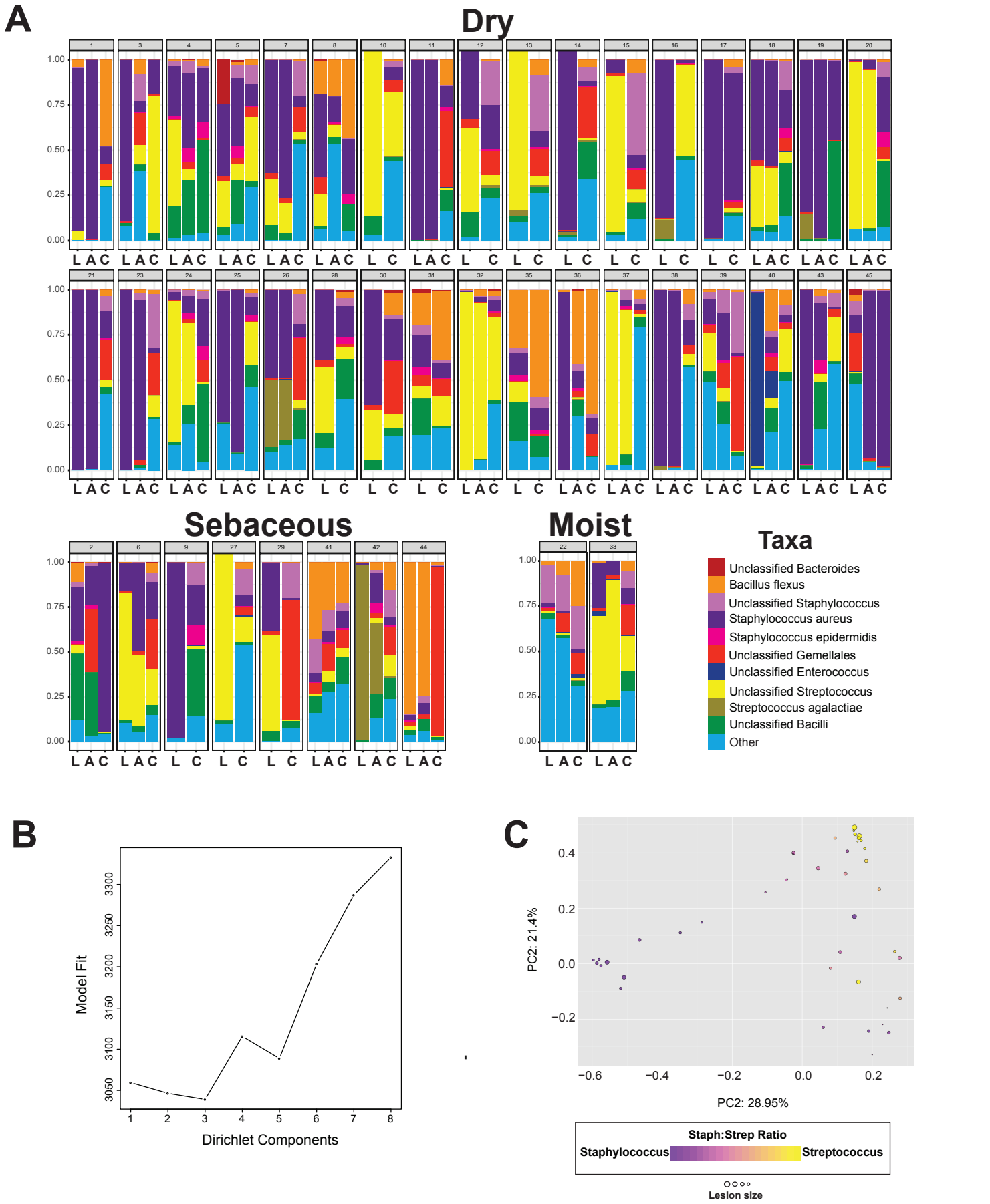
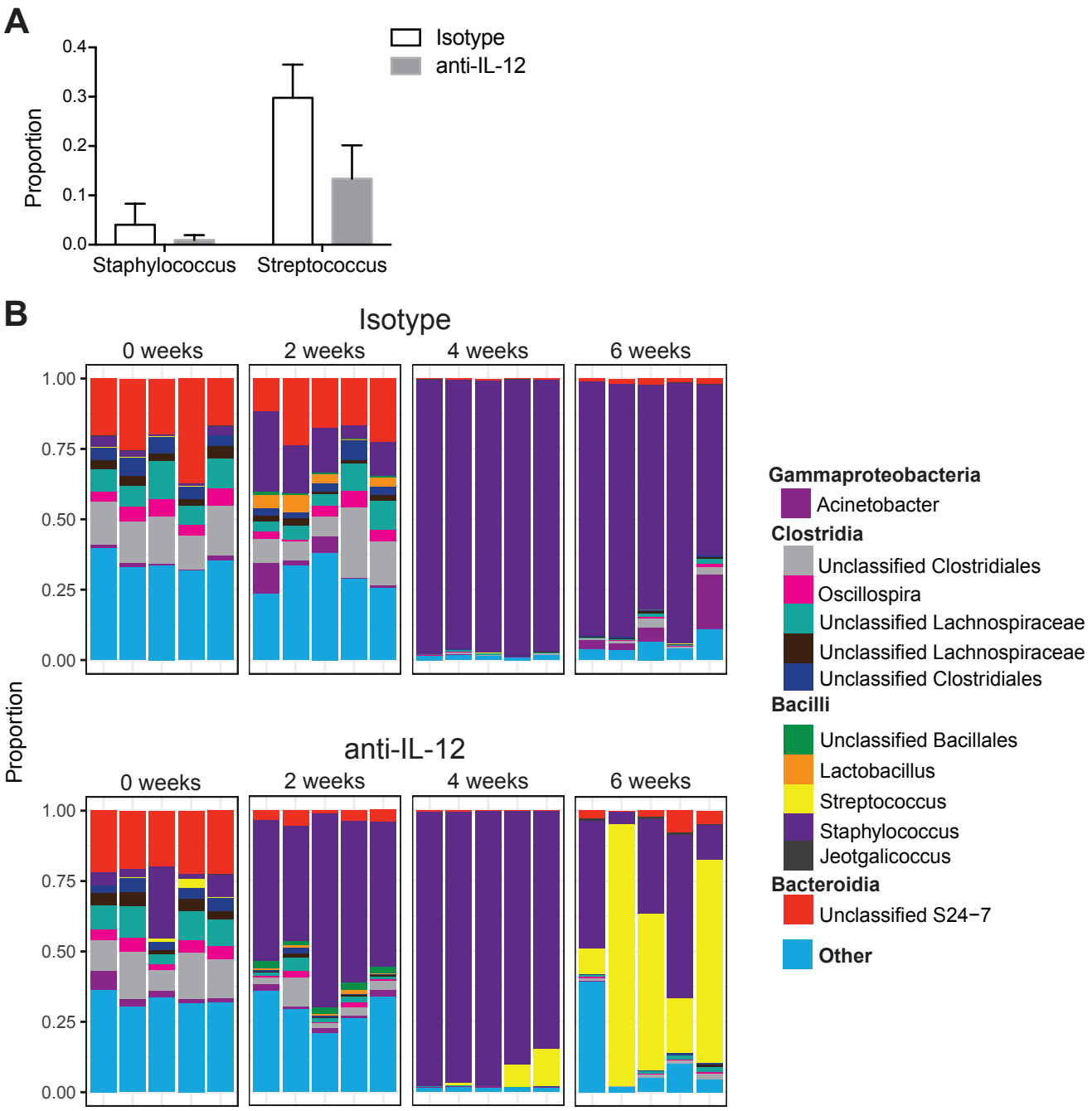
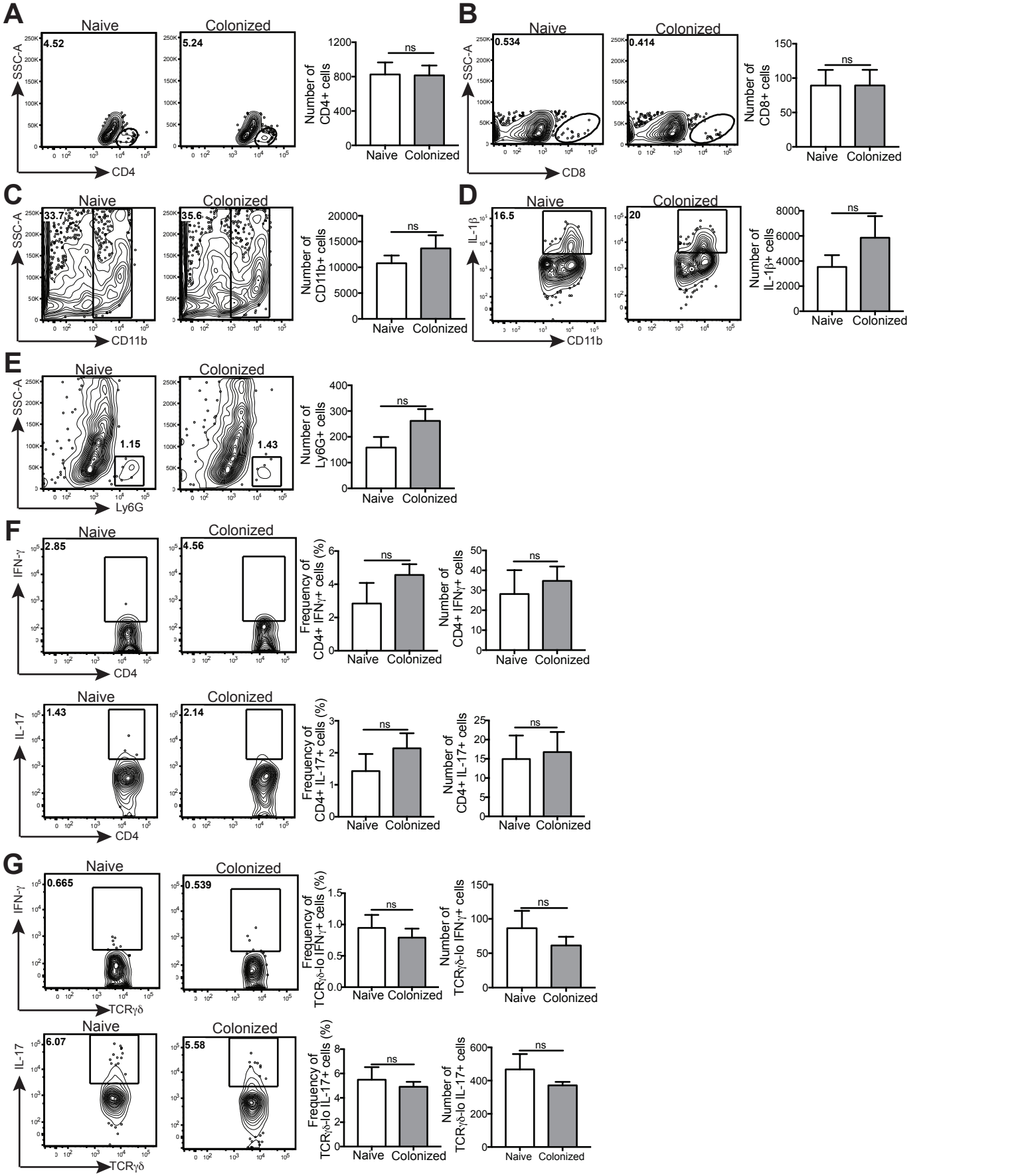


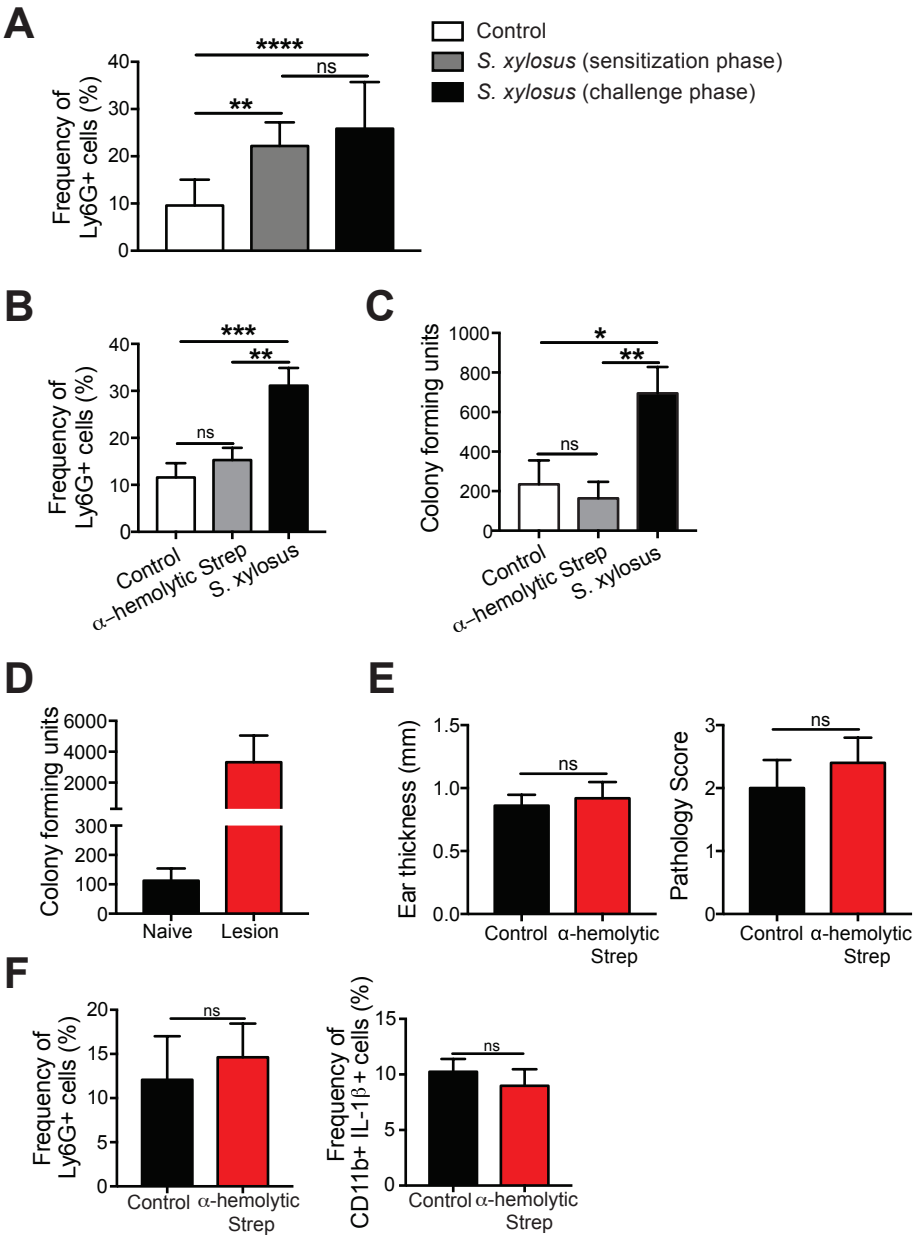
Supplemental Figure 1. Samples from patients are diverse and lesions cluster into 3 community types, Related to Figure 1. (A) Stacked bar charts represent the proportion of the top 10 taxa present in each sample. Patients are identified by number and skin type is identified as lesion (L), adjacent skin sites (A), or contralateral skin sites (C). (B) Laplace approximation of model evidence was used to measure the model fit. The lowest value (3) indicates the best fit for the model. (C) PCoA values for weighted UniFrac analysis were plotted and colored based on the ratio of the abundances of Staphylococcus spp. to Streptococcus spp. in each lesions sample and circle size is based on size of the lesion of each sample.



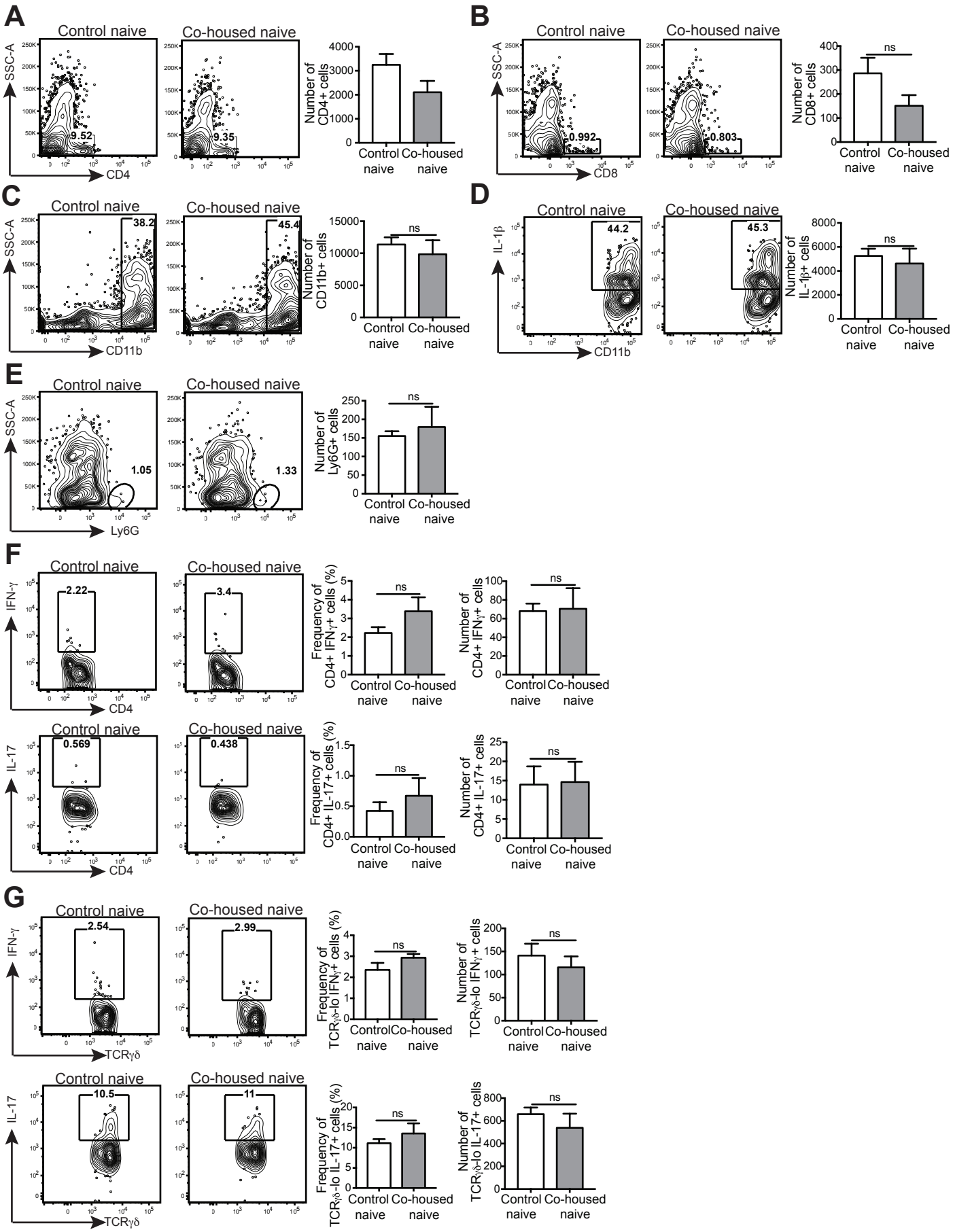
Supplemental Figure 2. Anti-IL-12 treatment alters the skin microbiota during *L. major* infection, but not on naive skin, Related to Figure 3. (A) C57BL/6 mice were treated with an isotype or anti-IL-12 mAB twice a week. Swabs were collected prior to treatment and at 2 weeks post-treatment to assess the proportion of Staphylococcus spp. and Streptococcus spp. by 16S rRNA gene analysis. Data are representative of one independent experiment (n = 1 swab of each ear from 3 mice in each group). (B) Isotype and anti-Il-12 mAB treated mice were intradermally infected in the ear with *L. major* parasites. Swabs were collected for 16S rRNA gene sequencing at 0 weeks (before treatment and infection) and at 2, 4, and 6 weeks post-infection. Stacked bar charts represent the proportion of each taxa present within the samples. Data are representative of two independent experiments (n = 1 lesional swab from 10 mice in each group).



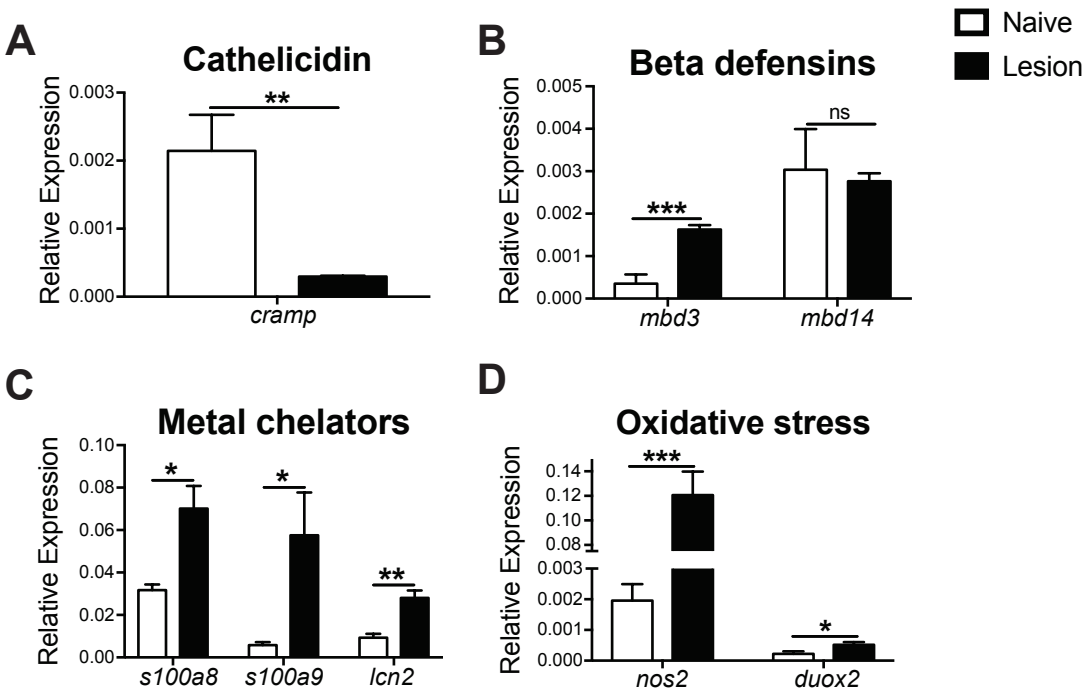
Supplemental Figure 3. Dysbiosis due to *S. xylosus* colonization does not alter the immune response or cytokine production in naive skin, Related to Figure 4. C57BL/6 mice were topically colonized with 10^8-10^9 *S. xylosus* every other day for a total of 4 applications; naïve mice were unassociated. Flow cytometry analysis was performed for the frequency and total cell number of (A) CD4+ T cells (B) CD8+ T cells (C) CD11b+ cells (D) CD11b+ IL-1β+ cells (E) Ly6G+ cells (F) CD4+ IFNγ+ and CD4+ IL-17+ and (G) TCRγδ+ IFNγ+ and TCRγδ+ IL-17+ cells in the ears of naïve or colonized mice 14 days post-association. Cells were pregated on live, singlet, CD45+ cells. Flow cytometry plots are representatives of each group. Data are representative of two independent experiments (n = 1 ear tissue from 4 mice in each group). ns = not significant.



Supplemental Figure 4. *S. xylosus* only exacerbates inflammation during a barrier breach, while *Streptococcus* does not, Related to Figure 5. (A) C57BL/6 mice were topically colonized with 10^8-10^9 CFU of *S. xylosus* prior to the sensitization phase or on each day of the challenge phase of DNFB treatment. Control mice were unassociated, then sensitized and challenged with DNFB. Bar graphs of skin cells depict the frequency of Ly6G+ cells present in the ear skin on day 8. Data are representative of one experiment (n = 1 ear tissue from 5 mice in each group). (B) C57BL/6 mice were topically associated with 10^8-10^9 CFU of an alpha hemolytic *Streptococcus* isolate or *S. xylosus* every other day for 4 applications and control C57BL/6 mice were left unassociated. The next day, all mice were treated on the belly with DNFB. Five days later, mice were challenged with DNFB. Bar graphs depict the frequency of Ly6G+ cells present in the ear skin. (C) Colony forming units were measured after skin homogenates were cultured on tryptic soy blood agar plates overnight from the ears of control and alpha hemolytic *Streptococcus* or *S. xylosus* associated mice. Data are representative of two independent experiments (n = 1 ear tissue from 5 mice in each group). (D) C57BL/6 mice were intradermally infected with *L. major*. At 3 weeks post-infection, mice were topically associated with 10^8-10^9 CFU of an alpha hemolytic *Streptococcus* isolate every other day for 4 applications and control C57BL/6 mice were left unassociated. Colony forming units were measured after skin homogenates were cultured on tryptic soy blood agar plates overnight from the ear skin of control and alpha hemolytic *Streptococcus* associated mice. (E) Lesion size and pathology were assessed after colonization. (F) Bar graphs of skin cells depict the frequency of Ly6G+ and IL-1β+ cells present in the ear skin. Data are representative of one experiment (For colonized naive mice, n = 1 ear tissue from 3 mice; for colonized infected mice, n = 1 ear tissue from 5 mice; for uncolonized control mice, n = 1 ear tissue from 5 mice). ns = not significant; *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; ****, $p < 0.0001$.



Supplemental Figure 5. Dysbiosis due to co-housing does not alter the immune response or cytokine production in naive skin, Related to Figure 6. Naïve C57BL/6 mice were co-housed with L. major infected mice for 6 weeks, while control naïve mice were housed separately. Cells were isolated from the ears of co-housed naïve mice and control naïve mice. Flow cytometry analysis was performed for the frequency and total cell number of (A) CD4+ T cells (B) CD8+ T cells (C) CD11b+ cells (D) CD11b+ IL-1β+ cells (E) Ly6G+ cells (F) CD4+ IFNγ+ and CD4+ IL-17+ and (G) TCRγδ+ IFNγ+ and TCRγδ+ IL-17+ cells in the ears of naïve or co-housed mice. Cells were pregated on live, singlet, CD45+ cells. Flow cytometry plots are representatives of each group. Data are representative of one experiment (Co-housed naïve, n = 1 ear tissue from 4 mice; control naïve, n = 1 ear tissue from 5 mice). ns = not significant.



Supplemental Figure 6. *L. major* infection alters the expression of antimicrobial peptides in the skin, Related to Figure 1. C57BL/6 mice were intradermally infected with *L. major* in the ear for 5 weeks. Ear skin was harvested from naive and infected mice and mRNA expression was assessed for (A) the murine cathelicidin gene, (B) beta defensin genes, (C) metal chelators genes and (D) oxidative stress genes. Data are representative of two independent experiments (For naive group, n = 1 ear tissue from 4 mice; for infected mice n = 1 ear tissue from 7 mice). ns = not significant; *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$.

Subject ID	Sex	Age	Body Site	Lesion Size (mm2)	Duration of Lesion (Days)	Skin Test (mm2)
1	Male	22	Leg	396	30	440
2	Male	43	Neck	216	30	225
3	Male	18	Ankle	NA	40	300
4	Male	24	Leg	225	40	144
5	Male	20	Leg	660	90	725
6	Male	16	Back	500	30	440
7	Female	30	Leg	544	21	225
8	Male	36	Thigh	437	30	Negative
9	Male	31	Face	840	60	300
10	Male	22	Arm	49	30	400
11	Female	24	Thigh	25	30	210
12	Female	39	Leg	70	30	130
13	Male	22	Leg	3300	40	110
14	Female	45	Leg	180	30	378
15	Male	26	Leg	90	10	260
16	Male	21	Arm	200	60	400
17	Female	33	Leg	380	40	NA
18	Male	21	Leg	780	21	228
19	Female	20	Leg	80	30	100
20	Male	29	Leg	500	60	180
21	Female	35	Leg	100	60	255
22	Male	37	Foot	24	60	300
23	Female	26	Arm	130	30	285
24	Male	25	Leg	150	21	180
25	Male	50	Leg	270	30	272
26	Male	55	NA	1575	60	1085
27	Male	18	Head	192	34	130
28	Male	19	Leg	480	14	208
29	Female	24	Abdomen	325	NA	700
30	Male	40	Leg	130	20	460
31	Male	57	Leg	35	45	132
32	Male	18	Leg	49	20	400
33	Male	19	Foot	306	15	441
34	Male	28	Leg	25	15	49
35	Male	39	Leg	77	30	255
36	Male	31	Leg	330	90	130
37	Female	24	Leg	1476	60	625
38	Male	63	Leg	272	20	196
39	Male	20	Arm	1377	45	225
40	Female	16	Chest	30	20	156
41	Female	24	Back	255	30	144
42	Female	64	Leg	216	30	NA
43	Male	33	Abdomen	207	40	289
44	Male	59	Thigh	340	90	255

Supplemental Table 1. Information about samples collected from cutaneous leishmaniasis patients, Related to Figure 1. Swabs were collected from these cutaneous leishmaniasis patients prior to treatment. All cutaneous leishmaniasis patients were seen at the health post in Corte de Pedra, Bahia, Brazil, which is a well-known area of L. braziliensis transmission. The criteria for diagnosis were a clinical picture characteristic of cutaneous leishmaniasis in conjunction with parasite isolation or a positive delayed-type hypersensitivity response to Leishmania antigen, plus histological features of cutaneous leishmaniasis.

Taxa	Cluster 1	Cluster 2	Cluster 3
Staphylococcus aureus	0.788992731	0.16077901	0.049802691
Unclassified Streptococcus 1	0.022511662	0.11087683	0.814618671
Unclassified Bacilli	0.04901982	0.10691883	0.018451401
Unclassified Gemellales	0.030965307	0.06667456	0.013448359
Unclassified Staphylococcus 1	0.013819064	0.06478127	0.005975455
Bacillus flexus	0.002613152	0.06594624	0.00479366
Unclassified Staphylococcus 2	0.010710605	0.02253503	0.004936899
Unclassified Streptococcus 2	0.007199348	0.0130796	0.01322084
Unclassified Bacillales	0.002463076	0.02473744	0.001617316
Staphylococcus epidermidis	0.001303855	0.02767135	0.001574108

Supplemental Table 2. DMN Clusters top 10 discriminating taxa, Related to Figure 1.
Bacteria represent the top 10 discriminating taxa present in each DMN cluster. Numbers depict the proportion of each taxa in clusters 1-3.

Primer	Sequence
Rps11, forward	5’-CGTGACGAAGATGAAGATGC-3’
Rps11, reverse	5’-GCACATTGAATCGCACAGTC-3
Il17, forward	5'-CATGAGTCCAGGGAGAGCTT-3'
Il17, reverse	5'-GCTGAGCTTTGAGGGATGAT-3'
Tnfa, forward	5'-TCACTGGAGCCTCGAATGTC-3'
Tnfa, reverse	5'-GTGAGGAAGGCTGTGCATTG-3'
Il1b, forward	5'-TTGACGGACCCCAAAAGAT-3’
Il1b, reverse	5’- GATGTGCTGCTGCGAGATT-3’
Cxcl1, forward	5'-GCACCCAAACCGAAGTCATA-3'
Cxcl1, reverse	5'-CTTGGGGACACCTTTTAGCA-3'
Ccl2, forward	5’-GCTTCTGGGCCTGCTGTTCA-3
Ccl2, reverse	5’-AGCTCTCCAGCCTACTCATT-3’

Supplemental Table 3. Oligonucleotide sequences, Related to Figure 4.
Primers used for RT-PCR on whole ear skin tissue.