Toshiba and Revorf Advance Computational Drug Discovery Evaluationwith Quantum-Inspired SQBM+™ Optimization Solution

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News

Aim to significantly expand druggable targets through new allosteric regulation prediction technology

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Toshiba Digital Solutions Corporation
Revorf Co., Ltd.

Toshiba Digital Solutions Corporation ("TDSL") and Revorf Co., Ltd. ("Revorf") have developed a computational drug discovery[1] technology that can identify proteins susceptible to treatment with drugs, an advance that will support progress in creating innovative drug therapies. The technology uses TDSL's SQBM+[2], an advanced combinatorial optimization solver developed during research into quantum computing, to achieve much improved accuracy in predicting allosteric regulation[3], the mechanism that realizes functional diversity in proteins by regulating their structure and activities

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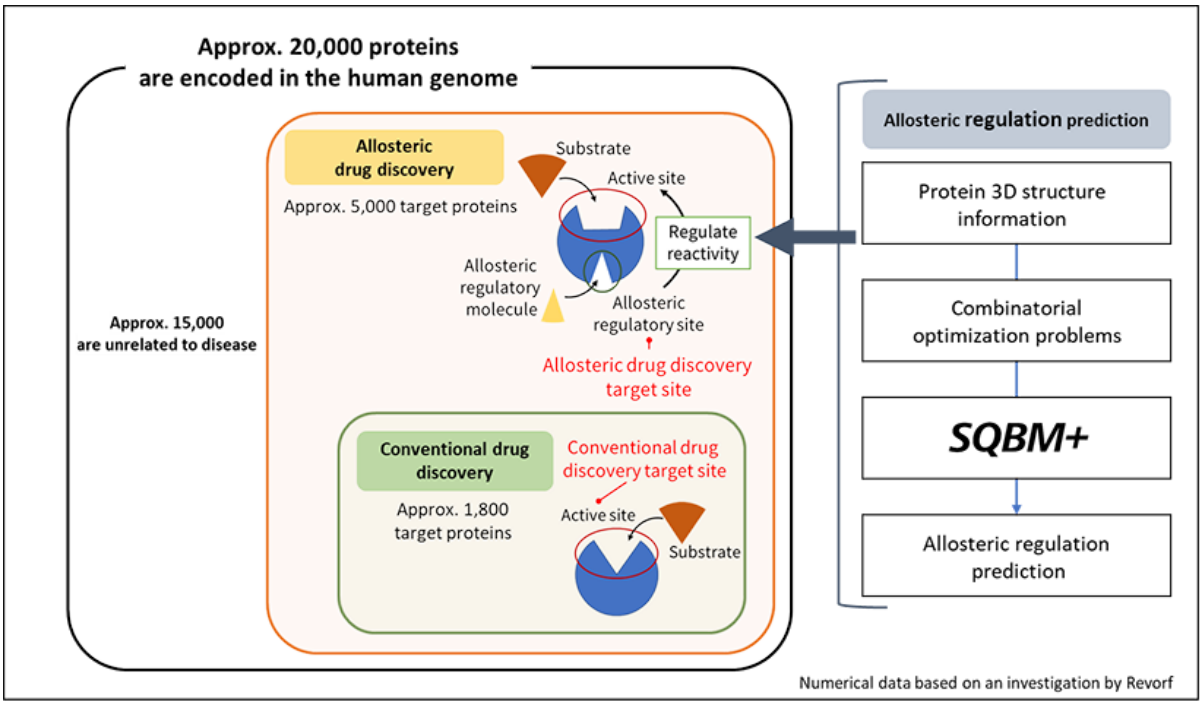
Effective drug target depletion[4], the targeting of a protein to induce a therapeutic effect, is a concern in the drug discovery process. Discovery of allosteric regulatory sites[5] in proteins requires labor- and time-consuming *in vitro*[6] experiments, which is driving demand for an alternative calculation technology. Methods based on allosteric regulation can now identify certain druggable proteins that can be targeted by drugs among proteins that, until now, had been considered undruggable, raising expectations for resolution of the target depletion problem.

TDSL's SQBM+ uses the Simulated Bifurcation Algorithm, invented in the course of research into quantum computing at Toshiba's R&D Center, to solve combinatorial optimization problems at very high speeds. SQBM+ finds optimal solutions to problems that require enormous numbers of calculations and that are beyond the capabilities of conventional computers. TDSL and Revorf together developed technology that solves predictions for allosteric regulation as a combinatorial optimization problems, and have succeeded in predicting allosteric regulatory sites that could not be identified using current methods.

Comparisons of allosteric regulatory sites predicted by SQBM+ with known allosteric regulatory sites for multiple proteins, including KRAS[7], have confirmed that SQBM+ achieves accurate prediction of sites that could not be identified with current calculation methods. Realizing discovery of sites through calculation alone increases the possibility of accelerating the search for drug candidates.

Using calculation to predict allosteric regulation

The evaluation technology uses information on the three-dimensional structure of proteins to formulate the allosteric regulation mechanism of proteins as a combinatorial optimization, and performs calculations to predict their regulation. Recent years have seen dramatic breakthroughs in technology for analyzing the 3D structure of proteins, including cryogenic electron microscopy[8] and structural predictions using AlphaFold2[9] and other AI. These advances are driving a rapid accumulation of 3D structural information for more and more proteins, creating a big data source that can be used to predict allosteric regulation with SQBM+. This new allosteric drug discovery method will accelerate drug development and raise the probability of success.



The evaluation technology is the outcome of building on the results of a research theme, “Formulation of drug discovery solutions using combinatorial optimization solvers,” proposed by Revorf and Ahead Biocomputing, Co. Ltd. at the Toshiba OPEN INNOVATION PROGRAM 2021[10], held from July to September 2021. Moving forward, the evaluation results will be shared with pharmaceutical companies and third-party organizations, the effectiveness of the technology in the drug discovery process will be further investigation through demonstration use in *in vitro* experiments. This initiative will enable drug discovery for proteins that were previously considered difficult to discover.

“Revorf contributes to people’s health by analyzing and applying biological information, such as genetic information and protein information,” explained Shinichi Sueta, the CEO of Revorf Co., Ltd. “Many patients suffer from unmet medical needs without appropriate medication. It is difficult to create effective therapeutic drugs due to the difficulty in finding druggable targets. We intend to combine this evaluation technology with our technology for analyzing protein functions, with the aim of making undruggable targets druggable and provide new drug targets.”

Commenting on the research results, Shunsuke Okada, President and CEO of Toshiba Digital Solutions Corporation said: “TDSL’s success in using SQBM+ in protein evaluation underlines that this versatile quantum-inspired optimization solution can be applied to complex issues in diverse fields. In this case, it has made a clear and valuable contribution by broadening the ability to identify druggable proteins, opening the way to innovations in drug development. Looking to the future, we look forward to using SQBM+ in various drug discovery situations.”

・About Revorf Co., Ltd.

Revorf aims to establish a new medical technology and drug discovery platform method by combining its unique technology for detecting and analyzing genes such as RNA, technology for analyzing protein information, and data analysis and AI technology.

1：
Computational drug discovery: A drug discovery method that uses computational science to develop drugs.

2：
Toshiba Digital Solutions Press Release（March 2022): Announcing the Launch of the Quantum-Inspired Optimization Solution SQBM+™:
https://www.global.toshiba/ww/company/digitalsolution/news/2022/0302.html

3：
Protein functions are controlled by enzymes that act as regulators, a mechanism called allosteric regulation. Targeting sites that regulator bind to (allosteric regulatory sites) brings benefits that include more drug targets, the formulation of highly specific drugs, and the possibility of fewer side effects. Technology that identifies allosteric regulatory sites is seen as fundamental for increasing the success rate in new drug development.

4：
Drug target: A protein consider to be responsible for a disease, and the target in therapeutic drug design.

5：
Allosteric regulatory site: A region other than the active center of a protein to which a regulatory molecule (allosteric modulator) binds.

6：
In vitro experiment: *In vitro* is Latin for “within the glass.” An *in vitro* experiment creates an artificial environment in a test tube or an incubator that reproduces conditions within the body.

7：
KRAS: A type of oncogene. Oncogenes are genes with the potential to trigger cancer, and are found in all cells.

8：
Cryogenic electron microscope: A transmission electron microscope that can observe biomolecules, such as proteins, cooled by liquid nitrogen. Realizes high resolution observation of protein structures.

9：
AlphaFold2: An AI system developed by DeepMind Technologies that analyzes the structure of proteins from amino acid sequences.

10：
Toshiba OPEN INNOVATION PROGRAM 2021: This program recruits companies that are enthusiastic about creating innovation. In the program, we utilize the business assets and advanced technologies of the Group to support accelerated commercialization of applicant companies through collaboration with the Group.

Quantum-Inspired Optimization Solution SQBM+ (English site)
https://www.global.toshiba/ww/products-solutions/ai-iot/sbm.html