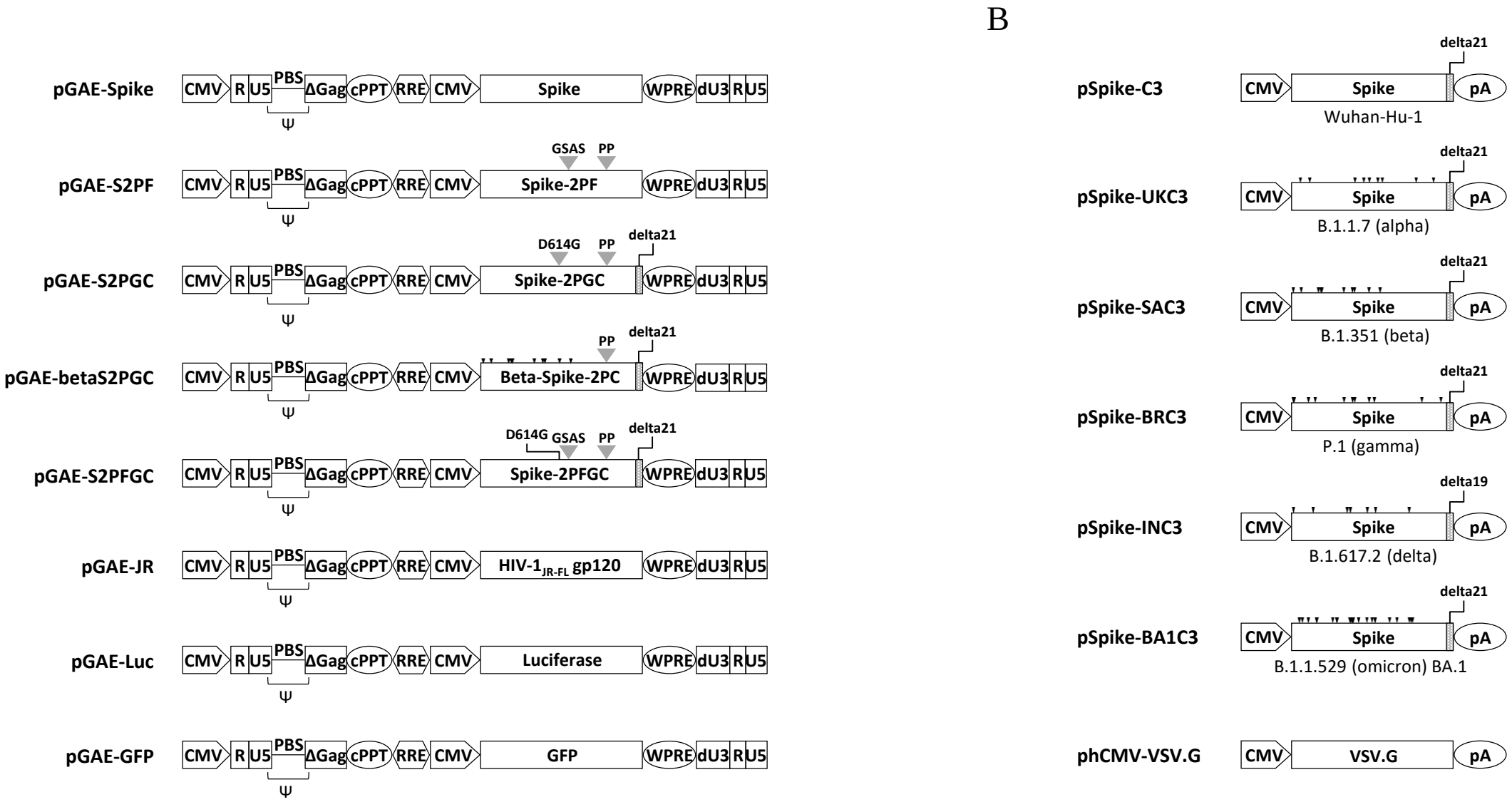
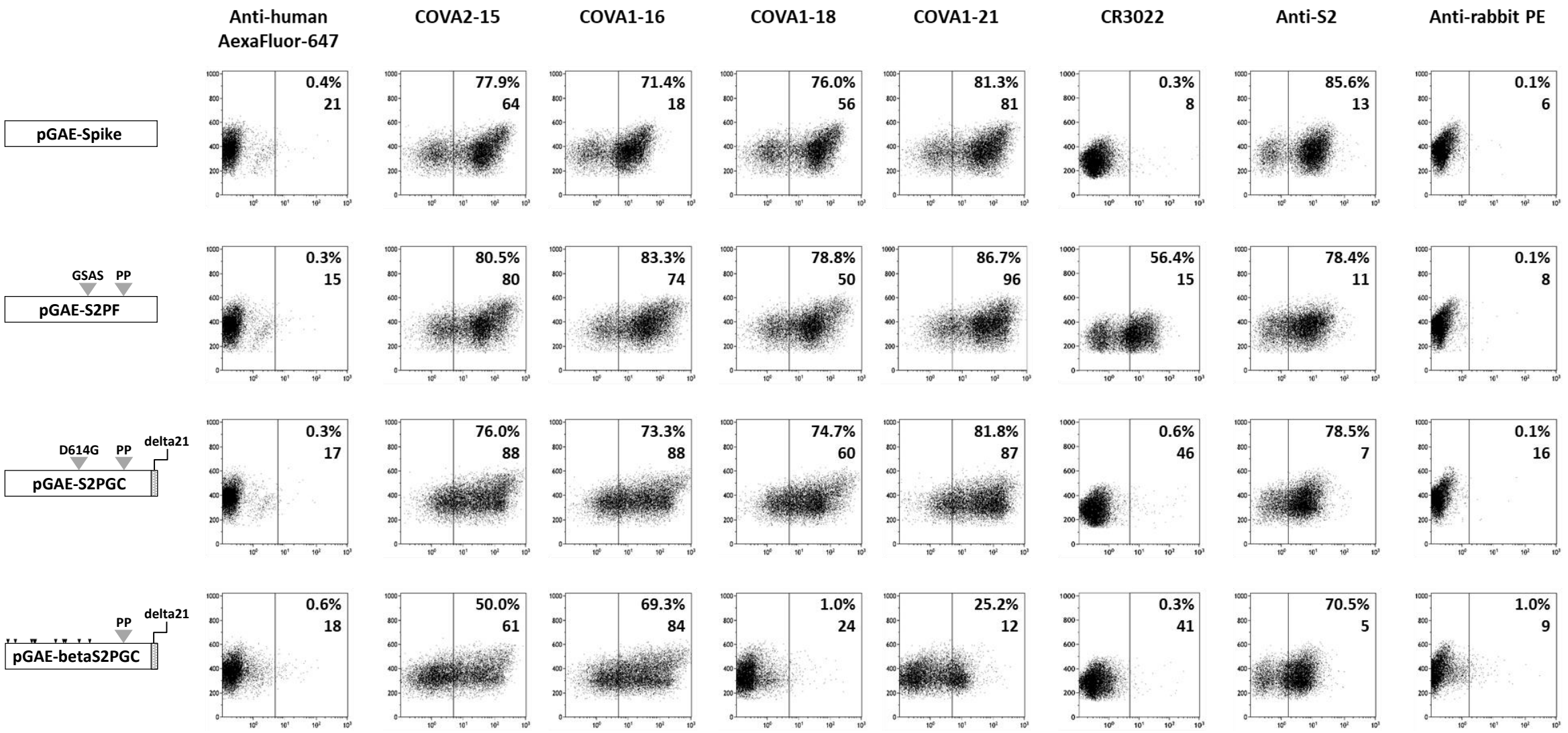
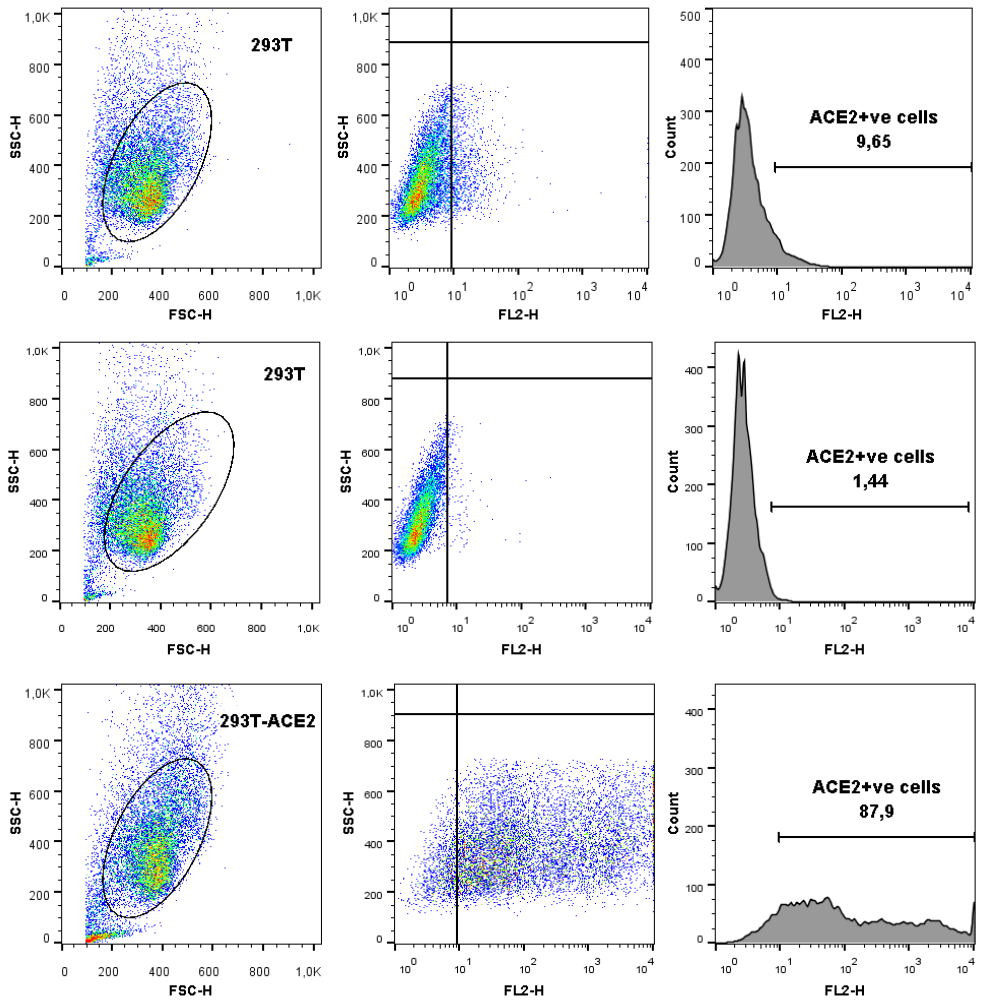


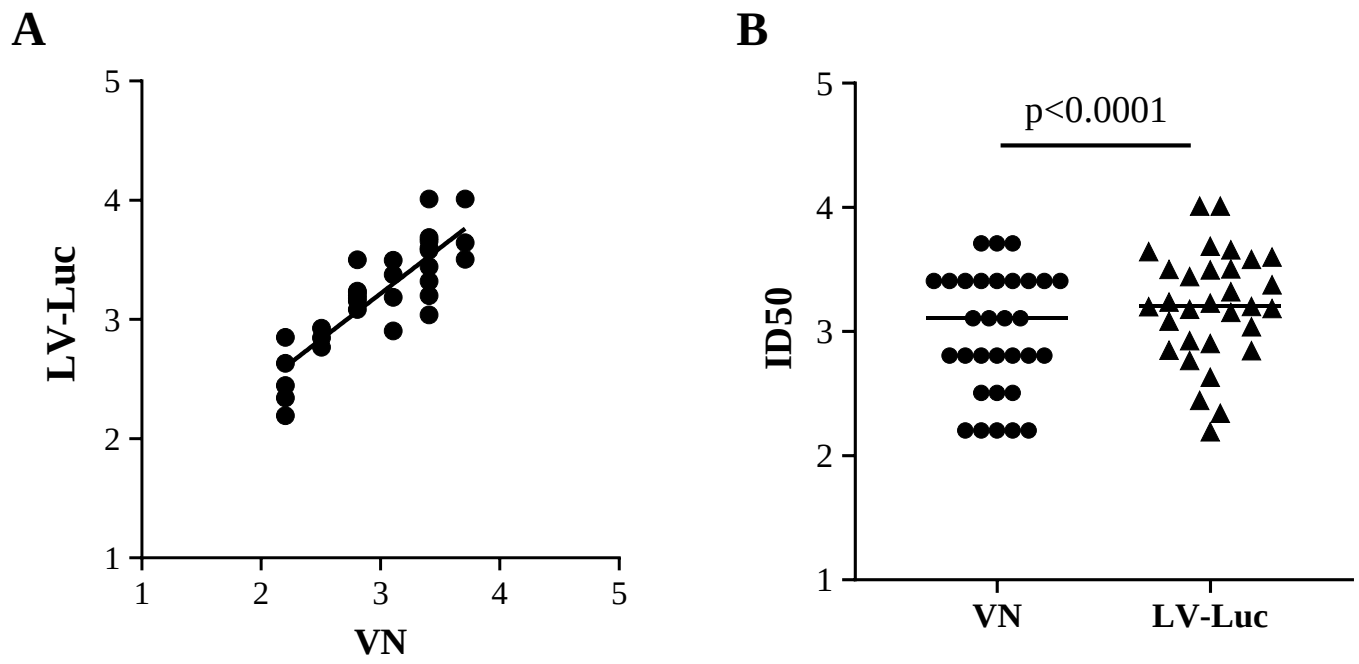
Supplementary Figure 1. **Schematic representation of transfer vectors and plasmids used in this study**. (**A**) Lentiviral transfer vectors expressing Spike proteins, HIV-1_{JR-FL} gp120, Luciferase and GFP. (**B**) Pseudotyping plasmids expressing cytoplasmic tail truncated wild-type Spike (pSpike-C3), VoC (pSpike-UKC3, pSpike-SAC3, pSpike-BRC3, pSpike-INC3, pSpike-BA1C3) and VSV.G envelope (phCMV-VSV.G). CMV, cytomegalovirus immediate-early promoter; R, repeat element; U5, 5' untranslated region; U3, 3' untranslated region; PBS, primer binding site; Ψ, packaging signal; cPPT, central polypurine tract; RRE, Rev response element; dU3, SIN deletion in U3 region of 3' LTR; WPRE, woodchuck hepatitis virus post-transcriptional regulatory element. See Methods for details on construction.



Supplementary Figure 2. **Spike expression in 293T Lenti-X transfected with Spike-expressing lentiviral transfer vector plasmids.** Cells transfected with the indicated pSpike plasmids were stained with anti-RBD neutralizing mAbs (COVA2-15, COVA1-16 and COVA1-18), one non-RBD-binding neutralzing mAb (COVA1-21), the SARS-CoV-1 neutralizing mAb CR3022, a commercial anti-S2 polyclonal antibody and secondary antibodies alone Anti-human AexaFluor-647 and Anti-rabbit PE). The number within the histogram plot indicates the % of positive cells and the mean fluorescence intensity (MFI). Shown are results from one representative of n = 3 experiments.

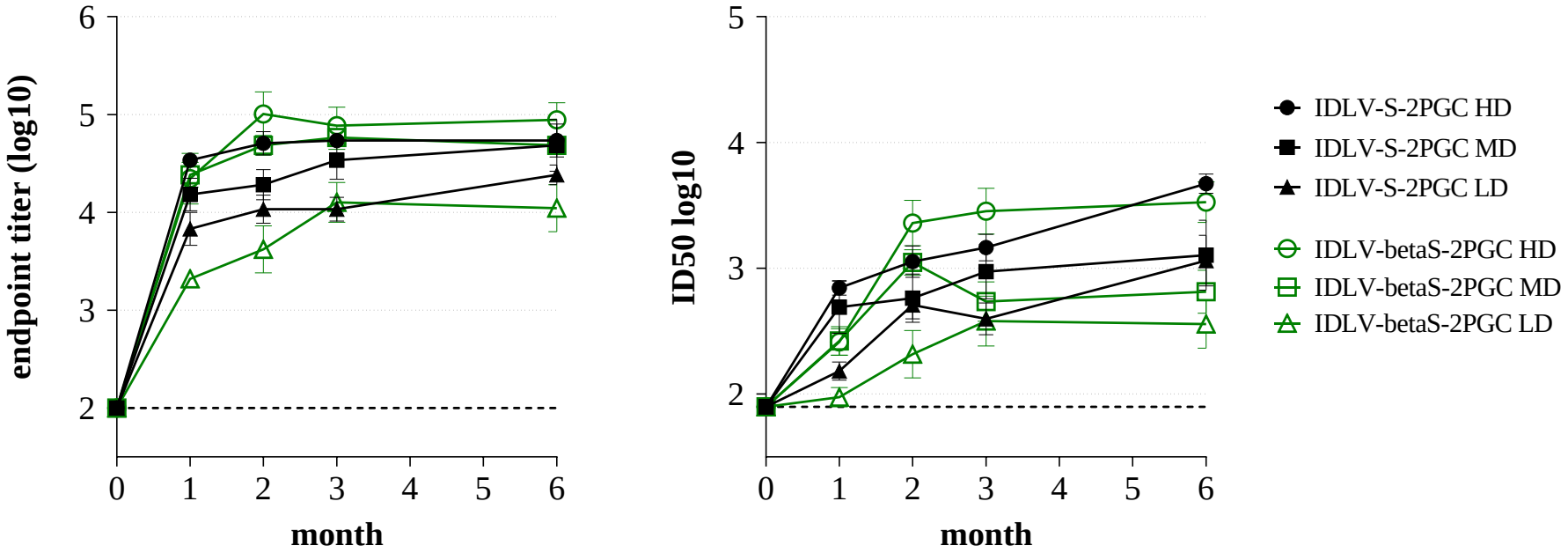


Supplementary Figure 3 . Human ACE2 expression in 293T Lenti-X cells. The identification of ACE2 positive cells was performed by using a primary mouse anti-human ACE2 antibody (Millipore, Catalog Number: MAB5676) followed by a secondary goat anti-mouse IgG-PE (SoutherBiotech; Catalog Number: 1030-09). Staining with secondary antibody only (goat anti-mouse, GAM PE) was used as negative control to set the gate of negative cells and quantify the percentage of positive cells expressing ACE2. 293T cells transfected with ACE2 expressing plasmid (phACE2 plasmid from Addgene, Cat# 1786) were used as positive control (293T-ACE2). The number within the histogram plot indicates the % of ACE2 positive cells.

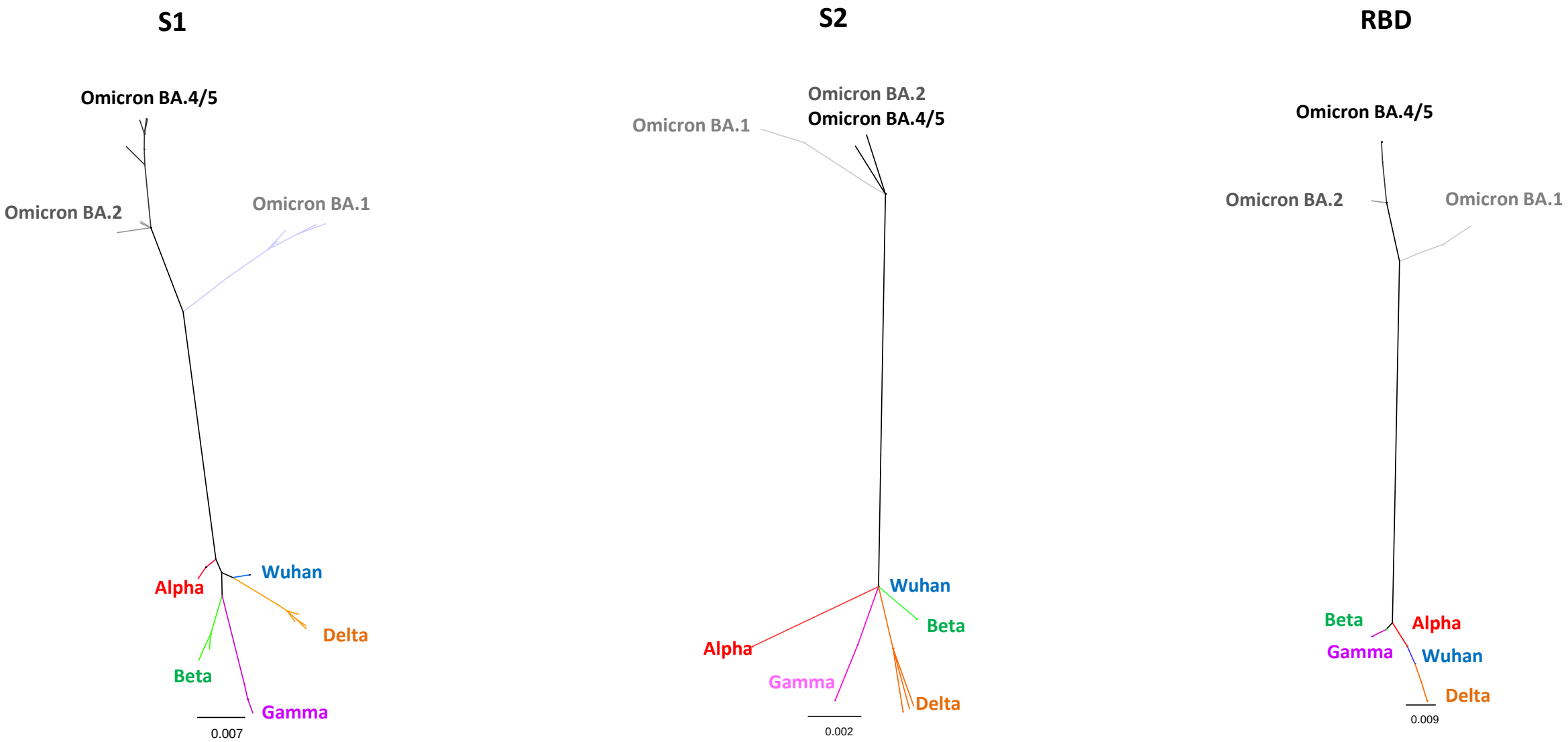


test	Spearman	Pearson
r	0,8344	0,8486
95% CI	0,6757-0,9192	0,7068-0,9249
p Value (two-tailed)	<0,0001	<0,0001

Supplementary Figure 4. Correlation between neutralization assays. Serum samples (N=31) collected from immunized animals were assayed using neutralization assays based on infectious SARS-CoV-2 (VN) and on lentiviral vector pseudotyped with Spike (LV-Luc). (**A**) Correlation between the ID50 (log10) values obtained from the two assays. Dots correspond to individual measurements; the black line represents the regression line. The table below shows the statistical analysis based on Spearman and Pearson correlation. (**B**) Comparison of ID50 (log10) values obtained using the two assays. A Wilcoxon matched-pairs signed rank test was used to compare the assays. The black line indicates the median ID50.



Supplementary Figure 5. Comparison between IDLV vaccines expressing Wuhan or Beta Spike. Kinetics of anti-RBD binding Abs (left panel) and anti-Wuhan nAbs (right panel) in mice immunized with IDLV-S-2PGC (black) and IDLV-betaS-2PGC (green).



Supplementary Figure 6. Maximum likelihood phylogenetic tree inferred from S1, S2 and RBD amino acid sequences. The ancestral SARS-CoV-2 sequence (Wuhan-Hu-1), the Alpha, Beta, Gamma, Delta and the Omicron (BA.1, BA.2, BA.4/5) variants are highlighted with different colors. The scale bar at the bottom of the tree correspond to amino acid substitutions per site.

Supplementary Table 1.
We gratefully acknowledge the authors, originating and submitting laboratories of the genetic sequences and metadata made available through GISAID on which this research is based.

GISAID EpiCoV accession(s)	Originating laboratory	Submitting laboratory	Authors
EPI_ISL_14471503	Max von Pettenkofer Institute, Virology, National Reference Center for Retroviruses, LMU Munich	Laboratory for Functional Genome Analysis; Dept. Genomics; Gene Center of the LMU Munich	Max Muenchhoff; Stefan Krebs; Alexander Graf; Oliver Keppler; Helmut Blum
EPI_ISL_14616786	Biogroup-Labo-Biolam	Laborizon Centre	Julien Baillus, Christian Chillou, Alyssia Francois, Friconnet Marion, Eve Haguenoer, Anne Holstein, Mélanie Jimenez, Karolina Modzelewska, Claire Vignault, Stephane Watt
EPI_ISL_14672772	KU Leuven, Rega Institute, Clinical and Epidemiological Virology	KU Leuven, Rega Institute, Clinical and Epidemiological Virology	Tony Wawina-Bokalanga, Anne-Sophie Logist, Bram Van Holm, Robbe Sinnesael, Jens Verlinden, Levi Ysebaert, Bert Vanmechelen, Piet Maes
EPI_ISL_15108686	Servicio de Microbiologia, Hospital Puerta del Mar, Cadiz, Spain	Clinical Bioinformatics Area, Fundación Progreso y Salud	María Lara on behalf of SARS-CoV-2 whole genome sequencing circuit of Andalusia
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EPI_ISL_13567182	Rosalind Franklin Laboratory	Wellcome Sanger Institute for the COVID-19 Genomics UK (COG-UK) Consortium	Donald Fraser, Suki Lee, Rob Howes, The Rosalind Franklin Laboratory and Alex Alderton, Roberto Amato, Jeffrey Barrett, Sonia Goncalves, Ewan Harrison, David K. Jackson, Ian Johnston, Dominic Kwiatkowski, Cordelia Langford, John Sillitoe on behalf of the Wellcome Sanger Institute COVID-19 Surveillance Team
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EPI_ISL_15141596	Biogroup Laboratoire Biorylis Saint Gilles	Laborizon Centre	Julien Baillus, Christian Chillou, Alyssia Francois, Friconnet Marion, Eve Haguenoer, Anne Holstein, Mélanie Jimenez, Karolina Modzelewska, Claire Vignault, Stephane Watt
EPI_ISL_15147441	Robert Koch-Institut ZBS1 (Zentrum für biologische Gefahren und spezielle Pathogene hochpathogene Viren)	Robert Koch Institute	Drechsel, Oliver
EPI_ISL_15153853	Lifebrain Covid Labor GmbH	Lifebrain Covid Labor GmbH	Filip Sima, Alexandra Wagner, Kristina Bavrka Kolenc, Lucia Castello, Sojung Han, Anna Edermayr
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EPI_ISL_15287572	Servicio de Microbiología. Hospital Clínico Universitario de Valencia	FISABIO_DGSP_COVIDSurveillance	David Navarro Ortega, Eliseo Albert Vicent, Ignacio Torres and Consortium for Genomic Surveillance of SARS-CoV-2 in Comunitat Valenciana
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EPI_ISL_15147701	Labor ZOTZ|KLIMAS; MVZ Düsseldorf-Centrum	Robert Koch Institute	Drechsel, Oliver
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EPI_ISL_15137335	Labor Dr. Heidrich & Kollegen MVZ GmbH Hamburg	Robert Koch Institute	Drechsel, Oliver

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EPI_ISL_7806545	MEPHI, Aix Marseille University	MEPHI, Aix Marseille University	Anthony LEVASSEUR
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EPI_ISL_14022807	Regional Virus Laboratory, Belfast Health and Social Care Trust; and: Genomics Core Technology Unit, Queen's University Belfast.	COVID-19 Genomics UK (COG-UK) Consortium	[Regional Virus Laboratory, BHSCT]: Conall McCaughey, James McKenna, Tanya Curran, Susan Feeney, Alison Watt, Ciara Cox, Mairead Connor, Zoltan Molnar, David Simpson, Derek Fairley; [Genomics Core Technology Unit, QUB]: Marc Fuchs, Clara Radulescu, Miao Tang, Arun Mahesh, Deborah Lavin, Syed Umbreen, Sarah

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EPI_ISL_2281368	Microbiology Department, Laboratori Clínic Metropolitana Nord. Hospital Universitari Germans Trias i Pujol	Can Ruti SARS-CoV-2 Sequencing Hub (HUGTiP/IrsiCaixa/IGTP)	Marc Noguera-Julian, Pilar Armengol, Ignacio Blanco, Antoni E Bordoy, Francesc Catala-Moll, Pere-Joan Cardona, Maria Casadellà, Cristina Casañ, Gemma Clara, Bonaventura Clotet, Cristina Esteban, Montserrat Giménez, Mercedes Guerrero, Anna Not, Roger Paredes, Mariona Parera, Verónica Saludes, Alba Sánchez, and Elisa Martró on behalf of the Can Ruti SARS-CoV-2 Sequencing Hub.
EPI_ISL_12655397	Pharmgenetix GmbH	Pharmgenetix GmbH	S. Vanoni, A. Matulevicius, B. Avdiu, G. Scantamburlo, C. Nofziger