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## HSC-Engineered Off-The-Shelf iNKT Cell Therapy For Cancer

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### INVENTORS

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### OTHER INFORMATION

#### KEYWORDS

invariant natural killer T cells, iNKT,  
hematopoietic stem cell, HSC, cell  
therapy, immunotherapy, cancer

#### CATEGORIZED AS

- ▶ **Medical**
- ▶ [Disease: Cancer](#)
- ▶ [Therapeutics](#)

#### RELATED CASES

[2018-594-0](#)

## SUMMARY

UCLA researchers in the Department of Microbiology, Immunology, and Molecular Genetics, and the Department of Pathology & Laboratory Medicine have developed novel methods to produce invariant natural killer T (iNKT) cells from hematopoietic stem cells (HSCs) at high efficiency and yield for the development of off-the-shelf universal HSC-engineered iNKT cell therapy for cancer.

## BACKGROUND

The success of using chimeric antigen receptor (CAR)-engineered adoptive T cell to target certain blood cancers have set the foundation for cell-based immunotherapy to become the new generation of cancer medicine. However, most of the current protocols for cell-based therapy consist of autologous adoptive cell transfer, wherein immune cells collected from a patient are manufactured and used to treat this single patient. This type of approach is costly, labor intensive, and difficult to deliver to all patients in need. Thus, allogenic immune cellular products that can be manufactured at large scale and readily distributed to treat a broad range of cancer patients are in great demand.

Invariant natural killer T (iNKT) cells target multiple types of cancer independent of tumor antigen- and major histocompatibility complex (MHC)-restrictions, and they can deploy multiple mechanisms to attack tumor cells through direct killing and adjuvant effects. Most importantly, they do not cause graft-versus-host disease (GvHD), making them attractive candidates for the development of universal off-the-shelf cellular therapy for cancer. However, because of their extremely low numbers and high variabilities in humans, it is challenging to grow therapeutic numbers of iNKT cells from peripheral blood cells of allogenic human donors.

## INNOVATION

Researchers at UCLA have developed a novel method to generate iNKT cells from hematopoietic stem cells (HSCs) through iNKT T cell receptor gene engineering. An artificial thymic organoid in vitro culture system further supports the differentiation of human HSCs into T cells at high efficiency and high yield. Using this approach, G-CSF-mobilized CD34+ HSCs harvested from a single healthy donor can be used to produce 10<sup>12</sup> scale of homogenous human iNKT cells of potent tumor killing capacity, which is equivalent to 1,000 to 10,000 doses of therapeutic cellular products.

## APPLICATIONS

- ▶ Production of universal off-the-shelf iNKT cells for cancer immunotherapy for patients with cancers that have been clinically indicated to be subject to iNKT cell regulation
  - Multiple types of solid tumors (melanoma, colon, lung, breast, head and neck cancer)
  - Blood cancers (leukemia, multiple myeloma, myelodysplastic syndromes)

## ADVANTAGES

- ▶ iNKT cells are capable of attacking tumor cells via multiple mechanisms, independent of tumor antigen- and major MHC-restrictions
- ▶ iNKT cells do not cause graft-versus-host disease, making it an ideal candidate for developing universal off-the-shelf cell therapy
- ▶ The artificial thymic organoid in vitro culture system can reliably generate a homogenous population of iNKT cells in large quantities

## STATE OF DEVELOPMENT

The artificial thymic organoid in vitro culture system has been experimentally validated, and the produced HSC-iNKT cells have shown to mediate robust tumor killing capabilities in mouse model.

## PATENT STATUS

Country	Type	Number	Dated	Case
Japan	Issued Patent	7730569	08/20/2025	2018-594
Australia	Issued Patent	2019287483	06/27/2024	2018-594
Japan	Published Application	2025-78723	05/20/2025	2018-594
United States Of America	Published Application	<a href="#">20210123022</a>	04/29/2021	2018-594
European Patent Office	Published Application	3806869A	04/21/2021	2018-594
China	Published Application	CN112512536A	03/16/2021	2018-594

## RELATED MATERIALS

- ▶ [Smith, D.J., Liu, S., Ji, S., Li, B., McLaughlin, J., Cheng, D., Witte, O.N. and Yang, L., 2015. Genetic engineering of hematopoietic stem cells to generate invariant natural killer T cells. Proceedings of the National Academy of Sciences, 112\(5\), pp.1523-1528.](#)
- ▶ [Seet, C.S., He, C., Bethune, M.T., Li, S., Chick, B., Gschweng, E.H., Zhu, Y., Kim, K., Kohn, D.B., Baltimore, D. and Crooks, G.M., 2017. Generation of mature T cells from human hematopoietic stem and progenitor cells in artificial thymic organoids. Nature methods, 14\(5\), p.521.](#)

## ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- ▶ [Invariant Natural Killer T Cell Receptor \(iNKT TCR\) Gene-Based Immunotherapy](#)

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