Conscience Announces Results of CACHE Challenge #4, Targeting Cancer Immunotherapy

CACHE Challenge #4 focused on using computational methods to predict novel chemical matter for CBLB, an E3 ubiquitin-protein ligase

Keunwan Park of the Korea Institute of Science and Technology successfully identified a molecule that was both bioactive and chemically novel

Results show that innovative AI-driven workflows can overcome barriers in drug discovery

Toronto, ON, Canada, June 16, 2025 — Conscience, a non-profit that uses open science and true collaboration to enable drug discovery and development where market solutions are limited, is pleased to announce the results of its fourth CACHE (Critical Assessment of Computational Hit-Finding Experiments) Challenge, and the identification of a chemically novel and bioactive molecule. CACHE Challenge #4 focused on the difficult task of identifying novel molecules that bind to CBLB, a cancer immunotherapy target with an existing patent landscape.

The standout result of CACHE Challenge #4 came from Keunwan Park of the Korea Institute of Science and Technology, who was the only participant to identify a molecule that was both bioactive and chemically novel. Park did so by combining machine learning and structure-based methods. His approach encompassed learning patterns from existing patented molecules to generate new, distinct scaffolds. From this, he used the Structural Genomics Consortium (SGC)'s protein structure to refine the selection. This two-step pipeline led to the discovery of a novel, active compound, which is especially noteworthy given that pharmaceutical companies have struggled to find new chemical scaffolds – or frameworks of a molecule – for this target.

"At the outset of CACHE #4, all known CBLB patent molecules shared a common chemical scaffold, underscoring the difficulty of identifying novel templates," said

Matthieu Schapira, CACHE's Scientific Coordinator, Principal Investigator at the Structural Genomics Consortium and Professor at University of Toronto. "The recent crystal structure from Levon Halabelian's lab at the SGC offered new hope for structure-based discovery, and resulted in one of the 23 participating computational groups succeeding in identifying a truly novel molecule. This highlights the potential of open science challenges to drive innovation, but also the hurdles in reliably predicting biologically relevant compounds. Congratulations to Cheryl Arrowsmith's biophysics team, who screened over a thousand predicted compounds and validated Keunwan Park's winning molecule."

Another notable result came from Wei Lu, Research Lead at Galixir. Lei identified the most potent compound in the challenge; however, it offered limited novelty as it closely resembled known patented molecules.

The CACHE Challenges are governed by Conscience, along with pharmaceutical companies AstraZeneca, Bayer, Boehringer Ingelheim, and UCB, and tap into small molecule design expertise across continents.

Park's finding builds on his track record in previous CACHE challenges. In CACHE Challenge #3, he identified the only novel, active hit, but there were no chemical analogs to further support the finding, and in CACHE Challenge #2, he found the most potent molecule, but it was deemed chemically unstable. With Park's successful discovery in CACHE Challenge #4, the promising new molecule – along with the overall dataset generated from the competition – is now available publicly on the CACHE Challenges website for researchers anywhere to develop further without patent or restriction.

Conscience has now announced the results of four CACHE Challenges. The first CACHE Challenge found potential drug targets for familial Parkinson's disease and succeeded in recognizing that AI techniques offer promise in identifying hits. The second CACHE Challenge focused on identifying molecules that would bind to a highly conserved site on a SARS-CoV-2 protein, which, if successfully developed into a drug, could be used to treat all coronaviruses. In the third CACHE Challenge, researchers from across the globe used computational methods to predict molecules to bind on a potential target to develop medicines against another round of COVID, SARS-CoV-2. Four molecules were identified that were chemically novel and showed promise as starting points for drug development. The fourth CACHE Challenge focused on cancer immunotherapy. Other challenges in progress focus on developing treatments to address obesity and other forms of cancer, and the seventh CACHE Challenge will be launched this year.

Additional Quotes

“Support for initiatives like CACHE helps spur the kind of outside-the-box thinking that will help position Canada as a world-leading hub for science and innovation. Through this program, Conscience is harnessing the best minds in the world to develop new medicines and therapeutics. I want to congratulate Keunwan Park and the Korea Institute of Science and Technology on identifying a novel molecule to bind cancer immunotherapy targets that will aid in the development of new cancer treatments.”

- The Honourable Mélanie Joly, Minister of Industry and Minister responsible for Canada Economic Development for Quebec Regions

”To have successfully identified a bioactive and chemically novel molecule for CBLB is a huge achievement, and one that is particularly meaningful to me as a computational scientist. This is my third time participating in a CACHE Challenge, and through these experiences, I’ve had valuable opportunities to sharpen our approach and apply what we’ve learned, ultimately leading to a successful outcome. I am grateful to showcase that AI-driven workflows can overcome barriers in drug discovery, and I appreciate CACHE’s efforts in driving open science and collaboration through these impactful initiatives.”

- Keunwan Park, Principal Researcher at the Korea Institute of Science and Technology

“The CACHE Challenges offer a unique opportunity to accelerate early-stage drug discovery. As seen in CACHE Challenge #4, identifying novel molecules that bind to CBLB was a significant challenge. Yet, the effort illustrates both the complexity of the task and the promise of open science in tackling it together. Every new step or connection we make brings us closer to advancing drug discovery and builds greater awareness of the power of open science. I’m proud to contribute to this collective effort, and be a part of an initiative that demonstrates the real potential of harnessing AI as a tool for drug discovery, and ultimately driving scientific progress.”

- Wei Lu, Research Lead at Galixir

About Conscience

Conscience is a non-profit focused on enabling drug discovery and development in areas where open sharing and collaboration are key to advancement and where market solutions are limited, such as rare or neglected diseases, pandemic preparedness, and antimicrobial resistance. It does so by encouraging teamwork, the open sharing of knowledge and tools, the use and improvement of artificial intelligence, and the development of policies that break down barriers of traditional drug development models. Powered by a network that includes academics, industry,

technologists, policy experts, and public support, Conscience seeks to drive innovation by turning drug discovery and development into a team sport. Through key initiatives, such as its DMOS (Developing Medicines through Open Science) program and CACHE (Critical Assessment of Computation Hit-finding Experiments) Challenges, Conscience is accelerating the path to treatments for those who need them most so no patient is left behind. For more information, visit www.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 small 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/.

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