

## Supplementary Material



**Supplementary Figure 1.** Morphological evaluation of BAL samples. (A) Two neutrophils in the cytological smear; OM 100x. (B) Cell block characterized by macrophages, epithelial cells, neutrophils and cellular/nuclear debris; H&E OM 40x. (C) Histological evaluation of lung tissue with macrophages, epithelial cells, neutrophils and cellular/nuclear debris in alveolar spaces; H&E OM 40x.



**Supplementary Figure 2.** Confocal images of neutrophils activated or not towards NETosis. (A-I) Neutrophils isolated from peripheral blood of healthy donors without any treatment or (J-S) treated with 100 nM of PMA for 4 h. All samples were then labeled with (B,K) anti-H3 or (E,N) anti-HNE or (H,R) anti-MPO Ab (red signal). (A,D,G,J,M,P) DAPI (blue signal) was used to label DNA. (C,F,I,L,O,S). Images of merged channels. Scale bar = 50  $\mu$ m.



**Supplementary Figure 3.** (A) Representative optical images of A549 incubated with TGF- $\beta$ , 2.5 x 10<sup>6</sup> PMA-Neu and pure NETs isolated from 2.5 x 10<sup>6</sup> PMA-Neu. Images were acquired with a 40X magnification. (B) Quantification of immunoblots and RT-PCR analysis of A549 treated with TGF- $\beta$  for 24 h. (C) Cell death analysis of A549 incubated with 100 nM PMA, 2.5 x 10<sup>6</sup> PMA-Neu or NETs (24 h) was evaluated by flow cytometry labeling A549 with PI before the acquisition. Data are represented as mean  $\pm$  SD of three independent replicates. \*\*\*, p<0.001 vs. CTR; \*, p<0.05 vs. CTR.



**Supplementary Figure 4.** (A) IL8 and (B) IL1 $\beta$  quantification in culture media of A549 *in vitro* airway model by ELISA assay. (C) free-DNA quantified in culture media of A549 *in vitro* airway model. Data are represented as mean  $\pm$  SD. \*\*\*, p<0.001 vs. CTR; ^, p<0.001 vs. SARS-CoV2.



**Supplementary Figure 5.** (A) Representative immunoblots of 16HBE incubated with SARS-CoV2, AM+SARS-CoV2, Neu+SARS-CoV2, or Neu+AM+SARS-CoV2 for 48 h. (B) Quantification of immunoblots and RT-PCR analysis after 48 h of treatment. (C) CitH3 quantification in cell culture medium of *in vitro* model. (D) TGF- $\beta$  quantified in culture media of 16HBE *in vitro* airway model. Data are represented as mean  $\pm$  SD. \*\*\*, p<0.001 vs. CTR; \*, p<0.05 vs. CTR.