**Supplementary Figure Captions**

**Supp. Figure 1. Cell viability following Tg treatment or HCoV-229E infection. (A)** A549 cells were treated with the indicated concentrations of Tg for 30 minutes, then washed and incubated in normal media for 48 hours. (B) A549 cells were mock-treated, or treated with DMSO or Tg (0.5 μM) for 30 minutes, then washed and mock-infected or infected with HCoV-229E (MOI 0.05 or MOI 0.5) for 48 h. Cell viability was assessed by Alamar blue assay. Graphs show means +/- SD from 2 independent experiments performed in technical triplicate. Statistical significance was assessed by one-way or two-way ANOVA.

Supp. Figure 2. Effect of Tg on HCoV-229E infection and UPR activation in Huh7 cells. (A-D) Huh7 cells were primed with DMSO or Tg at the indicated concentrations for 30 minutes, then washed and infected with HCoV-229E. At 24 hpi, cell lysates and supernatants were collected. (A, D) Expression of HCoV-229E N gene or UPR target genes (CHOP, HERPUD1 and Xbp1s) was assessed by RT-qPCR. (B) Extracellular viral titers were determined by plaquing assay on Huh7 cells. (C) Cell viability was assessed by Alamar blue assay. Graphs show means +/- SD from 2-3 independent experiments, with qPCR performed in technical triplicate. Statistical significance was assessed by one-way ANOVA (*$p<0.05$, **$p<0.01$, ****$p<0.0001$).

**Supp. Figure 3. Silencing of UPR sensors and the effect on HCoV-229E protein expression in the presence or absence of Tg**. **(A-D)** Band density analysis was performed in Fiji ImageJ and are expressed relative to the band density ratio obtained in shCTRL DMSO condition. Representative western blots are shown in Figure 3B-D. (B) Xbp1s expression was evaluated in shCTRL or shIRE1 cells following priming with DMSO or Tg. Graphs show means +/- SD from

2 independent experiments. Statistical significance was assessed by two-way ANOVA (*p<0.05, **p<0.01, ***p<0.001).

**Supp. Figure 4. Cell viability following treatment with UPR activators.** A549 cells were primed with Tg for 30 minutes, or treated with the indicated UPR activators (10 μM IXA5; 10 μM AA147; 5 μM CCT020312; or a combination of all three) for 24 h. Cell viability was then assessed by Alamar blue assay and is expressed as percentage relative to DMSO. Graph shows means +/- SD from 1-3 independent experiments performed in technical triplicate. Statistical significance was assessed by one-way ANOVA (****p<0.0001).