

# Hesperidin is a potential inhibitor against SARS-CoV-2 infection

Fang-Ju Cheng<sup>1</sup>, Thanh Kieu Huynh<sup>2</sup>, Chia-Shin Yang<sup>3</sup>, Dai-Wei Hu<sup>2</sup>, Yi-Cheng Shen<sup>2,4</sup>, Chih-Yen Tu<sup>4,5</sup>, Yang-Chang Wu<sup>6</sup>, Chih-Hsin Tang<sup>2,5</sup>, Wei-Chien Huang<sup>1,2,7,8,\*</sup>, Yeh Chen<sup>1,3,\*</sup>, Chien-Yi Ho<sup>9,10,\*</sup>

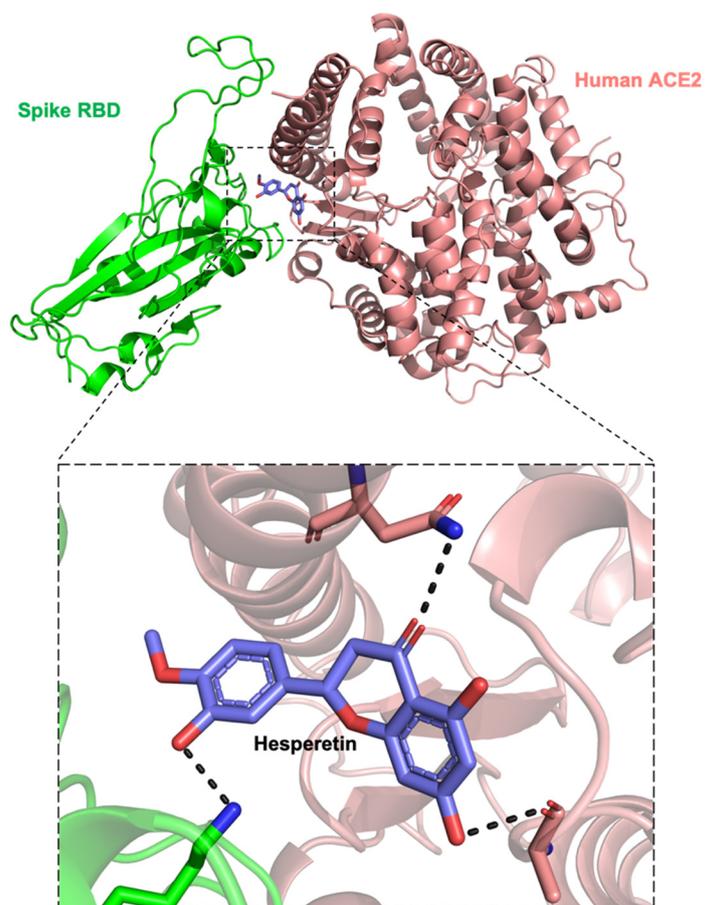
## **This PDF file includes:**

**Figure S1.** The docking simulation of hesperetin in the pocket of human ACE2 bound to viral S protein.

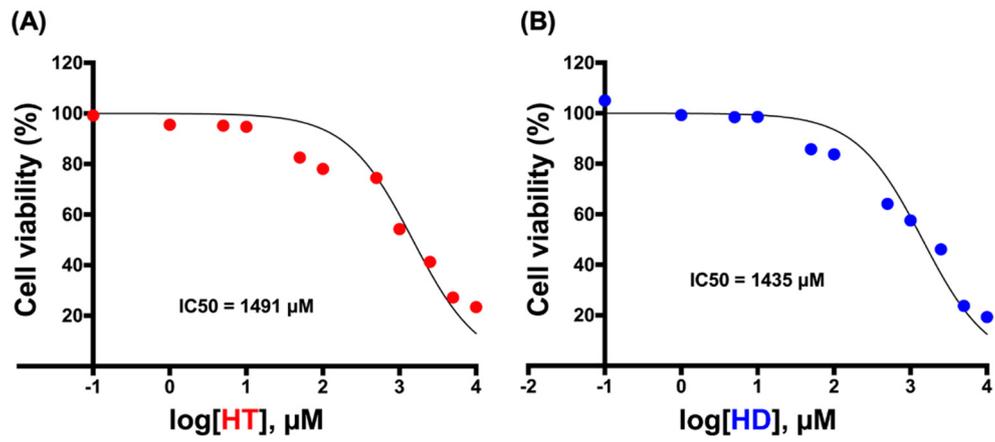
**Figure S2.** The effect of HT/HD on the viability of VeroE6 cells.

**Figure S3.** The effect of HT and HD on the mRNA expressions of ACE2 and TMPRSS2.

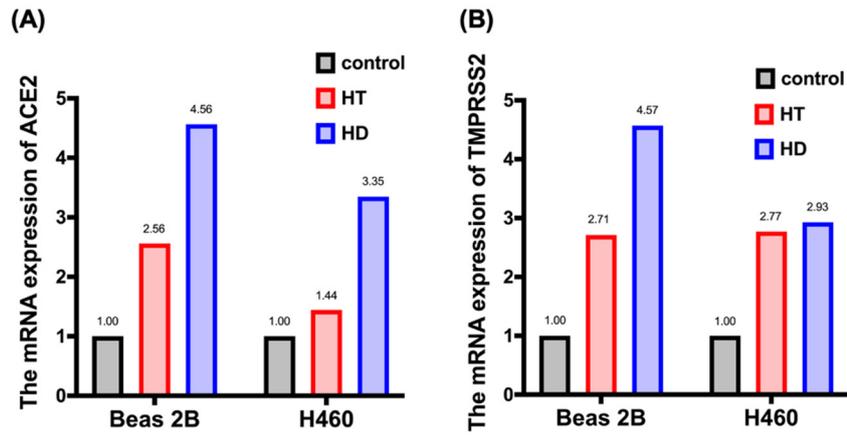
**Figure S4.** Short term treatment with HT impedes the infection of SARS-CoV-2 pseudovirus into VeroE6 cells.



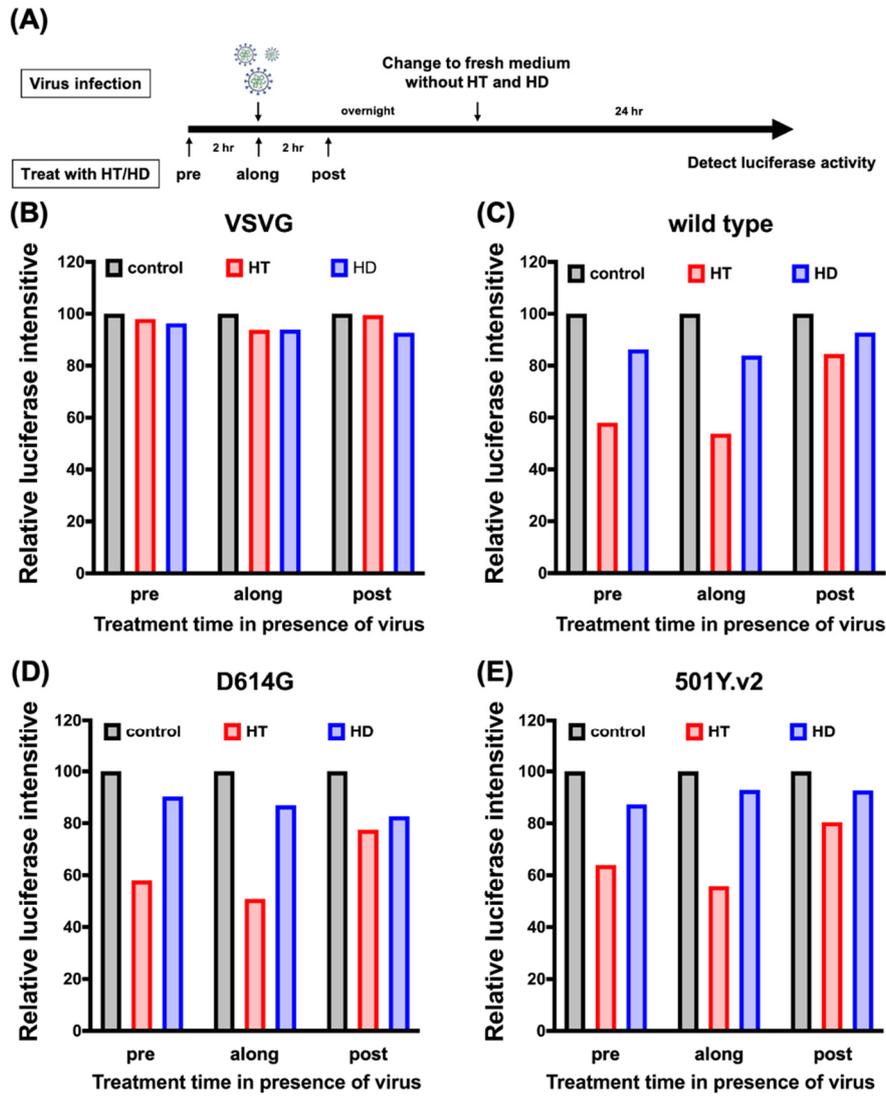
**Figure S1.** The docking simulation of hesperetin in the pocket of human ACE2 bound to viral S protein. Compound-protein interaction of HT with the site of ACE2 bound to S protein was generated by using Discovery Studio.



**Figure S2.** The effect of HT/HD on the viability of VeroE6 cells. VeroE6 cell line was treated with HT and HD in a dose-dependent manner for 2 days and the viability was determined in MTT assays.



**Figure S3.** The effect of HT and HD on the mRNA expressions of ACE2 and TMPRSS2. Beas 2B and H460 cell lines were treated with 100  $\mu$ M of HT or HD for 2 days, and the mRNA expressions of ACE2 (A) and TMPRSS2 (B) were examined in RT-qPCR analysis.



**Figure S4.** Short term treatment with HT impedes the infection of SARS-CoV-2 pseudovirus into VeroE6 cells. VeroE6 cells were treated with 100  $\mu$ M of HT or HD 2 hours before (as indicated as “pre”), along (as indicated as “along”), or after (as indicated as “post”) virus infections of VSVG pseudotyped vector (B), or SARS-CoV-2 pseudoviruses with wild type (C), D614G (D), and 501Y.v2 (E) of S protein followed by the measurement of luciferase activity.