

Advanced Clinical Research Center

Division of Innovative Cancer Therapy

先端がん治療分野

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Our Laboratory focuses on developing oncolytic virus therapies for various malignant tumors. Oncolytic viruses are genetically engineered to kill tumor cells without affecting normal cells. G47Δ, a triple-mutated oncolytic herpes simplex virus type 1 (HSV-1), exhibits potent antitumor efficacy while maintaining safety. Three clinical trials using G47Δ and one using IL-12-expressing HSV-1 (T-hIL12) are currently being conducted at IMSUT Hospital.

Development of novel recombinant oncolytic HSV-1

With a steady increase in the number of deaths caused by cancer, there is an urgent need for novel therapeutics. Oncolytic virus therapy utilizing genetically engineered viruses not only destroy tumor cells in the course of tumor cell-specific viral replication, but also exhibit robust antitumor effect by eliciting systemic and specific antitumor immunity. HSV-1 is particularly useful for cancer therapy, because of following favorable characteristics; (1) a high specificity for tumor cells while maintaining safety to normal cells, (2) a high stability of viral genome, (3) a potent oncolytic activity in a wide variety of cancer, (4) a minimal impact of antiviral antibodies on cell-to-cell spread of virus, (5) antiviral drugs are available that can terminate therapy if necessary, and (6) a high capacity for large or multiple transgenes owing to its large genome size of virus (<152kb). We developed G47Δ, an oncolytic HSV-1 with triple gene mutations with high efficacy and safety. While conventional homologous recombination techniques require time-consuming processes to create a new recombinant HSV-1, our original system, T-BAC, enables

quick and accurate generation of a new recombinant HSV-1 with desired transgenes inserted into a specific locus by utilizing BAC and two sets of recombinases (Cre/loxP and FLP/FRT). Using T-BAC, we generated human IL-12-expressing oncolytic HSV-1 (T-hIL2) that is currently used in the first-in-human clinical trial for malignant melanoma.

While developing G47Δ as the first-in-the-world, Japan-originated, oncolytic virus product for malignant brain tumors, we have meticulously accumulated pre-clinical data with the intention to expand the application of G47Δ to 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. Our research has revealed that G47Δ is universally effective for all types of solid tumors, and is expected as an innovative treatment for cancer in the near future.

Publications

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