

Reviewers' comments:

Reviewer #1 (Remarks to the Author):

Fyhrquist et al. perform a matched 16S rRNA and host transcriptome profiling on AD, psoriasis, and healthy controls at two different skin sites of disease occurrence. Major findings cited confirmed previous reports that *Staphylococcus aureus* is significantly associated with AD (Kong et al) with depletion of anaerobes (Myles et al), and that a strong microbial signature is lacking in psoriasis. Reassuringly, the transcriptional data is largely consistent with previous reports of AD or psoriasis transcriptomes, and the authors found that the host transcriptome was a stronger predictor of skin disease severity than different microbiome metrics.

We commend the authors on the size of the cohort, the care taken with negative controls and confounders, and a clear and well-presented paper. However, the study itself represents a relatively modest advance for the field, with the major contribution being a correlation analysis with microbial features with host skin transcriptome data. The size of the cohort is an asset and allows the author to break down the AD patients into yes/no *S. aureus* groups which allows them to further refine transcriptome correlates. Like these previous studies, different classifier methods were used to define host or microbial features characteristic of the disease, with the major advantage again being the size of the study.

A major point of revision would be to include additional covariate analysis for different skin treatments that the patients had undergone prior to the washout period with Dove, and to describe with more detail the different features of the matched healthy controls. This is because the authors observed that there were likely different community states/microbiome 'types' for AD because some individuals were characterized by a prevalence of *S. aureus* while others not. Kong et al. reported that intermittent treatment shifts the microbiome towards one with significantly less *S. aureus*, and it is likely that this could be one of the factors that could explain the variation.

Also, why were OTUs clustered at the 99.3% identity level? Which is fairly atypical and naturally resulted in a very large number of OTUs. There should be some justification of this in the methods, and/or also performed at more conventional levels (e.g., 97%).

Reviewer #2 (Remarks to the Author):

In the paper by Fyhrquist et al., “Microbe-host interplay in atopic dermatitis and psoriasis”, the authors assemble a large cohort of cases and controls (over 300 individuals), for which they perform 16S rRNA sequencing and microarray-based analysis of transcriptomes. They find that AD is dominated by *S. aureus* and immune activation, whereas PSO was associated with assemblages of organisms.

I was able to review the technicality of the manuscript as my expertise is in microbial community analysis and gut microbiomes, though I was able to only touch upon the conclusions regarding changes in the immune system pertaining to skin disease and the originality of the work from someone in the microbiome field, but an outsider to these specific areas.

My biggest issue with the manuscript is that it overall lacked details about the study design, sample collection and most importantly, statistical analyses, which made it both hard to review and also gave the impression that many of these choices were made without sufficient consideration. These include the method of DNA extraction (crucial for comparing across studies), the methods for performing skin swabs (Fig. S1 implies some buffer but none was discussed), whether there were any exclusion criteria, how samples were matched, and what affymetrix plates were used for transcriptomics, to name a few. In terms of statistical analysis, it was unclear why some choices were made—99.3% identity for clustering, how controlling for confounders was done, but also what tests were used (see Figure 1A, a p-value is reported with a vague descriptor of ‘nonparametric score’, but the text only says ‘significantly associated’, yet this repeats in multiple results of the paper, and this is unclear whether this is significantly associated with one of the conditions or if multiple are being compared etc.). Similarly, in the transcriptomics section, the only thing that was mentioned was “Differential gene expression analysis” (line 347) rather than the specific method used. There wasn’t mention about false-discovery corrections for some analyses, though mentioned for others (i.e. Fig 4), or whether any normalization was performed on gene abundances. Since the devil is in the details for microbiome analyses, this can potentially be a major issue.

My other issue with the manuscript is the novelty of the results. Despite my disclaimer that I don’t work entirely in this field, it seems obvious both from quick lit searches and their own statements that there have been a number of studies that have done community analysis of psoriasis and AD and their analysis doesn’t particularly add much. The *S. aureus*-association with AD is not a new finding, and this has been reported on many times. There have also been RNA-seq experiments performed on both AD (Suarez-Farinas et al, 2015 and even a metaanalysis of transcriptome analyses (Ding et al., 2015) and PSO (Li et al., 2014). They find many of the same co-occurrences and pathway regulation, even according to their own statements (lines 552, 574). It was hard to decipher whether direct comparison could be made between the two disease cohorts because of the ambiguity of the matching scheme, and also the difference in body sampling sites. I can’t comment whether their results significantly improve or change our understand of PSO or AD.

Other issues:

- It was not clear how samples were matched, especially since large differences in gender underlie the Psoriasis and HV cohorts. Similarly, age-related dysbioses have been reported for skin microbiomes which are thought to predispose individuals to AD. This wasn't tested (or mentioned) within this cohort.
- Were there any exclusion criteria? Atopic dermatitis and psoriasis can be treated in many ways, including topical medications (including corticosteroids), oral immunosuppressant therapies, antibiotics, vitamin therapies, and oral steroids as well as immunomodulators. These were never mentioned in the patient recruitment or analysis.

Minor issues:

- Hard to follow what is being plotted in many of the figures. I mentioned Fig. 1A above, but this is the same for Fig 1B. Is this some aggregate of all of the samples, masking inter-personal variability? This is abnormal to group individual compositions into one composite composition.
- The data display was very confusing—like Figure 3B is very confusing—are these genes up or down in these different conditions and the same direction in these different conditions. This was a confusing figure. Figure 3C/D are also confusing visually. Or what are the yellow edges in Fig 4F?

Reviewer #3 (Remarks to the Author):

In this manuscript, the authors conducted 16s rRNA sequencing identification of the skin microbiome of patients with atopic dermatitis and psoriasis as well as host transcriptome characterization using microarrays of skin biopsies at the same sites. They showed that *S. aureus* is significantly associated with atopic dermatitis and that multiple species, such as *Corynebacterium* spp and anaerobes are associated with psoriatic skin. They also made classifiers to identify the microbial species that could most differentiate between atopic dermatitis vs normal and psoriasis vs normal skin. They then analyze the host skin transcriptome at these sites.

Many of the findings in this paper confirm previously known studies. The skin microbiome findings for atopic dermatitis reflect what is already known in the literature<sup>1,2</sup>. Some findings for the psoriatic skin microbiome are also already known, such as the overrepresentation of *Streptococcus* spp and overabundance of *Corynebacterium* species (reviewed in 3) although this study has a

different way of presenting the data (Figures 1-2). The approach of defining microbial classifiers of AD and psoriatic skin is novel, but without any mechanistic data to suggest why particular species in the classifier are disease-defining, the finding has less impact. Additionally, even if species within the classifier are not disease-defining but are in fact secondary effects of a particular type of inflammation, without mechanistic data suggesting why AD vs psoriatic inflammation might bias towards one set of bacteria vs another, it is hard to assess the biological significance of the classifier.

The atopic dermatitis transcriptomic data reveal similar pathways as previous skin transcriptome studies<sup>4,5</sup> and confirms known involved pathways, such as Th1 and Th2 pathways (Figure 3). The psoriasis transcriptomic data also confirm known involved pathways and prior studies (reviewed in 6,7), such as IL-17 signaling and IFN- $\gamma$  signaling (Figure 3). Although Figures 3-4 were clear and beautiful representations of the data, they did not offer new hypothesis-generating insight into disease pathogenesis.

The main novelty of this study is that skin microbiome and transcriptome data were collected at the same time, to allow for analysis of microbiome-transcriptome correlations. However, in their analysis, the authors did not reveal surprising information. By comparing the transcriptomes in AD samples with high abundance of *S. aureus* to those with low abundance of *S. aureus*, the authors found an enrichment of pathways such as "Keratinization" and enrichment in gene expression of IL18, IL1a, TNF, IFN $\gamma$ , and other expected pro-inflammatory cytokines (Figure 4C-D).

The analysis of psoriatic microbiomes to transcriptomes revealed that *Corynebacterium* spp may be negatively associated with inflammatory pathways in psoriasis (p.17, line 441-461). However, there are no mechanistic studies to suggest that *Corynebacterium* is protective. Additionally, earlier in the microbiome study, *Corynebacterium* was shown to be overrepresented in psoriatic lesions, which seems contradictory. Perhaps, some *Corynebacterium* species are immunoregulatory or help resistance towards more inflammatory bacteria and are therefore protective, whereas other *Corynebacterium* species are positive associated with psoriasis because they are more pro-inflammatory. This idea would be interesting, but would need additional studies in order to be validated.

There is another finding in the paper that I thought was interesting: abundance of anaerobic bacteria in AD was decreased suggesting that there is increased O<sub>2</sub> tension in AD lesions (Figure 1D, discussed in line 555-557). An analysis of metabolic pathways upregulated in disease states was a very successful approach to show that utilization of formate and aerobic respiration by *E. coli* was increased in gut inflammation<sup>(8)</sup> and then that blocking this particular microbial metabolic pathway using tungsten could ameliorate colitis<sup>(9)</sup>. Therefore, if the authors were to use metagenomic sequencing instead of 16s rRNA sequencing to look at the microbial metabolic pathways that were changed in disease states and correlate this to host transcriptome signatures, this study would be much more informative and more likely to generate hypotheses for further mechanistic studies.



The approach and intent of the study was commendable and as a field, we do need to move toward connecting microbiota changes to host epithelial or immunologic changes. However, the data presented here did not reveal many distinctive positive results. If the authors were to re-focus on some of the more interesting findings highlighted above and develop further mechanistic insight instead of presenting a broad overview of findings without specific hypotheses, this would greatly improve the impact of this study.

#### References:

1. Byrd, A. L. et al. *Staphylococcus aureus* and *Staphylococcus epidermidis* strain diversity underlying pediatric atopic dermatitis. *Sci. Transl. Med.* 9, eaal4651 (2017).
2. Kong, H. H. et al. Temporal shifts in the skin microbiome associated with disease flares and treatment in children with atopic dermatitis. *Genome Res.* 22, 850–859 (2012).
3. Yan, D. et al. The Role of the Skin and Gut Microbiome in Psoriatic Disease. *Curr. Dermatol. Rep.* 6, 94–103 (2017).
4. Ghosh, D. et al. Multiple Transcriptome Data Analysis Reveals Biologically Relevant Atopic Dermatitis Signature Genes and Pathways. *PLOS ONE* 10, e0144316 (2015).
5. Ewald, D. A. et al. Meta-analysis derived atopic dermatitis (MADAD) transcriptome defines a robust AD signature highlighting the involvement of atherosclerosis and lipid metabolism pathways. *BMC Med. Genomics* 8, (2015).
6. Jiang, S., Hinchliffe, T. E. & Wu, T. Biomarkers of An Autoimmune Skin Disease—Psoriasis. *Genomics Proteomics Bioinformatics* 13, 224–233 (2015).
7. Lowes, M. A., Suárez-Fariñas, M. & Krueger, J. G. Immunology of Psoriasis. *Annu. Rev. Immunol.* 32, 227–255 (2014).
8. Hughes, E. R. et al. Microbial Respiration and Formate Oxidation as Metabolic Signatures of Inflammation-Associated Dysbiosis. *Cell Host Microbe* 21, 208–219 (2017).
9. Zhu, W. et al. Precision editing of the gut microbiota ameliorates colitis. *Nature* 553, 208–211 (2018).

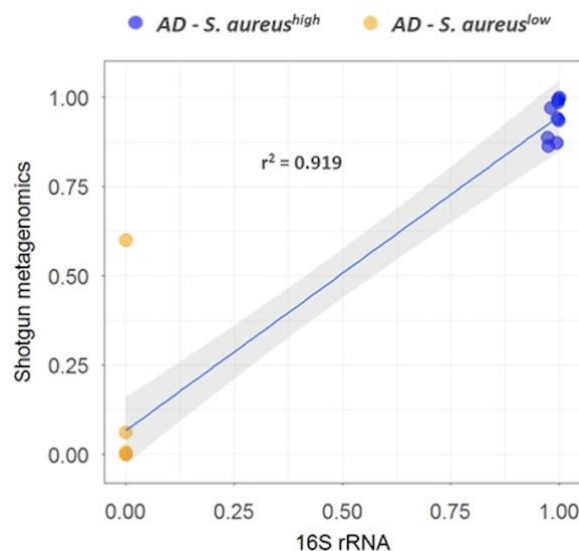
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**ANSWER:** Thank you for reviewing our manuscript and for raising this comment. We would like to point out that next to its size a main novelty of this study is that the cutaneous microbiome and the host's transcriptome data were collected at the same location and time, to allow for analysis of microbe-host-interactions (microbiome-transcriptome correlations). The approach and intent of the study is commendable and as a field, we do need to move towards connecting changes in microbiota to host epithelial or immunologic homeostasis and disease.

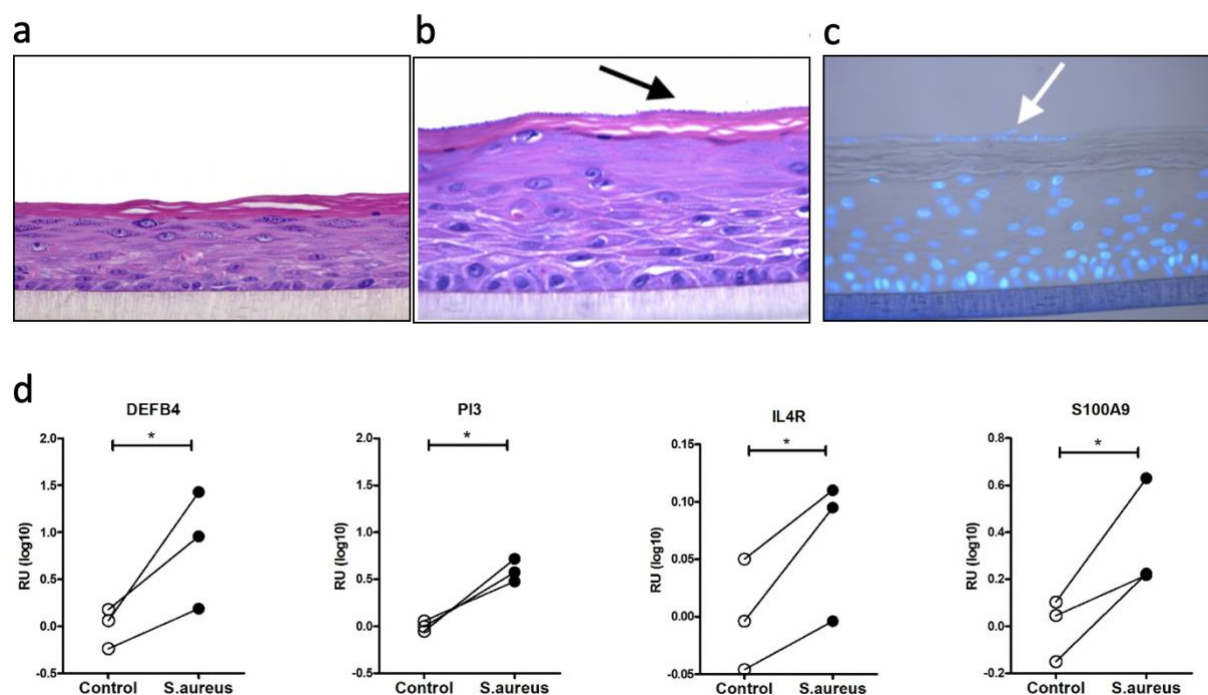
We have now revised the manuscript and added/ included:

1. Preliminary data from whole genome sequencing (WGS), to validate 16S based OTU classification and functional predictions based on the 16S marker. The results show close agreement between the two sequencing methods (Fig. 1) and are now included in the manuscript in Fig.S9 and in the text on p.17.



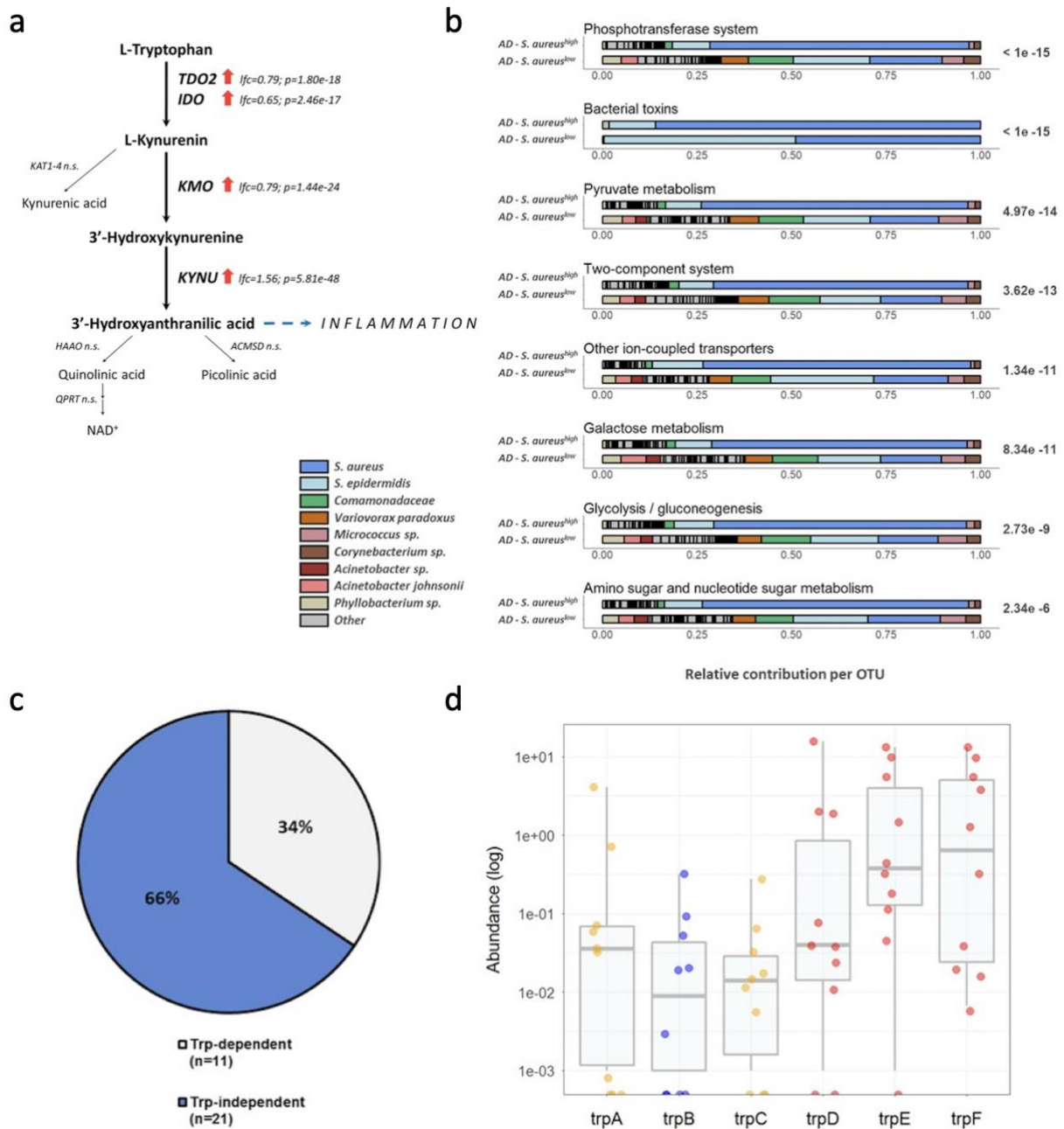
**Fig. 1. Validation of 16S-based OTU classification by WGS.** Correlation of relative abundance of *S. aureus* between 16S rRNA sequencing and WGS metagenomics. For validation of 16S OTU classification, preliminary data of WGS metagenomic sequencing of 20 randomly selected samples from 10 *S. aureus* 'high' and 10 *S. aureus* 'low' patients were used. The significant correlation ( $r^2=0.919$ ) shows agreement of taxonomic classification between the independent sequencing methods.

- Mechanistic validation of the observed host-microbe-interactions, including exposure of human 3D epidermal equivalents with viable *S. aureus*, showing the induction of key *S. aureus* signature genes (Fig. 2). The results are now included in the manuscript in Fig S10 and in the text on p. 17.



**Fig. 2. Mechanistic validation of host-microbe interactions.** **a** Morphological analysis of human epidermal equivalents (HEEs). **b** H&E and **c** immuno-fluorescence staining of microbial colonization of HEEs cultured for 8 days at the air-liquid interface. *S. aureus* bacteria were exposed to the skin equivalent. Arrows indicate visible bacteria on top of the stratum corneum. **d** Keratinocyte response following bacterial stimulation, qPCR measurement of selected *S. aureus* signature genes.

- In depth analysis of tryptophan (trp) metabolism, where we observed significant upregulation of the kynurenine pathway in the *S. aureus* ‘high’ cohort, and reconstructed trp breakdown in atopic skin inflammation (Fig. 3a), indicating the accumulation of the metabolite 3-hydroxyanthranilic acid (3-HAA), which is considered an inflammatory mediator. Moreover, the depletion of the essential amino acid, trp, may be a mode of host defense during bacterial colonization. Since certain microbes, including staphylococci, are susceptible to the depletion of trp by the host, we investigated whether such mechanisms are at play in AD, during *S. aureus* overcolonization. First we cultured *S. aureus* strains from the skin of an independent group of AD patients, and carried out trp-dependence screening. The results indicate that 66% of isolated *S. aureus* strains were independent of trp (Fig 3c). Second, while we did not have access to bacterial isolates from the MAARS cohort, we examined preliminary whole-genome shotgun metagenomic sequencing (WGS) data, and found that on average, 73% of samples carried members of the trp gene family (Fig. 3d). These results are now included in the manuscript as Fig. S11, and in the text on p.17-18 and discussed on p. 24-25.

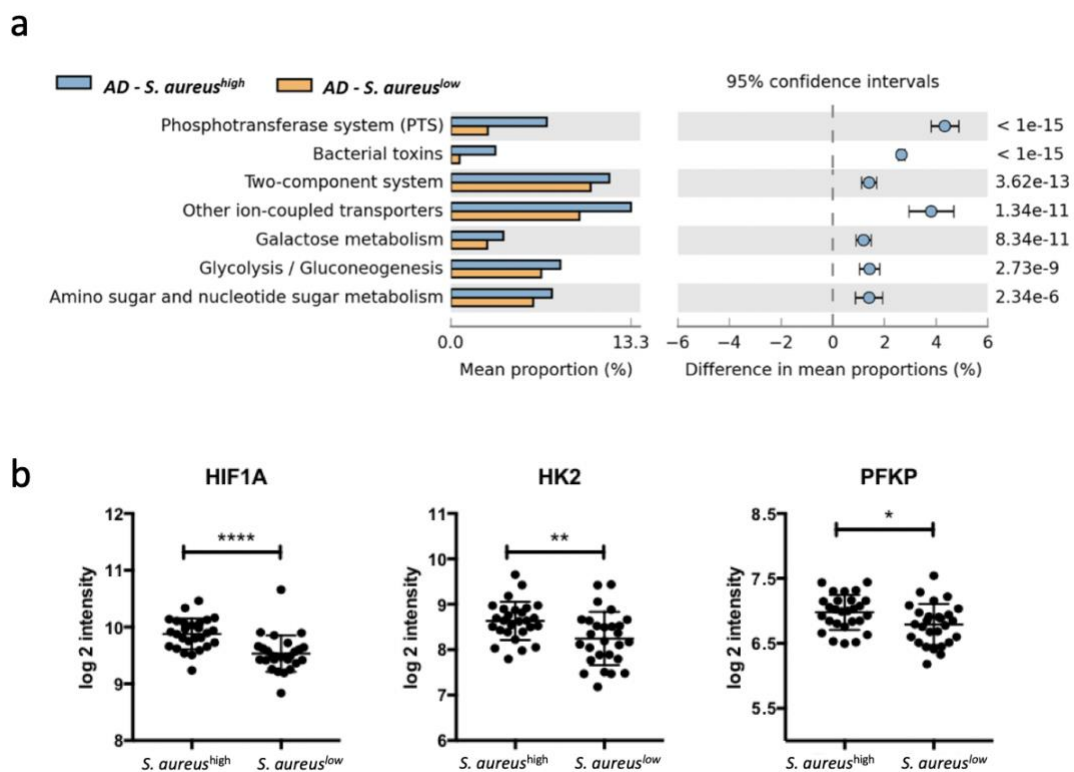


**Fig. 3. Inference of functional metagenomic features based on 16S rRNA and whole genome sequencing.** **a** Regulation of the kynureninase pathway of tryptophan degradation on the mRNA level between HV and the *S. aureus* 'high' cohort. Red arrows: significantly regulated genes, n.s.: not significant. Arrow and font thickness correspond to significance. **b** Contribution of individual OTUs to relevant microbial pathways. The gene content of individual OTUs was inferred using the Greengenes v.13.5 database, and subsequently used to predict enriched microbial pathways in the respective disease groups. Horizontal bars represent the percentage of genes contributed by the most abundant microbes in the dataset. X-axis: sum of relative contributions per sample. Y-axis: contribution across *S. aureus* 'high' and *S. aureus* 'low' cohorts, respectively. **c** Culture-based tryptophan dependence assay of 32 *S. aureus* strains isolated from moderate-to-severe atopic dermatitis patients. Overall, 66% of colonizing *S. aureus* strains were shown to grow independent of tryptophan in Trp-depleted culture medium. **d** Presence of tryptophan biosynthesis-related gene families in WGS sequencing results of *S. aureus* 'high' samples. Y axis: relative abundance of UniRef50-defined *trp* gene families.

4. In order to investigate whether sensitivity to tryptophan depletion is at play in AD during *S. aureus* overcolonization, we sought to identify differences in the metabolic capacity of the microbiome, and generated 16S rRNA-based prediction of the metagenome using the PICRUSt tool (Langille et al., 2013). As a result, we found significantly overrepresented

microbial functions in *S. aureus* ‘high’ compared to ‘low’ groups, such as: ‘bacterial toxins’ (ko02042), ‘phosphotransferase system’ (ko02060), ‘two-component system’ (ko02022), among others (Fig3b, Fig.S11b in the manuscript, Fig.4a). It is notable that due to the great difference in beta diversity, the *S. aureus* ‘high’ cohort represents the bacterial functions of mainly a single species, *S. aureus*, with little contributions from other microbes, while this is contrasted by the functional capacity of a relatively high diversity of microbes in *S. aureus* ‘low’. These results are included in the manuscript as Fig. S11b and Fig.S14a, and in the text on p.17, and discussed on p.24.

- Furthermore, 16S rRNA-based prediction of the metagenome revealed a shift towards glycolysis in the *S. aureus* ‘high’ associated microbiome (Fig. 4a, Fig.S14a in the manuscript). *S. aureus* is known to impose metabolic stress on keratinocytes, resulting in HIF1alpha signaling in the skin, which in turn promotes the generation of inflammatory cytokines, particularly mature IL-1beta (Wickersham et al., 2017). Indeed, in the *S. aureus* ‘high’ samples HIF1a signaling was significantly induced, including HIF1A and HIF1A-dependent genes HK2 and PFKP (Figure 4b, Fig. S14b in the manuscript), and functional analysis predicted IL-1beta as a top upstream regulator, based on the gene expression profiles in the skin (Figure 4d). The results support the notion that metabolic stress, caused by microbial overcolonization as the microorganisms and skin compete for limited oxygen and glucose, drives inflammatory signaling through the induction of HIF1A. These results are included in the manuscript in Fig 14S, and in the text on p. 17 and p. 24-25.



**Fig. 4. Prediction of the *S. aureus* metagenome and gene expression in the skin.** **a** Significantly enriched microbial pathways between *S. aureus* ‘high’ and *S. aureus* ‘low’ groups. Gene content of individual OTUs was inferred using the Greengenes v.13.5 database, and subsequently used to predict enriched microbial pathways in the respective disease groups. **b** Expression of HIF1A and HIF1A dependent genes in the skin in the *S. aureus* ‘high’ cohort.



**Comment 2:** A major point of revision would be to include additional covariate analysis for different skin treatments that the patients had undergone prior to the washout period with Dove, and to describe with more detail the different features of the matched? healthy controls. This is because the authors observed that there were likely different community states/microbiome 'types' for AD because some individuals were characterized by a prevalence of *S. aureus* while others not. Kong et al. reported that intermittent treatment shifts the microbiome towards one with significantly less *S. aureus*, and it is likely that this could be one of the factors that could explain the variation.

**ANSWER:** The patients were carefully (with strict inclusion and exclusion criteria) selected for this study, omitting those who used systemic antibiotics within 2 weeks, or systemic immunosuppressive therapy, phototherapy, or systemic biologic agents within the previous 12 weeks prior to screening.

We agree this is an important issue to explore, and suggest including it in subsequent studies/analyses of this patient cohort.

**Comment 3:** Also, why were OTUs clustered at the 99.3% identity level? Which is fairly atypical and naturally resulted in a very large number of OTUs. There should be some justification of this in the methods, and/or also performed at more conventional levels (eg. 97%).

**ANSWER:** The traditional 97% threshold proposed in 1994 is conservative and could safely be increased, without a significant risk of wrongly differentiated species. In the V4 region, which is one of the two regions (V3-V4) we use in this study, the threshold can be risen much higher, due to stable variable regions as previously described (Meier-Kolthoff JP et al Arch Microbiol. 2013, doi: 10.1007/s00203-013-0888-4).

Importantly, we have now used preliminary data from whole genome sequencing (WGS), to validate 16S based OTU classification and functional predictions based on the 16S marker. The results show close agreement between the two sequencing methods (see Figure 1 above), and are included in the manuscript on p.17 and in Fig. S9D.

## **Reviewer #2 (Remarks to the Author):**

**Comment 1:** In the paper by Fyhrquist et al., "Microbe-host interplay in atopic dermatitis and psoriasis", the authors assemble a large cohort of cases and controls (over 300 individuals), for which they perform 16S rRNA sequencing and microarray-based analysis of transcriptomes. They find that AD is dominated by *S. aureus* and immune activation, whereas PSO was associated with assemblages of organisms.

I was able to review the technicality of the manuscript as my expertise is in microbial community analysis and gut microbiomes, though I was able to only touch upon the conclusions regarding changes in the immune system pertaining to skin disease and the originality of the work from someone in the microbiome field, but an outsider to these specific areas.

My biggest issue with the manuscript is that it overall lacked details about the study design, sample collection and most importantly, statistical analyses, which made it both hard to review and also gave the impression that many of these choices were made without sufficient consideration. These include the method of DNA extraction (crucial for comparing across studies), the methods for performing skin swabs (Fig. S1 implies some buffer but none was discussed), whether there were any exclusion criteria, how samples were matched, and what Affymetrix plates were used for transcriptomics, to name a few.

**ANSWER:** This information is available in great detail in the Supplementary material p61-69.

**Comment 2:** *In terms of statistical analysis, it was unclear why some choices were made—99.3% identity for clustering, how controlling for confounders was done, but also what tests were used (see Figure 1A, a p-value is reported with a vague descriptor of ‘nonparametric score’, but the text only says ‘significantly associated’, yet this repeats in multiple results of the paper, and this is unclear whether this is significantly associated with one of the conditions or if multiple are being compared etc.).*

**ANSWER:** Concerning 99.3%, please see the answer above.

Confounders were tested and removed as described and illustrated on in the main text on p. 8, in Supplementary material on page 63, last paragraph, in Table S1, and in FigS3C. The analysis of 16S rRNA including the use of statistical tests is described in detail in Supplementary materials, p. 61-64. Differentially abundant OTUs were identified by comparing the abundance distribution of each OTU across the clinical groups (AD, PSO, HV) with the Kruskal-Wallis test (FDR, p-value<0.05). Microbe-disease specific associations were detected testing for the differences in the abundances with the Mann-Whitney U-test (FDR, p-value<0.05).

**Comment 3:** *Similarly, in the transcriptomics section, the only thing that was mentioned was “Differential gene expression analysis (line 347) rather than the specific method used. There wasn’t mention about false-discovery corrections for some analyses, though mentioned for others (i.e. Fig 4), or whether any normalization was performed on gene abundances. Since the devil is in the details for microbiome analyses, this can potentially be a major issue.*

**ANSWER:** Affymetrix microarray data were normalized and technical batch effects corrected during preprocessing of the data using state-of-the-art methods, and all critical biological variables were adjusted and tested in the final linear model. Furthermore, Benjamini & Hochberg correction for multiple testing was used throughout the microarray analysis. This information is available in great detail in the Supplementary material p. 65-66.

**Comment 4:** *My other issue with the manuscript is the novelty of the results. Despite my disclaimer that I don’t work entirely in this field, it seems obvious both from quick lit searches and their own statements that there have been a number of studies that have done community analysis of psoriasis and AD and their analysis doesn’t particularly add much. The S. aureus-association with AD is not a new finding, and this has been reported on many times. There have also been RNA-seq experiments performed on both AD (Suarez-Farinas et al, 2015 and even a metaanalysis of transcriptome analyses (Ding et al., 2015) and PSO (Li et al., 2014). They find many of the same co-occurrences and pathway regulation, even according to their own statements (lines 552, 574). It was hard to decipher whether direct comparison could be made between the two disease cohorts because of the ambiguity of the matching scheme, and also the difference in body sampling sites. I can’t comment whether their results significantly improve or change our understand of PSO or AD.*

**ANSWER:** We have now added predictions of bacterial pathways, validation of 16S based taxonomy by WGS, functional predictions and mechanistic validations of the observed host-microbe interactions. The analysis brings in several novel aspects of microbe-host-interplay. For more details, please see the answer to reviewer #1 starting on p. 2.

**Comment 5:** *Other issues:*

- *It was not clear how samples were matched, especially since large differences in gender underlie the Psoriasis and HV cohorts. Similarly, age-related dysbiosis have been reported for skin microbiomes which are thought to predispose individuals to AD. This wasn't tested (or mentioned) within this cohort.*
- *Were there any exclusion criteria? Atopic dermatitis and psoriasis can be treated in many ways, including topical medications (including corticosteroids), oral immunosuppressant therapies, antibiotics, vitamin therapies, and oral steroids as well as immunomodulators. These were never mentioned in the patient recruitment or analysis.*

**ANSWER:**

Matching of samples: As indicated in Figure S1, the mean ages in the AD, PSO and HV groups are 44.5, 48.8 and 34.9 y, respectively. Women are slightly overrepresented in HV, and men in PSO. To account for these differences, age, gender, anatomical location and clinical center were used as covariates during the extrapolation of differentially expressed genes, and OTUs were corrected for gender, age, anatomical location and clinical center (Table S1). The analysis which combined the transcriptome and the microbiome data, included only individuals which had both types of samples available – a high-quality microbiome sample, and high-quality transcriptome sample.

Exclusion criteria: The exclusion criteria included concomitant autoimmune diseases (e.g. rheumatoid arthritis, diabetes, alopecia areata, etc.) the use of systemic antibiotics within 2 weeks and systemic immunosuppressive therapy or phototherapy or systemic biologic agents within the previous 12 weeks prior to screening. Before skin sampling, the biopsy sites were left untreated for at least 2 weeks and cleansing with only the non-antibacterial Dove soap was allowed and washing was avoided for 24 hours prior to sampling. The patients or healthy volunteers who did not match these clinical exclusion criteria were removed from the study.

This information is available in Supplementary information, p.61.

*Minor issues:*

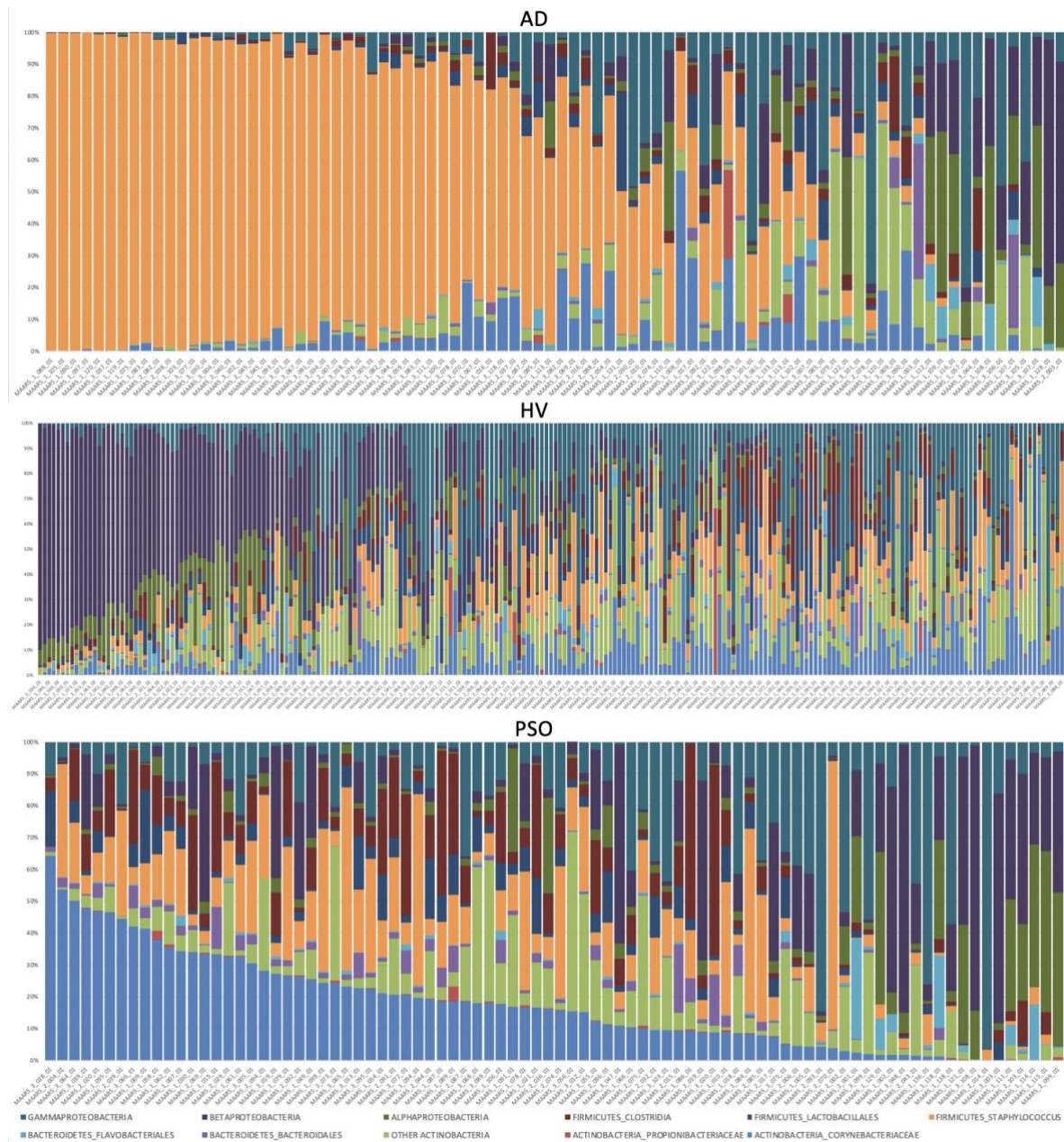
**Comment 6:** - *Hard to follow what is being plotted in many of the figures. I mentioned Fig 1A above, but this is the same for Fig 1B. Is this some aggregate of all of the samples, masking inter-personal variability? This is abnormal to group individual compositions into one composite composition.*

**ANSWER:** We generated individual compositions of the skin microbiota and included these in the supplementary information (see Fig. 5 below, included in the manuscript as Fig. S2). However, as this study includes 316 samples, we chose to show average microbial compositions of AD, PSO and HV in main Figure 1B in the manuscript.

**Comment 7:** - *The data display was very confusing—like Figure 3B is very confusing—are these genes up or down in these different conditions and the same direction in these different conditions. This was a confusing figure. Figure 3C/D are also confusing visually. Or what are the yellow edges in Fig 4F?*

**ANSWER:** The yellow hue inside the dark borders in Fig. 3C and 3D indicate significance, in -log p-values. The yellow edges without a dark border in Fig. 3D indicate log fold change (LogFC). To simplify Fig. 3, we moved panel D to supplementary materials (Figure S7), and included instead dot plots of key genes in HV, AD and PSO.





**Fig. 5.** Individual compositions of the skin microbiota in AD lesions, HV normal skin and PSO lesions. The most abundant bacterial groups depicted for HV, AD and PSO based on 16S sequences.

**Reviewer #3** (Remarks to the Author):

**Comment 1:** In this manuscript, the authors conducted 16S rRNA sequencing identification of the skin microbiome of patients with atopic dermatitis and psoriasis as well as host transcriptome characterization using microarrays of skin biopsies at the same sites. They showed that *S. aureus* is significantly associated with atopic dermatitis and that multiple species, such as *Corynebacterium* spp and anaerobes are associated with psoriatic skin. They also made classifiers to identify the microbial species that could most differentiate between atopic dermatitis vs normal and psoriasis vs normal skin. They then analyze the host skin transcriptome at these sites.

Many of the findings in this paper confirm previously known studies. The skin microbiome findings for atopic dermatitis reflect what is already known in the literature<sup>1,2</sup>. Some findings

for the psoriatic skin microbiome are also already known, such as the overrepresentation of *Streptococcus* spp and overabundance of *Corynebacterium* species (reviewed in 3) although this study has a different way of presenting the data (Figures 1-2). The approach of defining microbial classifiers of AD and psoriatic skin is novel, but without any mechanistic data to suggest why particular species in the classifier are disease-defining, the finding has less impact. Additionally, even if species within the classifier are not disease-defining but are in fact secondary effects of a particular type of inflammation, without mechanistic data suggesting why AD vs psoriatic inflammation might bias towards one set of bacteria vs another, it is hard to assess the biological significance of the classifier.

**ANSWER:** The reviewer raised an important question which unfortunately cannot be addressed here, as it would require a whole new study on its own. However, we believe that our by far largest patient material ever reported in the context of the integration of skin microbiome with the host's cutaneous transcriptome - obtained simultaneously from the same individuals and from the same anatomical locations - provides novel information regarding how microbial communities in the skin are involved in the regulation of skin inflammation in AD and PSO.

**Comment 2:** *The atopic dermatitis transcriptomic data reveal similar pathways as previous skin transcriptome studies<sup>4,5</sup> and confirms known involved pathways, such as Th1 and Th2 pathways (Figure 3). The psoriasis transcriptomic data also confirm known involved pathways and prior studies (reviewed in 6,7), such as IL-17 signaling and IFN-g signaling (Figure 3). Although Figures 3-4 were clear and beautiful representations of the data, they did not offer new hypothesis-generating insight into disease pathogenesis.*

**ANSWER:** Since the main focus in this paper is on host-microbe-transcriptome interactions, the transcriptomics data *per se* serves mainly as proof of concept.

**Comment 3:** *The main novelty of this study is that skin microbiome and transcriptome data were collected at the same time, to allow for analysis of microbiome-transcriptome correlations. However, in their analysis, the authors did not reveal surprising information. By comparing the transcriptomes in AD samples with high abundance of *S. aureus* to those with low abundance of *S. aureus*, the authors found an enrichment of pathways such as "Keratinization" and enrichment in gene expression of IL18, IL1a, TNF, IFNg, and other expected pro-inflammatory cytokines (Figure 4C-D).*

*The analysis of psoriatic microbiomes to transcriptomes revealed that *Corynebacterium* spp may be negatively associated with inflammatory pathways in psoriasis (p.17, line 441-461). However, there are no mechanistic studies to suggest that *Corynebacterium* is protective. Additionally, earlier in the microbiome study, *Corynebacterium* was shown to be overrepresented in psoriatic lesions, which seems contradictory. Perhaps, some *Corynebacterium* species are immunoregulatory or help resistance towards more inflammatory bacteria and are therefore protective, whereas other *Corynebacterium* species are positive associated with psoriasis because they are more pro-inflammatory. This idea would be interesting, but would need additional studies in order to be validated.*

*There is another finding in the paper that I thought was interesting : abundance of anaerobic bacteria in AD was decreased suggesting that there is increased O<sub>2</sub> tension in AD lesions. (Figure 1D, discussed in line 555-557). An analysis of metabolic pathways upregulated in disease states was a very successful approach to show that utilization of formate and aerobic respiration by *E. coli* was increased in gut inflammation<sup>(8)</sup> and then that blocking this particular microbial metabolic pathway using tungsten could ameliorate colitis <sup>(9)</sup>. Therefore, if the authors were to use metagenomic sequencing instead of 16s rRNA sequencing to look at the*

*microbial metabolic pathways that were changed in disease states and correlate this to host transcriptome signatures, this study would be much more informative and more likely to generate hypotheses for further mechanistic studies.*

**ANSWER:** We thank reviewer for this interesting viewpoint. We address now the loss of anaerobes by citing work by Zeeuwen et al (2017) in the manuscript, who introduce a hypothesis regarding the ability of gram-positive anaerobe cocci to induce high levels of antimicrobial peptides in human keratinocytes, thereby strengthening the skin barrier. A complete or partial absence of these organisms, may therefore potentially favor colonization by *S. aureus*. Moreover, we observe metabolic shifts in the AD-associated microbiome (Figures 3-4), generating hypotheses for further mechanistic studies. For further details regarding these, please see above our response to reviewer #1, p. 2.

**Comment 4:** *The approach and intent of the study was commendable and as a field, we do need to move toward connecting microbiota changes to host epithelial or immunologic changes. However, the data presented here did not reveal many distinctive positive results. If the authors were to re-focus on some of the more interesting findings highlighted above and develop further mechanistic insight instead of presenting a broad overview of findings without specific hypotheses, this would greatly improve the impact of this study.*

**ANSWER:** We believe that we report here the by far largest patient material ever in the context of integrating the skin microbiome with the host's cutaneous transcriptome in AD and PSO – sampled simultaneously in the same individuals and anatomical locations. Making use of this exceptional resource, we present an overview of our observations, together with novel insights gained from observed correlations between the skin microbiota and host physiology. We have now added validations of 16S based taxonomy by whole genome sequencing (WGS), functional predictions based on the 16S markers, as well as functional insight based on WGS preliminary data. Moreover, we bring in mechanistic validation of the observed host-microbe interactions. Henceforth, this great resource will provide an exceptional asset for continued studies, digging deeper into the interplay between microbial communities in the skin and the regulation of atopic and psoriatic skin inflammation.

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9. Zhu, W. et al. Precision editing of the gut microbiota ameliorates colitis. *Nature* 553, 208–211 (2018).

Reviewers' comments:

Reviewer #1 (Remarks to the Author):

The manuscript has improved, but my impression remains that the value of this manuscript is not from new biological insights, but rather from the size of the dataset investigating simultaneously the microbiome (metagenome) and transcriptome, albeit the microbiome analysis is conducted at the 16S level where metagenomic data would have been desirable. It remains, as I previously noted, a clean, high quality, and well-written study, nonetheless.

One of the potential additional findings of the paper - the link between trp depletion and AD skin response has also been studied (most recently in Dec 2019 the decrease in trp/trp-related metabolites in AD skin was recently published - "A tryptophan metabolite of the skin microbiota attenuates inflammation in atopic dermatitis via the aryl hydrocarbon receptor" that needs to be cited).

The authors did attempt to provide additional data by sequencing 20 of their samples using shotgun metagenomics - how many millions of reads? How many after removal of human DNA? This is important to evaluate the potential depth and whether the trp pathway is actually present or absent. Was trp pathway analysis presence/absence, or can you say something about the relative abundance of the occurrence of the pathway. More generally, the use of PiCrust for strain-specific phenotypes (trp auxotrophy in a portion of strains) is not advised, as in this case, as it can lead to misleading inferences.

I maintain that looking at previous treatment as confounders is important given the high/low *S. aureus* categorization and previous literature on this point. This is a relatively straightforward analysis and there is not really a good reason that it has to be pushed to a second manuscript.

I am not convinced about the rebutting argument to use the 99.4% similarity by looking at the correlation in relative abundance of *S. aureus*. Basically that figure says that the classifications of *S. aureus* are OK (which I agree with), but it remains that the number of OTUs identified is highly inflated. Because the bulk of the analysis doesn't use the data at the OTU level, there is really no value to using this threshold that yields all these OTUs, and I would be sure that many of them are sequencing/technical/artifacts. Phylotyping would be largely fine given the point of the paper. While this is a technical point, it is a trivial one to correct towards a more conservative estimate of microbial diversity.

Reviewer #2 (Remarks to the Author):

I am satisfied with the additional data, information and conclusions in this revised manuscript. The focus on the tryptophan metabolism and the anaerobe discussion improves the unique conclusions of the paper. The inclusion of the metagenomic data is good, although since the PiCRUST stuff is still in there, the authors should show more validation, i.e. check to see if the genes they find in the PiCRUST analysis also correlate in these samples. Even 10 samples of each *S. aureus* high and low cohort, would be nice validation to show. The additional experimental detail is good. I would recommend making sure that the number of samples and the statistical tests used are in the figures. It takes a lot of searching to find this data and makes it hard to interpret at first glance. Another small comment—what immunofluorescence was used in Fig S10C—is the antibody specific to *S. aureus*? (It looks like it could just be DAPI?) I don't think details on the microscopy were included.

Reviewer #3 (Remarks to the Author):

In the revised manuscript, the authors used their transcriptomic data from AD samples with high vs low *S. aureus* abundance to define a host tissue “*S. aureus* signature”. They found the GO term “Tryptophan degradation” to be enriched in the *S. aureus* high group and they also found that *S. aureus* strains in the “high” group seemed to have more tryptophan biosynthesis genes and a majority grew independently of tryptophan.

Here, the authors are trying to draw a more direct connection between their host transcriptome data and their microbe 16s sequencing data, but the logic of this section was confusing to read. Specifically:

- Line 459 – may have a fragment of a sentence or a misplaced comma.
- Line 460-463 – I don't understand how enrichment of microbial pathways like “Phosphotransferase system” etc relate to tryptophan metabolism, which is what this paragraph seems to be mainly about.
- In Figure S11C, Table S4, they found that 66% of isolated *S. aureus* strains grew independently of tryptophan, and I think they are implying that this microbial trait was selected for by decreased host availability of tryptophan due to increased tryptophan metabolism. However, I

don't see in Figures S11C-D a comparison to *S. aureus* "low" AD samples. What if 66% of skin-associated *S. aureus* strains in AD are generally tryptophan-independent, whether or not they exist in a "high *S. aureus*" or "low *S. aureus*" microbial environment?

Additionally, the results regarding upregulated microbial pathways is based on inference from their 16s rRNA sequencing data using PICRUSt. My understanding is that this inference is only as good as the database of sequenced microbial genomes and the ability to match the sequenced strain genomes to the 16s rRNA sequence-generated OTU. Given that different strains of the same skin-colonizing bacterial species can have highly variable behavior in terms of virulence and immune stimulation, that a great number of skin bacterial strains are not sequenced (even if some members of the species have been sequenced), and that 16s rRNA sequencing cannot fully resolve strain-specific differences, how can the authors feel confident in their metagenomic inferences?

I do think, on page 25, the authors present an interesting idea. That is, the host attempt to limit available tryptophan as a defense mechanism against higher *S. aureus* colonization may then cause increased metabolites (such as 3-HAA), which are pro-inflammatory. It is then interesting to wonder if such metabolites like 3-HAA continue to help the host maintain a defensive immune barrier or if they backfire and feed into AD pathology. It is also interesting to wonder if the host defense mechanism of limiting tryptophan is unable to repress *S. aureus* colonization but does in fact repress colonization by benign commensal bacteria, and thus also inadvertently creates more dysbiosis. I wonder if the novelty of these points could be better expressed if the authors condensed lines 658-673 (which seem to mainly restate the results) and highlighted the implications of their data more.



Responses to the reviewers' comments:

**Reviewer #1 (Remarks to the Author):**

1. *The manuscript has improved, but my impression remains that the value of this manuscript is not from new biological insights, but rather from the size of the dataset investigating simultaneously the microbiome (metagenome) and transcriptome, albeit the microbiome analysis is conducted at the 16S level where metagenomic data would have been desirable. It remains, as I previously noted, a clean, high quality, and well-written study, nonetheless.*

*One of the potential additional findings of the paper - the **link between trp depletion and AD skin response** has also been studied (most recently in Dec 2019 the decrease in trp/trp-related metabolites in AD skin was recently published - "A tryptophan metabolite of the skin microbiota attenuates inflammation in atopic dermatitis via the aryl hydrocarbon receptor" that needs to be cited).*

*Was trp pathway analysis presence/absence, or can you say something about the relative abundance of the occurrence of the pathway. More generally, the use of PiCrust for strain-specific phenotypes (trp auxotrophy in a portion of strains) is not advised, as in this case, as it can lead to misleading inferences.*

*The authors did attempt to provide additional data by sequencing 20 of their samples using shotgun metagenomics - how many millions of reads? How many after removal of human DNA? This is important to evaluate the potential depth and whether the trp pathway is actually present or absent.*

**Answer:** The authors thank the reviewer for referring to the recent study by Yu *et al.* In the revised manuscript, we have now cited the study, please see page 26, lines 698-700. Although in the present work we did not investigate trp metabolites, we maintain that the simultaneous high-throughput characterization of trp metabolism genes in the host transcriptome and microbiome provides novel insights.

Detailed information on sequencing read counts for human and microbial DNA is provided in Table 1 of our point-by-point (please see below). Shotgun metagenomic libraries contained between 2-18.5% microbial DNA while read counts ranged from 0.15-5.5 million and were comparable to those achieved in recent large-scale microbiome studies by Chng *et al* or Tett *et al*<sup>1,2</sup>. Thus, taking into account the quality of WGS libraries, together with the additional information of independent culture-based Trp-dependence assays (Figure S12b), the authors feel confident in their WGS validation presented in Figure S12c in the manuscript. However, we agree that the role of Trp metabolites in host-microbial interactions in AD is an important issue to further explore in subsequent studies.

Sample ID	Million reads sequenced	Filtered reads	Percentage microbiome
MB1	26.05	725865	2.79
MB2	78.64	2086180	2.65
MB3	54.77	2772356	5.06
MB4	33.03	2373752	7.19
MB5	43.94	1728968	3.93
MB6	29.11	5390992	18.52
MB7	19.94	1354057	6.79
MB8	10.31	208857	2.03
MB9	31.43	2161375	6.88
MB10	18.9	807488	4.27
MB11	52.6	4442216	8.45
MB12	4.51	149775	3.32
MB13	9.38	1053178	11.23
MB14	21.55	823947	3.82
MB15	52.28	1323858	2.53
MB16	30.4	1795493	5.91
MB17	28.23	960793	3.40
MB18	34.17	1408536	4.12
MB19	0.86	136668	15.89
MB20	32.56	2887738	8.87
Average	30.633	1729604.6	6.38

**Table 1.** Sequence reads before and after removing human DNA.

**2.** *I maintain that looking at previous treatment as confounders is important given the high/low S. aureus categorization and previous literature on this point. This is a relatively straightforward analysis and there is not really a good reason that it has to be pushed to a second manuscript.*

**Answer:** We analyzed the potential effect of treatments according to the reviewer suggestions, as shown in Table 2 or our point-by-point reply (please see TABLE 2 at the end of this document). Analysis was carried out in the same manner as confounding factor analysis for age, gender, sampling institution and body site, applying Wilcoxon rank-sum test followed by Benjamini-Hochberg multiple testing correction. We have found no significant associations between treatments and the top 95 most abundant microbiota in atopic dermatitis. In the case of psoriasis, a single *Acinetobacter* OTU showed an association ( $p=0.019$ ) with topical coal tar treatment. Topical coal tar treatment was only used in a small subset within the psoriasis cohort ( $n=24$ ). The specific *Acinetobacter* OTU did not demonstrate any significant associations with the host transcriptome and was not used or referenced in any analyses of the present study. Hence we decided not to include this information into the revised manuscript.

**3.** *I am not convinced about the rebutting argument to use the 99.4% similarity by looking at the correlation in relative abundance of S. aureus. Basically that figure says that the classifications of S. aureus are OK (which I agree with), but it remains that the number of OTUs identified is highly inflated. Because the bulk of the analysis doesn't use the data at the OTU level, there is really no value to using this threshold that yields all these OTUs, and I would be sure that many of them are sequencing/technical/artifacts. Phylotyping would be largely fine given the point of the paper. While this is a technical point, it is a trivial one to correct towards a more conservative estimate of microbial diversity.*

**Answer:** We appreciate this concern and we appreciate that the reviewer agrees that the OTU classifications are correct using the higher cutoff. We agree though, that the OTU number we have reported is unnecessarily high as a result. After careful analysis, we have found that the





**3. Another small comment—what immunofluorescence was used in Fig S10C—is the antibody specific to *S. aureus*? (It looks like it could just be DAPI?) I don't think details on the microscopy were included.**

**Answer:** In this experiment, a single *S. aureus* strain (ATCC 29213) was applied onto sterile 3D human epidermal equivalents. We indeed use DAPI (DAPI Fluoromount-G, Southern Biotech) to detect all DNA in the sample, hence the staining of both human DNA (keratinocyte nuclei) and the bacterial DNA on top of the stratum corneum. This staining allows for a visualization of the bacteria to determine the distribution of bacteria topically applied, but does not specifically discriminate bacterial species. Since we in this case applied a single bacterial strain, the DAPI stain herein used is sufficient to discriminate the bacteria in the 3D culture model.

**Reviewer #3 (Remarks to the Author):**

**1. In the revised manuscript, the authors used their transcriptomic data from AD samples with high vs low *S. aureus* abundance to define a host tissue “*S. aureus* signature”. They found the GO term “Tryptophan degradation” to be enriched in the *S. aureus* high group and they also found that *S. aureus* strains in the “high” group seemed to have more tryptophan biosynthesis genes and a majority grew independently of tryptophan.**

*Here, the authors are trying to draw a more direct connection between their host transcriptome data and their microbe 16s sequencing data, but the logic of this section was confusing to read. Specifically:*

*- Line 459 – may have a fragment of a sentence or a misplaced comma.*

*- Line 460-463 – I don't understand how enrichment of microbial pathways like “Phosphotransferase system” etc relate to tryptophan metabolism, which is what this paragraph seems to be mainly about.*

**Answer:** The authors thank the reviewer for this suggestion. The section has been rewritten. Please see page 18, lines 461-470, and page 26-27, lines 696-717. Figures S8 and S12 have been revised accordingly and rearranged for a clearer presentation of the referenced data.

**2. - In Figure S11C, Table S4, they found that 66% of isolated *S. aureus* strains grew independently of tryptophan, and I think they are implying that this microbial trait was selected for by decreased host availability of tryptophan due to increased tryptophan metabolism. However, I don't see in Figures S11C-D a comparison to *S. aureus* “low” AD samples. What if 66% of skin-associated *S. aureus* strains in AD are generally tryptophan-independent, whether or not they exist in a “high *S. aureus*” or “low *S. aureus*” microbial environment?**

**Answer:** In *S. aureus* ‘low’ samples, the pathogen is indeed absent, or present at extremely low abundance. Hence, isolation of *S. aureus* strains from these patients is not possible and the coverage of metagenomic shotgun sequencing for the species is also too shallow to identify *S. aureus*-specific Trp gene sequences with the necessary confidence. Trp-dependence assays were performed in *S. aureus* strains isolated from an independent AD collective and findings were confirmed by whole-genome metagenomic sequencing in the MAARS *S. aureus* ‘high’ cohort. On the other hand, assessment of the general independence of *S. aureus* strains from Trp requires analysis and data collection beyond the scope of our present study.

However, the hypothesis that the particular means of host defense by Trp depletion is ineffective against the majority of skin colonizing *S. aureus* strains in the *S. aureus* 'high' group is not affected by these limitations.

**3.** *Additionally, the results regarding upregulated microbial pathways is based on inference from their 16s rRNA sequencing data using PICRUSt. My understanding is that this inference is only as good as the database of sequenced microbial genomes and the ability to match the sequenced strain genomes to the 16s rRNA sequence-generated OTU. Given that different strains of the same skin-colonizing bacterial species can have highly variable behavior in terms of virulence and immune stimulation, that a great number of skin bacterial strains are not sequenced (even if some members of the species have been sequenced), and that 16s rRNA sequencing cannot fully resolve strain-specific differences, how can the authors feel confident in their metagenomic inferences?*

**Answer:** Although a significant limitation of prediction methods is, naturally, the missing information on yet unsequenced bacterial strains, the extended ancestral state-reconstruction algorithm developed for PICRUSt has produced up to  $r=0.8-0.9$  correlation with WGS datasets<sup>3</sup>. As our present study focused on a condition dominated by a single, well-studied and well-annotated species, we aimed to gain preliminary insight into the mechanisms of *S. aureus* colonization using the PICRUSt method. Furthermore, we have provided experimental validation of microbial genes predicted to show significantly higher abundance in *S. aureus*-high compared to *S. aureus*-low samples, using preliminary data from 10 whole-genome shotgun sequencing samples of each group. Our validation dataset shows a strikingly high concordance with the findings of 16S rRNA gene-based predictions.

**4.** *I do think, on page 25, the authors present an interesting idea. That is, the host attempt to limit available tryptophan as a defense mechanism against higher *S. aureus* colonization may then cause increased metabolites (such as 3-HAA), which are pro-inflammatory. It is then interesting to wonder if such metabolites like 3-HAA continue to help the host maintain a defensive immune barrier or if they backfire and feed into AD pathology. It is also interesting to wonder if the host defense mechanism of limiting tryptophan is unable to repress *S. aureus* colonization but does in fact repress colonization by benign commensal bacteria, and thus also inadvertently creates more dysbiosis. I wonder if the novelty of these points could be better expressed if the authors condensed lines 658-673 (which seem to mainly restate the results) and highlighted the implications of their data more.*

**Answer:** The authors thank the reviewer for this suggestion. The paragraph has been revised accordingly, on page 18, lines 461-470, and page 26-27, lines 696-717. Figures S8 and S12 have been rearranged for a clearer representation of supporting data.

## References

- 1 Chng, K. R. *et al.* Whole metagenome profiling reveals skin microbiome-dependent susceptibility to atopic dermatitis flare. *Nat Microbiol* **1**, 16106, doi:10.1038/nmicrobiol.2016.106 (2016).
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- 3 Langille, M. G. *et al.* Predictive functional profiling of microbial communities using 16S rRNA marker gene sequences. *Nat Biotechnol* **31**, 814-821, doi:10.1038/nbt.2676 (2013).

TABLE 2. Analysis of the effect of medical treatments on the microbial diversity analyses.

AD				PSO			
Wilcoxon rank-sum test statistic	P.adjusted	Treatment	OTU	Wilcoxon rank-sum test statistic	P.adjusted	Treatment	OTU
438	0.14435989	Phototherapy	OTU4422405	1697	0.01960517	TAR.topical.	OTU4021335
483	0.27270111	Topicalcalcineurininhbitors	OTU1004369	1796	0.09405471	LocalCorticosteroids	OTU4456068
560.5	0.32639065	Topicalcalcineurininhbitors	OTU3841245	819	0.25029678	LocalCorticosteroids	OTU820692
543	0.32639065	Topicalcalcineurininhbitors	OTU4411187	2280,05,01	0.25029678	VitaminDanalogs	OTU4411187
555	0.33906797	Phototherapy	OTU4411187	1614	0.25259955	TAR.topical.	OTU4482598
459.5	0.56347641	SystemicCorticosteroids	OTU4446521	1702.5	0.27002811	LocalCorticosteroids	OTU4346894
554	0.59970951	Phototherapy	OTU1004369	716	0.27002811	LocalCorticosteroids	OTU837884
635	0.59970951	Phototherapy	OTU4348347	1542	0.3601251	Methotrexate	OTU496787
615.5	0.59970951	Topicalcalcineurininhbitors	OTU4408996	1573	0.3601251	LocalCorticosteroids	OTU4411187
589.5	0.59970951	Topicalcalcineurininhbitors	OTU4446521	936	0.3601251	Fumaricacid	OTU282360
583	0.59970951	Topicalcalcineurininhbitors	OTU912997	2309	0.3601251	VitaminDanalogs	OTU4422405
527	0.59970951	SystemicCorticosteroids	OTU4439089	1526	0.3601251	TAR.topical.	OTU279980
264	0.59970951	Antibiotics	OTU378096	1470.5	0.3601251	TAR.topical.	OTU4348347
223	0.59970951	Antibiotics	OTU4440643	1506	0.3601251	TAR.topical.	OTU4468125
214	0.60647265	LocalCorticosteroids	OTU4346894	743.5	0.3601251	Cyclosporin	OTU4476950
214	0.60647265	LocalCorticosteroids	OTU4346894	1379	0.40496133	VitaminDanalogs	OTU820692
646	0.60647265	Phototherapy	OTU2110555	1116	0.40496133	Dithranol.minute	OTU4468125
627	0.60647265	Phototherapy	OTU3841245	1057	0.40496133	Dithranol.minute	OTU883806
632.5	0.60647265	Topicalcalcineurininhbitors	OTU25478	1524	0.41132963	TAR.topical.	OTU1036883
1061.5	0.60647265	Topicalcalcineurininhbitors	OTU4482598	1518.5	0.55130905	TAR.topical.	OTU4047452
473	0.60647265	SystemicCorticosteroids	OTU4349859	1098	0.62742789	Dithranol.minute	OTU4309323
301	0.60647265	Cyclosporin	OTU4294554	888	0.65432936	Fumaricacid	OTU247720
270.5	0.60647265	Cyclosporin	OTU4476950	888	0.65432936	TAR.topical.	OTU3841245
299	0.60647265	Cyclosporin	OTU565753	1142	0.66960777	Dithranol.minute	OTU4456068
252.5	0.60647265	Antibiotics	OTU940083	672	0.67189545	Retinoids	OTU4408996
1015.5	0.70370445	Topicalcalcineurininhbitors	OTU3208510	1369	0.67189545	Methotrexate	OTU987144
259	0.70370445	Antibiotics	OTU755148	589.5	0.67189545	Topicalcalcineurininhbitors	OTU4369229
256	0.75101766	LocalCorticosteroids	OTU4411187	203	0.67189545	Topicalcalcineurininhbitors	OTU4422718
256	0.75101766	LocalCorticosteroids	OTU4411187	196	0.67189545	Topicalcalcineurininhbitors	OTU851917
629	0.75101766	Topicalcalcineurininhbitors	OTU1131523	420	0.67189545	Fumaricacid	OTU4411187
637	0.75101766	Topicalcalcineurininhbitors	OTU403853	2182	0.67189545	VitaminDanalogs	OTU4474056
661	0.75101766	Topicalcalcineurininhbitors	OTU4309323	2169	0.67189545	VitaminDanalogs	OTU851917
611	0.75101766	Topicalcalcineurininhbitors	OTU4346894	2212	0.67189545	VitaminDanalogs	OTU912997
650	0.75101766	Topicalcalcineurininhbitors	OTU4474056	1442.5	0.67189545	TAR.topical.	OTU103810
996	0.75101766	Topicalcalcineurininhbitors	OTU819937	804	0.67189545	Photochemotherapy	OTU4408996
607	0.75101766	Topicalcalcineurininhbitors	OTU837884	696.5	0.67189545	Cyclosporin	OTU4309323
280	0.75101766	Cyclosporin	OTU1036883	1094	0.67189545	Dithranol.minute	OTU4021335
302	0.75101766	Cyclosporin	OTU4303697	206.5	0.70787186	Topicalcalcineurininhbitors	OTU360483
280	0.75101766	Cyclosporin	OTU4482598	1959,05,01	0.71306337	Phototherapy	OTU25478
265	0.75101766	Antibiotics	OTU1081372	783.5	0.73211584	Photochemotherapy	OTU4301457
257	0.75101766	Antibiotics	OTU1131523	557	0.78626063	Dithranol.minute	OTU20360
296	0.75101766	Antibiotics	OTU4294554	564.5	0.78626063	Dithranol.minute	OTU4349519
64	0.75101766	Methotrexate	OTU4021335	1536	0.79423233	LocalCorticosteroids	OTU4369229
62	0.75101766	Methotrexate	OTU4294554	584	0.79423233	Topicalcalcineurininhbitors	OTU4480063
63	0.75101766	Methotrexate	OTU565753	549	0.83709956	Topicalcalcineurininhbitors	OTU4350124
294.5	0.75972604	Cyclosporin	OTU4299324	547	0.83709956	Dithranol.minute	OTU285376
305	0.75972604	Cyclosporin	OTU625320	1463	0.8447206	TAR.topical.	OTU4346894
281	0.81474028	LocalCorticosteroids	OTU1004369	346.5	0.86593812	SystemicCorticosteroids	OTU378096
304	0.81474028	LocalCorticosteroids	OTU2901965	703	0.86795704	Cyclosporin	OTU995817
284	0.81474028	LocalCorticosteroids	OTU403853	868	0.87688108	Fumaricacid	OTU4440643
299	0.81474028	LocalCorticosteroids	OTU4309323	1527.5	0.89311589	LocalCorticosteroids	OTU4480063
280.5	0.81474028	LocalCorticosteroids	OTU4317476	114	0.89311589	Antibiotics	OTU987144
260	0.81474028	LocalCorticosteroids	OTU4422405	416	0.90423024	Fumaricacid	OTU4354809
267	0.81474028	LocalCorticosteroids	OTU4456068	575	0.90423024	Dithranol.minute	OTU370309
276	0.81474028	LocalCorticosteroids	OTU837884	841	0.91128509	Methotrexate	OTU279980
297	0.81474028	LocalCorticosteroids	OTU851917	221	0.91128509	Topicalcalcineurininhbitors	OTU4474056
281	0.81474028	LocalCorticosteroids	OTU1004369	757	0.91605862	Retinoids	OTU1107940
304	0.81474028	LocalCorticosteroids	OTU2901965	756.5	0.91605862	Retinoids	OTU13445
284	0.81474028	LocalCorticosteroids	OTU403853	1174	0.91605862	Retinoids	OTU205025
299	0.81474028	LocalCorticosteroids	OTU4309323	687.5	0.91605862	Retinoids	OTU4301457
280.5	0.81474028	LocalCorticosteroids	OTU4317476	1219	0.91605862	Retinoids	OTU4349859
260	0.81474028	LocalCorticosteroids	OTU4422405	1147	0.91605862	Retinoids	OTU565753
267	0.81474028	LocalCorticosteroids	OTU4456068	1210.5	0.91605862	Retinoids	OTU837884
276	0.81474028	LocalCorticosteroids	OTU837884	1157	0.91605862	Retinoids	OTU851925
297	0.81474028	LocalCorticosteroids	OTU851917	745	0.91605862	Retinoids	OTU912906
970.5	0.81474028	Phototherapy	OTU1003210	1326.5	0.91605862	Methotrexate	OTU247720
695	0.81474028	Phototherapy	OTU25259	1375	0.91605862	Methotrexate	OTU282360
703	0.81474028	Phototherapy	OTU2901965	1344	0.91605862	Methotrexate	OTU625320
714	0.81474028	Phototherapy	OTU360483	1372	0.91605862	Methotrexate	OTU995817
697.5	0.81474028	Phototherapy	OTU4299324	949.5	0.91605862	LocalCorticosteroids	OTU1003210
959	0.81474028	Phototherapy	OTU4306540	920	0.91605862	LocalCorticosteroids	OTU1081372
636.5	0.81474028	Phototherapy	OTU4349859	949.5	0.91605862	LocalCorticosteroids	OTU282360
694	0.81474028	Phototherapy	OTU4354809	969	0.91605862	LocalCorticosteroids	OTU4294554
698.5	0.81474028	Phototherapy	OTU4440643	916.5	0.91605862	LocalCorticosteroids	OTU505749
673.5	0.81474028	Phototherapy	OTU4446521	536	0.91605862	Topicalcalcineurininhbitors	OTU1036883
662.5	0.81474028	Phototherapy	OTU4456068	250	0.91605862	Topicalcalcineurininhbitors	OTU370134
689.5	0.81474028	Phototherapy	OTU4467218	531	0.91605862	Topicalcalcineurininhbitors	OTU4021335



715	0.81474028	Phototherapy	OTU4473201
677	0.81474028	Phototherapy	OTU4480063
670.5	0.81474028	Phototherapy	OTU496787
693	0.81474028	Phototherapy	OTU511475
951	0.81474028	Topicalcalcineurininhibitors	OTU164003
669.5	0.81474028	Topicalcalcineurininhibitors	OTU20360
738	0.81474028	Topicalcalcineurininhibitors	OTU4294554
706	0.81474028	Topicalcalcineurininhibitors	OTU4299324
704.5	0.81474028	Topicalcalcineurininhibitors	OTU4318084
690	0.81474028	Topicalcalcineurininhibitors	OTU4349519
650.5	0.81474028	Topicalcalcineurininhibitors	OTU4349859
980	0.81474028	Topicalcalcineurininhibitors	OTU4353642
980	0.81474028	Topicalcalcineurininhibitors	OTU4421536
636	0.81474028	Topicalcalcineurininhibitors	OTU4422405
946	0.81474028	Topicalcalcineurininhibitors	OTU505749
695	0.81474028	Topicalcalcineurininhibitors	OTU511475
704.5	0.81474028	Topicalcalcineurininhibitors	OTU940083
680	0.81474028	Topicalcalcineurininhibitors	OTU995817
575	0.81474028	SystemicCorticosteroids	OTU1131523
821	0.81474028	SystemicCorticosteroids	OTU14278
841	0.81474028	SystemicCorticosteroids	OTU205025
564	0.81474028	SystemicCorticosteroids	OTU3841245
827	0.81474028	SystemicCorticosteroids	OTU4306540
564	0.81474028	SystemicCorticosteroids	OTU4309323
587.5	0.81474028	SystemicCorticosteroids	OTU4411187
526	0.81474028	SystemicCorticosteroids	OTU4422405
546	0.81474028	SystemicCorticosteroids	OTU4440643
836	0.81474028	SystemicCorticosteroids	OTU4468125
573	0.81474028	SystemicCorticosteroids	OTU4480063
534	0.81474028	SystemicCorticosteroids	OTU837884
604	0.81474028	SystemicCorticosteroids	OTU851925
298	0.81474028	Cyclosporin	OTU1081372
335.5	0.81474028	Cyclosporin	OTU247720
316	0.81474028	Cyclosporin	OTU2901965
316.5	0.81474028	Cyclosporin	OTU370309
349	0.81474028	Cyclosporin	OTU4021335
330	0.81474028	Cyclosporin	OTU4353642
530	0.81474028	Cyclosporin	OTU4354809
557.5	0.81474028	Cyclosporin	OTU4369229
344	0.81474028	Cyclosporin	OTU4422718
320	0.81474028	Cyclosporin	OTU4439089
296	0.81474028	Cyclosporin	OTU4440643
318	0.81474028	Cyclosporin	OTU4474056
300.5	0.81474028	Cyclosporin	OTU912997
301	0.81474028	Cyclosporin	OTU995817
306	0.81474028	Antibiotics	OTU2901965
286	0.81474028	Antibiotics	OTU370134
497	0.81474028	Antibiotics	OTU403853
271	0.81474028	Antibiotics	OTU4301457
295	0.81474028	Antibiotics	OTU4349519
291.5	0.81474028	Antibiotics	OTU4482598
299	0.81474028	Antibiotics	OTU565753
308.5	0.81474028	Antibiotics	OTU820692
278	0.81474028	Antibiotics	OTU837884
489.5	0.81474028	Antibiotics	OTU987144
172.5	0.81474028	Methotrexate	OTU4317476
174	0.81474028	Methotrexate	OTU4354809
178.5	0.81474028	Methotrexate	OTU4369229
72	0.81474028	Methotrexate	OTU4439089
1965,05,01	0.81474028	Methotrexate	OTU4481323
54	0.81474028	Methotrexate	OTU883806
597.5	0.82412327	SystemicCorticosteroids	OTU25478
300	0.82412327	Antibiotics	OTU4474056
311	0.8289316	Cyclosporin	OTU4422405
612	0.83018581	SystemicCorticosteroids	OTU114999
729.5	0.8326991	Topicalcalcineurininhibitors	OTU4349522
575	0.8326991	SystemicCorticosteroids	OTU1004369
503	0.8326991	Cyclosporin	OTU205025
691	0.8334532	Topicalcalcineurininhibitors	OTU1096610
329	0.8334532	Cyclosporin	OTU4349519
325	0.8334532	Cyclosporin	OTU4446521
333.5	0.8334532	Cyclosporin	OTU940083
471	0.8334532	Antibiotics	OTU4327286
319.5	0.8334532	Antibiotics	OTU912906
699	0.83440212	Topicalcalcineurininhibitors	OTU4301457
599	0.83440212	SystemicCorticosteroids	OTU4299324
294.5	0.83686604	LocalCorticosteroids	OTU4349859
459	0.83686604	LocalCorticosteroids	OTU4353642
299	0.83686604	LocalCorticosteroids	OTU4369229
318	0.83686604	LocalCorticosteroids	OTU4460228
297	0.83686604	LocalCorticosteroids	OTU4480063
294.5	0.83686604	LocalCorticosteroids	OTU4349859

545	0.91605862	Topicalcalcineurininhibitors	OTU4449324
248.5	0.91605862	Topicalcalcineurininhibitors	OTU761594
522	0.91605862	Topicalcalcineurininhibitors	OTU912906
845.5	0.91605862	Fumaricacid	OTU285376
800	0.91605862	Fumaricacid	OTU4294554
459	0.91605862	Fumaricacid	OTU4306540
110	0.91605862	Antibiotics	OTU205025
118	0.91605862	Antibiotics	OTU360483
117	0.91605862	Antibiotics	OTU4021335
2110,05,01	0.91605862	VitaminDanalogs	OTU164003
2005	0.91605862	VitaminDanalogs	OTU3841245
1449	0.91605862	VitaminDanalogs	OTU4301457
2083	0.91605862	VitaminDanalogs	OTU4349519
2081	0.91605862	VitaminDanalogs	OTU4446521
1442	0.91605862	VitaminDanalogs	OTU4482598
1411	0.91605862	TAR.topical.	OTU4421536
889	0.91605862	TAR.topical.	OTU625320
1337.5	0.91605862	Photochemotherapy	OTU114999
1342	0.91605862	Photochemotherapy	OTU4327286
1370	0.91605862	Photochemotherapy	OTU851917
120	0.91605862	SystemicCorticosteroids	OTU1003210
98	0.91605862	SystemicCorticosteroids	OTU4346894
106	0.91605862	SystemicCorticosteroids	OTU4474056
345	0.91605862	SystemicCorticosteroids	OTU4482598
118	0.91605862	SystemicCorticosteroids	OTU851917
1283	0.91605862	Phototherapy	OTU4349859
1334	0.91605862	Phototherapy	OTU4353642
346.5	0.91605862	Cyclosporin	OTU13445
307	0.91605862	Cyclosporin	OTU4480063
656	0.91605862	Dithranol.minute	OTU3841245
1016	0.91605862	Dithranol.minute	OTU4299324
1067	0.91605862	Dithranol.minute	OTU4346894
652	0.91605862	Dithranol.minute	OTU820692
605	0.91605862	Dithranol.minute	OTU851917
122	0.91743109	SystemicCorticosteroids	OTU4422718
1100	0.91868516	Retinoids	OTU1036883
765	0.91868516	Retinoids	OTU1081372
849.5	0.91868516	Retinoids	OTU1096610
817.5	0.91868516	Retinoids	OTU1131523
844	0.91868516	Retinoids	OTU14278
775	0.91868516	Retinoids	OTU25259
1111.5	0.91868516	Retinoids	OTU25478
806	0.91868516	Retinoids	OTU279980
852	0.91868516	Retinoids	OTU2901965
773	0.91868516	Retinoids	OTU362390
1109.5	0.91868516	Retinoids	OTU378096
1036	0.91868516	Retinoids	OTU4047452
796	0.91868516	Retinoids	OTU4294554
843	0.91868516	Retinoids	OTU4299324
1124.5	0.91868516	Retinoids	OTU4327286
790	0.91868516	Retinoids	OTU4327300
813	0.91868516	Retinoids	OTU4349519
758.5	0.91868516	Retinoids	OTU4349522
1048	0.91868516	Retinoids	OTU4350124
848	0.91868516	Retinoids	OTU4353642
866	0.91868516	Retinoids	OTU4421536
863.5	0.91868516	Retinoids	OTU4440643
1066.5	0.91868516	Retinoids	OTU4449324
1063	0.91868516	Retinoids	OTU4456068
759	0.91868516	Retinoids	OTU4460228
1081.5	0.91868516	Retinoids	OTU4468125
1051	0.91868516	Retinoids	OTU4473201
867	0.91868516	Retinoids	OTU4474056
844.5	0.91868516	Retinoids	OTU4476950
785.5	0.91868516	Retinoids	OTU4480063
1107	0.91868516	Retinoids	OTU4481323
1117	0.91868516	Retinoids	OTU4482598
796	0.91868516	Retinoids	OTU505749
763.5	0.91868516	Retinoids	OTU610043
865	0.91868516	Retinoids	OTU654307
844	0.91868516	Retinoids	OTU755148
861	0.91868516	Retinoids	OTU819937
1037	0.91868516	Retinoids	OTU820692
826	0.91868516	Retinoids	OTU851668
811.5	0.91868516	Retinoids	OTU939571
1035	0.91868516	Retinoids	OTU940083
1115	0.91868516	Retinoids	OTU987144
1112	0.91868516	Retinoids	OTU995817
1297.5	0.91868516	Methotrexate	OTU1003210
1349	0.91868516	Methotrexate	OTU1004369
966	0.91868516	Methotrexate	OTU1107940
1206	0.91868516	Methotrexate	OTU1131523

459	0.83686604	LocalCorticosteroids	OTU4353642
299	0.83686604	LocalCorticosteroids	OTU4369229
318	0.83686604	LocalCorticosteroids	OTU4460228
297	0.83686604	LocalCorticosteroids	OTU4480063
723.5	0.83686604	Phototherapy	OTU4309323
953	0.83686604	Phototherapy	OTU755148
697	0.83686604	Phototherapy	OTU837884
742	0.83686604	Topicalcalcineurininhibitors	OTU4306540
704	0.83686604	Topicalcalcineurininhibitors	OTU4480063
734.5	0.83686604	Topicalcalcineurininhibitors	OTU74351
623.5	0.83686604	SystemicCorticosteroids	OTU360483
341.5	0.83686604	Cyclosporin	OTU4481323
493.5	0.83686604	Cyclosporin	OTU4367144
290	0.83686604	Antibiotics	OTU4349859
482	0.83686604	Antibiotics	OTU4369229
464	0.84847136	Antibiotics	OTU2110555
940.5	0.86477402	Phototherapy	OTU610043
632	0.87530452	SystemicCorticosteroids	OTU4294554
313	0.87530452	Antibiotics	OTU4299324
739	0.87835509	Phototherapy	OTU851925
748	0.87835509	Topicalcalcineurininhibitors	OTU4422718
715	0.88522086	Phototherapy	OTU403853
340	0.88522086	Cyclosporin	OTU4327300
321	0.90452158	LocalCorticosteroids	OTU205025
321	0.90452158	LocalCorticosteroids	OTU205025
608	0.90452158	SystemicCorticosteroids	OTU4474056
348	0.90452158	Cyclosporin	OTU25259
318.5	0.91840204	LocalCorticosteroids	OTU3841245
315	0.91840204	LocalCorticosteroids	OTU4468125
324	0.91840204	LocalCorticosteroids	OTU4473664
465	0.91840204	LocalCorticosteroids	OTU4482598
474	0.91840204	LocalCorticosteroids	OTU883806
318.5	0.91840204	LocalCorticosteroids	OTU3841245
315	0.91840204	LocalCorticosteroids	OTU4468125
324	0.91840204	LocalCorticosteroids	OTU4473664
465	0.91840204	LocalCorticosteroids	OTU4482598
474	0.91840204	LocalCorticosteroids	OTU883806
727	0.91840204	Phototherapy	OTU20360
723.5	0.91840204	Phototherapy	OTU4317476
965	0.91840204	Phototherapy	OTU883806
727.5	0.91840204	Topicalcalcineurininhibitors	OTU4317476
791	0.91840204	SystemicCorticosteroids	OTU1003210
615	0.91840204	SystemicCorticosteroids	OTU1036883
602	0.91840204	SystemicCorticosteroids	OTU4346894
482	0.91840204	Cyclosporin	OTU114999
350	0.91840204	Cyclosporin	OTU13445
352	0.91840204	Cyclosporin	OTU2110555
462	0.91840204	Cyclosporin	OTU279980
341.5	0.91840204	Cyclosporin	OTU4318084
492	0.91840204	Cyclosporin	OTU4471315
349	0.91840204	Cyclosporin	OTU755148
324	0.91840204	Antibiotics	OTU103810
471.5	0.91840204	Antibiotics	OTU4467218
1980,05,01	0.91840204	Methotrexate	OTU4299324
1981,05,01	0.91840204	Methotrexate	OTU4309323
164	0.91840204	Methotrexate	OTU4449324
157.5	0.91840204	Methotrexate	OTU4471315
74	0.91840204	Methotrexate	OTU995817
352	0.92031903	LocalCorticosteroids	OTU279980
440	0.92031903	LocalCorticosteroids	OTU4294554
314	0.92031903	LocalCorticosteroids	OTU4301457
319	0.92031903	LocalCorticosteroids	OTU4449324
319	0.92031903	LocalCorticosteroids	OTU496787
334	0.92031903	LocalCorticosteroids	OTU74351
332	0.92031903	LocalCorticosteroids	OTU851925
323.5	0.92031903	LocalCorticosteroids	OTU939571
352	0.92031903	LocalCorticosteroids	OTU279980
440	0.92031903	LocalCorticosteroids	OTU4294554
314	0.92031903	LocalCorticosteroids	OTU4301457
319	0.92031903	LocalCorticosteroids	OTU4449324
319	0.92031903	LocalCorticosteroids	OTU496787
334	0.92031903	LocalCorticosteroids	OTU74351
332	0.92031903	LocalCorticosteroids	OTU851925
323.5	0.92031903	LocalCorticosteroids	OTU939571
924	0.92031903	Phototherapy	OTU13445
918.5	0.92031903	Phototherapy	OTU14278
749.5	0.92031903	Phototherapy	OTU4481323
758.5	0.92031903	Phototherapy	OTU74351
743	0.92031903	Phototherapy	OTU851917
925.5	0.92031903	Topicalcalcineurininhibitors	OTU103810
923	0.92031903	Topicalcalcineurininhibitors	OTU13445
898	0.92031903	Topicalcalcineurininhibitors	OTU279980

917	0.91868516	Methotrexate	OTU13445
965.5	0.91868516	Methotrexate	OTU164003
1322.5	0.91868516	Methotrexate	OTU20360
1278	0.91868516	Methotrexate	OTU205025
1213	0.91868516	Methotrexate	OTU2110555
1199.5	0.91868516	Methotrexate	OTU25478
1334	0.91868516	Methotrexate	OTU285376
1215.5	0.91868516	Methotrexate	OTU2901965
1257	0.91868516	Methotrexate	OTU3208510
1242.5	0.91868516	Methotrexate	OTU360483
1210	0.91868516	Methotrexate	OTU362390
1272	0.91868516	Methotrexate	OTU378096
1289.5	0.91868516	Methotrexate	OTU403853
1229	0.91868516	Methotrexate	OTU4294554
863	0.91868516	Methotrexate	OTU4301457
912	0.91868516	Methotrexate	OTU4306540
1254.5	0.91868516	Methotrexate	OTU4309323
1195	0.91868516	Methotrexate	OTU4317476
1229.5	0.91868516	Methotrexate	OTU4327286
930	0.91868516	Methotrexate	OTU4346894
943	0.91868516	Methotrexate	OTU4348347
1026	0.91868516	Methotrexate	OTU4350124
986	0.91868516	Methotrexate	OTU4354809
1010	0.91868516	Methotrexate	OTU4408996
1221	0.91868516	Methotrexate	OTU4411187
1283	0.91868516	Methotrexate	OTU4422718
1020	0.91868516	Methotrexate	OTU4439089
1006	0.91868516	Methotrexate	OTU4456068
984	0.91868516	Methotrexate	OTU4468125
1189	0.91868516	Methotrexate	OTU4471315
923	0.91868516	Methotrexate	OTU4473664
1241	0.91868516	Methotrexate	OTU4476950
920.5	0.91868516	Methotrexate	OTU4480063
1290	0.91868516	Methotrexate	OTU565753
1021	0.91868516	Methotrexate	OTU654307
1326	0.91868516	Methotrexate	OTU755148
964.5	0.91868516	Methotrexate	OTU761594
1207.5	0.91868516	Methotrexate	OTU819937
940.5	0.91868516	Methotrexate	OTU851668
1276	0.91868516	Methotrexate	OTU851925
993	0.91868516	Methotrexate	OTU912906
1009	0.91868516	Methotrexate	OTU912997
1010	0.91868516	LocalCorticosteroids	OTU1004369
1340.5	0.91868516	LocalCorticosteroids	OTU103810
1426	0.91868516	LocalCorticosteroids	OTU1131523
1007	0.91868516	LocalCorticosteroids	OTU114999
1417.5	0.91868516	LocalCorticosteroids	OTU164003
964	0.91868516	LocalCorticosteroids	OTU20360
1313	0.91868516	LocalCorticosteroids	OTU205025
1069	0.91868516	LocalCorticosteroids	OTU2110555
1081	0.91868516	LocalCorticosteroids	OTU247720
1007	0.91868516	LocalCorticosteroids	OTU25259
1334	0.91868516	LocalCorticosteroids	OTU25478
1003	0.91868516	LocalCorticosteroids	OTU279980
1099	0.91868516	LocalCorticosteroids	OTU285376
1114	0.91868516	LocalCorticosteroids	OTU3208510
1365	0.91868516	LocalCorticosteroids	OTU3841245
1313	0.91868516	LocalCorticosteroids	OTU4021335
1079.5	0.91868516	LocalCorticosteroids	OTU4047452
1353	0.91868516	LocalCorticosteroids	OTU4299324
1116	0.91868516	LocalCorticosteroids	OTU4301457
1313	0.91868516	LocalCorticosteroids	OTU4303697
1400	0.91868516	LocalCorticosteroids	OTU4306540
1401.5	0.91868516	LocalCorticosteroids	OTU4309323
1038	0.91868516	LocalCorticosteroids	OTU4317476
1323.5	0.91868516	LocalCorticosteroids	OTU4327286
1096	0.91868516	LocalCorticosteroids	OTU4327300
1341	0.91868516	LocalCorticosteroids	OTU4348347
1066.5	0.91868516	LocalCorticosteroids	OTU4349522
1345	0.91868516	LocalCorticosteroids	OTU4349859
1103	0.91868516	LocalCorticosteroids	OTU4350124
1104	0.91868516	LocalCorticosteroids	OTU4353642
1106	0.91868516	LocalCorticosteroids	OTU4421536
1398	0.91868516	LocalCorticosteroids	OTU4422405
994	0.91868516	LocalCorticosteroids	OTU4422718
1314	0.91868516	LocalCorticosteroids	OTU4439089
1077.5	0.91868516	LocalCorticosteroids	OTU4440643
996	0.91868516	LocalCorticosteroids	OTU4460228
1057.5	0.91868516	LocalCorticosteroids	OTU4467218
1379.5	0.91868516	LocalCorticosteroids	OTU4468125
1025	0.91868516	LocalCorticosteroids	OTU4473201
1038	0.91868516	LocalCorticosteroids	OTU4473664

720.5	0.92031903	Topicalcalcineurininhibitors	OTU285376
925.5	0.92031903	Topicalcalcineurininhibitors	OTU4327286
736	0.92031903	Topicalcalcineurininhibitors	OTU4369229
758	0.92031903	Topicalcalcineurininhibitors	OTU4439089
760	0.92031903	Topicalcalcineurininhibitors	OTU4460228
732.5	0.92031903	Topicalcalcineurininhibitors	OTU496787
610.5	0.92031903	SystemicCorticosteroids	OTU912997
360	0.92031903	Cyclosporin	OTU164003
356.5	0.92031903	Cyclosporin	OTU25478
364	0.92031903	Cyclosporin	OTU4348347
362	0.92031903	Cyclosporin	OTU4473664
341	0.92031903	Antibiotics	OTU4021335
458	0.92031903	Antibiotics	OTU511475
448	0.92031903	Antibiotics	OTU74351
151.5	0.92031903	Methotrexate	OTU103810
150	0.92031903	Methotrexate	OTU205025
150	0.92031903	Methotrexate	OTU2110555
151.5	0.92031903	Methotrexate	OTU2901965
150	0.92031903	Methotrexate	OTU4303697
151.5	0.92031903	Methotrexate	OTU4327286
150	0.92031903	Methotrexate	OTU4421536
1985,05,01	0.92031903	Methotrexate	OTU4476950
339	0.93187609	LocalCorticosteroids	OTU114999
339	0.93187609	LocalCorticosteroids	OTU114999
450.5	0.93187609	Antibiotics	OTU4471315
441	0.93187609	Antibiotics	OTU819937
916.5	0.93681361	Topicalcalcineurininhibitors	OTU14278
332.5	0.94192026	LocalCorticosteroids	OTU4299324
332.5	0.94192026	LocalCorticosteroids	OTU4299324
758.5	0.94192026	Topicalcalcineurininhibitors	OTU2901965
756	0.94192026	Topicalcalcineurininhibitors	OTU851917
800	0.94192026	SystemicCorticosteroids	OTU4354809
645	0.94192026	SystemicCorticosteroids	OTU4473201
636	0.94192026	SystemicCorticosteroids	OTU4476950
460	0.94192026	Antibiotics	OTU4346894
148.5	0.94192026	Methotrexate	OTU4408996
924	0.94476845	Phototherapy	OTU4349519
766	0.94476845	Topicalcalcineurininhibitors	OTU247720
752.5	0.94476845	Topicalcalcineurininhibitors	OTU4440643
637	0.94476845	SystemicCorticosteroids	OTU4327300
778	0.94476845	SystemicCorticosteroids	OTU4353642
349	0.94476845	Cyclosporin	OTU1096610
368	0.94476845	Cyclosporin	OTU4460228
480	0.94476845	Cyclosporin	OTU4468125
438	0.94476845	Antibiotics	OTU1003210
355.5	0.94476845	Antibiotics	OTU1107940
339	0.94476845	Antibiotics	OTU13445
444.5	0.94476845	Antibiotics	OTU4309323
332	0.94476845	Antibiotics	OTU4411187
341	0.94476845	Antibiotics	OTU4439089
145.5	0.94476845	Methotrexate	OTU14278
147	0.94476845	Methotrexate	OTU370134
145.5	0.94476845	Methotrexate	OTU74351
145.5	0.94476845	Methotrexate	OTU987144
424.5	0.9462391	LocalCorticosteroids	OTU851668
337.5	0.9462391	LocalCorticosteroids	OTU940083
424.5	0.9462391	LocalCorticosteroids	OTU851668
337.5	0.9462391	LocalCorticosteroids	OTU940083
762	0.9462391	Phototherapy	OTU25478
912.5	0.9462391	Phototherapy	OTU4473664
483	0.9462391	Cyclosporin	OTU403853
763	0.9462448	Topicalcalcineurininhibitors	OTU362390
336	0.94820623	Antibiotics	OTU4327300
144	0.94929792	Methotrexate	OTU164003
144	0.94929792	Methotrexate	OTU4353642
144	0.94929792	Methotrexate	OTU4473201
449	0.95678303	Antibiotics	OTU4354809
438	0.9591508	LocalCorticosteroids	OTU25259
333	0.9591508	LocalCorticosteroids	OTU4354809
438	0.9591508	LocalCorticosteroids	OTU25259
333	0.9591508	LocalCorticosteroids	OTU4354809
887.5	0.9591508	Phototherapy	OTU851668
774.5	0.9591508	Phototherapy	OTU987144
898	0.9591508	Topicalcalcineurininhibitors	OTU4021335
760.5	0.9591508	Topicalcalcineurininhibitors	OTU939571
641	0.9591508	SystemicCorticosteroids	OTU511475
773.5	0.9591508	SystemicCorticosteroids	OTU987144
386	0.9591508	Cyclosporin	OTU851668
151	0.9591508	Methotrexate	OTU4467218
142.5	0.9591508	Methotrexate	OTU819937
358	0.96584504	Cyclosporin	OTU1004369
775.5	0.97030547	Phototherapy	OTU4350124

1011	0.91868516	LocalCorticosteroids	OTU4474056
1014.5	0.91868516	LocalCorticosteroids	OTU610043
1099	0.91868516	LocalCorticosteroids	OTU625320
1120	0.91868516	LocalCorticosteroids	OTU654307
1327	0.91868516	LocalCorticosteroids	OTU74351
1040	0.91868516	LocalCorticosteroids	OTU761594
1061	0.91868516	LocalCorticosteroids	OTU851668
1064	0.91868516	LocalCorticosteroids	OTU851917
1279	0.91868516	LocalCorticosteroids	OTU883806
977.5	0.91868516	LocalCorticosteroids	OTU939571
1406	0.91868516	LocalCorticosteroids	OTU940083
1367	0.91868516	LocalCorticosteroids	OTU987144
332	0.91868516	Topicalcalcineurininhibitors	OTU1003210
505	0.91868516	Topicalcalcineurininhibitors	OTU1004369
308	0.91868516	Topicalcalcineurininhibitors	OTU1096610
294	0.91868516	Topicalcalcineurininhibitors	OTU1107940
313.5	0.91868516	Topicalcalcineurininhibitors	OTU114999
447	0.91868516	Topicalcalcineurininhibitors	OTU205025
314	0.91868516	Topicalcalcineurininhibitors	OTU247720
444	0.91868516	Topicalcalcineurininhibitors	OTU25259
315.5	0.91868516	Topicalcalcineurininhibitors	OTU25478
293.5	0.91868516	Topicalcalcineurininhibitors	OTU282360
296.5	0.91868516	Topicalcalcineurininhibitors	OTU2901965
325	0.91868516	Topicalcalcineurininhibitors	OTU3208510
309.5	0.91868516	Topicalcalcineurininhibitors	OTU370309
455	0.91868516	Topicalcalcineurininhibitors	OTU378096
318.5	0.91868516	Topicalcalcineurininhibitors	OTU3841245
494.5	0.91868516	Topicalcalcineurininhibitors	OTU4039323
330	0.91868516	Topicalcalcineurininhibitors	OTU4294554
329	0.91868516	Topicalcalcineurininhibitors	OTU4299324
512	0.91868516	Topicalcalcineurininhibitors	OTU4303697
481	0.91868516	Topicalcalcineurininhibitors	OTU4306540
441	0.91868516	Topicalcalcineurininhibitors	OTU4309323
472	0.91868516	Topicalcalcineurininhibitors	OTU4317476
456	0.91868516	Topicalcalcineurininhibitors	OTU4318084
458	0.91868516	Topicalcalcineurininhibitors	OTU4327300
456	0.91868516	Topicalcalcineurininhibitors	OTU4346894
458	0.91868516	Topicalcalcineurininhibitors	OTU4348347
329.5	0.91868516	Topicalcalcineurininhibitors	OTU4349519
330.5	0.91868516	Topicalcalcineurininhibitors	OTU4349522
474	0.91868516	Topicalcalcineurininhibitors	OTU4349859
489	0.91868516	Topicalcalcineurininhibitors	OTU4354809
452	0.91868516	Topicalcalcineurininhibitors	OTU4411187
473	0.91868516	Topicalcalcineurininhibitors	OTU4422405
465	0.91868516	Topicalcalcineurininhibitors	OTU4456068
298.5	0.91868516	Topicalcalcineurininhibitors	OTU4467218
323	0.91868516	Topicalcalcineurininhibitors	OTU4471315
315	0.91868516	Topicalcalcineurininhibitors	OTU4473201
503.5	0.91868516	Topicalcalcineurininhibitors	OTU4496787
287	0.91868516	Topicalcalcineurininhibitors	OTU565753
321.5	0.91868516	Topicalcalcineurininhibitors	OTU610043
512	0.91868516	Topicalcalcineurininhibitors	OTU74351
314.5	0.91868516	Topicalcalcineurininhibitors	OTU819937
294	0.91868516	Topicalcalcineurininhibitors	OTU820692
322	0.91868516	Topicalcalcineurininhibitors	OTU883806
274	0.91868516	Topicalcalcineurininhibitors	OTU995817
793	0.91868516	Fumaricacid	OTU1003210
512	0.91868516	Fumaricacid	OTU1036883
764	0.91868516	Fumaricacid	OTU1081372
741	0.91868516	Fumaricacid	OTU1096610
712	0.91868516	Fumaricacid	OTU1107940
754.5	0.91868516	Fumaricacid	OTU1131523
723	0.91868516	Fumaricacid	OTU14278
747.5	0.91868516	Fumaricacid	OTU20360
736	0.91868516	Fumaricacid	OTU205025
726	0.91868516	Fumaricacid	OTU25259
498	0.91868516	Fumaricacid	OTU25478
707	0.91868516	Fumaricacid	OTU370134
749.5	0.91868516	Fumaricacid	OTU378096
581.5	0.91868516	Fumaricacid	OTU3841245
765	0.91868516	Fumaricacid	OTU4021335
759	0.91868516	Fumaricacid	OTU4047452
557.5	0.91868516	Fumaricacid	OTU4301457
722	0.91868516	Fumaricacid	OTU4318084
729.5	0.91868516	Fumaricacid	OTU4327286
484.5	0.91868516	Fumaricacid	OTU4346894
577	0.91868516	Fumaricacid	OTU4348347
729.5	0.91868516	Fumaricacid	OTU4349519
729	0.91868516	Fumaricacid	OTU4349522
555.5	0.91868516	Fumaricacid	OTU4349859
584	0.91868516	Fumaricacid	OTU4353642
541	0.91868516	Fumaricacid	OTU4369229



331	0.97162011	LocalCorticosteroids	OTU1096610
341.5	0.97162011	LocalCorticosteroids	OTU282360
427	0.97162011	LocalCorticosteroids	OTU654307
331	0.97162011	LocalCorticosteroids	OTU1096610
341.5	0.97162011	LocalCorticosteroids	OTU282360
427	0.97162011	LocalCorticosteroids	OTU654307
771	0.97162011	Phototherapy	OTU940083
757.5	0.97162011	Topicalcalcineurininhibitors	OTU4456068
777	0.97162011	SystemicCorticosteroids	OTU1081372
632	0.97162011	SystemicCorticosteroids	OTU1096610
651	0.97162011	SystemicCorticosteroids	OTU13445
779	0.97162011	SystemicCorticosteroids	OTU282360
654	0.97162011	SystemicCorticosteroids	OTU370309
371.5	0.97162011	Cyclosporin	OTU4309323
478	0.97162011	Cyclosporin	OTU4480063
382	0.97162011	Cyclosporin	OTU654307
334	0.97162011	Antibiotics	OTU995817
139.5	0.97162011	Methotrexate	OTU360483
97	0.97162011	Methotrexate	OTU378096
149	0.97162011	Methotrexate	OTU403853
139.5	0.97162011	Methotrexate	OTU505749
88	0.97162011	Methotrexate	OTU912997
352	0.97342505	Antibiotics	OTU4422718
354	0.97546845	LocalCorticosteroids	OTU378096
432.5	0.97546845	LocalCorticosteroids	OTU4327286
427	0.97546845	LocalCorticosteroids	OTU565753
354	0.97546845	LocalCorticosteroids	OTU378096
432.5	0.97546845	LocalCorticosteroids	OTU4327286
427	0.97546845	LocalCorticosteroids	OTU565753
904	0.97546845	Phototherapy	OTU4327286
913	0.97546845	Phototherapy	OTU4369229
762	0.97546845	Phototherapy	OTU995817
778	0.97546845	Topicalcalcineurininhibitors	OTU2110555
766	0.97546845	Topicalcalcineurininhibitors	OTU4467218
775.5	0.97546845	Topicalcalcineurininhibitors	OTU761594
676	0.97546845	SystemicCorticosteroids	OTU279980
645	0.97546845	SystemicCorticosteroids	OTU403853
651	0.97546845	SystemicCorticosteroids	OTU851917
465	0.97546845	Cyclosporin	OTU4327286
354	0.97546845	Antibiotics	OTU4306540
340.5	0.97546845	Antibiotics	OTU496787
1991,05,01	0.97546845	Methotrexate	OTU4440643
138	0.97546845	Methotrexate	OTU654307
880.5	0.97553677	Topicalcalcineurininhibitors	OTU851668
380	0.97691141	Cyclosporin	OTU4350124
97	0.97691141	Methotrexate	OTU4349522
897	0.97740412	Phototherapy	OTU4460228
776.5	0.97740412	Topicalcalcineurininhibitors	OTU4471315
759	0.97740412	SystemicCorticosteroids	OTU378096
365.5	0.97740412	Cyclosporin	OTU285376
890	0.97760614	Phototherapy	OTU505749
774.5	0.97760614	SystemicCorticosteroids	OTU4482598
384.5	0.97760614	Cyclosporin	OTU378096
356	0.98870701	LocalCorticosteroids	OTU4306540
356	0.98870701	LocalCorticosteroids	OTU4306540
377.5	0.98870701	Cyclosporin	OTU761594
897	0.98882508	Topicalcalcineurininhibitors	OTU205025
146	0.99481531	Methotrexate	OTU4346894
430.5	0.99785764	LocalCorticosteroids	OTU4476950
343	0.99785764	LocalCorticosteroids	OTU995817
430.5	0.99785764	LocalCorticosteroids	OTU4476950
343	0.99785764	LocalCorticosteroids	OTU995817
793	0.99959501	Topicalcalcineurininhibitors	OTU360483
901	0.99959501	Topicalcalcineurininhibitors	OTU4468125
428	0.99959501	Antibiotics	OTU4303697
94	0.99959501	Methotrexate	OTU4047452
381.5	1	LocalCorticosteroids	OTU1003210
431	1	LocalCorticosteroids	OTU1036883
360.5	1	LocalCorticosteroids	OTU103810
366	1	LocalCorticosteroids	OTU1081372
385	1	LocalCorticosteroids	OTU1107940
359	1	LocalCorticosteroids	OTU1131523
401	1	LocalCorticosteroids	OTU13445
411	1	LocalCorticosteroids	OTU14278
374	1	LocalCorticosteroids	OTU164003
404	1	LocalCorticosteroids	OTU20360
396	1	LocalCorticosteroids	OTU2110555
375.5	1	LocalCorticosteroids	OTU247720
386	1	LocalCorticosteroids	OTU25478
424.5	1	LocalCorticosteroids	OTU285376
410	1	LocalCorticosteroids	OTU3208510
395.5	1	LocalCorticosteroids	OTU360483

724	0.91868516	Fumaricacid	OTU4421536
534	0.91868516	Fumaricacid	OTU4422405
733	0.91868516	Fumaricacid	OTU4422718
772	0.91868516	Fumaricacid	OTU4446521
523	0.91868516	Fumaricacid	OTU4449324
486.5	0.91868516	Fumaricacid	OTU4456068
809	0.91868516	Fumaricacid	OTU4460228
777.5	0.91868516	Fumaricacid	OTU4467218
522	0.91868516	Fumaricacid	OTU4468125
529	0.91868516	Fumaricacid	OTU4480063
775.5	0.91868516	Fumaricacid	OTU4496787
770	0.91868516	Fumaricacid	OTU505749
699	0.91868516	Fumaricacid	OTU511475
767	0.91868516	Fumaricacid	OTU625320
775	0.91868516	Fumaricacid	OTU755148
727	0.91868516	Fumaricacid	OTU851917
709	0.91868516	Fumaricacid	OTU883806
715	0.91868516	Fumaricacid	OTU987144
755	0.91868516	Fumaricacid	OTU995817
2019,05,31	0.91868516	Antibiotics	OTU1003210
30	0.91868516	Antibiotics	OTU1036883
96	0.91868516	Antibiotics	OTU103810
29	0.91868516	Antibiotics	OTU1081372
30	0.91868516	Antibiotics	OTU1096610
1934,05,01	0.91868516	Antibiotics	OTU1131523
1935,05,01	0.91868516	Antibiotics	OTU114999
40	0.91868516	Antibiotics	OTU14278
80	0.91868516	Antibiotics	OTU164003
112	0.91868516	Antibiotics	OTU2110555
1937,05,01	0.91868516	Antibiotics	OTU247720
33	0.91868516	Antibiotics	OTU25259
1935,05,01	0.91868516	Antibiotics	OTU25478
37	0.91868516	Antibiotics	OTU279980
1933,05,01	0.91868516	Antibiotics	OTU282360
97	0.91868516	Antibiotics	OTU2901965
40	0.91868516	Antibiotics	OTU3208510
1939,05,01	0.91868516	Antibiotics	OTU362390
1933,05,01	0.91868516	Antibiotics	OTU370134
2019,05,28	0.91868516	Antibiotics	OTU370309
102	0.91868516	Antibiotics	OTU403853
92	0.91868516	Antibiotics	OTU4047452
40	0.91868516	Antibiotics	OTU4299324
34	0.91868516	Antibiotics	OTU4303697
1933,05,01	0.91868516	Antibiotics	OTU4306540
1939,05,01	0.91868516	Antibiotics	OTU4309323
30	0.91868516	Antibiotics	OTU4317476
100	0.91868516	Antibiotics	OTU4318084
101	0.91868516	Antibiotics	OTU4327286
29	0.91868516	Antibiotics	OTU4327300
98	0.91868516	Antibiotics	OTU4346894
1932,05,01	0.91868516	Antibiotics	OTU4349519
1936,05,01	0.91868516	Antibiotics	OTU4349522
97	0.91868516	Antibiotics	OTU4350124
41	0.91868516	Antibiotics	OTU4353642
24	0.91868516	Antibiotics	OTU4354809
37	0.91868516	Antibiotics	OTU4408996
1940,05,01	0.91868516	Antibiotics	OTU4411187
93	0.91868516	Antibiotics	OTU4421536
97	0.91868516	Antibiotics	OTU4422405
32	0.91868516	Antibiotics	OTU4422718
35	0.91868516	Antibiotics	OTU4439089
2019,05,27	0.91868516	Antibiotics	OTU4440643
86	0.91868516	Antibiotics	OTU4446521
98	0.91868516	Antibiotics	OTU4456068
34	0.91868516	Antibiotics	OTU4460228
2019,05,22	0.91868516	Antibiotics	OTU4467218
1940,05,01	0.91868516	Antibiotics	OTU4468125
82	0.91868516	Antibiotics	OTU4471315
80	0.91868516	Antibiotics	OTU4473201
33	0.91868516	Antibiotics	OTU4473664
28	0.91868516	Antibiotics	OTU4474056
1936,05,01	0.91868516	Antibiotics	OTU4476950
2019,05,18	0.91868516	Antibiotics	OTU4480063
106	0.91868516	Antibiotics	OTU4481323
104	0.91868516	Antibiotics	OTU4482598
85	0.91868516	Antibiotics	OTU4496787
29	0.91868516	Antibiotics	OTU505749
35	0.91868516	Antibiotics	OTU625320
40	0.91868516	Antibiotics	OTU654307
89	0.91868516	Antibiotics	OTU74351
31	0.91868516	Antibiotics	OTU755148
1938,05,01	0.91868516	Antibiotics	OTU761594



395	1	LocalCorticosteroids	OTU362390
372	1	LocalCorticosteroids	OTU370134
423	1	LocalCorticosteroids	OTU370309
396	1	LocalCorticosteroids	OTU4021335
410	1	LocalCorticosteroids	OTU4047452
358	1	LocalCorticosteroids	OTU4303697
375.5	1	LocalCorticosteroids	OTU4318084
378	1	LocalCorticosteroids	OTU4327300
377.5	1	LocalCorticosteroids	OTU4348347
402	1	LocalCorticosteroids	OTU4349519
375.5	1	LocalCorticosteroids	OTU4349522
405	1	LocalCorticosteroids	OTU4350124
394	1	LocalCorticosteroids	OTU4408996
390	1	LocalCorticosteroids	OTU4421536
392	1	LocalCorticosteroids	OTU4422718
381	1	LocalCorticosteroids	OTU4439089
393.5	1	LocalCorticosteroids	OTU4440643
369.5	1	LocalCorticosteroids	OTU4446521
353.5	1	LocalCorticosteroids	OTU4467218
376	1	LocalCorticosteroids	OTU4471315
386	1	LocalCorticosteroids	OTU4473201
407	1	LocalCorticosteroids	OTU4474056
394	1	LocalCorticosteroids	OTU4481323
399.5	1	LocalCorticosteroids	OTU505749
413	1	LocalCorticosteroids	OTU511475
380.5	1	LocalCorticosteroids	OTU610043
395	1	LocalCorticosteroids	OTU625320
378	1	LocalCorticosteroids	OTU755148
388	1	LocalCorticosteroids	OTU761594
380.5	1	LocalCorticosteroids	OTU819937
385.5	1	LocalCorticosteroids	OTU820692
390.5	1	LocalCorticosteroids	OTU912906
410.5	1	LocalCorticosteroids	OTU912997
415	1	LocalCorticosteroids	OTU987144
381.5	1	LocalCorticosteroids	OTU1003210
431	1	LocalCorticosteroids	OTU1036883
360.5	1	LocalCorticosteroids	OTU103810
366	1	LocalCorticosteroids	OTU1081372
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401	1	LocalCorticosteroids	OTU13445
411	1	LocalCorticosteroids	OTU14278
374	1	LocalCorticosteroids	OTU164003
404	1	LocalCorticosteroids	OTU20360
396	1	LocalCorticosteroids	OTU2110555
375.5	1	LocalCorticosteroids	OTU247720
386	1	LocalCorticosteroids	OTU25478
424.5	1	LocalCorticosteroids	OTU285376
410	1	LocalCorticosteroids	OTU3208510
395.5	1	LocalCorticosteroids	OTU360483
395	1	LocalCorticosteroids	OTU362390
372	1	LocalCorticosteroids	OTU370134
423	1	LocalCorticosteroids	OTU370309
396	1	LocalCorticosteroids	OTU4021335
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378	1	LocalCorticosteroids	OTU4327300
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405	1	LocalCorticosteroids	OTU4350124
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390	1	LocalCorticosteroids	OTU4421536
392	1	LocalCorticosteroids	OTU4422718
381	1	LocalCorticosteroids	OTU4439089
393.5	1	LocalCorticosteroids	OTU4440643
369.5	1	LocalCorticosteroids	OTU4446521
353.5	1	LocalCorticosteroids	OTU4467218
376	1	LocalCorticosteroids	OTU4471315
386	1	LocalCorticosteroids	OTU4473201
407	1	LocalCorticosteroids	OTU4474056
394	1	LocalCorticosteroids	OTU4481323
399.5	1	LocalCorticosteroids	OTU505749
413	1	LocalCorticosteroids	OTU511475
380.5	1	LocalCorticosteroids	OTU610043
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378	1	LocalCorticosteroids	OTU755148
388	1	LocalCorticosteroids	OTU761594
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31	0.91868516	Antibiotics	OTU851917
92	0.91868516	Antibiotics	OTU851925
40	0.91868516	Antibiotics	OTU912906
15	0.91868516	Antibiotics	OTU912997
82	0.91868516	Antibiotics	OTU939571
1626	0.91868516	VitaminDanalogs	OTU1004369
2055	0.91868516	VitaminDanalogs	OTU1036883
1998,05,01	0.91868516	VitaminDanalogs	OTU103810
2066	0.91868516	VitaminDanalogs	OTU1096610
1852	0.91868516	VitaminDanalogs	OTU1107940
1912,05,01	0.91868516	VitaminDanalogs	OTU1131523
1664	0.91868516	VitaminDanalogs	OTU14278
1959	0.91868516	VitaminDanalogs	OTU205025
1534	0.91868516	VitaminDanalogs	OTU25259
2019	0.91868516	VitaminDanalogs	OTU25478
1980	0.91868516	VitaminDanalogs	OTU279980
1648	0.91868516	VitaminDanalogs	OTU282360
2043	0.91868516	VitaminDanalogs	OTU370134
1578	0.91868516	VitaminDanalogs	OTU403853
1638	0.91868516	VitaminDanalogs	OTU4047452
1571	0.91868516	VitaminDanalogs	OTU4294554
1582	0.91868516	VitaminDanalogs	OTU4303697
1939,05,01	0.91868516	VitaminDanalogs	OTU4306540
1895	0.91868516	VitaminDanalogs	OTU4309323
1590	0.91868516	VitaminDanalogs	OTU4317476
1627	0.91868516	VitaminDanalogs	OTU4318084
1880	0.91868516	VitaminDanalogs	OTU4327286
2019,05,01	0.91868516	VitaminDanalogs	OTU4346894
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1980	0.91868516	VitaminDanalogs	OTU4349859
1663.5	0.91868516	VitaminDanalogs	OTU4353642
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1933,05,01	0.91868516	VitaminDanalogs	OTU4369229
1600	0.91868516	VitaminDanalogs	OTU4408996
1983	0.91868516	VitaminDanalogs	OTU4422718
1954	0.91868516	VitaminDanalogs	OTU4439089
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1962,05,01	0.91868516	VitaminDanalogs	OTU4456068
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1905,05,01	0.91868516	VitaminDanalogs	OTU4468125
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1241	0.91868516	TAR.topical.	OTU205025
1226	0.91868516	TAR.topical.	OTU25259
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880	1	Phototherapy	OTU103810
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840	1	Phototherapy	OTU1107940
844	1	Phototherapy	OTU1131523
861	1	Phototherapy	OTU114999
842	1	Phototherapy	OTU164003
830	1	Phototherapy	OTU205025
840	1	Phototherapy	OTU247720
819	1	Phototherapy	OTU279980
867.5	1	Phototherapy	OTU282360
807	1	Phototherapy	OTU285376
812	1	Phototherapy	OTU3208510
892.5	1	Phototherapy	OTU362390
878	1	Phototherapy	OTU370134
793	1	Phototherapy	OTU370309
816	1	Phototherapy	OTU378096
870	1	Phototherapy	OTU4021335
794	1	Phototherapy	OTU4047452
840	1	Phototherapy	OTU4294554
776	1	Phototherapy	OTU4301457
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853	1	Phototherapy	OTU4327300
793	1	Phototherapy	OTU4346894
876	1	Phototherapy	OTU4349522
861	1	Phototherapy	OTU4353642
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818	1	Phototherapy	OTU4421536
871	1	Phototherapy	OTU4422718
856	1	Phototherapy	OTU4439089
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837	1	Phototherapy	OTU4474056
856	1	Phototherapy	OTU4476950
847	1	Phototherapy	OTU4482598
856	1	Phototherapy	OTU565753
882.5	1	Phototherapy	OTU625320
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852	1	Phototherapy	OTU819937
846	1	Phototherapy	OTU820692
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796	1	Topicalcalcineurininhibitors	OTU378096
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773	1	Topicalcalcineurininhibitors	OTU4449324
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832	1	Topicalcalcineurininhibitors	OTU4473664
806.5	1	Topicalcalcineurininhibitors	OTU4476950
817.5	1	Topicalcalcineurininhibitors	OTU4481323
805	1	Topicalcalcineurininhibitors	OTU565753
835.5	1	Topicalcalcineurininhibitors	OTU610043
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808	1	Topicalcalcineurininhibitors	OTU654307
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877.5	1	Topicalcalcineurininhibitors	OTU820692
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882	1	Topicalcalcineurininhibitors	OTU987144
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691	1	SystemicCorticosteroids	OTU1107940

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1316	0.91868516	TAR.topical.	OTU74351
962	0.91868516	TAR.topical.	OTU820692
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965	0.91868516	TAR.topical.	OTU851917
1292	0.91868516	TAR.topical.	OTU851925
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947	0.91868516	Photochemotherapy	OTU360483
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1240.5	0.91868516	Photochemotherapy	OTU4306540
1270	0.91868516	Photochemotherapy	OTU4309323
1306	0.91868516	Photochemotherapy	OTU4317476
974.5	0.91868516	Photochemotherapy	OTU4346894
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1005	0.91868516	Photochemotherapy	OTU4354809
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717	1	SystemicCorticosteroids	OTU4318084
675.5	1	SystemicCorticosteroids	OTU4327286
708.5	1	SystemicCorticosteroids	OTU4408996
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755	1	SystemicCorticosteroids	OTU761594
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692	1	SystemicCorticosteroids	OTU851668
678	1	SystemicCorticosteroids	OTU883806
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423.5	1	Cyclosporin	OTU1107940
410	1	Cyclosporin	OTU1131523
446	1	Cyclosporin	OTU14278
400	1	Cyclosporin	OTU20360
386.5	1	Cyclosporin	OTU282360
402.5	1	Cyclosporin	OTU3208510
422	1	Cyclosporin	OTU360483
433.5	1	Cyclosporin	OTU362390
447	1	Cyclosporin	OTU370134
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424	1	Cyclosporin	OTU4301457
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465	1	Cyclosporin	OTU4317476
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438	1	Cyclosporin	OTU4349522
387.5	1	Cyclosporin	OTU4349859
457	1	Cyclosporin	OTU4408996
459	1	Cyclosporin	OTU4411187
432	1	Cyclosporin	OTU4421536
434	1	Cyclosporin	OTU4449324
464.5	1	Cyclosporin	OTU4456068
465.5	1	Cyclosporin	OTU4467218
443	1	Cyclosporin	OTU4473201
399.5	1	Cyclosporin	OTU496787
422	1	Cyclosporin	OTU505749
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434	1	Cyclosporin	OTU819937
432	1	Cyclosporin	OTU820692

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297.5	0.91868516	SystemicCorticosteroids	OTU4476950
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186.5	0.91868516	SystemicCorticosteroids	OTU496787
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171.5	0.91868516	SystemicCorticosteroids	OTU610043
134	0.91868516	SystemicCorticosteroids	OTU625320
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138	0.91868516	SystemicCorticosteroids	OTU74351
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179.5	0.91868516	SystemicCorticosteroids	OTU939571
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1793.5	0.91868516	Phototherapy	OTU20360
1472	0.91868516	Phototherapy	OTU205025
1773	0.91868516	Phototherapy	OTU2110555
1819	0.91868516	Phototherapy	OTU247720
1792.5	0.91868516	Phototherapy	OTU2901965
1738	0.91868516	Phototherapy	OTU362390
1419	0.91868516	Phototherapy	OTU4294554
1784	0.91868516	Phototherapy	OTU4299324
1775.5	0.91868516	Phototherapy	OTU4309323
1716	0.91868516	Phototherapy	OTU4317476
1805.5	0.91868516	Phototherapy	OTU4327286
1851.5	0.91868516	Phototherapy	OTU4349519
1815.5	0.91868516	Phototherapy	OTU4349522
1875	0.91868516	Phototherapy	OTU4369229
1463	0.91868516	Phototherapy	OTU4408996
1702	0.91868516	Phototherapy	OTU4411187
1389	0.91868516	Phototherapy	OTU4421536
1738	0.91868516	Phototherapy	OTU4446521
1732	0.91868516	Phototherapy	OTU4471315
1749	0.91868516	Phototherapy	OTU4473664
1711	0.91868516	Phototherapy	OTU4480063
1840	0.91868516	Phototherapy	OTU625320
1466	0.91868516	Phototherapy	OTU654307
1757	0.91868516	Phototherapy	OTU74351
1460	0.91868516	Phototherapy	OTU761594
1799	0.91868516	Phototherapy	OTU819937
1439	0.91868516	Phototherapy	OTU820692
1444	0.91868516	Phototherapy	OTU837884
1494	0.91868516	Phototherapy	OTU851925
1472	0.91868516	Phototherapy	OTU883806
1487	0.91868516	Phototherapy	OTU912906
1789	0.91868516	Phototherapy	OTU987144
420	0.91868516	Cyclosporin	OTU1003210
569	0.91868516	Cyclosporin	OTU1004369
652	0.91868516	Cyclosporin	OTU1036883
573.5	0.91868516	Cyclosporin	OTU103810
433	0.91868516	Cyclosporin	OTU1081372
570	0.91868516	Cyclosporin	OTU1096610
550	0.91868516	Cyclosporin	OTU1107940
620.5	0.91868516	Cyclosporin	OTU1131523
422	0.91868516	Cyclosporin	OTU14278
634	0.91868516	Cyclosporin	OTU205025
586	0.91868516	Cyclosporin	OTU247720
555	0.91868516	Cyclosporin	OTU25259
587	0.91868516	Cyclosporin	OTU25478
412	0.91868516	Cyclosporin	OTU279980
549.5	0.91868516	Cyclosporin	OTU362390
396.5	0.91868516	Cyclosporin	OTU370309
625	0.91868516	Cyclosporin	OTU378096
549	0.91868516	Cyclosporin	OTU4294554
560	0.91868516	Cyclosporin	OTU4299324
380.5	0.91868516	Cyclosporin	OTU4301457
402	0.91868516	Cyclosporin	OTU4306540
586.5	0.91868516	Cyclosporin	OTU4318084
577	0.91868516	Cyclosporin	OTU4327286
434	0.91868516	Cyclosporin	OTU4327300
370	0.91868516	Cyclosporin	OTU4346894



421	1	Cyclosporin	OTU837884
409	1	Cyclosporin	OTU851917
445	1	Cyclosporin	OTU851925
409	1	Cyclosporin	OTU883806
399.5	1	Cyclosporin	OTU912906
462	1	Cyclosporin	OTU939571
376	1	Antibiotics	OTU1004369
375	1	Antibiotics	OTU1036883
362	1	Antibiotics	OTU1096610
365	1	Antibiotics	OTU114999
378	1	Antibiotics	OTU14278
403	1	Antibiotics	OTU164003
426	1	Antibiotics	OTU20360
412	1	Antibiotics	OTU205025
385	1	Antibiotics	OTU247720
369	1	Antibiotics	OTU25259
360.5	1	Antibiotics	OTU25478
390	1	Antibiotics	OTU279980
405.5	1	Antibiotics	OTU282360
343.5	1	Antibiotics	OTU285376
402.5	1	Antibiotics	OTU3208510
394.5	1	Antibiotics	OTU360483
415	1	Antibiotics	OTU362390
375	1	Antibiotics	OTU370309
391	1	Antibiotics	OTU3841245
364	1	Antibiotics	OTU4047452
403.5	1	Antibiotics	OTU4317476
379.5	1	Antibiotics	OTU4318084
411.5	1	Antibiotics	OTU4348347
406.5	1	Antibiotics	OTU4349522
419.5	1	Antibiotics	OTU4350124
376	1	Antibiotics	OTU4353642
411.5	1	Antibiotics	OTU4408996
413	1	Antibiotics	OTU4421536
344	1	Antibiotics	OTU4422405
401	1	Antibiotics	OTU4446521
436	1	Antibiotics	OTU4449324
424.5	1	Antibiotics	OTU4456068
417	1	Antibiotics	OTU4460228
358	1	Antibiotics	OTU4468125
360	1	Antibiotics	OTU4473201
420.5	1	Antibiotics	OTU4473664
365.5	1	Antibiotics	OTU4476950
421	1	Antibiotics	OTU4480063
406.5	1	Antibiotics	OTU4481323
381.5	1	Antibiotics	OTU505749
410.5	1	Antibiotics	OTU610043
390	1	Antibiotics	OTU625320
421	1	Antibiotics	OTU654307
356.5	1	Antibiotics	OTU761594
392	1	Antibiotics	OTU851668
395	1	Antibiotics	OTU851917
368	1	Antibiotics	OTU851925
410	1	Antibiotics	OTU883806
369.5	1	Antibiotics	OTU912997
412.5	1	Antibiotics	OTU939571
102	1	Methotrexate	OTU1003210
125	1	Methotrexate	OTU1004369
96	1	Methotrexate	OTU1036883
130	1	Methotrexate	OTU1081372
142	1	Methotrexate	OTU1096610
130.5	1	Methotrexate	OTU1107940
102	1	Methotrexate	OTU1131523
104	1	Methotrexate	OTU114999
114	1	Methotrexate	OTU13445
119	1	Methotrexate	OTU20360
111	1	Methotrexate	OTU247720
116	1	Methotrexate	OTU25259
114	1	Methotrexate	OTU25478
129	1	Methotrexate	OTU279980
126	1	Methotrexate	OTU282360
129	1	Methotrexate	OTU285376
108	1	Methotrexate	OTU3208510
114	1	Methotrexate	OTU362390
109	1	Methotrexate	OTU370309
116	1	Methotrexate	OTU3841245
123	1	Methotrexate	OTU4301457
104	1	Methotrexate	OTU4306540
131	1	Methotrexate	OTU4318084
118	1	Methotrexate	OTU4327300
104	1	Methotrexate	OTU4348347
115	1	Methotrexate	OTU4349519

432.5	0.91868516	Cyclosporin	OTU4349522
611.5	0.91868516	Cyclosporin	OTU4349859
560	0.91868516	Cyclosporin	OTU4353642
598	0.91868516	Cyclosporin	OTU4422405
338	0.91868516	Cyclosporin	OTU4422718
404	0.91868516	Cyclosporin	OTU4446521
579	0.91868516	Cyclosporin	OTU4473664
407	0.91868516	Cyclosporin	OTU4474056
401	0.91868516	Cyclosporin	OTU4481323
648	0.91868516	Cyclosporin	OTU4482598
404	0.91868516	Cyclosporin	OTU505749
553	0.91868516	Cyclosporin	OTU565753
375	0.91868516	Cyclosporin	OTU654307
364	0.91868516	Cyclosporin	OTU74351
606	0.91868516	Cyclosporin	OTU851925
574	0.91868516	Cyclosporin	OTU883806
427	0.91868516	Cyclosporin	OTU912906
613	0.91868516	Cyclosporin	OTU912997
368	0.91868516	Cyclosporin	OTU939571
594	0.91868516	Cyclosporin	OTU940083
555	0.91868516	Cyclosporin	OTU987144
722	0.91868516	Dithranol.minute	OTU1081372
689.5	0.91868516	Dithranol.minute	OTU1096610
755.5	0.91868516	Dithranol.minute	OTU13445
748	0.91868516	Dithranol.minute	OTU14278
970	0.91868516	Dithranol.minute	OTU205025
710	0.91868516	Dithranol.minute	OTU247720
895.5	0.91868516	Dithranol.minute	OTU25478
640	0.91868516	Dithranol.minute	OTU282360
692	0.91868516	Dithranol.minute	OTU3208510
712	0.91868516	Dithranol.minute	OTU360483
653.5	0.91868516	Dithranol.minute	OTU362390
912	0.91868516	Dithranol.minute	OTU370134
705	0.91868516	Dithranol.minute	OTU403853
918.5	0.91868516	Dithranol.minute	OTU4301457
923	0.91868516	Dithranol.minute	OTU4306540
699.5	0.91868516	Dithranol.minute	OTU4327286
731	0.91868516	Dithranol.minute	OTU4327300
644	0.91868516	Dithranol.minute	OTU4349522
685	0.91868516	Dithranol.minute	OTU4349859
715.5	0.91868516	Dithranol.minute	OTU4350124
992	0.91868516	Dithranol.minute	OTU4421536
690	0.91868516	Dithranol.minute	OTU4422405
685	0.91868516	Dithranol.minute	OTU4422718
699	0.91868516	Dithranol.minute	OTU4439089
714	0.91868516	Dithranol.minute	OTU4446521
749	0.91868516	Dithranol.minute	OTU4460228
731.5	0.91868516	Dithranol.minute	OTU4467218
666	0.91868516	Dithranol.minute	OTU4471315
920	0.91868516	Dithranol.minute	OTU4473664
929.5	0.91868516	Dithranol.minute	OTU4480063
891	0.91868516	Dithranol.minute	OTU4481323
975	0.91868516	Dithranol.minute	OTU4482598
699.5	0.91868516	Dithranol.minute	OTU505749
760.5	0.91868516	Dithranol.minute	OTU511475
747	0.91868516	Dithranol.minute	OTU565753
657	0.91868516	Dithranol.minute	OTU625320
717	0.91868516	Dithranol.minute	OTU654307
928	0.91868516	Dithranol.minute	OTU74351
677	0.91868516	Dithranol.minute	OTU755148
717.5	0.91868516	Dithranol.minute	OTU851668
982	0.91868516	Dithranol.minute	OTU912997
730	0.91868516	Dithranol.minute	OTU939571
704	0.91868516	Dithranol.minute	OTU940083
713	0.91868516	Dithranol.minute	OTU987144
665.5	0.91868516	Dithranol.minute	OTU995817
440	0.91986716	Topicalcalcineurininhibitors	OTU4408996
1682	0.91986716	Phototherapy	OTU1107940
342	0.91996795	Topicalcalcineurininhibitors	OTU164003
1941,05,01	0.91996795	Antibiotics	OTU378096
1221	0.91996795	TAR.topical.	OTU4408996
1195.5	0.91996795	Photochemotherapy	OTU496787
757	0.91996795	Dithranol.minute	OTU4473201
1195	0.92200647	Photochemotherapy	OTU4349859
267	0.92200647	SystemicCorticosteroids	OTU25478
1178	0.92215085	Methotrexate	OTU4353642
869.5	0.92286155	Retinoids	OTU4369229
38	0.92286155	Antibiotics	OTU995817
194	0.92286155	SystemicCorticosteroids	OTU4408996
42	0.92365539	Antibiotics	OTU4294554
193.5	0.92365539	SystemicCorticosteroids	OTU114999
345.5	0.92492995	Topicalcalcineurininhibitors	OTU4476950

100	1	Methotrexate	OTU4349859
109	1	Methotrexate	OTU4350124
133	1	Methotrexate	OTU4411187
128	1	Methotrexate	OTU4422405
103	1	Methotrexate	OTU4422718
139	1	Methotrexate	OTU4446521
134.5	1	Methotrexate	OTU4456068
109	1	Methotrexate	OTU4460228
127	1	Methotrexate	OTU4468125
110	1	Methotrexate	OTU4473664
128	1	Methotrexate	OTU4474056
100	1	Methotrexate	OTU4480063
1997,05,01	1	Methotrexate	OTU4482598
124	1	Methotrexate	OTU496787
96	1	Methotrexate	OTU511475
104	1	Methotrexate	OTU610043
110	1	Methotrexate	OTU625320
109	1	Methotrexate	OTU755148
120	1	Methotrexate	OTU761594
103	1	Methotrexate	OTU820692
120	1	Methotrexate	OTU837884
130.5	1	Methotrexate	OTU851668
119	1	Methotrexate	OTU851917
101	1	Methotrexate	OTU851925
106	1	Methotrexate	OTU912906
127	1	Methotrexate	OTU939571
104	1	Methotrexate	OTU940083

580	0.92492995	Fumaricacid	OTU610043
584	0.92492995	Fumaricacid	OTU761594
442	0.92492995	Cyclosporin	OTU114999
876	0.92496879	Retinoids	OTU370134
1942,05,01	0.92496879	Antibiotics	OTU13445
1863	0.92496879	VitaminDanalogs	OTU625320
264	0.92496879	SystemicCorticosteroids	OTU362390
748	0.92496879	Dithranol.minute	OTU1004369
1017	0.92578655	Retinoids	OTU4411187
1191.5	0.92578655	Methotrexate	OTU837884
1182	0.92578655	Methotrexate	OTU851917
1131.5	0.92578655	LocalCorticosteroids	OTU4476950
1276	0.92578655	LocalCorticosteroids	OTU851925
437.5	0.92578655	Topicalcalcineurininhibitors	OTU1131523
345.5	0.92578655	Topicalcalcineurininhibitors	OTU851668
577.5	0.92578655	Fumaricacid	OTU403853
79	0.92578655	Antibiotics	OTU1004369
1864	0.92578655	VitaminDanalogs	OTU1081372
1851	0.92578655	VitaminDanalogs	OTU13445
1026	0.92578655	Photochemotherapy	OTU4349519
1020.5	0.92578655	Photochemotherapy	OTU4480063
1183	0.92578655	Photochemotherapy	OTU610043
1161	0.92578655	Photochemotherapy	OTU883806
266.5	0.92578655	SystemicCorticosteroids	OTU360483
1499.5	0.92578655	Phototherapy	OTU4047452
1701	0.92578655	Phototherapy	OTU4346894
547	0.92578655	Cyclosporin	OTU282360
447.5	0.92578655	Cyclosporin	OTU4350124
756	0.92578655	Dithranol.minute	OTU4317476
754	0.92578655	Dithranol.minute	OTU4474056
446	0.92698449	Cyclosporin	OTU4408996
355	0.9285878	Topicalcalcineurininhibitors	OTU511475
699	0.9285878	Fumaricacid	OTU164003
44	0.9285878	Antibiotics	OTU565753
76	0.9285878	Antibiotics	OTU940083
1070	0.9285878	TAR.topical.	OTU4473201
1178	0.9285878	Photochemotherapy	OTU4460228
194	0.9285878	SystemicCorticosteroids	OTU1081372
192	0.9285878	SystemicCorticosteroids	OTU912997
1511	0.9285878	Phototherapy	OTU4439089
442	0.9285878	Cyclosporin	OTU4440643
444	0.9285878	Cyclosporin	OTU851917
886	0.9285878	Dithranol.minute	OTU279980
762	0.9285878	Dithranol.minute	OTU4476950
1029	0.92881133	Methotrexate	OTU4327300
437	0.92881133	Topicalcalcineurininhibitors	OTU1081372
438	0.92881133	Topicalcalcineurininhibitors	OTU4482598
440	0.92881133	Topicalcalcineurininhibitors	OTU912997
588	0.92881133	Fumaricacid	OTU940083
1944,05,01	0.92881133	Antibiotics	OTU4348347
1944,05,01	0.92881133	Antibiotics	OTU511475
1221	0.92881133	TAR.topical.	OTU912997
1179	0.92881133	Photochemotherapy	OTU4327300
1185.5	0.92881133	Photochemotherapy	OTU837884
442.5	0.92881133	Cyclosporin	OTU4467218
1126.5	0.92938841	LocalCorticosteroids	OTU1096610
347	0.92938841	Topicalcalcineurininhibitors	OTU2110555
696	0.92938841	Fumaricacid	OTU819937
45	0.92938841	Antibiotics	OTU1107940
45	0.92938841	Antibiotics	OTU820692
540	0.92938841	Cyclosporin	OTU4473201
885	0.93132145	Retinoids	OTU4473664
1052	0.93132145	Methotrexate	OTU3841245
1174	0.93132145	Methotrexate	OTU4460228
1034	0.93132145	Methotrexate	OTU610043
1148.5	0.93132145	LocalCorticosteroids	OTU511475
1214	0.93132145	TAR.topical.	OTU4440643
1089	0.93132145	TAR.topical.	OTU883806
1027.5	0.93132145	Photochemotherapy	OTU403853
264	0.93132145	SystemicCorticosteroids	OTU4354809
199	0.93132145	SystemicCorticosteroids	OTU940083
1508	0.93132145	Phototherapy	OTU4449324
1515	0.93132145	Phototherapy	OTU4460228
545	0.93132145	Cyclosporin	OTU4047452
1039	0.93135251	Methotrexate	OTU4021335
1134.5	0.93135251	LocalCorticosteroids	OTU370309
696.5	0.93135251	Fumaricacid	OTU370309
1853.5	0.93135251	VitaminDanalogs	OTU505749
1067	0.93135251	TAR.topical.	OTU2110555
1031	0.93135251	Photochemotherapy	OTU4047452
1035	0.93321	Methotrexate	OTU1036883
1032.5	0.93321	Methotrexate	OTU4369229

1131	0.93321	LocalCorticosteroids	OTU496787
426	0.93321	Topicalcalcineurininhibitors	OTU987144
593	0.93321	Fumaricacid	OTU279980
1858.5	0.93321	VitaminDanalogs	OTU285376
1215	0.93321	TAR.topical.	OTU1004369
1074.5	0.93321	TAR.topical.	OTU247720
771	0.93321	Dithranol.minute	OTU912906
1177.5	0.93459596	Methotrexate	OTU1096610
1136	0.93586675	LocalCorticosteroids	OTU4482598
430	0.93586675	Topicalcalcineurininhibitors	OTU279980
433.5	0.93586675	Topicalcalcineurininhibitors	OTU4301457
1038	0.93586675	Photochemotherapy	OTU4421536
202.5	0.93586675	SystemicCorticosteroids	OTU4468125
1164	0.93621294	Photochemotherapy	OTU4299324
1165	0.93842995	Methotrexate	OTU103810
1844	0.93842995	VitaminDanalogs	OTU114999
1006	0.94041046	Retinoids	OTU4318084
687	0.94041046	Fumaricacid	OTU654307
1204.5	0.94041046	TAR.topical.	OTU819937
891.5	0.94044152	Retinoids	OTU1003210
893.5	0.94044152	Retinoids	OTU164003
890	0.94044152	Retinoids	OTU4422718
892	0.94044152	Retinoids	OTU4439089
894	0.94044152	Retinoids	OTU851917
1170	0.94044152	Methotrexate	OTU370309
1166	0.94044152	Methotrexate	OTU4421536
1272.5	0.94044152	LocalCorticosteroids	OTU4349519
1155	0.94044152	LocalCorticosteroids	OTU4481323
355	0.94044152	Topicalcalcineurininhibitors	OTU20360
430.5	0.94044152	Topicalcalcineurininhibitors	OTU4047452
356	0.94044152	Topicalcalcineurininhibitors	OTU4473664
356	0.94044152	Topicalcalcineurininhibitors	OTU940083
686.5	0.94044152	Fumaricacid	OTU362390
683	0.94044152	Fumaricacid	OTU4299324
687	0.94044152	Fumaricacid	OTU4471315
1948,05,01	0.94044152	Antibiotics	OTU3841245
1841.5	0.94044152	VitaminDanalogs	OTU360483
1828.5	0.94044152	VitaminDanalogs	OTU4348347
1845	0.94044152	VitaminDanalogs	OTU755148
1688.5	0.94044152	VitaminDanalogs	OTU761594
1079	0.94044152	TAR.topical.	OTU4471315
1079.5	0.94044152	TAR.topical.	OTU610043
1085	0.94044152	TAR.topical.	OTU654307
1073.5	0.94044152	TAR.topical.	OTU939571
1164	0.94044152	Photochemotherapy	OTU1131523
1043	0.94044152	Photochemotherapy	OTU939571
205	0.94044152	SystemicCorticosteroids	OTU4294554
205.5	0.94044152	SystemicCorticosteroids	OTU4411187
1525.5	0.94044152	Phototherapy	OTU370309
1535	0.94044152	Phototherapy	OTU378096
1537	0.94044152	Phototherapy	OTU4348347
1678	0.94044152	Phototherapy	OTU4422405
1523.5	0.94044152	Phototherapy	OTU610043
1667	0.94044152	Phototherapy	OTU940083
524.5	0.94044152	Cyclosporin	OTU3841245
771	0.94044152	Dithranol.minute	OTU164003
778	0.94044152	Dithranol.minute	OTU4294554
876	0.94044152	Dithranol.minute	OTU4318084
871	0.94044152	Dithranol.minute	OTU4353642
772	0.94044152	Dithranol.minute	OTU4408996
773	0.94044152	Dithranol.minute	OTU610043
685	0.94088258	Fumaricacid	OTU74351
1675	0.94088258	Phototherapy	OTU995817
1151	0.94113559	Methotrexate	OTU820692
49	0.94113559	Antibiotics	OTU883806
1838	0.94113559	VitaminDanalogs	OTU1003210
1827	0.94113559	VitaminDanalogs	OTU4481323
1080.5	0.94113559	TAR.topical.	OTU505749
1156	0.94113559	Photochemotherapy	OTU4350124
201	0.94113559	SystemicCorticosteroids	OTU285376
259	0.94113559	SystemicCorticosteroids	OTU4422405
453	0.94113559	Cyclosporin	OTU4456068
876	0.94113559	Dithranol.minute	OTU4047452
1666.5	0.9416623	Phototherapy	OTU370134
899	0.94264371	Retinoids	OTU282360
1004	0.94264371	Retinoids	OTU370309
1006	0.94264371	Retinoids	OTU4422405
1162.5	0.94264371	Methotrexate	OTU4047452
1162	0.94264371	Methotrexate	OTU939571
1146	0.94264371	LocalCorticosteroids	OTU912997
1055	0.94264371	Photochemotherapy	OTU4353642
1045	0.94264371	Photochemotherapy	OTU4467218

204.5	0.94264371	SystemicCorticosteroids	OTU164003
204	0.94264371	SystemicCorticosteroids	OTU20360
207	0.94264371	SystemicCorticosteroids	OTU912906
1529	0.94264371	Phototherapy	OTU4482598
455	0.94264371	Cyclosporin	OTU4449324
896.5	0.94388727	Retinoids	OTU4467218
1155	0.94388727	LocalCorticosteroids	OTU4408996
45	0.94388727	Antibiotics	OTU4349859
1826	0.94388727	VitaminDanalogs	OTU912906
1531.5	0.94388727	Phototherapy	OTU4301457
1532.5	0.94388727	Phototherapy	OTU505749
1660.5	0.94390535	Phototherapy	OTU4476950
783	0.94390535	Dithranol.minute	OTU378096
425	0.94438696	Topicalcalcineurininhibitors	OTU4440643
423	0.94438696	Topicalcalcineurininhibitors	OTU625320
205.5	0.94438696	SystemicCorticosteroids	OTU4349519
1264	0.94528897	LocalCorticosteroids	OTU360483
1155	0.94528897	LocalCorticosteroids	OTU819937
1268	0.94574249	LocalCorticosteroids	OTU4449324
254	0.94574249	SystemicCorticosteroids	OTU25259
256	0.94574249	SystemicCorticosteroids	OTU995817
423	0.94596241	Topicalcalcineurininhibitors	OTU4421536
460.5	0.9460888	Cyclosporin	OTU370134
364	0.9465208	Topicalcalcineurininhibitors	OTU14278
422	0.9465208	Topicalcalcineurininhibitors	OTU4439089
530	0.9465208	Cyclosporin	OTU755148
1267	0.94741399	LocalCorticosteroids	OTU403853
1057	0.9479187	Methotrexate	OTU4318084
604	0.9479187	Fumaricacid	OTU851668
1089	0.9479187	TAR.topical.	OTU370134
204.5	0.9479187	SystemicCorticosteroids	OTU837884
1154	0.94834179	Methotrexate	OTU1081372
605	0.94834179	Fumaricacid	OTU4439089
677.5	0.94834179	Fumaricacid	OTU4476950
676	0.94834179	Fumaricacid	OTU912906
1194	0.94834179	TAR.topical.	OTU4422405
1091	0.94834179	TAR.topical.	OTU4473664
1055	0.94834179	Photochemotherapy	OTU755148
1156.5	0.94834179	Photochemotherapy	OTU995817
1651	0.94834179	Phototherapy	OTU13445
1545	0.94834179	Phototherapy	OTU4318084
1660	0.94834179	Phototherapy	OTU4327300
523	0.94834179	Cyclosporin	OTU4348347
458.5	0.94834179	Cyclosporin	OTU496787
522	0.94834179	Cyclosporin	OTU511475
784.5	0.94834179	Dithranol.minute	OTU103810
1700	0.94992251	VitaminDanalogs	OTU4467218
1822	0.94992251	VitaminDanalogs	OTU74351
1153.5	0.94992251	Photochemotherapy	OTU4440643
366.5	0.95089257	Topicalcalcineurininhibitors	OTU4468125
1710	0.95089257	VitaminDanalogs	OTU4299324
1818	0.95089257	VitaminDanalogs	OTU654307
1660	0.95371818	Phototherapy	OTU1004369
70	0.95691009	Antibiotics	OTU610043
1711	0.95691009	VitaminDanalogs	OTU362390
915.5	0.95725431	Retinoids	OTU4348347
909	0.95725431	Retinoids	OTU625320
607.5	0.95725431	Fumaricacid	OTU360483
1708.5	0.95725431	VitaminDanalogs	OTU819937
211	0.95725431	SystemicCorticosteroids	OTU14278
251	0.95725431	SystemicCorticosteroids	OTU4471315
792	0.95725431	Dithranol.minute	OTU1107940
1103	0.95854109	TAR.topical.	OTU1107940
991	0.95974721	Retinoids	OTU20360
907.5	0.95974721	Retinoids	OTU403853
1146	0.95974721	Methotrexate	OTU4303697
1249	0.95974721	LocalCorticosteroids	OTU362390
368	0.95974721	Topicalcalcineurininhibitors	OTU654307
614	0.95974721	Fumaricacid	OTU4481323
70	0.95974721	Antibiotics	OTU4449324
1097	0.95974721	TAR.topical.	OTU114999
1094.5	0.95974721	TAR.topical.	OTU4449324
1063.5	0.95974721	Photochemotherapy	OTU103810
1066	0.95974721	Photochemotherapy	OTU14278
1061	0.95974721	Photochemotherapy	OTU164003
1143	0.95974721	Photochemotherapy	OTU205025
1148	0.95974721	Photochemotherapy	OTU2110555
1147	0.95974721	Photochemotherapy	OTU25259
249	0.95974721	SystemicCorticosteroids	OTU4303697
1549	0.95974721	Phototherapy	OTU4303697
1650	0.95974721	Phototherapy	OTU4306540
466.5	0.95974721	Cyclosporin	OTU4349519

784.5	0.95974721	Dithranol.minute	OTU4440643
367	0.9601394	Topicalcalcineurininhibitors	OTU4327286
1185.5	0.9601394	TAR.topical.	OTU403853
1067	0.9609343	Methotrexate	OTU14278
1146	0.9609343	Methotrexate	OTU4474056
1252	0.9609343	LocalCorticosteroids	OTU1036883
1651.5	0.9609343	Phototherapy	OTU4456068
523	0.9609343	Cyclosporin	OTU2110555
524.5	0.9609343	Cyclosporin	OTU403853
521.5	0.9609343	Cyclosporin	OTU851668
787	0.9609343	Dithranol.minute	OTU4354809
1147.5	0.96113607	Methotrexate	OTU4349859
1800	0.96113607	VitaminDanalogs	OTU883806
1141	0.9616637	Methotrexate	OTU114999
1065.5	0.9616637	Methotrexate	OTU4349519
1066	0.9616637	Methotrexate	OTU74351
1175	0.9616637	LocalCorticosteroids	OTU13445
1169	0.9616637	LocalCorticosteroids	OTU755148
1252.5	0.9616637	LocalCorticosteroids	OTU995817
666	0.9616637	Fumaricacid	OTU565753
675	0.9616637	Fumaricacid	OTU837884
1807.5	0.9616637	VitaminDanalogs	OTU4350124
1177.5	0.9616637	TAR.topical.	OTU25478
1102	0.9616637	TAR.topical.	OTU4303697
1648	0.9616637	Phototherapy	OTU4354809
1644	0.9616637	Phototherapy	OTU4422718
1640	0.9616637	Phototherapy	OTU4481323
520	0.9616637	Cyclosporin	OTU4303697
471	0.9616637	Cyclosporin	OTU761594
792	0.9616637	Dithranol.minute	OTU4303697
918.5	0.96259709	Retinoids	OTU761594
416	0.96259709	Topicalcalcineurininhibitors	OTU285376
1066.5	0.96259709	Photochemotherapy	OTU20360
244	0.96259709	SystemicCorticosteroids	OTU820692
1643	0.96259709	Phototherapy	OTU282360
519.5	0.96259709	Cyclosporin	OTU164003
668.5	0.96330929	Fumaricacid	OTU114999
1069.5	0.96330929	Photochemotherapy	OTU4476950
854.5	0.96330929	Dithranol.minute	OTU1131523
856.5	0.96330929	Dithranol.minute	OTU4369229
68	0.96377545	Antibiotics	OTU4369229
1642	0.96377545	Phototherapy	OTU851917
1641	0.96422706	Phototherapy	OTU25259
1070	0.9664714	Photochemotherapy	OTU819937
413	0.96714331	Topicalcalcineurininhibitors	OTU755148
979	0.96726303	Retinoids	OTU4309323
916	0.96726303	Retinoids	OTU912997
618	0.96726303	Fumaricacid	OTU103810
68	0.96726303	Antibiotics	OTU285376
243	0.96726303	SystemicCorticosteroids	OTU1107940
1557	0.96726303	Phototherapy	OTU939571
980	0.96861598	Retinoids	OTU360483
928	0.96861598	Retinoids	OTU3841245
981	0.96861598	Retinoids	OTU4354809
1072	0.96861598	Methotrexate	OTU4446521
1132	0.96861598	Methotrexate	OTU4481323
410	0.96861598	Topicalcalcineurininhibitors	OTU362390
618	0.96861598	Fumaricacid	OTU4473664
662	0.96861598	Fumaricacid	OTU820692
1804	0.96861598	VitaminDanalogs	OTU4471315
1107	0.96861598	TAR.topical.	OTU755148
241	0.96861598	SystemicCorticosteroids	OTU883806
516	0.96861598	Cyclosporin	OTU4421536
516	0.96861598	Cyclosporin	OTU625320
516	0.96861598	Cyclosporin	OTU819937
796	0.96861598	Dithranol.minute	OTU2110555
797	0.96861598	Dithranol.minute	OTU25259
1171	0.97052901	TAR.topical.	OTU282360
979	0.97056003	Retinoids	OTU1004369
923	0.97056003	Retinoids	OTU2110555
925	0.97056003	Retinoids	OTU247720
976	0.97056003	Retinoids	OTU4021335
977	0.97056003	Retinoids	OTU4471315
930	0.97056003	Retinoids	OTU883806
1074	0.97056003	Methotrexate	OTU370134
1183	0.97056003	LocalCorticosteroids	OTU565753
664	0.97056003	Fumaricacid	OTU4303697
1802	0.97056003	VitaminDanalogs	OTU2110555
1133.5	0.97056003	Photochemotherapy	OTU370309
1074	0.97056003	Photochemotherapy	OTU4482598
243	0.97056003	SystemicCorticosteroids	OTU1131523
243	0.97056003	SystemicCorticosteroids	OTU282360



218	0.97056003	SystemicCorticosteroids	OTU3208510
1632	0.97056003	Phototherapy	OTU114999
1634	0.97056003	Phototherapy	OTU279980
1563	0.97056003	Phototherapy	OTU755148
515	0.97056003	Cyclosporin	OTU4439089
845	0.97056003	Dithranol.minute	OTU851925
927	0.97123767	Retinoids	OTU3208510
924.5	0.97123767	Retinoids	OTU4306540
1180	0.97123767	LocalCorticosteroids	OTU2901965
1184	0.97123767	LocalCorticosteroids	OTU378096
623.5	0.97123767	Fumaricacid	OTU4350124
619	0.97123767	Fumaricacid	OTU912997
1736	0.97123767	VitaminDanalogs	OTU565753
1623	0.97123767	Phototherapy	OTU3841245
1635	0.97123767	Phototherapy	OTU496787
846.5	0.97123767	Dithranol.minute	OTU819937
798.5	0.97123767	Dithranol.minute	OTU837884
1130	0.97270009	Photochemotherapy	OTU4446521
1129.5	0.97339847	Photochemotherapy	OTU282360
242	0.97339847	SystemicCorticosteroids	OTU4473664
217.5	0.97405353	SystemicCorticosteroids	OTU4369229
1233	0.97418992	LocalCorticosteroids	OTU14278
622	0.97418992	Fumaricacid	OTU4327300
1081	0.97433502	Photochemotherapy	OTU362390
1127	0.97825737	Photochemotherapy	OTU247720
1082	0.97844062	Photochemotherapy	OTU3208510
378.5	0.97854183	Topicalcalcineurininhibitors	OTU103810
1166.5	0.97854183	TAR.topical.	OTU496787
1235	0.97964384	LocalCorticosteroids	OTU4354809
626.5	0.97964384	Fumaricacid	OTU13445
1118	0.97964384	TAR.topical.	OTU761594
479	0.97964384	Cyclosporin	OTU4317476
929	0.97977109	Retinoids	OTU4303697
1738.5	0.97977109	VitaminDanalogs	OTU378096
1788	0.97999566	VitaminDanalogs	OTU987144
927.5	0.98135141	Retinoids	OTU4346894
403	0.98135141	Topicalcalcineurininhibitors	OTU851925
479.5	0.98135141	Cyclosporin	OTU2901965
221	0.98248499	SystemicCorticosteroids	OTU4481323
1083	0.98365272	Methotrexate	OTU25259
1119	0.98365272	Methotrexate	OTU883806
1083.5	0.98365272	Photochemotherapy	OTU4349522
1126	0.98365272	Photochemotherapy	OTU4474056
1621.5	0.98365272	Phototherapy	OTU4468125
509	0.98365272	Cyclosporin	OTU4460228
1124	0.98378876	Methotrexate	OTU4440643
1122	0.98378876	Methotrexate	OTU4473201
1120.5	0.98378876	Methotrexate	OTU511475
657	0.98378876	Fumaricacid	OTU4317476
1741	0.98378876	VitaminDanalogs	OTU4021335
1119	0.98378876	TAR.topical.	OTU4467218
1084	0.98378876	Photochemotherapy	OTU625320
1623.5	0.98378876	Phototherapy	OTU4467218
1619	0.98378876	Phototherapy	OTU565753
1576	0.98378876	Phototherapy	OTU851668
508	0.98378876	Cyclosporin	OTU4471315
841	0.98378876	Dithranol.minute	OTU1036883
509	0.98448982	Cyclosporin	OTU837884
934.5	0.98530666	Retinoids	OTU103810
966	0.98530666	Retinoids	OTU4446521
932.5	0.98530666	Retinoids	OTU496787
656	0.98530666	Fumaricacid	OTU2110555
653	0.98530666	Fumaricacid	OTU851925
1785.5	0.98530666	VitaminDanalogs	OTU4476950
1158	0.98530666	TAR.topical.	OTU360483
1579	0.98530666	Phototherapy	OTU4473201
1618	0.98530666	Phototherapy	OTU912906
508	0.98530666	Cyclosporin	OTU4354809
485	0.98530666	Cyclosporin	OTU820692
965	0.987455	Retinoids	OTU114999
1121	0.987455	Photochemotherapy	OTU1036883
1619.5	0.9874968	Phototherapy	OTU4440643
937.5	0.98835338	Retinoids	OTU511475
1125.5	0.98835338	TAR.topical.	OTU378096
631	0.98847033	Fumaricacid	OTU3208510
1117	0.98847033	Photochemotherapy	OTU820692
810	0.98847033	Dithranol.minute	OTU2901965
937	0.98891134	Retinoids	OTU74351
1194	0.98891134	LocalCorticosteroids	OTU4318084
630	0.98891134	Fumaricacid	OTU4474056
63	0.98891134	Antibiotics	OTU20360
63	0.98891134	Antibiotics	OTU4301457

1153	0.98891134	TAR.topical.	OTU4294554
1118	0.98891134	Photochemotherapy	OTU4021335
1088	0.98891134	Photochemotherapy	OTU4422405
653	0.98987863	Fumaricacid	OTU2901965
652	0.98987863	Fumaricacid	OTU4309323
1126	0.98987863	TAR.topical.	OTU851668
812	0.99051617	Dithranol.minute	OTU1003210
1116	0.99067792	Methotrexate	OTU4299324
1195	0.99067792	LocalCorticosteroids	OTU4471315
385	0.99067792	Topicalcalcineurininhibitors	OTU4481323
1613	0.99067792	Phototherapy	OTU14278
1583	0.99067792	Phototherapy	OTU4474056
811.5	0.99067792	Dithranol.minute	OTU4449324
651	0.99146669	Fumaricacid	OTU4473201
503.5	0.99146669	Cyclosporin	OTU610043
1152	0.99172584	TAR.topical.	OTU940083
812.5	0.99172584	Dithranol.minute	OTU496787
939	0.99373266	Retinoids	OTU4317476
1779	0.99373266	VitaminDanalogs	OTU939571
1116	0.99465828	Methotrexate	OTU4422405
1115	0.99465828	Methotrexate	OTU505749
502	0.99465828	Cyclosporin	OTU3208510
815.5	0.99465828	Dithranol.minute	OTU4411187
815	0.99465828	Dithranol.minute	OTU761594
1752	0.9949947	VitaminDanalogs	OTU3208510
1114	0.99621042	Methotrexate	OTU4467218
1201	0.99621042	LocalCorticosteroids	OTU1107940
1149	0.99621042	TAR.topical.	OTU4439089
1112.5	0.99621042	Photochemotherapy	OTU4318084
234	0.99621042	SystemicCorticosteroids	OTU851925
1610	0.99621042	Phototherapy	OTU164003
1611	0.99621042	Phototherapy	OTU285376
1609	0.99621042	Phototherapy	OTU3208510
501.5	0.99621042	Cyclosporin	OTU20360
1610	0.99797008	Phototherapy	OTU403853
1590.5	0.99797008	Phototherapy	OTU511475
1095	0.99800556	Methotrexate	OTU4449324
949.5	1	Retinoids	OTU285376
1110	1	Methotrexate	OTU4349522
1111	1	Methotrexate	OTU4482598
1110	1	Methotrexate	OTU940083
1211.5	1	LocalCorticosteroids	OTU370134
1208	1	LocalCorticosteroids	OTU4446521
1209	1	LocalCorticosteroids	OTU912906
389.5	1	Topicalcalcineurininhibitors	OTU13445
390	1	Topicalcalcineurininhibitors	OTU4353642
393	1	Topicalcalcineurininhibitors	OTU4446521
391	1	Topicalcalcineurininhibitors	OTU4460228
393	1	Topicalcalcineurininhibitors	OTU505749
388	1	Topicalcalcineurininhibitors	OTU837884
395.5	1	Topicalcalcineurininhibitors	OTU939571
638	1	Fumaricacid	OTU1004369
639	1	Fumaricacid	OTU4408996
638	1	Fumaricacid	OTU4482598
642	1	Fumaricacid	OTU939571
1760.5	1	VitaminDanalogs	OTU20360
1766	1	VitaminDanalogs	OTU247720
1762.5	1	VitaminDanalogs	OTU2901965
1761	1	VitaminDanalogs	OTU370309
1770	1	VitaminDanalogs	OTU4327300
1769	1	VitaminDanalogs	OTU4421536
1755	1	VitaminDanalogs	OTU4449324
1146	1	TAR.topical.	OTU14278
1145	1	TAR.topical.	OTU4317476
1135	1	TAR.topical.	OTU4460228
1138	1	TAR.topical.	OTU4474056
1139	1	TAR.topical.	OTU511475
1098	1	Photochemotherapy	OTU1107940
1103.5	1	Photochemotherapy	OTU13445
1105	1	Photochemotherapy	OTU2901965
1107	1	Photochemotherapy	OTU4294554
1108	1	Photochemotherapy	OTU4473201
1100	1	Photochemotherapy	OTU505749
1100	1	Photochemotherapy	OTU511475
1099	1	Photochemotherapy	OTU851925
230	1	SystemicCorticosteroids	OTU4327300
233.5	1	SystemicCorticosteroids	OTU4350124
229	1	SystemicCorticosteroids	OTU4353642
229.5	1	SystemicCorticosteroids	OTU511475
227	1	SystemicCorticosteroids	OTU565753
230	1	SystemicCorticosteroids	OTU819937
1596	1	Phototherapy	OTU360483

1592	1	Phototherapy	OTU4021335
1602	1	Phototherapy	OTU4350124
494.5	1	Cyclosporin	OTU285376
499	1	Cyclosporin	OTU360483
498	1	Cyclosporin	OTU4021335
498	1	Cyclosporin	OTU4369229
494	1	Cyclosporin	OTU4411187
495	1	Cyclosporin	OTU4468125
818.5	1	Dithranol.minute	OTU114999
823	1	Dithranol.minute	OTU4348347

## REVIEWERS' COMMENTS:

Reviewer #1 (Remarks to the Author):

We feel the authors have sufficiently addressed my concerns for the manuscript. Congratulations on a great paper.

Reviewer #2 (Remarks to the Author):

I am satisfied with what the authors have done to address the comments.

Reviewer #3 (Remarks to the Author):

The manuscript has improved; the sections in the results and discussion regarding interpretation of the *S. aureus* and host transcriptional signatures is now much better explained.

For Figure S8b, I could not find the methods about how you picked the genes shown in Figure S8b. For example, under "Two\_Component\_System", only 15 genes have abundance data shown. Were these ones picked because they showed the best differences across the SA high vs low categories? Or were these the ones that had the best WGS coverage? I'm sorry if the methods are clearly stated somewhere, but I couldn't find it easily.

Responses to the reviewers' comments:

**Reviewer #3 (remarks to the author):**

*For Figure S8b, I could not find the methods about how you picked the genes shown in Figure S8b. For example, under "Two\_Component\_System", only 15 genes have abundance data shown. Were these ones picked because they showed the best differences across the SA high vs low categories? Or were these the ones that had the best WGS coverage? I'm sorry if the methods are clearly stated somewhere, but I couldn't find it easily.*

**Answer:**

Indeed, the heatmap presented in Figure S8b shows the top most significantly differentially abundant set of microbial genes between the *S. aureus*-high and *S. aureus*-low, with a cutoff of log<sub>2</sub> fold-change > 1 and adjusted p-value < 0.05, annotated with the relevant KEGG pathway categories. The statistical test used was the zero-inflated Gaussian model implemented in the metagenomeSeq R package with adjustment for sampling site, body site, age, sex and library preparation. The figure legend has been updated accordingly (Supplementary Fig. 8b).