Structure-Based Repurposing of FDA-Approved Antiviral Drugs targeting hMPV F Protein: Insights from Molecular Docking and Dynamics Analysis

Jeyanthi Sankar[1], Dr. M. Karthikeyan[1,2*]

[1]Pharmacogenomics and CADD Lab, Department of Bioinformatics, Alagappa University, Karaikudi-630 003, Tamil Nadu, India.

[1.2*]Research officer, TamilNadu Council for Higher Education (TANSCHE), Kamarajar Salai, Triplicane, Chennai-600 005, Tamil Nadu, India.

Email ID: mkbioinformatics@gmail.com

Abstract

Humanmetapneumovirus (hMPV) infection can pose a serious threat since it leads to a number of respiratory diseases and other complications HMPV is a major contributor to pneumonia in infants, older adults, and immunocompromised populations worldwide with high mortality. The lack of approved antiviral therapies or vaccines for HMPV places a significant strain on global healthcare systems. Drug repurposing has emerged as a promising strategy for managing both emerging and established diseases, as it offers a faster and more cost-effective alternative to conventional drug discovery. This study employs advanced computational approaches to identify promising antiviral candidates against HMPV, with a particular focus on FDA-approved antiviral drugs and selected control compounds. Considering the essential role of the co-receptor heparan sulfate (HS) in facilitating hMPV F attachment and host-cell entry, selected FDA-approved drugs was screened as potential hMPV F inhibitors using structure-based computational approaches targeting the fusion protein of hMPV. Key findings highlight Raltegravir and Sofosbuvir as the most promising candidates, with superior binding energies (-9.2 kcal/mol and – 7.0 kcal/mol, respectively), and stable interaction profiles. ADMET profiling confirmed their high bioavailability and low toxicity, positioning these drugs for repurposing against HMPV. Furthermore, 100-ns MD simulations revealed that Raltegravir forms a stable and persistent complex with the hMPV F protein. This integrative study underscores the potential of computational tools in streamlining drug discovery and advancing therapeutic interventions. Overall, the findings highlight Raltegravir as promising repurposed therapeutic candidates for targeting hMPV F.

Keywords: Human Metapneumovirus (HMPV), Drug Repurposing, Antiviral Therapeutics, Molecular Docking, Molecular Dynamics Simulations.