Crowdsourcing drug discovery for pandemics

To the Editor — In 2002 and 2003 the SARS-CoV pandemic paralysed the Far East[1]. However, drug discovery efforts into the virus largely halted after the crisis subsided. The COVID-19 pandemic might have been avoided if those efforts against SARS-CoV had persisted. Despite many warnings, we have not made headway in anti-infective medicines more generally. Relying on commercial promise has clearly not worked: even after discovering a novel antibiotic and taking it to market, the antibiotics-focused company Achaogen collapsed due to lack of market incentives[2]. A new approach is needed for pandemic preparedness, in which society's investment in health is decoupled from commercial interests. Our initiative — the COVID Moonshot (https://postera.ai/covid) — is trying to implement such a solution.

Our approach is a non-profit, open-science drug-discovery model. COVID Moonshot is an international consortium of scientists drawn from academia, biotechs, contract research organizations (CROs) and pharma, all working pro bono or at cost with funding generated from crowdfunding (https://www.gofundme.com/f/covidmoonshot), philanthropy and bootstrapped grants. Unencumbered by intellectual property concerns, it aims to rapidly develop easily manufacturable antiviral drugs that can inhibit the SARS-CoV-2 main protease. All data and structures are made publicly available.

The project began with our large crystallographic and mass-spectrometry fragment screen, resulting in over 71 protein–ligand crystal structures[3]. We are now crowdsourcing molecular designs inspired by these fragments and have so far received over 4,500 submissions from 250 scientists (https://postera.ai/covid/submissions). We use machine learning and computational tools to rapidly triage compounds and design synthetic routes, enabling us to decrease the time it takes to find those with most promise. CROs are freely contributing both raw materials and their synthetic chemists' time, while scientists in pharma and academia offer chemistry expertise at no cost. Over 500 compounds are now being synthesized and tested, with several promising novel hits confirmed by crystal structures and activity assays (https://postera.ai/covid/activity_data).

With original crystallography being done in China, fragment screens conducted in Oxford and The Weizmann Institute in Israel, computational methods spearheaded by PostEra in California and Memorial Sloan Kettering Cancer Center in New York, and chemical synthesis carried out in Ukraine, India and China, we are seeking to combat a global pandemic in a global fashion whilst developing a future-proof infrastructure for pandemic preparedness. Breakthroughs in high-throughput synthesis and crystallography, as well as machine learning and computational science, make this vision possible. We invite like-minded scientists and organizations to join our global effort. ❐

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Competing interests

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