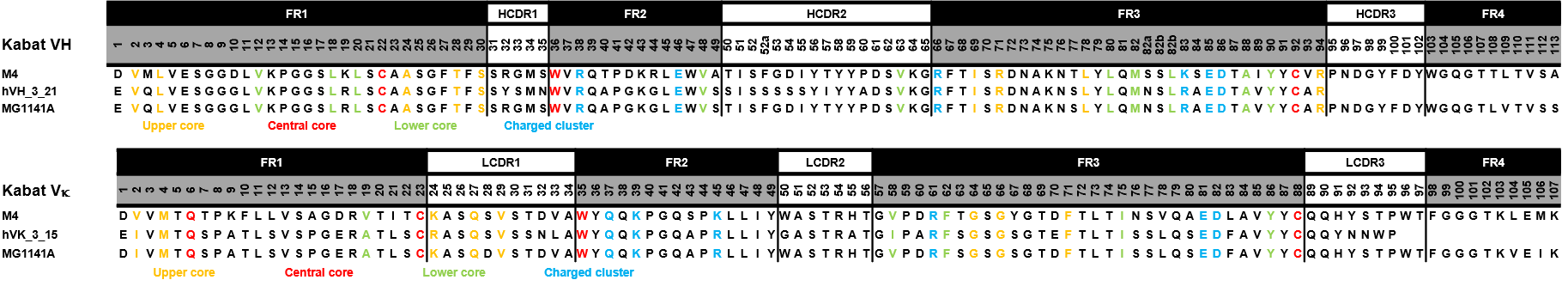
***Supplementary Material***



**Supplementary Figure 1. Amino-acid sequence alignment between mouse and humanized variable domains.** Mouse CDR sequences were grafted onto human VH3-21 and Vk3-15 germline sequences.The sequences are numbered according to Kabat numbering. Core residues are marked by different colors: upper core (orange), central core (red), lower core (green), and charged cluster (blue).



**Supplementary Figure 2. SDS-PAGE results of the purified antibodies.** The purity of in-house antibodies was verified using SDS-PAGE. The clone names of the antibodies are indicated above the SDS-PAGE gel. SDS-PAGE was performed under reducing (A) and non-reducing (B) conditions.



**Supplementary Figure 3. Binding characterization of anti-SARS-CoV-2 mAbs used in clinical trials.** Binding analysis of mAbs captured on a protein-A chip at 25 °C using Biacore T-200. S protein serial diluted (2-fold) from 0.3125 nM to 20 nM was run on the chip for 180 sec for association and 1,800 sec for dissociation. Equilibrium dissociation constants (KD) were calculated from Koff/Kon. At least four concentrations of S proteins were used.



**Supplementary Figure 4. A** Representative flow-cytometry plots of ACE2 expression from the ACE2-HEK293 stable cell line. **B** Representative flow cytometry of SARS-CoV-2 Spike protein expression from the HT1080-S stable cell line.

Chart, timeline

Description generated with high confidence

**Supplementary Figure 5. Schematic figure of mutation sequences of SARS-CoV-2 variants.** The SARS-CoV-2 S protein consists of two subunits (S1 and S2). The S1 subunit contains a receptor-binding domain (RBD), and the S2 subunit contains a fusion peptide (FP), two heptad repeats (HR1 and HR2), and a transmembrane region. Each SARS-CoV-2 pseudovirus variant was generated with mutated representative sequences in the S protein. The UK variant additionally had the deletion of residues 69-70 and 144. The mutations are located in the receptor-binding motif (RBM) and are highlighted by yellow boxes in the mutated sequences.



**Supplementary Figure 6. Epitope binning of MG1141A.** Trace data of epitope binning performed using the in-tandem method. The steps of antigen immobilization, 1st association, and 2nd association are shown by a dashed line. Among the traces, the 2nd binding trace was observed only in the reference trace. Based on this, the binding percentages were classified into 3 stages: < 33%, complete competition; 33%–66 %, intermediate competition; > 66 %, no competition.

**Chart, histogram

Description generated with very high confidence**

**Supplementary Figure 7. Donor screening.** Human sera and peripheral blood mononuclear cells (PBMCs) were collected and isolated from the 19 COVID-19 convalescent donors. Serum was separated from the collected blood and the antibody titer was analyzed against the S protein extracellular domain (ECD) and receptor-binding domain (RBD)-Fc. A 96-well ELISA plate was coated with S protein ECD and RBD protein at 0.15 µg in each well in phosphate-buffered saline (PBS) overnight at 4 °C. After washing with 0.05% Tween 20 in PBS (PBST) and blocking with 5% bovine serum albumin in PBS, the plasmas were incubated for 2 h at room temperature. The plasma from donors was diluted 1:100. After washing with PBST, anti-human Fc-HRP (1:1000) was used as the secondary antibody. Tetramethylbenzidine solution and stop solution were used for detection. Antibody titers showed higher binding to the S protein ECD than to RBD-Fc. Antibody titers were slightly correlated with the median plaque reduction neutralization result (PRNT50). Donor numbers 3, 5, 7, 8, 16, 17, 18, and 19 were chosen to construct the phage display library. The PRNT50 method is included in the Materials and Methods.

**Supplementary Table 1.** **Information on RBD variant proteins**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variant** | **Name** | **Mutation** | **Cat. no.** |
| WT | SARS-CoV Spike/RBD Protein (RBD, His Tag) | - | Sino Biologics, 40150-V08B2 |
| UK variant | B.1.1.7 | SARS-CoV-2 (2019-nCoV) Spike RBD(N501Y)-His Recombinant Protein | N501Y | Sino Biologics, 40592-V08H82 |
| South Africa variant | B.1.351 | SARS-CoV-2 (2019-nCoV) Spike RBD(K417N, E484K, N501Y)-His Recombinant Protein | K417N, E484K, N501Y | Sino Biologics, 40592-V08H85 |
| Brazil variant | P.1 | SARS-CoV-2 (2019-nCoV) Spike RBD (K417T, E484K, N501Y) Protein (His Tag) | K417T, E484K, N501Y | Sino Biologics, 40592-V08H86 |

**Supplementary Table 2. Screening results of anti-SARS-CoV-2 chimeric and fully human antibodies**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Origin** | **Clone name** | **Germlinea** | | **EC50, nMb** | **Affinity (*k*D, nM)c** | |
| **Heavy chain** | **Light chain** | **RBD** | **S protein ECD** |
| **Mouse**  **chimeric Ab** | M4 | IGHV 5-6 | IGKV 6-32 | 0.08 | 0.263 | 0.107 |
| **Human Ab** | 2 | IGHV3-23 | IGKV1-33 | >100 | 0.459 | 0.37 |
| 3 | IGHV3-23 | IGKV1-33 | >100 | 0.468 | 0.323 |
| 4 | IGHV3-23 | IGKV1-33 | >50 | 0.45 | 0.381 |
| 5 | IGHV3-23 | IGKV1-33 | >50 | 0.71 | 0.259 |
| 8 | IGHV3-48 | IGLV1-44 | n.d. | n.d. | 0.626 |
| 10 | IGHV3-48 | IGLV1-44 | n.d. | n.d. | 0.265 |
| 11 | IGHV3-7 | IGLV2-11 | n.d. | n.d. | 0.44 |
| 13 | IGHV3-30 | IGLV1-40 | >100 | n.d. | 0.207 |
| 14 | IGHV3-7 | IGLV1-40 | >100 | n.d. | 0.119 |
| 15 | IGHV3-23 | IGLV1-50 | n.d. | n.d. | 0.34 |
| 16 | IGHV3-23 | IGLV1-40 | n.d. | n.d. | 0.996 |
| 17 | IGHV3-7 | IGLV1-40 | >100 | n.d. | 0.373 |
| 18 | IGHV3-23 | IGLV1-40 | n.d. | n.d. | 0.293 |
| 21 | IGHV3-7 | IGLV1-40 | n.d. | n.d. | 0.453 |
| 22 | IGHV3-7 | IGLV1-40 | n.d. | n.d. | 0.904 |
| 23 | IGHV3-7 | IGLV1-40 | n.d. | n.d. | 1.825 |
| 25 | IGHV3-7 | IGLV1-40 | n.d. | n.d. | 0.99 |
| 27 | IGHV3-7 | IGLV1-40 | n.d. | n.d. | 1.55 |
| 28 | IGHV3-7 | IGKV1-39 | n.d. | n.d. | 0.632 |
| 29 | IGHV3-7 | IGLV1-40 | n.d. | n.d. | 1.16 |
| 30 | IGHV3-7 | IGLV1-40 | n.d. | n.d. | 2.43 |
| 31 | IGHV3-7 | IGLV1-40 | n.d. | n.d. | 1.481 |
| 32 | IGHV3-7 | IGLV1-40 | n.d. | n.d. | 3.216 |
| 33 | IGHV3-7 | IGKV1-39 | >100 | n.d. | 0.111 |
| 35 | IGHV3-9 | IGLV2-14 | n.d. | 1.104 | 0.667 |
| 38 | IGHV1-46 | IGLV1-51 | n.d. | n.d. | 1.095 |
| 41 | IGHV4-4 | IGKV1-39 | n.d. | n.d. | 0.473 |
| 42 | IGHV3-48 | IGLV3-21 | n.d. | n.d. | 2.177 |
| **Control Ab** | REGN10933 | IGHV3-11 | IGKV1-33 | 0.08 | 0.466 | 0.359 |
| REGN10987 | IGHV3-30 | IGLV2-14 | 0.08 | 0.534 | 0.493 |

a Antibody germline sequences were identified using an IgBLAST search.

b The EC50 values of antibodies against clinical SARS-CoV-2 isolates (Korea/KUMC45/2020, clade GH) were determined by the plaque reduction neutralization test (PRNT).

c The affinity of antibodies was determined by ELISA.