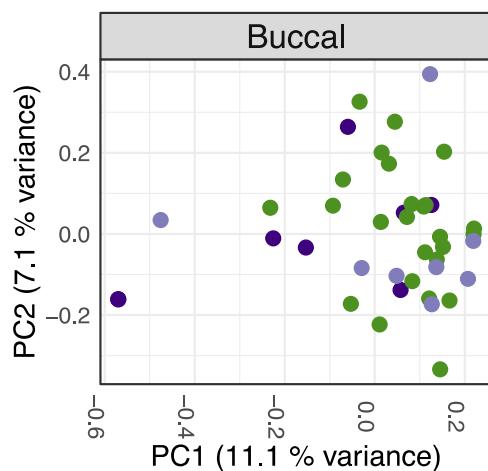
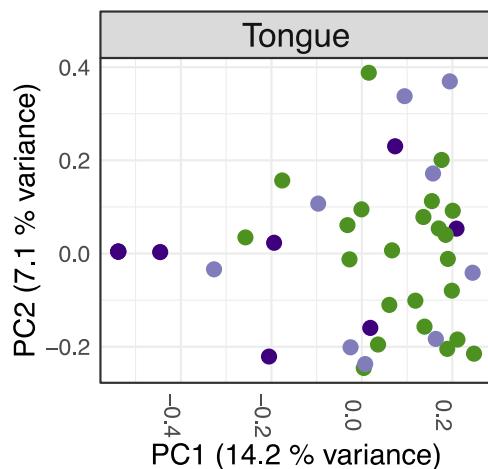


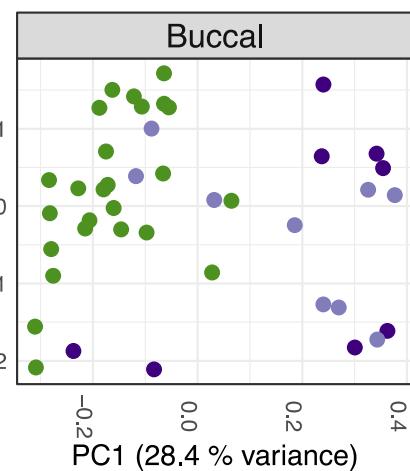
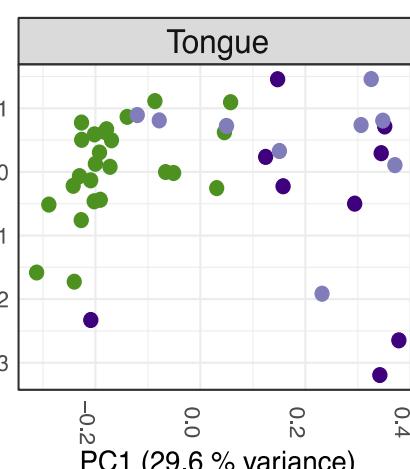
Supplementary Figure 1. Defects in STAT3-mediated immunity in AD-HIES are associated recurrent candidiasis. A) Quantification of S100A9 protein (constituent of Calprotectin; S100A8/9) in saliva of patients with Autosomal-Dominant Hyper IgE Syndrome (AD-HIES, n=16) and healthy controls (HC, n=24). * $P < 0.01$ as determined by Mann-Whitney test. Boxes extend from the 25th to 75th percentiles and the whiskers were plotted from the minimum to maximum value. All outlying values were shown. B) Representative image of oral candidiasis in a AD-HIES patient affecting the tongue dorsum. C) Representative image of oral candidiasis in a AD-HIES patient affecting the buccal mucosa.

A**Fungi****B****Bacteria**

● HC ● U_HIES ● A_HIES

Tongue
 $P < 0.01$ HC vs HIES combined
 $P = 0.081$ (ns) U_HIES vs A_HIES

Buccal
 $P < 0.01$ HC vs HIES combined
 $P = 0.063$ (ns) U_HIES vs A_HIES

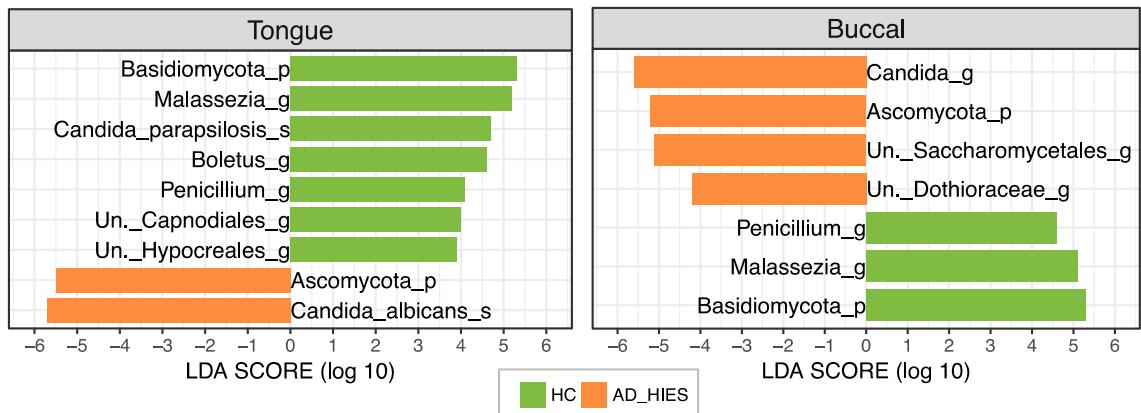
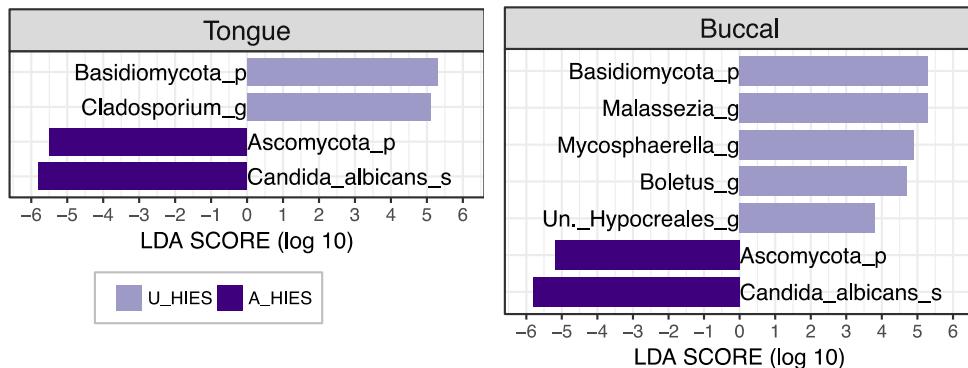


● HC ● U_HIES ● A_HIES

Tongue
 $P < 0.001$ HC vs HIES combined
 $P = 0.186$ (ns) U_HIES vs A_HIES

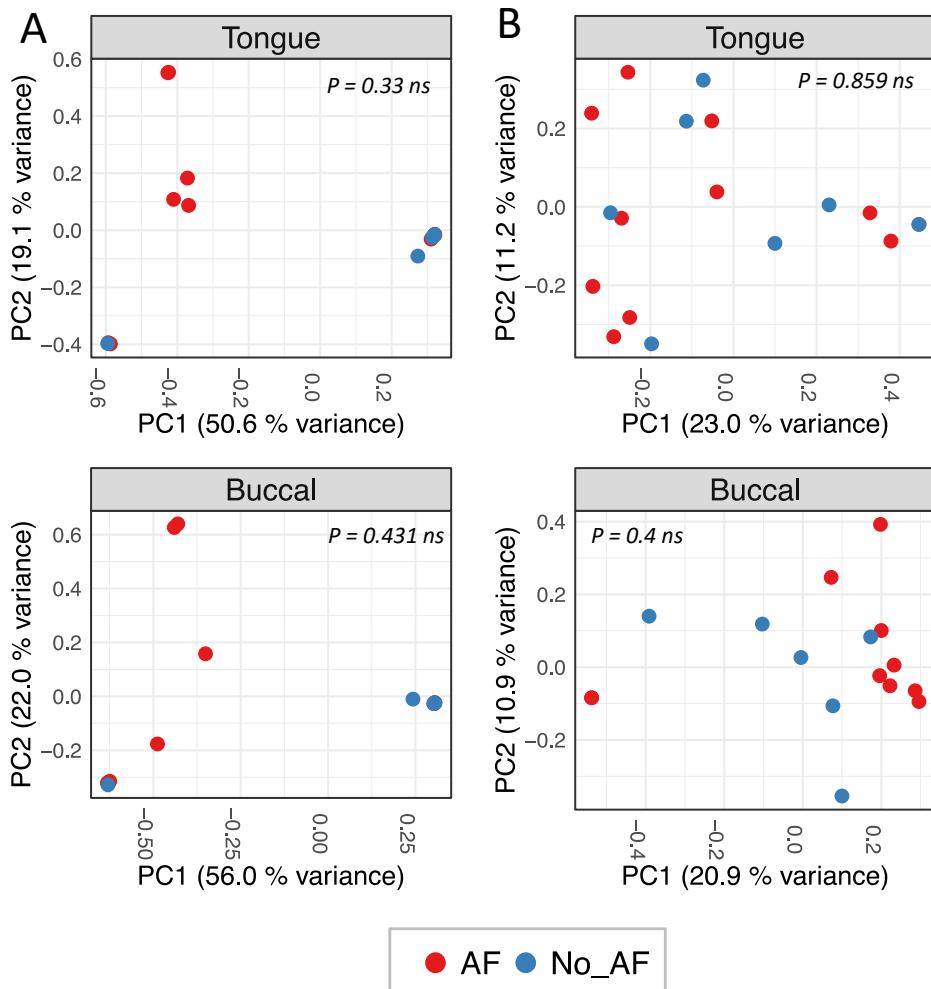
Buccal
 $P < 0.001$ HC vs HIES combined
 $P = 0.194$ (ns) U_HIES vs A_HIES

Supplementary Figure 2. Fungal and bacterial communities from AD-HIES patients separate from healthy controls according to community membership. Graphs depict Principal Coordinate Analysis (PCoA) plots of community membership (based on the Jaccard Index). (A) Fungal communities and (B) bacterial communities from tongue and buccal sites. Each circle represents one sample. (A and B) The number of samples per group included in graphs of fungal communities for healthy controls (HC) were n=23 for tongue and n=25 for buccal. For Uninfected AD-HIES (U_HIES) and actively infected AD-HIES (A_HIES), the number of samples was n=9 for tongue and n=8 for buccal for both groups. The number of samples per group included in graphs of bacterial communities were for HC, n=25 for tongue and buccal, for U_HIES n=9 for tongue and buccal and for A_HIES n=9 for tongue and n=8 for buccal. P values were calculated using AMOVA (details of each P value are in the figure). Some data points are not visible as they get superimposed due to tight clustering

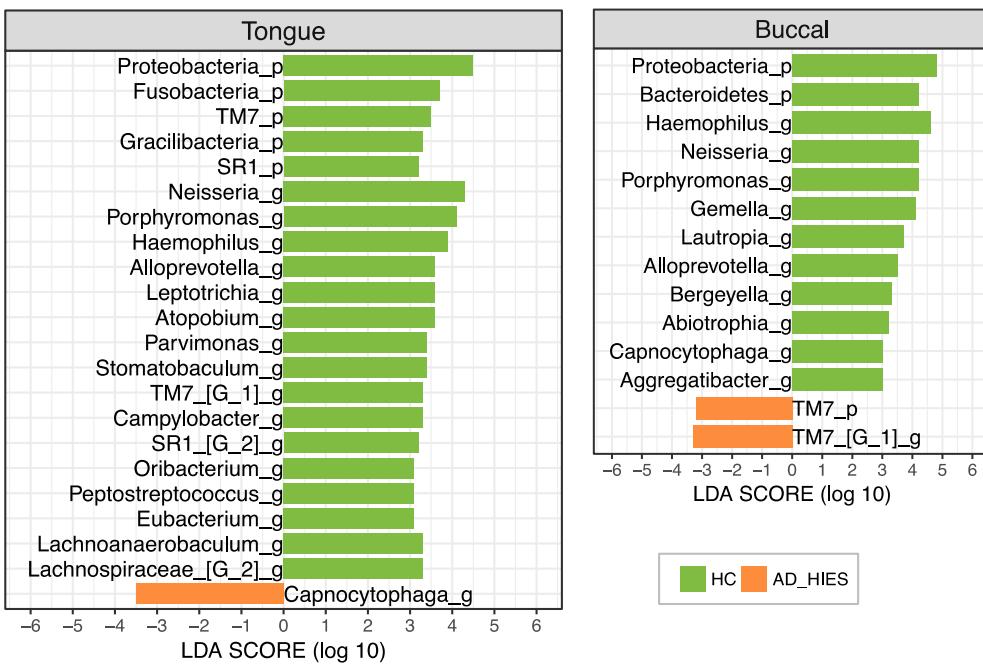
A**B**

Supplementary Figure 3. Differential representation of fungal taxa in AD-HIES and healthy controls. A) Graph shows taxa differentially represented according to LEfSe analysis comparing fungal taxa in healthy controls (HC) and all samples from patients with Autosomal Dominant Hyper IgE Syndrome (AD-HIES) in both tongue (HC, n=23 and AD-HIES, n=18) and buccal surfaces (HC, n=25 and AD-HIES, n=16).

B) Graph depicts taxa found in significantly different proportions via LEfSe analysis comparing fungal taxa between actively infected AD-HIES patients (A_HIES) and uninfected AD-HIES patients (U_HIES) in both tongue (U_HIES and A_HIES, n=9) and buccal surfaces (U_HIES and A_HIES, n=8). The taxonomical level corresponding to each taxa is indicated by _s (species), _g (genus) and _p (phylum).



Supplementary Figure 4. Antifungal prophylaxis does not affect fungal AD-HIES community structure and composition. Graphs depict Principal Coordinate Analysis (PCoA) of patients with Autosomal Dominant Hyper IgE Syndrome (AD-HIES) samples from patients receiving antifungal prophylaxis (AF) or not (No_AF), irrespective of their candidiasis status. PCoA are based on the community structure metric (Theta YC distances) (A) and on the community membership measure (Jaccard Index) (B). Each circle represents one patient. For Tongue graphs (AF, n=11 and No_AF, n=7). For buccal plots (AF, n=10 and No_AF, n=6). Some data points are not visible as they get superimposed due to tight clustering. P values were calculated using AMOVA (details of each P value are in the figure).



Supplementary Figure 5. Differentially represented bacterial genera in healthy controls and AD-HIES. A) Graph shows taxa differentially represented according to LEfSe analysis comparing bacterial taxa in healthy controls (HC) and all samples from patients with Autosomal Dominant Hyper IgE Syndrome (AD-HIES) in both tongue (HC, n=25 and AD-HIES, n=18) and buccal surfaces (HC, n=25 and AD-HIES, n=17) .

TABLE S1. Demographic and Clinical Information of Healthy Controls and AD-HIES cohort for microbiome study

	Healthy Controls	AD-HIES patients
Subjects analyzed, (n)	25	18
Age, mean (SD)	33.1 (12.3)	35.1 (12.6) [^]
Gender, (female:male)	(16:9)	(11:7) [#]
Race, n (%)		
Caucasian	15 (60%)	15 (83.3%)
African American	5 (20%)	2 (11.1%)
Other	5(20%)	1 (5.6%)
Active oral candidiasis at time of sampling, n (%)	0	* 9 (50%)
Antifungal prophylaxis, n (%)	0	11 (61.1%)
Posaconazole		6
Fluconazole		3
Itraconazole		1
Voriconazole		1
Antibacterial prophylaxis, n (%)	0	17 (94.4%)
Sulfamethoxazole/Trimethoprim		8
Azithromycin		4
Doxycycline		2
Amoxicillin/Clavulanate		2
Levofloxacin		1
History of recurrent oral candidiasis, n (%)	0	15 (83.3%)
History of recurrent oral ulcers, n (%)	0	7 (38.8%)
Severe dental caries, n (%)	0	8 (44.4%)
Xerostomia, n (%)	0	2 (11.1%)

[^] $P = 0.5807$ (ns), [#] $P > 0.9999$ (ns)

* From those, 4 patients were receiving antifungal prophylaxis and 5 did not.