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LIGAND-BASED AND MACHINE LEARNING VIRTUAL SCREENING FOR ANTIVIRAL REPURPOSING TARGET TO SARS COV-2 REPLICASE POLYPROTEIN 1A
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ABSTRACT

COVID-19 is an infectious disease caused by the SARS-CoV-2 virus, which belongs to the B lineage of beta-coronavirus related to SARS-CoV. It primarily infects human respiratory system, proved by the initial clinical sign of pneumonia. RP1a is a complex protein consisting of NSPs, especially PLpro and 3CLpro, which are essential and highly conserved proteins. It has become a promising candidate and its pivotal role has been cited by many studies, yet published research is limited, thus presenting an opportunity.

This study aims to repurpose 10,692 drugs in DrugBank to seek potential therapy for RP1a inhibitors through LBVS using KNIME. A total of 272 active ligands were retrieved to obtain 96 MCS for substructure screening. The study indicated 3,166 compound candidates inhibiting 3CLpro and none for PLpro, with the highest confidence being 0.95 (Bromo-7-Nitroindazole) from the RF MACCS ML model. Through literature analysis, six compound classes with potential activity to 3CLpro were discovered, namely benzopyrazole, azole, pyrazolopyrimidine, carboxylic acids and derivatives, benzene and substituted derivatives, and diazine. Four pathologies based on the 3CLpro PPI network were discovered as well. The results demonstrate the efficiency of the LBVS strategy, which can quickly discover therapy for novel or orphan diseases with existing drugs.

Keywords: *COVID-19, drug repurposing, RP1a, ligand-based virtual screening, KNIME*