Repurposed drugs present new strategy for treating COVID-19

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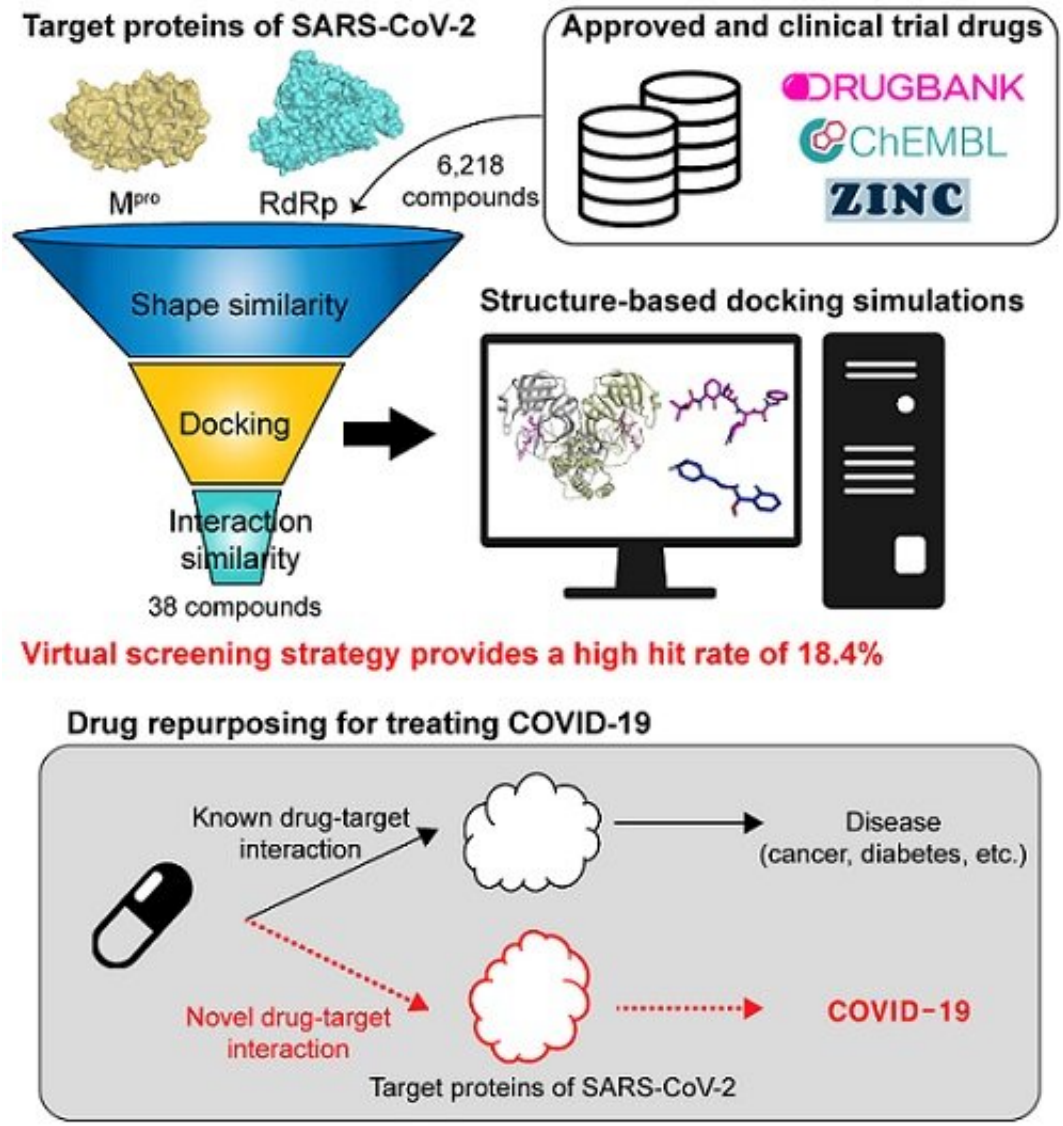

Figure: A schematic representation of computational drug repurposing strategy. Docking-based virtual screening can rapidly identify novel compounds for

COVID-19 treatment among from the collection of approved and clinical trial drugs. Credit: Korea Advanced Institute of Science and Technology

A joint research group from KAIST and Institut Pasteur Korea has identified repurposed drugs for COVID-19 treatment through virtual screening and cell-based assays. The research team suggested the strategy for virtual screening with greatly reduced false positives by incorporating pre-docking filtering based on shape similarity and post-docking filtering based on interaction similarity. This strategy will help develop therapeutic medications for COVID-19 and other antiviral diseases more rapidly. This study was reported at the *Proceedings of the National Academy of Sciences* of the United States of America (*PNAS*).

Researchers screened 6,218 drugs from a collection of FDA-approved drugs or those under clinical trial and identified 38 potential repurposed drugs for COVID-19 with this strategy. Among them, seven compounds inhibited SARS-CoV-2 replication in Vero cells. Three of these drugs, emodin, omipalisib, and tipifarnib, showed anti-SARS-CoV-2 activity in human lung cells, Calu-3.

Drug repurposing is a practical strategy for developing antiviral drugs in a short period of time, especially during a global pandemic. In many instances, drug repurposing starts with the virtual screening of approved drugs. However, the actual hit rate of virtual screening is low and most of the predicted drug candidates are false positives.

The research group developed effective filtering algorithms before and after the docking simulations to improve the hit rates. In the pre-docking filtering process, compounds with similar shapes to the known active compounds for each target protein were selected and used for docking simulations. In the post-docking filtering process, the chemicals

identified through their docking simulations were evaluated considering the docking energy and the similarity of the protein-ligand interactions with the known active compounds.

The experimental results showed that the virtual screening strategy reached a high hit rate of 18.4%, leading to the identification of seven potential drugs out of the 38 drugs initially selected.

"We plan to conduct further preclinical trials for optimizing drug concentrations as one of the three candidates didn't resolve the toxicity issues in preclinical trials," said Woo Dae Jang, one of the researchers from KAIST.

"The most important part of this research is that we developed a platform technology that can rapidly identify novel compounds for COVID-19 treatment. If we use this technology, we will be able to quickly respond to new infectious diseases as well as variants of the coronavirus," said Distinguished Professor Sang Yup Lee.

More information: Woo Dae Jang et al, Drugs repurposed for COVID-19 by virtual screening of 6,218 drugs and cell-based assay, *Proceedings of the National Academy of Sciences* (2021). DOI: 10.1073/pnas.2024302118

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