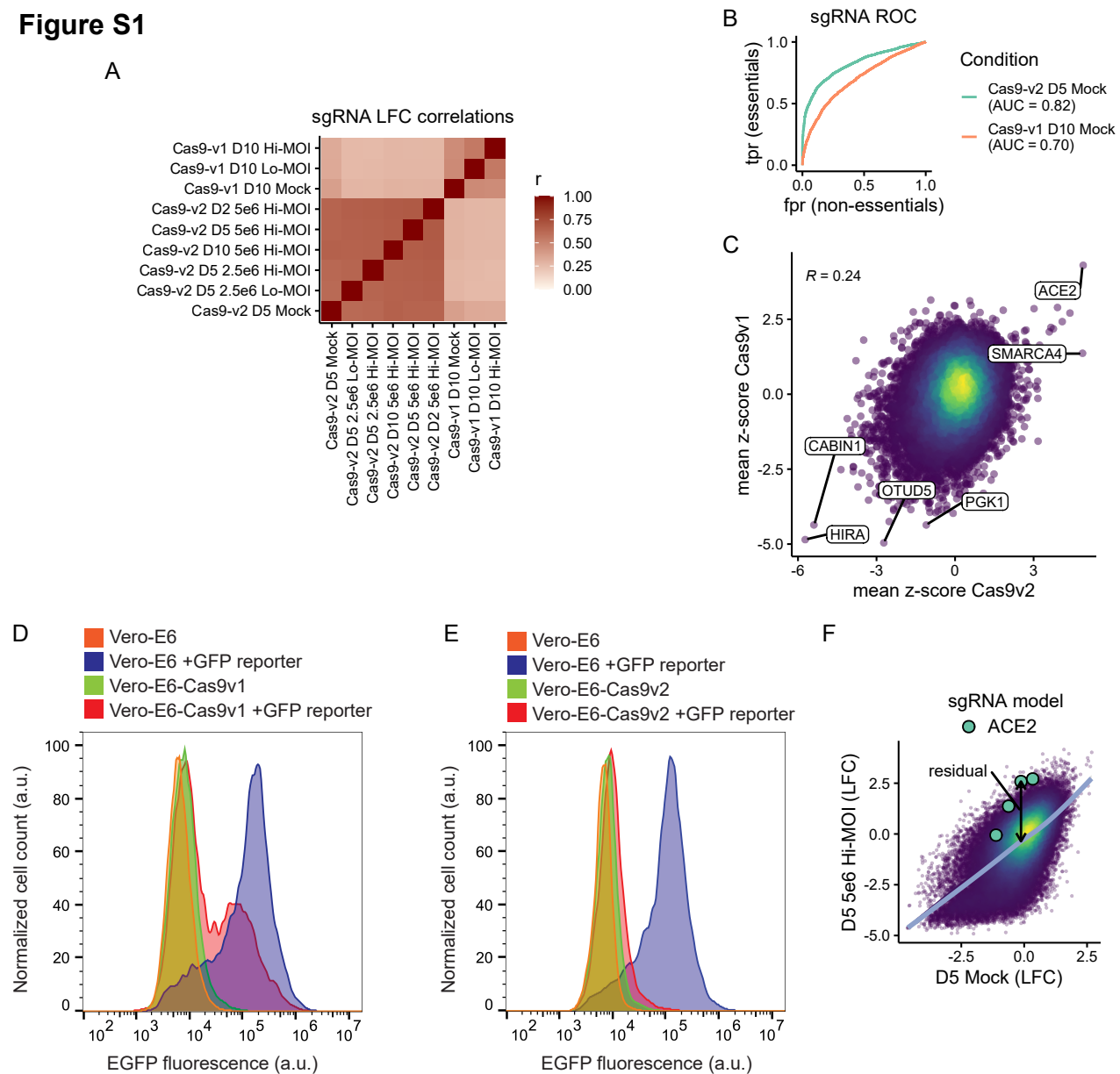# Figure S1

Fig. S1. Quality control metrics for CRISPR screen. (A) Correlation matrix depicting the Pearson correlation between the guide-level log-fold change values relative to the plasmid DNA. Cells were cultured in DMEM with 2% FBS (D2), 5% FBS (D5), 10% FBS (D10), plated at 2.5 x 10⁶ or 5.0 x 10⁶ cells per flask and infected at a MOI 0.1 (Hi) or MOI 0.01 (Lo). (B) Receiver-operator characteristic (ROC) curve for the recovery of guides targeting essential genes in the mock-treated condition of the Cas9-v1 and Cas9-v2 screens. True positives are n = 1,528 essential genes (n = 6,178 guides); true negative genes are n = 622 non-essential genes (n = 2,504 guides). We mapped essential and non-essential genes, which were derived for human cell lines, to the African green monkey genome simply by matching gene symbols. AUC = area under curve. (C) Correlation between gene enrichment in Cas9-v1 and Cas9-v2 screens. Pearson correlation is reported. (D-E) GFP-based Cas9 activity assay in Vero-E6 cells stably expressing either Cas9-v1 (D) or Cas9-v2 (E). The pXPR_047 construct expresses GFP and an sgRNA targeting GFP; therefore, cells without Cas9 activity will express GFP, whereas cells with high Cas9 activity will knock out GFP and resemble parental cells. (F) Approach to calculate residuals from log-fold change data, using ACE2 and the 5%FBS, 5 x 10⁶ cells/flask, MOI 0.1 condition as an example. A natural cubic spline with four degrees of freedom is shown in blue, and a residual for each sgRNA is calculated to be the vertical distance from the fit spline.
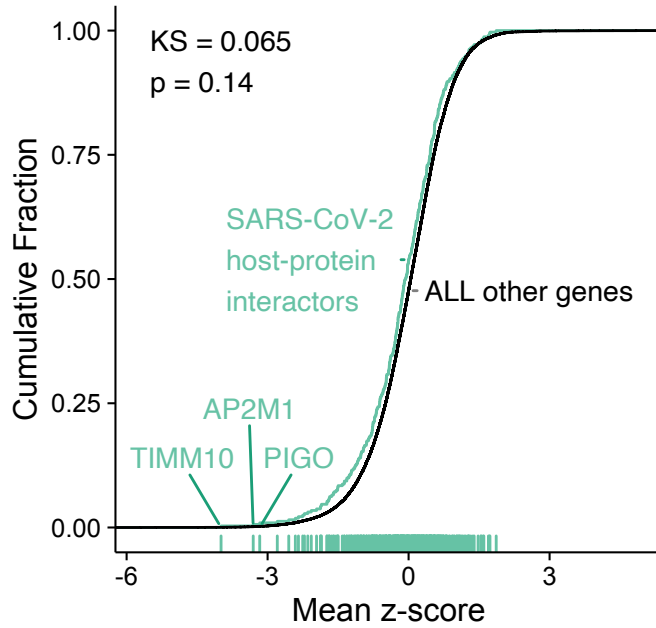
Figure S2

Fig. S2. Comparison to SARS-CoV-2 protein interactome. Cumulative distribution of mean z-scores for SARS-CoV-2 protein interactors from (7) (n=321; green) compared with all other genes (n = 21,351; black). Interactors with an absolute z-score greater than 3 are labelled. The KS-statistic and corre- sponding p-value are indicated for a two-sided KS-test. We mapped interactors to the African Green Monkey genome by matching gene symbols.
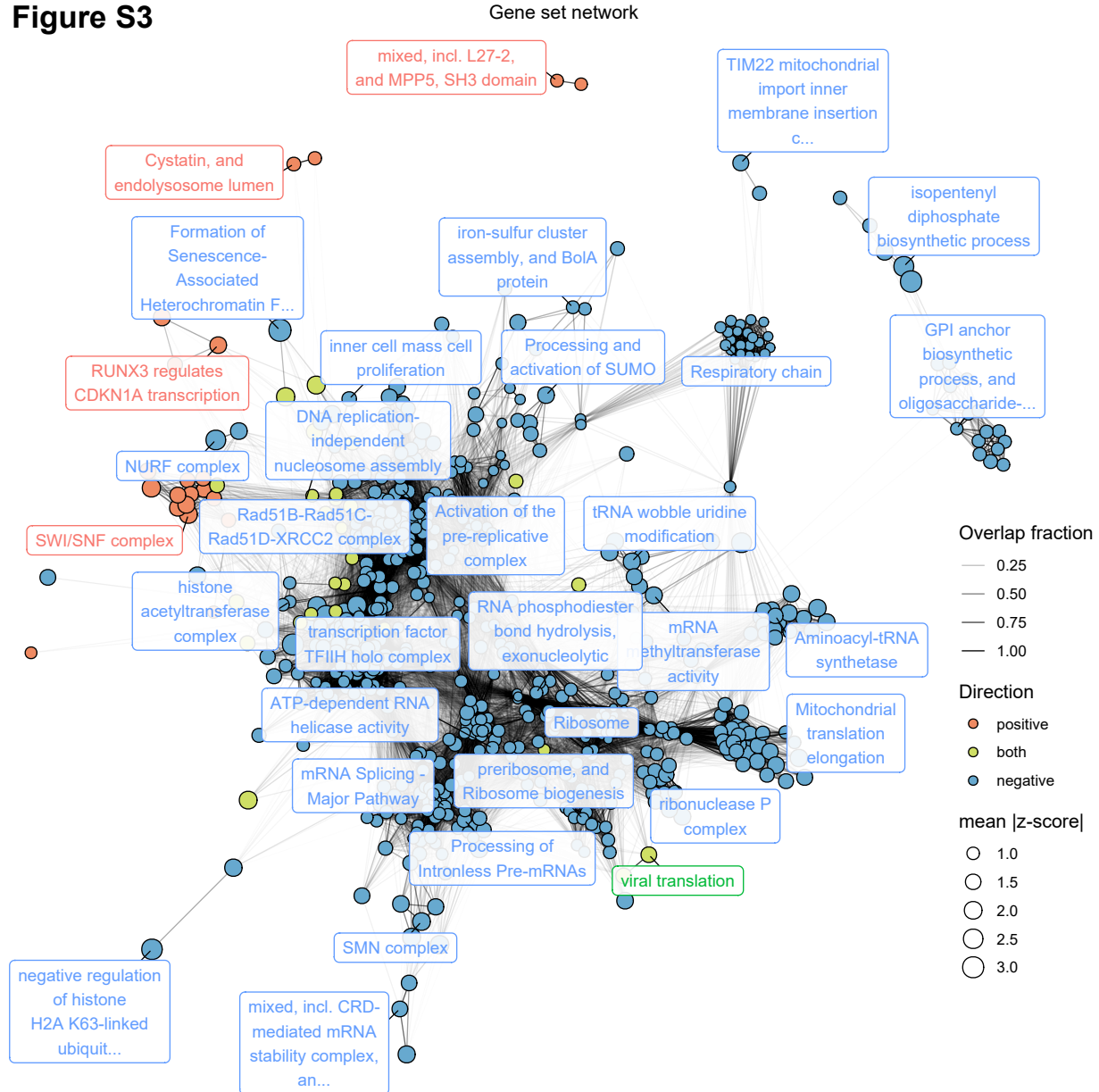
Figure S3

Fig. S3. Network of gene sets. Nodes represent significantly enriched gene sets. The size of each gene set is proportional to its mean absolute z-score. Gene sets are colored by the direction in which they score. Edges represent significant overlap between gene sets. The transparency of each edge is proportional to the fraction of genes shared by two gene sets. Gene sets were clustered using the infomap algorithm and the most central set by PageRank is labelled for each cluster. The Fruchterman–Reingold algorithm was used to lay out the network.
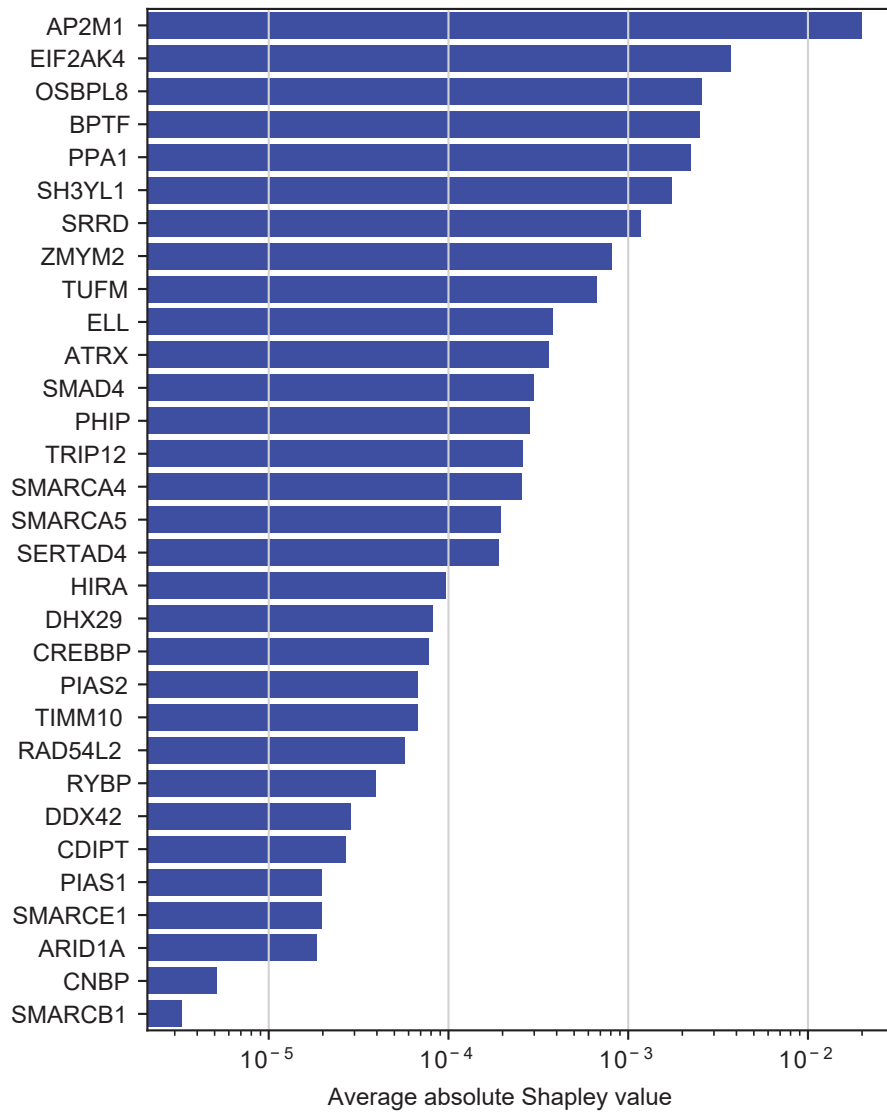
Figure S4

Fig. S4. Feature importance of an infection prediction model trained on single-cell RNA sequencing analysis of infected human bronchial epithelial cells. Genes are ranked by mean of absolute Shapley values, computed from a gradient boosting model.

Table S5. sgRNAs for secondary validation genes

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sgRNA name	Target sequence
ACE2 sgRNA	CCAAAGGCGAGAGATAGTTG
ACVR1B sgRNA	AAGAGATTATTGGCAAGGGT
ARID1A sgRNA #1	CAGCAGAACTCTCACGACCA
ARID1A sgRNA #2	TTTGAATGCAAGATTGAACG
ARID1A sgRNA #3	CCTGTTGACCATACCCGCTG
ATRX sgRNA #1	TGAATTCTATACGATCAAGG
ATRX sgRNA #2	GAAAATCTCAAAAAACGCGG
CABIN1 sgRNA #1	CTGGAGAACCTAACCAACGG
CABIN1 sgRNA #2	TGAAATGATAATCAGCCAGG
CTSL sgRNA	CTGGGGGCCTCATAAAACAG
DOLK sgRNA	GCCAGGGTAGGACCACACCA
DPF2 sgRNA #1	GAAGATACTCCCAAGCGTCG
DPF2 sgRNA #2	TGGATGGAAAAGCGACACCG
DYRK1A sgRNA #1	TGAGAAACACCAATTTCCGA
DYRK1A sgRNA #2	TTCAACCAAAATACACCCGA
DYRK1A sgRNA #3	GAGAAACACCAATTTCCGAG
HIRA sgRNA	TGTGTGCGGTGGTCAAACAG
HMGB1 sgRNA #1	GATACTCACGGAGGCCTCTT
HMGB1 sgRNA #2	AGATACTCACGGAGGCCTCT
HMGB1 sgRNA #3	GTAAGAAGTGTGGGTTTGCT
JMJD6 sgRNA #1	CGGAACCAGAAGTTCAAGTG
JMJD6 sgRNA #2	TGAAAGACCTTACAAGCCCG
KDM6A sgRNA #1	CCTAGCAATTCAGTAACACA
KDM6A sgRNA #2	TCTTTGTATGAACAGCTGGG
PCBD1 sgRNA #1	CACTCTTGTCATGAACCCAA
PCBD1 sgRNA #2	AACTGGACCACCATCCTGAA
PHF6 sgRNA #1	CTTTATCATGCAATGCACAG
PHF6 sgRNA #2	AAAACTGCACATAACTCCGA
PHIP sgRNA	TGGCCGTGAAAATTGCAGGG
PIAS1 sgRNA #1	TAGGACTTGAATGTACGTTG
PIAS2 sgRNA #1	ATACAGTCCAAGTTCAGTTG
PIAS2 sgRNA #2	GATGTGTACAAGTCACTGCA
RAD54L2 sgRNA	TCTGATTGGTGCCAACCGAG
SIAH1 sgRNA #1	CGAAGTGTCCACCATCCCAG
SIAH1 sgRNA #2	CCCATTCTTCAATGTCAGAG
SMAD3 sgRNA #1	AGAAGCGCTCCGAATTGGAG
SMAD3 sgRNA #2	CCACCAGATGAACCACAGCA
SMAD4 sgRNA	AGTCCTACTTCCAGTCCAGG
SMARCA4 sgRNA #1	CTAGGTATGAAGTAGCTCCG
SMARCA4 sgRNA #2	ACCCCCATCCAGAAGCCGCG
SMARCA4 sgRNA #3	GCATGCTCAGAGCCACCCAG
SMARCA5 sgRNA	ATGCATCTAGTAACCAACAG
SMARCE1 sgRNA	TATGTAAGCAAGGTACGCGG
TMPRSS4 sgRNA	CCTGGCGAGTATCATCATTG
UBXN7 sgRNA #1	GTGGCCGGAATAGATCTGCA
UBXN7 sgRNA #2	TCAGGTGCAAGTGAAAGTGT