Institute of DNA Medicine
Department of Molecular Cell Biology

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General Summary

The goal of our department is to perform medical science research based on the molecular biology of cells. For this reason, molecular events of cells under physiological and pathological conditions are analyzed. To achieve our goal, both morphological and biochemical approaches are applied, and methods for modifying the transcription and expression of nucleic acids are used. The methods include transfection of DNA or short interfering RNA to modulate gene expression. Also, to quantify target molecules, we use such methods as labeling with fluorescent nanoparticles, conjugation to sensors, and amplification with radiolabelled materials. By introducing the methods of molecular and cellular biology, we are addressing clinical problems.

Research Activities

Development of a nucleic acid delivery system for malignant glioma cells by acoustic energy

Malignant glioma is an intractable disease. Many adjuvant therapies, such as radiotherapy, chemotherapy, and immunotherapy, have been developed. Nevertheless, the prognoses of patients remain unsatisfactory. For this reason, we are exploring alternative strategies, such as sonodynamic therapy. Despite the poor prognosis of patients with malignant glioma, metastasis outside the central nervous system is rare, and the cause of death in most cases is local recurrence. Therefore, if an effective local therapy were established, patients would live longer, and even complete cure could be expected. Against this background, we have developed a theragnosis system, which is a combination of therapy and diagnosis, for glioma. With this system, ultrasound is applied to local glioma lesions for both diagnosis and treatment. In addition, we are developing a nucleic acid delivery system based on the theragnosis system. We found that down-regulation of Rho-associated kinase 2 (ROCK2) by short hairpin RNA inhibited tumor growth *in vitro* and increased sensitivity to the antineoplastic agent temozolomide. Also, forced expression of phosphatase and tensin homologue (PTEN) demonstrated the same effects. Both methods prolonged the G2 phase of the cell cycle and increased sensitivity to alkylating agents. While these molecules are key targets for therapy, other candidates and other types of malignancy are being screened.

The antioxidative actions of urocortin I on cardiac myocytes

Oxidative stress is a major pathological factor in heart disease. Recently, many protective cardiovascular agents, such as atrial/brain natriuretic peptides, are used to treat heart disease. The protein urocortin I exerts several beneficial effects involved in cytoprotec-

tion, including the antioxidative action. The antioxidative action of urocortin I, however, has not been thoroughly investigated. Therefore, the antioxidative action of urocortin I in HL-1 cardiomyocytes induced by cardiovascular pathological agents was investigated with nicotine. We found that urocortin I, not urocortin II, attenuated nicotine-induced oxidative stress. The mechanism of the antioxidative action of urocortin I is also being investigated.

Development of a high-accuracy, high-sensitivity, and rapid diagnosis system for thyroid carcinoma

We developed biomedical applications for histochemistry and cytochemistry using a biotinylated JT-95 monoclonal antibody that recognizes an antigen of thyroid carcinomas. Moreover, we optimized the enzyme-linked immunosorbent assay system for blood tests with both JT-95 and biotinylated JT-95. To support the clinical use of these applications, we have been studying the accuracy of the detection system.

Publications

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