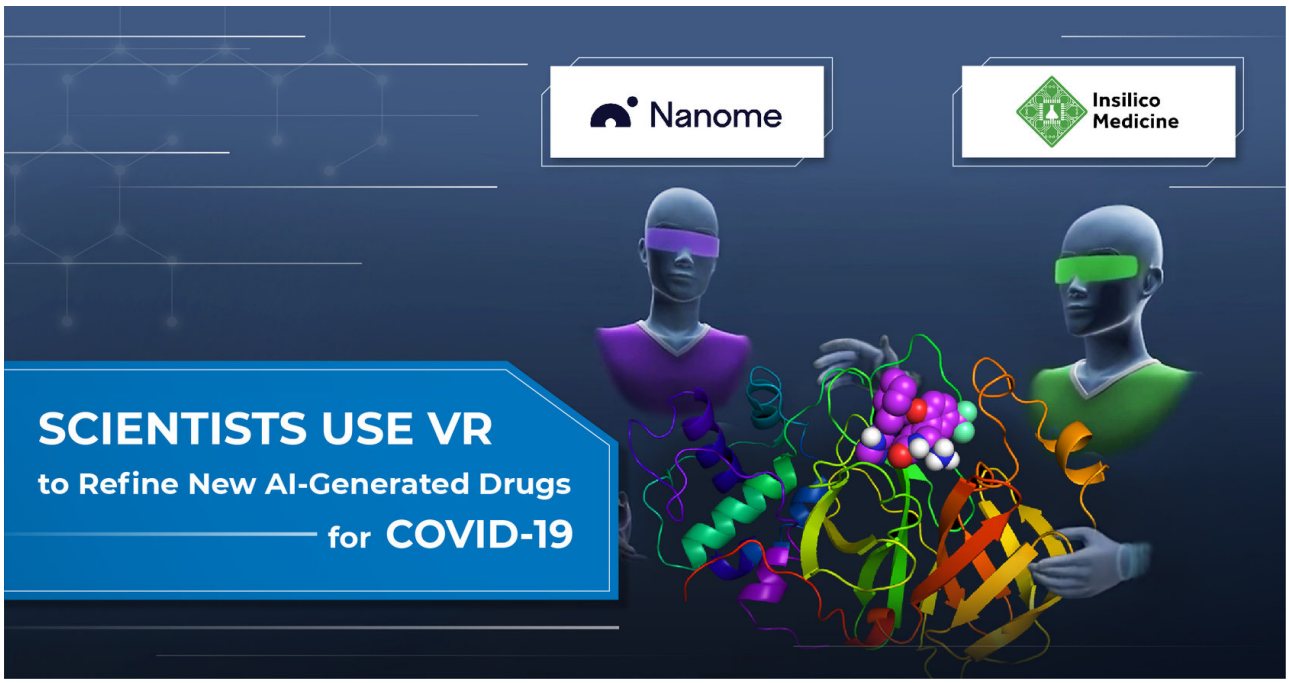

Scientists Use Virtual Reality to Refine New AI-Generated Drugs for COVID-19

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San Diego, California – Nanome, Inc., a virtual reality (VR) startup whose signature product is a computational chemistry software platform, has co-authored a paper describing 10 potential small molecule inhibitors targeting the SARS-CoV-2 main protease that were generated by artificial intelligence (AI). The study was conducted in collaboration with Insilico Medicine, an artificial intelligence company based in Hong Kong, and could reveal as-yet-undiscovered methods for attacking the virus that have eluded scientists working with existing drug candidates.

Many potential therapeutics aimed at containing the spread of SARS-CoV-2 have targeted the S, or spike, protein, a surface protein that plays a vital role in viral entry into host cells, since that is the approach that was taken with both SARS and MERS coronaviruses. However, according to the authors, two-thirds of the SARS-CoV-2 genome comprises non-structural proteins, such as the viral protease (the protein necessary for viral replication), which shouldn't be overlooked as potential therapeutic targets.

"The SARS-CoV-2 main protease is a much more druggable protein than the spike protein. It contains a pocket perfect for small molecule inhibitors."

Alex Zhavoronkov, PhD
CEO of Insilico Medicine and lead author on the paper

Initial investigations into therapeutics to treat COVID-19 patients relied mostly on the identification of drug repurposing candidates, but new attempts are being made to develop novel drug-like molecules that are active against SARS-CoV-2. Previous studies on SARS-CoV and MERS-CoV focused on the development of small molecule therapeutics using protease inhibitors (which handicap the virus by interfering with its ability to replicate), but since the beginning of the COVID-19 outbreak, only a few studies on SARS-CoV-2 protease inhibitors have been published.

One reason for the relatively few number of studies is the daunting number of chemical structures that can be generated from scratch. "Consequently, conventional computational drug design approaches tend to include a limited number of fragments and/or employ sophisticated search strategies to sample hit compounds from a predefined area of the chemical space," said Zhavoronkov.

To enable scientists to exploit the whole drug-like chemical space, scientists have developed a new type of computational method for drug discovery using recent advances in deep learning and artificial intelligence (AI). These "generative" models can utilize large datasets for training and perform *in silico* design of *de novo* molecular structures with predefined properties—something Zhavoronkov calls "AI imagination".

"The approach involves teaching the machine what the target protein looks like, and then letting it 'sniff' out the binding pockets. Then, we let it 'imagine' molecules with certain features having to do with the likelihood that a molecule will fit inside, and stay inside, a binding pocket."

Alex Zhavoronkov, PhD
CEO of Insilico Medicine and lead author on the paper

Generative chemistry approaches to drug design have had several recent successes, demonstrating that it is possible to generate molecules that can be synthesized, are active *in vitro*, metabolically stable, and elicit *in vivo* activity in disease-relevant models.

At the end of January 2020, Insilico Medicine launched a program to start generating the structures of inhibitors targeting the SARS-CoV-2 main protease, and has since become a pioneer in applying generative chemistry for the development of potential treatments for COVID-19.

Insilico's proprietary platform has already been successfully applied to design small molecule drugs for a wide range of human diseases, such as cancer, fibrosis, and immunological diseases.

In this study, published to ResearchGate (May 11, 2020) and ChemRxiv (May 19, 2020), the authors used a protein structure published to the Protein Data Bank (PDB) website by Purdue University to generate and refine a number of non-covalent drug candidates, 10 of which are described.

"The vast majority of small molecule drugs on the market are non-covalent. Covalent inhibitors form a strong bond with a protein, but they aren't very selective and usually cause severe side effects. To date, the most potent inhibitors of the SARS-CoV-2 protease are covalent. We set out to generate non-covalent drug candidates due to their higher levels of safety and efficacy."

Alex Zhavoronkov, PhD
CEO of Insilico Medicine and lead author on the paper

The generation was followed by the selection of representative examples and medicinal chemistry analysis provided by Nanome.

"We saw on YouTube that the guys at Nanome had looked at some of our molecules in VR, so we reached out and asked if we could collaborate. While AI can come up with novel and diverse drug-like molecules, it is important for medicinal chemists to look at these molecules closely before placing a billion-dollar, life-or-death wager. VR enables medicinal chemists to do this while unleashing creativity and encouraging collaboration across both disciplinary and physical borders. We are looking forward to continuing our collaboration with Nanome."

Alex Zhavoronkov, PhD
CEO of Insilico Medicine and lead author on the paper

A comparison of the newly generated molecules to existing databases revealed that there is no molecule with the same core structure. The authors hope their compounds will be synthesized and tested *in vitro* and *in vivo* in the future.

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Nanome, the first virtual reality (VR) software company to launch an immersive real-time collaboration platform for scientific discovery, is changing the way we understand and interact with science at the molecular level. The software environment allows users to visualize, modify, and simulate proteins, chemical compounds, and nucleic acids to accelerate scientific decision making. The platform facilitates effective communication of data and integrates with existing computational chemistry workflows—features that have led to the adoption of the San Diego–based company's enterprise solution by several pharmaceutical and biotech companies worldwide. For more information, visit nanome.ai

Insilico Medicine

Since 2014 Insilico Medicine is focusing on generative models, reinforcement learning (RL), and other modern machine learning techniques for the generation of new molecular structures with the specified parameters, generation of synthetic biological data, target identification, and prediction of clinical trials outcomes. Recently, Insilico Medicine secured $37 million in series B funding. Since its inception, Insilico Medicine raised over $52 million, published over 80 peer-reviewed papers, applied for over 25 patents, and received multiple industry awards. Website insilico.com. For further information, images or interviews, please contact: ai@insilico.com.