PRESS RELEASE
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Conscience Announces Top Performers in Its Third Open Drug Discovery Challenge, Targeting Coronaviruses

- *23 teams used computational methods to predict molecules to bind a potential drug target on SARS-CoV-2 as starting points for developing coronavirus drugs*
- *Four teams, hailing from Canada, Germany, Korea and the U.S., named as top performers*
- *Full high-quality dataset from challenge publicly available for further research*

TORONTO (10 December 2024) — The nonprofit drug discovery biotech Conscience today announced the results of its third CACHE open science challenge to find molecules that could be developed into drugs that prevent coronaviruses from evading the immune system. Out of 1739 molecules predicted by 23 teams, four molecules were chemically novel and showed promise as starting points for drug development.

Four teams ranked highest based on the experimental confirmation and chemical novelty of the molecules they discovered. Those teams were led by: Francesco Gentile (University of Ottawa and Ottawa Institute of Systems Biology) and Artem Cherkasov (Vancouver General Hospital and University of British Columbia), Gerhard Wolber (Freie Universitat Berlin), Minghu Song (University of Connecticut), and Keunwan Park (Korea Institute of Science and Technology). Another five teams had at least one confirmed molecule each but scored lower in terms of chemical novelty. The researchers used various computational methods including artificial intelligence to make their predictions.

The dataset generated from the competition, including the promising new molecules, is now available publicly on the CACHE Challenges website for researchers anywhere to develop further without patent or restriction.

This edition of the CACHE (Critical Assessment of Computational Hit-Finding Experiments) Challenges, governed by Conscience, along with pharmaceutical companies AstraZeneca, Bayer and Boehringer Ingelheim, was sponsored by the U.S. National Institutes of Health and tapped into small molecule design expertise across continents.

“While attention and resources have shifted away from COVID-19, the threat of future coronavirus pandemics continue,” said Ryan Merkley, CEO of Conscience. “AI and open science tools can help identify potential drugs against pandemic threats like COVID, as well as for treating rare diseases and addressing antimicrobial resistance, and these research teams from around the world have shared their skills to advance much-needed discovery in under-studied areas.”

Participants in this CACHE Challenge were asked to design molecules that bind to the ADPr site of SARS-CoV-2 Nsp3 macrodomain (Mac1). This site on a coronavirus protein enables the virus to evade the immune system. All the submitted molecules were evaluated in the lab by the biophysics team at the Structural Genomics Consortium at the University of Toronto for their ability to bind to the target.

While the top four experimentally confirmed molecules in this Challenge were deemed to be chemically novel by the CACHE Hit Evaluation Committee, three of them were remotely related to molecules discovered by the lab led by James Fraser at the University of California San Francisco. Fraser is a collaborator in the CACHE Challenge and an expert on the target protein.

“CACHE participants were successful in finding a few novel hits targeting SARS-CoV-2 Nsp3-Mac1, but discovering truly novel chemical scaffolds proved to be a nearly insurmountable challenge,” said Dr. Matthieu Schapira from the Structural Genomics Consortium at the University of Toronto and the lead scientist for the CACHE program.

Schapira noted that the Fraser Lab published a preprint paper in August describing a potent molecule targeting Nsp3-Mac1 that shows promising in vivo effects. Evaluating such highly customized molecules is beyond the scope of the CACHE Challenges, which require the selected molecules to be in the catalog of commercial vendors.

“The experimentally confirmed molecules from this CACHE Challenge complement the data generated by other groups such as the Fraser Lab and will hopefully spur further research and development toward novel immune-restoring drugs against coronaviruses,” said Schapira. “Between the results of our second CACHE Challenge, which targeted the SARS-CoV-2 Nsp13 helicase to prevent the virus from replicating, and these Nsp3-Mac1 hits to weaken the virus against the immune system, we are opening avenues for future combination therapies.”

Conscience has now announced the results of three CACHE Challenges: the first found potential drug targets for familial Parkinson’s disease and second and third for COVID. Other Challenges in progress focus on developing treatments to address multiple forms of cancer and obesity.

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About Conscience
Conscience is a nonprofit biotech focused on changing the game on drug development, by enabling new discoveries for diseases that have received limited attention from the

pharmaceutical industry. Using collaborative approaches and artificial intelligence, it breaks down barriers and inefficiencies imposed on profit-driven models. Powered by a network that includes academics, industry, technologists, and public support, a key initiative is the CACHE Challenge. It empowers scientists worldwide to unlock promising drug targets, accelerating the path to treatments for those who need them most. For more information, visit conscience.ca.

About the CACHE Challenges

The CACHE (Critical Assessment of Computation Hit-finding Experiments) Challenges offer an open competition platform to help accelerate one of the early stages of drug discovery. Researchers from academia, industry, and nonprofits are invited to deploy their best computational methods to predict molecules that will bind to a predefined target linked to a specific disease, a critical step in the drug discovery pipeline known as hit-finding. Their predictions are evaluated and benchmarked in a state-of-the-art laboratory, by our partners at the Structural Genomics Consortium (SGC). All the benchmarked results are shared openly and publicly with the world, and all chemical structures are made available without patent to all. Visit conscience.ca/cache-challenge.