Institute of DNA Medicine
Department of Molecular Cell Biology

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General Summary

Our research goal is to analyze the molecular events of cells under physiological and pathological conditions. To achieve this goal, we use morphological and biochemical approaches combined with nucleic acid modification. We have used transfection of naked DNA or short interfering RNA to modulate protein expression and have used fluorescent nanoparticle conjugates to visualize or quantify target molecules. By combining methods of molecular and cellular biology, we are exploring medical life sciences.

Research Activities

Development of nucleic acids delivery into malignant glioma cells by acoustic energy
Malignant glioma is an intractable disease of the human brain. Although many adjuvant therapies, such as radiotherapy, chemotherapy, and immunotherapy, have been developed, the prognoses of patients remain unsatisfactory. Therefore, we are exploring alternative therapies, such as sonodynamic therapy. A characteristic of the malignant glioma is that in spite of the poor prognosis, distant metastasis seldom occurs and death is due mostly to local recurrence. In this situation, we developed a theragnosis system, which combines therapy and diagnosis, for glioma. The system enables radiotherapeutic ultrasound to be applied to a glioma as a local treatment while the process is monitored. This year, we attempted to develop another combination of nucleic acid delivery to the theragnosis system. We selected several intracellular signal molecules as targets. First, we found that in most glioma cell lines, Rho kinase isoforms (ROCK1 and ROCK2), epidermal growth factor receptor (EGFR), and signal transducer and activator of transcription (STAT) 3 were expressed and phosphatase and tensin homologue (PTEN) was down-regulated. Next we found that transduction of short hairpin RNA (shRNA) to ROCK1, ROCK2, EGFR and STAT3 down-regulated the expressions of respective molecules, and forced expression of PTEN inhibited cell proliferation. We also found that down-regulation of ROCK1 and expression of PTEN prolonged the G2 phase of the cell cycle and increased sensitivity to alkylating agents. Because these molecules are potential therapeutic targets, acoustic conditions for delivery were evaluated.

Biochemical application of thyroid carcinoma specific antibody
Diagnosis of thyroid cancer involves such methods as palpation, ultrasonography, fine-needle aspiration cytology, scintigraphy, and blood tests. To increase diagnostic precision and to alleviate the burdens on both patients and physicians, we have developed detection systems with a thyroid carcinoma-specific antibody (JT95) and fluorescent nanoparticles (quantum dots). The direct binding of quantum dots and JT95 monoclonal

antibodies was applicable to Western blotting analysis, an enzyme-linked immunosorbent assay-like system, and fluorescent microscopic analysis of the SW1736 thyroid carcinoma cell line. These easily handled techniques may increase diagnostic precision.

Function of proopiomelanocortin in cardiomyocytes

The expression of proopiomelanocortin (POMC) in HL-1 cardiomyocytes was studied. An overexpression vector plasmid of POMC was constructed and will be used to study the release of ACTH from HL-1 cardiomyocytes overexpressing POMC. In addition, the effects of Ca^{2+} channel blockers on the expression of steroidogenic enzymes were investigated using NCI-H295R adrenocortical carcinoma cells.

Publications

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