UNIVERSITY OF BRESCIA

PhD Program
in
TECHNOLOGY FOR HEALTH

DISCOVERY OF SARS-CoV-2 ANTIVIRAL DRUGS: DEVELOPMENT OF SPECIFIC DATASETS FOR DRUG REPURPOSING AND DEEP LEARNING MODELS

PhD Candidate: Alessandro Rondina

Email: *a.rondina001@unibs.it*

XXXVII Cycle

Tutor: full professor Marco Rusnati

Co-Tutor: associate professor Francesca Caccuri

Background

In December 2019, the global health emergency caused by the spread of the new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has urgently required the discovery of a treatment capable of stopping the pandemic. To date there is no effective pharmacological treatment for SARS-CoV-2 infection, and the development of new drugs is likely to require years of research. It is therefore essential to find faster methodologies. Computer science comes up against this need thanks to the development of in silico techniques, such as drug repositioning and the creation of prediction models by means of Artificial Intelligence. However, there are several limitations as the models are often poorly interpretable or lack explanations relevant to certain biological mechanisms, or even the type of data used in the construction of the model is not sufficient.

Objectives

My PhD proposal fits into this scientific context aimed to solve the problems related to the construction of specific datasets for drug repurposing and machine learning studies, to be applied in the search for effective antivirals against SARS-CoV-2.

Methodologies

The project consists of three work-packages (WP), each of which presents different tasks to be completed. Initially, I will take care of specific datasets to be used for drug repositioning and for the creation of Deep Learning (DL) models. The main purpose will be to use AI to implement a repositioning pipeline on three distinct levels: i) identification of the suitable 3D target structures and (ii) of specific binding pockets; iii) identification of putative antiviral candidates.

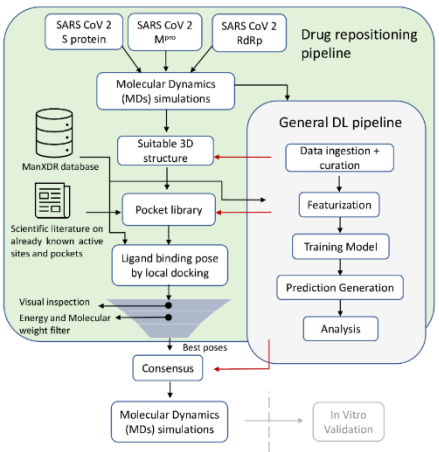

Figure 1 - Schematic representation of the combined drug repositioning-DL pipeline

Expected Results and Impact

The results obtained from drug repositioning approaches will be combined through a consensus procedure to improve the quality of results compared to the single drug repositioning method. The molecules thus obtained will be validated through an accurate analysis of the interaction between ligand protein target and cell assays.