Structural proteomics-driven targeted design of favipiravir-binding site in the RdRp of SARS-CoV-2 unravels susceptible hotspots and resistance mutations

Aditya K. Padhi[1], Jagneshwar Dandapat[2,3], Vladimir N. Uversky[4], and Timir Tripathi[5*]

[1]Laboratory for Structural Bioinformatics, Center for Biosystems Dynamics Research, RIKEN, Yokohama, Kanagawa 230-0045, Japan

[2]Centre of Excellence in Integrated Omics and Computational Biology, Utkal University, Bhubaneswar 751004, Odisha, India

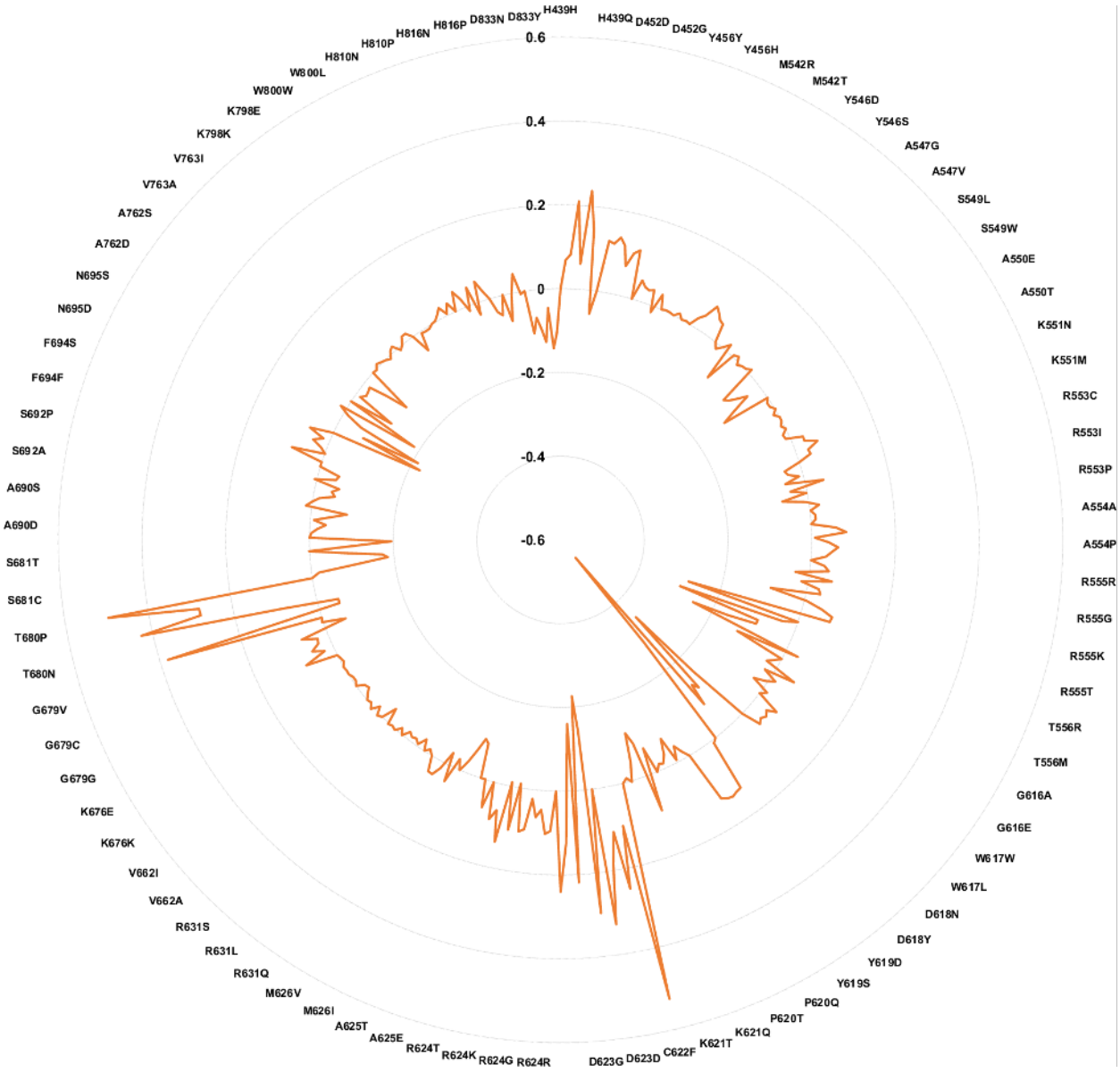
[3]Post Graduate Department of Biotechnology, Utkal University, Bhubaneswar 751004, Odisha, India

[4]Department of Molecular Medicine and Byrd Alzheimer's Research Institute, Morsani College of Medicine, University of South Florida, Tampa, FL 33620, United States

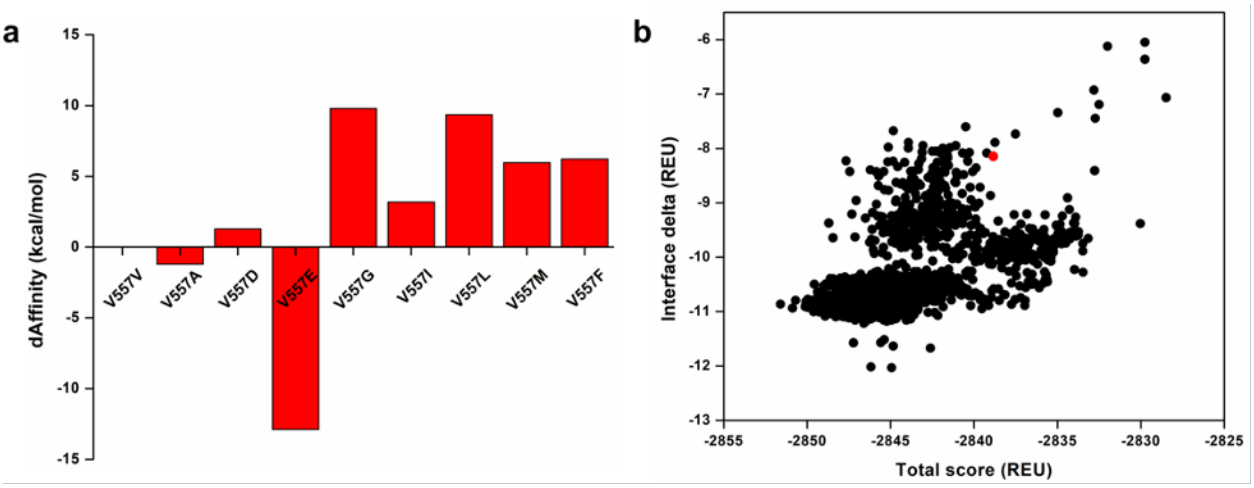
[5]Molecular and Structural Biophysics Laboratory, Department of Biochemistry, North-Eastern Hill University, Shillong- 793022, India

***Corresponding author:**

Dr. Timir Tripathi, Department of Biochemistry, North-Eastern Hill University, Shillong-793022, India. Email: timir.tripathi@gmail.com, Tel: +91-364-2722141; Fax: +91-364-2550108



Supplementary Figure 1. Relative binding affinities of all the 350 designs from the favipiravir-interacting nsp12 residues. Radar plot showing the MOE-computed relative binding affinities (dAffinities) for all the 350 favipiravir-interacting nsp12 designs. The dAffinity values range from -0.54 to 0.52 kcal/mol.



Supplementary Figure 2. MOE- and Rosetta-based binding affinity scores for the V557L remdesivir-resistant mutant of SARS-CoV. (a) MOE- and (b) Rosetta-based binding affinity scores showing the V557L design was among the low-affinity designs against remdesivir, indicating its potential role in the emergence of drug resistance.