

## REBIRTHEL CO., LTD.

Developing a novel allogeneic T cell therapy with cytotoxic T lymphocytes regenerated from induced pluripotent stem cells (iPSCs)

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Founded in 2019  
Founder & CTO: KAWAMOTO Hiroshi MD PhD  
President & CEO: KAJIKAWA Masunori  
No. of employees: 8  
Type of Ownership: Private  
Primary stock exchange: N/A

**October 2023:** Preparing the first clinical trial conducted in humans for acute myeloid leukemia to evaluate safety and efficacy.



Venture Valuation (VV) interviewed, Mr. Kajikawa Masunori, President & CEO.

**VV:** **There are reports that the use of iPSCs in regenerative medicine potentially causes the formation of tumors. Please explain what your solution is.**

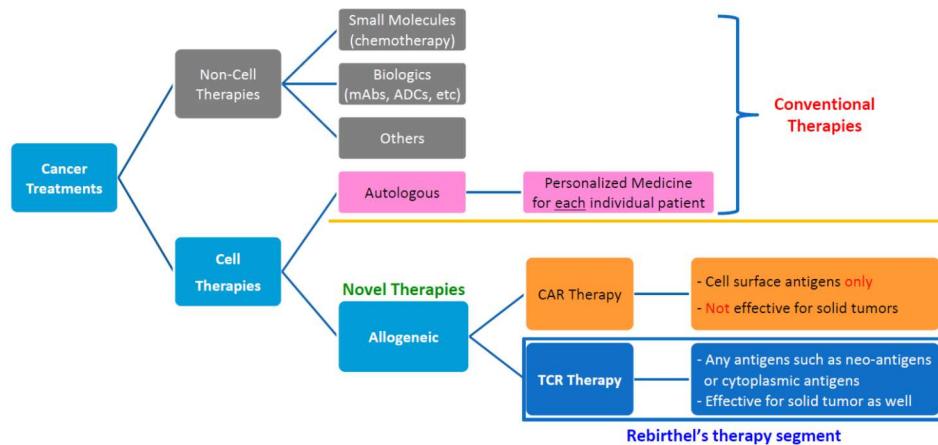
**Kajikawa:** It is known that contamination of undifferentiated iPSCs causes the formation of tumors. Those cells have not yet acquired a specific structure and function just like mature cells do. It is essential to eliminate them for successful iPSC-derived cell therapy.

Led by our founder, Prof. Kawamoto of Kyoto University, we have learned how to control and check the quality of cells to eradicate undifferentiated iPSCs. Furthermore, we have constantly controlled the quality of iPSCs-derived cell preparation used for cell therapy in a year-long safety test.

**VV:** **Your novel allogeneic iPSC-derived T cell therapy technology will be an advanced cancer treatment. How do you position your technology in the cancer treatment field?**

**Kajikawa:** To treat various cancers, we need a greater variety of treatments that include non-cell therapies and cell therapies. Our technology is for the cell therapy field that consists of autologous and allogeneic. (see the chart on the next page)

Autologous cell therapy is a treatment in which patient-derived T cells are strengthened ex vivo by activation or genetic modification and introduced back into the patient. The process of autologous cell therapy is known to be time-consuming, costly, and heterogeneous in quality.



Allogeneic T cell therapies are currently TCR (T Cell Receptor), in which our technology is classified, and CAR (Chimeric Antigen Receptor). CAR technology is an artificial receptor to recognize tumor cell surface antigens. It is not effective for solid tumors.

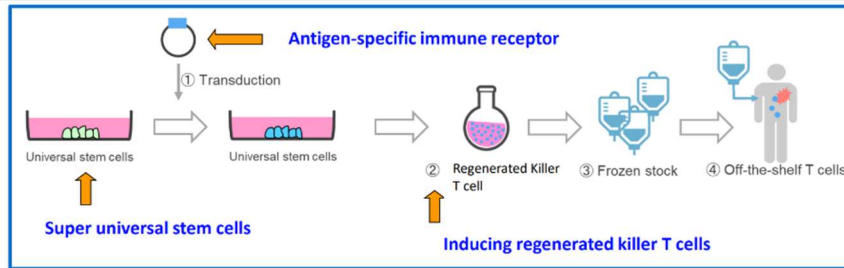
Meanwhile, our allogeneic TCR therapy uses pluripotent stem cell as a material and TCR therapy is transduced to recognize cancer antigens. It is applicable to any cancer including solid cancer.

**VV:** Among various allogeneic approaches that other companies are developing, your technology excels in suppression of immune rejection, antigen specificity, and induction of antigen specific T cells.

**Kajikawa:** Those fields are our intellectual property. The chart below illustrates the process of transduction, differentiation, mass-production, and frozen stock to provide off-the-shelf T cells to patients. We already have patented technologies at each critical step in all schemes.

We have the advantage of producing large quantity of T cells to make our therapy available to patients suffering from cancer at affordable prices and delivered without delay.

**Rebirthel's key innovations and IP**



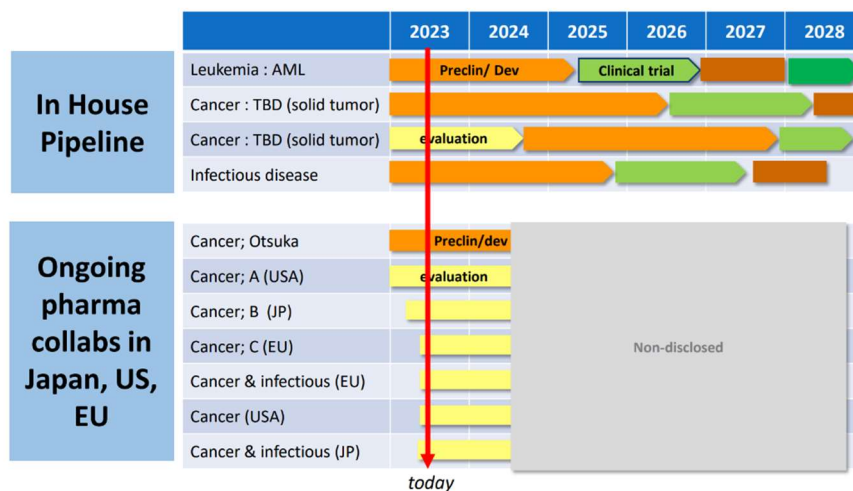
title	Patent #/status	description
<b>Antigen-specific immune receptor</b> TCR-iPSC method	PCT/JP2015/070623 Patented in EU, AU, and Japan	PRODUCTION METHOD FOR PLURIPOTENT STEM CELLS HAVING ANTIGEN-SPECIFIC T CELL RECEPTOR GENE *Molecular Therapy: Methods & Clinical Development Vol. 19 December 2020
TCR-Cassette method	PCT/JP2019/029537 Applied a patent	METHOD FOR PRODUCING FOREIGN ANTIGEN RECEPTOR GENE-INTRODUCED CELL *Unpublished paper
<b>Inducing regenerated killer T cells</b> Differentiation method	PCT/JP2017/015358 Patented in EU, USA, Japan, and AU	METHOD FOR INDUCING CD8+ T CELL *Cell Stem Cell 12, 31–36, January 3, 2013 *Cancer Res; 76(23) December 1, 2016 *Molecular Therapy: Methods & Clinical Development Vol. 19 December 2020
<b>Super Universal Stem Cells</b> Suppression of immune rejection	In prep	SUPPRESSION OF IMMUNE REJECTION FROM BOTH OF T CELLS AND NK CELLS *Unpublished paper

**VV:** Your first target of the in-house pipeline projects is acute myeloid leukemia. Why not a solid cancer?

**Kajikawa:** Our vision is to pioneer a new era of cancer treatment. For the purpose of that, we understand that solid cancer is the most targeted field.

However, as this is a brand-new cancer treatment, we selected acute myeloid leukemia to demonstrate the safety and efficacy of our technology. CAR T-cell therapy has become a promising treatment for various types of blood cancer like leukemia.

**Rebirthel has a robust in-house pipeline and several pharma collaborations**



**VV:** On the pipeline chart above, you are listing several partnering business projects for cancer and infectious diseases. What is your business development plan?

**Kajikawa:** We intend to submit an IND (Investigational New Drug) application in Japan when the first-in-human clinical trial for acute myeloid leukemia will start in late 2025. Raising funds of US\$ 20 to 30 million is our objective.

Currently we are proactively in discussions with pharma and biotech companies as well as investors worldwide for licensing and collaboration opportunities. Any inquiries and suggestions are welcome.

**VV Comments after the interview:**

A report on the market of cell therapies published on August 2022<sup>1</sup> mentions that more than 250 companies in the world are engaged in the development of more than 1,200 early and late-stage T cell therapies. Over 6,800 patents are related to CAR-T therapy. TCR therapies and others such as TIL (Tumor Infiltrating Lymphocyte) therapy have been demonstrating continued innovation.

Considerable funding is indispensable. The same report points out that “... to fund product development initiatives in this domain, capital investments worth USD 30 billion have been made by various private and public sector investors in the last few years. Driven by the ongoing pace of innovation in this field, sufficient financial support from investors and encouraging clinical results, the T-cell immunotherapy market is anticipated to witness substantial growth in the mid to long-term.”

CAR-T therapy is working in liquid tumors but not the solid tumors representing approximately 90 percent of adult human cancers<sup>2</sup>. Rebirthel’s allogeneic T cell therapy for treatment of solid tumors will be a significant breakthrough for the cancer treatment field. An affordable price and speedy delivery to patients are a pathway to democratizing cancer care.

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Venture Valuation specializes in independent assessment and valuation of technology-driven companies in growth industries, such as the Life Sciences (Biotech, Pharma, and Medtech), ICT, Femtech, Nanotech, Cleantech and Renewable Energy. In addition to valuation products, Venture Valuation offers high-quality, focused information services like the Global Life Sciences Database, Biotechgate.com and this “*Let’s Interview Series*” with companies with

<sup>1</sup> <https://www.rootsanalysis.com/reports/t-cell-therapies-market/261.html>

<sup>2</sup> <https://themedicinemaker.com/discovery-development/completing-the-cell-therapy-revolution>

interesting technologies and services. We select and interview thriving companies and organizations especially in Switzerland and Japan.