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How machines could mine forgotten data

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Drug discovery is getting harder, and some companies are turning to machine learning to look for new targets.

The low-hanging fruit has already been picked, and discovering novel drugs is getting harder. But some in biopharma are convinced that the new targets and therapies are already out there; it's just that they are hidden amid reams of data, and need to be uncovered by artificial intelligence.

“We already have the cure for motor neurone disease, and pretty much every tumour, somewhere in a file. We just have to find it,” Alex McMullan, regional chief technology officer of the machine learning specialist Pure Storage, told *Vantage* on the sidelines of the AI Summit in London in June.

Forgotten but not gone

Many of the big pharma groups appear to have come to the same conclusion, with Novartis, Glaxosmithkline, Astrazeneca and Johnson & Johnson all presenting at the same conference on their plans to use machine learning in drug discovery.

Novartis’s head of global development operations, Badhri Srinivasan, admitted that some of the raw data from the company’s clinicial trials had been sitting, unused, at CROs and other third-party companies – and it now wants to tap into this resource.

George Okafo, senior director of Glaxosmithkline’s in silico drug discovery unit, outlined his company’s plan to look for new targets in existing datasets, with an initial focus on hard-to-treat disorders. Glaxo hopes to be able to go from concept to candidate in 12-18 months.

And Glaxo’s recent deal with the consumer testing specialist 23andme, which aims to discover new drug targets, shows that the UK company is putting its money where its mouth is.

So how is machine learning being used in practice? One approach, being taken by the AI specialist GNS Healthcare, is homing in on clinical trial subjects who do not respond to a given therapy.

“We want to learn who those patients are and what’s causing that lack of response on a molecular level,” the group’s co-founder and chief commercial officer, Iya Khalil, told *Vantage*. “If we can learn that then we have a new target.”

She believes that this approach would not be possible without machine learning, which allows the analysis of vastly more data than could be comprehended by a human. GNS is working with 30% of the top pharma

companies at any given time on various activities including target discovery, according to Ms Khalil.

Reuse and recycle

But finding new therapies does not always involve new targets – or even new drugs. The UK company Healx is using machine learning to identify existing therapies that could be repurposed for rare diseases.

The approach involves comparing transcriptomes – the full set of RNA molecules – in patients with rare diseases versus healthy controls. This could identify new targets, which are then matched against a database of approved drugs, to find a product that hits this target.

Repurposing older drugs is a strategy that has not always gone smoothly for other companies such as Axovant and Retrophin. This might be a more efficient way of going about it.

Healx's co-founder, David Brown, told *Vantage* that the company's "hypothesis free" approach was what made it different. "We don't start with favoured targets or modes of action," he said, adding that picking the wrong target at the beginning of the process was often where companies went wrong under the traditional drug discovery model.

The company does not even begin with a specific rare disease, he added. "We'll let the algorithms and the data decide which one to go for – I think that's really different than the traditional biotech."

The advantage of Healx's approach is that these drugs have already proven safe, so their development could be fast tracked, keeping costs down. Still, lack of intellectual protection for old, marketed drugs is a problem, and new method-of-use patents are notoriously unreliable. Mr Brown reckons his company could develop new formulations or combinations, with stronger IP protection.

However, it is hard to see this approach being adopted throughout the entire biopharma world, particularly if the thirst for riskier projects like cell and gene therapy continues.

Modelling

Another technological advance that could transform drug discovery is the development of in silico models enabling the rapid generation of data on potential candidates, which could help weed out duds quickly and allow a greater focus on more promising projects.

This feeds into biopharma's obsession with "failing fast" – a term that came up more than once at the AI Summit. Companies obviously hope that hard data could give them better reason to bail out of doomed projects early, but it would take a big shift in the current mindset; biopharma has historically found it hard to let go of stuttering drug candidates.

An *in silico* human being, "a model that fully explains the human body from a molecular level", would be the ultimate goal here. Alan Louie, an analyst at IDC Health Insights with a focus on AI, told *Vantage* that this could become reality in the next five to 10 years, even if it currently sounds like science fiction.

But Ray Barlow, chief executive of the UK company E-therapeutics, which is using AI for drug discovery, is not sure that regulators are ready to embrace *in silico* models. "I don't see the FDA letting you go straight into a human based upon an *in silico* prediction," he told *Vantage*.

But he added: "The FDA's waking up – regulatory agencies are now accepting that you can use *in silico* predictions of toxicology as a guide".

And Pure Storage's Mr McMullan thinks that regulators will get more comfortable with these simulations: "There's always going to be a risk, but at different stages of different diseases you'll find the patient more willing to take that risk." The company provides machine learning technology across various sectors, including pharma.

New era?

It is undeniable that big pharma is increasingly looking towards machine learning to improve the drug discovery process (*Big pharma piles into machine learning, but what will it get out of it?, July 31, 2018*).

And Mr Brown of Healx contended that the old method – picking a disease, then a target, then generating chemical leads against that target – needed turning on its head.

GNS's Ms Khalil reckons that the number-crunching capabilities of machine learning will become invaluable. "With the traditional method of target discovery, you think a gene might be involved. You knock it down; it may or may not be involved. And now you're going to pick another gene. Well, there are 30,000 genes – that's way too many possibilities to go through one gene at a time."

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