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**Title**

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# SARS-CoV-2 metagenomics for identification of microbial superinfection

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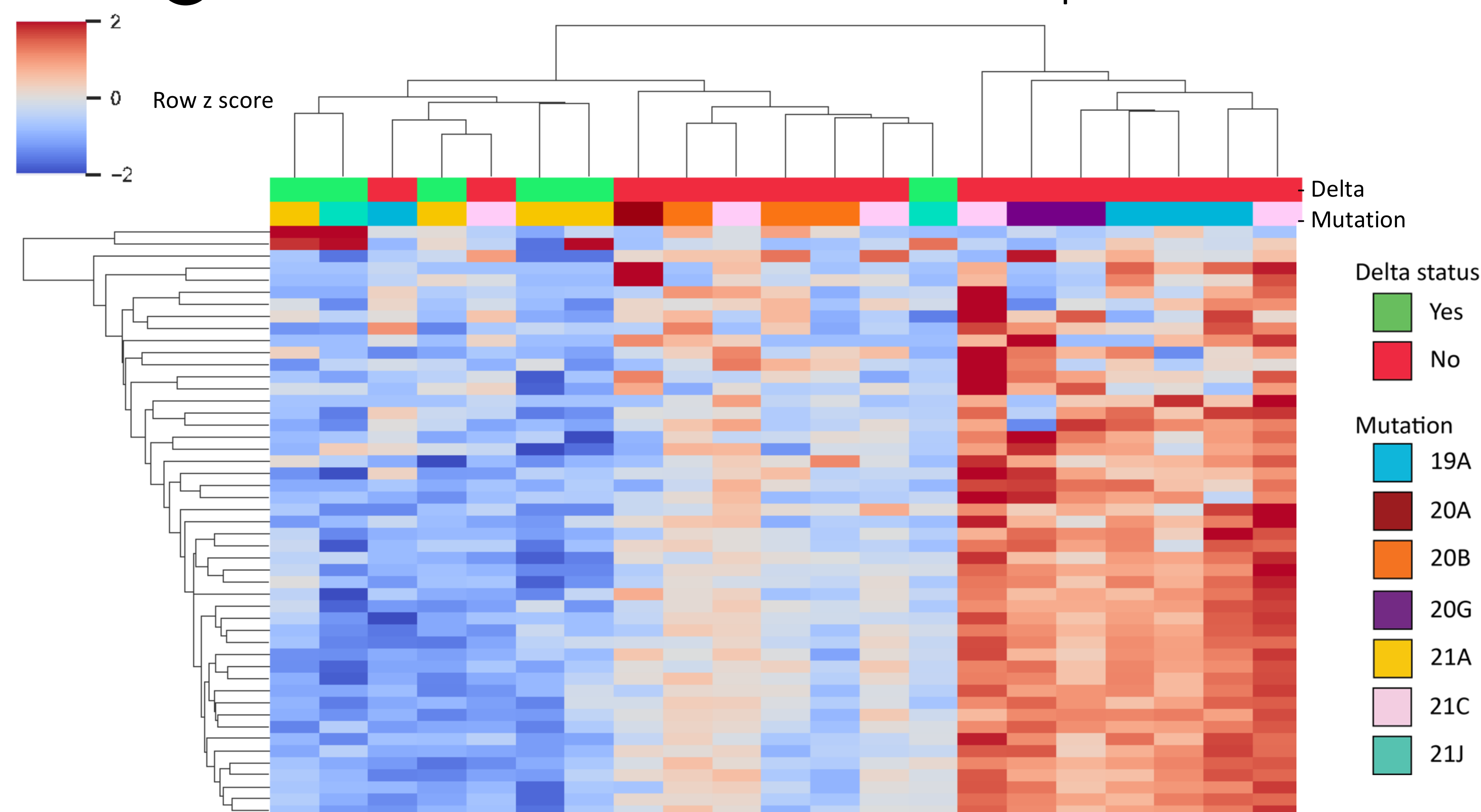
## Background

- SARS-CoV-2 superinfection can masquerade as COVID-19 flare or non-infectious ARDS
- No method of diagnosis of bacterial pneumonia exists for non-intubated patients
- Lower respiratory culture results in ~1 week and not all pathogens can be cultured
- Differential diagnoses have contradictory treatments
- We aimed to compare host transcriptomics of Delta variant versus other variants
- We aimed to characterize microbiome of upper and lower airway in patients with COVID-19 with

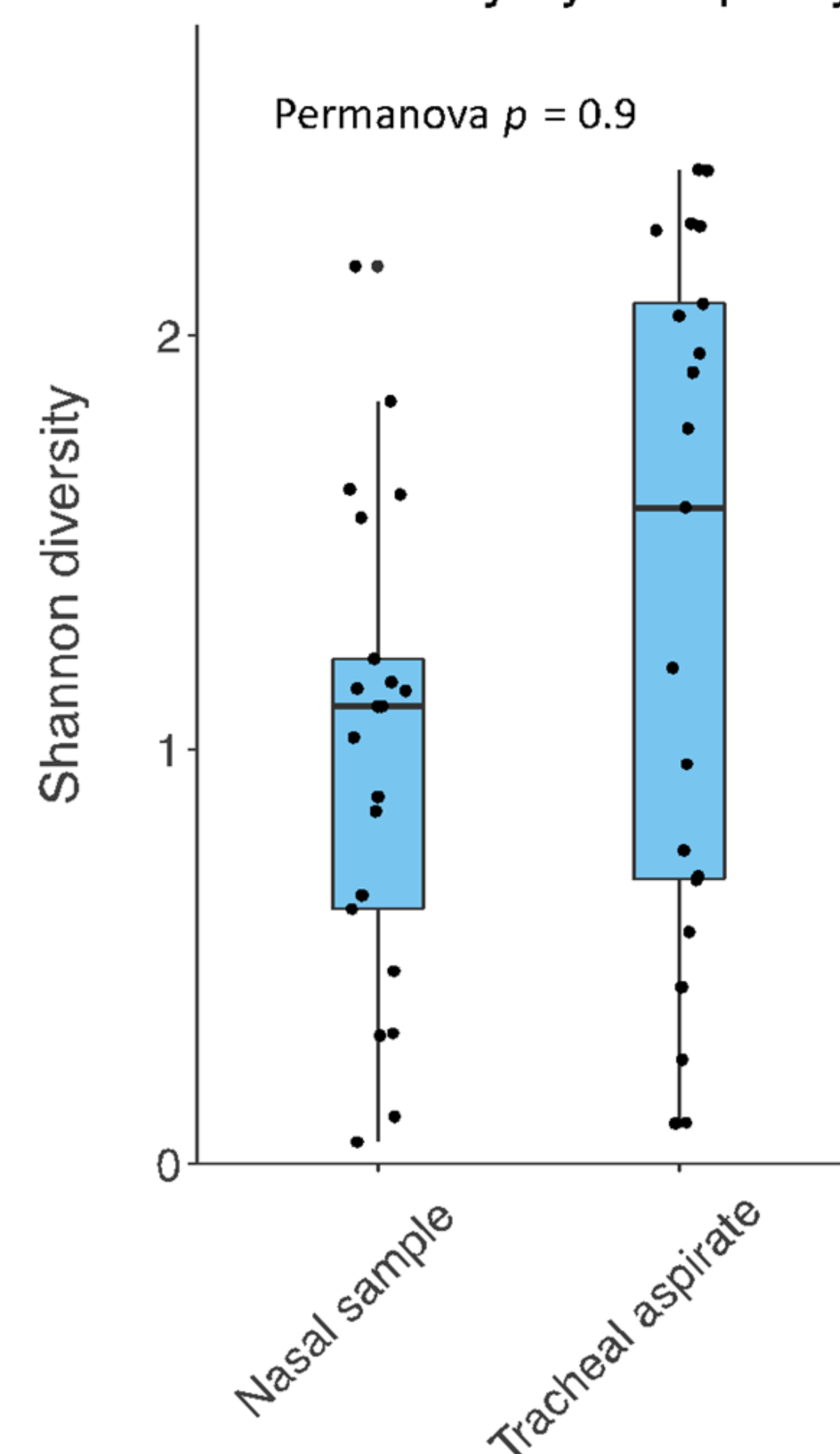
## Results

- VAP RNA-seq of Delta variant versus other variants showed 49 differentially expressed genes (DEGs) at threshold of 5-fold change and FDR < 0.05 **1**
- Gene Set Enrichment Analysis (GSEA) highlighted downregulation of flagellar transport and possible upregulation of neutrophil degranulation **2**
- $\alpha$ -diversity and  $\beta$ -diversity did not significantly differ between NS and TA samples **3**, **4**
- In COVID-VAP, nasal swab microbiome correlates with tracheal aspirate microbiome **5**, **6**

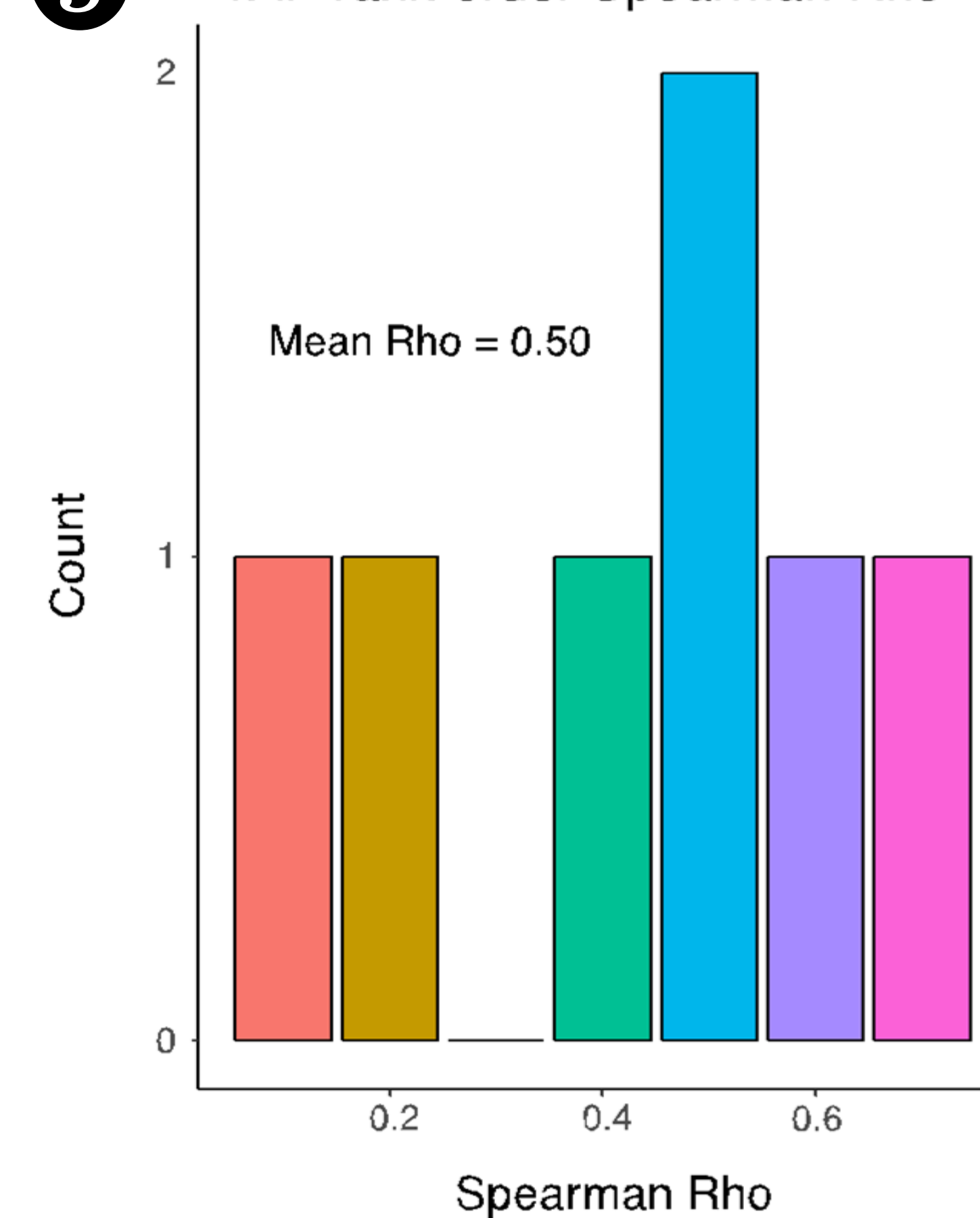
**1** Delta variant vs. other variants differential expression



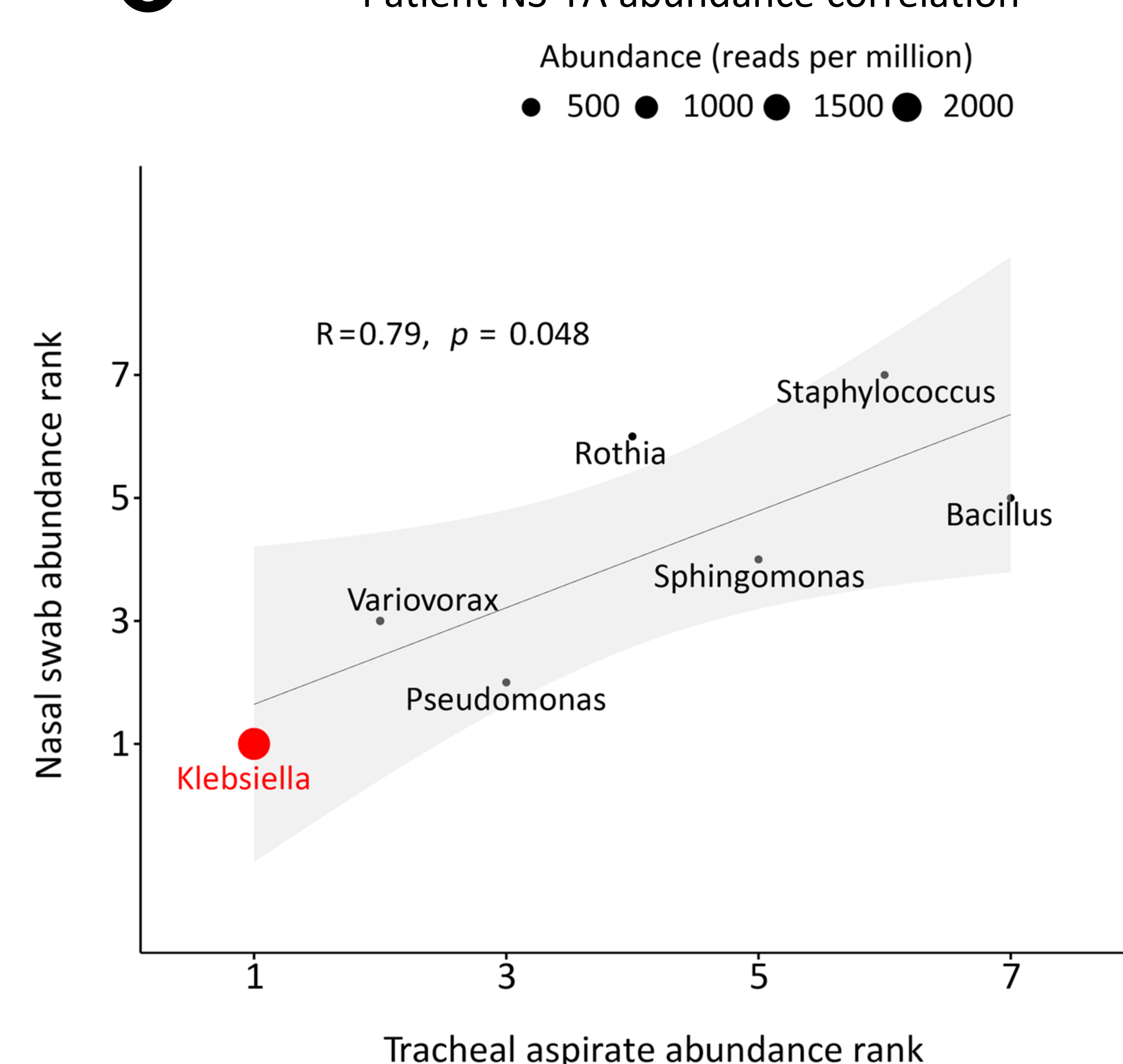
**3** Shannon diversity by sample type



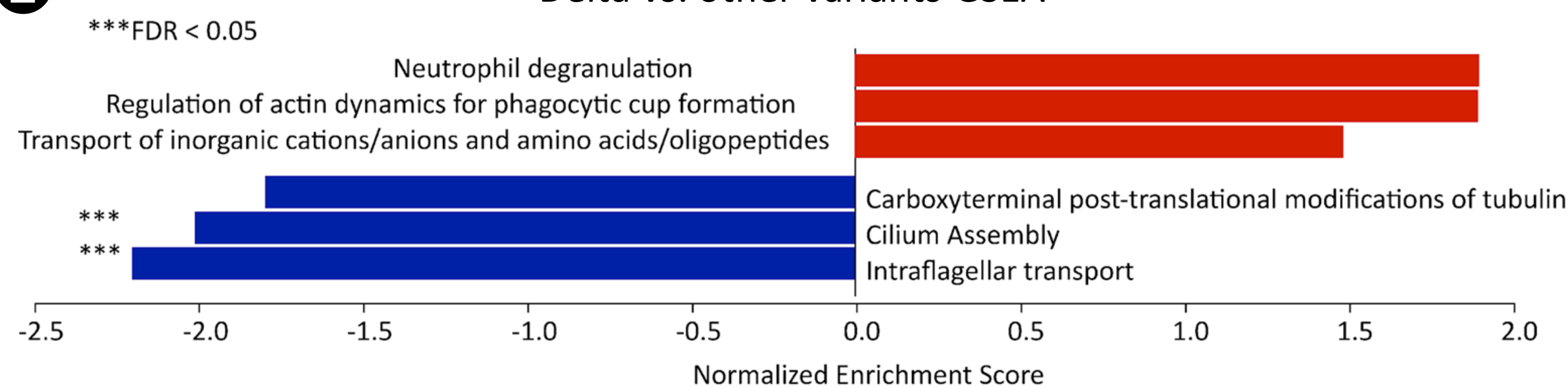
**5** VAP rank-order Spearman Rho



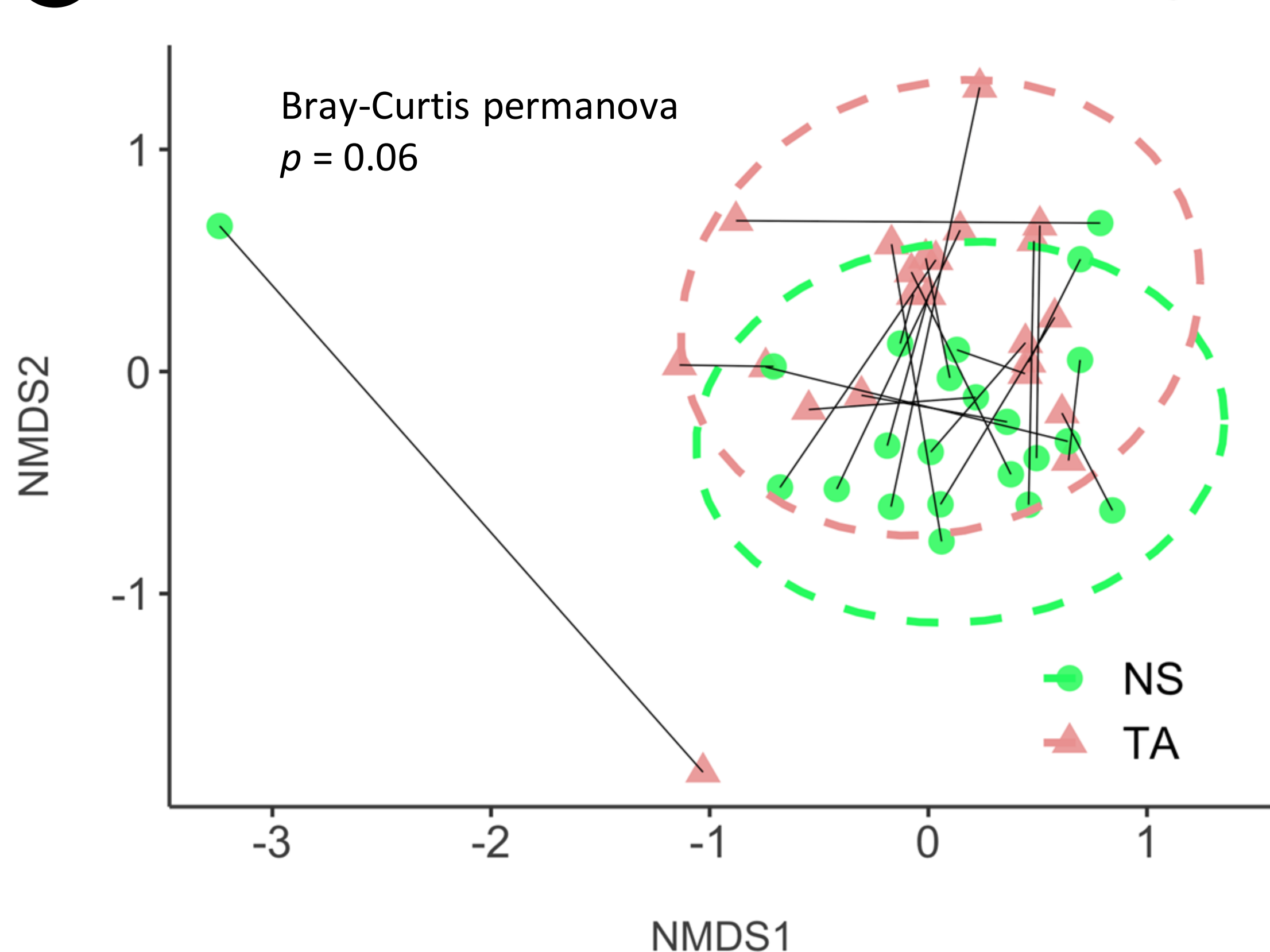
**6** Patient NS-TA abundance correlation



**2** Delta vs. other variants GSEA



**4** Non-metric Multi-Dimensional Scaling



## Conclusions

- Delta variant generates a unique host response most likely implicated in its enhanced virulence
- NS serves as surrogate for TA in COVID-VAP
- Metagenomics show promise as a method for rapid detection of COVID superinfection

## Future Steps

- Calculate Spearman rank-order correlation of established respiratory pathogens between NS and TA samples
- Identify NS host gene signature to rapidly predict bacterial or fungal superinfection
- Compare host response of symptomatic versus asymptomatic patients with positive SARS-CoV-2 test
- Determine the utility of NS for predicting antibiotic