Impact of the use of biologics and their discontinuation on the gut microbiota of psoriasis patients

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Introduction

Increasing number of studies have shown that the imbalance of gut microbial populations or dysbiosis may be implicated in psoriasis pathogenesis[1].

Psoriasis treatment can shift the abundance of specific taxa, however the effect of treatment discontinuation on gut microbiota has not been investigated.

At the start of the COVID-19 pandemic in March 2020, it was unclear whether patients on biologics were at risk of complications from COVID-19 infection. The decision to continue or stop treatment in a group of patients under secukinumab treatment was individualised and agreed with the patient. According to Blauvelt *et al*, the median time to loss of PASI 50 after secukinumab withdrawal was 28 weeks, so patients were not at increased risk of relapse[2].

The aim of this study was to investigate whether there were differences in gut microbiota of psoriasis patients treated with secukinumab (IL-17 A inhibitor) compared to controls, non-treated moderate-to-severe psoriasis patients and psoriasis patients after 3 months of secukinumab discontinuation (discontinuation group).

Methods

We evaluated 27 non-psoriasis (control group) and 58 psoriasis fecal samples (27 moderate to severe psoriasis, 19 secukinumab treated patients -300 mg every 4 weeks- and 12 drug discontinuation.

Fecal microbial diversity and composition were analyzed using the Illumina MiSeq sequencing platform by targeting the hypervariable V3-V4 regions of the 16S rRNA gene. Bioinformatic analysis was performed using Qiime2.

Results

The median treatment time for secukinumab-treated patients was 21 months. Absolute PASI ≤3 and PASI ≤1 were achieved by 14 patients (73.7%) and 8 patients (42.1%) on secukinumab treatment, respectively. The background of patients and controls are shown in **Table 1**. Secukinumab-treated patients showed greater biodiversity (Shannon index) and higher number of observed features than moderate-to-severe psoriasis patients and controls. **Figure 1, table 2**. Bacteroides was the most prevalent genera in all groups. **Figure 2**. We found no differences in beta diversity between groups (weighted and unweighted Unifrac) **Figures 3 and 4**. When comparing the major genera detected (ANCOM), we found that secukinumab-treated patients differed from controls without psoriasis in *Marvinbryantia* abundance (p <0.05). Samples taken after treatment discontinuation showed lower alpha diversity compared to samples under secukinumab treatment, although the difference was not statistically significant. **Figure 1**.

Table 1. Characteristics of the sample.

	Moderate-to-severe Psoriasis (not treated)	Secukinumab treatment (x̄ 21 months)	non Psoriasis controls
	n:27	n:19	n: 27
Age (x̄±SD)	48.6 (18.9)	51.9 (12.4)	48.7 (18.8)
Female (%)	55,6	31.6	57,7
Male (%)	44,4	68.4	42,3
Age of Psoriasis onset (x̄±SD)	29.9 (19.8)	29.3 (11.1)	NA
Type 1 Psoriasis (%)	52,6	78.5	NA
Years with Psoriasis (x̄±SD)	18.6 (13.4)	22.7 (9.1)	NA
Weight (x̄±SD)	79.1 (20.2)	86.5 (19.1)	75.0 (15.1)
Heigh (x̄±SD)	1.64 (0.1)	1.68 (0.1)	1.63 (0.1)
BMI (x̄±SD)	29.5 (5.3)	30.7 (5.9)	28.1 (5.2)
Overweight (%)	29,6	31.6	42.3
Obesity (%)	44,4	63.2	30.7
PASI (x̄±SD)	16.3 (4.8)	2.2 (2.4)	NA
BSA (x̄±SD)	27.5 (19.2)	1.8 (2.3)	NA

Table 2. Main genera and observed features.

	Taxaplot			
Group	**% Bacteroides**	**% Prevotella**	**% Faecalibacterium**	**Observed features**
Non-Psoriasis	34.14	14.02	4.87	167
Severe-Psoriasis	20.62	19.63	8.19	167
Secukinumab-Treated	20.91	10.83	8.72	206
Drug-Discontinuation	22.28	11.03	8.32	203

Figure 1. Biodiversity. Shannon Index.

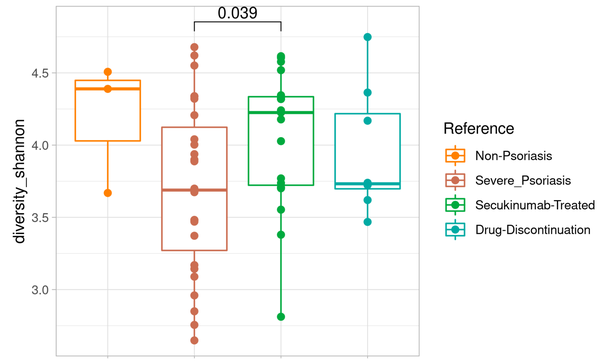


Figure 2. Relative abundance (genera level).

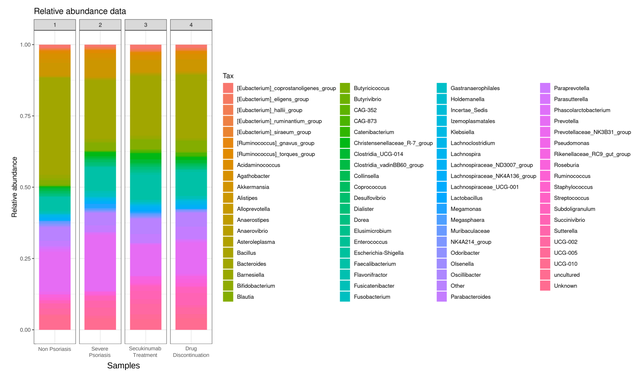


Figure 3. Weighted Unifraq distance.

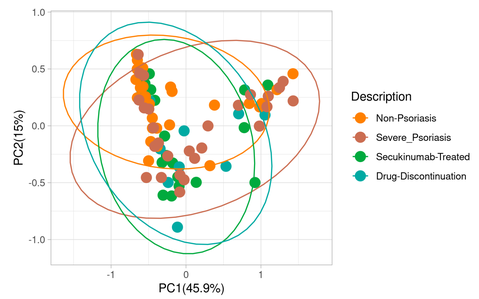
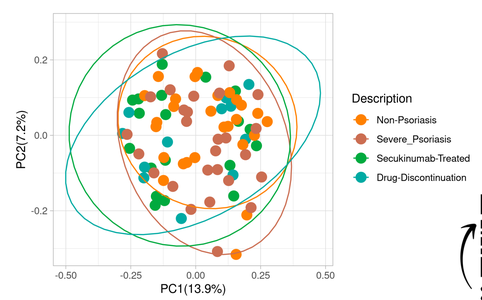


Figure 4. Unweighted Unifraq distance.



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Discussion

Secukinumab has been reported to be able to alter gut microbiome composition in psoriatic patients. However, the alteration of gut microbiota and related functional changes caused by successful secukinumab therapy in psoriatic patients remains unclear. Yeh *et al* showed a tendency of clustering of samples from patients receiving secukinumab treatment for 6 months, separating from samples at baseline or healthy control samples, but no significant differences in the α-diversity of microbiota were observed among fecal samples collected at different time points during treatment[3]. In a recent study, Du *et al* found that secukinumab treatment resulted in significantly elevated microbiota richness and biodiversity and altered gut microbiota composition than untreated psoriasis and healthy controls[4].

In this study, we found that secukinumab increased the biodiversity of the gut microbiota of psoriasis patients and promoted shifts in the abundance of specific taxa, which tended to disappear after treatment discontinuation. Genera *Marvinbryantia* was increased in secukinumab treated patients. *Marvinbryantia* is a beneficial intestinal bacterium that maintains the diversity and function of gut microbiota and can improve human health.

According to our knowledge this is the first study that investigated gut microbiota changes after secukinumab withdrawal in patients with satisfactory response to therapy. Therefore, the role of biologics on the gut microbiota of psoriasis patients deserves further study.

References

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