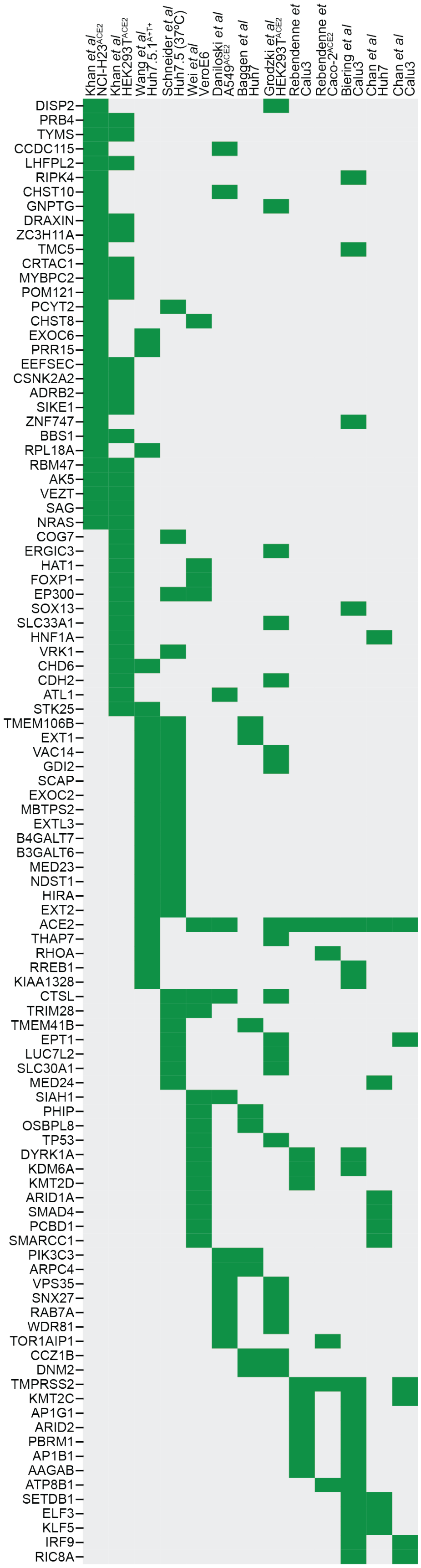

Figure S1. Meta-analysis of multiple CRISPR screens identify common SARS-CoV-2 host-dependency factors. A complete meta-analysis of 10 CRISPR KO studies done between 2020 to 2023, in multiple cell lines (as labelled above the graph) [21-29], reveal overlapping gene hits, represented as green blocks; with the genes labelled on the left. The genes are arranged according to the p-value calculated for NCI-H23^{ACE2} and HEK293T^{ACE2} screen in our study, followed by common clusters of genes from other groups.

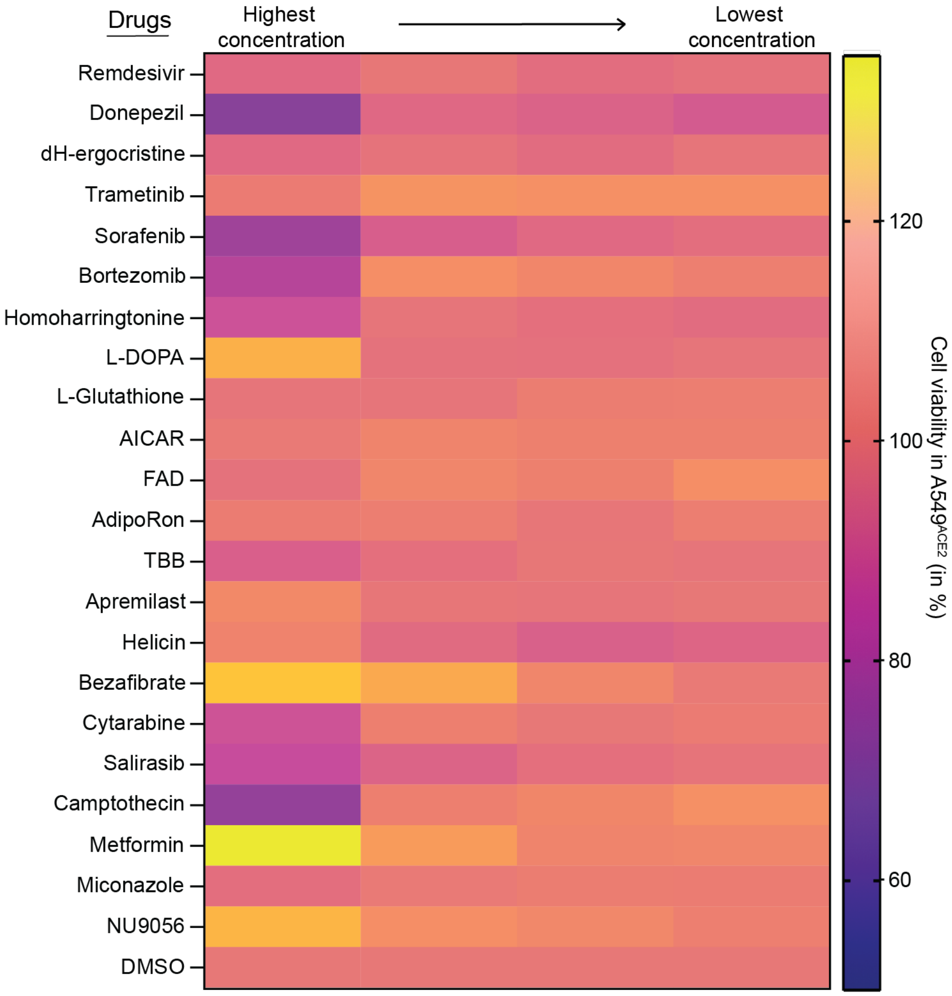

Figure S2. Treatment with drugs from the antiviral screen did not adversely affect cell viability in A549^{ACE2} cells. Using an ATP based cell viability assay, all the drugs tested in the antiviral screen in Figure 2a, were confirmed to not be toxic to A549^{ACE2} cells at corresponding concentrations. Cells were incubated with the drug for 48 hours before testing the cell viability and is represented in the heatmap as relative cell viability (in %), normalized to DMSO treated cells (represented at 100% as orange bars). The scale of cell viability is indicated on the right, with all drugs maintaining cell viability of >70%. The data represent an average of at least three independent experiments.

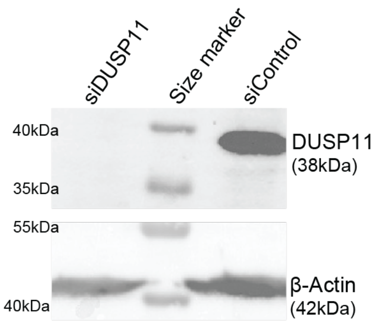

Figure S3. siRNA knockdown and transfection competency of NCI-H23^{ACE2} cells was confirmed by DUSP11 knockdown. Western blot analysis confirmed the knockdown of protein expression of DUSP11 (38kDa), normalized to expression of β-actin (42kDa). The figure is representative of three independent experiments.

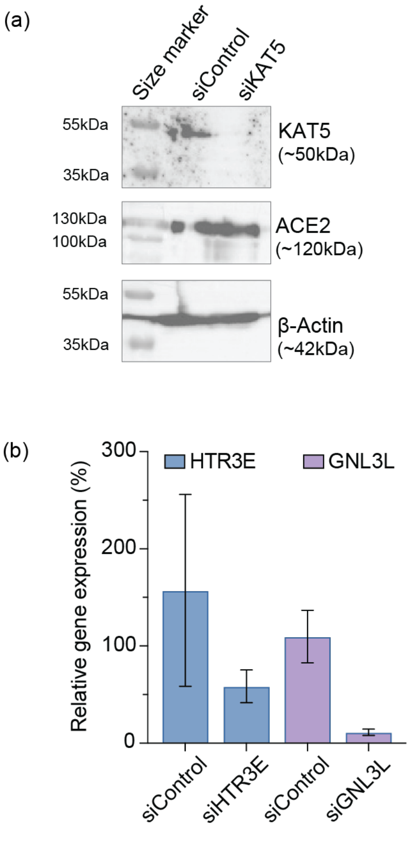

Figure S4. Validation of siRNA knockdown in NCI-H23^{ACE2} cells was performed by Western blot analysis or qPCR quantification. (a) Western blot analysis confirmed complete knockdown of protein expression of KAT5 (50kDa), normal to expression of β-actin (42kDa). ACE2 protein expression was confirmed to remain unchanged post siRNA knockdown. (b) qPCR quantification confirmed the siRNA knockdown by showing reduction in mRNA expression of HTR3E by about 60% (blue bars) and GNl3L by about 90% (purple bars), as compared to mRNA expression in cells targeted by a non-targeting siRNA, siControl.