COVID.SI – An Citizen Science project for HTVS for SARS-CoV-2 Inhibitors

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The SARS-CoV-2 virus has been with us for more than two years. In a little over two years, more than half a billion people have contracted the virus, and more than six million people have died from the virus. Since the virus can not seem to say goodbye fast enough, we must learn to coexist with it. [1] Subsequent pandemic waves of the disease can be prevented by consistent distancing during local outbreaks and by vaccinating as wide a population as possible. Since the first announcement of the existence of the new virus, many scientific groups around the world began an intensive search for a suitable drug that would inhibit the effects of the virus with as few side effects as possible. With great research effort, scientists used supercomputers, which soon deciphered the structures of the main viral targets (mostly proteins). With the help of computers, we can determine and analyze the structure of the virus in detail, study how mutations in the virus affect its properties, study its interactions with the body, which is important for the development of vaccines. Computer methods can also be used to search for molecules in a chemical space that could effectively inhibit the virus.

Some of these computational projects have been carried out by volunteers; the most prominent example is Folding@ HOME, in which exascale computational power has been achieved to accurately characterize some of the specific functions of SARS-CoV-2 - such as the movement of its critical spike protein - and to identify a wide range of "pockets" that researchers say will expand options for drug development to combat COVID -19. [2]

Early in the pandemic, we joined the initiative to cure COVID-19 with the COVID.SI Citizen Science Distribution Computing project (https://covid.si). An important part of the COVID.SI project is virtual screening using the docking method. In this project, we are performing molecular docking on more than 100 different target models associated with the life cycle of SARS-CoV-2 and related viruses. In total, we have already performed nearly 1 billion independent molecular docking experiments as part of the COVID.SI project. The use of our methodology has been successfully demonstrated for prioritizing compounds for the development of 3CL-Pro inhibitors for SARS-CoV variants. [3] Next, we introduce the SiDock@home volunteer computing project (https://sidock.si) and its place among other BOINC-based projects in the fight against SARS-CoV-2. The SiDock@Home project is an organic extension of the COVID.SI project that has been very well received by the worldwide BOINC community. Having grown into a state-of-the-art grid-based supercomputer in a matter of months, SiDock@home is now evolving into an independent, general-purpose drug discovery project. Its first mission targets SARS-CoV-2 and other life-threatening viruses in the Coronaviridae family, such as SARS-CoV and MERS-CoV. [4]

An example of the use of silico methods in conjunction with experimental affinity determination is presented based on the study of the binding of polyphenolic compounds to the main protease of SARS-CoV-2 virus. [5]

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