Title : Applying Pharmacoinformatics, Virtual Screening, and Molecular Dynamics Simulation are being Used to Find Best Inhibitors for the Human Infectious Lujo Virus 6GH8 Target.

Mohammed Emon[1]*, Jovel Varghese Jose[1], Eshaan Agarwal[1], Mosadoluwa Agbonyin[1], Sanjana Fatema Chowdhury[1], Karthika R[1], Ayush Panda[1], Maurya Sharma[1], Ayesha Saman Hawaldar[1], Jaskeerat Singh[1], Anjali Sharma[1], Hameed Sanusi [1], Emmanuel Ifeanyi Attah[1], Siddhant Sharma[1]

[1]The Hackbio, Lagos, Nigeria

Corresponding author email: siddhaantsharma.ss@gmail.com

Introduction

Lujo Hemorrhagic Fever Virus (LUHFV) has emerged as a human pathogenic viral infectious disease with a high mortality rate. Our study aims to identify molecules with appreciable inhibition through molecular modeling against Lujo Hemorrhagic Fever Virus. These compounds can further serve as potential drug candidates for the treatment of viral hemorrhagic fever by validating them through rigorous wet laboratory studies.

Methods

We identified a 3D crystal structure of the GP1 domain of the Lujo virus in combination with the first CUB domain of neuropilin-2 of 6GH8 protein using 6GH8 viral protein with a specific chain refinement that carries NRP2, VEGF165R2 genes with a homo sapiens host. We utilized our study workflow to analyze the protein-protein interaction (PPI) using STRING, predict protein bioactivity using Molinspiration, and cytotoxic effects of compounds via CLC tools. We selected the three main ligands from PubChem: Rivabirin, N-acetylcysteine, and Atorvastatin through intensive literature studies. We then analyzed the absorption, distribution, metabolism, and excretion and toxicity (ADMET) characteristics of all three main control ligands with their similar compounds by utilizing Ambinter as default 80% similarity searching, yielding a total of 276 compounds for further validation in our study. Filtering of the 276 total compounds was done according to the Lipinsky rule. The PyRx tool and AutoDock Vina were used for performing the docking study. The top three docking binding affinity compounds with main ligands total of 12 compounds were selected for protein-ligand interaction analysis. The molecular dynamic (MD) simulation was done for the top 12 compounds of three ligands according to the docking results.

Results

Rivabirin, N-acetylcysteine, and Atorvastatin were chosen as control ligands with 276 compounds being curated based on similarity search. After rigorous ADMET filtration and molecular docking, about 12 compounds were identified as potential Lujo viral inhibitors. Molecular dynamics simulation results proved the stability of the ligand–protein complex. The risk posed by this virus has necessitated the design and development of the associated viral inhibitor. The 12 identified compounds have the potential of being a target to this virus and thus should further be developed through wet laboratory studies

Conclusion

Lujo is a novel arenavirus, genetically different from other members of the family, including the Lassa virus, according to sequence research. The risk posed by this virus has necessitated the design and development of the associated viral inhibitor. The 12 identified compounds have the potential of being a target to this virus and thus should further be developed through wet laboratory studies.

Funding

No received any funding .

References

Cohen-Dvashi H, Kilimnik I, Diskin R. Structural basis for receptor recognition by Lujo virus. Nat Microbiol. 2018;3(10):1153-1160. doi:10.1038/s41564-018-0224-5