

March 29, 2018  
BrightPath Biotherapeutics, Co., Ltd.

## **Collaborative research agreement concluded with RIKEN on iPS cell-derived NKT cell therapy**

Tokyo, March 29, 2018 — BrightPath Biotherapeutics, Co., Ltd. (“BrightPath”) hereby announces that it has entered into a collaborative research agreement with RIKEN regarding a natural killer T (NKT) cell therapy. Under this agreement, BrightPath will participate in the project pursued by the RIKEN Center for Integrative Medical Sciences that aims at technology development and clinical application of this novel allogeneic cancer immunotherapy using NKT cells redifferentiated from induced pluripotent stem (iPS) cells (“iPS-NKT cell therapy”).

This is a RIKEN-led project from the “Center for development of cancer immunotherapy technology by regenerating natural killer T-cells,” which was accepted as a Center for Clinical Application Research on Specific Disease/Organ (Type B) of the Research Center Network for Realization of Regenerative Medicine of the Japan Agency for Medical Research and Development. This project is also part of the RIKEN Program for Drug Discovery and Medical Technology Platforms. An investigator-initiated clinical trial targeting head and neck cancers is slated to start within fiscal year 2019.

NKT cells are immune cells that are capable of directly attacking cancer cells and activating other immune cells via an adjuvant process. Activated NKT cells produce various types of cytokines that elicit activation of natural killer (NK) cells and maturation of dendritic cells of the innate immune system.\* Mature dendritic cells then cause killer T cells of the adaptive immune system\* to proliferate and become activated, resulting in a synergistically enhanced anti-tumor effect. By activating innate immune system, NKT cells are capable of killing major histocompatibility complex (MHC)-negative cancer cells, which T cells are incapable of killing. This is one feature that is unique to iPS-NKT cell therapy.

Despite their significant anti-cancer potential, current cell therapies using NKT cells have their downsides. Unlike with chimeric antigen receptor T-cell therapy (CAR-T, where patients’ own T cells are employed to treat cancer), they are extremely difficult to harvest from the body and culture and grow to quantities that are adequate for clinical treatment, since NKT cells make up only from 0.01% to 0.1% of total blood T cells. Overcoming this limitation is what prompted RIKEN to initiate research in iPS cell technology. Dr. Haruhiko Koseki, Group Director of the Laboratory for Developmental Genetics, and associates sought to realize the timely production of NKT cells in sufficient and stable quality and quantity for treatment with iPS cell technology, in which unlimited numbers of NKT cell derived pluripotent stem cells are grown and then induced to re-differentiate into NKT cells.

As a research partner and proprietor of the option to acquire the exclusive rights to develop, manufacture, and market iPS-NKT cell therapy research products, BrightPath is set to fully support the aforementioned investigator-initiated trial towards the world’s first clinical application of this therapy.

[Explanation of terms]

\*Innate and adaptive immune systems—The immune system is classified into two types: innate and adaptive. The innate immune system quickly responds to and attacks foreign substances that have entered the body (e.g., bacteria, viruses) or formed within it (e.g., cancer cells). The adaptive immune system takes longer to respond but is more specific; based on information gathered on the foreign invaders, B and T cells are mobilized to fight their specific targets. The innate system not only eliminates foreign substances but also assumes another important role of passing on information that is specific to such substances to the adaptive system through antigen-presenting cells, e.g., dendritic cells.

### **BrightPath Biotherapeutics**

BrightPath is a clinical stage biopharmaceutical company focused on the development of novel cancer immunotherapies to transform cancer treatment for refractory or progressive cancers that cannot be treated with conventional standard therapies. In addition to cancer peptide vaccines currently in clinical trials in Japan and the United States, BrightPath is actively involved in developing cell therapies, immunomodulatory antibodies and new drugs targeted at cancer specific neoantigens.

### **RIKEN**

RIKEN is Japan's largest and most comprehensive research organization for basic and applied science, and a world leader in a diverse array of scientific disciplines, including physics, engineering, chemistry, computational science, biology, and medical science. In an effort to contribute to society by disseminating their research achievements, RIKEN is active in joint research and contract research, supported by partnerships with universities and businesses, and also engages in activities involving technology transfer to industry, such as intellectual property transfer.

### **Contact**

• BrightPath Biotherapeutics Co., Ltd.

Business Administration

Phone: +81-3-5840-7697

E-mail: [irpr05@brightpathbio.com](mailto:irpr05@brightpathbio.com)

<https://www.brightpathbio.com/english/index.html>

---

## Supplementary Information

---

March 29, 2018

# Characteristics of iPS-NKT cell therapy

This is an induced pluripotent stem (iPS) cell technology-based Natural killer T (NKT) cell therapy. NKT cells are believed to possess multifaceted antitumor effects, but have proven difficult to supply in adequate amounts for therapy. iPS cell technology has enabled the timely provision of NKT cells in sufficient quantity for clinical use in allogeneic immunotherapy.

## NKT cells

Immune cells with multifaceted antitumor effects

- Activate innate immunity
- Induce adaptive immunity
- Alter immunosuppressive environment

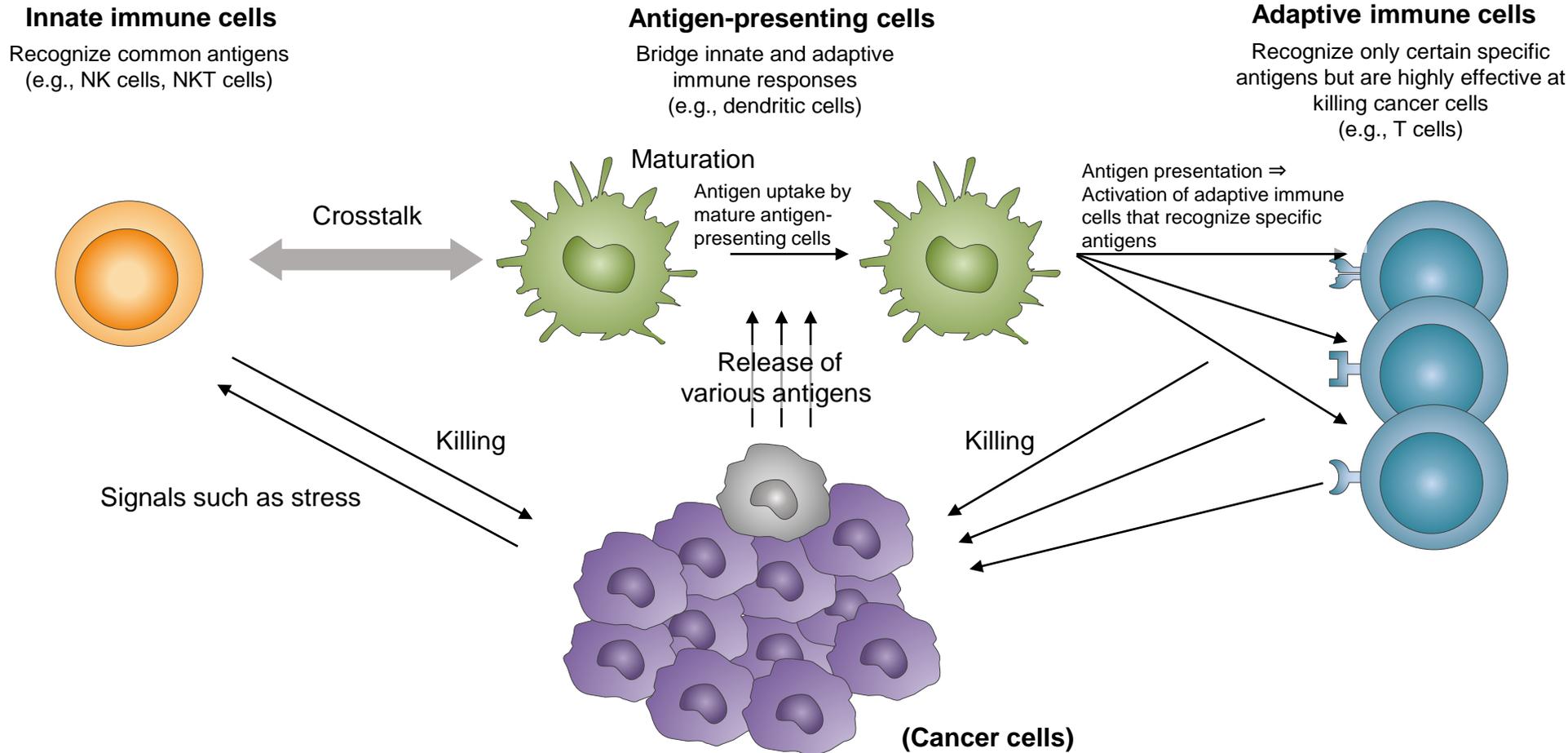


## iPS technology

Enables cell banking as pre-differentiated stage and therefore an as-needed supply of cells in quantities sufficient for clinical treatment

# Antitumor effects of innate and adaptive immunity (general overview)

The innate immune system not only possesses direct antitumor activity but also induces a cancer-specific adaptive immune system through cancer antigen presentation by antigen-presenting cells. Effective activation of the innate system, located upstream of multiple immune responses, is expected to lead to synergistic antitumor effects.



# Multifaceted effects of NKT cells

In addition to the above-mentioned innate-immunity activities in general, NKT cells are equipped with several properties that allow for further potent antitumor effects

Presented below in black are general innate-immunity activities, while NKT cell specific properties are in red

