

**Cell, Volume 185**

## **Supplemental information**

**T cell reactivity to the SARS-CoV-2**

**Omicron variant is preserved in most**

**but not all individuals**

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**Table S1: Baseline characteristics of included samples (N=101 from 76 unique donors), related to Figure 1.**

	Unvaccinated, N = 21	pre- boost, N = 36 <sup>#</sup>	post- boost, N = 44 <sup>#</sup>
<b>Age</b>	34 (28, 58)	46 (38, 54)	48 (40, 64)
<b>Sex</b>			
Female	9 (43%)	26 (72%)	30 (68%)
Male	12 (57%)	10 (28%)	14 (32%)
<b>Prior infection</b>			
PCR/Antibody confirmed prior infection	11 (52%)	12 (33%)	13 (30%)
No prior infection	10 (48%)	24 (67%)	31 (70%)
<b>Vaccine type</b>			
None	21 (100%)	0 (0%)	0 (0%)
Ad26.COVS2.S	NA	4 (11%)	7* (16%) 27**
BNT-162b2	NA	24 (67%)	(61%) 10***
mRNA-1273	NA	8 (22%)	(23%)
<b>Duration after primary vaccination series (median days (IQR))</b>	NA	220 (207, 243)	232 (216, 250)
<b>Booster type</b>			
heterologous	NA	NA	7 (16%)
homologous	NA	NA	37 (84%)
<b>Duration after booster (median days (IQR))</b>	NA	NA	10 (9, 15)

<sup>#</sup> includes paired pre-boost and post-boost samples from 25 individuals

\* includes 3 boosted with Ad26.COVS2.S, 2 with mRNA-1273 and 2 with BNT162b2

\*\* includes 25 boosted with BNT162b2 and 2 with mRNA-1273

**Table S2: Details of variant peptide pools for spike and non-spike structural proteins, related to Figure 1.**

	Wildtype	Spike Delta	Omicron	Nucleocapsid, Membrane, Envelope, ORF3A	
				Wildtype	Omicron
<b>Number of peptides in pool</b>	315	315	315	237	237
<b>Peptides shared with wildtype</b>	Ref	288 (91.4%)	229 (72.7%)	Ref	213 (89.9%)
<b>Peptides unique to variant</b>	Ref	27 (8.6%)	86 (27.3%)	Ref	24 (10.1%)

**Table S3: Multivariate regression of total T-cell response to SARS-CoV-2 spike peptides in vaccinated individuals, related to Figures 1 and 2.**

		<b>Effect estimate on total T-cell response (in log<sub>10</sub> CFU/10<sup>6</sup> PBMC)</b>	<b>95% Confidence Interval</b>	<b>p- value</b>
<b>Age (per 10 year increase)</b>		-0.03	-0.09, 0.03	0.3
<b>Sex</b>				
Female	Ref			
Male		-0.03	-0.21, 0.15	0.7
<b>SARS-CoV-2 variant</b>				
ancestral	Ref			
Delta (B.1.617.2)		-0.09	-0.27, 0.09	0.3
Omicron (B.1.1529)		-0.03	-0.21, 0.15	0.7
<b>Prior infection</b>				
No prior infection	Ref			
PCR/Antibody confirmed prior infection		0.55	0.38, 0.72	<0.001
<b>Vaccine type</b>				
mRNA-1273	Ref			
BNT-162b2		0.09	-0.10, 0.28	0.3
Ad26.COVS.S		-0.05	-0.32, 0.22	0.7
<b>Duration after primary vaccination series in weeks</b>		-0.02	-0.05, 0.00	0.028
<b>Booster group</b>				
pre-boost	Ref			
post-boost		1.1	0.91, 1.2	<0.001

**Table S4. Frequency of individuals with greater than 50% ( $0.3\log_{10}$ ) reduction in circulating effector T-cell response to variant, relative to wildtype, related to Figures 1 and 2.**

		<b>Unvaccinated</b>	<b>Pre-booster</b>	<b>Post-booster</b>	<b>Overall</b>
<b>Omicron</b>	<b>Prior infected</b>	27.3% (3/11)	8.3% (1/12)	15.4% (2/13)	15.3%
	<b>No prior infection</b>	-	25% (6/24)	6.5% (2/31)	(14/91)*
<b>Delta</b>	<b>Prior infected</b>	18.2% (2/11)	0% (0/12)	0% (0/13)	5.9%
	<b>No prior infection</b>	-	16.7% (3/18)	0% (0/31)	(5/85)

\*Fisher's exact test comparing frequency for Omicron vs. Delta in 85 individuals with both measured, i.e. 13/85 5/85; p-value 0.024.

**Table S5: Multivariate regression of CD4<sup>+</sup> and CD8<sup>+</sup> T-cell proliferative response to SARS-CoV-2 spike peptides in vaccinated individuals, related to Figures 1 and 2.**

	CD4+ Memory T cell response			CD8+ Memory T cell response		
	Effect estimate	95% Confidence Interval	p-value	Effect estimate	95% Confidence Interval	p-value
<b>Age (per 10 year increase)</b>	0.16	-1.2, 1.5	0.8	-0.67	-2.2, 0.88	0.4
<b>Sex</b>						
Female	Ref					
Male	0.72	-3.1, 4.5	0.7	0.72	-3.1, 4.5	0.7
<b>SARS-CoV-2 variant</b>						
ancestral Omicron (B.1.1529)	Ref					
(B.1.1529)	-1	-4.5, 2.5	0.6	-3.4	-7.4, 0.58	0.093
<b>Prior infection</b>						
No prior infection	Ref					
PCR/Antibody confirmed prior infection	0.42	-3.2, 4.1	0.8	3.6	-0.54, 7.8	0.087
<b>Vaccine type</b>						
mRNA-1273	Ref			4.1	-0.79, 9.0	0.1
BNT-162b2	1.6	-2.7, 5.9	0.5	0.28	-9.0, 9.6	>0.9
Ad26.COV2.S	2	-6.2, 10	0.6			
<b>Duration after primary vaccination series in weeks</b>	-0.28	-0.74, 0.18	0.2	-0.01	-0.53, 0.51	>0.9
<b>Booster group</b>						
pre-boost	Ref					
post-boost	3.2	-1.2, 7.5	0.2	5.4	0.48, 10	0.032

**Table S7: HLA genotypes of representative participants who demonstrated >50% decline in T-cell reactivity to SARS-CoV-2 Omicron, related to Table 1.**

<b>Participant</b>	<b>HLA-A Allele 1</b>	<b>HLA-A Allele 2</b>	<b>HLA-B Allele 1</b>	<b>HLA-B Allele 2</b>	<b>HLA-C Allele 1</b>	<b>HLA-C Allele 2</b>	<b>Number of HLA-I alleles predicted to be affected by loss in Omicron binding</b>
1	<b>11:01</b>	<b>30:01</b>	<b>15:01</b>	<b>42:02</b>	<b>01:02</b>	17:01	5
2	<b>01:01</b>	<b>29:02</b>	<b>08:01</b>	44:03	07:01	<b>16:01</b>	4
3	02:01	<b>26:01</b>	<b>08:01</b>	<b>38:01</b>	07:01	<b>12:03</b>	4
4	<b>23:01</b>	80:01	18:01	44:03	<b>02:02</b>	<b>04:01</b>	3
5	02:01	<b>32:01</b>	<b>35:01</b>	58:01	<b>04:01</b>	07:01	3
6	<b>24:02</b>	<b>24:02</b>	<b>15:20</b>	<b>15:20</b>	<b>01:02</b>	<b>01:02</b>	6
7	<b>01:01</b>	<b>68:01</b>	50:02	<b>52:01</b>	<b>06:02</b>	<b>12:02</b>	5
8	02:01	<b>29:02</b>	<b>35:01</b>	51:01	<b>04:01</b>	<b>15:09</b>	4
9	31:01	68:03	<b>39:05</b>	<b>40:02</b>	03:05	<b>07:02</b>	3
10	<b>23:01</b>	<b>30:02</b>	40:01	51:01	03:04	<b>15:02</b>	3

*Bolded HLA class I alleles are those where binding to wildtype epitopes is affected by mutations in Omicron.*