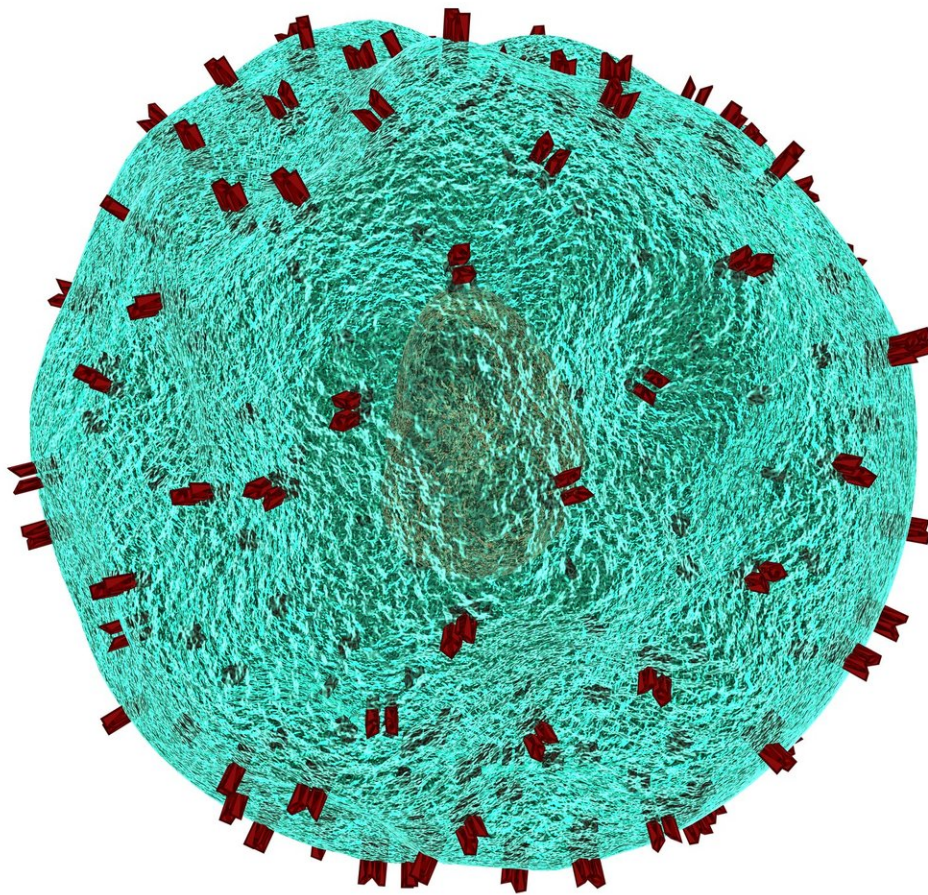


Researchers identify experimental immunotherapy approach to target acute myeloid leukemia

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University of North Carolina Lineberger Comprehensive Cancer Center researchers have identified a potential way to target a subtype of acute myeloid leukemia (AML) using chimeric antigen receptor (CAR) T-cell therapy, a form of immunotherapy in which patients' immune cells are genetically engineered to recognize and track their cancer.

At the 60th American Society of Hematology Annual Meeting in San Diego on Dec. 3, researchers presented preliminary findings from preclinical studies of CAR T-cells directed towards a potential target called B7-H3, which is found on the [cell surface](#) in certain types of AML. They believe they can genetically engineer a patient's normal white blood cells to create CAR T-cells that will home in on this target and kill AML cells.

"Acute myeloid leukemia is the most common acute leukemia in adults," said the study's first author Eben Lichtman, MD, a clinical instructor in the UNC School of Medicine Division of Hematology/Oncology. "The prognosis is poor, with only about a quarter of patients surviving more than five years from diagnosis. CAR T-cell therapy has emerged as an important and successful component of therapy for [acute lymphoblastic leukemia](#), or ALL, but CAR T-cell treatment has been more elusive for AML. This is partly because no good targets have been identified on the surface of AML cells that allow us to use CAR T-cells to target them without also targeting normal components of our immune system."

Studying a group of 10 patients with monocytic AML, the researchers found that most patients had B7-H3 expressed on a high proportion of

their leukemia cells, with a median of 62.5 percent of the target on their leukemia cells. In a separate experiment of leukemic cancer cell lines commonly studied in the laboratory, B7-H3 was also shown to be "highly" expressed.

"We found that this protein, B7-H3, appears to be over-expressed in a certain subtype of AML that is clinically, often quite aggressive," Lichtman said.

The researchers created CAR T-cells that tracked the B7-H3 marker that proved effective in both controlling tumor cell growth and prolonging survival in mouse models with this disease. And while this marker can be found on certain immune cells called "antigen presenting cells" that act as scouts for the immune system, targeting the cancer with CAR T-cell therapy did not cause significant toxicity in their preclinical experiments.

"This target is present on normal immune cells called antigen-presenting cells, but usually they express a lower level compared to tumors," said UNC Lineberger's Gianpietro Dotti, MD. "That is why we believe we can kill the tumor, but spare the normal antigen-presenting cells."

Dotti said this marker may be a promising target in other cancers in addition to AML, including ovarian and pancreatic cancers.

"This antigen is highly expressed in solid tumors like pancreatic, ovarian and prostate cancer," he said.

The researchers said the next step is to develop early-stage clinical studies of CAR T-cells designed to target the B7-H3 antigen.

"Allogeneic transplant, and the associated graft versus leukemia effect—which is where donor cells attack the leukemia—are already

important ways of controlling AML," Lichtman said. "If we are able to engineer our own T-cells to attack the leukemia cells, it could be a much safer, and more effective, way to treat this disease."

He added that there are additional questions to be answered about potential toxicities, as well as about whether the therapy would be effective alone, or in combination with other treatment modalities used in AML.

"The expression of B7-H3 on this subtype of AML is relatively high, however there is still a possibility that the protein may not be present on a certain subset of [leukemia](#) cells, and that those cells could lead to resistance," Lichtman said. "It remains to be seen whether this will be effective in treating people with AML. To prevent such resistance, it may be necessary to develop CAR-T cells which simultaneously [target](#) two different antigens."

More information: 701 Pre-Clinical Evaluation of B7-H3-Specific Chimeric Antigen Receptor T-Cells for the Treatment of Acute Myeloid Leukemia. [ash.confex.com/ash/2018/webpro ... ram/Paper113468.html](http://ash.confex.com/ash/2018/webpro...ram/Paper113468.html)

Provided by University of North Carolina at Chapel Hill School of Medicine

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