



FIG S6 The ABSL3 SARS-CoV-2 infection model and associated viral titers. (A) 50 female mice were housed at a ratio of 5 mice/cage in an ABSL3 facility. Three cages of mice were infected with each variant ($n=45$ mice, $n=15$ per variant) and one cage of mice was uninfected ($n=5$ mice). One cage of mice was sacrificed for each variant at days 2, 4, and 7 for lung viral titer assessment. Any mice reaching a sacrificial endpoint (weight loss of 15% or body conditioning scale (BCS) < 2) were euthanized and removed from the experiment on days 5 and 6. All remaining mice were sacrificed on day 7. (B) Lung viral titers for each variant are shown as described in (23) with mean \pm sem plotted at each timepoint. Statistics represent 2 way-ANOVA and where titer is a function of variant and time, and the p -value for variant between the indicated comparisons is displayed. The limit of detection (LOD) for viral plaques is indicated by a gray, dashed line (LOD=10 plaque forming units (PFU) per mL). SARS-CoV-2 envelope (E) gene qPCR (C) or nucleocapsid (N) gene qPCR (D) was conducted on tissue from animals harvested at day 7 post infection. The unadjusted Dunn's post-test of Kruskal Wallis analysis of variance is displayed for the groups with $p<0.05$ and all non-displayed comparisons are not significant. Uninfected mice were sacrificed and included as controls; given they were never infected with SARS-CoV-2 a day of infection of 0 was assigned in the figure. For (A) $n=10$ unique cages with 55 total samples from 50 mice. In (B) $n=12$ mice for WA1, $n=13$ mice for Delta, and $n=15$ mice for Omicron infected mice. In (C-D) each data point reflects one mouse ($n=2-4$ mice per group and timepoint). (E) Experimental design for C57BL/6J background infected mice. (F) PFUs from indicated body sites ($n=5$ mice per group) and statistics reflect Mann-Whitney U test between groups for lung samples. Live virus was not detected (nd) from Gut and Stool. LOD=10 PFU per mL and is indicated by a gray, dashed line.