Core Research Facilities

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General Summary

The Core Research Facilities were reorganized on April 1, 2009, as the Research Center for Medical Sciences and consists of the Division of Fine Morphology, the Division of Biochemistry, and the Division of Advanced-Research Laboratory. The mission of the facilities is the facilitation of research in the university. Two systems are constituted for the use of the facilities

1. Annual Registration System

This system is intended to supply research space, benches, and other equipment to researchers of the university to perform experiments. Once registered, researchers can freely use the various devices, such as fluorescent microscopes, optical microscopes, and equipment for the preparation of samples for histological examinations, high-performance liquid chromatographs, and nucleic acid amplification systems (polymerase chain reaction). Because inspections and maintenance are regularly performed by the staff, the equipment is reliable and available at any time. This system also provides technical advice and guidance on specific fine-morphological or biochemical approaches to a registrant's experiment, if necessary.

2. System for Providing Research Services

Advances in research technologies and equipment enable us to perform more precise and accurate observations of specimens in medical sciences. However, the various new high technologies and devices require specialized knowledge. These advances can cost the researchers both time and money. Also, all researchers are not necessarily familiar with all the equipment for medical experiments. For researchers who cannot perform experiments owing to limits of time and funds, our staff can prepare samples for scanning electron microscopy and transmission electron microscopy, record images, or perform high-performance liquid chromatography and mass spectrometry. By using this system, researchers can proceed efficiently. The service fee is minimal because services are limited to the university.

Research Activities

Monoclonal antibody to thyroid papillary carcinoma for patient screening

A monoclonal antibody against thyroid papillary carcinoma has been used to detect antigens in the membrane fraction of tumor cells or secreted by tumors in tumor-bearing patients. With the conjugation of the antibody, we developed a measuring method with the sandwich enzyme-linked immunosorbent assay. However, when the tumor is too small, the antigen might not be detected, especially in the blood of patients. Therefore, assay methods that are more sensitive need to be developed. We are trying to apply

thermal reacting magnetic beads and immunochromatography to the detective system.

Analysis of mitochondrial DNA of the genus Nycticebus
Slow lorises (*Nycticebus* ssp.) have been kept, bred, and exhibited for many years in many Japanese facilities. However, because of their endangered status, in 2007 slow lorises were shifted from Appendix II to Appendix I of the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES). Since then, international trade in slow lorises has been prohibited. However, illegal trade continues. The problem is that when slow lorises are confiscated while being illegally transported, the country of origin and even the name of the species is often unclear. Previously, we determined the species by examining DNA nucleotide sequences, as requested by the Asian Wildlife Research Center. This examination includes amplification, sequencing of mitochondrial DNAs of cytochrome oxidase subunit 1 (COI), and comparison with standard individuals, animals can be classified into the 5 present species of *Nycticebus*. This year, we sequenced the whole mitochondrial DNA of the Bengal slow loris (*Nycticebus bengalensis*). This information will facilitate more accurate identification of the species of each animal.

Functional analysis of 3 novel cell lines derived from human papillary thyroid carcinomas with 3 different clinical courses
Papillary thyroid carcinoma (PTC) is the most frequent thyroid carcinoma. Cell lines derived from PTC have been of considerable value in studying various aspects of thyroid cancer, such as gene expression, cell proliferation, and differentiation. Here we report 3 novel PTC lines established from 3 patients with different backgrounds.
Patient 1 was a 38-year-old woman with a PTC of the right thyroid lobe which had not metastasized. The cell line consisted of epithelial cells with few lysosomes and showed a pavement structure. The secretion of free thyroxine (fT4) and thyroglobulin were increased by thyroid-stimulating hormone or treatment with growth hormone (GH) and insulin-like growth factor (IGF) I.
Patient 2 was a 22-year-old woman with PTC initially in the right thyroid lobe, but 4 years after resection of the right lobe, the PTC had metastasized to the left lobe. This cell line consisted of small epithelial cells with evident lysosomes. The secretion of fT4 and thyroglobulin were slightly increased by TSH or by treatment with GH and IGF-I.
Patient 3 was an 85-year-old man with PTC and acromegaly. The PTC had metastasized to the cervical lymph nodes. This cell line consisted of small epithelial cells with many lysosomes. The cells frequently piled up. The secretion of fT4 and thyroglobulin was significantly increased by treatment with GH and IGF-I. We have established 3 PTC cell lines with substantial variations in phenotype. The cell lines may be useful for thyroid cancer research.

Biophysical characterization of branched amphilic peptide capsules.
Branched amphiphilic peptide capsules (BAPCs) are peptide nanospheres comprised of equimolar proportions of 2 branched peptide sequences — (FLIVI) 2-K-KKKK and (FLIVIGSII) 2-K-KKKK — that self-assemble in water to form bilayer-delimited poly-

cationic capsules capable of trapping solutes. We examined the lipid-like properties of this system including assembly, fusion, solute encapsulation, and resizing by membrane extrusion and also examined their capability to be maintained at a specific size by storage at 4˚C. These studies demonstrated that the capsules, while sharing many properties with lipid vesicles, were much more robust. We also investigated the stability, size limitations of encapsulation, cellular localization, retention, and biodistribution of the BAPCs. We demonstrated that the BAPCs are readily taken up by epithelial cells in culture, escape or evade the endocytotic pathway, and accumulate in the perinuclear region, where they persist without apparent degradation. The BAPCs encapsulated alpha particle-emitting radionuclides without apparent leakage, were taken up by cells, and were retained for extended periods of time. Their potential for clinical application is being examined.

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