

Modulations of Homeostatic ACE2, CD147, GRP78 Pathways Correlate with Vascular and Endothelial Performance Markers during Pulmonary SARS-CoV-2 Infection

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Supplementary Table S1. List of the hamster gene-specific primer sequences used for RT-PCR studies.

Gene name		Gene sequence (5' – 3')
ACE2	Forward	GGGACGCTACCATTCACTTAC
	Reverse	GCTTCATCTCCCACCACTTT
CD147	Forward	GACTATGCCTGCATCTTCCTT
	Reverse	ACTGGAATGCTCTGACTTCTTC
GRP78	Forward	TCTTGTCGGTGGGTCTACT
	Reverse	ACAGCCTCATCTGGGTTTATG
TF	Forward	CCTATCTGTCCCACGGAATAAC
	Reverse	GGATTACAGGCTTCCGAGTT
PLAT	Forward	GGAAGAAGTGAGGACTGCTATG
	Reverse	TGCTGTGTAACCTTGCCTATC
THBD	Forward	GGATCCGTGCTTCGGAAATA
	Reverse	CCTCGGGTTTGGGTCTAAAG
vWF	Forward	GATGTACGGTCTCTGTGGAATC
	Reverse	GCACAGTCCATTCTGGATAA
PAI-1	Forward	CGTGAACACAGAACGAGATTAG
	Reverse	GTCCGGAAGAGCTTGAAGAAG
ESAM	Forward	GCCACCCTTGTCATAGCCT
	Reverse	GCGAGGGAAGCAAAGGTACT
PROCR/CD201	Forward	ACCTGTGTGCAGTTTGTGGA
	Reverse	GAAGTGTAAGAGCGGCCTGT
VCAM-1/CD106	Forward	TCCATTTTCGTCACCACAGCA
	Reverse	AGCTTGAGAGGCTGCAAACA
VEGF-A	Forward	TGCATTGGACCCTGGCTTTA
	Reverse	CTGCTCTCCTTCTGTCGTGG
VEGFR-2/CD309	Forward	CAGTGGGATGGTCCTTGCAT
	Reverse	GTACCCAGACTGATAGCCGC
GAPDH	Forward	AGAACGGGAAGCTTGTCATC
	Reverse	GCCAGTAGACTCCACAACATAC
β-actin	Forward	CCCAGAGCAAGAGAGGTATTC
	Reverse	GGTGCCAGATCTTCTCCATATC

Supplementary Table S2. List of the genes and corresponding probe sequences used for smFISH studies.

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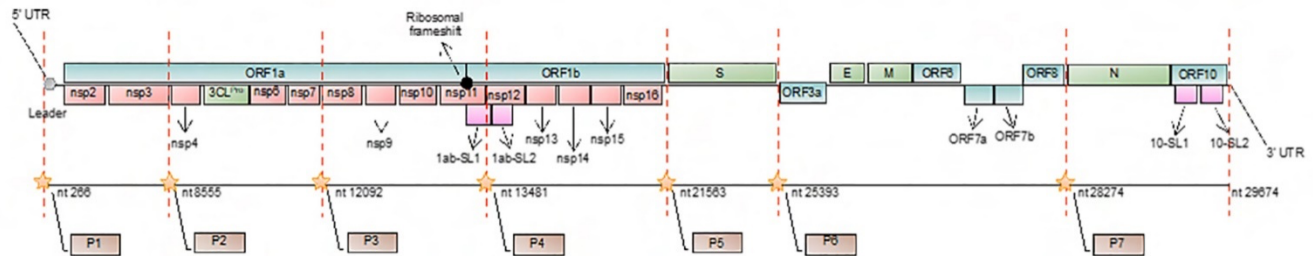
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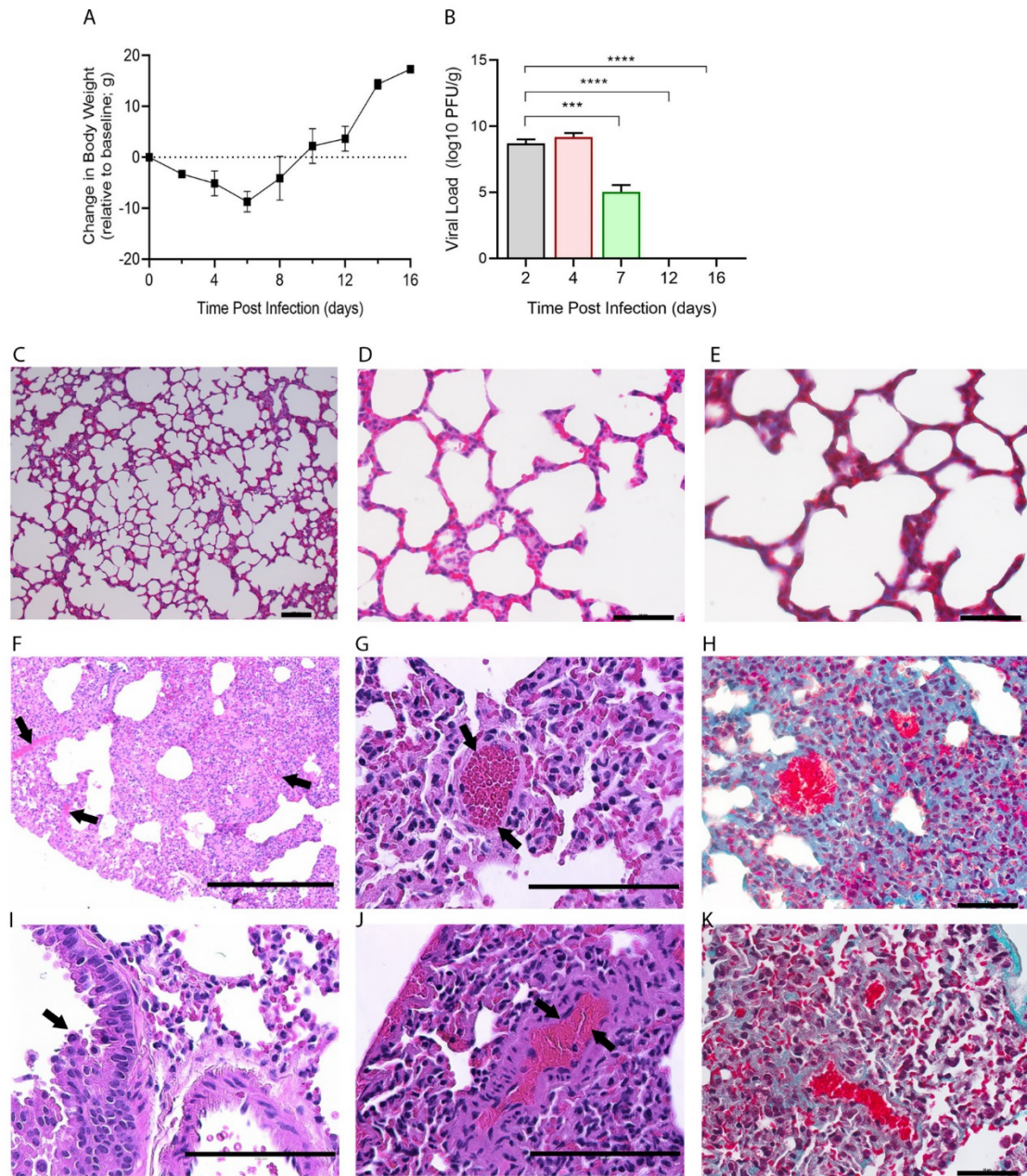
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Supplementary Figure S1.



Supplementary Figure S1. Organization and expression of SARS-CoV-2 complete genome and FISH probe diagram targeting its genes. The virus ORFs are defined by the genomic sequence of SARS-CoV-2 isolate Wuhan-Hu-1 (NCBI Reference Sequence: NC_045512.2). The ORFs are depicted in blue (ORF1ab, ORF3a, ORF6, ORF7ab, ORF8 and ORF10), non-structural proteins in orange (nsp2-3, nsp 6-11, nsp12 (RNA-dependent RNA polymerase; NiRAN and RdRp), nsp 13 (helicase), nsp14 (3' → 5' exonuclease), nsp15 (endoRNase) and nsp16 (2'-O-ribose methyltransferase)), structural proteins in green (3C-like proteinase, spike (S), envelope (E), membrane (M) and nucleocapsid (N) proteins) as well as frameshifting stimulation elements in pink (ORF1ab – SL1, SL2, and ORF10 – SL1, SL2). The open grey box represents the common 5' leader sequence and the black circle represents another programmed frameshifting element in the ORF1 fragment. P1 – P7 represent probe set designs with each set containing 43-48 probes (details in Supplementary Table 2.) targeting specific regions of SARS-CoV-2 genes.

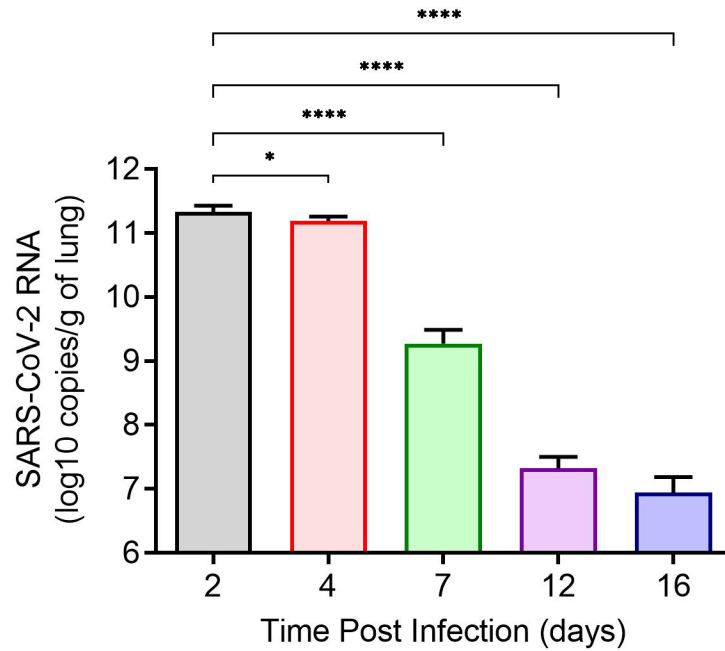
Supplementary Figure S2.



Supplementary Figure S2. Clinical pathology of SARS-CoV-2 infected hamsters. **A.** Body weight changes in SARS-CoV-2 infected hamsters up to 16 dpi. **B.** Replicative viral load in the lungs as determined by the number of viral plaque-forming units (PFU). No replicative virus was noted at 12 and 16 dpi. Values plotted are mean $\pm$ SD (n=3-4 animals per group). Only statistically significant differences were shown in the figure. *** $P < 0.001$ and **** $P < 0.0001$ by unpaired *t*-test. **C,D,F,G,I,J.** Representative H&E-stained histologic image of lung sections from SARS-CoV-2 infected hamsters at 4dpi showing key pathological features related to COVID-19 in humans. **E, H, K** are representative images of lung sections stained with Masson's Trichrome to visualize tissue remodeling, fibrin and collagen deposition. No clinicopathological signs were noted in the uninfected/control hamster lung sections (**C, D, E**). SARS-CoV-2 infected hamster lungs show pulmonary occlusion (arrows in **F**), extravasation of platelets in the pulmonary tissues and adherence of RBCs on the wall of a blood vessel (arrows in **G** and **H**), loss of endothelial cells in the vasculature (arrows in **I**), and red-thrombus tightly

adhered to the walls of pulmonary arterioles and occluded the lumen (arrows in J and K). Image C is 40x, image D and F are 100x and images E, G-K are 400x. The scale bar represents 100 μ m in images G, I, J, 400 μ m in C, F, 200 μ m in D and 50 μ m in E, H, K.

Supplementary Figure S3.



Supplementary Figure S3. Number of total viral RNA copies in the lung of SARS-CoV-2 infected hamsters. Total RNA from lungs harvested over time post-infection was analyzed using SARS-CoV-2 N-specific primers. Values plotted are mean $\pm$ SD (n=3-4 animals per group). Only statistically significant differences were shown in the figure. * $P < 0.01$ and **** $P < 0.0001$ by unpaired t test.