Opinion

When is AI useful for biomarker discovery in cancer?

By Dr Uzma Asghar, Prof Andrew Biankin, Prof Philip Beer

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What is a biomarker?

Put simply, a biomarker is something that can be measured to provide information about a disease. Biomarkers determine not only the condition but also the optimal treatment for that condition and are used as ‘readouts’ for response to treatment. Understandably, in complex diseases like cancer, biomarkers are of particular importance and must be reliable, informative and cost-effective.

This is especially important for drug development, as each new investigational drug is inherently linked to biomarkers as a measure of its efficacy and toxicity. A recent study in JAMA[1] estimated that the clinical trial success rate from Phase 1 to Approval in oncology was a shocking 3.4% - by far the lowest across all therapeutic areas. The cost of failed drugs is high - socially and economically. To improve drug success rates and reduce the cost of development, drug developers must generate robust and predictive biomarkers. Recent advances in machine learning, advanced analytics and artificial intelligence are set to make this process substantially more efficient and effective.

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[1]Wouters OJ, McKee M, Luyten J. Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018. JAMA. 2020;323(9):844–853. doi:10.1001/jama.2020.1166

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Types of biomarkers

Biomarkers must be robustly measurable. Measurable features of the disease include biochemical attributes, genetic changes, radiological imaging, and histopathological features. A biomarker may be a single analyte or a composite measurement of several different analytes.

Biomarkers fall into one or more of the following categories:

1. Diagnostic biomarkers are required for accurate diagnosis, for example, ATRX mutation and genomic deletion of 1p/19q in adult gliomas.
2. Prognostic biomarkers predict clinical outcomes, for example, a TP53 mutation is associated with worse outcomes in appendiceal cancer and KRAS mutations are associated with worse outcomes in colorectal cancers.
3. Predictive biomarkers indicate the likelihood of response to a specific therapy, for example, protein expression of the oestrogen receptor and response to hormone suppression in breast cancer, EGFR mutation and response to EGFR inhibitors in lung cancer, and high tumour mutation burden and response to immune checkpoint inhibitors across multiple cancer types.
4. Pharmacogenomic biomarkers guide correct drug dosing to ensure that individual patients receive an effective dose without risk of serious side effects, for example, DPYD genotype and dosing of fluorouracil.

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How can AI positively impact the cancer biomarker landscape?

Diagnostic biomarkers

In cancer of unknown primary (CUP), machine learning adds value by processing large amounts of complex molecular data from tumours to help identify the tissue of origin when conventional clinical approaches fail.

Prognostic biomarkers

Knowledge about prognostic biomarkers in cancer is rapidly increasing, with multiple candidates identified in different datasets, based on testing multiple analytes using different platforms at different time points. Machine learning algorithms can integrate multi-omics data and clinical data to make accurate survival predictions and quantify the prognostic significance of each specific feature.

The automation of digital whole slide imaging of tumours and efficient quantification of cell populations has widened the prospect for biomarker discovery beyond genomics. For example, machine learning makes the routine evaluation of tumour infiltrating lymphocytes (TILS), an established prognostic biomarker in triple negative breast cancer, feasible for delivery as part of routine clinical practice.

AI-driven companion diagnostic platforms hold strong potential for identifying target patient populations within clinical trials.

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Predictive biomarkers

Phase 1 clinical studies taking a personalised medicine approach have greater success with higher drug response rates. Hence pharmaceutical and biotech companies are investing heavily in biomarker programmes and embedding them within their drug development pipelines.

Challenging drug classes for the discovery of predictive biomarkers include cytotoxic agents and immunotherapy drugs. Machine learning approaches can identify key biological pathways to help narrow the search for biomarkers. In addition, AI-driven companion diagnostic platforms hold strong potential for identifying target patient populations within clinical trials.

Target discovery

Understanding mechanisms that cause resistance to treatment has the potential to be novel targets for new therapies.

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The way forward

Using AI as a biomarker discovery tool, coupled with experimental laboratory approaches and clinical outcome data, has the ability to accelerate drug discovery and development, including the better application of current therapeutic strategies. The next natural step in the evolution of precision oncology is the use of artificial intelligence-driven biomarker platforms for diagnostic pathways and the characterisation of target patient populations to better select the best treatment option for a patient.

It is clear that biomarker strategies that better select patients for appropriate therapy are the way forward. Many forget that targeting the oestrogen receptor, initially with tamoxifen, and now with newer strategies that target the oestrogen pathway, has likely helped more cancer patients than all other drug treatments combined. Tamoxifen was developed in the 1970s. Several other examples of low-hanging fruit that target specific genetic aberrations such as EGFR mutations reaffirm the strategy. We now need to move to more complex biomarkers that guide drug development as the old one-size-fits-all approach is failing and unsustainable.

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