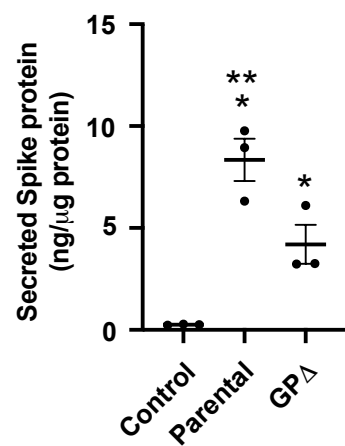


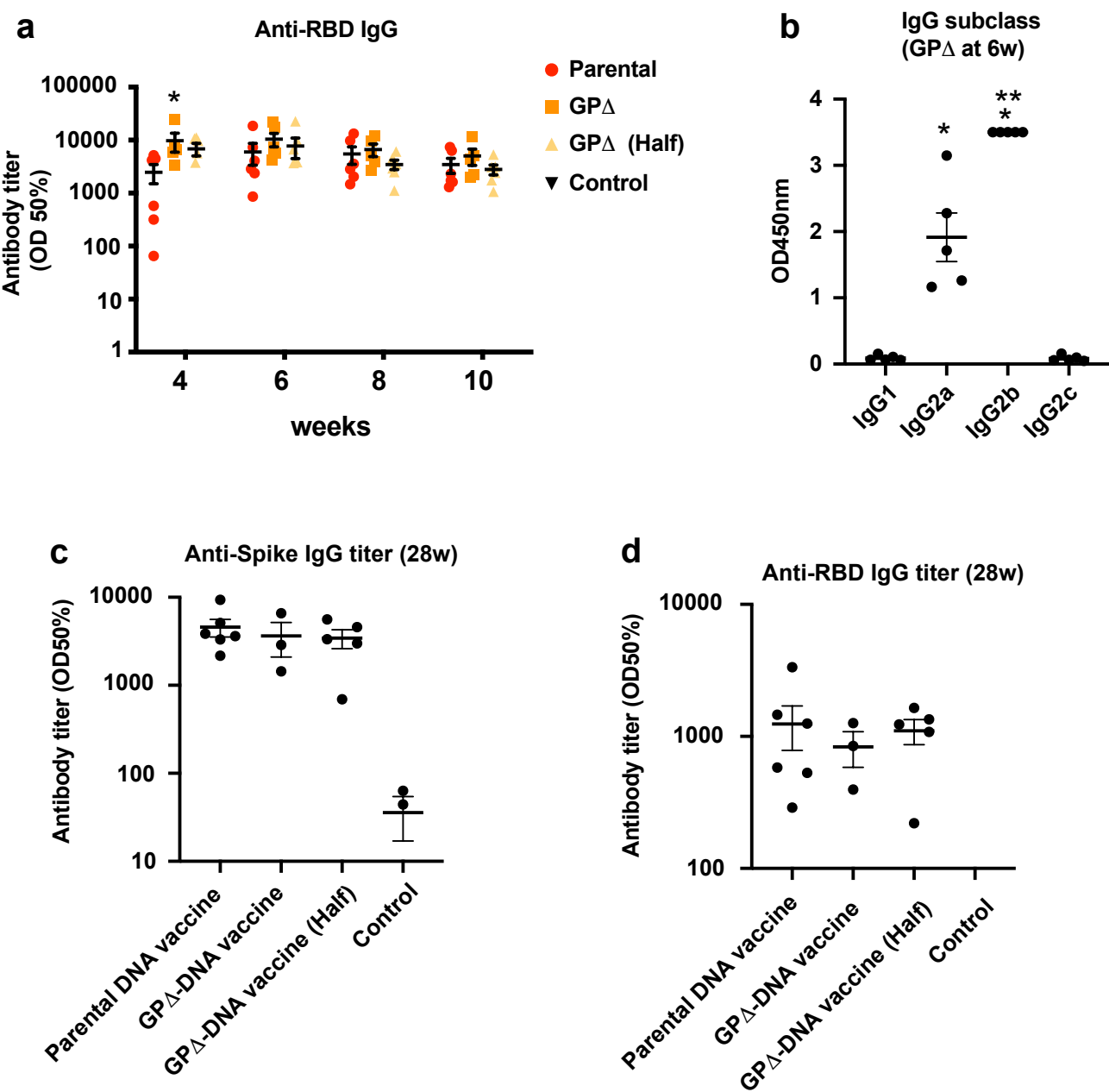
Supplementary Fig.1 Secreted spike protein from parental or GPΔ-DNA vaccine.



Supplementary Fig.1 Secreted spike protein from parental or GPΔ-DNA vaccine.

Secreted Spike protein in supernatant of HEK293 transfected with parental DNA vaccine or GPΔ-DNA vaccine. . *p<0.05 vs.Control, **p<0.05 vs.GPΔ (one-way ANOVA with Tukey’s multiple comparison test). See also Fig.1.

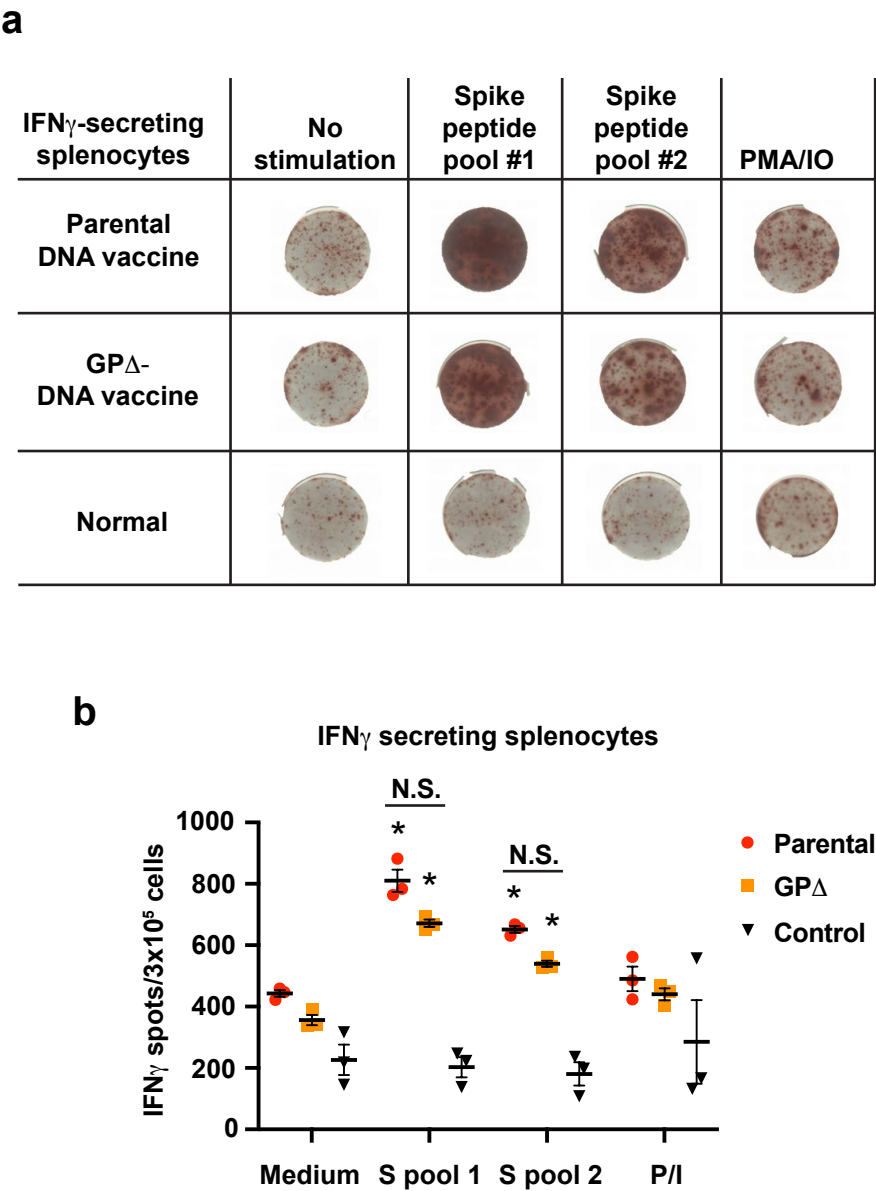
Supplementary Fig.2 GP Δ -DNA vaccine induced quick antibody production.



Supplementary Fig.2 GP Δ -DNA vaccine induced quick antibody production.

(a) anti-RBD IgG titer was measured by ELISA from 4 to 10 week after 1st dose of GP Δ -DNA vaccine. Parental DNA vaccine (666.6 μ g); Parental, GP Δ -DNA vaccine (666.6 μ g); GP Δ or half amount of GP Δ -DNA vaccine (333.3 μ g); GP Δ (Half), with alum adjuvant was intramuscularly injected into male SD rats three times at 2-week intervals. Control rats were not treated. *p<0.05 vs. Control (two-way ANOVA with Tukey's multiple comparison test). (b) IgG subclass (IgG1, IgG2a, IgG2b, and IgG2c) for spike was analyzed by ELISA. Sera collected at 6 weeks after 1st dose of GP Δ -DNA vaccine was used. *p<0.001 vs. IgG1, IgG2c, **p<0.001 vs. IgG1, IgG2a, respectively (one-way ANOVA with Tukey's multiple comparison test). (c-d) Antibody titer for spike (c) or RBD (d) was analyzed at 28 w after 1st dose of GP Δ -DNA vaccine. See also Fig.1.

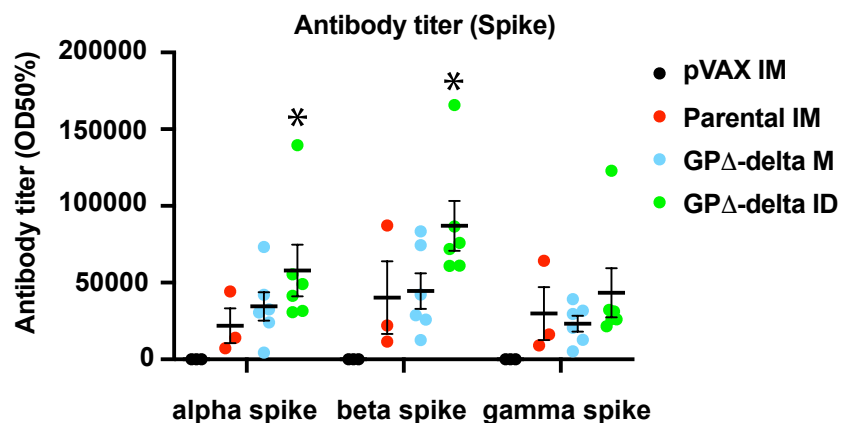
Supplementary Fig.3 GPΔ-DNA vaccine elicited SARS-CoV-2 specific cellular immune response.



Supplementary Fig.3 GPΔ-DNA vaccine elicited SARS-CoV-2 specific cellular immune response.

(a) SARS-CoV-2 spike-specific IFN γ secreting splenocytes were analyzed by ELISPOT assay. Splenocytes were collected from spleen of immunized rats at 7 weeks after three doses at 2 weeks interval. Splenocytes were stimulated with spike peptide pool for 48 h. (b) IFN γ secreting splenocytes were counted in each wells. *p<0.001, vs Control, respectively (two-way ANOVA with Tukey's multiple comparison test). N.S.: not significant between parental and GPΔ group. See also Fig.1.

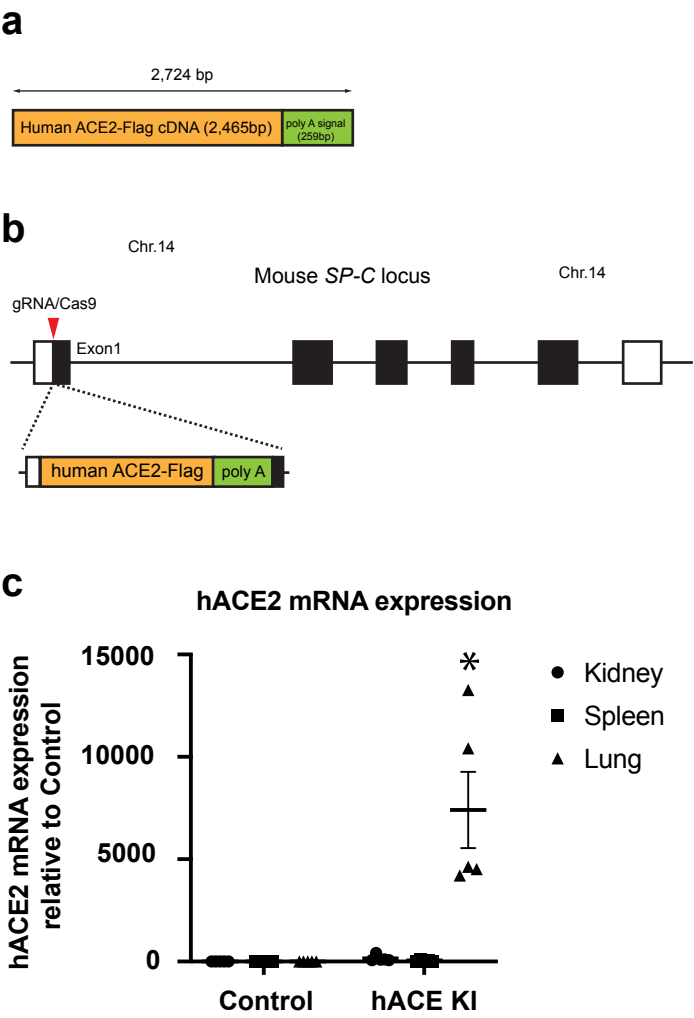
Supplementary Fig.4 Intradermal GP Δ -delta DNA vaccine induced higher antibody titer for VOCs.



Supplementary Fig.4 Intradermal GP Δ -DNA vaccine-induced antibody titer for VOCs was higher than intramuscular injection.

Antibody titer for VOCs spike (B.1.1.7; alpha, B.1.351; beta, P.1; gamma) was measured by ELISA using serum at 6 weeks. Data are shown as mean $\pm$ SEM. * $p < 0.01$ vs. pVAX IM (two-way ANOVA with Tukey's multiple comparison test). See also Fig.3.

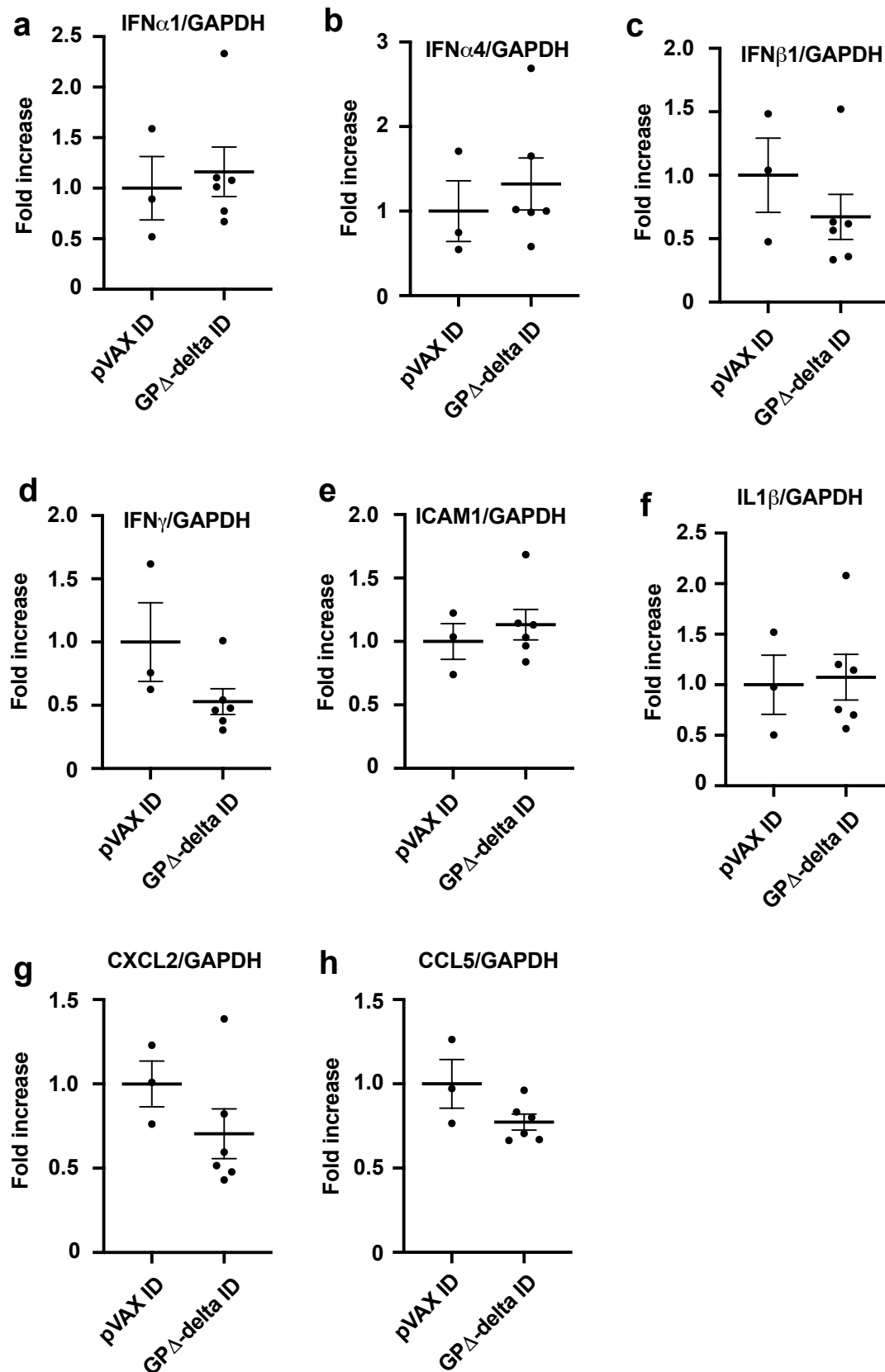
Supplementary Fig.5 Generation of mouse SP-C hACE KI mice.



Supplementary Fig.5 Generation of mouse SP-C hACE KI mice.

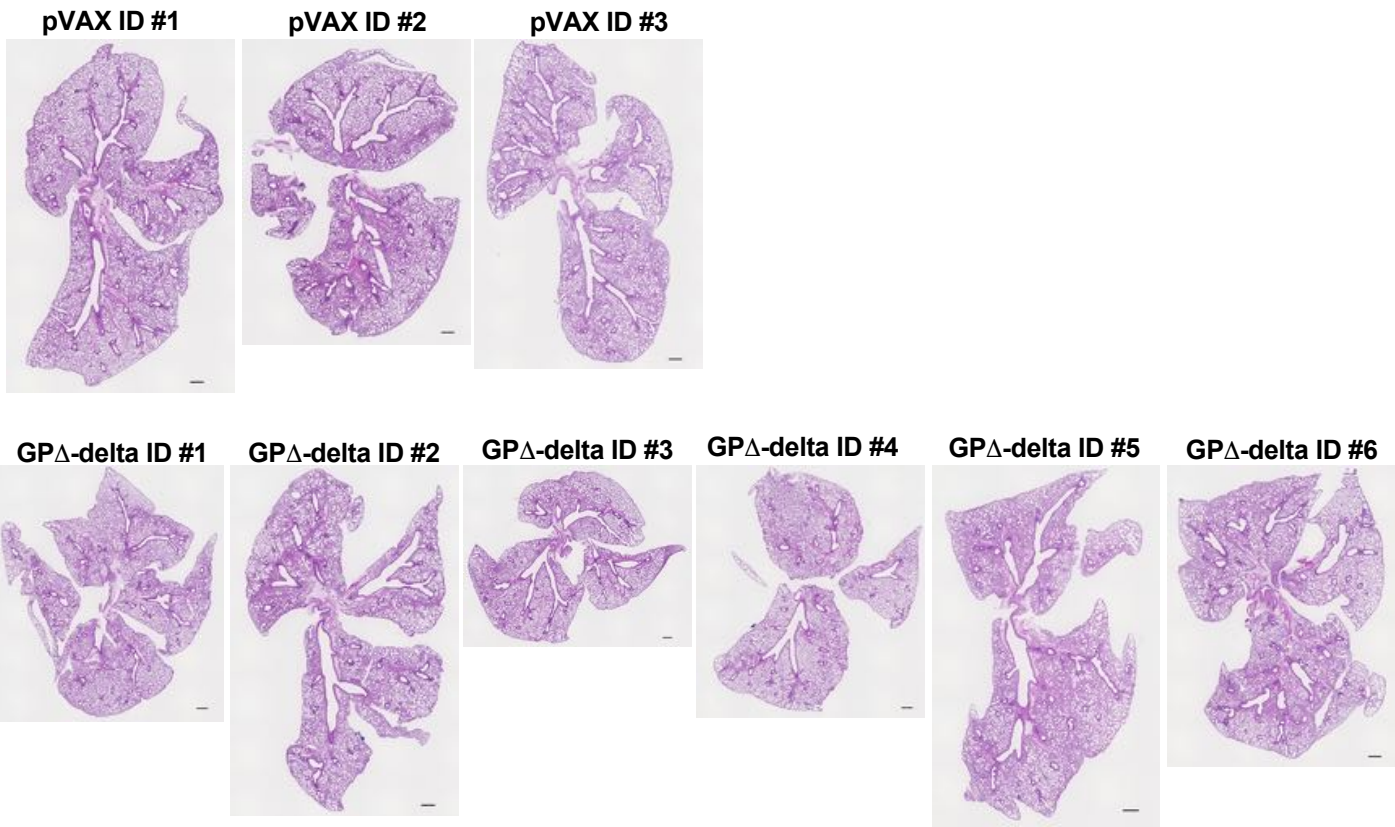
(a) Human ACE2 cDNA and bovine albumin poly A signal sequence used in this study. (b) Targeting strategy for the insertion of hACE2 in the murine *sp-c* locus. (c) Quantitative RT-PCR analysis for detection of human ACE2 mRNA expression in the indicated organs from Control (wild-type) or mouse SP-C hACE2 KI mice. * $p < 0.001$ vs. Control (two-way ANOVA with Bonferroni's multiple comparison test). See also Fig.4.

Supplementary Fig.6 The expression profile of cytokines in the lung after SARS-CoV-2 infection.



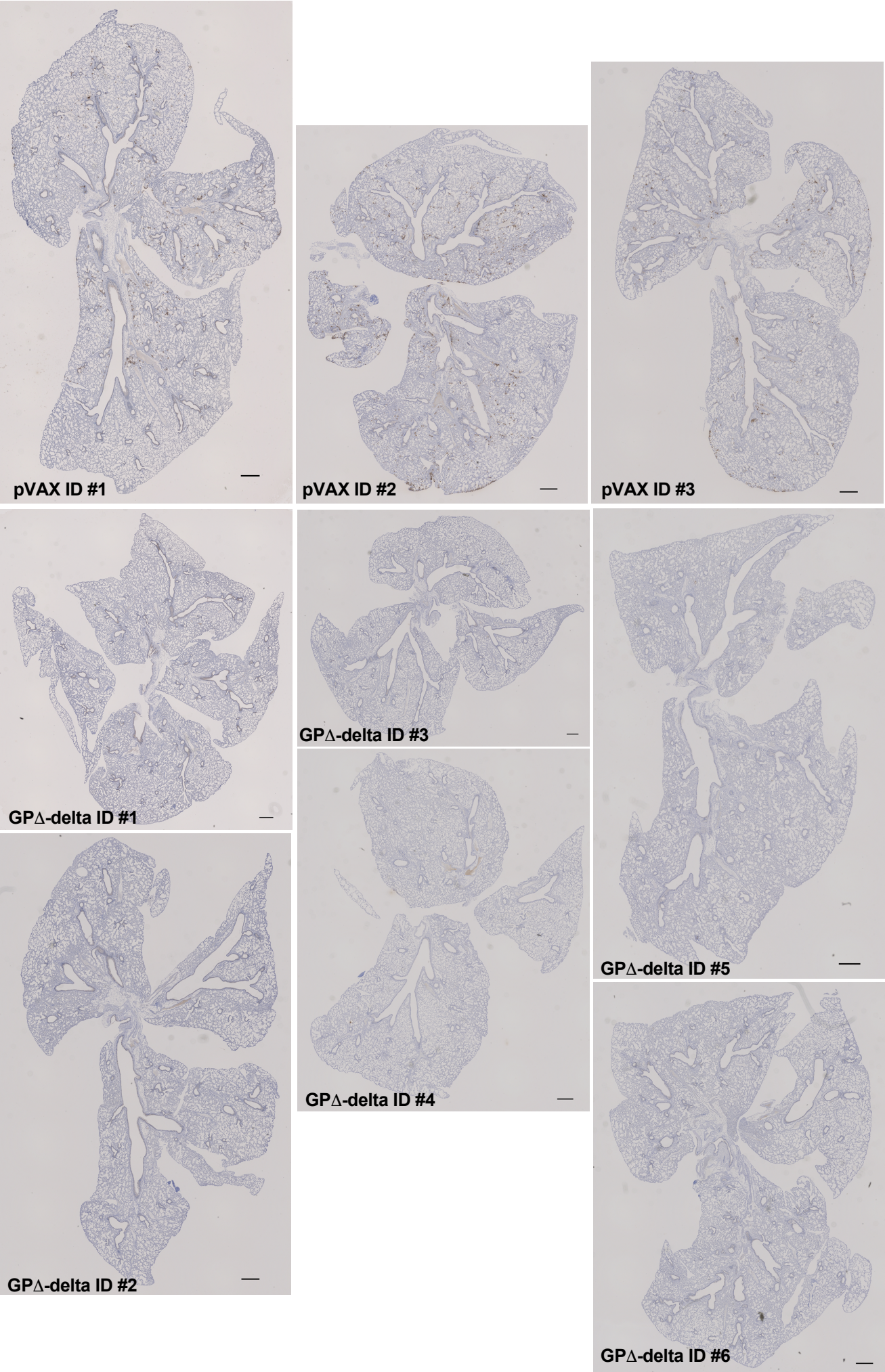
Supplementary Fig.6 The expression profile of cytokines in the lung after SARS-CoV-2 infection. The cytokines (a) IFN α , (b) IFN α 4, (c) IFN β 1, (d) IFN γ , (e) ICAM1, (f) IL1 β , (g) CXCL2, (h) CCL5 expression in the lung after SARS-CoV-2 infectino was evaluated by realtime qPCR. The value was normalized with GAPDH. See also Fig.4.

Supplementary Fig.7 Histological analysis of lung at 2 dpi.



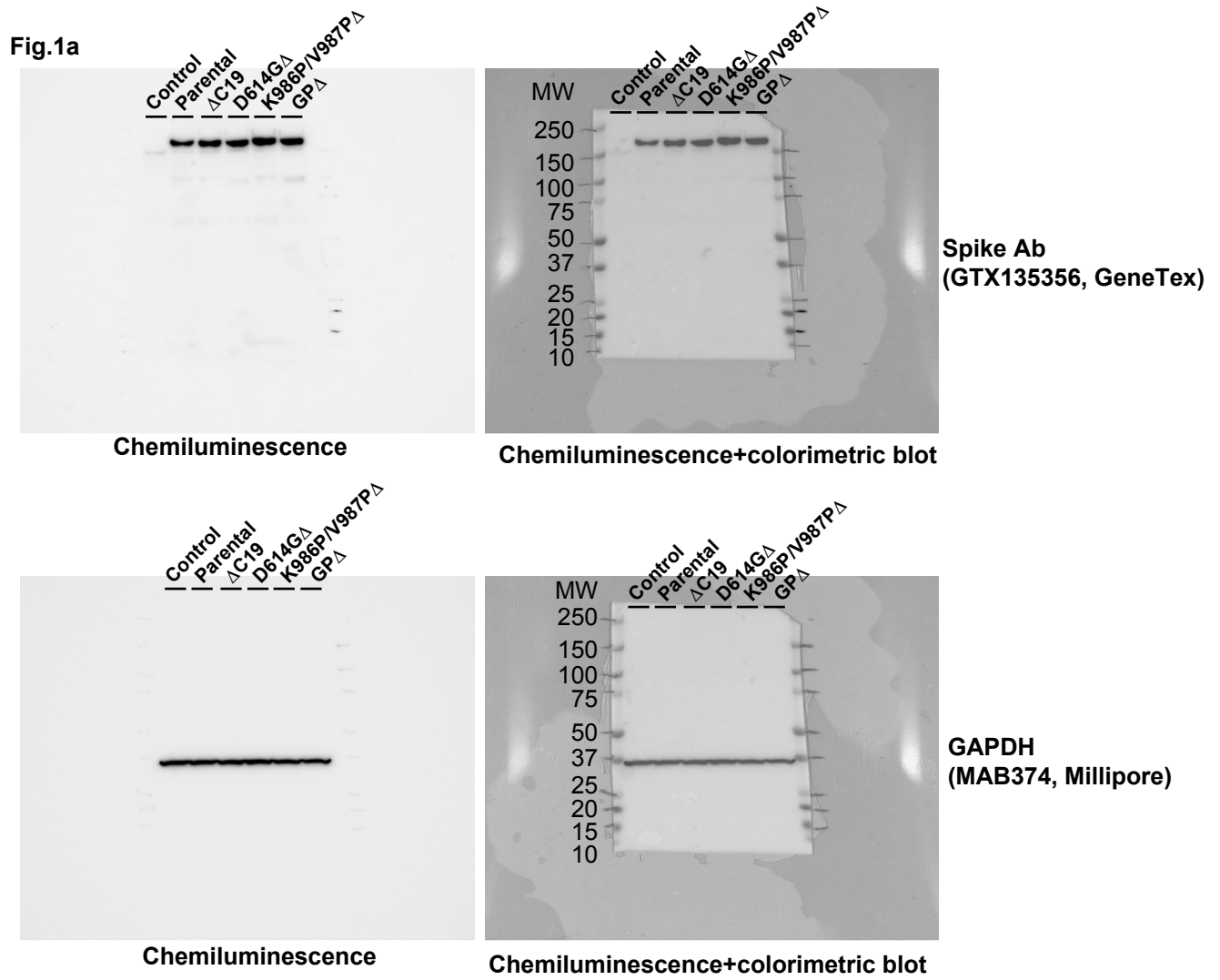
Supplementary Fig.7 Histological analysis of lung at 2 dpi.
Whole lung image of H&E staining. See also Fig.4.

Supplementary Fig.8 SARS-CoV-2 nucleoprotein expression in the lung 2 dpi.



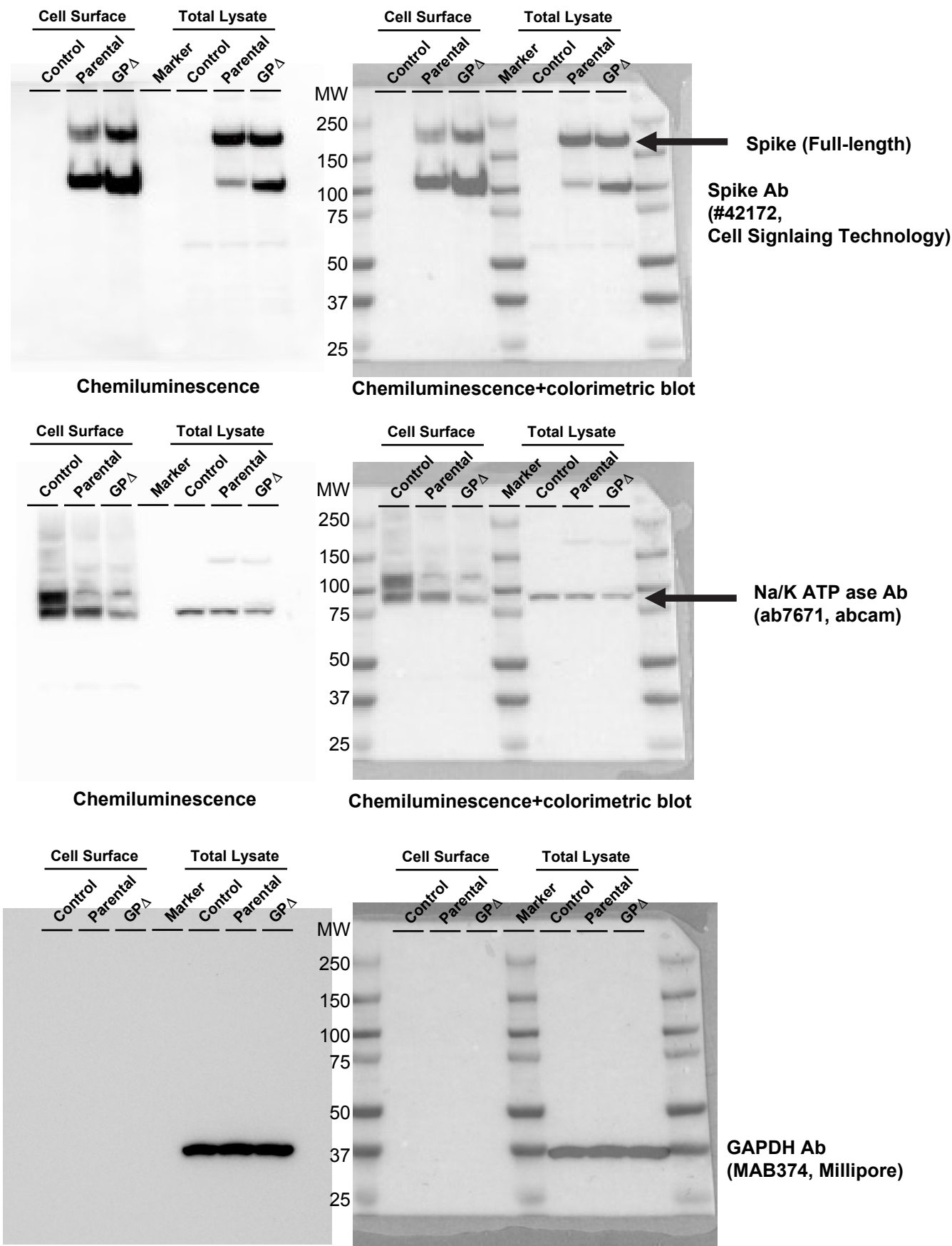
Supplementary Fig.8 SARS-CoV-2 nucleoprotein in the lung 2 dpi.
Whole lung image of SARS-CoV-2 nucleoprotein staining. See also Fig.4.

Supplementary Fig.9 Uncropped western blots related to Fig.1a.



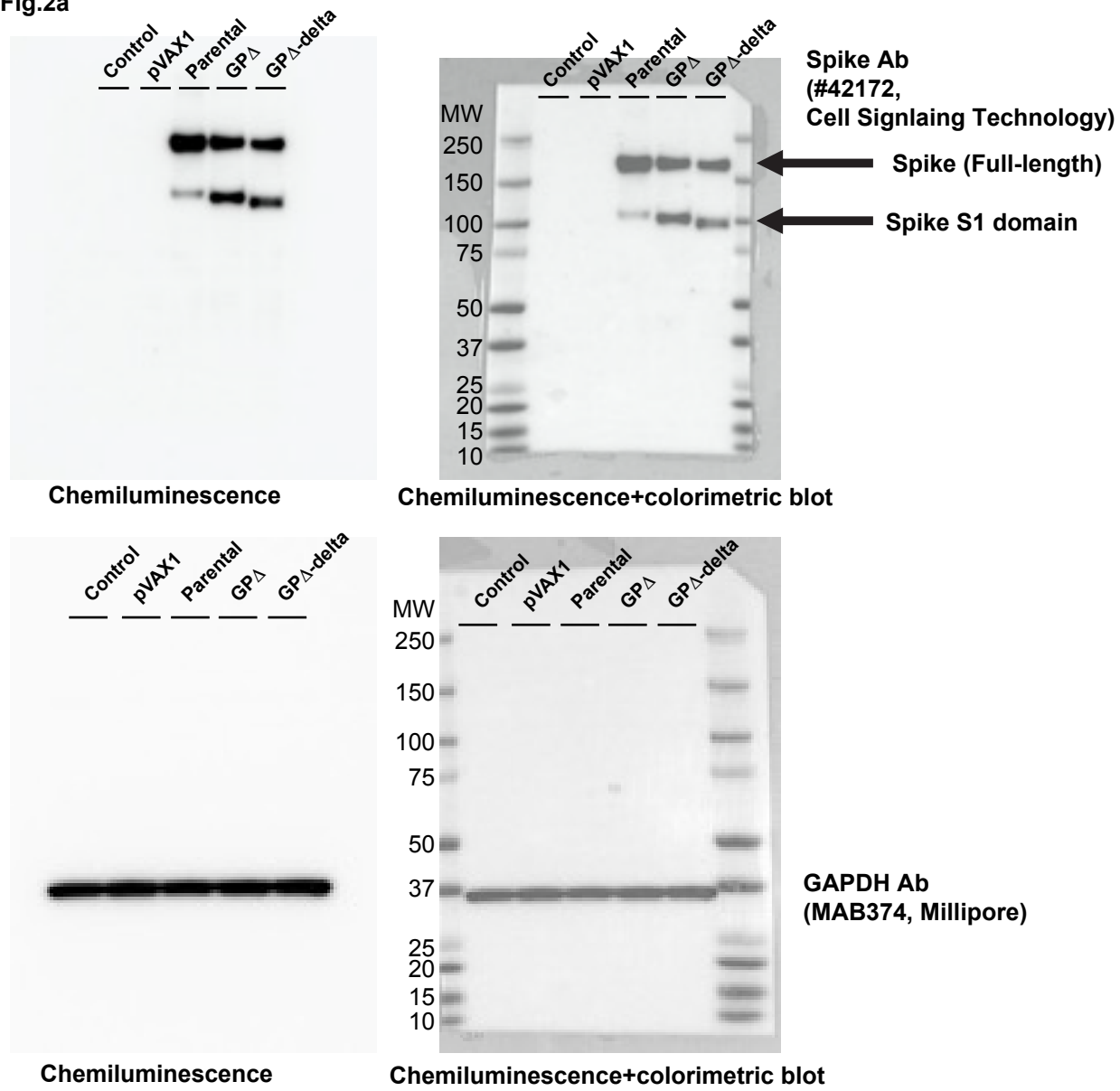
Supplementary Fig.10 Uncropped western blots related to Fig.1c.

Fig.1c



Supplementary Fig.11 Uncropped western blots related to Fig.2a.

Fig.2a



Supplementary Information

Sequences of pVAX1-SARS-CoV-2 Spike (GPA) plasmid

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Sequences of pVAX1-**SARS-CoV-2 delta Spike** (GPA) plasmid

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