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 these goals, we have used morphological and biochemical approaches. Our department has two sections: biochemistry and fine morphology. Through the activities of both sections, we are exploring medical life sciences.

Research Activities

Development of sonodynamic therapy and diagnostics for malignant glioma

Ultrasound has been widely used as a diagnostic tool. It is handy, convenient, and inexpensive. It is also safe, because no ionizing radiation or other harmful energies are emitted. Thus, many clinicians and medical technologists use ultrasound. Recently, therapeutic ultrasound irradiation, or insonation, has been developed. Insonation is a potentially useful cancer treatment. One application is sonodynamic therapy. When sonodynamic agents are enhanced with ultrasound, insonation has cytocidal effects on nearby malignant tissues. With this method, we are developing a therapeutic strategy for malignant brain tumors. A microbubble agent, Levovist, is used as an ultrasound enhancer, and both therapy and diagnosis can be simultaneously achieved.

Three-dimensional cell culture of malignant glioma cells

Cell culture is a basic tool for understanding the characteristics of tissues and organs in the human body. The procedure is also essential for the development of diagnostics and therapeutics for human disease. However, vital cellular functions that are present in tissues or organs are missed by ordinary flask-based or culture dish-based cell cultures. From this point of view, we have established a culture method that mimics the human intracranial environment. This year, we compared 4 different malignant glioma cell lines. A bioadaptable and biodegradable gelatin was used as a scaffold upon which cells were cultivated. Some morphologic features observed in 3-dimensional (3D) culture could not be observed in conventional cell culture. When the 4 glioma lines were compared, each cell line demonstrated distinct characteristics. For example, 1 cell line conglomerated and formed balloon-like structure, and cells of another line dispersed and grew separately immediately after cell division. These characteristics were unpredictable and could be revealed only with the current culture method. We conclude that this culture method is useful for evaluating characteristics of individual glioma cell lines in the human body.

Functional analysis of tight junctions

Tight junctions (TJs) in the epithelia and endothelia restrict the paracellular flux of water and solutes. In the epidermis, the significance of the TJ is largely unknown because of the structural complexity of the epidermis. To understand TJ functions in the epidermis, a specific method for TJ disruption would be useful. Sodium caprate is a well-known absorption enhancer that causes dilatation of the TJ and increases paracellular permeability in the intestine. We investigated the effects of sodium caprate on 3D cultures of human skin to help understand TJ functions in the epidermis. After treatment with sodium caprate, transepidermal resistance decreased, indicating paracellular barrier disruption. Treatment with sodium caprate decreased claudin-1 and occludin expression and fragmented their localization in 3D skin cells. Cell polarity was disrupted in 3D skin as well. These results suggest that sodium caprate induces TJ disruption in 3D cultures of human skin and can be applied to further studies of epidermal TJ function.

Photoluminescent silicon quantum dots

In nanotechnology research, we assessed biochemical applications of photoluminescent silicon (Si) quantum dots (QDs). Si-QDs have been used as biological labels for imaging living cells at nontoxic concentrations. We have shown that Si-QDs have no toxicity against living cells at a concentration of 112 μg/mL and that Si-QDs are less toxic than current cadmium-selenium (CdSe)-QDs at high concentrations both in modified methylthiotetrazol assays and with lactate dehydrogenase assays. We found that under ultraviolet light CdSe-QDs released cadmium and were more toxic than nonirradiated CdSe-QDs or Si-QDs. In addition, we found that the toxicity mechanisms of Si-QDs at high concentrations were related to radical production. These results will be useful for the future application of Si-QDs in biology and medicine.

Publications

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