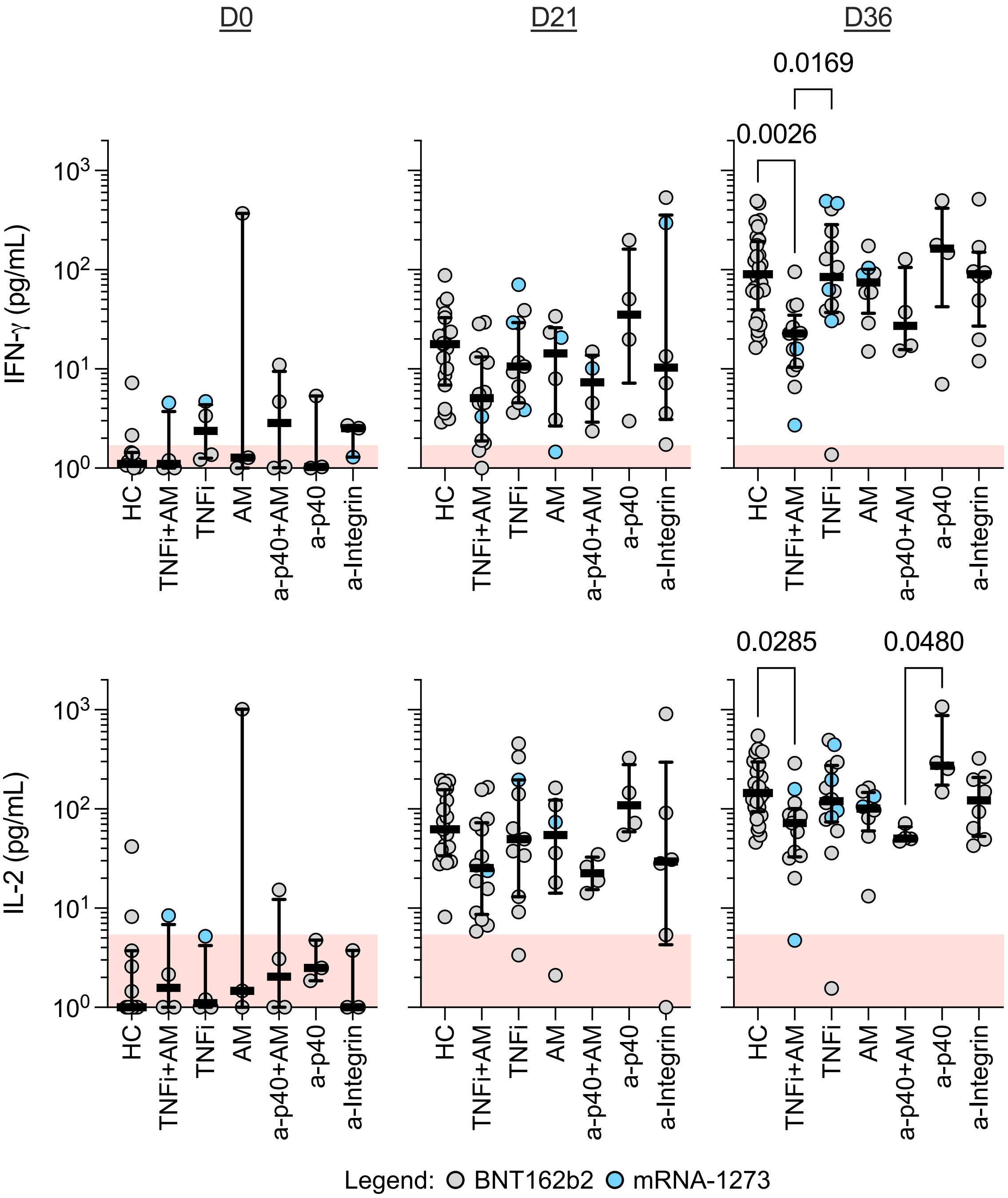

Figure S1. Early T cell responses in patients under different immunotherapies. (**A**) Dot plots with median line (middle bar) and interquartile range (whiskers) of quantified IFN-γ or IL-2 concentrations (pg/mL) from S pool-stimulated whole blood supernatants of HC and IBD patients grouped by treatment and faceted according to timepoint. Shaded red region denotes the area under the threshold for a positive test. Statistical analyses were performed by Kruskal-Wallis and Dunn's test with p values shown above the comparison lines when significant (α=0.05). For D 0: HC (n=10), TNFi+AM (n=4), TNFi (n=4), AM (n=3), a-p40+AM (n=4), a-p40 (n=3), a-Integrin (n=3). For D 21: HC (n=19), TNFi+AM (n=14), TNFi (n=11), AM (n=6), a-p40+AM (n=4), a-p40 (n=4), a-Integrin (n=6). For D 36: HC (n=28), TNFi+AM (n=14), TNFi (n=14), AM (n=8), a-p40+AM (n=5), a-p40 (n=4), a-Integrin (n=8).

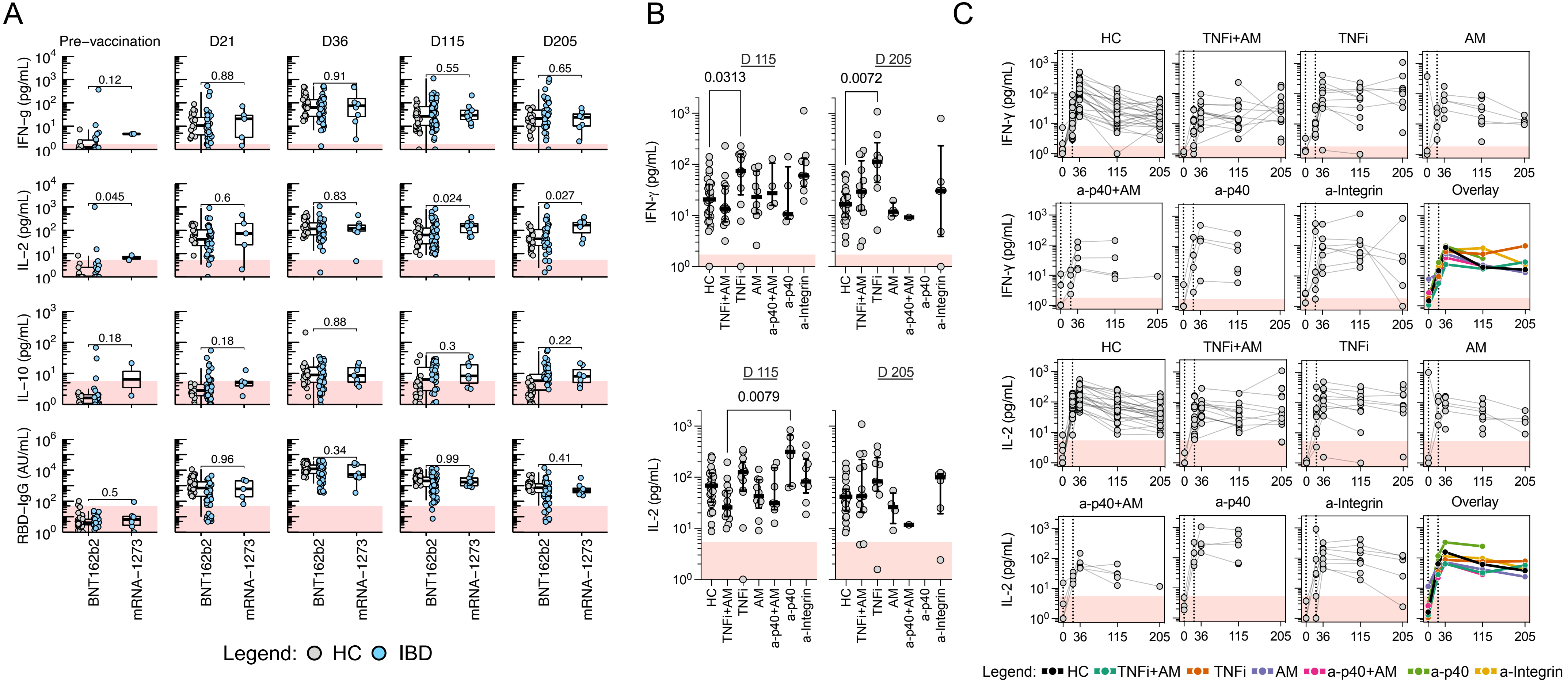

Figure S2. Vaccine-induced T cell responses based on mRNA vaccine administered. (**A**) Box and whisker plots with median line. Statistical analyses were performed by Wilcoxon signed rank test with p values indicated above the comparison line when significant (α=0.05). For RBD-IgG D0-D205: BNT162b2 (n=86, 91, 96, 110, 98), mRNA-1273 (n=6, 5, 8, 9, 8). For RBD-IgG D0-D205: BNT162b2 (n=86, 91, 96, 110, 98), mRNA-1273 (n=6, 5, 8, 9, 8). For IFN-γ/IL-2 D0-D205: BNT162b2 (n=29, 59, 73, 87, 61), mRNA-1273 (n=2, 5, 8, 9, 7). For IL-10 D0-D205: BNT162b2 (n=29, 59, 72, 66, 58), mRNA-1273 (n=2, 5, 7, 7, 7). (**B**) Dot plots with median line (middle bar) and interquartile range (whiskers) of quantified IFN-γ or IL-2 concentrations (pg/mL) from S pool-stimulated whole blood supernatants of HC and IBD patients without mRNA-1273 vaccinees grouped by treatment 3 and 6 months after completing their two-dose vaccination. Statistical analyses were performed by Kruskal-Wallis and Dunn's test with p values shown above the comparison lines when significant (α=0.05). For D 115: HC (n=29), TNFi+AM (n=15), TNFi (n=13), AM (n=10), a-p40+AM (n=5), a-p40 (n=6), a-Integrin (n=9). For D 205: HC (n=25), TNFi+AM (n=13), TNFi (n=9), AM (n=4), a-p40+AM (n=1), a-p40 (n=6), a-Integrin (n=9). **(C)** Quantified IFN-γ or IL-2 concentrations (pg/mL) plotted against time of HC and IBD patients grouped by treatment without mRNA-1273 vaccinees. Datapoints originating from the same participant are connected by gray lines. Data is summarized in the 'Overlay' plot with lines connecting the geometric means of each group at each sampling interval. (**A-C**) Shaded red regions denote the area under the threshold for a positive test.

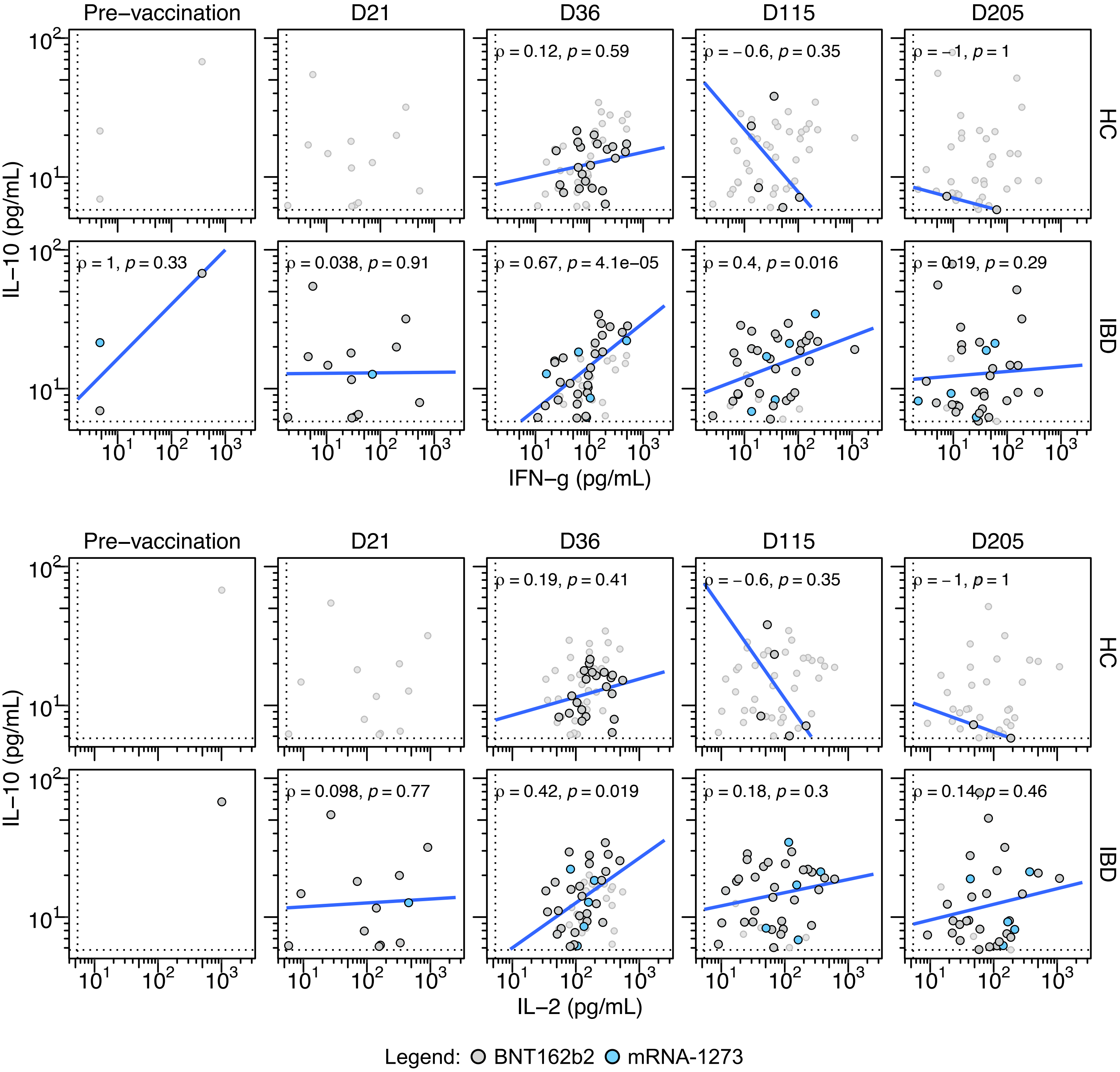

Figure S3. 2-D Correlation plots between peptide-induced IFN-γ/IL-2 and IL-10 from whole blood cytokine release assay between the HC and IBD cohorts. Data from each donor are faceted by cohort (rows) and timepoint (columns). All points from the same timepoint are displayed in each plot, which points originating from the designated cohort (row titles) highlighted. Datapoints below the threshold defined for each analyte (broken horizontal and vertical lines) for a positive response have been excluded from the nonparametric Spearman correlation analysis. Spearman's rho (ρ) and p values are inscribed into the plots when calculations are appropriate. Regression lines are drawn in blue (linear regression) used for visualisation purposes.

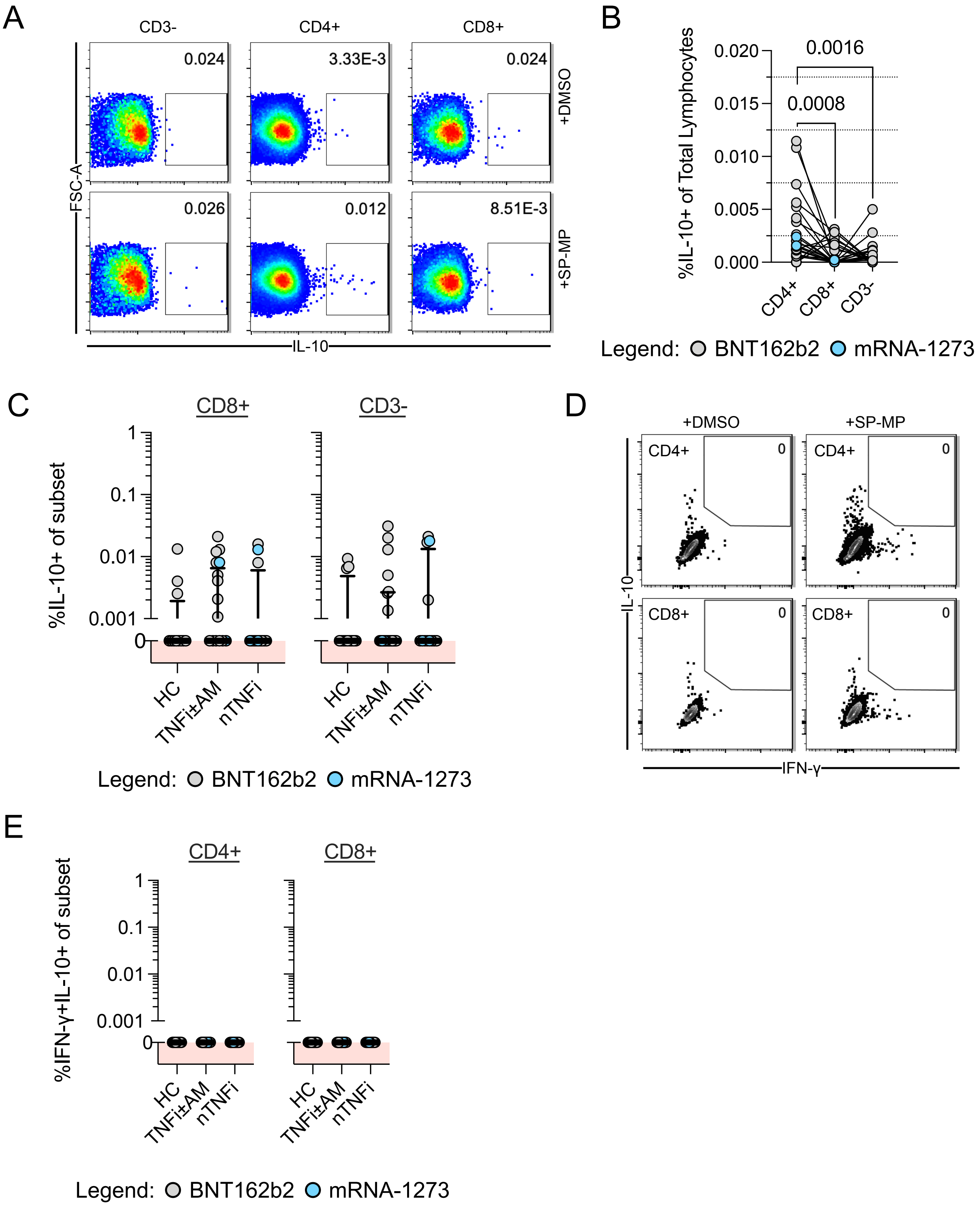

Figure S4. IL-10 production in peripheral blood lymphocytes. (**A** and **D**) Representative flow cytometry plots from intracellular cytokine staining to identify IL-10+ (**A**) or IFN-γ+ IL-10+ (**D**) T cell populations with or without stimulation with Spike peptides (drawn in gate). (**B**) Summary frequencies of paired background-subtracted IL-10+ frequencies identified from IBD patient PBMCs (n=30). Only samples with at least one subset of IL-10+ cells above background were included in the analysis. Statistical analysis was performed using multiple Wilcoxon matched-pairs signed rank test with p values indicated above the comparison line when significant (α=0.05). (**C** and **E**) Dot plots with median line (middle bar) and interquartile range (whiskers) of cellular frequencies of intracellular CD8+ or CD3- IL-10+ (**C**) and CD4+ or CD8+ IFN-γ+IL-10+ (**E**) cells from HC (n=12) or IBD donors on TNFi±AM (n=21) or nTNFi therapy (n=12). Statistical analyses were performed by Wilcoxon signed rank test with p values indicated above the comparison line when significant (α=0.05). Shaded red regions denote responses below background levels (denoted as 0).

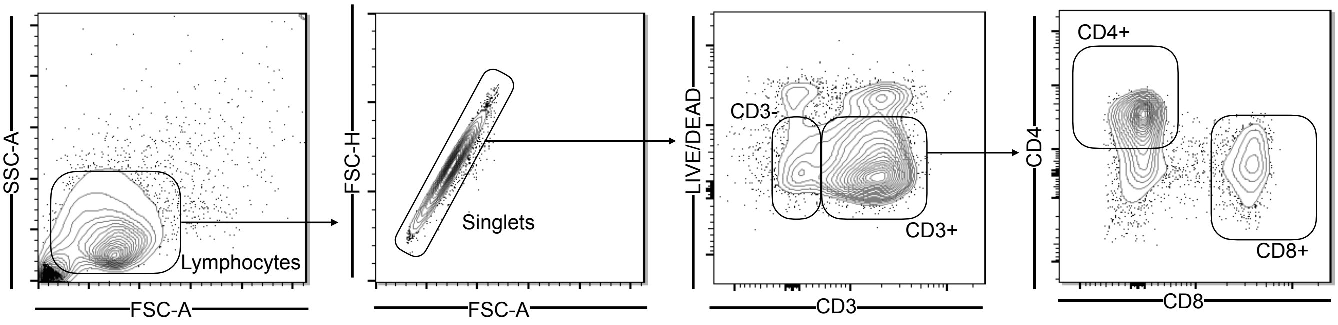

Figure S5. Representative gating strategy of T cell subsets for activation-induced markers assay/intracellular cytokine staining. Bivariate contour plots with outliers displaying a measured parameter obtained from flow cytometry indicated at the lower left corner of each plot. Gates are outlined in each plot. Similar gating strategies for T cell subsets are used for AIM and ICS assays.

Table S1. SARS-CoV-2 S pool peptide library

Peptide #	Peptide Sequence	aa
1	IRGWIFGTTLDSKTQ	101-115
2	FGTTLDSKTQSLLIV	106-120
3	CTFEYVSQPFLMDLE	166-180
4	VSQPFLMDLEGKQGN	171-185
5	TRFQTLLALHRSYLT	236-250
6	LLALHRSYLTPGDSS	241-255
7	RSYLTPGDSSSGWTA	246-260
8	CALDPLSETKCTLKS	291-305
9	LSETKCTLKSFTVEK	296-310
10	CTLKSFTVEKGIYQT	301-315
11	FTVEKGIYQTSNFRV	306-320
12	GIYQTSNFRVQPTES	311-325
13	SASFSTFKCYGVSPT	371-385
14	TFKCYGVSPTKLNDL	376-390
15	YNYKLPDDFTGCVIA	421-435
16	WNSNNLDSKVGGNYN	436-450
17	LDSKVGGNYNYLYRL	441-455
18	GGNYNYLYRLFRKSN	446-460
19	YLYRLFRKSNLKPFE	451-465
20	FRKSNLKPFERDIST	456-470
21	LKPFERDISTEIYQA	461-475
22	GPKKSTNLVKNKCVN	526-540
23	TNLVKNKCVNFNFNG	531-545
24	FNFNGLTGTGVLTES	541-555
25	LTGTGVLTESNKKFL	546-560
26	RAGCLIGAEHVNNSY	646-660
27	IGAEHVNNSYECDIP	651-665
28	SVASQSIIAYTMSLG	686-700
29	SIIAYTMSLGAENSV	691-705
30	TMSLGAENSVAYSNN	696-710
31	STECSNLLLQYGSFC	746-760
32	NLLLQYGSFCTQLNR	751-765
33	KNTQEVFAQVKQIYK	776-790
34	VFAQVKQIYKTPPIK	781-795

Peptide #	Peptide Sequence	aa
35	KQIYKTPPIKDFGGF	786-800
36	TPPIKDFGGFNFSQI	791-805
37	NFSQILPDPSKPSKR	801-815
38	AGFIKQYGDCLGDIA	831-845
39	QYGDCLGDIAARDLI	836-850
40	GAALQIPFAMQMAYR	891-905
41	QMAYRFNGIGVTQNV	901-915
42	FNGIGVTQNVLYENQ	906-920
43	DSLSSTASALGKLQD	936-950
44	TASALGKLQDVVNQN	941-955
45	AQALNTLVKQLSSNF	956-970
46	VLNDILSRLDKVEAE	976-990
47	LITGRLQSLQTYVTQ	996-1010
48	QLIRAAEIRASANLA	1011-1025
49	AEIRASANLAATKMS	1016-1030
50	APHGVVFLHVTYVPA	1056-1070
51	HWFVTQRNFYEPQII	1101-1115
52	KEIDRLNEVAKNLNE	1181-1195
53	LNEVAKNLNESLIDL	1186-1200
54	KNLNESLIDLQELGK	1191-1205
55	IWLGFIAGLIAIVMV	1216-1230

Table S2: SARS-CoV-2 SP-MP pool peptide library

Peptide #	Peptide Sequence	aa
1	MFVFLVLLPLVSSQC	1-15
2	VLLPLVSSQCVNLTT	6-20
3	VSSQCVNLTTRTQLP	11-25
4	VNLTTRTQLPPAYTN	16-30
5	RTQLPPAYTNSFTRG	21-35
6	PAYTNSFTRGVYYPD	26-40
7	SFTRGVYYPDKVFRS	31-45
8	VYYPDKVFRSSVLHS	36-50
9	KVFRSSVLHSTQDLF	41-55
10	SVLHSTQDLFLPFFS	46-60
11	TQDLFLPFFSNVTWF	51-65
12	LPFFSNVTWFHAIHV	56-70
13	NVTWFHAIHVSGTNG	61-75
14	HAIHVSGTNGTKRFD	66-80
15	SGTNGTKRFDNPVLP	71-85
16	TKRFDNPVLPFNDGV	76-90
17	NPVLPFNDGVYFAST	81-95
18	FNDGVYFASTEKSNI	86-100
19	YFASTEKSNIIRGWI	91-105
20	EKSNIIRGWIFGTTL	96-110
21	IRGWIFGTTLDSKTQ	101-115
22	FGTTLDSKTQSLLIV	106-120
23	DSKTQSLLIVNNATN	111-125
24	SLLIVNNATNVVIKV	116-130
25	NNATNVVIKVCEFQF	121-135
26	VVIKVCEFQFCNDPF	126-140
27	CEFQFCNDPFLGVYY	131-145
28	CNDPFLGVYYHKNNK	136-150
29	LGVYYHKNNKSWMES	141-155
30	HKNNKSWMESEFRVY	146-160
31	SWMESEFRVYSSANN	151-165
32	EFRVYSSANNCTFEY	156-170
33	SSANNCTFEYVSQPF	161-175
34	CTFEYVSQPFLMDLE	166-180

Peptide #	Peptide Sequence	aa
35	VSQPFLMDLEGKQGN	171-185
36	LMDLEGKQGNFKNLR	176-190
37	GKQGNFKNLREFVFK	181-195
38	FKNLREFVFKNIDGY	186-200
39	EFVFKNIDGYFKIYS	191-205
40	NIDGYFKIYSKHTPI	196-210
41	FKIYSKHTPINLVRD	201-215
42	KHTPINLVRDLPQGF	206-220
43	NLVRDLPQGFSALEP	211-225
44	LPQGFSALEPLVDLP	216-230
45	SALEPLVDLPIGINI	221-235
46	LVDLPIGINITRFQT	226-240
47	IGINITRFQTLLALH	231-245
48	TRFQTLLALHRSYLT	236-250
49	LLALHRSYLTPGDSS	241-255
50	RSYLTPGDSSSGWTA	246-260
51	PGDSSSGWTAGAAAY	251-265
52	SGWTAGAAAYYVGYL	256-270
53	GAAAYYVGYLQPRTF	261-275
54	YVGYLQPRTFLLKYN	266-280
55	QPRTFLLKYNENGTI	271-285
56	LLKYNENGTITDAVD	276-290
57	ENGTITDAVDCALDP	281-295
58	TDAVDCALDPLSETK	286-300
59	CALDPLSETKCTLKS	291-305
60	LSETKCTLKSFTVEK	296-310
61	CTLKSFTVEKGIYQT	301-315
62	FTVEKGIYQTSNFRV	306-320
63	GIYQTSNFRVQPTES	311-325
64	SNFRVQPTESIVRFP	316-330
65	QPTESIVRFPNITNL	321-335
66	IVRFPNITNLCPFGE	326-340
67	NITNLCPFGEVFNAT	331-345
68	CPFGEVFNATRFASV	336-350
69	VFNATRFASVYAWNR	341-355

Peptide #	**Peptide Sequence**	**aa**
70	RFASVYAWNRKRISN	346-360
71	YAWNRKRISNCVADY	351-365
72	KRISNCVADYSVLYN	356-370
73	CVADYSVLYNSASFS	361-375
74	SVLYNSASFSTFKCY	366-380
75	SASFSTFKCYGVSPT	371-385
76	TFKCYGVSPTKLNDL	376-390
77	GVSPTKLNDLCFTNV	381-395
78	KLNDLCFTNVYADSF	386-400
79	CFTNVYADSFVIRGD	391-405
80	YADSFVIRGDEVRQI	396-410
81	VIRGDEVRQIAPGQT	401-415
82	EVRQIAPGQTGKIAD	406-420
83	APGQTGKIADYNYKL	411-425
84	GKIADYNYKLPDDFT	416-430
85	YNYKLPDDFTGCVIA	421-435
86	PDDFTGCVIAWNSNN	426-440
87	GCVIAWNSNNLDSKV	431-445
88	WNSNNLDSKVGGNYN	436-450
89	LDSKVGGNYNYLYRL	441-455
90	GGNYNYLYRLFRKSN	446-460
91	YLYRLFRKSNLKPFE	451-465
92	FRKSNLKPFERDIST	456-470
93	LKPFERDISTEIYQA	461-475
94	RDISTEIYQAGSTPC	466-480
95	EIYQAGSTPCNGVEG	471-485
96	GSTPCNGVEGFNCYF	476-490
97	NGVEGFNCYFPLQSY	481-495
98	FNCYFPLQSYGFQPT	486-500
99	PLQSYGFQPTNGVGY	491-505
100	GFQPTNGVGYQPYRV	496-510
101	NGVGYQPYRVVVLSF	501-515
102	QPYRVVVLSFELLHA	506-520
103	VVLSFELLHAPATVC	511-525

Peptide #	Peptide Sequence	aa
104	ELLHAPATVCGPKKS	516-530
105	PATVCGPKKSTNLVK	521-535
106	GPKKSTNLVKNKCVN	526-540
107	TNLVKNKCVNFNFNG	531-545
108	NKCVNFNFNGLTGTG	536-550
109	FNFNGLTGTGVLTES	541-555
110	LTGTGVLTESNKKFL	546-560
111	VLTESNKKFLPFQQF	551-565
112	NKKFLPFQQFGRDIA	556-570
113	PFQQFGRDIADTTDA	561-575
114	GRDIADTTDAVRDPQ	566-580
115	DTTDAVRDPQTLEIL	571-585
116	VRDPQTLEILDITPC	576-590
117	TLEILDITPCSFGGV	581-595
118	DITPCSFGGVSVITP	586-600
119	SFGGVSVITPGTNTS	591-605
120	SVITPGTNTSNQVAV	596-610
121	GTNTSNQVAVLYQDV	601-615
122	NQVAVLYQDVNCTEV	606-620
123	LYQDVNCTEVPVAIH	611-625
124	NCTEVPVAIHADQLT	616-630
125	PVAIHADQLTPTWRV	621-635
126	ADQLTPTWRVYSTGS	626-640
127	PTWRVYSTGSNVFQT	631-645
128	YSTGSNVFQTRAGCL	636-650
129	NVFQTRAGCLIGAEH	641-655
130	RAGCLIGAEHVNNSY	646-660
131	IGAEHVNNSYECDIP	651-665
132	VNNSYECDIPIGAGI	656-670
133	ECDIPIGAGICASYQ	661-675
134	IGAGICASYQTQTNS	666-680
135	CASYQTQTNSPRRAR	671-685
136	TQTNSPRRARSVASQ	676-690
137	PRRARSVASQSIIAY	681-695

Peptide #	Peptide Sequence	aa
138	SVASQSIIAYTMSLG	686-700
139	SIIAYTMSLGAENSV	691-705
140	TMSLGAENSVAYSNN	696-710
141	AENSVAYSNNSIAIP	701-715
142	AYSNNSIAIPTNFTI	706-720
143	SIAIPTNFTISVTTE	711-725
144	TNFTISVTTEILPVS	716-730
145	SVTTEILPVSMTKTS	721-735
146	ILPVSMTKTSVDCTM	726-740
147	MTKTSVDCTMYICGD	731-745
148	VDCTMYICGDSTECS	736-750
149	YICGDSTECSNLLLQ	741-755
150	STECSNLLLQYGSFC	746-760
151	NLLLQYGSFCTQLNR	751-765
152	YGSFCTQLNRALTGI	756-770
153	TQLNRALTGIAVEQD	761-775
154	ALTGIAVEQDKNTQE	766-780
155	AVEQDKNTQEVFAQV	771-785
156	KNTQEVFAQVKQIYK	776-790
157	VFAQVKQIYKTPPIK	781-795
158	KQIYKTPPIKDFGGF	786-800
159	TPPIKDFGGFNFSQI	791-805
160	DFGGFNFSQILPDPS	796-810
161	NFSQILPDPSKPSKR	801-815
162	LPDPSKPSKRSFIED	806-820
163	KPSKRSFIEDLLFNK	811-825
164	SFIEDLLFNKVTLAD	816-830
165	LLFNKVTLADAGFIK	821-835
166	VTLADAGFIKQYGDC	826-840
167	AGFIKQYGDCLGDIA	831-845
168	QYGDCLGDIAARDLI	836-850
169	LGDIAARDLICAQKF	841-855
170	ARDLICAQKFNGLTV	846-860
171	CAQKFNGLTVLPPLL	851-865

Peptide #	Peptide Sequence	aa
172	NGLTVLPPLLTDEMI	856-870
173	LPPLLTDEMIAQYTS	861-875
174	TDEMIAQYTSALLAG	866-880
175	AQYTSALLAGTITSG	871-885
176	ALLAGTITSGWTFGA	876-890
177	TITSGWTFGAGAALQ	881-895
178	WTFGAGAALQIPFAM	886-900
179	GAALQIPFAMQMAYR	891-905
180	IPFAMQMAYRFNGIG	896-910
181	QMAYRFNGIGVTQNV	901-915
182	FNGIGVTQNVLYENQ	906-920
183	VTQNVLYENQKLIAN	911-925
184	LYENQKLIANQFNSA	916-930
185	KLIANQFNSAIGKIQ	921-935
186	QFNSAIGKIQDSLSS	926-940
187	IGKIQDSLSSTASAL	931-945
188	DSLSSTASALGKLQD	936-950
189	TASALGKLQDVVNQN	941-955
190	GKLQDVVNQNAQALN	946-960
191	VVNQNAQALNTLVKQ	951-965
192	AQALNTLVKQLSSNF	956-970
193	TLVKQLSSNFGAISS	961-975
194	LSSNFGAISSVLNDI	966-980
195	GAISSVLNDILSRLD	971-985
196	VLNDILSRLDKVEAE	976-990
197	LSRLDKVEAEVQIDR	981-995
198	KVEAEVQIDRLITGR	986-1000
199	VQIDRLITGRLQSLQ	991-1005
200	LITGRLQSLQTYVTQ	996-1010
201	LQSLQTYVTQQLIRA	1001-1015
202	TYVTQQLIRAAEIRA	1006-1020
203	QLIRAAEIRASANLA	1011-1025
204	AEIRASANLAATKMS	1016-1030
205	SANLAATKMSECVLG	1021-1035

Peptide #	Peptide Sequence	aa
206	ATKMSECVLGQSKRV	1026-1040
207	ECVLGQSKRVDFCGK	1031-1045
208	QSKRVDFCGKGYHLM	1036-1050
209	DFCGKGYHLMSFPQS	1041-1055
210	GYHLMSFPQSAPHGV	1046-1060
211	SFPQSAPHGVVFLHV	1051-1065
212	APHGVVFLHVTYVPA	1056-1070
213	VFLHVTYVPAQEKNF	1061-1075
214	TYVPAQEKNFTTAPA	1066-1080
215	QEKNFTTAPAICHDG	1071-1085
216	TTAPAICHDGKAHFP	1076-1090
217	ICHDGKAHFPREGVF	1081-1095
218	KAHFPREGVFVSNGT	1086-1100
219	REGVFVSNGTHWFVT	1091-1105
220	VSNGTHWFVTQRNFY	1096-1110
221	HWFVTQRNFYEPQII	1101-1115
222	QRNFYEPQIITTDNT	1106-1120
223	EPQIITTDNTFVSGN	1111-1125
224	TTDNTFVSGNCDVVI	1116-1130
225	FVSGNCDVVIGIVNN	1121-1135
226	CDVVIGIVNNTVYDP	1126-1140
227	GIVNNTVYDPLQPEL	1131-1145
228	TVYDPLQPELDSFKE	1136-1150
229	LQPELDSFKEELDKY	1141-1155
230	DSFKEELDKYFKNHT	1146-1160
231	ELDKYFKNHTSPDVD	1151-1165
232	FKNHTSPDVDLGDIS	1156-1170
233	SPDVDLGDISGINAS	1161-1175
234	LGDISGINASVVNIQ	1166-1180
235	GINASVVNIQKEIDR	1171-1185
236	VVNIQKEIDRLNEVA	1176-1190
237	KEIDRLNEVAKNLNE	1181-1195
238	LNEVAKNLNESLIDL	1186-1200
239	KNLNESLIDLQELGK	1191-1205

Peptide #	Peptide Sequence	aa
240	SLIDLQELGKYEQYI	1196-1210
241	QELGKYEQYIKWPWY	1201-1215
242	YEQYIKWPWYIWLGF	1206-1220
243	KWPWYIWLGFIAGLI	1211-1225
244	IWLGFIAGLIAIVMV	1216-1230
245	IAGLIAIVMVTIMLC	1221-1235
246	AIVMVTIMLCCMTSC	1226-1240
247	TIMLCCMTSCCSCLK	1231-1245
248	CMTSCCSCLKGCCSC	1236-1250
249	CSCLKGCCSCGSCCK	1241-1255
250	GCCSCGSCCKFDEDD	1246-1260
251	GSCCKFDEDDSEPVL	1251-1265
252	FDEDDSEPVLKGVKL	1256-1270
253	SEPVLKGVKLHYT	1261-1273

Table S3. SARS-CoV-2 Spike Hotspot-Ancestral and Hotspot-Omicron peptide libraries used to study responses to the Omicron variant (BA.1)

Peptide #	Spike Hotspot-Ancestral	Spike Hotspot-Omicron	aa
1	LPFFSNVTWFHAIHV	LPFFSNVTWFHVISG	56-70
2	NVTWFHAIHVSGTNG	NVTWFHVISGTNGTK	61-75
3	HAIHVSGTNGTKRFD	HVISGTNGTKRFDNP	66-80
4	FNDGVYFASTEKSNI	FNDGVYFASIEKSNI	86-100
5	YFASTEKSNIIRGWI	YFASIEKSNIIRGWI	91-105
6	CEFQFCNDPFLGVYY	CEFQFCNDPFLDHKN	131-145
7	CNDPFLGVYYHKNNK	CNDPFLDHKNNKSWM	136-150
8	LGVYYHKNNKSWMES	LDHKNNKSWMESEFR	141-155
9	FKIYSKHTPINLVRD	FKIYSKHTPIIVEPE	201-215
10	KHTPINLVRDLPQGF	KHTPIIVEPERDLPQ	206-220
11	NLVRDLPQGFSALEP	IVEPERDLPQGFSAL	211-225
12	IVRFPNITNLCPFGE	IVRFPNITNLCPFDE	326-340
13	NITNLCPFGEVFNAT	NITNLCPFDEVFNAT	331-345
14	CPFGEVFNATRFASV	CPFDEVFNATRFASV	336-350
15	CVADYSVLYNSASFS	CVADYSVLYNLAPFF	361-375
16	SVLYNSASFSTFKCY	SVLYNLAPFFTFKCY	366-380
17	SASFSTFKCYGVSPT	LAPFFTFKCYGVSPT	371-385
18	EVRQIAPGQTGKIAD	EVRQIAPGQTGNIAD	406-420
19	APGQTGKIADYNYKL	APGQTGNIADYNYKL	411-425
20	GKIADYNYKLPDDFT	GNIADYNYKLPDDFT	416-430
21	PDDFTGCVIAWNSNN	PDDFTGCVIAWNSNK	426-440
22	GCVIAWNSNNLDSKV	GCVIAWNSNKLDSKV	431-445
23	WNSNNLDSKVGGNYN	WNSNKLDSKVSGNYN	436-450
24	LDSKVGGNYNYLYRL	LDSKVSGNYNYLYRL	441-455
25	GGNYNYLYRLFRKSN	SGNYNYLYRLFRKSN	446-460
26	RDISTEIYQAGSTPC	RDISTEIYQAGNKPC	466-480
27	EIYQAGSTPCNGVEG	EIYQAGNKPCNGVAG	471-485
28	GSTPCNGVEGFNCYF	GNKPCNGVAGFNCYF	476-490
29	NGVEGFNCYFPLQSY	NGVAGFNCYFPLRSY	481-495
30	FNCYFPLQSYGFQPT	FNCYFPLRSYSFRPT	486-500
31	PLQSYGFQPTNGVGY	PLRSYSFRPTYGVGH	491-505
32	GFQPTNGVGYQPYRV	SFRPTYGVGHQPYRV	496-510
33	NGVGYQPYRVVVLSF	YGVGHQPYRVVVLSF	501-515
34	NKCVNFNFNGLTGTG	NKCVNFNFNGLKGTG	536-550
35	FNFNGLTGTGVLTES	FNFNGLKGTGVLTES	541-555
36	LTGTGVLTESNKKFL	LKGTGVLTESNKKFL	546-560

Peptide #	Spike Hotspot-Ancestral	Spike Hotspot-Omicron	aa
37	GTNTSNQVAVLYQDV	GTNTSNQVAVLYQGV	601-615
38	NQVAVLYQDVNCTEV	NQVAVLYQGVNCTEV	606-620
39	LYQDVNCTEVPVAIH	LYQGVNCTEVPVAIH	611-625
40	NVFQTRAGCLIGAEH	NVFQTRAGCLIGAEY	641-655
41	RAGCLIGAEHVNNSY	RAGCLIGAEYVNNSY	646-660
42	IGAEHVNNSYECDIP	IGAEYVNNSYECDIP	651-665
43	IGAGICASYQTQTNS	IGAGICASYQTQTKS	666-680
44	CASYQTQTNSPRRAR	CASYQTQTKSHRRAR	671-685
45	TQTNSPRRARSVASQ	TQTKSHRRARSVASQ	676-690
46	PRRARSVASQSIIAY	HRRARSVASQSIIAY	681-695
47	SIIAYTMSLGAENSV	SIIAYTMSLGVENSV	691-705
48	TMSLGAENSVAYSNN	TMSLGVENSVAYSNN	696-710
49	AENSVAYSNNSIAIP	VENSVAYSNNSIAIP	701-715
50	NLLLQYGSFCTQLNR	NLLLQYGSFCTQLKR	751-765
51	YGSFCTQLNRALTGI	YGSFCTQLKRALTGI	756-770
52	TQLNRALTGIAVEQD	TQLKRALTGIAVEQD	761-775
53	KQIYKTPPIKDFGGF	KQIYKTPPIKYFGGF	786-800
54	TPPIKDFGGFNFSQI	TPPIKYFGGFNFSQI	791-805
55	DFGGFNFSQILPDPS	YFGGFNFSQILPDPS	796-810
56	ARDLICAQKFNGLTV	ARDLICAQKFKGLTV	846-860
57	CAQKFNGLTVLPPLL	CAQKFKGLTVLPPLL	851-865
58	NGLTVLPPLLTDEMI	KGLTVLPPLLTDEMI	856-870
59	TASALGKLQDVVNQN	TASALGKLQDVVNHN	941-955
60	GKLQDVVNQNAQALN	GKLQDVVNHNAQALN	946-960
61	VVNQNAQALNTLVKQ	VVNHNAQALNTLVKQ	951-965
62	AQALNTLVKQLSSNF	AQALNTLVKQLSSKF	956-970
63	TLVKQLSSNFGAISS	TLVKQLSSKFGAISS	961-975
64	LSSNFGAISSVLNDI	LSSKFGAISSVLNDI	966-980
65	GAISSVLNDILSRLD	GAISSVLNDIFSRLD	971-985
66	VLNDILSRLDKVEAE	VLNDIFSRLDKVEAE	976-990
67	LSRLDKVEAEVQIDR	FSRLDKVEAEVQIDR	981-995

Table S4. List of labelling reagents used for flow cytometry

Target	Organism	Color	Clone	Label	RRID/Cat. no	Dilution (in 100µL)
CD3	anti-Human	BV650	SP34-2	BD Horizon™	AB_2738486	2.5
CD4	anti-Human	AF700	RPA-T4	Biolegend	AB_493743	2.5
CD8	anti-Human	V500	RPA-T8	BD Horizon™	AB_1937333	0.5
CD69	anti-Human	PE/Dazzle594	FN50	Biolegend	AB_2564276	2
CD134/OX40	anti-Human	PerCP-Cy5.5	Ber-ACT35	Biolegend	AB_10720986	2
CD137/4-1BB	anti-Human	PE-Cy5	4B4-1	BD Horizon™	AB_394067	5
IL-10	anti-Human	BV421	JES3-9D7	Biolegend	AB_10896947	6
IFN-gamma	anti-Human	PE-Cy7	4S.B3	eBioscience™	AB_1659719	6
IL-2	anti-Human	PerCP-Cy5.5	MQ1-17H12	BD Pharmingen™	AB_1727543	5
LIVE/DEAD™ Fixable Yellow Dead Cell Stain Kit (405nm excitation)				ThermoFisher	Cat. L34959	0.1