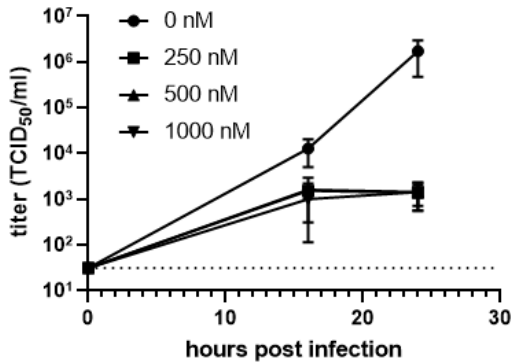


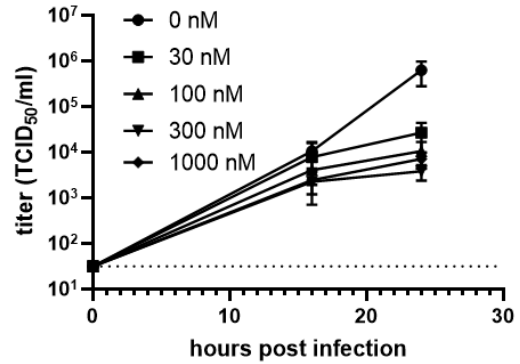
Supporting information

Fig. S1. PTC299 inhibition of SARS-CoV-2 is via inhibition of DHODH

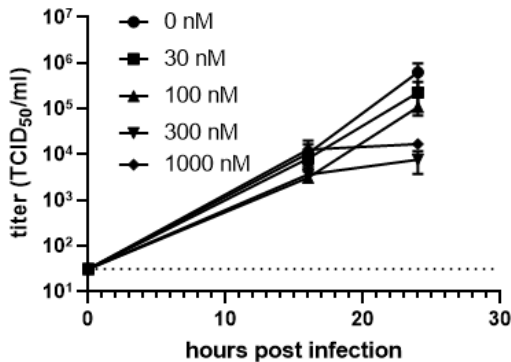
A. 18 hours preincubation with PTC299 prior to viral infection



B. Addition of PTC299 at same time as viral infection



C. Treatment with PTC299 2 hours after viral infection



Legend: Vero cells were treated with PTC299 at the indicated concentrations for 18 hours before, at the same time as, or 2 hours after infection. Cells were inoculated with SARS-CoV-2 (USA-WA1/2020) at a MOI of 0.05. Viral titer was determined by collecting the medium from the infected cells and assessing the concentration required for 50% infectivity of Vero cells (the 50% tissue culture infectious dose assay or TCID₅₀). Data is plotted as the mean and standard deviation of 3 independent replicate.

Table S1. PTC299 potently inhibits cytokine production (p<0.01) – summary of BioMap profile results

Cytokine	Co-culture system	Dose (nM) with p<0.01	% Inhibition
MCP-1	SAg	10, 100	31, 45
CD40	SAg	100	29
IL-8	SAg	10, 100	27, 29
Endothelial Cell Proliferation	SAg	100	23
slgG	BT	10, 100	97, 98
sIL-17A	BT	10, 100	68, 83
s-IL-17F	BT	10, 100	58, 74
s-IL-6	BT	10, 100	53, 72
sTNF α	BT	10, 100	49, 66
B cell proliferation	BT	100	31
MCP-1	HDFSAg	100	33
IL-8	HDFSAg	10, 100	25, 44
MMP-1	HDFSAg	100	23
sIL-10	HDFSAg	10, 100	73, 81
sIL-17A	HDFSAg	10, 100	57, 74
sIL-17F	HDFSAg	1, 10, 100	46, 86, 83
sIL-2	HDFSAg	10, 100	47, 68
sIL-6	HDFSAg	1, 10, 100	33, 91, 96
sTNF α	HDFSAg	100	35
sVEGF	HDFSAg	1, 10, 100	90, 84, 60
MCP-1	/TH2	10, 100	21, 25
sIL-17	/TH2	100	23

Abbreviations: BCR, B-cell receptor; BT System, co-culture of CD19+ B cells and PBMC that utilizes BCR stimulation and sub-mitogenic TCR stimulation; HDFSAg system, co-culture of human primary dermal fibroblasts and PBMC that is stimulated with sub-mitogenic TCR levels; IL, interleukin; PBMC, Peripheral Blood Mononuclear Cell; SAg system, co-culture of endothelial cells and PBMC stimulated with mitogenic levels of TCR ligands; TCR, T-cell receptor; /TH2 system, co-culture of endothelial cells and Th2 blasts stimulated with TCR ligands and cytokines; Th2, T helper type 2; VEGF, vascular endothelial growth factor.

Each BioMap assay was performed once. The dose response is consistent across all four different model systems that assessed cytokine production and release into the cell culture medium, suggesting that the results are robust.