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RESEARCH NEWS STORY

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Combination Therapy with Stem Cell-Derived Immune Cells Boost Anti-Cancer Response

When properly activated using a specific lipid compound, these immune cells can trigger lasting, tumor-targeting immunity

Invariant natural killer T (iNKT) cells are promising for cancer immunotherapy because they can coordinate broader immune responses, but sourcing enough functional cells is challenging. In a recent study, researchers from Japan showed that combining stem cell-derived iNKT cells with an immune-activating lipid compound can strongly suppress tumors in mice by training the body's own T cells to recognize and remember cancer. These findings point to a more effective and scalable form of immunotherapy.

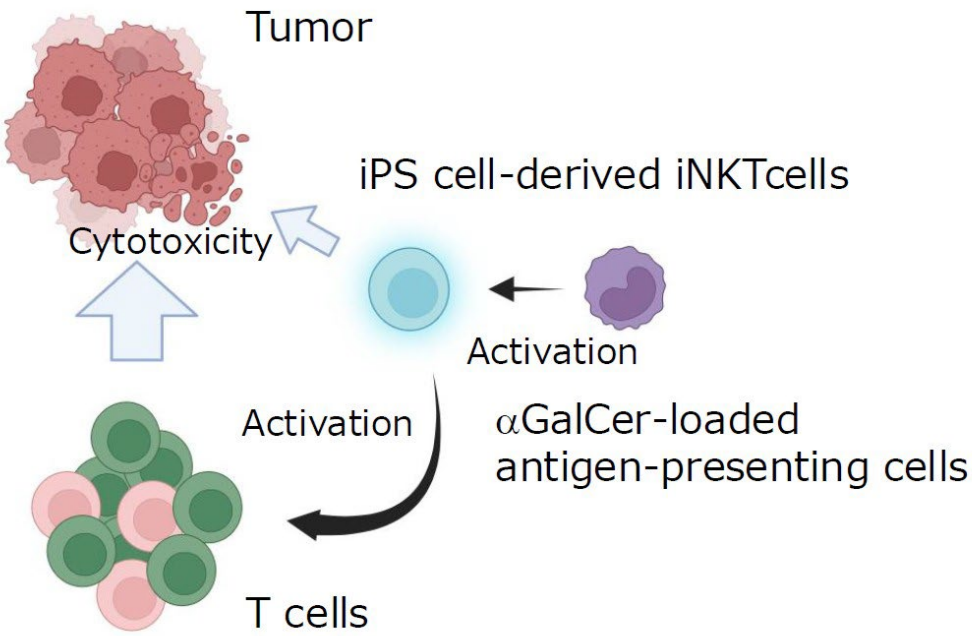

Image title: Overview of how iNKT cells drive an antitumor immune response
Image caption: Antigen-presenting cells activate invariant natural killer T (iNKT) cells, and this combination with α-galactosylceramide subsequently activates the body's own T cells to fight tumors. This image was created using BioRender.
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Cancer immunotherapy is built on a simple but powerful idea: the immune system can recognize and destroy cancer cells if it is properly activated. In many patients, however, this response is too weak or too slow to be effective. Recently, a type of immune cell called invariant natural killer T (iNKT) cells has attracted attention because of their ability to act as coordinators of immune responses, rapidly activating and rallying other immune cells to fight cancer.

One of the major obstacles holding back iNKT cell-based therapies is that patients with cancer often cannot produce enough iNKT cells on their own for therapeutic use. Scientists have worked around this issue by generating iNKT cells using donor-sourced induced pluripotent stem cells (iPSCs); these are reprogrammed cells obtained from healthy donors that can be grown in the laboratory. But an important question remains unanswered: when these lab-derived iNKT cells are introduced into a patient, do they actually set off the intended immune response?

In a recent study, a research team led by Assistant Professor Takahiro Aoki from the Department of Medical Immunology, Chiba University, Japan, set out to answer this question. They tested whether iPSC-derived iNKT cells could trigger effective antitumor immunity when combined with antigen-presenting cells (APCs) loaded with α-galactosylceramide (αGalCer), a lipid compound known to activate iNKT cells. Their paper, published in the journal *Stem Cell Research & Therapy* on March 29, 2026, was co-authored by Dr. Haruhiko Koseki from RIKEN Center for Integrative Medical Sciences and Professor Shinichiro Motohashi from Chiba University.

Dr. Aoki shares the motivation behind his study: "*I began my research after feeling powerless while treating pediatric patients with cancer who could not be cured even with multidisciplinary treatment of chemotherapy, including stem cell transplantation, radiation therapy, and surgery.*"

The team used a mouse model designed to reflect a human immune environment. These mice were transplanted with both patient-derived lung cancer cells and human immune cells, allowing the researchers to observe how iNKT cell therapy would interact with a human-like immune system. The animals were divided into four groups: each group received either iPSC-derived iNKT cells alone, APCs loaded with αGalCer, both cell types combined, or no treatment at all.

The combined therapy clearly outperformed all other groups in suppressing tumor growth. Notably, when human immune cells were excluded from the model, the antitumor effect largely disappeared. This implies that the benefit came not from direct tumor killing by the iNKT cells themselves but from the broader immune response they triggered.

Using single-cell RNA sequencing, the researchers found that the combined therapy generated a population of memory-phenotype T cells, a type of long-lasting immune cell that can recognize, remember, and respond to a specific threat repeatedly. These memory-phenotype T cells carried receptors that were confirmed to be specifically reactive to the tumor cells used in the study. When the researchers removed these memory-phenotype T cells, the antitumor effect was significantly reduced, thus confirming their central role.

Looking ahead, the findings point toward more personalized forms of immunotherapy. By using APCs derived from a patient and combining them with iPSC-derived iNKT cells, it may be possible to tailor immune responses to the specific characteristics of an individual's tumor via genetic modification. "*This approach could potentially save the lives of patients with intractable cancers that are difficult to cure with existing treatments, and a clinical trial is currently being conducted on patients with advanced head and neck cancer,*" concludes Dr. Aoki.

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About Assistant Professor Takahiro Aoki from Chiba University

Dr. Takahiro Aoki obtained his Ph.D. from Chiba University in 2019. He currently serves as an assistant professor at the Department of Medical Immunology, Graduate School of Medicine, Chiba University. He is also affiliated with the Laboratory for Developmental Genetics at the RIKEN Center for Integrative Medical Sciences. His research focuses on the development of novel cancer immunotherapies, particularly using induced pluripotent stem cell-derived invariant natural killer T cells, as well as the immunobiology of hematologic malignancies and pediatric cancers. He has over 20 publications to his name on these topics.

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Reference:

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Authors: Takahiro Aoki[1,2], Midori Kobayashi[1,2], Momoko Okoshi[1], Munechika Yamaguchi[1], Hiroko Okura[1], Satoko Sasaki[1], Yoshie Sasako[1], Sachiko Kira[1], Yun-Hsuan Chang[1], Nayuta Yakushiji-Kaminatsui[1], Jafar Sharif[1], Masashi Matsuda[1], Masahiro Kiuchi[4], Kiyoshi Hirahara[4], Motoko Y. Kimura[5], Shinichiro Motohashi[2], Haruhiko Koseki[1,3]

Affiliations: [1]Laboratory for Developmental Genetics, RIKEN Center for Integrative Medical Sciences

[2]Department of Medical Immunology, Graduate School of Medicine, Chiba University

[3]Department of Cellular and Molecular Medicine, Graduate School of Medicine, Chiba University

[4]Department of Immunology, Graduate School of Medicine, Chiba University

[5]Department of Experimental Immunology, Graduate School of Medicine, Chiba University

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Contact: Takahiro Aoki
Department of Medical Immunology, Graduate School of Medicine, Chiba University
Email: aokitakahiro@chiba-u.jp

Academic Research & Innovation Management Organization (IMO), Chiba University
Address: 1-33 Yayoi, Inage, Chiba 263-8522, Japan
Email: cn-info@chiba-u.jp