Supplementary Information for:

A single dose of recombinant VSV-ΔG-spike vaccine provides protection against SARS-CoV-2 challenge

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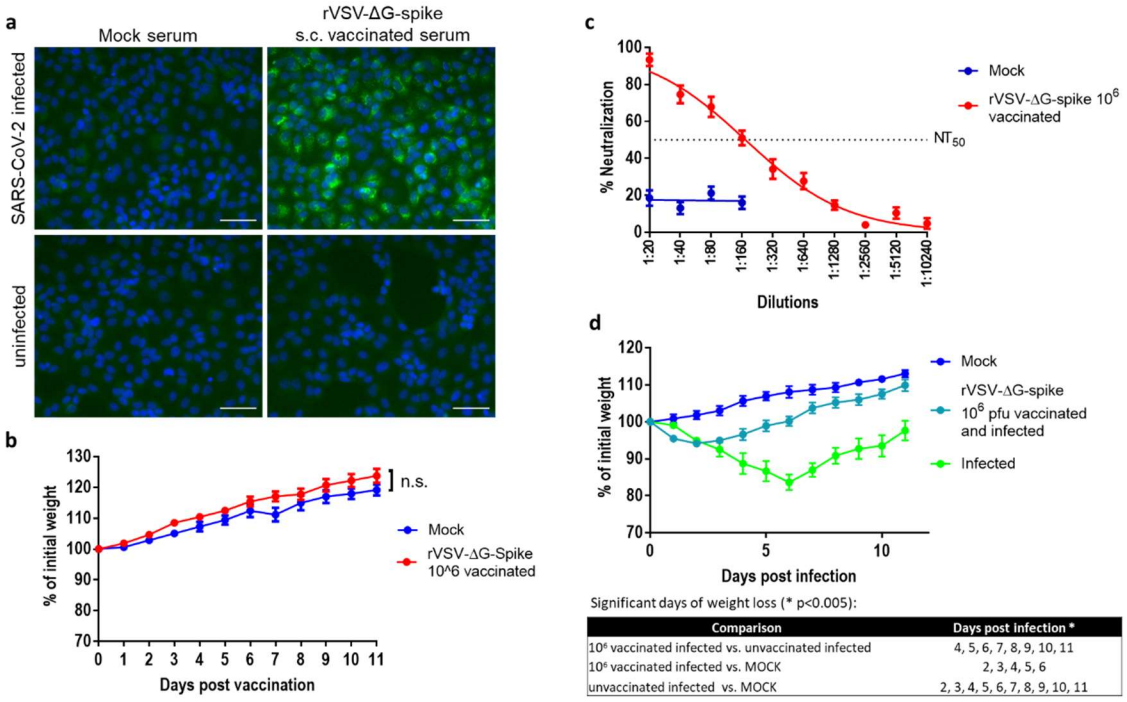
Supplementary Figure 1:

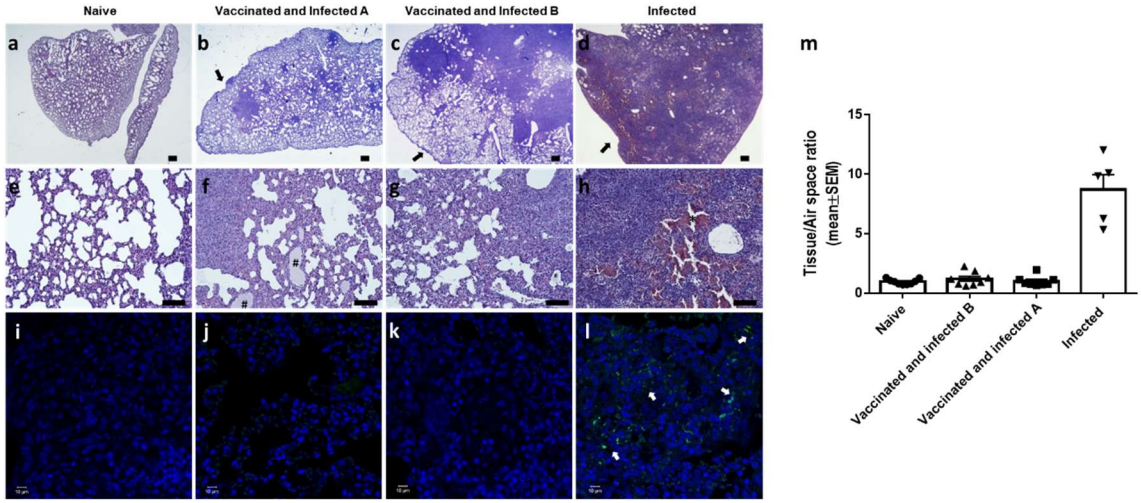


Significant days of weight loss (* p<0.005):

Comparison	Days post infection *
10^6 vaccinated infected vs. unvaccinated infected	4, 5, 6, 7, 8, 9, 10, 11
10^6 vaccinated infected vs. MOCK	2, 3, 4, 5, 6
unvaccinated infected vs. MOCK	2, 3, 4, 5, 6, 7, 8, 9, 10, 11

Supplementary Figure 1. A single-dose s.c. rVSV-ΔG-spike vaccine safety and efficacy in hamsters following SARS-CoV-2 challenge. a Immunofluorescent images of Vero E6 cells infected with SARS-CoV-2, stained with sera from either mock-vaccinated hamsters (left panel) or rVSV-ΔG-spike vaccinated-hamsters (right panel). Representative images of three experiments are presented. Scale bars: 50 µm. **b** Body weight changes of naïve hamsters (Mock, n=4; these animals also served as the Mock group in Fig. 4a), and hamsters vaccinated s.c. with rVSV-ΔG-spike (n=16 in days 0-7, n=12 in days 8-12). Statistical analysis was performed using two-tailed one unpaired t-test per row with correction for multiple comparisons using Holm-Sidak method. No statistical difference was observed (n.s.). **c** PRNT of hamster sera collected from mock-vaccinated hamsters (n=5) or hamsters vaccinated s.c. with rVSV-ΔG-spike (n=5). **d** Body weight changes of hamsters infected with SARS-CoV-2 (n=4), and hamsters vaccinated and infected with SARS-CoV-2 ($5x10^6$ pfu/hamster, n=14) 25 days post-vaccination, compared to mock hamsters (n=4). Three hamsters from vaccinated and infected group, and one hamster from infected group, were sacrificed at 5dpi for additional analyses. Statistical significance was determined by two-tailed one unpaired t-test per row, with correction for multiple comparisons using Holm-Sidak method. * p<0.005. Data for (**b**, **c**, **d**) are presented as mean values ± SEM. Source data are provided as a Source Data file.

Supplementary Figure 2:



Supplementary Figure 2. Histopathological analysis of SARS-CoV-2 infected lungs following s.c. rVSV-ΔG-spike vaccination. General histology (H&E) and SARS-CoV-2 Immunolabeling of naïve, unvaccinated infected ($5x10^6$), and vaccinated and infected (10^6 pfu) hamsters' lungs. Lungs were isolated and processed for paraffin embedding from naïve (**a**, **e**, **i**), vaccinated and infected (**b**, **f**, **j**, **c**, **g**, **k**), and infected ($5x10^6$ pfu) (**d**, **h**, **l**) 5 dpi. Sections (5 µm) were taken for H&E staining (**a**-**h**) and SARS-CoV-2 immunolabeling (**i**-**l**, DAPI-Blue, SARS-CoV-2-Green). Images **a**-**d**: bar= 100µm; images **e**-**h**: bar= 100µm; images **i**-**l**: bar= 10µm. Black arrows indicate patches of focal inflammation, pleural invagination and alveolar collapse. "*"- indicates hemorrhagic areas. "#"- indicates edema and protein rich exudates. Black arrow heads indicate pulmonary mononuclear cells. White arrows indicate SARS-CoV-2 positive staining. **m** Tissue/Air space ratio. Each column represents one hamster. The data were analyzed from at least 5ROIs per animal, and is presented in bars as mean ± SEM. Naïve group: n=1, vaccinated and infected: n=2, infected: n=1. Source data are provided as a Source Data file.