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## Supplemental information

## Reduced pathogenicity of the SARS-CoV-2

## omicron variant in hamsters

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Figure S1. Vascular, pulmonary, and nasal turbinate pathology in hamsters on day 4 following SARS-CoV-2 infection. Related to Figure 1. Lung tissue from hamsters infected with SARS-CoV-2 WA1/2020 and Omicron variants was stained with H&E. Vascular inflammatory infiltrates and endothelialitis of small and medium sized arteries were observed in both WA1/2020 and Omicron infected hamsters but reduced in Omicron infected hamsters. (A) Pulmonary arteries show vascular margination of inflammatory infiltrates and endothelialitis in Omicron variant infected hamsters.

**(B)** Similar but decreased pathology observed at the 1:100 dilution challenge dose of the Omicron variant.

(C, D) Similar vascular endothelialitis in WA1/2020 SARS-CoV-2 infected hamsters.

(E-H) Macrophage infiltrates in lungs of Omicron infected hamsters. Immunohistochemistry for Iba-1 (macrophages) in Omicron (E, F) and WA1/2020 (G, H) infected hamsters 4 days following challenge.

(I-K) Nasal turbinate pathology in SARS-CoV-2 Omicron infected hamsters.

(I) H&E and SARS-N immunohistochemistry from hamsters infected with WA1/2020 (upper) or Omicron (middle), as compared to uninfected hamsters (lower). Significant degeneration and necrosis of ciliated epithelium with the presence of intraepithelial neutrophils and degenerative and karyorrhectic debris adhered along regions of epithelial loss and attenuation, and SARS-N positivity (brown) is observed in both WA1/2020 and Omicron infections.

(J) Semi-quantitative scoring of nasal turbinate pathology and (K) SARS-N (brown) positivity in WA1/2020 and Omicron infected hamsters at 4 days following challenge: Scores= 0 none seen; 1 mild; 2 moderate; 3 severe.