

BrightPath Biotherapeutics Co., Ltd.

www.brightpathbio.com/english/index.html

BrightPath
Biotherapeutics

Personalizing cancer immunotherapy

BrightPath, formerly known as GreenPeptide, is moving beyond peptides to push the boundaries of cancer immunotherapy toward more personalized treatments.

The ongoing battle against cancer has taken many forms, but in recent years, immunotherapy—reprogramming the body's immune system—has shown great promise, and the field has grown significantly. Recent market studies suggest that by the mid-2020s, immunotherapy agents will make up roughly half of all available cancer treatments.

Seeing the opportunities of this new wave of developing therapies, BrightPath Biotherapeutics is at the forefront of cancer immunotherapy research in Japan (Fig. 1). Now under a new name, BrightPath was formerly known as GreenPeptide. Since 2003, this clinical-stage biopharmaceutical company has focused on the development of cancer peptide vaccines, including its ITK-1 for castration-resistant prostate cancer and GRN-1201 for melanomas and non-small-cell lung cancer (NSCLC), both of which are currently in clinical trials.

"Our focus is shifting from just peptide vaccines to other modalities," said Kenichi Nagai, president and CEO of BrightPath, which is based in Tokyo. "We are backed by more than 10 years of peptide development, and now we are in a very good position to expand our pipeline."

BrightPath's expanding pipeline

Since 2003, researchers at BrightPath—then GreenPeptide—have been developing their lead product ITK-1, which is a peptide-based cancer vaccine that is designed to stimulate the patient's immune system to attack cancer cells by boosting the presentation of tumor-associated antigens (TAAs). This product, licensed to Fujifilm Corporation, is now in a phase 3 clinical trial in Japan for prostate cancer. Data from this trial are expected in 2018.

ITK-1 consists of 12 pre-arranged TAAs, and it aims to increase the activation of tumor-specific cytotoxic T cells, which attack the tumor. The vaccine can be tailored to each patient, however, by choosing a maximum of four peptides from the pre-arranged 12 TAAs that will be selected based on the patient's immunity before vaccination. If a patient has immunological memory to the vaccine antigens, they are likely to show a quick, strong immune response to the antigens, which will increase the efficacy.

Another BrightPath product, GRN-1201, is in a phase 1 trial for melanoma and a phase 2 trial for NSCLC in the United States. This is a cancer peptide vaccine that stimulates the patient's immune system by targeting four novel TAAs restricted to human leukocyte antigen A2 (HLA-A2) that are shared across many types of cancers.

BrightPath believes that GRN-1201 could be promising in combination with an immune-checkpoint inhibitor that uncloaks a tumor and

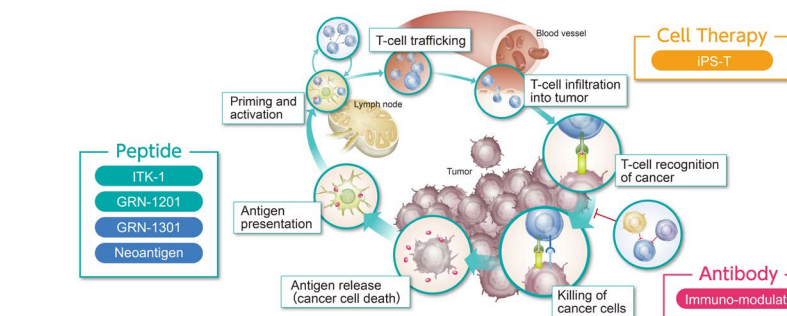


Figure 1: Both BrightPath's target area of cancer immunotherapy and products in development.

makes it recognizable to the immune system. This 'one-two punch' method is the focus of the clinical trial in patients with NSCLC. "Further improvement in efficacy by combining a cancer vaccine can be expected," said Nagai, describing BrightPath's work as the exploration of the new frontier of cancer therapy.

Transformed cells express some tumor-specific proteins, and also accumulate somatic mutations during proliferation and progression. The antigens derived from these tumor-specific proteins appear as foreign to the immune system when they contain the somatic mutations as neoantigens. Researchers believe neoantigens are important markers that flag transformed neoplastic cells—making them recognizable to the immune system. In addition, tumor-specific gene mutation-derived neoantigens are recognized as 'foreign' by the body, so they have strong immunogenicity and may have an important part in spurring an effective immune response. BrightPath has been conducting neoantigen research in conjunction with Kanagawa Cancer Center since 2016.

BrightPath's GRN-1301 is a neoantigen peptide vaccine that is derived from HLA-A2-restricted antigenic T cell epitopes that contain a mutation in the epidermal growth factor receptor (EGFR-T790M), which is directly related to the development of drug-resistant NSCLC. Because of its tumor-specificity, GRN-1301 has high immunogenicity, and it induces a patient's immune system to attack tumor cells expressing EGFR-T790M. GRN-1301 prevents the cancer from becoming immune-resistant and aims to prevent tumor growth.

To truly branch out beyond peptide-based therapies, BrightPath is developing a novel application of induced pluripotent stem cell (iPSC)-derived rejuvenated T cells. Through this new therapy, called iPS-T, the T cells circulating in the blood are then gathered, reprogrammed to pluripotency and redifferentiated to antigen-specific T cells with a high proliferative capacity. This collection of new cytotoxic T cells is administered back to the patient, delivering an onslaught of anticancer therapy.

To move toward a clinical application of iPS-T, BrightPath has initiated a joint study with the Institute of Medical Science of Tokyo University and Juntendo University Hospital for the treatment of lymphomas associated with Epstein-Barr virus.

Toward personalized medicine

Many factors determine if immunotherapy will be effective against immune-resistant tumors, including the number of genetic mutations, the state of the immune system and the microenvironmental conditions of the tumor. By targeting multiple steps in the cancer immune cycle, BrightPath is focused on profiling patients, developing immune monitoring methods and designing patient-specific combination therapies, which means treatments with predictable effects for individual patients.

"I believe the next big thing in immuno-oncology is fully personalized therapy," said Nagai. "We have already had experience with the vaccination approach that is semi-personalized. Looking to the future, BrightPath is in a great position to move toward the development of a fully personalized cancer vaccine immunotherapy, including the integration of immune-checkpoint inhibitors."

The new frontier

BrightPath is poised to progress toward the development of an even broader pipeline based on its clinical trial successes as well as the promise that its other new products have shown.

contact

Masashi Fukuari, Leader,
Business Development
BrightPath Biotherapeutics Co., Ltd.
Tokyo, Japan
Tel +81 3 5840 7697
Email: fukuari_m@brightpathbio.com