August 19, 2019

Shinshu University and BrightPath Conclude Joint R&D Agreement for CAR-T Cell Therapy for Solid Tumors

Tokyo, August 19, 2019 — National University Corporation Shinshu University and BrightPath Biotherapeutics Co., Ltd., an immuno-oncology company, announced the conclusion of a joint research and development agreement aiming at the clinical development of CAR-T cell therapy for solid tumors.

A cancer antigen called “HER2” is overexpressed in many cases of solid tumors. While anti-HER2 antibody drugs have already been put into practical use, HER2 continues to draw attention as a promising target antigen in cancer treatment. In cooperation with Shinshu University, BrightPath will start preparations for an investigator initiated trial treating patients with osteosarcoma using HER2-CAR-T cells as an investigational drug. These cells recognize HER2 antigens, and are produced using a method established by Professor Yozo Nakazawa, Department of Pediatrics, Shinshu University School of Medicine, Assistant Professor Shigeki Yagyu, Department of Pediatrics, Kyoto Prefectural University of Medicine, and others.

CAR-T cells, which have been transduced with a viral vector or the like, recognize cancer antigens via chimeric antigen receptors (CARs) and have the ability to kill cancer cells. CAR-T cell therapy has already been approved in Japan, the US and Europe for certain hematologic cancers, and its substantial benefits have recently been clinically demonstrated. In the pursuit of further clinical effects, development of next-generation CAR-T cell therapy is already in progress around the world. While its effects are evident in an expanding range of hematologic cancers, there is still room for improvement in the area of solid tumors.

The difficulty in using CAR-T cell therapy targeted to treat solid tumors is due to the fact that sustained anti-tumor effects of CAR-T cells are required for them to be effective in the fierce environment specific to solid tumors, known as the “tumor microenvironment,” where the functions of immune cells are suppressed. One solution to overcome this difficulty is to use the non-viral gene transfer method established by Professor Yozo Nakazawa’s team and the new CAR-T cell culture method jointly developed by Professor Nakazawa’s team and other groups (joint patent pending). It is suggested that CAR-T cells created by these methods have more sustained anti-tumor effects in comparison with CAR-T cells created by

conventional viral methods. This new approach is therefore expected to achieve sustained activity in the immunosuppressive tumor microenvironment and thereby exhibit greater efficacy against solid tumors.

Shinshu University is now preparing an investigator initiated trial treating osteosarcoma, a representative pediatric cancer. Although recent progress in osteosarcoma treatment has been remarkable, development of new therapeutic options is awaited in order to cure those with severe symptoms or distant metastases and prevent cancer recurrence. In the US, clinical trials for such cases of refractory osteosarcoma have been conducted using HER2-CAR-T cells, which are created through traditional genetic modification using conventional viral vectors. In some cases reported from those clinical trials, promising results, including complete remission, have been observed. With the clinical concept already proven, BrightPath expects that CAR-T cell therapy targeting HER2 antigens but using the more durable platform technology invented by Professor Nakazawa, will broaden future therapeutic options for such patients, and has decided to commit its support to Shinshu University's upcoming investigator initiated clinical trial, which is scheduled to start in fiscal 2020.

Shinshu University

Shinshu University is a national university with eight faculties (Arts, Education, Economics and Law, Science, Medicine, Engineering, Agriculture, and Textile Science and Technology) on five campuses, which are located in four municipalities in Nagano Prefecture (Nagano, Matsumoto, Ueda, and Minamiminowa). The university marks its 70th anniversary in 2019. Shinshu University Hospital is the only national university hospital in Nagano Prefecture, with 32 clinical departments and 707 beds. It provides safe and secure medical services as a government-designated advanced treatment hospital, performs leading-edge medical practice based on state-of-the-art research achievements, and endeavors to develop next generation international healthcare human resources.

BrightPath

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

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CAR-T Cell Therapy for Solid Tumors (BP2301)

Supplemental Information

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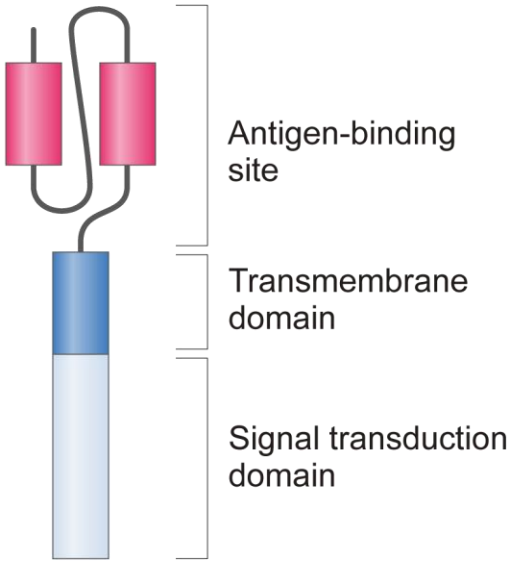
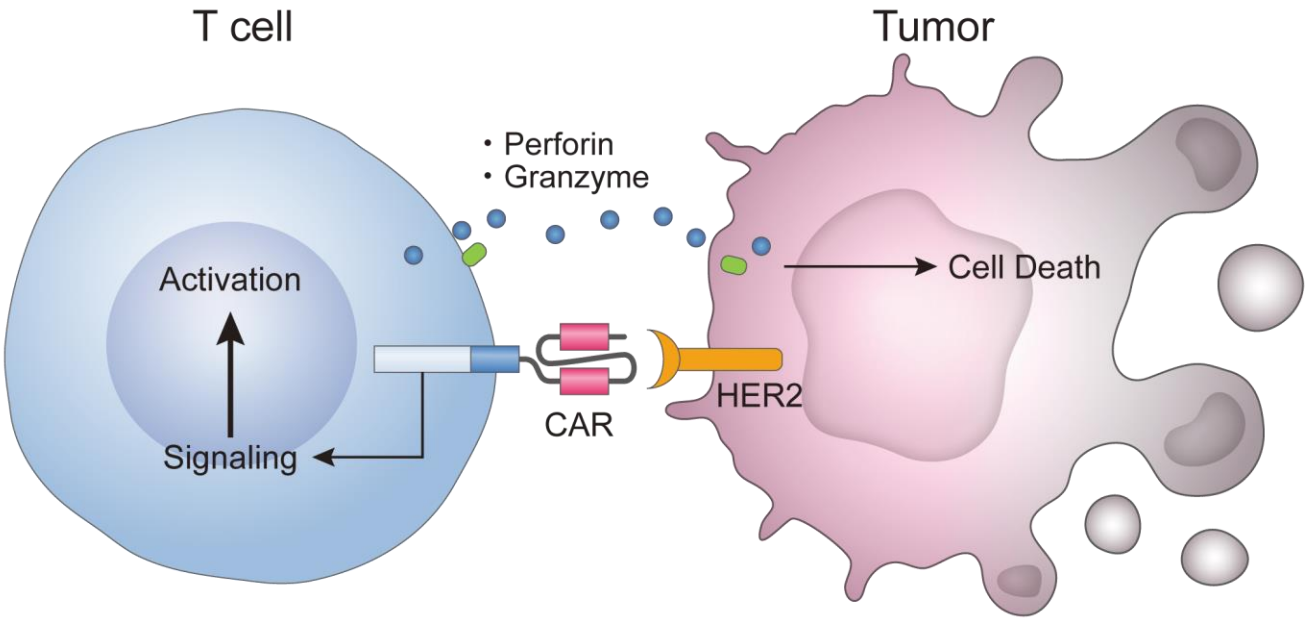
Mechanism of the Anti-Tumor Effect of CAR-T Cells

A chimeric antigen receptor (CAR) is a protein designed to bind to certain tumor antigens on cancer cells. It also contains a signal transmitting domain to activate T cells. By transducing a CAR into a T cell, the CAR-T cell can come to recognize tumors and exert anti-tumor effects.

CAR structure

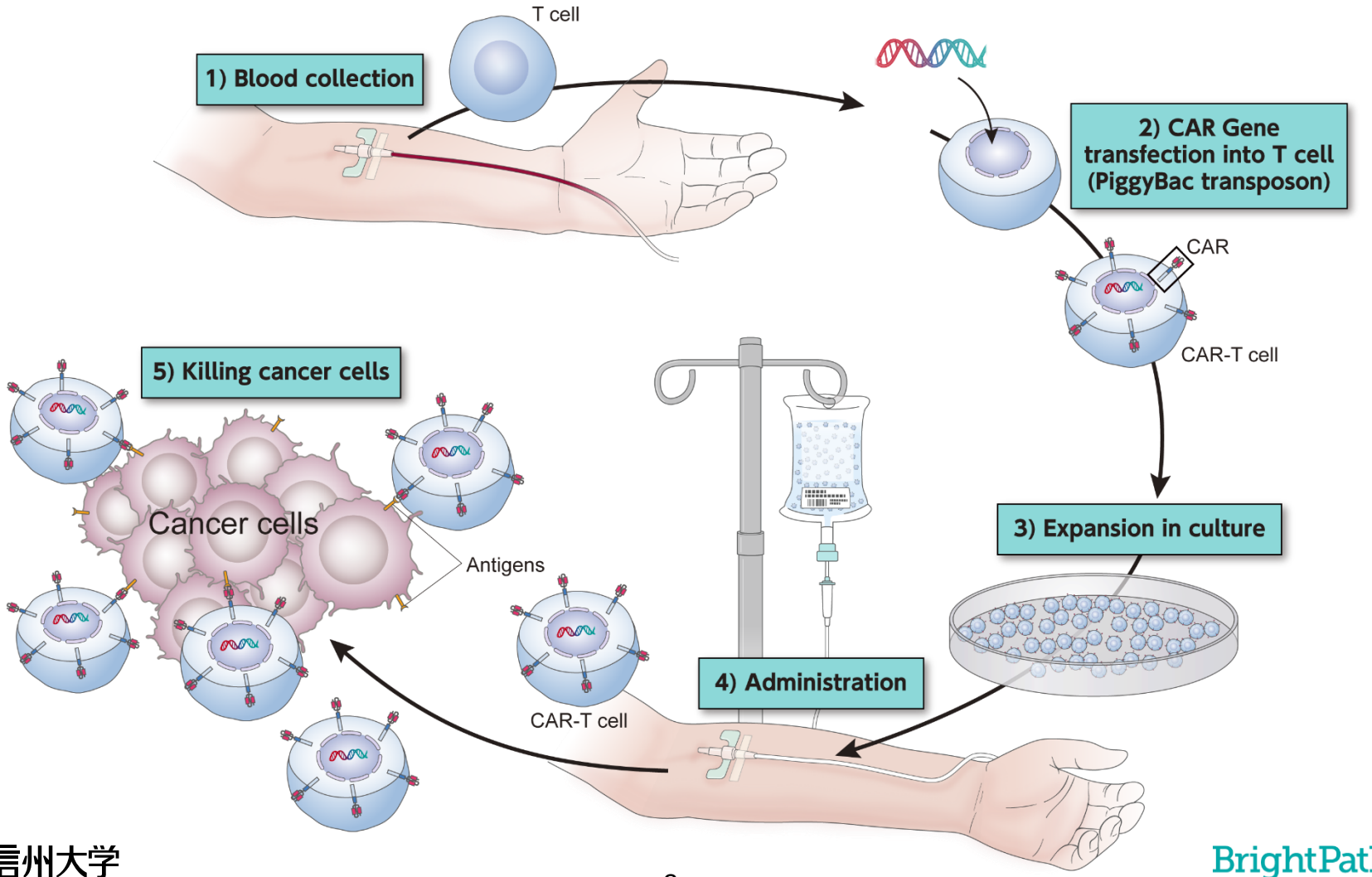


Mechanism of action



Flow of Treatment in CAR-T Cell Therapy

An anti-tumor effect is achieved by transfecting CAR genes into T cells collected from the patient's blood, growing them in culture and returning the CAR-T cells into the patient's body.

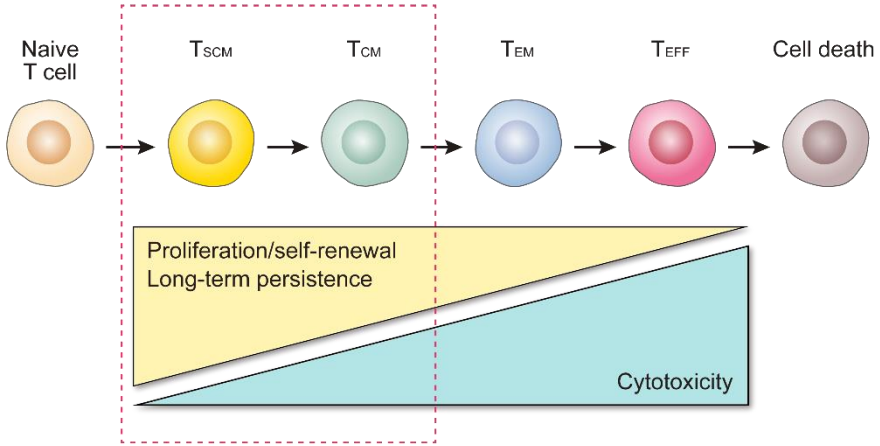


Characteristics of BP2301

BP2301 is largely comprised of young memory T cells with high proliferative capacity and long-term persistence, leading to durable anti-tumor effects.

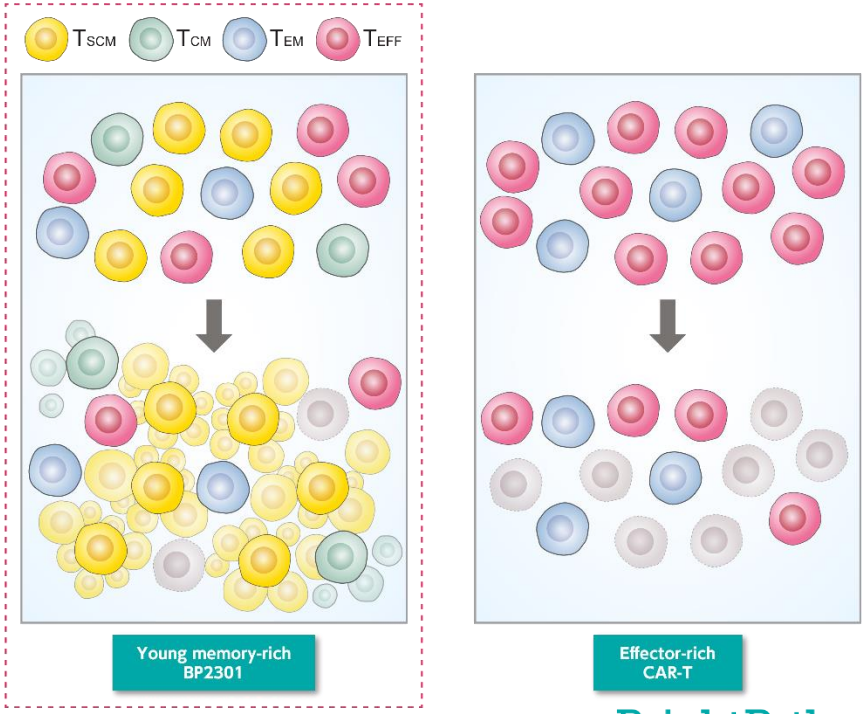
T cell subset and differentiation

Effector function (anti-tumor function) is enhanced upon T cell differentiation, while memory function and proliferation capacity are gradually lost.



BP2301 T cell subset

The young memory-rich BP2301 cell subset maintains proliferative capacity to produce cytotoxic effector T cells after administration (left figure), while the effector-rich CAR-T subset has transient proliferative capacity and effector function (right figure).



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