## Supplementary Materials

# The impacts of antivirals on the coronavirus genome structure and subsequent pathogenicity, virus fitness and antiviral design 

Ching-Hung Lin ${ }^{1}$, Cheng-Yao Yang ${ }^{1}$, Shan-Chia $\mathbf{O u}^{2}$, Meilin Wang ${ }^{3}$, Chen-Yu Lo ${ }^{1}$, Tsung-Lin Tsai ${ }^{1}$, Hung-Yi Wu ${ }^{1 *}$<br>1 Graduate Institute of Veterinary Pathobiology, College of Veterinary Medicine, National Chung Hsing University, Taichung 40227, Taiwan; tw23whale@hotmail.com (C.-H.L.); yangchengyao@nchu.edu.tw (C.-Y. Y); axfbji7917@gmail.com (C.-Y.L.); windtaker10@msn.com (T.-L.T.)<br>2 Graduate Institute of Microbiology and Public Health, College of Veterinary Medicine, National Chung Hsing University, Taichung 40227, Taiwan; scou@dragon.nchu.edu.tw (S.-C.O.)<br>3 Department of Microbiology and Immunology, School of Medicine, Chung-Shan Medical University and Clinical Laboratory, Chung-Shan Medical University Hospital, Taichung 40201, Taiwan ; wml@csmu.edu.tw (M. W.)<br>* Correspondence; E-Mail: hwu2@dragon.nchu.edu.tw (H.-Y.W.); Telephone: +886-4-22840369; Fax: +886-4-22862073

## Supplementary Figures


$S_{1}$ subunit

|  | 331 | 617618 |  |  | 686687 |  |  | 768 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | B |  | C |  |  | D |  |  |
| a.a. position |  |  |  | 677 |  |  |  | 768 |
| Wt10-HRT |  |  |  | R |  |  | G | R |
| Wt10-ML |  |  |  | R |  |  | v | R |
| WtGS10-ML |  |  |  | K |  |  | G | S |
| WtIC10-ML |  |  |  | T |  |  | G | S |



$S_{1}$ subunit

$\mathrm{S}_{2}$ subunit


Figure S1. Comparison of the $S$ protein aa sequences identified from HRT-18 cells and ML cells infected with wt BCoV and its variants. (A) Linear schematic of BCoV S protein showing the comparison of the aa sequences for Wt10-ML, WtGS10-ML and WtIC10-ML identified from ML cells infected with Wt10, WtGS10 and WtIC10, respectively, at VP10. (B) Linear schematic of BCoV S protein showing the comparison of the aa sequences identified from HRT-18 cells under the treatments of antiviral GS5734 (WtGS10-HRT, i.e., WtGS10 in Figure 1) and poly IC-induced innate immunity (WtIC10-HRT, i.e., WtIC10 in Figure 4) at VP10. Wt10-HRT (i.e., Wt10 in Figures 1 and 4): Viral RNA collected from HRT-18 cells infected with wt BCoV at VP10.

