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National Institutes of Biomedical Innovation, Health and Nutrition

The University of Chicago

Japanese Foundation for Cancer Research

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CD4+ T cells with convergent TCR recombination reprogram stroma and halt tumor progression in adoptive therapy

Laboratory of Immunogenomics at National Institutes of Biomedical Innovation, Health and Nutrition (Ibaraki, Osaka, Japan), in collaboration with the University of Chicago (Chicago, IL, USA) and Japanese Foundation for Cancer Research (Tokyo, Japan), revealed that neoantigen-specific CD4+ T cells destroyed established tumors through reprogramming of tumor stroma.

With the advancement of immune checkpoint inhibitors, the importance of CD8+ T cells in cancer immunotherapy has been widely recognized. Recently, it is reported that CD4+ T cells also play an important role in cancer therapies. In particular, we reported that CD4+ T cells genetically modified to recognize cancer-specific neoantigens showed long-term tumor suppressive effects, although the detailed mechanism behind this effect remained largely unknown.

In this study, we used a mouse tumor model to find neoantigens that serve as landmarks in cancer cells, generated genetically-engineered CD4+ T cells with T cell receptors (TCRs) recognizing the specific neoantigen, and assessed their antitumor activity in mice.

Our findings include:

- (1) The TCR-engineered CD4+ T cells suppress the tumor growth via reprogramming of stromal cells, but not directly targeting cancer cells.
- (2) The TCR of CD4+ T cells, exhibiting long-term tumor suppression, showed convergent TCR recombination.

These results open new possibilities of developing cancer immunotherapies using CD4+ T cells targeting neoantigens, in addition to CD8+ T cells, and will significantly contribute to future advances of cancer immunotherapy.

The results of this research were published online in *Science Immunology* on September 13, 2024 (U.S. Eastern Time).

Website: <https://www.science.org/doi/10.1126/sciimmunol.adp6529>

❖ Keywords

CD8+ T cells: T cells that express the CD8 molecule on their cell surface, also called cytotoxic T cells. These cells recognize, attack, and destroy cancer cells and virus-infected cells.

CD4+ T cells: T cells that express the CD4 molecule on their cell surface, often as helper T cells that promote the function of cytotoxic T cells and B cells.

Neoantigens: Cancer-specific antigens caused by somatic gene alteration in cancer cells. T cells recognize neoantigens as non-self antigens and attack the cancer cells.

Stromal cells: Cells that provide the supportive structures surrounding cancer cells or tumor microenvironment and are involved in tumor growth and metastasis. Stroma is consisted of various types of cells, including macrophages, dendritic cells and fibroblasts.

❖ Paper information

Title:

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❖ About NIBIOHN

The National Institutes of Biomedical Innovation, Health and Nutrition (NIBIOHN) was established on April 1, 2015 through the merger of the National Institute of Biomedical Innovation and the National Institute of Health and Nutrition. This institute specializes in a wide range of research from medicine to health sciences, and is positioned as a national research and development agency aimed to contribute to the improvement of the health of the Japanese people by preparing the foundation for the enhancement of technologies related to drugs and medical devices and by promoting public health.

For further information: <https://www.nibiohn.go.jp/en/>

❖ About The University of Chicago Medicine & Biological Sciences

The University of Chicago Medicine & Biological Sciences is one of the nation's leading academic medical institutions. It comprises the Pritzker School of Medicine, a top medical school in the nation; the University of Chicago Biological Sciences Division; and the University of Chicago Medical Center. Twelve Nobel Prize winners in physiology or medicine have been affiliated with the University of Chicago Medicine.

For further information: <https://www.uchicago.edu/>

❖ About Japanese Foundation for Cancer Research

Japanese Foundation for Cancer Research (JFCR) was founded in 1908 as the first organization in Japan specialized for study and control of cancer. JFCR has been playing a leading role in cancer research and treatment for a long time.

We have three research centers and a hospital, which are “Cancer Institute” for basic cancer research, “Cancer Chemotherapy Center” for drug development, “Cancer Precision Medicine Center” (CPM Center) and “Cancer Institute Hospital of JFCR” for development of novel cancer treatments. These centers and a hospital are working together to achieve our common goal which is cancer control.

For further information: <https://www.jfcr.or.jp/english/>

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