Supplementary Information

Serological fingerprints link antiviral activity of therapeutic antibodies to affinity and concentration

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**Table S1.** Mutations within the spike protein shared among SARS-CoV-2 variants\(^4\)4.

| Domain | Region | SARS-CoV-2 variant |
|--------|--------|--------------------|
|        |        | Alpha Beta Gamma Delta Kappa Omicron (BA.1) Omicron (BA.2) Eta Iota Lambda Mu |
| NTD    |        | L18F L18F T19R T19I P26S P26- A67V A67V H69- H69- V70- V70- T95I T95I T95I G142- G142- V143- V143- Y144- Y144- Y144- Y144- Y145D Y145D Y145 D253G D253N |
| S1     |        | G339D G339D S371L S371F S373P S373P S375F S375F K417N K417T K417N K417N N440K N440K L452R L452R T478K T478K E484K E484K E484Q E484A E484A E484K E484K Q493R Q493R Q498R Q498R N501Y N501Y N501Y N501Y N501Y N501Y N501Y Y505H Y505H |
| SD2    |        | D614G D614G D614G D614G D614G D614G D614G D614G D614G D614G D614G D614G D614G H655Y H655Y H655Y H655Y N679K N679K N679K P681H P681R P681R P681R P681H P681H P681H P681H |
| S2     |        | A701V A701V N764K N764K D796Y D796Y |
| HR1    |        | D950N D950N Q954H Q954H N969K N969K |
Table S2. Mutations within the spike protein unique among SARS-CoV-2 variants\textsuperscript{44}.

| SARS-CoV-2 variant | Alpha | Beta | Gamma | Delta | Kappa | Omicron (BA.1) | Omicron (BA.2) | Eta | Lota | Lambda | Mu |
|--------------------|-------|------|-------|-------|-------|----------------|----------------|-----|------|--------|----|
|                    |       |      |       |       |       | Unique mutations |                |     |      |        |    |
|                    | A570D | D80A | T20N  | E156- | E154K | N211-          | L24-           | Q52R| L5F  | G75V   | R346K |
|                    | T716I | D215G| D138Y | F157- | Q1071H| L212I         | P25-           | Q677H| T76I | R246-  |     |
|                    | S982A | L241-| R190S | R158G | G446S | A275           | F888L          |     |      |        |    |
|                    | D1118H| L242-| T1027I|       | G496S | V213G          |                |     |      | S247-  |     |
|                    | A243- | V1176F|      |       | T547K | T376A          |                |     |      | Y248-  |     |
|                    |       |       |       |       |       | N856K          | D405N          | L249-| T250-| P251-  |     |
|                    |       |       |       |       |       | L981F          | R408S          |     |      | G252-  |     |
|                    |       |       |       |       |       |                |                |     |      | F490S  |     |
|                    |       |       |       |       |       |                |                |     |      | T859N  |     |
### Table S3

Summary of unpublished microfluidic antibody affinity profiling data from SARS-CoV-2 convalescent samples shown in Figure 3. Results from samples collected by Blutspendedienst (BDS) Kanton Zürich and University Hospital Zurich (CH) have been published previously in *Life Sci. Alliance* 2021, 5 (2), e202101270.

| Sample source: Working reagent for anti-SARS-CoV-2 immunoglobulin, NIBSC code 21/234. National Institute for Biological Standards and Control (UK) | $K_D$ (nM) | [antibody] (nM) |
|---|---|---|
| antigen | best fit | lower 95% CI | upper 95% CI | best fit | lower 95% CI | upper 95% CI |
| SARS-CoV-2 wt spike RBD | 12.3 | 9.3 | 16.4 | 110 | 130 | 93.9 |
| SARS-CoV-2 delta spike RBD | 17.5 | 13 | 24.3 | 119 | 138 | 98.1 |
| SARS-CoV-2 omicron spike RBD | 30.1 | 23 | 39.9 | 59.3 | 71.7 | 46.4 |

| Sample source: Fred Hutchinson Cancer Research Center, Seattle WA, USA | $K_D$ (nM) | [antibody] (nM) |
|---|---|---|
| antigen | best fit | lower 95% CI | upper 95% CI | best fit | lower 95% CI | upper 95% CI |
| SARS-CoV-2 wt spike RBD | 11.2 | 3.2 | 26.8 | 246 | 76.7 | 452 |
| SARS-CoV-2 wt spike RBD | 9.3 | 4.1 | 18.9 | 70.5 | 40.5 | 110 |
| SARS-CoV-2 wt spike RBD | 6.9 | 3.6 | 12.2 | 676.8 | 597 | 813 |
| SARS-CoV-2 wt spike RBD | 9.4 | 5.8 | 13.2 | 240 | 196 | 281 |
| SARS-CoV-2 wt spike RBD | 17.4 | 12.4 | 23.1 | 495 | 414 | 583 |
| SARS-CoV-2 wt spike RBD | 8.6 | 3.2 | 25.9 | 424 | 230 | 777 |
| SARS-CoV-2 wt spike RBD | 40.4 | 23.5 | 64.9 | 239 | 161 | 324 |
| SARS-CoV-2 wt spike RBD | 15.1 | 0.29 | 37.0 | 104 | 3.1 | 202 |
| SARS-CoV-2 wt spike RBD | 4.5 | 0.01 | 11.2 | 190 | 67.7 | 349 |
| SARS-CoV-2 wt spike RBD | 10.9 | 3.9 | 27.4 | 170 | 77.3 | 275 |
| SARS-CoV-2 wt spike RBD | 9.3 | 0.06 | 28.5 | 71.7 | 22.0 | 127 |
| SARS-CoV-2 wt spike RBD | 5.8 | 1.9 | 11.0 | 140 | 99.6 | 192 |
| SARS-CoV-2 wt spike RBD | 25.4 | 11.9 | 60.9 | 249 | 127 | 400 |
| SARS-CoV-2 wt spike RBD | 9.7 | 0.01 | 1108 | 9.7 | 0.09 | 1416 |
| SARS-CoV-2 wt spike RBD | 9.4 | 3.4 | 16.1 | 1778 | 1176 | 2270 |
| SARS-CoV-2 wt spike RBD | 30.7 | 11.8 | 62.5 | 275 | 146 | 788 |
| SARS-CoV-2 wt spike RBD | 6.8 | 1.4 | 19.6 | 26.7 | 11.3 | 46 |
| SARS-CoV-2 wt spike RBD | 48.3 | 1.0 | 278 | 326 | 4.5 | 804 |
| SARS-CoV-2 wt spike RBD | 9.2 | 0.01 | 294 | 373 | 0.0 | 3441 |
| SARS-CoV-2 wt spike RBD | 6.5 | 2.8 | 11.7 | 135 | 108 | 178 |
| SARS-CoV-2 wt spike RBD | 51.8 | 20.0 | 124 | 340 | 103 | 1014 |
| SARS-CoV-2 wt spike RBD | 16.3 | 10.5 | 24.1 | 297 | 224 | 383 |
| SARS-CoV-2 wt spike RBD | 7.4 | 0.02 | 14.3 | 96.0 | 32.0 | 151 |
| SARS-CoV-2 wt spike RBD | 29.2 | 17.2 | 47.7 | 430 | 241 | 583 |
| SARS-CoV-2 wt spike RBD | 18.5 | 8.1 | 37.7 | 92.0 | 39.0 | 153 |

Sample source: Mayo Clinic, Rochester, MN, USA
| antigen                        | $K_o$ (nM) | [antibody] (nM) |
|-------------------------------|------------|----------------|
|                               | best fit   | lower 95% CI   | upper 95% CI   | best fit   | lower 95% CI | upper 95% CI |
| SARS-CoV-2 wt spike RBD       | 0.55       | 0.011          | 1.5            | 2.3        | 1.2          | 5.6          |
| SARS-CoV-2 wt spike RBD       | 0.02       | 0.010          | 1.98           | 22.3       | 14.6         | 66.5         |
| SARS-CoV-2 wt spike RBD       | 1.0        | 0.013          | 2.8            | 19.4       | 13.1         | 26.2         |
| SARS-CoV-2 wt spike RBD       | 0.02       | 0.010          | 0.67           | 3.3        | 2.0          | 10.4         |