Institute of DNA Medicine
Department of Oncology

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General Summary

The research goal of our department is to develop novel and modified therapeutic approaches for cancers and to explore new tumor markers indicating the presence of a cancer. We focused our efforts on studies of tumor immunology and cancer cell biology. Two clinical studies have been in progress to assess the therapeutic strategies in tumor immunology.

Research Activities

Mechanisms of synergistic effect of Wilms tumor 1 peptide vaccine and gemcitabine against pancreatic cancer

Clinical studies of Wilms tumor 1 (WT1) peptide and gemcitabine for the treatment of pancreatic cancer have achieved good responses. We investigated the basic mechanisms of these effects. Gemcitabine upregulates WT1 messages in human pancreatic cells through a nuclear factor kappa B pathway. The WT1 protein was shown to move from the nucleus to the cytoplasm. Furthermore, mass spectrometric measurement has shown an increase in the amount of WT1 peptide expressed on HLA-A*2402 molecules. These results indicate that gemcitabine-induced upregulation of WT1 can contribute to enhancement of immune responses.

Clinical immunotherapy for brain tumors

Treatment with the combination of fusion-cell therapy and temozolomide is in progress. Fusion cells were produced according to Good Manufacturing Practice procedures.

Crafting novel proteins composed of functional peptides for immunotherapy

To improve the efficiency of immunotherapy, we have started to develop artificial proteins to provide multiple candidates for antigens. As an initial trial, the proteins have been designed to contain WT1 peptide and α helix protein-stabilizing sequences, and the immunogenicity of these proteins is being examined. Once a library of designed proteins has been constructed and screened for immunogenicity, the association between the immune responses and physiochemical structure of the proteins can been studied.

Molecular mechanisms toward megakaryocytic differentiation induce by adhesion

A member of the ets transcription factor family, Friend leukemia virus integration 1 (FLI-1), has been investigated in human leukemia JAS-R cells, which can be induced to the megakaryocytic lineage by adhesion. Adhesion induces transcription of FLI-1, and

once this induction has occurred, the FLI-1 gene promoter is further activated through the positive feedback of FLI-1.

Confirmation of novel tumor markers for urological malignancies using tissue microarrays

Tissue microarrays were produced by rearranging paraffin-embedded blocks of cancerous and noncancerous tissue which were used as samples for histological studies. This system provides an efficient tool for studying possible tumor markers. Two candidates, Minichromosome maintenance 5 and glucosidase alpha neutral AB proteins, previously identified as tumor markers with proteomic methods, were confirmed with tissue microarray analysis to be upregulated in cancer tissues.

Publications

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