Università degli Studi di Napoli Federico II

Phd program in Computational and Quantitative Biology

Project Proposal

Title *Development of AI platforms for repositioning currently available drugs for new diseases*

Project Description

From the past two decades, the development of efficient and advanced systems for the identification of therapeutic approaches with maximum efficiency and minimum risks has imposed a great challenge among chemical and biological scientists. Artificial intelligence (AI), including deep learning (DL) and machine learning (ML) algorithms, has emerged as a powerful approach, which can overcome problems and hurdles in the drug design and discovery process, speeding the discovery and improving the efficiency of the discovery process.

Computational modeling based on AI and ML principles provides a great avenue in all the steps of drug discovery, including the identification and validation of chemical compounds, target identification, peptide synthesis, evaluation of drug toxicity and physiochemical properties, drug monitoring, drug efficacy and effectiveness, and drug repositioning.

In recent years polypharmacology, referred to a single drug capable of interacting with multiple targets, has emerged as a very valuable therapeutic approach for complex diseases such as cancer, heart failure, metabolic and neurodegenerative diseases. The design and/or the discovery of drugs targeting two or more biological target is a great challenge considering the amount of data that should be correlated to improve multitargeting features.

In this context we aim to establish AI based methods to improve the efficacy of the drug discovery process in the design of a polypharmacology strategy exploiting the drug repurposing approach to identify novel agents for metabolic disorders. In particular, the project aim to: i) exploit ML approaches that integrate the biochemical and structural properties of individual proteins and their role within global protein-protein interaction networks, in order to identify for drug target prioritization [1,2]; ii) develop deep learning (DL) techniques, such as multi-level deep neural networks (DNN), to foster and improve accuracy of high throughput virtual screening methods (HTVS) of databases of compounds with demonstrated safety profiles, such as the ReFRAME database, including 12000 safe compounds [3], in the frame of a drug repositions strategy. AI protocols will be designed to analyze HTVS results on different targets to improve the selection of hits showing potential multitargeting profile [4]. The results of the screening will be finally tested in vitro and in vivo in the group of Prof. Fiorucci of the University of Perugia, in the frame of a well-established collaboration. The results of the pharmacological evaluation will be used as further input for the optimization of the hit selection procedure, in an iterative process.

Project Description

Supervisor(s), Lab/Group details, other additional info.

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Horizon-2020 ERC-CoG-2018 “Order and Disorder at the Surface of Biological Membranes” BioDisOrder-819644

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