Section S3: Immunohistochemical validation

Immunohistochemical staining were validated with positive and negative controls. Validated with neutralizing antibodies, a positive control lung from a vaccine study was used as positive control (Ethical approval: Date: 24.08.2020 No: 2020-4) (Alp Onen et al., 2022). As a negative control, the primary antibody was replaced with non-immune serum. Anti-SARS-CoV-2 Spike Glycoprotein antibody (ab275759, ABCAM, Cambridge, UK) at 1:500 dilution was used as the primary antibody.

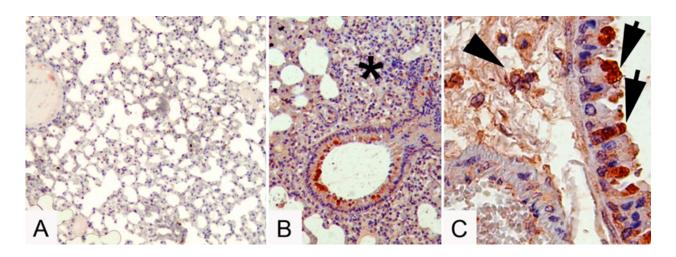


Fig. S3-1. IHC validation. The results of positive and negative control immunostaining of the lungs from Balb/c mice that were either vaccinated or infected with SARS-CoV-2. A. Besides the mild damage caused by the inactivated virus vaccine, the bronchioles and alveoli were negative for SARS-CoV-2. B&C. In SARS-CoV-2 infected mice had interstitial pneumonitis (asterisk), and bronchiolar exocrine cells and stromal cells were positive for SARS-CoV-2. A 4x, B 10x, and C 40x magnification.

REFERENCES

- Alp Onen, E., Sonmez, K., Yildirim, F., Demirci, E. K., & Gurel, A. Development, analysis, and preclinical evaluation of inactivated vaccine candidate for prevention of Covid-19 disease. *All Life*. 15(1), 771-793, 2022.
- Hübner, R. H., Gitter, W., El Mokhtari, N. E., Mathiak, M., Both, M., Bolte, H., Freitag-Wolf, S., & Bewig, B. Standardized quantification of pulmonary fibrosis in histological samples. *Biotechniques*. 44(4), 507-511, 514-507, 2008.
- Moreau, G. B., Burgess, S. L., Sturek, J. M., Donlan, A. N., Petri, W. A., & Mann, B. J. Evaluation of K18hACE2 Mice as a Model of SARS-CoV-2 Infection. *Am J Trop Med Hyg. 103*(3), 1215-1219, 2020.
- van Griensven, M., Dahlweid, F. M., Giannoudis, P. V., Wittwer, T., Böttcher, F., Breddin, M., & Pape, H. C.
 Dehydroepiandrosterone (DHEA) modulates the activity and the expression of lymphocyte subpopulations induced by cecal ligation and puncture. *Shock*. 18(5), 445-449, 2002.