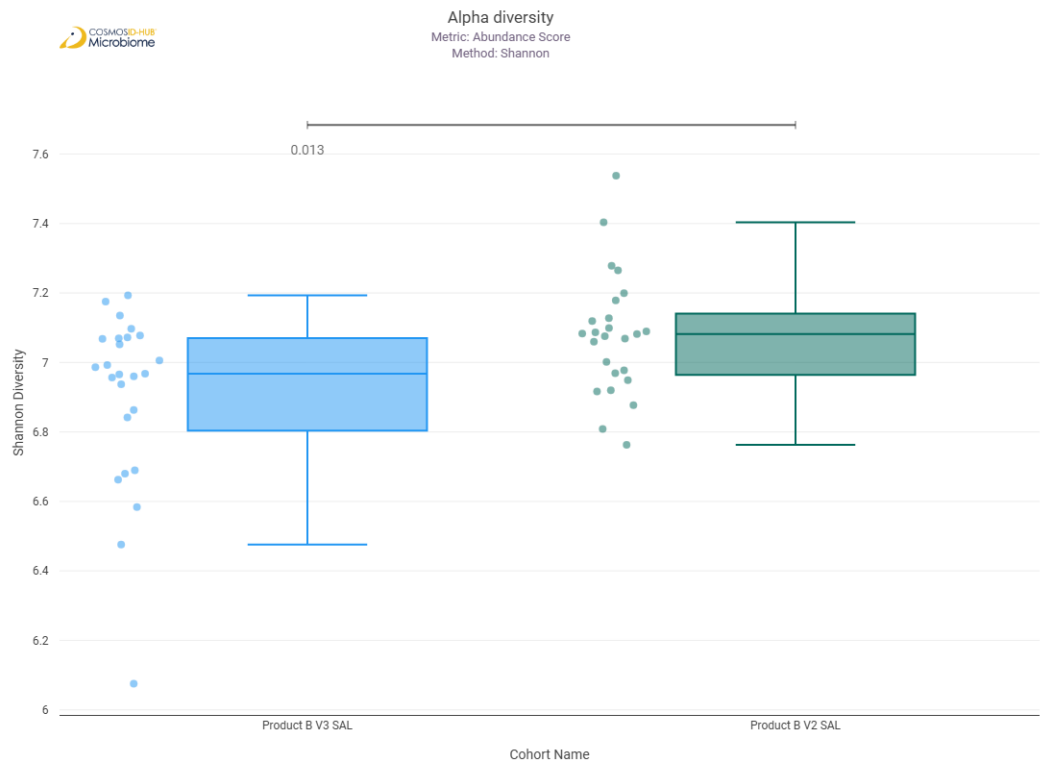
No differentially abundant features detected

## MetaCyc Pathways

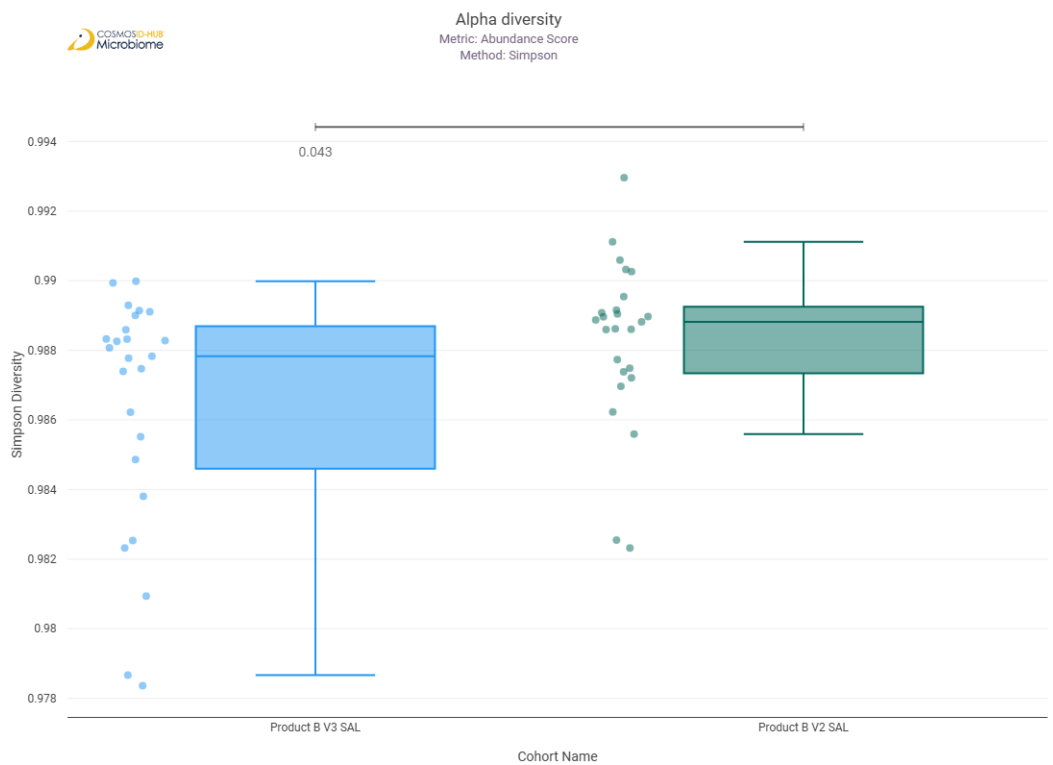
### Alpha Diversity (MetaCyc)



# Shannon

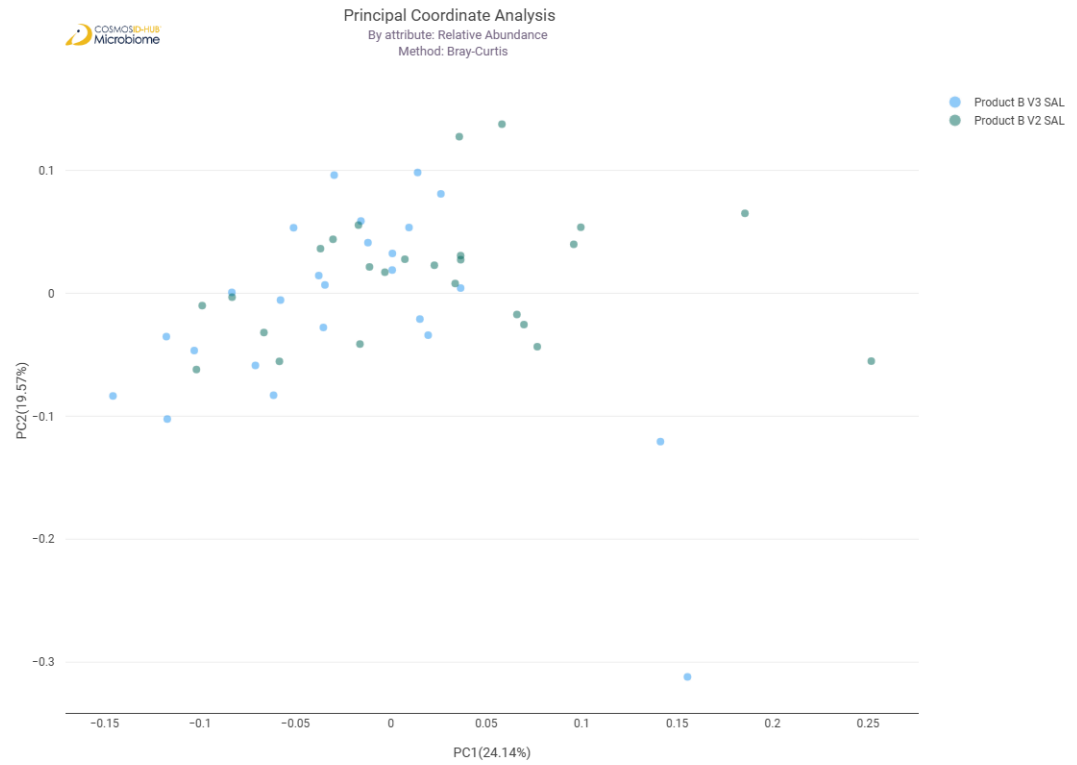


# Simpson

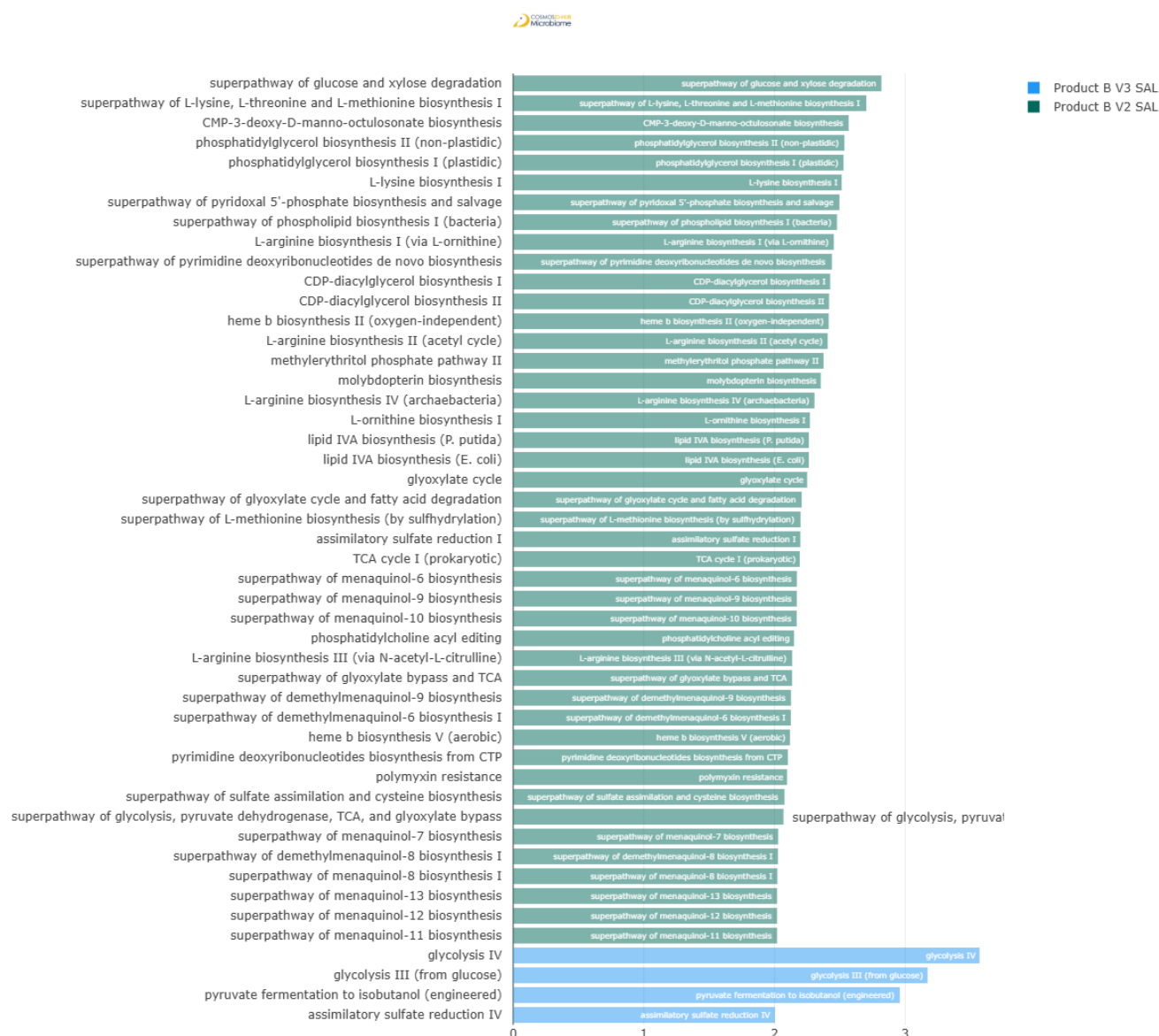


## Beta Diversity (MetaCyc)

Bray-Curtis  
PERMNOVA  
 $p = 0.040$



## Differential Abundance (LEfSe) (MetaCyc)



Feature	Enriched Cohort	LDA Score	P-value
superpathway of glucose and xylose degradation	Product B V2 SAL	2.818172394	0.003199335
superpathway of L-lysine, L-threonine and L-methionine biosynthesis I	Product B V2 SAL	2.702332952	0.001268472
CMP-3-deoxy-D-manno-octulosonate biosynthesis	Product B V2 SAL	2.567217917	0.021478913
phosphatidylglycerol biosynthesis II (non-plastidic)	Product B V2 SAL	2.534565735	0.011339073
phosphatidylglycerol biosynthesis I (plastidic)	Product B V2 SAL	2.527633184	0.011339073
L-lysine biosynthesis I	Product B V2 SAL	2.513475321	0.044617455
superpathway of pyridoxal 5'-phosphate biosynthesis and salvage	Product B V2 SAL	2.496575918	0.045855823
superpathway of phospholipid biosynthesis I (bacteria)	Product B V2 SAL	2.47795577	0.040658018
L-arginine biosynthesis I (via L-ornithine)	Product B V2 SAL	2.453409033	0.028209048
superpathway of pyrimidine deoxyribonucleotides de novo biosynthesis	Product B V2 SAL	2.43911832	0.035179233

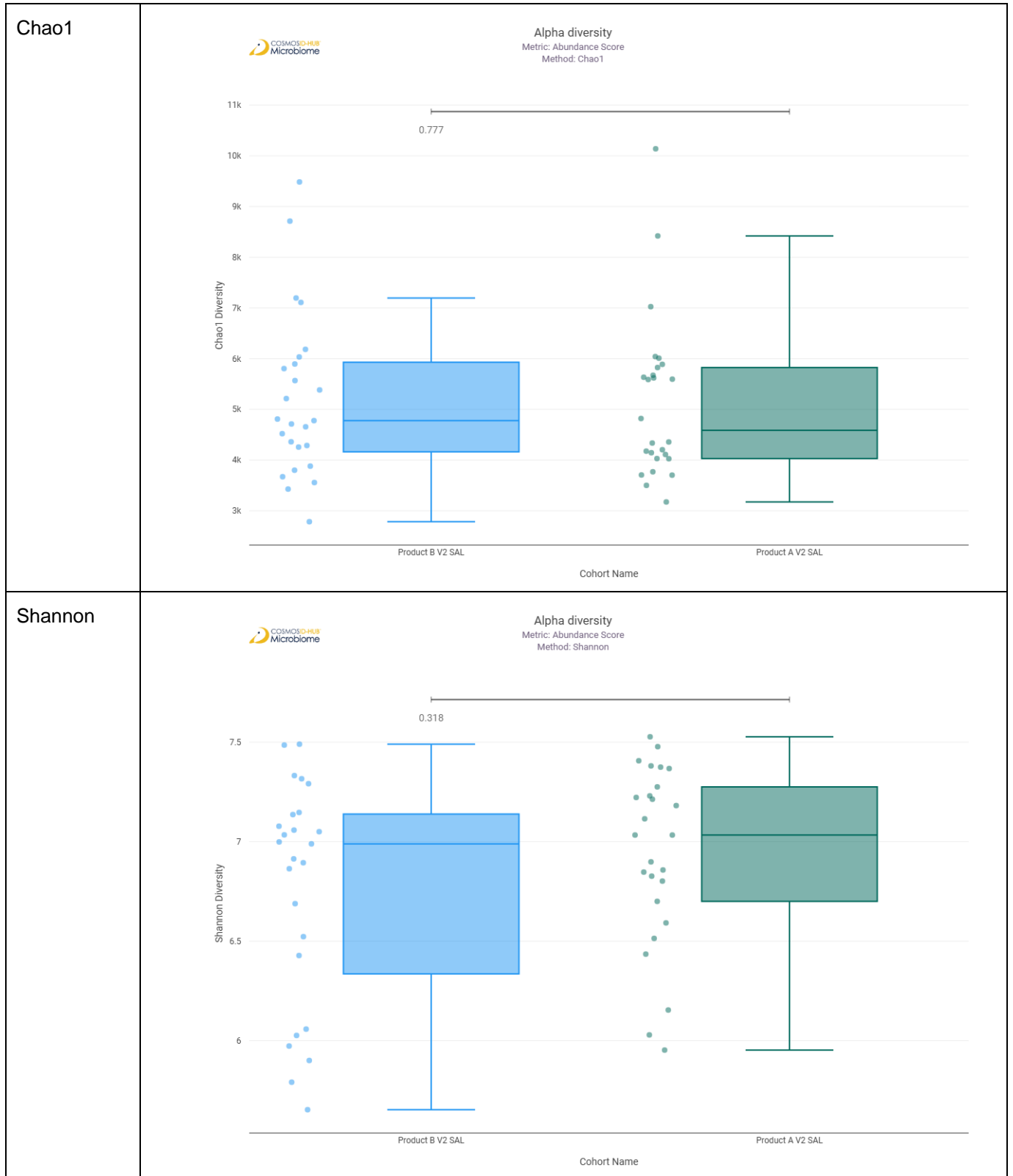


CDP-diacylglycerol biosynthesis I	Product B V2 SAL	2.425530852	4.07E-02
CDP-diacylglycerol biosynthesis II	Product B V2 SAL	2.417219654	0.0352731
heme b biosynthesis II (oxygen-independent)	Product B V2 SAL	2.414277056	0.009055969
L-arginine biosynthesis II (acetyl cycle)	Product B V2 SAL	2.406610684	0.012881271
methylerythritol phosphate pathway II	Product B V2 SAL	2.374746616	0.038785713
molybdopterin biosynthesis	Product B V2 SAL	2.353869718	0.004474919
L-arginine biosynthesis IV (archaeobacteria)	Product B V2 SAL	2.30565784	0.046662482
L-ornithine biosynthesis I	Product B V2 SAL	2.270426756	0.034286155
lipid IVA biosynthesis (E. coli)	Product B V2 SAL	2.262174403	0.013543566
lipid IVA biosynthesis (P. putida)	Product B V2 SAL	2.262174403	0.013543566
glyoxylate cycle	Product B V2 SAL	2.249728953	1.84E-03
superpathway of glyoxylate cycle and fatty acid degradation	Product B V2 SAL	2.20753772	0.030301371
superpathway of L-methionine biosynthesis (by sulfhydrylation)	Product B V2 SAL	2.19885117	0.011392734
assimilatory sulfate reduction I	Product B V2 SAL	2.197446182	0.010334085
TCA cycle I (prokaryotic)	Product B V2 SAL	2.192838295	0.027140444
superpathway of menaquinol-6 biosynthesis	Product B V2 SAL	2.171045532	6.09421E-05
superpathway of menaquinol-9 biosynthesis	Product B V2 SAL	2.170593917	6.09421E-05
superpathway of menaquinol-10 biosynthesis	Product B V2 SAL	2.169649613	6.09421E-05
phosphatidylcholine acyl editing	Product B V2 SAL	2.149186255	0.043498937
L-arginine biosynthesis III (via N-acetyl-L-citrulline)	Product B V2 SAL	2.134965514	0.031737021
superpathway of glyoxylate bypass and TCA	Product B V2 SAL	2.134203058	0.044486372
superpathway of demethylmenaquinol-9 biosynthesis	Product B V2 SAL	2.1257968	6.09421E-05
superpathway of demethylmenaquinol-6 biosynthesis I	Product B V2 SAL	2.124841397	6.09421E-05
heme b biosynthesis V (aerobic)	Product B V2 SAL	2.118223752	0.031887431
pyrimidine deoxyribonucleotides biosynthesis from CTP	Product B V2 SAL	2.102099596	0.044416899
polymyxin resistance	Product B V2 SAL	2.095875541	0.00741426
superpathway of sulfate assimilation and cysteine biosynthesis	Product B V2 SAL	2.076167827	0.004912845
superpathway of glycolysis, pyruvate dehydrogenase, TCA, and glyoxylate bypass	Product B V2 SAL	2.068575031	0.002366655
superpathway of menaquinol-7 biosynthesis	Product B V2 SAL	2.028076494	0.030318736
superpathway of demethylmenaquinol-8 biosynthesis I	Product B V2 SAL	2.026100386	0.013730328
superpathway of menaquinol-8 biosynthesis I	Product B V2 SAL	2.021614503	0.009305995
superpathway of menaquinol-11 biosynthesis	Product B V2 SAL	2.019480361	0.016137021
superpathway of menaquinol-12 biosynthesis	Product B V2 SAL	2.019480361	0.016137021
superpathway of menaquinol-13 biosynthesis	Product B V2 SAL	2.019480361	0.016137021
glycolysis IV	Product B V3 SAL	3.567908932	0.002551693
glycolysis III (from glucose)	Product B V3 SAL	3.170717244	0.011339073
pyruvate fermentation to isobutanol (engineered)	Product B V3 SAL	2.958214564	0.036996166
assimilatory sulfate reduction IV	Product B V3 SAL	2.00338347	0.006173676

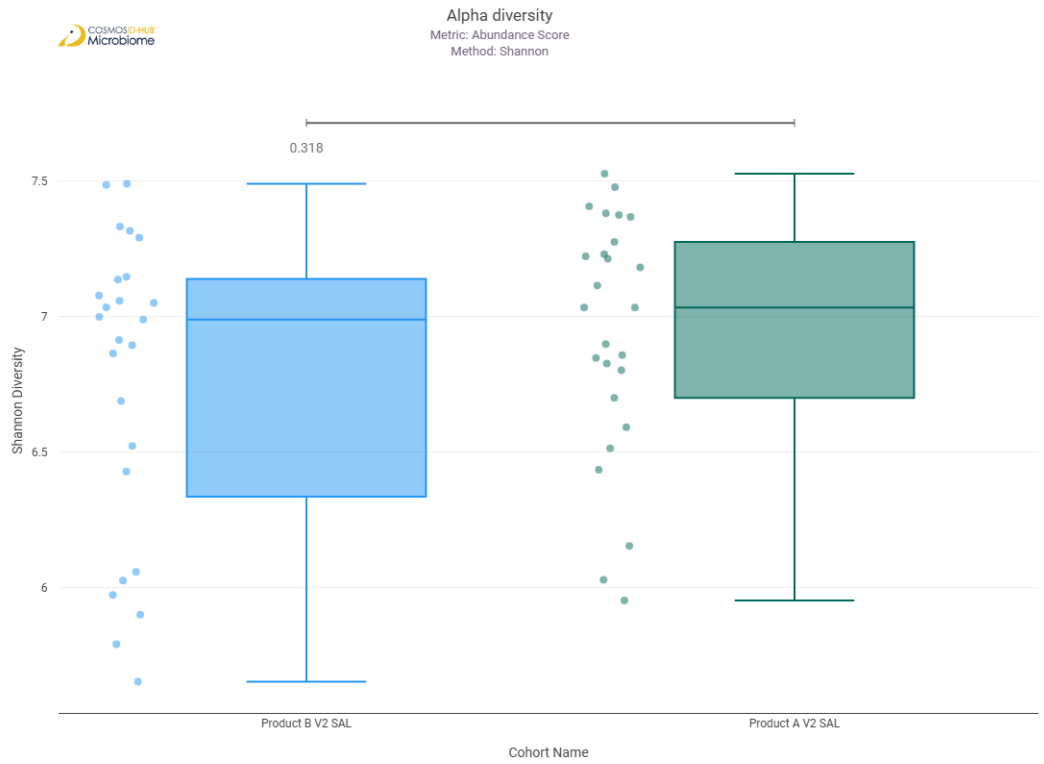
# Comparison 7: Product A V2 SAL vs Product B V2 SAL

## Gene Ontology

### Alpha Diversity (GO)

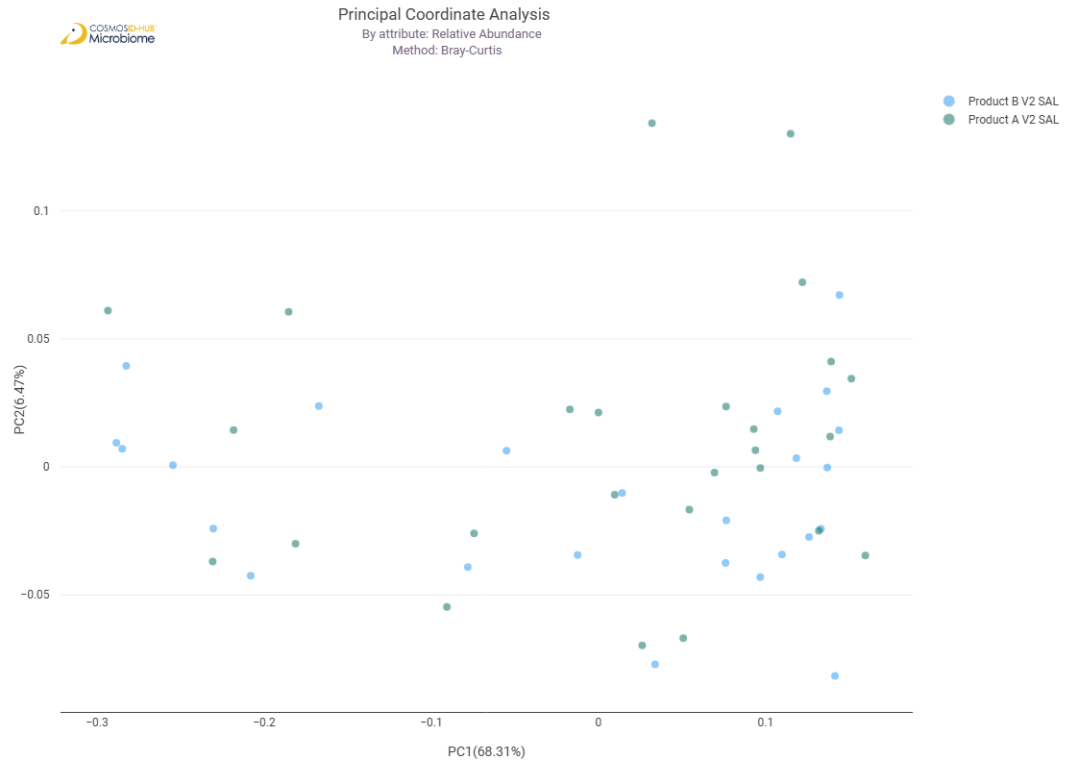


Simpson

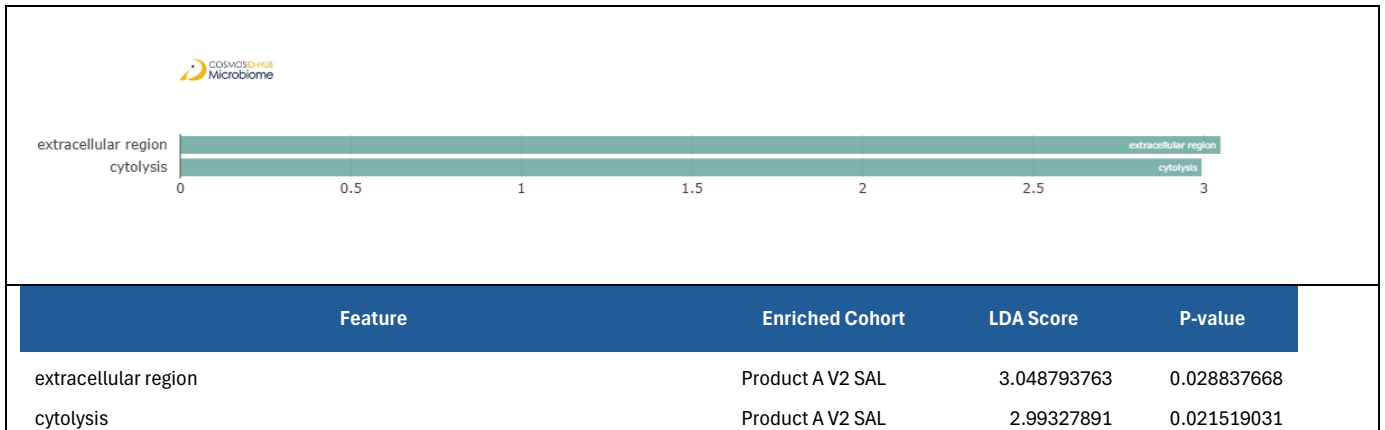


Beta Diversity (GO)

Bray-Curtis  
PERMNOVA  
p = 0.573

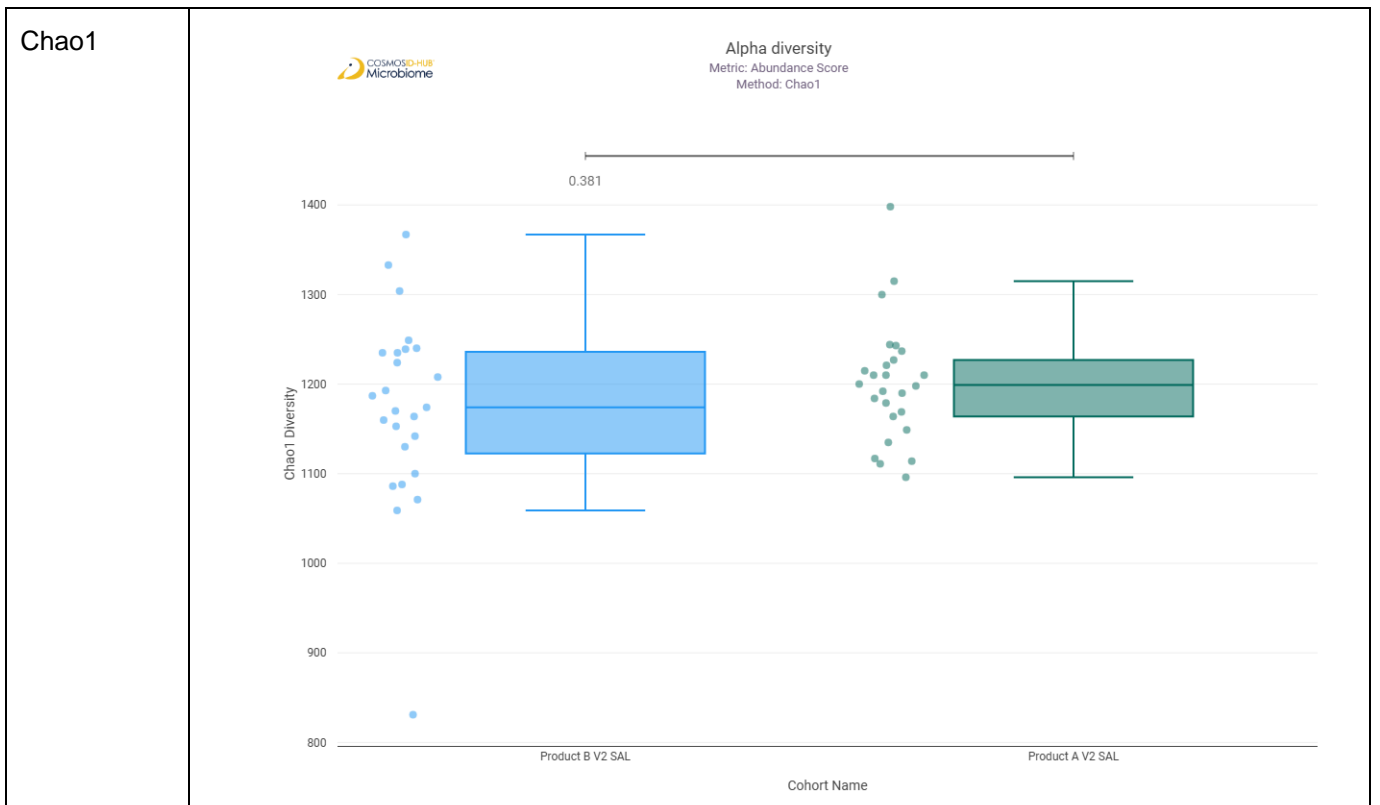


## Differential Abundance (LEfSe) (GO)

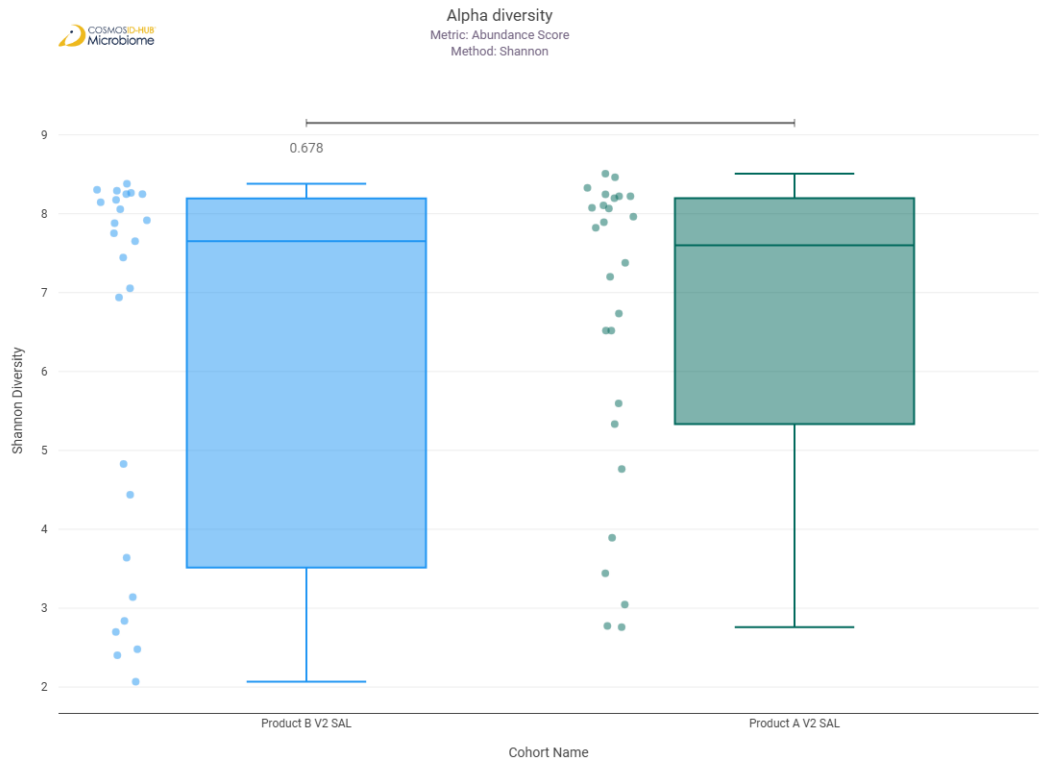


## Enzyme Commission

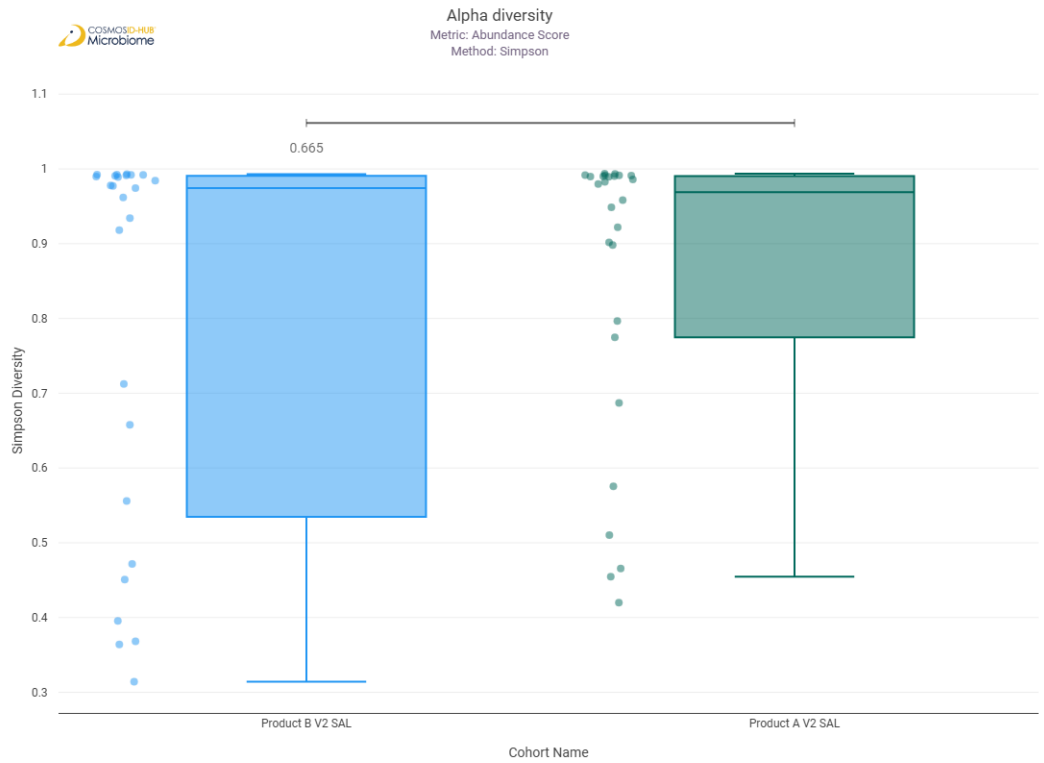
### Alpha Diversity (EC)



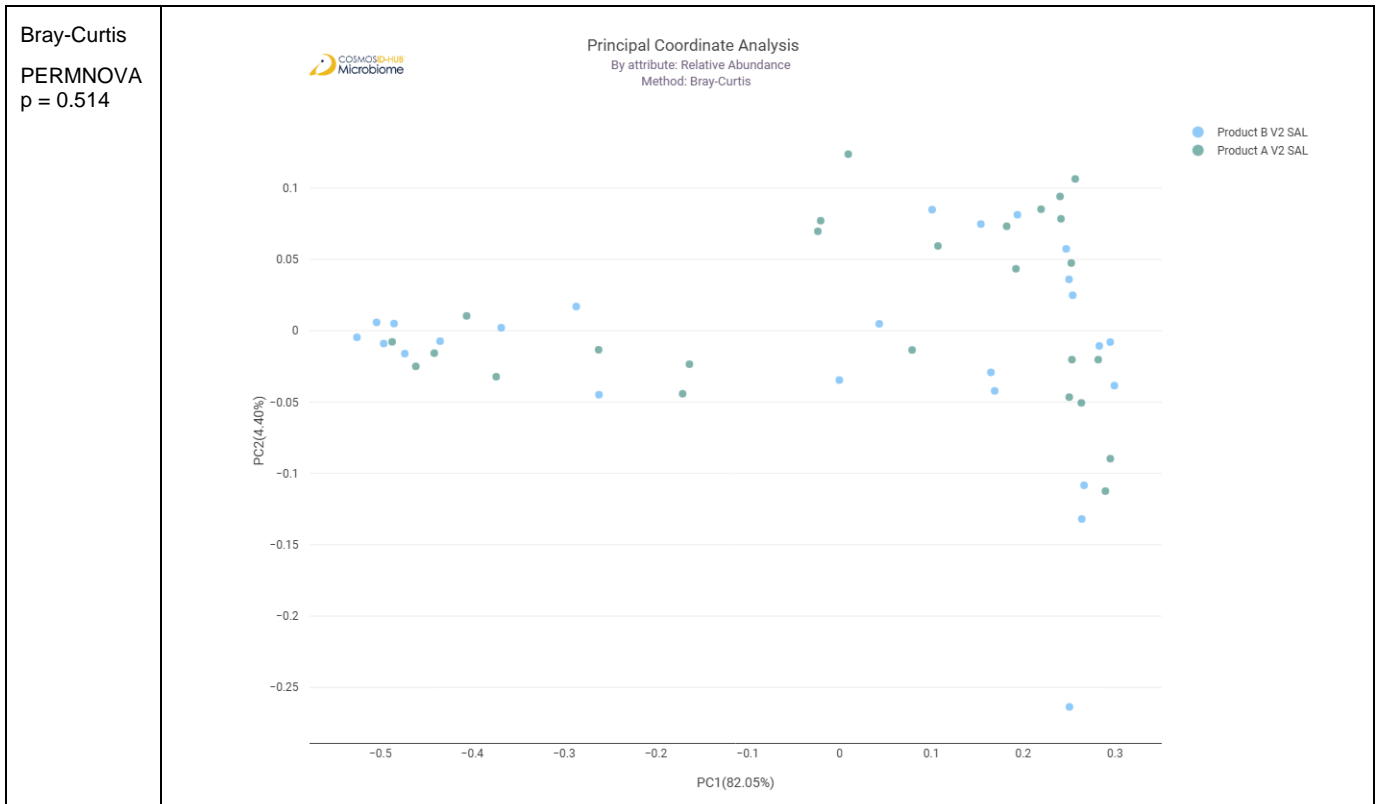
# Shannon



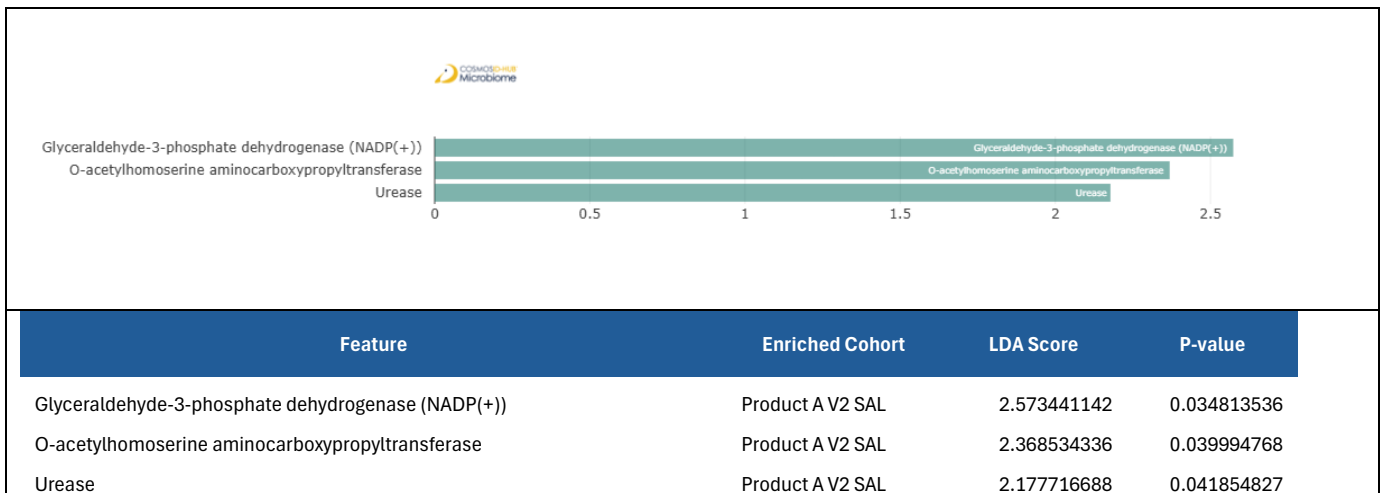
# Simpson



## Beta Diversity (EC)



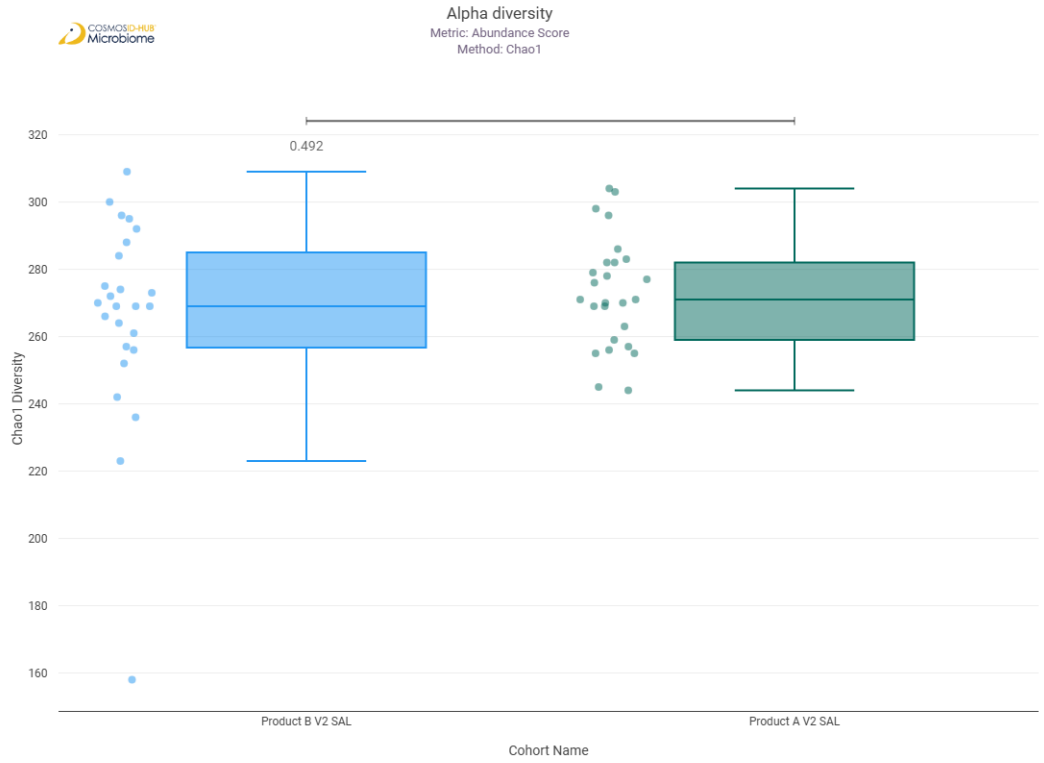
## Differential Abundance (LEfSe) (EC)



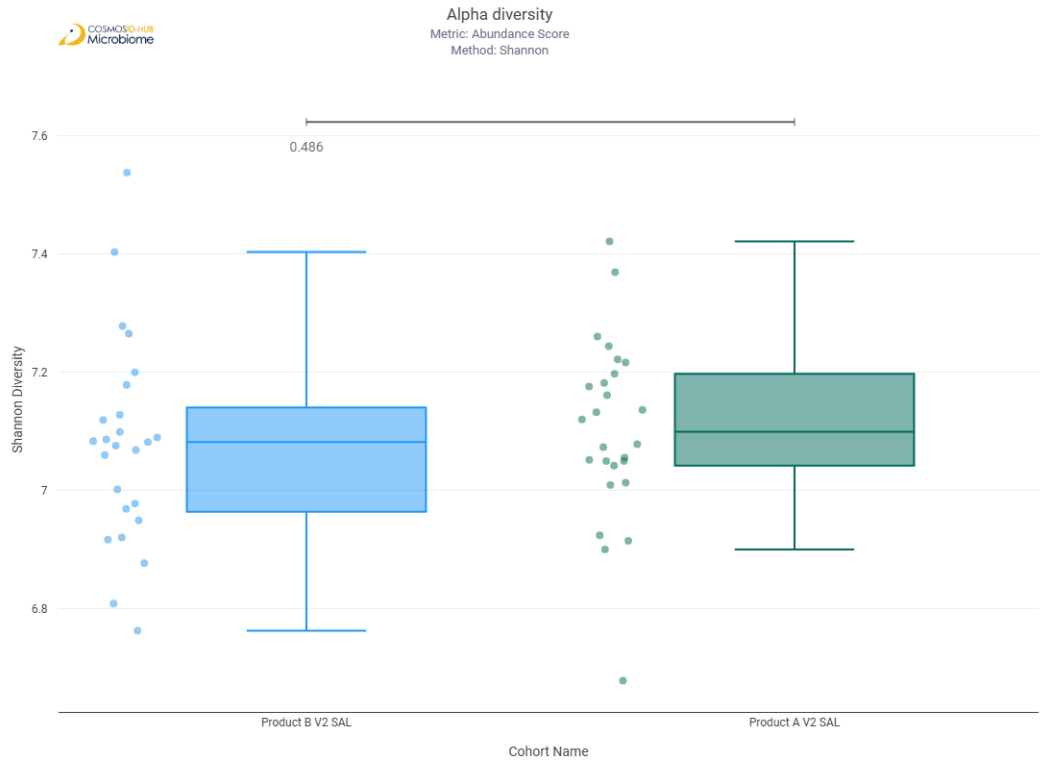
## MetaCyc Pathways

# Alpha Diversity (MetaCyc)

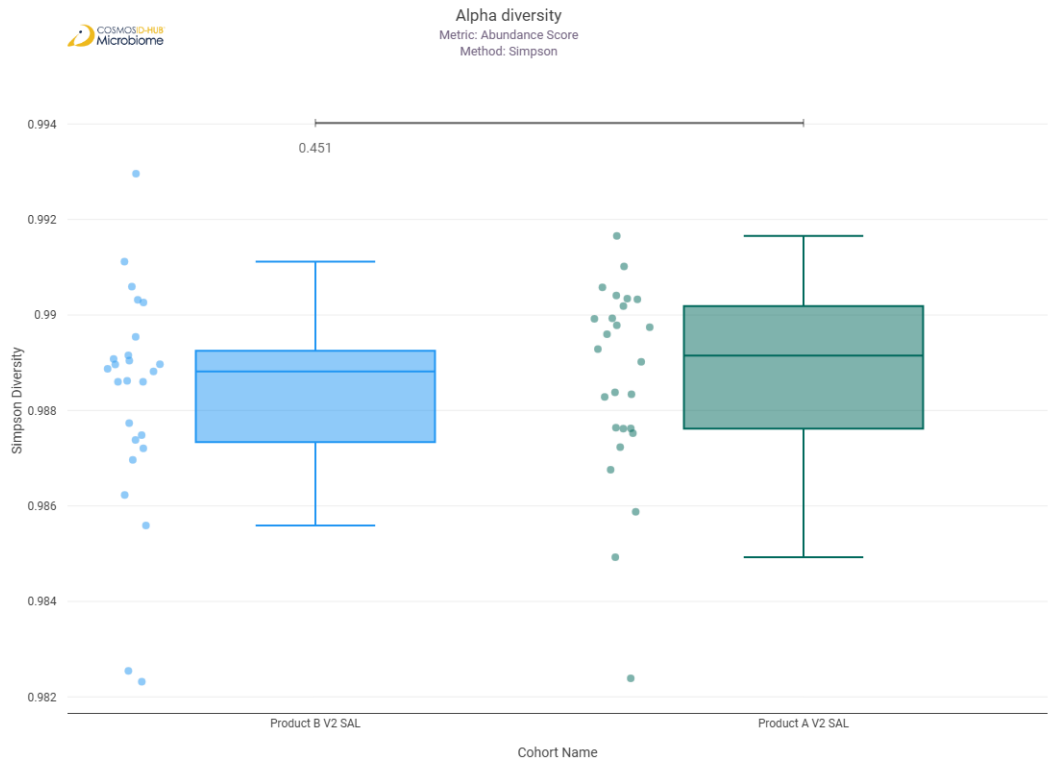
Chao1



Shannon

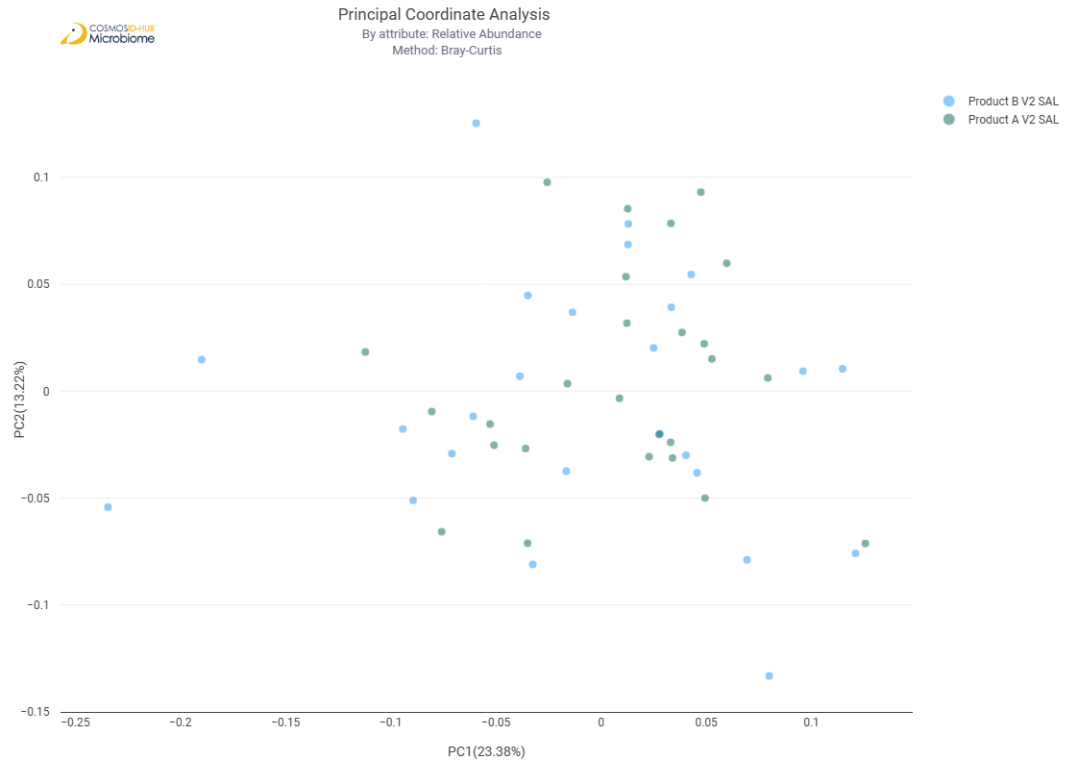


Simpson



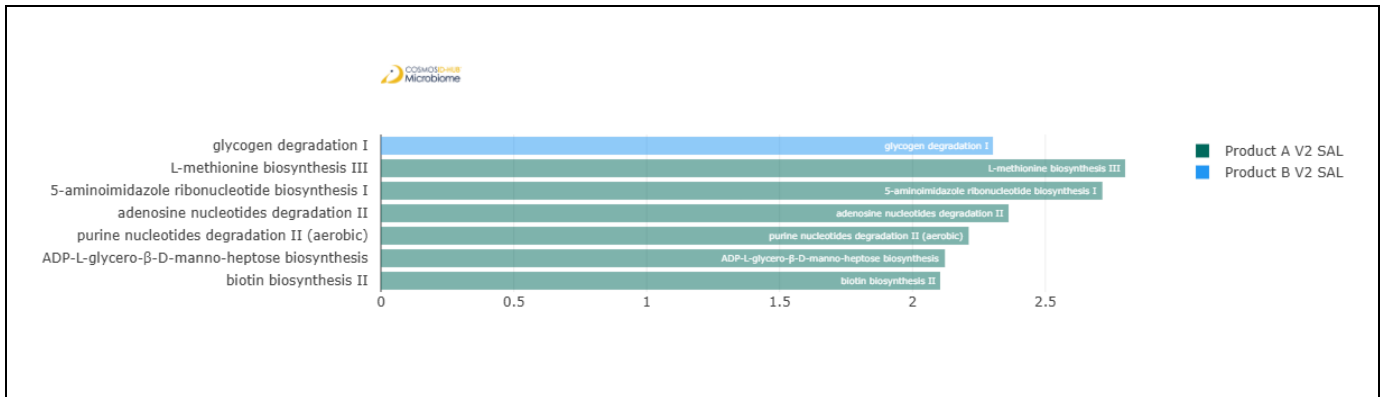
Beta Diversity (MetaCyc)

Bray-Curtis  
PERMNOVA  
p = 0.588





## Differential Abundance (LEfSe) (MetaCyc)

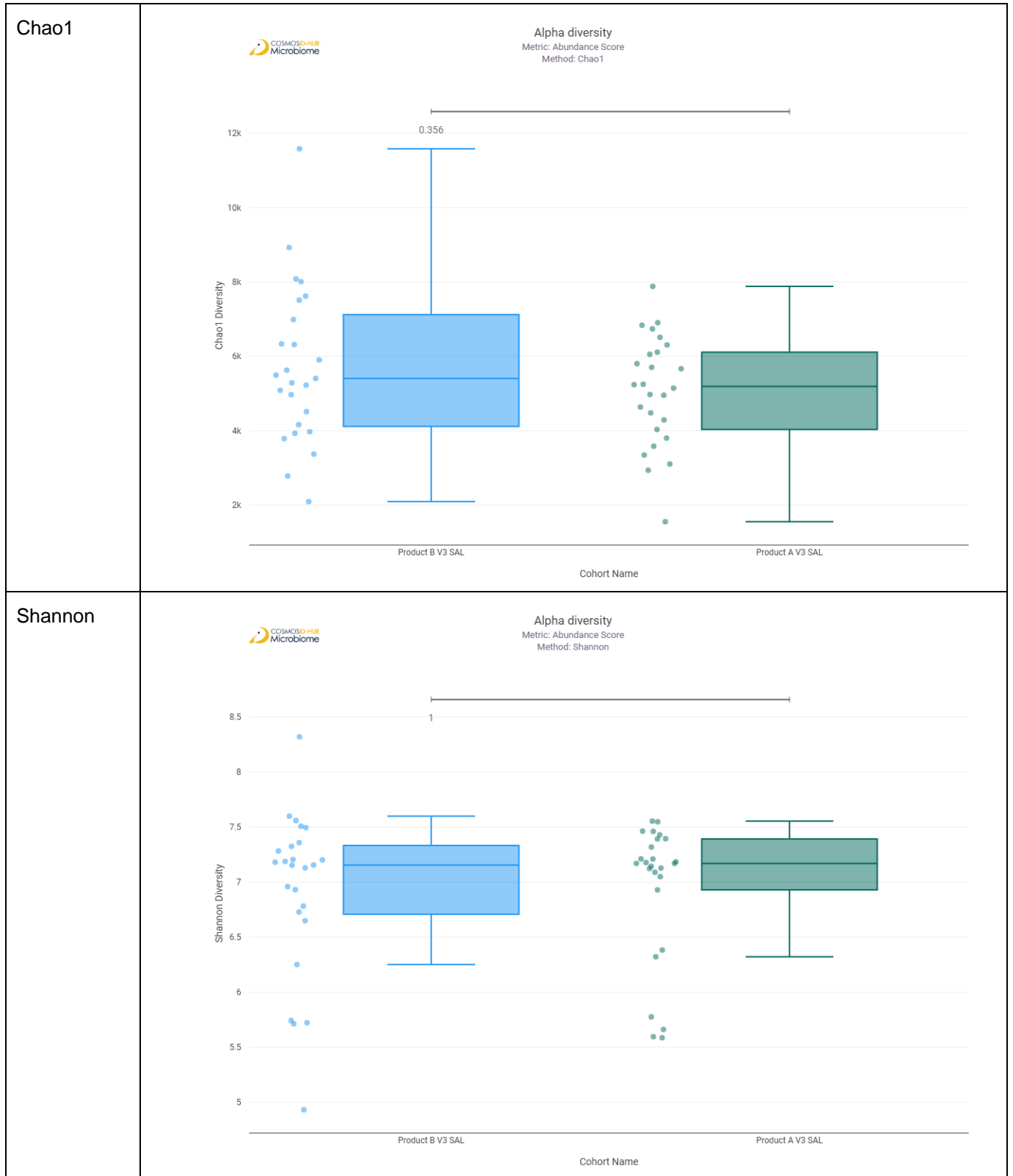


Feature	Enriched Cohort	LDA Score	P-value
glycogen degradation I	Product B V2 SAL	2.302816818	0.038205314
L-methionine biosynthesis III	Product A V2 SAL	2.800174369	0.028837668
5-aminoimidazole ribonucleotide biosynthesis I	Product A V2 SAL	2.714616828	0.041854827
adenosine nucleotides degradation II	Product A V2 SAL	2.361586069	0.033160392
purine nucleotides degradation II (aerobic)	Product A V2 SAL	2.211547707	0.020887991
ADP-L-glycero-β-D-manno-heptose biosynthesis	Product A V2 SAL	2.122101305	0.026186596
biotin biosynthesis II	Product A V2 SAL	2.104231519	0.018951173

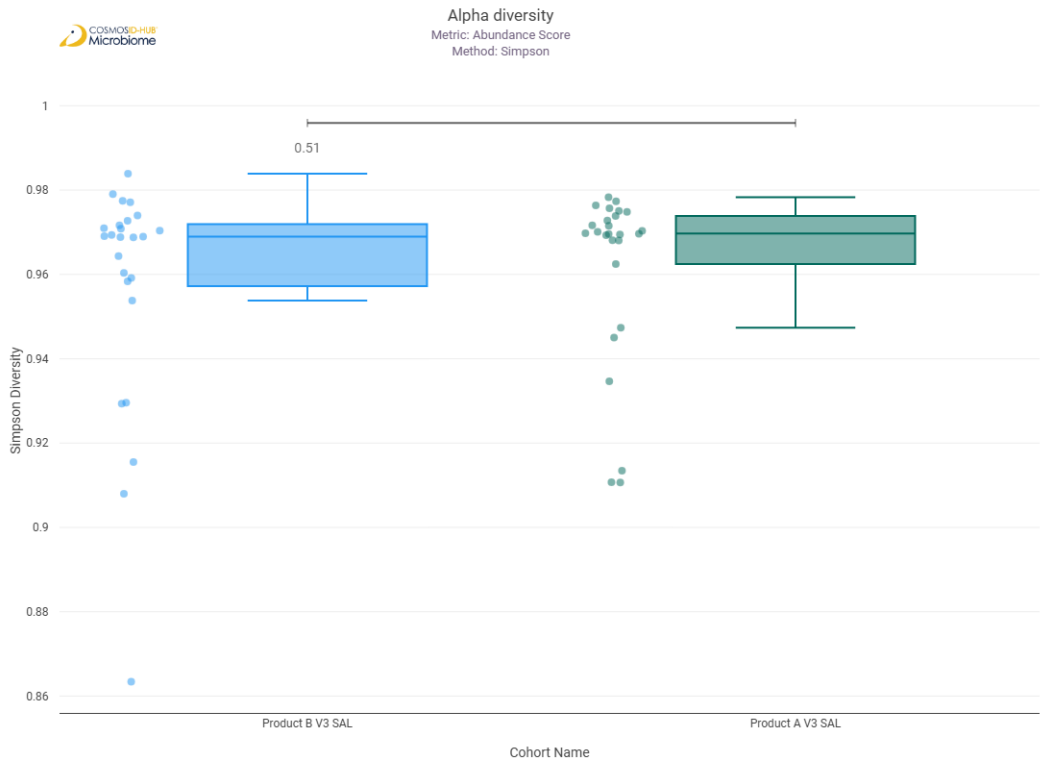
# Comparison 8: Product A V3 SAL vs Product B V3 SAL

## Gene Ontology

### Alpha Diversity (GO)



Simpson

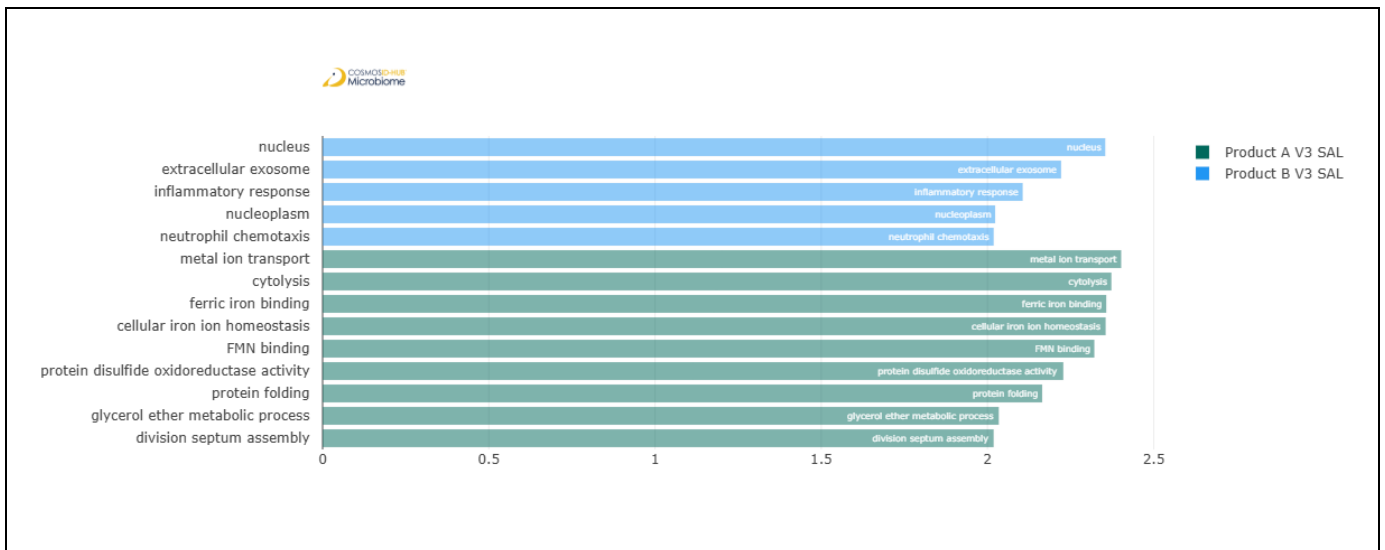


Beta Diversity (GO)

Bray-Curtis  
PERMNOVA  
p = 0.505



## Differential Abundance (LEfSe) (GO)

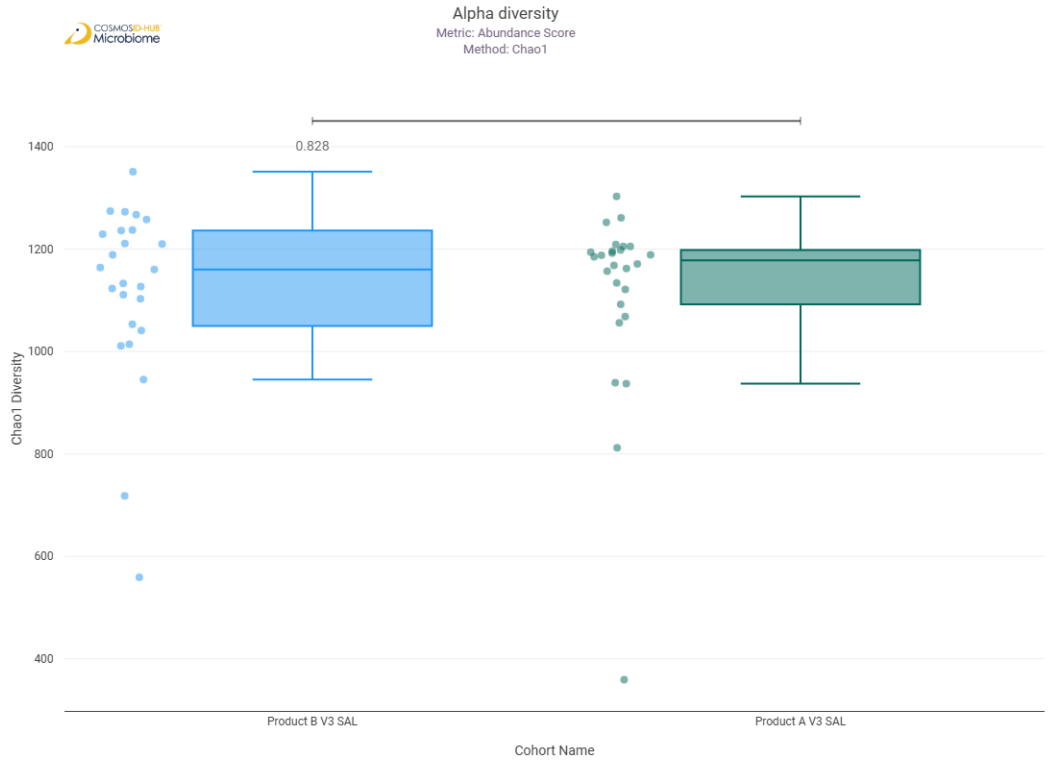


Feature	Enriched Cohort	LDA Score	P-value
nucleus	Product B V3 SAL	2.354393027	0.030245812
extracellular exosome	Product B V3 SAL	2.221604406	0.047879765
inflammatory response	Product B V3 SAL	2.106087975	0.033240045
nucleoplasm	Product B V3 SAL	2.023113821	0.038205314
neutrophil chemotaxis	Product B V3 SAL	2.01875955	0.045795182
metal ion transport	Product A V3 SAL	2.402291309	0.010390869
cytolysis	Product A V3 SAL	2.372871937	0.024341408
ferric iron binding	Product A V3 SAL	2.357375209	0.00745964
cellular iron ion homeostasis	Product A V3 SAL	2.355615079	0.00881699
FMN binding	Product A V3 SAL	2.321558848	0.028837668
protein disulfide oxidoreductase activity	Product A V3 SAL	2.228239528	0.030245812
protein folding	Product A V3 SAL	2.164657961	0.039994768
glycerol ether metabolic process	Product A V3 SAL	2.034126856	0.045795182
division septum assembly	Product A V3 SAL	2.018707201	0.009840467

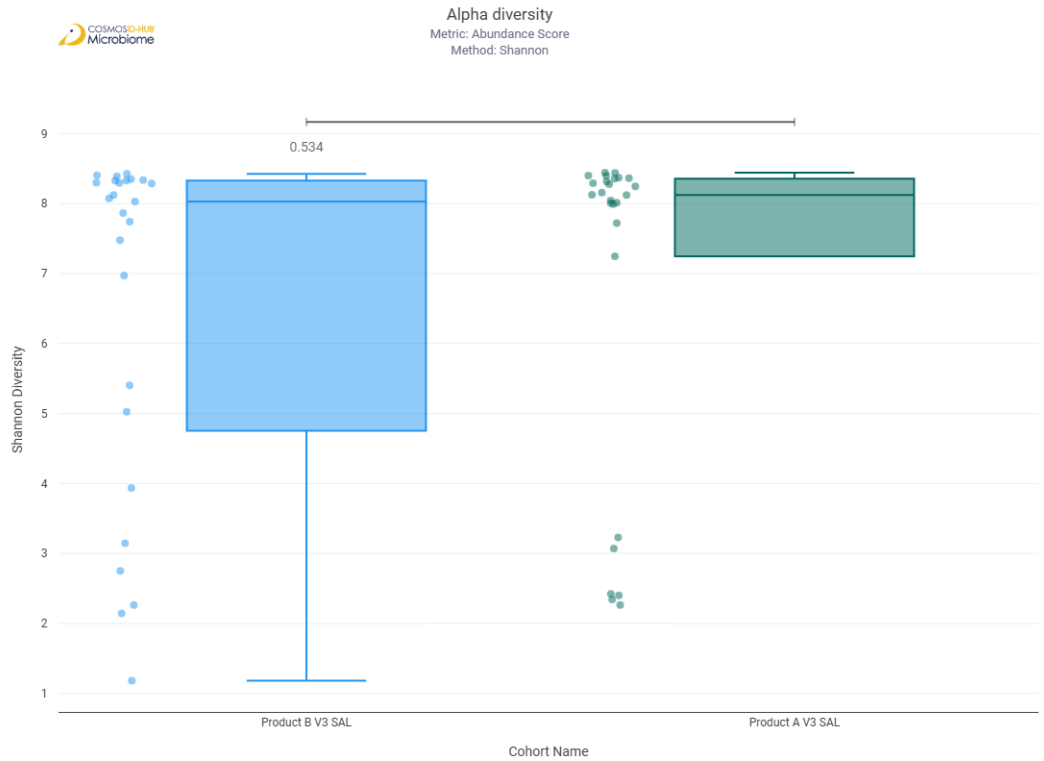
## Enzyme Commission

# Alpha Diversity (EC)

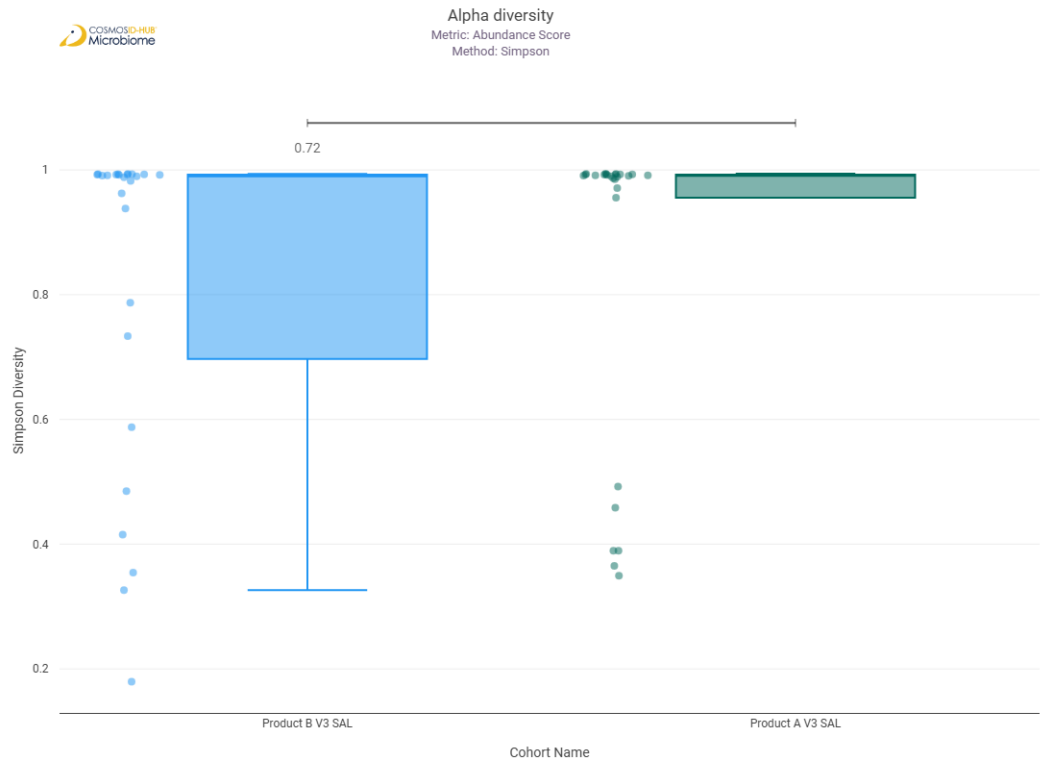
Chao1



Shannon

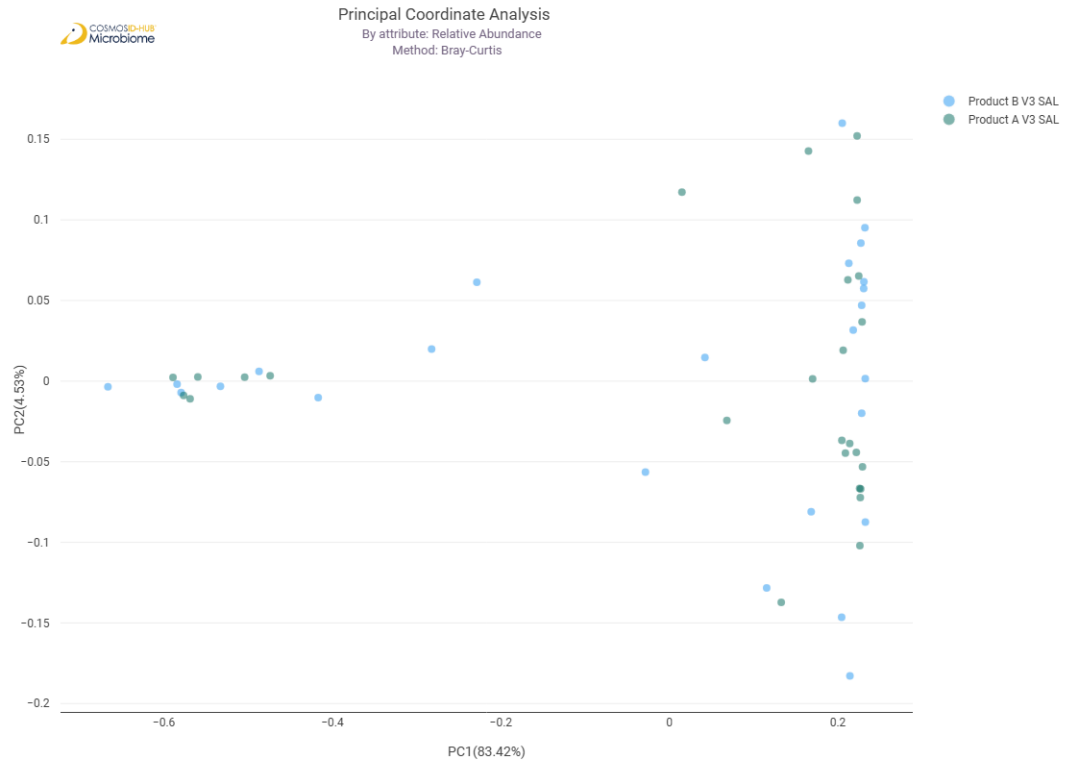


# Simpson

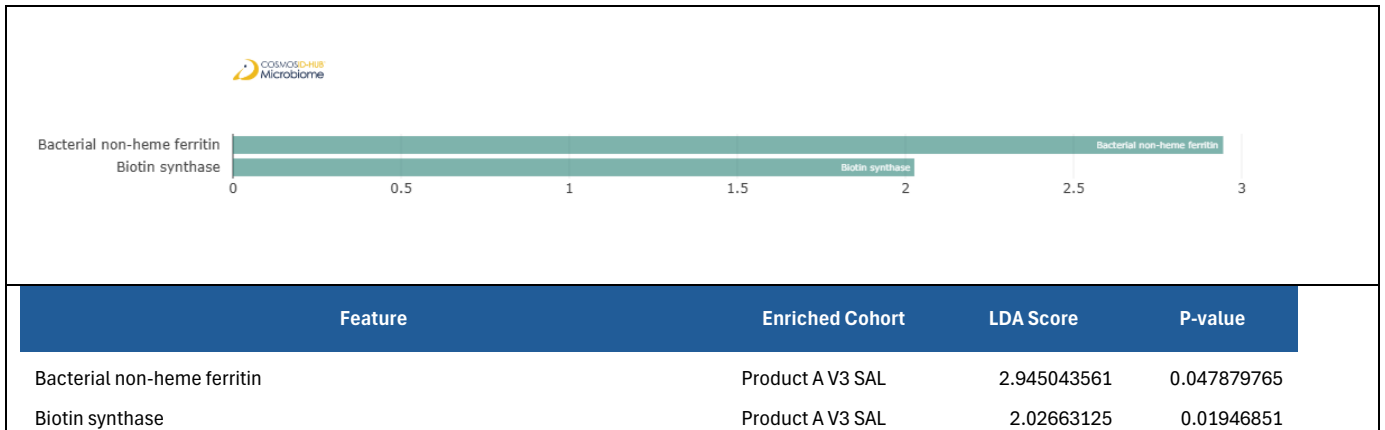


## Beta Diversity (EC)

Bray-Curtis  
PERMNOVA  
p = 0.676

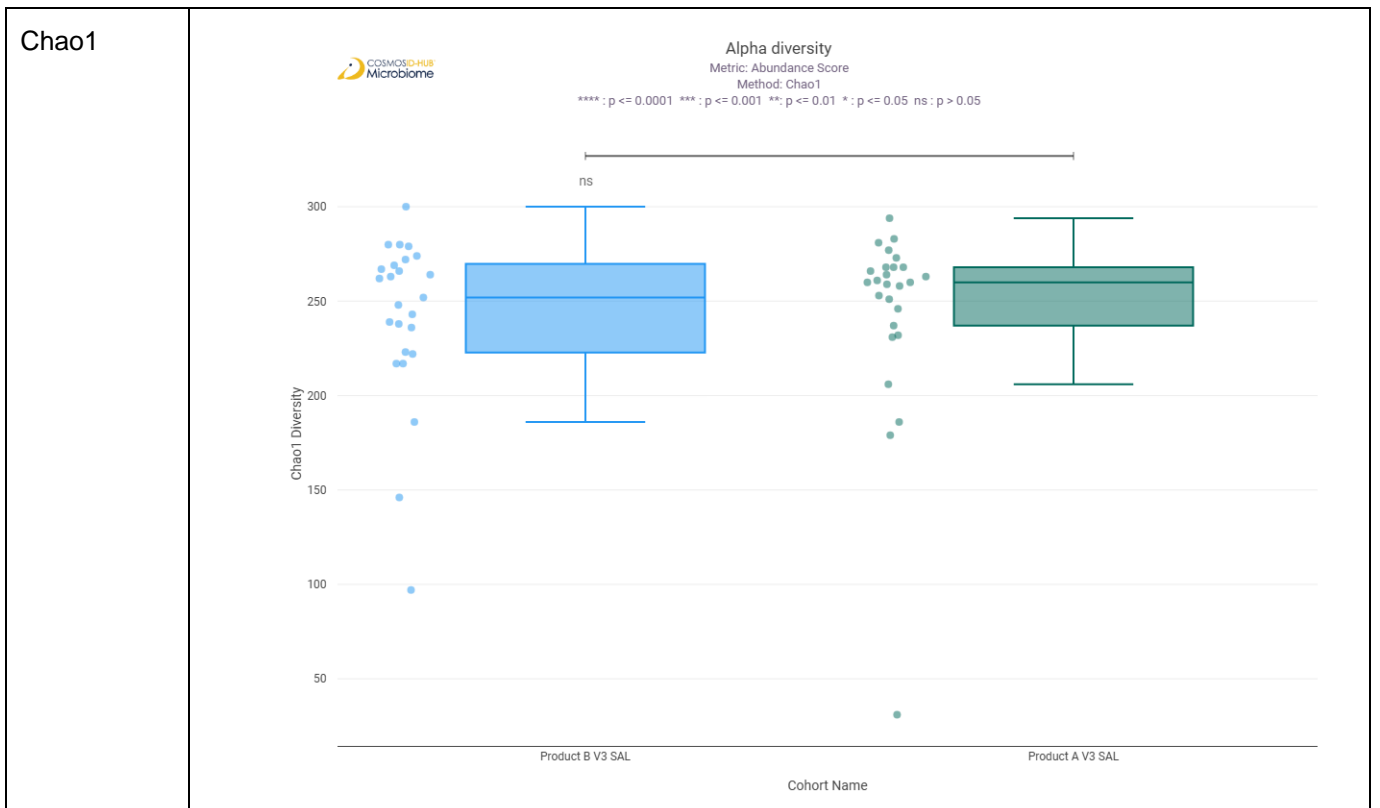


## Differential Abundance (LEfSe) (EC)

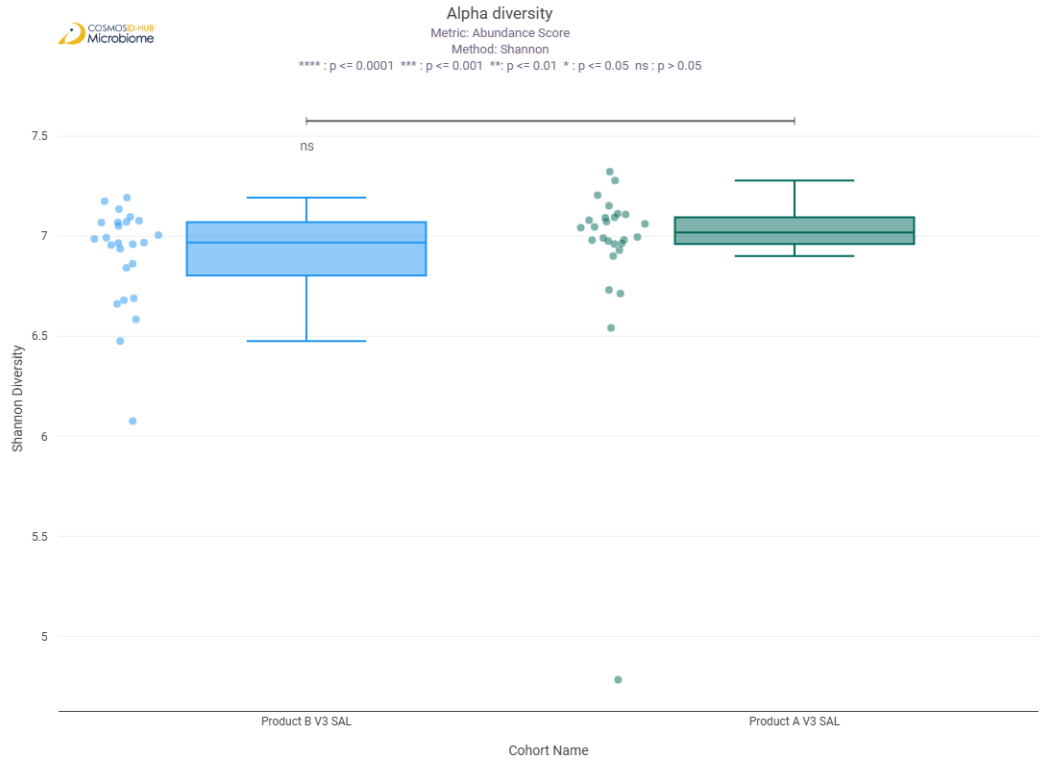


## MetaCyc Pathways

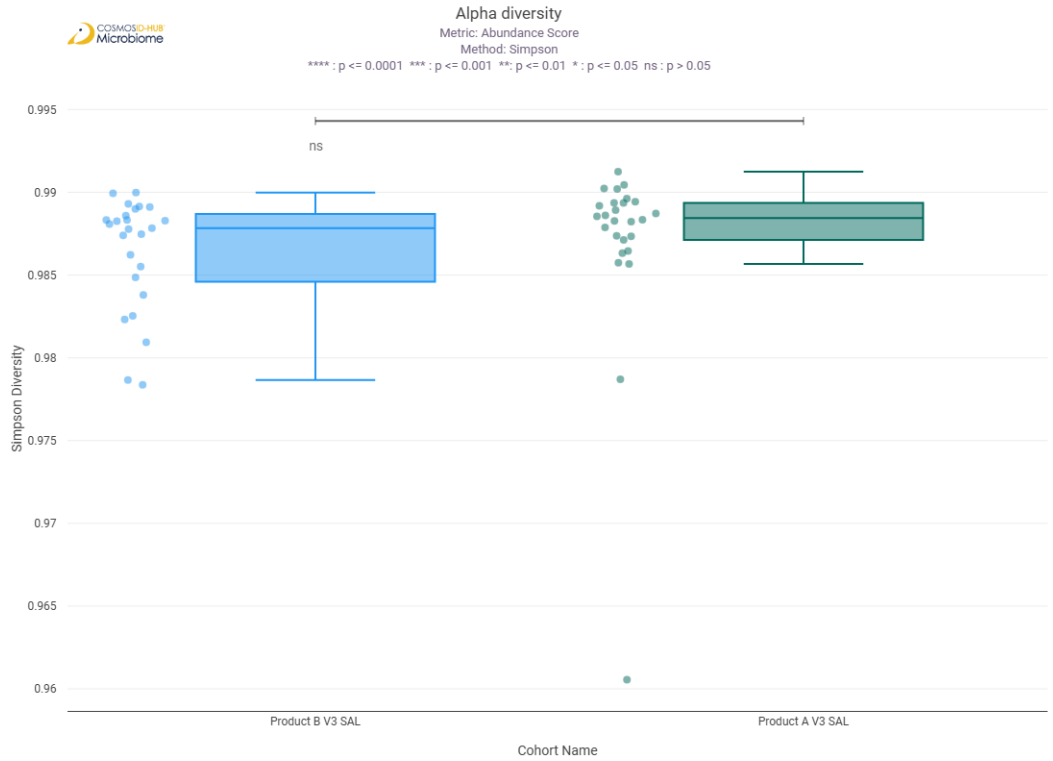
### Alpha Diversity (MetaCyc)



Shannon

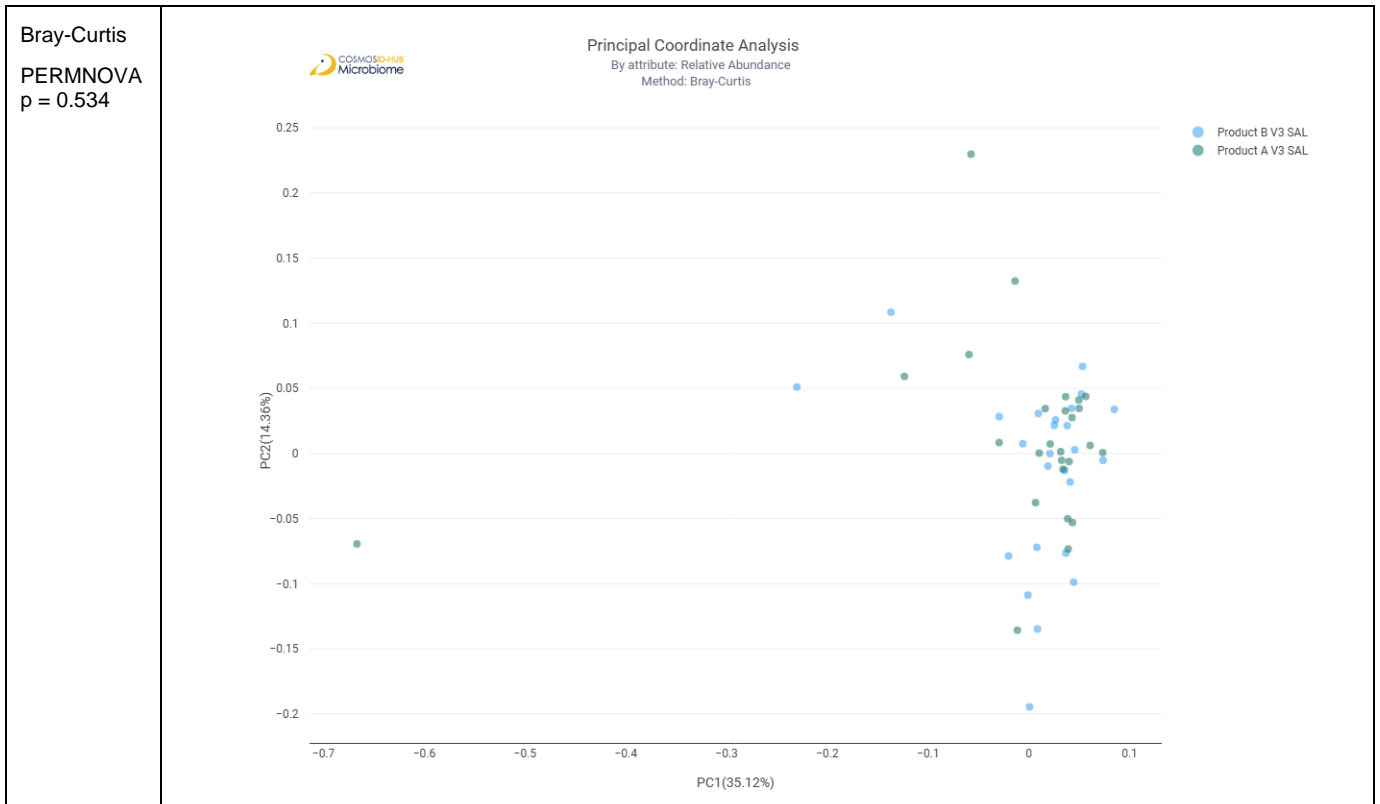


Simpson

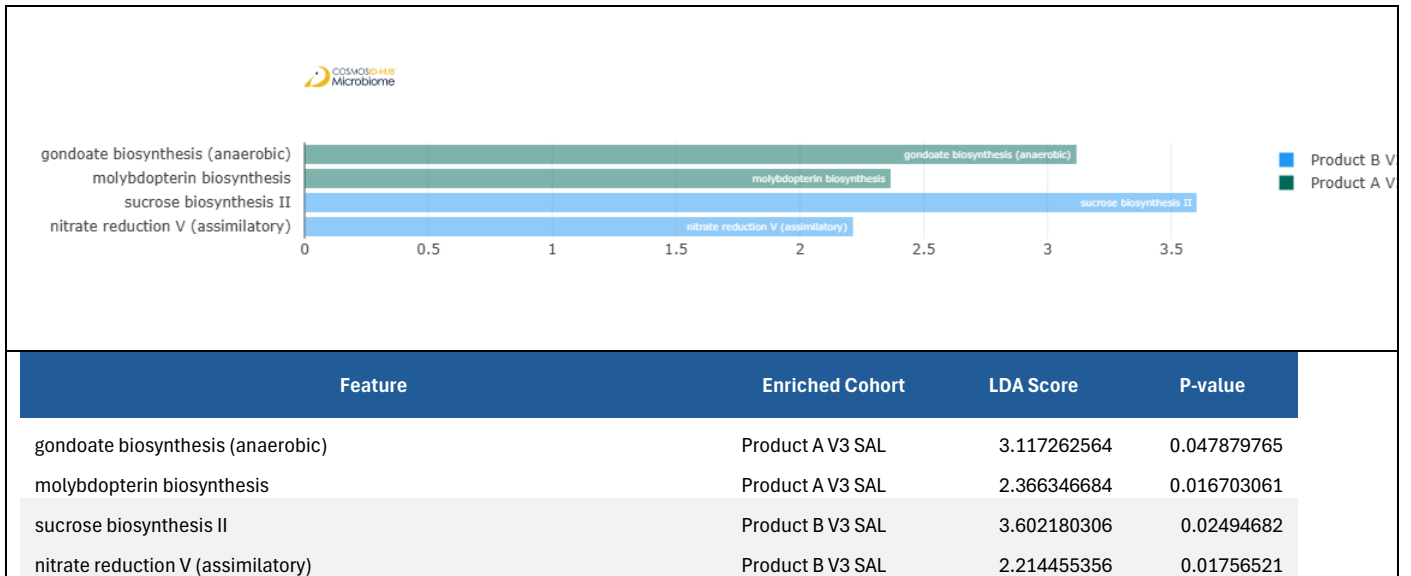




## Beta Diversity (MetaCyc)



## Differential Abundance (LEfSe) (MetaCyc)

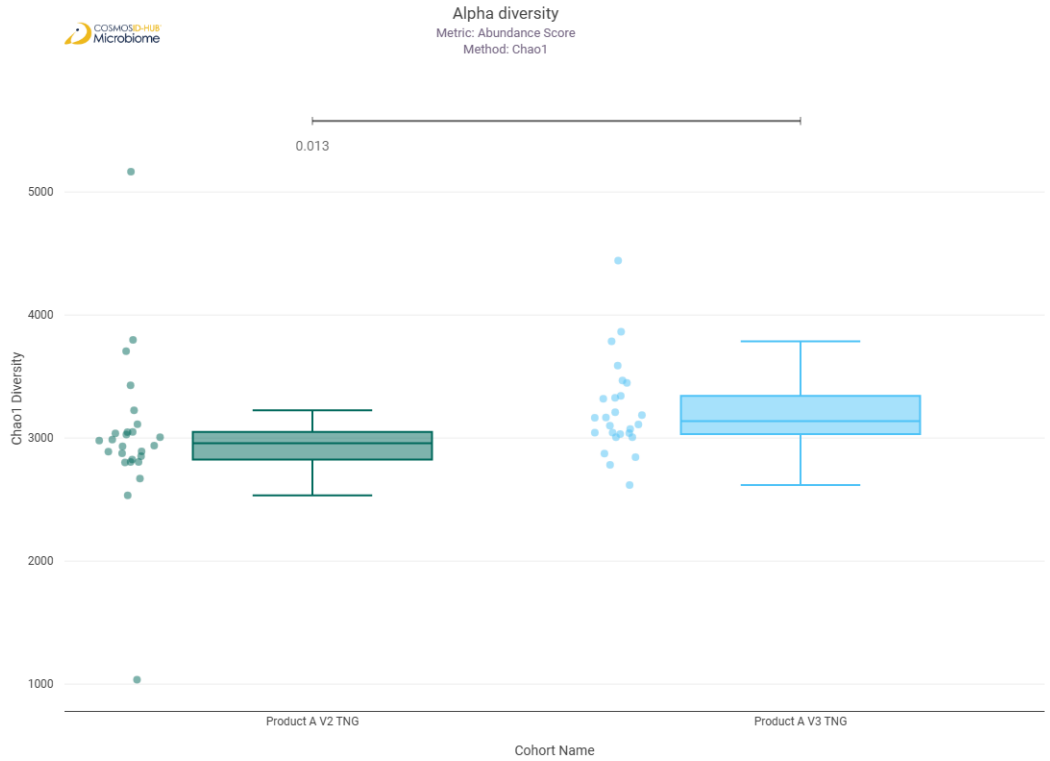


## Comparison 9: Product A V2 TNG vs Product A V3 TNG

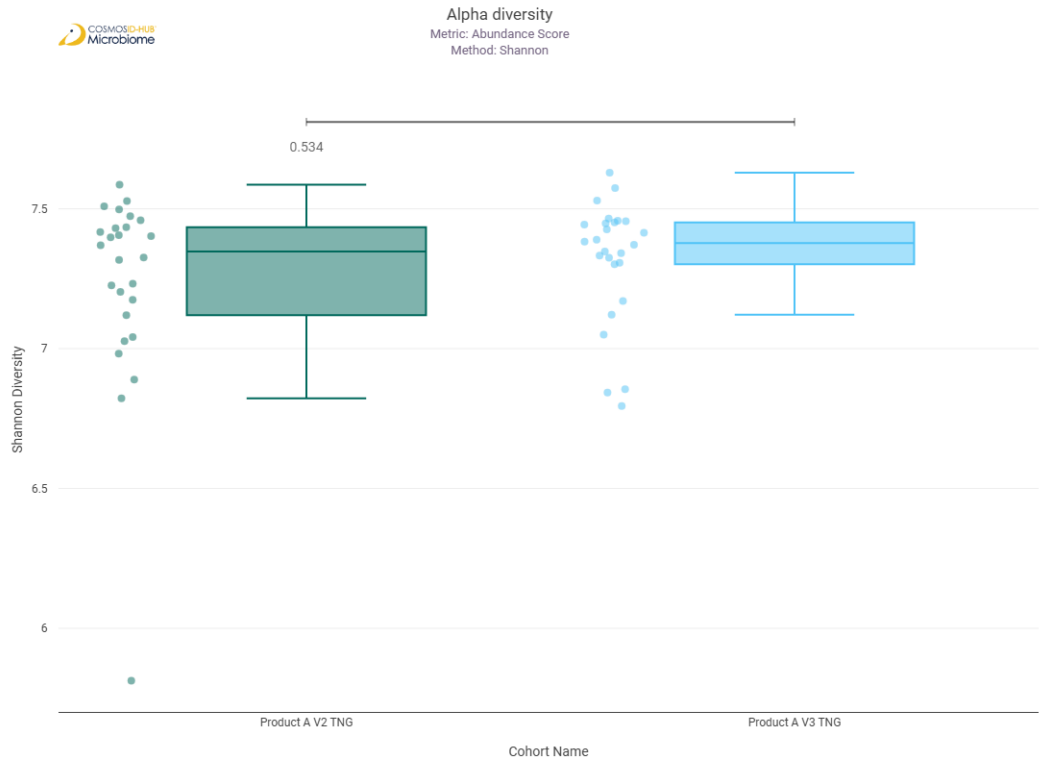
### Gene Ontology

# Alpha Diversity (GO)

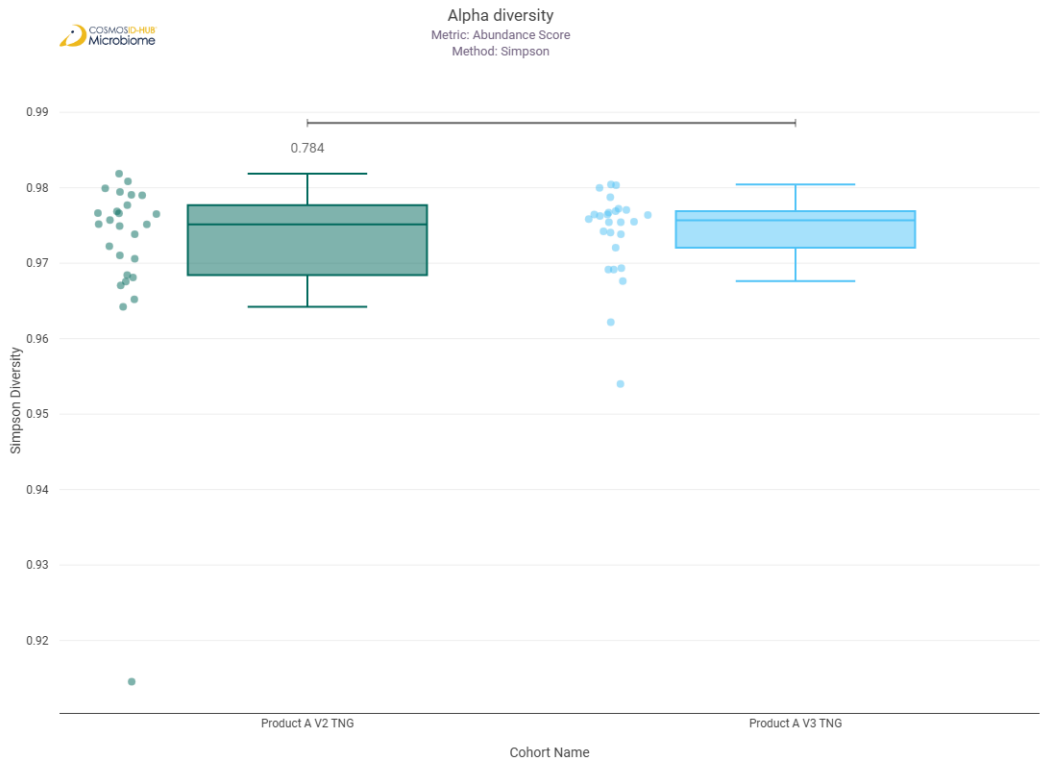
Chao1



Shannon

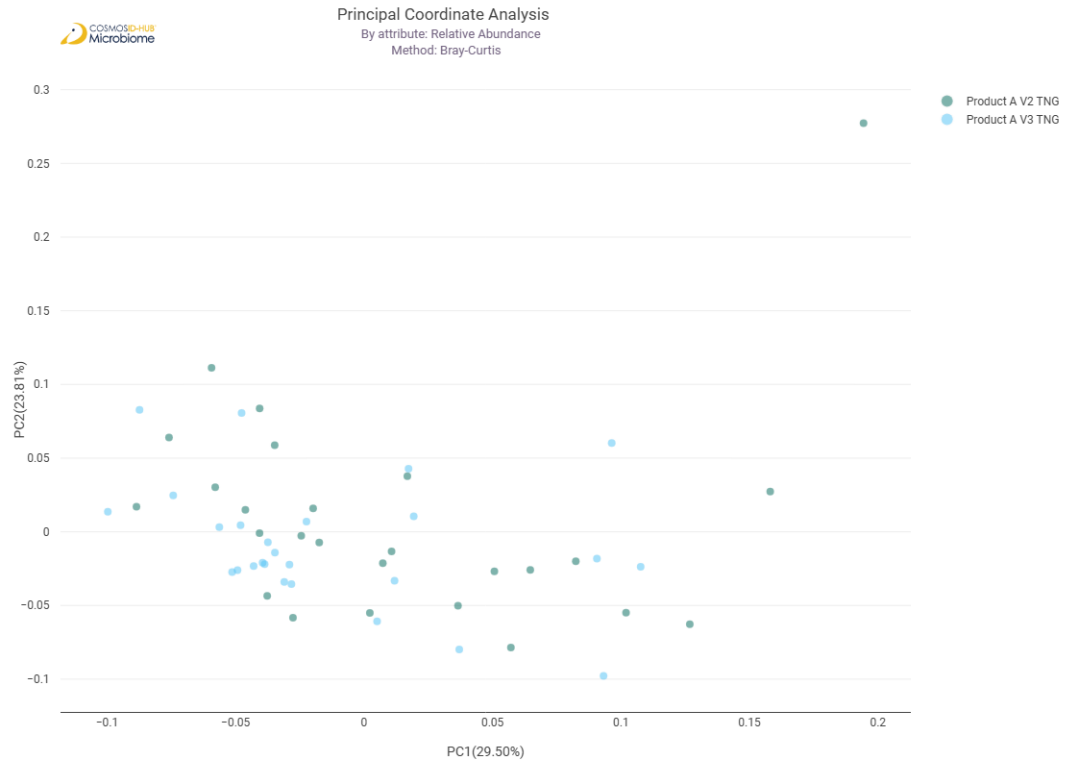


# Simpson

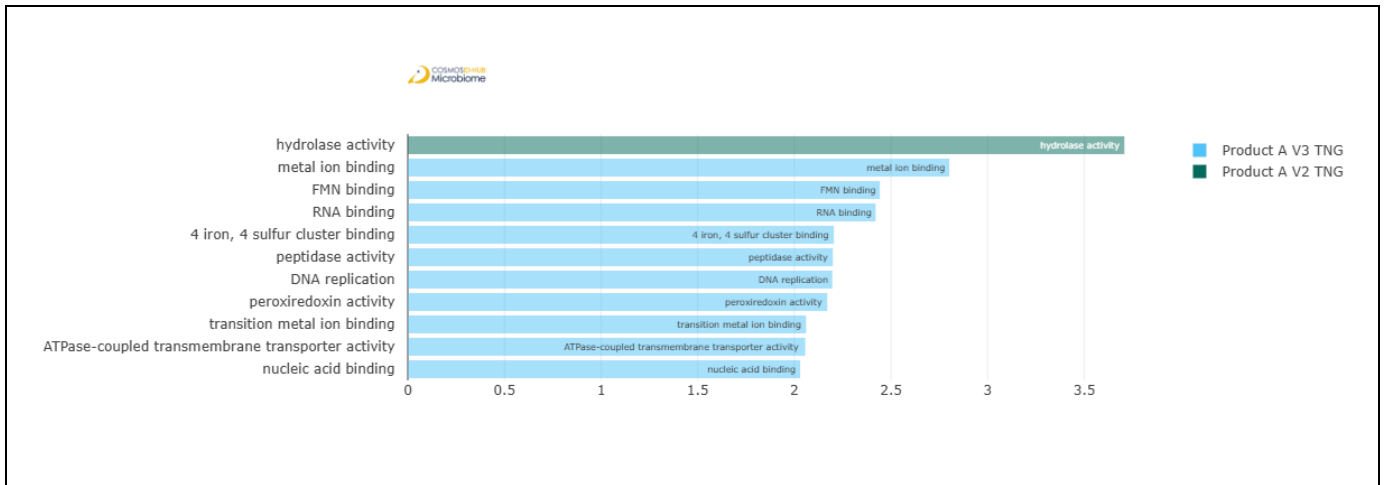


## Beta Diversity (GO)

Bray-Curtis  
PERMNOVA  
 $p = 0.170$



## Differential Abundance (LEfSe) (GO)

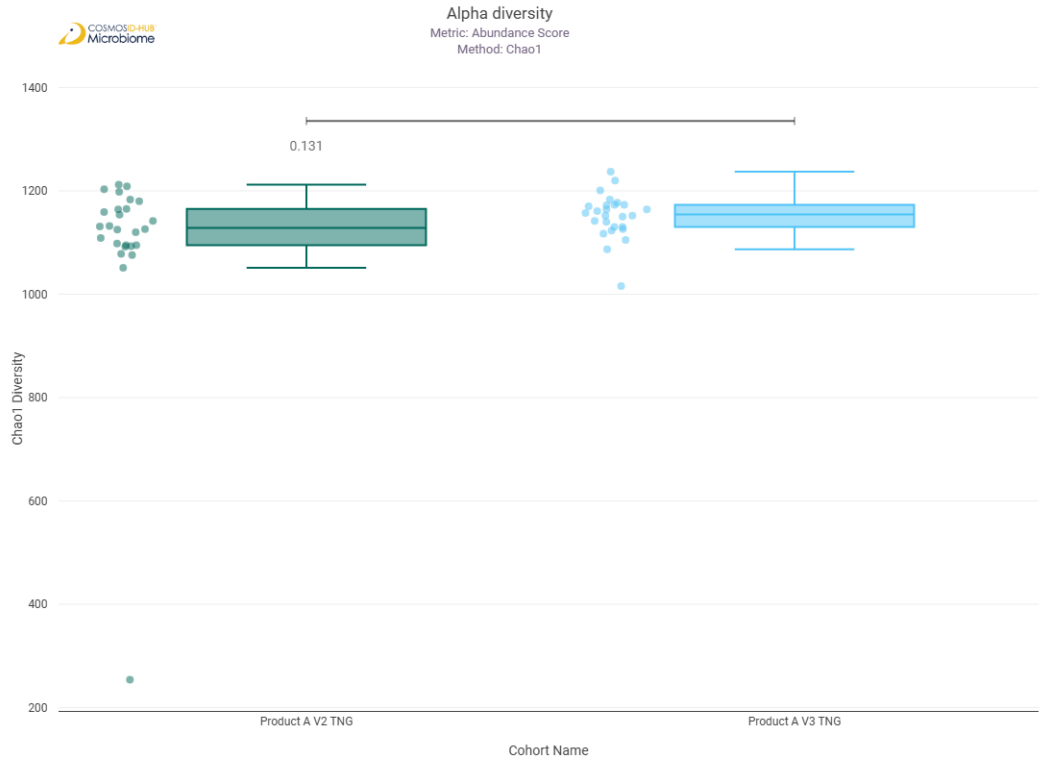


Feature	Enriched Cohort	LDA Score	P-value
hydrolase activity	Product A V2 TNG	3.707495081	0.016509366
metal ion binding	Product A V3 TNG	2.801446552	0.029417827
FMN binding	Product A V3 TNG	2.442148744	0.005108961
RNA binding	Product A V3 TNG	2.420090714	0.014930589
4 iron, 4 sulfur cluster binding	Product A V3 TNG	2.20433213	0.024382597
peptidase activity	Product A V3 TNG	2.198773629	0.003615568
DNA replication	Product A V3 TNG	2.196261075	0.005108961
peroxiredoxin activity	Product A V3 TNG	2.170304979	0.036948224
transition metal ion binding	Product A V3 TNG	2.060247577	0.035322927
ATPase-coupled transmembrane transporter activity	Product A V3 TNG	2.05653438	0.046061451
nucleic acid binding	Product A V3 TNG	2.029809755	0.005108961

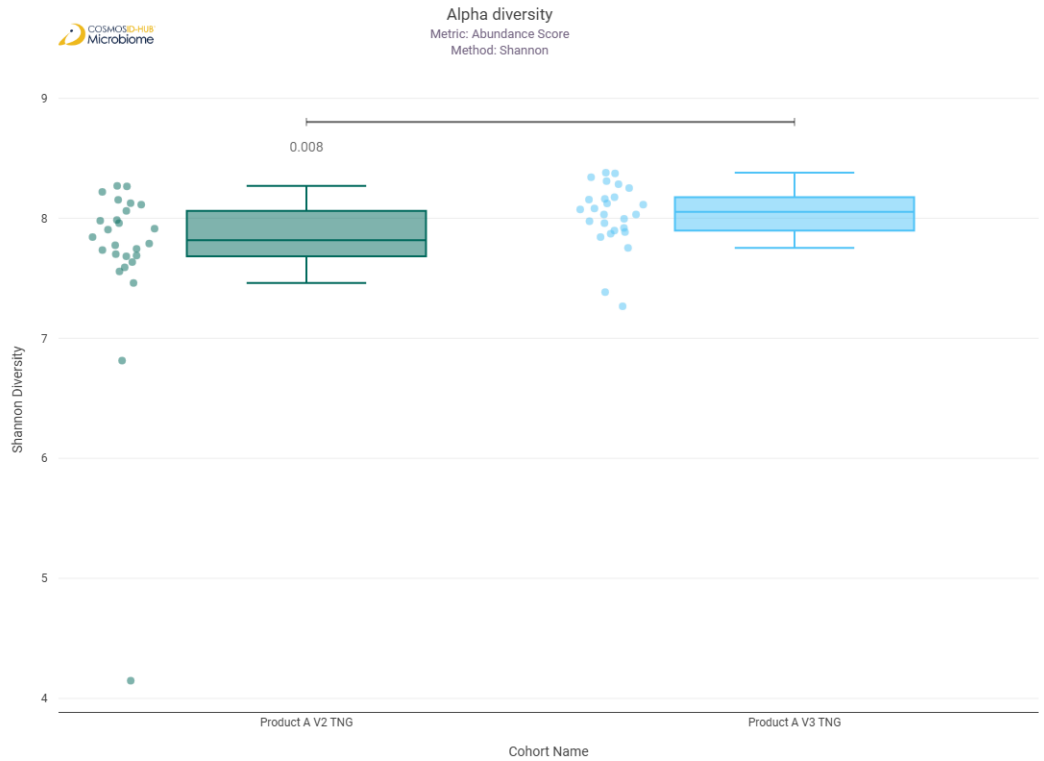
## Enzyme Commission

# Alpha Diversity (EC)

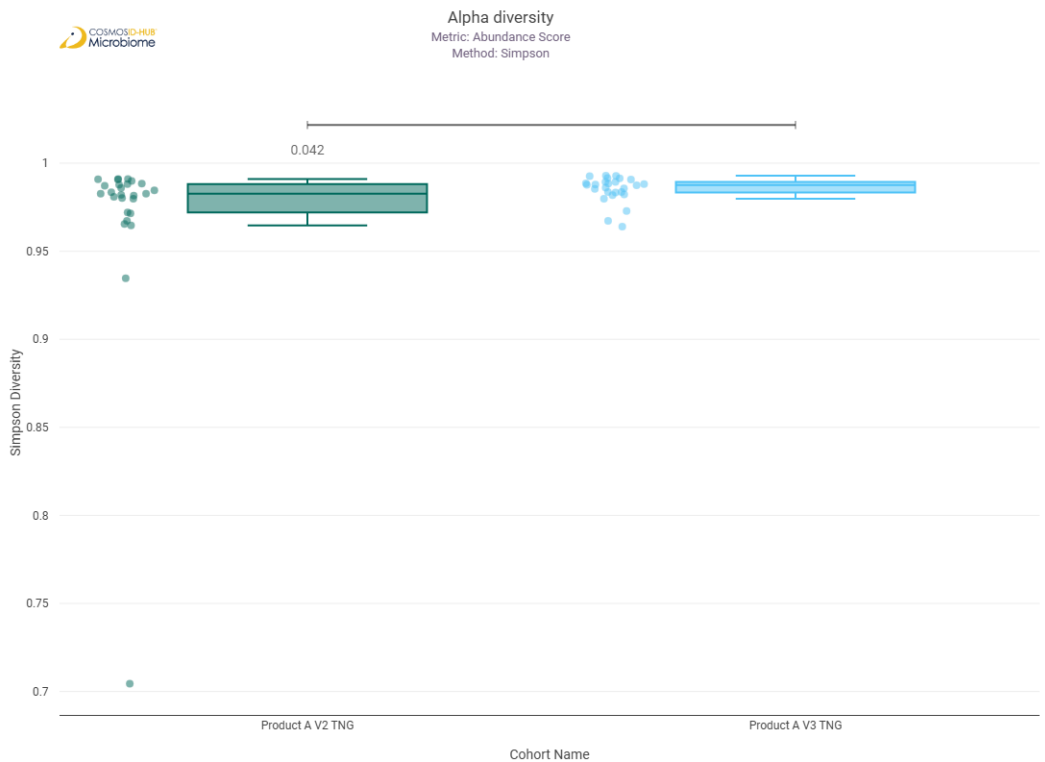
Chao1



Shannon

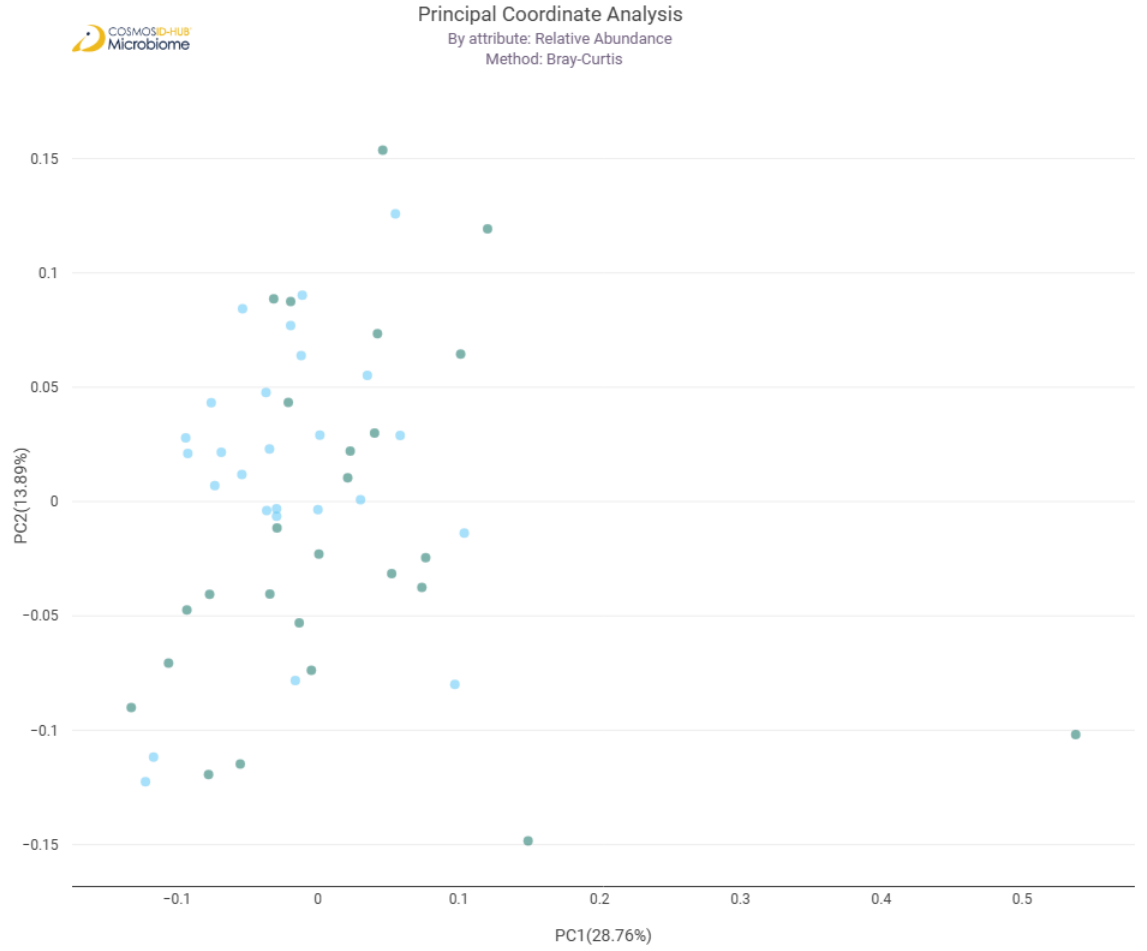


# Simpson

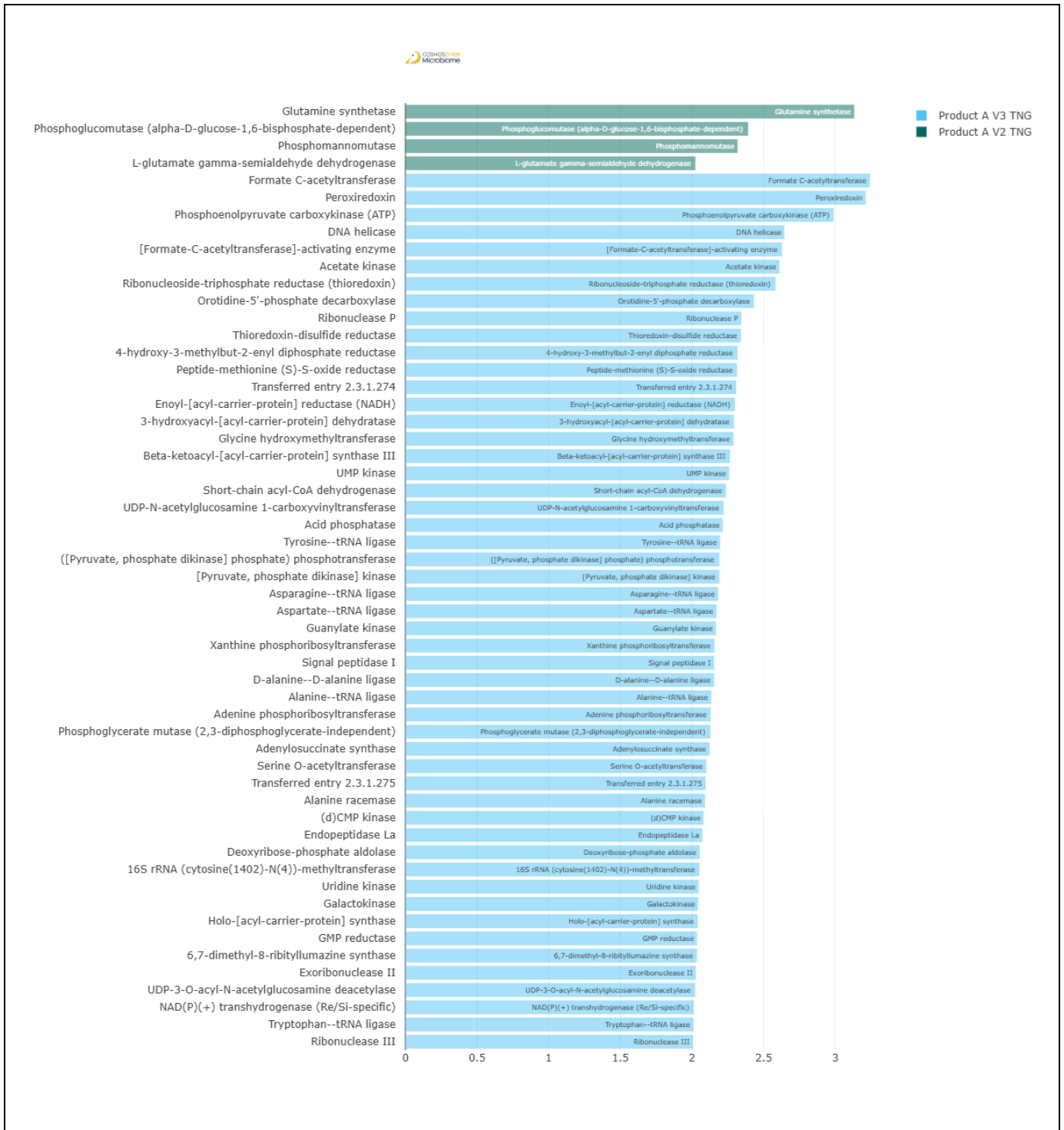


Beta Diversity (EC)

Bray-Curtis  
PERMNO  
VA p =  
0.053



## Differential Abundance (LEfSe) (EC)



Feature	Enriched Cohort	LDA Score	P-value
Glutamine synthetase	Product A V2 TNG	3.131773587	0.019152346
Phosphoglucosmutase (alpha-D-glucose-1,6-bisphosphate-dependent)	Product A V2 TNG	2.391780049	0.008404526
Phosphomannomutase	Product A V2 TNG	2.318057666	0.013486371
L-glutamate gamma-semialdehyde dehydrogenase	Product A V2 TNG	2.023541115	0.030808261
Formate C-acetyltransferase	Product A V3 TNG	3.242142189	0.02808172
Peroxioredoxin	Product A V3 TNG	3.210994816	0.036948224

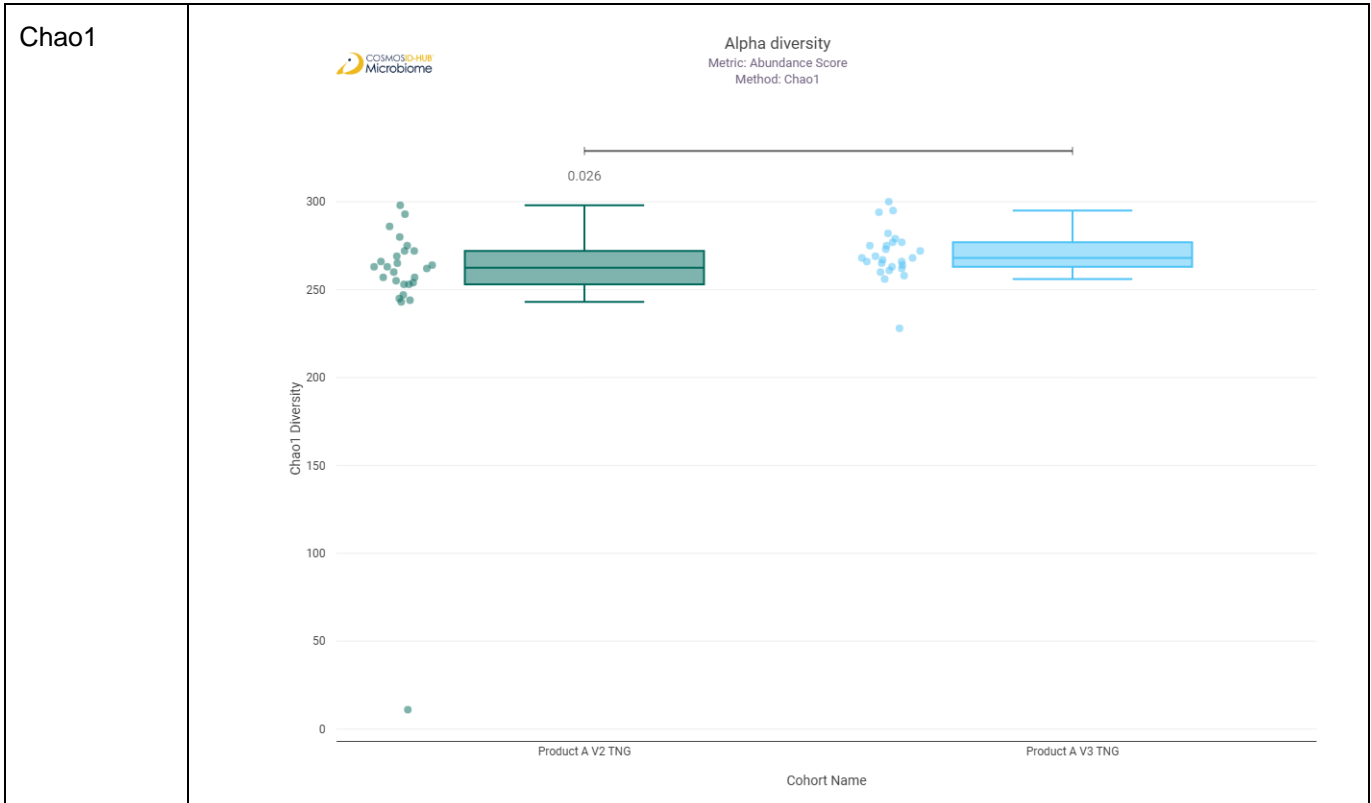


Phosphoenolpyruvate carboxykinase (ATP)	Product A V3 TNG	2.988111427	0.006393679
DNA helicase	Product A V3 TNG	2.644863609	0.004826615
[Formate-C-acetyltransferase]-activating enzyme	Product A V3 TNG	2.627544174	0.012167011
Acetate kinase	Product A V3 TNG	2.609351455	0.036948224
Ribonucleoside-triphosphate reductase (thioredoxin)	Product A V3 TNG	2.58250405	0.008404526
Orotidine-5'-phosphate decarboxylase	Product A V3 TNG	2.432550553	0.020112035
Ribonuclease P	Product A V3 TNG	2.344650231	0.006393679
Thioredoxin-disulfide reductase	Product A V3 TNG	2.341433821	0.029417827
4-hydroxy-3-methylbut-2-enyl diphosphate reductase	Product A V3 TNG	2.317067874	0.013486371
Peptide-methionine (S)-S-oxide reductase	Product A V3 TNG	2.313771424	0.015702531
Transferred entry 2.3.1.274	Product A V3 TNG	2.307913789	2.77761E-05
Enoyl-[acyl-carrier-protein] reductase (NADH)	Product A V3 TNG	2.299102917	0.024382597
3-hydroxyacyl-[acyl-carrier-protein] dehydratase	Product A V3 TNG	2.29215255	8.40E-03
Glycine hydroxymethyltransferase	Product A V3 TNG	2.289754924	0.020112035
Beta-ketoacyl-[acyl-carrier-protein] synthase III	Product A V3 TNG	2.265318101	0.038636777
UMP kinase	Product A V3 TNG	2.258348794	0.038636777
Short-chain acyl-CoA dehydrogenase	Product A V3 TNG	2.237427668	0.046061451
UDP-N-acetylglucosamine 1-carboxyvinyltransferase	Product A V3 TNG	2.221010504	0.012811669
Acid phosphatase	Product A V3 TNG	2.214868777	0.003833001
Tyrosine--tRNA ligase	Product A V3 TNG	2.195780873	0.038636777
[Pyruvate, phosphate dikinase] kinase	Product A V3 TNG	2.190769448	0.048090171
([Pyruvate, phosphate dikinase] phosphate) phosphotransferase	Product A V3 TNG	2.190769448	0.048090171
Asparagine--tRNA ligase	Product A V3 TNG	2.18153077	0.013486371
Aspartate--tRNA ligase	Product A V3 TNG	2.171000903	0.00675726
Guanylate kinase	Product A V3 TNG	2.167070883	0.002853503
Xanthine phosphoribosyltransferase	Product A V3 TNG	2.156672978	0.036948224
Signal peptidase I	Product A V3 TNG	2.154503472	0.010402139
D-alanine--D-alanine ligase	Product A V3 TNG	2.154118252	0.002381558
Alanine--tRNA ligase	Product A V3 TNG	2.134582965	0.046061451
Adenine phosphoribosyltransferase	Product A V3 TNG	2.130121973	0.026798248
Phosphoglycerate mutase (2,3-diphosphoglycerate-independent)	Product A V3 TNG	2.128669083	1.92E-02
Adenylosuccinate synthase	Product A V3 TNG	2.122998977	0.022157981
Serine O-acetyltransferase	Product A V3 TNG	2.100032319	0.022157981
Transferred entry 2.3.1.275	Product A V3 TNG	2.09535326	0.003615568
Alanine racemase	Product A V3 TNG	2.090745674	0.03375904
(d)CMP kinase	Product A V3 TNG	2.080791026	0.014192278
Endopeptidase La	Product A V3 TNG	2.072431	0.015702531
Deoxyribose-phosphate aldolase	Product A V3 TNG	2.054306578	0.01096333
16S rRNA (cytosine(1402)-N(4))-methyltransferase	Product A V3 TNG	2.05217557	0.042211177
Uridine kinase	Product A V3 TNG	2.046121636	0.000865916
Galactokinase	Product A V3 TNG	2.042511013	0.02808172
Holo-[acyl-carrier-protein] synthase	Product A V3 TNG	2.040422943	0.036948224
GMP reductase	Product A V3 TNG	2.035067493	0.029417827
6,7-dimethyl-8-ribityllumazine synthase	Product A V3 TNG	2.035018511	0.038636777
Exoribonuclease II	Product A V3 TNG	2.027495812	0.023247195
UDP-3-O-acyl-N-acetylglucosamine deacetylase	Product A V3 TNG	2.022030905	0.008868809

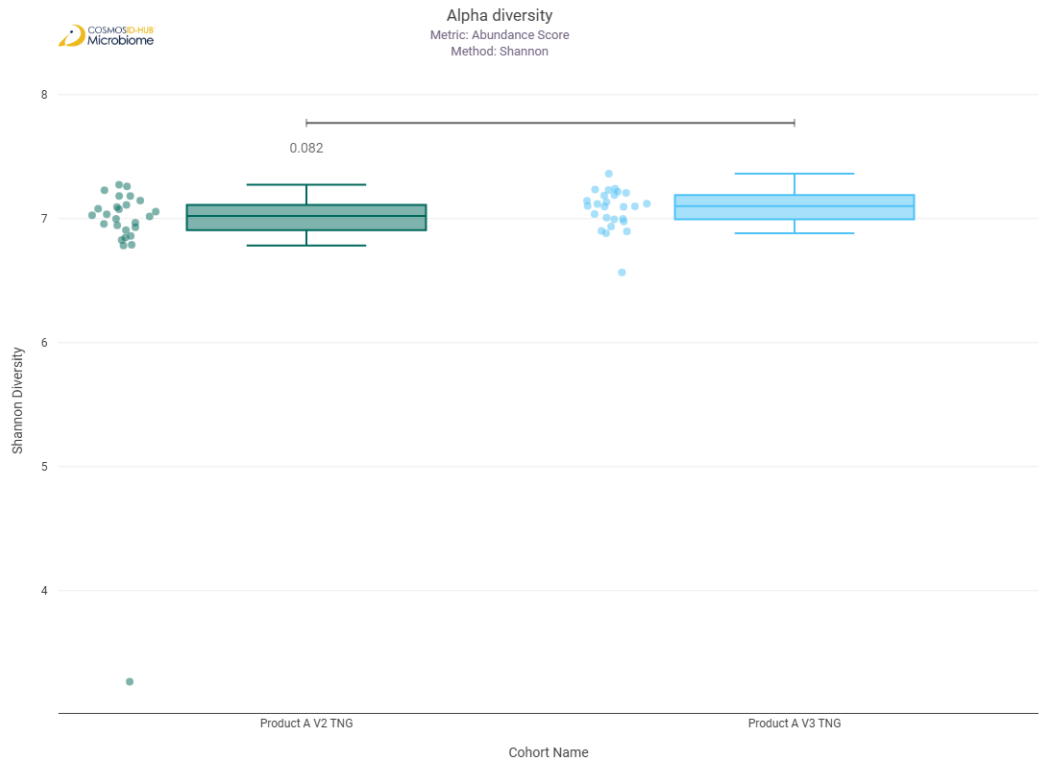
NAD(P)(+) transhydrogenase (Re/Si-specific)	Product A V3 TNG	2.011575686	0.01096333
Tryptophan--tRNA ligase	Product A V3 TNG	2.010476434	0.016509366
Ribonuclease III	Product A V3 TNG	2.006528818	0.024382597

## MetaCyc Pathways

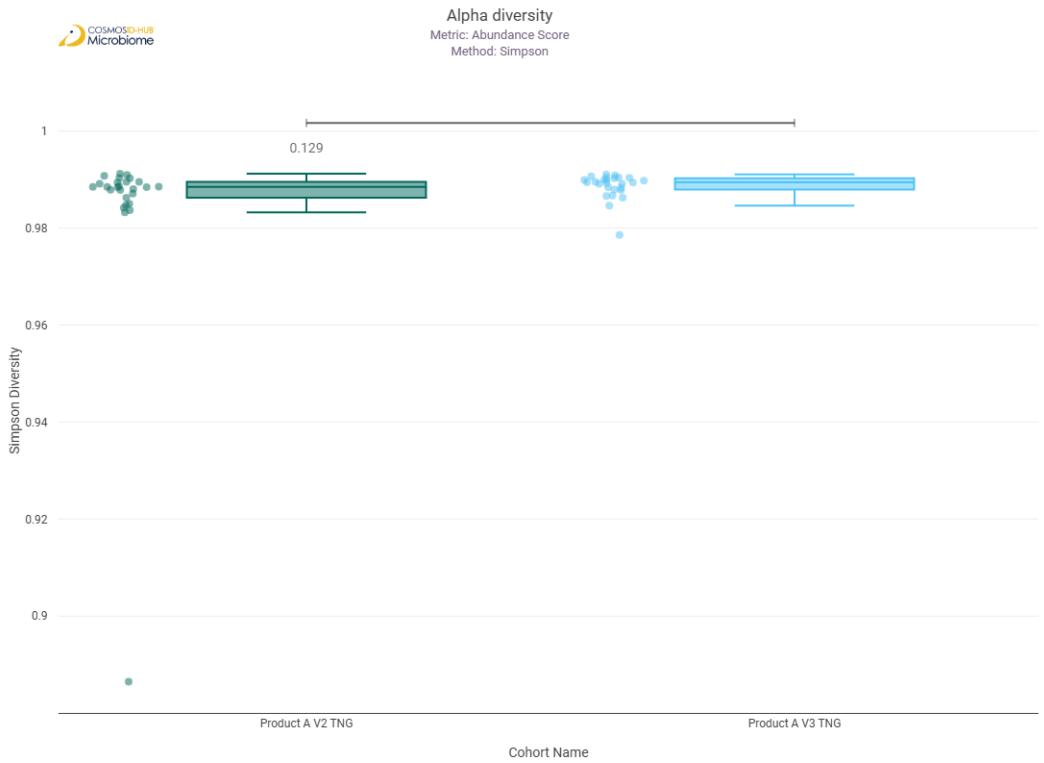
### Alpha Diversity (MetaCyc)



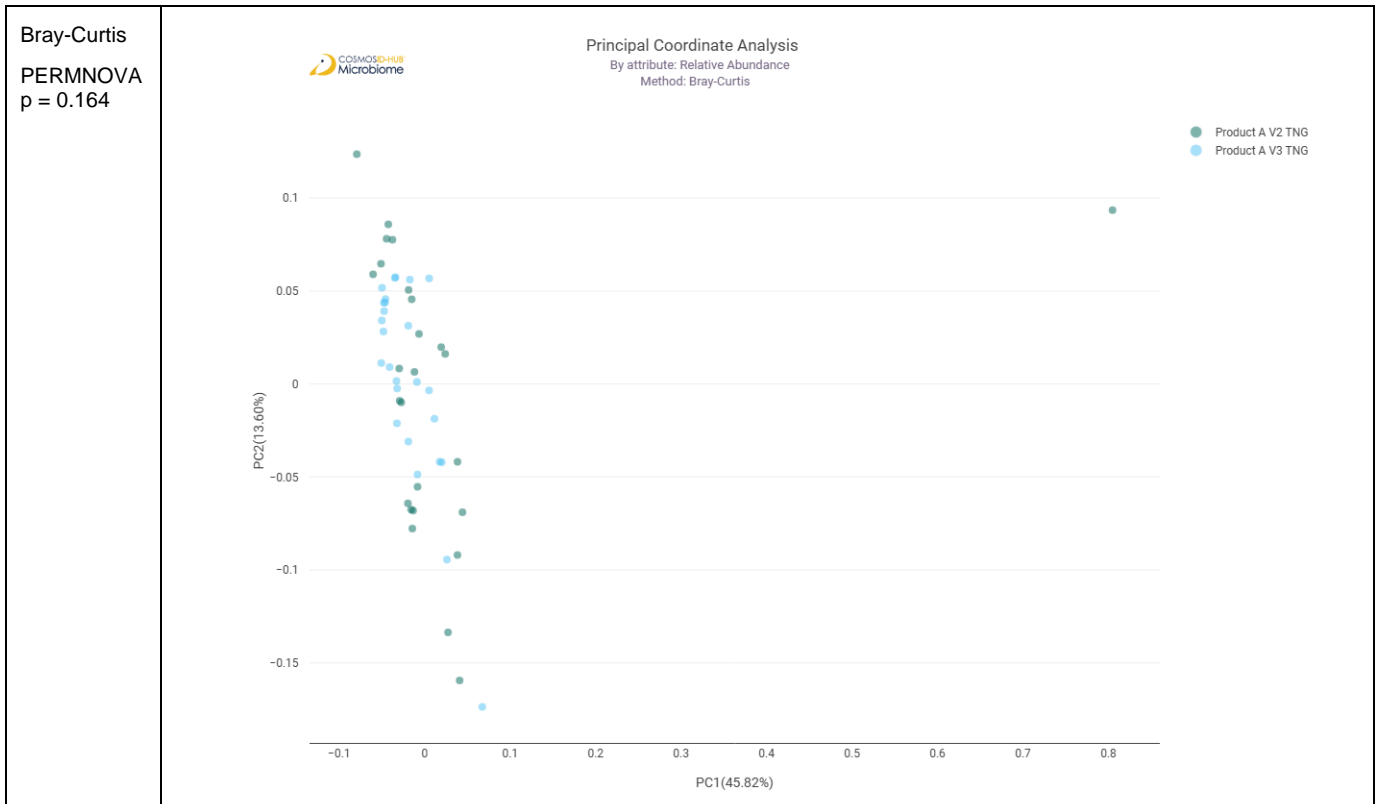
# Shannon



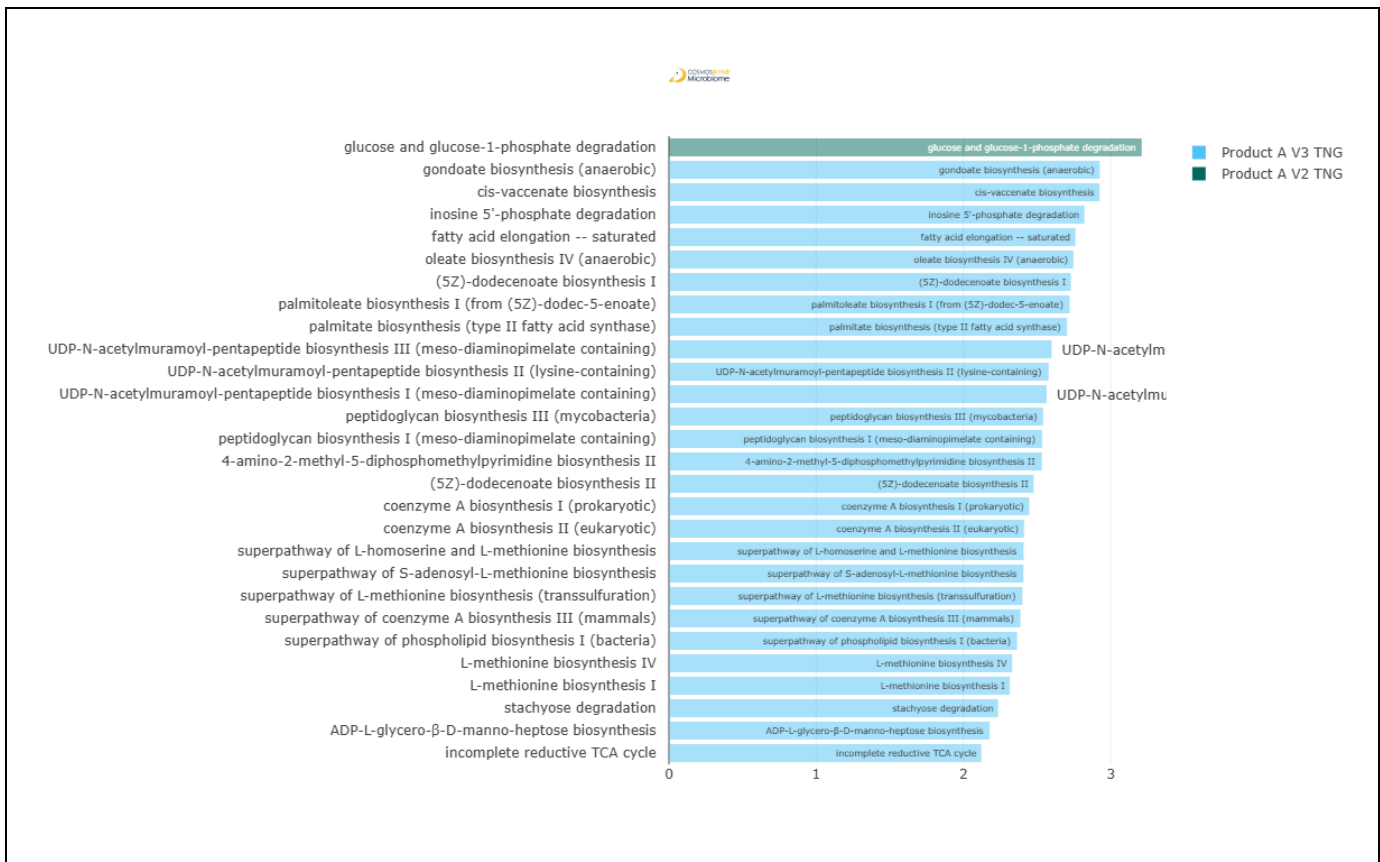
# Simpson



## Beta Diversity (MetaCyc)



## Differential Abundance (LEfSe) (MetaCyc)

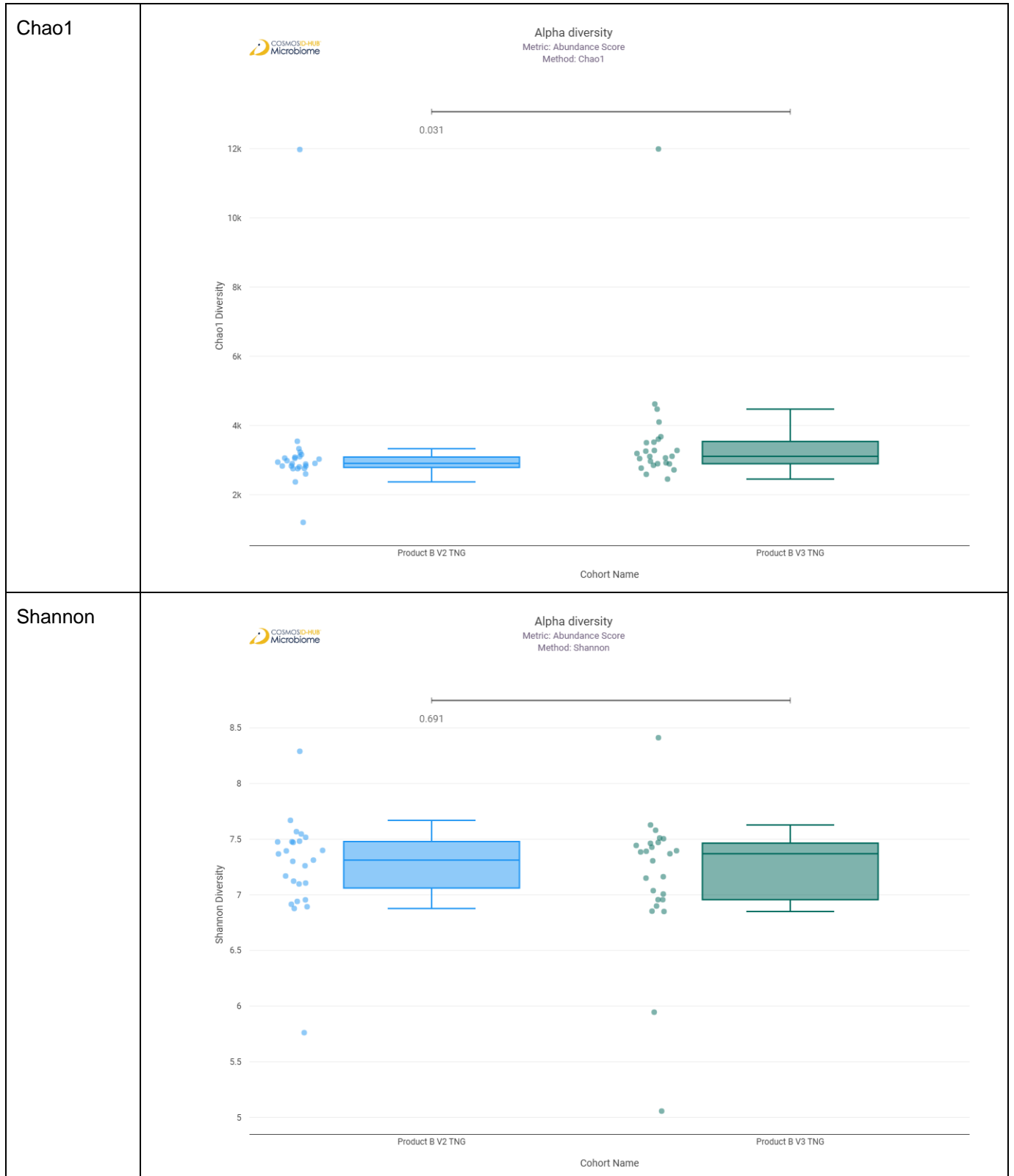


Feature	Enriched Cohort	LDA Score	P-value
glucose and glucose-1-phosphate degradation	Product A V2 TNG	3.209559052	0.00340667
gondoate biosynthesis (anaerobic)	Product A V3 TNG	2.924765578	0.012811669
cis-vaccenate biosynthesis	Product A V3 TNG	2.923502255	0.024382597
inosine 5'-phosphate degradation	Product A V3 TNG	2.820503146	0.007962104
fatty acid elongation -- saturated	Product A V3 TNG	2.759343308	0.02808172
oleate biosynthesis IV (anaerobic)	Product A V3 TNG	2.746062827	0.022157981
(5Z)-dodecenoate biosynthesis I	Product A V3 TNG	2.728547812	0.024382597
palmitoleate biosynthesis I (from (5Z)-dodec-5-enoate)	Product A V3 TNG	2.720034844	0.03375904
palmitate biosynthesis (type II fatty acid synthase)	Product A V3 TNG	2.702281934	0.032254747
UDP-N-acetylmuramoyl-pentapeptide biosynthesis III (meso-diaminopimelate containing)	Product A V3 TNG	2.597049045	0.008868809
UDP-N-acetylmuramoyl-pentapeptide biosynthesis II (lysine-containing)	Product A V3 TNG	2.578363977	0.02556575
UDP-N-acetylmuramoyl-pentapeptide biosynthesis I (meso-diaminopimelate containing)	Product A V3 TNG	2.563990058	0.019152346
peptidoglycan biosynthesis III (mycobacteria)	Product A V3 TNG	2.540069927	0.036948224
peptidoglycan biosynthesis I (meso-diaminopimelate containing)	Product A V3 TNG	2.533524177	0.026798248
4-amino-2-methyl-5-diphosphomethylpyrimidine biosynthesis II	Product A V3 TNG	2.531429766	0.003615568
(5Z)-dodecenoate biosynthesis II	Product A V3 TNG	2.475232712	0.030736851
coenzyme A biosynthesis I (prokaryotic)	Product A V3 TNG	2.446066864	0.02808172
coenzyme A biosynthesis II (eukaryotic)	Product A V3 TNG	2.410665002	0.00210785
superpathway of L-homoserine and L-methionine biosynthesis	Product A V3 TNG	2.407228434	3.08E-02
superpathway of S-adenosyl-L-methionine biosynthesis	Product A V3 TNG	2.406586807	0.014930589
superpathway of L-methionine biosynthesis (transsulfuration)	Product A V3 TNG	2.399360615	0.038636777
superpathway of coenzyme A biosynthesis III (mammals)	Product A V3 TNG	2.385903102	0.00406225
superpathway of phospholipid biosynthesis I (bacteria)	Product A V3 TNG	2.363206689	0.000664015
L-methionine biosynthesis IV	Product A V3 TNG	2.330041224	0.006393679
L-methionine biosynthesis I	Product A V3 TNG	2.313741316	0.029417827
stachyose degradation	Product A V3 TNG	2.234251147	0.044100855
ADP-L-glycero-β-D-manno-heptose biosynthesis	Product A V3 TNG	2.177105902	0.011551265
incomplete reductive TCA cycle	Product A V3 TNG	2.121158237	0.012466883

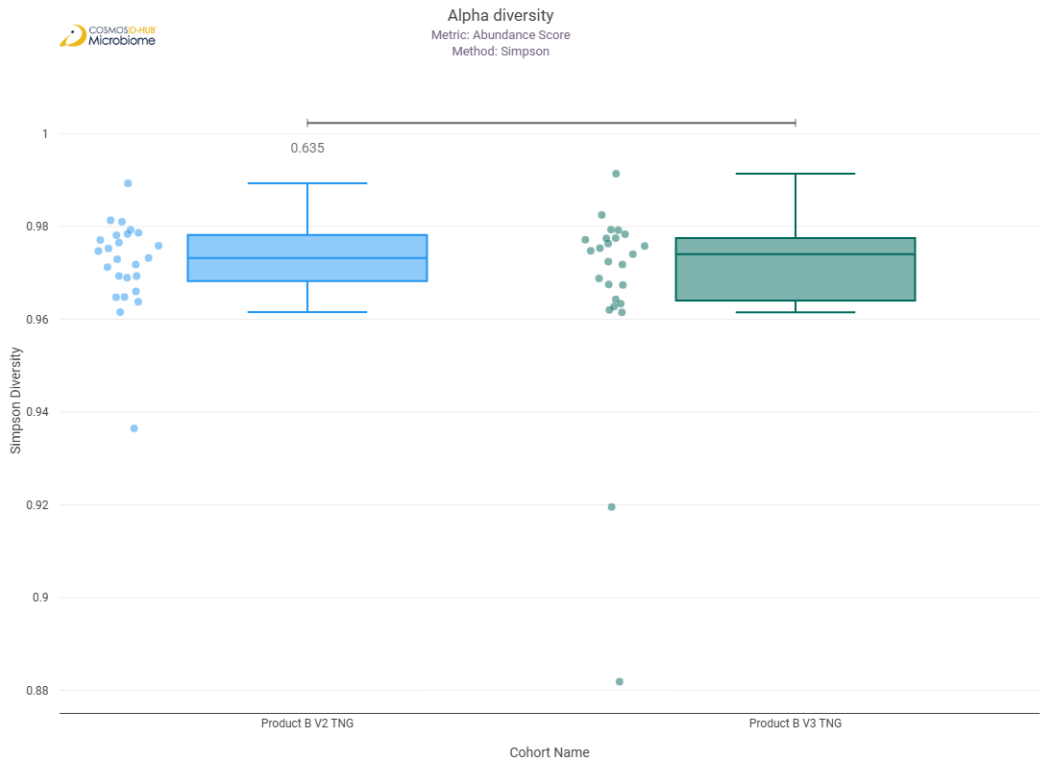
# Comparison 10: Product B V2 TNG vs Product B V3 TNG

## Gene Ontology

### Alpha Diversity (GO)

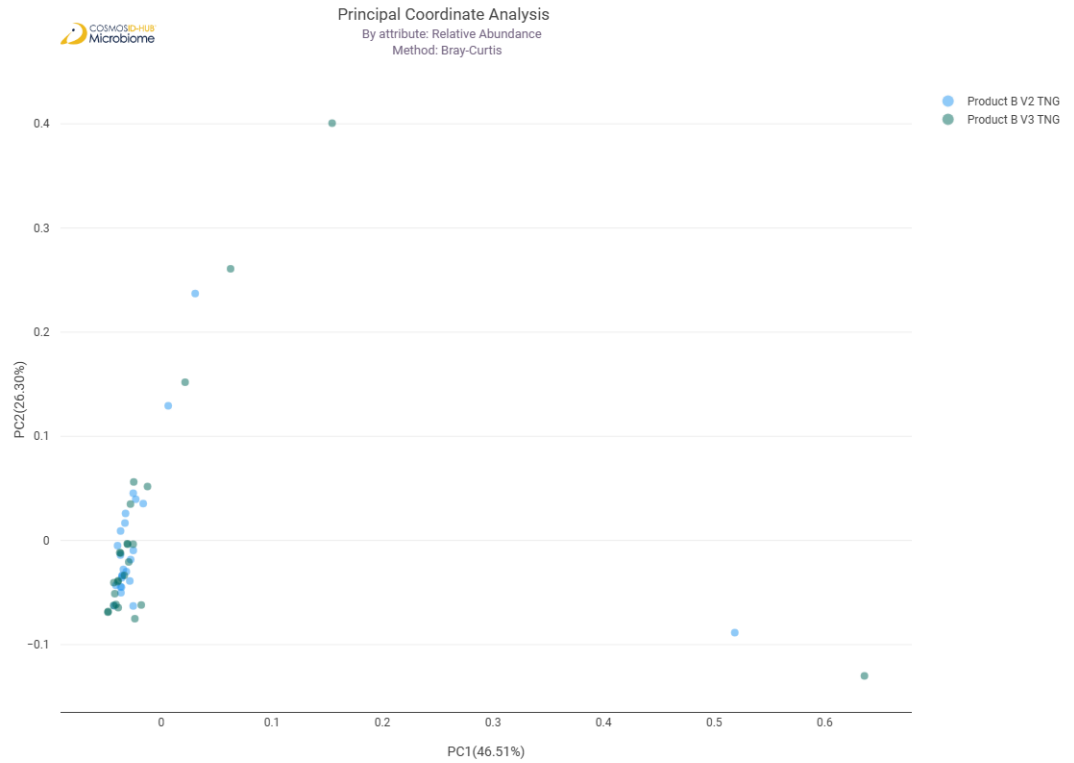


Simpson

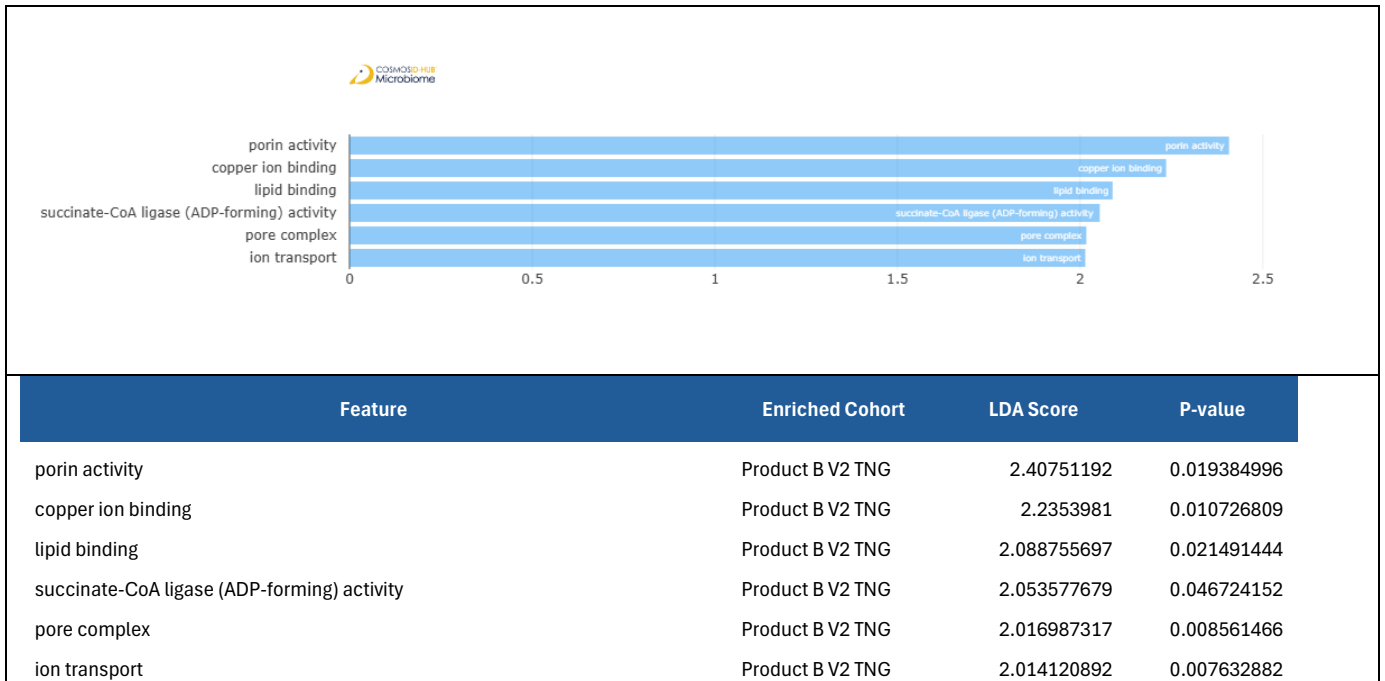


Beta Diversity (GO)

Bray-Curtis  
PERMNOVA  
p = 0.724

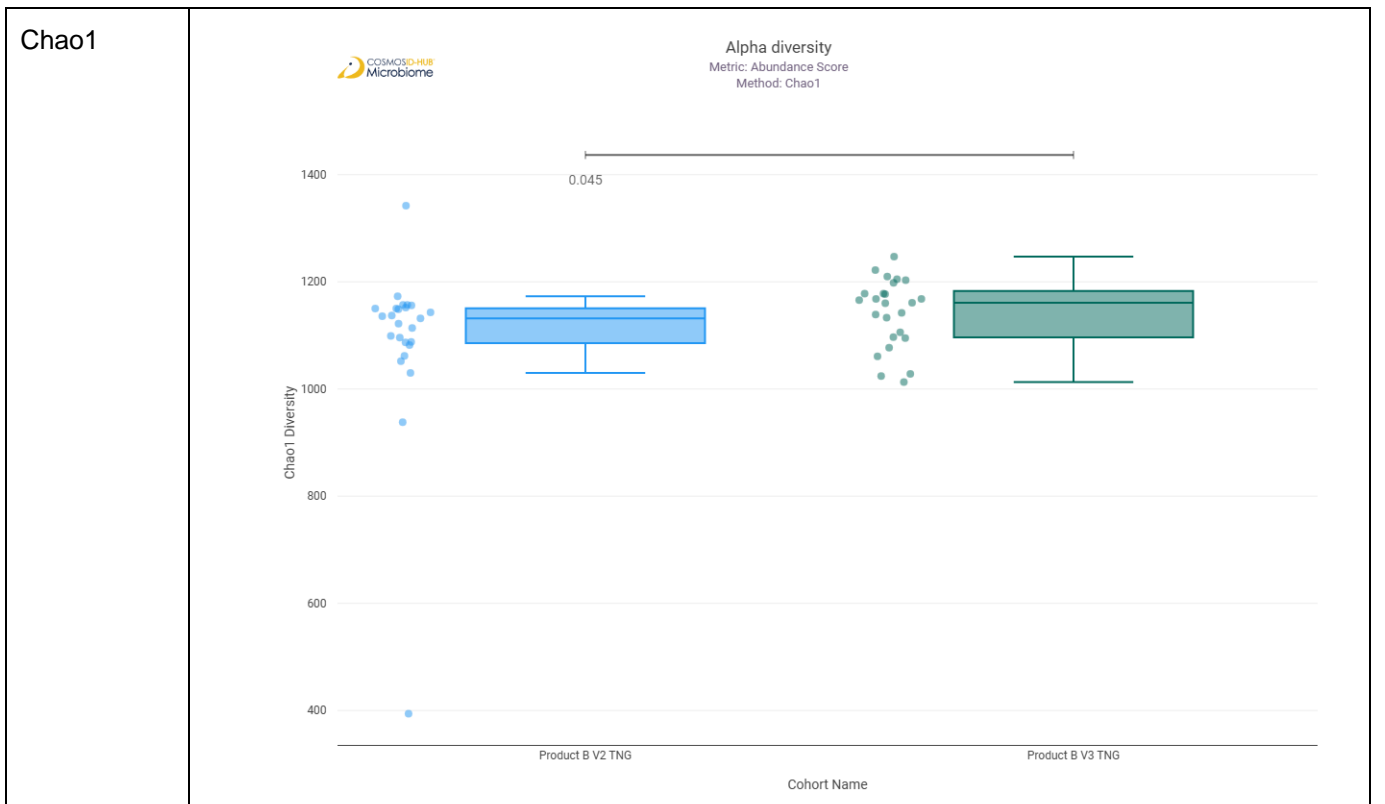


## Differential Abundance (LEfSe) (GO)



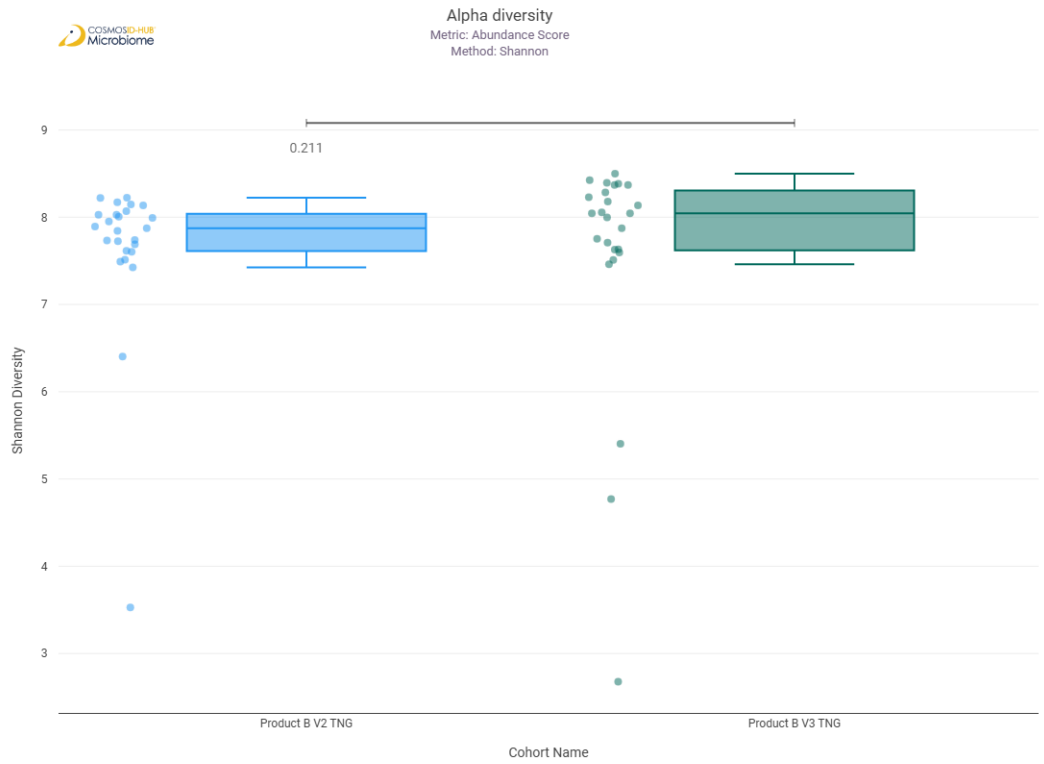
## Enzyme Commission

### Alpha Diversity (EC)

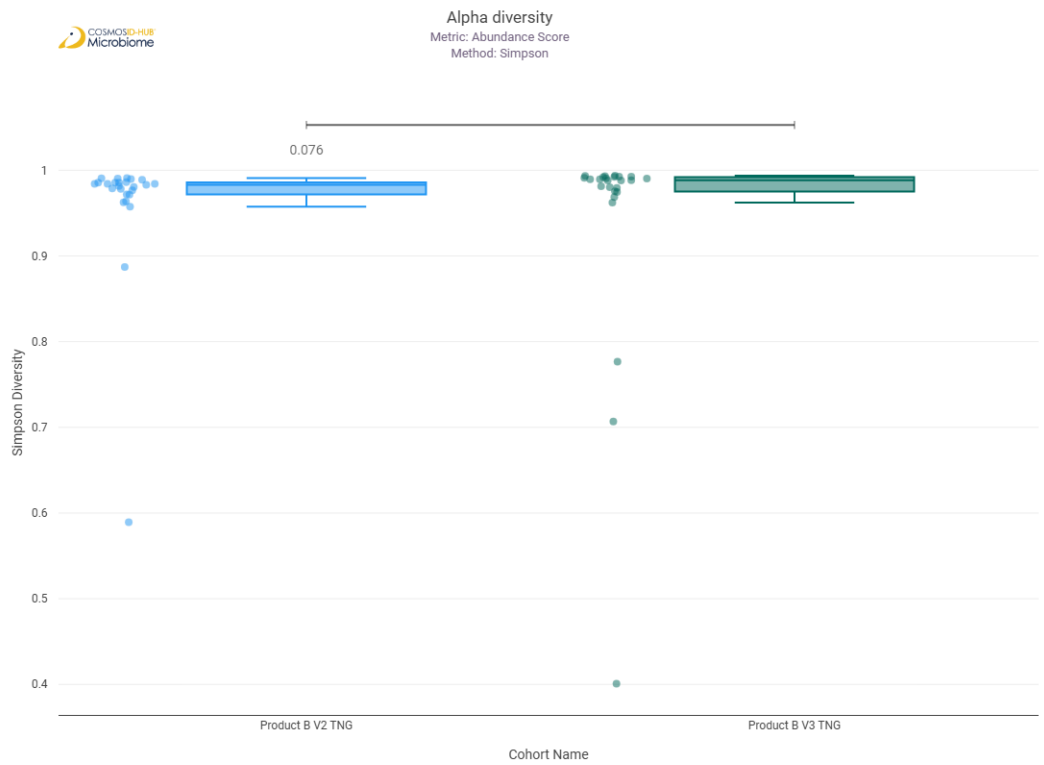




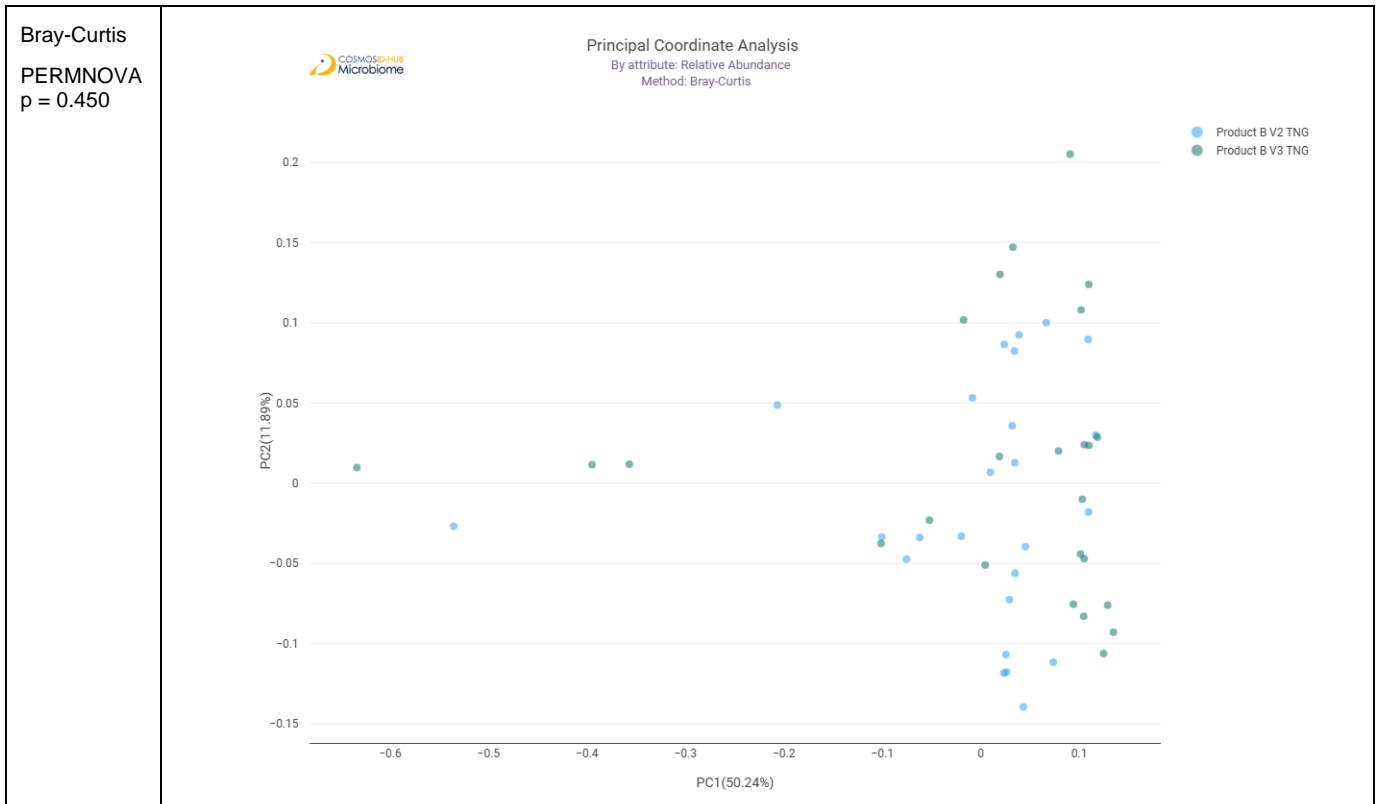
# Shannon



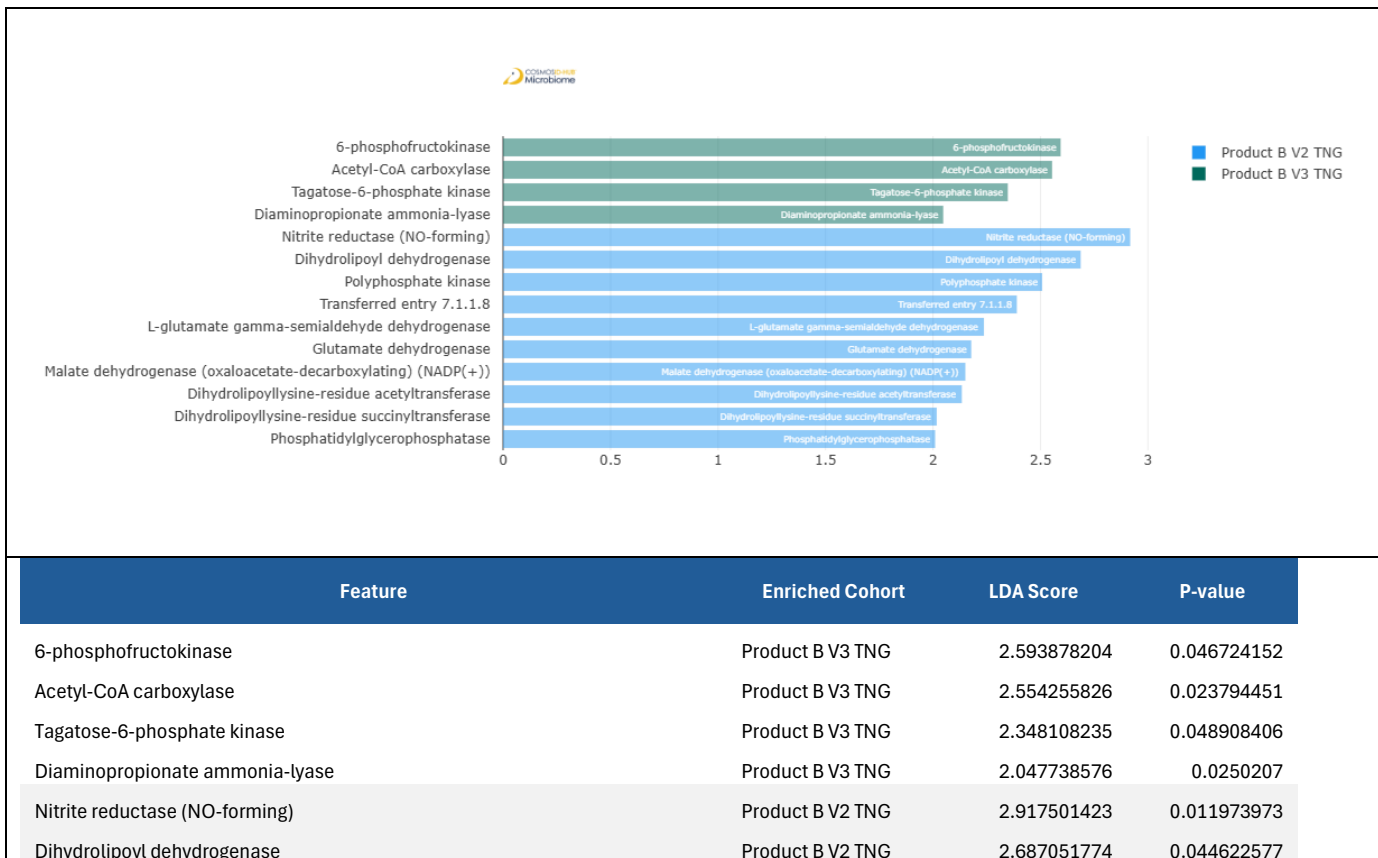
# Simpson



## Beta Diversity (EC)



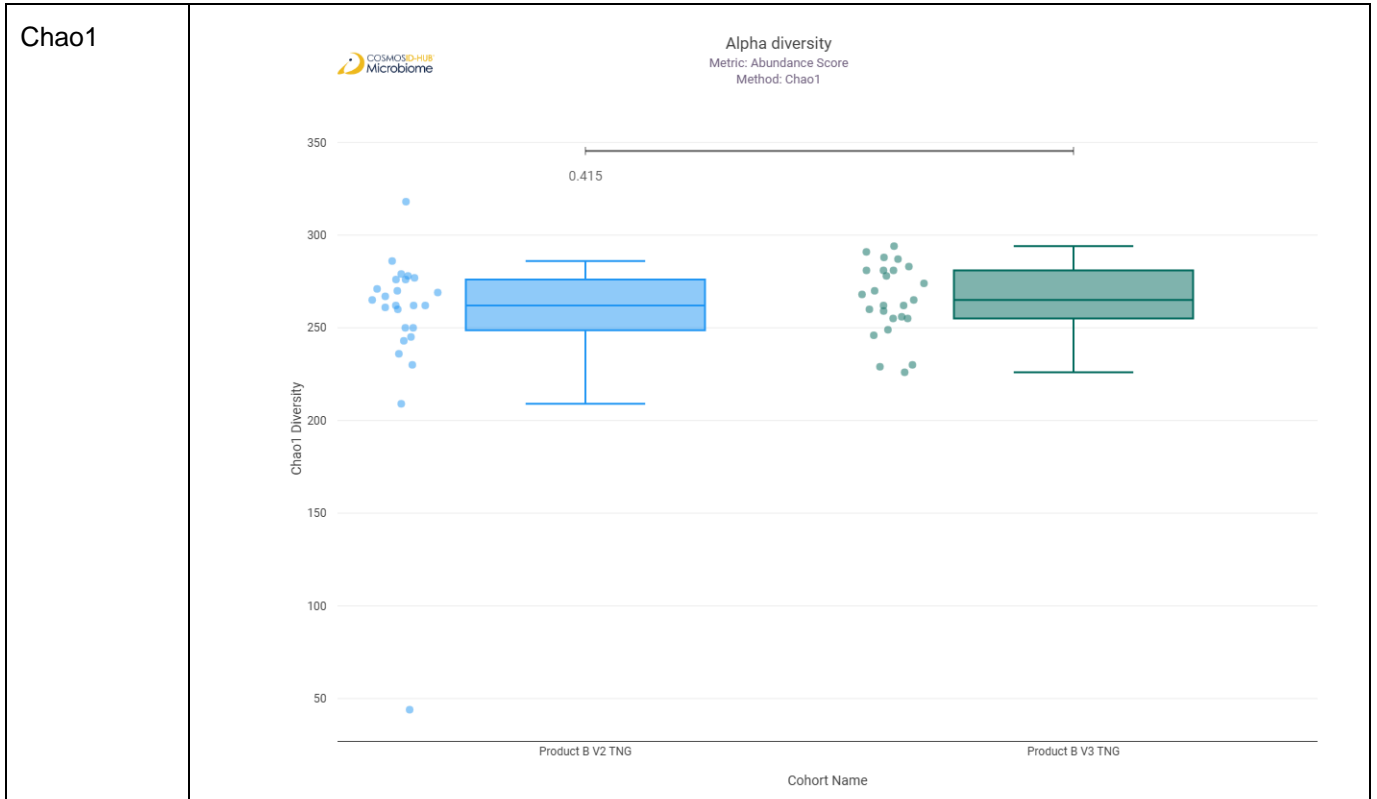
## Differential Abundance (LEfSe) (EC)



Polyphosphate kinase	Product B V2 TNG	2.50802902	0.019384996
Transferred entry 7.1.1.8	Product B V2 TNG	2.390039535	0.0352731
L-glutamate gamma-semialdehyde dehydrogenase	Product B V2 TNG	2.237146802	0.0352731
Glutamate dehydrogenase	Product B V2 TNG	2.178088537	0.016563699
Malate dehydrogenase (oxaloacetate-decarboxylating) (NADP(+))	Product B V2 TNG	2.150718273	0.044622577
Dihydrolipoyllysine-residue acetyltransferase	Product B V2 TNG	2.134159792	0.010726809
Dihydrolipoyllysine-residue succinyltransferase	Product B V2 TNG	2.017575362	0.019384996
Phosphatidylglycerophosphatase	Product B V2 TNG	2.010237144	0.001321949

## MetaCyc Pathways

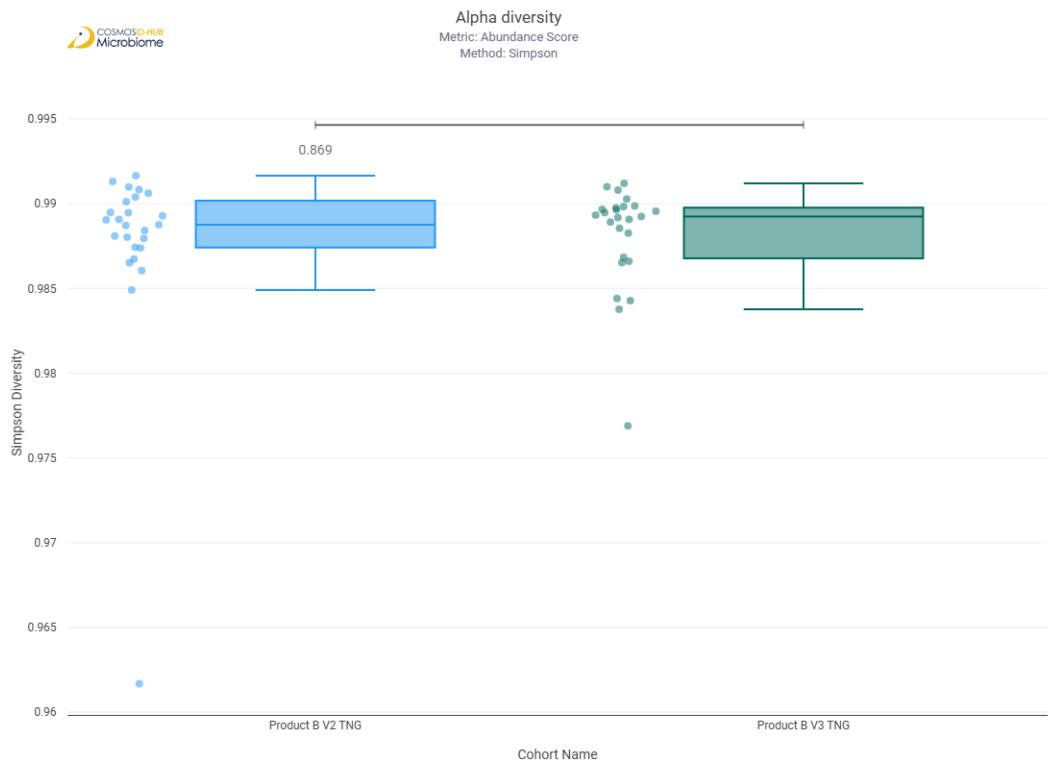
### Alpha Diversity (MetaCyc)



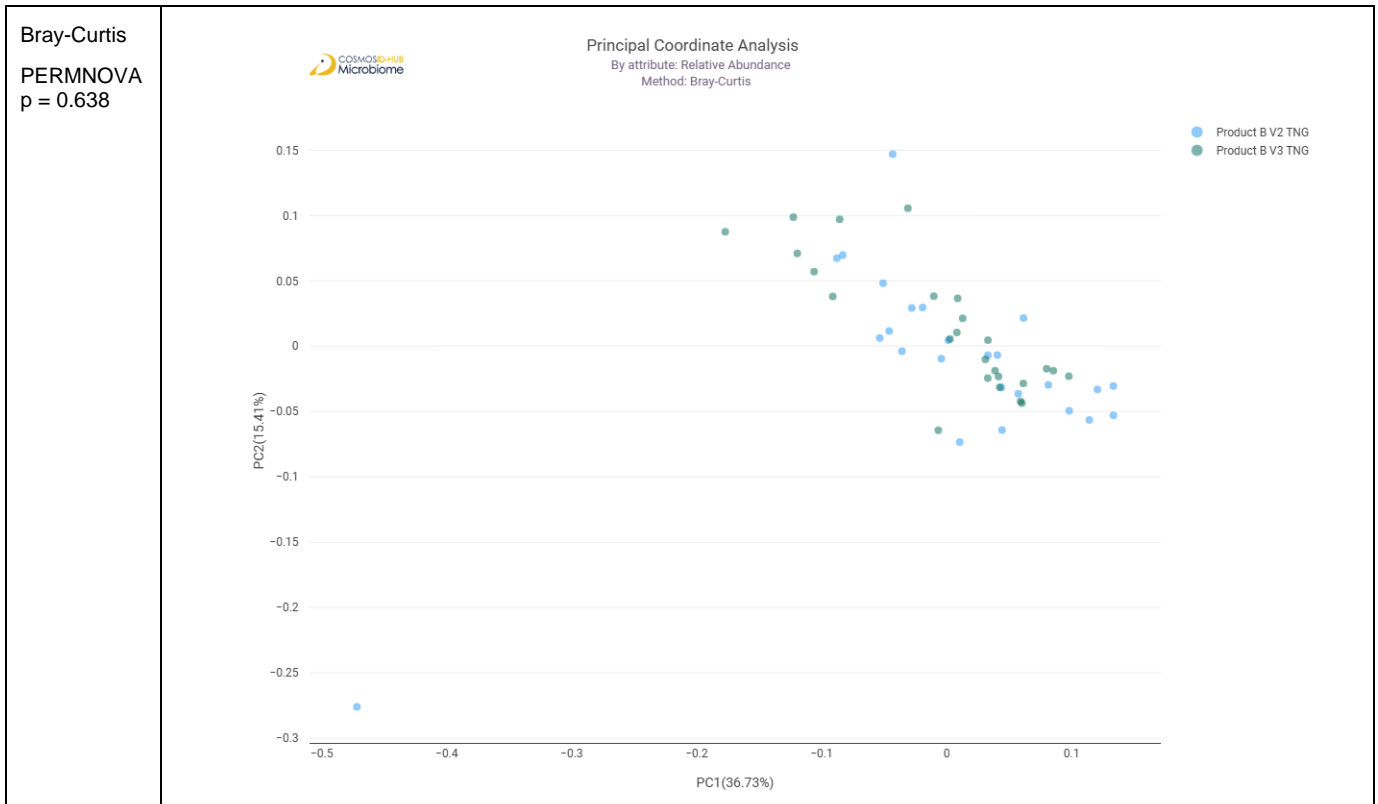
# Shannon



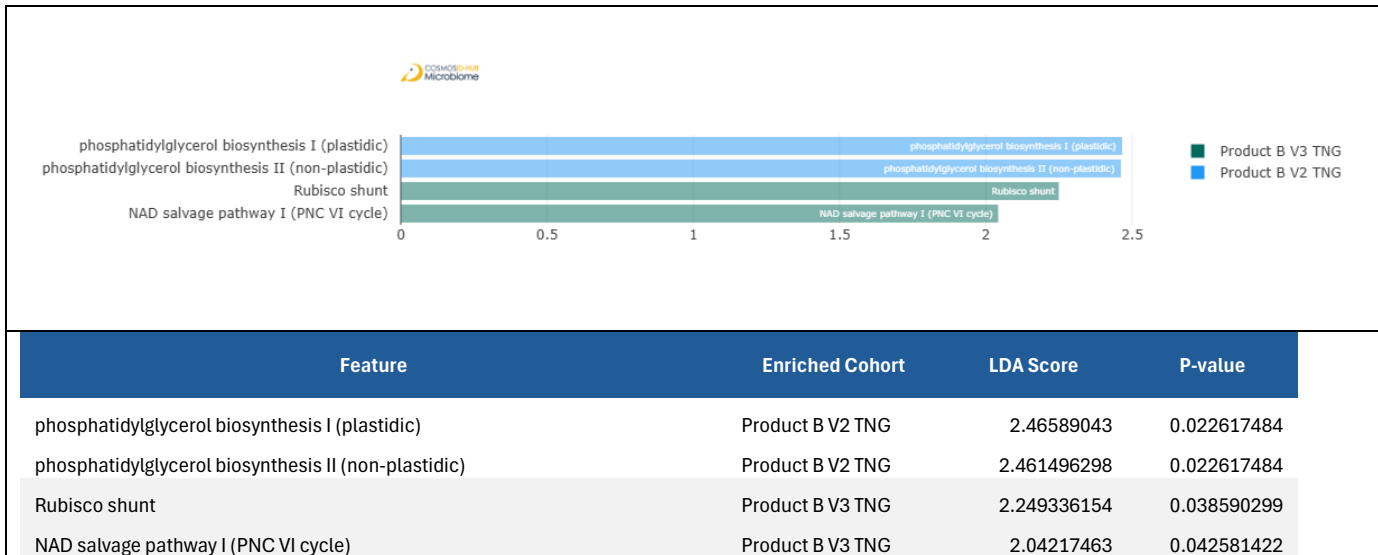
# Simpson



## Beta Diversity (MetaCyc)



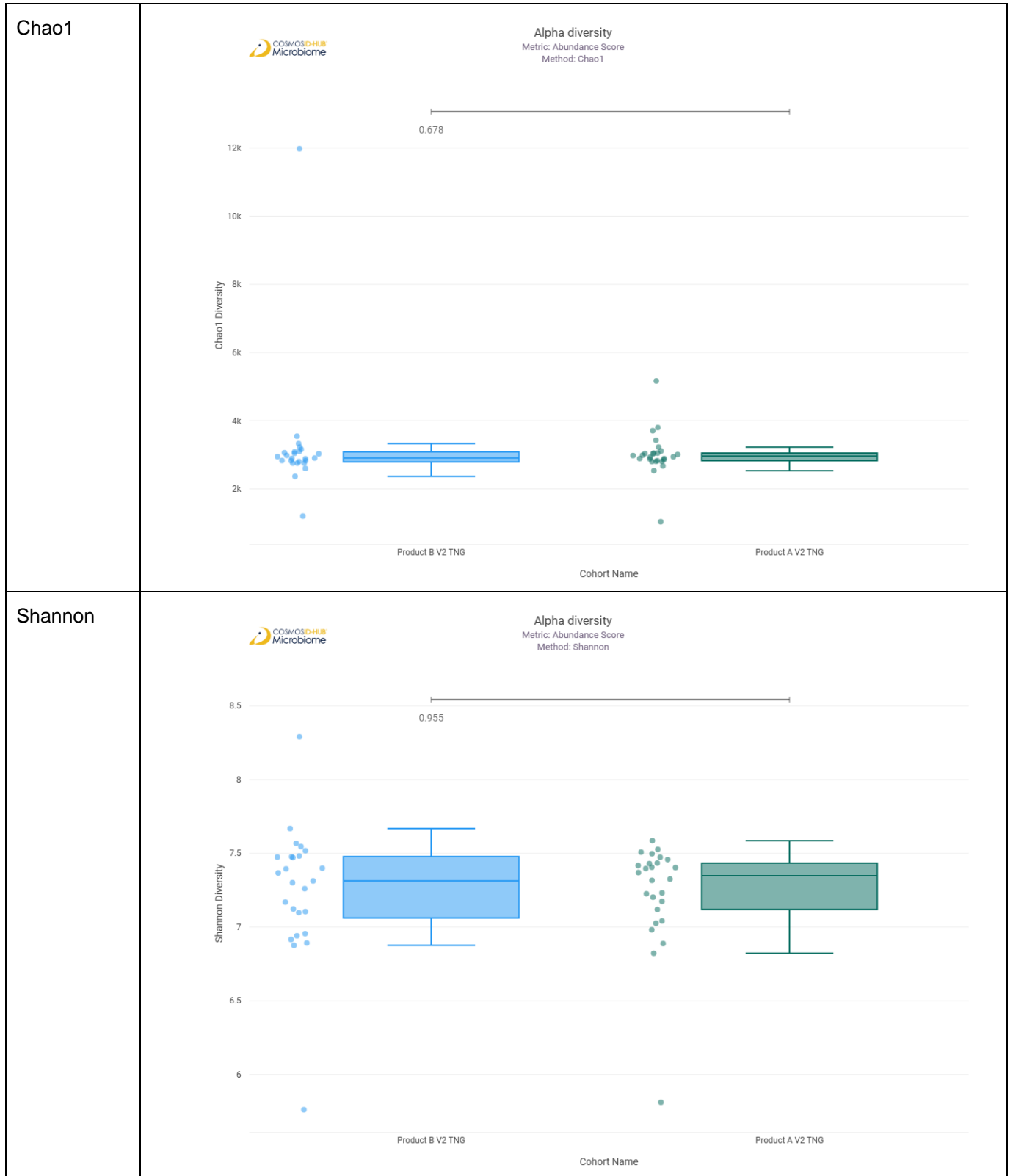
## Differential Abundance (LEfSe) (MetaCyc)



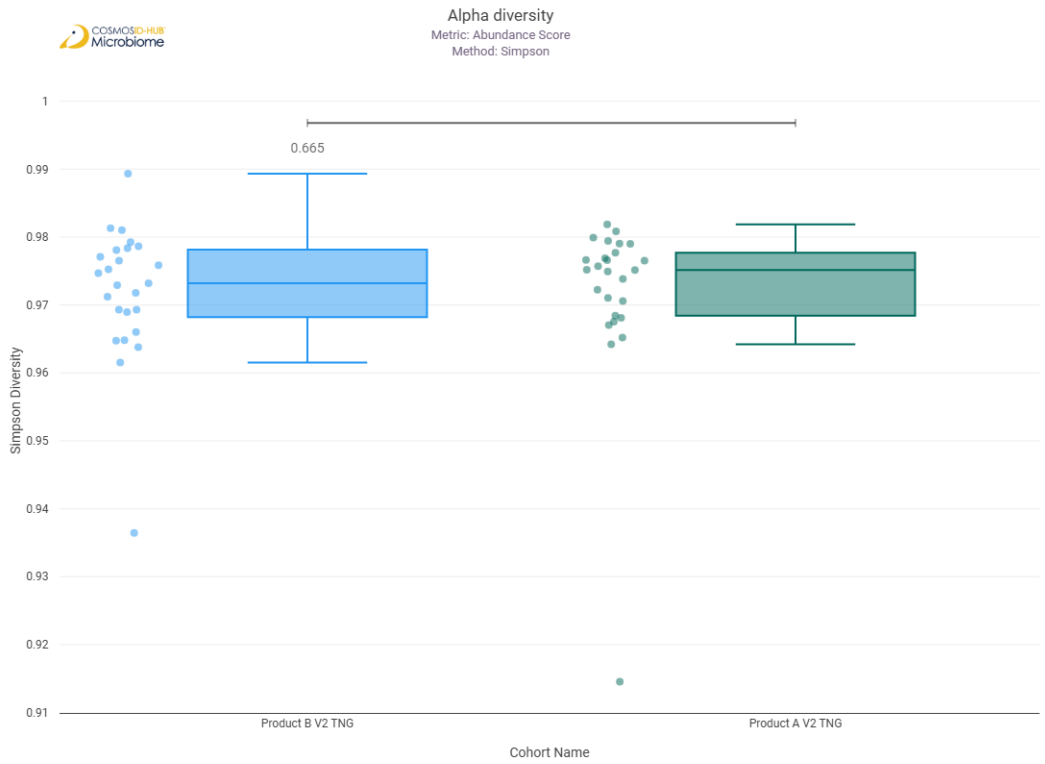
# Comparison 11: Product A V2 TNG vs Product B V2 TNG

## Gene Ontology

### Alpha Diversity (GO)

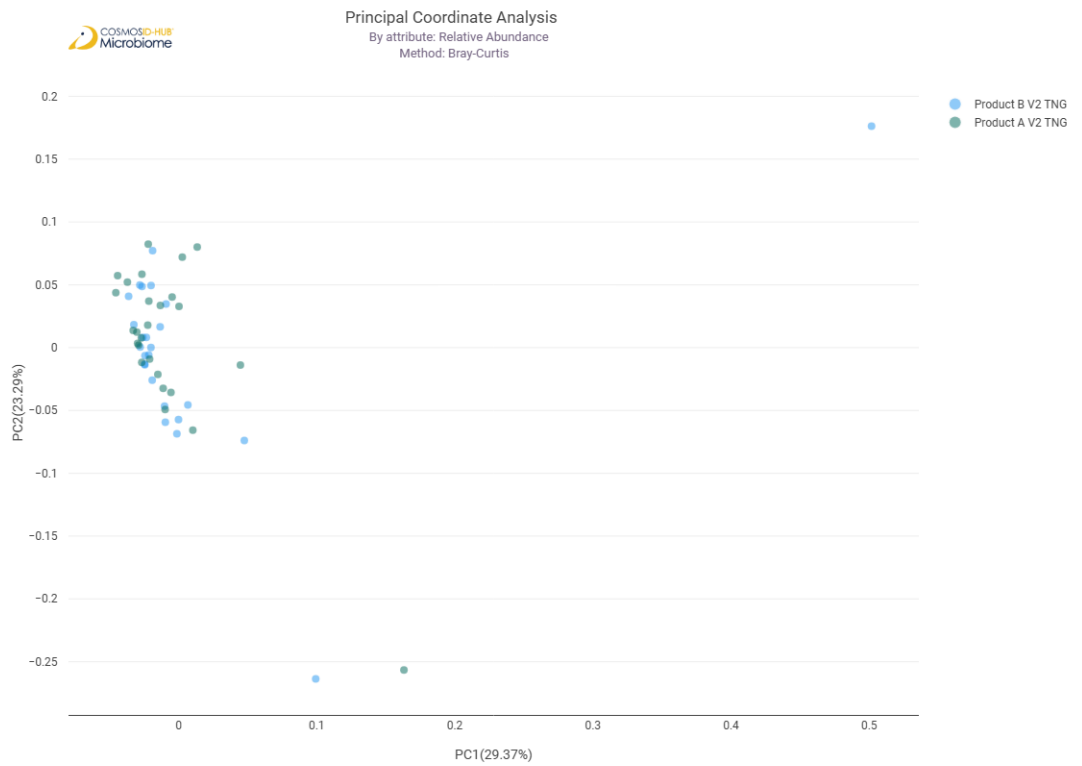


Simpson

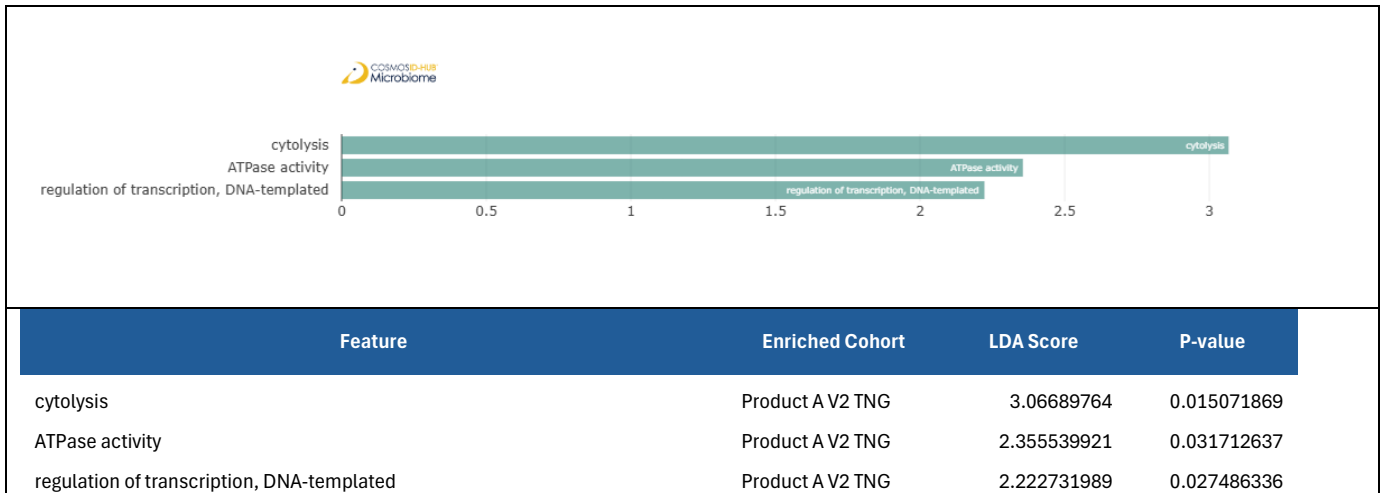


Beta Diversity (GO)

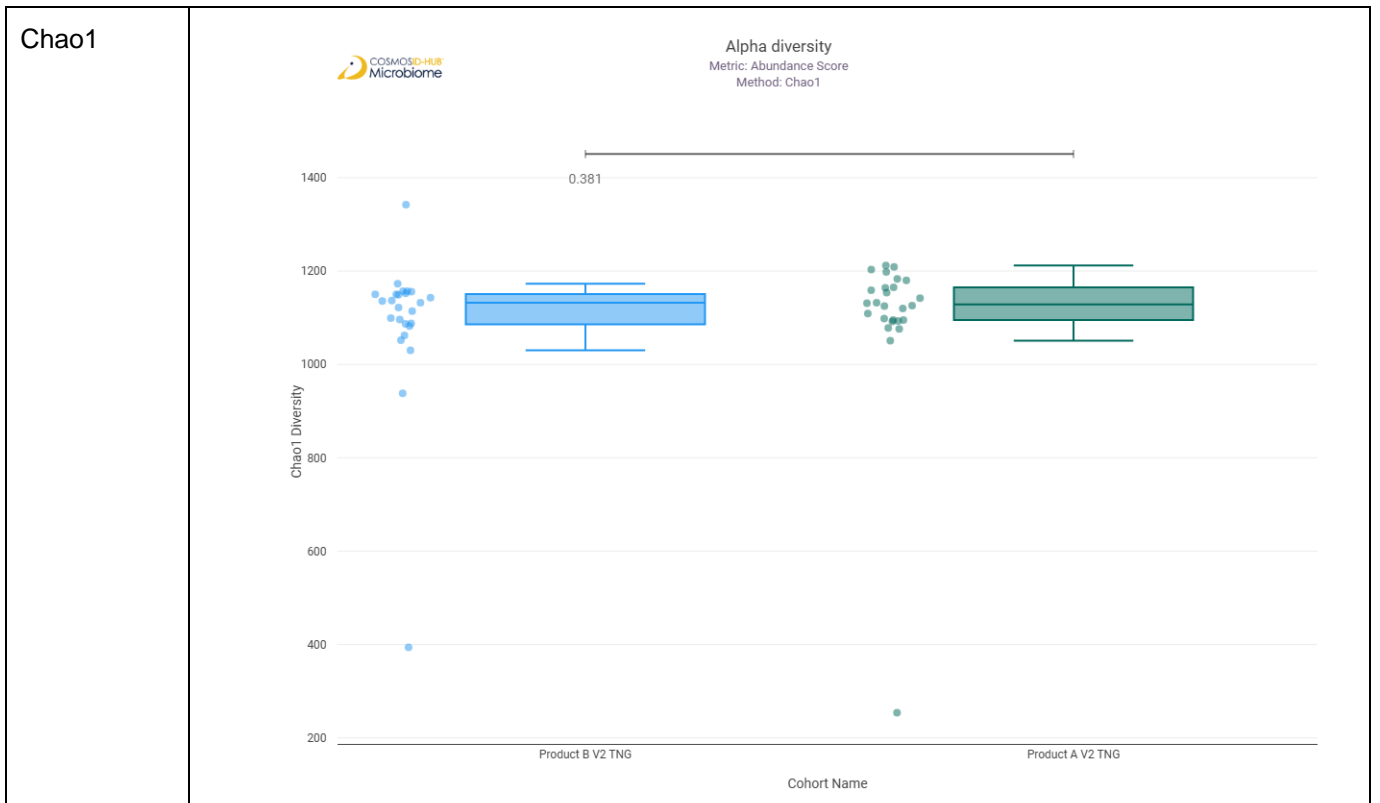
Bray-Curtis  
PERMNOVA  
 $p = 0.651$



## Differential Abundance (LEfSe) (GO)

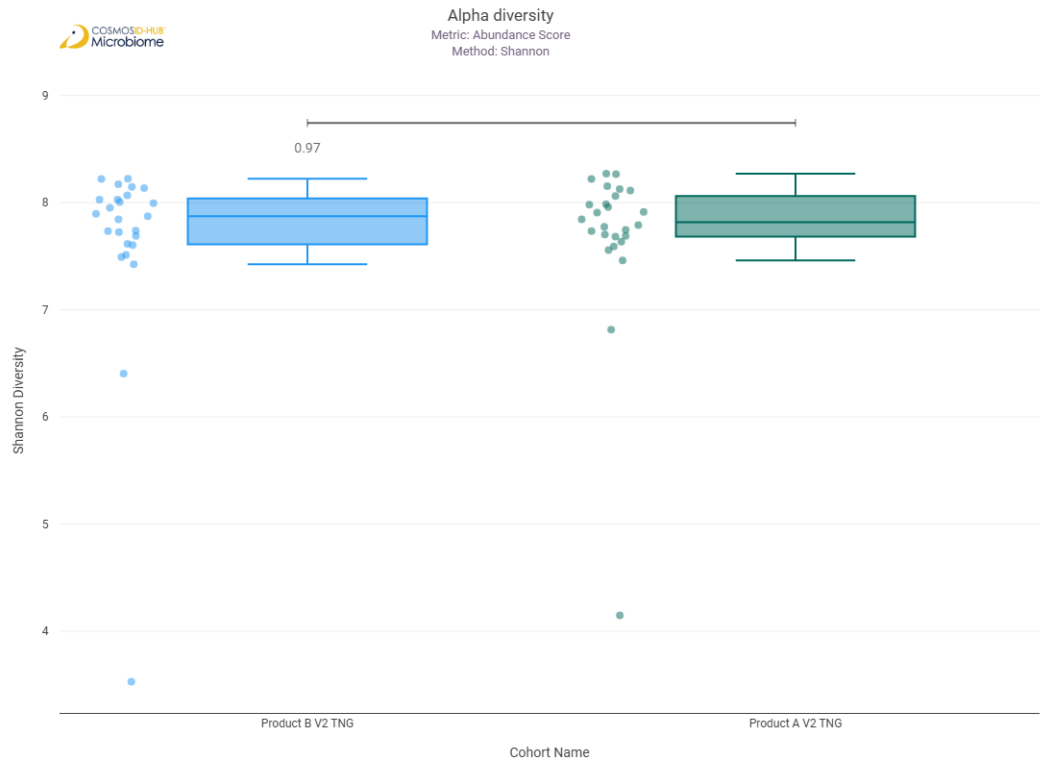


## Enzyme Commission Alpha Diversity (EC)





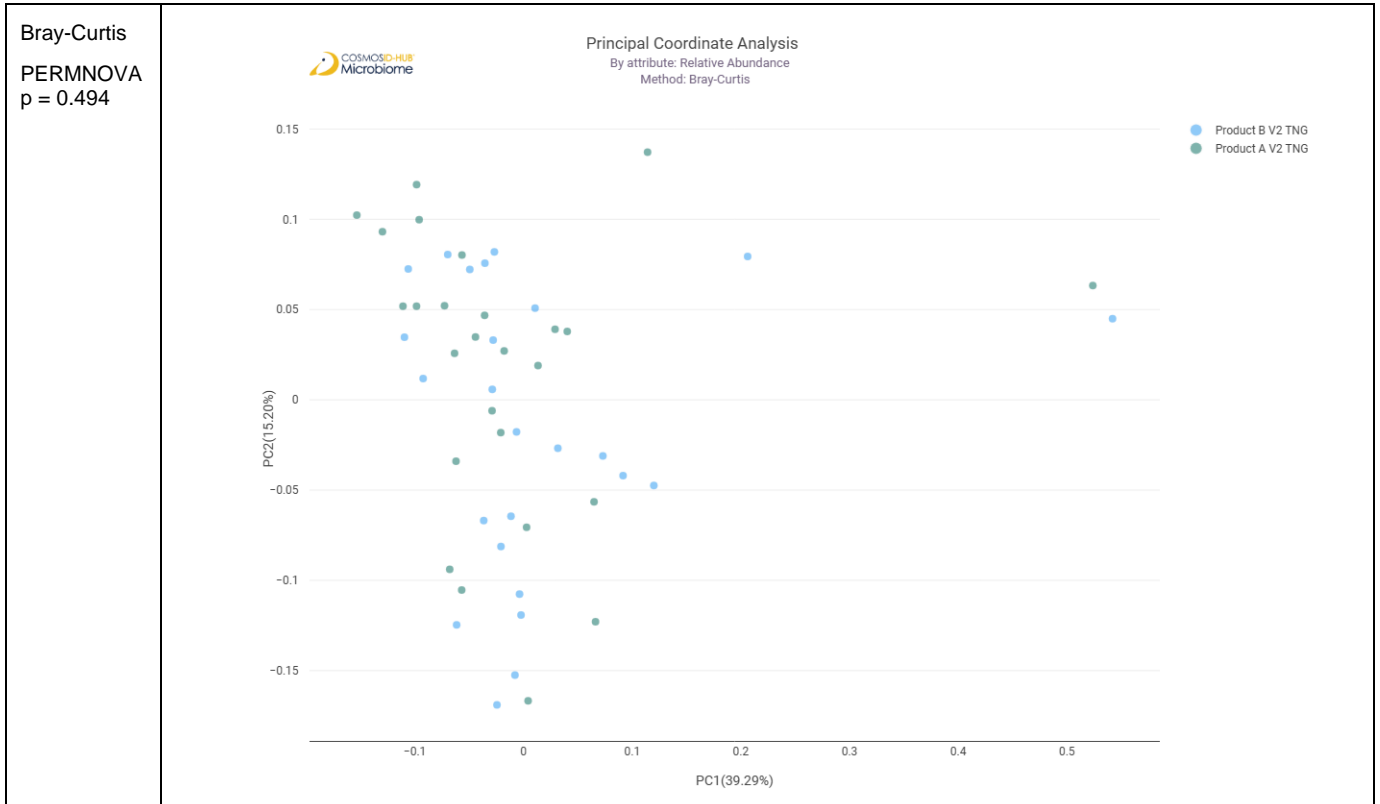
# Shannon



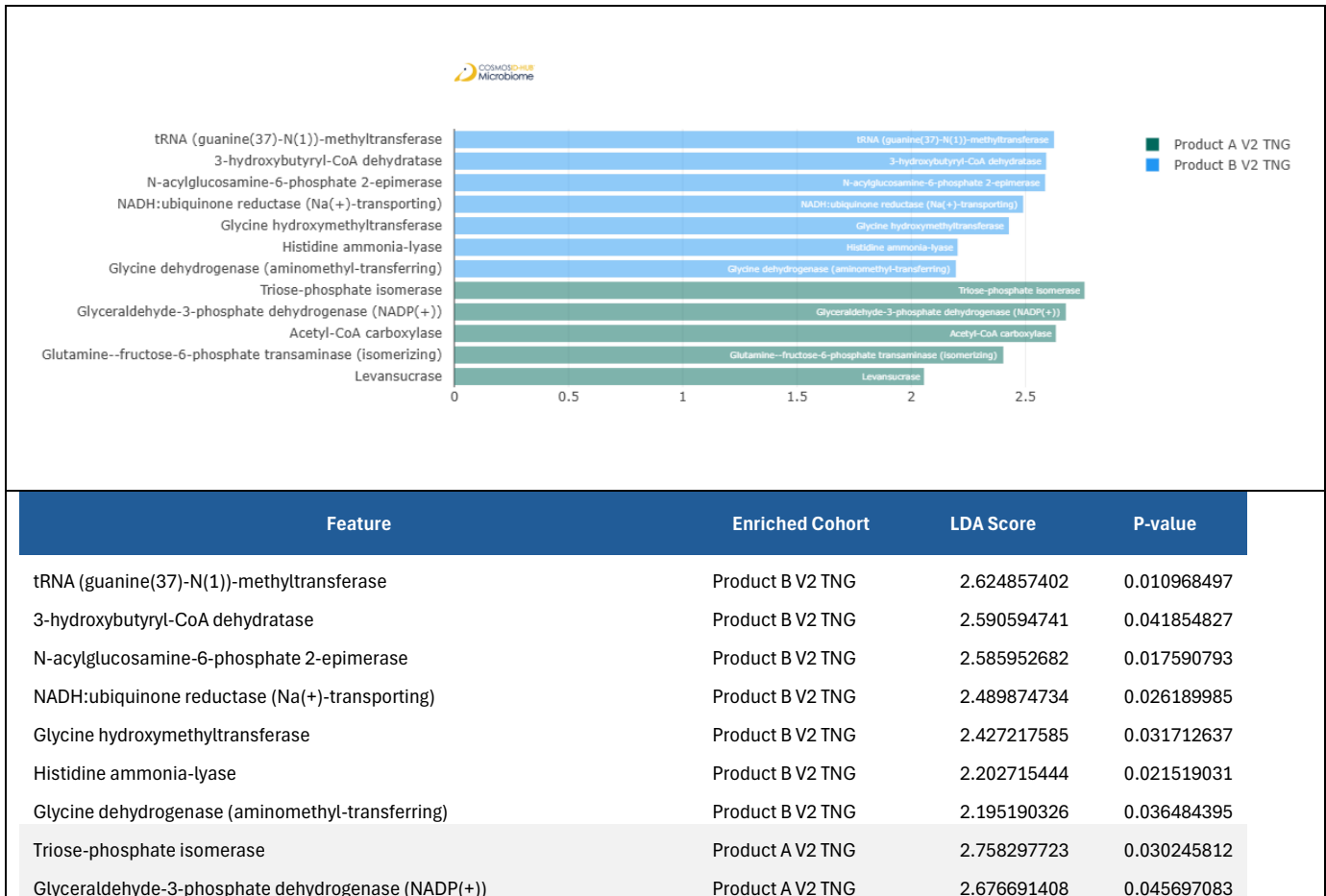
# Simpson



## Beta Diversity (EC)



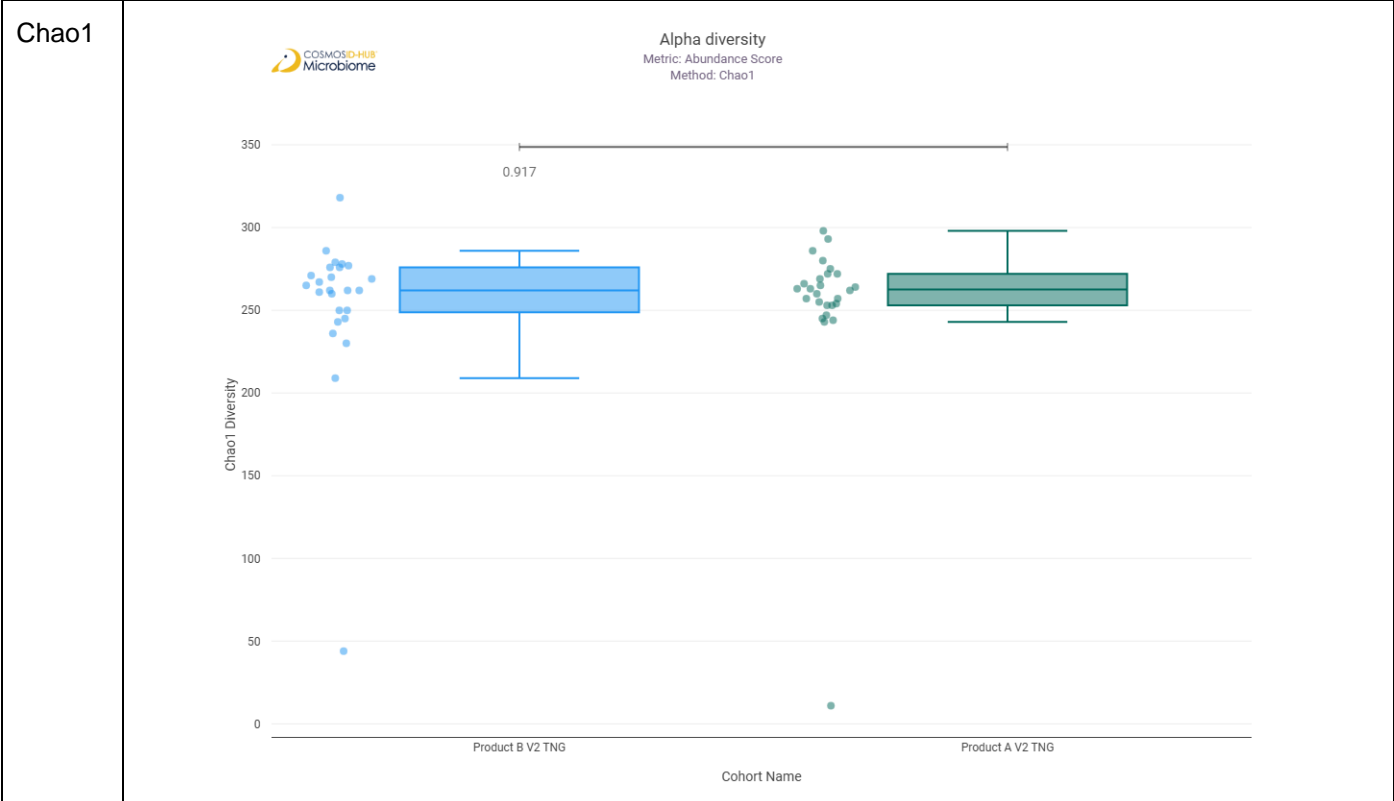
## Differential Abundance (LEfSe) (EC)



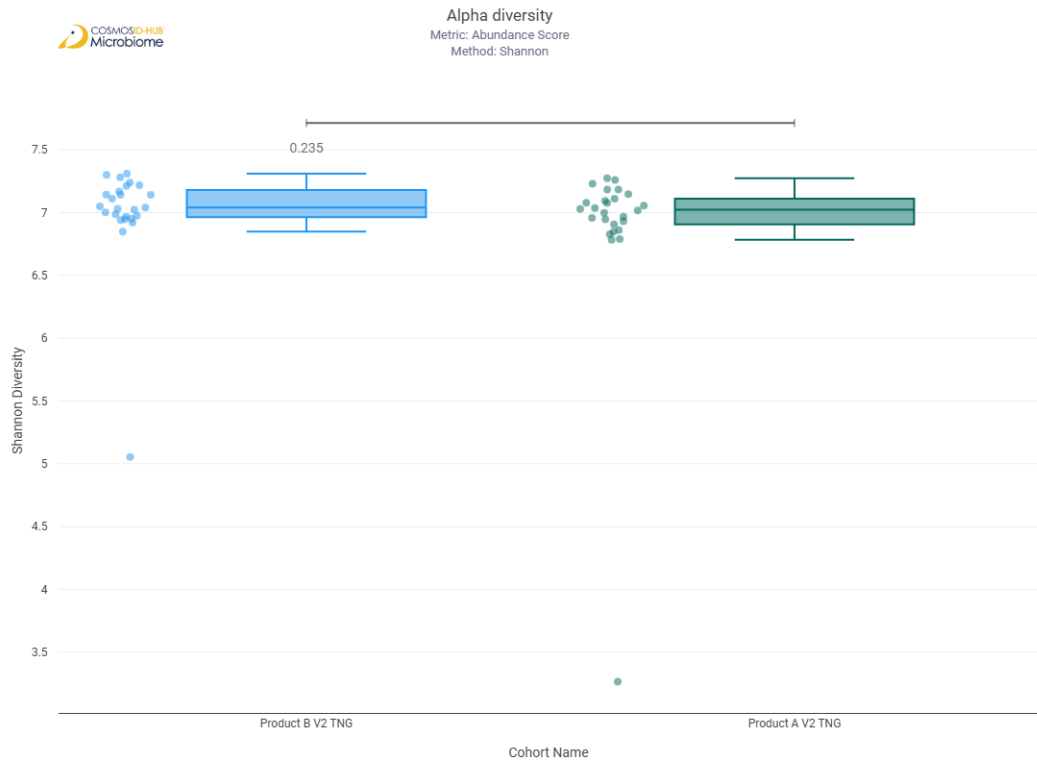
Acetyl-CoA carboxylase	Product A V2 TNG	2.63288439	0.00745964
Glutamine--fructose-6-phosphate transaminase (isomerizing)	Product A V2 TNG	2.403033073	0.045795182
Levansucrase	Product A V2 TNG	2.055940637	0.017552852

### MetaCyc Pathways

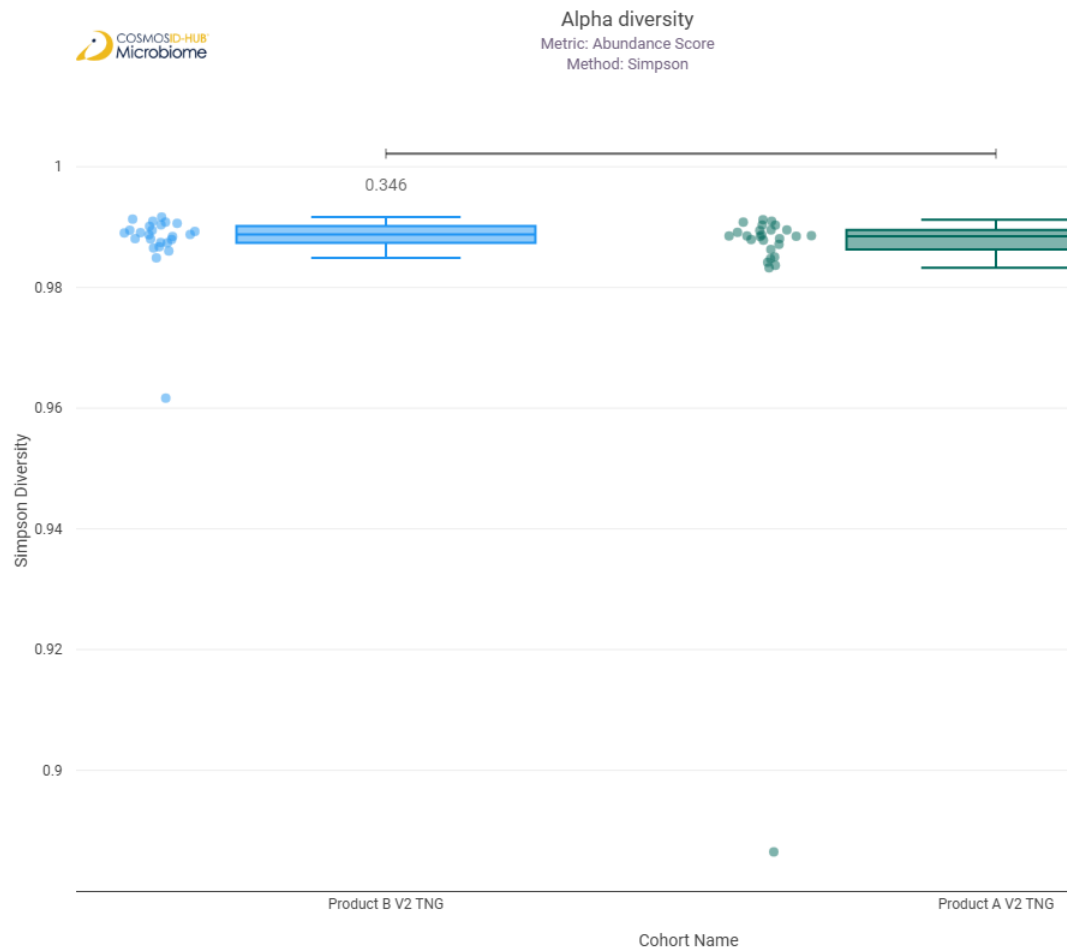
#### Alpha Diversity (MetaCyc)



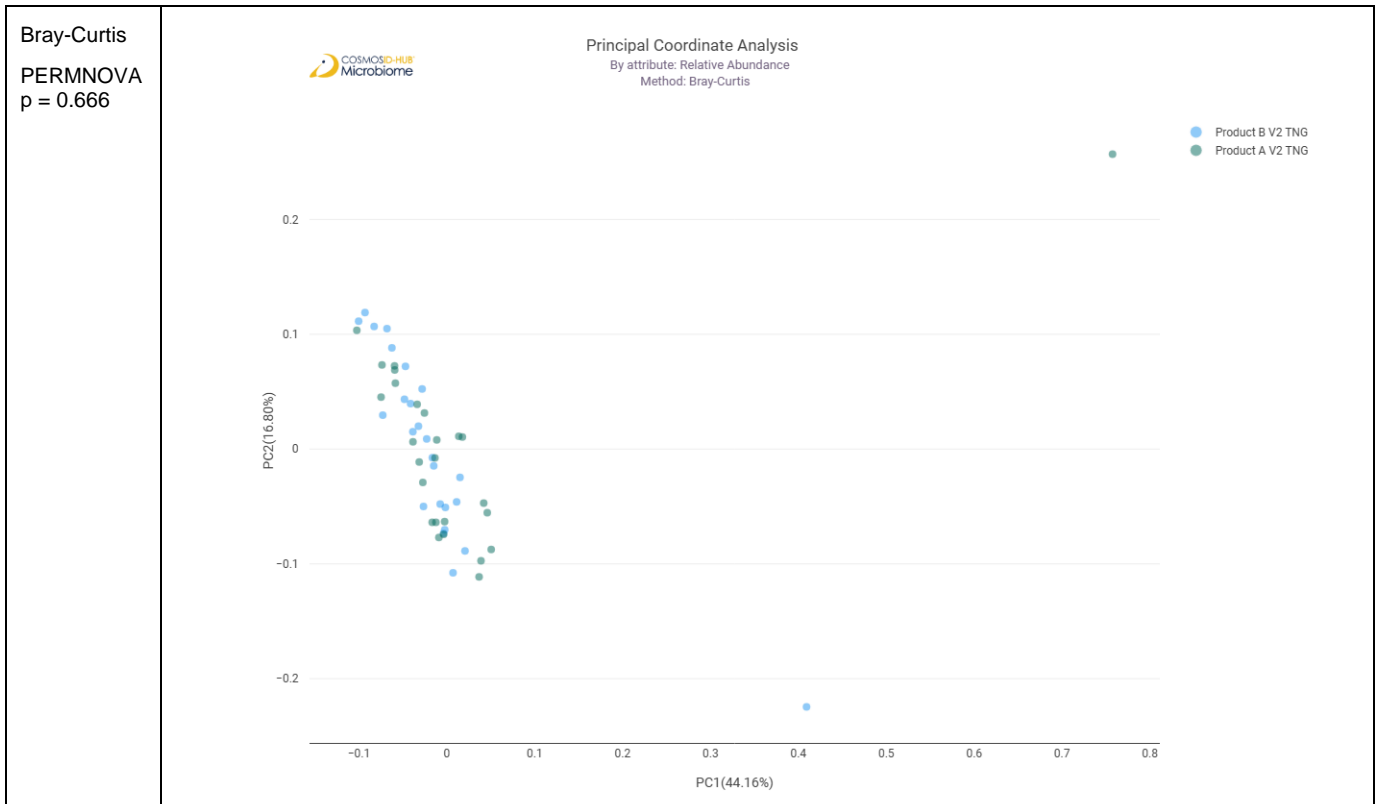
Shannon



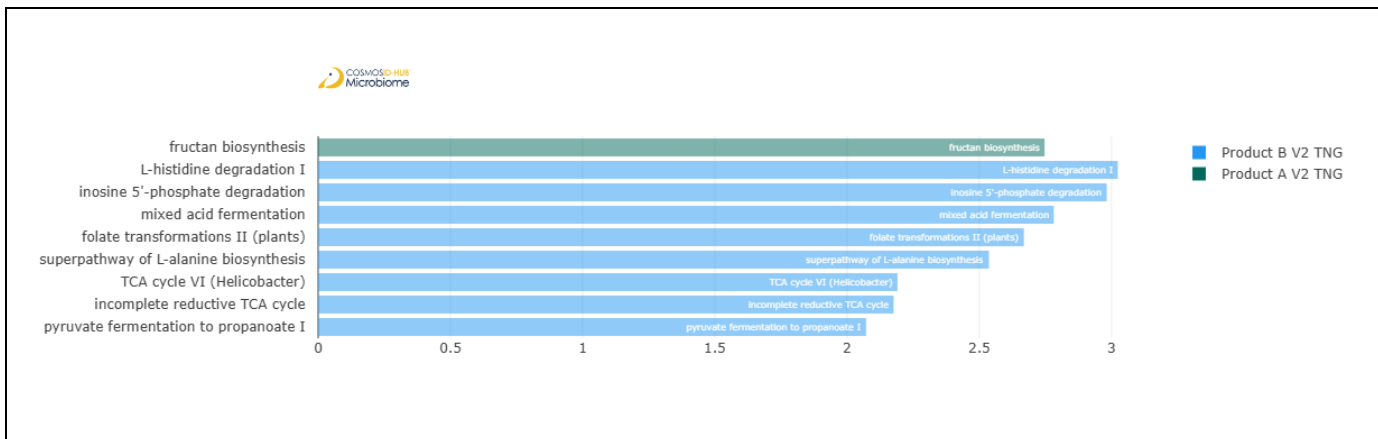
Simpson



## Beta Diversity (MetaCyc)



## Differential Abundance (LEfSe) (MetaCyc)

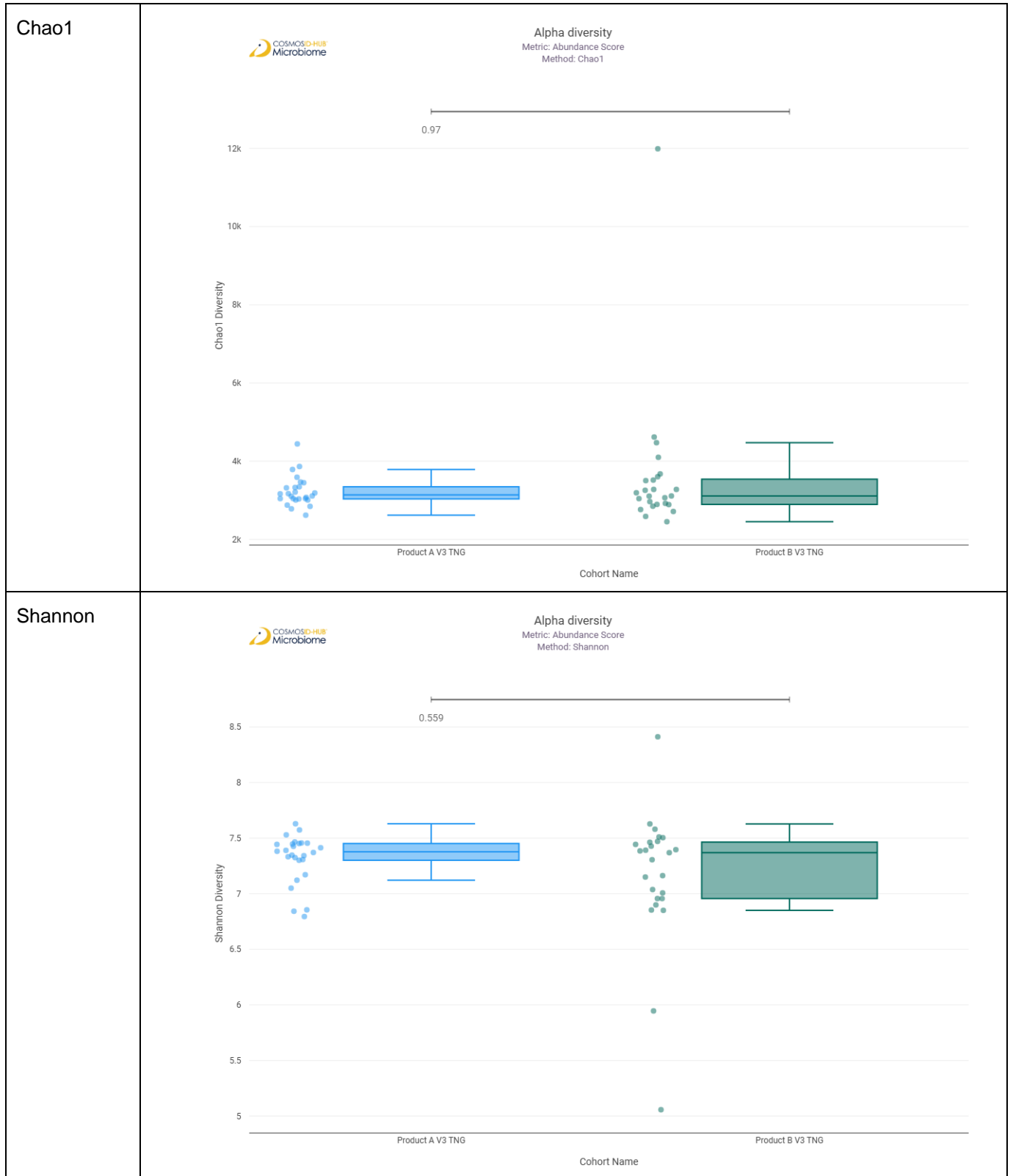


Feature	Enriched Cohort	LDA Score	P-value
fructan biosynthesis	Product A V2 TNG	2.746991997	0.019443383
L-histidine degradation I	Product B V2 TNG	3.02380233	0.021519031
inosine 5'-phosphate degradation	Product B V2 TNG	2.981940294	0.002269883
mixed acid fermentation	Product B V2 TNG	2.781796134	0.030967972
folate transformations II (plants)	Product B V2 TNG	2.668838629	0.026189985
superpathway of L-alanine biosynthesis	Product B V2 TNG	2.536575601	0.048946493
TCA cycle VI (Helicobacter)	Product B V2 TNG	2.190843266	0.00083361
incomplete reductive TCA cycle	Product B V2 TNG	2.17615078	0.018956342
pyruvate fermentation to propanoate I	Product B V2 TNG	2.071955954	0.010899265

# Comparison 12: Product A V3 TNG vs Product B V3 TNG

## Gene Ontology

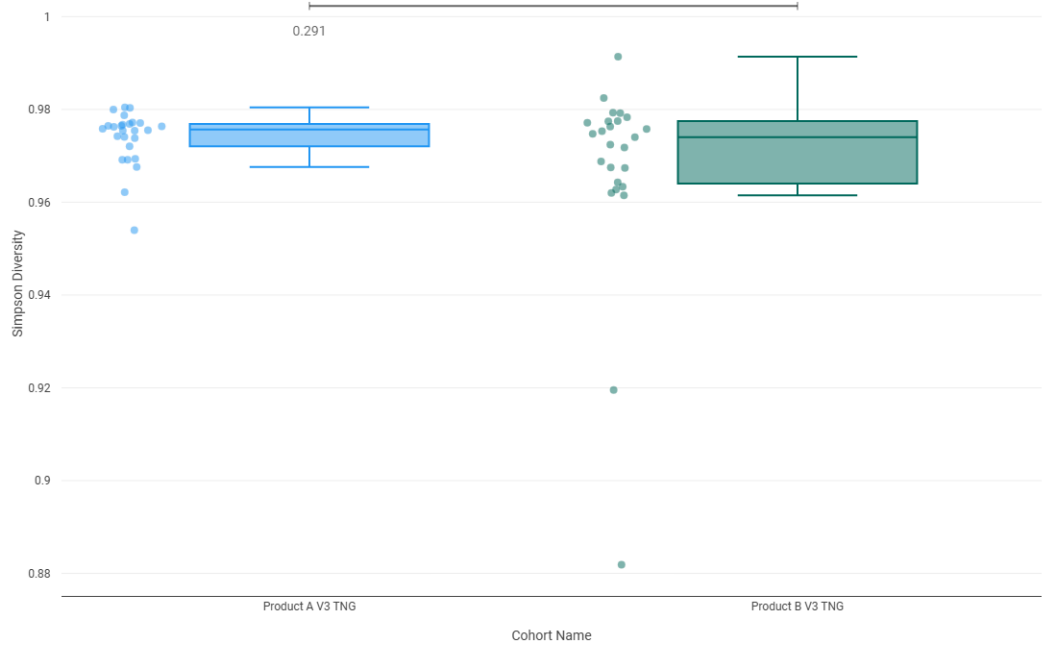
### Alpha Diversity (GO)



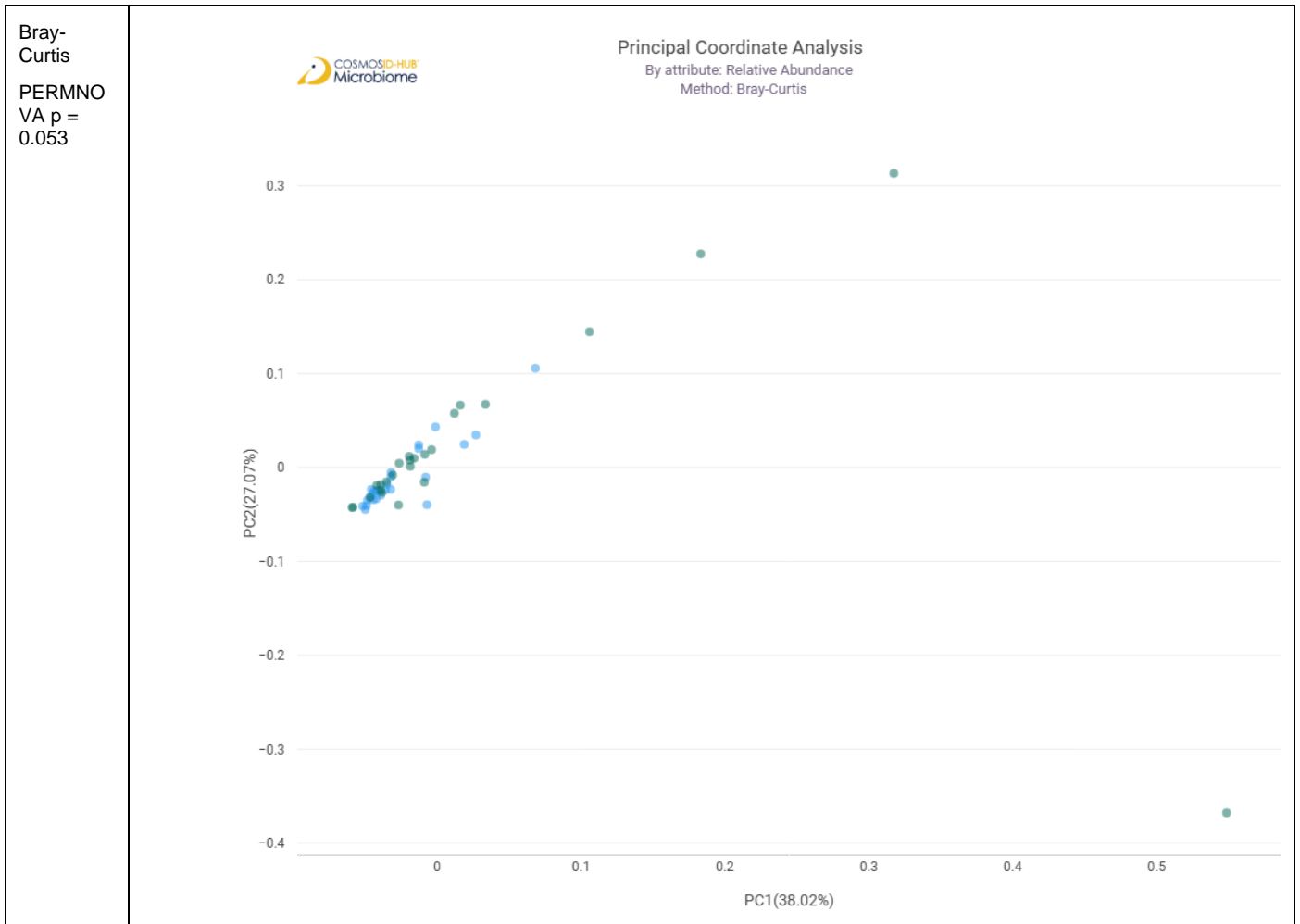
# Simpson



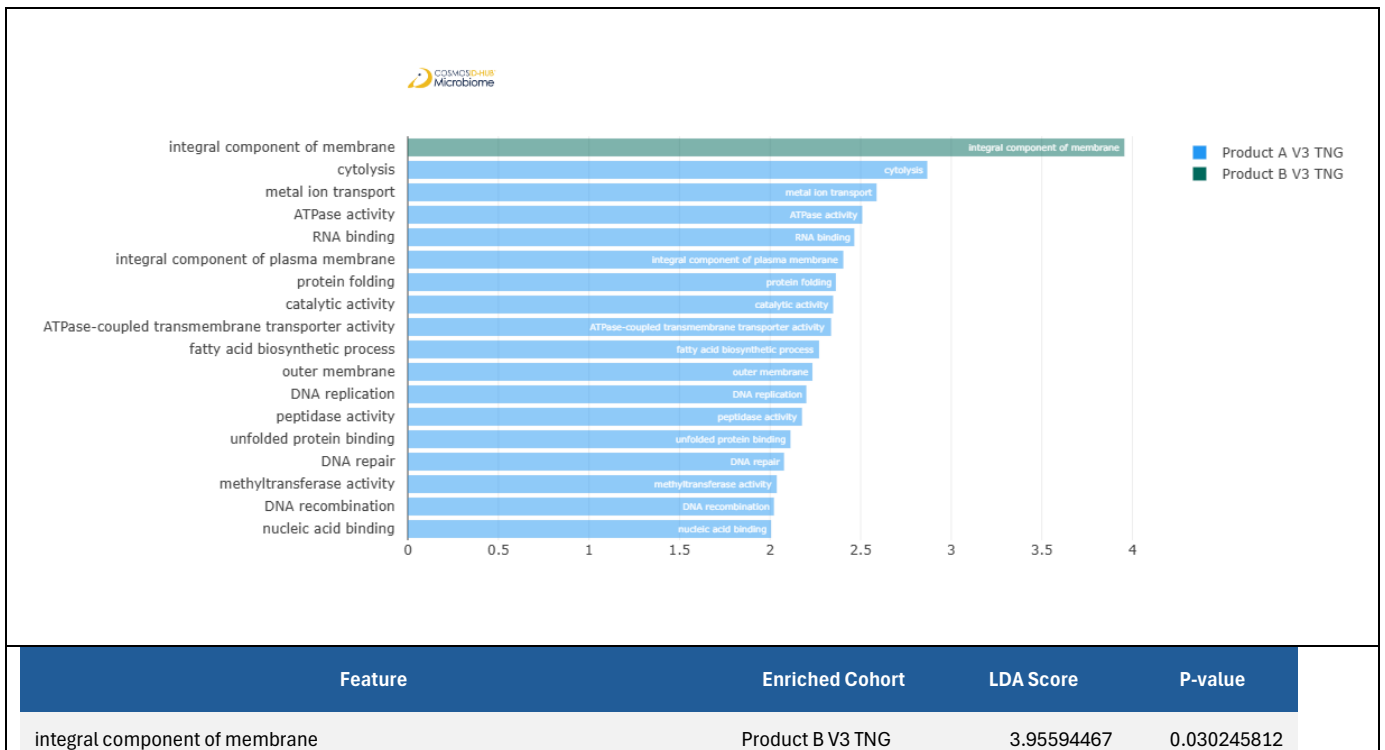
Alpha diversity  
Metric: Abundance Score  
Method: Simpson



## Beta Diversity (GO)



## Differential Abundance (LEfSe) (GO)

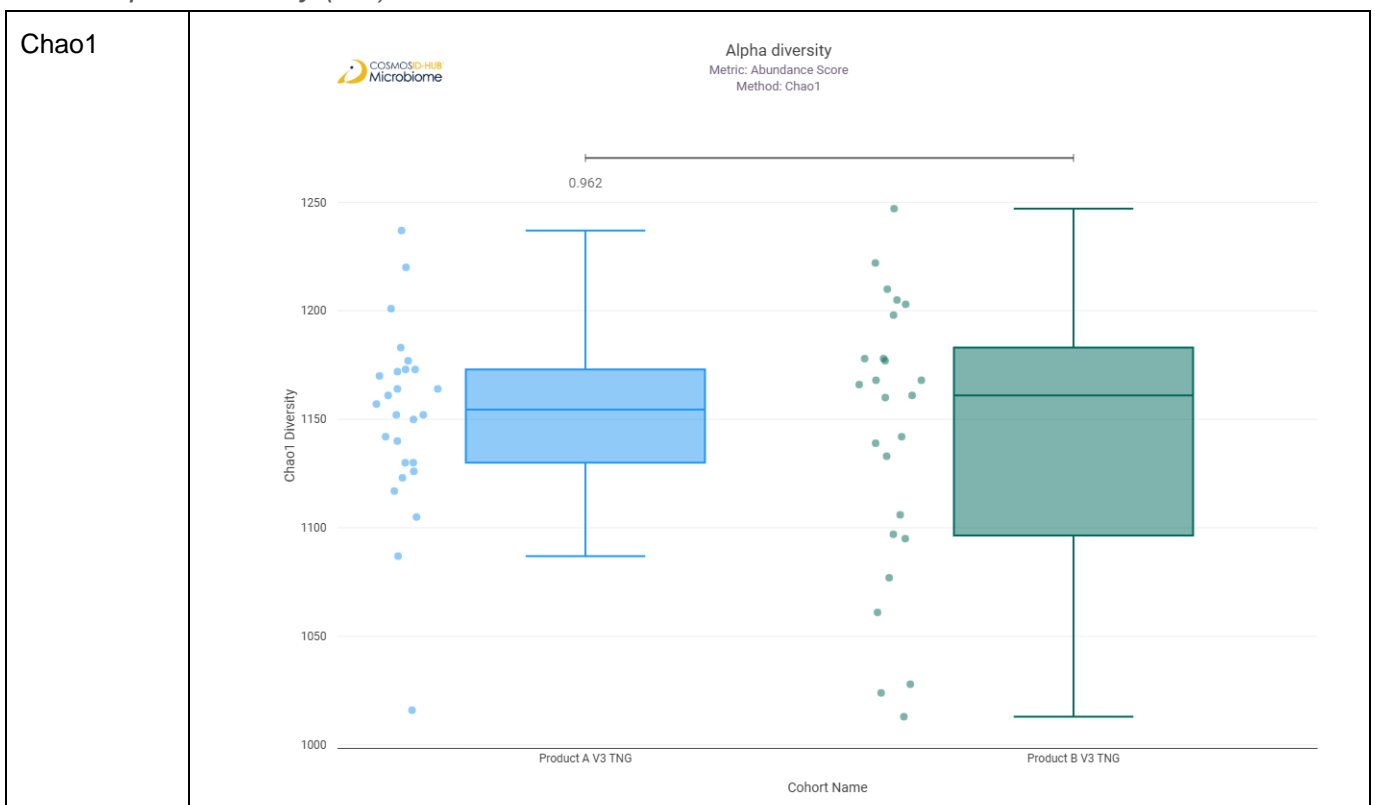




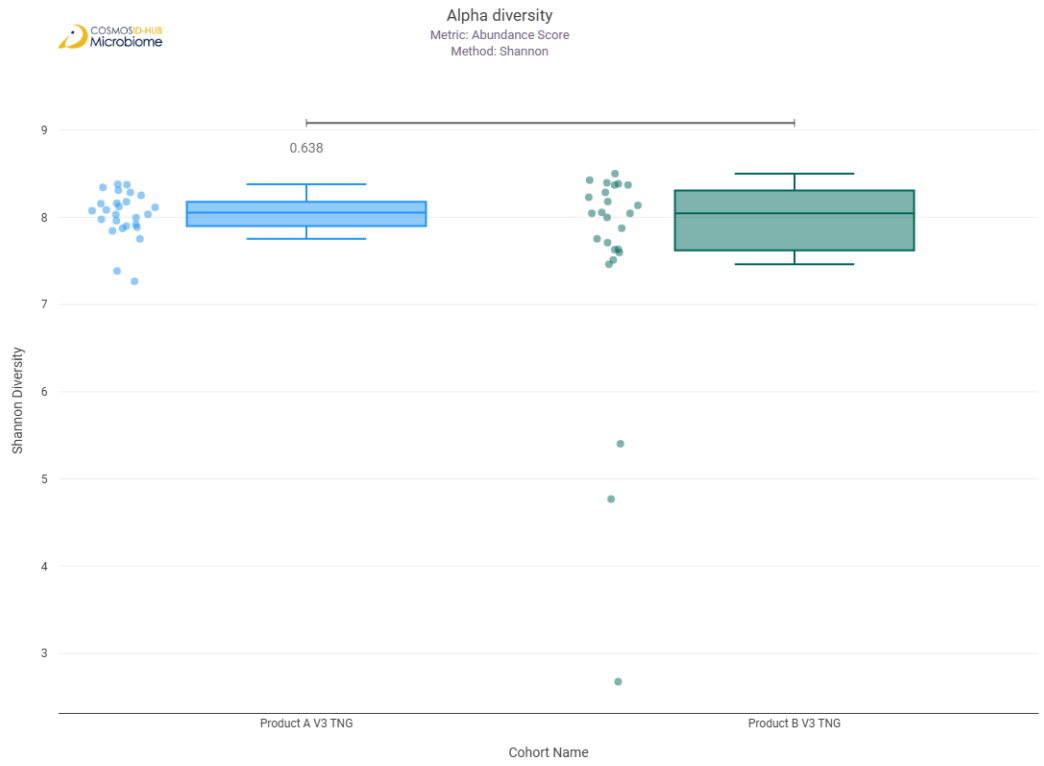
cytolysis	Product A V3 TNG	2.86819902	0.043787588
metal ion transport	Product A V3 TNG	2.588053047	0.000121136
ATPase activity	Product A V3 TNG	2.509036589	0.031712637
RNA binding	Product A V3 TNG	2.46499143	0.026189985
integral component of plasma membrane	Product A V3 TNG	2.404445655	0.004992891
protein folding	Product A V3 TNG	2.363291849	0.008341822
catalytic activity	Product A V3 TNG	2.348315829	0.045795182
ATPase-coupled transmembrane transporter activity	Product A V3 TNG	2.336885912	0.004438681
fatty acid biosynthetic process	Product A V3 TNG	2.27062913	0.045795182
outer membrane	Product A V3 TNG	2.233829492	0.030245812
DNA replication	Product A V3 TNG	2.200445561	0.036484395
peptidase activity	Product A V3 TNG	2.176299275	0.012209995
unfolded protein binding	Product A V3 TNG	2.112611698	0.033240045
DNA repair	Product A V3 TNG	2.07714937	0.026189985
methyltransferase activity	Product A V3 TNG	2.037014259	0.027486336
DNA recombination	Product A V3 TNG	2.02153966	0.00666206
nucleic acid binding	Product A V3 TNG	2.005813652	0.041854827

## Enzyme Commission

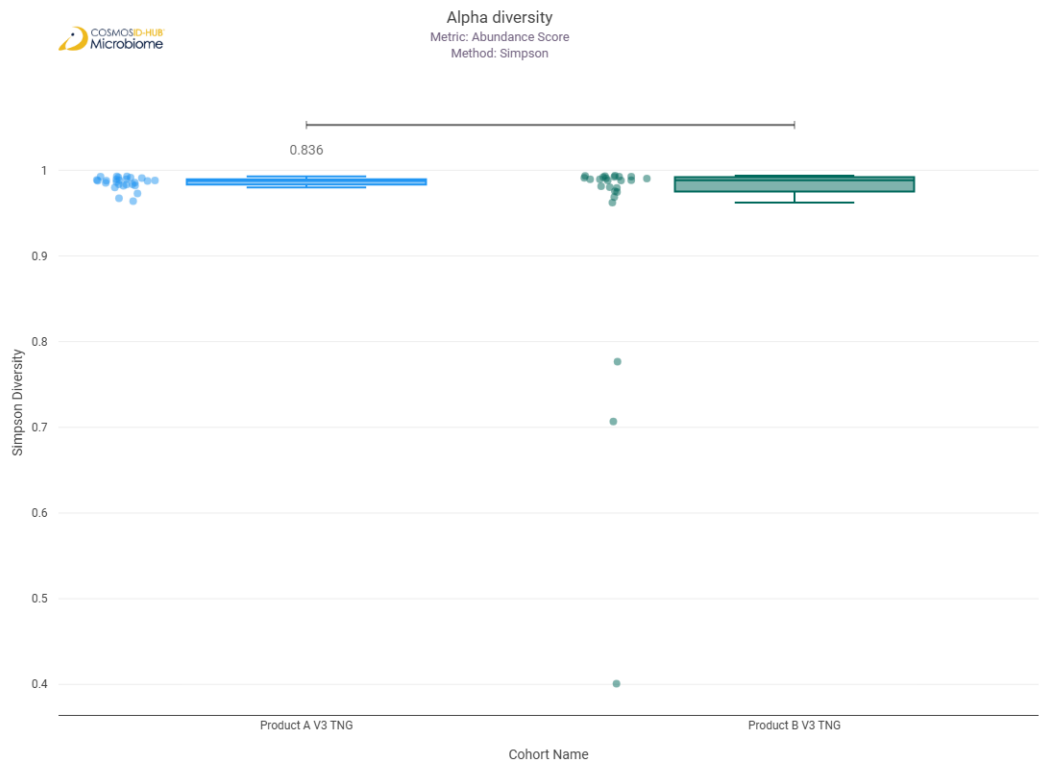
### Alpha Diversity (EC)



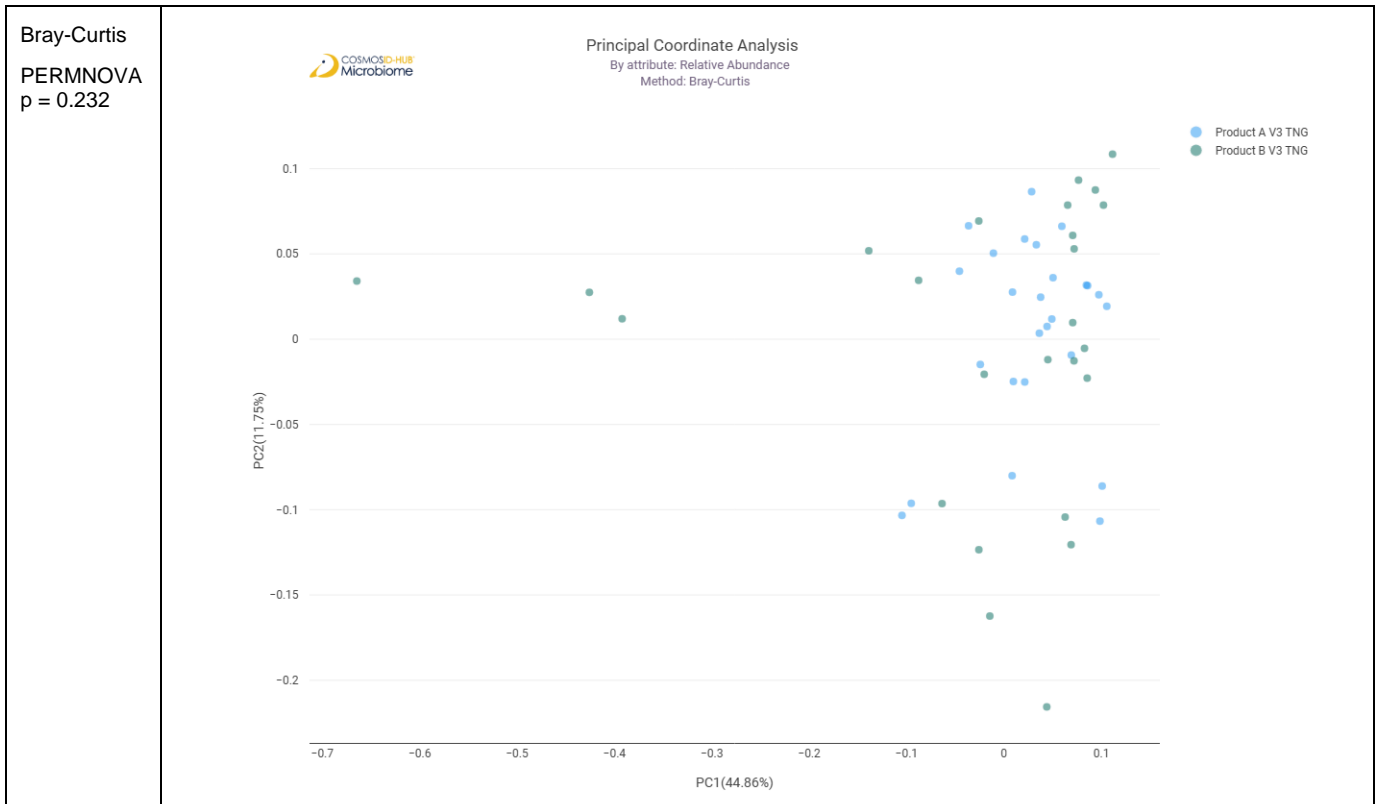
# Shannon



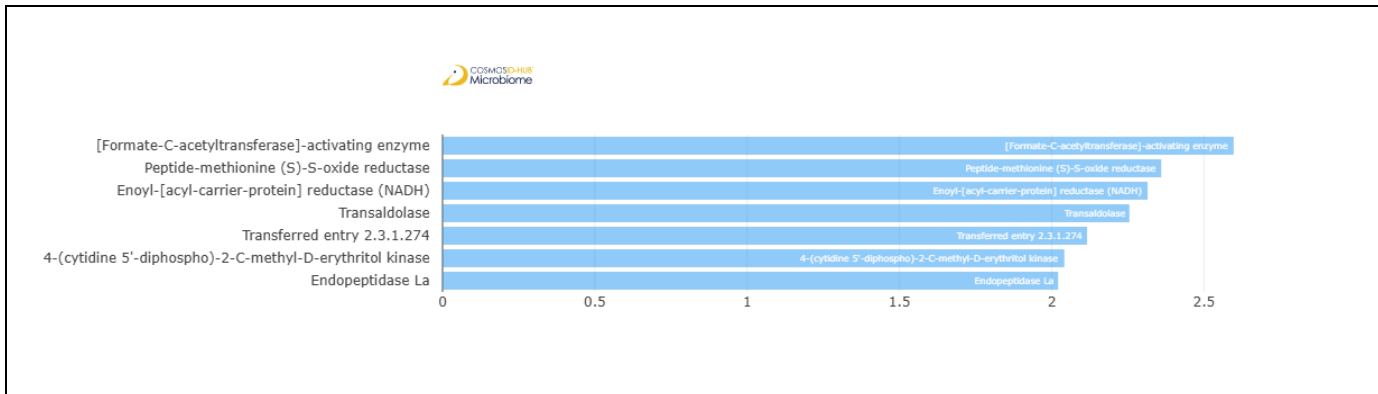
# Simpson



## Beta Diversity (EC)



## Differential Abundance (LEfSe) (EC)

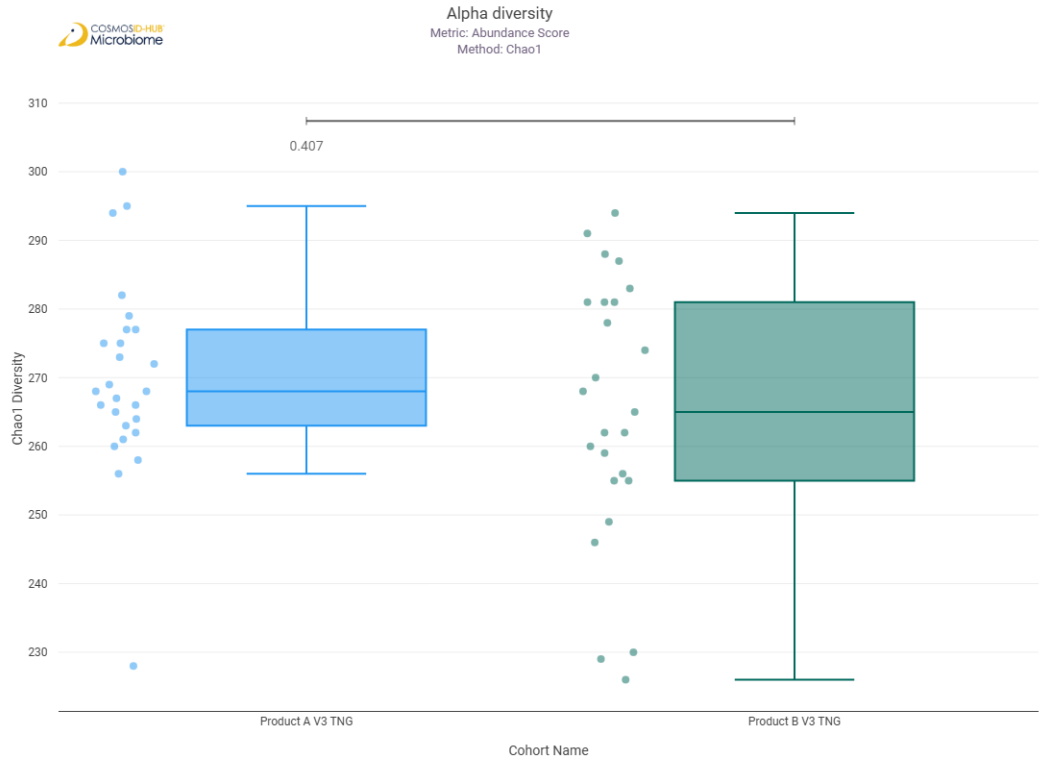


Feature	Enriched Cohort	LDA Score	P-value
[Formate-C-acetyltransferase]-activating enzyme	Product A V3 TNG	2.597387363	0.021519031
Peptide-methionine (S)-S-oxide reductase	Product A V3 TNG	2.359536073	0.009840467
Enoyl-[acyl-carrier-protein] reductase (NADH)	Product A V3 TNG	2.31483187	0.033240045
Transaldolase	Product A V3 TNG	2.254985266	0.033240045
Transferred entry 2.3.1.274	Product A V3 TNG	2.116157133	0.043787588
4-(cytidine 5'-diphospho)-2-C-methyl-D-erythritol kinase	Product A V3 TNG	2.041454779	0.008341822
Endopeptidase La	Product A V3 TNG	2.020895553	0.045795182

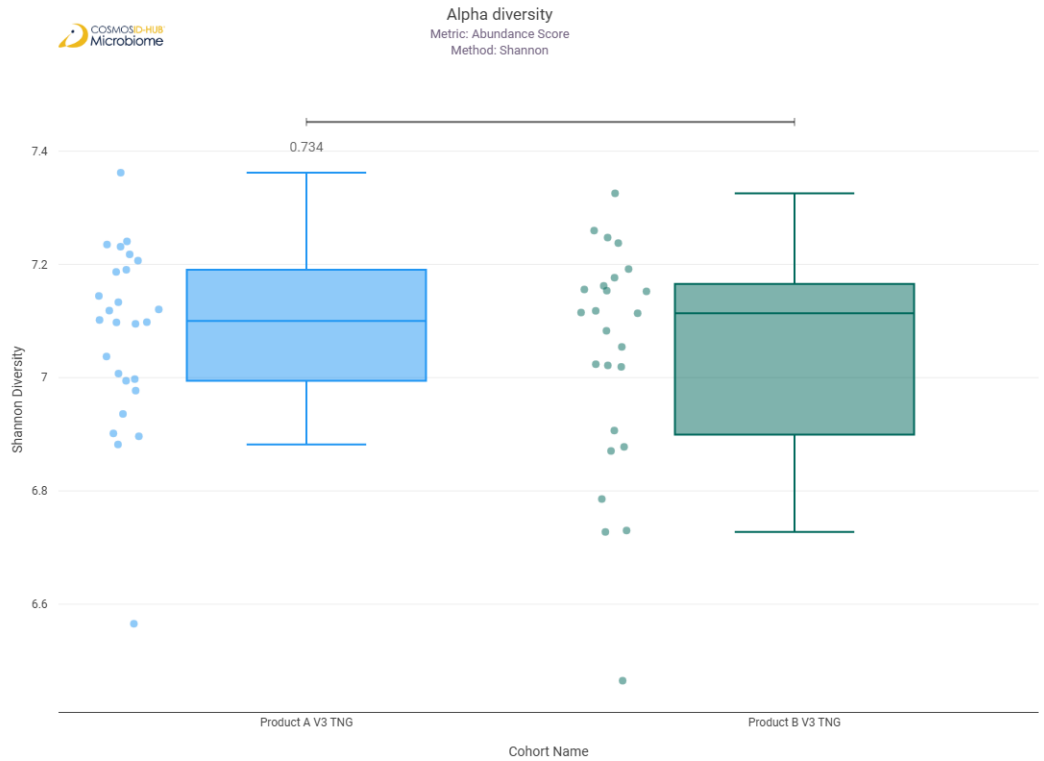
## MetaCyc Pathways

# Alpha Diversity (MetaCyc)

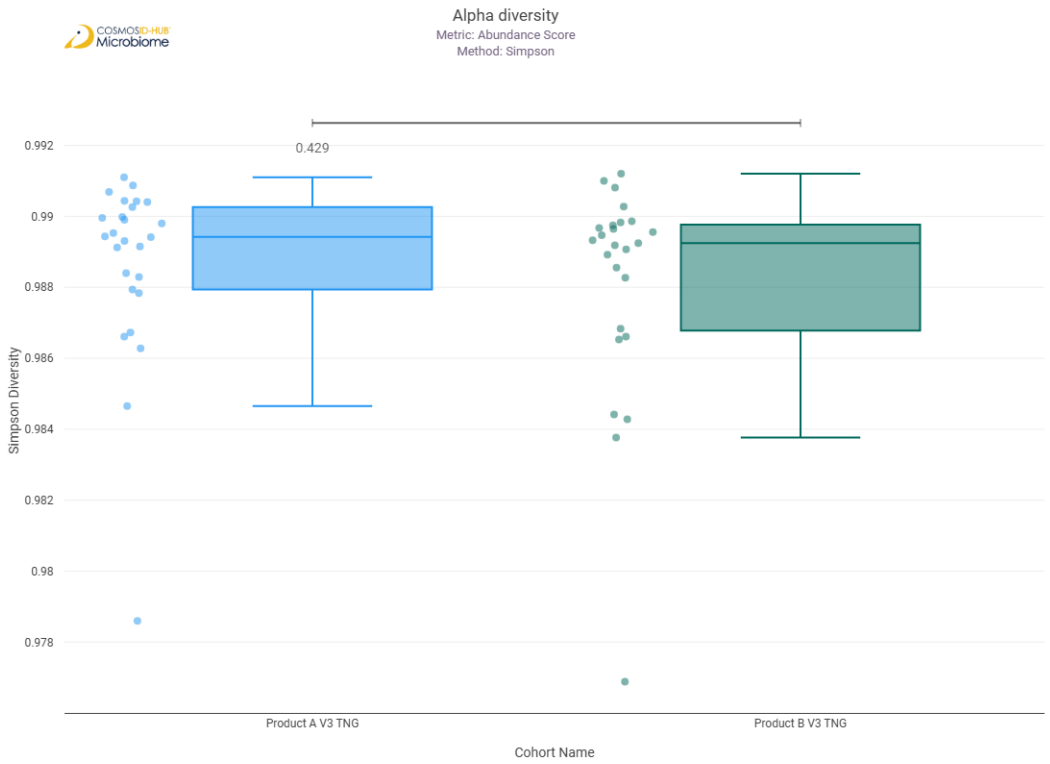
Chao1



Shannon

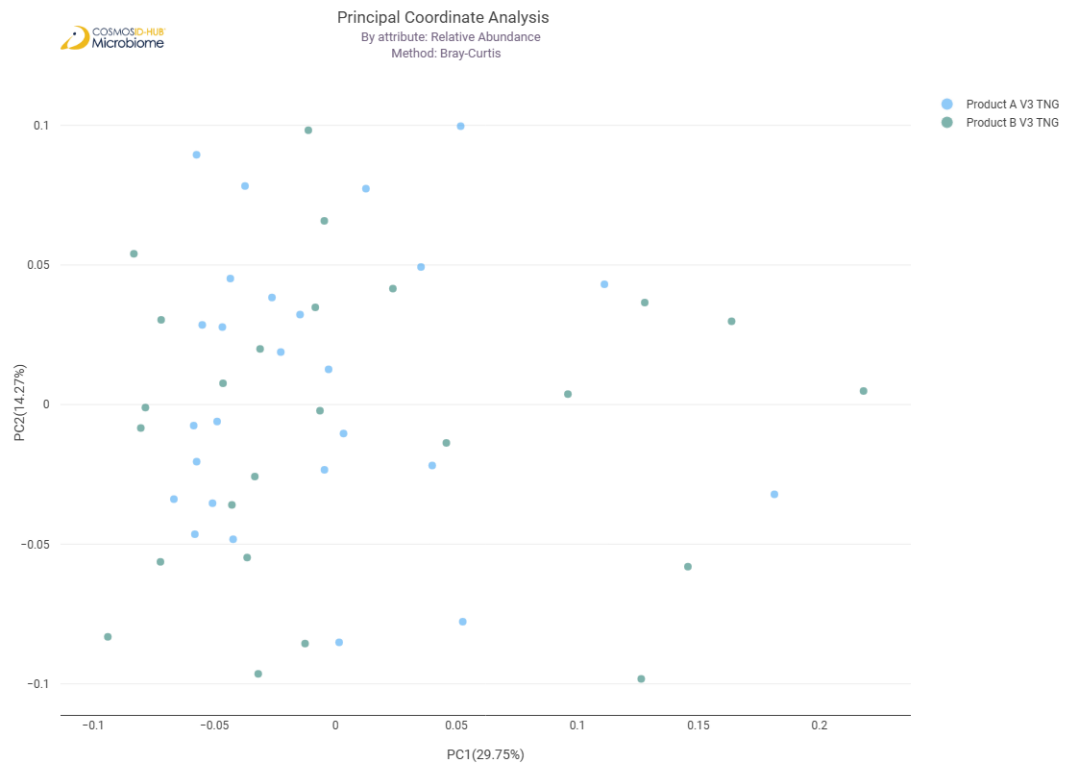


Simpson

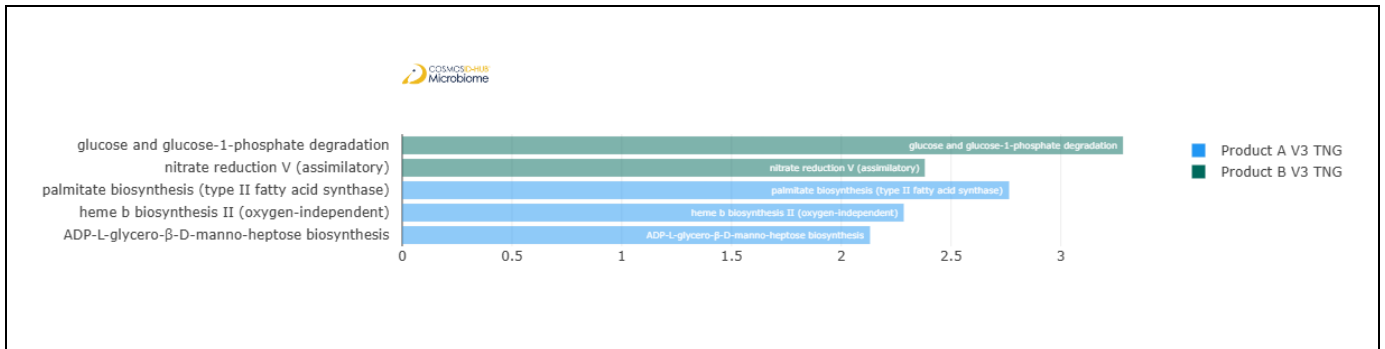


Beta Diversity (MetaCyc)

Bray-Curtis  
PERMNOVA  
p = 0.529



## Differential Abundance (LEfSe) (MetaCyc)

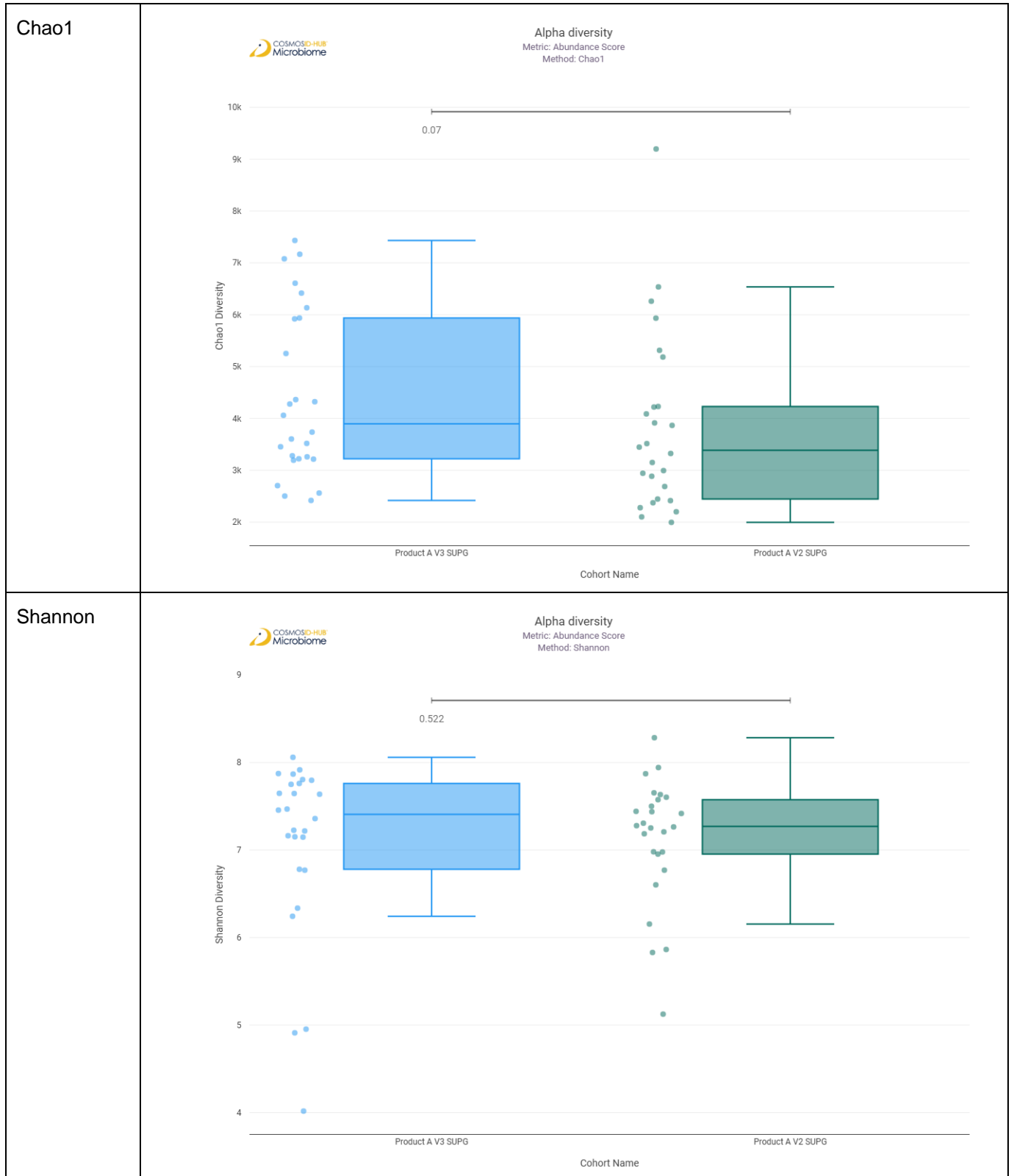


Feature	Enriched Cohort	LDA Score	P-value
glucose and glucose-1-phosphate degradation	Product B V3 TNG	3.28329517	0.039994768
nitrate reduction V (assimilatory)	Product B V3 TNG	2.380513641	0.027486336
palmitate biosynthesis (type II fatty acid synthase)	Product A V3 TNG	2.764475862	0.038200947
heme b biosynthesis II (oxygen-independent)	Product A V3 TNG	2.284637925	0.013574437
ADP-L-glycero-β-D-manno-heptose biosynthesis	Product A V3 TNG	2.130957279	0.045795182

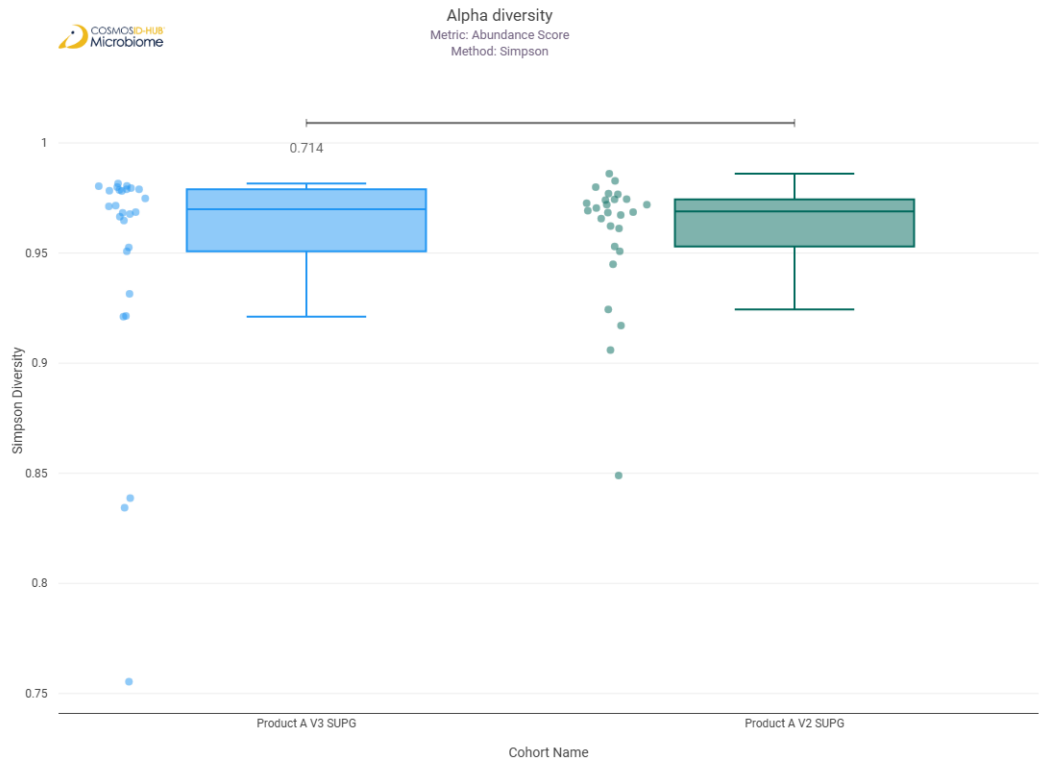
# Comparison 13: Product A V2 SUPG vs Product A V3 SUPG

## Gene Ontology

### Alpha Diversity (GO)

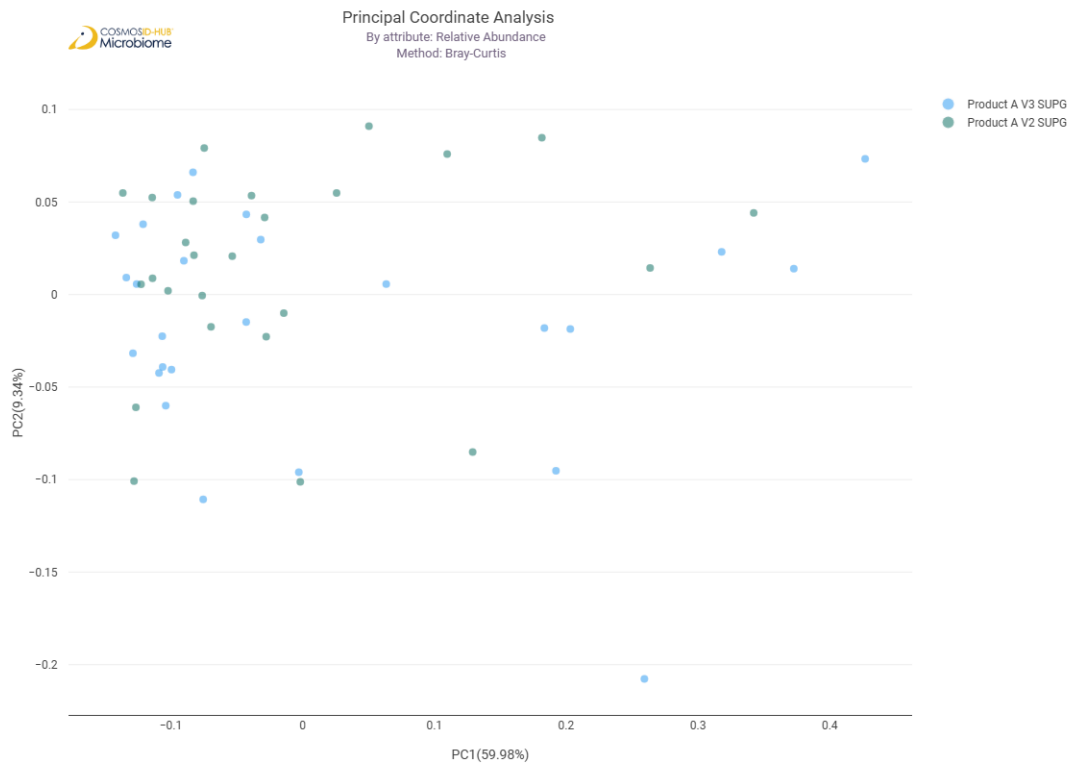


Simpson



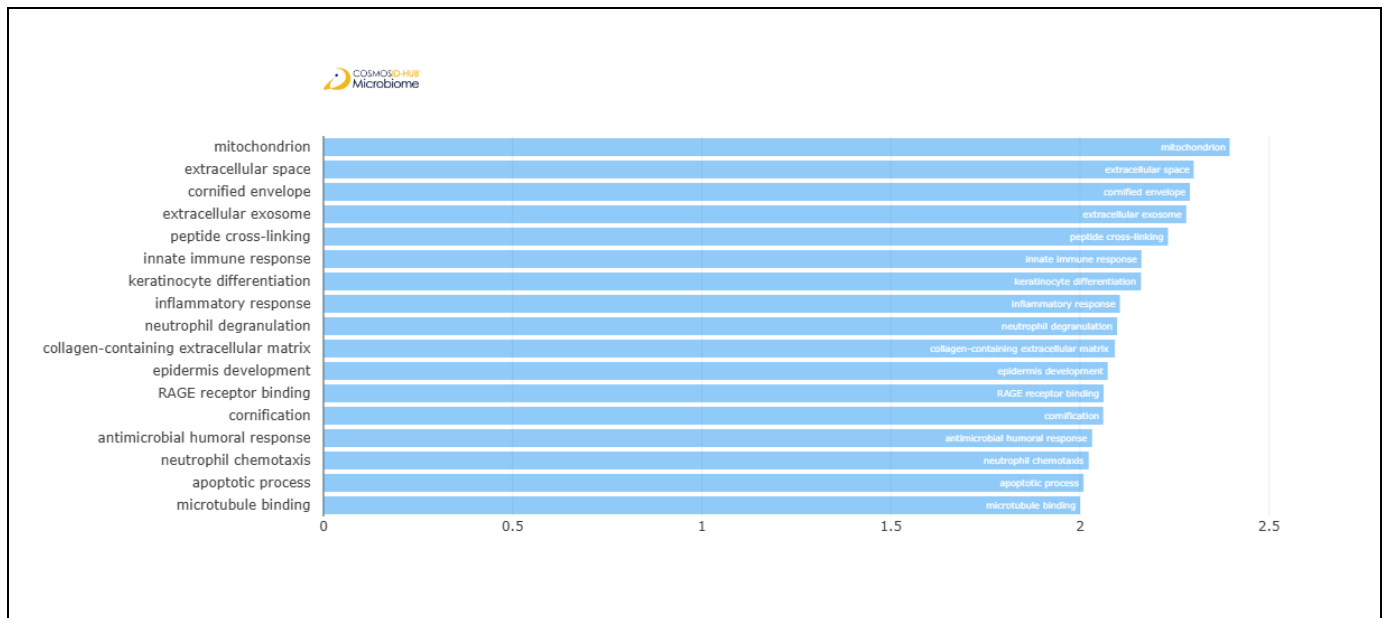
Beta Diversity (GO)

Bray-Curtis  
PERMNOVA  
p = 0.402





## Differential Abundance (LEfSe) (GO)

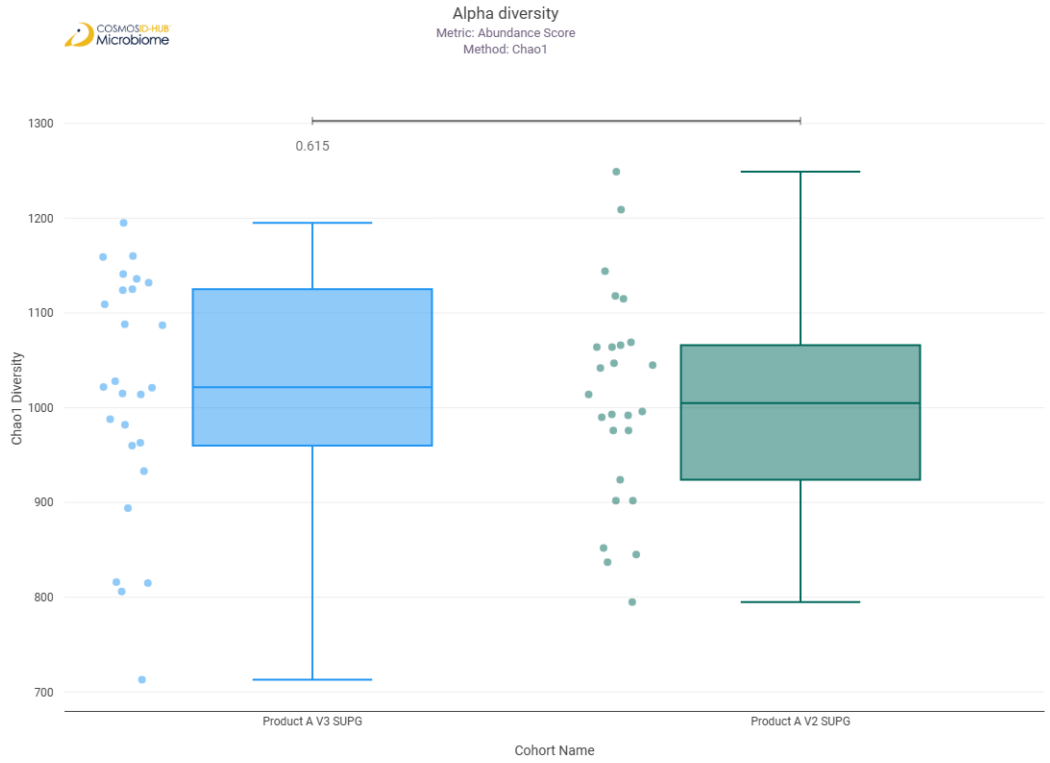


Feature	Enriched Cohort	LDA Score	P-value
mitochondrion	Product A V3 SUPG	2.395593333	0.044100855
extracellular space	Product A V3 SUPG	2.30062659	0.044100855
cornified envelope	Product A V3 SUPG	2.290652157	0.036807215
extracellular exosome	Product A V3 SUPG	2.280967867	0.035244686
peptide cross-linking	Product A V3 SUPG	2.232724206	0.042057434
innate immune response	Product A V3 SUPG	2.162582759	0.03077255
keratinocyte differentiation	Product A V3 SUPG	2.161426341	0.042057434
inflammatory response	Product A V3 SUPG	2.105579409	0.022101093
neutrophil degranulation	Product A V3 SUPG	2.098179782	0.028014666
collagen-containing extracellular matrix	Product A V3 SUPG	2.092271978	0.038553793
epidermis development	Product A V3 SUPG	2.073464904	0.03686763
RAGE receptor binding	Product A V3 SUPG	2.062537534	0.030683327
cornification	Product A V3 SUPG	2.06157641	0.036807215
antimicrobial humoral response	Product A V3 SUPG	2.032144347	0.033626203
neutrophil chemotaxis	Product A V3 SUPG	2.023076006	0.026684643
apoptotic process	Product A V3 SUPG	2.009510989	0.026684643
microtubule binding	Product A V3 SUPG	2.000388259	0.026684643

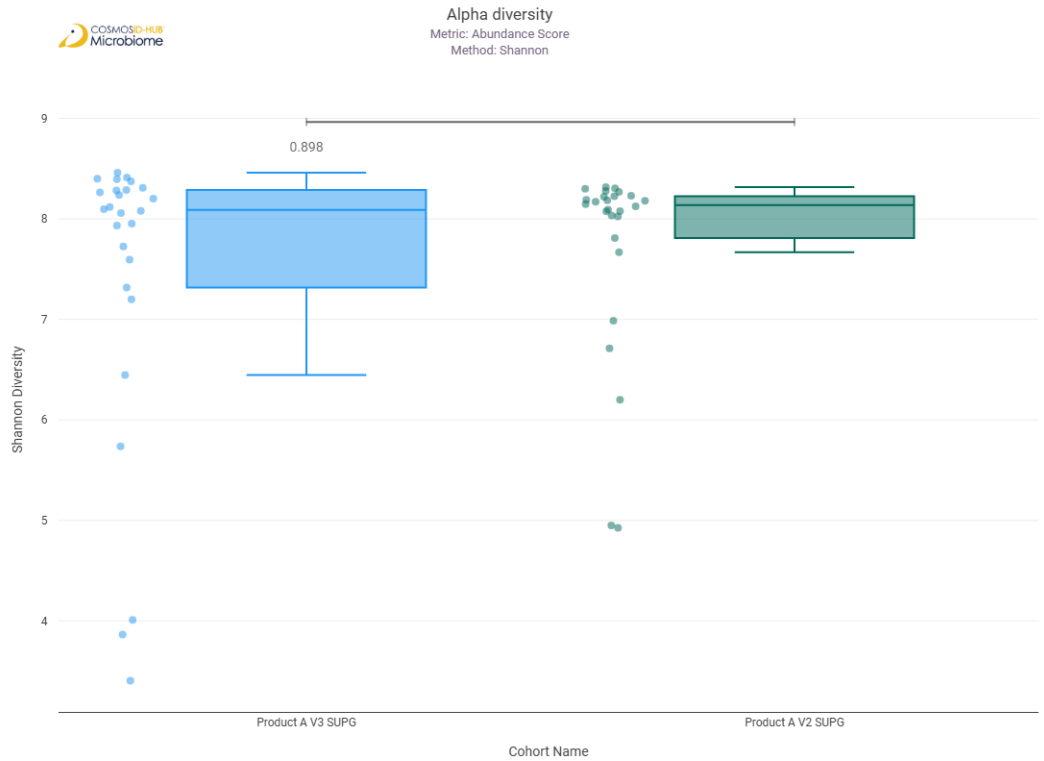
## Enzyme Commission

# Alpha Diversity (EC)

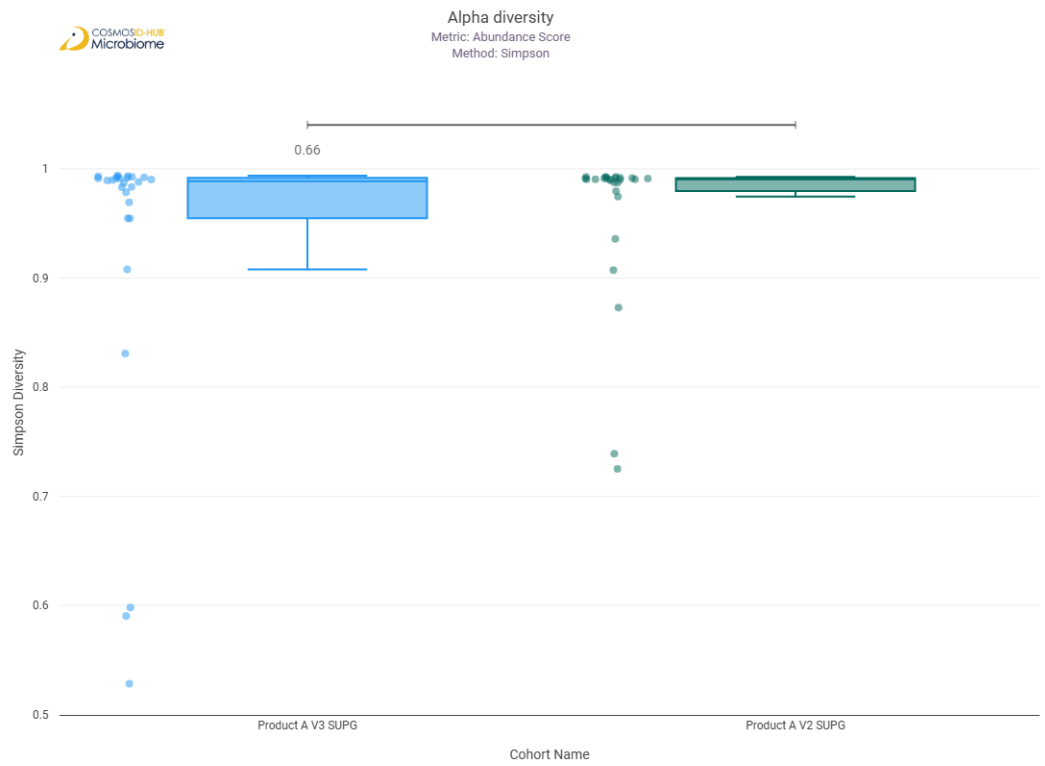
Chao1



Shannon

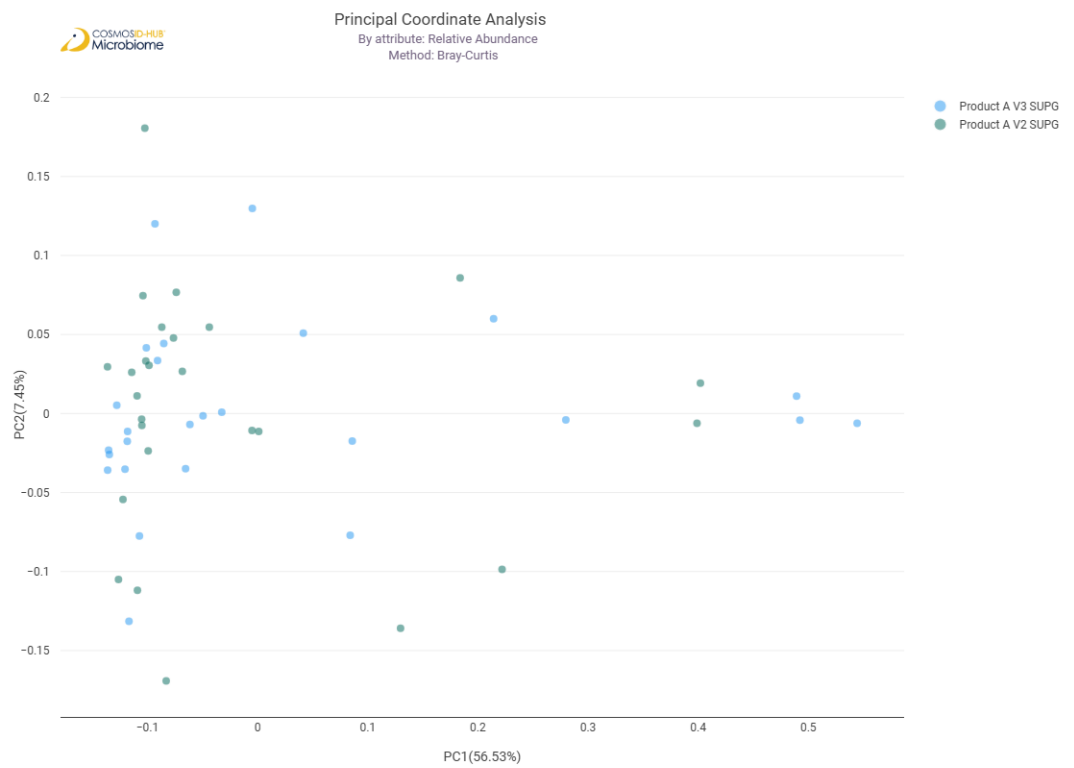


# Simpson

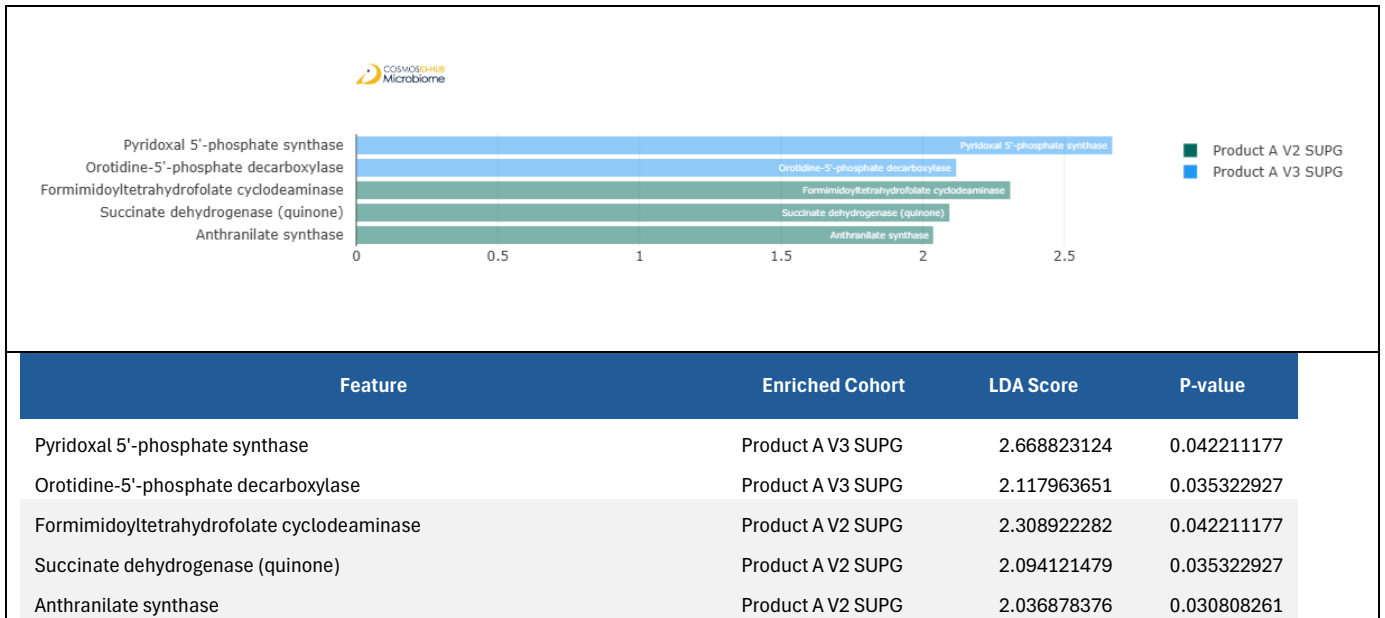


## Beta Diversity (EC)

Bray-Curtis  
PERMNOVA  
 $p = 0.609$

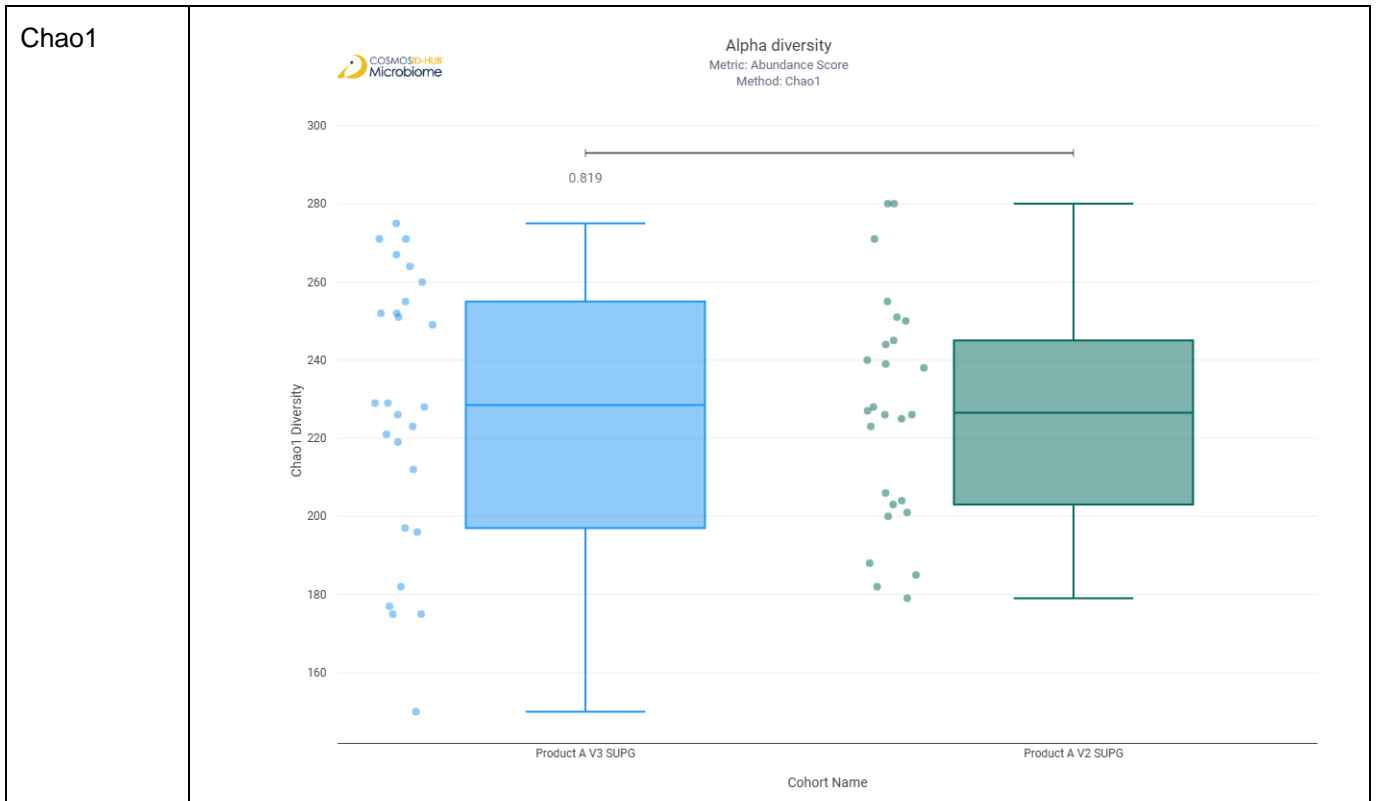


## Differential Abundance (LEfSe) (EC)

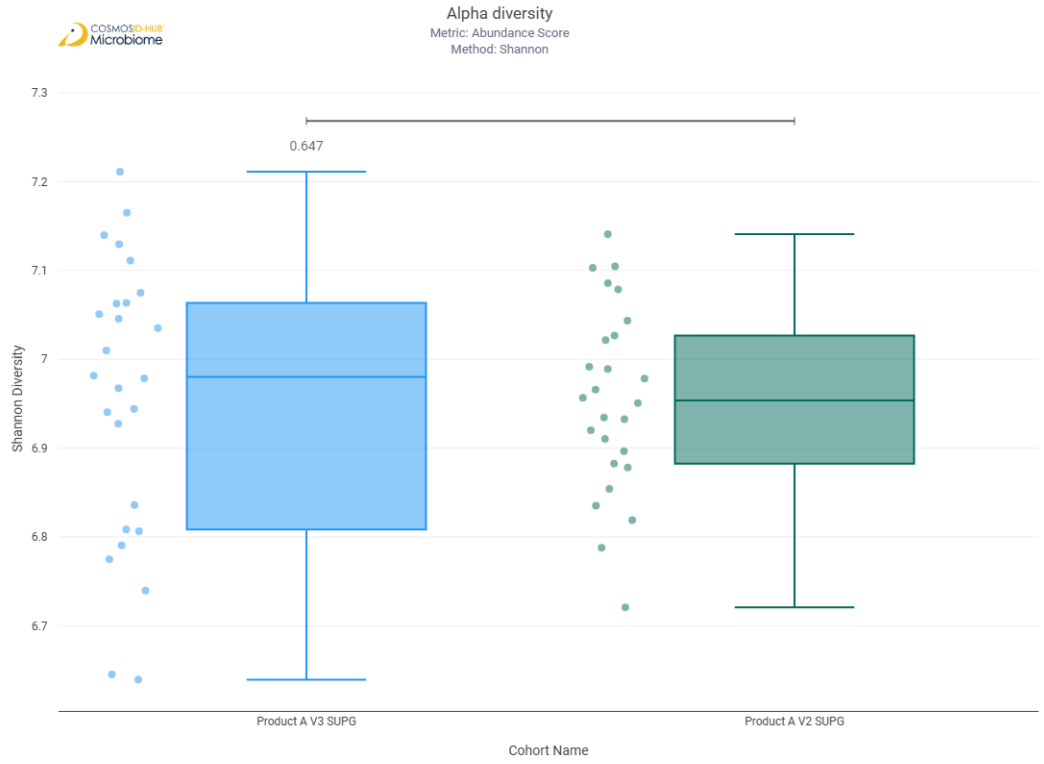


## MetaCyc Pathways

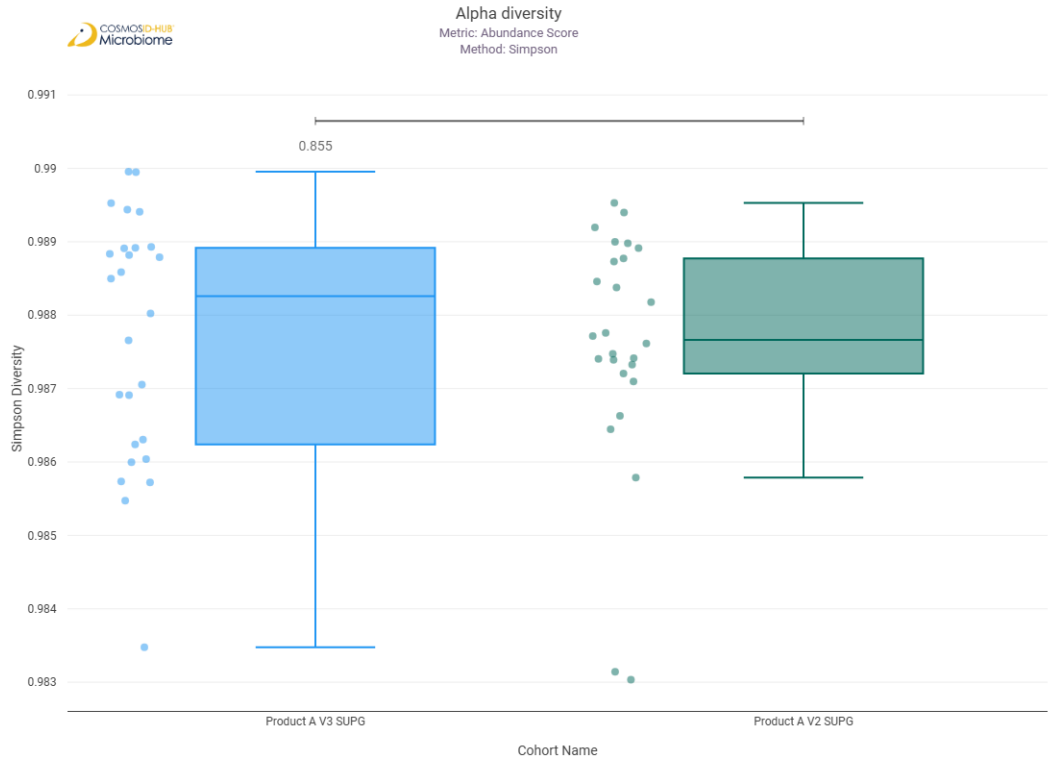
### Alpha Diversity (MetaCyc)



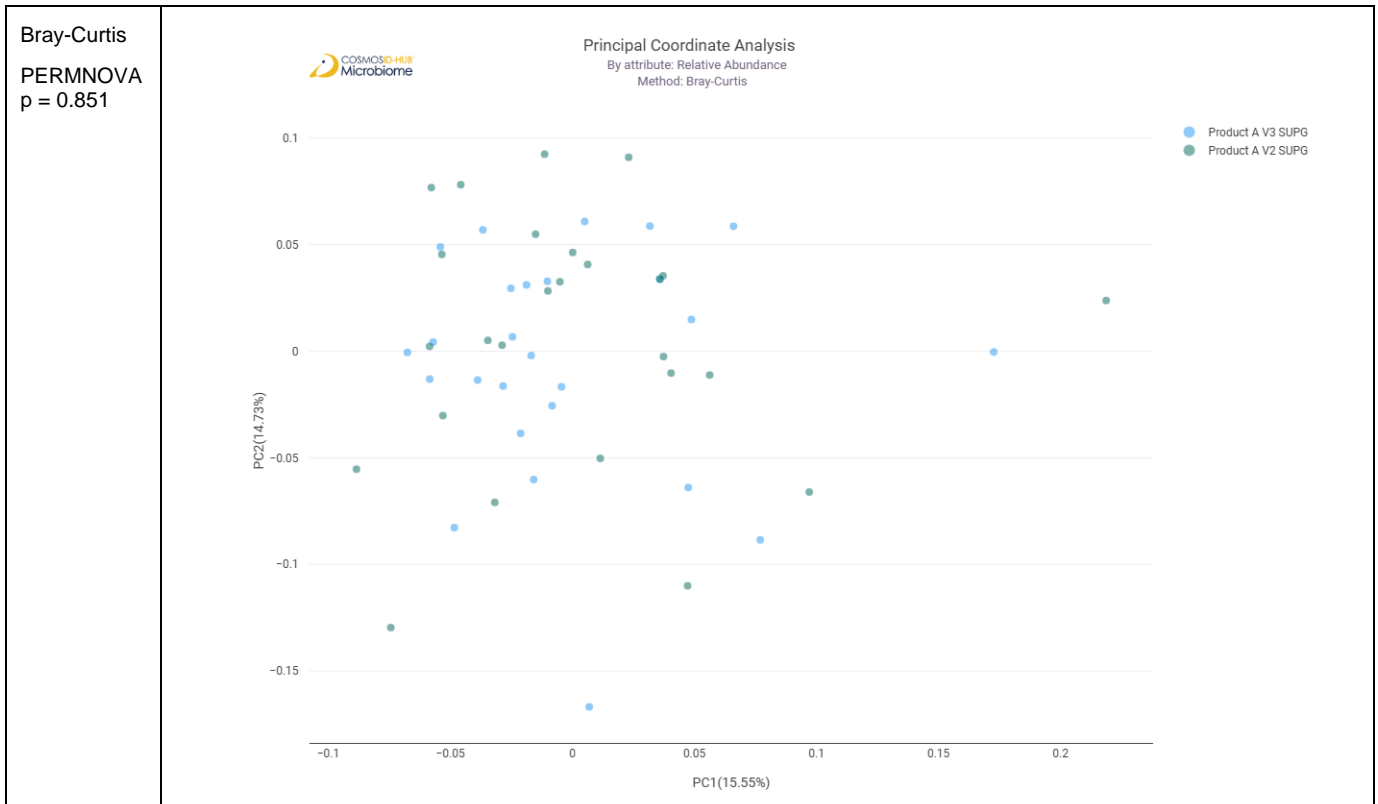
# Shannon



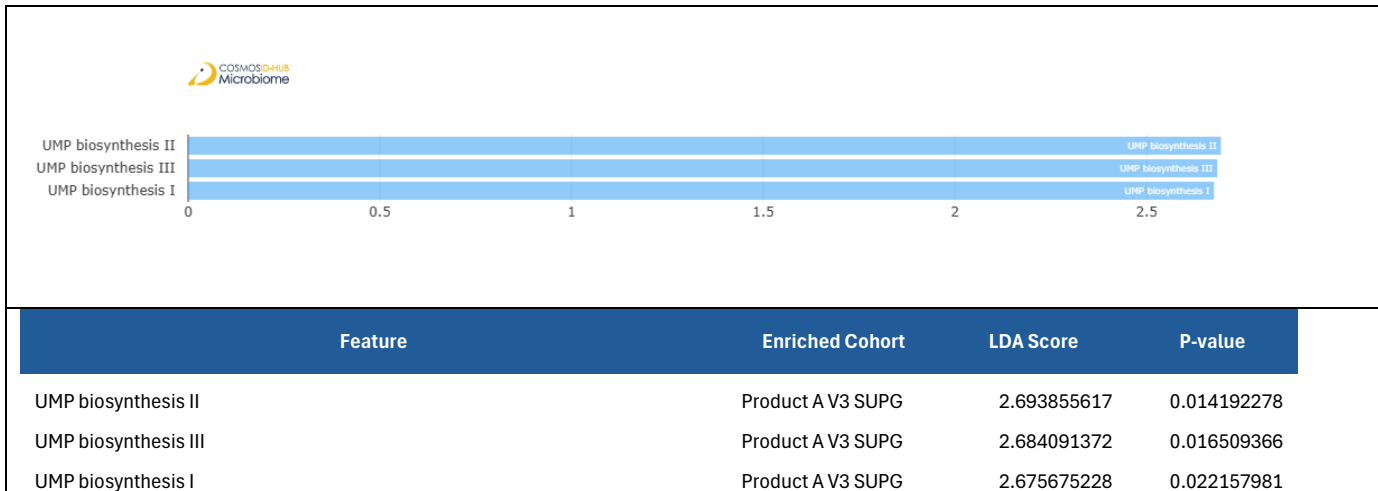
# Simpson



## Beta Diversity (MetaCyc)



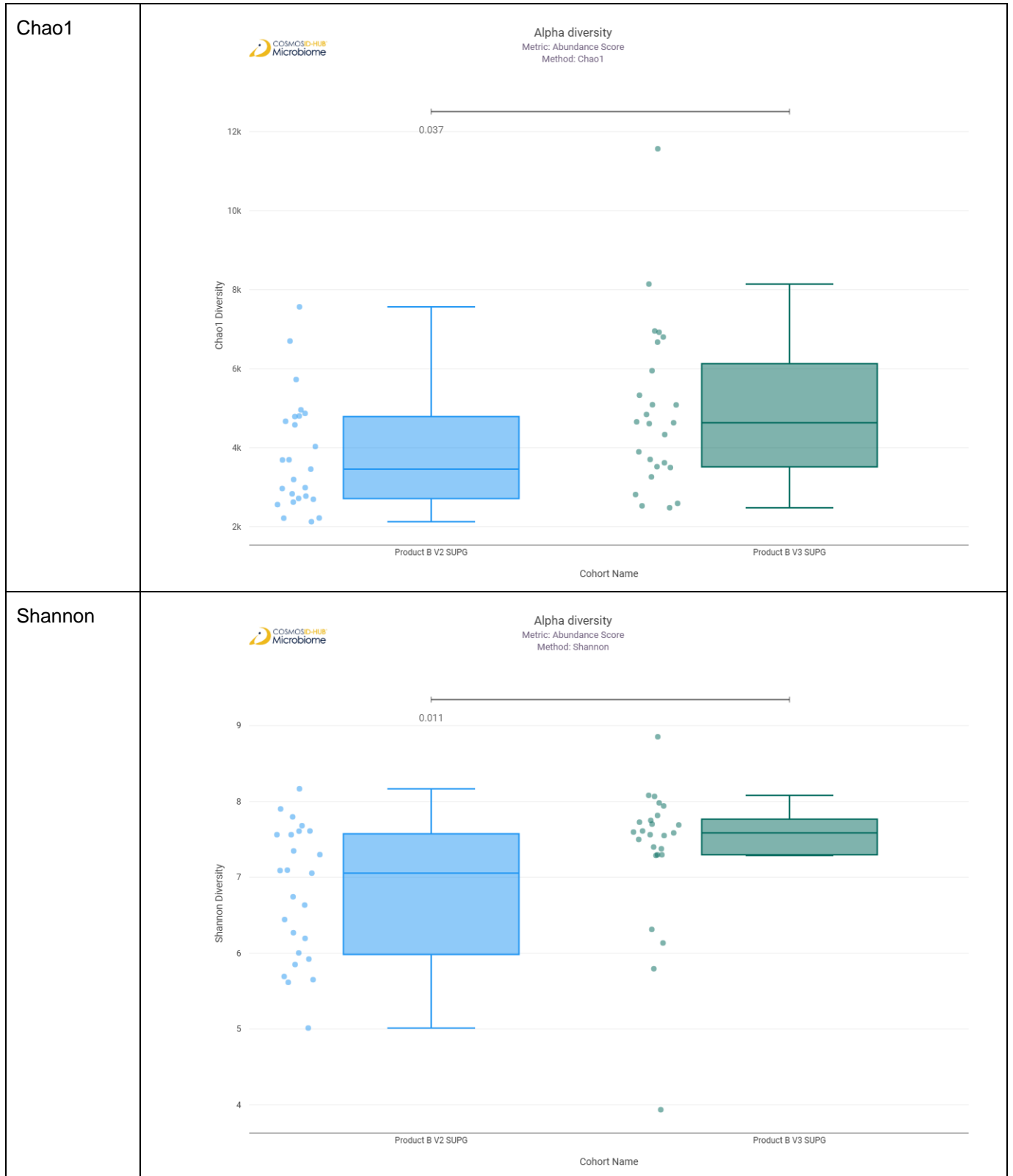
## Differential Abundance (LEfSe) (MetaCyc)



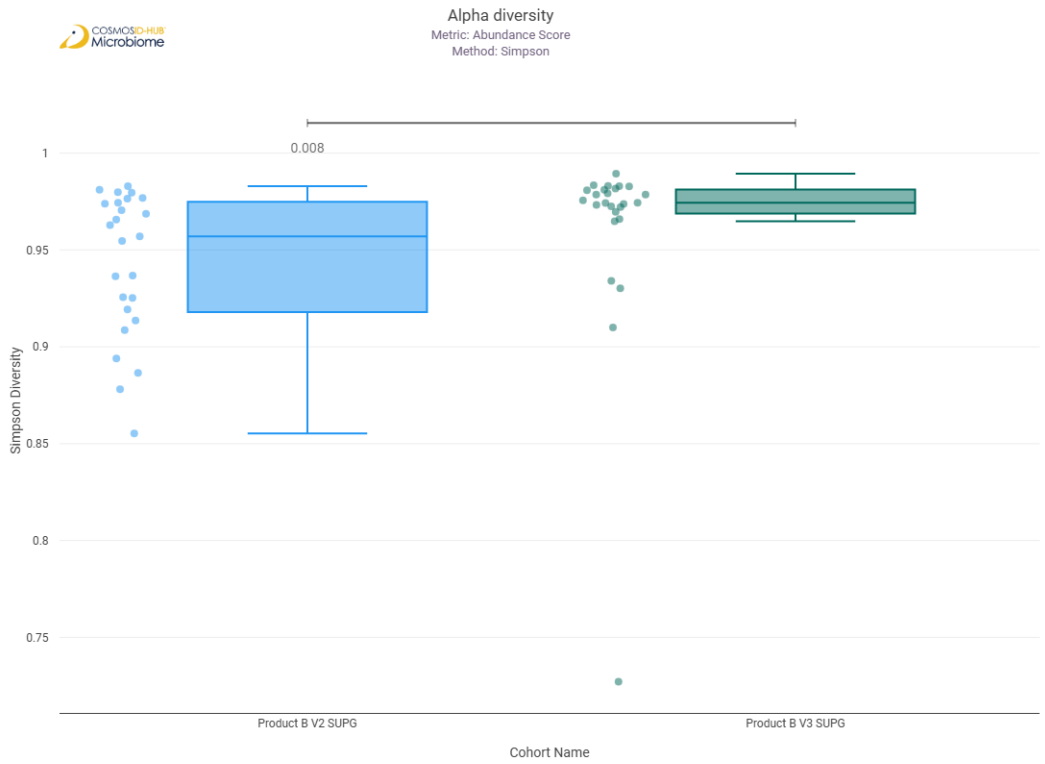
# Comparison 14: Product B V2 SUPG vs Product B V3 SUPG

## Gene Ontology

### Alpha Diversity (GO)

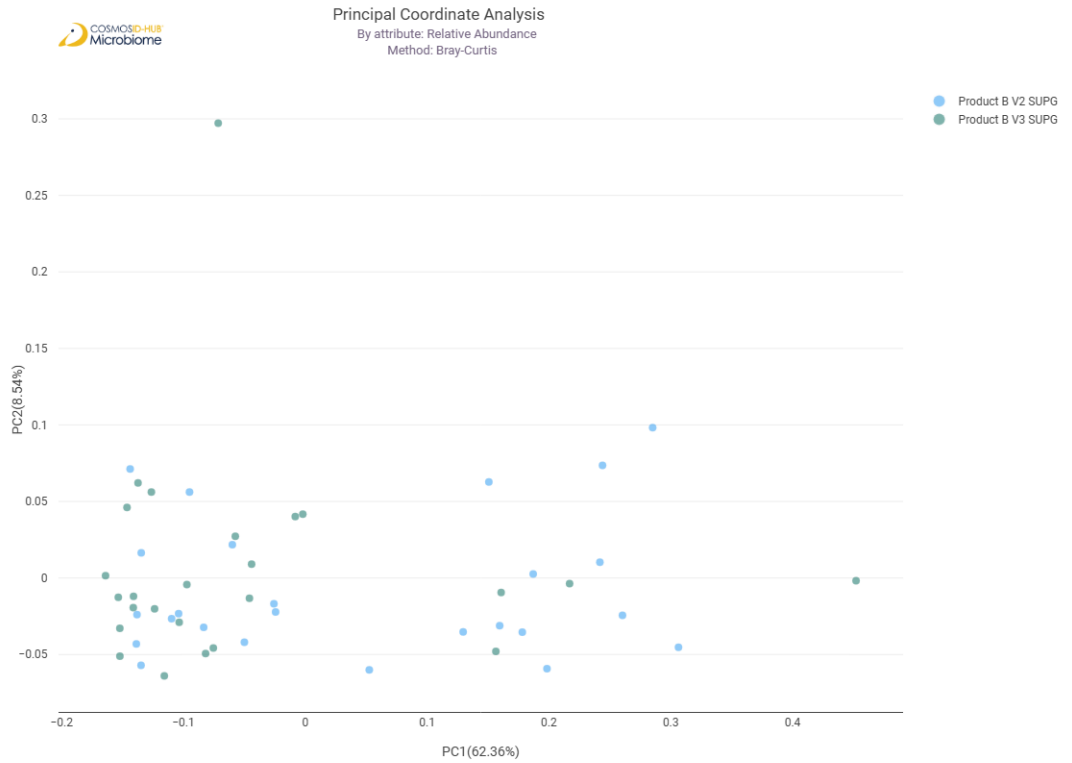


Simpson



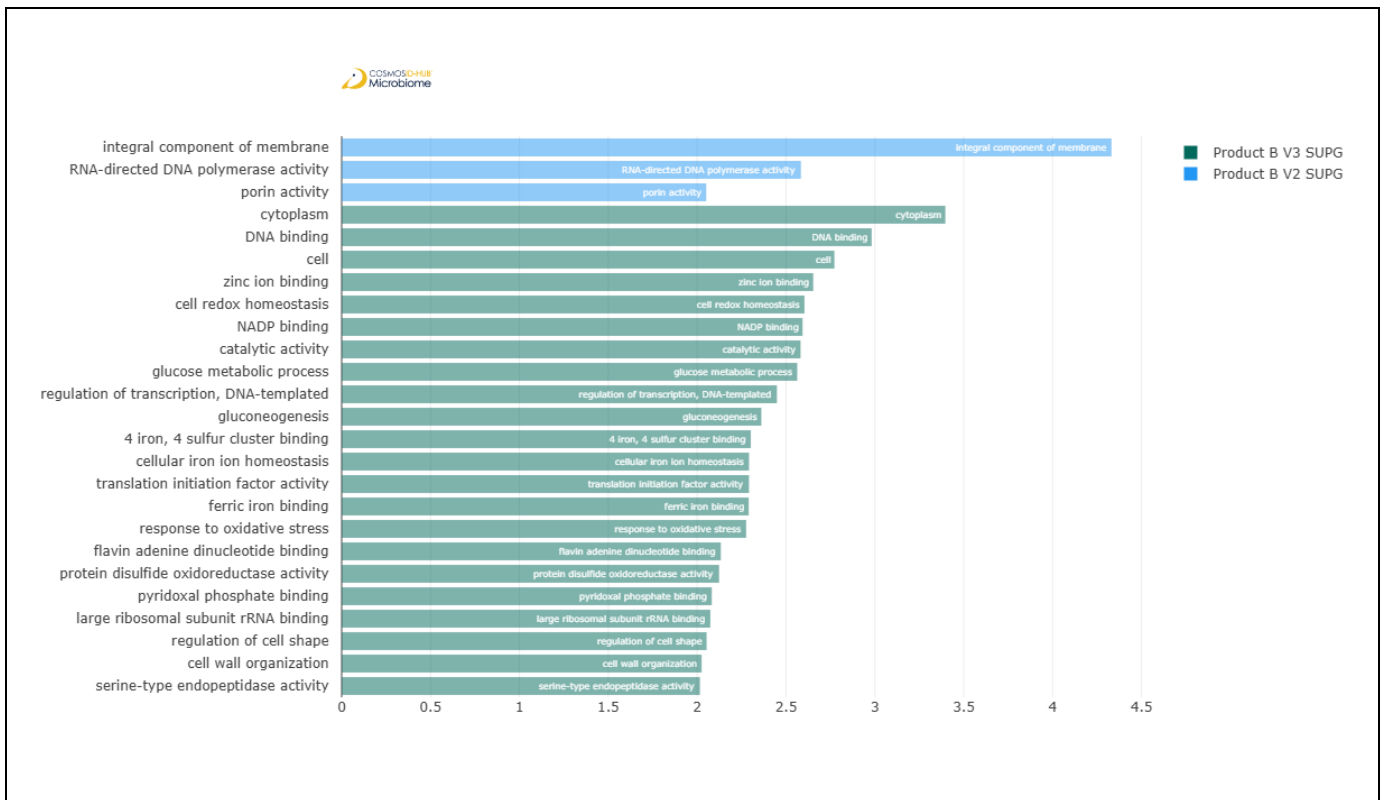
Beta Diversity (GO)

Bray-Curtis  
PERMNOVA  
 $p = 0.031$





## Differential Abundance (LEfSe) (GO)

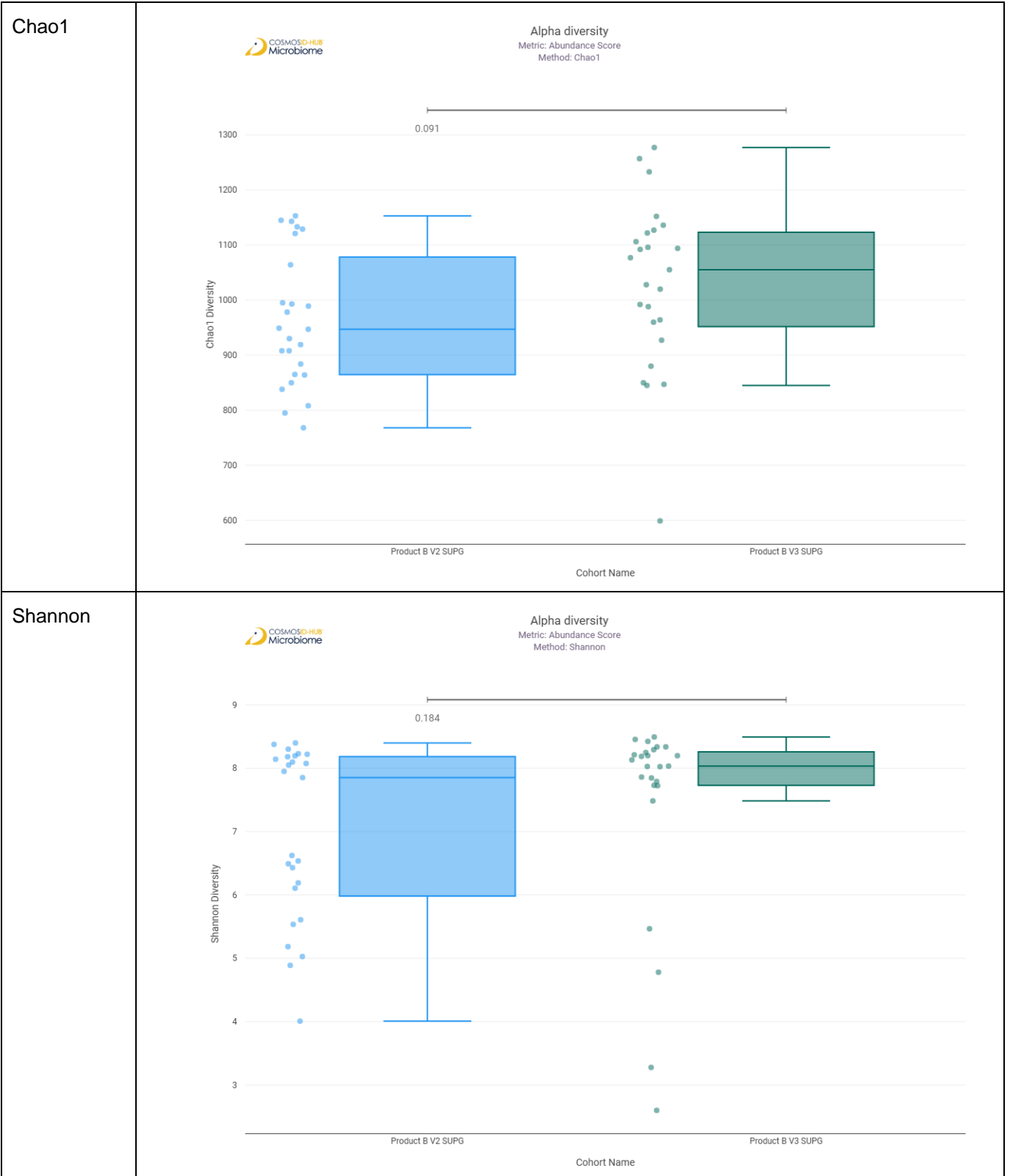


Feature	Enriched Cohort	LDA Score	P-value
integral component of membrane	Product B V2 SUPG	4.331239388	0.000876011
RNA-directed DNA polymerase activity	Product B V2 SUPG	2.583794457	0.021491444
porin activity	Product B V2 SUPG	2.051060432	0.000370258
cytoplasm	Product B V3 SUPG	3.396749929	0.009589776
DNA binding	Product B V3 SUPG	2.981994326	0.048908406
cell	Product B V3 SUPG	2.772339093	0.004210827
zinc ion binding	Product B V3 SUPG	2.653236004	0.033618995
cell redox homeostasis	Product B V3 SUPG	2.604058534	0.011982167
NADP binding	Product B V3 SUPG	2.593277033	0.044622577
catalytic activity	Product B V3 SUPG	2.581800698	0.014109615
glucose metabolic process	Product B V3 SUPG	2.563245358	0.048908406
regulation of transcription, DNA-templated	Product B V3 SUPG	2.448756977	0.029049022
gluconeogenesis	Product B V3 SUPG	2.361417944	0.046724152
4 iron, 4 sulfur cluster binding	Product B V3 SUPG	2.301918482	0.005364191
cellular iron ion homeostasis	Product B V3 SUPG	2.291981249	0.01265739
translation initiation factor activity	Product B V3 SUPG	2.291727599	0.010144117
ferric iron binding	Product B V3 SUPG	2.290111	0.010726809
response to oxidative stress	Product B V3 SUPG	2.275933055	0.019384996
flavin adenine dinucleotide binding	Product B V3 SUPG	2.133201392	0.038790393
protein disulfide oxidoreductase activity	Product B V3 SUPG	2.12366867	6.80E-03
pyridoxal phosphate binding	Product B V3 SUPG	2.082319369	0.0352731
large ribosomal subunit rRNA binding	Product B V3 SUPG	2.074326848	0.027649527
regulation of cell shape	Product B V3 SUPG	2.053444527	0.015706943

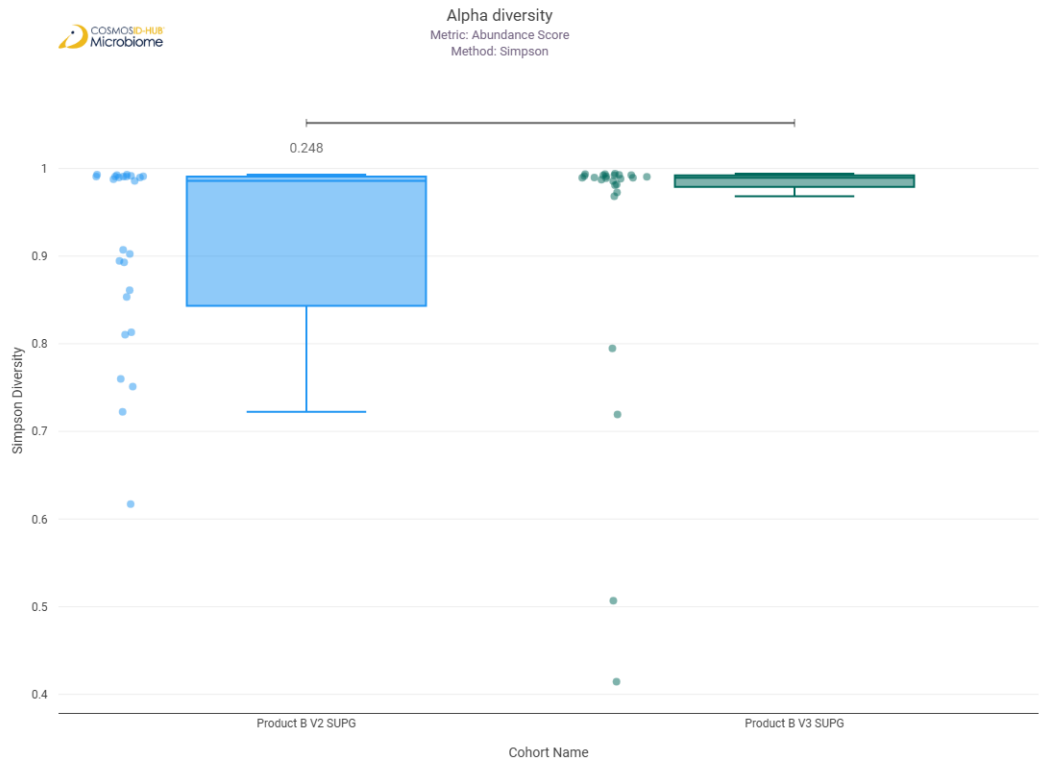
cell wall organization	Product B V3 SUPG	2.025283891	0.021491444
serine-type endopeptidase activity	Product B V3 SUPG	2.015887339	0.006795613

## Enzyme Commission

### Alpha Diversity (EC)

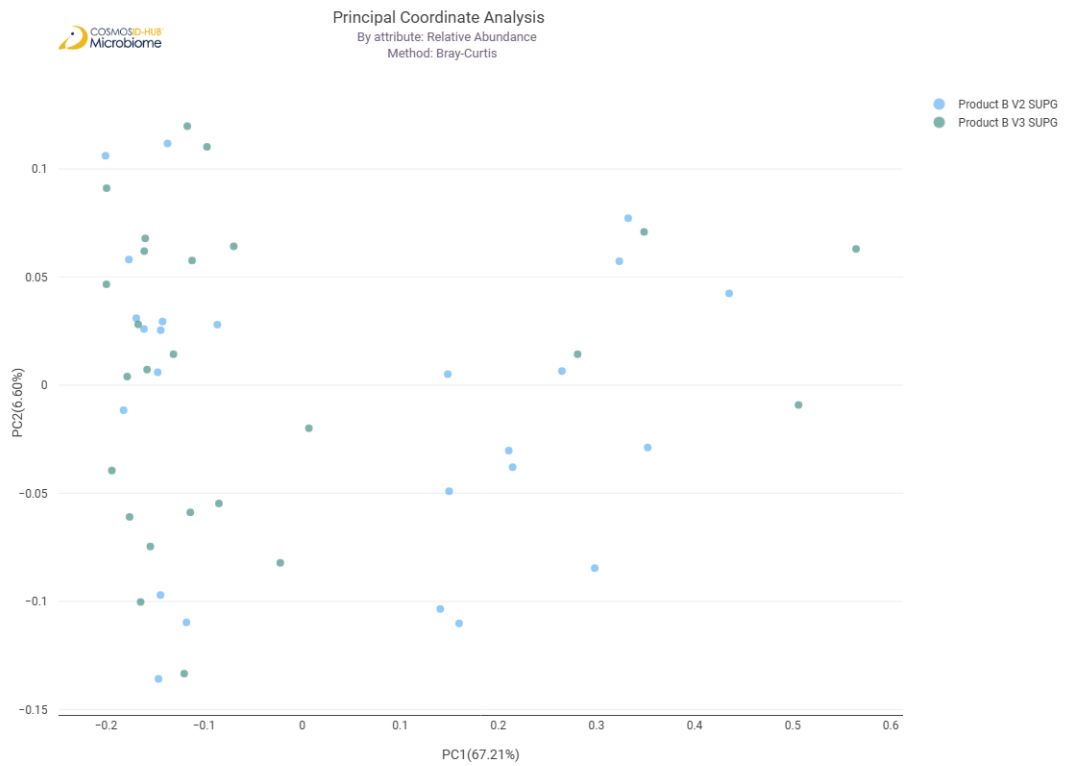


Simpson

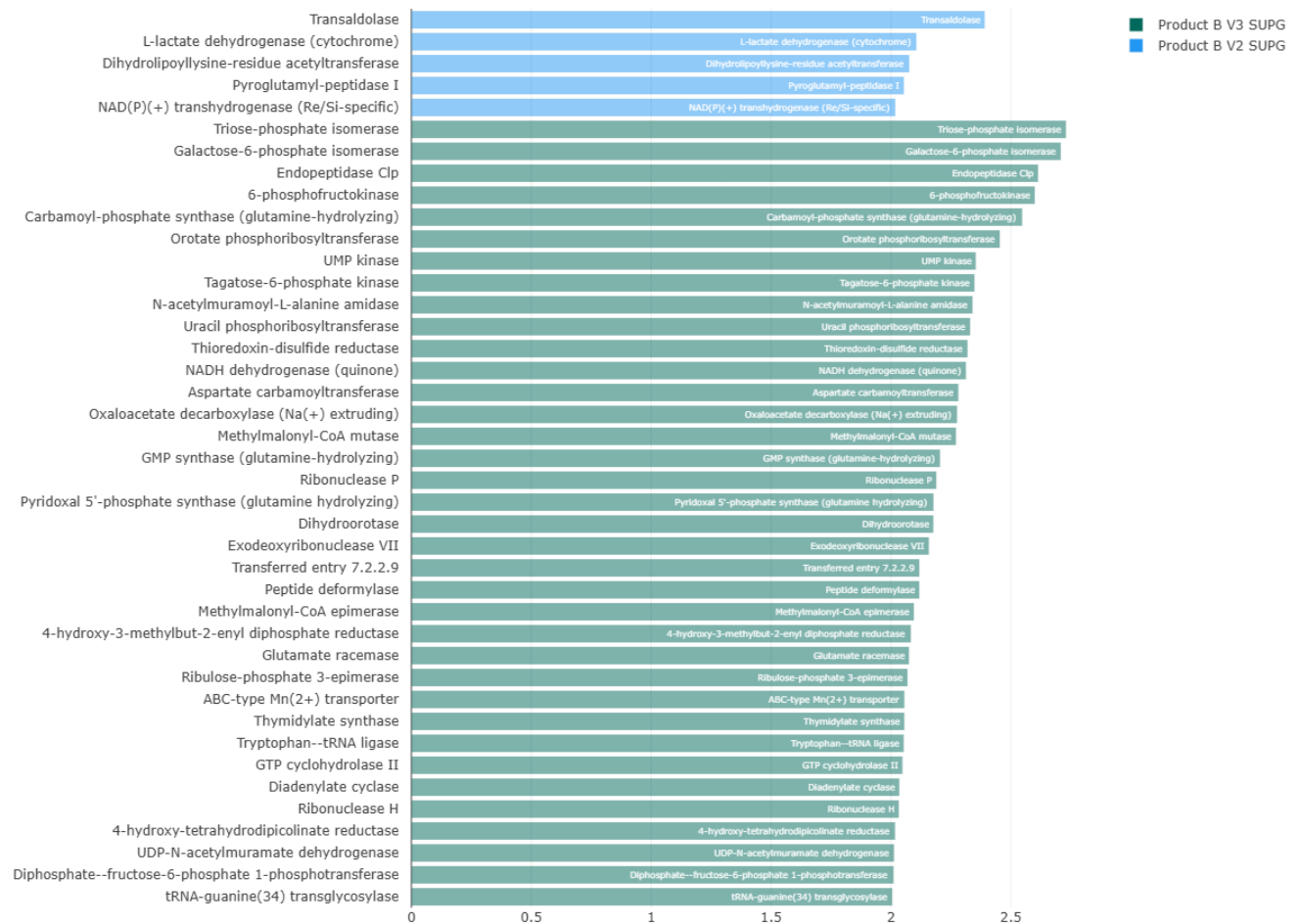


Beta Diversity (EC)

Bray-Curtis  
PERMNOVA  
 $p = 0.166$



## Differential Abundance (LEfSe) (EC)



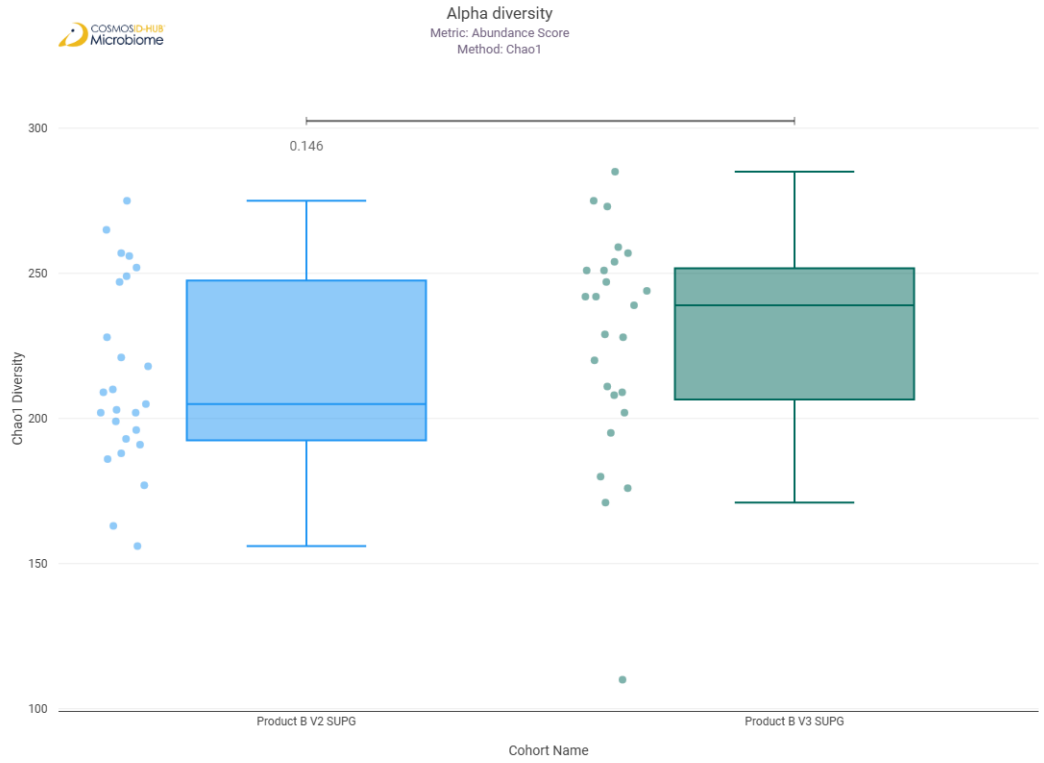
Feature	Enriched Cohort	LDA Score	P-value
Transaldolase	Product B V2 SUPG	2.390769552	0.042601311
L-lactate dehydrogenase (cytochrome)	Product B V2 SUPG	2.105776673	0.005364191
Dihydropyridyllysine-residue acetyltransferase	Product B V2 SUPG	2.07600155	0.0352731
Pyroglutamyl-peptidase I	Product B V2 SUPG	2.053847965	0.033618995
NAD(P)(+) transhydrogenase (Re/Si-specific)	Product B V2 SUPG	2.017837527	1.72E-04
Triose-phosphate isomerase	Product B V3 SUPG	2.729787667	0.042601311
Galactose-6-phosphate isomerase	Product B V3 SUPG	2.708214701	0.048908406
Endopeptidase Clp	Product B V3 SUPG	2.613478253	0.000428923
6-phosphofructokinase	Product B V3 SUPG	2.599739158	0.033618995
Carbamoyl-phosphate synthase (glutamine-hydrolyzing)	Product B V3 SUPG	2.547124164	0.010726809
Orotate phosphoribosyltransferase	Product B V3 SUPG	2.453677511	0.003722992
UMP kinase	Product B V3 SUPG	2.353643566	0.006795613
Tagatose-6-phosphate kinase	Product B V3 SUPG	2.348135378	0.040658018
N-acetylmuramoyl-L-alanine amidase	Product B V3 SUPG	2.34005959	0.008085247

Uracil phosphoribosyltransferase	Product B V3 SUPG	2.330251985	0.009062607
Thioredoxin-disulfide reductase	Product B V3 SUPG	2.319357948	0.032031691
NADH dehydrogenase (quinone)	Product B V3 SUPG	2.312617351	0.008085247
Aspartate carbamoyltransferase	Product B V3 SUPG	2.281069066	0.000709718
Oxaloacetate decarboxylase (Na(+)) extruding)	Product B V3 SUPG	2.275653684	0.014889416
Methylmalonyl-CoA mutase	Product B V3 SUPG	2.271006675	0.004210827
GMP synthase (glutamine-hydrolyzing)	Product B V3 SUPG	2.204584616	0.044622577
Ribonuclease P	Product B V3 SUPG	2.188896914	0.046724152
Pyridoxal 5'-phosphate synthase (glutamine hydrolyzing)	Product B V3 SUPG	2.177234182	0.021491444
Dihydroorotase	Product B V3 SUPG	2.176732496	2.38E-02
Exodeoxyribonuclease VII	Product B V3 SUPG	2.158007478	0.032031691
Transferred entry 7.2.2.9	Product B V3 SUPG	2.118208671	0.042601311
Peptide deformylase	Product B V3 SUPG	2.118113302	0.00640875
Methylmalonyl-CoA epimerase	Product B V3 SUPG	2.095581121	0.040658018
4-hydroxy-3-methylbut-2-enyl diphosphate reductase	Product B V3 SUPG	2.082886492	0.016563699
Glutamate racemase	Product B V3 SUPG	2.075228413	0.019384996
Ribulose-phosphate 3-epimerase	Product B V3 SUPG	2.069042333	0.015706943
ABC-type Mn(2+) transporter	Product B V3 SUPG	2.055859209	0.021460122
Thymidylate synthase	Product B V3 SUPG	2.055573227	0.003722992
Tryptophan--tRNA ligase	Product B V3 SUPG	2.053341932	0.033618995
GTP cyclohydrolase II	Product B V3 SUPG	2.047958835	0.011339073
Diadenylate cyclase	Product B V3 SUPG	2.034732305	0.015706943
Ribonuclease H	Product B V3 SUPG	2.032716664	0.017461229
4-hydroxy-tetrahydrodipicolinate reductase	Product B V3 SUPG	2.017088339	0.006041816
UDP-N-acetylmuramate dehydrogenase	Product B V3 SUPG	2.012642411	0.023794451
Diphosphate--fructose-6-phosphate 1-phosphotransferase	Product B V3 SUPG	2.010879805	0.01265739
tRNA-guanine(34) transglycosylase	Product B V3 SUPG	2.005209166	0.018401118

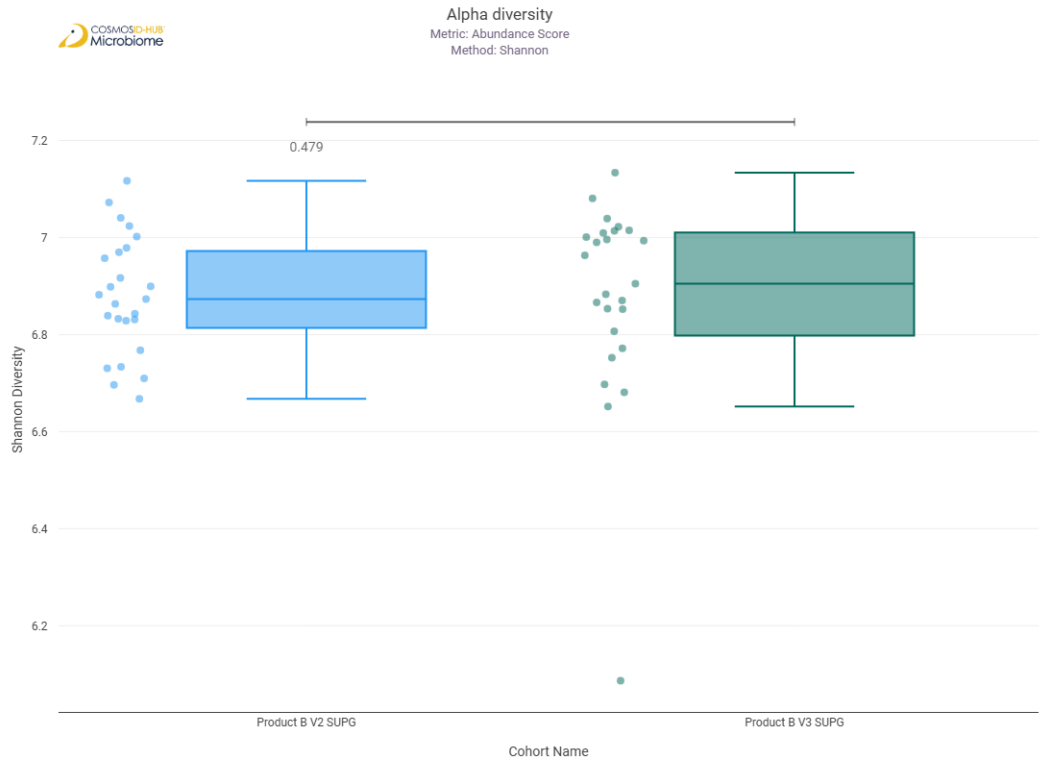
## MetaCyc Pathways

# Alpha Diversity (MetaCyc)

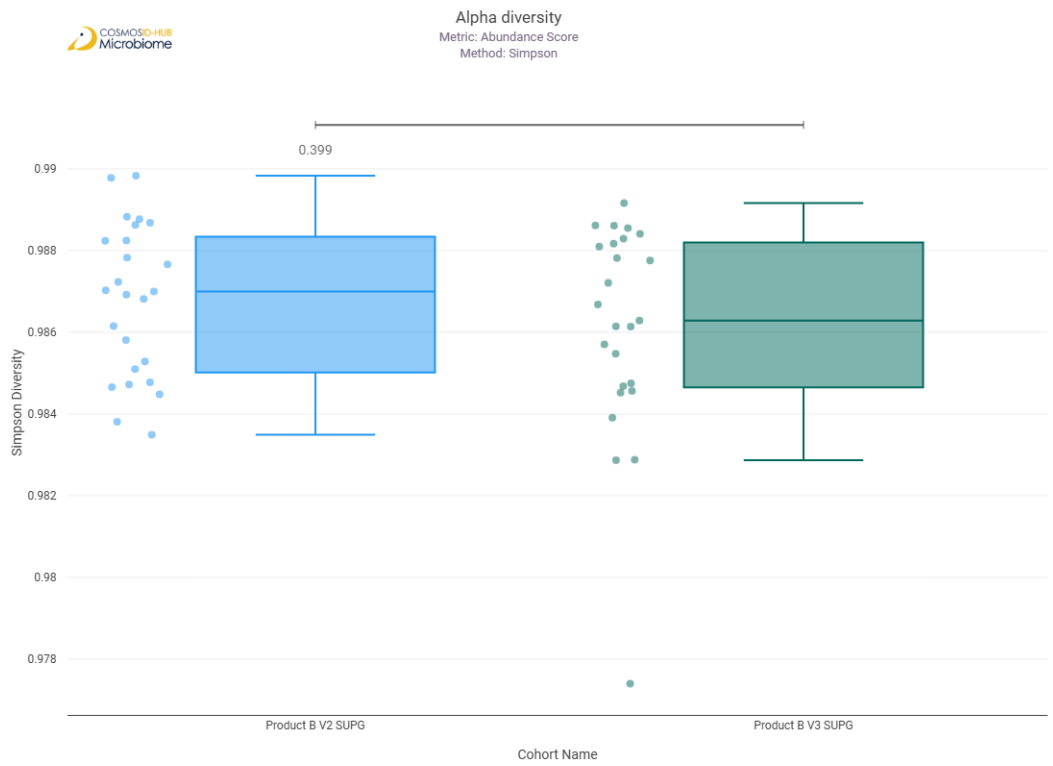
Chao1



Shannon

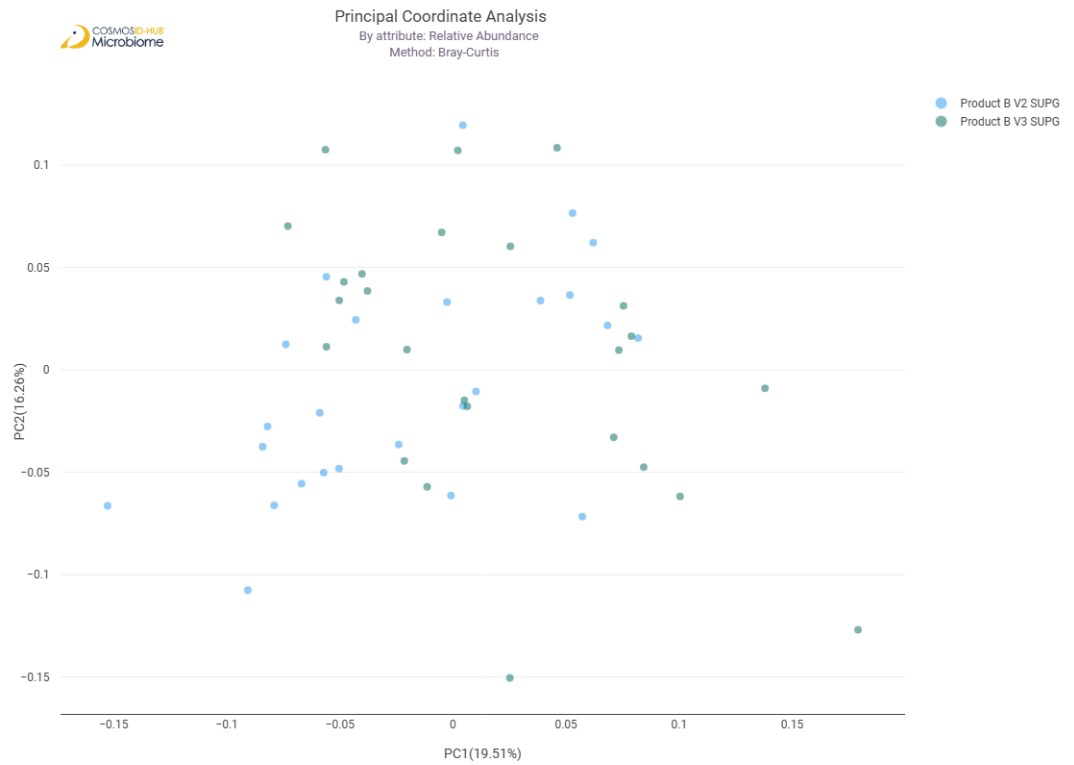


# Simpson

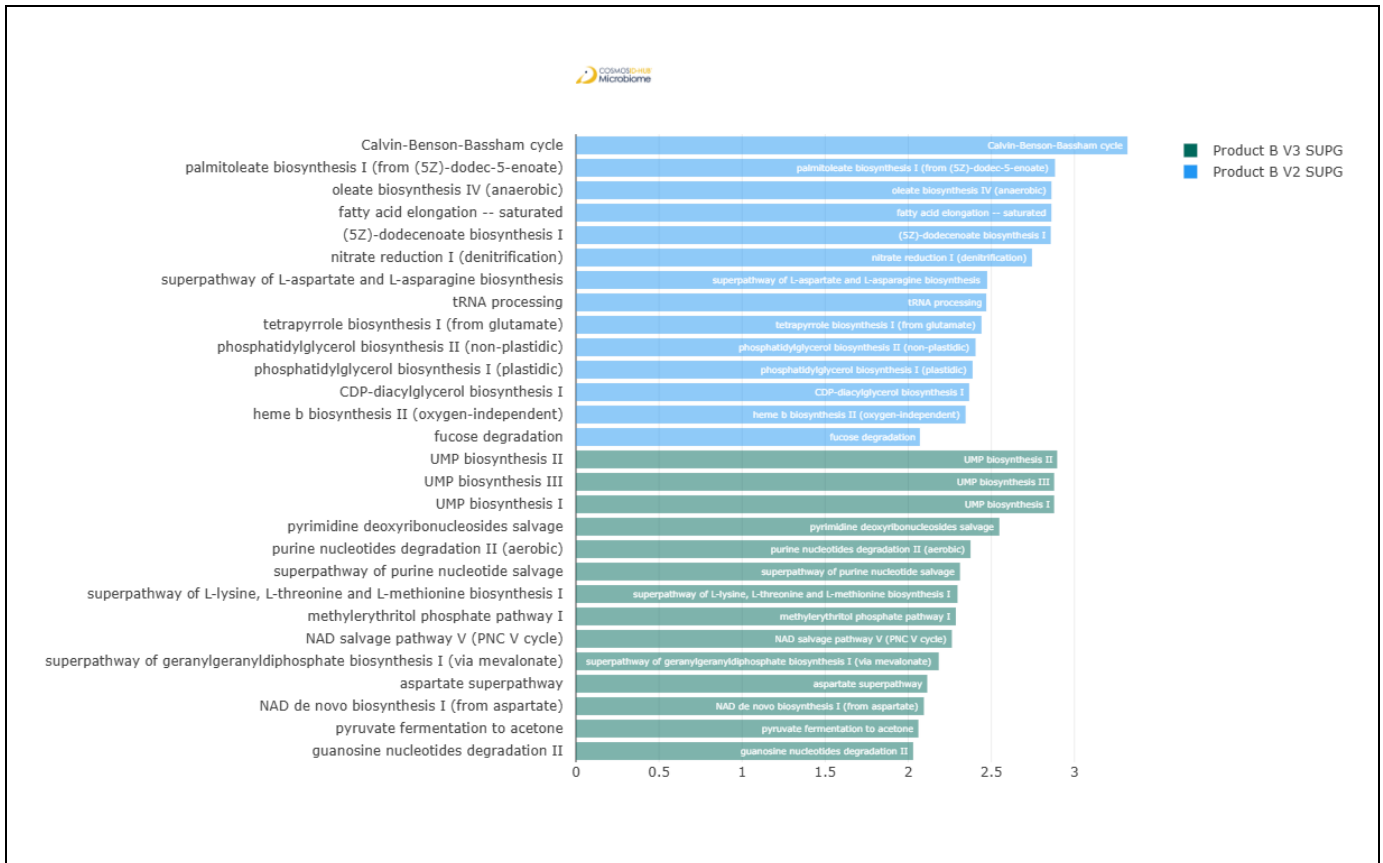


## Beta Diversity (MetaCyc)

Bray-Curtis  
PERMNOVA  
p = 0.044



## Differential Abundance (LEfSe) (MetaCyc)



Feature	Enriched Cohort	LDA Score	P-value
Calvin-Benson-Bassham cycle	Product B V2 SUPG	3.318964082	0.002102544
palmitoleate biosynthesis I (from (5Z)-dodec-5-enoate)	Product B V2 SUPG	2.883013913	0.018401118
oleate biosynthesis IV (anaerobic)	Product B V2 SUPG	2.86144877	0.020414533
fatty acid elongation -- saturated	Product B V2 SUPG	2.861077094	0.022617484
(5Z)-dodecenoate biosynthesis I	Product B V2 SUPG	2.857405063	0.025024185
nitrate reduction I (denitrification)	Product B V2 SUPG	2.744568111	0.022585015
superpathway of L-aspartate and L-asparagine biosynthesis	Product B V2 SUPG	2.474947946	0.026308569
tRNA processing	Product B V2 SUPG	2.469238055	0.029067013
tetrapyrrole biosynthesis I (from glutamate)	Product B V2 SUPG	2.440540879	0.039710137
phosphatidylglycerol biosynthesis II (non-plastidic)	Product B V2 SUPG	2.404869686	0.044602091
phosphatidylglycerol biosynthesis I (plastidic)	Product B V2 SUPG	2.387244196	0.048902981
CDP-diacylglycerol biosynthesis I	Product B V2 SUPG	2.366479671	0.048902981
heme b biosynthesis II (oxygen-independent)	Product B V2 SUPG	2.344926162	0.013357193
fucose degradation	Product B V2 SUPG	2.069795282	0.032608192
UMP biosynthesis II	Product B V3 SUPG	2.896161476	0.001077834
UMP biosynthesis I	Product B V3 SUPG	2.877911888	0.002243495
UMP biosynthesis III	Product B V3 SUPG	2.877911888	2.24E-03
pyrimidine deoxyribonucleosides salvage	Product B V3 SUPG	2.548343874	0.020414533
purine nucleotides degradation II (aerobic)	Product B V3 SUPG	2.374685324	0.012279495
superpathway of purine nucleotide salvage	Product B V3 SUPG	2.311473792	0.021218334
superpathway of L-lysine, L-threonine and L-methionine biosynthesis I	Product B V3 SUPG	2.296487754	0.042729021

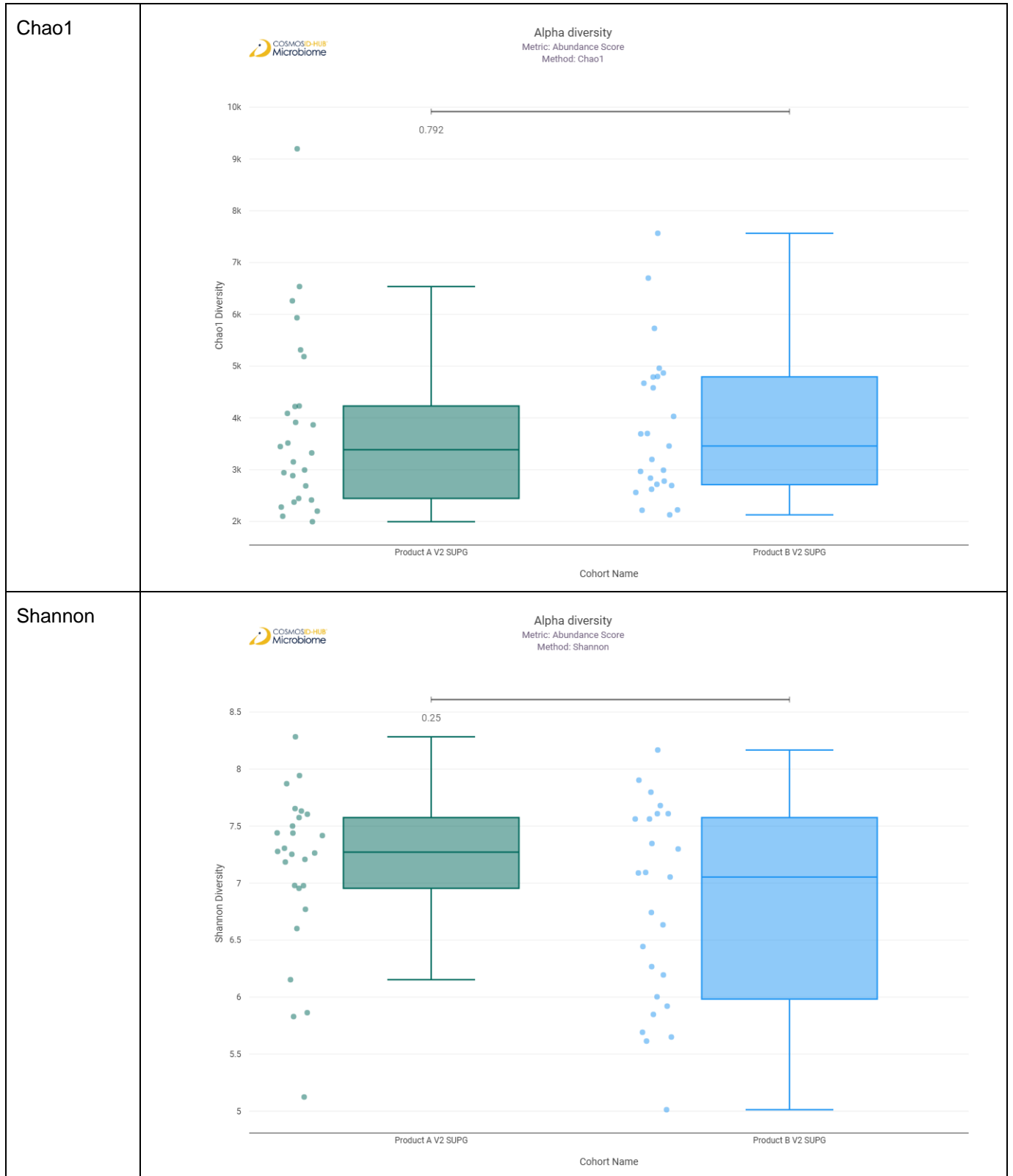


methylethritol phosphate pathway I	Product B V3 SUPG	2.286396655	0.033576403
NAD salvage pathway V (PNC V cycle)	Product B V3 SUPG	2.262555783	0.007877552
superpathway of geranylgeranyldiphosphate biosynthesis I (via mevalonate)	Product B V3 SUPG	2.183446506	0.037096259
aspartate superpathway	Product B V3 SUPG	2.114483365	1.29E-02
NAD de novo biosynthesis I (from aspartate)	Product B V3 SUPG	2.094212339	0.018497446
pyruvate fermentation to acetone	Product B V3 SUPG	2.061285087	0.040706043
guanosine nucleotides degradation II	Product B V3 SUPG	2.029587133	0.011292706

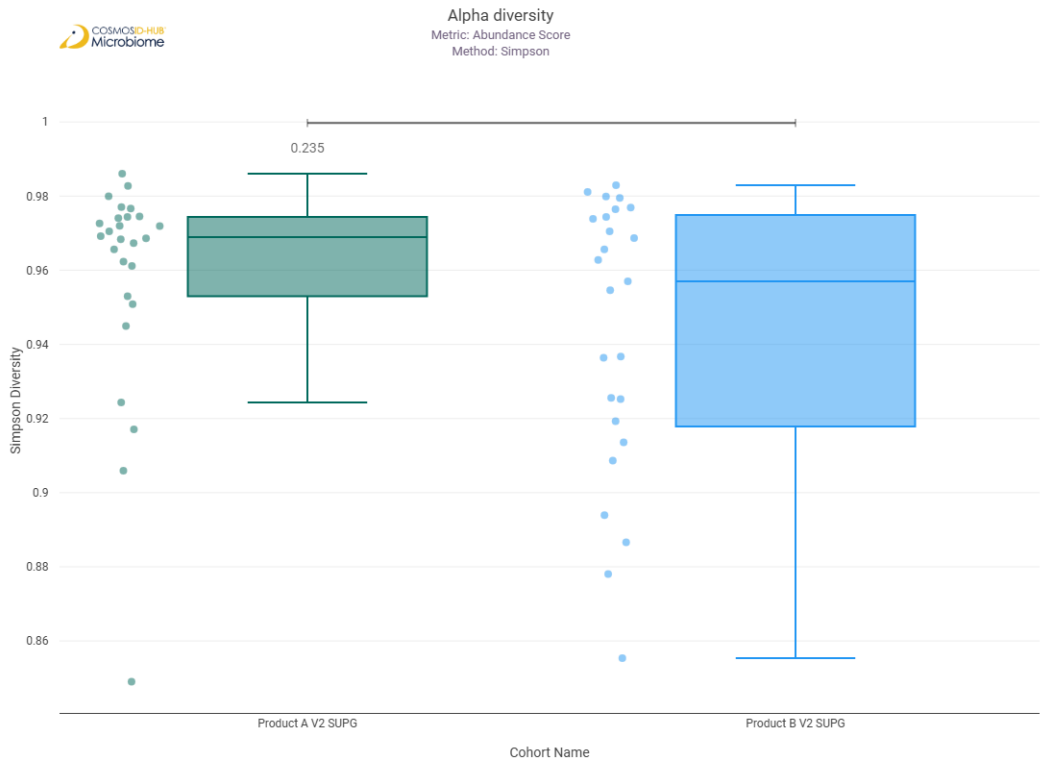
# Comparison 15: Product A V2 SUPG vs Product B V2 SUPG

## Gene Ontology

### Alpha Diversity (GO)

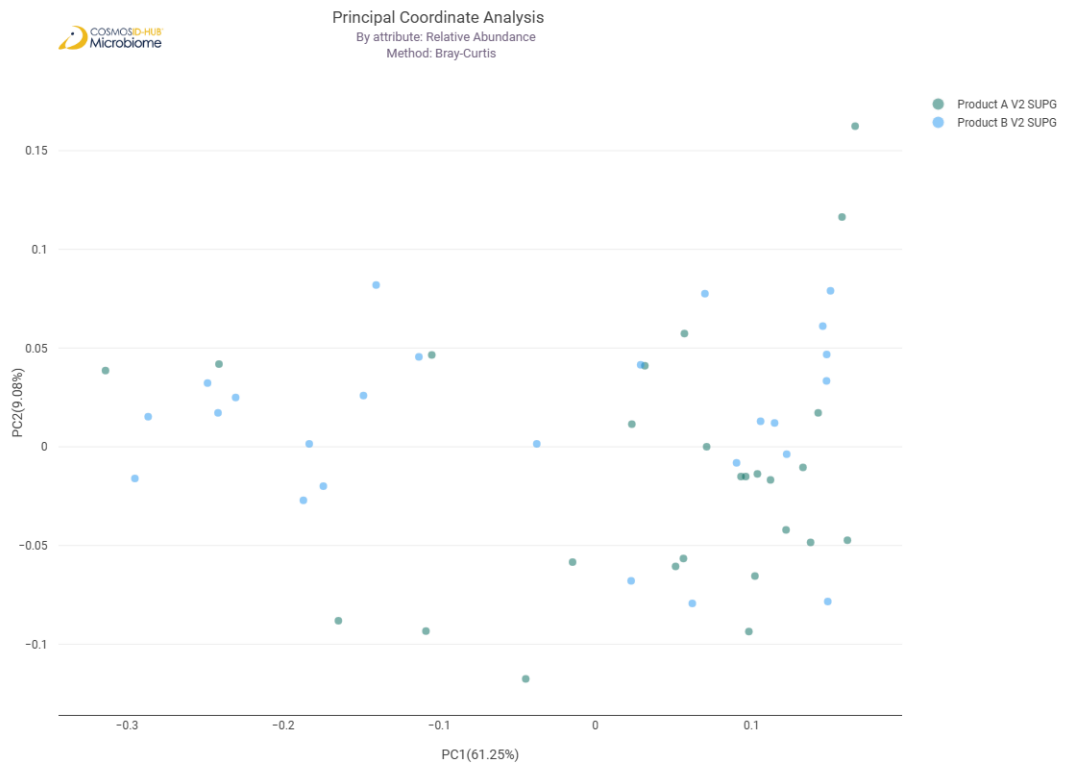


# Simpson

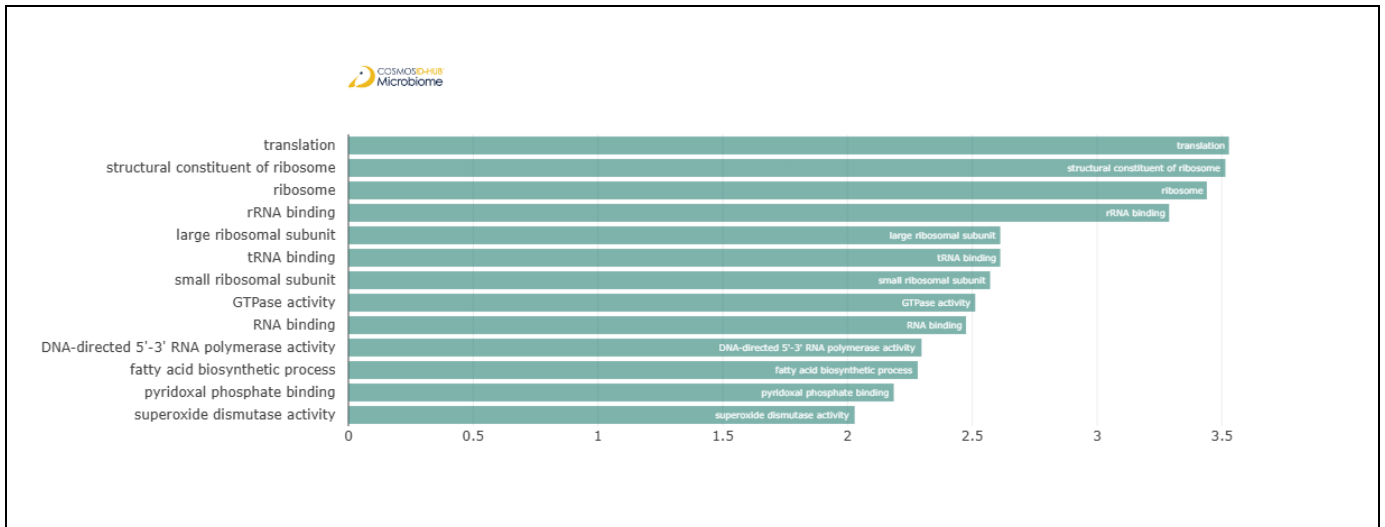


## Beta Diversity (GO)

Bray-Curtis  
PERMNOVA  
 $p = 0.067$



## Differential Abundance (LEfSe) (GO)

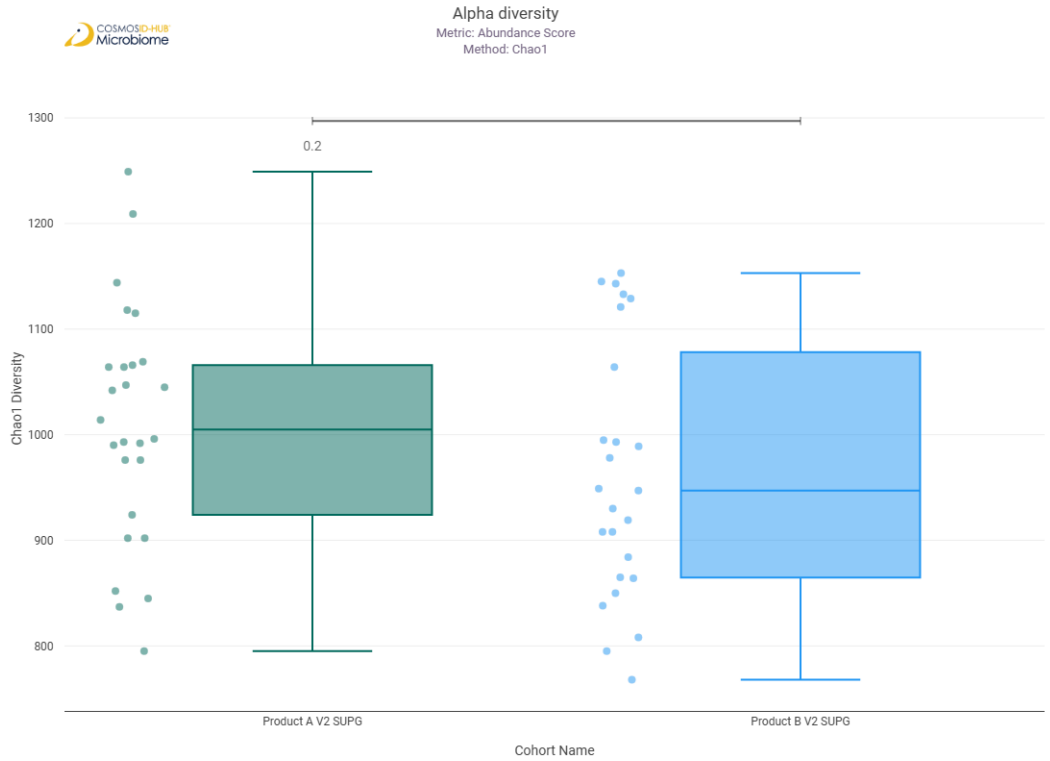


Feature	Enriched Cohort	LDA Score	P-value
translation	Product A V2 SUPG	3.528322109	0.020471389
structural constituent of ribosome	Product A V2 SUPG	3.514165407	0.022613046
ribosome	Product A V2 SUPG	3.439853578	0.017590793
rRNA binding	Product A V2 SUPG	3.288581331	0.033240045
large ribosomal subunit	Product A V2 SUPG	2.612173486	0.02494682
tRNA binding	Product A V2 SUPG	2.612099379	0.047879765
small ribosomal subunit	Product A V2 SUPG	2.571517429	0.034829974
GTPase activity	Product A V2 SUPG	2.511887932	0.036484395
RNA binding	Product A V2 SUPG	2.474828575	0.022613046
DNA-directed 5'-3' RNA polymerase activity	Product A V2 SUPG	2.296592301	0.038205314
fatty acid biosynthetic process	Product A V2 SUPG	2.281471017	0.009840467
pyridoxal phosphate binding	Product A V2 SUPG	2.185362531	0.036484395
superoxide dismutase activity	Product A V2 SUPG	2.028763107	0.020471389

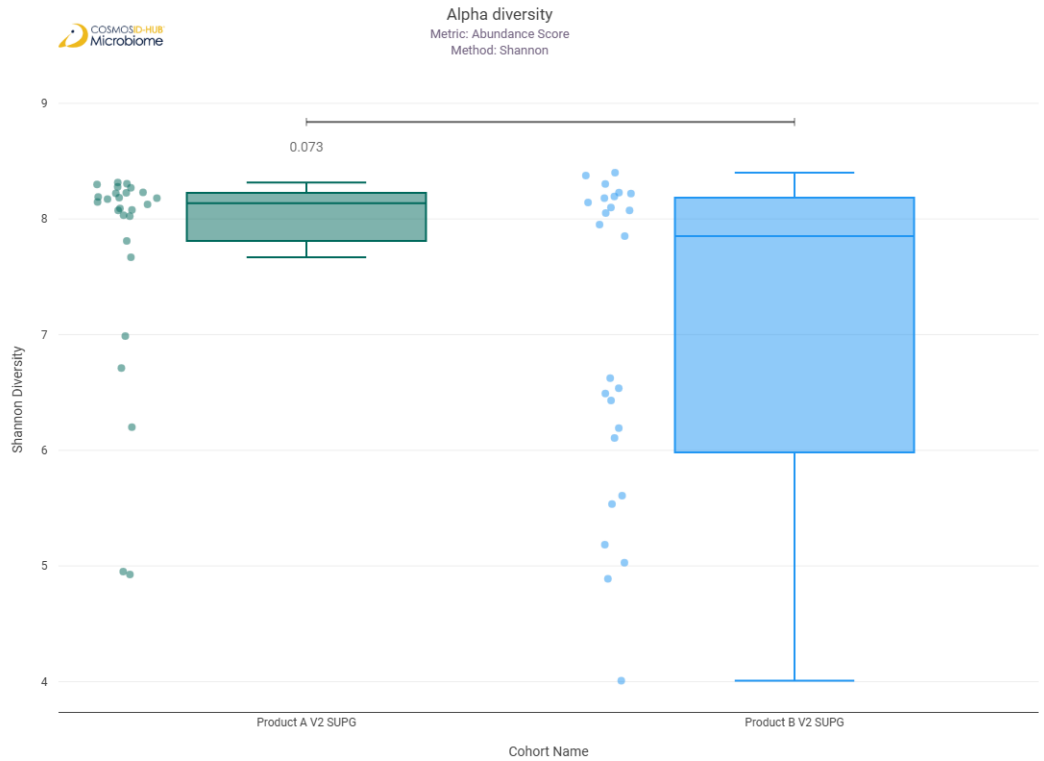
## Enzyme Commission

# Alpha Diversity (EC)

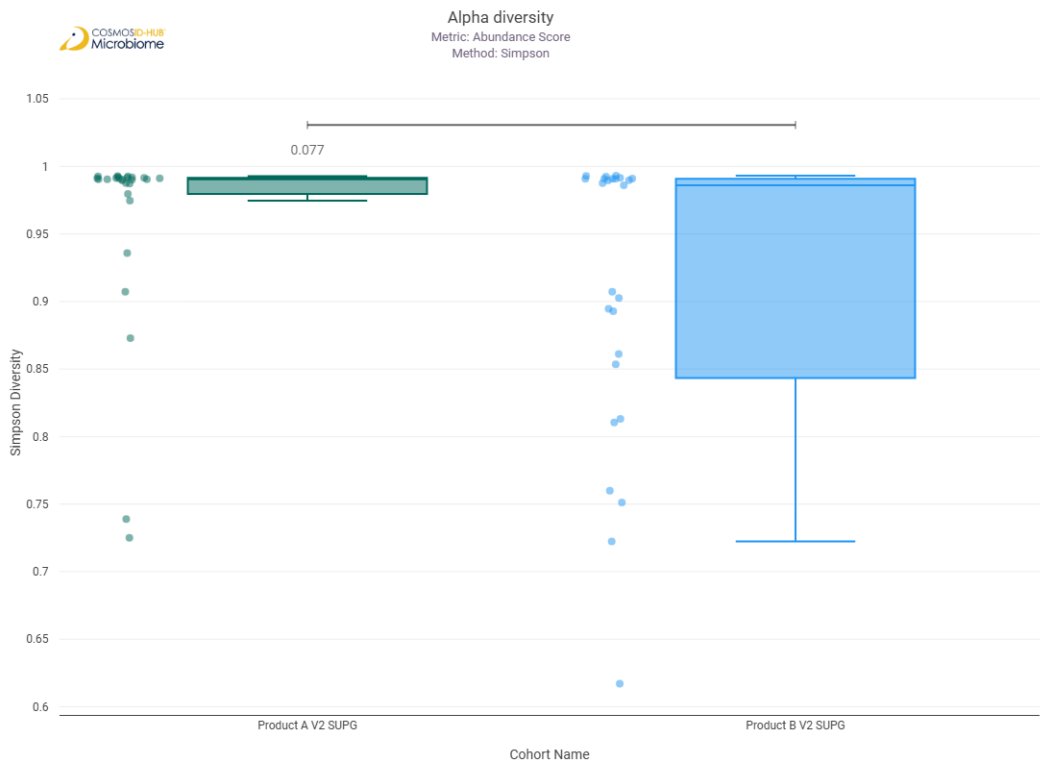
Chao1



Shannon

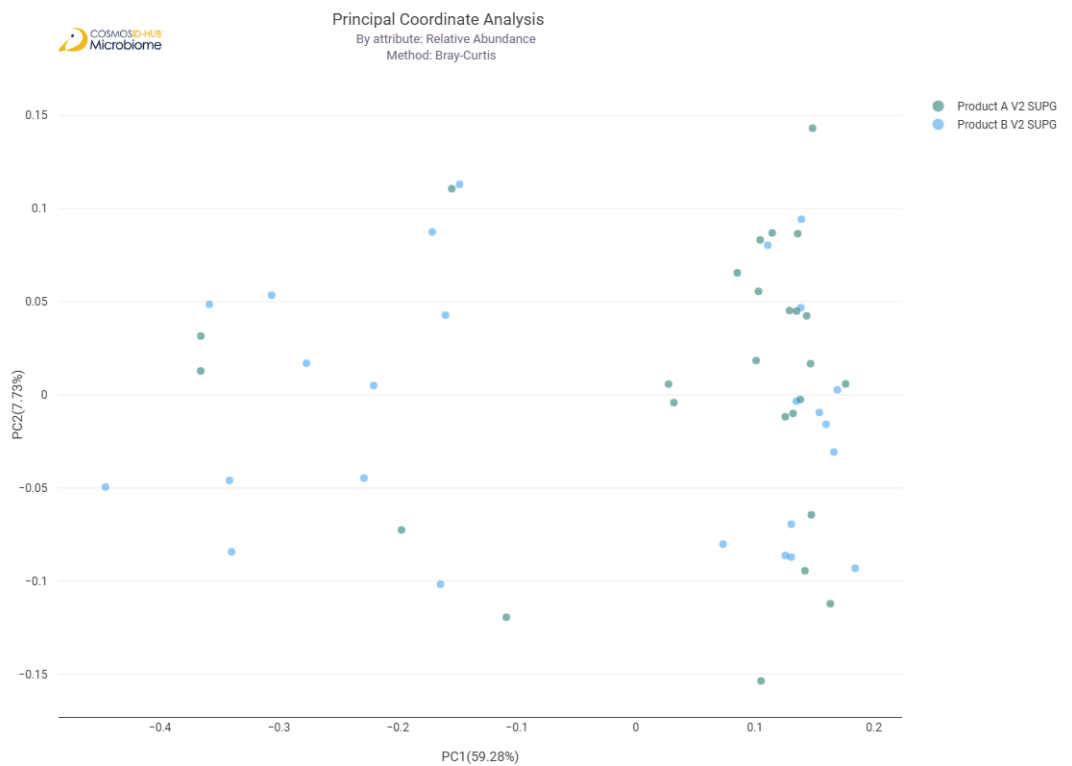


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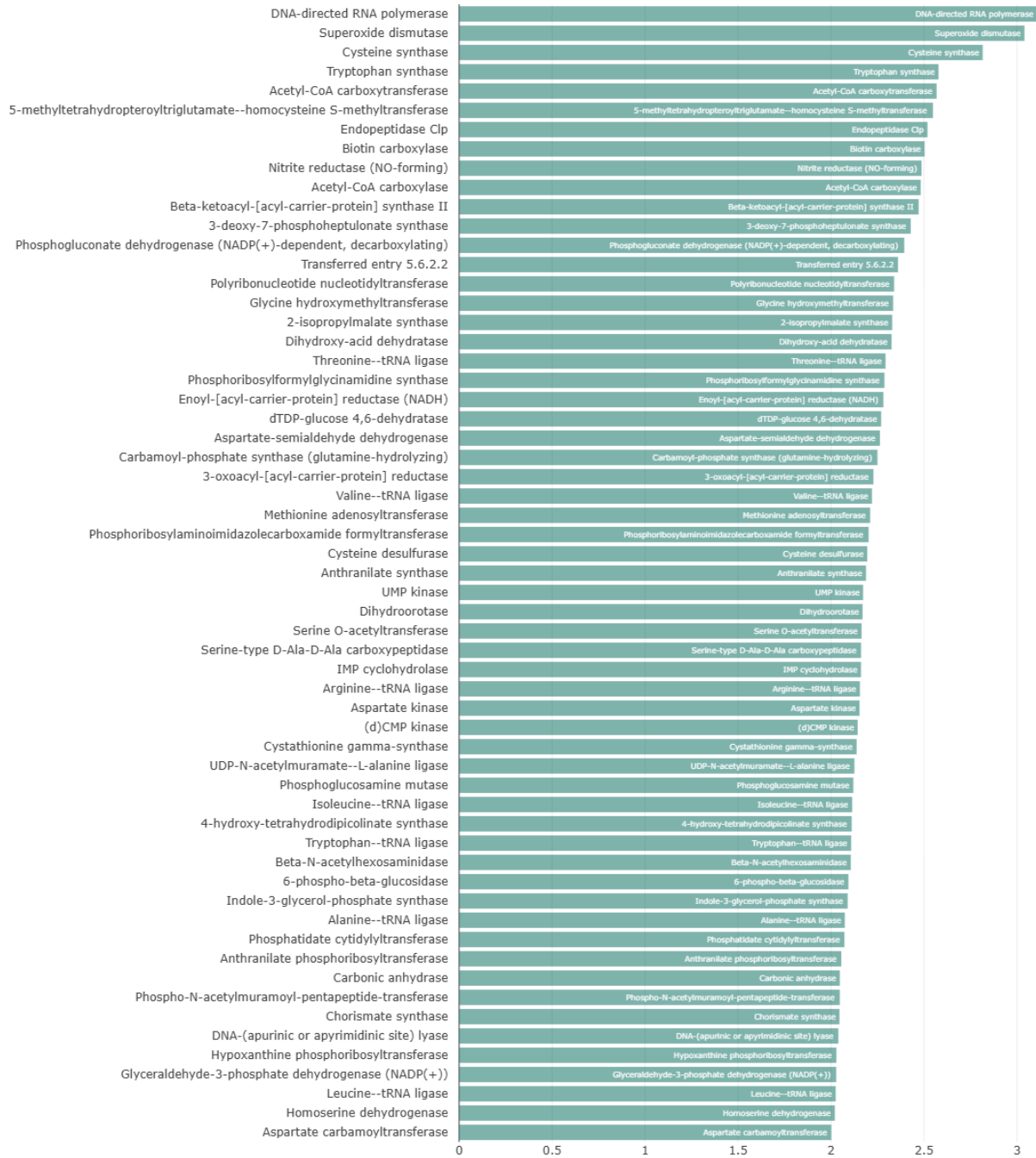


## Beta Diversity (EC)

Bray-Curtis  
PERMNOVA  
 $p = 0.036$



## Differential Abundance (LEfSe) (EC)



Feature	Enriched Cohort	LDA Score	P-value
DNA-directed RNA polymerase	Product A V2 SUPG	3.111020333	0.02375508
Superoxide dismutase	Product A V2 SUPG	3.040013385	0.011574483
Cysteine synthase	Product A V2 SUPG	2.815737109	0.001548196
Tryptophan synthase	Product A V2 SUPG	2.577744157	0.000276314

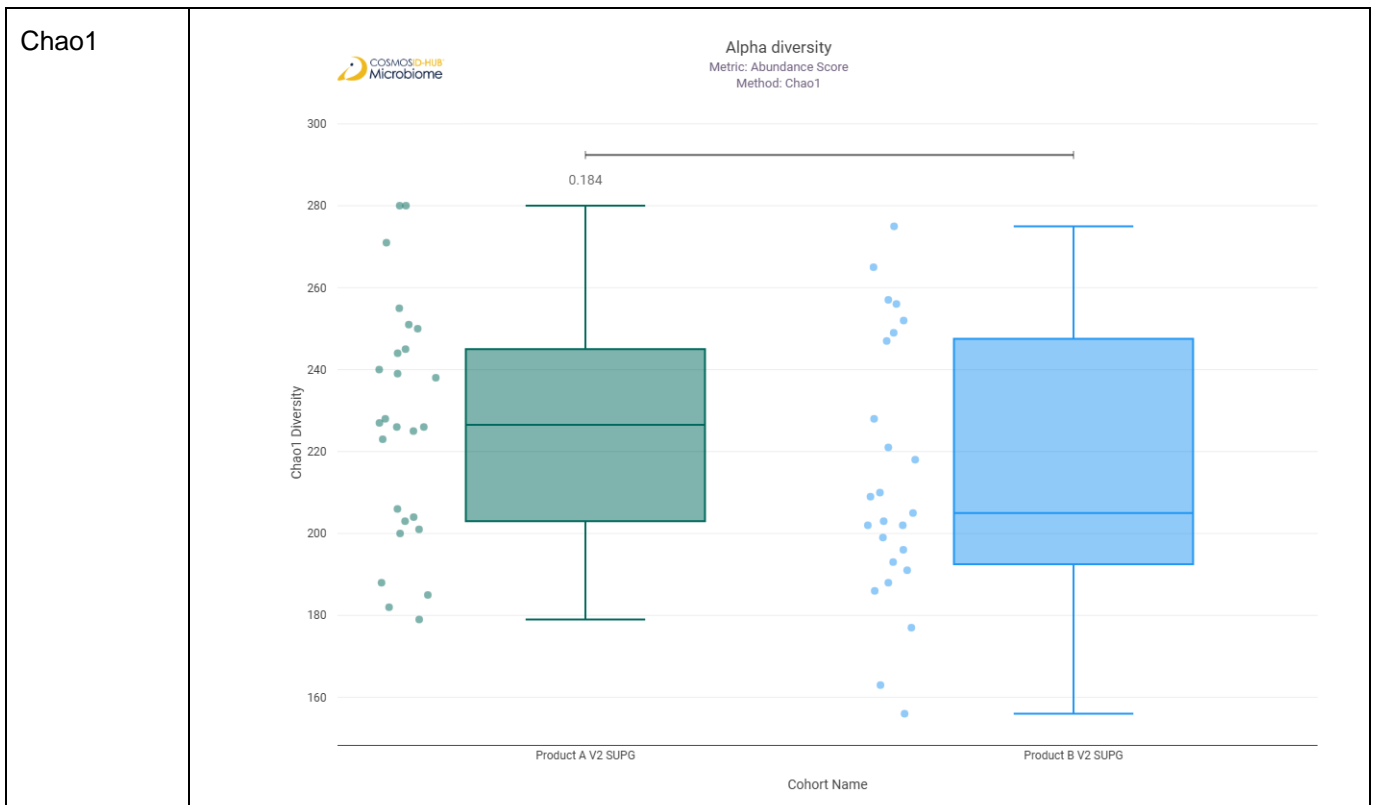
Acetyl-CoA carboxytransferase	Product A V2 SUPG	2.567719746	0.007889693
5-methyltetrahydropteroyltriglutamate--homocysteine S-methyltransferase	Product A V2 SUPG	2.547962006	0.036484395
Endopeptidase Clp	Product A V2 SUPG	2.518826283	0.006292761
Biotin carboxylase	Product A V2 SUPG	2.502821472	0.015873756
Nitrite reductase (NO-forming)	Product A V2 SUPG	2.486578655	0.030245812
Acetyl-CoA carboxylase	Product A V2 SUPG	2.482112113	0.038205314
Beta-ketoacyl-[acyl-carrier-protein] synthase II	Product A V2 SUPG	2.471132956	0.016712924
3-deoxy-7-phosphoheptulonate synthase	Product A V2 SUPG	2.428626553	0.020471389
Phosphogluconate dehydrogenase (NADP(+)-dependent, decarboxylating)	Product A V2 SUPG	2.393945069	0.039994768
Transferred entry 5.6.2.2	Product A V2 SUPG	2.360090893	0.010968497
Polyribonucleotide nucleotidyltransferase	Product A V2 SUPG	2.339073295	0.034829974
Glycine hydroxymethyltransferase	Product A V2 SUPG	2.334029314	0.038205314
2-isopropylmalate synthase	Product A V2 SUPG	2.328902169	1.43E-02
Dihydroxy-acid dehydratase	Product A V2 SUPG	2.325621312	0.015873756
Threonine--tRNA ligase	Product A V2 SUPG	2.293236056	0.016712924
Phosphoribosylformylglycinamide synthase	Product A V2 SUPG	2.287096387	0.02375508
Enoyl-[acyl-carrier-protein] reductase (NADH)	Product A V2 SUPG	2.281565459	0.013574437
dTDP-glucose 4,6-dehydratase	Product A V2 SUPG	2.269477405	0.005941992
Aspartate-semialdehyde dehydrogenase	Product A V2 SUPG	2.263052348	0.012209995
Carbamoyl-phosphate synthase (glutamine-hydrolyzing)	Product A V2 SUPG	2.249725795	0.010968497
3-oxoacyl-[acyl-carrier-protein] reductase	Product A V2 SUPG	2.228019455	4.58E-02
Valine--tRNA ligase	Product A V2 SUPG	2.220189052	0.005608941
Methionine adenosyltransferase	Product A V2 SUPG	2.210159621	0.002416555
Phosphoribosylaminoimidazolecarboxamide formyltransferase	Product A V2 SUPG	2.202152483	0.00881699
Cysteine desulfurase	Product A V2 SUPG	2.194846541	0.015873756
Anthranilate synthase	Product A V2 SUPG	2.188027235	0.000177114
UMP kinase	Product A V2 SUPG	2.17234657	0.038205314
Dihydroorotase	Product A V2 SUPG	2.169410392	0.02375508
Serine O-acetyltransferase	Product A V2 SUPG	2.164156919	0.031712637
Serine-type D-Ala-D-Ala carboxypeptidase	Product A V2 SUPG	2.161571218	0.026189985
IMP cyclohydrolase	Product A V2 SUPG	2.161164207	0.012209995
Arginine--tRNA ligase	Product A V2 SUPG	2.15520944	0.038205314
Aspartate kinase	Product A V2 SUPG	2.15326488	0.014305878
(d)CMP kinase	Product A V2 SUPG	2.143007637	0.017590793
Cystathionine gamma-synthase	Product A V2 SUPG	2.137563453	0.007889693
UDP-N-acetylmuramate--L-alanine ligase	Product A V2 SUPG	2.125778796	0.02375508
Phosphoglucosamine mutase	Product A V2 SUPG	2.120102518	0.028837668
Isoleucine--tRNA ligase	Product A V2 SUPG	2.113675052	0.002000719
4-hydroxy-tetrahydrodipicolinate synthase	Product A V2 SUPG	2.111127915	0.015071869
Tryptophan--tRNA ligase	Product A V2 SUPG	2.108140128	0.003711399
Beta-N-acetylhexosaminidase	Product A V2 SUPG	2.106142229	0.011574483
6-phospho-beta-glucosidase	Product A V2 SUPG	2.093597012	0.015873756
Indole-3-glycerol-phosphate synthase	Product A V2 SUPG	2.089718618	0.004183032
Alanine--tRNA ligase	Product A V2 SUPG	2.074156106	0.007050729
Phosphatidate cytidyltransferase	Product A V2 SUPG	2.071961346	0.003711399
Anthranilate phosphoribosyltransferase	Product A V2 SUPG	2.055331504	0.002910155



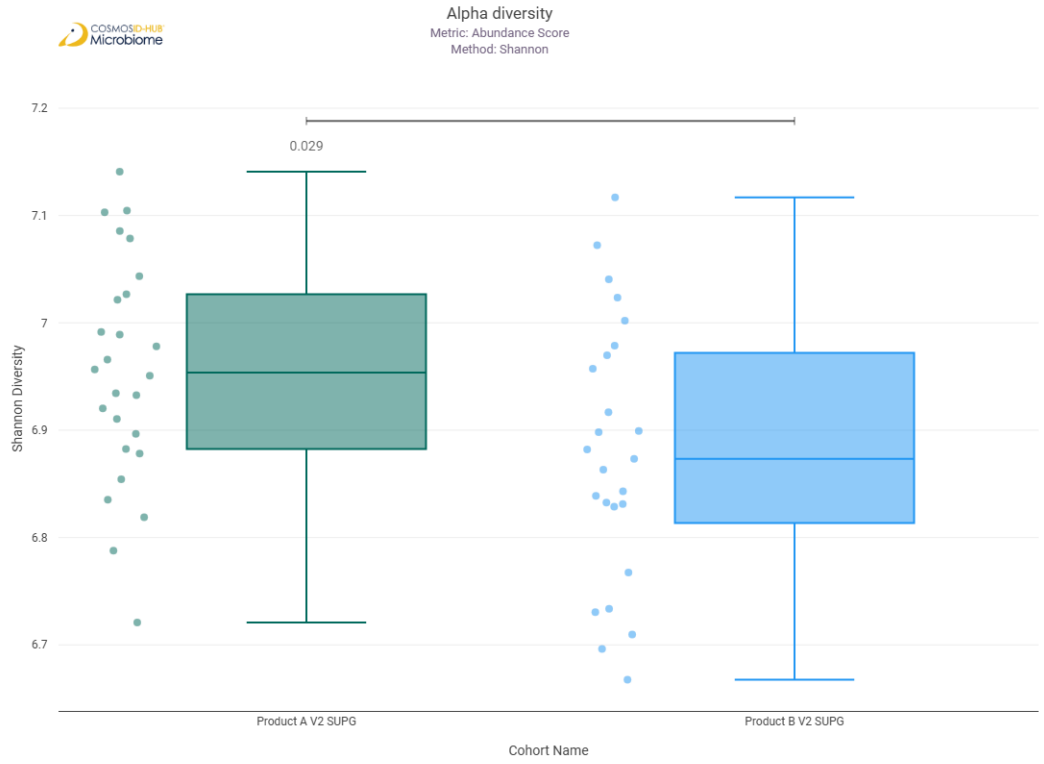
Carbonic anhydrase	Product A V2 SUPG	2.047193511	0.01946851
Phospho-N-acetylmuramoyl-pentapeptide-transferase	Product A V2 SUPG	2.04715419	0.045795182
Chorismate synthase	Product A V2 SUPG	2.045269032	0.034829974
DNA-(apurinic or apyrimidinic site) lyase	Product A V2 SUPG	2.039280143	0.015071869
Hypoxanthine phosphoribosyltransferase	Product A V2 SUPG	2.028740275	0.039994768
Glyceraldehyde-3-phosphate dehydrogenase (NADP(+))	Product A V2 SUPG	2.027884467	0.012762404
Leucine--tRNA ligase	Product A V2 SUPG	2.025092427	0.028837668
Homoserine dehydrogenase	Product A V2 SUPG	2.020459585	0.010390869
Aspartate carbamoyltransferase	Product A V2 SUPG	2.001420241	0.00745964

## MetaCyc Pathways

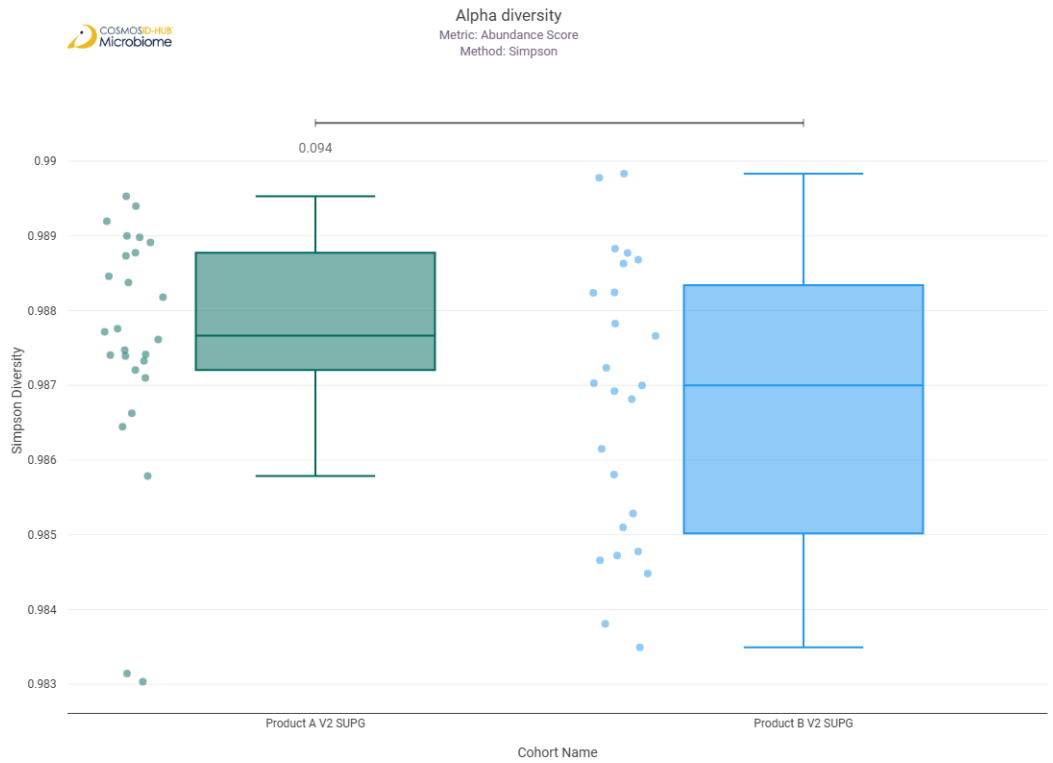
### Alpha Diversity (MetaCyc)



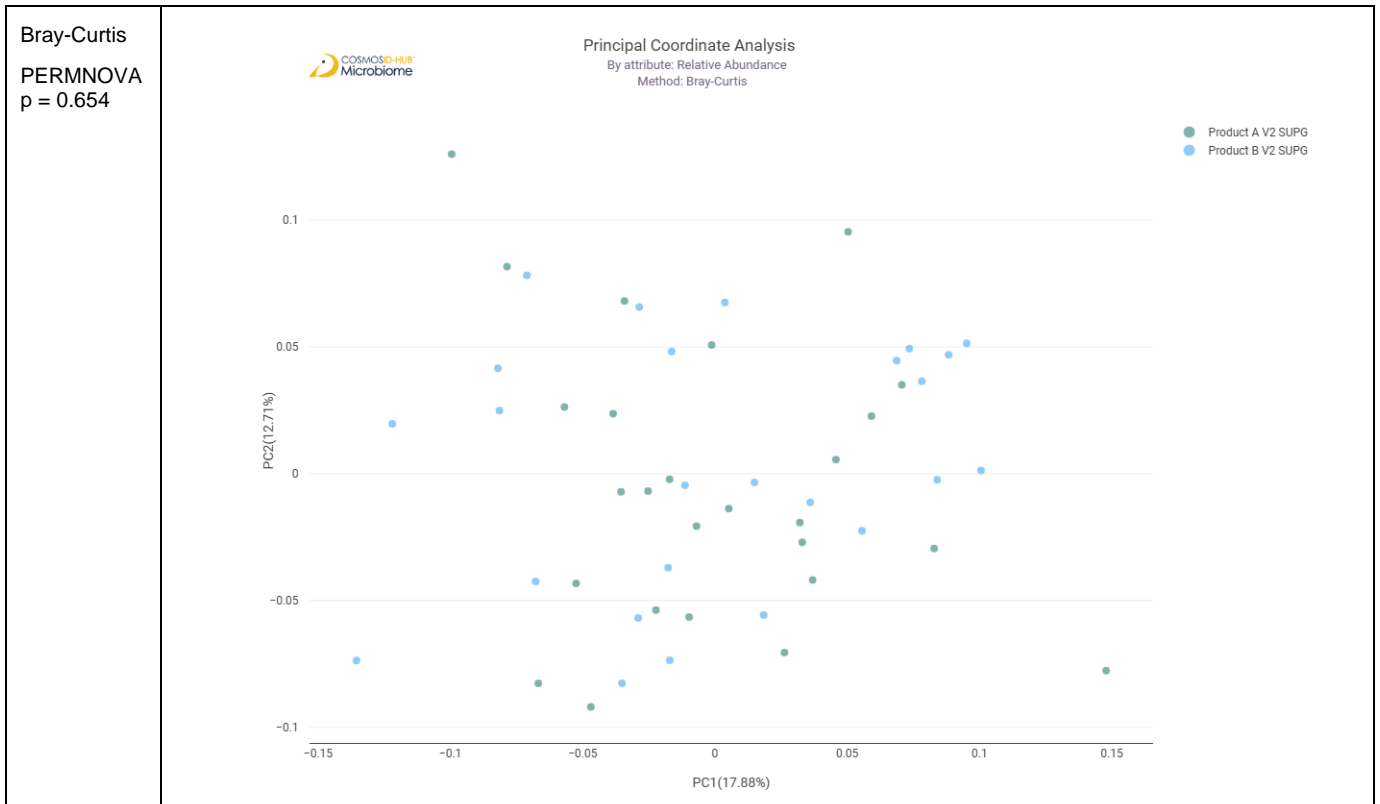
Shannon



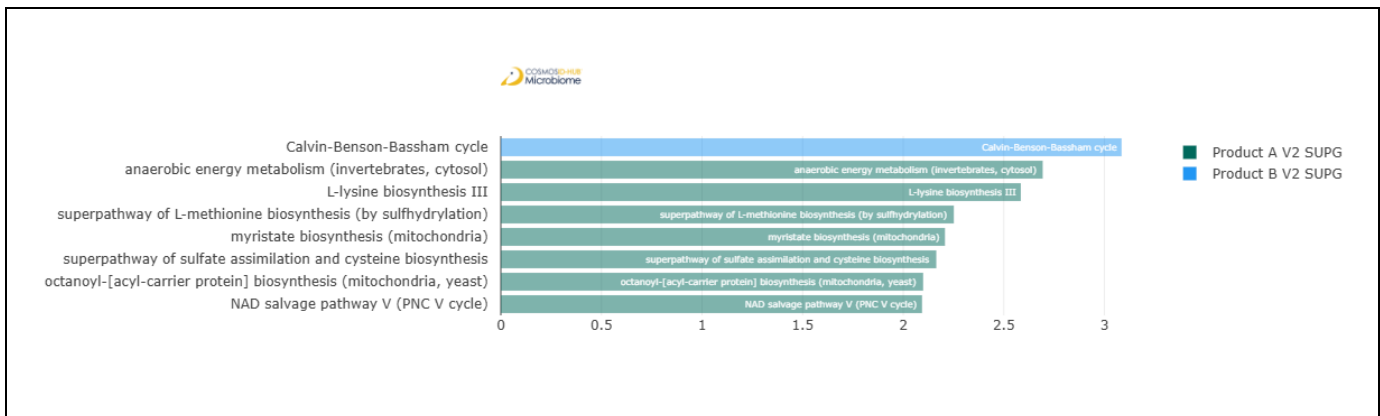
Simpson



## Beta Diversity (MetaCyc)



## Differential Abundance (LEfSe) (MetaCyc)

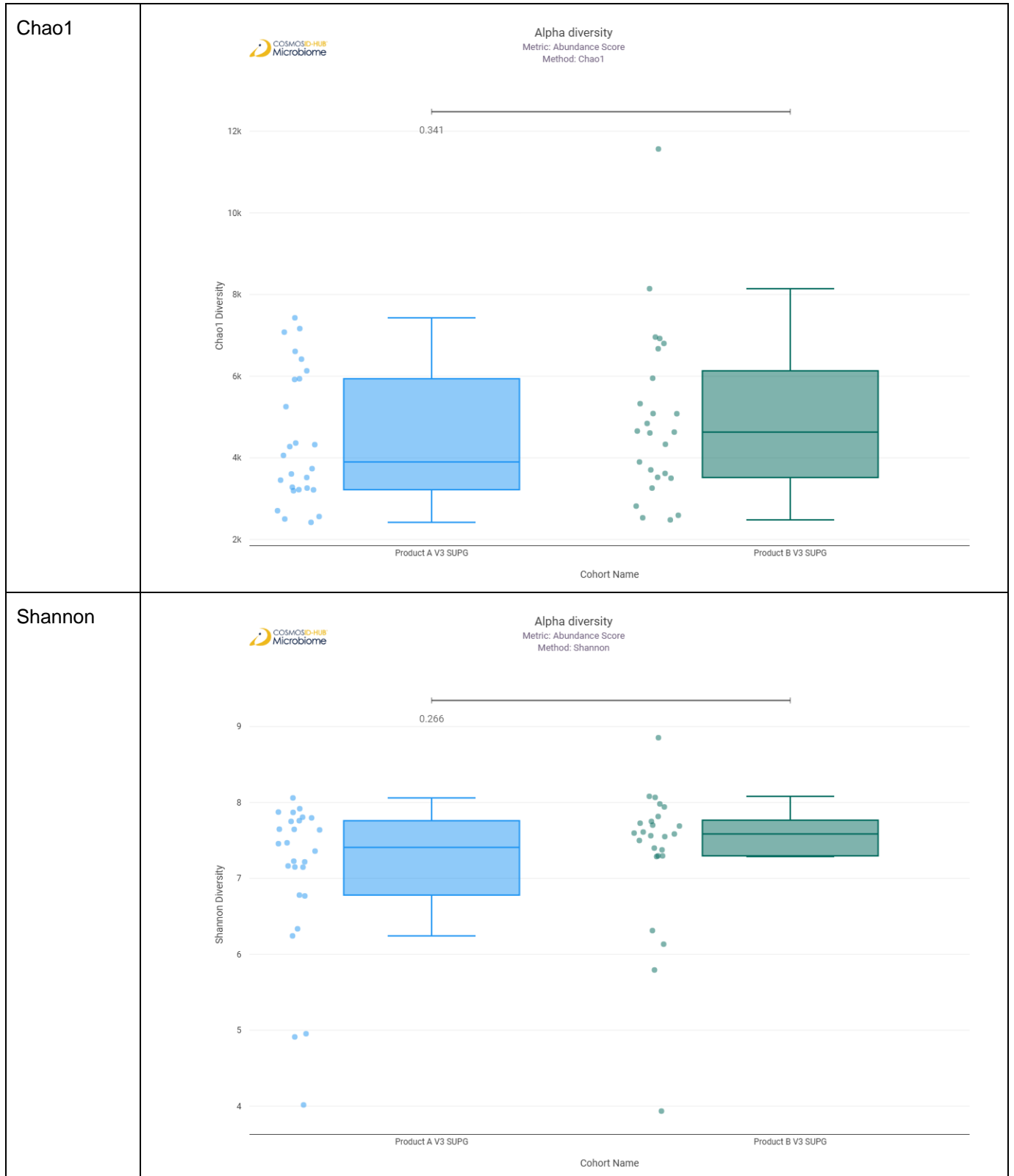


Feature	Enriched Cohort	LDA Score	P-value
Calvin-Benson-Bassham cycle	Product B V2 SUPG	3.085510466	0.047879765
anaerobic energy metabolism (invertebrates, cytosol)	Product A V2 SUPG	2.693616266	0.018508823
L-lysine biosynthesis III	Product A V2 SUPG	2.584864736	0.012209995
superpathway of L-methionine biosynthesis (by sulfhydrylation)	Product A V2 SUPG	2.251777445	0.005206458
myristate biosynthesis (mitochondria)	Product A V2 SUPG	2.207702327	0.001041621
superpathway of sulfate assimilation and cysteine biosynthesis	Product A V2 SUPG	2.164724922	0.003030685
octanoyl-[acyl-carrier protein] biosynthesis (mitochondria, yeast)	Product A V2 SUPG	2.099384673	0.005433155
NAD salvage pathway V (PNC V cycle)	Product A V2 SUPG	2.093878625	0.03882039

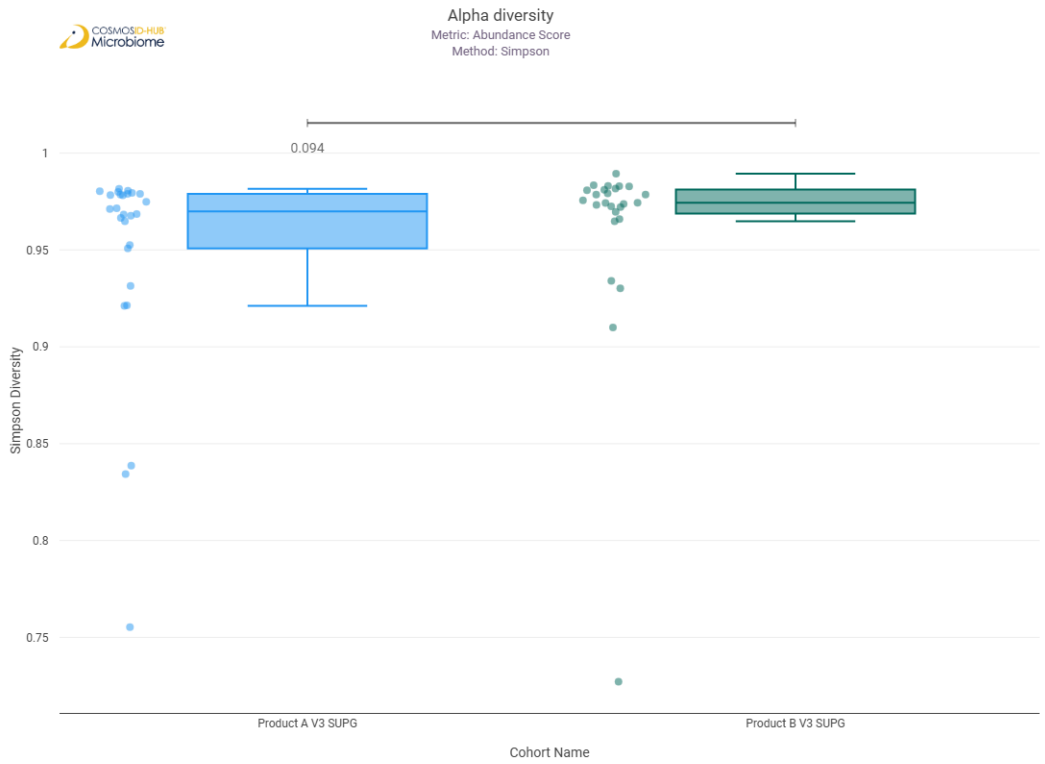
# Comparison 16: Product A V3 SUPG vs Product B V3 SUPG

## Gene Ontology

### Alpha Diversity (GO)

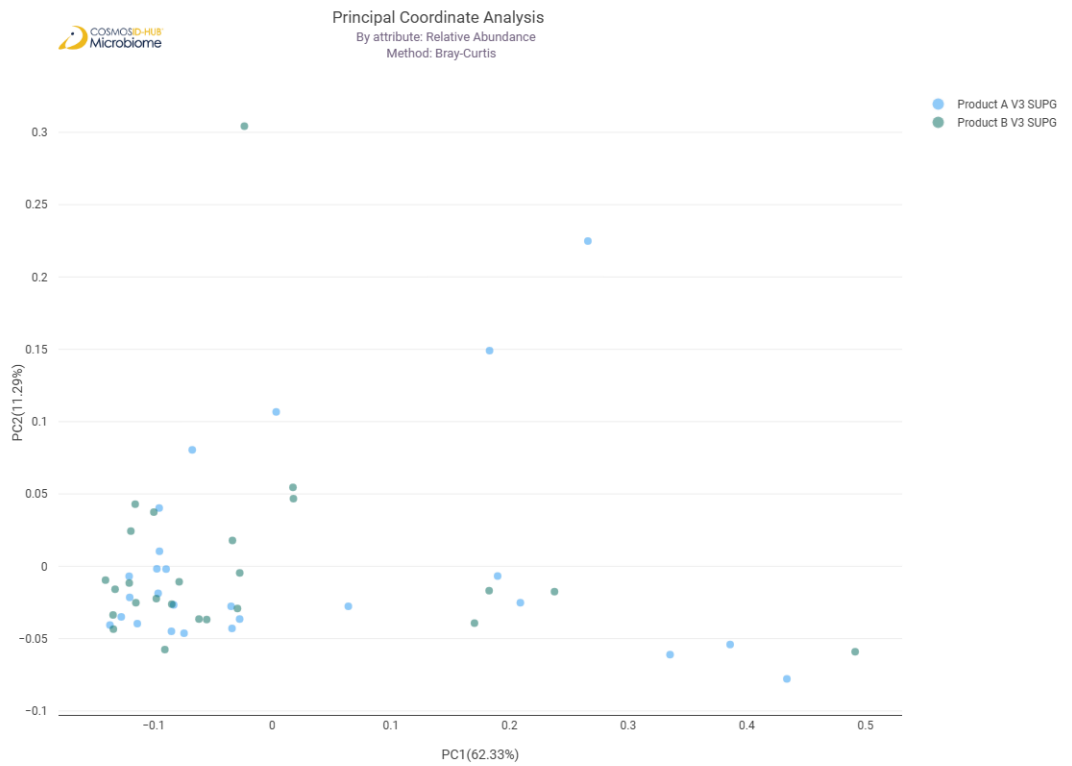


Simpson

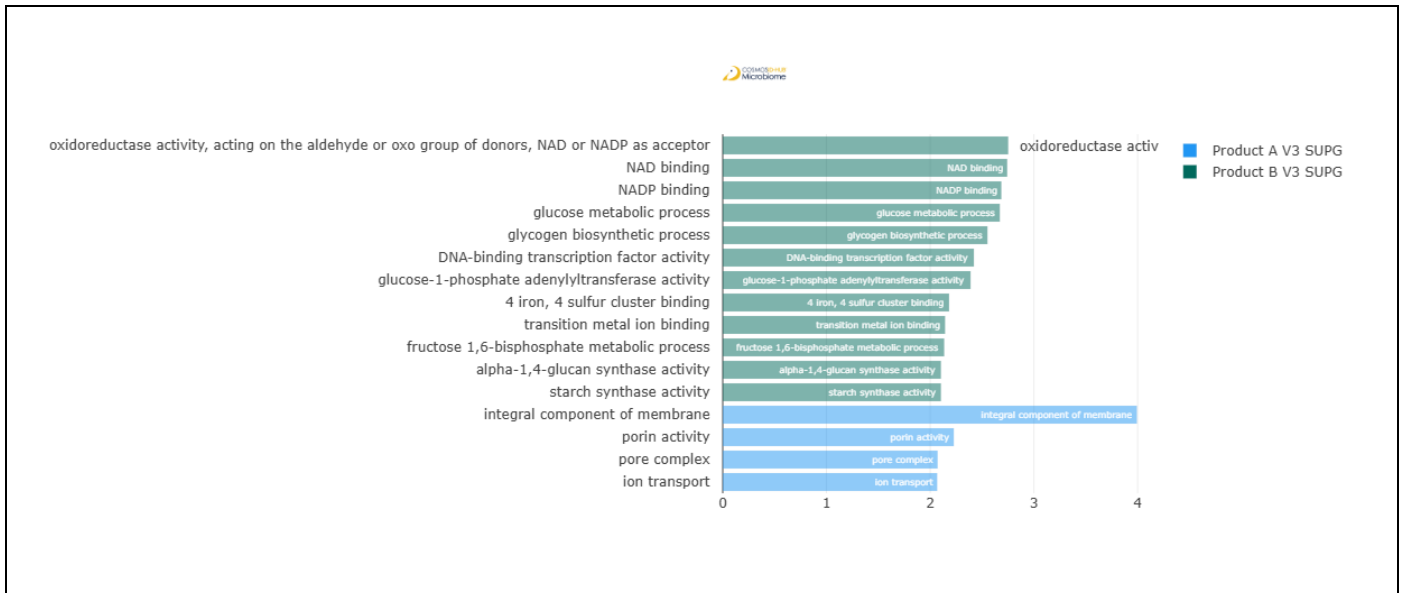


Beta Diversity (GO)

Bray-Curtis  
PERMNOVA  
 $p = 0.323$



## Differential Abundance (LEfSe) (GO)

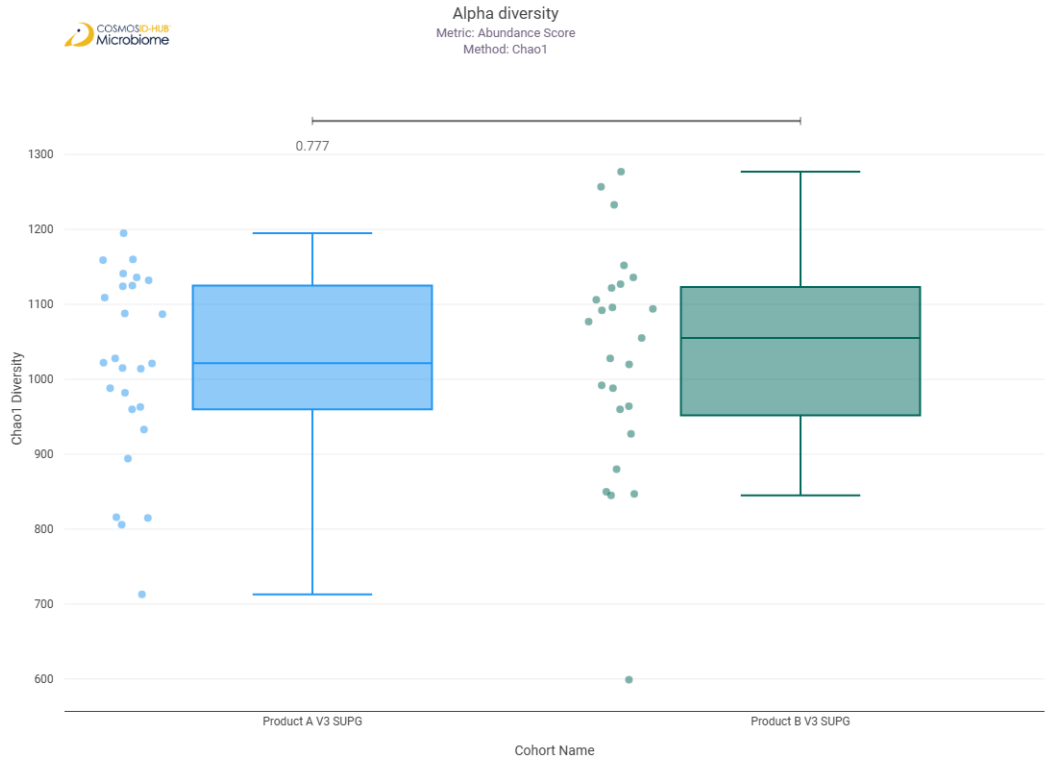


Feature	Enriched Cohort	LDA Score	P-value
oxidoreductase activity, acting on the aldehyde or oxo group of donors, NAD or NADP as acceptor	Product B V3 SUPG	2.752474797	0.012209995
NAD binding	Product B V3 SUPG	2.742648085	0.027486336
NADP binding	Product B V3 SUPG	2.686305478	0.013574437
glucose metabolic process	Product B V3 SUPG	2.671540978	0.015071869
glycogen biosynthetic process	Product B V3 SUPG	2.552404183	0.015873756
DNA-binding transcription factor activity	Product B V3 SUPG	2.42153675	0.020471389
glucose-1-phosphate adenylyltransferase activity	Product B V3 SUPG	2.389556209	0.011574483
4 iron, 4 sulfur cluster binding	Product B V3 SUPG	2.182217095	0.031712637
transition metal ion binding	Product B V3 SUPG	2.143807206	0.022613046
fructose 1,6-bisphosphate metabolic process	Product B V3 SUPG	2.135242629	0.02494682
starch synthase activity	Product B V3 SUPG	2.103901259	0.010390869
alpha-1,4-glucan synthase activity	Product B V3 SUPG	2.103901259	0.010390869
integral component of membrane	Product A V3 SUPG	3.993290893	0.030245812
porin activity	Product A V3 SUPG	2.227729313	0.000425892
pore complex	Product A V3 SUPG	2.071930111	0.004438681
ion transport	Product A V3 SUPG	2.067516171	0.004438681

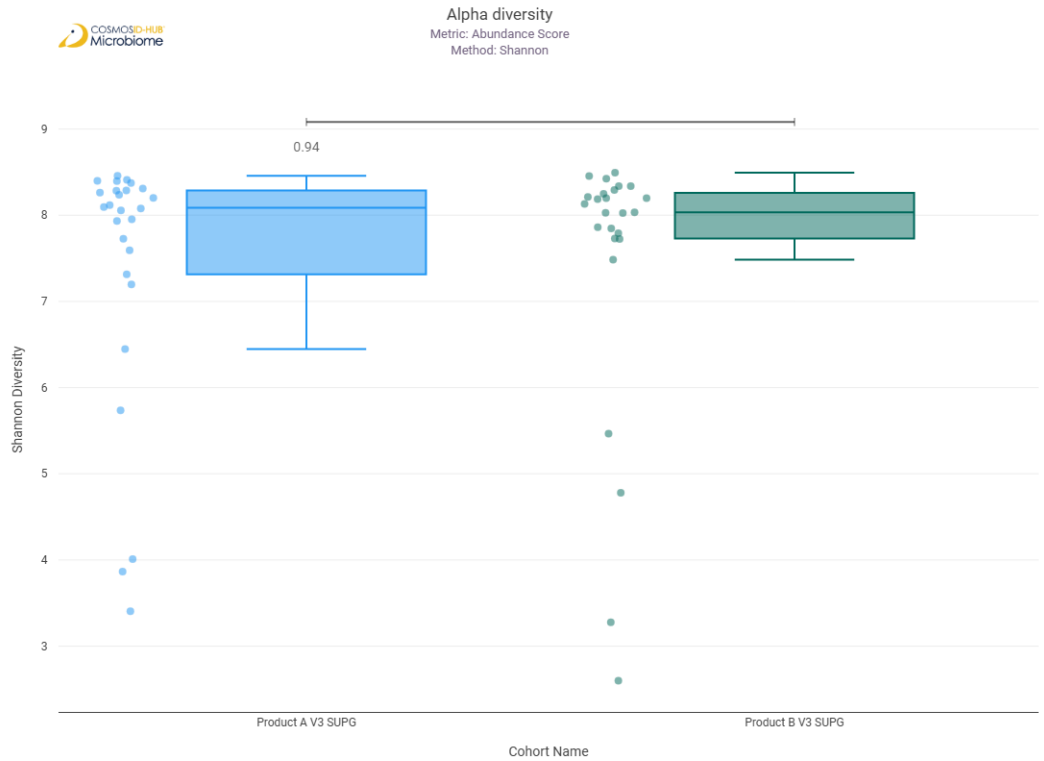
## Enzyme Commission

# Alpha Diversity (EC)

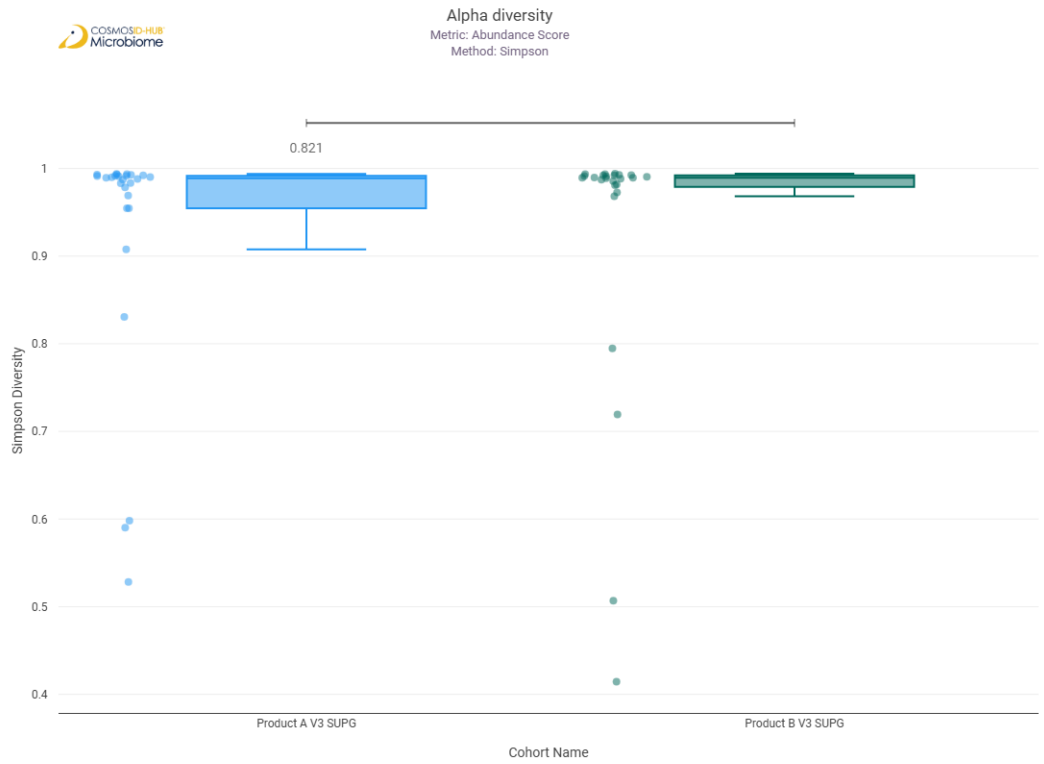
Chao1



Shannon

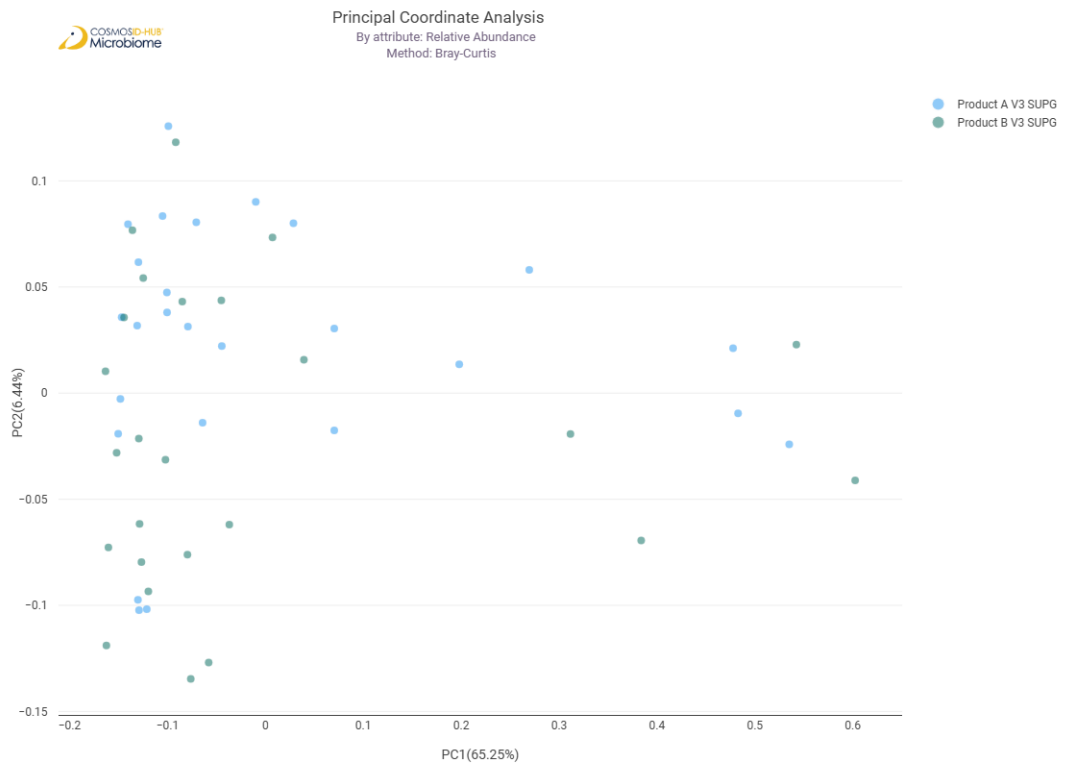


Simpson



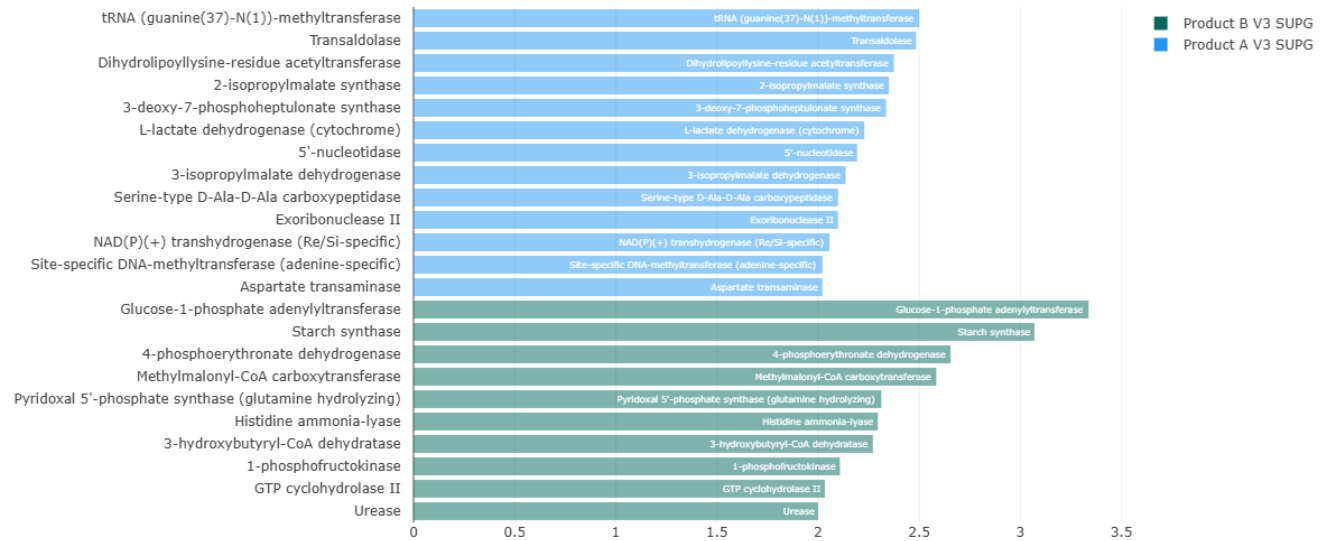
Beta Diversity (EC)

Bray-Curtis  
PERMNOVA  
 $p = 0.444$





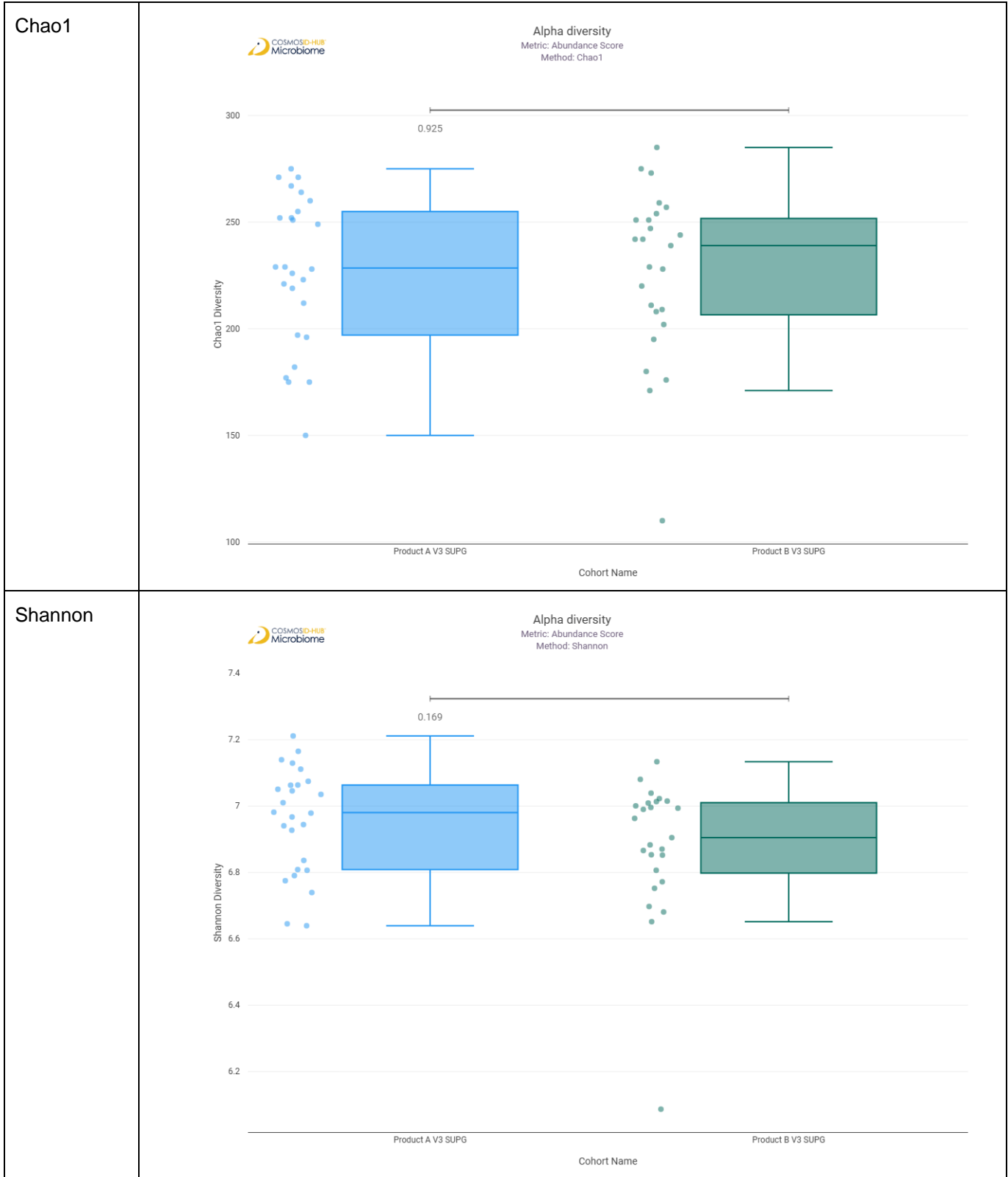
## Differential Abundance (LEfSe) (EC)



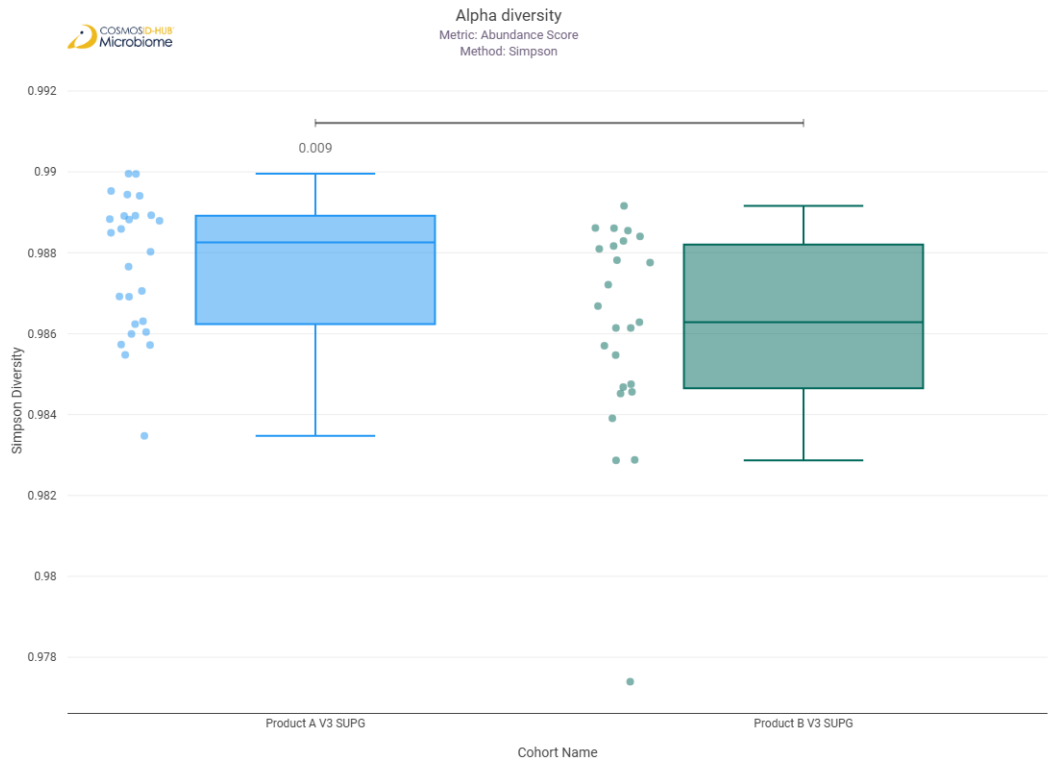
Feature	Enriched Cohort	LDA Score	P-value
tRNA (guanine(37)-N(1))-methyltransferase	Product A V3 SUPG	2.500264278	0.01946851
Transaldolase	Product A V3 SUPG	2.484762088	0.018508823
Dihydrolypoyllysine-residue acetyltransferase	Product A V3 SUPG	2.375737852	0.002269883
2-isopropylmalate synthase	Product A V3 SUPG	2.350585213	0.009316196
3-deoxy-7-phosphoheptulonate synthase	Product A V3 SUPG	2.337189254	0.012209995
L-lactate dehydrogenase (cytochrome)	Product A V3 SUPG	2.228905441	0.000975879
5'-nucleotidase	Product A V3 SUPG	2.193891563	0.017590793
3-isopropylmalate dehydrogenase	Product A V3 SUPG	2.136461137	0.034829974
Serine-type D-Ala-D-Ala carboxypeptidase	Product A V3 SUPG	2.099533029	3.65E-02
Exoribonuclease II	Product A V3 SUPG	2.098730123	0.00666206
NAD(P)(+) transhydrogenase (Re/Si-specific)	Product A V3 SUPG	2.057129937	9.12086E-05
Site-specific DNA-methyltransferase (adenine-specific)	Product A V3 SUPG	2.022241583	0.004708409
Aspartate transaminase	Product A V3 SUPG	2.022013886	0.007889693
Glucose-1-phosphate adenyltransferase	Product B V3 SUPG	3.338057083	0.014305878
Starch synthase	Product B V3 SUPG	3.070387876	0.010390869
4-phosphoerythronate dehydrogenase	Product B V3 SUPG	2.655965123	0.02375508
Methylmalonyl-CoA carboxytransferase	Product B V3 SUPG	2.585105624	0.030245812
Pyridoxal 5'-phosphate synthase (glutamine hydrolyzing)	Product B V3 SUPG	2.3131954	0.009840467
Histidine ammonia-lyase	Product B V3 SUPG	2.295994799	0.041854827
3-hydroxybutyryl-CoA dehydratase	Product B V3 SUPG	2.271443172	0.027416296
1-phosphofructokinase	Product B V3 SUPG	2.108726986	0.026189985
GTP cyclohydrolase II	Product B V3 SUPG	2.034218049	0.032464726
Urease	Product B V3 SUPG	2.000448337	0.036484395

# MetaCyc Pathways

## Alpha Diversity (MetaCyc)

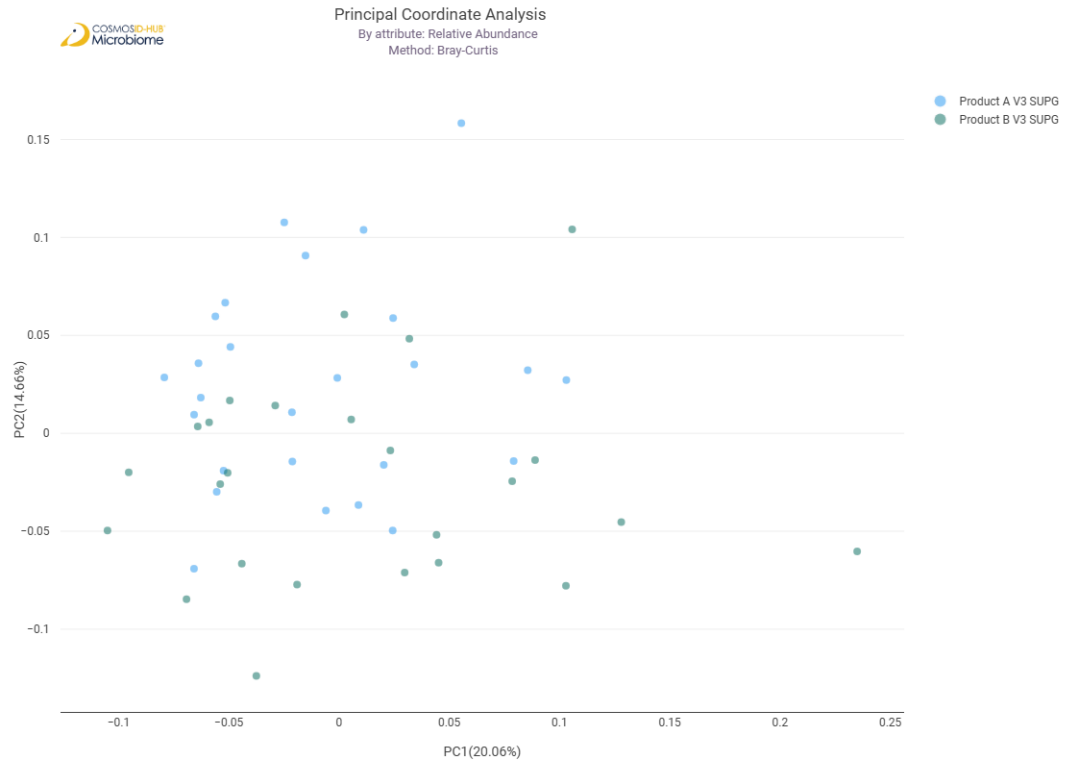


Simpson

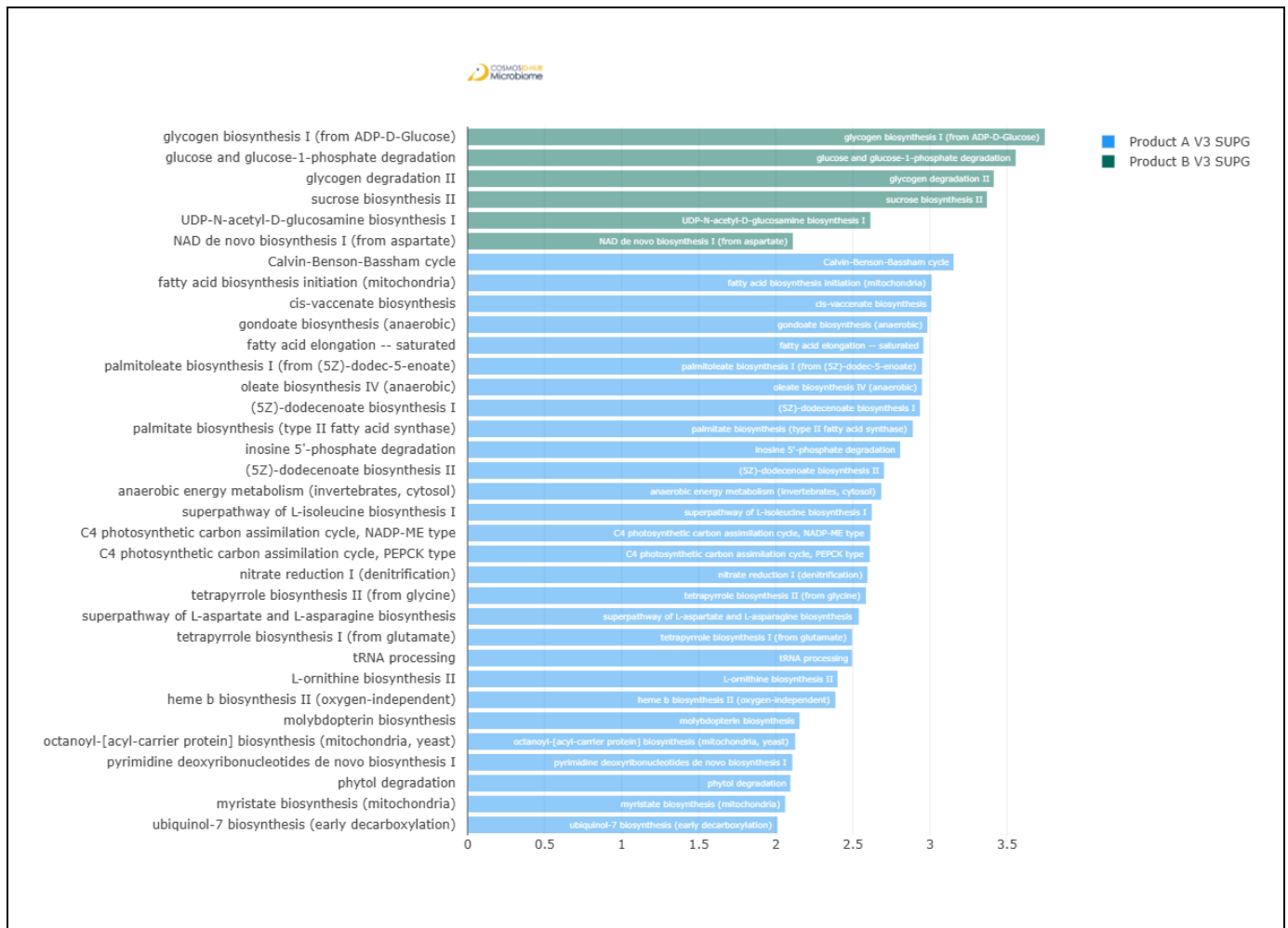


Beta Diversity (MetaCyc)

Bray-Curtis  
PERMNOVA  
p = 0.003



## Differential Abundance (LEfSe) (MetaCyc)



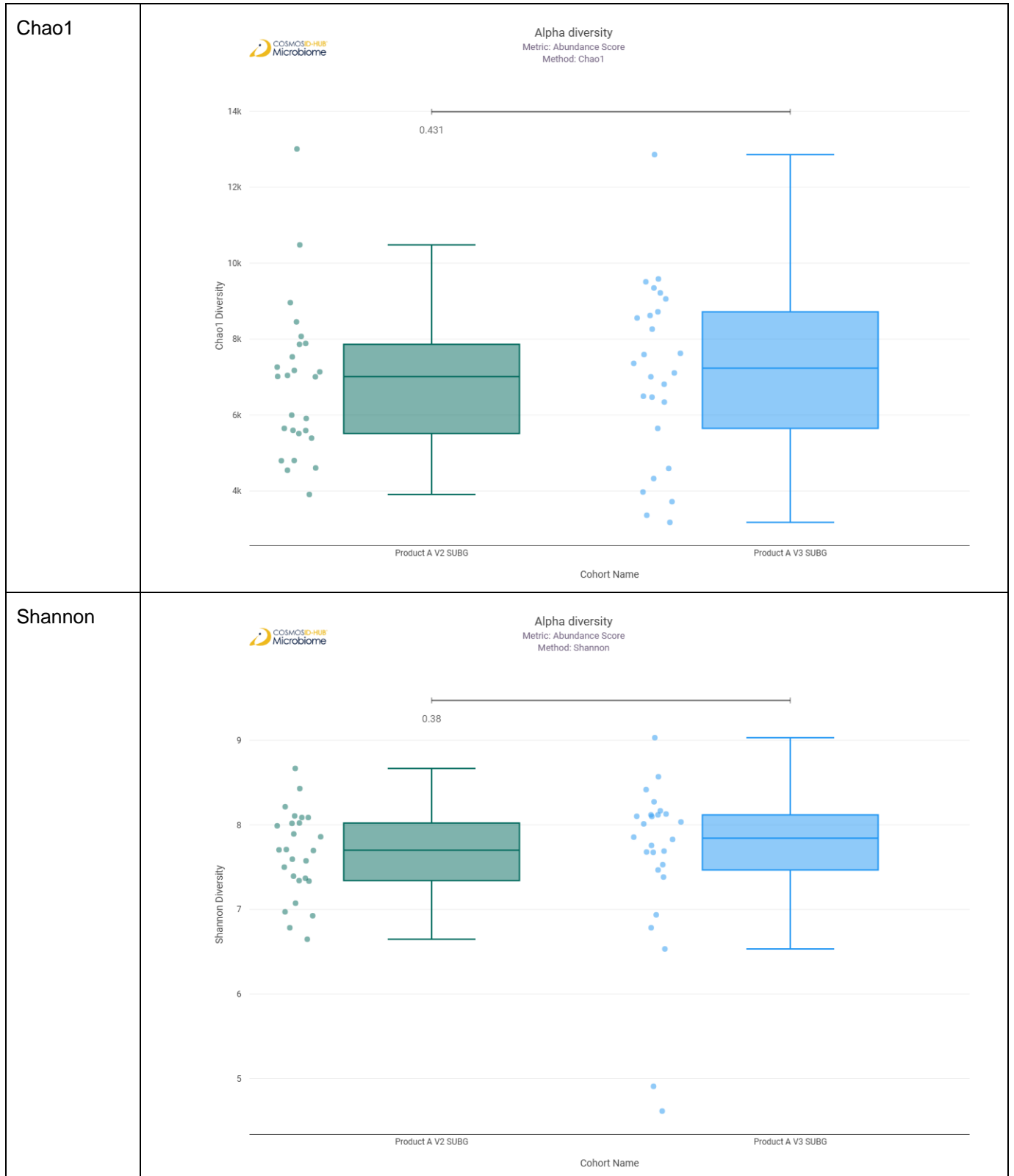
Feature	Enriched Cohort	LDA Score	P-value
glycogen biosynthesis I (from ADP-D-Glucose)	Product B V3 SUPG	3.745453908	0.004992891
glucose and glucose-1-phosphate degradation	Product B V3 SUPG	3.556342772	0.001185563
glycogen degradation II	Product B V3 SUPG	3.414064751	0.002416555
sucrose biosynthesis II	Product B V3 SUPG	3.369416045	0.043787588
UDP-N-acetyl-D-glucosamine biosynthesis I	Product B V3 SUPG	2.613767033	0.038205314
NAD de novo biosynthesis I (from aspartate)	Product B V3 SUPG	2.11061315	0.022998367
Calvin-Benson-Bassham cycle	Product A V3 SUPG	3.152784189	0.014305878
fatty acid biosynthesis initiation (mitochondria)	Product A V3 SUPG	3.01039182	0.045795182
cis-vaccenate biosynthesis	Product A V3 SUPG	3.009160863	0.002131408
gondoate biosynthesis (anaerobic)	Product A V3 SUPG	2.982772569	0.001651513
fatty acid elongation -- saturated	Product A V3 SUPG	2.957467752	1.55E-03
palmitoleate biosynthesis I (from (5Z)-dodec-5-enoate)	Product A V3 SUPG	2.9484708	0.001548196
oleate biosynthesis IV (anaerobic)	Product A V3 SUPG	2.947646008	0.001548196
(5Z)-dodecenoate biosynthesis I	Product A V3 SUPG	2.934424036	0.001450862
palmitate biosynthesis (type II fatty acid synthase)	Product A V3 SUPG	2.888494581	0.031388853
inosine 5'-phosphate degradation	Product A V3 SUPG	2.80641503	0.005608941
(5Z)-dodecenoate biosynthesis II	Product A V3 SUPG	2.70155732	0.001546672
anaerobic energy metabolism (invertebrates, cytosol)	Product A V3 SUPG	2.683835359	0.00176114

superpathway of L-isoleucine biosynthesis I	Product A V3 SUPG	2.622456465	0.00745964
C4 photosynthetic carbon assimilation cycle, NADP-ME type	Product A V3 SUPG	2.612696215	0.005608941
C4 photosynthetic carbon assimilation cycle, PEPCK type	Product A V3 SUPG	2.609269035	0.003940813
nitrate reduction I (denitrification)	Product A V3 SUPG	2.594250369	0.038117995
tetrapyrrole biosynthesis II (from glycine)	Product A V3 SUPG	2.583988202	0.002736233
superpathway of L-aspartate and L-asparagine biosynthesis	Product A V3 SUPG	2.537954679	0.01946851
tetrapyrrole biosynthesis I (from glutamate)	Product A V3 SUPG	2.494703731	0.021519031
tRNA processing	Product A V3 SUPG	2.494482922	3.04E-03
L-ornithine biosynthesis II	Product A V3 SUPG	2.400005683	0.001710728
heme b biosynthesis II (oxygen-independent)	Product A V3 SUPG	2.386491358	0.01038393
molybdopterin biosynthesis	Product A V3 SUPG	2.153352631	0.042764988
octanoyl-[acyl-carrier protein] biosynthesis (mitochondria, yeast)	Product A V3 SUPG	2.125495299	0.007588752
pyrimidine deoxyribonucleotides de novo biosynthesis I	Product A V3 SUPG	2.107076766	0.022483275
phytol degradation	Product A V3 SUPG	2.093939151	0.020872668
myristate biosynthesis (mitochondria)	Product A V3 SUPG	2.060356177	0.015762918
ubiquinol-7 biosynthesis (early decarboxylation)	Product A V3 SUPG	2.010244202	0.034572268

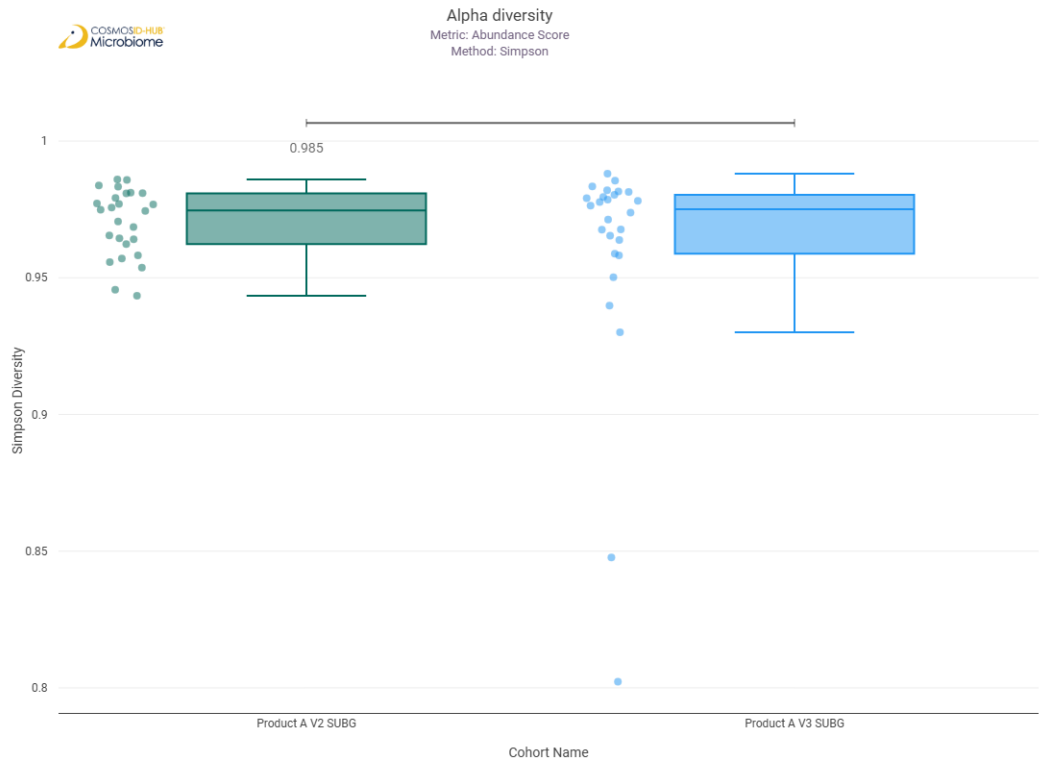
# Comparison 17: Product A V2 SUBG vs Product A V3 SUBG

## Gene Ontology

### Alpha Diversity (GO)

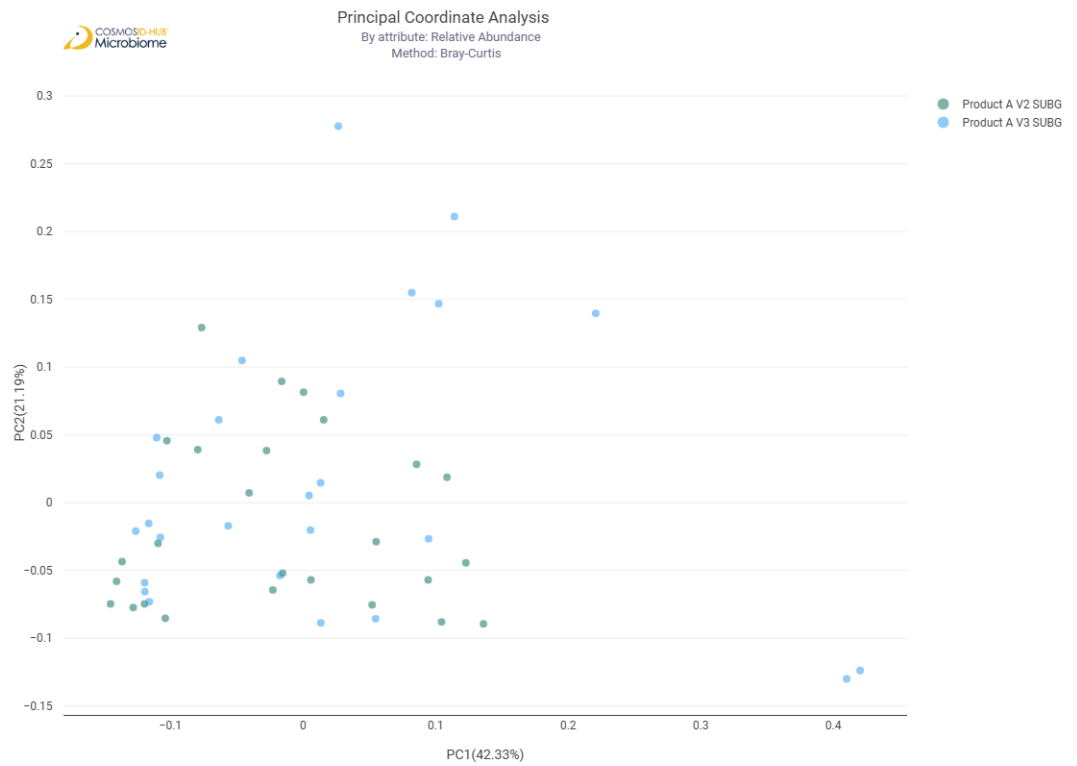


Simpson

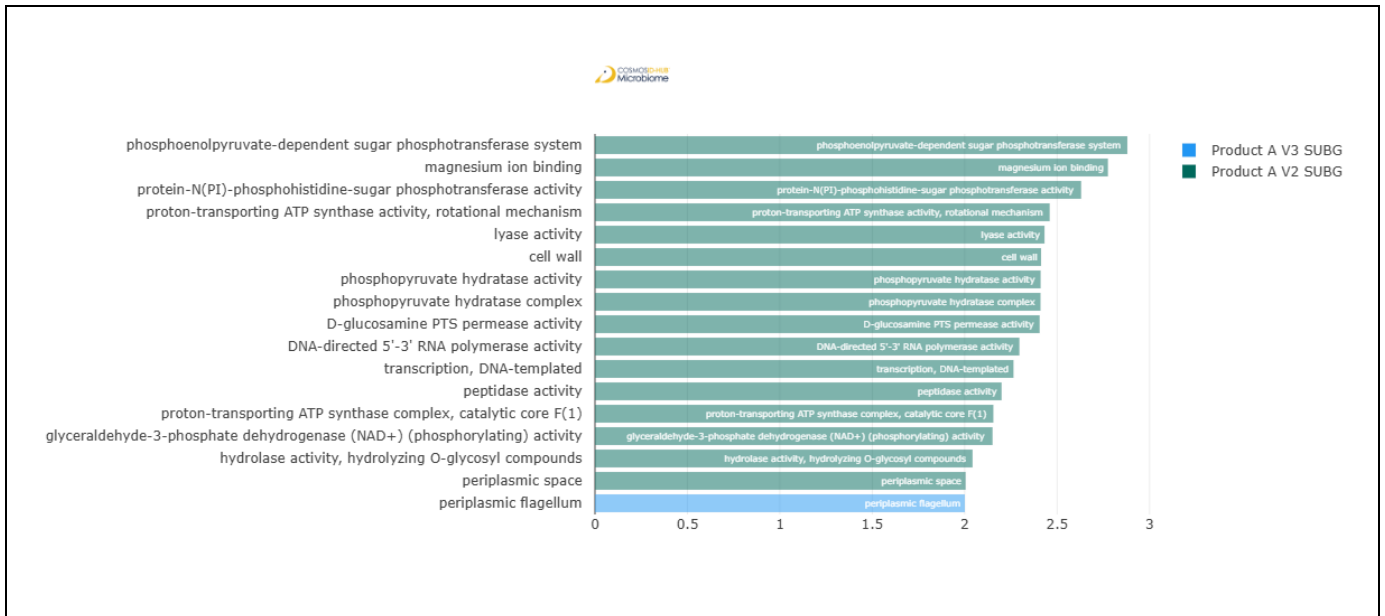


Beta Diversity (GO)

Bray-Curtis  
PERMNOVA  
p = 0.221



## Differential Abundance (LEfSe) (GO)



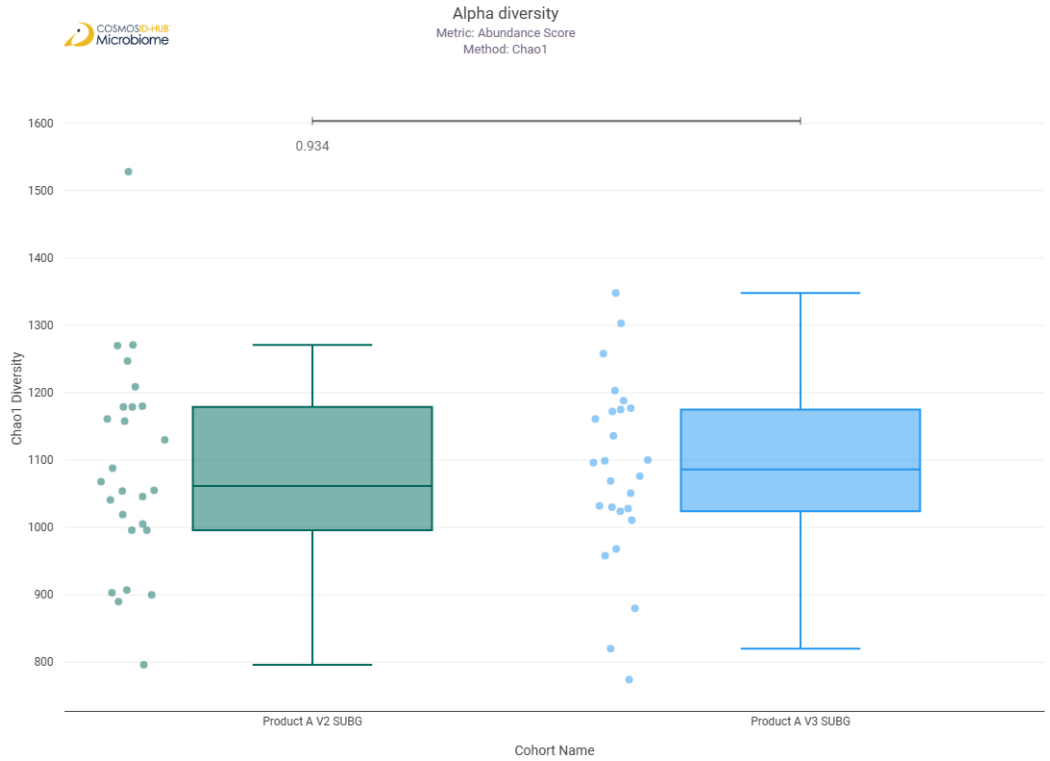
Feature	Enriched Cohort	LDA Score	P-value
phosphoenolpyruvate-dependent sugar phosphotransferase system	Product A V2 SUBG	2.879797903	0.032254747
magnesium ion binding	Product A V2 SUBG	2.774888442	0.036948224
protein-N(P1)-phosphohistidine-sugar phosphotransferase activity	Product A V2 SUBG	2.629946921	0.019152346
proton-transporting ATP synthase activity, rotational mechanism	Product A V2 SUBG	2.459822872	0.035322927
lyase activity	Product A V2 SUBG	2.431775521	0.020112035
cell wall	Product A V2 SUBG	2.413162378	0.00935587
phosphopyruvate hydratase activity	Product A V2 SUBG	2.410854956	0.029417827
phosphopyruvate hydratase complex	Product A V2 SUBG	2.410229337	0.032254747
D-glucosamine PTS permease activity	Product A V2 SUBG	2.405537558	0.030808261
DNA-directed 5'-3' RNA polymerase activity	Product A V2 SUBG	2.295963259	0.019152346
transcription, DNA-templated	Product A V2 SUBG	2.26404028	1.65E-02
peptidase activity	Product A V2 SUBG	2.199570388	0.044100855
proton-transporting ATP synthase complex, catalytic core F(1)	Product A V2 SUBG	2.155169223	0.030808261
glyceraldehyde-3-phosphate dehydrogenase (NAD+) (phosphorylating) activity	Product A V2 SUBG	2.150756046	0.01096333
hydrolase activity, hydrolyzing O-glycosyl compounds	Product A V2 SUBG	2.042624495	0.044100855
periplasmic space	Product A V2 SUBG	2.005080067	0.046061451
periplasmic flagellum	Product A V3 SUBG	2.000494506	0.029983145

## Enzyme Commission

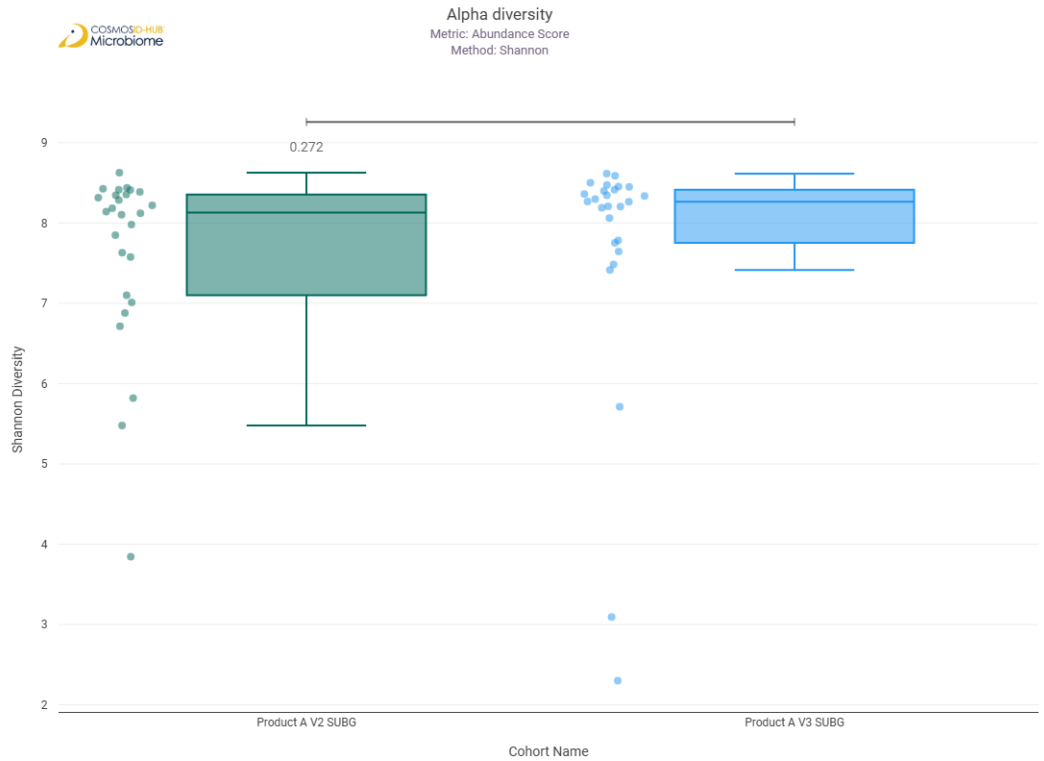


# Alpha Diversity (EC)

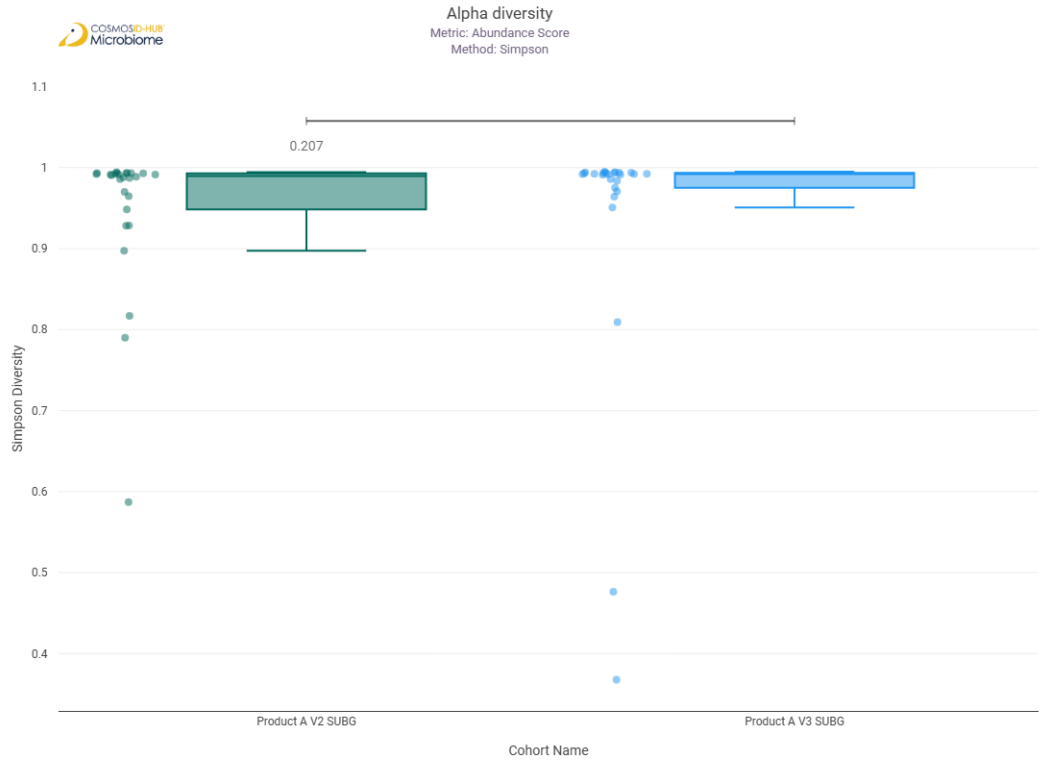
Chao1



Shannon

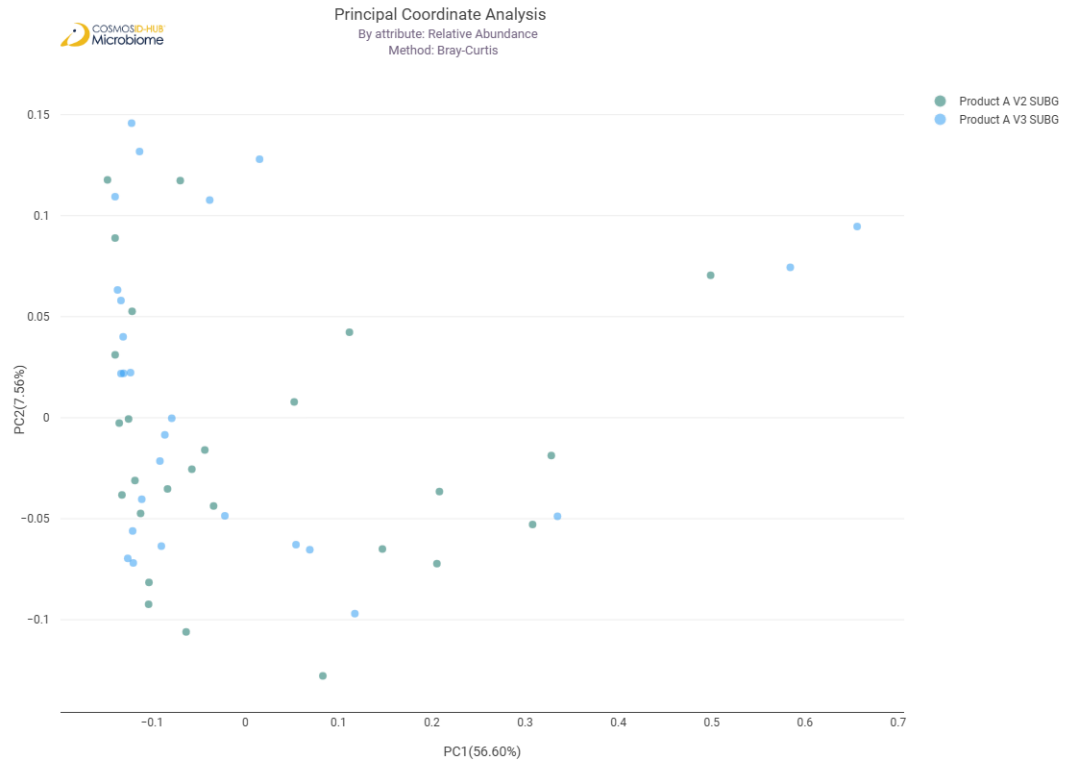


Simpson

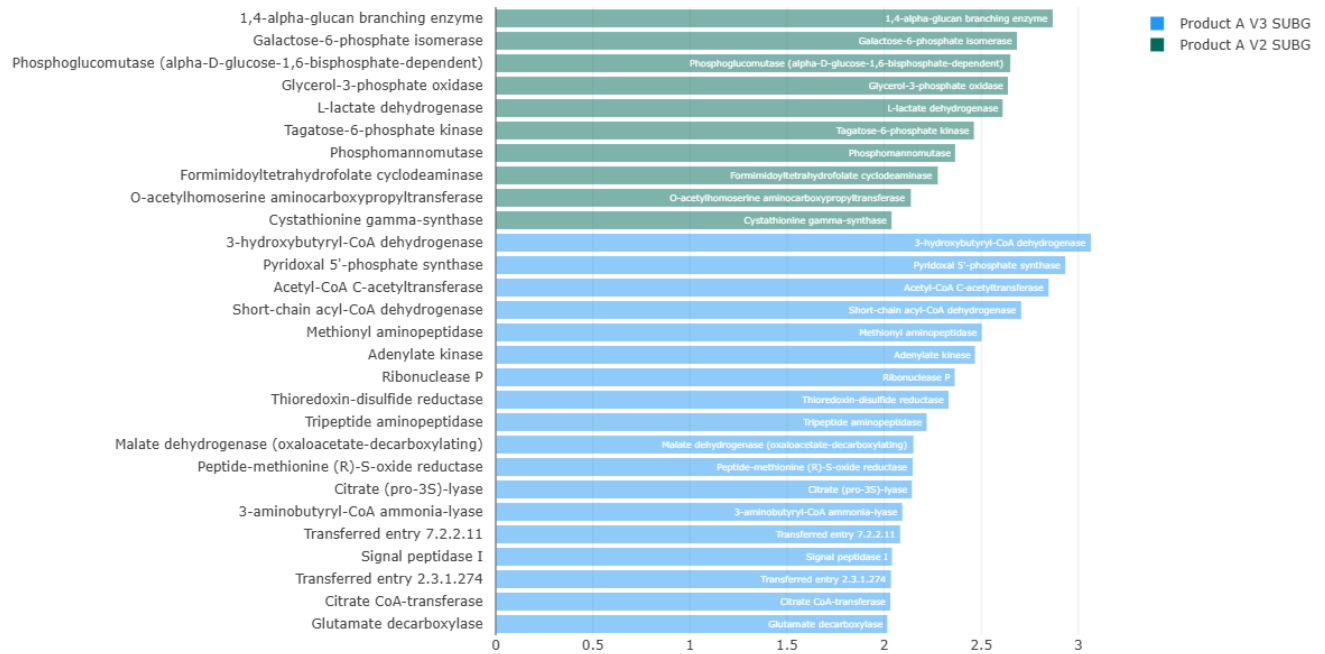


Beta Diversity (EC)

Bray-Curtis  
PERMNOVA  
 $p = 0.477$



## Differential Abundance (LEfSe) (EC)

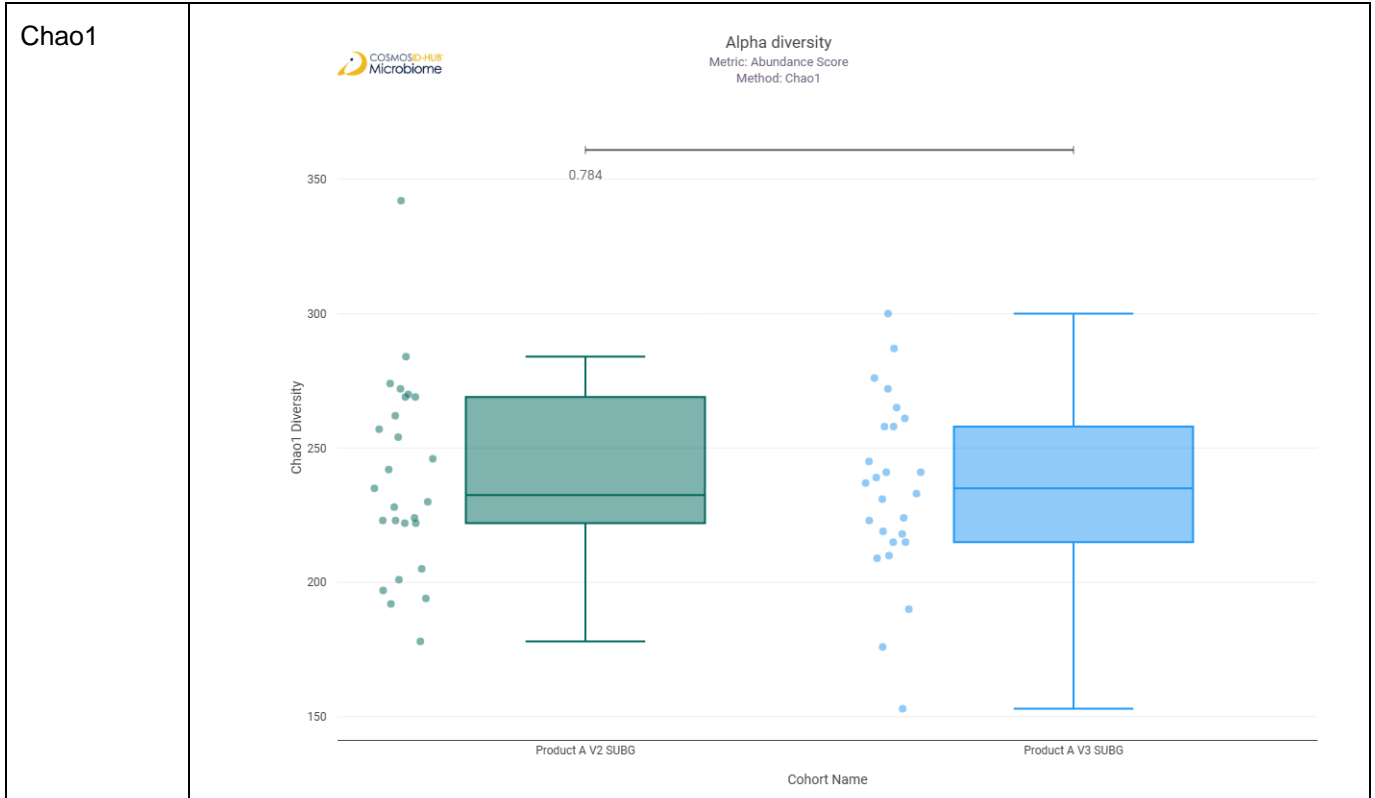


Feature	Enriched Cohort	LDA Score	P-value
1,4-alpha-glucan branching enzyme	Product A V2 SUBG	2.868316426	0.03375904
Galactose-6-phosphate isomerase	Product A V2 SUBG	2.684149527	0.030808261
Phosphoglucomutase (alpha-D-glucose-1,6-bisphosphate-dependent)	Product A V2 SUBG	2.649842397	0.02808172
Glycerol-3-phosphate oxidase	Product A V2 SUBG	2.637420912	0.016509366
L-lactate dehydrogenase	Product A V2 SUBG	2.610313421	0.040390461
Tagatose-6-phosphate kinase	Product A V2 SUBG	2.462341427	0.008404526
Phosphomannomutase	Product A V2 SUBG	2.365644114	0.026798248
Formimidoyltetrahydrofolate cyclodeaminase	Product A V2 SUBG	2.27631209	0.041248997
O-acetylhomoserine aminocarboxypropyltransferase	Product A V2 SUBG	2.137713911	0.004826615
Cystathionine gamma-synthase	Product A V2 SUBG	2.038346401	0.044100855
3-hydroxybutyryl-CoA dehydrogenase	Product A V3 SUBG	3.064708375	0.040390461
Pyridoxal 5'-phosphate synthase	Product A V3 SUBG	2.932292833	0.001450508
Acetyl-CoA C-acetyltransferase	Product A V3 SUBG	2.846871144	0.040390461
Short-chain acyl-CoA dehydrogenase	Product A V3 SUBG	2.705416934	0.023247195
Methionyl aminopeptidase	Product A V3 SUBG	2.502082155	0.03375904
Adenylate kinase	Product A V3 SUBG	2.467441243	4.04E-02
Ribonuclease P	Product A V3 SUBG	2.363351826	0.013486371
Thioredoxin-disulfide reductase	Product A V3 SUBG	2.331473944	0.029417827
Tripeptide aminopeptidase	Product A V3 SUBG	2.218866344	0.008404526
Malate dehydrogenase (oxaloacetate-decarboxylating)	Product A V3 SUBG	2.150705321	0.044100855
Peptide-methionine (R)-S-oxide reductase	Product A V3 SUBG	2.147252427	0.046061451

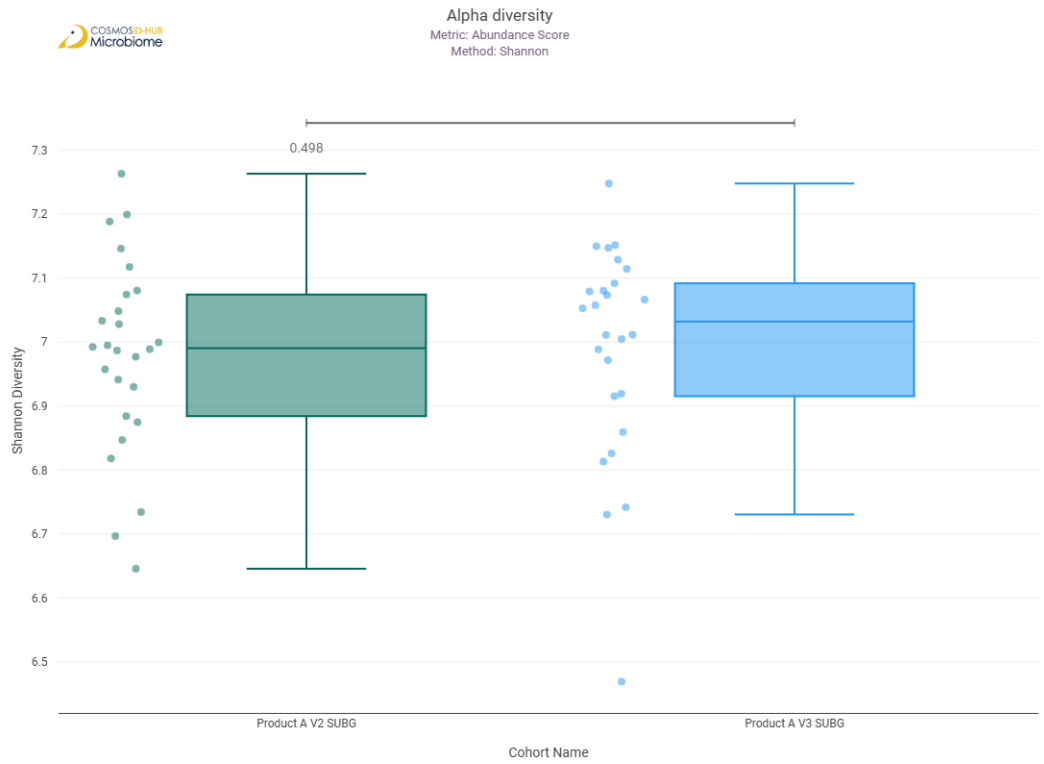
Citrate (pro-3S)-lyase	Product A V3 SUBG	2.143123658	0.019152346
3-aminobutyryl-CoA ammonia-lyase	Product A V3 SUBG	2.093593451	0.004825711
Transferred entry 7.2.2.11	Product A V3 SUBG	2.082564986	0.046061451
Signal peptidase I	Product A V3 SUBG	2.040245909	0.036948224
Transferred entry 2.3.1.274	Product A V3 SUBG	2.034991023	6.05E-03
Citrate CoA-transferase	Product A V3 SUBG	2.031605498	0.036948224
Glutamate decarboxylase	Product A V3 SUBG	2.016312006	0.042211177

## MetaCyc Pathways

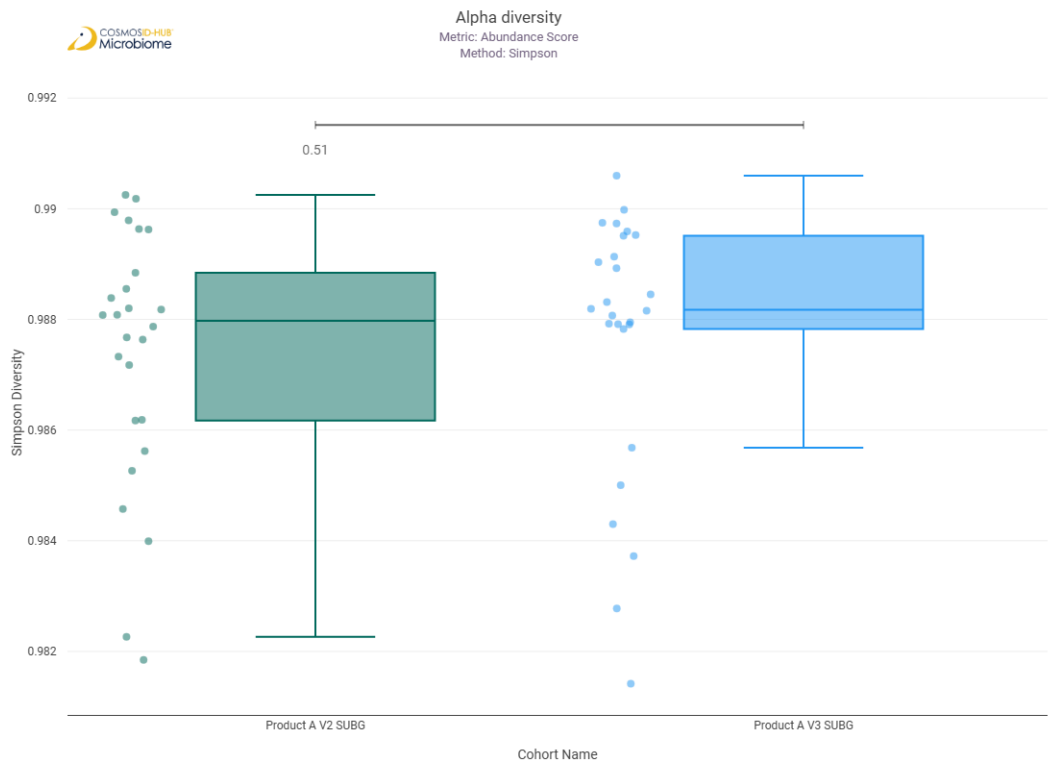
### Alpha Diversity (MetaCyc)



# Shannon

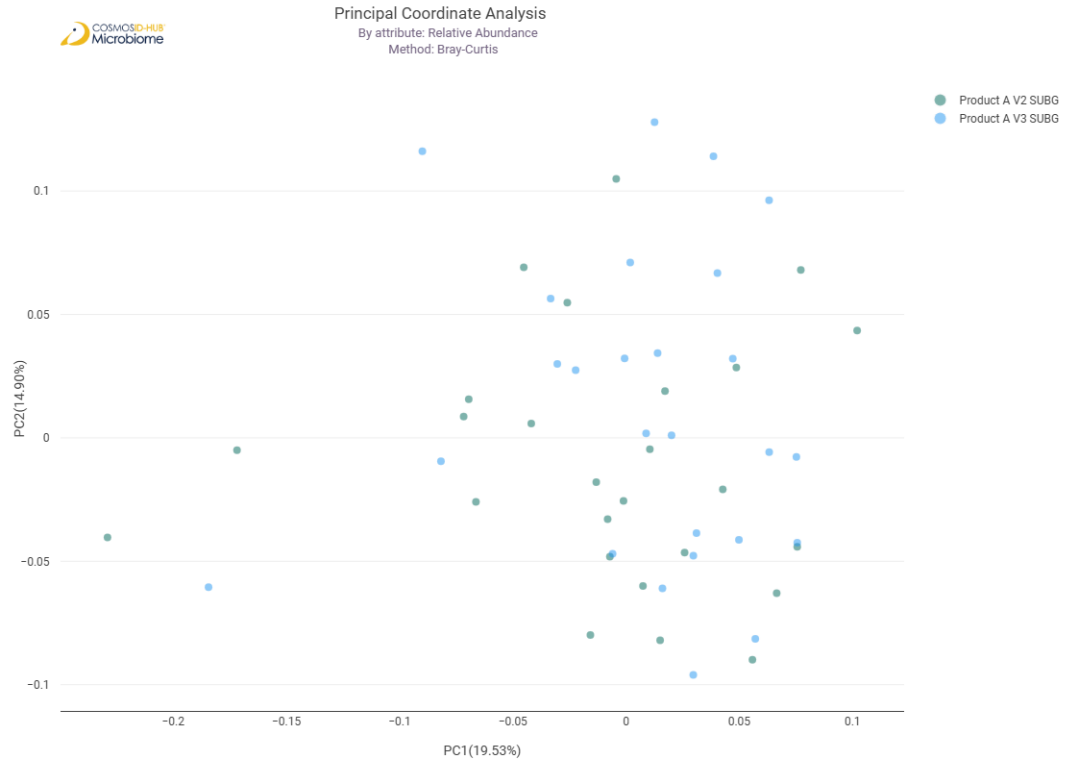


# Simpson

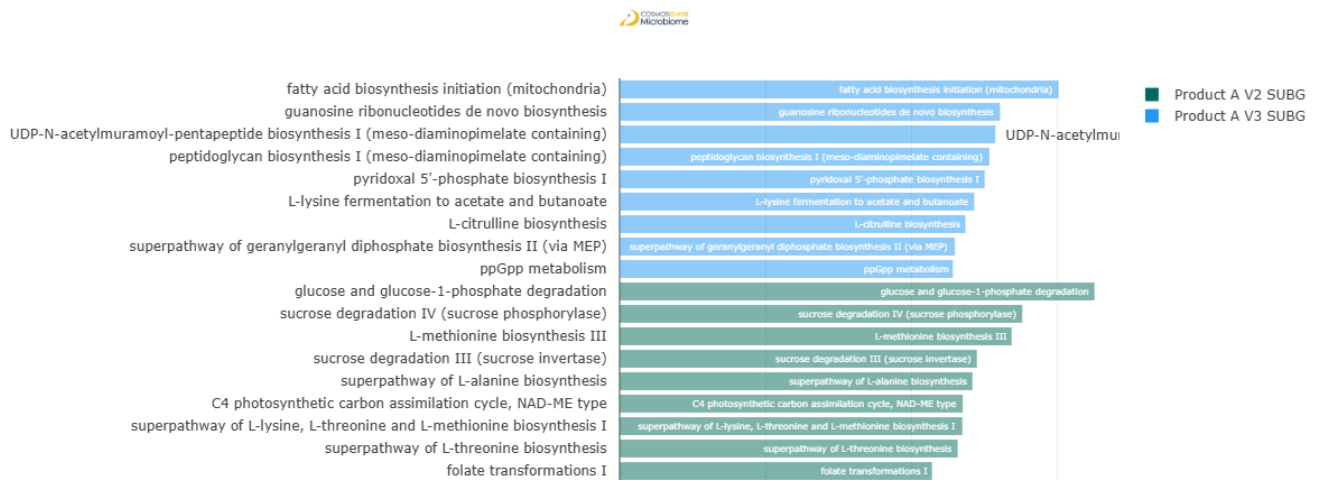


## Beta Diversity (MetaCyc)

Bray-Curtis  
PERMNOVA  
p = 0.351



## Differential Abundance (LEfSe) (MetaCyc)



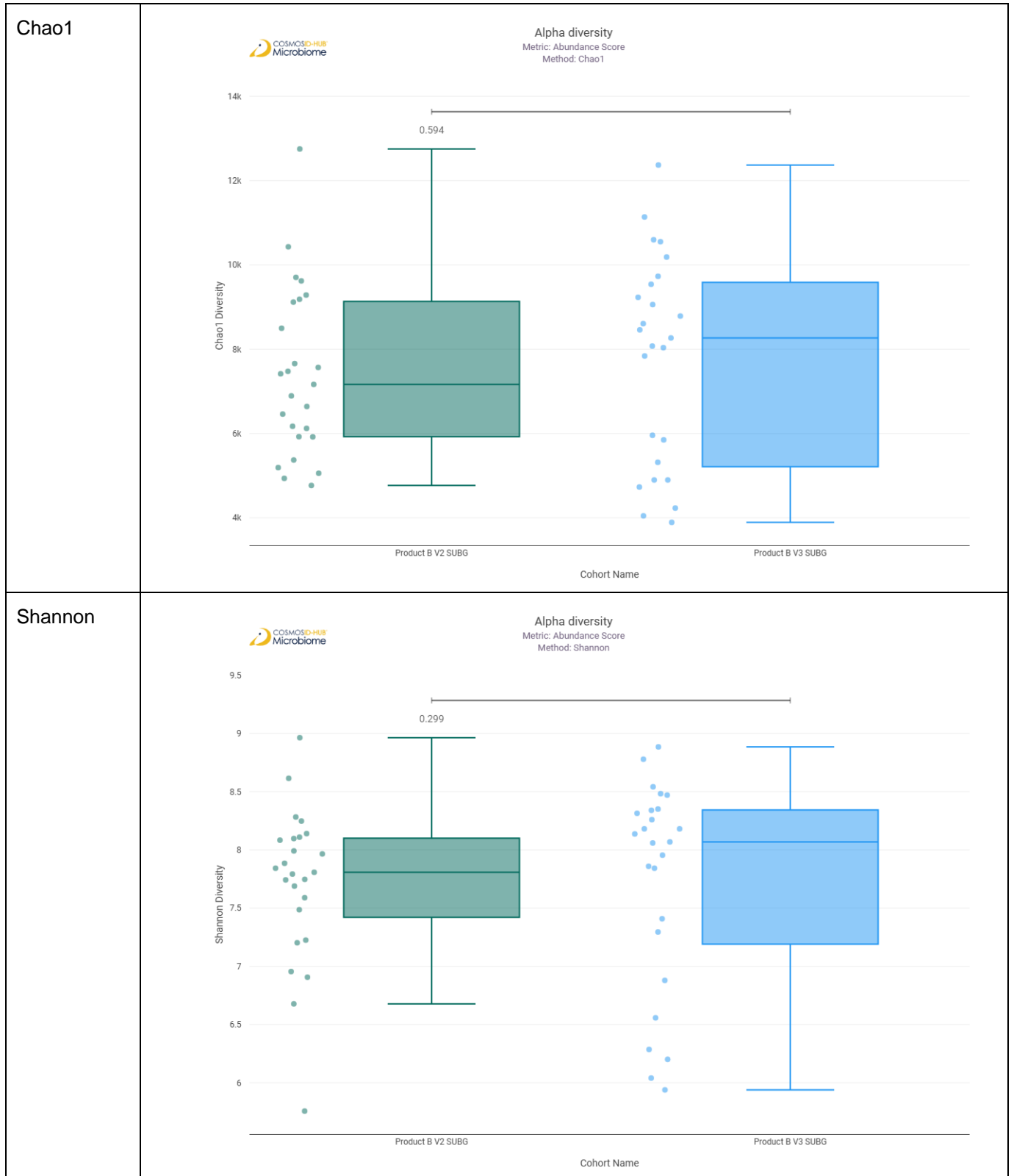
Feature	Enriched Cohort	LDA Score	P-value
fatty acid biosynthesis initiation (mitochondria)	Product A V3 SUBG	3.005949407	0.019152346
guanosine ribonucleotides de novo biosynthesis	Product A V3 SUBG	2.605116224	0.020112035
UDP-N-acetylmuramoyl-pentapeptide biosynthesis I (meso-diaminopimelate containing)	Product A V3 SUBG	2.572950032	0.023247195
peptidoglycan biosynthesis I (meso-diaminopimelate containing)	Product A V3 SUBG	2.53279651	0.032254747
pyridoxal 5'-phosphate biosynthesis I	Product A V3 SUBG	2.500028395	0.048970397

L-lysine fermentation to acetate and butanoate	Product A V3 SUBG	2.42853662	0.025907733
L-citrulline biosynthesis	Product A V3 SUBG	2.368319134	0.011551265
superpathway of geranylgeranyl diphosphate biosynthesis II (via MEP)	Product A V3 SUBG	2.29634489	4.91E-02
ppGpp metabolism	Product A V3 SUBG	2.281827361	0.044100855
glucose and glucose-1-phosphate degradation	Product A V2 SUBG	3.252312629	0.022595697
sucrose degradation IV (sucrose phosphorylase)	Product A V2 SUBG	2.757431708	0.015702531
L-methionine biosynthesis III	Product A V2 SUBG	2.685167724	0.026798248
sucrose degradation III (sucrose invertase)	Product A V2 SUBG	2.446760597	0.019152346
superpathway of L-alanine biosynthesis	Product A V2 SUBG	2.416704919	0.046061451
C4 photosynthetic carbon assimilation cycle, NAD-ME type	Product A V2 SUBG	2.350104694	0.026798248
superpathway of L-lysine, L-threonine and L-methionine biosynthesis I	Product A V2 SUBG	2.347295262	0.013505326
superpathway of L-threonine biosynthesis	Product A V2 SUBG	2.315420543	0.046061451
folate transformations I	Product A V2 SUBG	2.139570387	0.03927407

# Comparison 18: Product B V2 SUBG vs Product B V3 SUBG

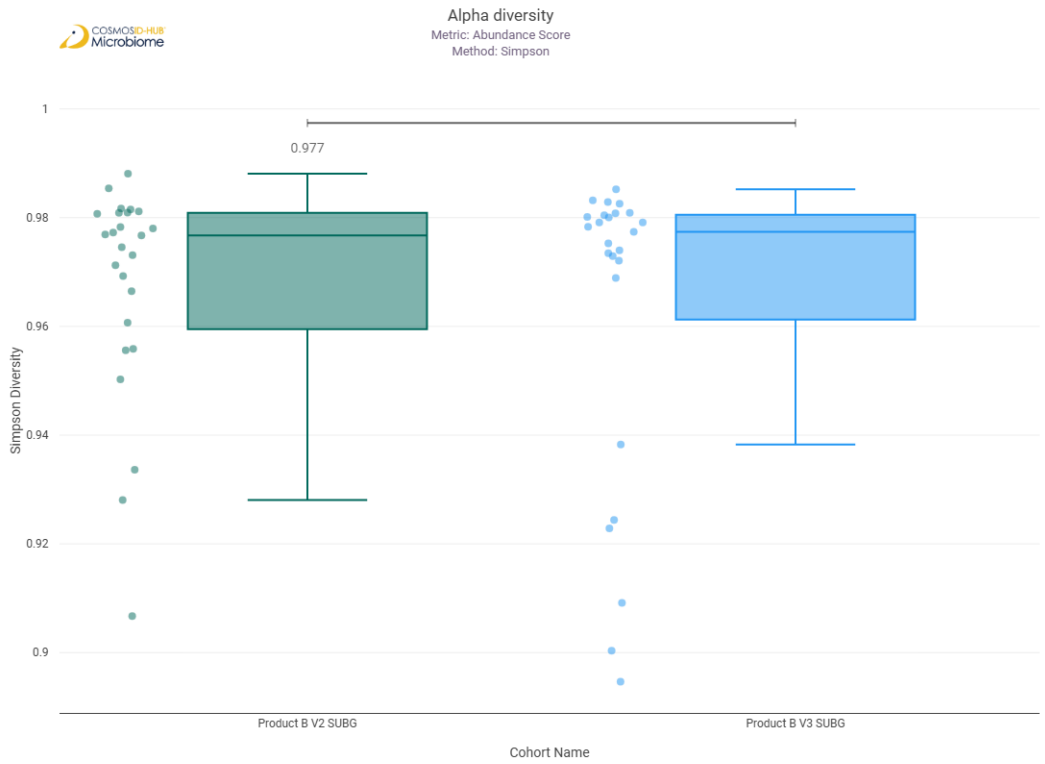
## Gene Ontology

### Alpha Diversity (GO)



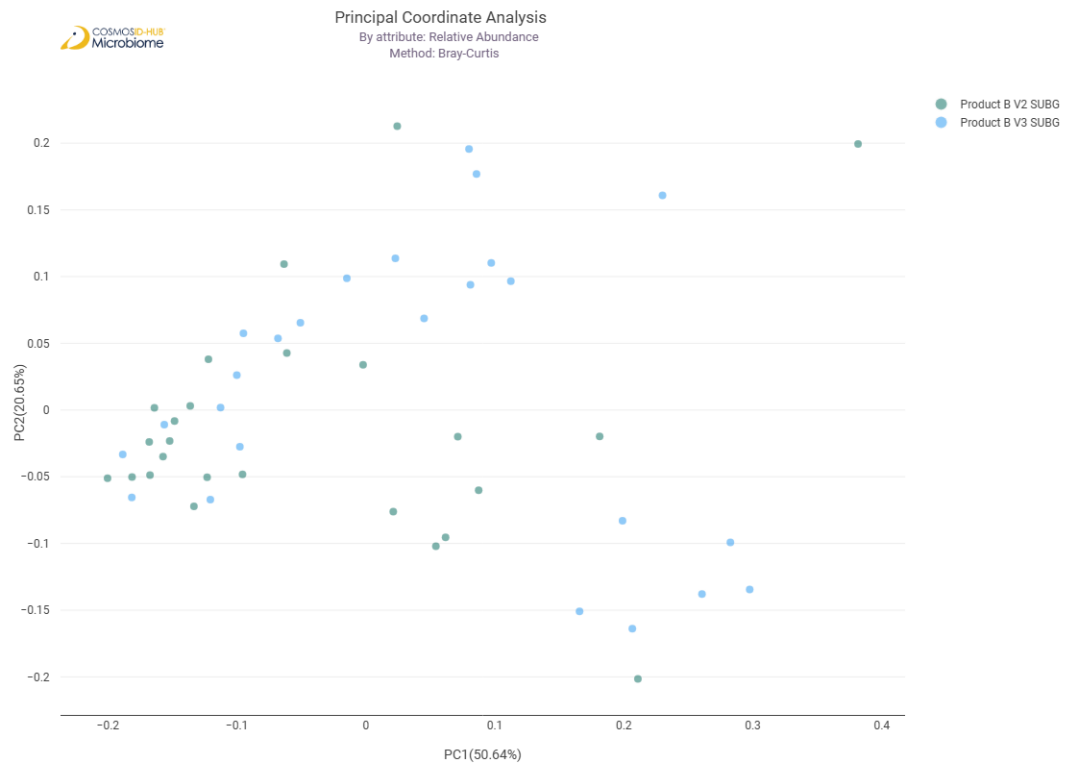


Simpson

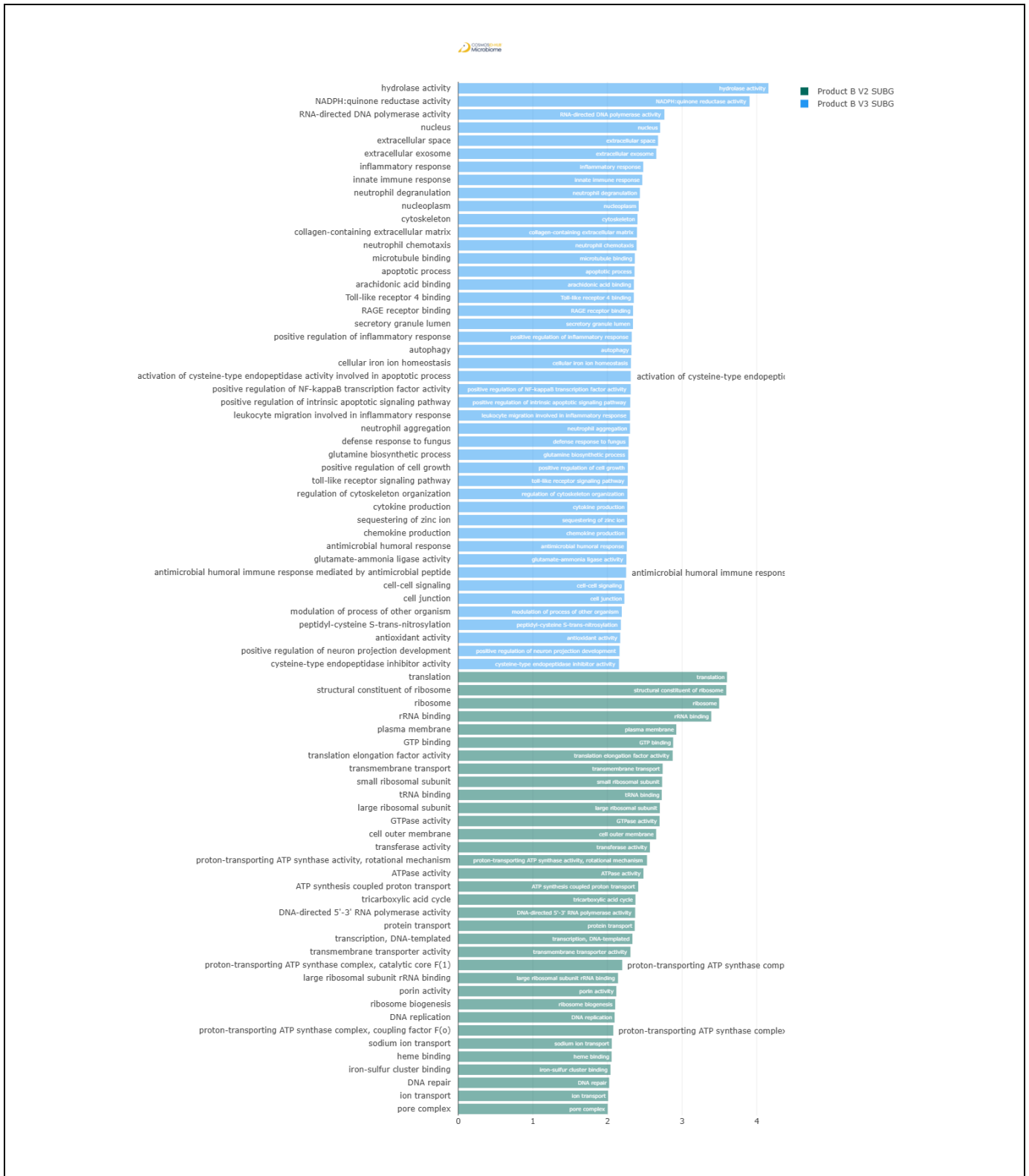


Beta Diversity (GO)

Bray-Curtis  
PERMNOVA  
 $p = 0.052$



# Differential Abundance (LEfSe) (GO)



Feature	Enriched Cohort	LDA Score	P-value
hydrolase activity	Product B V3 SUBG	4.156534105	0.046724152
NADPH:quinone reductase activity	Product B V3 SUBG	3.903411192	0.038790393
RNA-directed DNA polymerase activity	Product B V3 SUBG	2.762516384	0.010144117

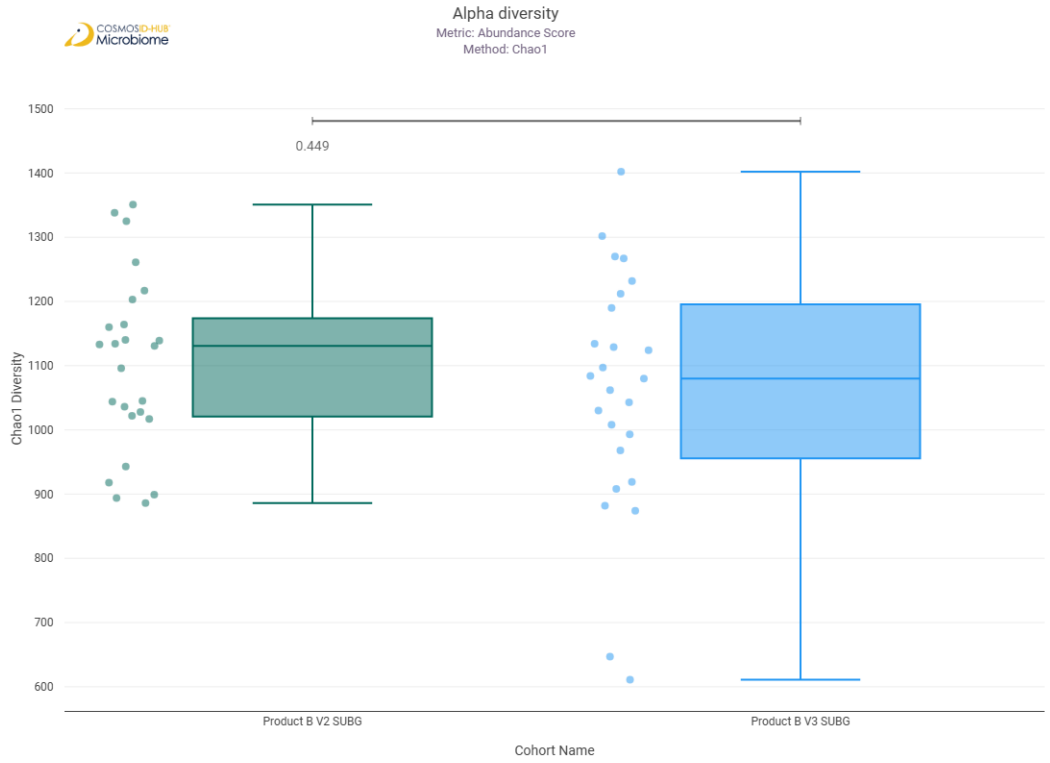
nucleus	Product B V3 SUBG	2.705824935	0.044622577
extracellular space	Product B V3 SUBG	2.677161463	0.032031691
extracellular exosome	Product B V3 SUBG	2.654055757	0.030509062
inflammatory response	Product B V3 SUBG	2.479045769	0.022617484
innate immune response	Product B V3 SUBG	2.466561032	0.025024185
neutrophil degranulation	Product B V3 SUBG	2.434546953	0.022617484
nucleoplasm	Product B V3 SUBG	2.418583258	1.84E-02
cytoskeleton	Product B V3 SUBG	2.402056268	0.007632882
collagen-containing extracellular matrix	Product B V3 SUBG	2.395453748	0.027649527
neutrophil chemotaxis	Product B V3 SUBG	2.390410925	0.020414533
microtubule binding	Product B V3 SUBG	2.366393497	0.014109615
apoptotic process	Product B V3 SUBG	2.362287574	0.014889416
arachidonic acid binding	Product B V3 SUBG	2.35381107	0.01265739
Toll-like receptor 4 binding	Product B V3 SUBG	2.352803461	0.01265739
RAGE receptor binding	Product B V3 SUBG	2.342847827	0.022617484
secretory granule lumen	Product B V3 SUBG	2.341644066	0.014109615
positive regulation of inflammatory response	Product B V3 SUBG	2.325368311	0.010144117
autophagy	Product B V3 SUBG	2.321122165	0.010144117
cellular iron ion homeostasis	Product B V3 SUBG	2.314227493	0.040658018
activation of cysteine-type endopeptidase activity involved in apoptotic process	Product B V3 SUBG	2.311541194	0.009589776
positive regulation of NF-kappaB transcription factor activity	Product B V3 SUBG	2.3110923	0.01265739
positive regulation of intrinsic apoptotic signaling pathway	Product B V3 SUBG	2.305115842	0.009062607
leukocyte migration involved in inflammatory response	Product B V3 SUBG	2.302179173	0.009062607
neutrophil aggregation	Product B V3 SUBG	2.301823987	0.009062607
defense response to fungus	Product B V3 SUBG	2.283744629	0.009589776
glutamine biosynthetic process	Product B V3 SUBG	2.27825556	0.014889416
positive regulation of cell growth	Product B V3 SUBG	2.272313134	0.009589776
toll-like receptor signaling pathway	Product B V3 SUBG	2.270650056	0.009062607
regulation of cytoskeleton organization	Product B V3 SUBG	2.267159509	0.010144117
cytokine production	Product B V3 SUBG	2.265455874	0.009589776
sequestering of zinc ion	Product B V3 SUBG	2.264105441	0.009062607
chemokine production	Product B V3 SUBG	2.264080101	0.009062607
antimicrobial humoral response	Product B V3 SUBG	2.260004794	0.027649527
glutamate-ammonia ligase activity	Product B V3 SUBG	2.253778074	0.019384996
antimicrobial humoral immune response mediated by antimicrobial peptide	Product B V3 SUBG	2.25017464	0.017461229
cell-cell signaling	Product B V3 SUBG	2.227194438	0.011339073
cell junction	Product B V3 SUBG	2.226507863	0.01336608
modulation of process of other organism	Product B V3 SUBG	2.191713031	0.007632882
peptidyl-cysteine S-trans-nitrosylation	Product B V3 SUBG	2.179649634	0.00640875
antioxidant activity	Product B V3 SUBG	2.170911949	0.003722992
positive regulation of neuron projection development	Product B V3 SUBG	2.161135069	0.007203336
cysteine-type endopeptidase inhibitor activity	Product B V3 SUBG	2.154679366	0.042601311
translation	Product B V2 SUBG	3.601581062	0.010726809
structural constituent of ribosome	Product B V2 SUBG	3.592047496	0.011339073
ribosome	Product B V2 SUBG	3.496305651	0.005051804
rRNA binding	Product B V2 SUBG	3.390564483	0.018401118

plasma membrane	Product B V2 SUBG	2.921973878	0.042601311
GTP binding	Product B V2 SUBG	2.880037294	1.84E-02
translation elongation factor activity	Product B V2 SUBG	2.873885039	0.01336608
transmembrane transport	Product B V2 SUBG	2.73919936	0.01265739
small ribosomal subunit	Product B V2 SUBG	2.732488352	0.010726809
tRNA binding	Product B V2 SUBG	2.727081355	0.044622577
large ribosomal subunit	Product B V2 SUBG	2.701633795	0.006041816
GTPase activity	Product B V2 SUBG	2.698296247	0.023794451
cell outer membrane	Product B V2 SUBG	2.652317031	0.027649527
transferase activity	Product B V2 SUBG	2.568598356	0.048908406
proton-transporting ATP synthase activity, rotational mechanism	Product B V2 SUBG	2.529987281	0.009062607
ATPase activity	Product B V2 SUBG	2.482085992	0.048908406
ATP synthesis coupled proton transport	Product B V2 SUBG	2.411899998	0.006041816
tricarboxylic acid cycle	Product B V2 SUBG	2.375045571	0.000148684
DNA-directed 5'-3' RNA polymerase activity	Product B V2 SUBG	2.371051842	0.003287086
protein transport	Product B V2 SUBG	2.365132113	0.030509062
transcription, DNA-templated	Product B V2 SUBG	2.334049907	0.005364191
transmembrane transporter activity	Product B V2 SUBG	2.307915949	0.030509062
proton-transporting ATP synthase complex, catalytic core F(1)	Product B V2 SUBG	2.197913979	0.01265739
large ribosomal subunit rRNA binding	Product B V2 SUBG	2.141433642	0.030509062
porin activity	Product B V2 SUBG	2.118878001	9.24207E-05
ribosome biogenesis	Product B V2 SUBG	2.103632447	0.022617484
DNA replication	Product B V2 SUBG	2.095886808	0.046724152
proton-transporting ATP synthase complex, coupling factor F(o)	Product B V2 SUBG	2.078331122	0.011982167
sodium ion transport	Product B V2 SUBG	2.057929399	0.001616222
heme binding	Product B V2 SUBG	2.055269007	0.001321949
iron-sulfur cluster binding	Product B V2 SUBG	2.040464006	0.044622577
DNA repair	Product B V2 SUBG	2.022758739	0.032031691
ion transport	Product B V2 SUBG	2.008697679	8.52725E-05
pore complex	Product B V2 SUBG	2.003123056	0.000160745

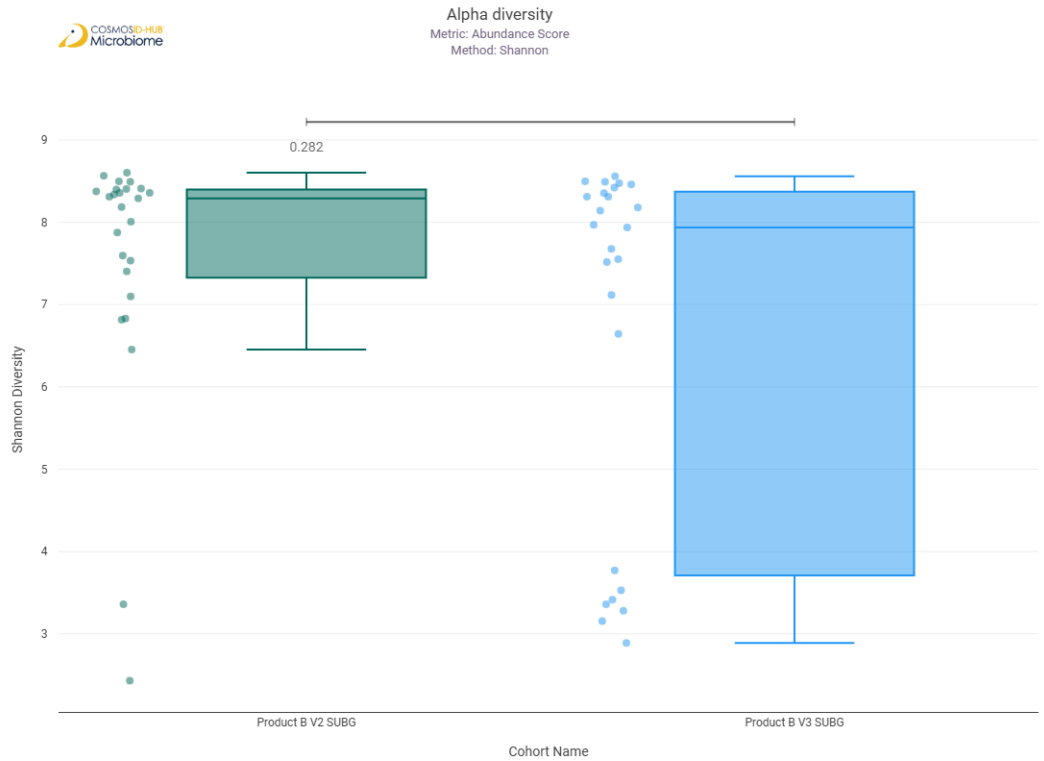
## Enzyme Commission

# Alpha Diversity (EC)

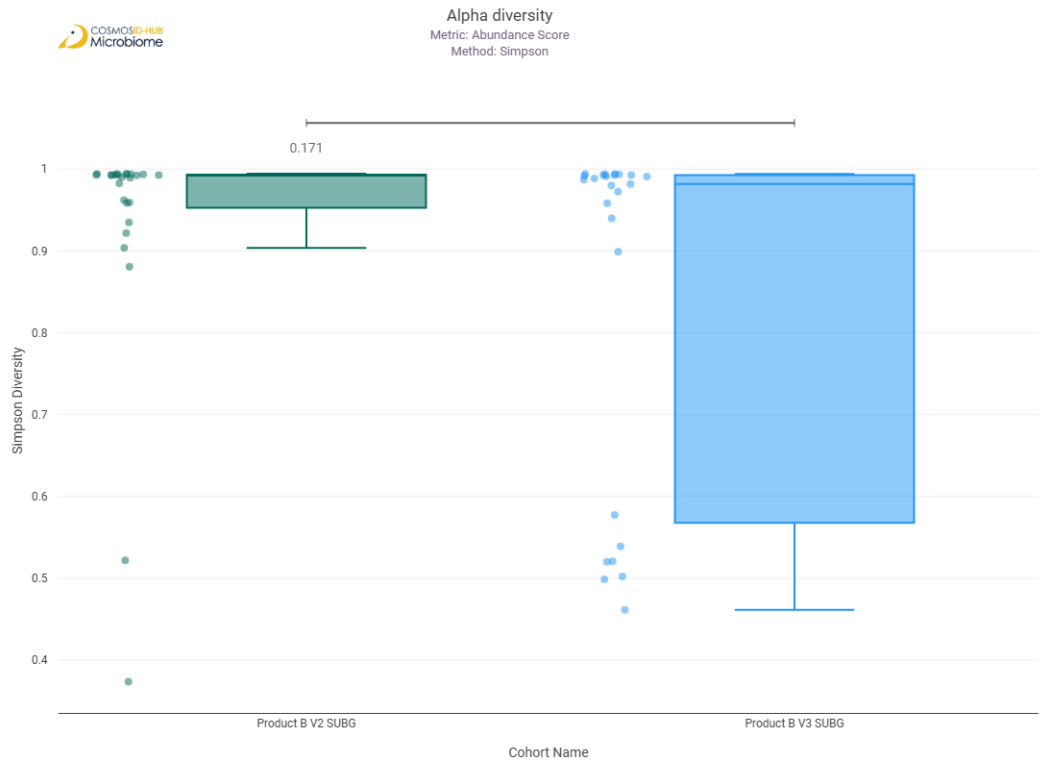
Chao1



Shannon

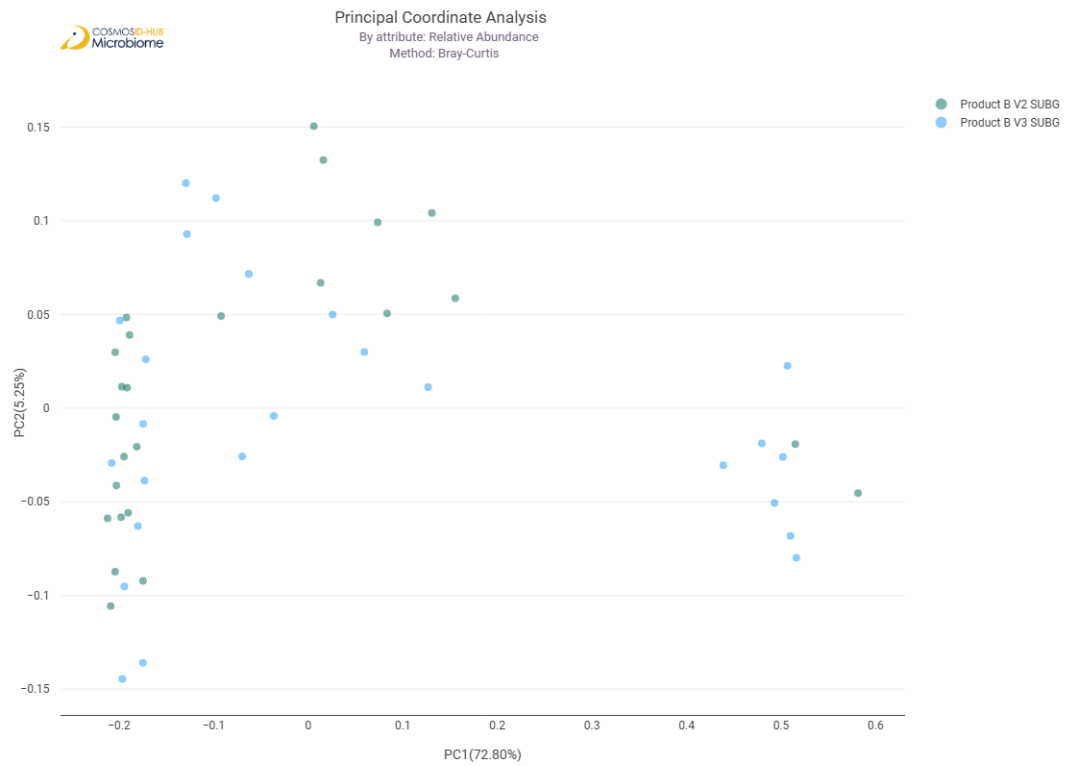


Simpson

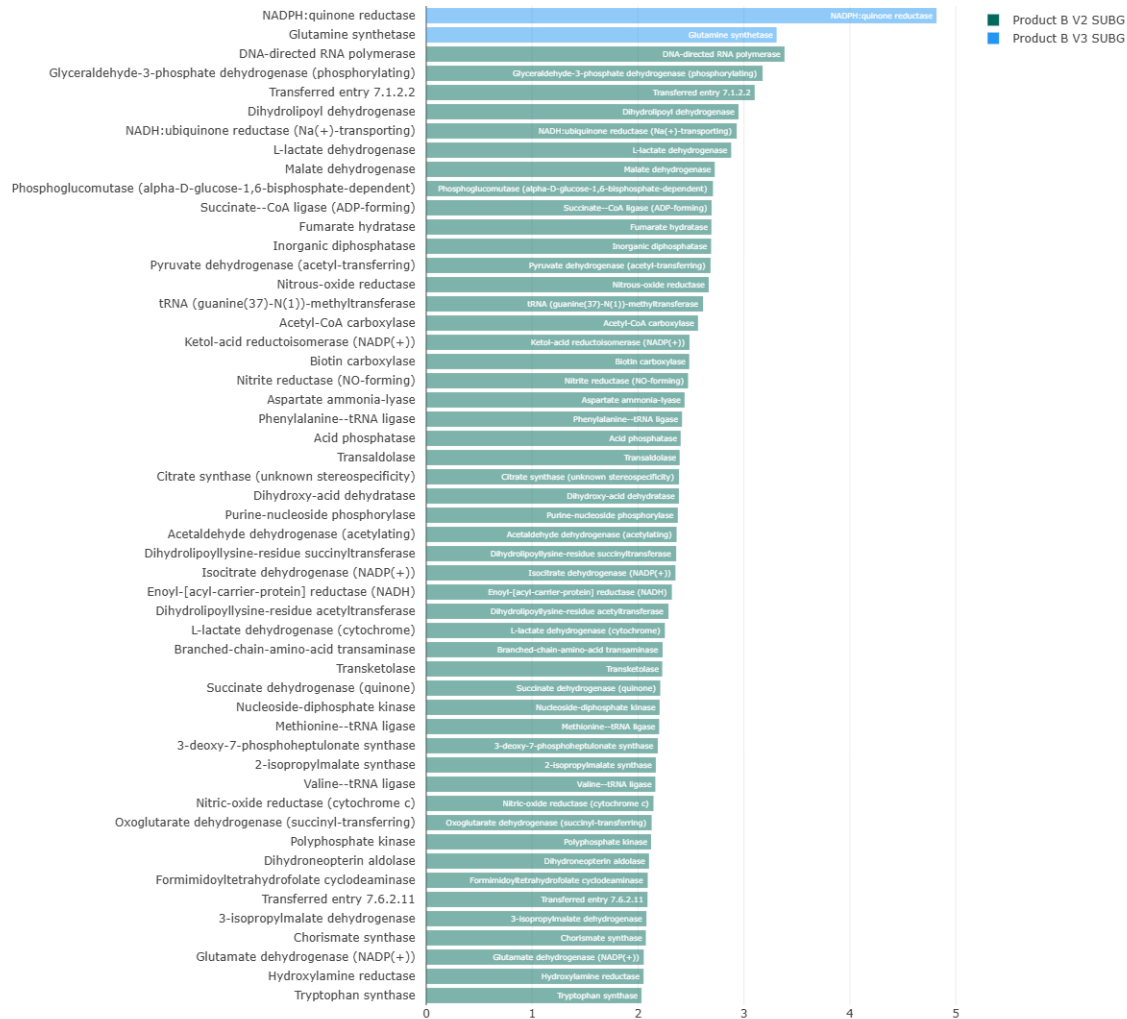


Beta Diversity (EC)

Bray-Curtis  
PERMNOVA  
 $p = 0.093$



## Differential Abundance (LEfSe) (EC)



Feature	Enriched Cohort	LDA Score	P-value
NADPH:quinone reductase	Product B V3 SUBG	4.817843052	0.032031691
Glutamine synthetase	Product B V3 SUBG	3.308540704	0.022617484
DNA-directed RNA polymerase	Product B V2 SUBG	3.383240925	0.019384996
Glyceraldehyde-3-phosphate dehydrogenase (phosphorylating)	Product B V2 SUBG	3.176211311	0.025024185
Transferred entry 7.1.2.2	Product B V2 SUBG	3.10148784	0.004210827
Dihydrolipoyl dehydrogenase	Product B V2 SUBG	2.948469076	5.22129E-05
NADH:ubiquinone reductase (Na(+)-transporting)	Product B V2 SUBG	2.931691645	0.004210827
L-lactate dehydrogenase	Product B V2 SUBG	2.879235232	0.048908406
Malate dehydrogenase	Product B V2 SUBG	2.724100617	0.005051804
Phosphoglucomutase (alpha-D-glucose-1,6-bisphosphate-dependent)	Product B V2 SUBG	2.707465232	1.27E-02
Succinate--CoA ligase (ADP-forming)	Product B V2 SUBG	2.694617006	0.023794451
Fumarate hydratase	Product B V2 SUBG	2.692816588	0.000160745
Inorganic diphosphatase	Product B V2 SUBG	2.690026587	0.003960093

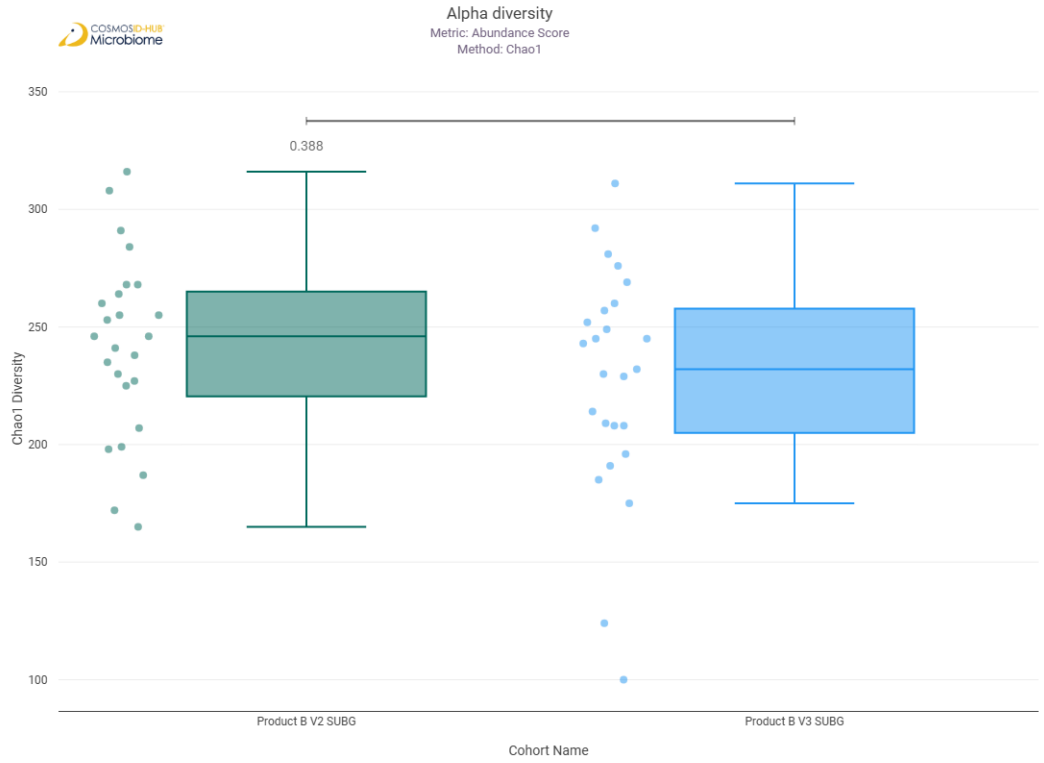
Pyruvate dehydrogenase (acetyl-transferring)	Product B V2 SUBG	2.684685914	0.000187679
Nitrous-oxide reductase	Product B V2 SUBG	2.667384781	0.018884597
tRNA (guanine(37)-N(1))-methyltransferase	Product B V2 SUBG	2.613982445	0.005364191
Acetyl-CoA carboxylase	Product B V2 SUBG	2.566500044	0.027649527
Ketol-acid reductoisomerase (NADP(+))	Product B V2 SUBG	2.485521905	0.046724152
Biotin carboxylase	Product B V2 SUBG	2.483332615	0.014889416
Nitrite reductase (NO-forming)	Product B V2 SUBG	2.47269739	0.005363085
Aspartate ammonia-lyase	Product B V2 SUBG	2.439522177	0.006795613
Phenylalanine--tRNA ligase	Product B V2 SUBG	2.415369545	0.030509062
Acid phosphatase	Product B V2 SUBG	2.402431779	0.003087046
Transaldolase	Product B V2 SUBG	2.392902202	0.007203336
Citrate synthase (unknown stereospecificity)	Product B V2 SUBG	2.38705336	0.003087046
Dihydroxy-acid dehydratase	Product B V2 SUBG	2.385655877	0.023794451
Purine-nucleoside phosphorylase	Product B V2 SUBG	2.375667367	0.040658018
Acetaldehyde dehydrogenase (acetylating)	Product B V2 SUBG	2.364135485	0.033618995
Dihydrolipoyllysine-residue succinyltransferase	Product B V2 SUBG	2.360073425	0.002719251
Isocitrate dehydrogenase (NADP(+))	Product B V2 SUBG	2.353143276	0.001152876
Enoyl-[acyl-carrier-protein] reductase (NADH)	Product B V2 SUBG	2.319528322	0.008561466
Dihydrolipoyllysine-residue acetyltransferase	Product B V2 SUBG	2.287414831	0.000319162
L-lactate dehydrogenase (cytochrome)	Product B V2 SUBG	2.253134982	5.67117E-05
Branched-chain-amino-acid transaminase	Product B V2 SUBG	2.232227272	0.036996166
Transketolase	Product B V2 SUBG	2.228748237	0.046724152
Succinate dehydrogenase (quinone)	Product B V2 SUBG	2.209898248	0.033618995
Nucleoside-diphosphate kinase	Product B V2 SUBG	2.203567512	0.026308569
Methionine--tRNA ligase	Product B V2 SUBG	2.199231134	0.033618995
3-deoxy-7-phosphoheptulonate synthase	Product B V2 SUBG	2.186770799	0.032031691
2-isopropylmalate synthase	Product B V2 SUBG	2.168032589	0.016563699
Valine--tRNA ligase	Product B V2 SUBG	2.16348786	0.046724152
Nitric-oxide reductase (cytochrome c)	Product B V2 SUBG	2.145805026	0.002884661
Oxoglutarate dehydrogenase (succinyl-transferring)	Product B V2 SUBG	2.12864016	0.000614953
Polyphosphate kinase	Product B V2 SUBG	2.122994623	0.001512023
Dihydroneopterin aldolase	Product B V2 SUBG	2.103839331	0.01336608
Formimidoyltetrahydrofolate cyclodeaminase	Product B V2 SUBG	2.091690116	0.044622577
Transferred entry 7.6.2.11	Product B V2 SUBG	2.089287505	0.010726809
3-isopropylmalate dehydrogenase	Product B V2 SUBG	2.079230739	0.008085247
Chorismate synthase	Product B V2 SUBG	2.073624143	0.01265739
Glutamate dehydrogenase (NADP(+))	Product B V2 SUBG	2.053517587	0.010144117
Hydroxylamine reductase	Product B V2 SUBG	2.052101267	3.70E-02
Tryptophan synthase	Product B V2 SUBG	2.032594664	0.036996166

## MetaCyc Pathway

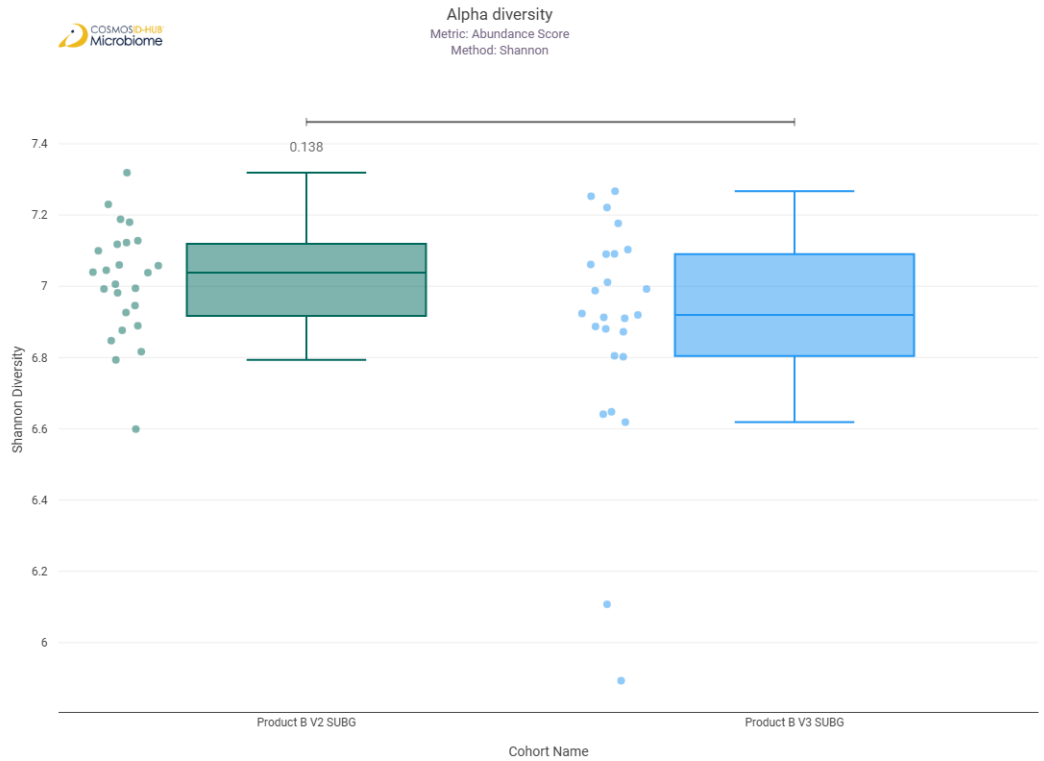


# Alpha Diversity (MetaCyc)

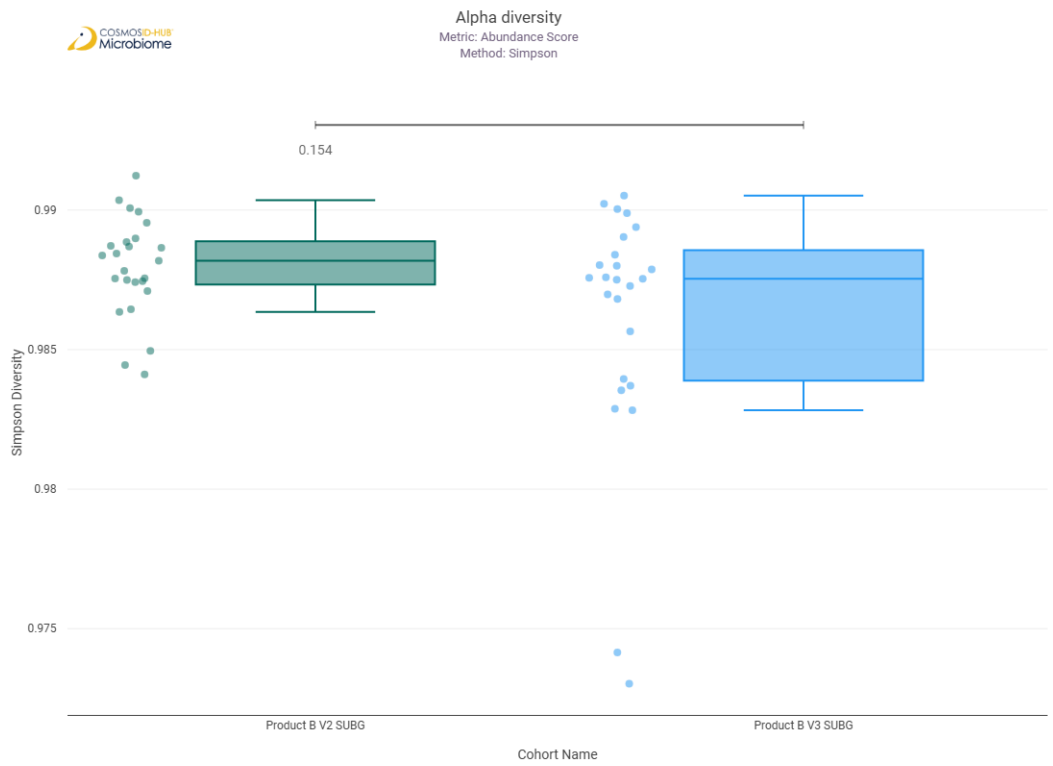
Chao1



Shannon

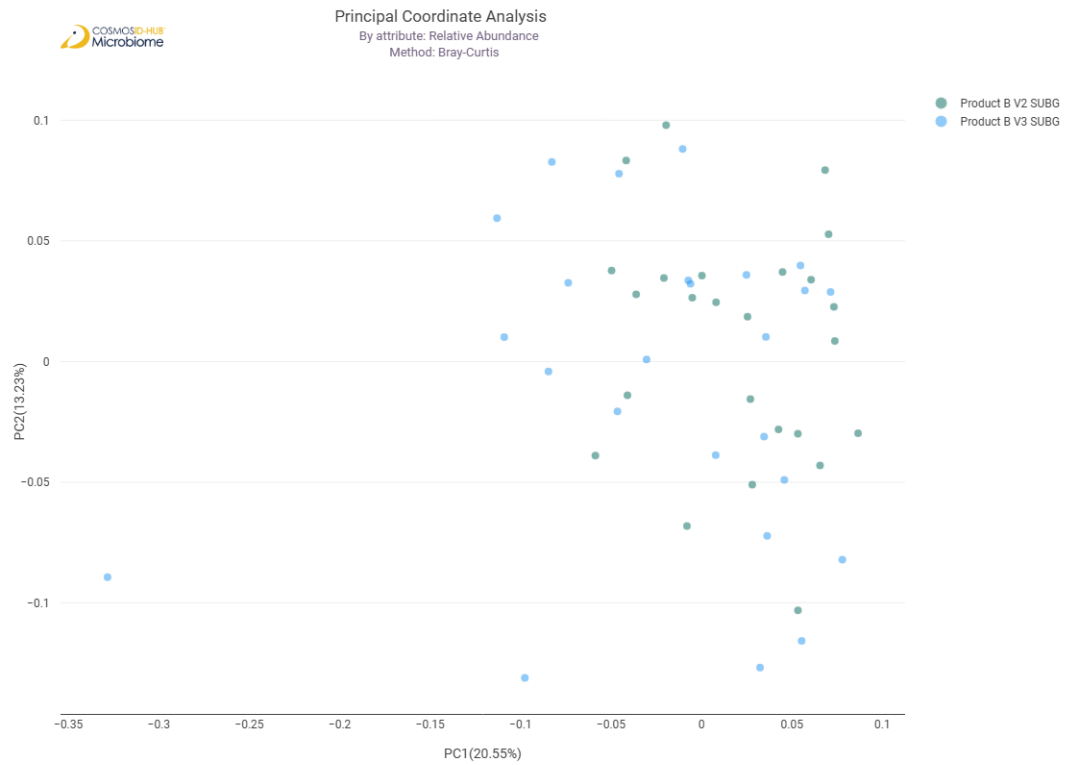


# Simpson

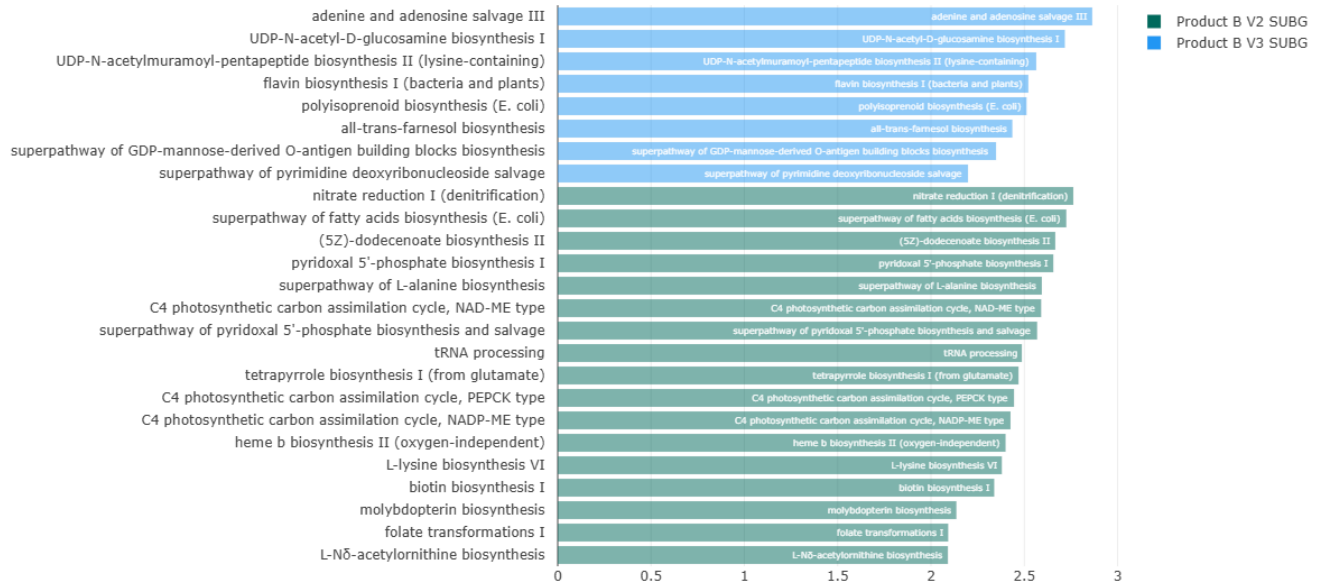


## Beta Diversity (MetaCyc)

Bray-Curtis  
PERMNOVA  
 $p = 0.107$



## Differential Abundance (LEfSe) (MetaCyc)



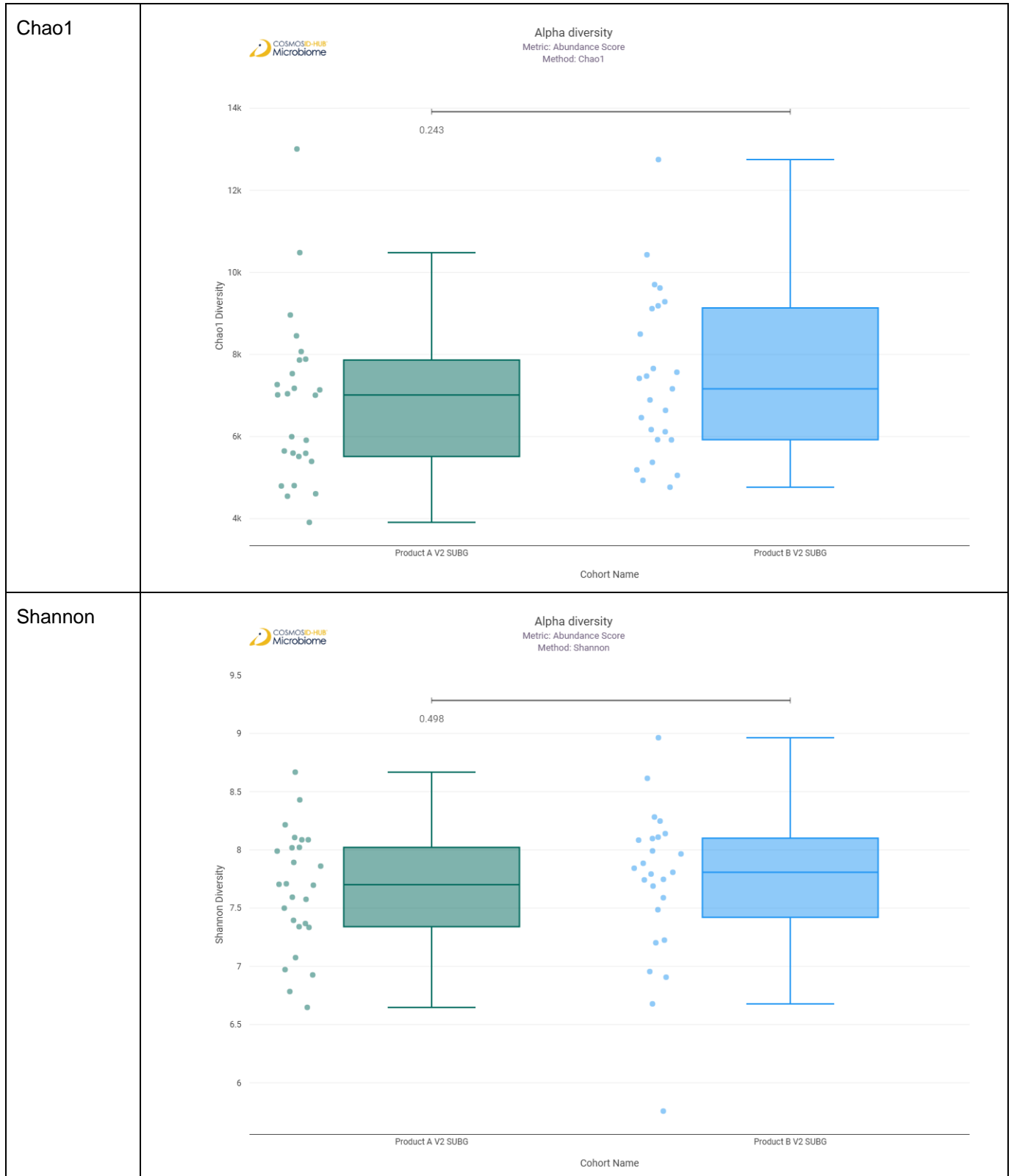
Feature	Enriched Cohort	LDA Score	P-value
adenine and adenosine salvage III	Product B V3 SUBG	2.863969812	0.048908406
UDP-N-acetyl-D-glucosamine biosynthesis I	Product B V3 SUBG	2.717396176	0.036996166
UDP-N-acetylmuramoyl-pentapeptide biosynthesis II (lysine-containing)	Product B V3 SUBG	2.564005299	2.15E-02
flavin biosynthesis I (bacteria and plants)	Product B V3 SUBG	2.521691982	0.021478913
polyisoprenoid biosynthesis (E. coli)	Product B V3 SUBG	2.511972274	0.009321172
all-trans-farnesol biosynthesis	Product B V3 SUBG	2.435974793	0.009321172
superpathway of GDP-mannose-derived O-antigen building blocks biosynthesis	Product B V3 SUBG	2.348650203	0.007288006
superpathway of pyrimidine deoxyribonucleoside salvage	Product B V3 SUBG	2.198461861	0.042804512
nitrate reduction I (denitrification)	Product B V2 SUBG	2.76268097	0.028209048
superpathway of fatty acids biosynthesis (E. coli)	Product B V2 SUBG	2.725110183	0.015664854
(5Z)-dodecenoate biosynthesis II	Product B V2 SUBG	2.666038782	0.000376802
pyridoxal 5'-phosphate biosynthesis I	Product B V2 SUBG	2.655506221	0.007401096
superpathway of L-alanine biosynthesis	Product B V2 SUBG	2.593947019	0.001489919
C4 photosynthetic carbon assimilation cycle, NAD-ME type	Product B V2 SUBG	2.590401904	0.000990491
superpathway of pyridoxal 5'-phosphate biosynthesis and salvage	Product B V2 SUBG	2.56884596	0.002984314
tRNA processing	Product B V2 SUBG	2.486859617	0.000545225
tetrapyrrole biosynthesis I (from glutamate)	Product B V2 SUBG	2.469081125	0.026304962
C4 photosynthetic carbon assimilation cycle, PEPC type	Product B V2 SUBG	2.445053069	0.044617455
C4 photosynthetic carbon assimilation cycle, NADP-ME type	Product B V2 SUBG	2.426092745	0.018401118
heme b biosynthesis II (oxygen-independent)	Product B V2 SUBG	2.399730809	0.011910559
L-lysine biosynthesis VI	Product B V2 SUBG	2.379651672	0.046703062
biotin biosynthesis I	Product B V2 SUBG	2.338785942	0.02096431
molybdopterin biosynthesis	Product B V2 SUBG	2.136102637	0.02751897

folate transformations I	Product B V2 SUBG	2.092205713	0.011137717
L-N $\delta$ -acetyloronithine biosynthesis	Product B V2 SUBG	2.090649307	0.006724272

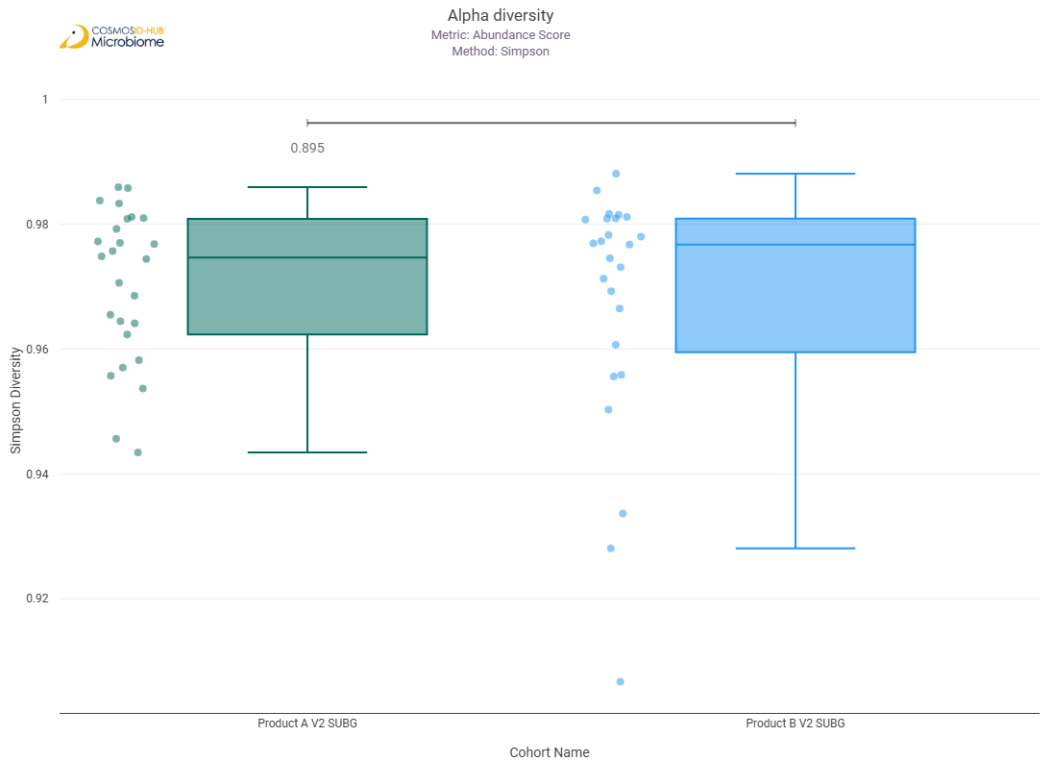
# Comparison 19: Product A V2 SUBG vs Product B V2 SUBG

## Gene Ontology

### Alpha Diversity (GO)

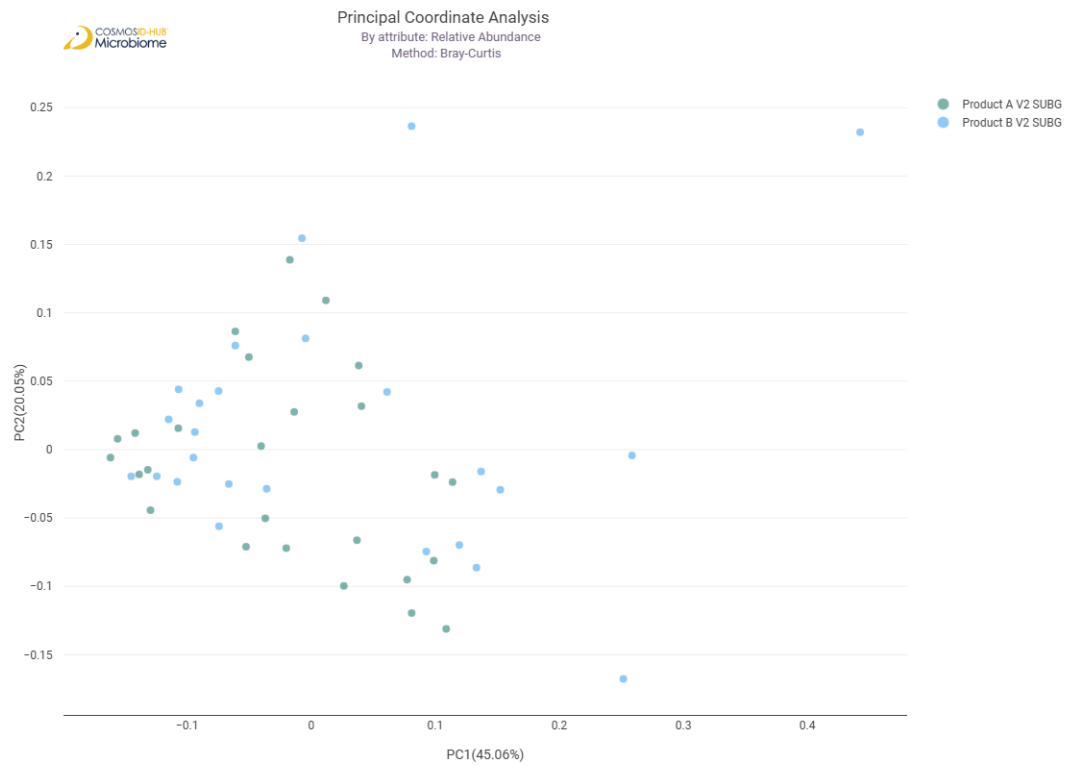


# Simpson

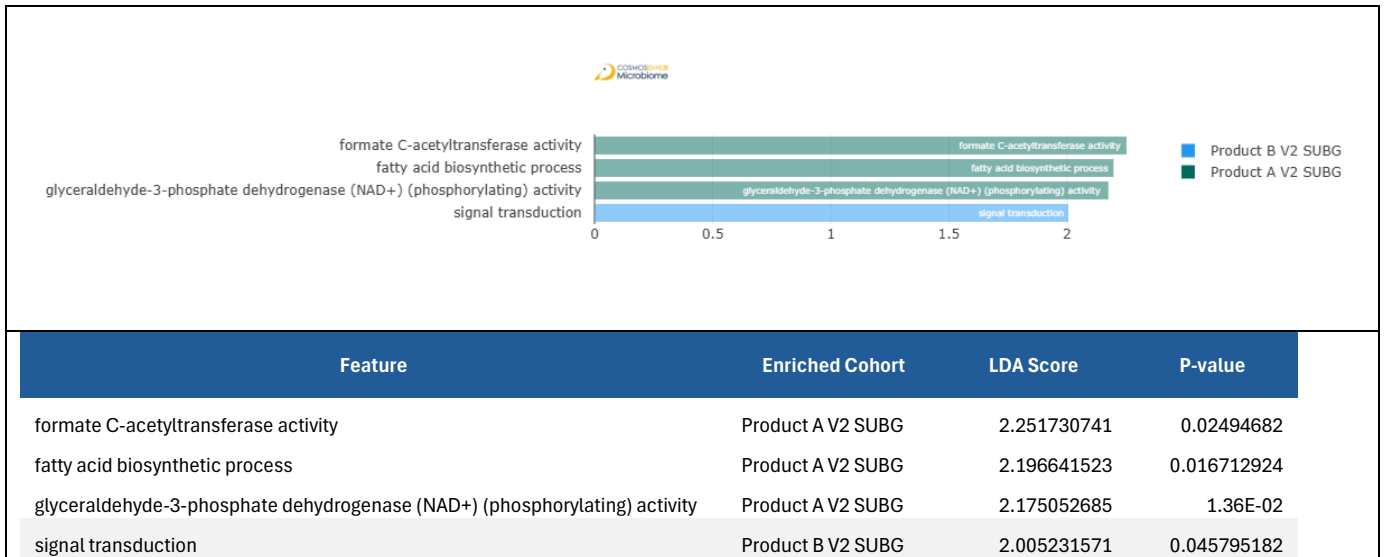


## Beta Diversity (GO)

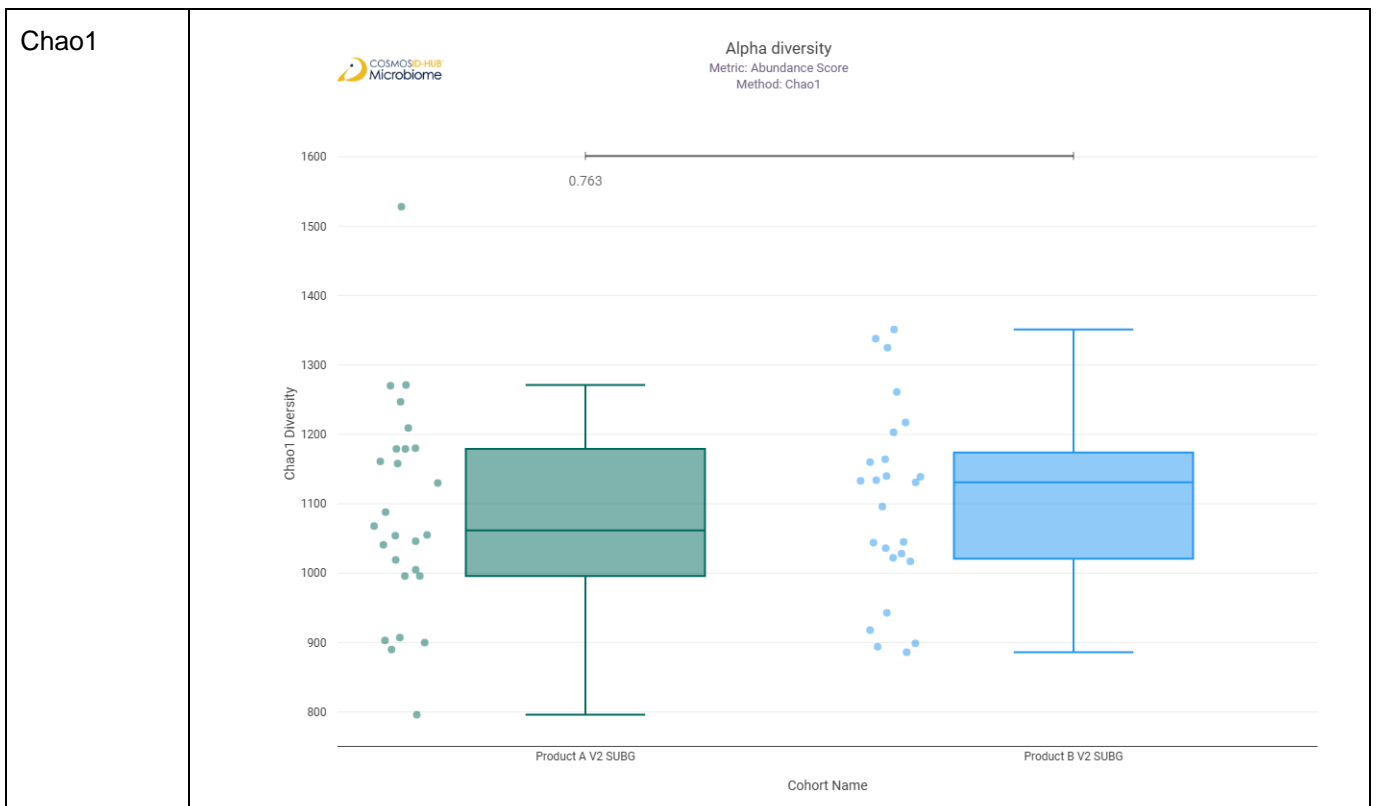
Bray-Curtis  
PERMNOVA  
 $p = 0.224$



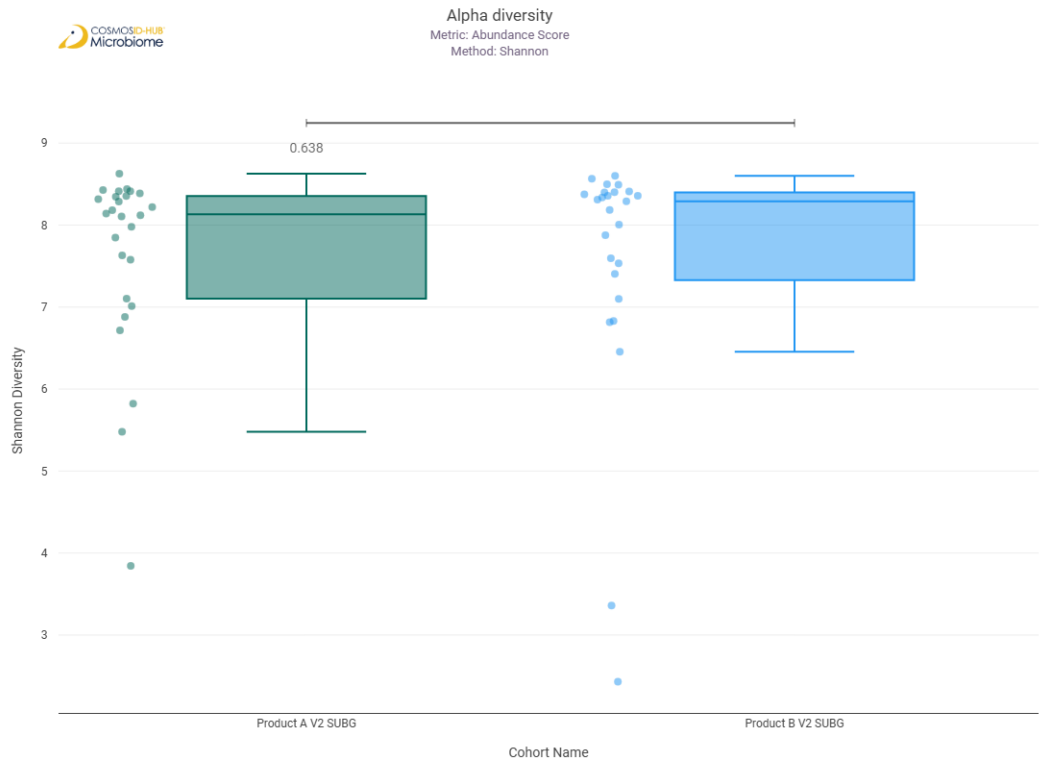
## Differential Abundance (LEfSe) (GO)



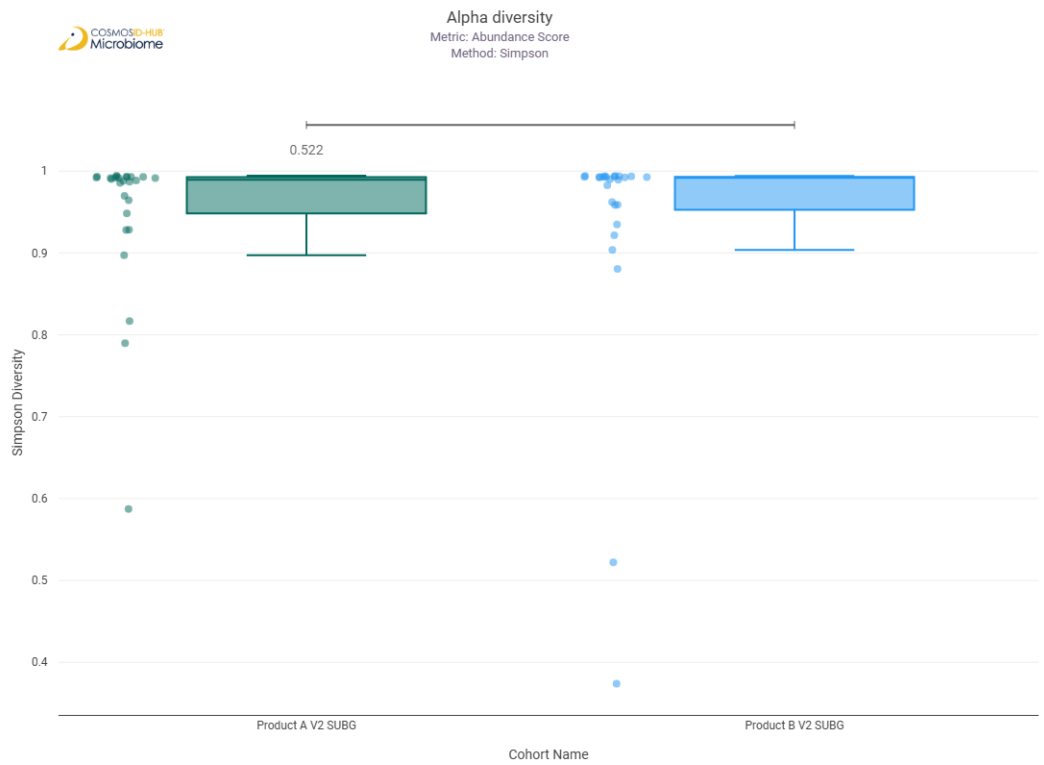
## Enzyme Commission Alpha Diversity (EC)



# Shannon



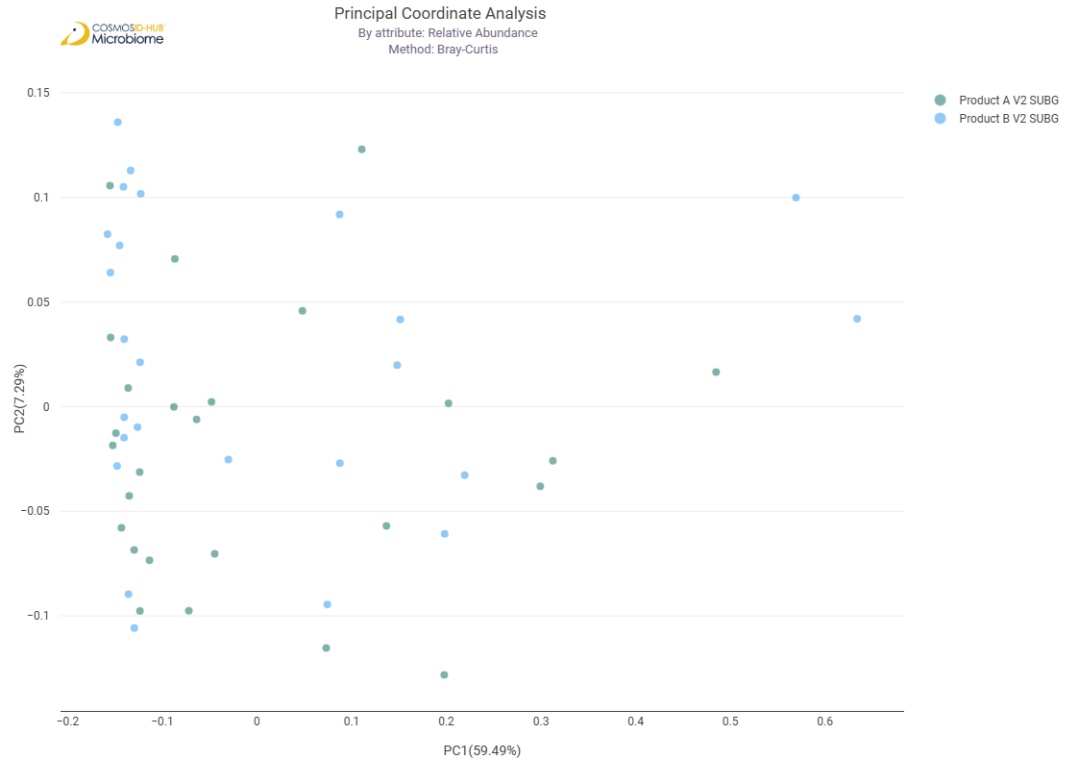
# Simpson



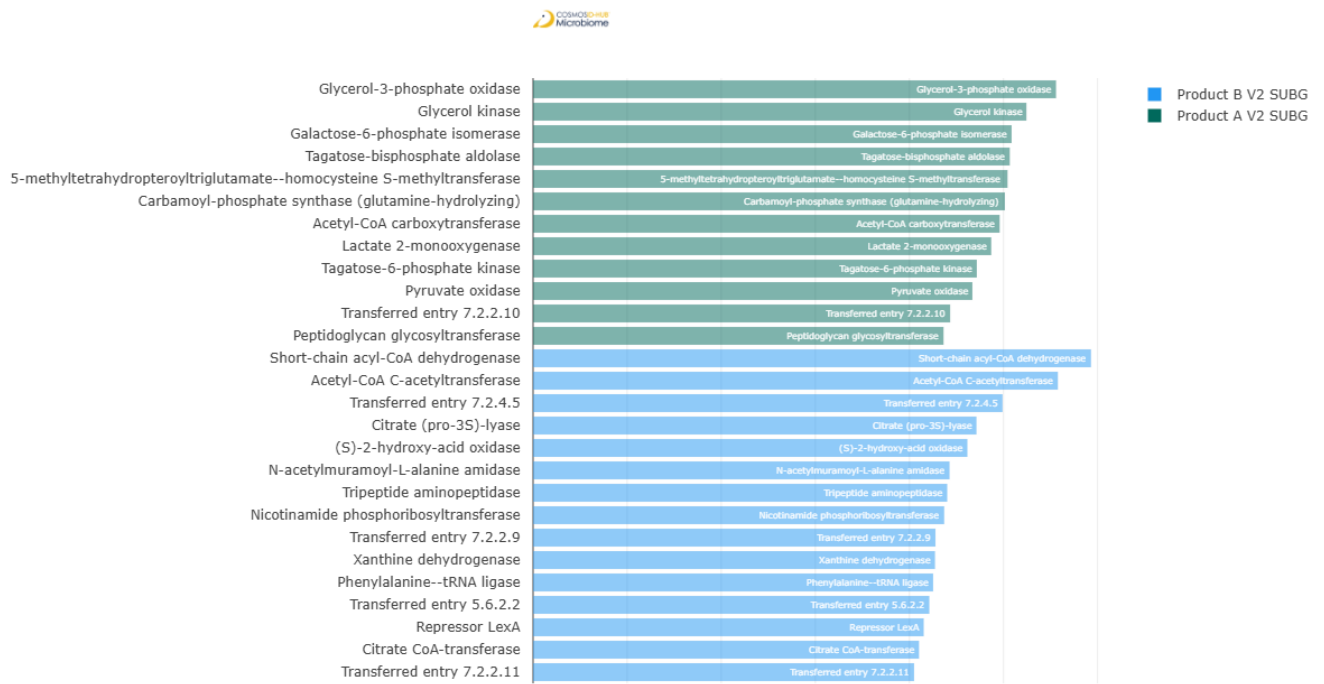


## Beta Diversity (EC)

Bray-Curtis  
PERMNOVA  
p = 0.594



## Differential Abundance (LEfSe) (EC)



Feature

Enriched Cohort

LDA Score

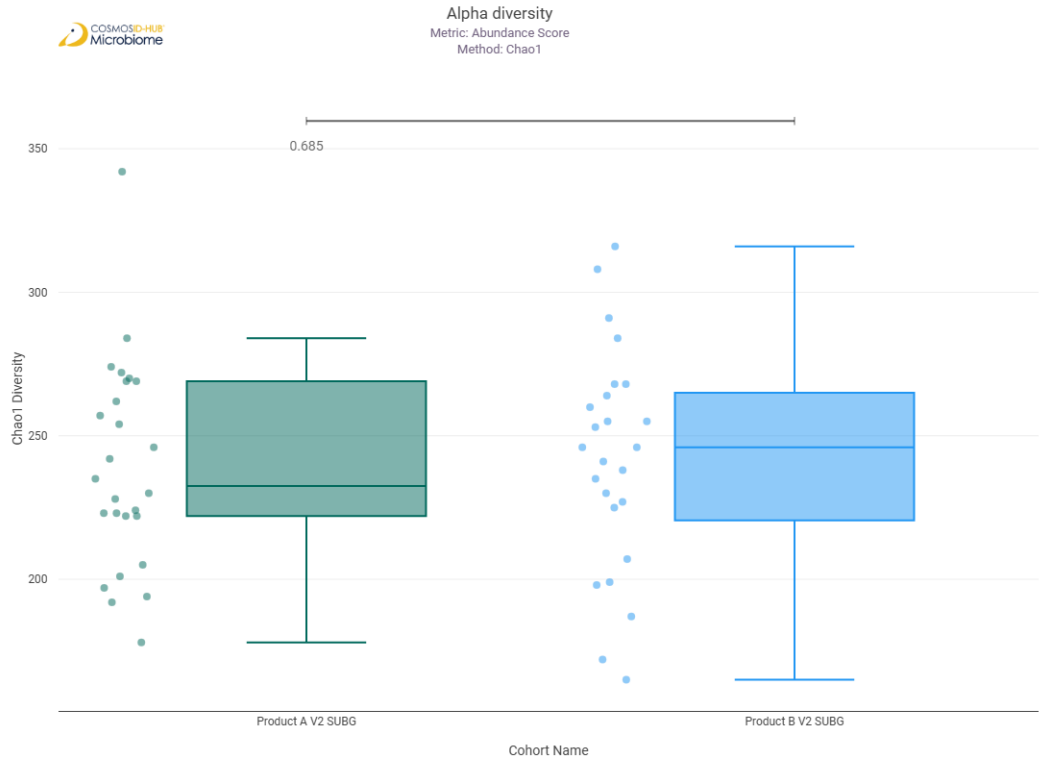
P-value

Glycerol-3-phosphate oxidase	Product A V2 SUBG	2.779339307	7.46E-03
Glycerol kinase	Product A V2 SUBG	2.621793949	0.047879765
Galactose-6-phosphate isomerase	Product A V2 SUBG	2.543170681	0.033240045
Tagatose-bisphosphate aldolase	Product A V2 SUBG	2.53337838	0.02375508
5-methyltetrahydropteroyltriglutamate--homocysteine S-methyltransferase	Product A V2 SUBG	2.521588181	0.038205314
Carbamoyl-phosphate synthase (glutamine-hydrolyzing)	Product A V2 SUBG	2.507544424	0.026189985
Acetyl-CoA carboxytransferase	Product A V2 SUBG	2.47958498	0.033240045
Lactate 2-monooxygenase	Product A V2 SUBG	2.434912862	0.026189985
Tagatose-6-phosphate kinase	Product A V2 SUBG	2.358412568	0.033240045
Pyruvate oxidase	Product A V2 SUBG	2.334779041	0.014305878
Transferred entry 7.2.2.10	Product A V2 SUBG	2.216544388	0.041854827
Peptidoglycan glycosyltransferase	Product A V2 SUBG	2.181459596	0.045795182
Short-chain acyl-CoA dehydrogenase	Product B V2 SUBG	2.965051957	0.007050729
Acetyl-CoA C-acetyltransferase	Product B V2 SUBG	2.788900518	0.031712637
Transferred entry 7.2.4.5	Product B V2 SUBG	2.494901524	0.045795182
Citrate (pro-3S)-lyase	Product B V2 SUBG	2.356485921	0.01946851
(S)-2-hydroxy-acid oxidase	Product B V2 SUBG	2.308306569	0.00104233
N-acetylmuramoyl-L-alanine amidase	Product B V2 SUBG	2.213349132	0.015873756
Tripeptide aminopeptidase	Product B V2 SUBG	2.201081091	0.010390869
Nicotinamide phosphoribosyltransferase	Product B V2 SUBG	2.184897207	0.047879765
Transferred entry 7.2.2.9	Product B V2 SUBG	2.138310427	0.039994768
Xanthine dehydrogenase	Product B V2 SUBG	2.136104068	0.045795182
Phenylalanine--tRNA ligase	Product B V2 SUBG	2.126179549	0.041854827
Transferred entry 5.6.2.2	Product B V2 SUBG	2.105945207	0.043787588
Repressor LexA	Product B V2 SUBG	2.076192914	0.045795182
Citrate CoA-transferase	Product B V2 SUBG	2.051022929	0.020471389
Transferred entry 7.2.2.11	Product B V2 SUBG	2.024983551	0.015071869

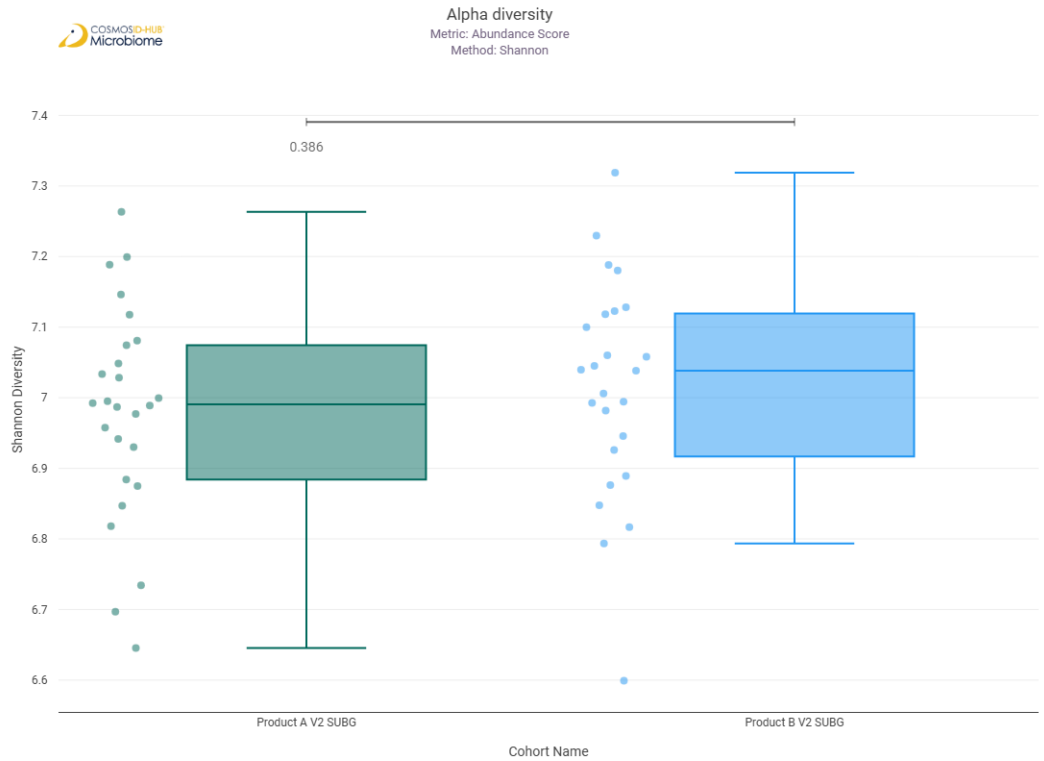
## MetaCyc Pathways

# Alpha Diversity (MetaCyc)

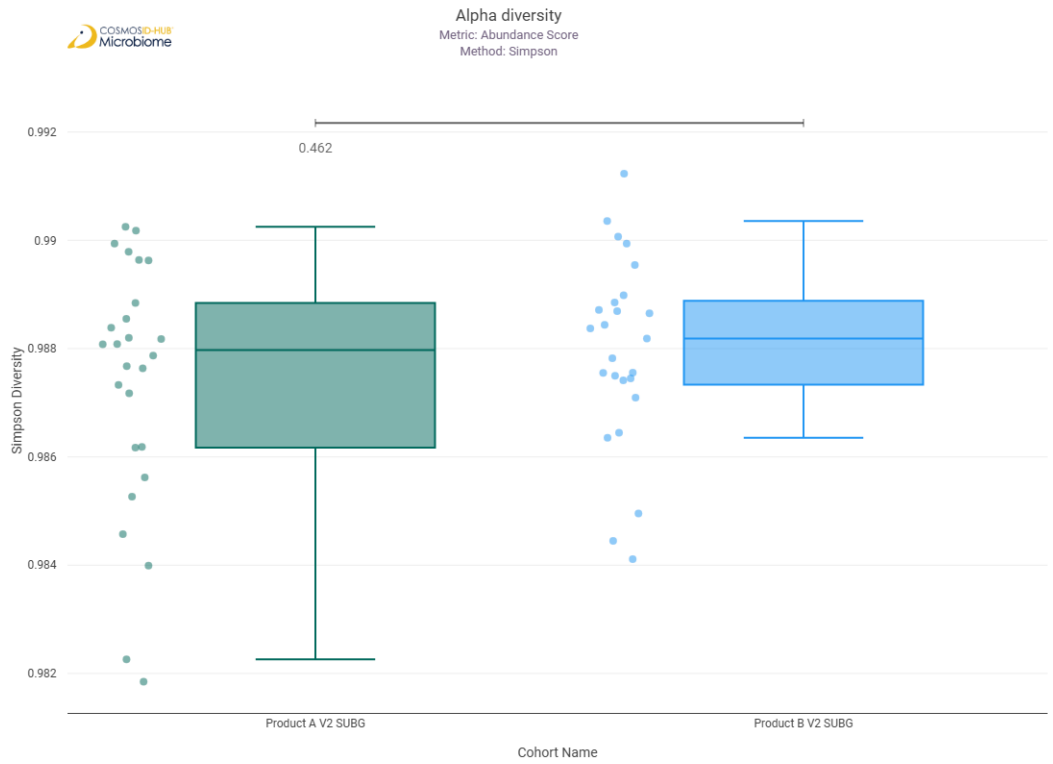
Chao1



Shannon

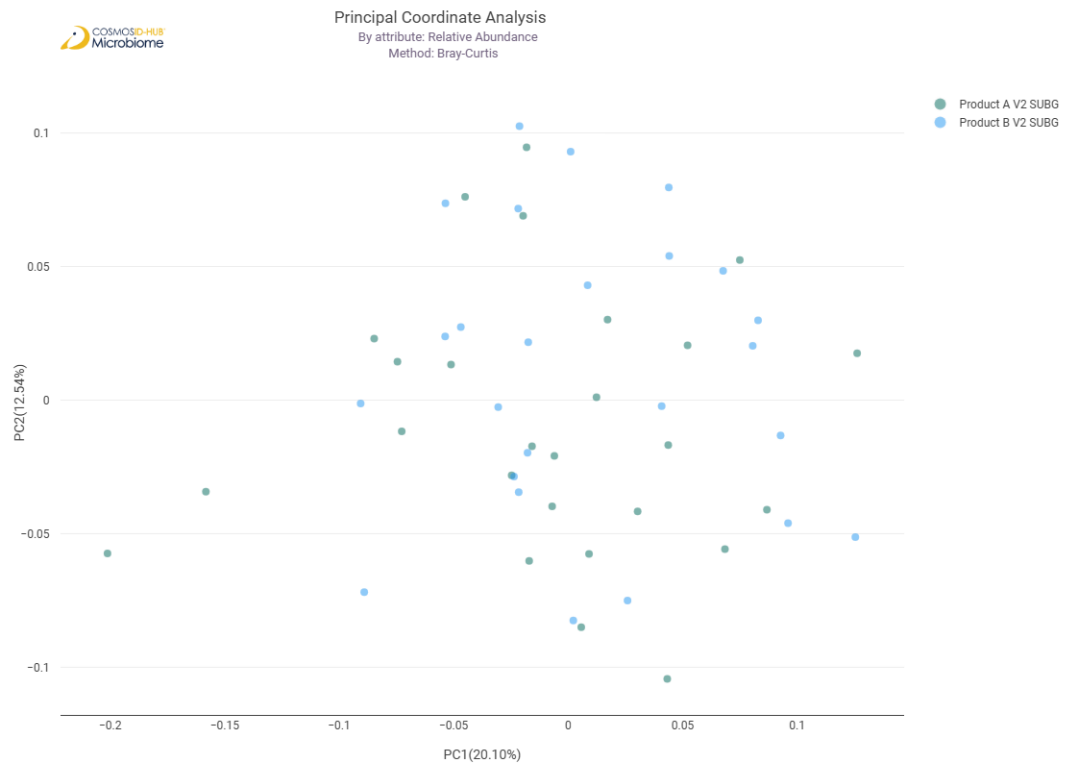


Simpson

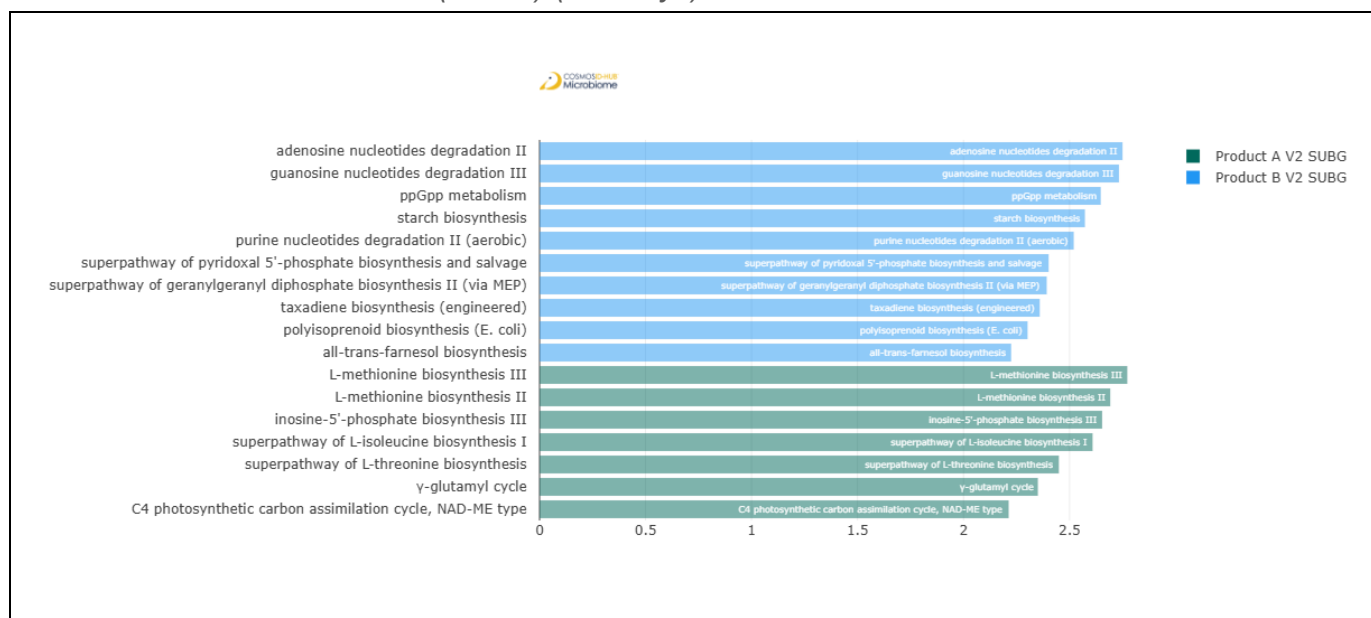


Beta Diversity (MetaCyc)

Bray-Curtis  
PERMNOVA  
p = 0.374



## Differential Abundance (LEfSe) (MetaCyc)

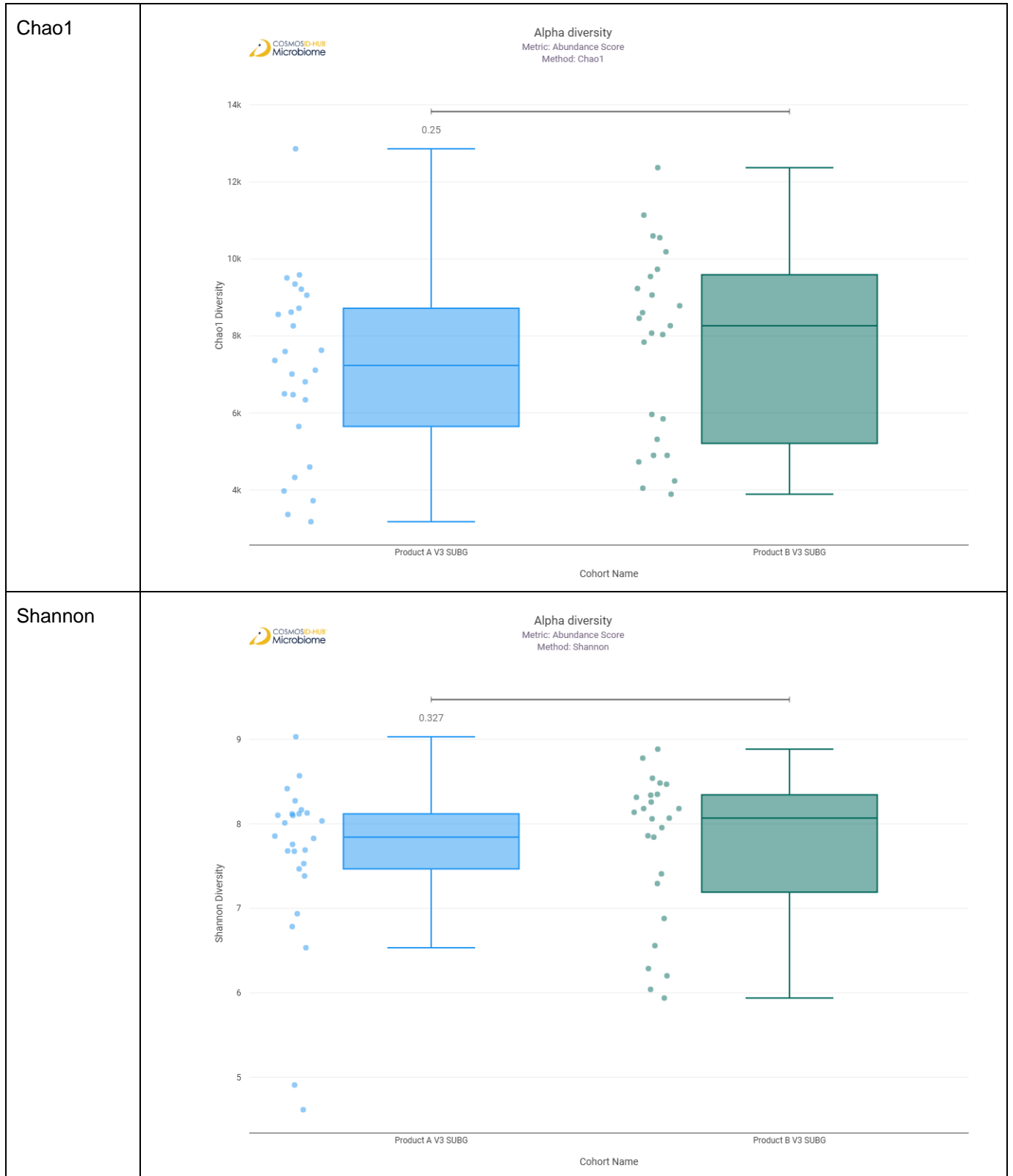


Feature	Enriched Cohort	LDA Score	P-value
adenosine nucleotides degradation II	Product B V2 SUBG	2.750057755	0.038205314
guanosine nucleotides degradation III	Product B V2 SUBG	2.733312194	0.047879765
ppGpp metabolism	Product B V2 SUBG	2.647451783	0.021519031
starch biosynthesis	Product B V2 SUBG	2.572844723	0.034763054
purine nucleotides degradation II (aerobic)	Product B V2 SUBG	2.520017744	0.018888853
superpathway of pyridoxal 5'-phosphate biosynthesis and salvage	Product B V2 SUBG	2.401578989	0.032429435
superpathway of geranylgeranyl diphosphate biosynthesis II (via MEP)	Product B V2 SUBG	2.392576475	0.003816582
taxadiene biosynthesis (engineered)	Product B V2 SUBG	2.359588815	0.005256809
polyisoprenoid biosynthesis (E. coli)	Product B V2 SUBG	2.302252108	0.015864256
all-trans-farnesol biosynthesis	Product B V2 SUBG	2.224778884	0.031697196
L-methionine biosynthesis III	Product A V2 SUBG	2.772698362	1.36E-02
L-methionine biosynthesis II	Product A V2 SUBG	2.692264645	0.039994768
inosine-5'-phosphate biosynthesis III	Product A V2 SUBG	2.65398707	0.008340354
superpathway of L-isoleucine biosynthesis I	Product A V2 SUBG	2.608969913	0.009840467
superpathway of L-threonine biosynthesis	Product A V2 SUBG	2.449856176	0.028837668
γ-glutamyl cycle	Product A V2 SUBG	2.35086058	0.03174462
C4 photosynthetic carbon assimilation cycle, NAD-ME type	Product A V2 SUBG	2.213100244	0.022057133

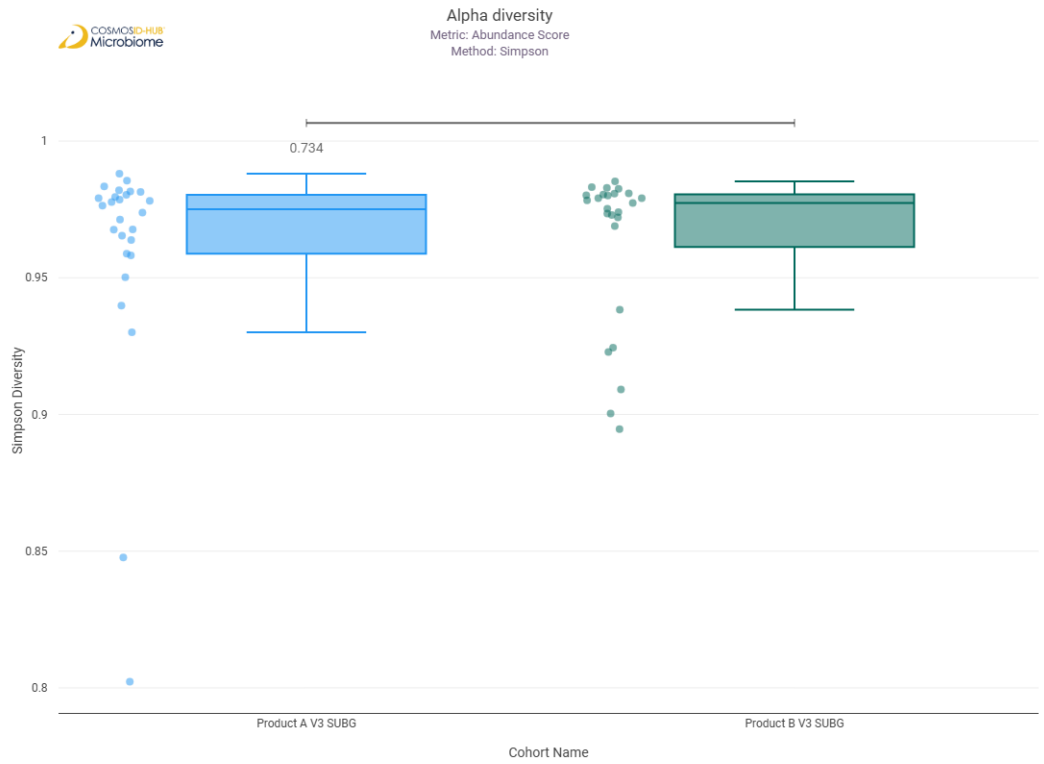
# Comparison 20: Product A V3 SUBG vs Product B V3 SUBG

## Gene Ontology

### Alpha Diversity (GO)

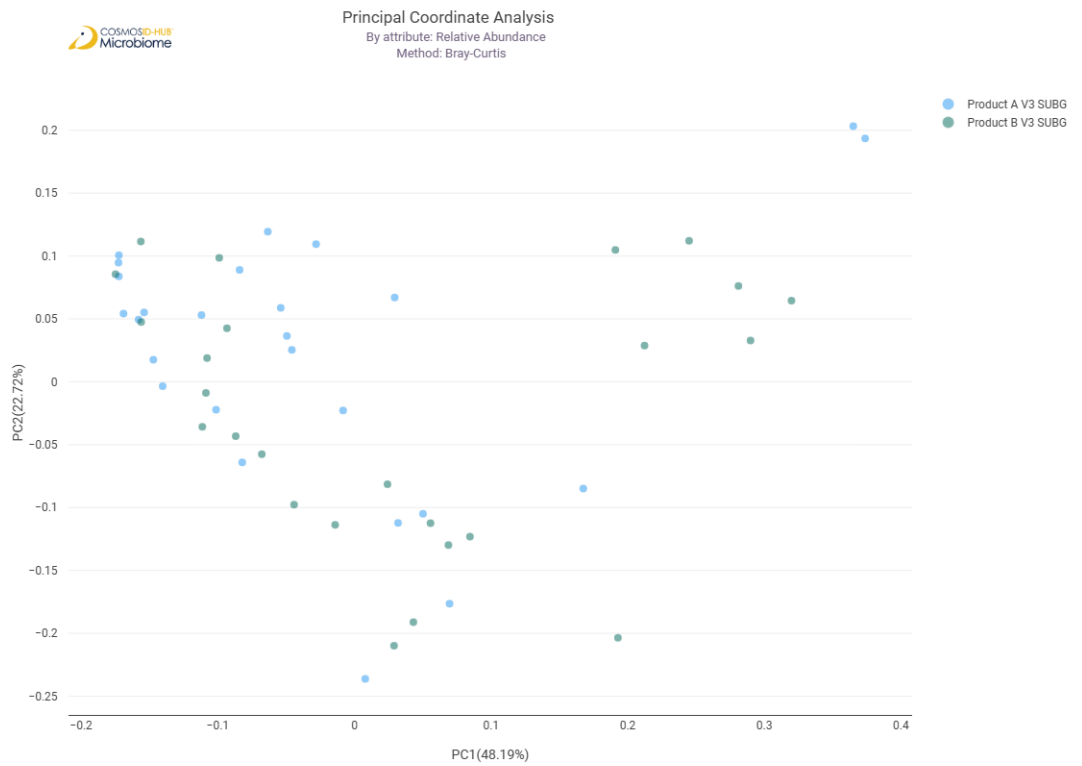


Simpson

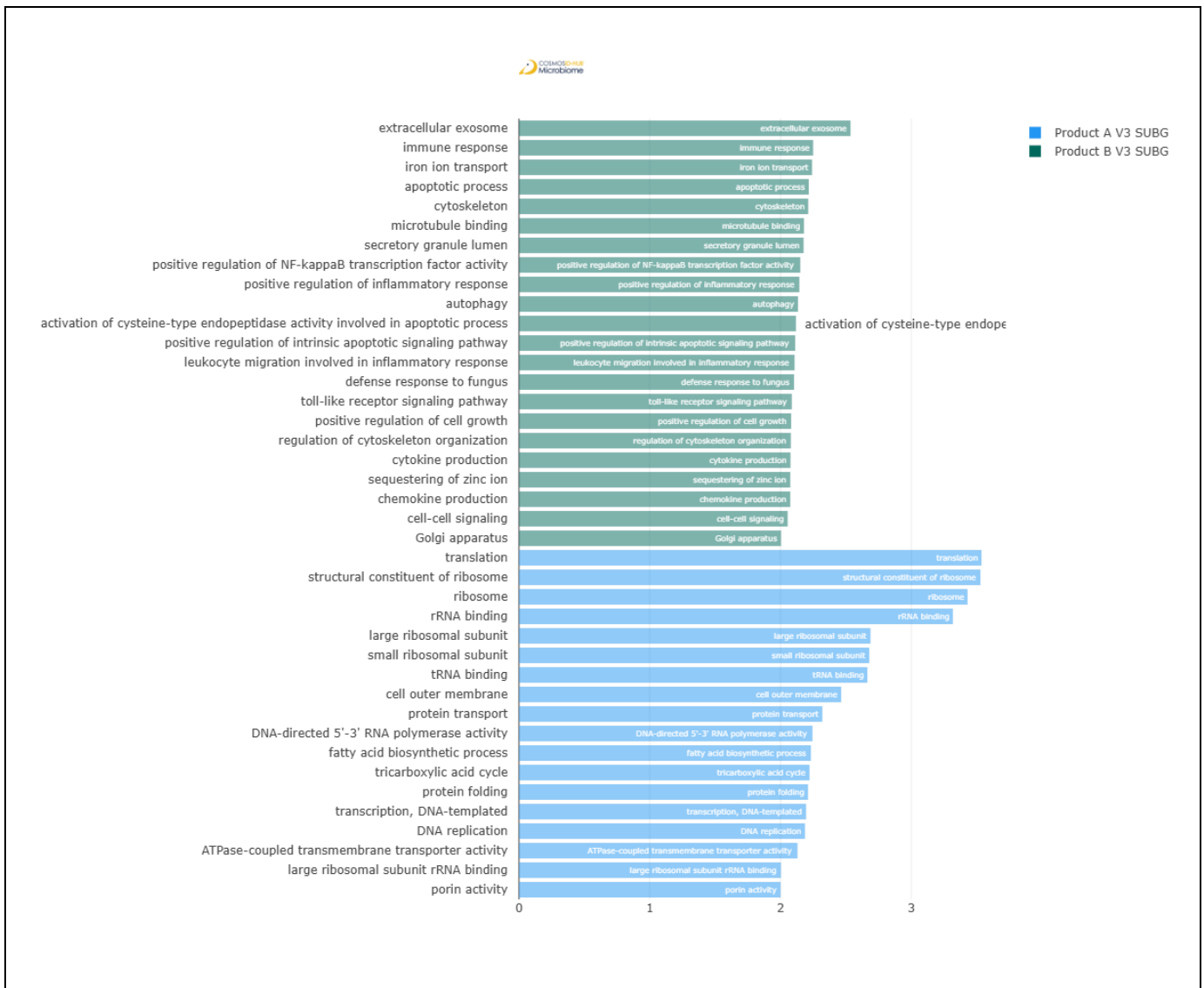


Beta Diversity (GO)

Bray-Curtis  
PERMNOVA  
 $p = 0.080$



## Differential Abundance (LEfSe) (GO)



Feature	Enriched Cohort	LDA Score	P-value
translation	Product A V3 SUBG	3.536687332	0.020471389
structural constituent of ribosome	Product A V3 SUBG	3.528572939	0.022613046
ribosome	Product A V3 SUBG	3.430131346	0.012876233
rRNA binding	Product A V3 SUBG	3.318350314	0.01946851
large ribosomal subunit	Product A V3 SUBG	2.688003944	0.008341822
small ribosomal subunit	Product A V3 SUBG	2.678502093	0.012876233
tRNA binding	Product A V3 SUBG	2.664213181	0.041854827
cell outer membrane	Product A V3 SUBG	2.463894606	0.041854827
protein transport	Product A V3 SUBG	2.319737363	0.016712924
DNA-directed 5'-3' RNA polymerase activity	Product A V3 SUBG	2.244648568	0.021519031
fatty acid biosynthetic process	Product A V3 SUBG	2.23219525	0.004183032
tricarboxylic acid cycle	Product A V3 SUBG	2.221672233	0.002000719
protein folding	Product A V3 SUBG	2.210436333	0.028837668
transcription, DNA-templated	Product A V3 SUBG	2.195364258	0.036484395

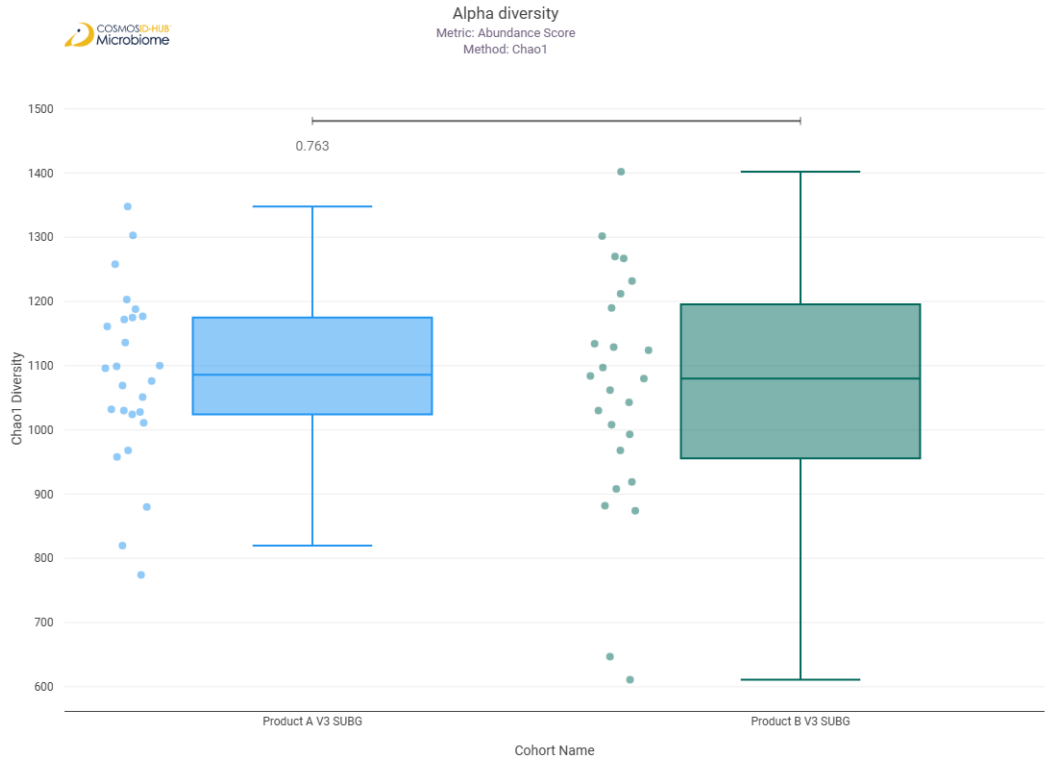


DNA replication	Product A V3 SUBG	2.187269297	0.033240045
ATPase-coupled transmembrane transporter activity	Product A V3 SUBG	2.130170003	0.028837668
large ribosomal subunit rRNA binding	Product A V3 SUBG	2.003191729	0.041854827
porin activity	Product A V3 SUBG	2.000393644	0.000744191
extracellular exosome	Product B V3 SUBG	2.535130566	0.039994768
immune response	Product B V3 SUBG	2.249850104	4.38E-02
iron ion transport	Product B V3 SUBG	2.241435289	0.012209995
apoptotic process	Product B V3 SUBG	2.216215889	0.045795182
cytoskeleton	Product B V3 SUBG	2.212010433	0.039994768
microtubule binding	Product B V3 SUBG	2.179482504	0.045795182
secretory granule lumen	Product B V3 SUBG	2.176539587	0.034829974
positive regulation of NF-kappaB transcription factor activity	Product B V3 SUBG	2.151381348	0.038205314
positive regulation of inflammatory response	Product B V3 SUBG	2.144302779	0.039994768
autophagy	Product B V3 SUBG	2.133749546	0.039994768
activation of cysteine-type endopeptidase activity involved in apoptotic process	Product B V3 SUBG	2.1181929	0.043787588
positive regulation of intrinsic apoptotic signaling pathway	Product B V3 SUBG	2.112289442	0.043787588
leukocyte migration involved in inflammatory response	Product B V3 SUBG	2.107427716	0.047879765
defense response to fungus	Product B V3 SUBG	2.103586985	0.039994768
toll-like receptor signaling pathway	Product B V3 SUBG	2.086746471	0.043787588
positive regulation of cell growth	Product B V3 SUBG	2.081484217	0.047879765
regulation of cytoskeleton organization	Product B V3 SUBG	2.079085603	0.047879765
cytokine production	Product B V3 SUBG	2.076455901	0.047879765
sequestering of zinc ion	Product B V3 SUBG	2.074832793	0.045795182
chemokine production	Product B V3 SUBG	2.074720372	0.045795182
cell-cell signaling	Product B V3 SUBG	2.054731602	0.038205314
Golgi apparatus	Product B V3 SUBG	2.003938769	0.038205314

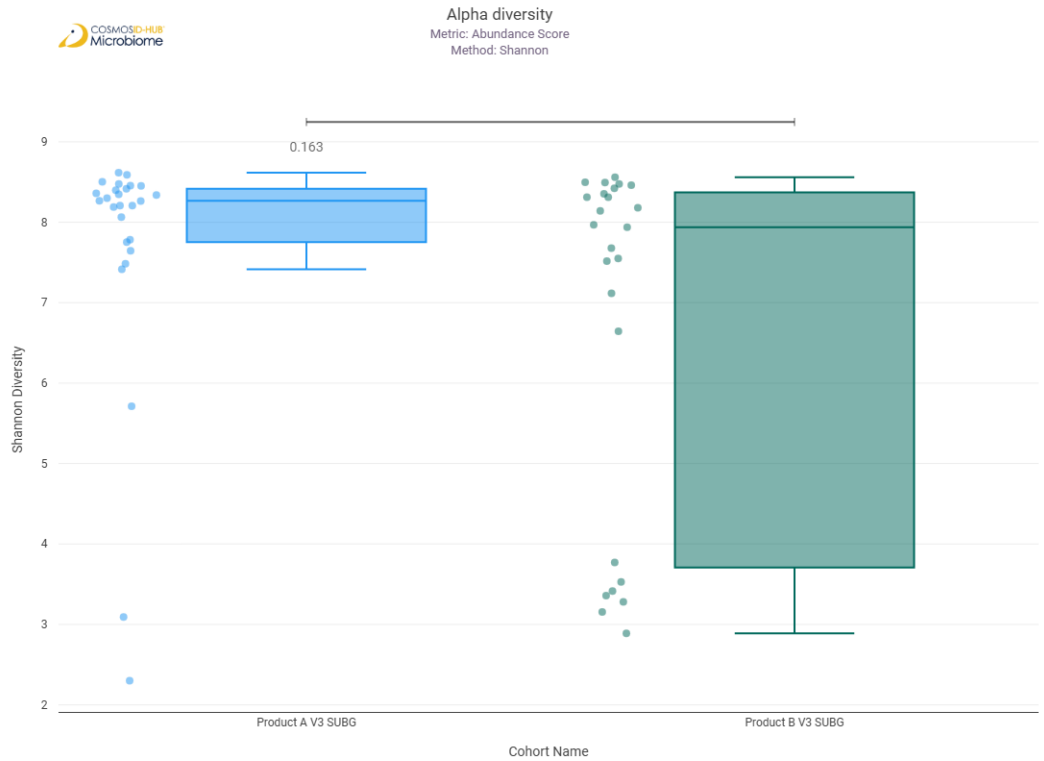
## Enzyme Commission

# Alpha Diversity (EC)

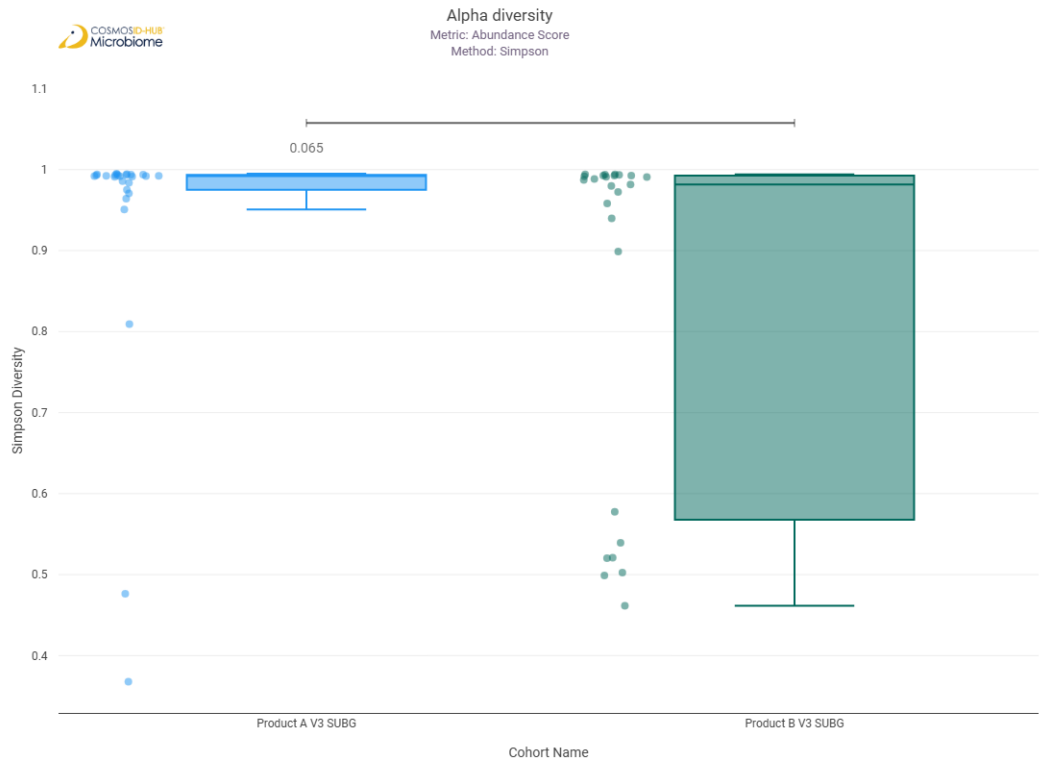
Chao1



Shannon

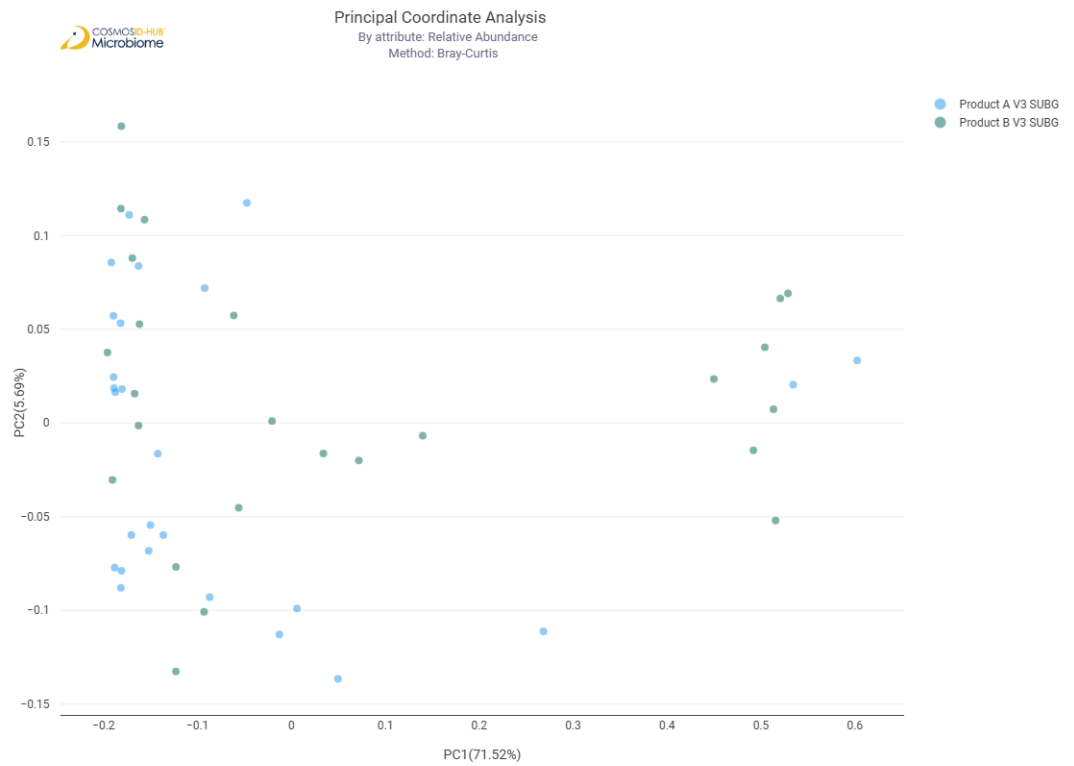


Simpson

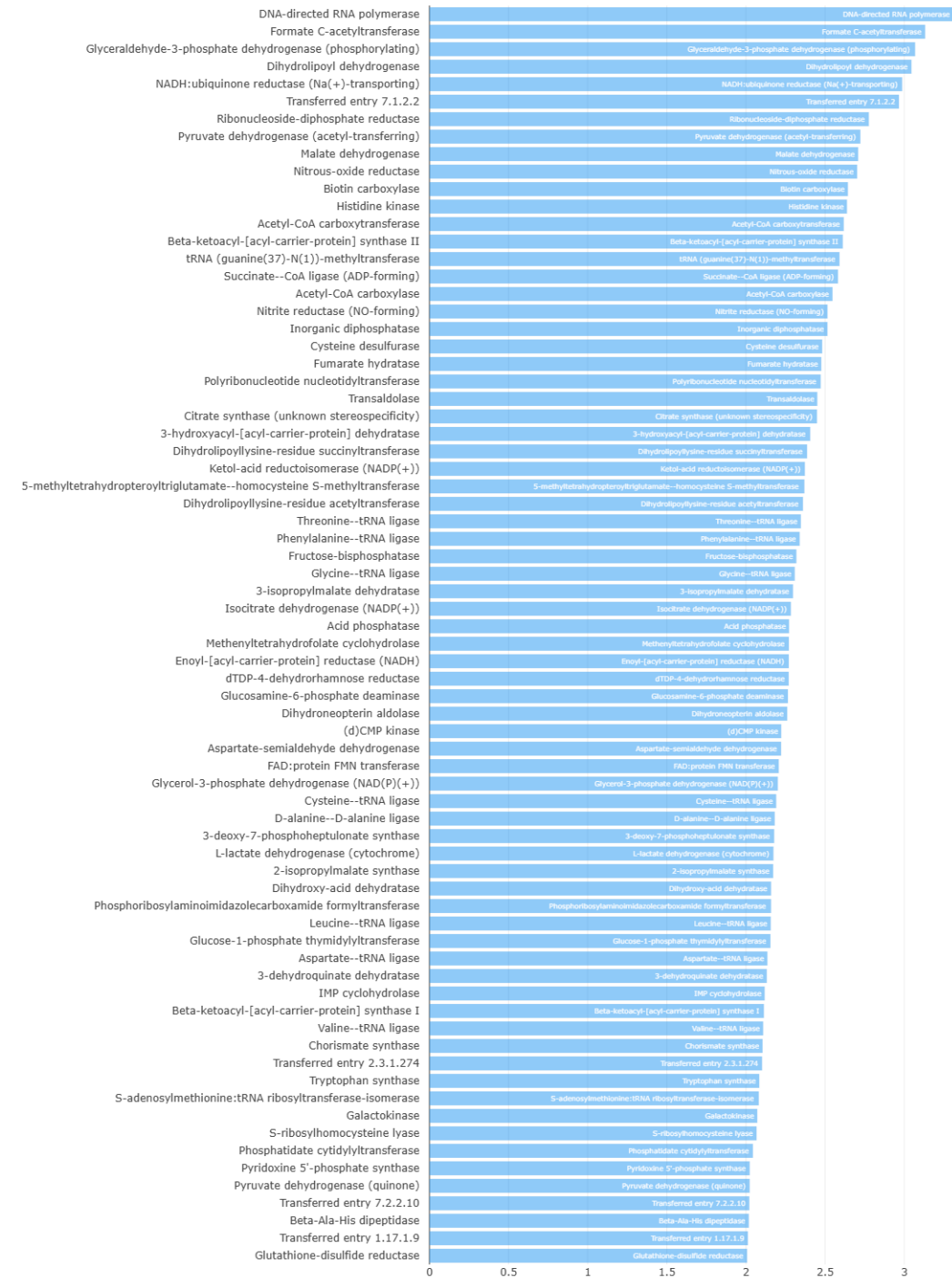


Beta Diversity (EC)

Bray-Curtis  
PERMNOVA  
 $p = 0.073$



# Differential Abundance (LEfSe) (EC)



Feature	Enriched Cohort	LDA Score	P-value
DNA-directed RNA polymerase	Product A V3 SUBG	3.312199282	0.007889693
Formate C-acetyltransferase	Product A V3 SUBG	3.13215656	0.039994768
Glyceraldehyde-3-phosphate dehydrogenase (phosphorylating)	Product A V3 SUBG	3.068813313	0.031712637

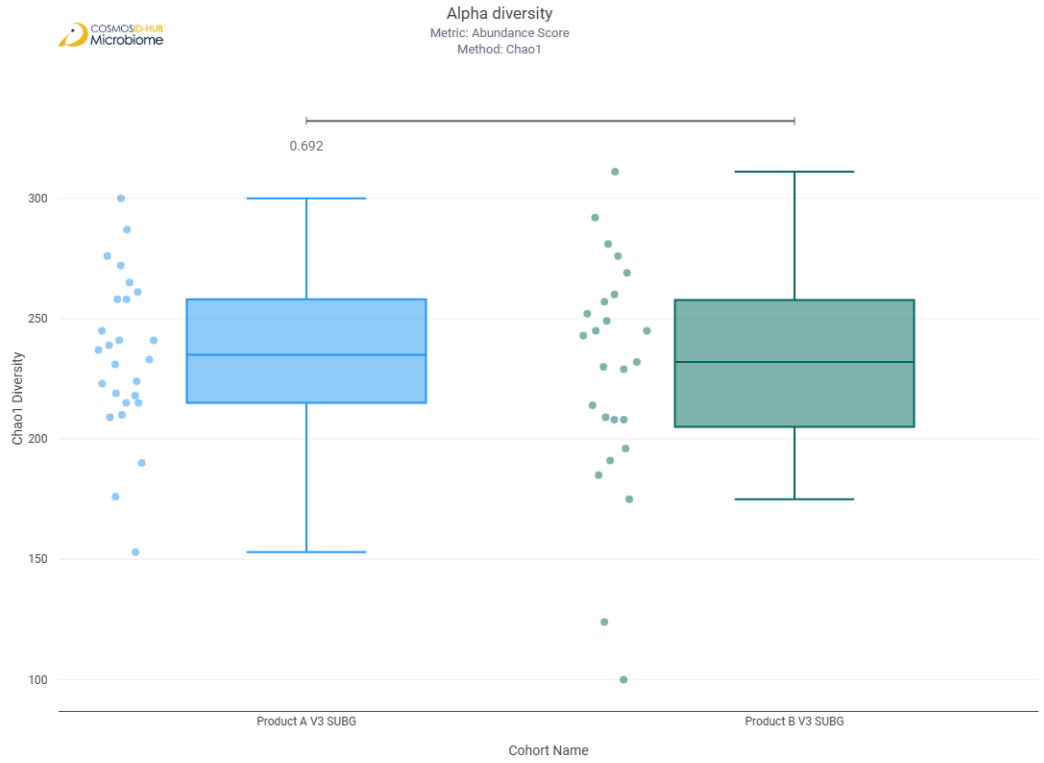
Dihydrolipoyl dehydrogenase	Product A V3 SUBG	3.045630912	1.46616E-05
NADH:ubiquinone reductase (Na(+)-transporting)	Product A V3 SUBG	2.986963277	0.000605172
Transferred entry 7.1.2.2	Product A V3 SUBG	2.966871817	0.020471389
Ribonucleoside-diphosphate reductase	Product A V3 SUBG	2.776516943	0.016712924
Pyruvate dehydrogenase (acetyl-transferring)	Product A V3 SUBG	2.723062614	0.000605172
Malate dehydrogenase	Product A V3 SUBG	2.709053579	0.005941992
Nitrous-oxide reductase	Product A V3 SUBG	2.702720573	0.021507212
Biotin carboxylase	Product A V3 SUBG	2.644235086	0.000852766
Histidine kinase	Product A V3 SUBG	2.638292954	0.041854827
Acetyl-CoA carboxyltransferase	Product A V3 SUBG	2.617952144	0.002736233
Beta-ketoacyl-[acyl-carrier-protein] synthase II	Product A V3 SUBG	2.611822632	0.015071869
tRNA (guanine(37)-N(1))-methyltransferase	Product A V3 SUBG	2.591202435	0.000694855
Succinate--CoA ligase (ADP-forming)	Product A V3 SUBG	2.581609521	0.02494682
Acetyl-CoA carboxylase	Product A V3 SUBG	2.546806449	0.004438681
Nitrite reductase (NO-forming)	Product A V3 SUBG	2.515556565	0.00628096
Inorganic diphosphatase	Product A V3 SUBG	2.515254374	0.020471389
Cysteine desulfurase	Product A V3 SUBG	2.48170098	1.88E-03
Fumarate hydratase	Product A V3 SUBG	2.475987752	0.008341822
Polyribonucleotide nucleotidyltransferase	Product A V3 SUBG	2.472260598	0.012876233
Transaldolase	Product A V3 SUBG	2.450906966	0.005292825
Citrate synthase (unknown stereospecificity)	Product A V3 SUBG	2.448881882	0.002269883
3-hydroxyacyl-[acyl-carrier-protein] dehydratase	Product A V3 SUBG	2.406150454	0.02494682
Dihydrolipoyllysine-residue succinyltransferase	Product A V3 SUBG	2.386412108	0.00097562
Ketol-acid reductoisomerase (NADP(+))	Product A V3 SUBG	2.372178573	0.047879765
5-methyltetrahydropteroyltriglutamate--homocysteine S-methyltransferase	Product A V3 SUBG	2.369261081	0.028837668
Dihydrolipoyllysine-residue acetyltransferase	Product A V3 SUBG	2.360242064	0.000319608
Threonine--tRNA ligase	Product A V3 SUBG	2.347096758	0.02494682
Phenylalanine--tRNA ligase	Product A V3 SUBG	2.339465697	0.028837668
Fructose-bisphosphatase	Product A V3 SUBG	2.318793495	0.016712924
Glycine--tRNA ligase	Product A V3 SUBG	2.308480299	0.038205314
3-isopropylmalate dehydratase	Product A V3 SUBG	2.297290891	0.01946851
Isocitrate dehydrogenase (NADP(+))	Product A V3 SUBG	2.28378722	0.000852534
Acid phosphatase	Product A V3 SUBG	2.272511228	0.009316196
Methenyltetrahydrofolate cyclohydrolase	Product A V3 SUBG	2.271222446	0.043787588
Enoyl-[acyl-carrier-protein] reductase (NADH)	Product A V3 SUBG	2.27078058	0.00881699
dTDP-4-dehydrorhamnose reductase	Product A V3 SUBG	2.270338236	0.004708409
Glucosamine-6-phosphate deaminase	Product A V3 SUBG	2.26535543	0.013574437
Dihydroneopterin aldolase	Product A V3 SUBG	2.260965749	0.001043427
(d)CMP kinase	Product A V3 SUBG	2.222871162	0.010390869
Aspartate-semialdehyde dehydrogenase	Product A V3 SUBG	2.222116087	0.036484395
FAD:protein FMN transferase	Product A V3 SUBG	2.207303025	0.021519031
Glycerol-3-phosphate dehydrogenase (NAD(P)(+))	Product A V3 SUBG	2.201487687	0.015071869
Cysteine--tRNA ligase	Product A V3 SUBG	2.191170276	0.004992891
D-alanine--D-alanine ligase	Product A V3 SUBG	2.181747657	0.027486336
3-deoxy-7-phosphoheptulonate synthase	Product A V3 SUBG	2.178294885	0.002571856
L-lactate dehydrogenase (cytochrome)	Product A V3 SUBG	2.173648975	0.000975879

2-isopropylmalate synthase	Product A V3 SUBG	2.172001333	0.010390869
Dihydroxy-acid dehydratase	Product A V3 SUBG	2.15868405	2.49E-02
Phosphoribosylaminoimidazolecarboxamide formyltransferase	Product A V3 SUBG	2.158625201	0.022613046
Leucine--tRNA ligase	Product A V3 SUBG	2.156558873	0.021519031
Glucose-1-phosphate thymidyltransferase	Product A V3 SUBG	2.154769362	0.018508823
Aspartate--tRNA ligase	Product A V3 SUBG	2.135805728	0.031712637
3-dehydroquininate dehydratase	Product A V3 SUBG	2.131724086	0.013574437
IMP cyclohydrolase	Product A V3 SUBG	2.118278512	0.028837668
Beta-ketoacyl-[acyl-carrier-protein] synthase I	Product A V3 SUBG	2.113359831	0.018508823
Valine--tRNA ligase	Product A V3 SUBG	2.108822781	0.033240045
Chorismate synthase	Product A V3 SUBG	2.104886081	0.00176114
Transferred entry 2.3.1.274	Product A V3 SUBG	2.101880318	0.030245812
Tryptophan synthase	Product A V3 SUBG	2.084119262	0.018508823
S-adenosylmethionine:tRNA ribosyltransferase-isomerase	Product A V3 SUBG	2.081182245	0.020471389
Galactokinase	Product A V3 SUBG	2.071628618	0.014305878
S-ribosylhomocysteine lyase	Product A V3 SUBG	2.06704668	0.030245812
Phosphatidate cytidyltransferase	Product A V3 SUBG	2.043892086	0.016712924
Pyridoxine 5'-phosphate synthase	Product A V3 SUBG	2.023792626	0.000275433
Pyruvate dehydrogenase (quinone)	Product A V3 SUBG	2.023536332	0.003703627
Transferred entry 7.2.2.10	Product A V3 SUBG	2.021427948	0.018506169
Beta-Ala-His dipeptidase	Product A V3 SUBG	2.018269524	0.015850009
Transferred entry 1.17.1.9	Product A V3 SUBG	2.012359892	0.008810865
Glutathione-disulfide reductase	Product A V3 SUBG	2.007145806	0.009316196

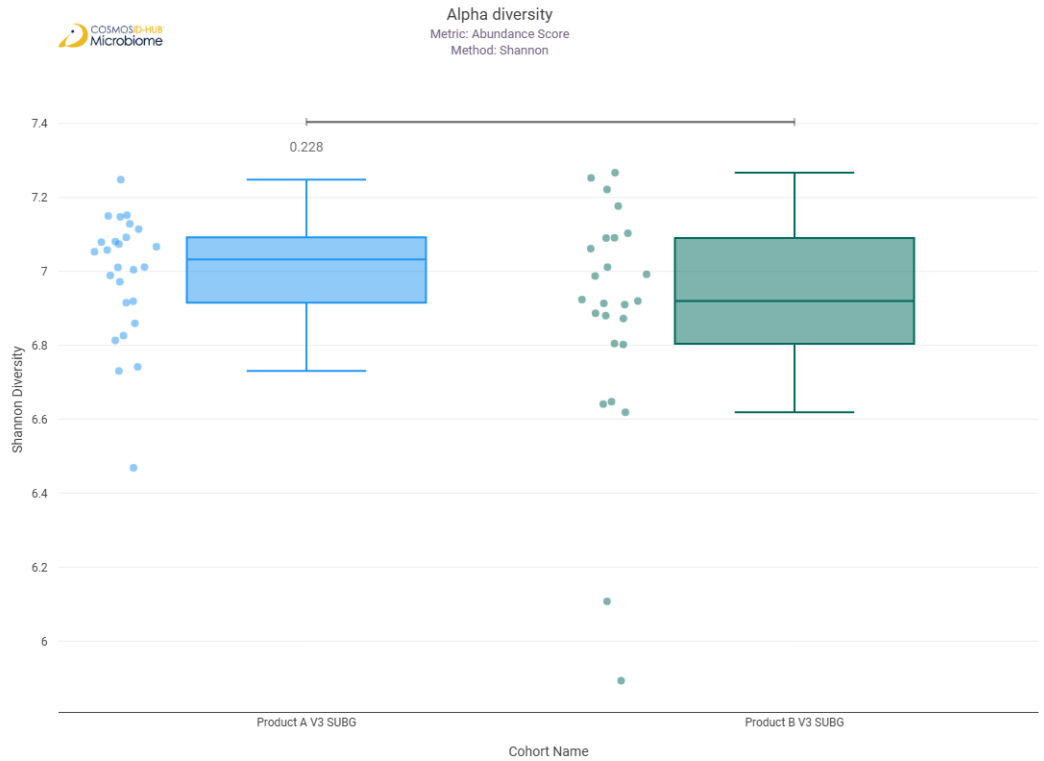
## MetaCyc Pathways

# Alpha Diversity (MetaCyc)

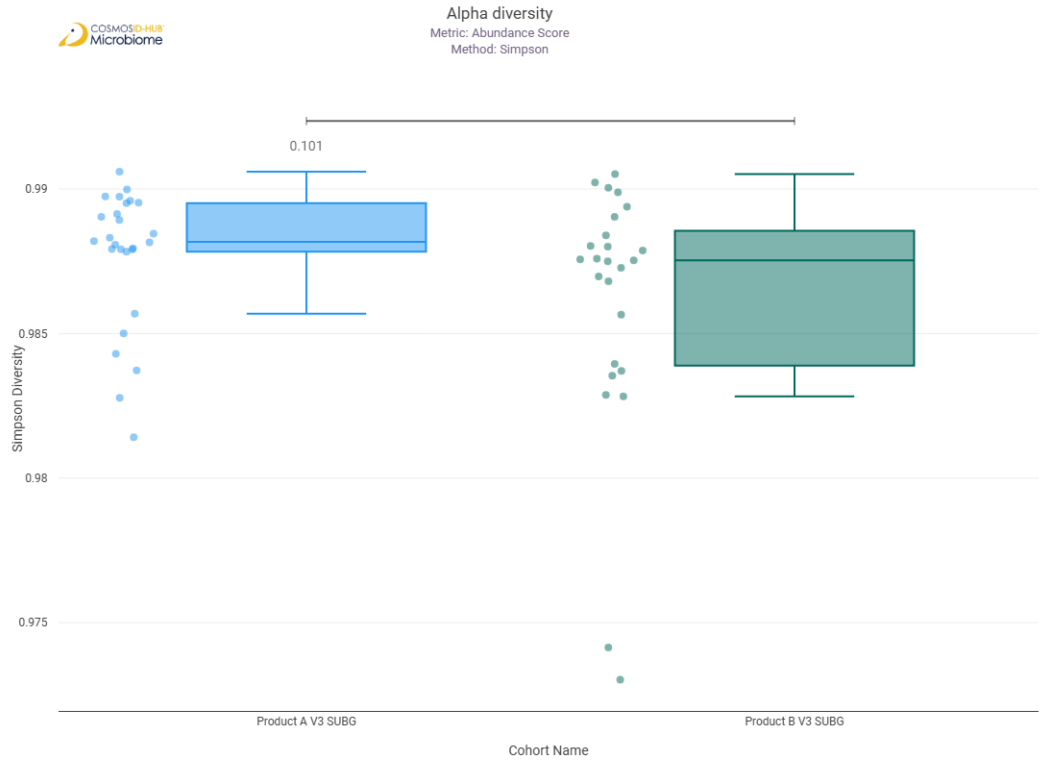
Chao1



Shannon

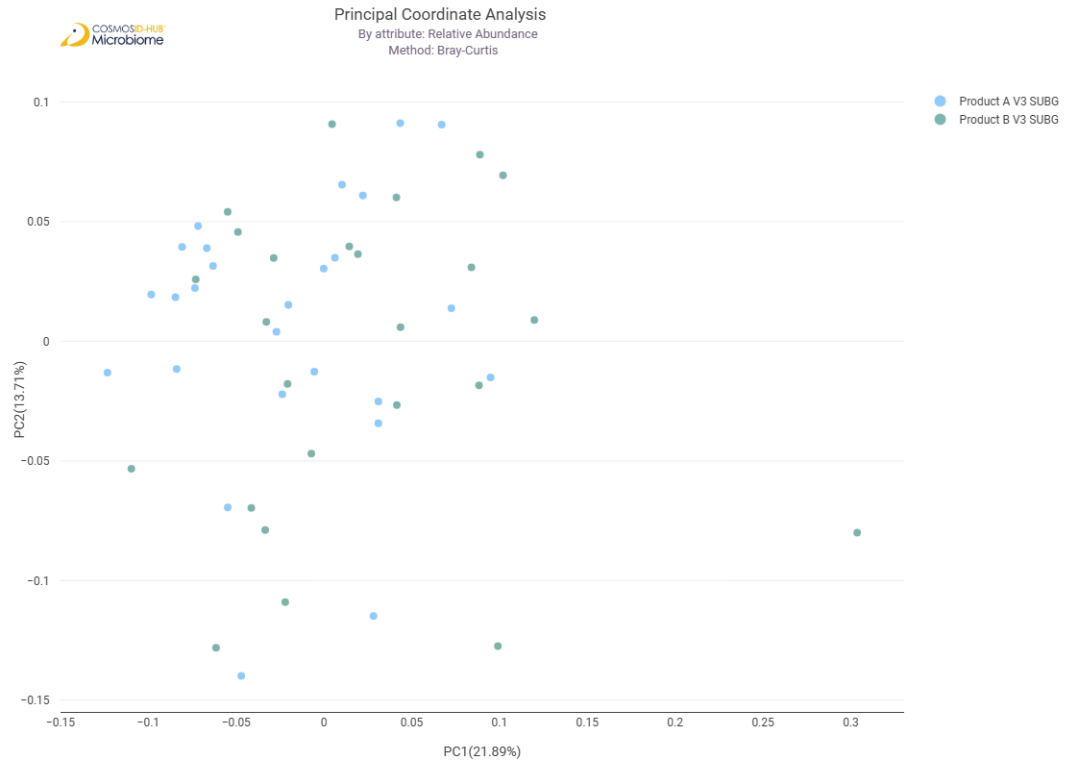


# Simpson



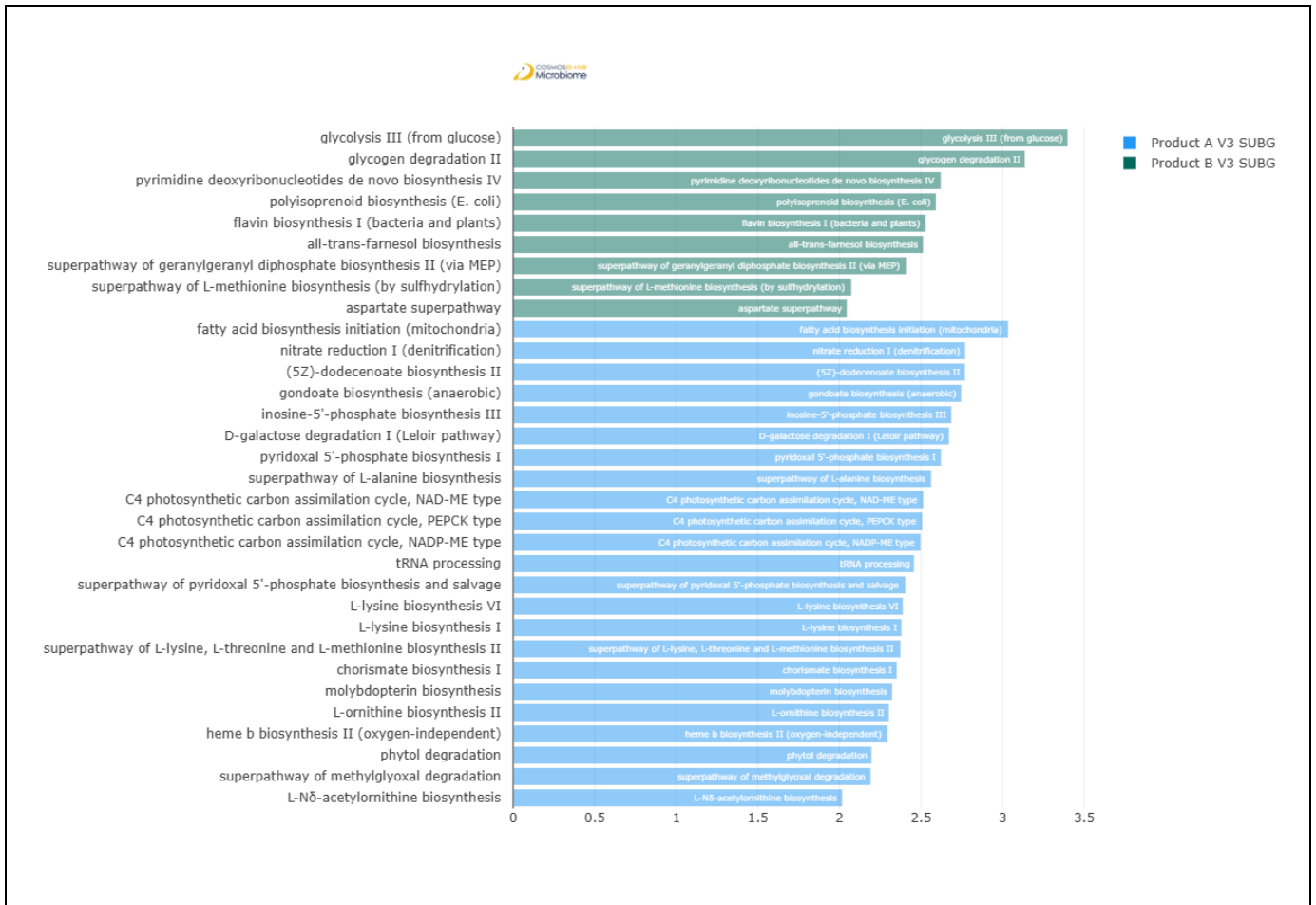
## Beta Diversity (MetaCyc)

Bray-Curtis  
PERMNOVA  
p = 0.058





## Differential Abundance (LEfSe) (MetaCyc)



Feature	Enriched Cohort	LDA Score	P-value
glycolysis III (from glucose)	Product B V3 SUBG	3.398008161	0.038205314
glycogen degradation II	Product B V3 SUBG	3.135718597	0.043787588
pyrimidine deoxyribonucleotides de novo biosynthesis IV	Product B V3 SUBG	2.620523396	0.008561476
polyisoprenoid biosynthesis (E. coli)	Product B V3 SUBG	2.590644283	0.002064632
flavin biosynthesis I (bacteria and plants)	Product B V3 SUBG	2.527895481	0.020459981
all-trans-farnesol biosynthesis	Product B V3 SUBG	2.512006003	0.002199138
superpathway of geranylgeranyl diphosphate biosynthesis II (via MEP)	Product B V3 SUBG	2.412732939	0.022030076
superpathway of L-methionine biosynthesis (by sulfhydrylation)	Product B V3 SUBG	2.072286136	0.038070937
aspartate superpathway	Product B V3 SUBG	2.044846563	0.035123508
fatty acid biosynthesis initiation (mitochondria)	Product A V3 SUBG	3.03335721	0.043787588
nitrate reduction I (denitrification)	Product A V3 SUBG	2.770074976	0.017447725
(5Z)-dodecenoate biosynthesis II	Product A V3 SUBG	2.768822004	0.000357175
gondoate biosynthesis (anaerobic)	Product A V3 SUBG	2.745818707	0.039994768
inosine-5'-phosphate biosynthesis III	Product A V3 SUBG	2.685496558	0.004437784
D-galactose degradation I (Leloir pathway)	Product A V3 SUBG	2.670583482	0.026189985
pyridoxal 5'-phosphate biosynthesis I	Product A V3 SUBG	2.621986388	0.00336473
superpathway of L-alanine biosynthesis	Product A V3 SUBG	2.562183598	0.003070652
C4 photosynthetic carbon assimilation cycle, NAD-ME type	Product A V3 SUBG	2.513144729	0.00186182
C4 photosynthetic carbon assimilation cycle, PEPC type	Product A V3 SUBG	2.506672461	0.023751913

C4 photosynthetic carbon assimilation cycle, NADP-ME type	Product A V3 SUBG	2.496833971	0.034829974
tRNA processing	Product A V3 SUBG	2.456212513	0.000875251
superpathway of pyridoxal 5'-phosphate biosynthesis and salvage	Product A V3 SUBG	2.403555807	3.55E-02
L-lysine biosynthesis VI	Product A V3 SUBG	2.38774424	0.036480158
L-lysine biosynthesis I	Product A V3 SUBG	2.379557703	0.012835527
superpathway of L-lysine, L-threonine and L-methionine biosynthesis II	Product A V3 SUBG	2.373267579	0.039990269
chorismate biosynthesis I	Product A V3 SUBG	2.350578747	0.041854827
molybdopterin biosynthesis	Product A V3 SUBG	2.322613992	0.003924514
L-ornithine biosynthesis II	Product A V3 SUBG	2.302634401	0.002370652
heme b biosynthesis II (oxygen-independent)	Product A V3 SUBG	2.292271137	0.014121484
phytol degradation	Product A V3 SUBG	2.196476941	0.005851078
superpathway of methylglyoxal degradation	Product A V3 SUBG	2.190473884	0.033160392
L-Nδ-acetylornithine biosynthesis	Product A V3 SUBG	2.016218191	0.006620791