

**Supplementary Figure 1:** K18-hACE2 mice were vaccinated via intra-nasal (vac i.n.) with the nasal vaccine formulation on days 0 and 7. Non-vaccinated mice (non-vac) received only PBS. Mice were infected intra-nasally with Wuhan strain (A, B, D, E) or Omicron strain (C) of SARS-CoV-2, 21 days after the first dose. **(A)** mRNA was isolated from the lungs and SARS-CoV-2 was quantitated by real-time PCR measuring spike protein gene copy number at four days after viral infection, DPI-6; **(B)** Concentration of Spike (S)-specific IgA in broncho-alveolar lavage (BAL) measured by ELISA at two and four days after viral infection, DPI2 and DPI-4 respectively; **(C)** mRNA was isolated from the lungs and SARS-CoV-2 was quantitated by real-time PCR measuring spike protein gene copy number four days after viral infection ((DPI-4) **(D - E)** RT-qPCR relative quantification of IL-1b, IL-6, TNFa mRNA contente four days after viral infection (DPI-4); in the olfactory bulb **(D)** and in the hippocampus **(E)**. Each symbol represents one biological replicate (animal). One-way ANOVA was performed in A-D. Error bars indicate SE; \* *p* < 0.05, \*\* *p* < 0.01, \*\*\* *p* < 0.001