Institute of DNA Medicine
Department of Oncology

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General Summary

The aim of our research is to develop and establish novel cancer therapies.   Concepts for new anticancer therapies, generated from the unique ideas of our researchers, would be verified by basic and clinical studies so that they could be applied clinically.   Most of our research has been based on antitumor immunity.

Research Activities

A phase I clinical study of immunotherapy against advanced pancreatic cancer using dendritic cells pulsed with Wilm's tumor 1 class I and II peptide
The activation of helper T cells should be an essential factor to induce effective antitumor immunity.   Vaccination with dendritic cells (DCs) pulsed with Wilm's tumor 1 (WT1) class I and II peptides would stimulate WT1-specific cytotoxic T cells, as well as helper T cells, leading to the induction of potent WT1-specifc antitumor immunity.   This clinical study is the first trial of treatment with DCs pulsed with WT1 class I and II peptides.   A 64-year-old man with advanced pancreatic cancer has received this treatment and has been well in good shape for 10 months.

A phase I clinical study of immunotherapy against glioblastoma using a DC/tumor fusion cell vaccine
The survival of patients with glioblastoma for more than 4 years has been achieved with the combined treatment with temozolomide and a DC-vaccine generated by the fusion of autologous DCs and irradiated glioblastoma cells.   The overall survival of patients with glioblastoma treated with the both temozolomide and DCs was significantly longer than that of patients treated with temozolomide alone.

Generation of an artificial protein vaccine inducing potent cellular immunity
Artificial proteins composed of a cytotoxic T-lymphocyte (CTL) epitopes, helper epitopes, and intercalated peptides of ovalbumin (OVA) were generated using the MolCraft system for protein evolution.   Vaccination of mice with the protein of the most proper peptide arrangement demonstrated strong induction of OVA-specific CTLs and elicited the inhibition of OVA-expressing tumor growth.   MolCraft-generated artificial proteins are promising future cancer vaccines.

Identification of unique cancer-associated molecules as candidates for novel cancer vaccines

HLA class I binding peptides were collected from cultured human prostate cancer cells and analyzed with liquid chromatography/tandem mass spectrometry. Several peptides derived from unique cancer-associated proteins were identified. The peptides of absent in melanoma 1-like protein (AIM1L), transmembrane protein-191C (TMEM 191C), and c20orf201 were expressed in various types of cancer cell but only in testis, cerebellum, and placenta among noncancerous tissues. These peptides are promising candidates for novel cancer vaccines.

A new molecularly targeted therapy against pancreatic cancer based on the up-regulation of human epidermal growth factor receptor 2 expression

Human pancreatic cancer frequently expresses human epidermal growth factor receptor 2 (HER2). We found that treatment of human pancreatic cancer cells with gemcitabine enhanced HER2 expression. Trastuzumab emtansine (T-DM1), a unique conjugate of a monoclonal antibody to HER2 and a chemotherapeutic agent, showed strong cytotoxic activity against gemcitabine-pretreated pancreatic cancer cells. This synergistic effect might be closely associated with enhanced T-DM1 binding to HER2, the expression of which was up-regulated by treatment with gemcitabine.

Inhibition of the expression of the immune-suppressive protein programmed cell death-ligand 1 on cancer cells by chemotherapeutic agents or molecularly targeted agents or both

The CTLs attacking tumor cells would be killed by the interaction between programmed cell death-ligand 1 (PD-L1) on cancer cells and programmed cell death 1 (PD1) on CTLs. We found that some inhibitors of nuclear factor-kB are able to reduce PD-L1 expression on cancer cells. Treatment with such agents might contribute to the inhibition of PD-L1-mediated immune suppression, leading to augmentation of the antitumor effect of cancer vaccines.

Publications

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