MedicalXpress

Testing blood metabolites could help tailor cancer treatment

June 3 2016

Testing for metabolic changes in the blood could indicate whether a cancer drug is working as designed, a new study reports.

Scientists have found that measuring how cancer treatment affects the levels of metabolites - the building blocks of fats and proteins - can be used to assess whether the drug is hitting its intended target.

This new way of monitoring cancer therapy could speed up the development of new targeted drugs - which exploit specific genetic weaknesses in cancer cells - and help in tailoring treatment for patients.

Scientists at The Institute of Cancer Research, London, measured the levels of 180 blood markers in 41 patients with advanced cancers in a phase I clinical trial conducted with The Royal Marsden NHS Foundation Trust.

They found that investigating the mix of metabolic markers could accurately assess how cancers were responding to the targeted drug pictilisib.

Their study was funded by the Wellcome Trust, Cancer Research UK and the pharmaceutical company Roche, and is published in the journal *Molecular Cancer Therapeutics*.

Pictilisib is designed to specifically target a molecular pathway in cancer cells, called PI3 kinase, which has key a role in cell metabolism and is

defective in a range of cancer types.

As cancers with PI3K defects grow, they can cause a decrease in the levels of metabolites in the bloodstream.

The new study is the first to show that blood metabolites are testable indicators of whether or not a new cancer treatment is hitting the correct target, both in preclinical mouse models and also in a trial of patients.

Using a sensitive technique called mass spectrometry, scientists at The Institute of Cancer Research (ICR) initially analysed the metabolite levels in the blood of mice with cancers that had defects in the PI3K pathway.

They found that the blood levels of 26 different metabolites, which were low prior to therapy, had risen considerably following treatment with pictilisib. Their findings indicated that the drug was hitting its target, and reversing the effects of the cancer on mouse metabolites.

Similarly, in humans the ICR researchers found that almost all of the metabolites - 22 out of the initial 26 - once again rose in response to pictilisib treatment, as seen in the mice.

Blood levels of the metabolites began to increase after a single dose of pictilisib, and were seen to drop again when treatment was stopped, suggesting that the effect was directly related to the drug treatment.

Metabolites vary naturally depending on the time of day or how much food a patient has eaten. But the researchers were able to provide the first strong evidence that despite this variation metabolites can be used to test if a drug is working, and could help guide decisions about treatment.

Dr Florence Raynaud, Senior Researcher in the Clinical Pharmacology and Trials Team at The Institute of Cancer Research, London, said:

"We have shown that assessing a patient's metabolites can be a quick and simple way of assessing whether a cancer drug is specifically hitting its intended target in the body. Our study is an important step in the development of new precision cancer therapies, and is the first to show that blood metabolites have real potential to monitor the effects of novel agents.

"Our method was developed specifically for pictilisib but could now be adapted to discover metabolite markers for other cancer treatments."

Co-author Professor Paul Workman, Chief Executive of The Institute of Cancer Research, London, said:

"In the modern world of precision cancer medicine it is really vital to understand a drug's mechanism of action, and to know how it is working not just overall but in individual cancer patients.

"By monitoring metabolic signals in the blood, we could make informed decisions about drug development without having to wait years to see the final results of large clinical trials. And our method could eventually be used to monitor patients routinely during the course of treatment, as a quick and easy way of assessing whether a drug is still working, or whether treatment needs to be adapted."

Provided by Institute of Cancer Research