

## 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 our 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 for diagnosis of thyroid papillary carcinoma*

Previously a monoclonal antibody recognizing thyroid carcinoma was established in the University by immunizing the membrane fraction of tumor cells from a patient with papillary thyroid carcinoma. This antibody recognizes an antigen produced by malignant thyroid carcinoma cells. By conjugating the antibody, we have attempted to develop an assay system from the blood of patients. The antibody was conjugated to streptavidin, and a method of sandwich enzyme-linked immunosorbent assay was devised. This

method enabled us to perform highly sensitive detection and quantification of the antigen. To test the relevancy of this assay, a clinical trial study is being performed.

*Analysis of the responsive gene of spontaneous mutant ICR Kuru<sup>2</sup> mouse*

We have established a mouse model of spontaneous deafness by sibling-inbreeding over 10 years. The mouse was designated as kuru<sup>2</sup> and is kept in the University. To identify the genetic abnormality, the mouse was back-crossed to *Mus musculus castaneus* (CAST), and myosine 15 or myoXV on chromosome 11 was assumed to be the responsive gene. This year, the background abnormality was identified with gene sequencing. A deletion of 2,446 base pairs was found in the mouse (from 28,795 to 31,241 in the complete sequence of the *M. musculus* unconventional myosin-15 gene; National Center for Biotechnology Information accession: AF144093). The myosin ATP-binding site is present in the deleted area. Considering the function that the affected area regulates and previous reports, hearing loss of the examined mouse is attributable to the abnormality of the myoXV gene, and we reported that the mouse might be another type of shaker-2 deaf mouse.

*Peptide nanovesicles formed by the self-assembly of branched amphiphilic peptides*

Peptide-based packaging systems show great potential as safer drug-delivery systems. They overcome problems associated with lipid-based or viral delivery systems in terms of stability, specificity, inflammation, antigenicity, and tuneability. Here, we describe a set of 15- and 23-residue branched, amphiphilic peptides that mimic phosphoglycerides in molecular architecture. These peptides undergo supramolecular self-assembly and form solvent-filled, bilayer-delimited spheres with 50.200-nm diameters as confirmed with transmission electron microscopy, scanning transmission electron microscopy, and dynamic light scattering. Whereas weak hydrophobic forces drive and sustain lipid bilayer assemblies, these all-peptide structures are stabilized potentially by both hydrophobic interactions and hydrogen bonds and remain intact at low micromolar concentrations and higher temperatures. A linear peptide lacking the branch point showed no self-assembly properties. We have observed that these peptide vesicles can trap fluorescent dye molecules within their interior and are taken up by N/N 1003A rabbit lens epithelial cells grown in culture. These assemblies are thus potential drug-delivery systems that can overcome some of the key limitations of the current packaging systems.

## Publications

**Yokoyama K, Ohkido I, Iwamoto T, Ishida M, Urashima M, Hosoya T.** Decrease of serum sphingosine-1-phosphate levels in hemodialysis patients with secondary hyperparathyroidism treated with cinacalcet. *Clin Nephrol.* 2012; **78**: 85-6.

**Gudlur S, Sukthankar P, Gao J, Avila LA, Hiro-masa Y, Chen J, Iwamoto T, Tomich JM.** Peptide nanovesicles formed by the self-assembly of branched amphiphilic peptides. *PLoS One.* 2012; **7**: e45374.

**Watanabe M, Akiyama N, Manome Y, Hasegawa N.** Spontaneous mutant ICR kuru2 might be another shaker-2 deaf mouse. *In Vivo.* 2012; **26**: 787-91.

**Kamada M, Ikeda K, Fujioka K, Akiyama N, Akiyoshi K, Inoue Y, Hanada S, Yamamoto K, Tojo Y, Manome Y.** Expression of mRNAs of urocortin and corticotropin-releasing factor receptors in malignant glioma cell lines. *Anticancer Res.* 2012; **32**: 5299-307.

**Fujioka K, Arakawa E, Kita J, Aoyama Y,**

**Manome Y, Ikeda K, Yamamoto K.** Detection of aeromonas hydrophila in liquid media by volatile production similarity patterns, using a FF-2A electronic nose. *Sensors (Basel)*. 2013; **1**: 736-45.

**Fujioka K, Hanada S, Inoue Y, Shiraishi K, Kanaya F, Manome Y.** Evaluation of nanotoxic effects on brain using in vitro models. *AATEX: Alternatives to Animal Testing and EXperimentation*. 2012; **17** Suppl: 156.

**Maruoka Y, Kanaya F, Hoshino A, Iimura T, Imai H, Otsuka R, Ueha S, Fujioka K, Katsuragawa Y, Shimbo T, Mimori A, Yamazaki T, Manome Y, Moriyama K, Omura K, Matsu-shima K, Yamamoto K.** Study of osteo/chondropenia caused by impaired chemokine receptor

and for progressive/idiopathic condylar resorption. *Nihon Gaku Henkeisho Gakkai Zasshi*. 2012; **22** Suppl: S15-22.

### Reviews and Books

**Ikeda K, Fujioka K, Manome Y, Tojo K.** Clinical Perspectives of urocortin and related agents for the treatment of cardiovascular disease. *Int J Endocrinol*. 2012; **2012**: 198628.

**Ikeda K, Isaka T, Fujioka K, Manome Y, Tojo K.** Suppression of aldosterone synthesis and secretion by Ca<sup>2+</sup> channel antagonists. *Int J Endocrinol*. 2012; **2012**: 519467.