NK cells with bispecific antibody show activity against lymphoma cells

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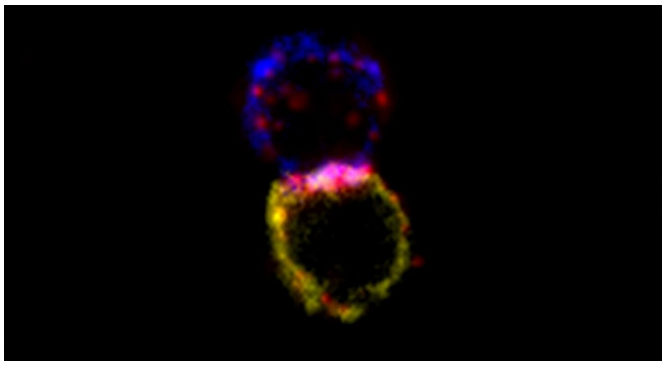

A CD16+ NK cell (blue) bound with AFM13 (red) works to eliminate a CD30+ lymphoma cell (yellow) through interactions at the immune synapse (pink). Credit: Pinaki Banerjee, Ph.D.

Cytokine-activated natural killer (NK) cells derived from donated umbilical cord blood, combined with an investigational bispecific antibody targeting CD16a and CD30 known as AFM13, displayed potent anti-tumor activity against CD30+ lymphoma cells, according to a new preclinical study from researchers at The University of Texas MD Anderson Cancer Center.

The findings were published today in *Clinical Cancer Research*, a journal of the American Association for Cancer Research. These results led to the launch of a Phase I clinical trial to evaluate the combination of cord blood-derived NK cells (cbNK cells) with AFM13 as an experimental cell-based immunotherapy in patients with CD30+ lymphoma.

"Developing novel NK cell therapies has been a priority for my team at MD Anderson to address unmet needs for the treatment of both hematologic cancers and solid tumors," said senior author Katy Rezvani, M.D., Ph.D., professor of Stem Cell Transplantation and Cellular Therapy. "This preclinical work provided proof of principle for NK cells precomplexed with AFM13, suggesting that they can effectively eliminate lymphoma cells expressing CD30 and warrant further clinical testing."

Natural killer cells are part of the innate immune system and work naturally to eliminate cancer cells in the body. However, they have limited persistence on their own, and tumors can develop mechanisms to evade NK cells, Rezvani explained. Therefore, her research team has worked to develop approaches to enhance the anti-tumor efficacy of NK cells.

Affimed's AFM13 is a proprietary bispecific antibody designed to bind to CD16a on NK cells and CD30 on lymphoma cells. Initial studies on NK cells isolated from the blood of patients with Hodgkin lymphoma found that AFM13 formed a stable complex with NK cells and could induce NK cell-mediated killing of CD30+ cells. However, the activity of these cells was modest, leading the researchers to evaluate alternative NK cell sources.

Further experiments suggested that cbNK cells, isolated from umbilical cord blood donations made to the MD Anderson Cord Blood Bank, displayed consistent and improved activity against lymphoma with AFM13 relative to other NK cell sources. The researchers were able to further stimulate the anti-tumor immune activity of cbNK cells by pre-activation with a combination of the cytokines IL-12/15/18.

In animal models, pre-activated and expanded cbNK cells complexed with AFM13 resulted in improved tumor control and survival relative to controls, with minimal side effects observed.

"These findings suggest that, in animal models, ex vivo pre-activated and expanded cord blood-derived NK cells complexed with AFM13 were able to safely eliminate CD30+ lymphoma cells,"

Rezvani said. "We look forward to learning if this investigational therapy may provide benefits to patients with advanced lymphoma in the ongoing clinical trial."

More information: Lucila N Kerbauy et al. Combining AFM13, a bispecific CD30/CD16 antibody, with cytokine-activated cord blood-derived NK cells facilitates CAR-like responses against CD30+ malignancies. *Clinical Cancer Research*. (2021) DOI: 10.1158/1078-0432.CCR-21-0164

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