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Supplemental information

SARS-CoV-2 variant B.1.1.7 is susceptible to neutralizing antibodies elicited by ancestral spike vaccines

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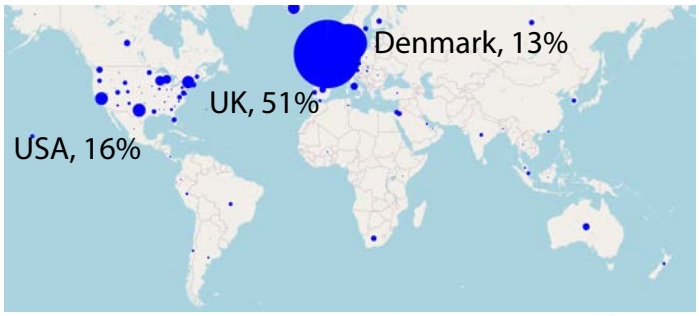
Contents of Supplemental Information

Figure S1



Global Sampling, Jun. 1, 2020 -Jan. 15, 2021

UK Scotland
UK England
UK Ireland
UK Wales
Europe, not Denmark
Australia
South Africa
Denmark
USA

B.1.1.7 (14,393, UK)
501Y.V2 (71, S. Africa)
N501Y (439, Wales)
N501T (233, Australia)
del69/70 (200, US, UK)
del69/70 + N439K (4,319, Denmark, UK)
N439K (1,253, Denmark, UK)
del69/70 + Y453F (791, Denmark, UK)
Y453F (150, Denmark, UK)
P681H (1552, US (Hawaii))

Figure S2

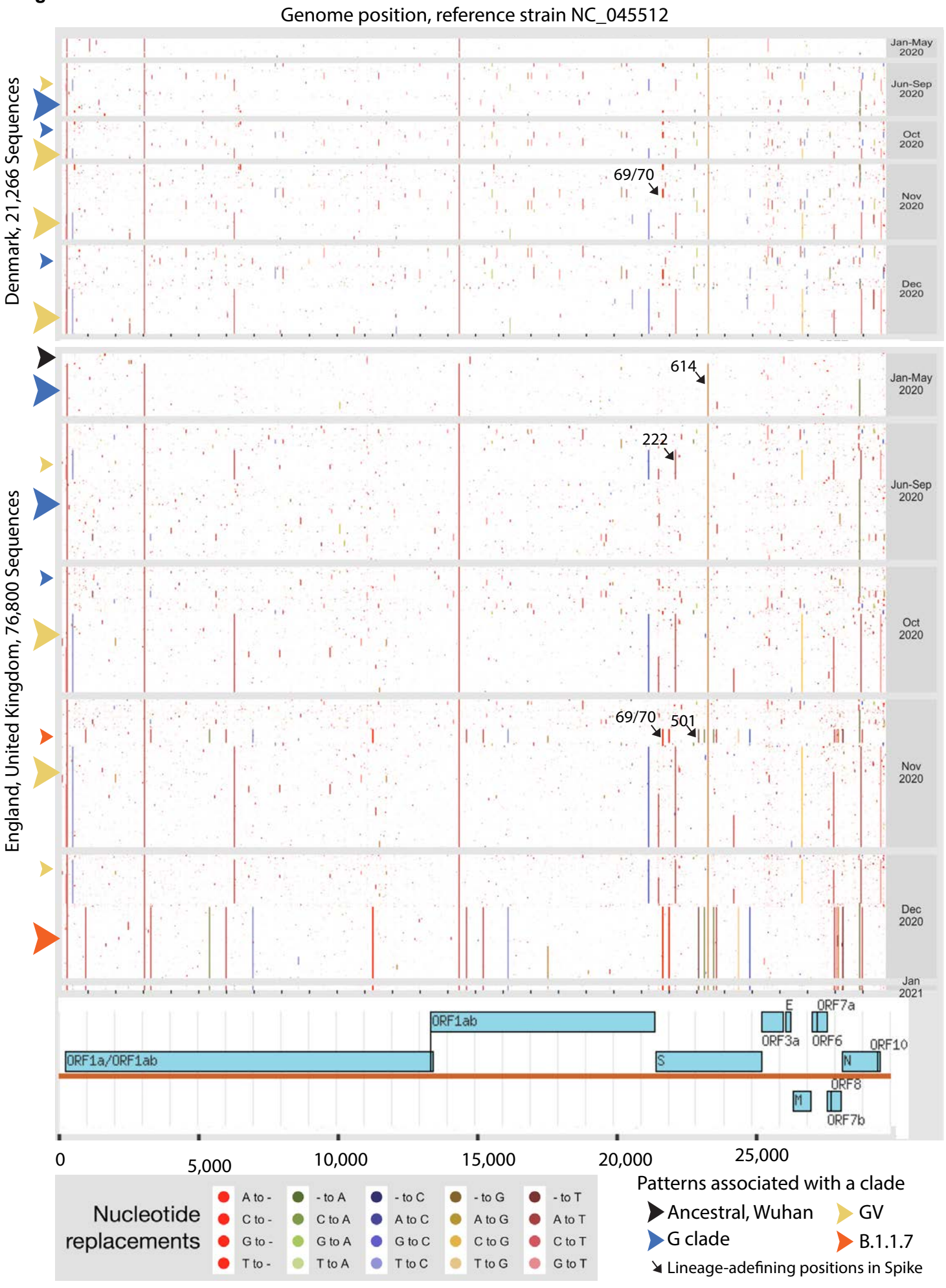
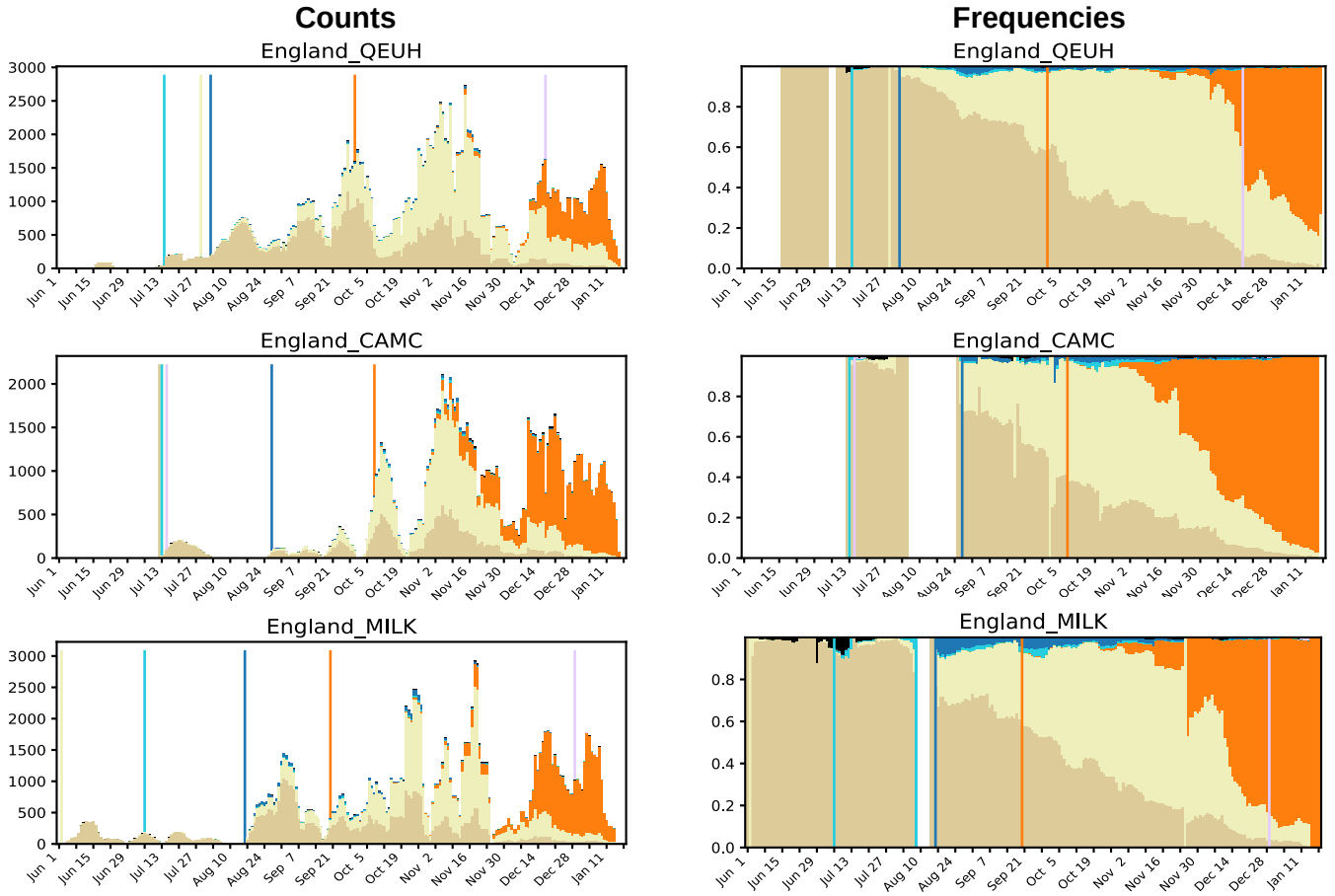
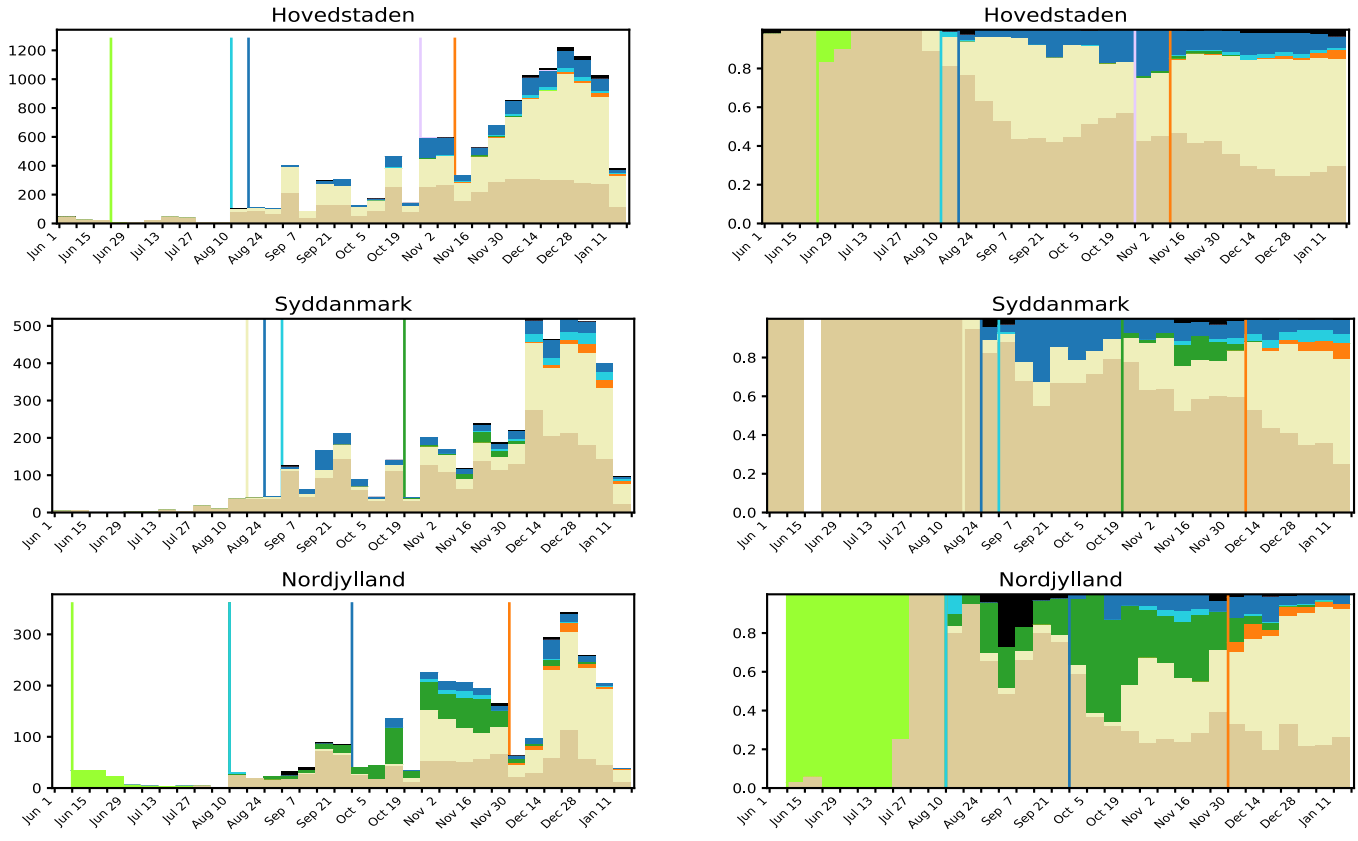

Genome position, reference strain NC_045512
Denmark, 21,266 Sequences
England, United Kingdom, 76,800 Sequences
Jan-May 2020
Jun-Sep 2020
Oct 2020
Nov 2020
Dec 2020
Jan 2021
69/70
614
222
501
ORF1ab
ORF1a/ORF1ab
S
E
ORF3a
ORF7a
ORF6
ORF10
N
M
ORF8
ORF7b
0
5,000
10,000
15,000
20,000
25,000
Nucleotide replacements
A to -
C to -
G to -
T to -
- to A
C to A
G to A
T to A
- to C
A to C
G to C
T to C
- to G
A to G
C to G
T to G
- to T
A to T
C to T
G to T
Patterns associated with a clade
Ancestral, Wuhan
G clade
GV
B.1.1.7
Lineage-adefining positions in Spike

Figure S3

A. Spike transitions within the UK: weekly running averages



B. Spike transitions within Denmark: weekly running averages



Common Forms in the UK and Denmark

D614G
A222V
B.1.1.7
Δ69/79 N439K
N439K
N501Y
Δ69/79 Y453F
Y453F
Other

Fig. S3

Fig. S1. Parsimony tree showing the relationships between B.1.1.7 and other variants with key mutations. 244,291 sequences were included in this tree, which is based on the GISAID data sampled on Jan.17th, 2021. Countries where the variants of interest are commonly found are indicated by branch color, key variants by symbols at the tips. The B.1.1.7 lineage is shown as pink open circles. The B.1.1.7 variant is still predominantly found in the UK, but by Jan. 24th 2021 had been sampled in 44 countries, and in 20 different states in the USA. Some of these geographically diverse samples were likely to have been detected as a consequence of sampling travelers from the UK and their contacts, due to the international interest in B.1.1.7 in late Dec. 2020 and early Jan. 2021; regardless of this potential sampling bias, the B.1.1.7 variant clearly has a global presence. The N501Y mutations is also found in the South African Variant of Interest, 501Y.V2, the red open triangles. N501Y has also transiently but significantly emerged in local populations, as a lone Spike mutation the D614G background, found in the early summer in Victoria, Australia, and also found in Wales (in this figure, and followed over time in Fig. 1). A distinct variant, N501T as been emerging in Sydney, New South Wales, Australia, that has become increasing common through December, 2020. Variants carrying the only the deletion in Spike at Δ69/70 on a D614G background; on the rare occasions they are found, they were primarily sampled in the UK and US. In contrast, Δ69/70 is frequently found coupled with other RBM mutations, either embedded in B.1.1.7 or coupled with N439K or Y453F, commonly circulating in both Denmark and UK as well as in other European counties; N439K and Y453F variants not coupled to Δ69/70 are found less frequently (see Fig. 1B). Of note, P681H is embedded in B.1.1.7, but is also frequently found independently, and is often found to increase in frequency regionally when it does arise, and it is recurrent throughout the phylogeny; it is the dominant form in the Hawaiian epidemic, and is found in many places throughout the US. All of the currently variants of interest are in the G clade, Spike D614G background. The map insert includes the subset of complete GISAID sequences with a known sampling date that were sampled since June 1, 2020, and the area of the circle is proportional to sample size, illustrating the strong sampling bias in the data: the UK is contributing over half of the sequences in the dataset, with the USA and Denmark following, these three nations account for 80% of the GISAID sequences that pass through the cov.lanl.gov quality control screen.

Fig. S2. Highlighter plot showing the mutations associated with major clade in the UK and Denmark transitioning over time. Distribution of mutations among SARS-CoV-2 sequences from Denmark and from England, UK. These figures are highly compressed pixel plots representing the full sampling of complete sequences from these countries, nearly 100,000 sequence in all, and full length genomes across the x-axis. Each row in the matrix represents a single genome sequence; each column, a genome position. Colored dots denote locations of nucleotide mutations relative to the Wuhan-Hu-1 isolate (GenBank accession NC_045512); unmutated bases are white to allow visualization of mutations. Sequences are presented in separate panels based on time of sampling. Within each panel, sequences are clustered phylogenetically, ordered top-to-bottom by position within a parsimony-based phylogenetic tree; therefore, mutations at a particular locus that are shared within a lineage are seen as vertical lines, and groupings of vertical lines that start and end at the same heights indicate coherent lineages defined by multiple mutations. Clades with more members are sorted lower. Colored arrowheads at the left margin indicate lineages of particular interest; smaller and larger arrowheads reflect the proportional representation of lineages among samples from a particular time window.

Fig. S3. Transitions in key mutational patterns over time in local regions in Denmark and in England. These figures are drawn as in Fig. 1C. Weekly running averages are plotted each day, with the actual counts on the left, and relative frequencies on the right. Regions with white banks indicate no sampling was done in that time frame. **A. English regional data over time.** The overall pattern seen in England in Fig. 1 was consistent across more local sampling in England (QUEH, CAMC, and MILK). The increased frequency of the GV clade, carrying the 4 G clade mutations plus an additional 8 mutations including the A222V mutation begins in early August, and it increases in prevalence relative to the G clade in each local region, but the transitions are more gradual than the later transition to the B.1.1.7 form indicated in orange. The lines indicate when a particular variant was introduced into the region, and the orange line indicates the first introduction of B.1.1.7, first sampled in late September and early October in each region. After the B.1.1.7 variant is first introduced, a very gradual increase in frequency is observed for a period, and then it begins to appreciably increase in frequency. **B. Danish regional data over time.** The B.1.1.7 form was introduced into Danish cites in November/December, and by mid-Jan was becoming more consistently observed. Danish sampling times are indicated on a weekly basis, UK daily, hence the broader bands. The N439K and N453Y variants, particularly in combination with the ∆69/70 deletion, were more prominent among Danish samples than among the UK samples; both these and the original D614G form becoming less frequently sampled, and the GV form more prominent, at the point when the B.1.1.7 form was introduced into Denmark.

GV defining mutations from **figure S2**. 12 mutations, include the following G clade mutations are highlighted

G00204T	C06286T	G21255C	C24334T
C00241T	A11533G	C21614T	T26424C
T00445C	C14408T	C22227T	C26801G
C03037T	C15352T	A23403G	C27944T

B.1.1.7 mutations: 40 mutations

C00241T	T11293-	A21768-	G24914C
C00913T	T11294-	T21769-	C27972T
C03037T	T11295-	G21770A	G28048T
C03267T	T11296-	T21992-	A28111G
C05388A	C14408T	A21993-	G28280C
C05986T	C14676T	T21994-	A28281T
T06954C	C15279T	A23063T	T28282A
T11288-	T16176C	C23271A	G28881A
C11289-	A21764-	A23403G	G28882A
T11290-	T21765-	C23604A	G28883C
G11291-	A21766-	C23709T	C28977T
G11292-	C21767-	T24506G	

Table S2. Statistical results.

Variable 1	Variable 2	[a]Group Identifier	Measurement	Sample Size	p value	q value	median_ Variable 1	median_ Variable 2	Figure referece	Test
D614G	B.1.1.7	MDP1.1	ID50	40	**5.80E-06**	7.73E-05	1374	687	2A	Wilcoxon signed-rank, paired, 2 tailed
D614G	B.1.1.7	NVVP1	ID50	28	**1.80E-05**	0.00018	975	448	2A	Wilcoxon signed-rank, paired, 2 tailed
D614G	B.1.1.7	Convalescent	ID50	15	0.041	0.065	1105	325	2A	Wilcoxon signed-rank, paired, 2 tailed
D614G	B.1.1.7	MDP1.1	ID80	40	**5.50E-12**	2.20E-10	347	188	2B	Wilcoxon signed-rank, paired, 2 tailed
D614G	B.1.1.7	NVVP1	ID80	28	**1.50E-06**	3.00E-05	209	142	2B	Wilcoxon signed-rank, paired, 2 tailed
D614G	B.1.1.7	Convalescent	ID80	15	**0.00061**	0.0022	218	106	2B	Wilcoxon signed-rank, paired, 2 tailed
D614G	D614G.N501Y	MDP1.2	ID50	11	0.24	0.30	1538	1604	2A	Wilcoxon signed-rank, paired, 2 tailed
D614G	D614G.N501Y	Convalescent	ID50	15	0.0012	0.0027	1105	412	2A	Wilcoxon signed-rank, paired, 2 tailed
D614G	D614G.N501Y	MDP1.2	ID80	11	0.46	0.53	453	347	2B	Wilcoxon signed-rank, paired, 2 tailed
D614G	D614G.N501Y	Convalescent	ID80	15	**0.00031**	0.0014	218	128	2B	Wilcoxon signed-rank, paired, 2 tailed
D614G	D614G.del69-70	MDP1.2	ID50	11	**0.00098**	0.0023	1538	2896	2A	Wilcoxon signed-rank, paired, 2 tailed
D614G	D614G.del69-70	Convalescent	ID50	15	0.25	0.30	1105	1244	2A	Wilcoxon signed-rank, paired, 2 tailed
D614G	D614G.del69-70	MDP1.2	ID80	11	**0.00098**	0.0023	453	617	2B	Wilcoxon signed-rank, paired, 2 tailed
D614G	D614G.del69-70	Convalescent	ID80	15	0.15	0.21	218	301	2B	Wilcoxon signed-rank, paired, 2 tailed
D614G	D614G.del69-70.N501Y	MDP1.2	ID50	11	0.002	0.0042	1538	1804	2A	Wilcoxon signed-rank, paired, 2 tailed
D614G	D614G.del69-70.N501Y	Convalescent	ID50	15	0.073	0.10	1105	923	2A	Wilcoxon signed-rank, paired, 2 tailed
D614G	D614G.del69-70.N501Y	MDP1.2	ID80	11	0.21	0.28	453	475	2B	Wilcoxon signed-rank, paired, 2 tailed
D614G	D614G.del69-70.N501Y	Convalescent	ID80	15	0.72	0.74	218	219	2B	Wilcoxon signed-rank, paired, 2 tailed
D614G	D614G.del69-70.Y453F	MDP1.2	ID50	11	0.24	0.30	1538	1365	2A	Wilcoxon signed-rank, paired, 2 tailed
D614G	D614G.del69-70.Y453F	Convalescent	ID50	15	0.012	0.023	1105	343	2A	Wilcoxon signed-rank, paired, 2 tailed
D614G	D614G.del69-70.Y453F	MDP1.2	ID80	11	0.58	0.62	453	351	2B	Wilcoxon signed-rank, paired, 2 tailed
D614G	D614G.del69-70.Y453F	Convalescent	ID80	15	0.0084	0.017	218	122	2B	Wilcoxon signed-rank, paired, 2 tailed
D614G	D614G.N439K	MDP1.2	ID50	11	0.76	0.76	1538	1312	2A	Wilcoxon signed-rank, paired, 2 tailed
D614G	D614G.N439K	Convalescent	ID50	15	**0.00061**	0.0022	1105	688	2A	Wilcoxon signed-rank, paired, 2 tailed
D614G	D614G.N439K	MDP1.2	ID80	11	0.46	0.53	453	481	2B	Wilcoxon signed-rank, paired, 2 tailed
D614G	D614G.N439K	Convalescent	ID80	15	**0.00085**	0.0023	218	151	2B	Wilcoxon signed-rank, paired, 2 tailed
D614G.N501Y	D614G.del69-70.N501Y	MDP1.2	ID50	11	0.042	0.065	1604	1804	2A	Wilcoxon signed-rank, paired, 2 tailed
D614G.N501Y	D614G.del69-70.N501Y	Convalescent	ID50	15	**6.10E-05**	0.00035	412	923	2A	Wilcoxon signed-rank, paired, 2 tailed
D614G.N501Y	D614G.del69-70.N501Y	MDP1.2	ID80	11	0.014	0.024	347	475	2B	Wilcoxon signed-rank, paired, 2 tailed
D614G.N501Y	D614G.del69-70.N501Y	Convalescent	ID80	15	**0.00018**	0.00090	128	219	2B	Wilcoxon signed-rank, paired, 2 tailed
D614G.del69-70	D614G.del69-70.N501Y	MDP1.2	ID50	11	0.042	0.065	2896	1804	2A	Wilcoxon signed-rank, paired, 2 tailed
D614G.del69-70	D614G.del69-70.N501Y	Convalescent	ID50	15	0.52	0.58	1244	923	2A	Wilcoxon signed-rank, paired, 2 tailed
D614G.del69-70	D614G.del69-70.N501Y	MDP1.2	ID80	11	0.014	0.024	617	475	2B	Wilcoxon signed-rank, paired, 2 tailed
D614G.del69-70	D614G.del69-70.N501Y	Convalescent	ID80	15	0.064	0.095	301	219	2B	Wilcoxon signed-rank, paired, 2 tailed
D614G.del69-70	D614G.del69-70.Y453F	MDP1.2	ID50	11	**0.00098**	0.0023	2896	1365	2A	Wilcoxon signed-rank, paired, 2 tailed
D614G.del69-70	D614G.del69-70.Y453F	Convalescent	ID50	15	**6.10E-05**	0.00035	1244	343	2A	Wilcoxon signed-rank, paired, 2 tailed
D614G.del69-70	D614G.del69-70.Y453F	MDP1.2	ID80	11	**0.00098**	0.0023	617	351	2B	Wilcoxon signed-rank, paired, 2 tailed
D614G.del69-70	D614G.del69-70.Y453F	Convalescent	ID80	15	**6.10E-05**	0.00035	301	122	2B	Wilcoxon signed-rank, paired, 2 tailed
Moderna D29	Moderna D57	B.1.1.7	D614G/B.1.1.7_ID50	11, 29	**0.00066**	0.0022	3.51	1.97	2C	Wilcoxon rank sum, 2 tailed
Moderna D29	Moderna D57	B.1.1.7	D614G/B.1.1.7_ID80	11, 29	0.59	0.62	1.75	1.7	2C	Wilcoxon rank sum, 2 tailed

[a]Group identifer: MDP1.1- Moderna Phase 1 Set 1; MDP1.2- Moderna Phase 1 set 2; NVVP1- Novavax Phase 1.

Underlined: p<0.01

Bold: p<0.001

Bold and underlined: p<0.0001

Grey shade: fold difference between median of two variables in comparison <1.3 and >0.77 (reflecting <30% difference in median values).

Table S3. Primers used for site-directed mutagenesis.

Primer	5'-Sequence-3'
H69-V70	5'-ccattggtgccgctgatggcgtggaacc-3'
H69-V70-anti	5'-ggttccacgccatcagcggcaccaatgg-3'
N501Y	5'-agcccacgccatatgttggctggaagccgtag-3'
N501Yanti	5'-ctacggcttccagccaacatatggcgtgggct-3'
N439K	5'-tgctatccagattcttagagttccaggcgatcacg-3'
N439K-anti	5'-cgtgatcgcctggaactctaagaatctggatagca-3'
Y453F	5'-ctaaacagccggaacagataattgtagttgccgccc-3'
Y453F-anti	5'-gggcggcaactacaattatctgttccggctgtttag-3'
A570D	5'-ggcgtctgtggtatcatcgatgtccctgccga-3'
A570D_anti	5'-tcggcagggacatcgatgataccacagacgcc-3'
P681H	5'-cagaccgtgctctcctatgggagtttgtctgggt-3'
P681H-anti	5'-acccagacaaactcccataggagagcacggtctg-3'
T716I	5'-cggagattgtgaagttgatagggatggcgatagaa-3'
T716I-anti	5'-ttctatcgccatccctatcaacttcacaatctccg-3'
S982A	5'-caccttgtccagccgggccaggatgtcattcagc-3'
S982A-anti	5'-gctgaatgacatcctggcccggctggacaaggtg-3'
D1118H	5'-cacgaatgtattgtgtgtggtgatgatctgtggc-3'
D1118H-anti	5'-gccacagatcatcaccacacacaatacattcgtg-3'
Y144-	5'-acttattgttcttgtgatacacgcccaggaatggatc-3'
Y144-anti	5'-gatccattcctgggcgtgtatcacaagaacaataagt-3'