TABLE 1 Patient characteristics at time of fecal collection, stratified by CD4 lymphocyte count

		CD4 lymphocyte count at time of fecal collection		
Characteristic	Total	< 350 cells/μL (low)	> 350 cells/μL (high)	*p**
number of participants (%)	49 (100)	14 (28.6)	35 (71.4)	
Female (%)	5 (10.2)	1 (7.1)	4 (11.4)	0.654
Age at time of fecal collection (years) [median (IQR)]	48 [39-61]	57 [48-62]	45 [39-57]	0.132
CD4 lymphocyte count at the time of fecal collection [median (IQR)]	459 [302-669]	240 [203-279]	615 [441-693]	<0.001
HIV transmission [n (%)]				0.125
MSM	31 (63.3)	7 (50.0)	24 (68.6)	
Heterosexual	15 (30.6)	7 (50.0)	8 (22.9)	
Blood products	3 (6.1)	0 (0)	3 (8.6)	
Ethnicity [n (%)]				
Asian	49 (100)	14 (28.6)	35 (71.4)	
cART duration (months) [median (IQR)]	79 [48-119]	59 [45-120]	85 [52-116]	0.550
Nadir CD4 lymphocyte count [median (IQR)]	185 [81-245]	102 [42-140]	204 [125-287]	0.003
Time since nadir CD4 (months) [median (IQR)]	61 [35-75]	51 [16-62]	62 [46-73]	0.135
Prior clinical AIDS [n (%)]	23 (46.9)	10 (71.4)	13 (37.1)	0.030
CVD risks				
Smoking, ever [n (%)]	10 (20.4)	1 (7.1)	9 (25.7)	0.145
Hypertention [n (%)]	8 (16.3)	5 (35.7)	3 (8.6)	0.020
Diabetes mellitus [n (%)]	3 (6.1)	1 (7.1)	2 (5.7)	0.851
Dyslipidaemia [n (%)]	6 (12.2)	1 (7.1)	5 (14.3)	0.491
Body mass index (kg/m^2) [median (IQR)]	23.5 [21.9-25.9]	22.4 [21.0-24.1]	24.2 [22.5-26.4]	0.043
number on cART regimen				
INTSTI [n (%)]	33 (67.3)	11 (78.6)	22 (62.9)	0.289
NRTI [n (%)]	48 (98.0)	14 (100)	34 (97.1)	0.232
NNRTI [n (%)]	6 (12.2)	1 (7.1)	5 (14.3)	0.491
PI [n (%)]	13 (23.5)	2 (14.3)	11 (31.4)	0.219

cART, combination antiretroviral therapy; CVD, cardiovascular disease; IQR, interquartile range; MSM, men who have sex with men; INTSTI, integrase strand transfer inhibitor; NRTI, nucleoside reverse transcriptaseinhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

*Nonparametric test for trend across CD4 count categories.

TABLE 2 Bacteria taxa ranked within the top 20 by relative abundance in patients with HIV infection

Bacterial taxa	Relative abundance (%)	
	HIV >350	HIV<350
Ranked within the top 20 in all two groups		
p, Firmicutes; c, Clostridia; o, Lachnospirales; f, *Lachnospiraceae*; g, *Blautia*	13.02	10.55
p, Actinobacteriota; c, Actinobacteria; o, Bifidobacteriales; f, *Bifidobacteriaceae*; g, *Bifidobacterium*	12.29	16.12
p, Firmicutes; c, Clostridia; o, Oscillospirales; f, *Ruminococcaceae*; g, *Faecalibacterium*	7.37	5.22
p, Actinobacteriota; c, Coriobacteriia; o, Coriobacteriales;f, *Coriobacteriaceae*; g, *Collinsella*	5.26	2.56
p, Firmicutes; c, Clostridia; o, Lachnospirales; f, *Lachnospiraceae*; g, *[Ruminococcus]_torques_group*	4.35	2.51
p, Firmicutes; c, Clostridia; o, Lachnospirales; f, *Lachnospiraceae*; g, *Dorea*	4.08	2.86
p, Firmicutes; c, Clostridia; o, Lachnospirales; f, Lachnospiraceae; g, *Agathobacter*	3.36	5.55
p, Firmicutes; c, Clostridia; o, Oscillospirales; f, *Ruminococcaceae*; g, *Subdoligranulum*	2.71	4.16
p, Firmicutes; c, Bacilli; o, Erysipelotrichales; f, *Erysipelotrichaceae*; g, *Holdemanella*	2.67	1.15
p, Firmicutes; c, Clostridia; o, Lachnospirales; f, *Lachnospiraceae*; g, *Fusicatenibacter*	2.52	4.25
p, Firmicutes; c, Bacilli; o, Lactobacillales; f, *Streptococcaceae*; g, *Streptococcus*	2.35	2.08
p, Bacteroidota; c, Bacteroidia; o, Bacteroidales; f, *Bacteroidaceae*; g, *Bacteroides*	2.21	3.98
p, Firmicutes; c, Clostridia; o, Oscillospirales; f, *[Eubacterium]_coprostanoligenes_group*; g, *[Eubacterium]_coprostanoligenes_group*	1.87	2.16
p, Firmicutes; c, Clostridia; o, Lachnospirales; f, *Lachnospiraceae*	1.79	3.14
p, Firmicutes; c, Clostridia; o, Lachnospirales; f, *Lachnospiraceae*; g, *Lachnoclostridium*	1.39	1.18
p, Firmicutes; c, Clostridia; o, Lachnospirales; f, *Lachnospiraceae*; g, *[Ruminococcus]_gnavus_group*	1.20	3.92
Ranked within the top 20 only in HIV patients with CD4 counts above 350		
p, Bacteroidota; c, Bacteroidia; o, Bacteroidales; f, *Prevotellaceae*; g, *Prevotella_9*	3.62	1.15
p, Firmicutes; c, Bacilli; o, Erysipelotrichales; f, *Erysipelatoclostridiaceae*; g, *Catenibacterium*	3.44	0.80
p, Firmicutes; c, Negativicutes; o, Veillonellales-Selenomonadales; f, *Selenomonadaceae*; g, *Megamonas*	3.09	0.20
p, Firmicutes; c, Negativicutes; o, Veillonellales-Selenomonadales; f, *Veillonellaceae*; g, *Megasphaera*	1.42	1.03
Ranked within the top 20 only in HIV patients with CD4 counts below 350		
p, Firmicutes; c, Bacilli; o, Lactobacillales; f, *Enterococcaceae*; g, *Enterococcus*	1.49	4.51
p, Firmicutes; c, Clostridia; o, Lachnospirales; f, *Lachnospiraceae*; g, *Anaerostipes*	1.92	3.74
p, Firmicutes; c, Clostridia; o, Lachnospirales; f, *Lachnospiraceae*; g, *Coprococcus*	1.13	1.47
p, Firmicutes; c, Clostridia; o, Oscillospirales; f, *Ruminococcaceae*; g, *Ruminococcus*	0.86	1.30

p, phylum; c, class; o, order; f, family; g, genus.

HIV>350, HIV patients with CD4 counts above 350 cells/μL; HIV<350, HIV patients with CD4 counts below 350 cells/μL.

Figure 1A: Alpha diversity (observed OTUs and chao1) in the high and low CD4 groups

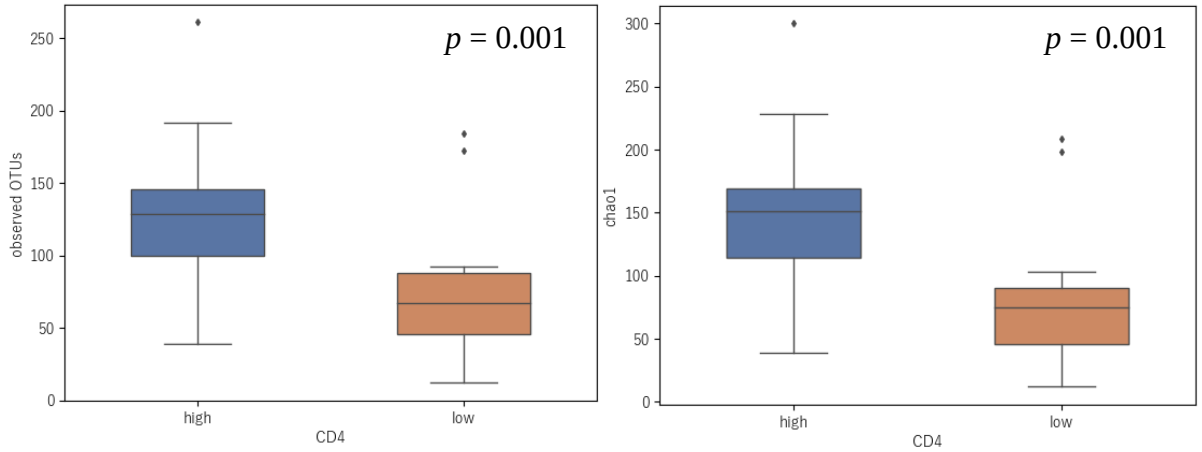


Figure 1B: Correlation between alpha diversity (chao1) and CD4 or nadir CD4 in HIV patients

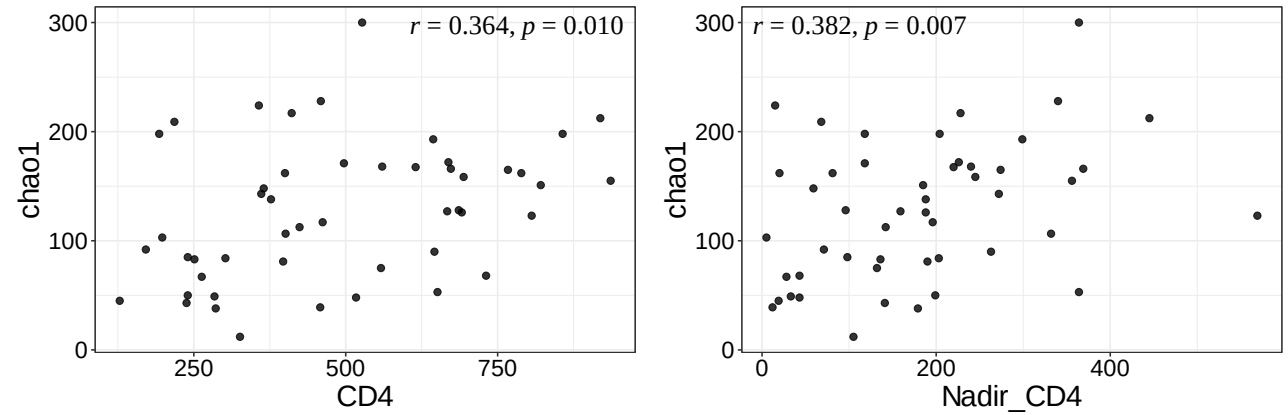


Figure 1C: Beta diversity comparisons between the low and high CD4 groups (Unweighted UniFrac : $p = 0.002$)

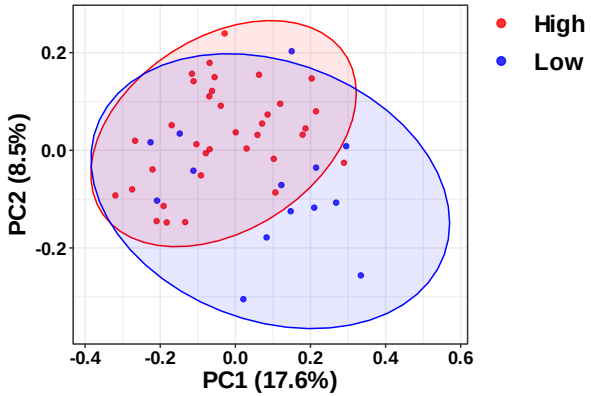


Figure 2: Heat map of significantly different bacterial flora composition between the low and high CD4 groups. Color intensity indicates row-scaled (z-score) relative abundance.

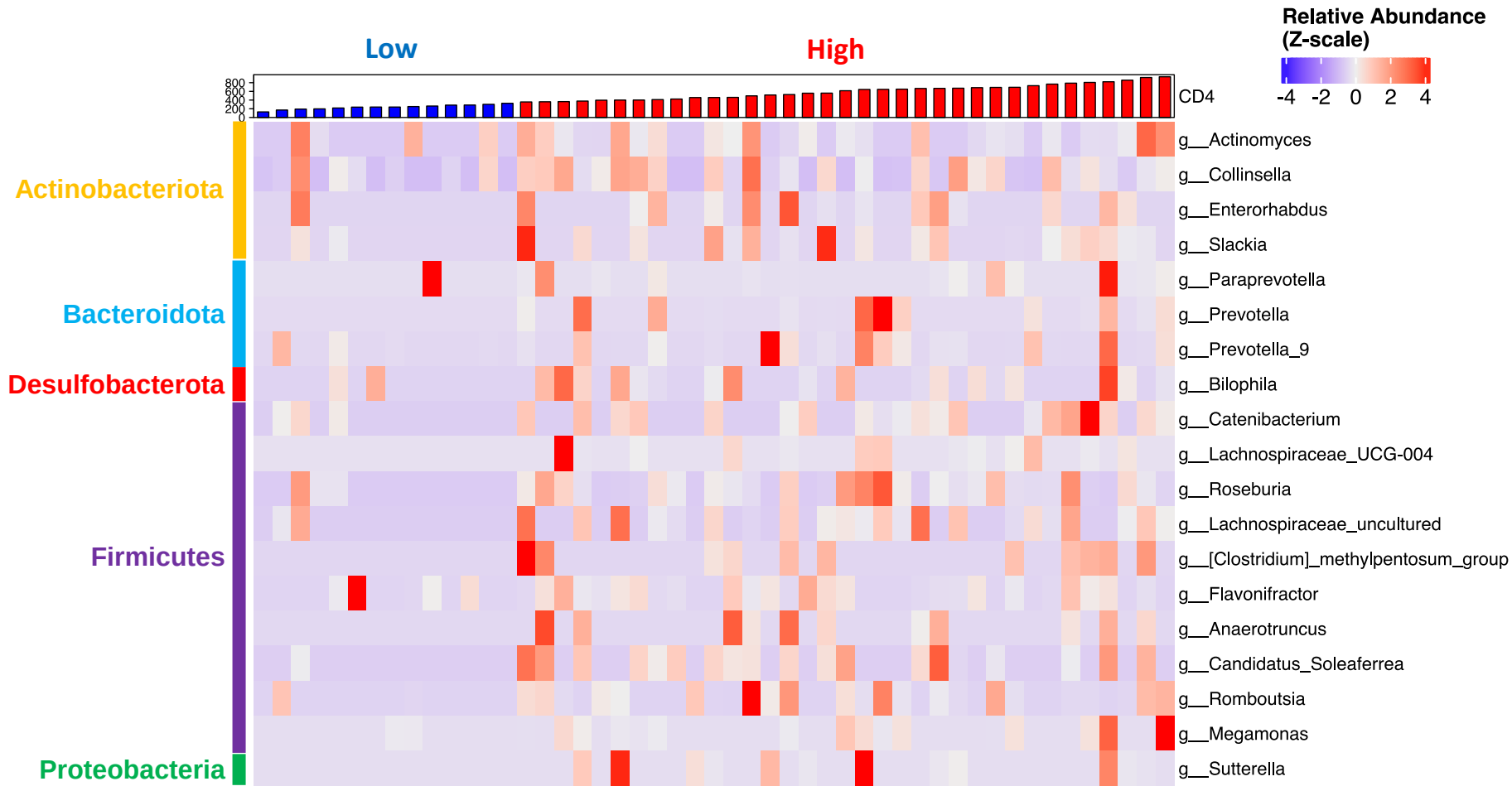


Figure 3A: The amount of organic acids in feces in the low and high CD4 groups.

The number above each bar is the *p*-value between the two groups.

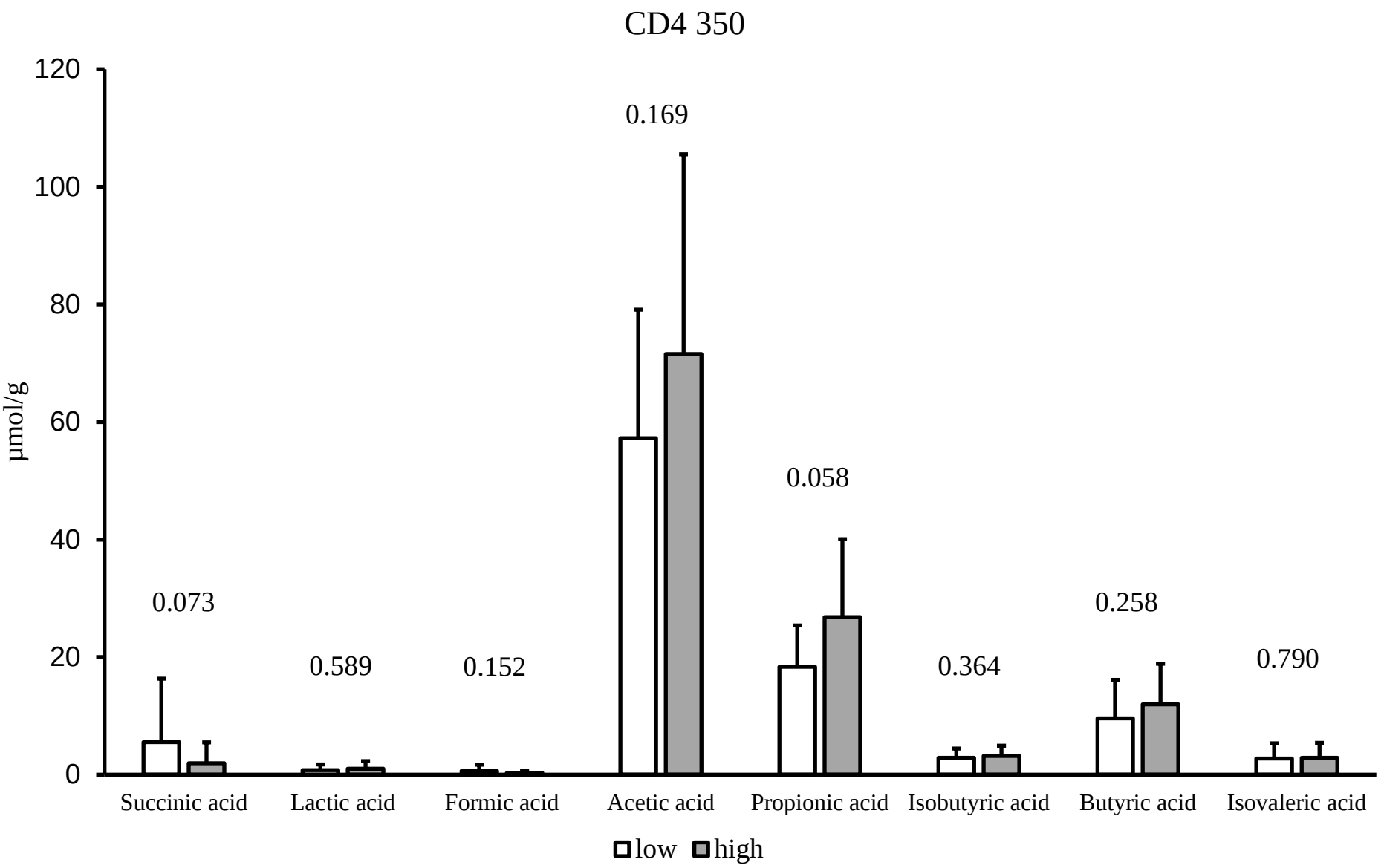


Figure 3B

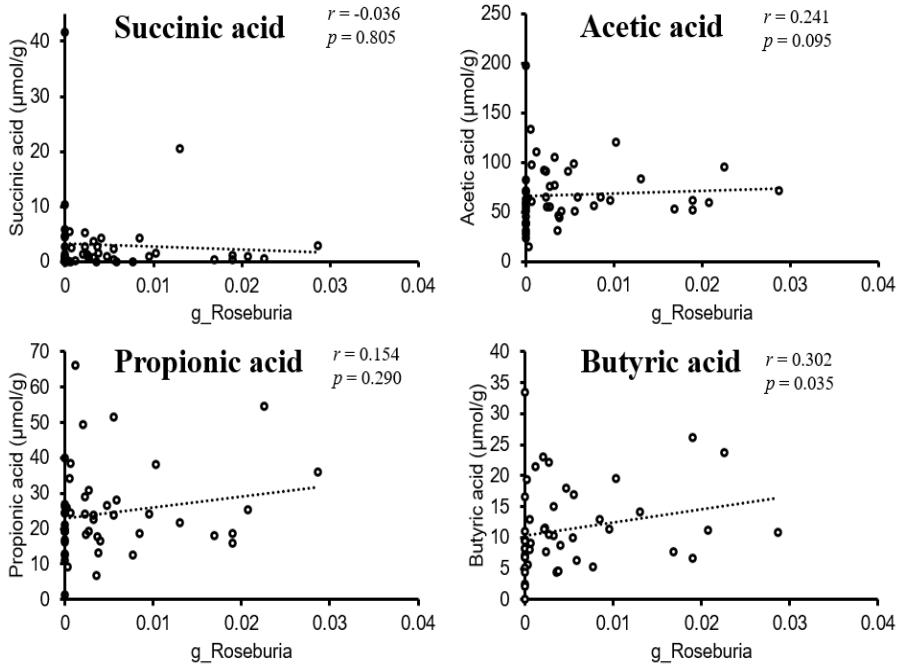


Figure 3C

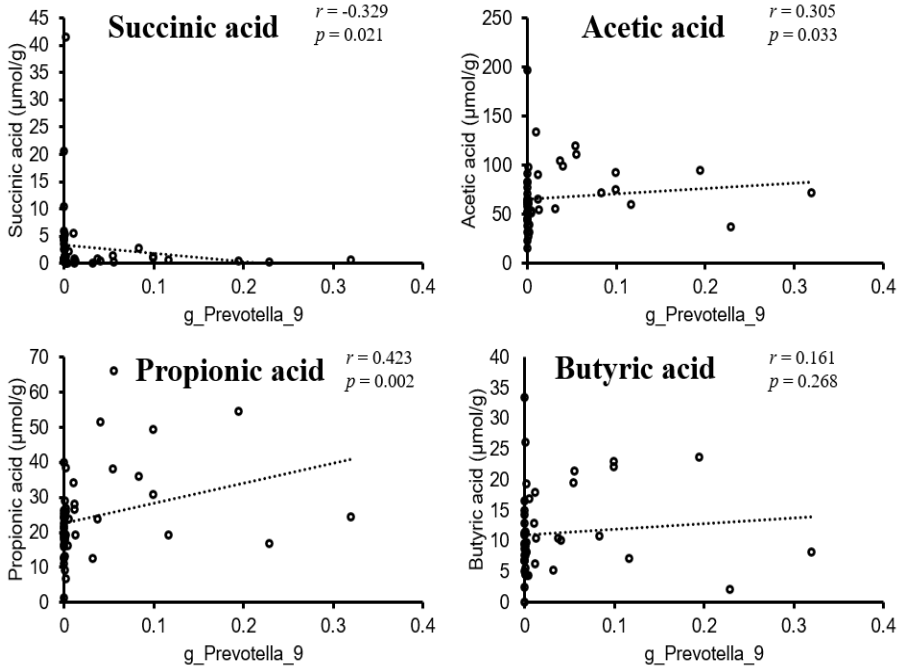


Figure 3D

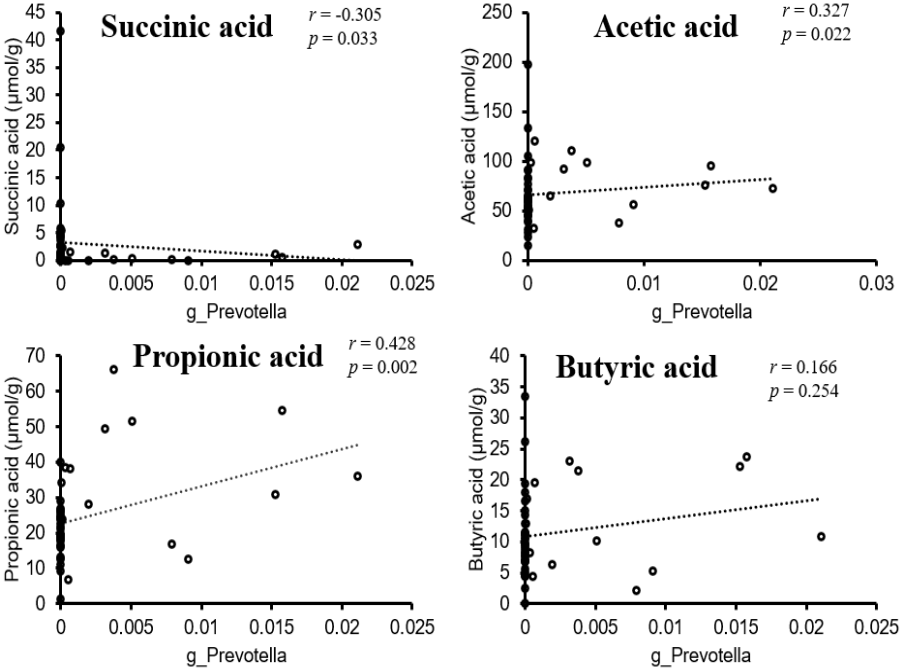
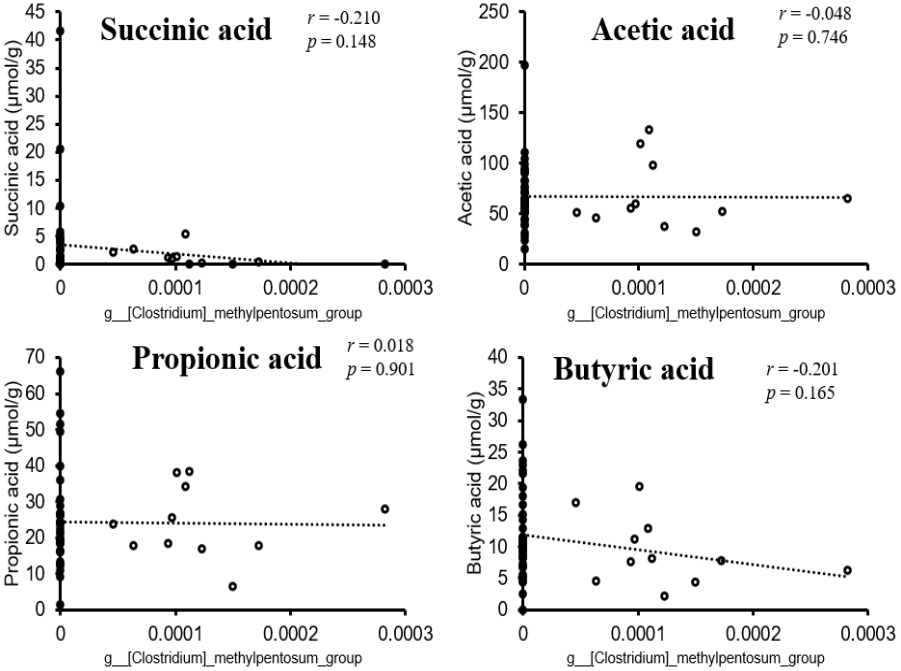


Figure 3E



Supplementary Table 1

Bacteria taxa ranked within the top 5 phyla by relative abundance in patients with HIV infection

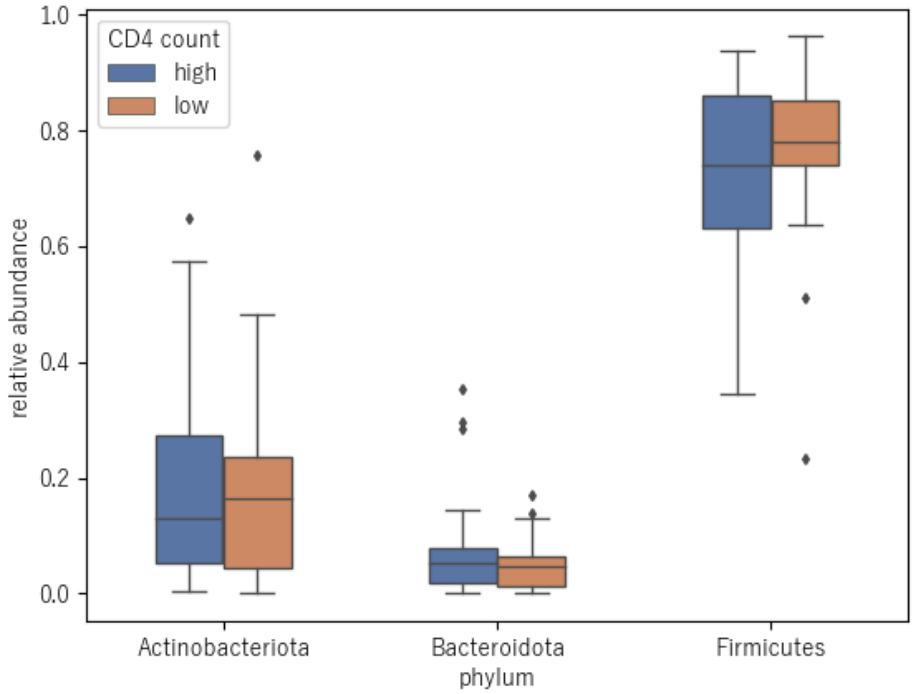
Bacterial taxa	Relative abundance (%)
	all
Phylum	
Firmicutes	72.58
Actinobacteria	18.85
Bacteroidota	6.59
Proteobacteria	1.71
Fusobacteriota	0.02

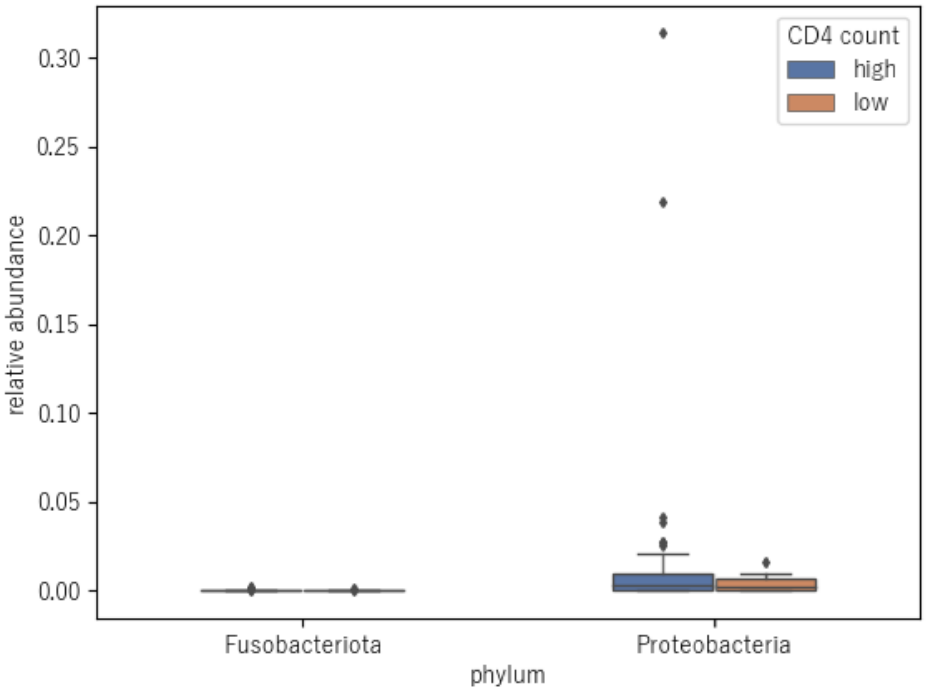
Supplementary Table 2

Correlations between the bacteria species treated in Figure 3 and various organic acids

	Succinic acid		Lactic acid		Formic acid		Acetic acid		Propionic acid		Isobutyric acid		Butyric acid		Isovaleric acid		total organic acids	
taxonomy	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p
g__Roseburia	-0.036	0.805	-0.131	0.368	-0.017	0.906	0.241	0.095	0.154	0.290	0.218	0.132	0.302	0.035	0.139	0.340	0.144	0.323
g__Prevotella	-0.305	0.033	0.175	0.229	-0.076	0.605	0.327	0.022	0.428	0.002	-0.011	0.939	0.166	0.254	-0.093	0.525	-0.077	0.597
g__Prevotella_9	-0.329	0.021	0.156	0.284	-0.086	0.555	0.305	0.033	0.423	0.002	-0.035	0.813	0.161	0.268	-0.037	0.801	-0.004	0.980
g__[Clostridium]_methylpentosum_group	-0.210	0.148	0.242	0.094	0.144	0.322	-0.048	0.746	0.018	0.901	-0.024	0.870	-0.201	0.165	0.055	0.710	0.048	0.744

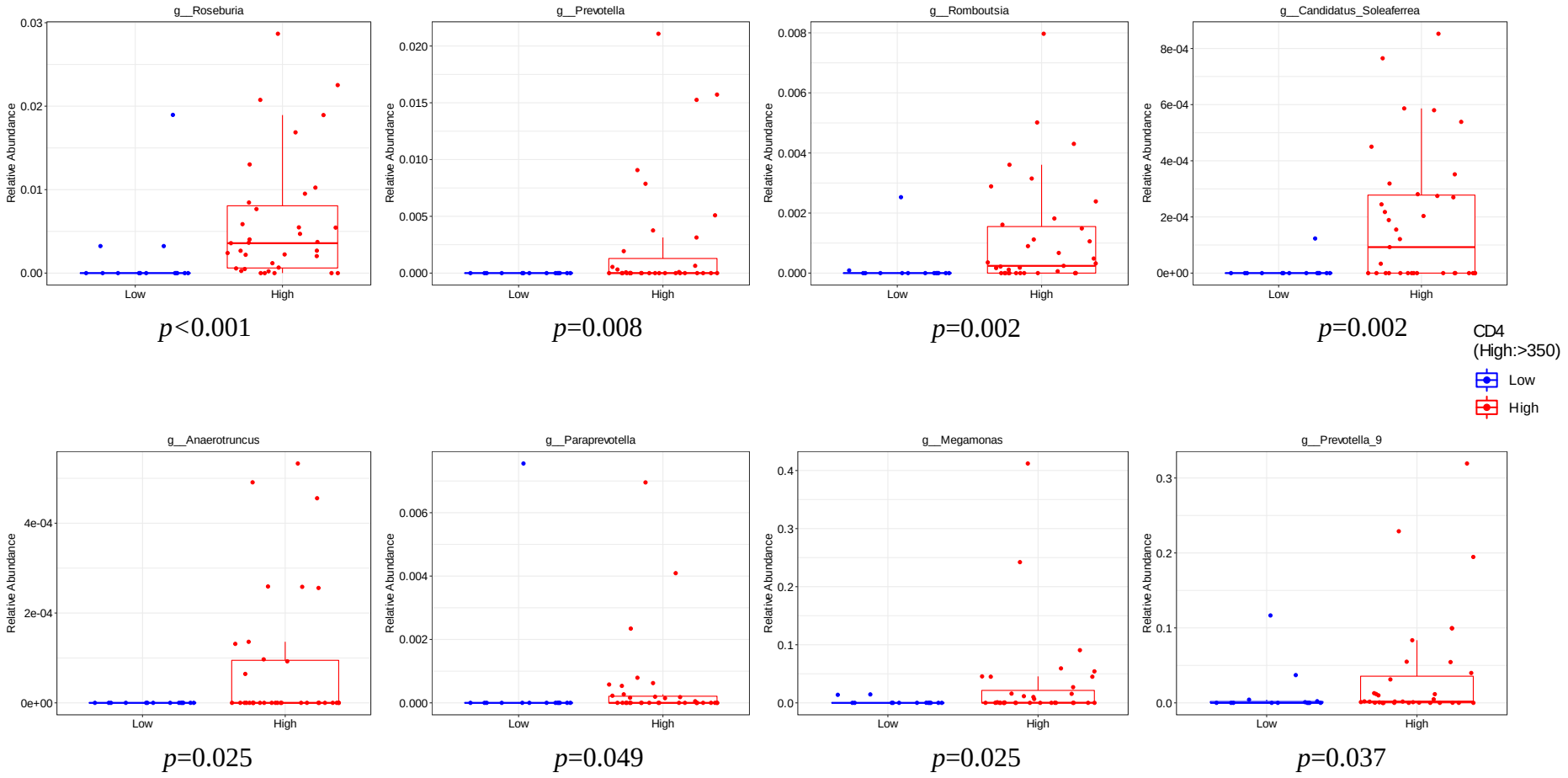
Supplementary Figure 1: Correlation between bacteria taxa at the phylum level and CD4 counts





Actinobacteria: $p = 0.903$
Bacteroidota: $p = 0.619$
Firmicutes: $p = 0.543$
Fusobacteriota: $p = 0.568$
Proteobacteria: $p = 0.485$

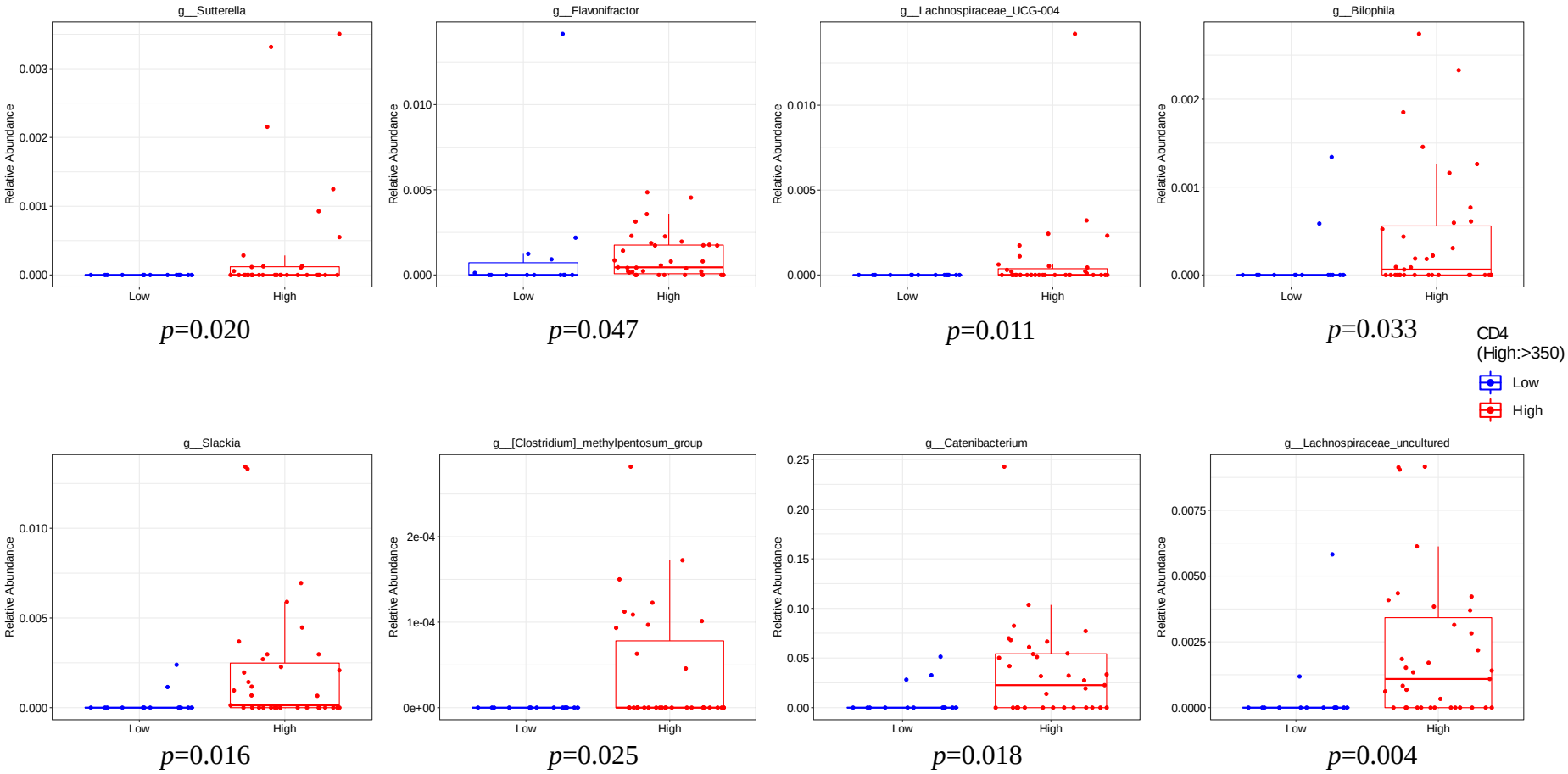
Supplementary Figure 2: The boxplot of bacterial taxa treated in Figure 2 between the low and high CD4 groups



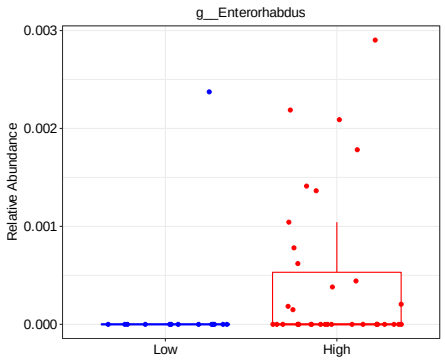
p<0.001 *p*=0.008 *p*=0.002 *p*=0.002

p=0.025 *p*=0.049 *p*=0.025 *p*=0.037

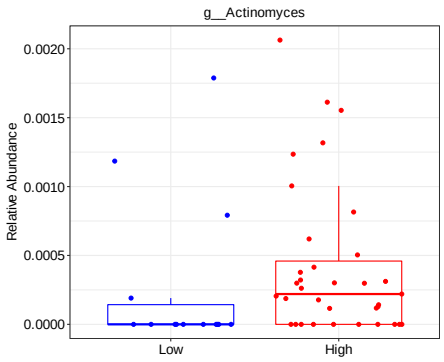
Supplementary Figure 2: The boxplot of bacterial taxa treated in Figure 2 between the low and high CD4 groups



Supplementary Figure 2: The boxplot of bacterial taxa treated in Figure 2 between the low and high CD4 groups



p=0.046



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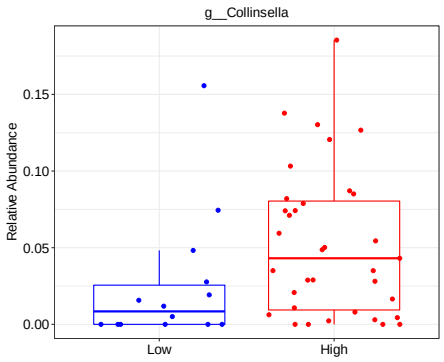

p=0.018