

**Supplementary Table S1. Biomarker values of patients with active TB disease**

ID	TB1-NIL	TB2-NIL	IP-10 pg/mL (log2)	MIG pg/mL (log2)	IL-1ra pg/mL (log2)
151	1.458	1.128	5,042.8 (12.3)	5,404.7 (12.4)	1,910.9 (10.9)
180	4.884	4.994	16,384.0 (14.0)	11,585.2 (13.5)	8,192.0 (13.0)
369	2.899	3.343	17,559.9 (14.1)	10,085.5 (13.3)	4,390.0 (12.1)
434	6.81	6.81	18,820.3 (14.2)	26,615.9 (14.7)	20,171.1 (14.3)
445	0.134	0.528	3,563.8 (11.8)	2,521.4 (11.3)	724.1 (9.5)

**Footnote**

TB1-NIL and TB2-NIL denote regular individual QuantiFERON Gold Plus (IFN- $\gamma$ ) values. Biomarker values in the table originate from the TB1-NIL/TB2-NIL with the highest IFN- $\gamma$  response.

**Supplementary Table S2. All biomarkers categorized by TB-endemicity**

Biomarkers	Low-negative			Borderline profile -*			Borderline profile +			Positive		
	Non TB-endemic	TB-endemic	p-value	Non TB-endemic	TB-endemic	p-value	Non TB-endemic	TB-endemic	p-value	Non TB-endemic	TB-endemic	p-value
β-NGF	0	0	0.955	0	0	0.775	0.7	1.35	0.683	0	0	0.850
CTACK	5	5.35	0.58	<b>5.1</b>	<b>0</b>	<b>0.039</b>	3.9	4.8	0.807	1.85	3.8	0.382
eotaxin	0	0	0.261	0	0	0.389	0	0	1.000	0	0	0.923
FGF-basic	2.3	3.75	0.087	3.1	2.2	0.621	2.1	3.1	0.835	3.55	4.3	0.661
G-CSF	4.2	3.95	1.000	6.1	5.15	0.696	0	6.5	0.347	0	6.3	0.193
GM-CSF	0	0	0.973	0	0	0.897	0	0	0.454	0.5	1.5	0.937
GRO-α	9.5	8.75	0.435	8.9	8.1	0.735	8.8	8.05	0.873	8.45	9.5	0.053
HGF	5.2	5.5	0.422	5.7	2.65	0.449	6.8	4.95	0.334	7.5	7	0.856
IFN-α2	0	2.55	0.505	2	1	0.515	0.9	0.8	0.910	1.5	2.9	0.648
IFN-γ	3.2	3.85	0.087	3.9	2.95	0.621	3.7	3.5	0.683	4.4	5	0.346
IL-1α	0	4.7	0.335	5.5	1.75	0.307	0	4.85	0.288	5.25	5.3	0.907
IL-1β	4.2	6.4	0.491	5.9	1.7	0.217	0	3.25	0.592	5.1	5.9	0.609
IL-1ra	10.3	10.1	0.596	9.3	7.45	0.389	11	10.35	0.098	11.95	11.8	0.140
IL-2	2.3	3.8	0.271	1.5	1.4	0.696	3.7	4.1	0.413	5.45	5.6	0.842
IL-2ra	5.5	5.7	0.710	0	4.75	0.856	5.2	5.1	0.936	4	5.8	0.161
IL-3	0	0	0.795	0	0	0.938	0	0	0.427	0	0	0.804
IL-4	0	0	0.884	0	0.15	0.856	0	0	0.475	0	1.1	0.156
IL-5	0	2.1	0.660	0	1.7	0.585	4.7	2.25	0.728	0	0	0.482
IL-6	7.8	7.5	0.565	4.9	6.2	0.696	0	6.9	0.458	0	7.5	0.054
IL-7	0	0	0.848	0	0	0.585	0	0	0.112	0	0	0.240
IL-8	11.9	13.15	0.324	12.3	10.75	0.775	12.1	12.05	0.457	12.25	12.1	0.916
IL-9	5.5	6.3	0.612	5.5	5.05	0.979	5.6	5.9	0.733	5	6.4	0.201
IL-10	0	0	0.973	0	0.25	0.621	0	0.85	0.051	0	0	0.703
IL-12p70	0	0	0.937	0	0	0.696	0	0	0.373	0	0	0.213
IL-12p40	4.6	4.5	0.884	6.3	4.8	1.000	4.2	0	0.962	0	5.6	0.195
IL-13	0	0	0.660	0	0	0.938	0	0	0.478	0	0	0.150
IL-15	0	2.5	0.123	0	0	0.621	0	0	0.161	0	0	0.490
IL-16	0	0	0.491	1.3	0	0.333	0	0	0.742	3.4	4.8	0.921
IL-17A	1.3	1.75	0.565	1.8	0.55	0.217	0.1	1.5	0.787	2.4	1.8	0.707
IL-18	3.3	3.5	0.693	3.4	0.4	0.119	2.6	3.05	0.578	3.7	4.2	0.901
IP-10	6.6	7.95	0.271	9.4	9.8	0.897	11.3	11.35	0.742	13.05	12.5	0.730
LIF	4.7	6.35	0.324	4.4	5.65	0.775	4.9	3.35	0.588	2.65	6.4	0.154
M-CSF	2.3	2.1	0.919	0	0	0.333	2.4	2.55	0.688	2.5	2.9	0.931
MCP-1	9.3	9.6	0.677	8.9	8.95	0.897	9.6	9.4	0.936	9.6	9.6	0.939
MCP-3	7	7.9	0.207	7.3	6.95	0.735	7.9	6.8	0.136	8.05	8	0.992
MIF	0	4.15	0.476	7.3	4.4	0.815	7.6	7	0.351	0	8.6	0.695
MIG	5.5	8.4	0.057	8.6	8.4	0.360	11.3	11.2	0.873	12.9	12.8	0.486
MIP-1α	5	3.25	0.848	4.1	6.5	0.389	0	1.05	0.156	0	0	0.238
MIP-1β	7.9	7.6	0.848	6.4	7	0.515	6.8	8	0.275	7.25	8.8	0.348
PDGF-bb	8.4	8.35	0.919	5.9	0	0.333	8.4	7.35	0.515	<b>6.85</b>	<b>9</b>	<b>0.038</b>
RANTES	9.2	8.7	0.919	0	4.4	0.775	9.3	9.85	0.781	<b>3.65</b>	<b>10.5</b>	<b>0.038</b>
SCF	3.6	4.25	0.313	3.3	1.85	0.585	3.3	2.65	0.619	3.65	4.6	0.752
SCGF-β	14.1	14.05	0.744	13.5	12.6	0.095	14	14.1	0.810	14.5	14.5	0.662
SDF-1α	4.9	7.05	0.092	6.6	0	0.217	4.6	1.95	0.278	4.4	6.3	0.344
TNF-α	4.9	8.05	0.168	4.7	5.05	1.000	5.3	6	0.928	6.1	7.1	0.756
TNF-β	5.8	6.9	0.313	5	5.6	0.856	5.8	5.75	0.929	5.9	6.9	0.201
TRAIL	4.9	6.65	0.079	5.1	2.2	0.360	4.7	5.6	0.971	4.95	5.6	0.985
VEGF	0	0	0.660	4.1	0	0.418	6	6.8	0.525	0	0	0.773

**Footnote**

Median values of all biomarkers classified based on TB-endemicity (defined as country with a TB incidence  $\geq 40$  cases of TB-infection with active disease/100,000 inhabitants). P-values were calculated using the Mann-Whitney U test. P-values  $< 0.05$  with their corresponding biomarker values are marked bold. Includes all data. Cytokine data are log2 transformed values.

Abbreviations used: TB: Tuberculosis

\*From one individual the country of origin could not be retrieved

**Supplementary Table S3. All biomarkers categorized by autoimmune disease**

Biomarkers	Low-negative			Borderline profile -			Borderline profile +			Positive		
	no AI N=29	AI N=28	p-value	no AI N=21	AI N=7	p-value	no AI N=41	AI N=18	p-value	no AI N=36	AI N=15	p-value
β-NGF	0	0	0.592	0	0	0.917	1.3	0.55	0.511	0.3	0	0.072
CTACK	4.3	5.25	0.889	0	6.2	0.172	4.5	5.1	0.314	1.6	4.7	0.974
eotaxin	0	0	0.373	0	0.9	0.080	0	0	0.464	0	0	0.371
FGF-basic	2.3	3.55	0.194	<b>2.7</b>	<b>4.4</b>	<b>0.048</b>	1.9	2.95	0.306	4.5	2.5	0.074
G-CSF	0	7.65	0.601	<b>5.5</b>	<b>9.7</b>	<b>0.017</b>	0	0	0.956	0	0	0.603
GM-CSF	0	0	0.779	0	0	0.466	0.3	0	0.499	<b>2.3</b>	<b>0</b>	<b>0.008</b>
GRO-α	8.8	9.4	0.712	6.5	9.9	0.678	8.4	6.3	0.080	9.45	8.8	0.122
HGF	4.3	6.3	0.479	4	6.9	0.126	<b>3.1</b>	<b>7.25</b>	<b>0.007</b>	7.5	6.9	0.917
IFN-α2	0	0.55	0.545	0	3.2	0.113	0	1.85	0.143	3.25	1.5	0.169
IFN-γ	3.2	3.4	0.968	2.6	4	0.296	3.7	3.35	0.348	4.95	4.4	0.475
IL-1α	0	4.85	0.421	4.4	5.5	0.113	2.3	2.3	0.759	5.7	0	0.186
IL-1β	4.2	5.25	0.928	4.1	6.8	0.071	0	4.15	0.70	5.8	0	0.130
IL-1ra	10.2	10.6	0.182	9.2	10.2	0.126	10.6	11	0.444	12.2	11.4	0.456
IL-2	3.1	2.3	0.492	1.3	2.7	0.296	4	3.35	0.499	5.75	5.5	0.264
IL-2ra	4.9	5.8	0.204	0	5.2	0.405	4.9	5.35	0.836	5	5.1	0.841
IL-3	0	0	0.523	0	0	0.604	0	0	0.437	<b>0</b>	<b>0</b>	<b>0.043</b>
IL-4	0	0	0.649	0	1	0.499	0	0.15	0.426	1	0	0.374
IL-5	0	0	0.423	0	0	0.717	4.5	2.35	0.663	<b>4.5</b>	<b>0</b>	<b>0.004</b>
IL-6	7.8	7.7	0.562	6	8.4	0.172	6.6	0	0.331	6.65	0	0.159
IL-7	0	0	0.591	0	2.2	0.376	0	0	0.621	0	0	0.752
IL-8	12.1	11.8	0.520	11.3	12.9	0.435	12.3	11.05	0.109	12.65	11.2	0.156
IL-9	5	6.2	0.122	5.3	5.7	0.640	5.7	5.15	0.703	<b>6.85</b>	<b>3.8</b>	<b>0.002</b>
IL-10	0	0	0.764	0	0	0.678	0	0	0.624	0	0	0.754
IL-12p70	0	0	0.309	0	0	0.272	0	0	0.166	0	0	0.539
IL-12p40	3.5	5.15	0.743	6.2	6.3	0.959	0	4.1	0.516	5.2	5	0.441
IL-13	0	0	0.543	0	0	0.499	0	0	0.762	<b>0.8</b>	<b>0</b>	<b>0.022</b>
IL-15	0	0	0.92	0	0	0.249	0	0	0.686	0	0	0.523
IL-16	0	3.25	0.365	0	3.5	0.126	0	0.95	0.497	5.05	0	0.265
IL-17A	0	1.5	0.293	<b>0</b>	<b>2.7</b>	<b>0.027</b>	0	1.2	0.331	2.1	2.7	0.785
IL-18	<b>3.1</b>	<b>4.15</b>	<b>0.037</b>	2.1	3	0.917	2.6	3.35	0.595	3.8	4.1	0.521
IP-10	6.6	7.05	0.754	9.1	10.2	0.055	11.3	11.4	0.974	12.95	12.1	0.059
LIF	5.4	5.4	0.895	3.4	5.8	0.208	3.9	5.65	0.261	6.25	0	0.093
M-CSF	1.7	2.6	0.139	0	1.6	0.272	2.4	2.4	0.747	2.95	2	0.292
MCP-1	9.3	9.25	0.420	8.8	8.9	0.876	9.6	9.3	0.263	9.55	9.7	0.764
MCP-3	7.5	7	0.968	7.2	7.3	0.678	7.8	7.85	0.908	8.1	7.7	0.780
MIF	0	5.9	0.444	<b>0</b>	<b>9.7</b>	<b>0.048</b>	6.8	8.05	0.565	9	0	0.113
MIG	6.2	5.7	0.551	8.5	8.6	0.678	11.2	11.4	0.837	13.2	12.6	0.115
MIP-1α	5	5.1	0.861	4.1	5.2	0.836	0	0	0.924	0	0	0.372
MIP-1β	6.8	8.05	0.384	6.4	7.7	0.466	7.5	7.05	0.340	8.5	8.4	0.454
PDGF-bb	7.7	8.65	0.135	3.3	5.1	0.568	7.9	8.5	0.907	8.8	6.1	0.308
RANTES	7.8	10	0.254	0	8.8	0.435	9.7	9.25	0.390	10.35	9	0.348
SCF	3.2	3.75	0.949	0	3.7	0.296	2.5	3.9	0.230	4.7	3	0.159
SCGF-β	13.9	14.15	0.690	13	14.3	0.208	14.3	13.8	0.098	14.4	14.7	0.756
SDF-1α	3.8	6.55	0.251	4.3	7.1	0.155	3.9	5.65	0.404	<b>6.3</b>	<b>0</b>	<b>0.046</b>
TNF-α	4.9	5.1	0.591	2.9	6.5	0.140	3.9	6.25	0.327	6.95	0	0.205
TNF-β	5.5	6.05	0.334	5	6.7	0.296	5.8	5.65	0.862	<b>6.9</b>	<b>5</b>	<b>0.029</b>
TRAIL	5.3	4.9	0.786	4.9	5.8	0.321	4.1	5.8	0.091	5.7	4.7	0.171
VEGF	0	0	0.314	0	7.1	0.376	6.7	2.65	0.088	3.2	0	0.440

**Footnote**

Median values of all biomarkers classified based on the presence of any autoimmune disease. P-values were calculated using the Mann-Whitney U test. P-values <0.05 with their corresponding biomarker values are marked bold. Includes all data. Cytokine data are log2 transformed values.

Abbreviations used: AI: autoimmune disease

**Supplementary Table S4. All biomarkers categorized by immunosuppressive therapy**

Biomarkers	Low-negative			Borderline profile -			Borderline profile +			Positive		
	No I.S. N=40	I.S. N=11	p-value	No I.S. N=15	I.S. N=8	p-value	No I.S. N=35	I.S. N=9	p-value	No I.S. N=36	I.S. N=5	p-value
β-NGF	0	0	0.673	0	0	0.591	1.7	1.1	0.422	0	0	0.954
CTACK	5.1	4.6	0.742	3.4	2.4	1.000	4.5	4.7	0.932	4.55	0	0.217
eotaxin	0	0	0.406	0	0	0.636	0	0	0.184	0	0	0.954
FGF-basic	1.65	3.4	0.098	3.1	3.95	0.875	2.1	3.7	0.606	3.9	5.1	0.232
G-CSF	1.75	8.9	0.127	<b>5.5</b>	<b>9.85</b>	<b>0.023</b>	0	0	0.567	0	8.4	0.202
GM-CSF	0	0	0.946	0	0	1.000	0	0	0.627	0.55	0	0.629
GRO-α	9.2	9.7	0.328	9.4	3.2	0.357	9.2	0	0.027	9.25	10	0.449
HGF	5.15	7.1	0.394	4	6.3	0.265	6	6.8	0.627	7.15	7.8	0.574
IFN-α2	0	0	0.831	2	2.95	0.466	0	2.4	0.300	2.05	3.4	0.449
IFN-γ	3.15	3.4	0.270	4	3.1	0.975	3.7	3.1	0.098	4.8	5.3	0.340
IL-1α	1.2	4.6	0.762	4.4	5.65	0.076	4.6	4	0.689	5.05	6.1	0.403
IL-1β	4.2	4.8	0.671	5.3	5.6	0.681	3.5	5.3	0.710	5.2	7.9	0.283
IL-1ra	10.3	10.9	0.191	9	9	0.506	11	11.1	0.977	11.85	11.4	0.713
IL-2	2.6	2.3	0.772	1.3	2.1	0.636	3.5	4	1.000	5.5	5.9	0.548
IL-2ra	5.5	5.7	0.729	0	5.35	0.466	5.3	3.1	0.287	4.75	6.3	0.574
IL-3	0	0	0.354	0	0	1.000	0	0	0.373	0	0	0.713
IL-4	0	0	0.687	0	0.35	0.975	0	0	0.474	0.05	1.4	0.340
IL-5	0	0	0.856	0	0	0.975	4.9	0	0.184	0	0	0.862
IL-6	7.8	7.7	0.917	6.4	5.45	0.548	7.2	0	0.076	3.95	8.4	0.522
IL-7	0	0	0.280	0	2.75	0.087	0	0	0.886	0	0	0.685
IL-8	12.1	11.5	0.890	12.6	11.4	0.925	11.8	11.8	0.864	11.75	11.8	0.954
IL-9	5.45	6.4	0.213	5.3	5.25	0.591	5.8	5.7	0.548	6	6.4	0.893
IL-10	0	1.3	0.160	0.7	0.25	0.825	<b>0.8</b>	<b>0</b>	<b>0.047</b>	0	2.5	0.301
IL-12p70	0	0	0.600	0	0	0.825	0	0	0.731	0	0	0.862
IL-12p40	2.3	6.3	0.374	6.4	6.6	1.000	4.9	0	0.689	2.45	6.5	0.320
IL-13	0	0	0.426	0	0	0.636	0	0	0.841	0	0	1.000
IL-15	0	0	0.814	0	0	0.728	0	0	0.529	0	0	0.574
IL-16	0	0	0.219	0	4.55	0.294	0	0	0.510	4.85	1.3	0.601
IL-17A	0.95	2.9	0.189	1.6	1.7	0.728	1.4	0.2	0.647	2.05	3.7	0.175
IL-18	3.35	3.2	0.881	3.5	1.15	0.065	2.6	3.5	0.422	4.25	2.5	0.283
IP-10	6.55	7.3	0.227	9.4	9.8	0.294	11.4	11.3	0.954	12.6	12.5	0.629
LIF	3.7	5.7	0.739	4.4	5.65	0.681	4.9	5.5	0.954	5.4	6.5	0.283
M-CSF	2.2	2.6	0.272	0	0	0.875	2.4	2.4	0.287	2.1	3.2	0.923
MCP-1	9.2	10.2	0.252	8.7	8.05	0.875	9.6	9.1	0.054	9.55	9.7	0.656
MCP-3	6.95	7.8	0.292	6.9	5.85	0.825	7.8	8	0.797	8.05	7.7	0.985
MIF	0	5.9	0.871	6.2	9.25	0.265	6.8	9	0.492	4.1	8.9	0.685
MIG	5.65	6	0.844	8.9	8.1	0.466	11.3	10.8	0.098	12.9	12.8	0.360
MIP-1α	1.7	6.7	0.177	4.1	5.2	0.776	0	0	0.647	0	8.2	0.426
MIP-1β	<b>6.8</b>	<b>8.9</b>	<b>0.042</b>	7.7	6.7	0.681	7.2	7.1	0.586	8.3	9.5	0.656
PDGF-bb	8.1	8.7	0.614	5.9	4.2	0.975	7.5	8.6	0.300	8.65	9.7	0.497
RANTES	9.25	10.3	0.972	0	4.4	0.975	10	5	0.111	10.65	7.3	0.629
SCF	3.35	3.8	0.853	3.3	3.5	0.925	3.4	3.3	0.932	4.7	4.3	0.923
SCGF-β	13.9	14.4	0.097	13.3	12.8	0.636	<b>14.3</b>	<b>12.9</b>	<b>0.015</b>	14.6	12.5	0.497
SDF-1α	6.2	6.5	0.917	0	6.9	0.325	4.2	2.8	0.797	5.45	2.9	0.656
TNF-α	4.65	6.4	0.841	4.3	6.15	0.428	5.6	6.8	0.886	6.05	8.5	0.188
TNF-β	5.65	6.3	0.204	4.6	6.45	0.506	5.8	5.8	0.405	6.75	6.1	0.985
TRAIL	4.9	4.9	0.571	6	4.85	0.636	5.2	5.7	0.775	5.4	6.3	0.381
VEGF	0	0	0.834	0	3.45	0.975	7.4	5.3	0.092	0	0	0.772

**Footnote**

Median values of all biomarkers classified based on concomitant use of immunosuppressive therapy.

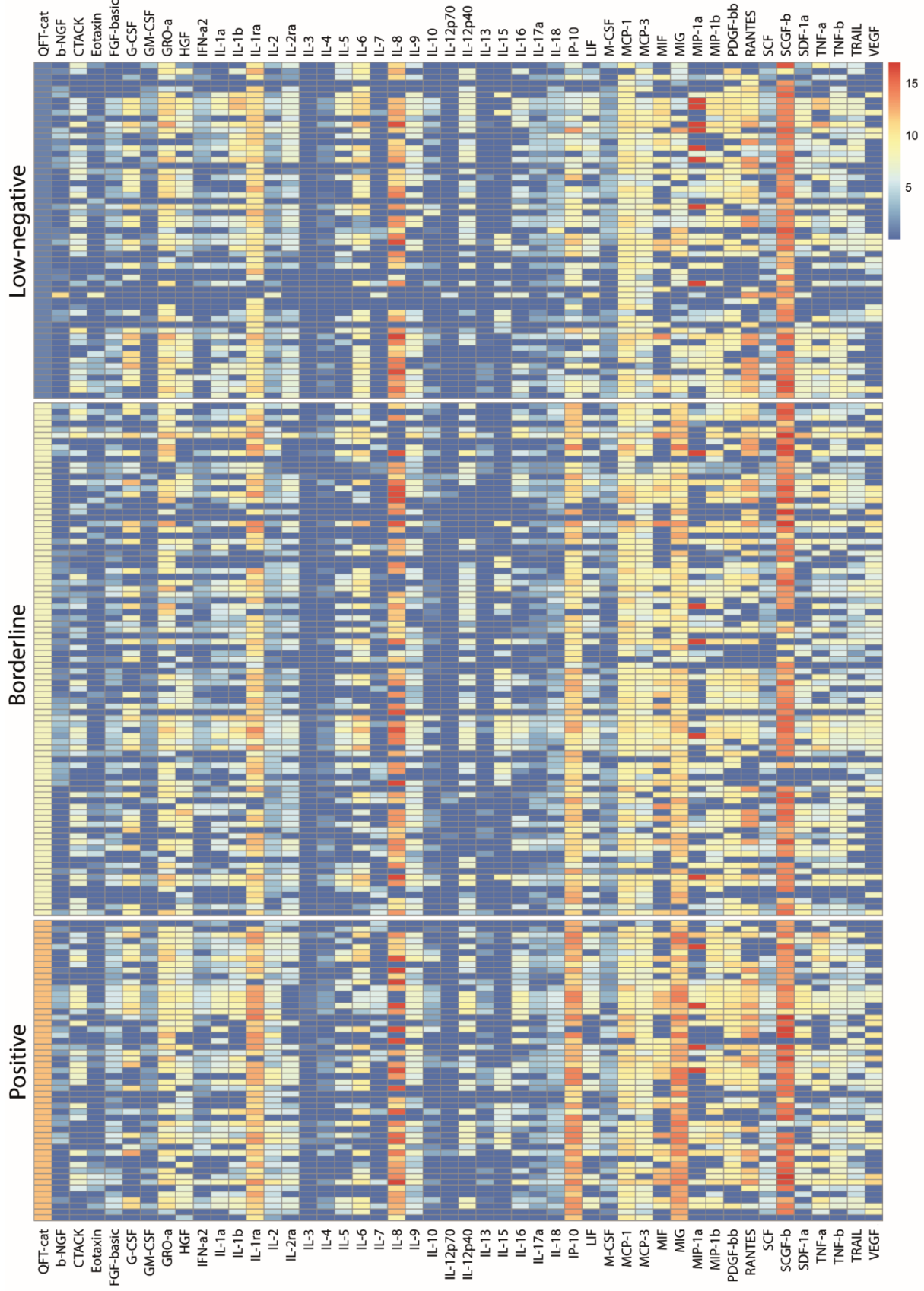
P-values were calculated using the Mann-Whitney U test. P-values <0.05 with their corresponding biomarker values are marked bold. Includes all data. Cytokine data are log<sub>2</sub> transformed values.

Abbreviations used: I.S.: immunosuppressive therapy

## **Supplementary Figures**

### **Figure S1. Heatmap of all measured biomarkers**

Heatmap including all maximal Log2-transformed values of each biomarker (by column), with omittance of IFN- $\gamma$ , for each included individual (by row). Includes all data.



**Figure S2. Correlation between all biomarker values in the TB1 and TB2 tubes**

Correlation matrix including all biomarkers measured in the TB1 tubes (X-axis) and TB2 tubes (Y-axis) from those with a low-negative (A), borderline profile – (B), borderline profile + (C), and positive QuantiFERON result (D). Numbers in the graph denote the Spearman's rank correlation coefficients. Correlations were calculated using Spearman's test for correlation. Includes all data.

**Figure S2A**

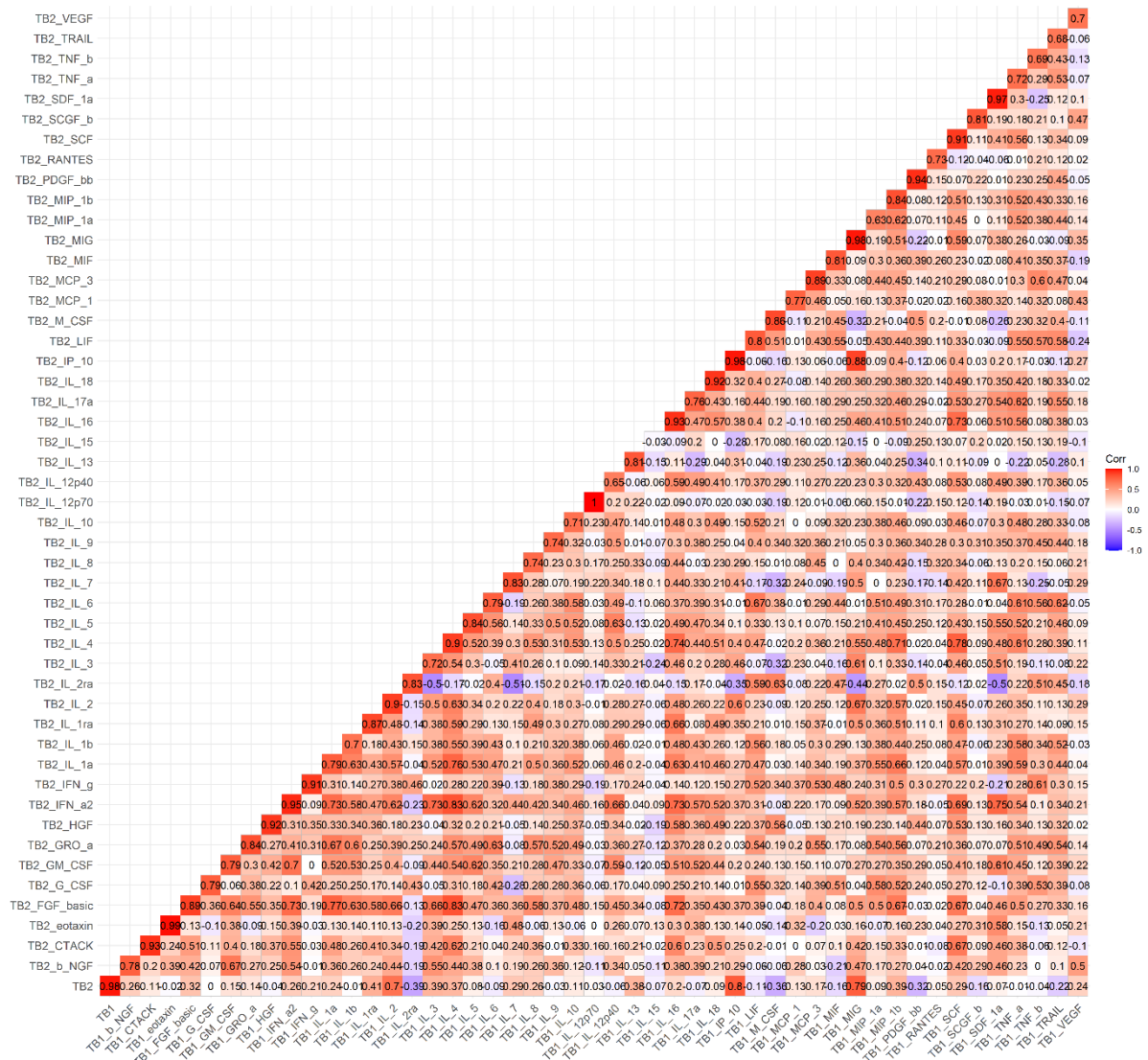


Figure S2B

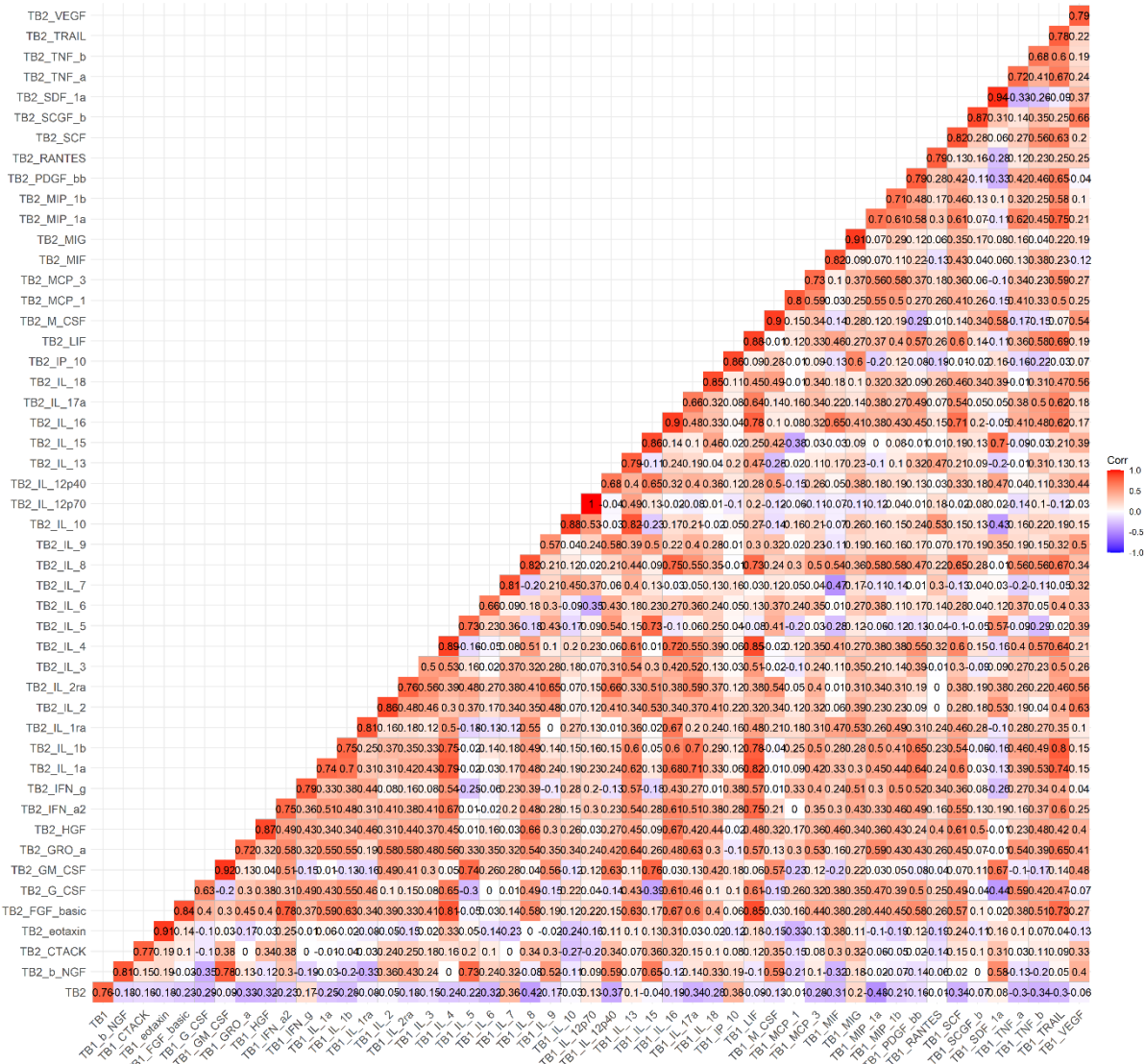
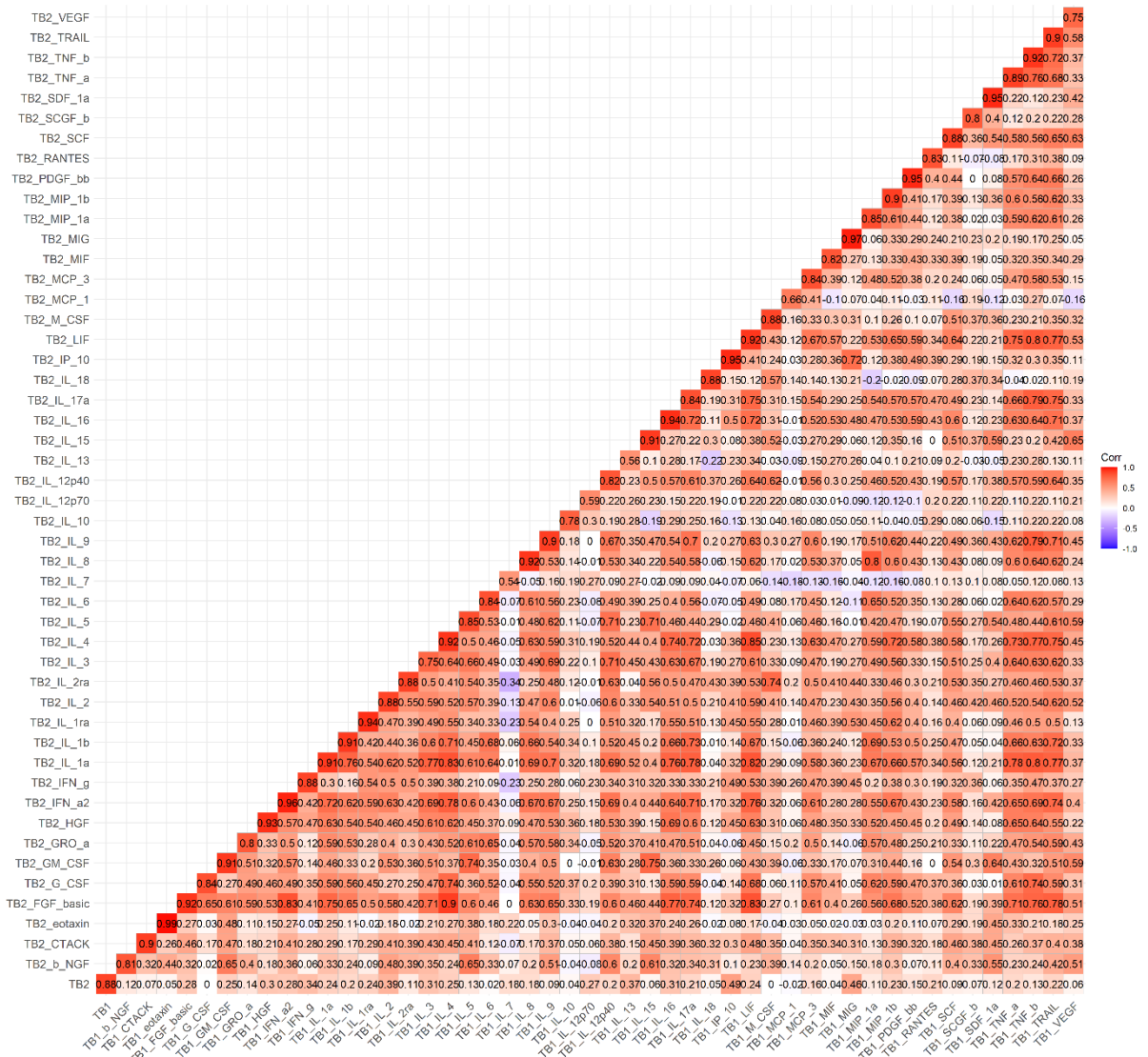
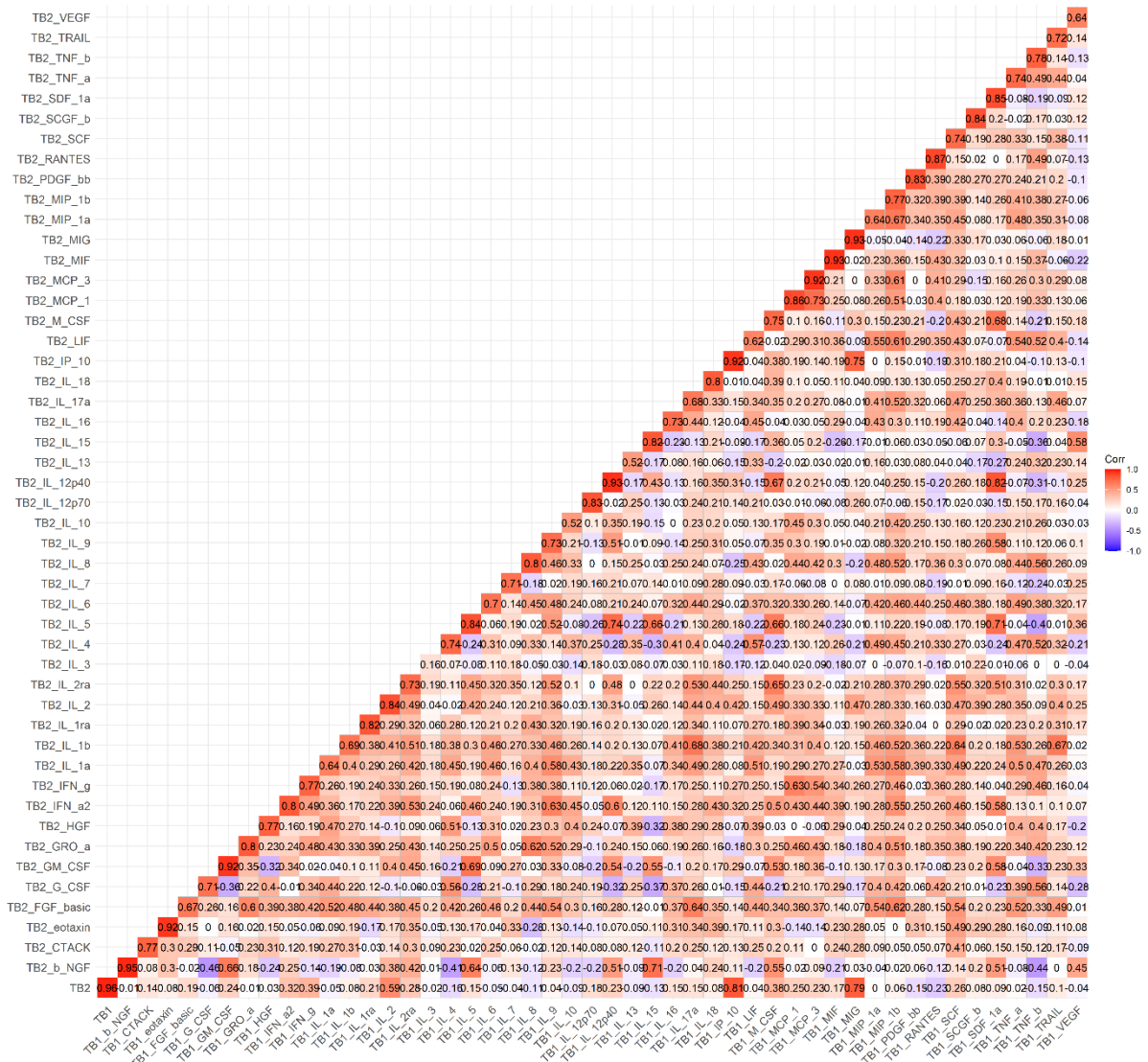




Figure S2C

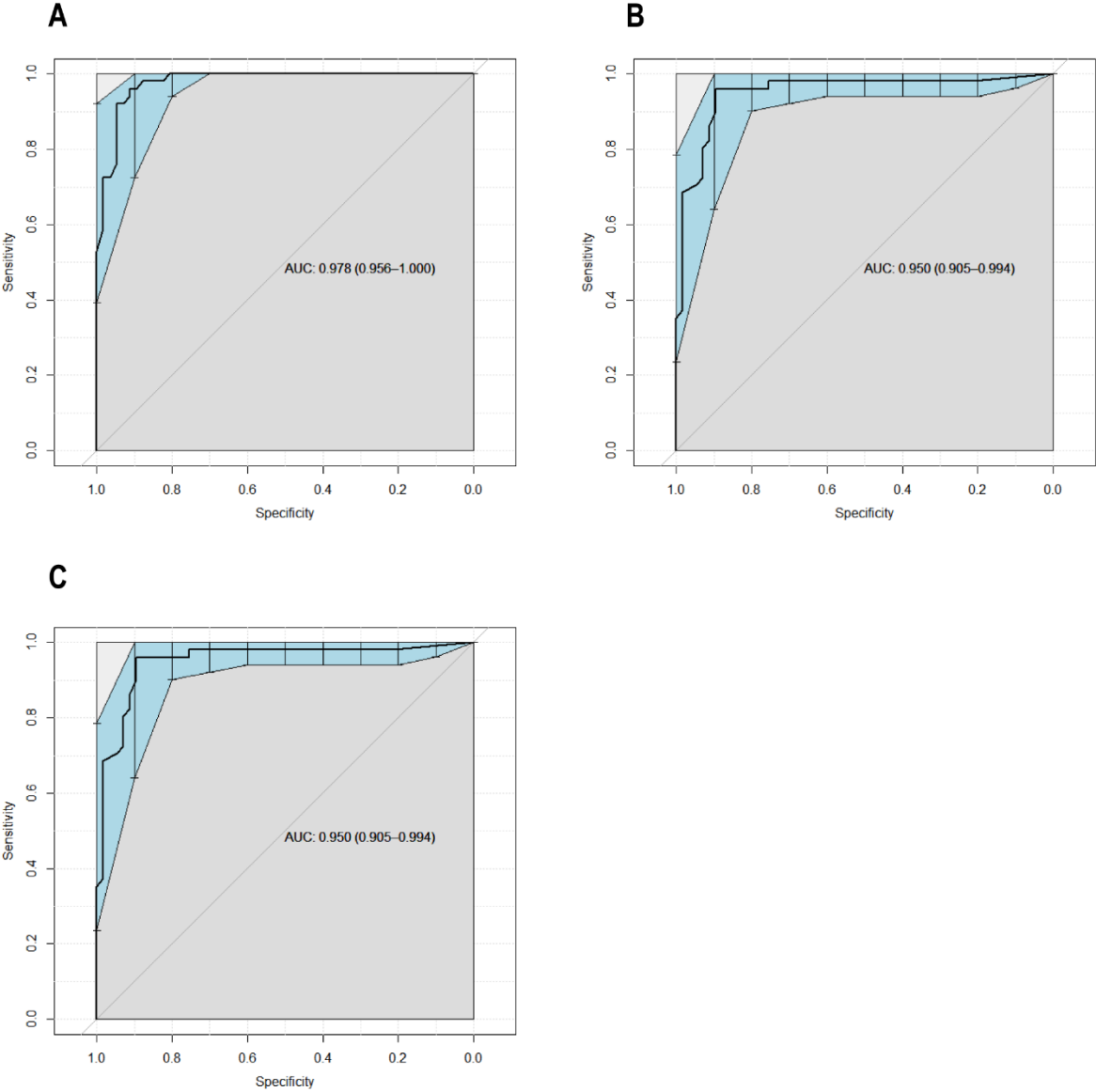


# Figure S2D



**Figure S3. Accuracy of IP-10, MIG and IL-1ra for TB-infection**

Receiver operating characteristic (ROC) curve plot showing the prediction accuracy of MIG (A), IP-10 (B) and IL-1ra (C) between patients with TB-infection (based on a positive QuantiFERON (QFT) result) and without TB-infection (based on a low-negative QFT result). Includes all data.



### Figure S4. Biomarker values by QuantiFERON-Plus categories

Median biomarker values displayed as box and whiskers (5%-95%). The lines represent the optimal cut-off (Youden Index) derived from receiver operating characteristic (ROC) curves (supplementary Figure 3). All data were log<sub>2</sub>-transformed prior to analysis. Includes all data.

