Six Potential Treatments for COVID-19 Identified

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Two brothers who started their careers in different fields are now working together to harness artificial intelligence (AI) to identify drugs that may be repurposed to fight COVID-19 — with some early success.

In the late 1980s and early 1990s, Aris and Andreas Persidis were studying for their doctorates in different fields — Aris in biochemistry at Cambridge, and Andreas in naval architecture and AI at the University of Strathclyde, both in the United Kingdom.

They had always wanted to work together. At the time, early versions of Al-driven telemedicine, called "medical expert systems," were being discussed as the next healthcare revolution. The brothers first collaborated by researching and writing a review of the subject, which they submitted to many journals. It was rejected by all except one.

Despite that early negative response, the Persidis brothers pushed on. In 2005, they started Biovista, a company that initially used early forms of AI to match research areas and scientists. This evolved into matching drugs and adverse effects, and then it morphed again into matching any and all drugs against any and all mechanisms, pathways, diseases, and clinical outcomes.

When COVID-19 hit, the brothers began applying novel AI approaches through Biovista's Project Prodigy AI platform to find treatments that would mitigate disease complications that can arise post infection.

Biovista has just announced that it has identified the antifibrinolytic agent aprotinin and the angiotensin II receptor blocker irbesartan as having potential for reducing the effects of cytokine storm and high viral load associated with COVID-19.

Biovista has also identified caplacizumab and ezetimibe/atorvastatin as potential treatments to address blood clotting and inflammation related to COVID-19.

The AI platform has also identified two bioactive compounds — lycopene and vitamin D — as potentially useful in treating COVID-19, bringing the total to date to six.



Dr Aris Persidis

Drug AI helps find that "needle in the haystack, and we are optimistic that we have found [several] of them to start," Aris Persidis, PhD, told *Medscape Medical News*.

These drugs are part of a "rolling release" of possible drugs identified by Project Prodigy that could potentially be repositioned for COVID-19, he noted.

"COVID-19 has rewritten the book on infectious diseases," Persidis said. Treating it has proven especially difficult because it causes multiple complications affecting nearly every organ system.

Persidis noted that typical machine learning AI isn't designed for a disease like COVID-19. "Machine learning only looks backwards based on what you've trained it in. If you change a tiny variable, you have to train it again," he explained.

In contrast to traditional machine learning AI, Project Prodigy is a "machine building AI that enables us to build, interrogate, and test possible and unanticipated scenarios," he explained. It's being used to map all known drugs against every possible mechanism in which SARS-CoV-2 operates to cause complications.

The company will continue to publicly release data on potential drugs for COVID-19 for scientists and clinicians to test "until we collectively" solve COVID-19, Persidis said.

It's the socially responsible thing to do, with some really badass science and AI behind to support the data. Dr Aris Persidis

"It's the socially responsible thing to do, with some really badass science and AI behind to support the data. We are also starting conversations with relevant companies to test these drugs against COVID-19," Persidis said.

Before COVID-19

Pre-COVID, Biovista was issued patents on the "unexpected uses of three drugs and their relatives against at least five diseases and their variations," Persidis told *Medscape Medical News*.

The first drug Biovista repositioned and tested in animal models was dimebolin, which the company's AI platform predicted would be helpful for patients with epilepsy and multiple sclerosis. This was confirmed with experiments in animal models, and Biovista was granted patents.

"It was an incredible moment to see an AI predict something new that a drug could do that nobody else had before, and then see it confirmed in animal models, a process that would be about 100 days in total," Persidis said.

Other repositioned drugs include pirlindole for multiple sclerosis, Friedreich's ataxia, Leber's hereditary optical neuropathy, and multiple related rare diseases of mitochondrial dysfunction; and linezolid for rare forms of cancer, including glioblastoma multiforme.

As part of their work with biotech and pharmaceutical companies, Biovista has worked on "at least 10 more drugs and drug classes, identifying over 17 diseases and their variations," Persidis noted.

"We can share that over 64% of our repositioning recommendations for our bio/pharmaceutical collaborators have been validated by third parties experimentally 1 to 3 years after Biovista originally predicted the new uses," he said.

AI Can Speed Time to Clinical Trial

Many methods are being used to identify currently existing drugs against COVID-19, from traditional clinical experience to different forms of AI.

A team at the National University of Singapore is currently using an AI-based platform called IDentif.AI (Identifying Infectious Disease Combination Therapy With Artificial Intelligence) to help accelerate the discovery of optimal combinations of existing drugs that might be effective against COVID-19.

Dean Ho, PhD, head of the university's Department of Biomedical Engineering and director of the N.1 Institute for Health and Institute for Digital Medicine, is leading the effort.

For COVID-19, using drug combinations in lieu of single-drug therapy is likely to be essential, he noted.



Dr Dean Ho

"This creates additional challenges because selecting the right drugs to combine and the right dose for each drug can mean the difference between maximal efficacy or no efficacy at all," Ho said.

"This is where AI can be particularly helpful," he said.

For example, testing 12 candidate drugs at 10 different doses each creates one trillion possible drug combinations, Ho explained. "Testing this many combinations is insurmountable for any laboratory or even [a] major pharma company."

Applying an AI platform toward COVID drug combination design "can potentially lead to rapid clinical trial initiation, as the ranked list of combinations is quite actionable," said Ho.

Ho's team has already shown the HIV drug lopinavir/ritonavir (Kaletra) to be "relatively ineffective" against COVID-19. The antiviral remdesivir was shown to be the most effective single drug therapy "but was still not extraordinarily effective."

However, combining lopinavir/ritonavir and remdesivir resulted in the "top-ranked combination with complete inhibition of infection," Ho said.

Actual experimental data confirmed the benefits of this drug combination, he added. "This is a completely unexpected interaction that was pinpointed with IDentif.AI, which further demonstrates the importance of leveraging AI to optimize combination therapy design."

Persidis has an equity stake in Biovista. Ho has pending intellectual property filings for AI-based drug development and personalized medicine and is co-founder and shareholder of KYAN Therapeutics, which has licensed intellectual property relating to AI-based drug development.

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