Advanced Clinical Research Center

Division of Innovative Cancer Therapy
先端がん治療分野

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Our Laboratory is focused on developing oncolytic virus therapies for various malignant tumors. Oncolytic viruses are engineered to kill tumor cells without affecting normal tissues. G47Δ, a recombinant, triple-mutated oncolytic herpes simplex virus type 1 (HSV-1), exhibits potent anti-tumor efficacy while maintaining safety. G47Δ was approved as the world's first oncolytic virus product for brain tumors in June 2021 and is now in clinical use since November 2021.

Development of novel recombinant oncolytic HSV-1

With a steady increase in cancer mortality, there has been a strong need for novel therapeutics for cancers. Oncolytic virus therapy utilizing genetically engineered virus not only destroys tumor cells by its lytic activity but also shows robust antitumor effect by eliciting systemic and specific antitumor immunity, and is expected as a promising novel therapeutic for cancer. Various kinds of virus have been modified and utilized as oncolytic viruses, but genetically engineered HSV-1 is particularly useful because of following favorable characteristics: (1) a highly selective replication in tumor cells while maintaining safety in normal tissues, (2) a high stability of the viral genome, (3) a potent oncolytic activity in a wide range of cancer cells, (4) cell-to-cell spread of the virus minimally affected by serum antiviral antibodies, (5) presence of antiviral drugs that serve as fail safe, (6) a high capacity for incorporating large or multiple transgenes owing to its large genome size (<152kb). We developed G47Δ, a triple-mutated oncolytic HSV-1 with high efficacy and safety. While conventional homologous recombination techniques had required time-consuming processes to create a new recombinant oncolytic HSV-1, our original recombinant HSV-1 construction system, T-BAC, enables quick and accurate generation of a new recombinant HSV-1 with desired transgenes inserted into a specific locus by utilizing two sets of recombinases (Cre/loxP and FLP/FRT).

Since 2003, translational research of G47Δ was initiated totally by this laboratory, including invention, preclinical studies, clinical lot manufacturing and clinical trials. G47Δ was approved as the world's first oncolytic virus product for malignant glioma in 2021. Besides malignant brain tumors, we have meticulously accumulated pre-clinical data with the intention to expand the application of G47Δ for other cancers, including renal cancer, prostate cancer, bladder cancer, malignant mesothelioma, tongue cancer, esophageal cancer, gastric cancer, colon cancer, lung cancer, breast cancer, nasopharyngeal cancer, cholangiocarcinoma, hepatic cancer, pancreatic cancer, malignant melanoma, and malignant lymphoma.

Preclinical research has revealed that G47Δ is universally effective for all types of solid tumors, and is expected a standard treatment option for cancer in

the near future. The clinical trials of G47Δ for malignant mesothelioma, olfactory neuroblastoma and prostate cancer, and that of human IL-12-expressing G47Δ (T-hIL12) for malignant melanoma have been steadily proceeding.

Publications

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