Discovery of potential compounds for active against coxsackievirus A16 and enterovirus A71 by virtual screening

Amita Sripattaraphan[1], Kamonpan Sanachai[1], Warinthorn Chavasiri[2], Siwaporn Boonyasuppayakorn[3] and Thanyada Rungrotmongkol[1,4] *

[1] Structural and Computational Biology Research Unit, Department of Biochemistry, Faculty of Science, Chulalongkorn University, Bangkok, Thailand
[2] Department of Chemistry, Faculty of Science, Chulalongkorn University, Bangkok 10330, Thailand
[3] Department of Microbiology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand
[4] Ph.D. Program in Bioinformatics and Computational Biology, Faculty of Science, Chulalongkorn University, Bangkok 10330, Thailand
* Correspondence: t.rungrotmongkol@gmail.com

Abstract: Outbreaks of hand, foot, and mouth disease (HFMD) occur around the world. It is caused by the Coxsackievirus-A16 (CV-A16) and Enterovirus-A71 (EV-A71) that belong to the Enterovirus genus. Unfortunately, neither an anti-HFMD drug nor a vaccine is currently available. Rupintrivir, one of the drug candidates for HFMD treatment, has been attractive for the development of its analogs with broad biological activities. This drug is an inhibitor for 3C protease of CV-A16 and EV-A71, an enzyme that plays a crucial role in the viral replication process. Pharmacophore modeling and structure-based virtual screenings have become the most effective method and are successfully applied in drug discovery. The virtual screening of a large number of compounds in the database can identify the best molecular structure. In the present study, pharmacophore models were generated using the LigandScout 4.2 program, starting from trajectories obtained from the last 50 ns of simulations of the 3Cprotease of EV-A71 and CV-A16 complexed with the rupintrivir. Subsequently, compound libralies i.e., drug database (Drugbank and flavonoids) were screened. The obtained hits compounds will be analyzed in more detail by molecular docking, followed by extensive MD simulations of the complexes. The highest-ranked compound from this procedure will be synthesized and tested on its inhibitory efficiency by experimental assays.

Keywords: Hand foot and mouth disease (HFMD), Coxsackievirus A16, Enterovirus A71, Rupintrivir, pharmacophore based virtual screening