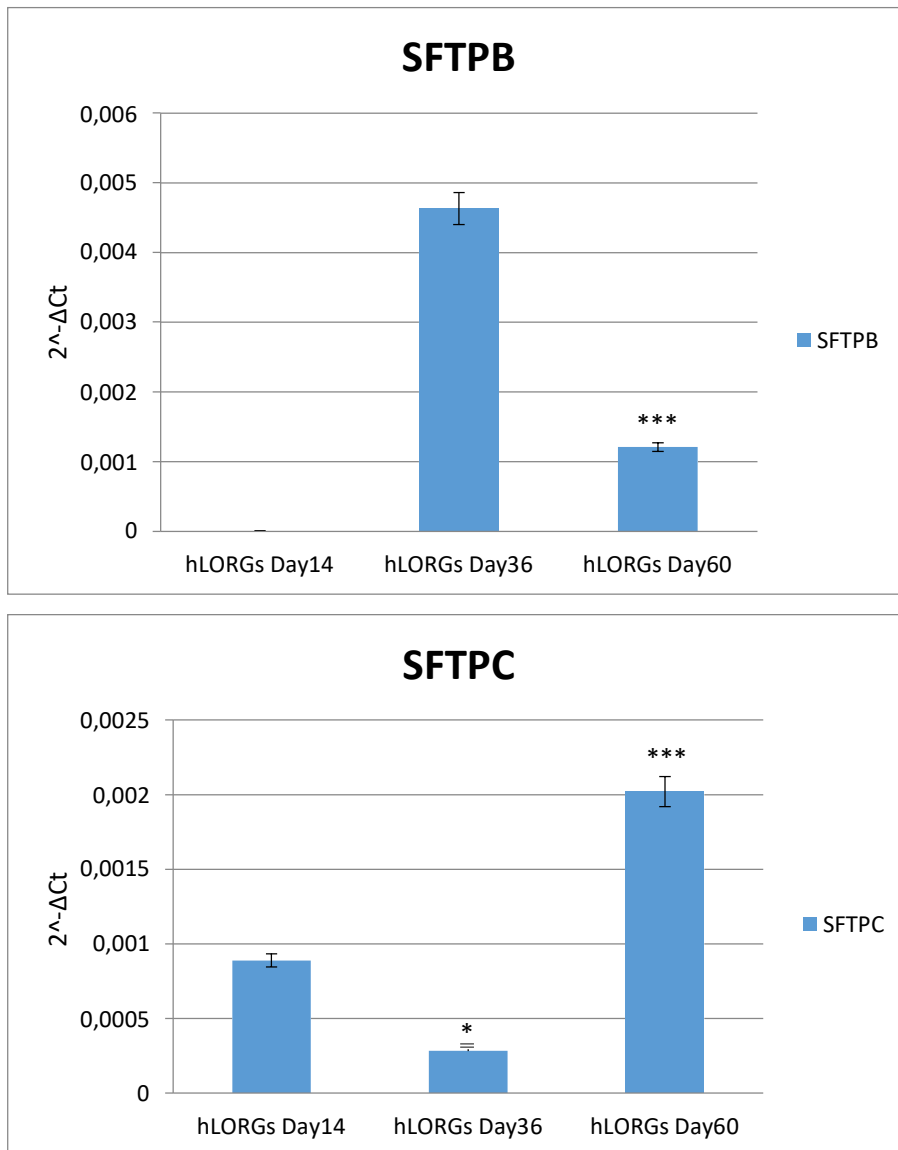
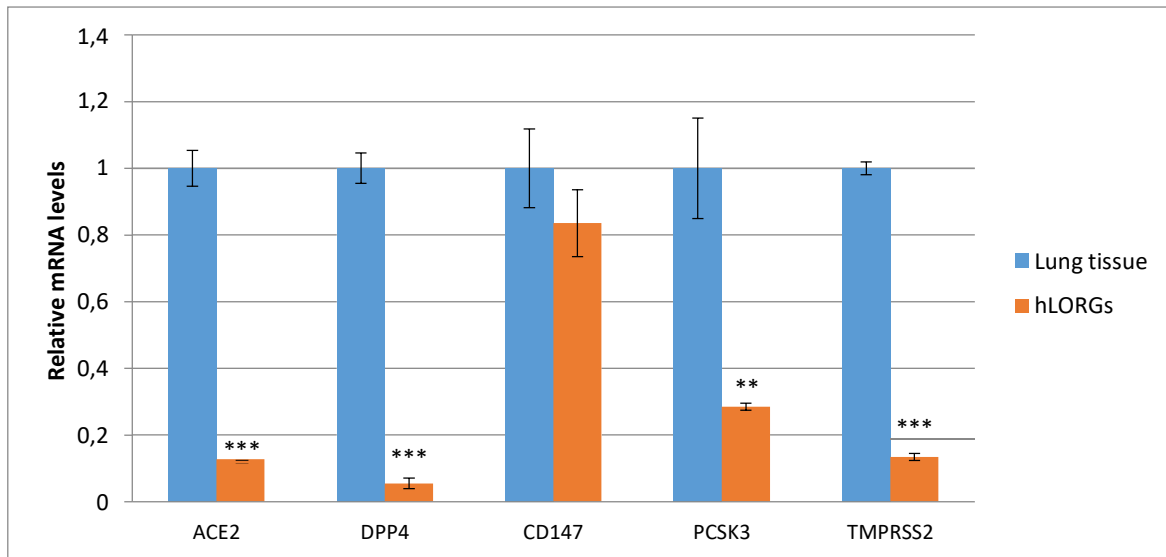


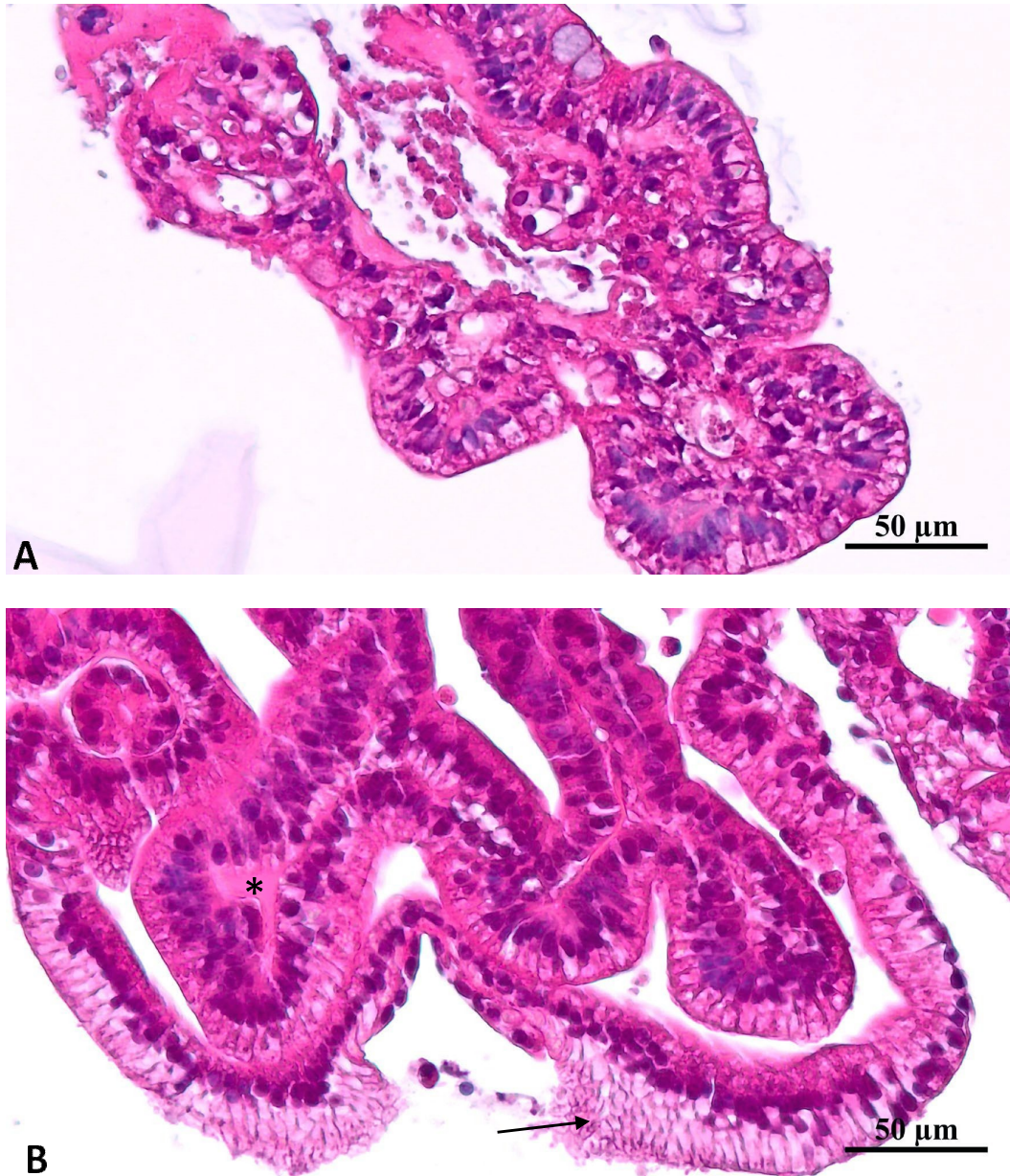
**Figure S1. Schematic for differentiation from hiPSCs to Lung Organoids (HLORGs)** (A) Flowchart protocol of hiPSCs differentiation to lung progenitors using StemDiff Lung Progenitor kit. (B) Workflow for lung progenitors into hLORGs: after characterization, hLORGs were infected and treated with Fab-IgG 15033-7 or DPP4<sub>270-295</sub> between days 60-67. The 3D cultures were maintained until day 105.



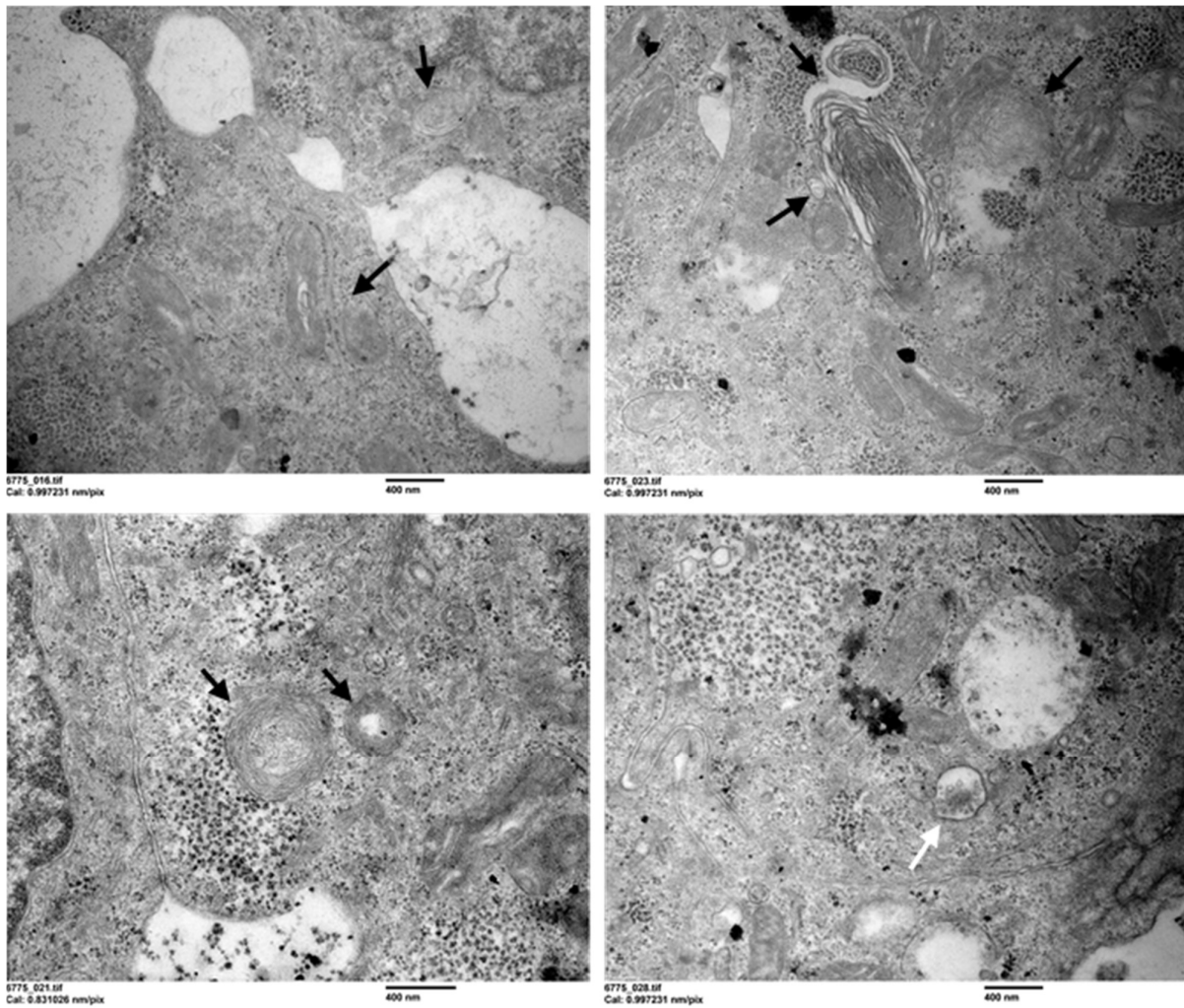
**Figure S2.** RT-qPCR analyses of *SFTPB* and *SFTPC* genes in hLORGs at days 14, 36 and 60 of differentiation. Data are reported as absolute values after normalization versus a housekeeping gene. The transcript SFTPB/C ratio is about 16: 1. Data are representative of three independent experiments and reported as mean  $\pm$  SD. (\* $p < 0.05$ ; \*\*\* $p < 0.001$  by one-way ANOVA test).



**Figure S3.** RT-qPCR analyses of proteins involved in SARS-CoV-2 entry (*ACE2*, *DPP4*, *CD147*, *PCSK3*, *TMPRSS2*) in hLORGs and human lung tissue. Data are representative of three independent experiments and reported as mean  $\pm$  SD. \*\* $p < 0.01$ , \*\*\* $p < 0.001$  by one way ANOVA test.



**Figure S4. Histological analysis of alveolocytes infected or not with pseudo-SARS-CoV-2S (A, B)** Haematoxylin and eosin-stained sections of infected or not alveolopheres with **pseudo-SARS-CoV-2S** (original magnification, 200X). Representative images show cellular damages of infected alveolocytes that display hyperplasia (arrow) with enlarged nuclei and prominent nucleoli with hyaline deposition (pink deposits, asterisk).



**Figure S5. Ultrastructural analysis of hLORGs infected with pseudo-SARS-CoV-2S.** TEM images of hLORGs (48 hours post-infection) show the presence of intracytoplasmic lamellar bodies (black arrows) and viral particles within a single membrane vesicle (white arrow).