Quris-AI
www.quris.ai

Quris-AI: an artificial intelligence innovator disrupting the drug development process

By integrating artificial intelligence, three-dimensional and multi-organ technology, Quris-AI is developing a ground-breaking clinical-prediction platform with the potential to revolutionize disease modelling and personalized medicine.

Drug discovery and development is an extremely lengthy and expensive process; yet drug safety, a fundamental part of this process, continues to be a major unaddressed problem. The problem of predicting which drug candidates will work safely in which humans—the so-called clinical-prediction challenge—remains unresolved: a staggering 92%[1] of all drugs fail in clinical trials, despite 'successfully' passing preclinical testing, costing pharma companies billions of dollars each year[2–4].

Artificial intelligence (AI) innovator Quris-AI is addressing this challenge. By integrating high-throughput three-dimensional (3D) and multi-organ technologies, real-time sensing, and stem-cell genomic diversity with state-of-the-art machine learning, the company is developing a Bio-AI Clinical Prediction Platform to reliably predict the clinical safety of drug candidates (Fig. 1). The first-of-its-kind system alleviates the need to fully rely on faulty animal-testing models and is designed to better predict which drug candidates will work safely in humans, eliminating the tremendous cost and wasted time associated with failed clinical trials.

A 3D multi-organ approach for better prediction

Predicting which drug candidates will be safe and efficacious in humans is a formidable challenge. Traditional preclinical data typically involve in vitro lab assays that rely on single-cell-type models, two-dimensional (2D) tissue-culture models, and/or tests in mouse and other animal models. Although easily accessible, these data have limited human biological relevance and, consequently, are very poor at predicting clinical safety in the human body.

> **Our Bio-AI Clinical Prediction Platform is the first system designed for multiple repeats and organs, and differs from traditional approaches in both the data that it uses and how it uses them... This is a radical new approach to predicting drug safety**
>
> Isaac Bentwich, Founder & CEO, Quris-AI

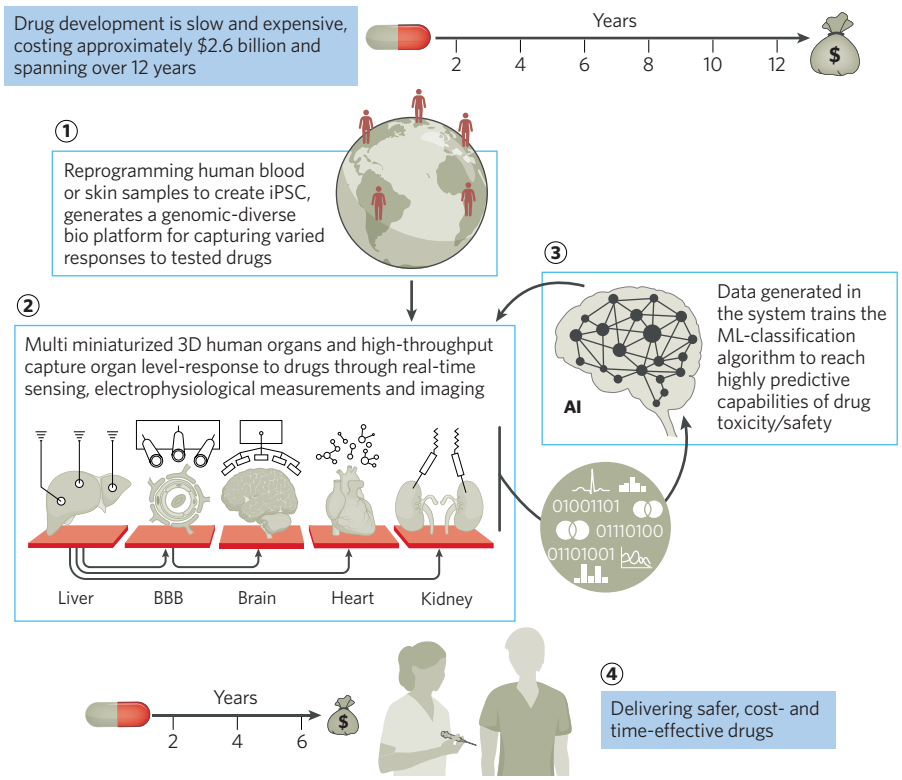

Fig. 1 | The Quris Bio-AI Clinical Prediction Platform. The platform is designed to reliably predict the clinical safety of drug candidates by integrating high-throughput three-dimensional and multi-organ technologies, real-time sensing, and stem-cell genomic diversity with state-of-the-art machine learning.

Despite promising progress in the development and validation of 3D miniaturized human-organ models in recent years, traditional organ-on-a-chip models still cannot fully solve the clinical safety-prediction challenge. While some can now functionally mimic the real organ response, expressing the same enzymes and producing similar metabolites to better imitate the response in the human body, current devices are low-throughput and poorly scalable.

Addressing this issue, Quris uses a high-throughput 3D and multi-organ approach involving various, separate miniaturized human organs—currently including the liver, blood–brain barrier, and brain—that can be interconnected to capture a systemic effect. When a therapeutic is administered to this 3D multi-organ model, the system mimics the functional effects of interacting organs, reproducing the complex metabolism that would occur in an actual patient. "Compared to old-school biology, our system is designed to have unprecedented response-assessment capabilities and far superior modelling of the systemic effect of drugs," said Isaac Bentwich, founder and CEO at Quris. "For example, we can assess the effect of a small molecule not only on the liver, but also after it has been metabolized in the liver and the metabolites have reached the brain. This often tells a very different story."

Moreover, Quris has incorporated sensors that continuously measure metabolites and other biomarkers produced by the high-throughput 3D and multi-organ system in real time. For each administered drug, this creates massive amounts of time-series data for every metabolite monitored.

Further setting the platform apart from cell lines typically used in lab assays and other organ-on-a-chip companies, Quris intends to leverage genomic diversity by deriving its 3D and multi-organ systems from stem cells from multiple donors to capture a wider picture of response patterns.

"These three components—a high-throughput 3D and multi-organ system, real-time sensing, and genomic diversity—can considerably improve data-safety predictability, but are missing from other organ-on-a-chip approaches," pointed out Amir Bein, VP of biology at Quris.

The power of AI

Despite the power of AI in solving complex problems, it has not taken-off commercially with organ-on-a-chip companies to date. "Current AI pharma companies rely primarily on 2D biology, which is an extremely poor predictor of drug safety, whereas organ-on-a-chip devices rely mainly on manual, non-AI analysis of their data, ignoring the tremendous power of machine learning and AI," explained Bein.

> **By integrating several disruptive technologies, our Bio-AI Platform holds the power to train AI to not only predict whether a drug is generally safe, but also to ascertain who can safely use it**
>
> Amir Bein, VP Biology, Quris-AI

Quris has taken the next logical step, integrating the unmatched power of AI with the unique data predictability of 3D and multi-organ technology. The Bio-AI Platform allows automated testing of thousands of known safe and unsafe drugs in genetically diverse, miniaturized multi-organoids, replicating and measuring their systemic metabolic effect as if in the human body. "In essence, this becomes a 'clinical-trial-on-a-chip', capturing the spectrum of responses of genetically diverse patients to each administered drug," said Bentwich.

The proprietary, classified data generated in this continuous high-throughput system is used for training the machine-learning classification algorithm to reach highly predictive capabilities for drug toxicity/safety. Then, when a new drug entity is applied to the model, the real-time data it generates are used by AI to predict whether or not it will be safe in humans.

"Traditional organ-on-a-chip approaches to detecting drug safety are modelled after antiquated animal studies, in that a single experiment generates primary end-point data that are analyzed manually. By contrast, our Bio-AI approach relies on thousands of experiments, which generate massive, real-time, time-series data, which cannot be assessed manually," said Bentwich. "Our Bio-AI Clinical Prediction Platform is the first system designed for multiple repeats and organs, and differs from traditional approaches in both the data that it uses and how it uses them, crucially generating predictive data. This is a radical new approach to predicting drug safety."

By harnessing the tremendous power of AI to predict drug toxicity, Quris has the potential to revolutionize clinical-safety prediction. Indeed, the platform has been shown to have an 85% sensitivity and a very high (78%) specificity when testing for liver toxicity. It is also significantly more cost effective than trying to do the same using a conventional organ-on-a-chip approach.

"By integrating several disruptive technologies, our Bio-AI Platform holds the power to train AI to not only predict whether a drug is generally safe, but also to ascertain who can safely use it," said Bein. "This has far-reaching implications for drug development, personalized medicine, repurposing drugs, and optimizing clinical trials."

Eminent scalability

Successfully tackling the complexities of clinical prediction requires machine-learning models to routinely run thousands, and eventually millions, of biological, multi-organ experiments for AI training, explained Bentwich. Limitations of older organ-on-a-chip devices preclude the ability to run such experiments. Quris' system, however, is highly scalable and tightly integrated with the AI, enabling massive experiments at a small fraction of the cost.

The Quris Bio-AI Clinical Prediction Platform (with 29 granted and pending patents) is currently running on liver, blood–brain barrier, and brain organoids, collecting millions of data points and covering nine genomes, said Bentwich. In the next two years, the platform will incorporate additional organ models (such as heart and kidney) with the aim of incorporating tens to hundreds of different genetic backgrounds. And although it initially focused on safety, the platform is also valid for assessing efficacy.

Furthermore, as a company that is focused on non-animal safety prediction, Quris is uniquely positioned to take advantage of a recent legislative landmark: the US Food and Drug Administration (FDA)'s Modernization Act 2.0. This was recently signed into law, ending the agency's mandated reliance on animal studies/modelling; after more than 80 years, it is allowing alternatives to animal testing in drug development. "It's a positive perfect-storm for us," said Bentwich. "3D organ models are coming of age, AI is becoming powerful and focused on this problem, and now regulators are acknowledging that animal studies are limited in their predictability."

Ready to partner with pharma

Based in Boston (MA, USA) and Tel Aviv (Israel), Quris is led by a stellar team of pioneers in the fields of machine learning, statistics, biology, software, genomics, engineering, and med-tech—all with a strong track-record of success.

> **We are striving to overcome one of the major obstacles in drug development—namely the poor capabilities of safety prediction using conventional models**
>
> Isaac Bentwich, Founder & CEO, Quris-AI

Corporate highlights

- Established collaborations with pharmaceutical and research institutes worldwide.
- Led by pharma and tech visionaries, including Moderna co-founder Robert Langer, Nobel laureate Aaron Ciechanover, and former Pfizer CEO Henry McKinnell.
- Backed by an exceptional mix of top investors and industry pioneers with $37 million in seed funding.
- Strong intellectual property portfolio protecting novel technology.

Harnessing the platform, the business has three synergistic revenue engines: expanding its drug pipeline by identifying promising drug candidates; providing personalized medicine services to patients; and forming pharmaceutical alliances to develop safe drugs, faster. To that end, Quris is already collaborating with Merck KGaA (Darmstadt, Germany), a leading science and technology company, to assess the Bio-AI Clinical Prediction Platform compared to traditional in vitro and in vivo approaches. The project is initially focusing on identifying potential liver-toxicity risks for several drug candidates, with special emphasis on those that preclinical experiments failed to identify. Quris is also in advanced dialogue with several other top pharmaceutical firms and is looking to partner with additional biopharma companies that would like to utilize its Bio-AI Platform to evaluate the safety profile of pre-clinical and clinical assets.

Quris' disruptive platform that marries machine learning with 3D/multi-organ technology has the potential to reduce the costly and inefficient practice of testing on animals and to be substantially better at predicting which drug candidates will work safely in humans. "We are striving to overcome one of the major obstacles in drug development—namely the poor capabilities of safety prediction using conventional models. Our Bio-AI Clinical Prediction Platform enables the testing of hundreds or thousands of compounds on human tissue in a very short time," said Bentwich. "Thus we are at the forefront of a revolution that has the potential to considerably improve disease modelling and personalized medicine, as well as to drastically cut the time and cost of developing safe drugs."

1. BIO, Informa Pharma Intelligence and QLS Advisors. *Clinical Development Success Rates and Contributing Factors 2011–2020* (2021).
2. DiMasi, J. A. et al. *Clin. Pharmacol. Ther.* **87**, 272–277 (2010).
3. DiMasi, J. A. et al. *J. Clin. Oncol.* **25**, 209–216 (2007).
4. Gupta Strategists. *The cost of opportunity.* https://gupta-strategists.nl/en/research/the-cost-of-opportunity (February 2019).

CONTACT
Isaac Bentwich, Founder & CEO
Quris-AI
Tel-Aviv, Israel
Email: bentwich@quris.ai