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AI test could predict effective cancer drug combinations in less than two days

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Scientists have created a prototype test that can predict which drug combinations are likely to work for cancer patients in as little as 24 to 48 hours.

Their cutting-edge technique uses artificial intelligence to analyze large-scale protein data from tumor samples, and is able to predict patients' response to drugs more accurately than is currently possible.

Genetic analysis of tumors can reveal mutations that are fueling cancers growth, some of which can be targeted with treatment—but genomics alone does not provide sufficiently accurate predictions to select drug combinations.

Scientists at The Institute of Cancer Research, London, tested the new technique on individual cancer cells in the lab and tumor cells freshly isolated from lung fluid in people with non-small cell lung cancer.

Their study is published in the journal *Molecular Cancer Therapeutics*, and was funded by the National Institute for Health Research (NIHR), Wellcome, Cancer Research UK and by The Institute of Cancer Research (ICR) – which as well as being a research institute is also a charity.

Training machine learning algorithms

Scientists carried out "proteomic" analyses—examining changes in 52 important proteins and how they interact with each other in response to drug treatments. Researchers then trained machine learning algorithms to define the key protein changes that predict drug responses.

First, the researchers used the algorithm to predict how sensitive cells were to individual cancer drugs. They found that the technique could predict individual drug responses more accurately than genetic features, such as mutations in key genes EGFR, KRAS and PIK3CA—three genetic markers currently used in the clinic to predict drug responses in lung cancer.

Researchers then used the same approach to predict sensitivity to drug combinations—using 21 different two-drug combinations in lung cancer cells with different gene faults, such as mutations in EGFR and KRAS.

Of 252 total drug combinations, 128 showed some level of synergy, meaning their combined effect exceeded the effect of each individual drug added together.

Of these, the AI test correctly identified the top five ranked combinations 57 percent of the time and the top 10 ranked combinations 83 percent of the time.

Identifying successful combinations

The test successfully identified combinations which have previously been shown to have promise—for example, combinations of trametinib and capivasertib, or gefitinib and everolimus, in non-small cell lung cancer cell lines with EGFR mutations.

Researchers were also able to identify possible new combinations such as vemurafenib and capivasertib, which the test found could potentially be effective for non-small cell lung cancer cell lines with no mutations in EGFR or KRAS.

This is therefore the first prototype test that can offer personalized predictions of which drug combinations are likely to work in different individuals. Researchers at the ICR believe the new technology could be crucial in overcoming cancer evolution and treatment resistance by allowing doctors to analyze how drugs work in combination.

The new study establishes proof of concept but the test will need further validation before it can be used in patients. The study looked at seven different drugs in multiple combinations, but researchers are already

planning a larger follow-up study which will test 15 drugs and look at 12,000 proteins involved in signal transduction instead of 52.

'Potential to guide doctors'

Study leader Professor Udai Banerji, professor of molecular cancer pharmacology at the Institute of Cancer Research, London, and Consultant Medical Oncologist at The Royal Marsden NHS Foundation Trust, said:

"Our test provides proof of concept for using AI to analyze changes in the way information flows within cancer cells and make predictions about how tumors are likely to respond to combinations of drugs.

"With a rapid turnaround time of less than two days, the test has the potential to guide doctors in their judgements on which treatments are most likely to benefit individual cancer patients. It is an important step to move forward from our current focus on using genetic mutations to predict response.

"Our findings show that our innovative approach is feasible, and makes more accurate predictions than genetic analysis for patients with non-small cell lung cancer. Before this test can enter the clinic and guide personalized treatment, we will need to further validate our findings—for example, by carrying out a study where we run the test in patients already getting a treatment to check if the predictions are correct."

'Combining therapies to overcome resistance'

Professor Kristian Helin, chief executive of the Institute of Cancer Research, London, said:

"One of the greatest challenges we face in cancer research and treatment is the ability of cancer to adapt, evolve and become drug resistant. We expect that the future of cancer treatment will be in combining therapies to overcome resistance—but we need to get much better at predicting which drug combinations will work best for individual patients.

"This new study is a great example of interdisciplinary collaboration, in integrating our understanding of cancer biology, AI and clinical medicine to provide proof of concept for a new test that can predict which combination treatments are most likely to work for patients. It demonstrates the potential power of AI and protein analysis to personalize treatment and could be an important step in helping us tackle drug resistance—hopefully helping us offer patients smarter, more personalized treatment options."

More information: Elizabeth A. Coker et al, Individualised prediction of drug response and rational combination therapy in NSCLC using artificial intelligence enabled studies of acute phosphoproteomic changes, *Molecular Cancer Therapeutics* (2022). DOI: 10.1158/1535-7163.MCT-21-0442

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