MedicalXpress

Study identifies biomarker that may predict treatment response to chemoimmunotherapy

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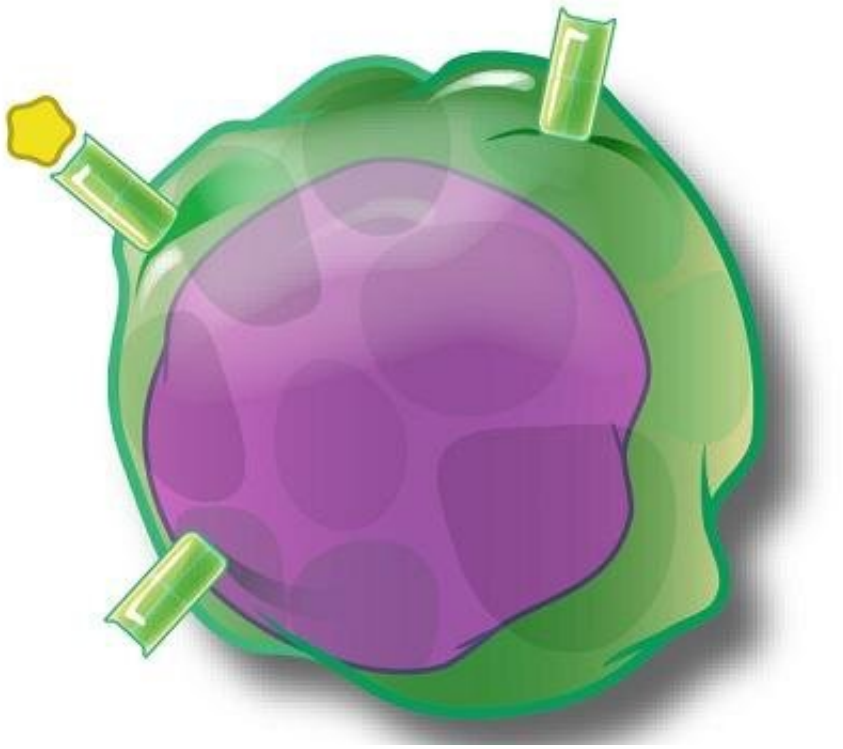

An artist’s depiction of a T cell. Credit: NIAID

Cutting-edge cancer treatments like immunotherapy are offering new hope for patients, often in combination with more common approaches such as chemotherapy. But determining the best treatment combination isn't always straightforward. Many patients spend valuable time on expensive therapies with serious side effects that aren't effective against their cancer.

Now, a new discovery is poised to help. Researchers from USC Norris Comprehensive Cancer Center have identified a biomarker that indicates which patients with non-small cell lung cancer (NSCLC) will respond well to chemoimmunotherapy. The biomarker, known as CX3CR1, is expressed on T-cells and can be detected with a simple blood test, six to nine weeks after a patient starts treatment. The results were published in the journal *Cancer Research Communications*.

"We found that T-cell CX3CR1 expression can be used to monitor treatment effectiveness, and can be used as a biomarker to predict treatment response and prognosis for these patients," said the study's lead author, Fumito Ito, MD, Ph.D., associate professor of surgery at the Keck School of Medicine of USC and co-leader of the Translational and Clinical Science Research program at the USC Norris cancer center.

Ito and his team collected a series of blood samples from 29 patients with NSCLC who received a combination of immune checkpoint inhibitor (ICI) therapy and chemotherapy. They found that patients with elevated levels of CX3CR1 after six and nine weeks of treatment were more likely to see long-terms benefits from chemoimmunotherapy, including tumor shrinkage and cancer remission.

The findings build on earlier work by Ito and his team, published in 2021, which found that CX3CR1 can be used to predict treatment response in NSCLC patients receiving immunotherapy only. The biomarker may also be useful for other cancers and therapies and could ultimately help doctors and patients determine the most effective cancer treatments while avoiding unnecessary side effects and invasive biopsies.

An "early-on" treatment biomarker

ICI therapy has revolutionized the treatment of lung and other cancers, but it doesn't work for all patients. For some, it can even trigger an

autoimmune reaction marked by life-threatening problems with the lungs, liver, kidneys, or other organs.

Current pre-treatment methods to determine which patients will benefit from ICI therapy—and which will experience harmful side effects—don't always work. CX3CR1 is the next best thing: an "early-on" treatment biomarker that is noninvasive. It can be measured when patients attend their first check-up and imaging appointment, typically about two months after starting ICI.

"If ICI is not working, we like to stop as soon as possible," Ito said. "We have other viable treatment options for NSCLC patients, so the biomarker can help us identify patients who might have better results with an alternative therapy."

Ito and his colleagues used a multi-omics approach, combining two cutting-edge sequencing methods to find the genomic and transcriptomic signature of T-cells. Each T-cell has a unique receptor pattern that can be used as a "barcode" to track them down in different parts of the body, including those attacking a tumor and those circulating in the blood.

"By combining two different types of next-generation sequencing, we found a way to characterize and monitor patients' T-cells," he said. "Next, we plan to use this analysis in a larger cohort to see if patients with other cancers will respond in a similar way."

More evidence for CX3CR1

Because ICI therapy targets a patient's immune system, rather than the tumor itself, the newly discovered biomarker could have broad utility across multiple types of cancer. In addition to testing other cancers, Ito and his colleagues also plan to explore whether CX3CR1 can predict treatment response to other types of immunotherapy, including adoptive

T-cell therapy and vaccine-based therapy.

The team will also collect additional evidence for CX3CR1 in a larger group of non-small cell lung cancer patients undergoing ICI, both with and without chemotherapy. If additional research is successful, a blood test for the biomarker could reach broader patient populations in two to three years, Ito said.

In addition to Ito, the study's other authors are Takayoshi Yamauchi from the Keck School of Medicine of USC; Eihab Abdelfatah from New York University Langone Health; and Mark D. Long, Ryutaro Kajihara and Takaaki Oba from the Roswell Park Comprehensive Cancer Center.

More information: Eihab Abdelfatah et al, Predictive and Prognostic Implications of Circulating CX3CR1+ CD8+ T Cells in Non–Small Cell Lung Cancer Patients Treated with Chemo-Immunotherapy, *Cancer Research Communications* (2023). DOI: 10.1158/2767-9764.CRC-22-0383

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