

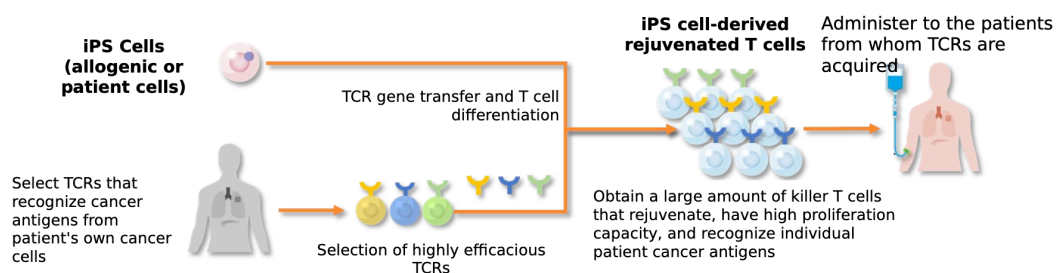


September 1, 2021

## Joint research on personalized cancer immunotherapy using regenerated T cells derived from iPS cells

Kyoto and Suita--- The Center for iPS Cell Research and Application, Kyoto University ("CiRA"; Headquarters: Sakyo-ku, Kyoto, Japan; Director: Shinya Yamanaka), KOTAI Biotechnologies, Inc. ("KOTAI"; Headquarters: Suita, Osaka, Japan; CEO, Kazuo Yamashita) and Thyas Co. Ltd. ("Thyas"; Headquarters: Sakyo-ku, Kyoto, Japan; CEO, Yasumichi Hitoshi) jointly announced today that Thyas has joined joint research initiated by CiRA and KOTAI on personalized cancer immunotherapy using regenerated T cells<sup>1</sup> derived from induced pluripotent stem (iPS) cells<sup>2</sup>.

The laboratory of Professor Shin Kaneko, CiRA, Department of Cell Growth and Differentiation, is conducting research on therapeutic regenerative T cells using iPS cells for cancer immune cell therapies. In these therapies, cytotoxic T cells<sup>3</sup> that can attack cancer cells are isolated from cancer patients and reprogrammed into iPS cells. These patients-derived iPS cells (or allogenic iPS cells transduced with these patients-derived TCR genes) are then used to produce large numbers of rejuvenated T cells with high anti-cancer function (see figure below). CiRA and KOTAI started the joint research in October, 2020 to establish more efficacious personalized cancer immune cell therapies using a surface antigens<sup>4</sup> specifically expressed on anti-cancer cytotoxic T cells and immuno-informatics technologies possessed by KOTAI.



### Personalized cancer immunotherapy with patients' own TCRs and iPSC-derived T cells

Thyas is developing robust and standardized manufacturing methods to produce regenerated T cells for industrial use using the research achievements by Professor Kaneko. It has also been manufacturing the clinical-grade batches of regenerated T cell products for clinical



studies. The inclusion of Thyas, well-experienced in the production of regenerated T cells, is expected to accelerate the clinical application of the joint research outcomes.

In this joint research, CiRA will isolate T cells from cancer tissue and conduct iPS cell induction, T cell redifferentiation, and functional evaluation, while KOTAI will provide information on the surface antigen for the T cell isolation and perform genetic analysis of the cells. Thyas will optimize the production of regenerated T cells for clinical trials. The first trials are scheduled to begin by 2025 and will be the world's first iPSC-derived therapeutic cells equipped with personalized TCRs<sup>5</sup>.

By conducting this joint research, CiRA, KOTAI, and Thyas aim to establish personalized cancer immunotherapy using regenerated T cells and contribute to the further development and popularization of cancer immune cell therapy through the efforts toward clinical trials.

The Center for iPS Cell Research and Application (CiRA), Kyoto University:

<https://www.cira.kyoto-u.ac.jp/e/index.html>

KOTAI Biotechnologies, Inc. : <https://www.kotai-bio.com/>

Thyas Co. Ltd.: <https://thyas.co.jp/en/>

(Note 1) T cells: A type of lymphocyte that acts in immunity by recognizing and eliminating infected cells and cancer cells. Each T cell responds to a specific antigen. There are various types of T cells, such as cytotoxic T cells, helper T cells and others.

(Note 2) iPS cells: Somatic cells, such as skin or blood cells are reprogrammed into the pluripotent state by introducing a few genes. iPS cells are a type of stem cell with almost indefinite capacity to multiply and can differentiate into almost any kind of cell in the body.

(Note 3) Cytotoxic T cells: A type of T cell. When antigen information is received from other immune cells, cytotoxic T cells attack the cells corresponding to the antigen.

(Note 4) Surface antigen: A substance on a cell surface recognized by an antibody.

(Note5) Thyas' Regenerated T Cell Products

Thyas aims to start clinical trials of allogeneic iPS cell-derived regenerated T cell therapy



targeting common antigens in 2023 as its first pipeline. Development of this personalized T cell therapy will be its second pipeline.

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