Institute of DNA Medicine
Department of Molecular Cell Biology

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General Summary

The department provides molecular tools for analyzing the medical problems under both physiological and pathological conditions. To elucidate the underlying mechanisms of such problems, molecular biological technologies using cells are useful. The methods include modification of nucleic acid transcription and expression by transfection of DNA or short interfering RNA. Also, labeling of molecules with fluorescent nanoparticles, conjugation to sensors, and amplification with radiolabelled materials are used. By introducing such methods of molecular and cellular biology, we are helping address clinical problems.

Research Activities

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

Glioma is an intractable disease of the central nervous system. Because the prognosis is poor, alternative therapies are required. Despite the poor prognosis, metastasis outside the central nervous system is rare, and the cause of the 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. Recently, local therapy using a therapeutic ultrasound irradiator was developed, and the beneficial effect of therapeutic insonation to glioma in combination with microbubbles was reported. In the present study, to enhance the therapeutic efficacy, a nucleic acid delivery system using ultrasound was developed. Ultrasound conditions for delivery as well as adjuvant factors and transcripts of target genes were examined. Also, the effects of ultrasound for gene transcriptions were examined.

Transcription of urocortin and corticotropin-releasing factors (CRFs) in human malignant glioma cells

Urocortin (Ucn) and corticotropin-releasing factors (CRFs) and their receptors are expressed in many organs, including the central nervous system. This year, the expression of the mRNAs of Ucn I, II, and III and CRF and CRF receptors 1 and 2 in malignant glioma was examined. The RNAs of 5 human and 3 rat glioma cell lines were isolated, and transcripts in these cells were analyzed on the basis of complementary DNAs. Human and rat cell transcripts of Ucn and CRF receptors were detected in human glioma cells. When human KNS42 cells were exposed to proliferative and cytotoxic stimulation, transcription altered according to the conditions. However, although the quantities of transcripts varied with the proliferative and cytotoxic stimulation, the

overall transcription pattern was not affected by these stimuli.

Possible involvement of Ucn I in the adaptation to oxidative stress in HL-1 cardiomyocytes

Our previous studies have revealed that Ucn I is regulated by oxidative stress and that Ucn I suppress oxidative stress in a murine atrial cell line, HL-1 cardiomyocytes. Therefore, we investigated the involvement of Ucn I in the suppressive action in HL-1 cardiomyocytes. Ucn I was knocked down by small interfering RNA, and knock-down of Ucn I in HL-1 cardiomyocytes resulted in enhancement of nicotine-induced oxidative stress. In addition, investigation of the effects of nicotine on promoter activity using an Ucn I promoter-driven reporter plasmid revealed that nicotine enhanced the promoter activity of Ucn I. These results may contribute to the future development of cardioprotective strategies for cardiac disease.

Carbohydrate analyses of thyroid carcinoma cell lines using lectins

In our previous studies, we have reported a potential marker for thyroid papillary carcinoma, sialylated fibronectin antigen, which was detected with "JT antibody," and developed applications for it. However, the details of the carbohydrate structure of the antigen in thyroid carcinoma remain unclear. Therefore, we investigated the structure of 5 thyroid carcinoma cell lines (K1 and IHH4 papillary carcinoma cell lines and SW1736, 8305C, and 8505C anaplastic carcinoma cell lines) using several lectins, which recognize specific carbohydrate structures. This research showed that SW1736 and IHH4 cells, which have high invasive capacity, were predominantly recognized by the lectin from *Datura stramonium*. Because *D. stramonium* lectin recognizes Galβ1-4GlcNAc carbohydrates, these cells could express these structures. The next step would be to determine the carbohydrate structures of the fibronectin antigen in thyroid carcinoma cell lines.

Publications

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