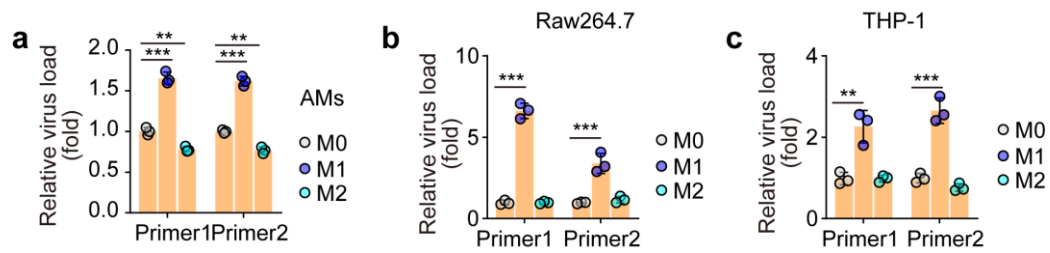


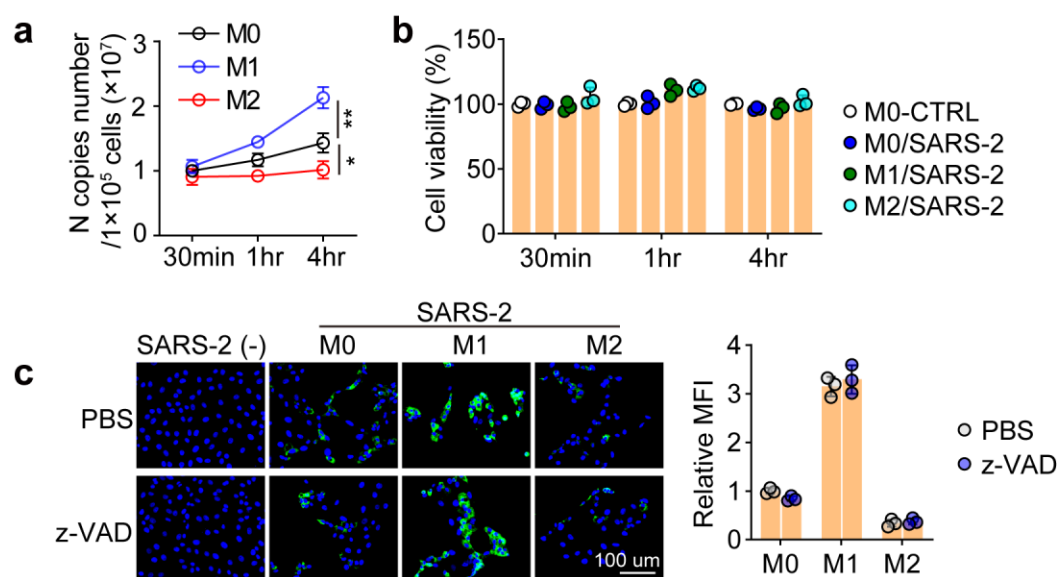
Supplementary figure legends

Figure S1



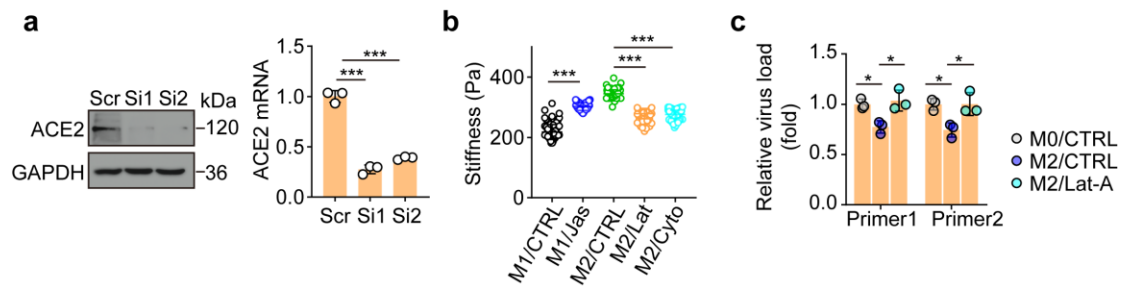
Supplementary Fig. S1 M1 macrophages facilitate SARS-CoV-2 infection. a, b Primary alveolar macrophages (AMs) or Raw264.7 were polarized to M1 by IFN- γ (20 ng/ml) and LPS (100 ng/ml) or M2 by IL-4 (20 ng/ml) for 24 hr, and then infected with SARS-CoV-2 at the ratio of 1:1 (TCID₅₀: cells) for 2 hr. The viral load was analyzed by real-time PCR with specific primers 1 and 2. **c** The same as (**a, b**), except that THP-1 were pretreated with PMA (100 ng/ml) for 48 hr. The data represent mean $\pm$ SD of 3 independent experiments. ** p < 0.01, *** p < 0.001, by one-way ANOVA (**a-c**).

Figure S2



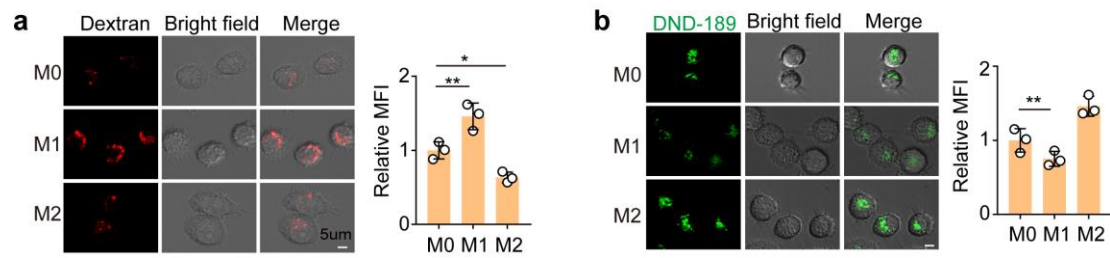
Supplementary Fig. S2 M1 AMs enable SARS-CoV-2 replication. **a, b** M0, M1 and M2 AMs were infected with SARS-CoV-2 for 30 min. Then, the viruses were removed and the cells were cultured with virus-free medium for another 30 min, 1 hr or 4 hr. The viral load was analyzed by real-time PCR (**a**). Cell viability was measured by a microplate luminometer (**b**). The M0 AMs without SARS-CoV-2 infection served as a control (M0-CTRL). **c** M0, M1 and M2 AMs pretreated with z-VAD-FMK (50 μ M) for 2 hr were infected with SARS-CoV-2 for 4 hr. The supernatants were collected to infect Vero E6 cells for 48 hr. Cells were stained with anti-NP antibody and observed by confocal microscopy (**c**). Scale bar, 100 μ m. The data represent mean $\pm$ SD of 3 independent experiments. * $p < 0.05$, ** $p < 0.01$, by one-way ANOVA (**a**).

Figure S3



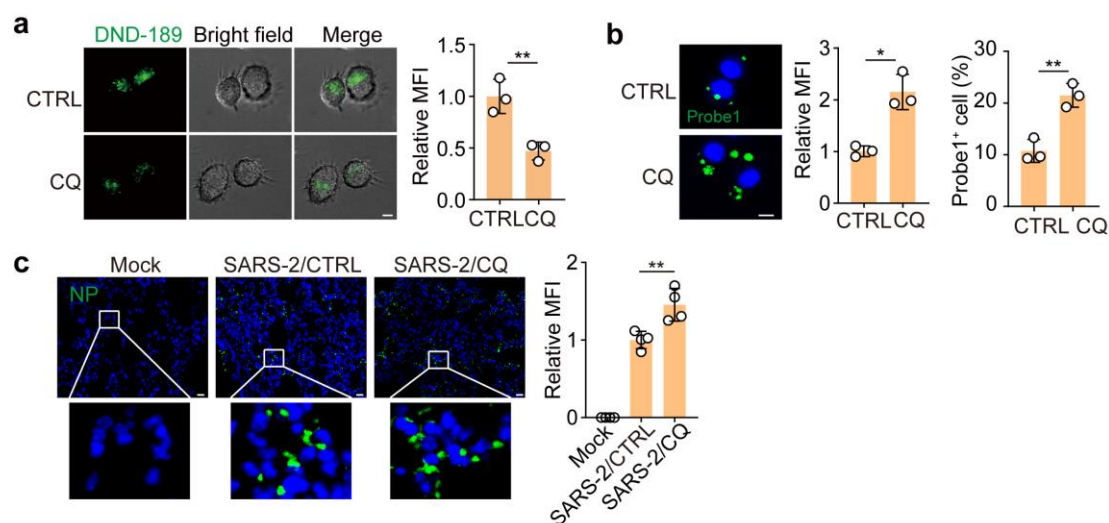
Supplementary Fig. S3 The stiffness of macrophages affected the uptake of viruses. **a** AMs isolated from hACE2 transgenic mice were transfected with scrambled or ACE2-siRNAs. The knockdown efficiency of ACE2 was evaluated by western blotting (left) and real-time PCR (right). **b** M1 or M2 AMs were treated with control vehicle (DMSO), jasplakinolide (Jas, 50 nM) for 12 hr, latrunculin A (Lat, 2 μ M) for 12 hr or cytochalasin D (Cyto, 1 μ M) for 4 hr. Cellular stiffness was detected by atomic force microscopy (AFM). **c** M2 AMs pretreated with Lat (2 μ M) for 12 hr were infected with SARS-CoV-2 for 2 hr. The viral load was analyzed by real-time PCR. The data represent mean $\pm$ SD of 3 independent experiments. * $p < 0.05$, *** $p < 0.001$, by one-way ANOVA (**a,c**) or Kruskal-Wallis test (**b**).

Figure S4



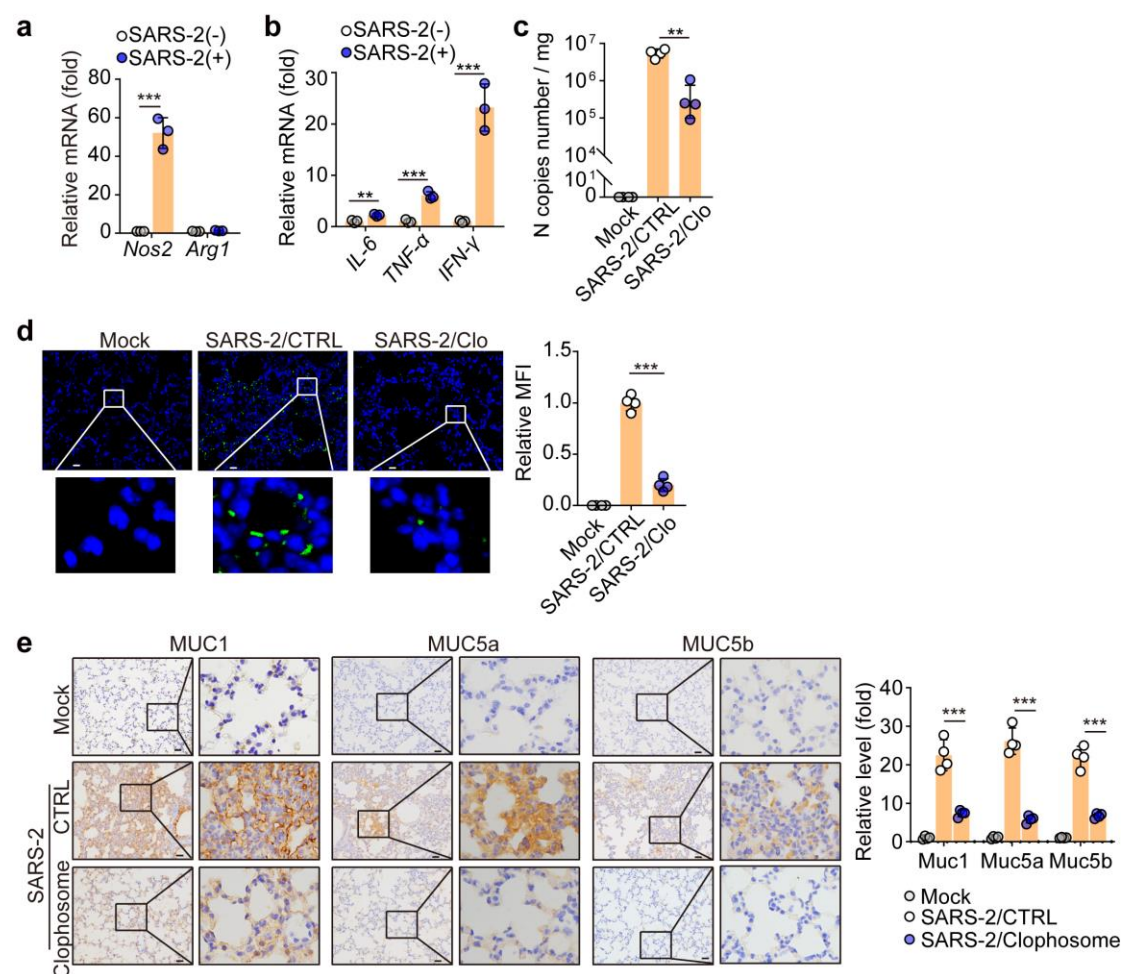
Supplementary Fig. S4 M0, M1 and M2 AMs showed different pH values in endosomes or lysosomes. a M0, M1 and M2 AMs were stained with pHrodo™ Red dextran (50 μg/ml) for 10 min at 37°C and observed by a confocal microscope. Scale bar, 5 μm. **b** The same as (a), except that cells were stained with LysoSensor™ Green DND-189 (5 μM) for 30 min at 37°C. Scale bar, 5 μm. The data represent mean ± SD of 3 independent experiments. * p<0.05, *** p<0.001, by one-way ANOVA (a, b).

Figure S5



Supplementary Fig. S5 CQ enhanced SARS-CoV-2 infection *in vivo*. **a** AMs pretreated with CQ (10 μ M) for 24 hr were stained with LysoSensor™ Green DND-189 and observed by confocal microscopy. Scale bar, 5 μ m. **b** M0 AMs pretreated with CQ (10 μ M) for 24 hr were infected with SARS-CoV-2 for 30min. Cells were fixed for RNAscope with specific Probe 1, which targets the positive-sense sequence. Scale bar, 5 μ m. **c** hACE2-transgenic mice were infected with SARS-CoV-2, and then treated with or without CQ (35 mg/kg, i.p.) once every day for 5 days. The lung tissues were fixed to perform the immunohistochemical staining of NP (n = 4 mice). The data represent mean $\pm$ SD. In **a** and **b**, n = 3 independent experiments. * p<0.05, ** p<0.01, by two-tailed student's t-test (**a**, **b**) or one-way ANOVA (**c**).

Figure S6



Supplementary Fig. S6 Macrophage depletion reduced the infection of SARS-CoV-2 and the production of mucins *in vivo*. **a-b** M0 AMs were infected with SARS-CoV-2 for 24 hr. The expression of *Nos2*, *Arg1* (**a**), *IL-6*, *TNF-α* or *IFN-γ* (**b**) was determined by real-time PCR. **c-e** hACE2-transgenic mice were infected with SARS-CoV-2, and then treated with a control liposome or clophosome-A (both i.v. 100 μl and nasally 50 μl). The lung tissues were used to perform the real-time PCR (**c**, n=4 mice), the immunohistochemical staining of NP (**d**, n = 4 mice) or mucins 1, 5a and 5b (**e**, n = 4 mice). The data represent mean ± SD. In **a**, **b** n = 3 independent experiments. * p<0.05, ** p<0.01, by two-tailed student's t-test (**a**, **b**) or one-way ANOVA (**c**, **d**, **e**).