

Repurposing of Approved Molecules against Chikungunya Virus Replication

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Chikungunya, a mosquito-borne viral disease is now a global public health problem. The chikungunya disease is potentially a global health intimidation and the therapeutic interventions are the immediate necessity. Since, the chikungunya disease has “sporadic outbreak/ re-emergence” across the world and hence the immediate potential therapeutics are obligatory. To curtail the virus in outbreak situation, a ready to use drug for chikungunya is necessary. We report the repurposing of approved molecules as an effective anti-chikungunya molecules conferring their antiviral effect validated through many biophysical, biochemical and in-vitro antiviral assays. Through this study we tried the repurposing approach against chikungunya which is a cost and time effective strategy with trust of safety due to continuous human use over time. Through this study, we have shown two approved molecules as an effective antiviral against chikungunya. These molecules were identified using the computational approaches, procured and validated for bimolecular interactions against the recombinantly purified full length nsP2 protein of chikungunya virus using surface plasmon resonance (SPR), thermofluor® assay and intrinsic tryptophan fluorescence titration experiments. The KD values as derived from the SPR experiments reported as 1.55 μ M and 35 μ M respectively. The anti-protease property of the molecules were assessed by the fluorescence resonance energy transfer (FRET) derived protease assay. The half of maximum activity (IC₅₀) and inhibition constant (K_i) for these molecules were found as ~ 1.25 μ M/ 2.27 \pm 0.5 μ M and ~ 2.20 μ M /3.46 \pm 0.3 μ M respectively. Moreover, the molecules displayed an effective suppression of the virus replication in post-treatment antiviral test assays with EC₅₀ values as 20.70 μ M and 48.58 μ M in both molecules.

Biography:

Ashok Patel is currently working as an Assistant Professor in Kusuma School of Biological Sciences, IIT Delhi. He has done his Ph.D. with Prof. J.V. Medicherla from M.B.U, Institute of Medical Sciences, BHU, India. He has been trained from Prof. David W. Rice, Prof B.W. Dijkstra and Prof. Petri Kursula through travel fellowship by Boehringer Ingelheim Fonds (BIF) Germany. He did postdoc with Prof. Gregory Bowman in Johns Hopkins University, USA. Ashok lab is interested to understand Chikungunya and dengue virus pathogenesis, structural and functional intricacies, host-virus interaction, identification and validation of inhibitors, compounds, medicinal plants against Chikungunya and dengue.