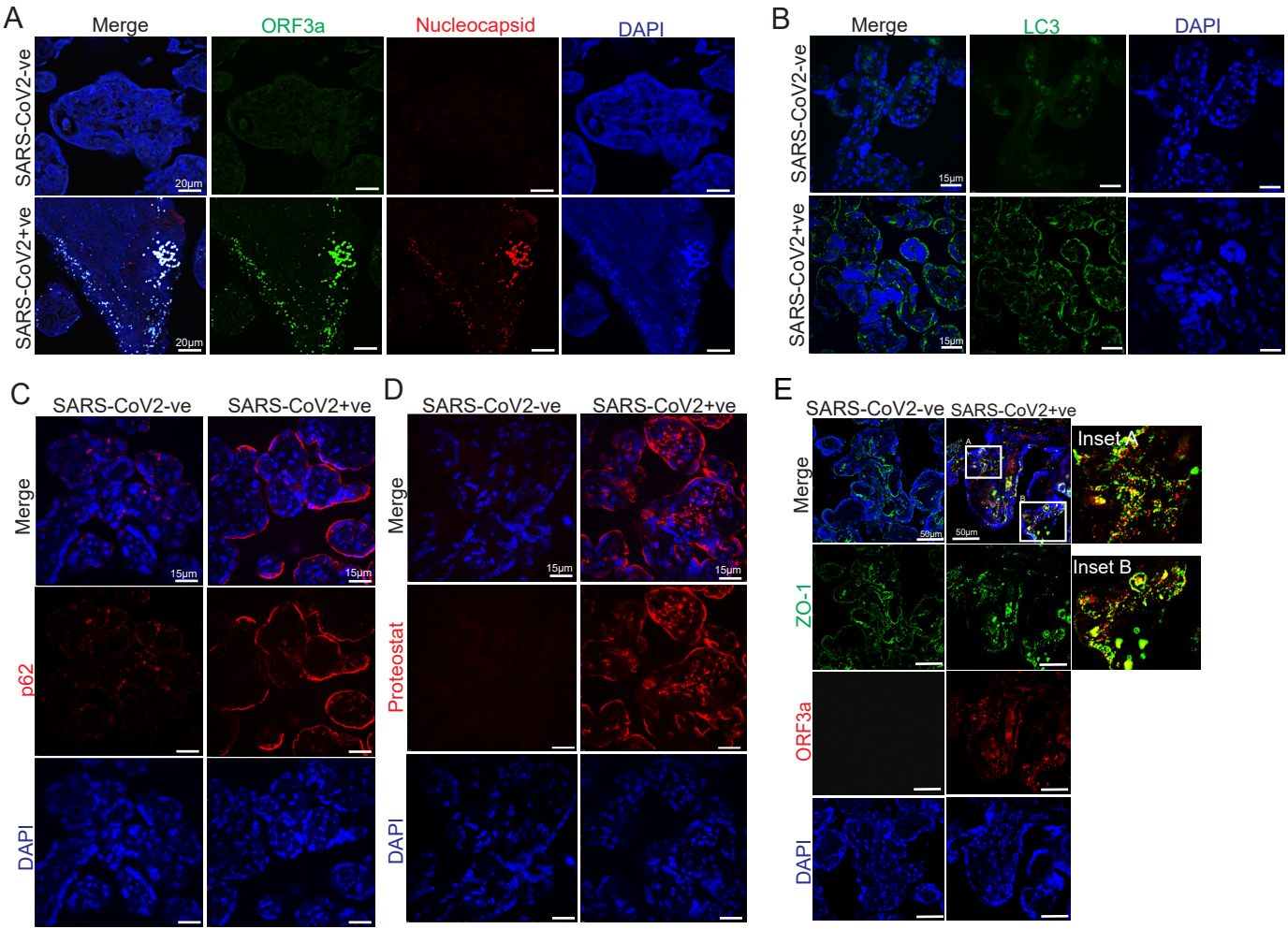
Supplementary Figure 1: SARS-CoV-2 infection of human term placenta. (A) Representative confocal microscopy images illustrating the presence of ORF3a (green) and Nucleocapsid (red) in term placentas infected with SARS-CoV-2. Scale bar = 20 μm; 20X magnification objective. **(B)** Immunostaining for the autophagy marker LC3 reveals heightened staining in SARS-CoV-2-infected term placenta relative to uninfected tissues. Scale bar = 15 μm; 60X magnification**. (C)** Representative image illustrating increased immunostaining for the autophagy adaptor protein p62 in SARS-CoV-2-positive term placentas relative to uninfected controls. Scale bar = 15 μm; 60X magnification. **(D)** Representative confocal image illustrating enhanced Proteostat staining, signifying higher protein aggregation, in SARS-CoV-2-positive placentas relative to uninfected term placentas. Scale bar = 15 μm; 60X magnification. **(E)** Representative confocal microscopy images of SARS-CoV-2 uninfected and infected term placenta demonstrate the co-localization of ORF3a (red) with ZO-1 (green), producing a merged yellow signal (inset A and B). Scale bar = 50 μm; 40X magnification.

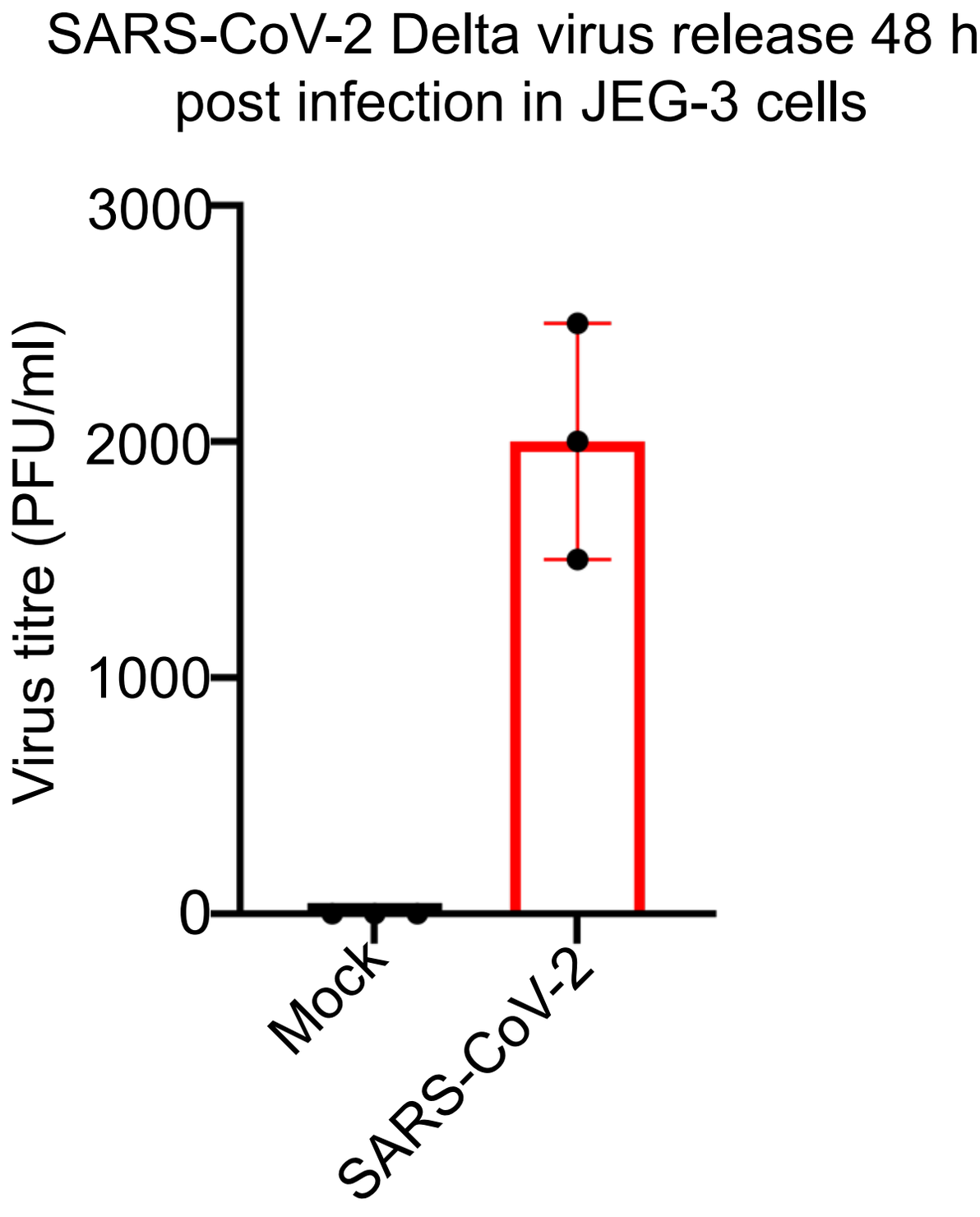
Supplementary Figure 2: Viral titer in JEG-3 cells. JEG-3 cells infected with Delta (MOI 1) and virus titer assayed though plaque assay 48 h post infection compared to mock.

Supplementary Figure 3: Impact of autophagy modulators on JEG-3 cells. JEG-3-LC3-EGFP-mCherry cells treated with bafilomycin or metformin were compared to untreated controls. Bafilomycin treatment led to the accumulation of yellow puncta (co-localized GFP-LC3 and mCherry-LC3), indicating a buildup of autophagosomes due to blocked autophagic flux. In contrast, metformin treatment showed fewer yellow puncta and more red-only vesicles (mCherry-LC3), consistent with increased autolysosome formation and ongoing autophagy

Supplementary Figure 1: SARS-CoV-2 infection of human term placenta.



Supplementary Figure 2: Viral titer in JEG-3 cells.



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