

Supplementary Figure 1: Cleaved Caspase 3 Staining in Retinal Cells.

Representative immunofluorescence (n=3) images showing immunostaining for Cleaved Caspase 3 (CL Casp.3, green), ZIKV (red), and DAP (blue) in ARPE19, MIO-M1, CEC, and 661W cells at 48h post ZIKV infection.



**Supplementary Figure 2: AXL Staining in Retinal Cells.** Representative immunofluorescence (n=3) images showing immunostaining for AXL (green), ZIKV (red), and DAP (blue) in ARPE19, MIO-M1, CEC, and 661W cells at 48h post ZIKV infection and mock treatment.



**Supplementary Figure 3: ISG15<sup>-/-</sup> Mice Have More Viral Antigens in the Retina as Compared to WT Mice.** The eyes of 57BL/6 and ISG15<sup>-/-</sup> mice (n=4) were challenged with ZIKV intravitreally at 10<sup>4</sup> PFU PRVABC59. Representative immunofluorescence images showing ZIKV (4G2 red, indicated by the yellow arrows) and DAP (blue) staining in various retinal layers of WT and ISG15<sup>-/-</sup> mice. RPE; retinal pigmented epithelial layer, ONL; outer nuclear layer, INL; inner nuclear layer, GCL; ganglion cell layer