

NIH Researchers Develop AI Tool With Potential to More Precisely Match Cancer Drugs to Patients

Proof-of-concept study analyzed a newer technology known as single-cell RNA sequencing.

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In a proof-of-concept study, researchers at the National Institutes of Health (NIH) have developed an artificial intelligence (AI) tool that uses data from individual cells inside tumors to predict whether a person's cancer will respond to a specific drug.

Researchers at the National Cancer Institute (NCI), part of NIH, published their work on April 18, 2024, in [Nature Cancer](#), and suggest that such single-cell RNA sequencing data could one day be used to help doctors more precisely match cancer patients with drugs that will be effective for their cancer.

Current approaches to matching patients to drugs rely on bulk sequencing of tumor DNA and RNA, which takes an average of all the cells in a tumor sample. However, tumors contain more than one type of cell and in fact can have many different types of subpopulations of cells. Individual cells in these subpopulations are known as clones. Researchers believe these subpopulations of cells may respond differently to specific drugs, which could explain why some patients do not respond to certain drugs or develop resistance to them.

In contrast to bulk sequencing, a newer technology known as single-cell RNA sequencing provides much higher resolution data, down to the single-cell level. Using this approach to identify and target individual clones may lead to more lasting drug responses. However, single-cell gene expression data are much more costly to generate than bulk gene expression data and not yet widely available in clinical settings.

In the new study, the researchers investigated whether they could use a machine learning technique called transfer learning to train an AI model to predict drug responses using widely available bulk RNA sequencing data but then fine-tune that model using single-cell RNA sequencing data. Using this approach on published cell-line data from large-scale drug screens, the researchers built AI models for 44 Food and Drug Administration-approved cancer drugs. The AI models accurately predicted how individual cells would respond to both single drugs and combinations of drugs.

The researchers then tested their approach on published data for 41 patients with multiple myeloma treated with a combination of four drugs, and 33 patients with breast cancer treated with a combination of two drugs. The researchers discovered that if just one clone were resistant to a particular drug, the patient would not respond to that drug, even if all the other clones responded. In addition, the AI model successfully predicted the development of resistance in published data from 24 patients treated with targeted therapies for non-small cell lung cancer.

The researchers cautioned that the accuracy of this technique will improve if single-cell RNA sequencing data become more widely available. In the meantime, the researchers have developed a research website and a guide for how to use the AI model, called Personalized Single-Cell Expression-based Planning for Treatments In Oncology (PERCEPTION), with new datasets.

This work was conducted by NCI's Center for Cancer Research and led by Alejandro Schaffer, PhD, and Sanju Sinha, PhD, previously at NCI, now at Sanford Burnham Prebys. Eytan Ruppin, MD, PhD, supervised the work.

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