New immunotherapy for multiple myeloma proves to be more effective in the lab than CAR-T treatment already in use

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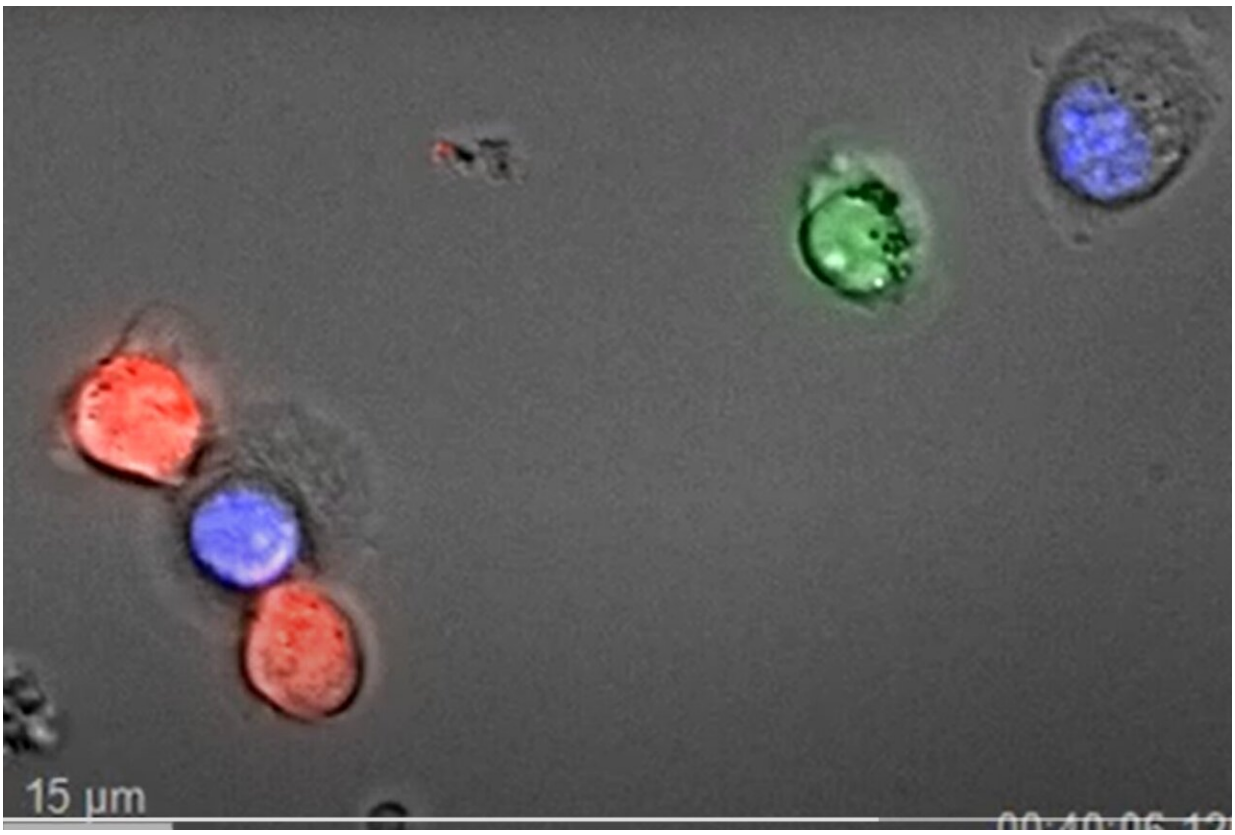

Credit: The Spanish National Cancer Research Centre

Immunotherapy is already improving treatment options for many cancer types, but research groups keep exploring ways to boost the body's

immune response against the tumor.

Researchers at the Spanish National Cancer Research Center (CNIO) and the 12 de Octubre University Hospital in Madrid have developed a new immunotherapy to treat multiple myeloma that shows, in the laboratory, to be more effective than the immunotherapy currently used as preferred treatment.

The new immunotherapy is based on the so-called STAb cells. It has yet to pass clinical trials and therefore it will be at least two years before it reaches the patients.

The study is published in *Science Translational Medicine,* with head of the H12O-CNIO Cancer Immunotherapy Clinical Research Unit Luis Álvarez-Vallina as senior author. It is a collaboration with the Josep Carreras Leukemia Research Institute; the Hospital Clínic of Barcelona; the University of Salamanca and the Complutense University of Madrid.

Multiple myeloma is the second most common hematological cancer in adults, just after lymphomas. "In recent years these cancers have begun to be treated with CAR-T cell immunotherapy," explains Luis Álvarez-Vallina, "which has meant a substantial improvement over previous therapeutic tools. In spite of this, and although patients now have longer survival times, a significant proportion of patients experience relapse, and relapse treatments are needed."

Advantages over conventional CAR-T

CAR-T cell therapy (Chimeric antigen receptor T-cell therapy, CAR-T for short), involves modifying the diseased person's T-lymphocyte immune cells (white blood cells) in the laboratory so that they acquire the capacity to recognize and fight tumor cells.

The new study compares this treatment with another cellular immunotherapy based on STAb-T cells. In both cases, the cells modified in the laboratory recognize the same antigen, called BCMA, which is only present in tumor cells. In this way, the modified cells target and attack only cancer cells.

The results show that STAb-T cells outperform CAR-T cells in that they recruit natural, non-modified T cells in the body, to also fight cancer cells, thus amplifying the effect of the therapy.

In addition, STAb-Ts overcome an element that slows down CAR-Ts. In some patients with multiple myeloma, the BCMA antigen –which identifies tumor cells—is found in soluble form when there is a high tumor burden. The fact that the antigen is soluble hinders the activity of CAR-T cells but does not affect STAb-T cells, the new result shows.

Immunological memory

"Finally, we also demonstrated that STAb-T cells generate immunological memory," says Álvarez-Vallina. After recapitulating the disease in animal models and treating them with STAb-T cells, the team obtained cells from various organs –mainly spleen and bone marrow– and observed new memory STAb-T cells being produced.

"This is important," explains Álvarez-Vallina, "because the persistence of CAR-T cells in the body, i.e. immunological memory, is related to the extent of the antitumor effect and, therefore, to a better control of the disease. The fact that we have shown that memory cells are also generated in STAb-T immunotherapy probably indicates that we could have long-term control of the disease in treated patients."

The research group aims to conduct a clinical trial with the 12 de Octubre University Hospital, in Madrid, to treat patients with this new

STAb-T immunotherapy.

More information: Laura Díez-Alonso et al, Engineered T cells secreting anti-BCMA T cell engagers control multiple myeloma and promote immune memory in vivo, *Science Translational Medicine* (2024). DOI: 10.1126/scitranslmed.adg7962. www.science.org/doi/10.1126/scitranslmed.adg7962

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