

Electronic supplementary information (ESI)

The Q41R mutation in HCV-protease enhances the reactivity towards MAVS by suppressing non-reactive pathways

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Supplementary Figures

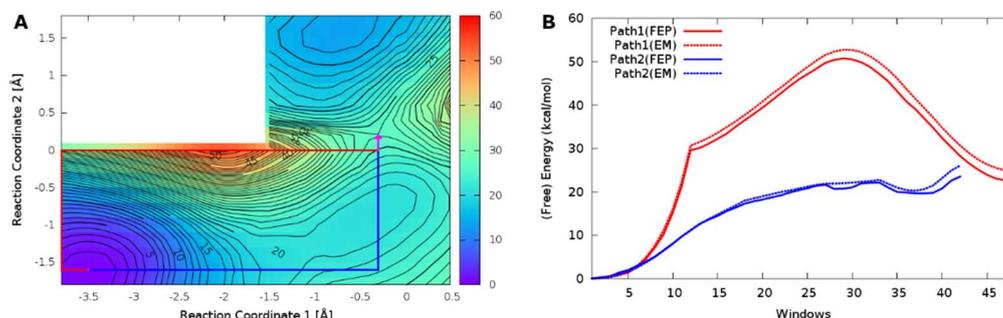


Figure S1. (A) Two paths connecting the reactant state and the second transition state on the potential energy surface of the acylation reaction for the wild type HCV NS3/4A protease bound to MAVS with non-reactive conformation calculated at the B3LYP/def2-TZVP level. (B) Free energy differences (solid lines) calculated by QM/MM FEP and energy differences (dashed lines) calculated by single point QM/MM calculations along two different paths. The scan path is shown in red and another path is shown in blue.

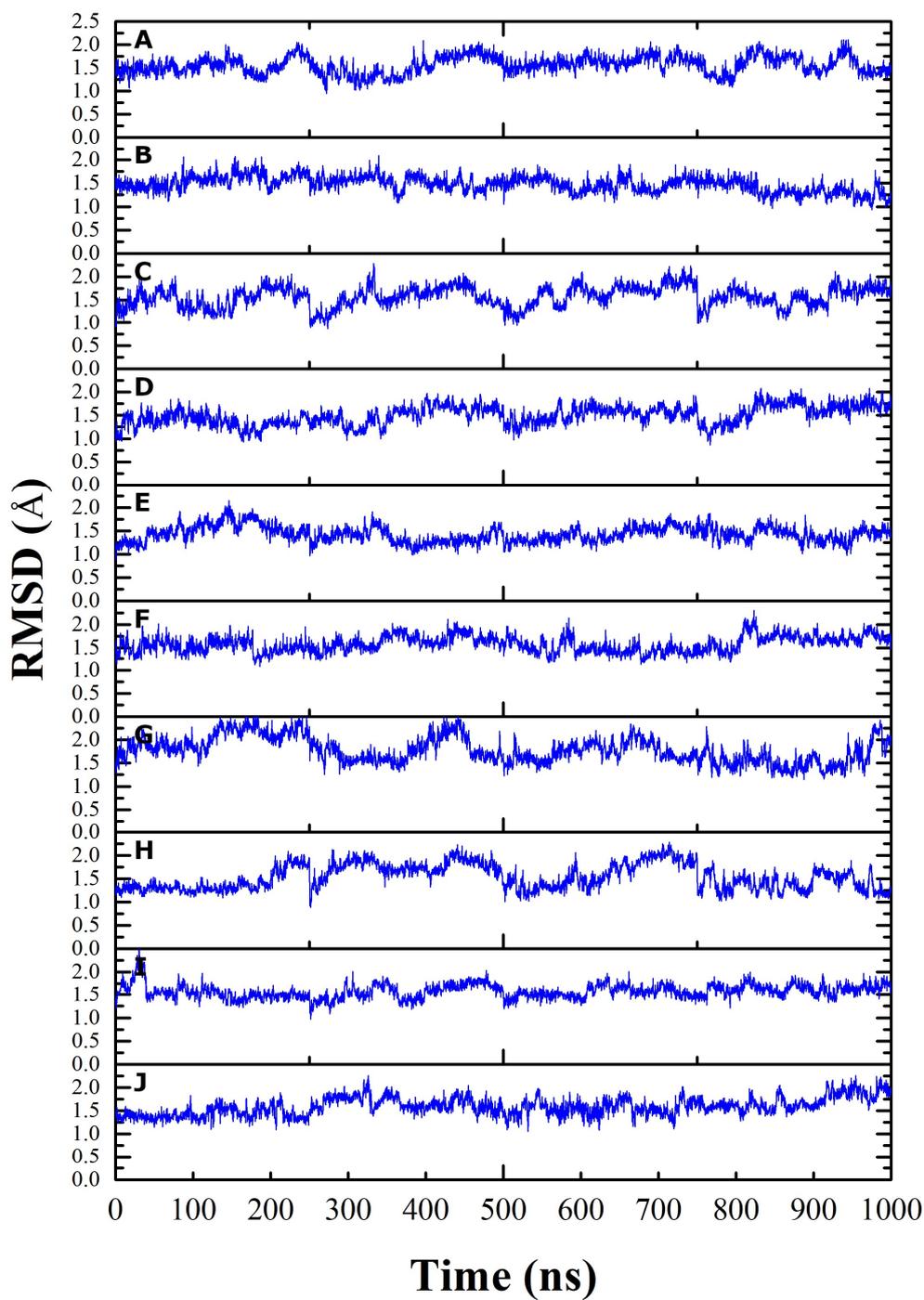


Figure S2. RMSD plots of the backbone of the protein-substrate complex with respect to its initial structure of production simulation for (A) WT-MAVS, (B) D168A-MAVS, (C) R155K-MAVS, (D) Q41R-MAVS, (E) Q41R-D168A-MAVS, (F) WT-NS4AB, (G) D168A-NS4AB, (H) R155K-NS4AB, (I) Q41R-NS4AB, and (J) Q41R-D168A-NS4AB.

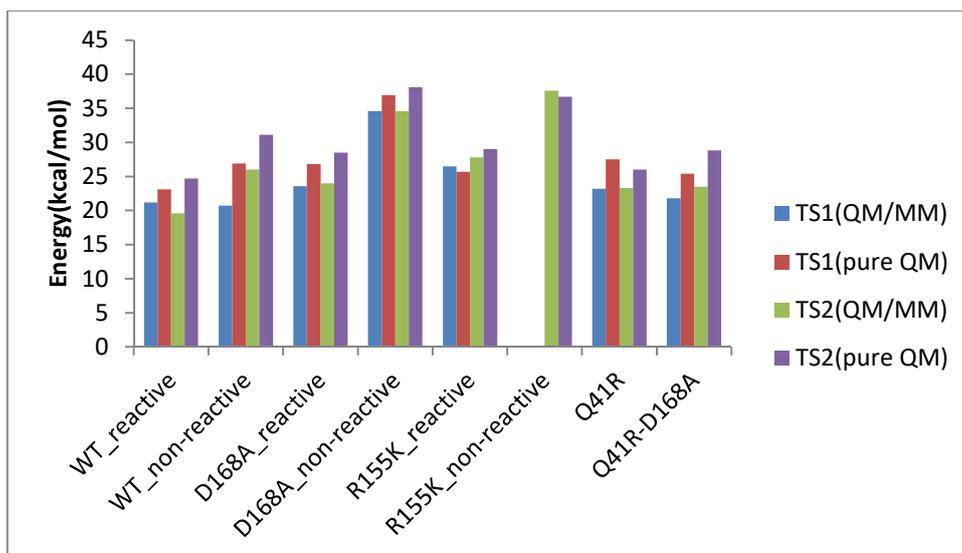


Figure S3. Relative QM/MM single point energies and pure QM energies (without MM part) of both transition states for HCV NS3/4A protease variants bound to MAVS.