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Abstract Book

DRUG REPURPOSING TO FIND INHIBITORS OF SARS-CoV-2 MAIN PROTEASE

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Background:

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the strain of coronavirus that causes coronavirus disease 2019 (COVID-19), the respiratory illness responsible for the COVID-19 pandemic. As of October 2021, with about 6 billion doses of COVID-19 vaccines administered globally, the world is slowly returning back to normality. However, there is still a need for novel therapeutics for people that contracted the disease either because they were not vaccinated or because the vaccine was not effective for them.

Drug repurposing is a strategy for identifying new uses for approved drugs that has the advantage, over conventional approaches that attempt to develop a drug from scratch, that the time frame of the overall process can be significantly reduced because of the few number of clinical trials required.

In this work, a structure-based virtual screening of FDA-approved drugs was performed for repositioning as potential inhibitors of the main protease Mpro of SARS-CoV-2.

Results:

12 drugs were prioritized from the Virtual Screening campaigns as potential inhibitors of the Mpro enzyme. Some of the selected compounds turned out to be antiviral drugs already being tested in COVID-19 clinical trials or used to alleviate symptoms of the disease. Curiously, the most promising candidate is the naturally occurring broad spectrum antibiotic Oxytetracycline (OTC). This drug has largely outperformed the remaining selected candidates along all filtering steps of the virtual screening workflow. The closely related tetracycline-derived drug Doxycycline (DOX) recently has proven to reduce the viral load in Vero cells infected with SARS-CoV-2. Since OTC but not DOX surpassed the more stringent filters in the late stages of our virtual screening pipeline, we suspect that OTC will show even higher antiviral activity than DOX in viral replication experiments.

Conclusions:

Considering our computational findings together with the proven antiviral properties of DOX, we believe it is worth testing OTC in prospective viral replication studies. We encourage the scientific community working on COVID-19 projects to include this repurposing candidate on their experimental screening pipelines.

Poster Session: http://bit.ly/cab2c-2021-posters
Poster Conti et al: https://youtu.be/WDp9o07Hjvc