Messenger RNA SARS-CoV-2 Vaccines Affect the Gut Microbiome

Sabine Hazan[1], Sonya Davé[2], Thomas J. Borody[3]

[1]ProgenaBiome, LLC, Ventura, CA, USA, [2]Microbiome Research Foundation, Ventura, CA, USA, [3]Centre for Digestive Diseases, Five Dock, NSW, AUS

Introduction

- Diverse populations of gut bacteria mediate several beneficial effects to health.
- Low *Bifidobacterium* levels have been linked with severe SARS-CoV-2 infection, inflammatory bowel disease, C. *difficile* infection, obesity, and aging.
- Differences in gut microbiome composition can affect immunity to vaccination, yet the effect of mRNA vaccines, for preventing SARS-CoV-2 infection, on the human gut microbiome is largely unknown.
- The purpose of the study was to examine changes in *Bifidobacterium* levels in fecal samples after mRNA SARS-CoV-2 vaccination.

Methods

Fecal matter samples were collected from 34 individuals before and after being vaccinated with Sars-CoV-2 mRNA vaccine; namely BNT162b2 mRNA (Pfizer-BioNTech) or mRNA-1273 (Moderna).

Metagenomic Next Generation Sequencing was performed on fecal samples, where DNA samples were extracted and normalized for library downstream fabrication using Shotgun methodology. The DNA sequences acquired were compared for bacterial species present before and after receiving the vaccine using One Codex database. The Wilcoxon Signed Rank test was used to compare changes in *Bifidobacterium* Relative Abundance over time.

Discussion

- *Bifidobacterium* levels were significantly reduced after receiving mRNA vaccination for SARS-CoV-2.
- This drop in *Bifidobacterium* levels may contribute to observed SARS-CoV-2 infection post vaccination.
- Future studies are needed in order to characterize how *Bifidobacterium* presence in the gut may change over time after SARS-CoV-2 vaccination, the impact on human health, and if these changes occur similarly post-vaccination for other diseases.

Results

Parameter	Value
Total Subjects (N)	34
Males	15/34 (44.11%)
Females	19/34 (55.88%)
Age (yrs) (mean ± SEM)	55.26 ± 2.65
BMI (kg/m^2) (mean ± SEM)	24.54 ± 0.96
Healthy medical history (%)	4/34 (11.76%)
Relative Abundance of *Bifidobacterium* (median, IQR)	
Pre-vaccination	1.13%, 0.0016-2.52%)
Post-vaccination	0.64% (0.0015-2.48%

Table 1. Subject characteristics and Relative Abundance of *Bifidobacterium*
- p = 0.0065 for comparing Relative Abundance pre- and post-vaccination.

Figure 1. Relative Abundance of various phyla before and after vaccination. Individual points correspond to individual subjects (n=34), and before vs. after vaccination points are connected. Blue and red bars indicate median values before and after vaccine, respectively. * = p < 0.05

Figure 2. Relative Abundance of various species before and after vaccination. Individual points correspond to individual subjects (n=34), and before vs. after vaccination points are connected. Blue and red bars indicate median values before and after vaccine, respectively. ** = p < 0.01, * = p < 0.05
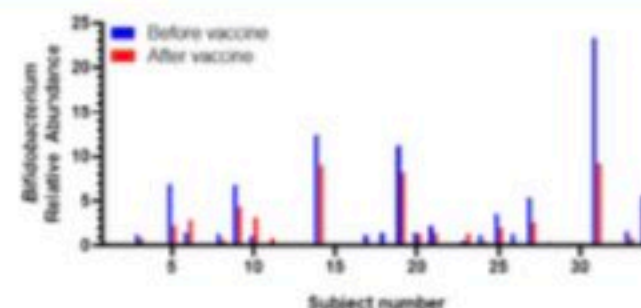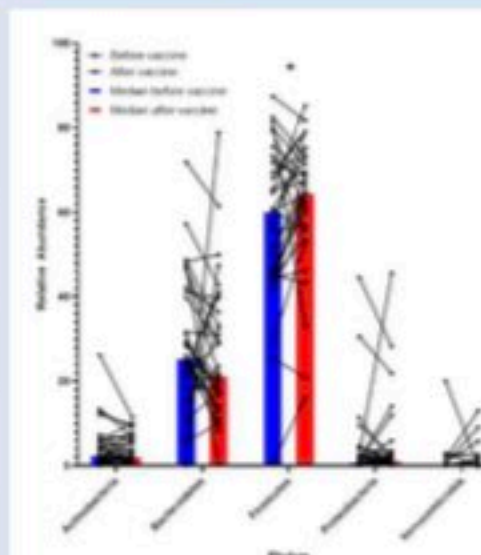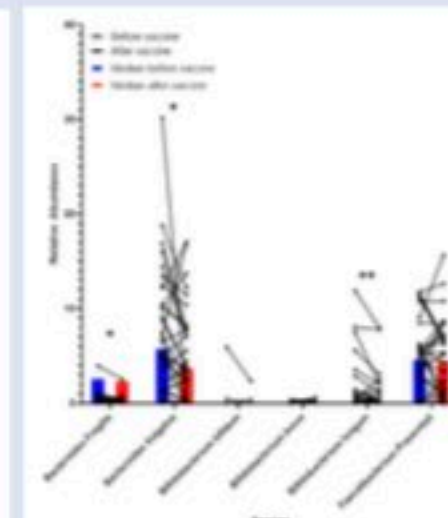

Figure 3. Relative Abundance of *Bifidobacterium* before and after vaccination. *Bifidobacterium* is the only genus whose relative abundances changes with vaccination significantly (p = 0.0065). Blue and red bars indicate median values after and before vaccination, respectively.
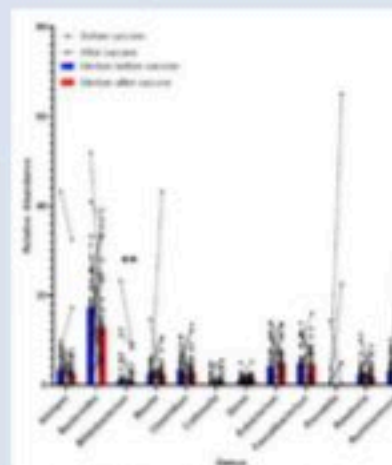

Figure 4. Relative Abundance of various genera before and after vaccination. Individual points correspond to individual subjects (n = 34), and before vs. after vaccination points are connected. Blue and red bars indicate median value before and after vaccine, respectively. ** = p<0.01, * = p<0.05
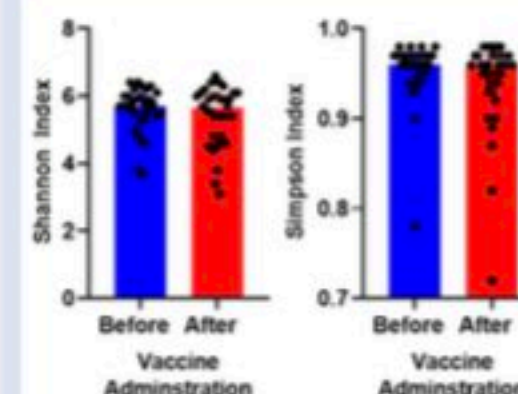

Figure 5. Alpha diversity at the genus level for subjects before and after vaccination. With vaccine administration, there was no significant change in A. Shannon index (p = 0.5441) or B. Simpson index (p = 0.0769).

Persistent Damage to the Gut Microbiome following Messenger RNA SARS-CoV-2 Vaccine

Sabine Hazan[1], Sonya Davé[2], Thomas J. Borody[3]

[1]ProgenaBiome, LLC, Ventura, CA, USA, [2]Microbiome Research Foundation, Ventura, CA, USA, [3]Centre for Digestive Diseases, Five Dock, NSW, AUS

Introduction

- The human gut microbiome is an essential determinant of human health.
- *Bifidobacterium* decline is associated with inflammatory bowel disease, obesity, neurological disorders, *C. difficile* infection and severe COVID-19 (1-3).
- Long-term effect of messenger RNA vaccines for SARS-CoV-2 on the human gut microbiome is unknown.
- The purpose of this study was to explore longitudinal changes in the Relative Abundance of *Bifidobacterium* after mRNA SARS-CoV-2 vaccination.

Methods

We longitudinally recorded the Relative Abundance of *Bifidobacterium* in four subjects before receiving a mRNA vaccine (Pfizer or Moderna) for SARS-CoV-2, approximately one post-vaccination, as well as 6-9 months post-vaccination. Additional SARS-CoV-2 vaccines were given during that period, totaling 2 to 3 doses. Samples were collected at the time points mentioned. No dietary changes or new medications were introduced throughout the study period. Metagenomic next generation sequencing-based methods were applied to samples obtained from fecal collection. DNA was extracted, and the library prepped, enriched and sequenced on an Illumina Nextseq 550 system. This study was IRB approved.

Results

Subject	Change in Relative Abundance of *Bifidobacterium* (% of pre-vaccine level)	
	1 month post-vaccine	6-9 months post-vaccine
1	38%	15%
2	258%	0%
3	49%	35%
4	90%	60%

Table 1. Change in Relative Abundance of *Bifidobacterium* after SARS-CoV-2 mRNA vaccination.

Discussion

- At 1 month post-vaccination, 3 of 4 subjects experienced a decrease in Relative Abundance of *Bifidobacterium* below pre-vaccination levels.
- At 6-9 months post-vaccination, all subjects experienced a decrease in Relative Abundance of *Bifidobacterium* below pre-vaccination levels.
- No subjects exhibited significant post-vaccine complications.
- The lasting decrease in *Bifidobacterium* levels may contribute to SARS-CoV-2 infection post vaccination.
- Gut dysbiosis after mRNA SARS-CoV-2 vaccination may be a future indication for restoration of *Bifidobacterium* via oral or fecal transplant routes.

References

1. Ruiz L, et al. *Front Microbiol.* 2017;8:2345.
2. Suganya K, Koo BS. *Int J Mol Sci.* 2020;21(20):7551.
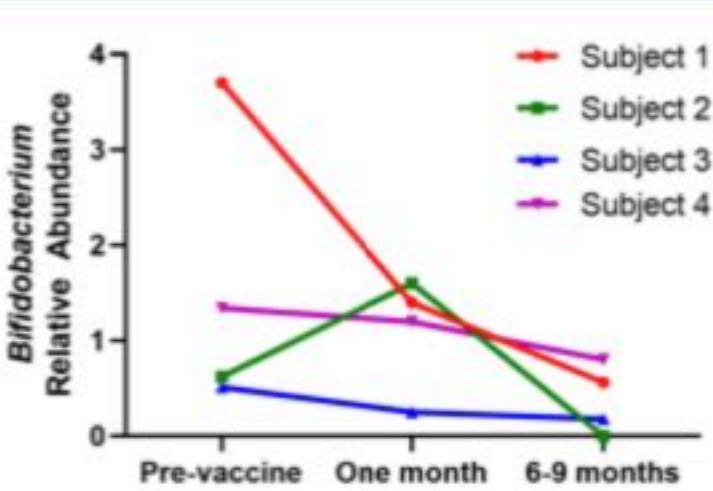3. Hazan S, et al. *BMJ Open Gastro.* 2022;9(1):e000871.

Figure 1. Decline in Relative Abundance of *Bifidobacterium* after SARS-CoV-2 mRNA vaccination.