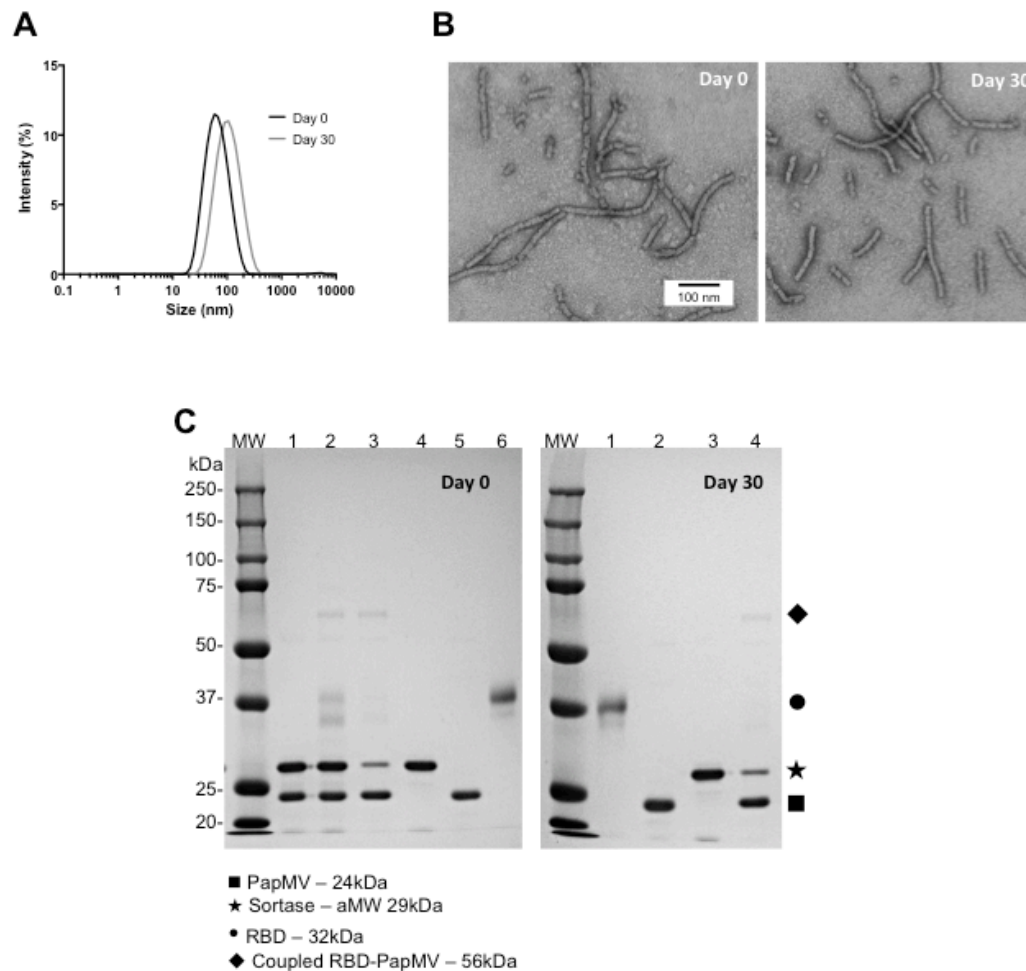
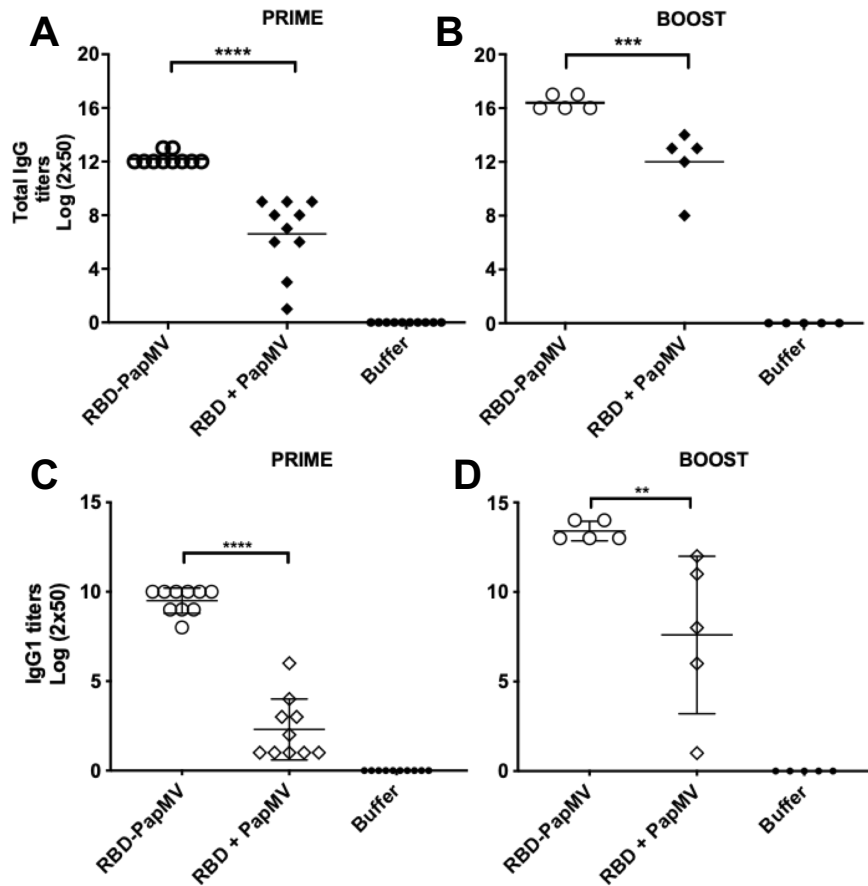


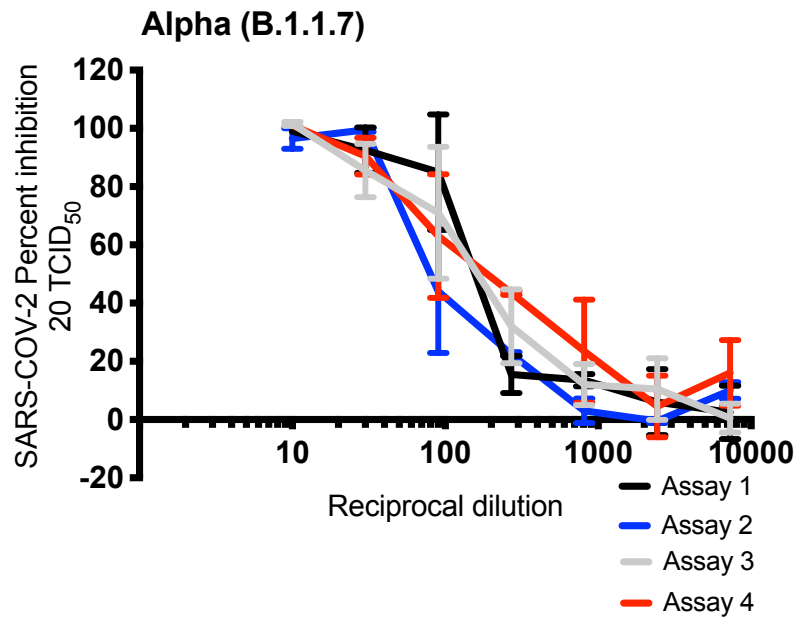
## SUPPLEMENTARY MATERIALS



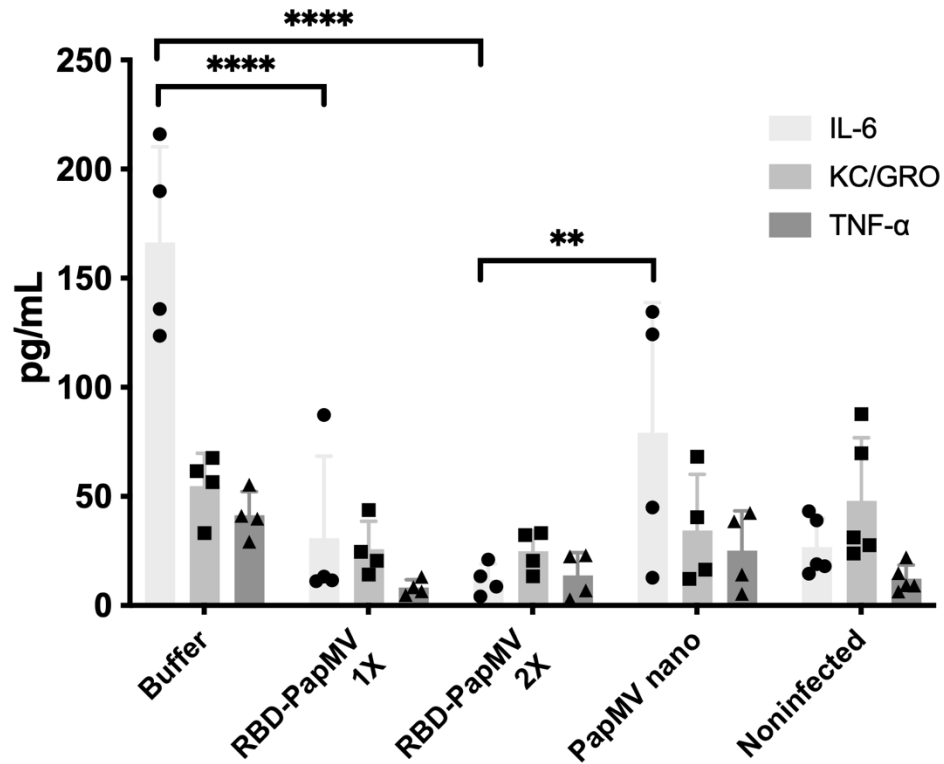
**Supplementary figure 1.** Stability of RBD-PapMV vaccine stored at 4 degrees Celsius for 30 days. The size, distribution, appearance, and coupling efficiency of RBD-PapMV batch#2 were monitored weekly for 30 days to assess the stability of the vaccine at 4 °C. A) Dynamic light scattering (DLS) shows the size and distribution of RBD-PapMV at day 0 right after production (80 nm) and 30 days after (99 nm). B) Electron micrographs of RBD-PapMV at day 0 (left) and 30 days after (right). (C) SDS-PAGE revealing the protein content of RBD-PapMV production at day 0 (Left), and RBD-PapMV after 30 days (Right). Molecular weight markers are shown to the left of each gel. Signals corresponding to the RBD-PapMV (◆ 56 kDa), the PapMV CP (■ 24 kDa), the SrtA (★ 29 kDa) and the free RBD (● 32 kDa) are shown. *Left panel*: lane 1; negative control of coupling reaction containing only PapMV nano and SrtA, lane 2; reaction containing PapMV nano, sortase A and the RBD (7% coupling efficiency), lane 3; coupling reaction after dialysis that removed free RBD and partially sortase A, lane 4; Sortase A, lane 5; PapMV CP, and lane 6; RBD. *Right panel*: lane 1; RBD, lane 2; PapMV CP, lane 3; Sortase A, lane 4; RBD-PapMV (8% coupling efficiency).



**Supplementary figure 2.** Assessment of the humoral response to the RBD-PapMV vaccine. A) Immunization schedule. Balb/C mice, five per group, were immunized twice, i.m., at day 0 and 21, with 100 $\mu$ g of the coupled RBD-PapMV (100 $\mu$ g)(RBD-PapMV), the uncoupled RBD (5.1 $\mu$ g) + PapMV (100 $\mu$ g) (RBD + PapMV) and the formulation buffer (Buffer). Bleeding occurred at day 0 and 20. At day 39, animal are sacrificed, the blood and the spleen were harvested. ELISA were performed to assess the total IgG titers to the RBD at day 20 (one immunization) (A) or day 39 (two immunizations) (B). Using the same sera, ELISA were performed to assess to assess the IgG1 titers to the RBD at day 20 (one immunization) (C) or day 39 (two immunizations) (D). \*\*p<0.01, \*\*\*p<0.001, \*\*\*\* p>0.0001.



**Supplementary figure 3.** Validation of the microneutralization assay using a commercial monoclonal antibody directed to the RBD protein. Four different assay performed with the same dilutions generated similar neutralization curve. The SARS-CoV-2 alpha (B.1.1.7) strain was used in this assay.



**Supplementary figure 4.** Assessment of the levels of IL-6, TNF- $\alpha$  and KC/Gro induced by SARS-CoV-2 infection in the lungs of infected animals. The lungs from animals presented at Fig. 6 were homogenized and used to assess the levels of the IL-6, TNF- $\alpha$  and KC/Gro a day 5 post infection. \*\*<math>p</math><math>< 0.01</math>, \*\*\*<math>p</math><math>< 0.001</math>, \*\*\*\*<math>p</math><math>< 0.0001</math>.

**Histologic technique and evaluation.** Four- $\mu$ m-thick histologic sections were obtained from formalin-fixed paraffin-embedded lung tissue stained by hematoxylin-eosin. For microphotographs, slides were digitalized at 40X magnification using a Nanozoomer slide scanner (Hamamatsu, Japan) and NDP viewer 2.0 software (Hamamatsu, Japan). Scoring of histologic parameters was performed by a pathologist (CC), blind to experimental data. A semiquantitative scale was used to score bronchial/endobronchial, peribronchial, perivascular, interstitial, pleural and intra alveolar inflammation, capillary vascular congestion and pulmonary edema.

**Table 1. Semiquantitative scoring scale of histologic parameters**

Parameter	Score			
	0	1	2	3
<b>Quality control</b>				
Tissue quality	inadequate	good	very good	excellent
<b>Inflammation intensity</b>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>
Bronchial/endobronchial	normal/absent	mild	moderate	marked
Peribronchial	normal/absent	mild	moderate	marked
Perivascular	normal/absent	mild	moderate	marked
Interstitial	normal/absent	mild	moderate	marked
Pleural	normal/absent	mild	moderate	marked
Intra alveolar	normal/absent	mild	moderate	marked
* Fractions of points allowed for very mild (0,5), mild to moderate (1,5) and moderate to marked (2,5)				
<b>Inflammatory cellular infiltrate</b>	<b>N/A</b>	<b>A</b>	<b>C</b>	<b>AC</b>
Type of cellular infiltrate	not applicable	acute (neutrophils)	chronic (lymphohistiocytic)	A and C
* Fractions of points allowed for very mild (0,5), mild to moderate (1,5) and moderate to marked (2,5)				
<b>Capillary vascular congestion</b>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>
Capillary vascular congestion	absent	mild	moderate	marked
* Fractions of points allowed for very mild (0,5), mild to moderate (1,5) and moderate to marked (2,5)				
<b>Pulmonary edema (intraalveolar)</b>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>
Pulmonary edema	absent	mild	moderate	marked
* Fractions of points allowed for very mild (0,5), mild to moderate (1,5) and moderate to marked (2,5)				

**Supplementary Table 1. Histologic scores parameters.**