Supplementary Information for

SARS-CoV-2 Couples Evasion of Inflammatory Response to Activated Nucleotide Synthesis

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Supplementary Materials and Methods

Cells and Viruses.
HEK293T (ATCC, cat. no. ACS-4500), HCT116 (ATCC, cat. no. CCL-247), mouse embryonic fibroblasts (MEFs) (isolated from the fetuses of different mouse strains) and Vero E6-hACE2 (a kind gift from Dr. Jae Jung, Cleveland Clinic Foundation, Cleveland, OH) were cultured in Dulbecco’s modified Eagle’s medium (DMEM, HyClone) supplemented with 10% fetal bovine serum (FBS; Gibco), penicillin (100 U/mL) and streptomycin (100 μg/mL). Caco-2 (ATCC, cat. no. HTB-37) and Calu-3 (ATCC, cat. no. HTB-55) were cultured in Minimum Essential Medium supplemented with 10% FBS and antibiotics. Normal human bronchial epithelial (NHBE) cells (ATCC, cat. no. PCS-300-010) were cultured in Airway Epithelial Cell Basal Medium (ATCC) supplemented with Bronchial Epithelial Cell Growth factors (ATCC) and antibiotics. Sendai Virus (Cantell strain) was purchased from Charles River (cat. no. 10100774).

Mice.
RelA-DD (N64D, N139D) and RelA-N64A knock-in C57BL/6 mice were genetically engineered by Cyagen using Cas9/CRISPR. Regular and K18-hACE2 C57BL/6 mice were purchased from the Jackson Laboratory. All strains were confirmed by genotyping.

Plasmids.
The nonsilencing (control) shRNA, shRNA for human CAD, and luciferase reporter plasmids for the NF-κB, RelA, MAVS were described previously (1). Lentiviral expression constructs containing hACE2 were generated from pCDH-CMV-EF1-Puro or pCDH-CMV-EF1-Hygro by molecular cloning.

SARS-CoV-2 Propagation and Plaque Assay.
T175 flaks of Vero E6-hACE2 cells were infected with SARS-CoV-2 at an MOI of 0.005 for 72 hours. Supernatants were collected after centrifuging at 2500 rpm for 5 min, aliquoted and stored at -80°C. Virus titer was determined by plaque assay. Briefly, Vero E6-hACE2 cells were infected in duplicate or triplicate with serial dilutions of virus for 45 min in serum-free DMEM, overlaid with 1× DMEM/1% agarose, and incubated at 37°C for 3 days. Cells were fixed with 4% paraformaldehyde for 1 h. Overlay was removed, and plates were stained with 0.2% crystal violet and washed with water.

Lentivirus-Mediated Stable Cell Line Construction.
Lentiviruses were produced as previously described (2). Briefly, HEK293T cells were transfected with the packaging plasmids psPAX2 and pMD2.G and the pCDH lentiviral expression vector or lentiviral shRNA plasmids. At 48 h post transfection, lentivirus-containing medium was harvested
and filtered (and concentrated by ultracentrifuge if necessary). MEFs, Caco-2, Calu-3, NHBE or HCT116 cells were infected with the virus-containing medium in the presence of polybrene (8 μg/mL) with centrifugation at 1800 rpm for 45 minutes. Cells were selected at 48 h post infection and maintained in corresponding medium supplemented with puromycin (1~2 μg/mL) or hygromycin (200 μg/mL).

**MEFs Extraction.**

MEFs were extracted from the fetuses of RelA-DD knock-in C57BL/6 mice (1) or RelA-N64A knock-in C57BL/6 mice at day 14 of gestation. Briefly, the head and liver were removed, and the embryo was washed with PBS, minced, and digested with trypsin (Corning). DMEM containing 10% FBS was subsequently added. Cells were cultured and genotypes were validated by sequencing using PCR products. Cells were then passaged for 3 generations before being used for experiments.

**qRT-PCR.**

qRT-PCR was performed as previously described (3, 4). Total RNA was extracted using TRIzol reagent (Invitrogen). Complementary DNA (cDNA) was synthesized from total RNA using reverse transcriptase (Invitrogen). cDNA was diluted and analyzed by qRT-PCR using SYBR Green Master Mix (Applied Biosystems) with CFX Connect PCR instrument (Bio-Rad Lab.). Relative mRNA expression for each target gene was calculated by the 2^{ΔΔCt} method using β-actin or Gapdh as an internal control. The sequences of qRT-PCR primers are listed in SI Appendix, Table S1.

**The 2-DGE.**

Cells were lysed in rehydration buffer (7 M Urea, 2 M Thiourea, 2% CHAPS, 0.5% IPG Buffer, 0.002% bromophenol blue) by two pulses of sonication, and whole cell lysates (WCLs) were centrifuged at 13k rpm for 15 min. Supernatants were loaded to IEF strips for focusing with a program comprising: 20 V, 10 h (rehydration); 500 V, 1 h; 1000 V, 1 h; 1000-5000 V, 4 h; 5000 V, 5 h. After IEF, strips were incubated with SDS equilibration buffer (50 mM Tris-HCl [pH8.8], 6 M urea, 30% glycerol, 2% SDS, 0.001% Bromophenol Blue) containing 10 mg/mL DTT for 15 min and then SDS equilibration buffer containing 2-iodoacetamide (25 mg/mL) for 15 min. Strips were washed with SDS-PAGE buffer, resolved by SDS-PAGE, and analyzed by immunoblotting.

**Metabolite Profiling and Isotope Tracing.**

Roughly, 2×10^6 cells per sample (in triplicates) were harvested for metabolomics analysis. For isotope tracing experiments, cells were cultured with medium containing [U-13C]glucose (Cambridge Isotope Lab, cat. no. CLM-1396) or [15N-amide]glutamine (Cambridge Isotope Lab,
Metabolite extraction was performed after labeling. Cells were washed on ice with 1 mL ice-cold 150 mM ammonium acetate (NH₄AcO, pH 7.3), and 1 mL of -80°C cold 80% MeOH was added to the wells. Samples were incubated at -80°C for 20 mins, and cells were scraped off and supernatant was transferred into microfuge tubes. Samples were pelleted at 4°C for 5 min at 15k rpm. The supernatant was transferred into new microfuge tubes. Metabolites were dried at room temperature under vacuum and re-suspended in water for LC-MS run.

Samples were randomized and analyzed on a Q-Exactive Plus hybrid quadrupole-Orbitrap mass spectrometer coupled to Vanquish UHPLC system (Thermo Fisher). The mass spectrometer was run in polarity switching mode (+3.00 kV/-2.25 kV) with an m/z window ranging from 65 to 975. Mobile phase A was 5 mM NH₄AcO, pH 9.9, and mobile phase B was acetonitrile. Metabolites were separated on a Luna 3 μm NH₂ 100 NH₂ 100Å` (150 x 2.0 mm) column (Phenomenex). The flow rate was 0.3 mL/min, and the gradient was from 15% A to 95% A in 18 min, followed by an isocratic step for 9 min and re-equilibration for 7 min. All samples were run in biological triplicate. Metabolites were detected and quantified as area under the curve based on retention time and accurate mass (5 ppm) using the TraceFinder 4.1 (Thermo Scientific) software. Raw data was corrected for natural isotope abundance and tracer impurity using the IsoCorrector package (5). Fractional enrichment represents the percentage of each labeled metabolites. The abundance of indicated metabolites in Fig. 3C and 5B is listed in SI Appendix, Datasets S1.

**Affinity Purification, Coimmunoprecipitation, and Immunoblotting.**

HEK293T cells were transfected with indicated expression plasmids for 48 h. Cells were harvested for experiments. Whole cell lysates (WCLs) were prepared with NP40 buffer (50 mM Tris-HCl, pH 7.4, 150 mM NaCl, 1% NP-40, 5 mM EDTA) supplemented with 20 mM β-glycerophosphate, 1 mM sodium orthovanadate and a protease inhibitor cocktail (Roche). WCLs were sonicated, centrifuged and the supernatant was pre-cleared with protein A/G agarose for 1 h. For pull-down assay, pre-cleared samples were incubated with StrepTactin agarose (GE Healthcare, cat. no. 28-9355-99) for 4 h at 4°C. For Co-IP, pre-cleared samples were incubated with indicated antibodies overnight and protein A/G agarose for 1 h at 4°C. The agarose beads were washed extensively, and samples were eluted by boiling at 95°C for 10 min. Precipitated proteins and WCLs were analyzed by SDS gel electrophoresis and immunoblotting.

All immunoblotting was performed using the following primary antibodies: RelA (Invitrogen, PA5-16545, 1:2000 dilution), GST (Santa Cruz, sc-53909, 1:1000 dilution), CAD (Bethyl Laboratories, A301-374A, 1:2000 dilution), Phospho-CAD (Ser1859) (Cell Signaling, 12662, 1:1000 dilution), Strep (BioLegend, 688202, 1:1000 dilution), Flag (Sigma, F3165, 1:1000 dilution), V5 (Bethyl Laboratories, A190-120A, 1:1000 dilution), and SARS-CoV-2 N (homemade). Proteins
were visualized by Odyssey infrared imaging system (LI-COR) after incubation with IRDye800-conjugated secondary antibodies (1:10,000 dilution, LI-COR).

**Dual-Luciferase Reporter Assay.**

HEK293T cells were transfected with NF-κB reporter plasmid cocktail (50 ng of luciferase reporter plasmid and 5 ng of pRL Renilla luciferase control vector) and expression plasmid (empty plasmid or one or multiple plasmids, depending on the experiment) by calcium phosphate precipitation. WCLs were used to determine the activity of firefly luciferase and Renilla luciferase by a microplate reader (FLUOstar Omega) at 24 hours post transfection.

**Cell Viability Test.**

Cell viability was measured with Cell Proliferation Kit II (XTT) according to the manufacturer’s recommendation (Sigma). Briefly, cells were seeded at a density of 1×10⁴ cells per well in 96-well culture plates. After 12 h, the medium was replaced with one that contains increasing concentrations of 2-TCPA, and cells were cultured for different hours. XTT was then added to the medium and cell viability in each well was measured by absorption at a wavelength of 475 nm, with 660 nm as the reference wavelength. Each data point was performed in triplicate.

**ELISA.**

The concentration of CCL5, IL6 and IL8 in culture supernatants were measured using ELISA kits (CCL5, R&D systems, cat. no. DRN00B; IL6, Proteintech, cat. no. KE00007; IL8, Proteintech, cat. no. KE00006).

**Mouse Infection and Treatment with Compounds.**

AAV9 encoding hACE2 was purchased from Vector Biolabs (AAV-CMV-hACE2). Mice (regular C57BL/6 mice or RelA-N64A knock-in C57BL/6 mice) were anesthetized with 2.5% isoflurane in O₂ (1 L/min). A volume of 40 μL AAV (10¹¹ GC) was delivered to mice intranasally. At 14 days post-infection, mice were intranasally infected with SARS-CoV-2 (5 x 10⁵ PFU) in a volume of 30 μL of DMEM. To determine the antiviral effect, a dose of 20 mg/kg/d of 2-TCPA or vehicle was intraperitoneally (i.p.) administered 2 hours before infection. All mice were monitored every day and euthanized at 4 dpi to collect lung tissues to determine viral titer by plaque assay and extract RNA for gene expression profiling.

Heterozygous K18-hACE2 C57BL/6J mice (Jackson laboratory) were intranasally infected with 10⁴ PFU of SARS-CoV-2. A dose of 40 mg/kg/d of 2-TCPA or vehicle was i.p. administered to the mice beginning at −1 dpi for a consecutive 3-d period. Mice were monitored and weighed
daily and sacrificed at 3 dpi to collect lung tissues for RNA extraction, plaque assay, H&E staining, immunofluorescence and metabolite analysis.

**Histology and Immunofluorescence Analysis.**

Fresh lung pieces were fixed with formalin solution for 24 h. The post-caval lobes of left lung were sent to histology lab in USC of School of Pharmacy Core Facilities for processing, and hematoxylin and eosin (H&E) staining. In brief, tissues were dehydrated and embedded in paraffin. Paraffin-embedded tissue blocks were sectioned with 5 μm thickness. Sections were processed by H&E staining and imaged by ZEISS Axio Scope.A1 microscope (Zeiss) and analyzed by ZEISS ZEN Blue software.

Pathological scoring on blinded H&E-stained sections was implemented via a semi-quantitative, 5-point grading scheme (0 - within normal limits, 1 - mild, 2 - moderate, 3 - marked, 4 severe) that considered four different histopathological parameters: 1) perivascular inflammation, 2) bronchial or bronchiolar epithelial degeneration or necrosis, 3) bronchiolar or bronchiolar inflammation, and 4) alveolar inflammation (6).

Immunofluorescence staining was performed on the middle lobes of left lung fixed with formalin solution. Tissues were embedded in optimal cutting temperature (OCT) compound and frozen immediately at -80°C. Subsequently, the frozen tissues were cut into 8 μm sections using a cryostat-microtome. Sections were blocked with 10 % normal goat serum diluted in PBST for 1 h, and incubated with primary antibodies diluted in 10% normal goat serum overnight at 4°C. After washing with PBST, sections were incubated with species-matched secondary antibodies for 30 min at room temperature. Then tissue sections were washed with PBST, mounted with Mounting Medium (Vector Laboratories), and analyzed with a confocal microscope (Nikon).

**Statistical Analysis.**

Statistical analyses were performed using GraphPad Prism software to perform Student’s t-test or analysis of variance (ANOVA) on at least three independent replicates. P values of <0.05 were considered statistically significant for each test.
Fig. S1. SARS-CoV-2 inhibits cytokine production. (A) Calu-3 cells were infected with SARS-CoV-2 (MOI = 0.1) or Sendai virus (SeV, 100 HAU/ml) for indicated hours. Total RNA was extracted and analyzed by real-time PCR with primers specific for indicated genes. (B) NHBE cells were mock-infected or infected with SARS-CoV-2 (MOI = 5) for 24 h and super-infected with SeV (100
HAU/ml) for 6 h. The expression of the indicated genes was analyzed by real-time PCR using total RNA. (C) Caco-2 cells were mock-infected or infected with SARS-CoV-2 (MOI = 0.1) for 72 and 96 h. Whole-cell lysates (WCLs) were analyzed by two-dimensional gel electrophoresis (2-DGE) and immunoblotting. (D) Wildtype, RelA-DD and RelA-N64A knock-in mouse embryonic fibroblasts (MEFs) were infected with letivirus carrying Flag-hACE2. hACE2 expression was analyzed by immunoblotting. (E and F) RelA wildtype, RelA-DD and RelA-N64A knock-in MEFs expressing hACE2 were infected with SARS-CoV-2 (MOI = 0.1) for 24 h. Indicated viral genes (E) and viral titer (F) were analyzed by real-time PCR and plaque assay, respectively. (G and H) Schematic of experimental plans (G). C57BL/6 mice (n=3) were transduced with an AAV coding for hACE2 (AAV-hACE2) and infected with SARS-CoV-2 for 2 weeks. Lung samples were collected at days 2, 4, 6, and 8 for analysis. Cytokine gene expression from lung homogenates was measured by real-time PCR (H). (I) AAV-hACE2-transduced wildtype and RelA-N64A knock-in mice (n=4) were intranasally infected with 5 x 10⁵ PFU of SARS-CoV-2. The expression of viral genes was analyzed by real-time PCR. Data are presented as means ± SD of biological triplicates (A, B, E, and F) and are representative of three independent experiments (C and D). Statistical analysis was performed by the one-way ANOVA test or unpaired, two-tailed Student’s t-test. *p < 0.05; **p < 0.01; ***p < 0.001.
Fig. S2. Infection rates of SARS-CoV-2 in different cells. (A-E) Indicated cells were infected with icSARS-CoV-2-mNG at indicated MOI. Cells were subjected to fluorescence microscopy analyses at indicated time points. Data are representative of three independent experiments. Scale bar, 100 μm.
Fig. S3. SARS-CoV-2 and Nsp9 promotes CAD-mediated RelA deamidation to inhibit NF-κB activation. (A) Caco-2 cells were depleted with shRNA targeting CAD by lentiviral infection. Cells were infected with SARS-CoV-2 (MOI = 0.1) for 72 h. Whole cell lysates (WCLs) were analyzed by two-dimensional gel electrophoresis and immunoblotting. WT and Deam denote wild-type and deamidated RelA, respectively. (B) Calu-3 cells were depleted with shRNA targeting CAD by lentiviral infection. Cells were infected with SARS-CoV-2 (MOI = 0.5) for 48 h. Total RNA was extracted for analysis by real-time PCR. (C-E) HEK293T cells were transfected with NF-κB
reporter plasmid cocktail, RelA or MAVS, along with increasing amounts of plasmids expressing Nsp9, ORF10 or ORF7a. Luciferase activity was determined at 24 h after transfection. (F) HCT116 cells were infected with control lentivirus or that carrying Nsp9 for 72 h. WCLs were analyzed by two-dimensional gel electrophoresis (2-DGE) and immunoblotting with indicated antibodies. (G) RelA-knockdown HCT116 cells reconstituted with wildtype RelA or RelA-DD (DD) were infected with control lentivirus or that carrying Nsp9 for 72 h. WCLs were analyzed by 2-DGE and immunoblotting with indicated antibodies. Data are presented as means ± SD of biological triplicates (B-E) and are representative of three independent experiments (A, F, and G). Statistical analysis was performed by the two-way ANOVA test or one-way ANOVA test. *p < 0.05; ***p < 0.001.
Fig. S4. CAD promotes SARS-CoV-2 replication. (A) Caco-2 cells were infected with SARS-CoV-2 (MOI = 0.1) for 72 and 96 h. Whole cell lysates (WCLs) were analyzed by immunoblotting with indicated antibodies. (B-D) Calu-3 cells were depleted with shRNA targeting CAD by lentiviral infection. Cells were infected with SARS-CoV-2 (MOI = 0.5) for indicated hours. WCLs were analyzed by immunoblotting with indicated antibodies (B). Total RNA extracted at 72 hpi was analyzed by real-time PCR (C) and viral titer was determined by plaque assay (D). (E-G) NHBE cells were depleted with shRNA targeting CAD by lentiviral infection. Cells were then infected with SARS-CoV-2 (MOI = 0.5) for 24 h. WCLs were analyzed by immunoblotting with indicated antibodies (E). Extracted total RNA was analyzed by real-time PCR (F) and viral titer was determined by plaque assay (G). Data are presented as means ± SD of biological triplicates (C, D, F, and G) and are representative of three independent experiments (A, B, and E). Statistical analysis was performed by the two-way ANOVA test or unpaired, two-tailed Student’s t-test. **p < 0.01; ***p < 0.001
Fig. S5. Nsp9 enhances the interaction between S6K1 and CAD. (A) Caco-2 cells were infected with control lentivirus or that carrying indicated viral genes. At 72 hpi, whole cell lysates (WCLs) were analyzed by immunoblotting with indicated antibodies. Red arrowheads indicate viral proteins. (B) Caco-2 cells were infected with control lentivirus or that carrying Nsp9. WCLs were analyzed by immunoblotting with indicated antibodies. (C) Control or Nsp9-expressing Caco-2
cells as described in (B) were used for metabolites analysis. Metabolites of the central carbon pathways were showed as metabolic map (normalized to the vector group). Black circles indicate undetected metabolites. (D) HEK293T cells were transfected with empty vector or that expressing Strep-tagged Nsp9. At 48 h post-transfection, WCLs were prepared and precipitated with StrepTacin beads. WCLs and precipitated proteins were analyzed by immunoblotting with indicated antibodies. (E) HEK293T cells were transfected with empty vector or that expressing Strep-tagged Nsp9. At 48 h post-transfection, WCLs were precipitated with anti-CAD or control rabbit IgG. Precipitated proteins and WCLs were analyzed by immunoblotting with indicated antibodies. (F) Caco-2 cells were infected with control lentivirus or that carrying Nsp9. At 72 hpi, cells were treated with DMSO or 20 μM S6K1 inhibitor (PF-4708671) for 2 h. WCLs were analyzed by two-dimensional gel electrophoresis (2-DGE) and immunoblotting. (G) Caco-2 cells were infected with control lentivirus or that carrying Nsp9. At 72 hpi, WCLs were analyzed by immunoblotting with indicated antibodies. Data are representative of three independent experiments.
Fig. S6. SARS-CoV-2 infection or Nsp9 expression promotes aerobic glycolysis. (A) Mouse embryonic fibroblasts (MEFs) expressing hACE2 were infected with SARS-CoV-2 (MOI = 0.1) for 24 h. Indicated genes were analyzed by real-time PCR. (B) Caco-2 cells were infected with SARS-CoV-2 (MOI = 1) for 72 h followed by labeling with [U-13C]glucose for 1 h. Indicated metabolites were determined by LC-MS. (C) Calu-3 cells were infected with control lentivirus or that carrying Nsp9 for 96 h followed by labeling with [U-13C]glucose for 1 h. Indicated metabolites were analyzed by LC/MS. (D) Control or CAD-knockdown Caco-2 cells were infected with control lentivirus or that carrying Nsp9. At 96 hpi, cells were harvested for immunoblotting analysis. Data are presented as means ± SD of biological triplicates (A-C) and are representative of three independent experiments (D). Statistical analysis was performed by unpaired, two-tailed Student’s t-test. *p < 0.05; **p < 0.01; ***p < 0.001.
Fig. S7. 2-TCPA inhibits SARS-CoV-2 replication. (A) HEK293T cells were transfected with NF-κB reporter plasmid cocktail, along with empty vector or that containing RelA. Luciferase activity was measured...
determined after treatment with DMSO or various TCP derivatives for 12 h. (B) DMSO- or 2-TCPA-treated HEK293T cells were infected with SeV for 6 h. Total RNA was extracted and analyzed by real-time PCR with primers specific for IFNB1. (C) DMSO- or 2-TCPA-treated control or CAD-knockout HEK293T cells were infected with SeV for 6 h. Total RNA was extracted and analyzed by real-time PCR with primers specific for IL-8 genes. (D) Caco-2 cells were treated with DMSO or 2-TCPA for 24 h. Metabolites of the central carbon metabolism altered by 2-TCPA were shown as metabolic map (normalized with DMSO). Black circles represent undetectable metabolites. (E) Caco-2 cells were treated with 2-TCPA at indicated concentration for every 24 h. Cells were enumerated under microscope at 72 h. (F) Protein levels of N were analyzed by immunoblotting in SARS-CoV-2-infected Caco-2 cells that were treated with DMSO or 4 µM 2-TCPA. (G) Calu-3 cells were treated with 2-TCPA at indicated concentration for every 24 h. Cells were enumerated under microscope at 72 h. (H) Abundance of S gene was analyzed by real-time PCR in SARS-CoV-2-infected Calu-3 cells that were treated with DMSO or indicated concentrations of 2-TCPA. (I) Viral titer was analyzed by plaque assay in SARS-CoV-2-infected NHBE cells that were treated with DMSO or indicated concentrations of 2-TCPA. (ND, not detectable) (J and K) NHBE cells were treated with 2-TCPA at indicated concentrations for every 24 h. Cell viability was determined by XTT at 48 h (J). Cells were enumerated under microscope (K). (L) Calu-3 cells were infected with SARS-CoV-2 (MOI = 0.1) and treated with DMSO, 2-TCPA (16 µM and 32 µM) or Uridine (150 µM) daily. At 72 hpi, viral titer was determined by plaque assay and viral RNA was analyzed by real-time PCR with primers specific for E gene. Data are presented as means ± SD of biological triplicates (A-E, G-L) and are representative of three independent experiments (F). Statistical analysis was performed by the two-way ANOVA test or the one-way ANOVA test. ***p < 0.001; ns, not significant.
Fig. S8. 2-TCPA impedes SARS-CoV-2 replication and alleviates pathogenesis in vivo. (A-C) K18-hACE2 mice (n=4) were intranasally infected with SARS-CoV-2 (1 x 10^4 PFU). A dosage of 40 mg/kg/d of 2-TCPA or vehicle was intraperitoneally administered to these mice at 1 day before
infection. Mice were sacrificed at 3 dpi and the lung was collected. Lung tissues were stained with DAPI or an antibody against SARS-CoV-2 N (A), analyzed by hematoxylin and eosin staining (C) and quantified by pathological severity scores (B) (scale bars: A, 100 μm; B, 100 μm). (D) Mouse peripheral blood mononuclear cells (PBMCs) were treated with DMSO or 2-TCPA with indicated concentration for 12 h. Total RNA was extracted and analyzed by real-time PCR with primers specific for indicated genes. Data are presented as means ± SD of biological triplicates.
### Table S1, primers used in this study

| Gene Name      | Forward Primer (5’-3’)                      | Reverse Primer (5’-3’)                       |
|----------------|---------------------------------------------|---------------------------------------------|
| Human IL-8     | GGCACAAACTTTTCAGAGACAG                      | ACACAGAGCTGCAGAAATCAGG                      |
| Human CXCL10   | GTGCCATTCAAGGAGTACCTC                       | TGATGGCCCTTCGATTCTGGATT                     |
| Human NFKB1A   | CTCGGAGACTTTTCGAGGAATAC                     | GCCATTGTAGTTGGTAGGCCCTCTCA                  |
| Human CCL5     | CGCTTTTGCCCTACATGCCC                       | TCGGGTGACAAAGACGACTG                       |
| Human TNFA     | AGGCCTTCCCCAAAGAGACA                       | TCTTGGCAAAATGCGACTCT                       |
| Human IL-6     | CCAGCTATAGACTCCTTTCTC                      | GCTTGGTCTCCTACATGCTCT                     |
| Human CXCL1    | CACAGCCGACAGACCC                           | CACGGACGCCTCCCTGCT                       |
| Human CXCL2    | CTCCTCCTCGCACAGGCC                        | AGGGGCCGCTCCTGCT                       |
| Human CCL2     | AAGATCTCAGTGCAAGGCTCG                      | TTGCTTGCAGAGGTGGAGGCTC                     |
| Human CAD      | AGTGGTTTTCAACCGGCAT                        | CAGAGGATCGTTGAAGCACTAAGA                  |
| Human IFNB1    | AGGACAGGATGAAGCTGAC                       | TGATAGACATTAGCCAGAG                        |
| Human β-actin  | CGCTTTTTTCAGCCATATG                        | TGAGGCATCCACACGGAGTACT                     |
| Mouse Il8      | TCGAGACCATTTACTGCACAG                      | CATTGCCGAGGCAATTTCTTCC                     |
| Mouse Cxcl1    | CTGGGATTCACCTCAAAGACATC                    | CAGGGTCAAGGCAAGCCT                        |
| Mouse Tnfa     | CAGGCAGTGCCTATGTCTC                       | CGATCAAGCGAAGTCTAGG                       |
| Mouse Il1b     | GAAATGCCCACCTTTGAGAG                     | TGGATGCTCCTCATCAAGGACAG                    |
| Mouse Cxcl2    | CTCTCAAGGGCGGTCAAAAAAGTT                  | TCAGACAGGGACAGCAGGCTAGGTA                 |
| Mouse Vcam     | TTGGGAGCCTCAAGCGATCT                      | GCAATCGTTTTGTATACAGGGGA                   |
| Mouse Il6      | CTCGAAGAGACTTCCAGCCAG                     | AGTGATAGACAGGTCTGTTGG                     |
| Mouse Gapdh    | AGGTCGCTGGTGAAAGGCTGAGT                  | GGGGTCGTTGATGGGAACAC                    |
| SARS-CoV-2 RdRp| AGAATAGAGCTCGCACCCTGA                    | CTCCTCAGTGCGGGCTATT                      |
| SARS-CoV-2 S   | GCTGGTCTGCTGGAGTTATTA                    | AGGGTCAAGGCAACGACTA                      |
| SARS-CoV-2 E   | ACTTCTTTTCTTCTTCTTGGT                    | GCAGGATACCGCACACATC                      |
| SARS-CoV-2 N   | GGGGAACTTTCTCGCTAGAAT                           | GGGGAACTTTCTCGCTAGAAT                           |
Legend for Datasets S1

Datasets S1 includes abundance of indicated metabolites in Fig. 5B and Fig. 3C.

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