



**Supplementary Figure 1.** No viral resistance in naïve ISG15-deficient cells. Near confluent A549 or A549-ISG15<sup>-/-</sup> (B8) cells in 6-well plates were infected with the indicated virus at dilution that allow the formation of discrete plaques. Following 6 days infection, cells were fixed and either stained with toluidine blue O (HPIV2 strain Collindale and PIV5 strain W3-infected cells) or immunostained (HPIV3 strain Washington using antibodies specific for HPIV3 nucleoprotein).