Cytokine_Analysis

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9/21/2018

Statistical Analysis

I wrote a function called pvals which evaluates the relevant two sample two-tailed p-values using the non-parametric Mann Whitney test (the command is wilcox.test in R). The function then corrects for multiple comparisons in two ways. The first uses a Bonferonni correction to control the Family Wise Error Rate. The second controls the False Discovery Rate, the expected proportion of false discoveries amongst the rejected hypotheses. The false discovery rate is a less stringent condition than the family-wise error rate, so these methods are more powerful than the others. The function is below if you would like to see the details.

```r
pvals<-function(data, column){

    data<-filter(data, SM!="N")
    data$SM<-factor(data$SM, levels=c("X","SM"))
    data$TB<-factor(data$TB, levels=c("HC","LTBI","TB"))

    x<-split(data,data$TB)
    A<-lapply(x, function(g) wilcox.test(g[,column]~g[,"SM"]))

    y<-split(data,data$SM)
    B<-lapply(y, function(g)
        wilcox.test((g[,column]~g[,"TB"]), subset=g$TB %in% c("HC", "LTBI")))
    C<- lapply(y, function(g)
        wilcox.test((g[,column]~g[,"TB"]), subset=g$TB %in% c("LTBI", "TB")))
    D<- lapply(y, function(g)
        wilcox.test((g[,column]~g[,"TB"]), subset=g$TB %in% c("HC", "TB")))

    labels<-c("HC SM+ to HC SM-", "LTBI SM+ to LTBI SM-", "TB SM+ to TB SM-",
             "HC SM+ to LTBI SM+", "LTBI SM+ to TB SM+", "HC SM+ to TB SM+",
             "HC SM- to LTBI SM-", "LTBI SM- to TB SM-", "HC SM- to TB SM-"
    )
    pvals<-c(A$HC$p.value, A$LTBI$p.value, A$TB$p.value,
            B$SM$p.value, C$SM$p.value,  D$SM$p.value,
            B$X$p.value,  C$X$p.value,   D$X$p.value)

    bonf_adj_pvals<-round(p.adjust(pvals, method="bonferroni"), 4)

    fdr_adj_pvals<-round(p.adjust(pvals, method="fdr"), 4)

    table<-(cbind(labels, round(pvals, 4), bonf_adj_pvals, fdr_adj_pvals))
    colnames(table)<-c("Comparison", paste(column,"p-values"," "),
                    "Bonferonni Corrected p-values", "FDR Corrected p-vales")
    table
}
```
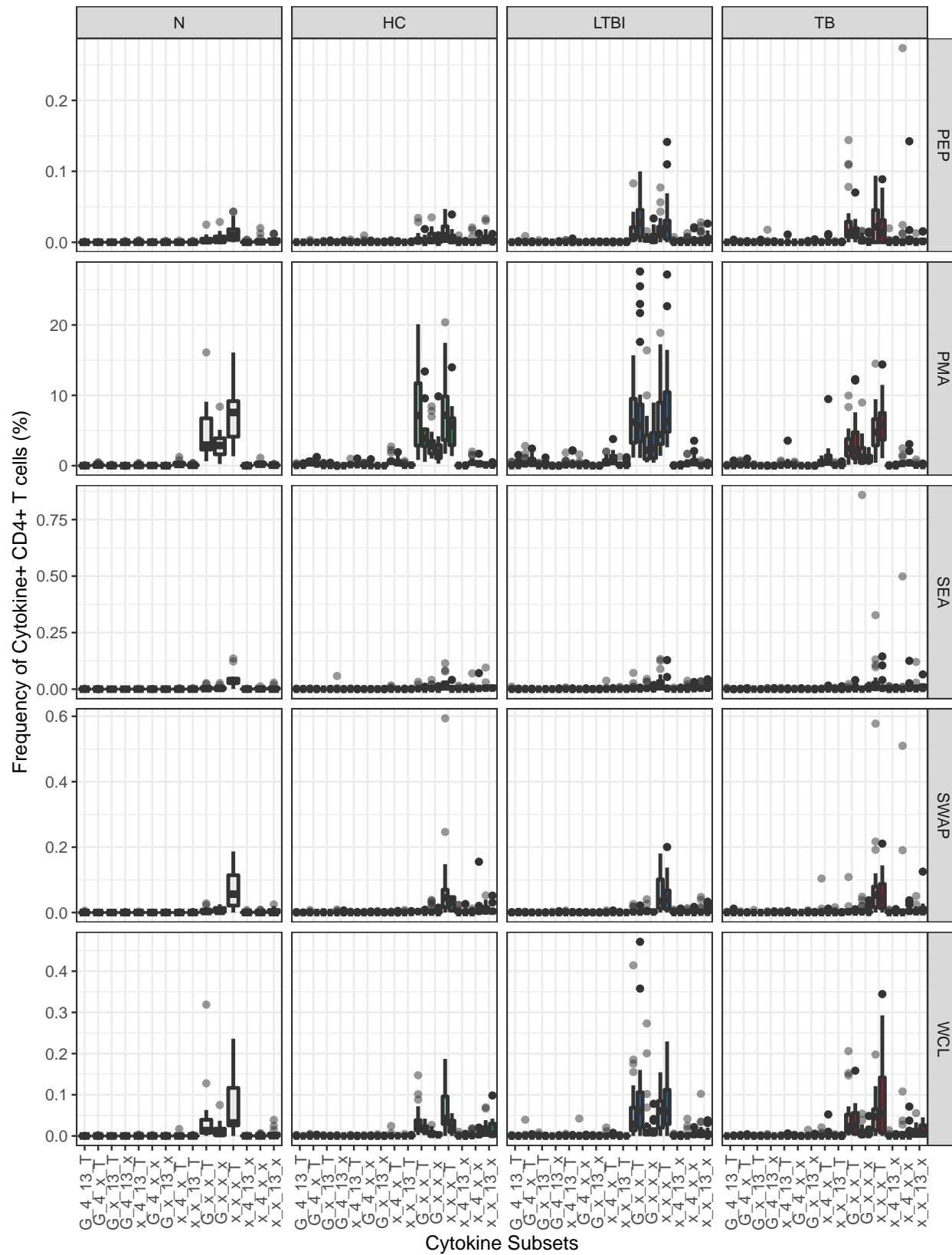
Boolean Graphs

The first graph is just meant to give a snapshot of all the data at once to see if there are weird anomalous data points that we will have to examine. I did not include all the individual data points on any of the graphs because it made it incredibly cluttered looking, however I did allow outliers to display.
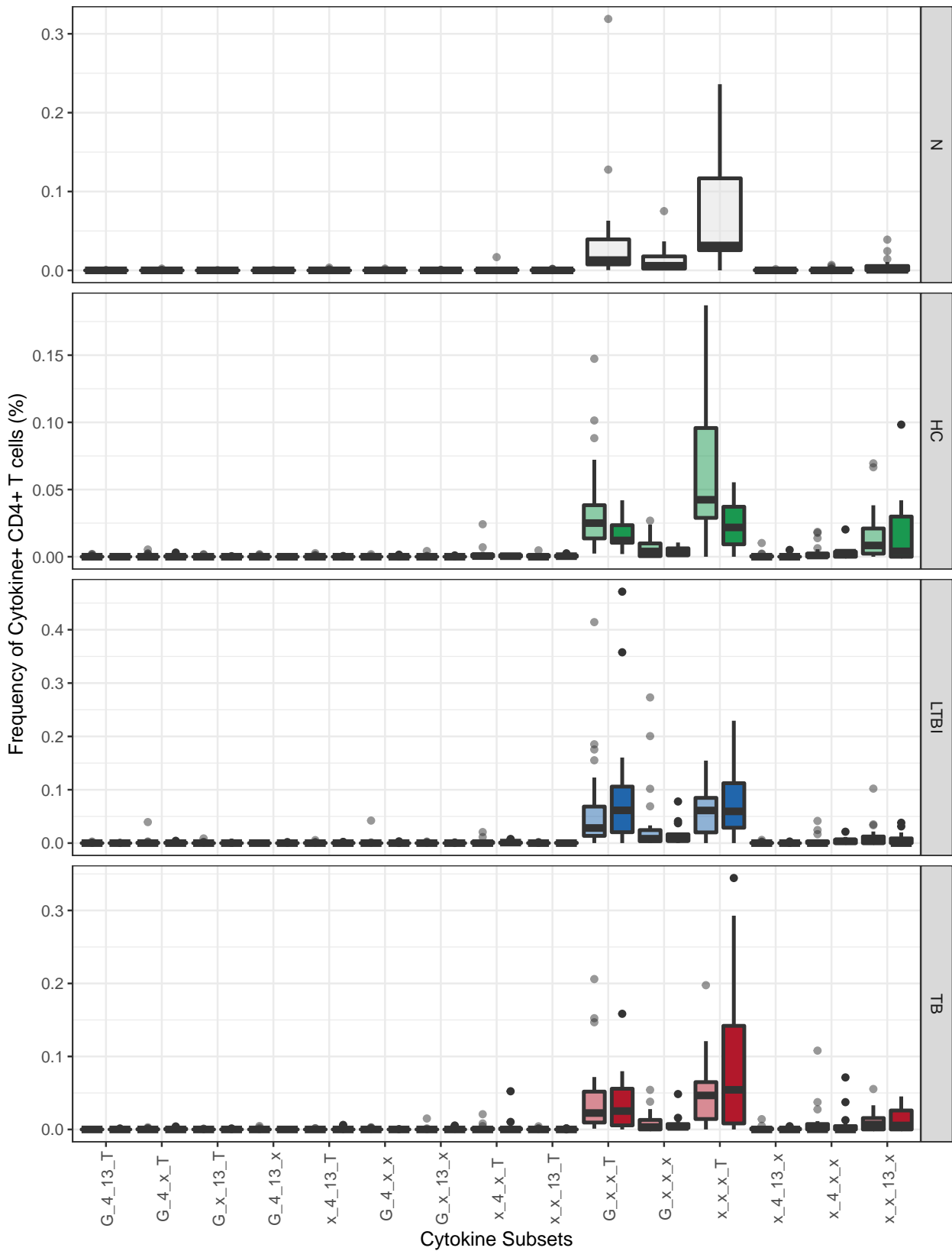
Cytokine Frequencies

PMA Cytokine Frequencies
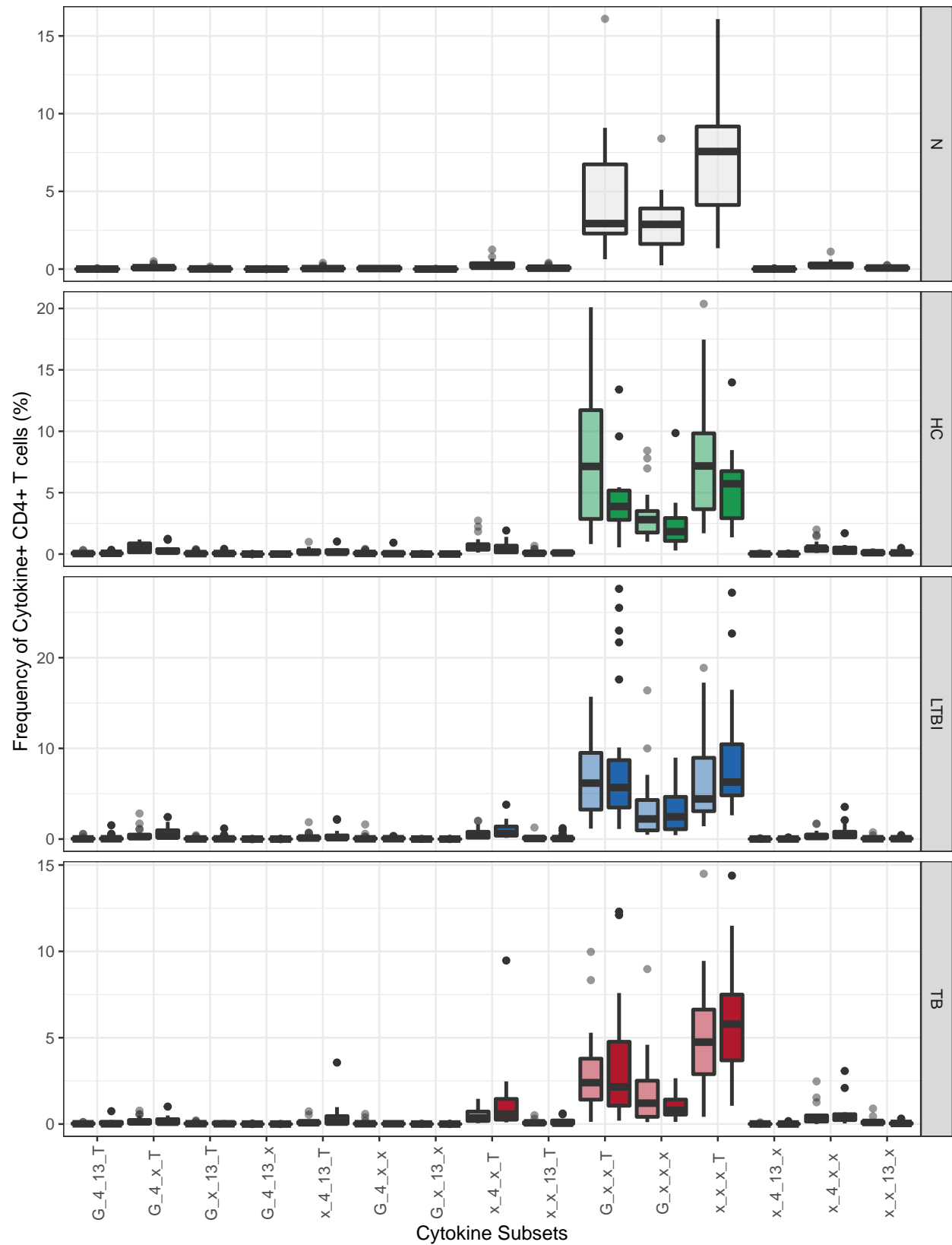
WCL Cytokine Frequencies

PEP Cytokine Frequencies
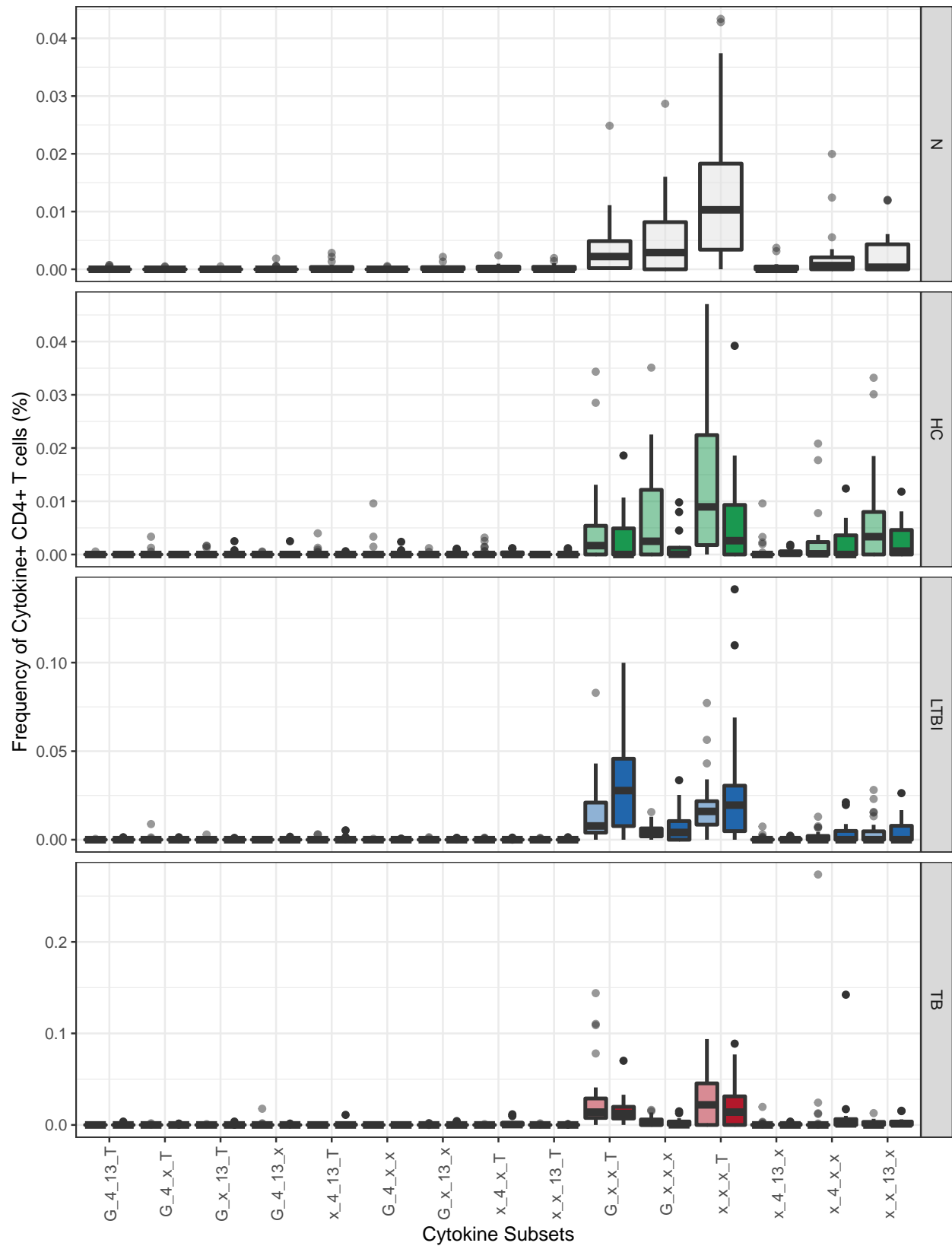
SEA Cytokine Frequencies
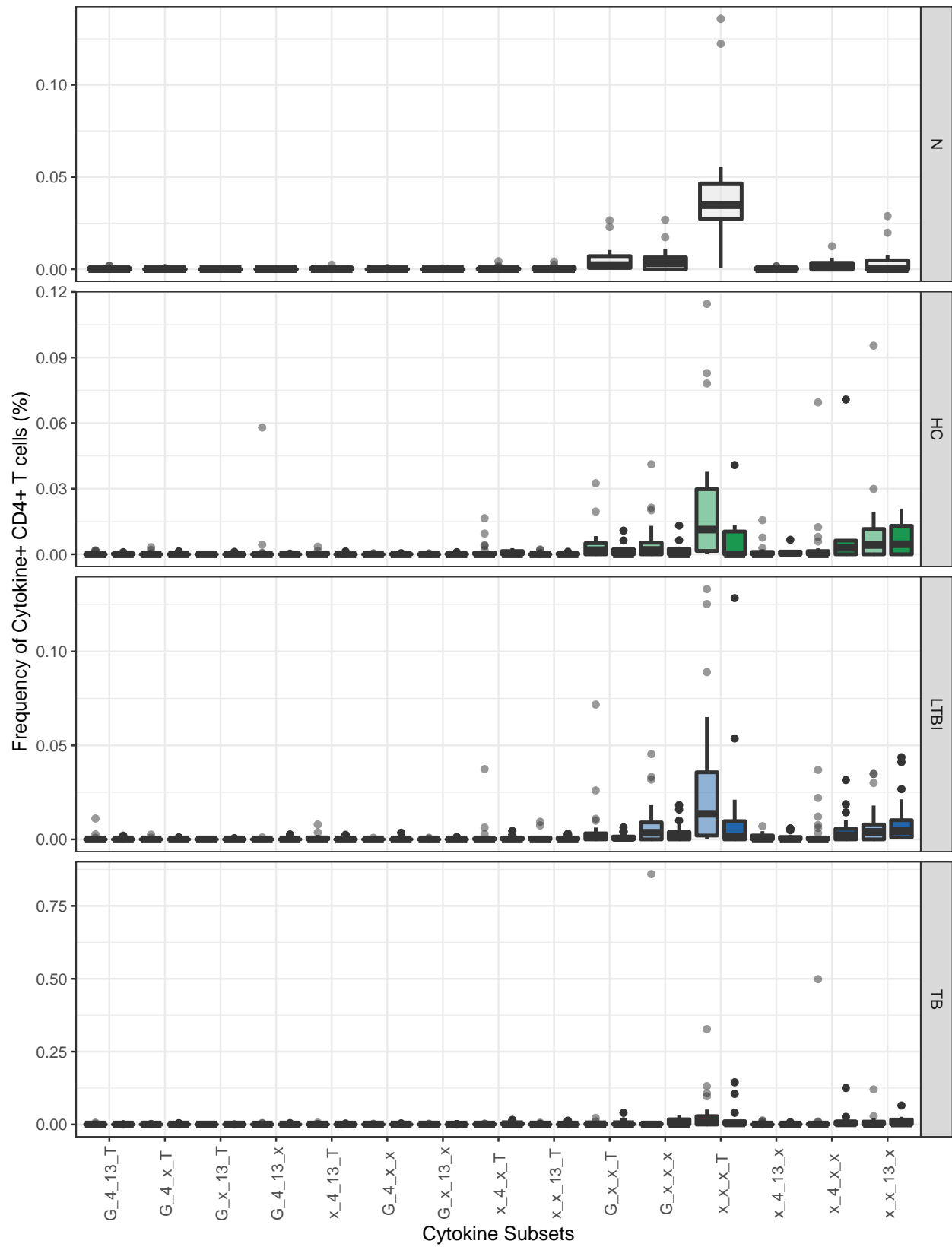
SWAP Cytokine Frequencies
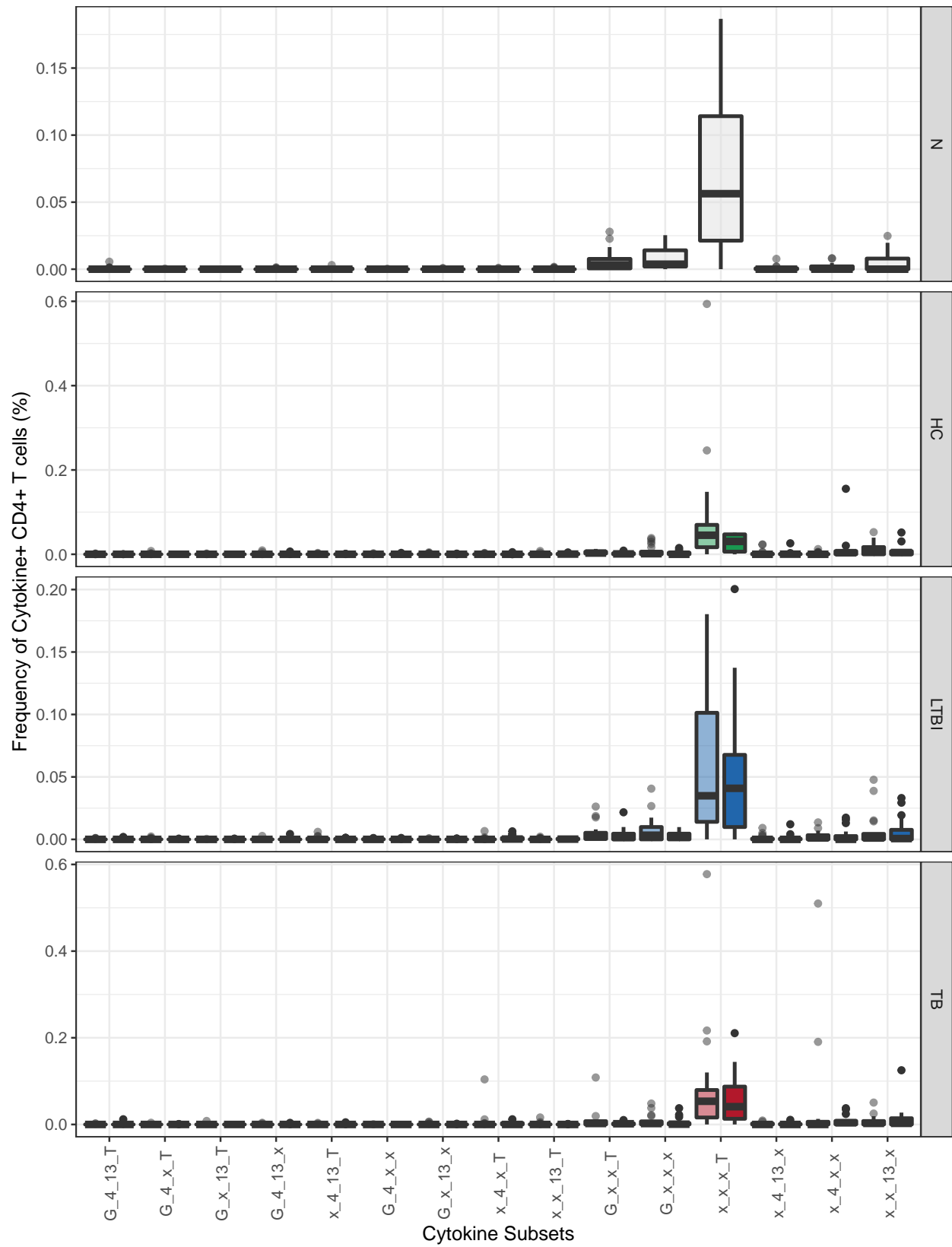
T cell Lineage Specific Grouped Analysis

These are my standard lineage specific groups.

	TH1 Type 1 Cytokines Only			TH2 Type 2 Cytokines Only			TH1/2 Any Combination of Type 1 and 2 Cytokines						
IFNγ	X	X					X	X	X	X			
TNFα	X		X				X	X	X		X	X	X
IL-4				X	X		X	X		X	X	X	
IL-13				X		X	X		X	X	X		X

Figure 1: Breakdown of Cytokine Definitions

Non Specific CD4+ T cell Responses

Table 1: Non Specific CD4+ T cell Responses

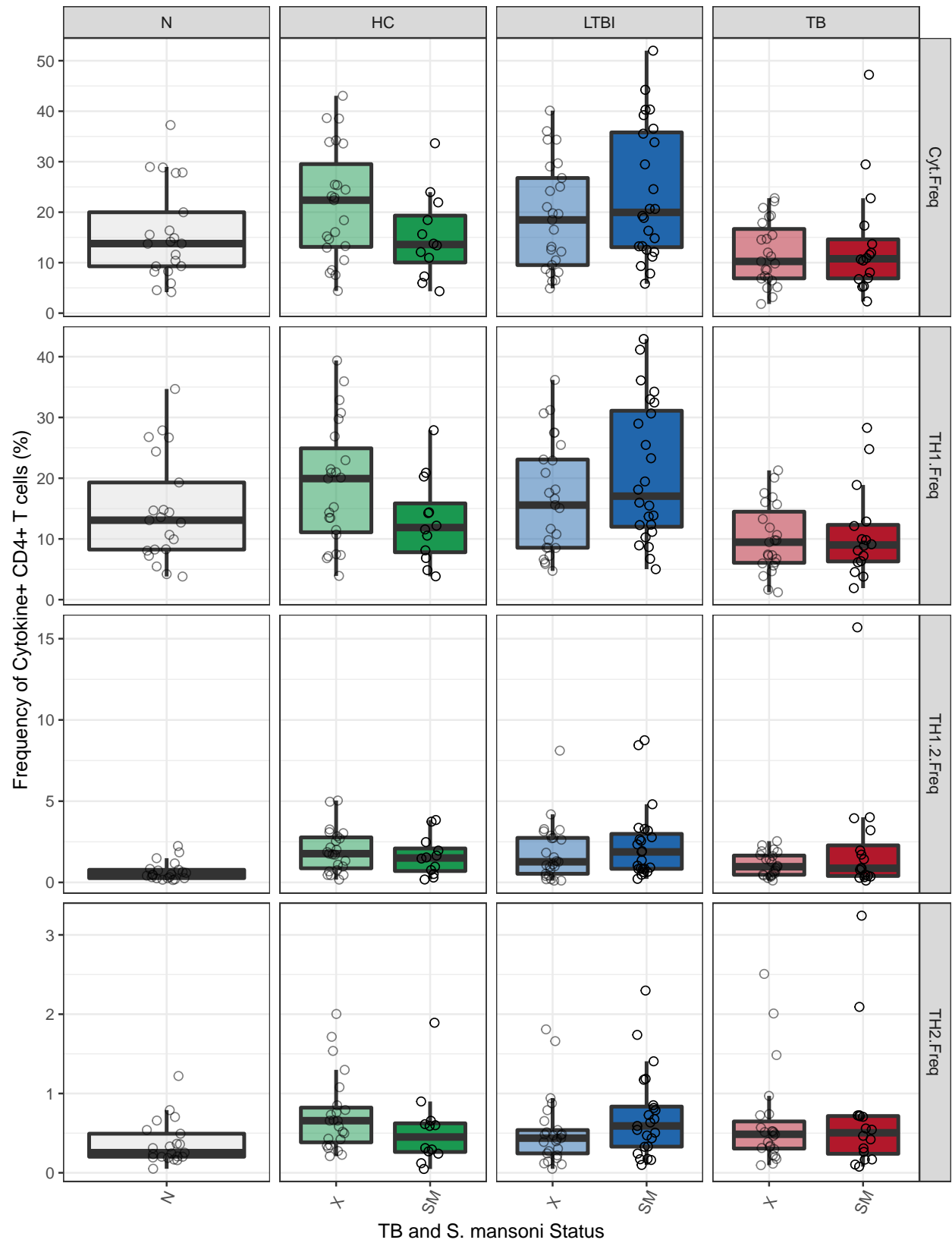| Comparison	TH1.Freq p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.1068	0.9613	0.1923
LTBI SM+ to LTBI SM-	0.1722	1	0.2583
TB SM+ to TB SM-	0.899	1	0.899
HC SM+ to LTBI SM+	0.0486	0.4375	0.1094
LTBI SM+ to TB SM+	0.0014	0.0122	0.0061
HC SM+ to TB SM+	0.2803	1	0.3604
HC SM- to LTBI SM-	0.4993	1	0.5617
LTBI SM- to TB SM-	0.0123	0.1108	0.0369
HC SM- to TB SM-	0.0012	0.0105	0.0061

Comparison	TH2.Freq p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.132	1	0.3504
LTBI SM+ to LTBI SM-	0.1558	1	0.3504
TB SM+ to TB SM-	0.9663	1	0.9663
HC SM+ to LTBI SM+	0.3101	1	0.5581
LTBI SM+ to TB SM+	0.3882	1	0.5824
HC SM+ to TB SM+	0.8017	1	0.9019
HC SM- to LTBI SM-	0.0493	0.4436	0.3504
LTBI SM- to TB SM-	0.5529	1	0.7108
HC SM- to TB SM-	0.1546	1	0.3504

Comparison	TH1.2.Freq p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.4398	1	0.6089
LTBI SM+ to LTBI SM-	0.4009	1	0.6089
TB SM+ to TB SM-	0.8082	1	0.8082
HC SM+ to LTBI SM+	0.4605	1	0.6089
LTBI SM+ to TB SM+	0.2392	1	0.6089
HC SM+ to TB SM+	0.7666	1	0.8082
HC SM- to LTBI SM-	0.4736	1	0.6089
LTBI SM- to TB SM-	0.2478	1	0.6089
HC SM- to TB SM-	0.0187	0.1686	0.1686

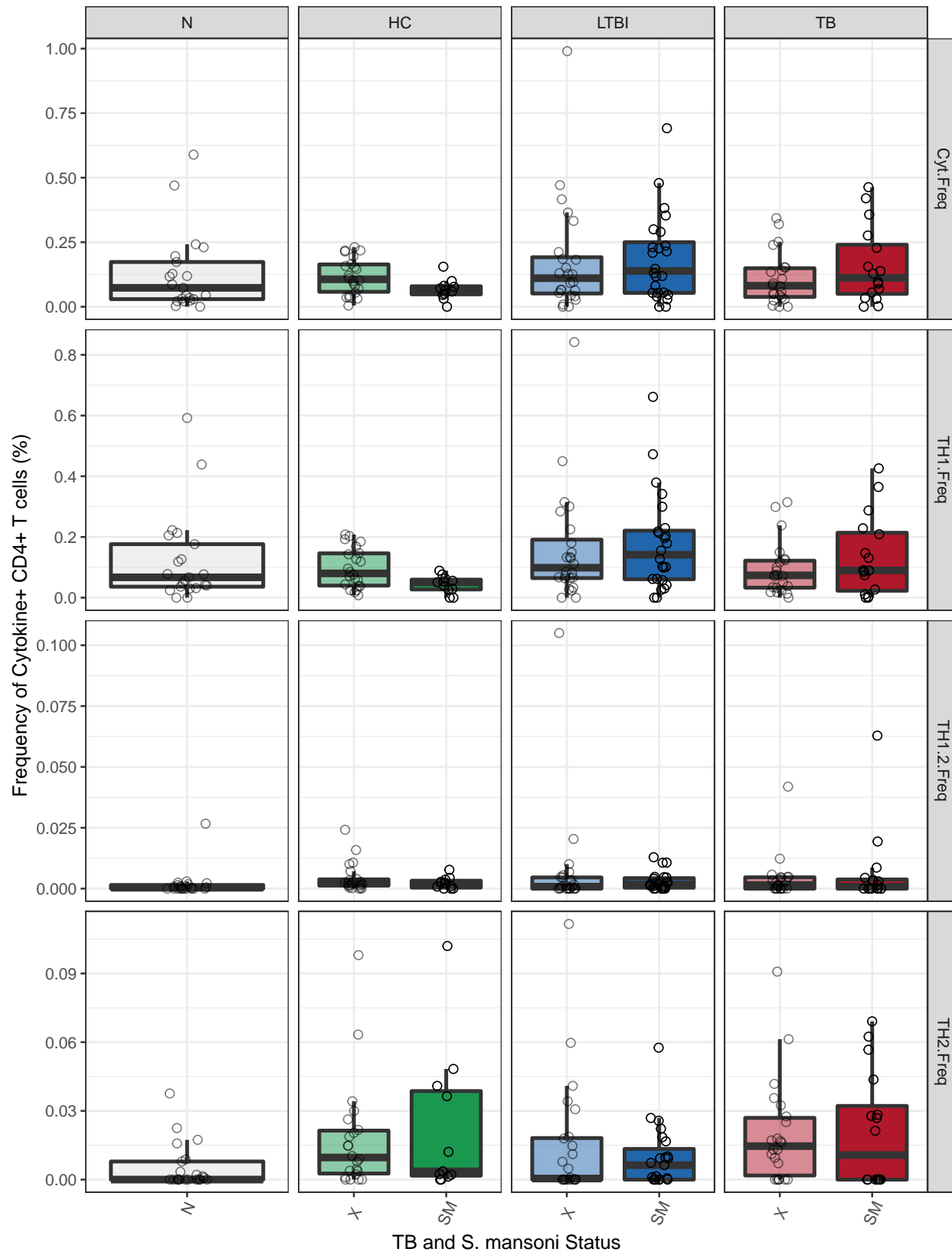# Mtb Whole Cell Lysate Specific CD4+ T cell Responses

Table 4: Mtb Whole Cell Lysate Specific CD4 T cell Responses

Comparison	TH1.Freq p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.041	0.3692	0.1712
LTBI SM+ to LTBI SM-	0.6133	1	0.6133
TB SM+ to TB SM-	0.5249	1	0.6133
HC SM+ to LTBI SM+	0.0038	0.0338	0.0338
LTBI SM+ to TB SM+	0.3995	1	0.5993
HC SM+ to TB SM+	0.0571	0.5137	0.1712
HC SM- to LTBI SM-	0.385	1	0.5993
LTBI SM- to TB SM-	0.2222	1	0.5
HC SM- to TB SM-	0.5652	1	0.6133

Comparison	TH2.Freq p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.9847	1	0.9847
LTBI SM+ to LTBI SM-	0.8688	1	0.9847
TB SM+ to TB SM-	0.9639	1	0.9847
HC SM+ to LTBI SM+	0.2633	1	0.7899
LTBI SM+ to TB SM+	0.4535	1	0.9847
HC SM+ to TB SM+	0.5631	1	0.9847
HC SM- to LTBI SM-	0.1585	1	0.7899
LTBI SM- to TB SM-	0.1757	1	0.7899
HC SM- to TB SM-	0.6968	1	0.9847

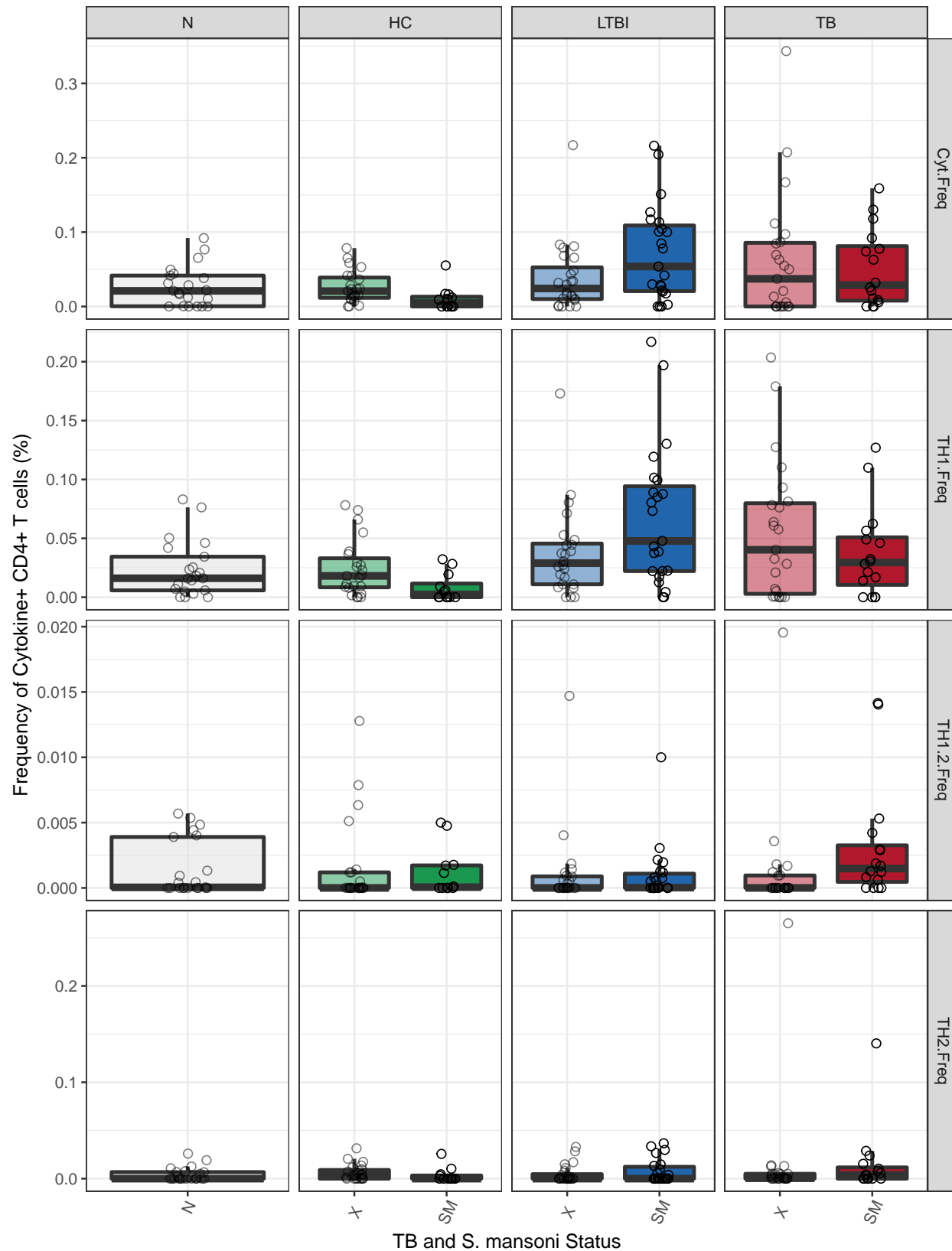| Comparison	TH1.2.Freq p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.5279	1	1
LTBI SM+ to LTBI SM-	0.4804	1	1
TB SM+ to TB SM-	0.9275	1	1
HC SM+ to LTBI SM+	0.8526	1	1
LTBI SM+ to TB SM+	0.8061	1	1
HC SM+ to TB SM+	1	1	1
HC SM- to LTBI SM-	0.1401	1	1
LTBI SM- to TB SM-	0.9183	1	1
HC SM- to TB SM-	0.3262	1	1

Mtb Peptide Specific CD4+ T cell Responses

Table 7: Mtb Peptide Specific CD4 T cell Responses

Comparison	TH1.Freq p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.0217	0.1953	0.0651
LTBI SM+ to LTBI SM-	0.0687	0.6179	0.1545
TB SM+ to TB SM-	0.3664	1	0.4122
HC SM+ to LTBI SM+	4e-04	0.0035	0.0035
LTBI SM+ to TB SM+	0.1061	0.9546	0.1909
HC SM+ to TB SM+	0.0187	0.1682	0.0651
HC SM- to LTBI SM-	0.183	1	0.2353
LTBI SM- to TB SM-	0.4884	1	0.4884
HC SM- to TB SM-	0.1526	1	0.2289

Comparison	TH2.Freq p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.139	1	0.6232
LTBI SM+ to LTBI SM-	0.8459	1	0.8459
TB SM+ to TB SM-	0.4344	1	0.6687
HC SM+ to LTBI SM+	0.4458	1	0.6687
LTBI SM+ to TB SM+	0.5434	1	0.6986
HC SM+ to TB SM+	0.1812	1	0.6232
HC SM- to LTBI SM-	0.2077	1	0.6232
LTBI SM- to TB SM-	0.7317	1	0.8232
HC SM- to TB SM-	0.3621	1	0.6687

Comparison	TH1.2.Freq p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.7762	1	0.9814
LTBI SM+ to LTBI SM-	0.6299	1	0.9734
TB SM+ to TB SM-	0.009	0.0813	0.0813
HC SM+ to LTBI SM+	0.894	1	0.9814
LTBI SM+ to TB SM+	0.035	0.3153	0.1577
HC SM+ to TB SM+	0.1611	1	0.4832
HC SM- to LTBI SM-	0.9814	1	0.9814
LTBI SM- to TB SM-	0.6489	1	0.9734
HC SM- to TB SM-	0.5575	1	0.9734

Comparison	TH1.2.Freq p-values	Bonferonni Corrected p-values	FDR Corrected p-vales

Individual Cytokines

These are the frequencies of cells producing individual cytokines without considering whether or not they are single positive, double positive etc. So any cell producing IL-4 is included in the IL-4 analysis.
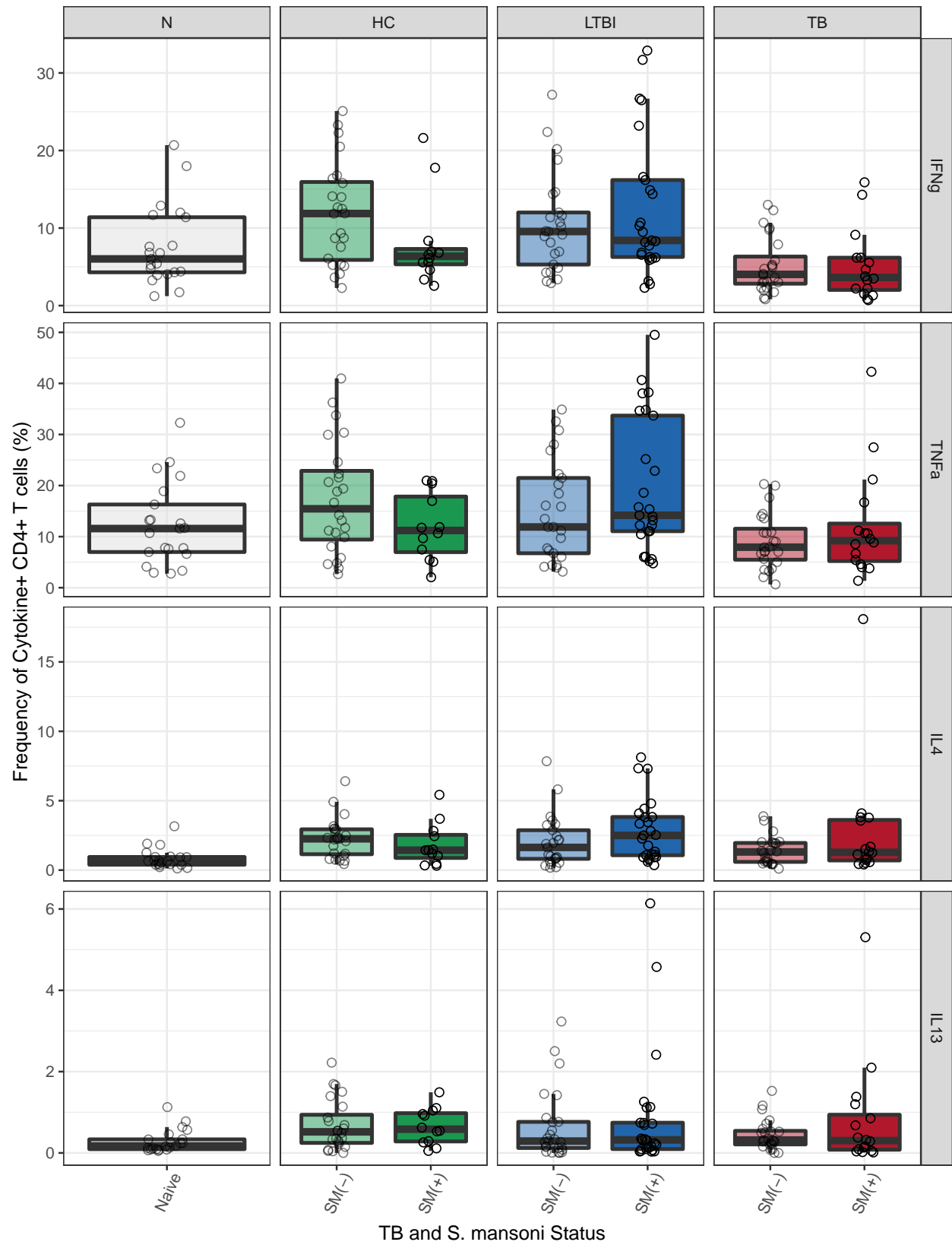
Non−Specific CD4+ T cell Responses

Table 10: Non Specific CD4 T cell Responses

Comparison	IFNg p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.0971	0.874	0.1457
LTBI SM+ to LTBI SM-	0.7437	1	0.7437
TB SM+ to TB SM-	0.6923	1	0.7437
HC SM+ to LTBI SM+	0.0768	0.6915	0.1383
LTBI SM+ to TB SM+	4e-04	0.0035	0.0017
HC SM+ to TB SM+	0.0473	0.4255	0.1064
HC SM- to LTBI SM-	0.4099	1	0.527
LTBI SM- to TB SM-	6e-04	0.0055	0.0018
HC SM- to TB SM-	1e-04	6e-04	6e-04

Comparison	TNFa p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.1994	1	0.2991
LTBI SM+ to LTBI SM-	0.1954	1	0.2991
TB SM+ to TB SM-	0.5944	1	0.5944
HC SM+ to LTBI SM+	0.0951	0.8559	0.214
LTBI SM+ to TB SM+	0.0227	0.2042	0.1021
HC SM+ to TB SM+	0.507	1	0.5704
HC SM- to LTBI SM-	0.4447	1	0.5704
LTBI SM- to TB SM-	0.0437	0.3935	0.1312
HC SM- to TB SM-	0.0048	0.0434	0.0434

Comparison	IL4 p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.3108	1	0.4182
LTBI SM+ to LTBI SM-	0.0916	0.824	0.412
TB SM+ to TB SM-	0.557	1	0.6267
HC SM+ to LTBI SM+	0.2273	1	0.4182
LTBI SM+ to TB SM+	0.1973	1	0.4182
HC SM+ to TB SM+	0.8372	1	0.8372
HC SM- to LTBI SM-	0.2526	1	0.4182
LTBI SM- to TB SM-	0.3252	1	0.4182
HC SM- to TB SM-	0.0094	0.0842	0.0842

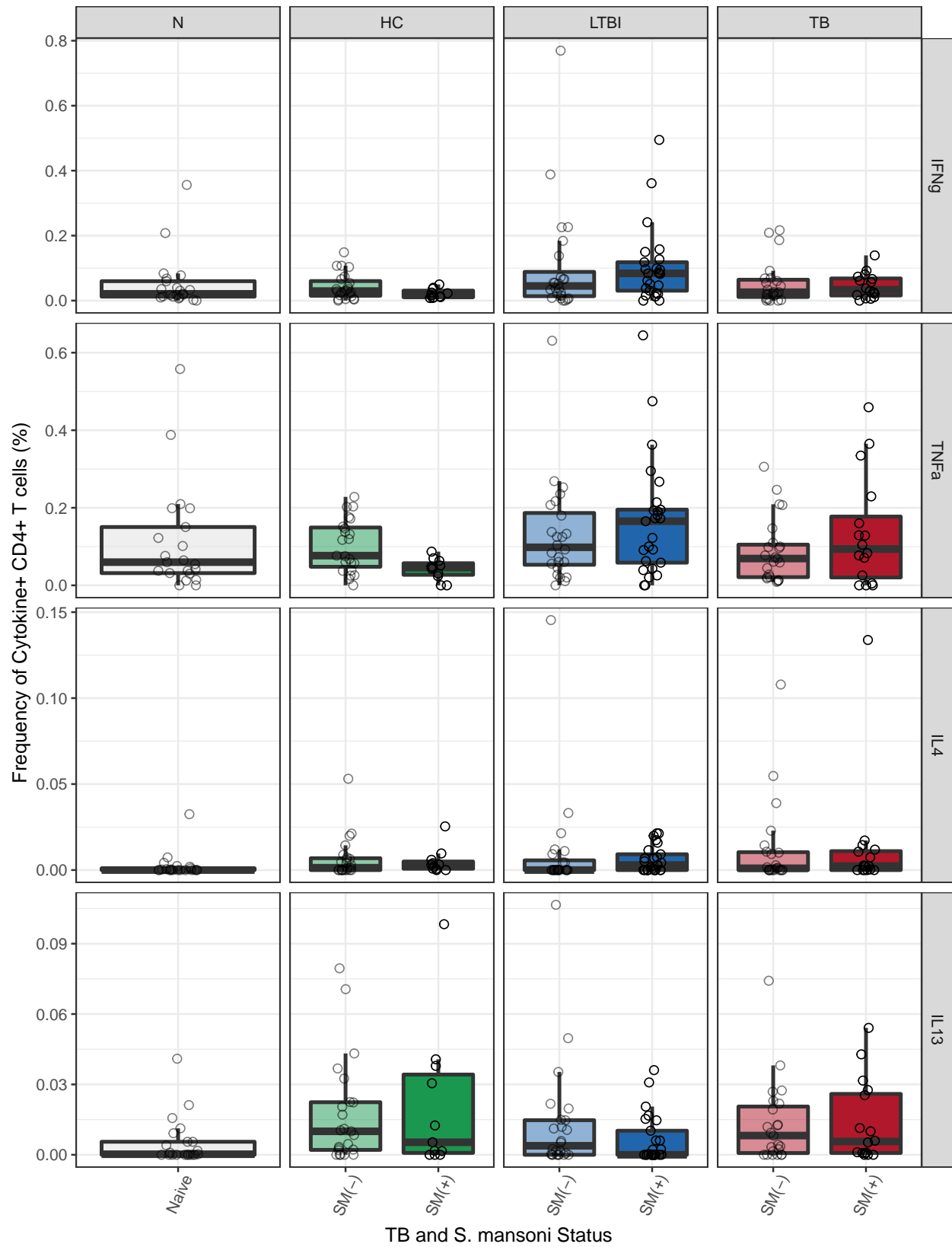| Comparison	IL13 p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.8041	1	0.989
LTBI SM+ to LTBI SM-	0.7583	1	0.989
TB SM+ to TB SM-	0.989	1	0.989
HC SM+ to LTBI SM+	0.4134	1	0.9302
LTBI SM+ to TB SM+	0.7412	1	0.989
HC SM+ to TB SM+	0.3713	1	0.9302
HC SM- to LTBI SM-	0.337	1	0.9302
LTBI SM- to TB SM-	0.8808	1	0.989
HC SM- to TB SM-	0.2357	1	0.9302

Mtb Whole Cell Lysate Specific CD4+ T cell Responses

Table 14: Mtb Whole Cell Lysate Specific CD4 T cell Responses

Comparison	IFNg p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.2283	1	0.3693
LTBI SM+ to LTBI SM-	0.2584	1	0.3693
TB SM+ to TB SM-	0.6071	1	0.683
HC SM+ to LTBI SM+	0.0028	0.0253	0.0253
LTBI SM+ to TB SM+	0.0436	0.3922	0.1961
HC SM+ to TB SM+	0.1623	1	0.3693
HC SM- to LTBI SM-	0.2872	1	0.3693
LTBI SM- to TB SM-	0.2822	1	0.3693
HC SM- to TB SM-	0.7835	1	0.7835

Comparison	TNFa p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.0184	0.1659	0.083
LTBI SM+ to LTBI SM-	0.4413	1	0.5547
TB SM+ to TB SM-	0.4931	1	0.5547
HC SM+ to LTBI SM+	0.0054	0.0484	0.0484
LTBI SM+ to TB SM+	0.3847	1	0.5547
HC SM+ to TB SM+	0.0634	0.5709	0.1903
HC SM- to LTBI SM-	0.617	1	0.617
LTBI SM- to TB SM-	0.2234	1	0.5026
HC SM- to TB SM-	0.3831	1	0.5547

Comparison	IL4 p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.7066	1	0.9801
LTBI SM+ to LTBI SM-	0.2506	1	0.9801
TB SM+ to TB SM-	0.5246	1	0.9801
HC SM+ to LTBI SM+	0.9442	1	0.9801
LTBI SM+ to TB SM+	0.9019	1	0.9801
HC SM+ to TB SM+	0.9801	1	0.9801
HC SM- to LTBI SM-	0.3741	1	0.9801
LTBI SM- to TB SM-	0.3625	1	0.9801
HC SM- to TB SM-	0.9448	1	0.9801

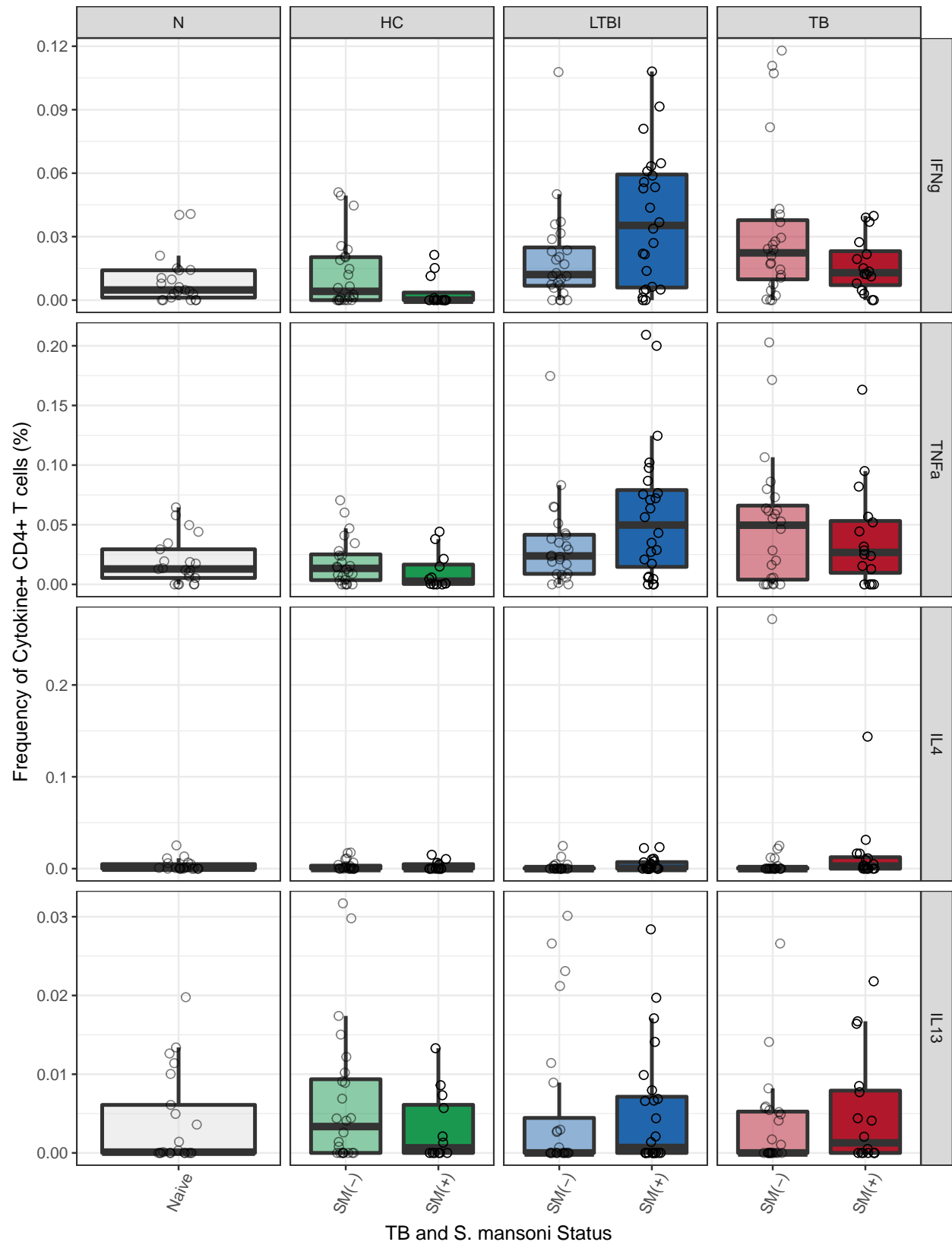| Comparison	IL13 p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.8968	1	0.9656
LTBI SM+ to LTBI SM-	0.1849	1	0.5547
TB SM+ to TB SM-	0.9656	1	0.9656
HC SM+ to LTBI SM+	0.1265	1	0.5547
LTBI SM+ to TB SM+	0.0778	0.7003	0.5547
HC SM+ to TB SM+	0.766	1	0.9656
HC SM- to LTBI SM-	0.303	1	0.6817
LTBI SM- to TB SM-	0.5614	1	0.9634
HC SM- to TB SM-	0.6423	1	0.9634

Mtb Peptide Specific CD4+ T cell Responses

Table 18: Mtb Peptide Specific CD4 T cell Responses

Comparison	IFNg p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.0618	0.5563	0.0927
LTBI SM+ to LTBI SM-	0.0442	0.3977	0.0814
TB SM+ to TB SM-	0.2404	1	0.2404
HC SM+ to LTBI SM+	2e-04	0.0019	0.0019
LTBI SM+ to TB SM+	0.0452	0.4071	0.0814
HC SM+ to TB SM+	0.0066	0.0598	0.0299
HC SM- to LTBI SM-	0.1523	1	0.1958
LTBI SM- to TB SM-	0.1764	1	0.1985
HC SM- to TB SM-	0.0142	0.1281	0.0427

Comparison	TNFa p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.2245	1	0.3078
LTBI SM+ to LTBI SM-	0.1487	1	0.2676
TB SM+ to TB SM-	0.5141	1	0.5424
HC SM+ to LTBI SM+	0.0043	0.0383	0.0383
LTBI SM+ to TB SM+	0.2394	1	0.3078
HC SM+ to TB SM+	0.0717	0.6451	0.1613
HC SM- to LTBI SM-	0.0676	0.6083	0.1613
LTBI SM- to TB SM-	0.5424	1	0.5424
HC SM- to TB SM-	0.0541	0.4866	0.1613

Comparison	IL4 p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.5015	1	0.5642
LTBI SM+ to LTBI SM-	0.1635	1	0.4474
TB SM+ to TB SM-	0.1266	1	0.4474
HC SM+ to LTBI SM+	0.4499	1	0.5642
LTBI SM+ to TB SM+	0.3729	1	0.5594
HC SM+ to TB SM+	0.1983	1	0.4474
HC SM- to LTBI SM-	0.1989	1	0.4474
LTBI SM- to TB SM-	0.99	1	0.99
HC SM- to TB SM-	0.2591	1	0.4664

Comparison	IL13 p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.3208	1	0.9255
LTBI SM+ to LTBI SM-	0.694	1	0.9255
TB SM+ to TB SM-	0.4697	1	0.9255
HC SM+ to LTBI SM+	0.7198	1	0.9255
LTBI SM+ to TB SM+	0.8839	1	0.9819
HC SM+ to TB SM+	0.6421	1	0.9255
HC SM- to LTBI SM-	0.2336	1	0.9255
LTBI SM- to TB SM-	0.9819	1	0.9819
HC SM- to TB SM-	0.1752	1	0.9255

True Single and Double Cytokine Positive CD4+ T Cells

These are the frequencies of cells truly ONLY producing:
1. IFNg or TNFa or the combination of both AND NOT IL4 or IL13
2. IL-4 or IL-13 or the combination of both AND NOT IFNg or TNFa
These are the subgroups within the grouped TH1 vs TH2 lineage analysis. They are essentially the last 6 groups of the boolean data.

Non−Specific CD4+ Cytokine Frequencies
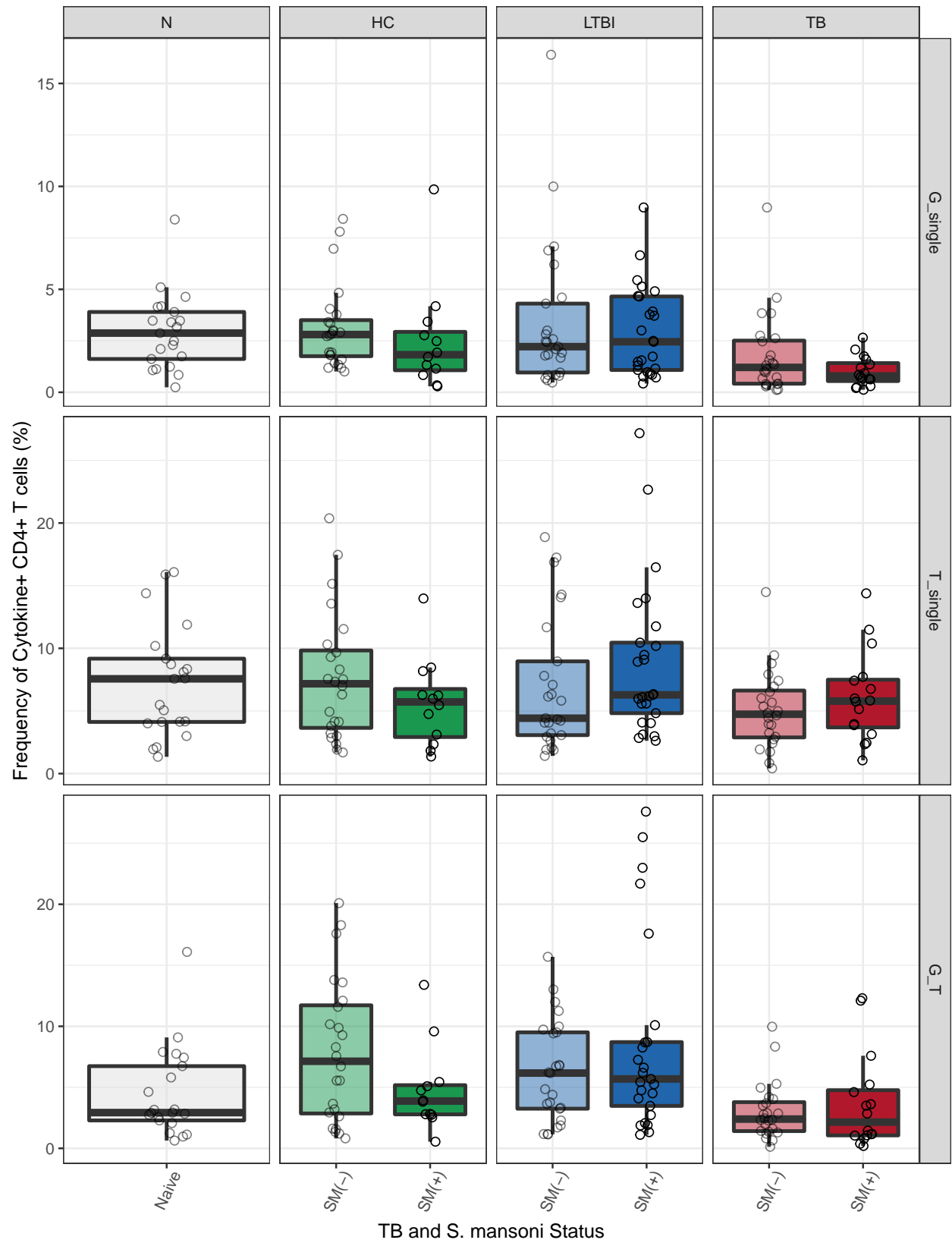
Non−Specific CD4+ Cytokine Frequencies

Table 22: Non-Specific CD4+ T cell Responses

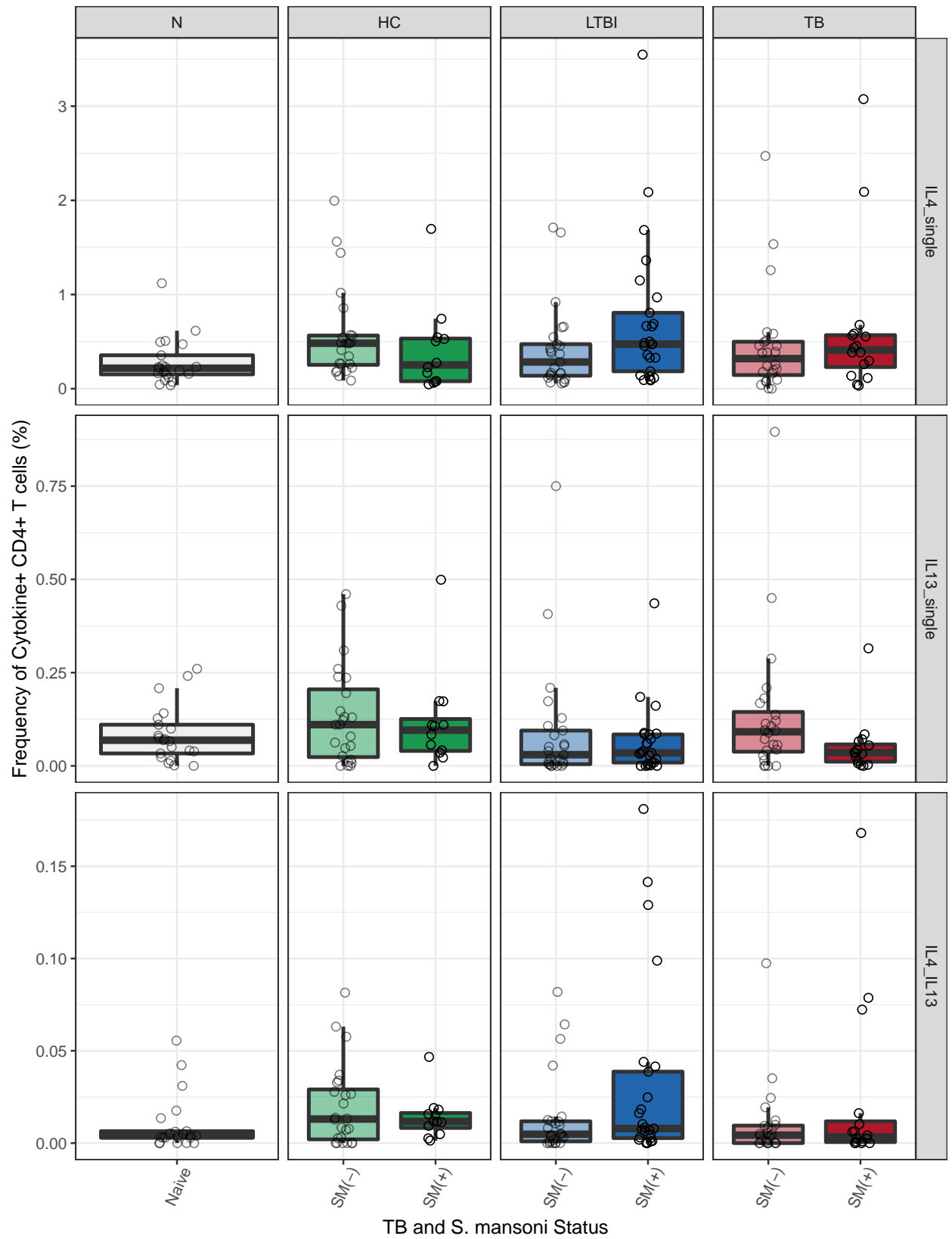| Comparison	G_single p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.1558	1	0.2805
LTBI SM+ to LTBI SM-	1	1	1
TB SM+ to TB SM-	0.2552	1	0.3828
HC SM+ to LTBI SM+	0.4708	1	0.5297
LTBI SM+ to TB SM+	0.001	0.0087	0.0072
HC SM+ to TB SM+	0.0331	0.2975	0.0744
HC SM- to LTBI SM-	0.3987	1	0.5126
LTBI SM- to TB SM-	0.0235	0.2115	0.0705
HC SM- to TB SM-	0.0016	0.0145	0.0072

Comparison	T_single p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.2509	1	0.4517
LTBI SM+ to LTBI SM-	0.2022	1	0.4517
TB SM+ to TB SM-	0.3888	1	0.5553
HC SM+ to LTBI SM+	0.1019	0.9169	0.4517
LTBI SM+ to TB SM+	0.1706	1	0.4517
HC SM+ to TB SM+	0.7666	1	0.7666
HC SM- to LTBI SM-	0.4936	1	0.5553
LTBI SM- to TB SM-	0.4329	1	0.5553
HC SM- to TB SM-	0.0852	0.7664	0.4517

Comparison	G_T p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.166	1	0.2988
LTBI SM+ to LTBI SM-	0.59	1	0.6638
TB SM+ to TB SM-	0.7745	1	0.7745
HC SM+ to LTBI SM+	0.1603	1	0.2988
LTBI SM+ to TB SM+	0.0062	0.0559	0.0186
HC SM+ to TB SM+	0.2226	1	0.3339
HC SM- to LTBI SM-	0.4688	1	0.6028
LTBI SM- to TB SM-	0.0043	0.0385	0.0186
HC SM- to TB SM-	0.002	0.0182	0.0182

Comparison	IL4_single p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.2373	1	0.4271
LTBI SM+ to LTBI SM-	0.0773	0.6961	0.348
TB SM+ to TB SM-	0.3888	1	0.5251
HC SM+ to LTBI SM+	0.1603	1	0.3606
LTBI SM+ to TB SM+	0.4668	1	0.5251
HC SM+ to TB SM+	0.4499	1	0.5251
HC SM- to LTBI SM-	0.0733	0.6594	0.348
LTBI SM- to TB SM-	0.9132	1	0.9132
HC SM- to TB SM-	0.1415	1	0.3606

Comparison	IL13_single p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.7118	1	0.9152
LTBI SM+ to LTBI SM-	0.9381	1	0.9381
TB SM+ to TB SM-	0.0369	0.3325	0.1375
HC SM+ to LTBI SM+	0.0597	0.5374	0.1375
LTBI SM+ to TB SM+	0.8725	1	0.9381
HC SM+ to TB SM+	0.0459	0.4129	0.1375
HC SM- to LTBI SM-	0.0611	0.55	0.1375
LTBI SM- to TB SM-	0.1156	1	0.2081
HC SM- to TB SM-	0.657	1	0.9152

Comparison	IL4_IL13 p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.933	1	0.933
LTBI SM+ to LTBI SM-	0.228	1	0.5059
TB SM+ to TB SM-	0.7476	1	0.841
HC SM+ to LTBI SM+	0.6851	1	0.841
LTBI SM+ to TB SM+	0.1483	1	0.445
HC SM+ to TB SM+	0.0989	0.8899	0.445
HC SM- to LTBI SM-	0.2811	1	0.5059
LTBI SM- to TB SM-	0.4851	1	0.7276
HC SM- to TB SM-	0.0742	0.6681	0.445

Mtb Whole Cell Lysate Specific CD4+ Cytokine Frequencies
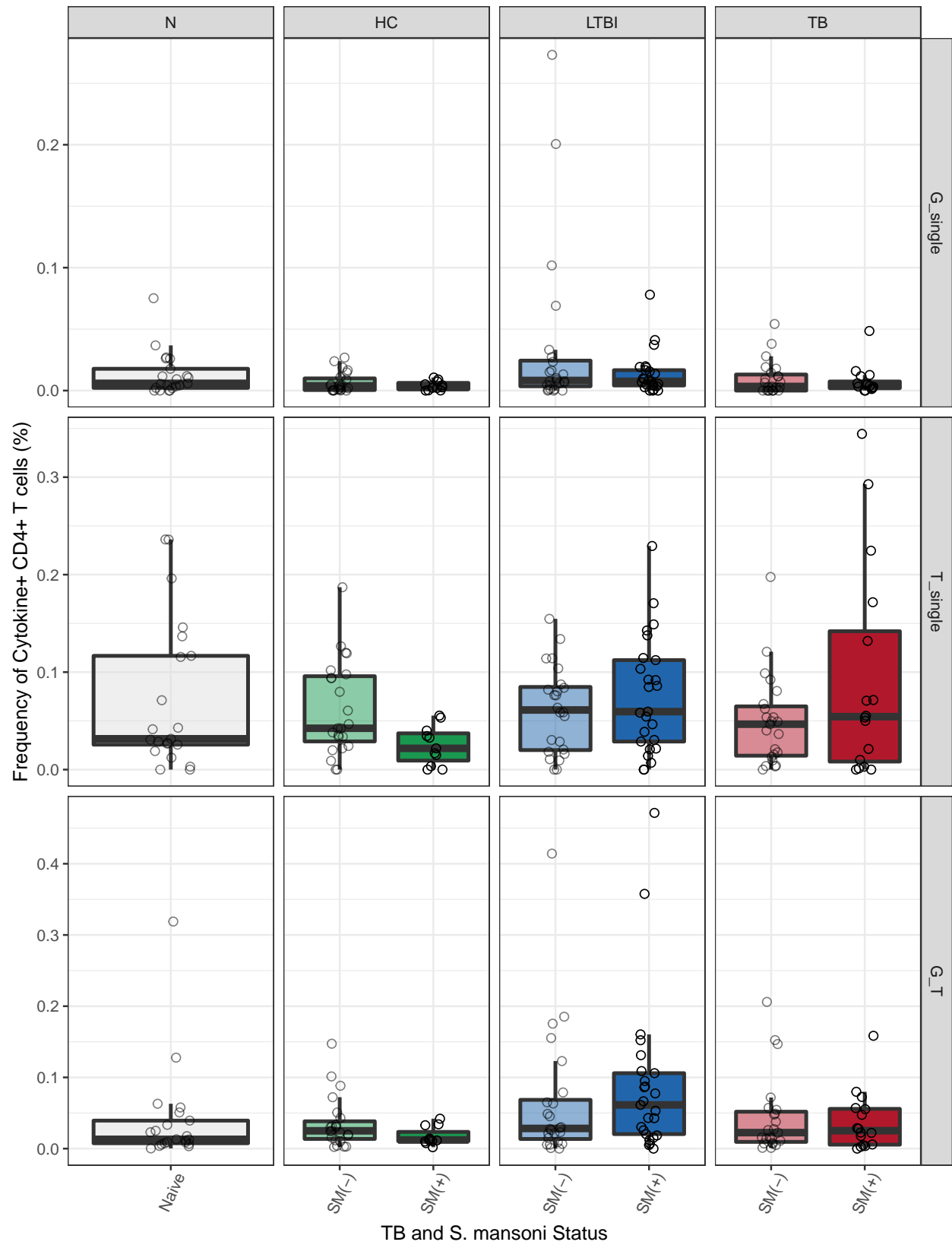
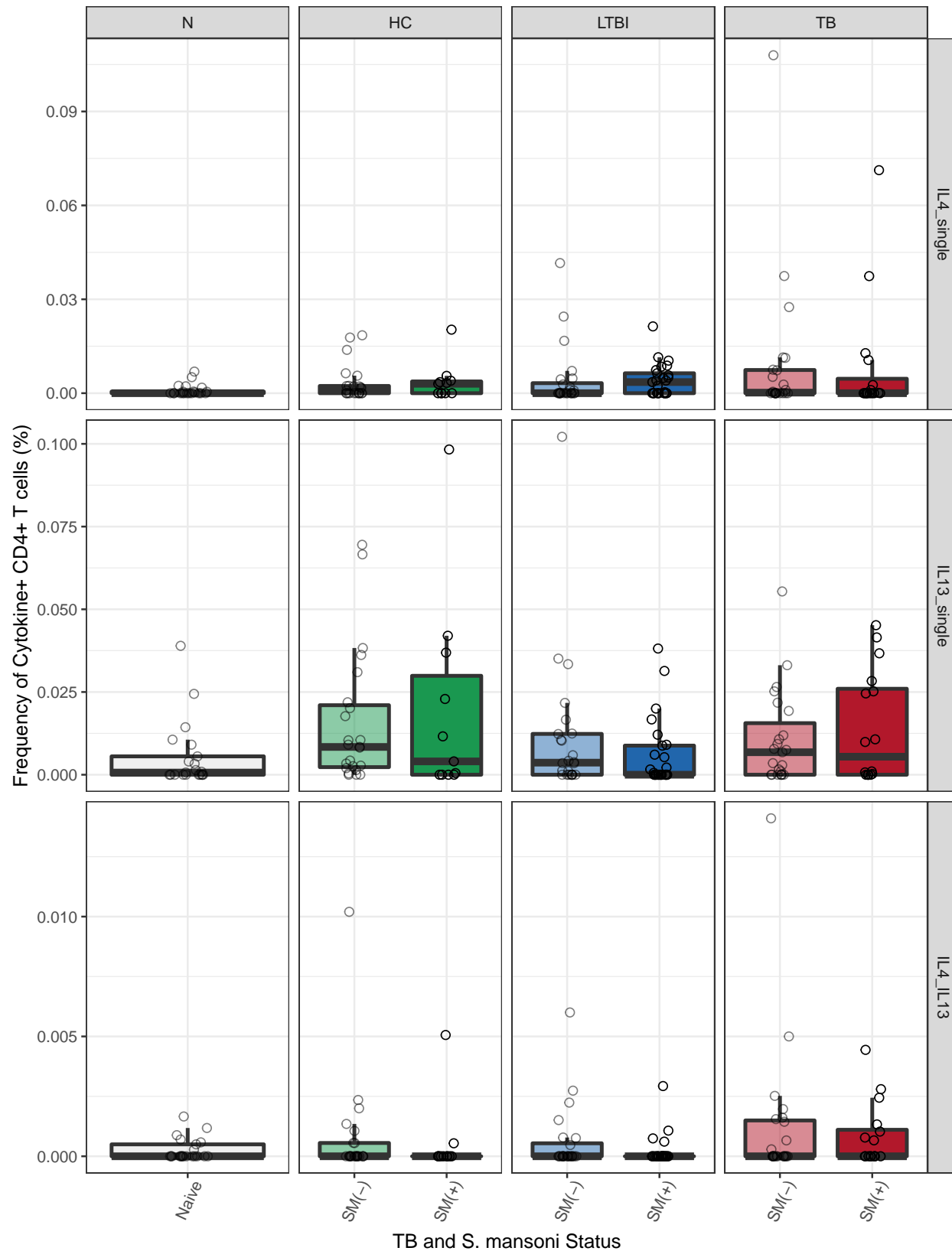# Mtb Whole Cell Lysate Specific CD4+ Cytokine Frequencies

Table 28: Mtb Whole Cell Lysate Specific CD4+ T cell Responses

Comparison	G_single p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.7823	1	1
LTBI SM+ to LTBI SM-	0.6309	1	0.9464
TB SM+ to TB SM-	1	1	1
HC SM+ to LTBI SM+	0.0444	0.3996	0.2608
LTBI SM+ to TB SM+	0.0946	0.851	0.2828
HC SM+ to TB SM+	0.5371	1	0.9464
HC SM- to LTBI SM-	0.058	0.5217	0.2608
LTBI SM- to TB SM-	0.1257	1	0.2828
HC SM- to TB SM-	0.9295	1	1

Comparison	T_single p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.0246	0.2216	0.1108
LTBI SM+ to LTBI SM-	0.4353	1	0.5997
TB SM+ to TB SM-	0.4665	1	0.5997
HC SM+ to LTBI SM+	0.0121	0.1091	0.1091
LTBI SM+ to TB SM+	0.7789	1	0.8763
HC SM+ to TB SM+	0.1195	1	0.3586
HC SM- to LTBI SM-	0.9406	1	0.9406
LTBI SM- to TB SM-	0.2131	1	0.4794
HC SM- to TB SM-	0.4037	1	0.5997

Comparison	G_T p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.1532	1	0.4597
LTBI SM+ to LTBI SM-	0.2543	1	0.5296
TB SM+ to TB SM-	1	1	1
HC SM+ to LTBI SM+	0.0025	0.0227	0.0227
LTBI SM+ to TB SM+	0.051	0.4594	0.2297
HC SM+ to TB SM+	0.2942	1	0.5296
HC SM- to LTBI SM-	0.5062	1	0.6508
LTBI SM- to TB SM-	0.4664	1	0.6508
HC SM- to TB SM-	0.879	1	0.9888

Comparison	IL4_single p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.5996	1	0.7357
LTBI SM+ to LTBI SM-	0.1905	1	0.7357
TB SM+ to TB SM-	0.6452	1	0.7357
HC SM+ to LTBI SM+	0.4329	1	0.7357
LTBI SM+ to TB SM+	0.4902	1	0.7357
HC SM+ to TB SM+	0.6705	1	0.7357
HC SM- to LTBI SM-	0.636	1	0.7357
LTBI SM- to TB SM-	0.4124	1	0.7357
HC SM- to TB SM-	0.7357	1	0.7357

Comparison	IL13_single p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.7116	1	0.904
LTBI SM+ to LTBI SM-	0.2151	1	0.4885
TB SM+ to TB SM-	0.7831	1	0.904
HC SM+ to LTBI SM+	0.2171	1	0.4885
LTBI SM+ to TB SM+	0.1178	1	0.4885
HC SM+ to TB SM+	0.9799	1	0.9799
HC SM- to LTBI SM-	0.2063	1	0.4885
LTBI SM- to TB SM-	0.8035	1	0.904
HC SM- to TB SM-	0.315	1	0.5671

Comparison	IL4_IL13 p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.4481	1	0.704
LTBI SM+ to LTBI SM-	0.2502	1	0.704
TB SM+ to TB SM-	0.8854	1	0.9475
HC SM+ to LTBI SM+	0.8948	1	0.9475
LTBI SM+ to TB SM+	0.0432	0.389	0.389
HC SM+ to TB SM+	0.1958	1	0.704
HC SM- to LTBI SM-	0.9475	1	0.9475
LTBI SM- to TB SM-	0.4573	1	0.704
HC SM- to TB SM-	0.4693	1	0.704

Mtb Peptide Specific CD4+ Cytokine Frequencies
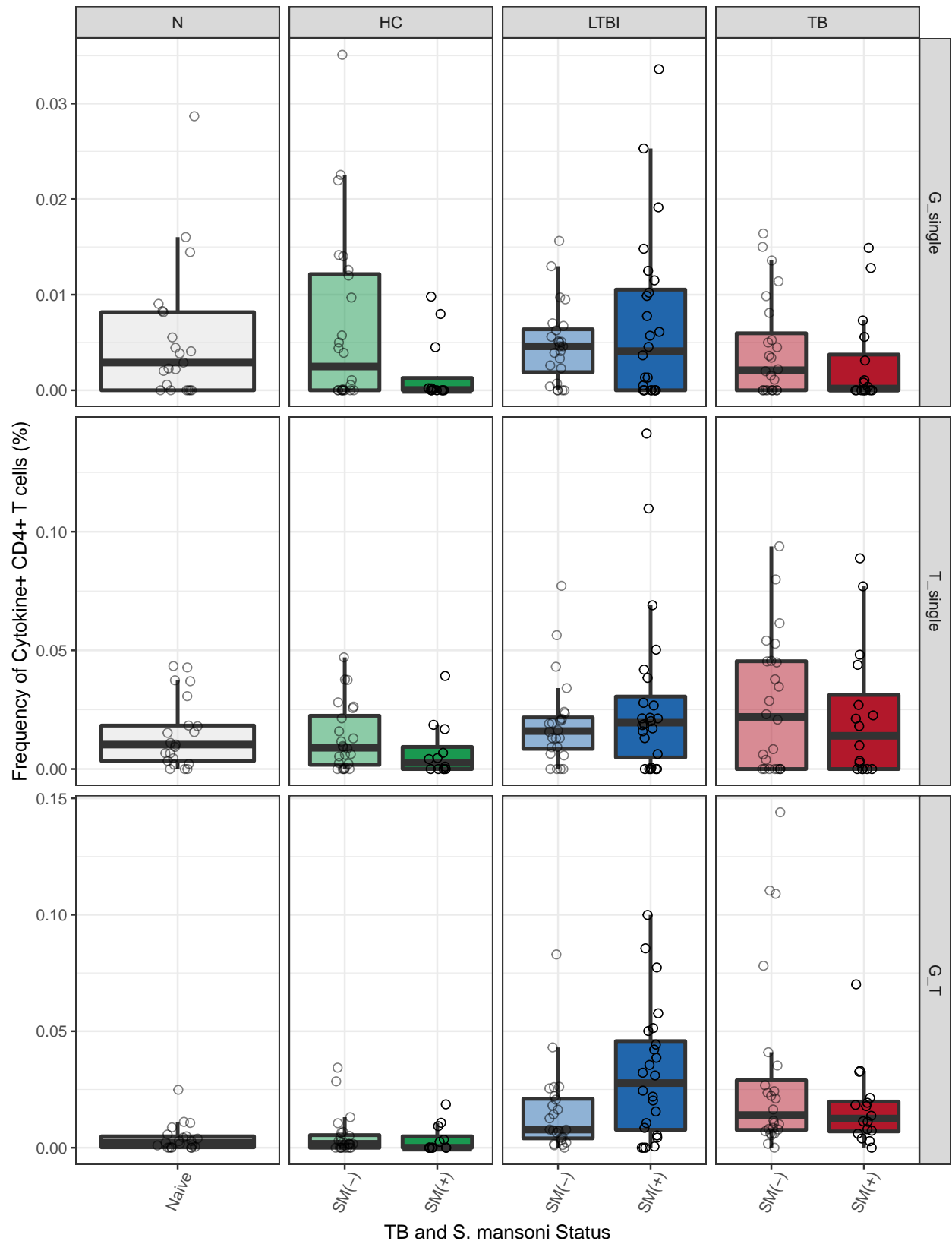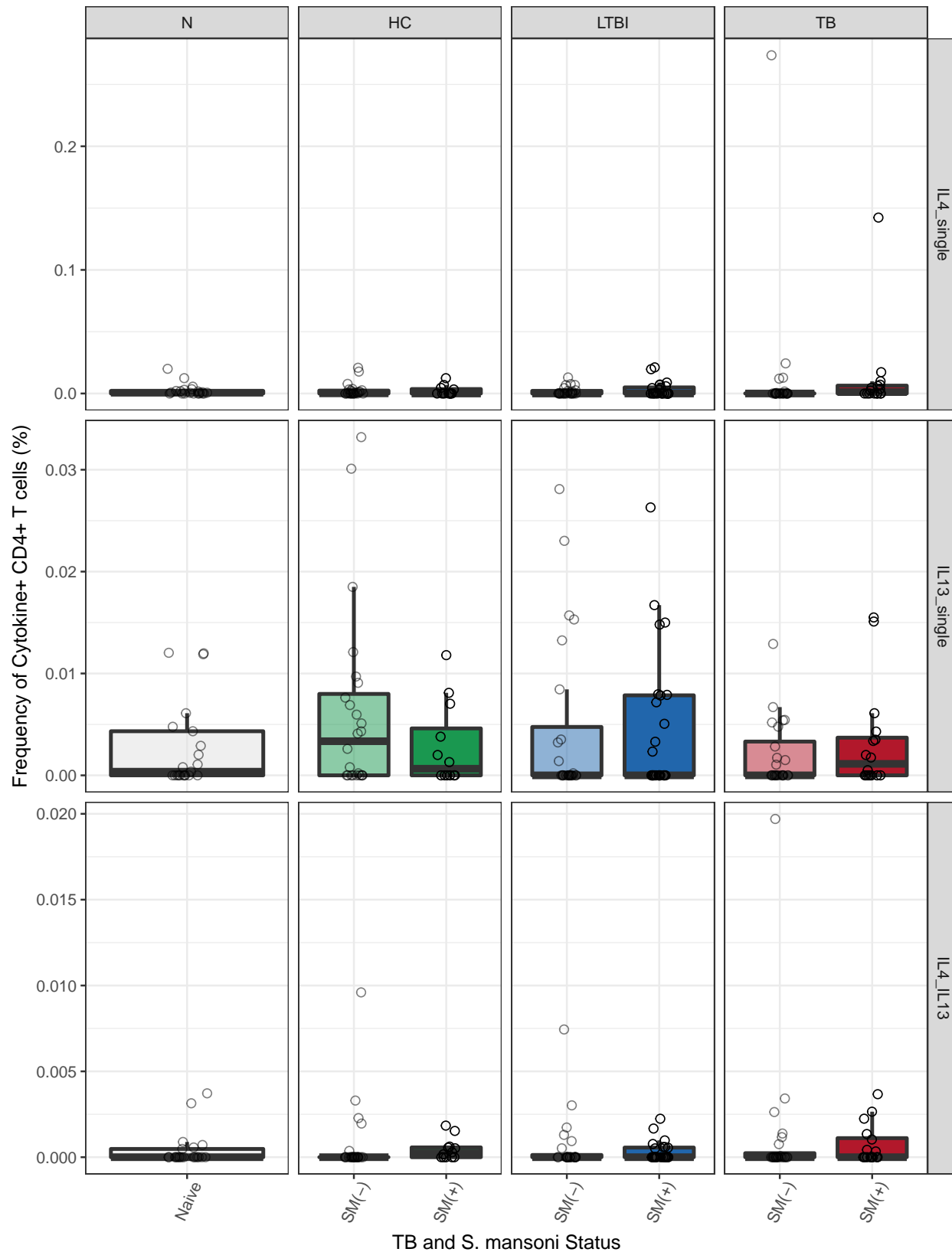
Mtb Peptide Specific CD4+ Cytokine Frequencies

Table 34: Mtb Peptide Specific CD4 T cell Responses

Comparison	G_single p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.1583	1	0.4748
LTBI SM+ to LTBI SM-	0.9751	1	0.9751
TB SM+ to TB SM-	0.2944	1	0.5298
HC SM+ to LTBI SM+	0.0749	0.674	0.4748
LTBI SM+ to TB SM+	0.1269	1	0.4748
HC SM+ to TB SM+	0.7098	1	0.7985
HC SM- to LTBI SM-	0.6618	1	0.7985
LTBI SM- to TB SM-	0.2652	1	0.5298
HC SM- to TB SM-	0.6641	1	0.7985

Comparison	T_single p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.1643	1	0.4826
LTBI SM+ to LTBI SM-	0.469	1	0.6701
TB SM+ to TB SM-	0.643	1	0.6701
HC SM+ to LTBI SM+	0.023	0.2074	0.2074
LTBI SM+ to TB SM+	0.5779	1	0.6701
HC SM+ to TB SM+	0.1834	1	0.4826
HC SM- to LTBI SM-	0.2145	1	0.4826
LTBI SM- to TB SM-	0.6701	1	0.6701
HC SM- to TB SM-	0.3026	1	0.5447

Comparison	G_T p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.4331	1	0.4395
LTBI SM+ to LTBI SM-	0.0454	0.4089	0.0818
TB SM+ to TB SM-	0.4395	1	0.4395
HC SM+ to LTBI SM+	6e-04	0.0055	0.0028
LTBI SM+ to TB SM+	0.1358	1	0.1746
HC SM+ to TB SM+	0.0019	0.0174	0.0045
HC SM- to LTBI SM-	0.002	0.0178	0.0045
LTBI SM- to TB SM-	0.1033	0.9298	0.155
HC SM- to TB SM-	0	4e-04	4e-04

Comparison	IL4_single p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.6716	1	0.6716
LTBI SM+ to LTBI SM-	0.5468	1	0.6716
TB SM+ to TB SM-	0.1492	1	0.6716
HC SM+ to LTBI SM+	0.524	1	0.6716
LTBI SM+ to TB SM+	0.6543	1	0.6716
HC SM+ to TB SM+	0.3411	1	0.6716
HC SM- to LTBI SM-	0.6368	1	0.6716
LTBI SM- to TB SM-	0.3829	1	0.6716
HC SM- to TB SM-	0.1727	1	0.6716

Comparison	IL13_single p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.3381	1	0.8886
LTBI SM+ to LTBI SM-	0.8113	1	0.9529
TB SM+ to TB SM-	0.395	1	0.8886
HC SM+ to LTBI SM+	0.7853	1	0.9529
LTBI SM+ to TB SM+	0.9529	1	0.9529
HC SM+ to TB SM+	0.8833	1	0.9529
HC SM- to LTBI SM-	0.2293	1	0.8886
LTBI SM- to TB SM-	0.6869	1	0.9529
HC SM- to TB SM-	0.068	0.6122	0.6122

Comparison	IL4_IL13 p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.101	0.9094	0.8817
LTBI SM+ to LTBI SM-	0.7482	1	0.8817
TB SM+ to TB SM-	0.4178	1	0.8817
HC SM+ to LTBI SM+	0.3027	1	0.8817
LTBI SM+ to TB SM+	0.3826	1	0.8817
HC SM+ to TB SM+	0.8817	1	0.8817
HC SM- to LTBI SM-	0.8336	1	0.8817
LTBI SM- to TB SM-	0.7619	1	0.8817
HC SM- to TB SM-	0.5691	1	0.8817

Lineage "Agnostic" Single and Double Cytokine Positive CD4+ T Cells

I don't really believe that this is an appropriate way to look at the data because the cells are technically shared between some of these groupings, but I'm almost certain someone would ask the question "What if you didn't consider Il-4 and IL-13 in defining Gamma and TNF single and double positive cells" so I did it for them.
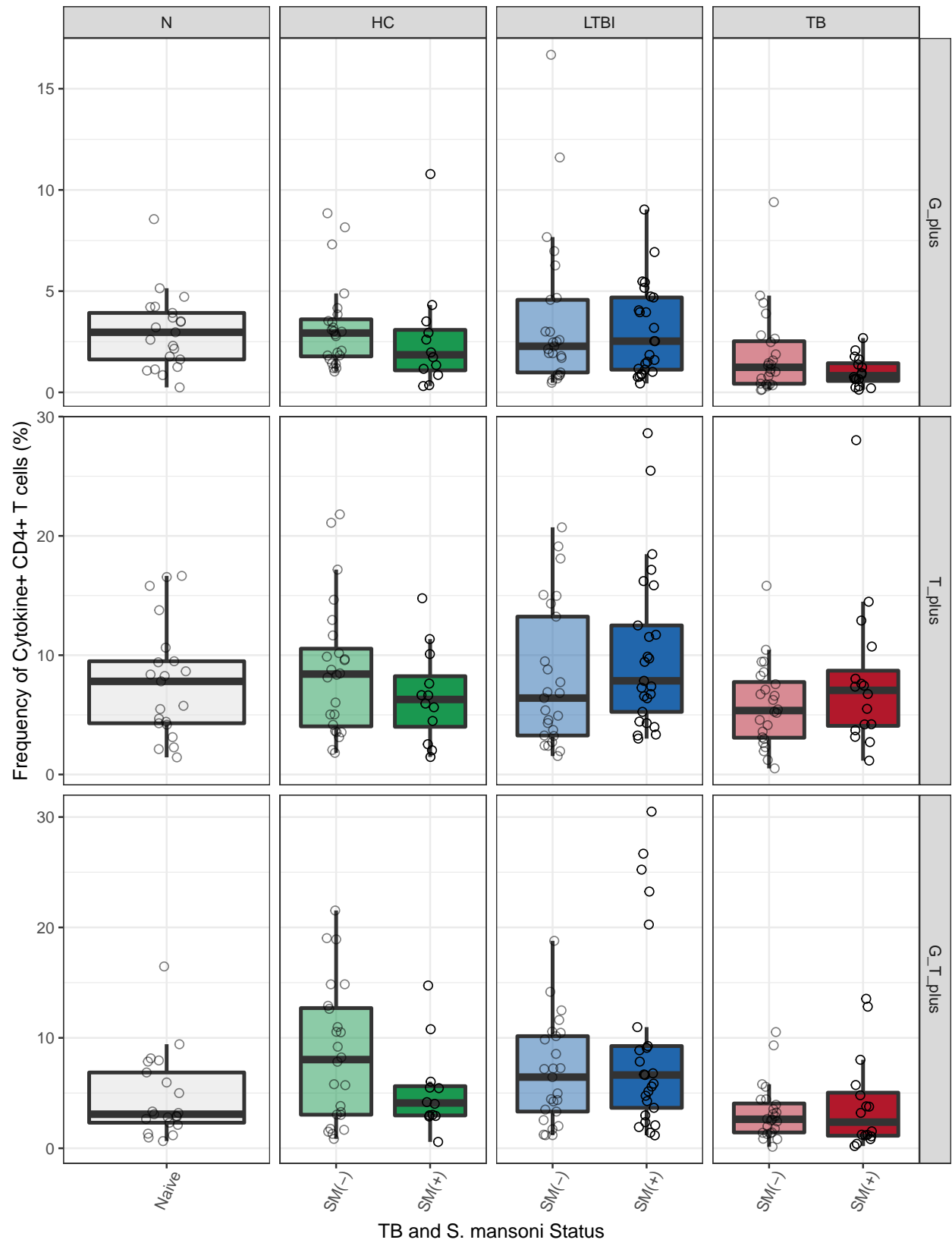
	IFNγ+				TNFα+				IFNγ+ TNFα+			
IFNγ	X	X	X	X					X	X	X	X
TNFα					X	X	X	X	X	X	X	X
IL-4		X		X		X		X		X		X
IL-13			X	X			X	X			X	X

Figure 2: Breakdown of TH1 Cytokine Definitions

	IL-4+				IL-13+				IL-4+ IL-13+			
IFNγ		X		X		X		X		X		X
TNFα			X	X			X	X			X	X
IL-4	X	X	X	X					X	X	X	X
IL-13					X	X	X	X	X	X	X	X

Figure 3: Breakdown of TH2 Cytokine Definitions

Non−Specific CD4+ T cell Cytokine Frequencies
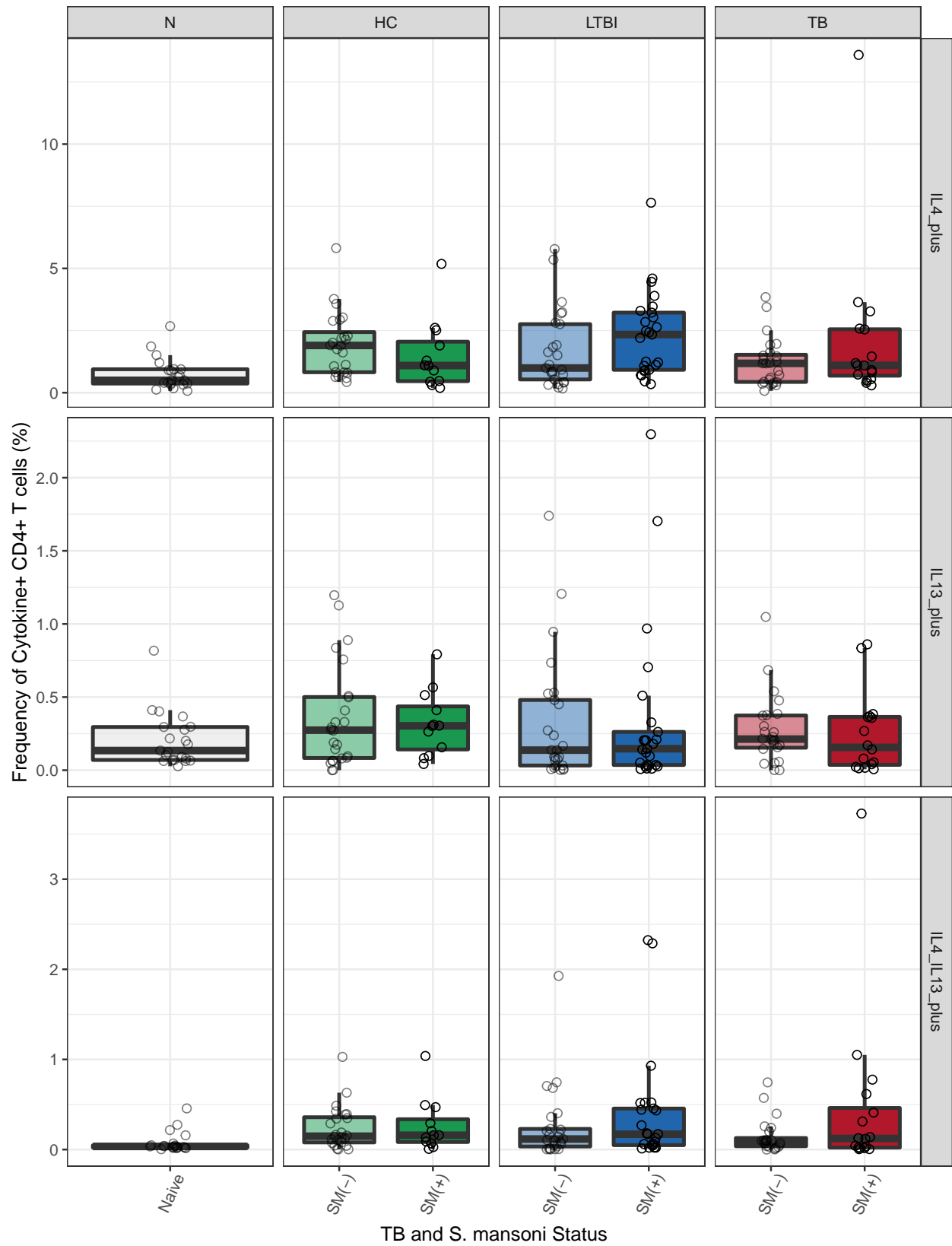
Non−Specific CD4+ T cell Cytokine Frequencies

Table 40: Non Specific CD4+ T cell Responses

Comparison	G_plus p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.166	1	0.2988
LTBI SM+ to LTBI SM-	0.9847	1	0.9847
TB SM+ to TB SM-	0.2438	1	0.3657
HC SM+ to LTBI SM+	0.4708	1	0.5297
LTBI SM+ to TB SM+	8e-04	0.0069	0.0069
HC SM+ to TB SM+	0.0292	0.2626	0.0657
HC SM- to LTBI SM-	0.3768	1	0.4844
LTBI SM- to TB SM-	0.0248	0.2232	0.0657
HC SM- to TB SM-	0.0017	0.0156	0.0078

Comparison	T_plus p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.3271	1	0.4206
LTBI SM+ to LTBI SM-	0.1698	1	0.4206
TB SM+ to TB SM-	0.2915	1	0.4206
HC SM+ to LTBI SM+	0.1166	1	0.4206
LTBI SM+ to TB SM+	0.2268	1	0.4206
HC SM+ to TB SM+	0.7319	1	0.7319
HC SM- to LTBI SM-	0.4936	1	0.5553
LTBI SM- to TB SM-	0.3252	1	0.4206
HC SM- to TB SM-	0.056	0.5037	0.4206

Comparison	G_T_plus p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.1767	1	0.318
LTBI SM+ to LTBI SM-	0.6169	1	0.694
TB SM+ to TB SM-	0.8166	1	0.8166
HC SM+ to LTBI SM+	0.1703	1	0.318
LTBI SM+ to TB SM+	0.0068	0.0611	0.0204
HC SM+ to TB SM+	0.2226	1	0.3339
HC SM- to LTBI SM-	0.4099	1	0.527
LTBI SM- to TB SM-	0.0037	0.0336	0.0168
HC SM- to TB SM-	0.002	0.0182	0.0168

Comparison	IL4_plus p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.1994	1	0.2991
LTBI SM+ to LTBI SM-	0.0916	0.824	0.2991
TB SM+ to TB SM-	0.5208	1	0.6133
HC SM+ to LTBI SM+	0.109	0.9813	0.2991
LTBI SM+ to TB SM+	0.1881	1	0.2991
HC SM+ to TB SM+	0.6642	1	0.6642
HC SM- to LTBI SM-	0.1989	1	0.2991
LTBI SM- to TB SM-	0.5452	1	0.6133
HC SM- to TB SM-	0.0205	0.1846	0.1846

Comparison	IL13_plus p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.7786	1	0.9474
LTBI SM+ to LTBI SM-	0.8929	1	0.9474
TB SM+ to TB SM-	0.4358	1	0.8439
HC SM+ to LTBI SM+	0.109	0.9813	0.8439
LTBI SM+ to TB SM+	0.9474	1	0.9474
HC SM+ to TB SM+	0.2408	1	0.8439
HC SM- to LTBI SM-	0.3661	1	0.8439
LTBI SM- to TB SM-	0.4688	1	0.8439
HC SM- to TB SM-	0.6062	1	0.9093

Comparison	IL4_IL13_plus p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.8298	1	0.9109
LTBI SM+ to LTBI SM-	0.3448	1	0.7702
TB SM+ to TB SM-	0.4689	1	0.7702
HC SM+ to LTBI SM+	0.9109	1	0.9109
LTBI SM+ to TB SM+	0.4999	1	0.7702
HC SM+ to TB SM+	0.5991	1	0.7702
HC SM- to LTBI SM-	0.5585	1	0.7702
LTBI SM- to TB SM-	0.4099	1	0.7702
HC SM- to TB SM-	0.0587	0.5286	0.5286

Mtb Whole Cell Lysate Specific CD4+ T cell Cytokine Frequencies
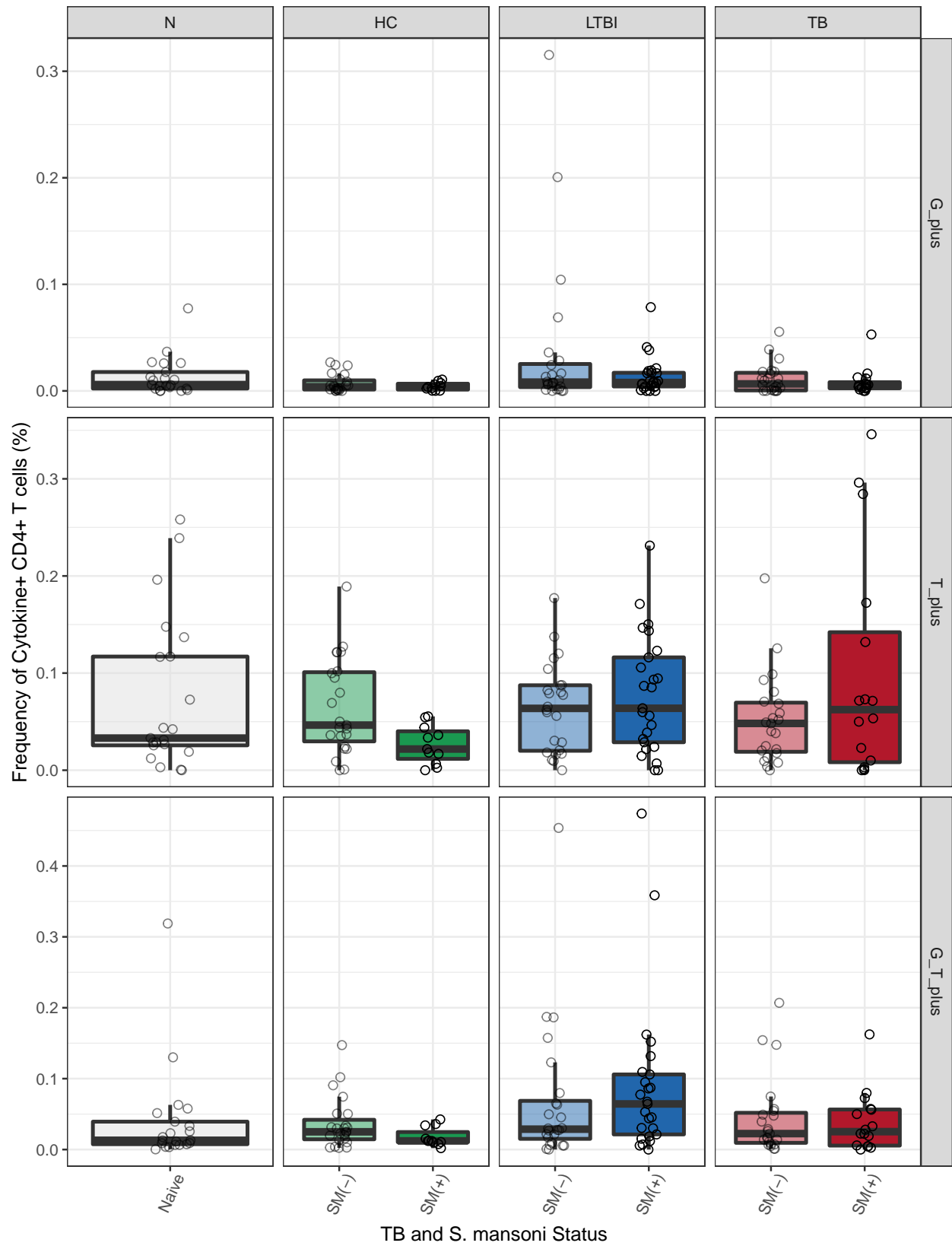
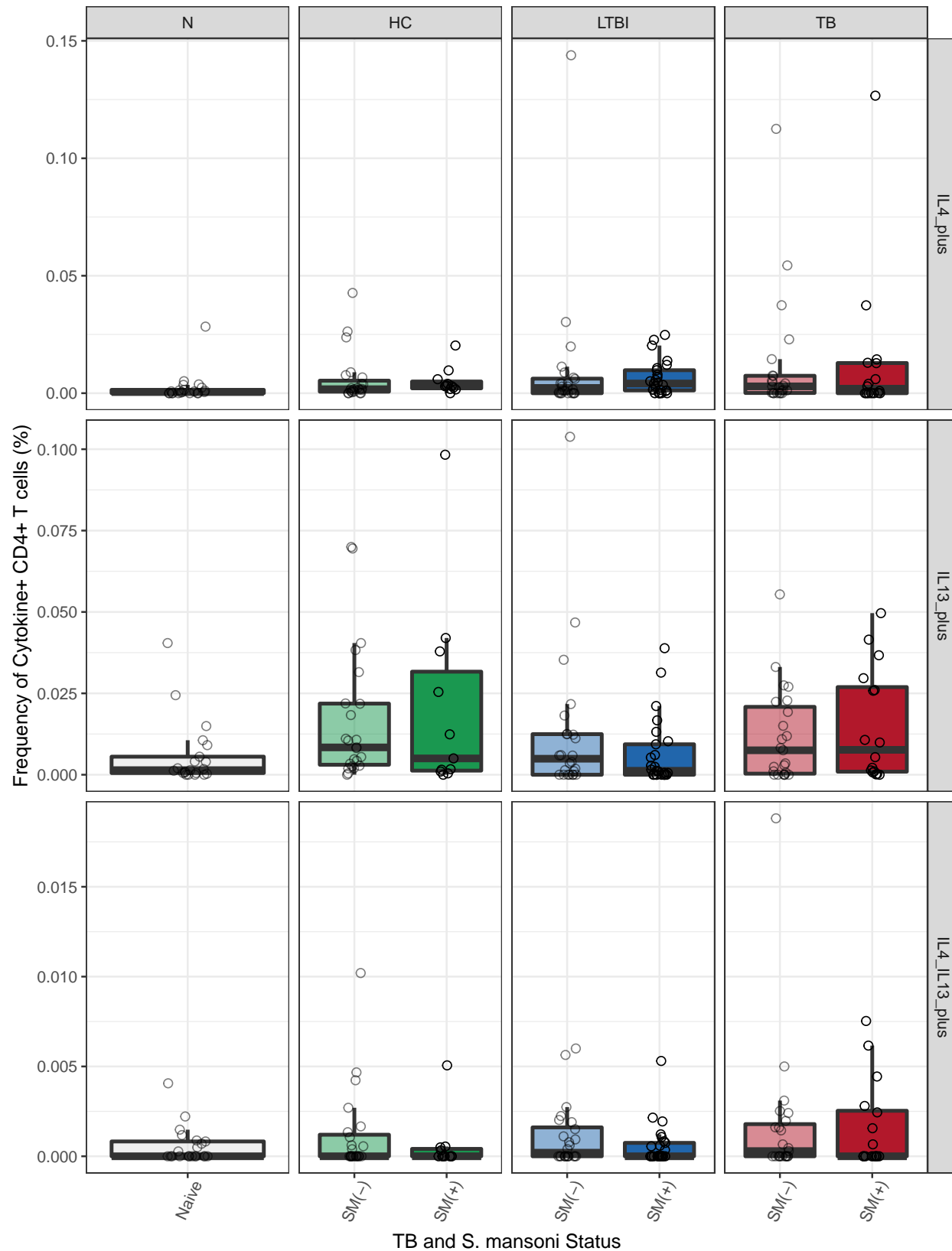Mtb Whole Cell Lysate Specific CD4+ T cell Cytokine Frequencies

Table 46: Mtb Whole Cell Lysate Specific CD4+ T cell Responses

Comparison	G_plus p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.7966	1	0.7966
LTBI SM+ to LTBI SM-	0.7336	1	0.7966
TB SM+ to TB SM-	0.6567	1	0.7966
HC SM+ to LTBI SM+	0.0636	0.5724	0.3529
LTBI SM+ to TB SM+	0.1176	1	0.3529
HC SM+ to TB SM+	0.6043	1	0.7966
HC SM- to LTBI SM-	0.0905	0.8144	0.3529
LTBI SM- to TB SM-	0.3104	1	0.6984
HC SM- to TB SM-	0.4947	1	0.7966

Comparison	T_plus p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.0214	0.1925	0.0963
LTBI SM+ to LTBI SM-	0.4532	1	0.6111
TB SM+ to TB SM-	0.4753	1	0.6111
HC SM+ to LTBI SM+	0.011	0.0992	0.0963
LTBI SM+ to TB SM+	0.8621	1	0.8816
HC SM+ to TB SM+	0.126	1	0.3781
HC SM- to LTBI SM-	0.8816	1	0.8816
LTBI SM- to TB SM-	0.2505	1	0.5635
HC SM- to TB SM-	0.3736	1	0.6111

Comparison	G_T_plus p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.1328	1	0.3983
LTBI SM+ to LTBI SM-	0.2005	1	0.4512
TB SM+ to TB SM-	1	1	1
HC SM+ to LTBI SM+	0.0033	0.0294	0.0294
LTBI SM+ to TB SM+	0.0577	0.5197	0.2598
HC SM+ to TB SM+	0.2942	1	0.5296
HC SM- to LTBI SM-	0.4927	1	0.6335
LTBI SM- to TB SM-	0.4284	1	0.6335
HC SM- to TB SM-	0.8962	1	1

Comparison	IL4_plus p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.2381	1	0.9244
LTBI SM+ to LTBI SM-	0.2938	1	0.9244
TB SM+ to TB SM-	0.6534	1	0.9244
HC SM+ to LTBI SM+	0.9314	1	0.9314
LTBI SM+ to TB SM+	0.5618	1	0.9244
HC SM+ to TB SM+	0.6363	1	0.9244
HC SM- to LTBI SM-	0.8217	1	0.9244
LTBI SM- to TB SM-	0.5676	1	0.9244
HC SM- to TB SM-	0.7572	1	0.9244

Comparison	IL13_plus p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.6454	1	0.813
LTBI SM+ to LTBI SM-	0.2898	1	0.5418
TB SM+ to TB SM-	0.5194	1	0.7791
HC SM+ to LTBI SM+	0.1065	0.9585	0.4406
LTBI SM+ to TB SM+	0.056	0.5036	0.4406
HC SM+ to TB SM+	0.8823	1	0.8823
HC SM- to LTBI SM-	0.1469	1	0.4406
LTBI SM- to TB SM-	0.7227	1	0.813
HC SM- to TB SM-	0.301	1	0.5418

Comparison	IL4_IL13_plus p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.4705	1	0.818
LTBI SM+ to LTBI SM-	0.3568	1	0.818
TB SM+ to TB SM-	0.9755	1	0.9755
HC SM+ to LTBI SM+	0.5144	1	0.818
LTBI SM+ to TB SM+	0.4706	1	0.818
HC SM+ to TB SM+	0.4057	1	0.818
HC SM- to LTBI SM-	0.6609	1	0.8497
LTBI SM- to TB SM-	0.812	1	0.9135
HC SM- to TB SM-	0.5453	1	0.818

Mtb Peptide Specific CD4+ T cell Cytokine Frequencies
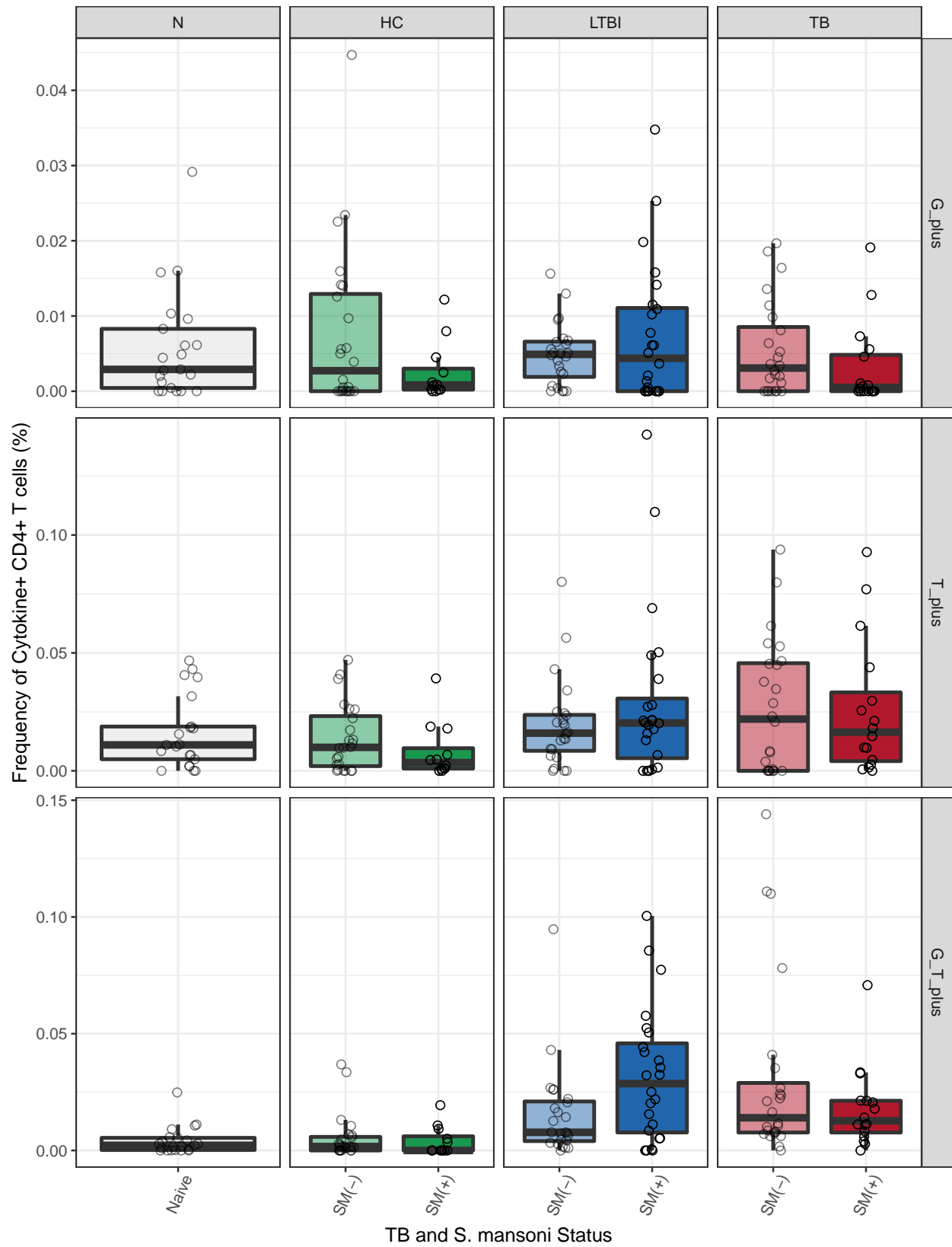
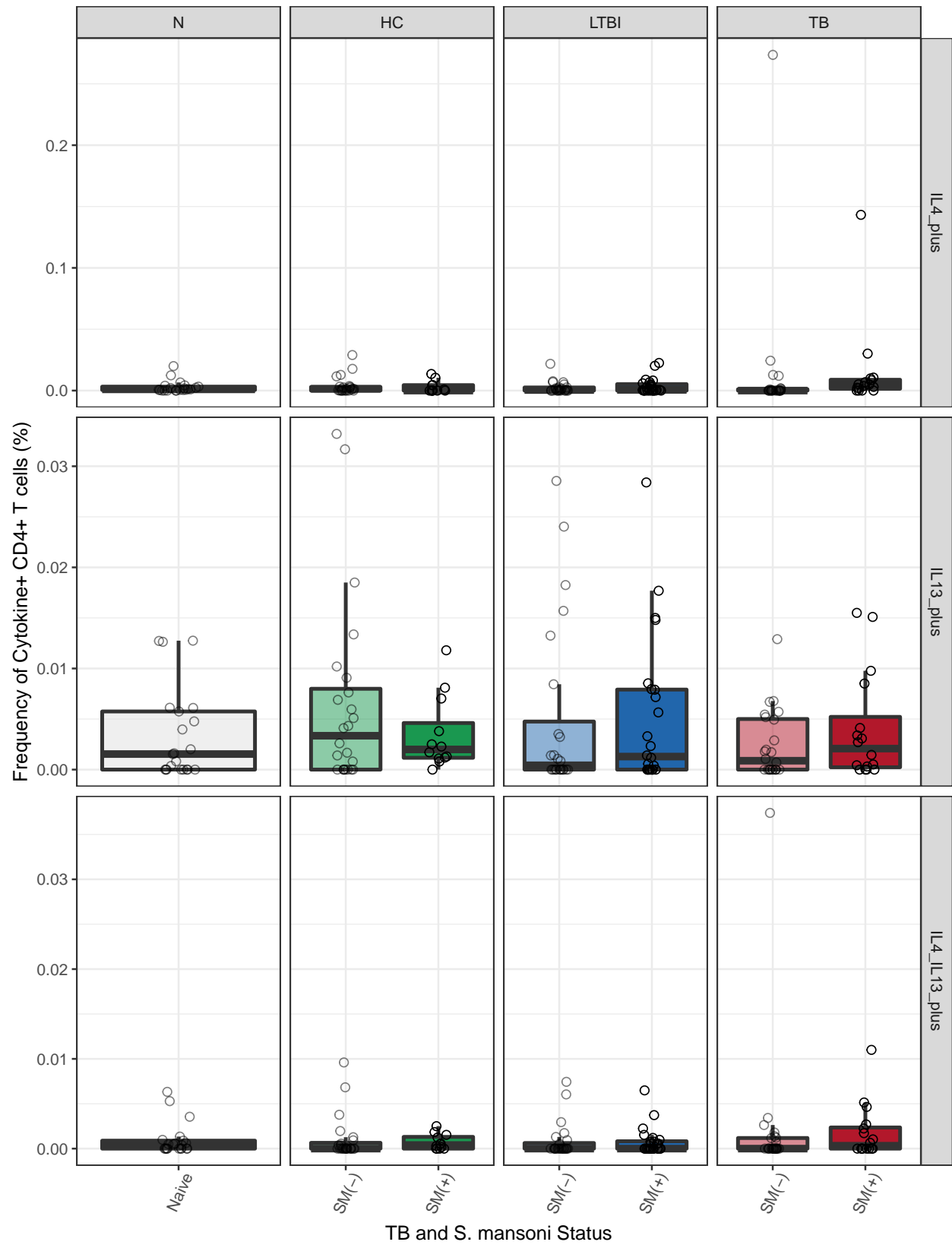# Mtb Peptide Specific CD4+ T cell Cytokine Frequencies

Table 52: Mtb Peptide Specific CD4+ T cell Responses

Comparison	G_plus p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.5528	1	0.9582
LTBI SM+ to LTBI SM-	0.9255	1	0.9582
TB SM+ to TB SM-	0.1756	1	0.7902
HC SM+ to LTBI SM+	0.3687	1	0.9582
LTBI SM+ to TB SM+	0.1689	1	0.7902
HC SM+ to TB SM+	0.5872	1	0.9582
HC SM- to LTBI SM-	0.7711	1	0.9582
LTBI SM- to TB SM-	0.6407	1	0.9582
HC SM- to TB SM-	0.9582	1	0.9582

Comparison	T_plus p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.2737	1	0.5378
LTBI SM+ to LTBI SM-	0.5154	1	0.773
TB SM+ to TB SM-	0.803	1	0.9034
HC SM+ to LTBI SM+	0.0419	0.3768	0.2177
LTBI SM+ to TB SM+	0.923	1	0.923
HC SM+ to TB SM+	0.0484	0.4353	0.2177
HC SM- to LTBI SM-	0.2471	1	0.5378
LTBI SM- to TB SM-	0.7403	1	0.9034
HC SM- to TB SM-	0.2988	1	0.5378

Comparison	G_T_plus p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.4263	1	0.4796
LTBI SM+ to LTBI SM-	0.0454	0.4089	0.0818
TB SM+ to TB SM-	0.5436	1	0.5436
HC SM+ to LTBI SM+	5e-04	0.0049	0.0024
LTBI SM+ to TB SM+	0.1589	1	0.2043
HC SM+ to TB SM+	0.0017	0.0149	0.005
HC SM- to LTBI SM-	0.0022	0.02	0.005
LTBI SM- to TB SM-	0.0949	0.8539	0.1423
HC SM- to TB SM-	0	4e-04	4e-04

Comparison	IL4_plus p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.5045	1	0.6361
LTBI SM+ to LTBI SM-	0.6453	1	0.6453
TB SM+ to TB SM-	0.0147	0.1324	0.1324
HC SM+ to LTBI SM+	0.5348	1	0.6361
LTBI SM+ to TB SM+	0.1311	1	0.2951
HC SM+ to TB SM+	0.0985	0.8866	0.2951
HC SM- to LTBI SM-	0.5654	1	0.6361
LTBI SM- to TB SM-	0.2707	1	0.4873
HC SM- to TB SM-	0.1229	1	0.2951

Comparison	IL13_plus p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.879	1	0.9043
LTBI SM+ to LTBI SM-	0.5754	1	0.9043
TB SM+ to TB SM-	0.3006	1	0.9017
HC SM+ to LTBI SM+	0.5873	1	0.9043
LTBI SM+ to TB SM+	0.8113	1	0.9043
HC SM+ to TB SM+	0.7622	1	0.9043
HC SM- to LTBI SM-	0.2433	1	0.9017
LTBI SM- to TB SM-	0.9043	1	0.9043
HC SM- to TB SM-	0.1334	1	0.9017

Comparison	IL4_IL13_plus p-values	Bonferonni Corrected p-values	FDR Corrected p-vales
HC SM+ to HC SM-	0.2679	1	0.8604
LTBI SM+ to LTBI SM-	0.4065	1	0.8604
TB SM+ to TB SM-	0.2552	1	0.8604
HC SM+ to LTBI SM+	0.478	1	0.8604
LTBI SM+ to TB SM+	0.3786	1	0.8604
HC SM+ to TB SM+	0.8277	1	0.8945
HC SM- to LTBI SM-	0.6582	1	0.8945
LTBI SM- to TB SM-	0.7729	1	0.8945
HC SM- to TB SM-	0.8945	1	0.8945