July 24, 2017
The University of Tokyo
BrightPath Biotherapeutics Co., Ltd.

Patent for rejuvenated antigen-specific T lymphocytes using iPS cells*1

Tokyo, July 24, 2017 – The University of Tokyo and BrightPath Biotherapeutics Co., Ltd., (TSE Mothers: 4594) jointly announced the issuance of a patent (P6164746, dated July 19th 2017) for generating rejuvenated antigen-specific T lymphocytes using iPS cells*1. This breakthrough was achieved in the laboratory of Professor Hiromitsu Nakauchi, at the Institute of Medical Science, University of Tokyo. This patent has been exclusively licensed to Advanced Immunotherapy Co., Ltd (a subsidiary of BrightPath Biotherapeutics) and is being co-developed for future use.

1. Summary of Patent

Patent No.	P6164746
Title of the Invention	Method for producing antigen-specific T cells
Patentee	The University of Tokyo
Licensee	Advanced Immunotherapy Co., Ltd.

2. Patent Description

T lymphocytes play an important role in acquired immunity by protecting us against pathogens and cancer. Cytotoxic T lymphocytes (CTLs), in particular, recognize various pathogenic antigens and specifically eliminate the cells that display these antigens. Numerous attempts to develop T lymphocyte therapieRs for treating viral infections and cancer have been made, albeit with less success. This is primarily due to the exhaustion of T lymphocytes. Moreover, these T lymphocytes are often rendered non-functional when collected from peripheral blood or processed outside the body, especially using the techniques which are available today.

The invention in the patent (P6164746) achieves the technical breakthrough by specifically producing antigen-specific CD8*2 or CD4*2 single-positive cells from iPS cells generated from human T lymphocytes. The iPS cells are generated from the T lymphocytes and then rejuvenated T lymphocytes are derived from these iPS cells. This process significantly increases the frequency of T lymphocytes with the same TCR gene*3 rearrangement pattern, similar to the donor's T lymphocytes. These rejuvenated T lymphocytes possess potent killing activity and can be limitlessly derived from the parent iPS cells.

Similar approaches have been tested previously but primarily resulted in the inefficient differentiation of active T-cells from iPS cells*1 and hit a dead end because they didn't use a specific method for generating CD8*2 or CD4*2 single-positive cells from iPS cells. The method allows us to mass-produce biologically rejuvenated T lymphocytes that maintain their antigen specificity, and markedly increases efficiency of T-lymphocyte therapy. Thus, this invention provides a technological breakthrough by overcoming the aforementioned issue and we ultimately envision establishing a viable commercial platform for effective cancer immune therapies.

Definitions of Terminology

*1 iPS (induced pluripotent stem) cells: Pluripotent stem cells induced by introducing certain genes (initially, the 4 transcription factors Oct3/4, Sox2, Klf4, and c-Myc were used) into somatic cells. Dr. Shinya Yamanaka and colleagues at Kyoto University established iPS cells from mice in 2006 and from humans in 2007.

*2 CD8/CD4 cells: T lymphocytes are broadly divided according to the CD8 and CD4 molecules they express during differentiation. Cells do not express CD4 or CD8 during early differentiation, a process termed as the double-negative (DN) stage. Cells then express both molecules in the double-positive (DP) stage, before maturing into cells that express either CD4 or CD8 in the single-positive (SP) stage. CD4 SP cells are T helper cells, and CD8 SP cells are cytotoxic T lymphocytes.

*3 TCR (T-cell receptor) gene: Expressed on the cell membrane of T lymphocytes, the T-cell receptor recognizes and binds to antigens. T lymphocytes form a great variety of TCR genes by rearranging the gene fragments by the process of recombination. This allows recognition of endless antigens presented on the surface of cancer cells, bacteria, and viruses.

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