Structure based drug designing approach reveals potential anti-coronaviral drugs targeting key proteins of SARS-CoV-2

An antiviral polymerase inhibitor PC786 targets key SARS-CoV-2 proteins with high binding affinity making it a stand-out among all the screened antiviral drugs

UPPSALA, SWEDEN, June 26, 2020 /EINPresswire.com/ -- The COVID-19 as of today has conquered almost all the countries in the world. The world has witnessed a surge of coronavirus cases with a high death rate. We urgently need effective drugs or vaccines for COVID-19, but what is the quickest way to find it? The quick and efficient development of active antiviral drugs or vaccines for therapeutic use is exceptionally challenging because traditional drug development methods usually take years of research and cost billions of dollars. Currently, the development of a new drug from basic research involves an enormous amount of money and time. The drug discovery process can be expedited significantly by computationally. This prompted the team led by Prof. Rajeev Ahuja, Uppsala University, Sweden in collaboration with Prof. Yogendra Kumar Mishra, University of South Denmark and Prof. Mrutyunjay Suar, KIIT School of Biotechnology, India to carry out a systematic finding of potent antiviral drugs and vaccine candidates based on state-of-the-art bioinformatics approaches as well as molecular dynamics to determine the binding of different drug molecules. We have used bioinformatics approaches to perform virtual screening of antiviral compounds to model their interactions with the SARS-CoV-2 virus that may enable scientists to more easily identify antiviral drugs that work against the virus while informing the search for viable vaccine candidates. The coronavirus needs a special type of protein (the spike protein) to infect a cell.

This spike protein acts as a key to enter into the human cells through an enzyme, ACE2, which is present on the surface of human cells (especially in the lungs). The virus can then fuse with the cell membrane and release its genetic material into the cell. The spike protein is the sharpest weapon of the virus; its exposed position makes it the preferred point of attack for the immune system. By screening for interactions with certain structural domains and active sites on the virus, this structure-based approach may help scientists identify existing drugs that can be repurposed, including therapies developed to treat MERS-CoV, SARS-CoV, Ebola, and HIV. Information about SARS-CoV-2 reported from its recent genome sequencing has revealed key targets for drugs and vaccines, including the spike protein complex, which helps mediate viral entry into host cells, as well as the main protease, an enzyme that enables viral replication and transcription. To test how these elements of the virus' structure may be used to search virtually for prospective drugs, the combinatorial drug-designing and immunoinformatics approaches

have been considered in this study. They have succeeded in identifying 38 anti-coronaviral drugs, from a pool of plausible antiviral drug candidates from virtual screening strategy using a bioinformatics approach. We have found that an antiviral polymerase inhibitor PC786 targets several SARS-CoV-2 receptors with high affinity, making it a standout among the antiviral drugs. They have also identified several additional antiviral drugs with strong binding affinities to the spike protein and main protease, revealing a number of drugs that may be candidates for further research in efforts to fight SARS-CoV-2. In addition to the drug screening approach, they have also proposed potential vaccine candidates (peptides) for SARS-CoV-2 using a structure-based immunoinformatics approach.

We have been engaged in research on Rapid DNA sequencing and Anti-cancer Drugs when it comes to the area of life sciences but amid the coronavirus pandemic, we are shifting gears in order to appropriately respond to the public health concerns posed by COVID-19. To mitigate the current pandemic, a combination of rationality and scientific insight with data-driven bioinformatics methods will give us our best shot. In the near future, our long experience in computational science in a combination with Artificial Intelligence (AI) will lead to more breakthroughs in data-driven drug discoveries to deal with the current pandemic. says Prof. Rajeev Ahuja. The combined drug-designing and immunoinformatics approach provides a detailed understanding of the vital structural domains of coronavirus involved in either acting as a drug-binding site or epitope recognition site. Our strategy will reduce the translational distance between preclinical test results and clinical outcomes, which is a significant challenge in the rapid development of practical treatment approaches for the ongoing coronavirus pandemic says Pritam Kumar Panda, a Ph.D. student from Rajeev's group. The computational approaches may also assist with the development of new drugs and protein-based SARS-CoV-2 vaccines with fewer experiments and higher reliability than traditional methods. We do acknowledge several limitations to validate our Insilco proposed work due to the lack of experimental support. However, the strategies mentioned above can reduce the resources and expenses for researchers involved directly with the experimental and clinical studies says, Pritam Kumar Panda. The findings have been published in Science Advances, AAAS (https://advances.sciencemag.org/content/early/2020/06/24/sciadv.abb8097).

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