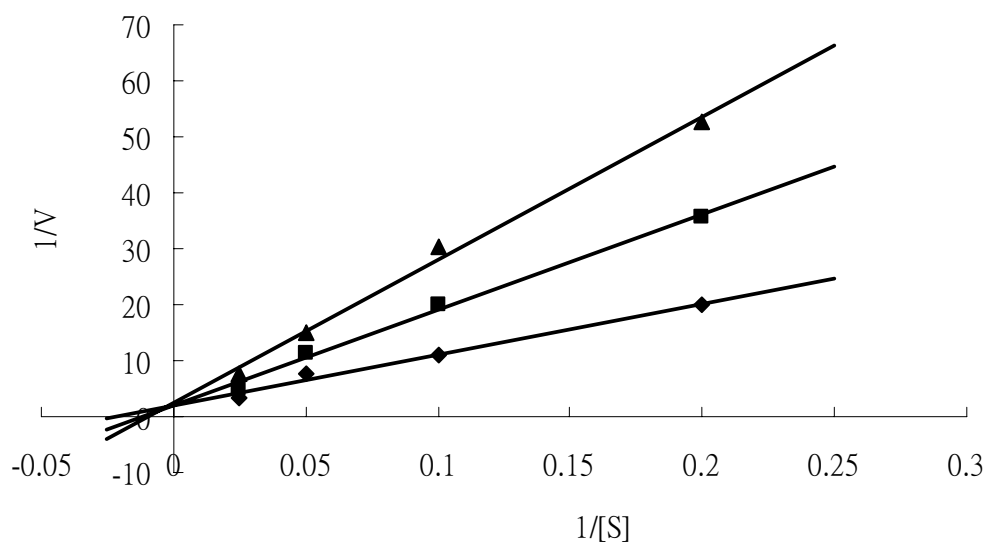
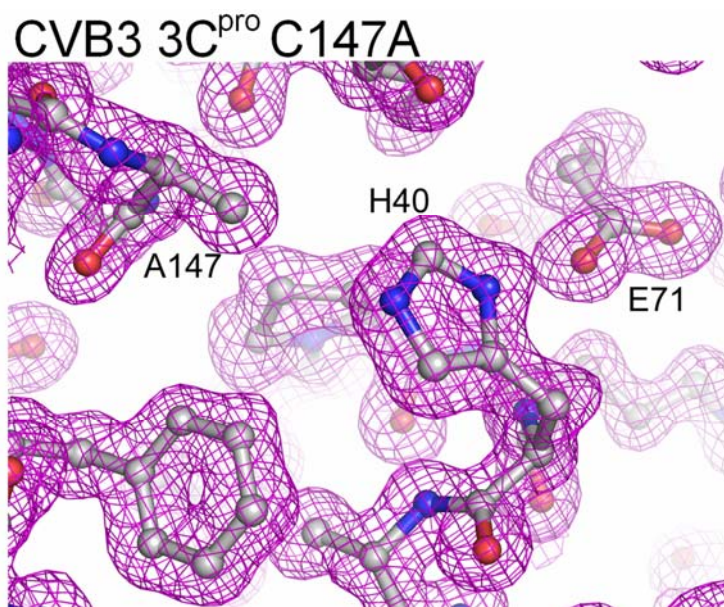


SUPPLEMENTARY



**Figure S1.  $K_i$  of EPDTC against CVB3 3C<sup>pro</sup>.** The CVB3 3C<sup>pro</sup> activities were measured under 5-40  $\mu$ M fluorogenic substrate in the absence ( $\blacklozenge$ ) or presence of 2.5  $\mu$ M ( $\blacksquare$ ) and 5  $\mu$ M ( $\blacktriangle$ ) EPDTC, respectively. The data gave the  $K_i$  value of  $4.4 \pm 0.7$   $\mu$ M. The inhibition pattern indicates that EPDTC is competitive with respect to the substrate.



**Figure S2. Electron density map of CVB3 3C<sup>pro</sup> C147A mutant.** The structure are superimposed on  $2F_o-F_c$  electron density maps (magenta) countered at  $1.0 \sigma$  level. In active site, the catalytic residue Cys<sup>147</sup> was mutated to Ala. The protein residues are shown as ball-and-stick model with gray carbon, the nitrogen and oxygen atoms are colored in blue and red, respectively.