Institute of DNA Medicine
Department of Molecular Cell Biology

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General Summary

Our research goals include molecular analysis and visualization of cellular events under both physiological and pathological conditions. To achieve our goals, we have used morphological and biochemical approaches combined with nucleic acid modification. We used transfection of DNA or short interfering RNA to modulate protein expression and fluorescent nanoparticles to visualize or quantify target molecules. Through the combination of molecular and cellular biology methods, we are exploring the medical life sciences.

Research Activities

Development of sonodynamic therapy and diagnostics for malignant glioma

Gliomas are common and intractable tumors of the brain. Because gliomas have an unfavorable prognosis, alternative therapies or treatments are needed. Despite the poor prognosis, distant metastasis is rare, and local recurrence is the most common cause of death. Therefore, long survival or even cure can be achieved only through the control of local recurrence. In this study, the prototype of a theragnosis system for glioma was produced. This system enables ultrasound to be applied to gliomas as a local treatment (therapy) while the process is monitored (diagnosis). The EUB6500 ultrasound diagnostic instrument (Hitachi Medical Corp., Tokyo, Japan) was used and combined with a therapeutic ultrasound generator and amplifier. The system can emit ultrasound at 500 kHz and 0 to 3 W/cm^2. The results demonstrated a beneficial effect of therapeutic insonation to gliomas in combination with microbubbles and suggested future clinical applications.

Three-dimensional cell culture of malignant glioma cells

Cell culture techniques are useful for observing the characteristics of tissues and organs in the human body. These techniques are also essential for the diagnosis and treatment of human disease. However, vital cell functions might be overlooked with ordinary 2-dimensional dish-based cell culture methods. For this reason, we used a culture method that mimics the human intracranial environment of gliomas. Structural changes have been observed in brain cell cultures using a gelatin scaffold as a bioabsorbable and biocompatible material. Because marked changes in morphological appearance can occur, we believe that signals or information of the cell membrane is important. Thus, expression of the transforming growth factor (TGF) β/SMAD system and matrix metalloproteinases (MMPs) was compared. The reverse transcriptase-polymerase chain reaction showed a difference in the expression of TGF-β, ALK5, ALK1, Smad 2, Smad

4, MMP-2, and p38 mitogen-activated protein kinase (MAPK). Among these, expression of genes ALK5, Smad 2, and Smad 4 differed considerably in 3-dimensional cultures. In contrast, differences in the expression of TGF-β, ALK5, MMP-2, and p38 MAPK were modest. Expression of these genes decreased in the 3-dimensional cell culture, and because the question of how the signal changes affect morphological differences in glioma needs to be answered, comprehensive analysis will be performed in combination with molecular targeting to the culture method. We also found that phosphorylation, but not the amount, of Akt significantly increased in the 3-dimensional culture. In addition, growth signals, such as platelet-derived growth factor subunit A of U118MG cells, which dispersed after cell division, increased more than 10 times compared with that of other cells, such as KNS42 and A172 forming agglomeration.

Detection of thyroid carcinoma antigen with quantum dots and JT 95 monoclonal antibody systems

Fluorescent nanoparticles, quantum dots (QDs), have been applied to biological studies and medical studies by taking advantage of their highly-intensity fluorescent properties. On the other hand, previous studies have shown the detection ability of the JT-95 IgM antibody with histological sections and the SW1736 thyroid carcinoma cell line. Therefore, we tested whether the combination of QDs and the JT-95 antibody could increase the ability to detect thyroid carcinoma. We showed that the combination of QDs and the JT-95 antibody could be used for biological analyses, such as Western blotting analysis and fluorescent microscopic analysis, of SW1736 cells. We have opened up the possibility that antibodies, even IgM, could be used to improve the ability to detect cancers.

Publications

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