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**Supplementary information**

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**High genetic barrier to SARS-CoV-2  
polyclonal neutralizing antibody escape**

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In the format provided by the  
authors and unedited

**Table S1. Substitutions enriched in rVSV/SARS-CoV-2 following selection in neutralizing plasma**

| Plasma | Parental virus                 | Dilution | Passage | Substitutions                                                                                         |
|--------|--------------------------------|----------|---------|-------------------------------------------------------------------------------------------------------|
| RU1    | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100      | 4       | I794T (11.7%), R246G (10.9%), T573I (10.3%)                                                           |
|        | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100      | 6       | I794T (5.7%), N536H (5.1%)                                                                            |
|        | rVSV/SARS-CoV-2 <sub>2E1</sub> | 100      | 2       | T604I (15.4%)                                                                                         |
|        | rVSV/SARS-CoV-2 <sub>2E1</sub> | 200      | 6       | L244P (57.2%), T604I (50.8%), G142E (30.7%), A623T (20.3%), P681S (20%), F759S (5.7%), Y248H (5.2%)   |
| RU2    | rVSV/SARS-CoV-2 <sub>1D7</sub> | 200      | 6       | N148K (37.3%), A264D (32.2%), N149T (19.5%), H146R (16.8%), N148S (9.6%), V1061A (8.7%), K150N (5.9%) |
|        | rVSV/SARS-CoV-2 <sub>2E1</sub> | 200      | 6       | P807H (68.5%), I931M (65.9%), N450D (63.2%), K150N (25.6%)                                            |
| RU3    | rVSV/SARS-CoV-2 <sub>1D7</sub> | 50       | 2       | P1213S (17.6%), W1212R (10.2%), K1211R (8.8%), I1210N (6%)                                            |
|        | rVSV/SARS-CoV-2 <sub>2E1</sub> | 50       | 2       | P1213S (29.5%), W1212R (19%), K1211R (16.2%), I1210N (12%), W64R (6%)                                 |
| RU4    | rVSV/SARS-CoV-2 <sub>1D7</sub> | 50       | 4       | R682G (23.7%), Y145D (12.5%), K147R (11.8%)                                                           |
|        | rVSV/SARS-CoV-2 <sub>2E1</sub> | 50       | 4       | W258R (58.3%), T604I (12.8%)                                                                          |
| RU5    | rVSV/SARS-CoV-2 <sub>1D7</sub> | 50       | 4       | K147E (6.4%), I1081V (5.4%)                                                                           |
|        | rVSV/SARS-CoV-2 <sub>2E1</sub> | 50       | 4       | T604I (10%), Y248D (5.4%)                                                                             |
|        | rVSV/SARS-CoV-2 <sub>2E1</sub> | 50       | 4       | T604I (14.9%), Y248D (10.5%)                                                                          |
| RU6    | rVSV/SARS-CoV-2 <sub>1D7</sub> | 400      | 6       | I794T (6%)                                                                                            |
|        | rVSV/SARS-CoV-2 <sub>2E1</sub> | 400      | 6       | T604I (27.2%), V1128A (9.2%)                                                                          |
| RU7    | rVSV/SARS-CoV-2 <sub>1D7</sub> | 50       | 4       | I794T (11.6%), P1213S (6.1%)                                                                          |
|        | rVSV/SARS-CoV-2 <sub>1D7</sub> | 200      | 4       | I794T (13%)                                                                                           |
|        | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100      | 6       | N709D (5.6%), I794T (5.3%)                                                                            |
|        | rVSV/SARS-CoV-2 <sub>2E1</sub> | 100      | 3       | T604I (6.5%)                                                                                          |
|        | rVSV/SARS-CoV-2 <sub>2E1</sub> | 100      | 4       | T604I (9.3%), V1061M (8.5%), E1188D (6.4%), C15Y (6%)                                                 |
|        | rVSV/SARS-CoV-2 <sub>2E1</sub> | 100      | 6       | L244P (26.5%), T604I (21.4%), I794T (6.1%), R1091S (5.1%)                                             |
| RU8    | rVSV/SARS-CoV-2 <sub>1D7</sub> | 50       | 4       | N450D (95.2%), R1091S (5.5%)                                                                          |
|        | rVSV/SARS-CoV-2 <sub>1D7</sub> | 200      | 6       | V445M (94.8%)                                                                                         |
|        | rVSV/SARS-CoV-2 <sub>2E1</sub> | 50       | 4       | K444T (67.9%), N450D (26.3%)                                                                          |
|        | rVSV/SARS-CoV-2 <sub>2E1</sub> | 100      | 4       | K444T (68.4%), N450D (27.8%)                                                                          |
|        | rVSV/SARS-CoV-2 <sub>2E1</sub> | 200      | 6       | I931M (46.1%), N450D (44.1%), P807H (32.6%)                                                           |
| RU9    | rVSV/SARS-CoV-2 <sub>1D7</sub> | 50       | 4       | P1213S (21%), W1212R (9.7%), K1211R (8.5%), I1210N (5.1%)                                             |
|        | rVSV/SARS-CoV-2 <sub>2E1</sub> | 100      | 4       | P792H (86.5%), Q992H (81%), P1213S (6%)                                                               |
| RU10   | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100      | 3       | R246G (18%), I794T (11.7%), V1128M (11.6%)                                                            |
|        | rVSV/SARS-CoV-2 <sub>1D7</sub> | 200      | 6       | P792H (22.6%), K147R (13.3%), I794T (7.3%)                                                            |
|        | rVSV/SARS-CoV-2 <sub>2E1</sub> | 50       | 4       | V143G (35.8%), Q1010R (30.5%), T604I (13.1%), S711R (7.2%)                                            |
|        | rVSV/SARS-CoV-2 <sub>2E1</sub> | 200      | 6       | S254Y (92.1%), N801D (91.5%)                                                                          |
| RU11   | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100      | 6       | I794T (29.3%), N969K (11.6%), K147R (10.3%)                                                           |
|        | rVSV/SARS-CoV-2 <sub>2E1</sub> | 100      | 6       | C136Y (52.5%), L141P (46.2%), V1128A (46.2%), R682K (6.1%)                                            |
| RU12   | rVSV/SARS-CoV-2 <sub>1D7</sub> | 50       | 4       | V143A (6.9%), P1213S (6.5%)                                                                           |
|        | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100      | 4       | E180K (9.3%), V143A (8.3%), H655Y (7.2%), P1213S (5.1%)                                               |

|      |                                |     |   |                                                                                                                                                             |
|------|--------------------------------|-----|---|-------------------------------------------------------------------------------------------------------------------------------------------------------------|
|      | rVSV/SARS-CoV-2 <sub>1D7</sub> | 50  | 6 | S813I (7%)                                                                                                                                                  |
|      | rVSV/SARS-CoV-2 <sub>2E1</sub> | 100 | 4 | L244P (21.3%), T604I (16.6%), N969K (8.7%), M740I (5.6%)                                                                                                    |
|      | rVSV/SARS-CoV-2 <sub>2E1</sub> | 200 | 6 | N801D (98.9%), S254Y (96.1%), Y144C (5.3%)                                                                                                                  |
| RU13 | rVSV/SARS-CoV-2 <sub>1D7</sub> | 50  | 4 | M153T (14.8%), I794T (10.2%), P1213S (6.5%)                                                                                                                 |
|      | rVSV/SARS-CoV-2 <sub>2E1</sub> | 50  | 3 | S247P (15.9%), N801D (14.5%), T604I (5.5%), P1213S (5.4%)                                                                                                   |
|      | rVSV/SARS-CoV-2 <sub>2E1</sub> | 50  | 4 | N801D (42.4%), S247P (41.3%), T604I (6.8%), P1213S (6.2%)                                                                                                   |
| RU14 | rVSV/SARS-CoV-2 <sub>1D7</sub> | 200 | 6 | I794T (6.8%), L212R (5.4%)                                                                                                                                  |
|      | rVSV/SARS-CoV-2 <sub>2E1</sub> | 400 | 6 | S399Y (44.9%), T604I (43.6%)                                                                                                                                |
| RU15 | rVSV/SARS-CoV-2 <sub>2E1</sub> | 100 | 4 | T604I (9.3%)                                                                                                                                                |
| RU16 | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 2 | N450D (35.8%), V445A (11.9%), K378R (11.8%), V445E (7.8%)                                                                                                   |
|      | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 6 | V445A (6.8%), G446E (6.1%)                                                                                                                                  |
|      | rVSV/SARS-CoV-2 <sub>2E1</sub> | 50  | 5 | G446R (67%), K444R (19%), K444T (9%)                                                                                                                        |
|      | rVSV/SARS-CoV-2 <sub>2E1</sub> | 50  | 6 | V445E (100%), T604I (100%)                                                                                                                                  |
| RU17 | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 2 | Q690H (7.8%)                                                                                                                                                |
|      | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 4 | Q690H (27.8%)                                                                                                                                               |
|      | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 6 | I794T (7.2%)                                                                                                                                                |
|      | rVSV/SARS-CoV-2 <sub>2E1</sub> | 100 | 2 | F797S (50.8%), L212R (47%), Q14H (19.6%), T604I (8.4%)                                                                                                      |
|      | rVSV/SARS-CoV-2 <sub>2E1</sub> | 100 | 4 | Q14H (50%), F797S (37.4%), L212R (36.2%)                                                                                                                    |
|      | rVSV/SARS-CoV-2 <sub>2E1</sub> | 200 | 6 | R102G (33.7%), T604I (33.3%), N87K (29%), H245N (27.2%), P792R (18.5%), I931M (8.3%), F140S (6.3%), R246M (5.4%)                                            |
| RU18 | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 2 | R246G (38%), Y248H (35.2%)                                                                                                                                  |
|      | rVSV/SARS-CoV-2 <sub>1D7</sub> | 50  | 4 | R246G (55.2%), Y248H (44.5%)                                                                                                                                |
|      | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 4 | R246G (56.9%), Y248H (43.1%)                                                                                                                                |
|      | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 6 | Y248H (26.7%), L176P (9.4%), R682G (8.6%), Y144H (6.3%)                                                                                                     |
|      | rVSV/SARS-CoV-2 <sub>2E1</sub> | 50  | 4 | P1162S (46.1%), L242P (39.1%), K147N (36.4%), S813I (6.6%)                                                                                                  |
|      | rVSV/SARS-CoV-2 <sub>2E1</sub> | 100 | 4 | K147N (54.1%), L242P (30%), P1162S (27%)                                                                                                                    |
|      | rVSV/SARS-CoV-2 <sub>2E1</sub> | 200 | 6 | Y144D (32.2%), L244P (27.3%), T604I (18.8%), P174S (16.4%), C136Y (13.9%), L141R (12.2%), G142R (11.2%), V687A (9%), N764S (8.6%), S813I (7%), G261R (5.5%) |
| RU19 | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 2 | I794T (11.8%), K150T (6.7%), I1013V (6%)                                                                                                                    |
|      | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 4 | I794T (44%), K150T (13.8%), Y837H (6%)                                                                                                                      |
|      | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 6 | I794T (6.4%)                                                                                                                                                |
|      | rVSV/SARS-CoV-2 <sub>2E1</sub> | 200 | 6 | N801D (83.2%), S254Y (79.1%), G142E (13.2%), T573I (6.1%)                                                                                                   |
| RU20 | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 6 | I794T (8.9%), K147R (7.6%)                                                                                                                                  |
|      | rVSV/SARS-CoV-2 <sub>2E1</sub> | 200 | 6 | T604I (82.9%), P25L (60.2%), G142E (30.9%), H69N (7.2%)                                                                                                     |
| RU21 | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 2 | Y248H (41.4%)                                                                                                                                               |
|      | rVSV/SARS-CoV-2 <sub>1D7</sub> | 50  | 4 | Y248H (81.2%)                                                                                                                                               |
|      | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 4 | Y248H (87.8%), G769S (5.5%)                                                                                                                                 |
|      | rVSV/SARS-CoV-2 <sub>2E1</sub> | 100 | 4 | C15G (74.1%)                                                                                                                                                |
|      | rVSV/SARS-CoV-2 <sub>2E1</sub> | 100 | 6 | A243D (95.3%), R190M (6.5%), L244P (5.3%)                                                                                                                   |
| RU22 | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 4 | V1065M (8.4%)                                                                                                                                               |

|           |                                |     |   |                                                                                                       |
|-----------|--------------------------------|-----|---|-------------------------------------------------------------------------------------------------------|
|           | rVSV/SARS-CoV-2 <sub>1D7</sub> | 50  | 6 | V1128A (8%)                                                                                           |
|           | rVSV/SARS-CoV-2 <sub>2E1</sub> | 100 | 4 | D808N (18%), T604I (12.4%)                                                                            |
|           | rVSV/SARS-CoV-2 <sub>2E1</sub> | 200 | 6 | R214S (86.1%)                                                                                         |
| RU23      | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 2 | E484K (16.6%)                                                                                         |
|           | rVSV/SARS-CoV-2 <sub>1D7</sub> | 50  | 4 | E484K (54.1%)                                                                                         |
|           | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 4 | T604I (8.4%)                                                                                          |
|           | rVSV/SARS-CoV-2 <sub>1D7</sub> | 50  | 6 | I794T (16.4%), Y248S (8.6%), T778N (5.9%)                                                             |
|           | rVSV/SARS-CoV-2 <sub>2E1</sub> | 100 | 4 | E484K (81.5%)                                                                                         |
| RU24      | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 2 | Q493K (10.4%)                                                                                         |
|           | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 4 | Y144C (24.7%), T604I (24.6%), I931M (19.9%), E154K (18%)                                              |
|           | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 6 | K147E (23.1%), L841Q (18.6%), K147R (14.4%)                                                           |
|           | rVSV/SARS-CoV-2 <sub>2E1</sub> | 100 | 4 | Q493K (40.5%), L18M (35.6%), N717D (8.3%), L226Q (6%)                                                 |
|           | rVSV/SARS-CoV-2 <sub>2E1</sub> | 100 | 6 | T604I (100%), Y144C (98.9%)                                                                           |
| RU25      | rVSV/SARS-CoV-2 <sub>1D7</sub> | 50  | 4 | E1092Y (5.1%), R1091S (5.1%)                                                                          |
|           | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 4 | R246G (5.6%)                                                                                          |
|           | rVSV/SARS-CoV-2 <sub>2E1</sub> | 100 | 4 | C15Y (27%), P1213S (13.5%), E1188D (8.6%), W1212R (7.7%), K1211R (6.5%), I1210N (5.6%)                |
|           | rVSV/SARS-CoV-2 <sub>2E1</sub> | 200 | 6 | P25L (65.3%), T604I (14.4%), L244P (10.7%), T734I (6.5%)                                              |
| RU26      | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 6 | A623T (78.9%), P681S (77.4%), G142E (54.2%), F759S (19.9%), I931M (12.3%), K113R (9.2%), T778N (5.7%) |
|           | rVSV/SARS-CoV-2 <sub>2E1</sub> | 200 | 6 | Y144C (71.7%), T604I (70.5%), I931M (30.6%), F759S (27.7%), F140S (26.4%)                             |
| RU27      | rVSV/SARS-CoV-2 <sub>1D7</sub> | 100 | 6 | K150N (51.5%), K147E (24.1%), L841Q (10.8%), K147R (9%)                                               |
|           | rVSV/SARS-CoV-2 <sub>2E1</sub> | 200 | 6 | L244P (79.3%), W64R (75.1%)                                                                           |
| No plasma | rVSV/SARS-CoV-2 <sub>1D7</sub> | 0   | 4 | S98R (31.7%)                                                                                          |
|           | rVSV/SARS-CoV-2 <sub>1D7</sub> | 0   | 6 | T604I (73.4%)                                                                                         |
|           | rVSV/SARS-CoV-2 <sub>2E1</sub> | 0   | 4 | W64R (31.6%), T604I (13.5%), H66R (7.5%)                                                              |
|           | rVSV/SARS-CoV-2 <sub>2E1</sub> | 0   | 6 | T604I (28.3%), H66R (17.4%), I931M (8.6%), S982R (8.4%), F759S (7.7%), W64R (6%)                      |