

ORGANIZATION OF MIE UNIVERSITY GRADUATE SCHOOL OF MEDICINE

三重大学大学院医学系研究科
生命医科学専攻（博士課程）

Graduate School of Medicine, Mie University
Medical Life Science (Doctoral Course)

基礎医学系講座		Department of Basic Medical Sciences (Research Fields)
1	幹細胞発生学	Stem Cell and Developmental Biology
2	統合薬理学	Integrative Pharmacology
3	分子病態学	Molecular Pathobiology & Cell Adhesion Biology
4	法医学科学	Forensic Medicine and Sciences

臨床医学系講座		Department of Clinical Medical Sciences (Research Fields)
5	皮膚科学	Dermatology
6	脳神経外科学	Neurosurgery
7	形成外科学	Plastic and Reconstructive Surgery
8	リハビリテーション医学	Rehabilitation Medicine

**Department
of
Basic Medical Sciences**

Stem Cell and Developmental Biology

Stem cells are defined as cells that are capable of self-renewal and differentiation to specialized cell types. Our laboratory is investigating on the ontogeny and the fate determination of stem cells, and how these stem cells contribute to the development of tissues or specific system. Currently, our research focuses are on development of neural crest-derived tissues and hematolymphoid system. The following projects are underway:

Research on organogenesis of thymus, bone marrow, and tooth tissues focusing on the contributions of neural crest stem cells and neural crest-derived cells.

The above projects involved the techniques of animal experiments, cell and tissue culture, and cell and molecular biology. The aim of the course is to master these basic techniques and to obtain scientific thinking skills required in the fields of developmental biology, stem cell biology, and immunology.

Department of Integrative Pharmacology

Many drugs have been developed to treat diseases. There are still several issues that need to be addressed, however, in the development of therapeutics and understanding the mechanisms. To tackle these problems, we take integrative approaches using different types of omics datasets, bioinformatics tools, and model animals. Our research aims to find new relationships between genes, diseases, and drugs through integrative approaches. Selected publications are shown below.

- 1) Primary cilia and lipid raft dynamics. *Open Biology* (2021)
- 2) Oxidative stress as a common key event in developmental neurotoxicity. *Oxidative Medicine and Cellular Longevity* (2021)
- 3) Primary cilia-dependent lipid raft/caveolin dynamics regulate adipogenesis. *Cell Reports* (2021)
- 4) An integrated in silico and in vivo approach to identify protective effects of palonosetron in cisplatin-induced nephrotoxicity. *Pharmaceuticals* (2020)
- 5) Targeting E3 ubiquitin ligases and deubiquitinases in ciliopathy and cancer *International Journal of Molecular Sciences* (2020)

Molecular Pathobiology

Roles of Integrins in Immune Cells, Cancers, and Their Exosomes

The Molecular Pathobiology Laboratory

(<http://www.medic.mie-u.ac.jp/molpath/en>) studies the fundamental mechanisms, by which integrins regulate leukocyte and extracellular vesicle (e.g., exosomes) trafficking and vascular biology in the context of inflammation, infection, and immunity. Integrins represent the largest family of cell adhesion molecules that mediate cell-to-cell, cell-to-extracellular matrix, and cell-to-pathogen interactions in a wide range of physiology and pathophysiology such as inflammation and immunity, host defense and cancer progression and metastasis, and vascular integrity and thrombosis. Integrins regulate leukocyte-endothelial cell interactions, thereby playing the pivotal roles in the pathogenesis of inflammatory tissue damages. Our laboratory has studied the roles of integrins in health and diseases as well as cells and exosomes using the state-of-the-art technologies such as CRISPR/Cas9 gene-editing, genetic engineering, nanoparticle tracking, stem cell-derived organoids and novel disease models.

We have a team of internationally diverse faculty members and students. All communications in the lab are done in English, thereby providing a friendly environment for international students who wish to study biomedical science in Japan. On-going research projects include:

- (1) How vascular inflammation is induced and how it causes remodeling of vascular walls? This question specifically addresses the underlying mechanisms of endothelial cell injury in severe infection and septic shock and vascular pathology in atherosclerosis.
- (2) How vascular endothelial cells communicate with immune cells (e.g., lymphocytes, monocytes, and innate lymphoid cells) via cell adhesion molecule integrins and exosomes? This question specifically addresses the underlying mechanisms of aberrant immune regulations observed

in immune deficiency and autoimmune diseases.

- (3) How SARS-CoV-2 induces vascular inflammation and lymphocyte deregulation? This question specifically is built on our recent discovery that SARS-CoV-2 spike protein bind to and signal through integrins.
- (4) How the immune system is interconnected to the regulation of coagulation (via a coagulation factor thrombomodulin) and skeletal muscle metabolism (via a myokine irisin). This question specifically addresses the molecular pathogenesis of septic shock and multiple organ failure seen in critically ill patients.

Ph.D. course students will be trained to master basic cellular and molecular biology techniques and involved in an independent research project under the full guidance of the faculty members of the department who have good command of English.

Motomu Shimaoka, M.D., Ph.D.

Professor and Chairman

shimaoka@med.mie-u.ac.jp

or

motomushimaoka@gmail.com

Forensic Medicine and Sciences

Staff: Hirokazu KOTANI, MD, PhD, Professor
Toru OSHIMA, MD, PhD, Associate Professor
Hidehisa SEKIJIMA, PhD, Assistant Professor

Research Interests:

The final goal of our department is to establish a field of pediatric forensic medicine in Japan. To achieve our goal, to foster pediatric forensic practitioners, and to save children's lives, we are currently developing models for prediction of sudden unexpected death in infancy (SUDI) risk, clinical prediction rules for abusive head trauma (AHT), and a child death review (CDR) system for Japan. On the practical side of forensic fields, we provide medico-legal reports and testify in court in relation to matters involving the medical aspects of child maltreatment. We are also conducting forensic researches in the fields of forensic pathology and toxicology to clarify pathophysiological mechanisms of trauma- and toxin-related deaths.

**Department
of
Clinical Medical Sciences**

Dermatology

We are focusing on molecular and histopathological analysis, molecular diagnosis and development of new therapies for resistant skin diseases, including atopic dermatitis, psoriasis, cancer, infectious diseases. We are currently performing several experiments as a group consisting with one instructor and five graduate students. Following issues are currently investigated;

1) Molecular analysis for skin diseases.

Skin disorders affect to systemic inflammation including abdominal aortic remodeling and systemic amyloidosis. We are trying to find the new evidence and therapies for these complications. Main focus: atopic dermatitis, psoriasis, and skin cancer.

2) The development of new drugs for skin neoplastic diseases.

New therapies will be required to overcome resistant cancer.

3) Mouse skin disease models by gene manipulation.

Main focus: atopic dermatitis mouse models

To perform projects described above, we can support molecular technique and instruct how to create and perform the immunological study.

Neurosurgery

Our graduate program includes the clinical and basic science research for developing new techniques for diagnosis and treatment of neurosurgical diseases, such as vascular lesions, malignant and benign tumors, traumas, infections, malformations and functional diseases of the central nervous system. Among them, we are focusing on the following projects.

Main Projects:

- 1) Development of devices for neuro-endovascular therapy.
- 2) Analysis of clinical data of neuro-endovascular therapy.
- 3) Biological response of the arterial wall to carotid artery stenting.
- 4) Molecular mechanism of cerebral vasospasm.
- 5) Neuroprotection against brain injury after subarachnoid hemorrhage.
- 6) Multimodality therapy for malignant brain tumors.
- 7) Neuroendoscopic treatment of pituitary tumors.
- 8) Computational flow dynamics (CFD) analysis of cerebral aneurysms concerning the growing and rupture risks.

Graduate students will research one or several areas of the projects using the techniques of neuropathology, neuroanatomy, neurochemistry, neurophysiology, neuropharmacology and neuroimaging.

Plastic and Reconstructive Surgery

1. Research contents

1) Development study on immediate neurological functional recovery therapy

A. Study on immediate neural function reconstruction using cell fusion methods

B. In vivo experimental study on an axonal transport using squid giant axons

C. An axonal regeneration study using mitochondrial GFP mouse

D. New drug therapy on axon regeneration

2) Research for a treatment of lymphatic function and lymphedema

A. Clinical and basic research on the mechanisms of lymphedema

B. Study on lymph node degeneration in lymphedema

3) Hemodynamics study on bone growth

4) Basic research on tissue regeneration of limbs

A comparative study on the wound healing process of newts and mammals with a focus on

A. Nerve regeneration

B. Muscle regeneration

C. Bone regeneration

D. Skin regeneration

E. Vascular regeneration

2. Instruction

Using biochemistry, histology, physiology, pathology and diagnostic imaging methods related to the above research contents, we aim for future clinical application of our laboratory results. We collaborate with other colleges / universities.

Rehabilitation Medicine

1. Research contents

- Early rehabilitation for acute in-hospital patients
- Prehabilitation before cancer surgery
- Total management of patients with dysphagia
- Nutritional care and medication therapy management for patients undergoing rehabilitation
- Real world research and health service research in rehabilitation medicine

2. Instructional contents

Based on each students' clinical question, we will teach them how to conduct a systematic review, study design, data handling, statistical analysis, medical writing, and how to get grant funding.

We welcome doctors as well as physical therapists, occupational therapists, speech and language therapists, dietitians, pharmacists, nurses, dentists, dental hygienists and many other professionals.