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Conscience Announces First Success in Open Science Challenge to Predict "Hits" for Parkinson's Disease Drugs

Structural Genomics Consortium and The Michael J. Fox Foundation celebrate the power of open science as an alternative to patents, as well as the promise of artificial intelligence as a new tool for drug discovery

TORONTO (16 January 2024) – As part of its pioneering approach to drug discovery, the Canadian nonprofit Conscience announced today that its first open science competition has resulted in the identification of seven promising molecules, or "hits," that show potential for new, more effective drugs for familial Parkinson's disease.

This first competition in Conscience's CACHE (Critical Assessment of Computational Hit-Finding Experiments) Challenge series was funded by The Michael J. Fox Foundation for Parkinson's Research (MJFF).

Six of the winning molecules were submitted by university laboratories and one from a pharmaceutical company. Specifically, the submissions were from the laboratories of David Koes at the University of Pittsburgh; Olexander Isayev (Carnegie Mellon University) and Artem Cherkasov (University of British Columbia); Christina Schindler and Lukas Friedrich at Merck KGaA; Dmitri Kireev at the University of Missouri; Didier Rognan at the Université Strasbourg; Pavel Polishchuk at Palacky University; and Christoph Gorgulla at Harvard University.

"Today's results are a win for open science, for collaboration in drug discovery, as opposed to a patent-driven approach where scientists work in isolation from competing laboratories," said Ryan Merkley, CEO of Conscience. "We can also celebrate the emergence of AI as a promising new tool for drug discovery. That's what makes these findings – even if preliminary – so exciting."

Parkinson's disease, which affects 8.5 million people worldwide and more than 1.1 million in North America, can cause tremor, slowness, stiffness, and walking and balance problems, as well as depression, memory problems and other symptoms. It is a disease that worsens over

time, and while current treatments offer symptom relief, they do not halt its advance or offer a cure.

"We celebrate today the scientific achievements of CACHE participants around the world and experimentalists at the Structural Genomics Consortium who together discovered new chemical starting points for drug discovery," said Dr. Matthieu Schapira, from the Structural Genomics Consortium at the University of Toronto, and lead scientist for the CACHE program. "These compounds have an entirely novel mode of action and may help explore new therapeutic strategies against Parkinson's disease."

Along with the announcement of the top seven hits, Conscience has now made the entire experimental dataset of the CACHE Challenge available to the public, including the chemical structures of all the molecules tested and associated computational methods.

By comparing dozens of computational methods against the same target protein, the CACHE Challenge provided a consistent benchmark and shed light on the most effective AI-generated, hit-finding algorithms.

"Core to our mission is to accelerate discoveries that lead to meaningful new treatments for people living with Parkinson's disease," said Brian Fiske, Co-Chief Scientific Officer at The Michael J. Fox Foundation for Parkinson's Research. "Working with partners like Conscience and their CACHE Challenge model is one way we have been able to tackle complex biology with innovative solutions."

The CACHE Challenge's transparency is intended to allow the entire scientific community to learn from and build upon the findings without the hindrance of patents or proprietary restraints. This promises to improve the efficiency and cost-effectiveness of the drug discovery process, which can typically take years, if not decades.

"The Strategic Innovation Fund and its networks provide major investments in innovative projects that help grow Canada's economy and generate benefits for the well-being of all Canadians. The application of artificial intelligence within a collaborative open science model is bearing fruit," said the Honourable François-Philippe Champagne, Canada's Minister of Innovation, Science and Industry. Canada announced CA $49 million in funding for Conscience in October. "These principles have successfully yielded a promising discovery in the treatment of Parkinson's Disease, and we applaud Conscience's commitment to this pioneering approach."

Two thousand molecules were predicted computationally by twenty-three academic and commercial organizations with expertise in computational chemistry or AI-driven computational algorithms to bind the WDR domain of LRRK2, the most mutated protein in familial Parkinson's disease. Seven molecules were later validated experimentally in a world-class laboratory at the Structural Genomics Consortium at the University of Toronto. These are the first seven molecules ever reported with this type of bioactivity.

An independent "hit evaluation committee" from industry then critically assessed the experimental data to determine the most convincing results. The process, including a second round of predictions and experimental validations to expand on the learnings from the first round, took two years.

"In an era where new therapies for many diseases have been scarce despite substantial investment, the CACHE Challenge provides an alternative, collaborative model for drug development," said Conscience's Ryan.

There are currently four CACHE Challenges underway. Two focus on developing medicines for COVID-19, the third seeks to develop new ways to enhance cancer treatments, the fourth explores MCHR1, which plays a role in obesity.

An inaugural CACHE Symposium will take place in Toronto, Canada, on March 6 and 7, 2024. It will bring together leading experts in the field of computational chemistry and artificial intelligence to share their insights and experiences about collaborating through Open Science and developing AI tools for drug discovery.

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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 www.conscience.ca