

# TOKYO MEDICAL AND DENTAL UNIVERSITY

Cultivating Professionals with Knowledge and Humanity, thereby Contributing to People's Well-being

# Institute of Biomaterials and Bioengineering

# OUTLINE 2018



# Message from the Director

# Achieving health and vitality in an aging society

Professor Yuji Miyahara, PhD More than 60 years have passed since the first institute for dental engineering was established at Tokyo Medical and carried out based on this framework

dental engineering was established at Tokyo Medical and Dental University (TMDU) in 1951. Since then, our institute, the Institute of Biomaterials and Bioengineering (IBB), has continued to develop. It has expanded its research fields from dental engineering to biomaterials and bioengineering, and has been making great contributions to academic fields as well as to the medical and dental industries through commercialization of several products. One of the unique features of our institute is its integration and cooperation among medicine, dentistry, and engineering. Research and education at IBB, TMDU have been carried out based on this framework to foster young researchers in the interdisciplinary crossroads of medical, dental, and engineering sciences.

Director of the Institute of Biomaterials and Bioengineering,

Japan is facing big challenges in the fields of energy and environment, and medicine. Through research and education, our institute will strive to overcome current problems, and to contribute to creating a healthy and secure aged society. We ask for your continuous support and encouragement in the years to come.



As an international research center in advanced medical and dental technology, the Institute of Biomaterials and Bioengineering (IBB) brings together established basic theory and frontier materials generation. At the same time, the IBB seeks a comprehensive approach to progress in pioneering applied research in the field, from drug discovery to biomedical devices.



## **Research Projects**

Every year at the IBB, we are vigorously promoting numerous research projects, joint research, and education programs. By conducting fundamental and developmental research in our

state-of-the-art research groups, we are providing practical training and education to develop human resources.

MEXT Funds for Function Reinforcement of the Education and Research
Research Center for Biomedical Engineering

Interdisciplinary and international project for development of advanced life-innovative materials and human resources

Cooperative project among medicine, dentistry, and engineering for medical innovation

- ~ Construction of creative scientific research of the viable material via integration of biology and engineering ~
- AMED Platform Project for Supporting Drug Discovery and Life Science Research Promotion of drug discovery and life science researches through advancement of synthetic technologies for expeditious development of molecular probes from screening hit compounds
- AMED Acceleration Transformative Research for Medical Innovation (ACT-M) Development of next-generation artificial pancreas for innovative therapy of diabetes
- Impulsing Paradigm Change through Disruptive Technologies Program Ultra high-speed multiplexed sensing system beyond evolution for detection of extremely small amount of substances
- AMED Development of Medical Devices and Systems for Advanced Medical Services Development of diagnosis-assistance devices and systems for intraoperative assessment and decision
- AMED Strategic Promotion of Innovative Research and Development (S-Innovation) Biofunctionalization of metallic biomaterials – A vital point of supporting long healthy life in musculoskeletal medicine –

In addition, with the Grants-in-aid for Scientific Research provided by the Ministry of Education, Culture, Sports, Science and Technology (MEXT) and the Ministry of Health, Labor and Welfare, and overseas research exchanges, we have undertaken various research projects.

## **Research Center of Biomedical Engineering (RCBE)**

The Research Center of Biomedical Engineering (RCBE) was established in April 2016 with the support of the Ministry of Education, Culture, Sports, Science and Technology (MEXT). It was established in collaboration with the IBB at TMDU, and three other research institutes: the Laboratory for Future Interdisciplinary Research of Science and Technology at Tokyo Institute of Technology, the Research Institute for Nanodevice and Biosystems at Hiroshima University, and the Research Institute of Electronics at Shizuoka University. The purpose of the RCBE is to promote interaction and collaboration among engineers and medical researchers to develop inno-

vative technologies that can revolutionize future medicine and healthcare. The four research institutes have core competencies in different areas of science and technology, and we aim to integrate and fuse them in the RCBE in order to strengthen and enhance them. We also seek to foster young researchers in the interdisciplinary field between medicine and engineering through collaboration with advanced research institutes around the world.

In the course of collaborative research in the RCBE, we discuss innovative technologies in areas such as minimally invasive treatment, prognosis and early diagnosis,

point-of-care testing, regenerative medicine, and personalized medicine, in order to realize a healthy aging society. The major areas of activity solicited and expected in the RCBE include, but are not limited to: biomaterials, biosensors, medical treatments, diagnostic devices, drug delivery systems, functional molecules, bioMEMS, robotics, biomedical instrumentation and systems, simulation and characterization, biomarkers, and nano/micro devices.



RCBE collaboration map

#### **Division of Biomedical Materials**

# **Department of Metallic Biomaterials**

Assistant Professor Peng Chen Yusuke Tsutsumi

Associate Professor

Assistant Professor Akira Umise

Technical Staff Shukan Okano Michiko Nakaishi

Assistant Professor

Hisashi Doi

#### Intermediary between medicine and engineering: metals

- 1. Development of Zr-based alloys for minimizing MRI artifacts
- 2. Bio-functionalization of metals with electrochemical surface modification
- 3. Development of titanium alloys by severe working
- 4. Establishment of nano/micro-topography that controls differentiation of stem cells
- 5. Effort to minimize metal allergy

1. Ishimoto T. Yamada K. Takahashi H. Takahata M. Ito M. Hanawa T. Nakano T: Trabecular health of vertebrae based on anisotropy in trabecular architecture and collagen/apatite micro-arrangement after implantation of intervertebral fusion cages in the sheep spine, Bone 108, 25-33, 2018.

Professor Takao Hanawa

Assistant Professor

Maki Ashida

Technical Staff

- 2. Takada R, Jinno T, Tsutsumi Y, Doi H, Hanawa T, Okawa A: Inhibitory effect of zirconium coating to bone bonding of titanium implants in rat femur, Mater Trans 58, 113-117, 2017.
- 3. Chen P, Aso T, Sasaki R, Tsutsumi Y, Ashida M, Doi H, Hanawa T: Micron/submicron hybrid topography of titanium surfaces influences adhesion and differentiation behaviors of the mesenchymal stem cells, J Biomed Nanotechnol 13, 324-336, 2017.
- 4. Sato M, Chen P, Tsutsumi Y, Hanawa T, Kasugai S: Effect of strontium ions on calcification of preosteoblasts cultured on porous calcium- and phosphate-containing titanium oxide layers formed by micro-arc oxidation, Dent Mater J 35, 627-634, 2016.
- 5. Tsutsumi Y, Niinomi M, Nakai M, Shimabukuro M, Ashida M, Chen P, Doi H, Hanawa T: Electrochemical surface treatment of a  $\beta$ -titanium alloy to realize an antibacterial property and bioactivity, Metals 6, 76, 2016.

To improve the performance of metals that occupy 70% of implant devices, we are striving to develop new alloy designs and manufacturing processes and to create new surface treatments and modification techniques. We base our work on the accumulated knowledge and the techniques of research and evaluation in materials science and engineering. Furthermore, we pursue a variety of collaborative research projects to commercialize the results.

Cells

#### **Development of MRI-compatible zirconium alloys**

To decrease MRI artifacts caused by the magnetization of metallic implants, zirconium alloys with low magnetic susceptibility are being developed: Large-scale melting, forging, swaging and heattreatment processes are being investigated based on an evaluation of crystal structure, mechanical properties, corrosion mechanisms, cytocompatibility, and etc.

#### Strengthening of titanium alloys for narrow dental implants

Narrow dental implants are applied in situations with limited horizontal space, and they require thin diameters and high strength. We have succeeded in strengthening titanium alloys through grain refinement while retaining almost the same elongation, by applying high-pressure torsion or high-pressure sliding.



#### based on electrochemical techniques are being developed. In addition to hard-tissue compatibility, antibacterial properties are successfully obtained through micro-arc oxidation with small amounts of antibacterial agents (Ag, Cu, Zn, etc.) on Ti.

**Development of multi-biofunctional implant surfaces** 

To achieve multiple biofunctional surfaces, surface treatments



A highly orientated and extended cellular morphology was achieved on the hierarchical topography, which also modulated the multi-lineage differentiation, such as osteogenic and chondrogenic differentiation.





#### **Division of Biomedical Materials**

# **Department of Inorganic Biomaterials**

#### Professor Kimihiro Yamashita



Miho Nakamura Assistant Professor Naohiro Horiuchi

Associate Professo

#### Advanced bioceramics for biomanipulation

- 1. Development of implantable devices through ceramic technology
- 2. Development of bioceramic electret
- 3. Manipulation of biological responses with bioceramics
- 4. Local control of bio-interfaces on bioceramics
- 5. Improvement of bioceramics on the basis of biomineralization
- Horiuchi N, Madokoro K, Nozaki K, Nakamura M, Katayama K, Nagai A, Yamashita K: Electrical conductivity of polycrystalline hydroxyapatite and its application to electret formation, Solid State Ionics 315, 19-25, 2018.
- Nakamura M, Hori N, Ando H, Namba S, Toyama T, Nishimiya N, Yamashita K: Surface free energy predominates in cell adhesion to hydroxyapatite through wettability, Mater Sci Eng C 62, 283-292, 2016.
- Horiuchi N, Wada N, Nozaki K, Nakamura M, Nagai A, Yamashita K: Dielectric relaxation in monoclinic hydroxyapatite: Observation of hydroxide ion dipoles, J Appl Phys 119 (8), 084903, 2016.
- Nagai A, Hattori T, Hirose M, Ogura A, Nozaki K, Aizawa M, Yamashita K: Mouse embryonic stem cells cultured under serum- and feeder-free conditions maintain their self-renewal capacity on hydroxyapatite, Mater Sci Eng C 34, 214-220, 2014.
- Wada N, Horiuch N, Nakamura M, Hiyama T, Nagai A, Okura T, Yamashita K: Effect of polyacrylic acid and polarization on the controlled crystallization of calcium carbonate on single-phase calcite substrates, Cryst Growth & Des 13 (7), 2928-2937, 2013.

Yamashita Laboratory evaluates electric field intensity and electric field distribution in polarized bioceramics from the viewpoint of materials, and electrochemical and crystal chemistry. Based on this, it is pursuing elucidation of the mechanism by which polarization is generated, and the establishment of local polarization control technology. We conduct fundamental research on protein adsorption, bacterial adsorption, cultured cell growth, adhesion, differentiation and bone tissue repair by locally controlling the electrostatic energy of the surfaces of bioceramics, and at the same time, we are developing clinical devices by collaborating with experts in clinical fields.

#### Development of bioceramic electrets

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Some ceramics, such as a hydroxyapatite, can be ionically polarized by thermoelectrical treatments. The polarized ceramics have large and time-durable induced electrostatic charges on their surfaces. The effects of the induced charges profoundly dominate the proximate regions up to a few millimeters. We have named these effects, "Electrovector Effects" and developed Electrovector ceramics, defined as ceramics that emit Electrovector Effects.





#### Application of bioceramic electrets to biomineralization

We have attempted to produce novel biomaterials by using a biomimetic approach. Biomaterials are formed through the cooperative interaction of inorganic materials with organic macromolecules having reactive functional groups. Hence, an understanding of the cooperation of electric fields due to the electrets and soluble organic additives during crystallization is important to developing strategies for controlled synthesis with biomimetics.



#### distances Acceleration of cell behaviors Electret 0 2. Migration. 3.Differer 1. Adhe Acceleration effects on various tissues Blood vessel Skin Nerve Bone h leration of n of (3-fold si regeneration ed HA > HA ed HA > HA ANHA A, et al. Life Sci

Polarization effects on various tissues over long

#### Development of hydroxyapatite nanoparticles with higher therapeutic potential

The surface and electric properties of hydroxyapatite are favorable for use in biomedical devices. However, these properties depend on the anisotropic nature of the crystals. Therefore, specific oriented structures are required to optimize performance. We focused on development of new synthesis methods to produce nano-sized particles with higher therapeutic potential, obtained by the anisotropic shape.



#### **Division of Biomedical Materials**

# **Department of Organic Biomaterials**

#### yui.org@tmd.ac.jp

## Emerging design of supramolecular biomaterials

- 1. Regulation of cell functions by dynamic surfaces
- 2. Therapeutic applications of biocleavable polyrotaxanes for metabolic diseases
- 3. Nanomedicine applications of biomolecules by complexation with polyrotaxanes
- 4. Design of smart dental materials based on biocleavable polyrotaxanes
- 1. Oova T. Equchi M. Yui N: Supramolecular design for multivalent interaction; high mobility of maltose groups in polyrotaxanes enhanced binding with concanavalin A, J Am Chem Soc 125 (43), 13016 -13017, 2003

Professor Nobuhiko Yui

Assistant Professo

Yoshinori Arisaka

Associate Professor

Atsushi Tamura

- 2. Ooya T, Choi H S, Yamashita A, Yui N, Sugaya Y, Kano A, Maruyama A, Akita H, Kogure K, Harashima H: Biocleavable polyrotaxane-plasmid DNA polyplex for enhanced gene delivery, J Am Chem Soc 128 (12), 3852 -3853, 2006.
- 3. Seo J-H, Kakinoki S, Inoue Y, Yamaoka T, Ishihara K, Yui N: Inducing rapid cellular response on RGD-binding threaded macromolecular surfaces, J Am Chem Soc 135 (15), 5513-5516, 2013. 4. Seo J-H, Kakinoki S, Yamaoka T, Yui N: Directing stem cell differentiation by changing the molecular mobility of supramolecular surfaces, Adv Healthcare Mater 4 (2), 215-222, 2015.
- 5. Tamura A, Yui N: Polyrotaxane-based systemic delivery of  $\beta$ -cyclodextrins for potentiating therapeutic efficacy in a mouse model of Niemann-Pick type C disease, J Control Release 269 148-158 2018

We are developing biomedical applications using supramolecular polyrotaxanes, in which many cyclic molecules (cyclodextrins) are threaded onto a linear polymer that is capped at both terminals with bulky end-groups, as biomaterials. We are aiming to create biomaterials that can demonstrate unprecedented functions by utilizing various characteristics derived from the structure of polyrotaxanes, such as the mobility of cyclic molecules, the rigidity of the frameworks, responsive degradability and others.

#### Regulation of cell functions by dynamic surfaces

Cyclic molecules threaded in polyrotaxanes are expected to move and rotate along a polymer axle. Focusing on the mobility of the cyclic molecules in polyrotaxanes, our group has designed biomaterials surfaces with dynamic properties by utilizing the movable architecture on the molecular level of polyrotaxanes. We have examined their effects on a variety of interactions with biological systems, such as proteins and cells. Interestingly, we have clarified that the molecular mobility on these surfaces is critical to directing the differentiation of stem cells.



#### Nanomedicine applications of biomolecules by complexation with polyrotaxanes

Biopharmaceutical agents, such as nucleic acids and proteins, have recently attracted much attention as a new class of drug. To enhance the stability and biological activities of such biopharmaceutical agents, supramolecular polyelectrolyte complexes with polyrotaxanes have been designed, and their therapeutic efficacy has been evaluated in vitro and in vivo.



#### Therapeutic applications of biocleavable polyrotaxanes for metabolic diseases

Biocleavable polyrotaxanes that can release threaded  $\beta$ -cyclodextrins ( $\beta$ -CDs) in cellular environments have been developed as a therapeutic agent for various intractable diseases. The intracellular release of  $\beta$ -CDs from the polyrotaxanes leads the interaction with the intracellular lipids and cholesterol to modulate the cellular metabolic functions. Our group has found that the polyrotaxanes showed significant therapeutic effects in model mice of Niemann-Pick disease type C, which is a rare metabolic disorder in which cholesterols accumulate in lysosomes.



#### Design of smart dental materials based on biocleavable polyrotaxanes

In current dental treatment, a variety of photocurable resins are used such as in composite resins and dental adhesives. However, these conventional resins and adhesives are difficult to remove after polymerization. Our group has developed photo-labile polyrotaxanes that can dissociate under UV-light irradiation and we have investigated their application as a component of dental adhesives for orthodontics. For instance, by using polyrotaxanes, it will become possible to remove orthodontic brackets by simple light irradiation.



#### **Division of Biofunctional Restoration**

# **Department of Biofunction Research**

Professor Keiji Itaka Assistant Professor Kosuke Nozaki



#### **Recovering and reconstructing sensorimotor functions**

- 1. mRNA-based therapeutics as a new paradigm for gene therapy
- 2. Regenerative medicine using gene and oligonucleotide therapeutics
- 3. Cell therapy using genetically modified spheroid transplantation
- 4. Creating osseointegrated dental implants by regulating micro/nano structure
- Uchida S, Yoshinaga N, Yanagihara K, Yuba E, Kataoka K, Itaka K: Designing immunostimulatory double stranded messenger RNA with maintained translational activity through hybridization with poly A sequences for effective vaccination, Biomaterials 150, 162-170, 2018.
- Anraku Y, Kuwahara H, Fukusato Y, Mizoguchi A, Ishii T, Nitta K, Matsumoto Y, Toh K, Miyata K, Uchida S, Nishina K, Osada K, Itaka K, Nishiyama N, Mizusawa H, Yamasoba T, Yokota T, Kataoka K: Glycaemic control boosts glucosylated nanocarrier crossing the BBB into the brain, Nature Communications 8, 1001, 2017.
- Lin CY, Perche F, Ikegami M, Uchida S, Kataoka K, Itaka K: Messenger RNA-based therapeutics for brain diseases: An animal study for augmenting clearance of beta-amyloid by intracerebral administration of neprilysin mRNA loaded in polyplex nanomicelles, J Control Release 235, 268-275, 2016.
- 4. Aini H, Itaka K, Fujisawa A, Uchida H, Uchida S, Fukushima S, Kataoka K, Saito T, Chung U, Ohba S: Messenger RNA delivery of a cartilage-anabolic transcription factor as a diseasemodifying strategy for osteoarthritis treatment, Sci Rep 6, 18743, 2016.
- Itaka K, Uchida S, Matsui A, Yanagihara K, Ikegami M, Endo T, Ishii T, Kataoka K: Gene transfection toward spheroid cells on micropatterned culture plates for genetically-modified cell transplantation, J Vis Exp 10, e52384, 2015.

Itaka Laboratory focuses on the development of innovative medical technologies based on the science of biomaterials, drug delivery systems (DDS), and molecular biology. We aim at regulating the biofunctions of host cells and biomaterials, obtaining proof-of-concept of therapeutic strategies through animal studies, and pursuing their clinical applications in collaboration with hospitals and companies.

# mRNA-based therapeutics:

#### a new paradigm of gene therapy

Gene therapy is defined as introducing genetic information for therapeutic purposes. Gene therapy may have wide application, including: vaccination against cancer and infectious diseases; regenerative medicine through in situ cell regulation by introducing "therapeutic" gene(s); and, the ultimate goal of "gene" therapy, through the technology of gene editing. Messenger RNA (mRNA) is a new tool for introducing genetic information. Direct delivery of mRNA into cells is highlighted as a safe and effective method that avoids the risk of random integration into the genome. Despite the fact that mRNA delivered in the body would be susceptible to highly active RNases that are ubiquitous in extracellular space, we have established a drug delivery system (DDS) based on synthesized polymers -- polyplex nanomicelles -- to transport mRNA into target cells while preventing its degradation. We achieved in vivo mRNA administration for therapeutic purposes to various organs and tissues, including brain, spinal cord, bone, articular cartilage, skeletal muscle, and liver. This mRNA-based therapy is indicated for the treatment of various diseases within the fields of gene therapy, cell therapy, and regenerative medicine.



Treatment of osteoarthritis by intra-articular injection of mRNA

# Genetically-modified spheroid cell culture system for cell transplantation

Cell transplantation therapy is an attractive strategy for various medical fields. We are developing an injectable spheroid system for cell transplantation therapy that preserves cell-to-cell interaction. It is based on a 3D spheroid cell culture system using micropatterned plates coated with a thermosensitive polymer. In addition, we have augmented the therapeutic effects of cell transplantation by integrating the genetic modification of the cells using a biocompatible non-viral gene carrier.



Micropatterned substrate for spheroid culture

# Osseointegrated dental implants created by regulating micro/nano structure

Although dental implant treatment has already been clinically applied and excellent clinical progress has been reported, some cases demonstrate unexpected disorders. Because natural teeth integrate with bone via periodontal ligaments to perform their functions, the osseointegration, which occurs during healing in current

dental implants, is thought to be one of the causes of disorders. In this department, we are working on the development of periodontal ligament-bonded dental implant materials, and we are trying to elucidate the mechanism of periodontal tissue homeostasis.



Micro/nano structure for controlling cell cycle of osteoblasts

# int of Material-based Medical Engineering

Associate Professor Tsuyoshi Kimura

At the forefront of biomaterials

- 1. Novel biological tissues for regenerative medicine (Bioscaffold)
- 2. Cell-specific capture and release technology for immunological regulation
- 3. Regulation of stem cells by controlling cellular microenvironments
- 4. Elucidation of the physiological effects of basement membrane structures and applications to tissue restructuring
- Nakamura N, Kimura T, Kishida A: Overview of the development, applications, and future perspectives of decellularized tissues and organs, ACS Biomater Sci Eng 3(7), 1236–1244, 2017.
  Kimura T, Nakamura N, Sasaki N, Hashimoto Y, Sakaguchi S, Kimura S, Kishida A: Capture and release of target cells using a surface that immobilizes an antibody via desthiobiotinavidin interaction, Sensor and Materials 28, 1255-1263, 2016.

Professor Akio Kishida

Research Scientist

Zhang Yongei

Assistant Professor

Yoshihide Hashimoto

- Hashimoto Y, Hattori S, Sasaki S, Honda T, Kimura T, Funamoto S, Kobayashi H, Kishida A: Ultrastructural analysis of the decellularized cornea after interlamellar keratoplasty and microkeratome-assisted anterior lamellar keratoplasty in a rabbit model, Sci Rep 6, 27734, 2016.
  Akazawa K, Iwasaki K, Nagata M, Yokoyama N, Ayame H, Yamaki K, Tanaka Y, Honda I, Morioka C, Kimura T, Komaki M, Kishida A, Izumi Y, Morita I: Double-layered cell transfer technology for bone regeneration, Sci Rep 6, 33286, 2016.
- Suwa Y, Nam K, Ozeki K, Kimura T, Kishida A, Masuzawa T: Thermal denaturation behavior of collagen fibrils in wet and dry environment, J Biomed Mater Res B Appl Biomater 104(3), 538-545, 2016.

The policies of our department are "Contribution to medical care" and "Exploration of basic science". Based on the policies, our research field extends from basic research of biomaterials as raw material, to the research and development of therapeutic equipment, leading to creating useful medical devices. We observe biological reactions to biomaterials and explore the mechanisms that control those reactions, and based on our findings, we are aiming to create new biomaterials. We are conducting research on developing decellularized tissues and organs with high biocompatibility, methodologies to achieve immune response regulation through surface modification techniques, stem cell control, and control of the process of tissue reconstruction. We believe our work can bear fruit in the form of new therapeutic biomaterials.

# Novel biological tissues for regenerative medicine (Bioscaffold)

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Decellularized tissue can be made from various tissues and organs from humans and animals by removing cells. Such tissue has at-

tracted attention for various purposes: as a material that can substitute for natural tissue, as a scaffold material for regenerative medicine, and as a material to promote tissue repair. We undertake analysis of the fundamental physical properties of decellularized tissue, *in vivo* analysis of function, and the creation of composites with dissimilar materials, and apply the results to creating new biomaterials for medical implants.



Top left: Application of decellularized bone to dental prosthetic material Top right: Percutaneous device made from decellularized skin Bottom: Fiber-composite smalldiameter decellularized blood vessel

# Regulation of stem cells by controlling cellular microenvironments

When decellularized tissue is transplanted into a living body, a phenomenon occurs called "cell homing", in which the cells originally present in the tissue invade and return to their original form. When decellularized bone marrow cells are implanted subcutaneously, they form bone marrow-like tissue ectopically. We are investigating such phenomena to clarify the cause of cell recruitment and "homing" *in* 

vivo, which will contribute not only to regenerative medicine, but also to wound healing and the embryology of organs and tissues.



# Cell-specific capture and release technology for immunological regulation

Regulatory T cells (Tregs) are known to be a controlling factor in inhibiting cancer immunotherapy. When Tregs are removed from tumor-bearing organisms, anti-tumor immune responses are enhanced and cancer can be rejected. Tregs also play an important role in transplantation immunity and autoimmune diseases. Techniques for induction and collection of Tregs are attracting attention for applications of Tregs. We are developing technology to capture and recover intact Tregs in a specific and highly efficient manner.



Selective cell capture and release system through extracorporeal circulation

# Elucidation of the physiological effects of basement membrane structures and applications to tissue restructuring

Epithelial and endothelial cells are present in tissue such as blood vessels, skin, cornea, etc. They are located at the boundaries with the outer environment and with other tissues, and they perform functions such as antithrombogenicity and moisture management. These epithelial cells exist on a special extracellular matrix called the basement membrane. We study the function of the basement membrane, which is an important factor in tissue

remodeling. We also conduct basic research in order to establish the basement membrane function on biomaterial surfaces, and enable the creation of new biomaterials.



# Department of Biomechanics

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Assistant Professor Tetsuro Miyazaki



Assistant Professor Takahiro Kanno

Development of medical devices based on mechanical control

- 1. Forceps manipulator for minimally invasive surgery
- 2. Power-assist device using pneumatic artificial rubber muscle
- 3. Development of soft actuators and their application to medical devices
- 4. Evaluation of surgical robot system
- 5. Teleoperation of robots using biological information
- 1. Watanabe K. Kanno T. Ito K. Kawashima K: Single-master dual-slave surgical robot with automated relay of suture needle, IEEE Trans. on Industrial Electronics 65(8), 6343-6351, 2018.
- 2. Takizawa T, Kanno T, Miyazaki R, Tadano K, Kawashima K: Grasping force estimation in robotic forceps using a soft pneumatic actuator with a built-in sensor, Sensors & Actuators: A. Physical 271, 124-130, 2018.
- 3. Li H, Kawashima K: Bilateral teleoperation with delayed force feedback using time domain passivity controller, Robotics and Computer-Integrated Manufacturing 37, 188-196, 2016.
- 4. Kanno T, Haraguchi D, Yamamoto M, Tadano K, Kawashima K: A forceps manipulator with flexible 4-DOF mechanism for laparoscopic surgery, IEEE/ASME Trans. on Mechatronics 20(3), 1170-1178, 2015.
- 5. Tadano K, Kawashima K: A pneumatic laparoscope holder controlled by head movement, The International Journal of Medical Robotics and Computer Assisted Surgery 11(3), 331-340, 2015.

Kawashima Laboratory focuses on the development of medical devices and systems based on control engineering, robotics and fluid dynamics. Our keywords are integration of hardware and software, electrical and pneumatic actuation, human and machine.

Forceps manipulator for surgical robot

We are developing forceps manipulators that are driven by pneumatic actuators. The forceps manipulator has a highly simplified flexible distal joint, which is actuated by push-pull motions of superelastic wires. The pneumatic system is backdrivable and suitable for applications that need force control. Furthermore, force can be measured using pressure sensors at the cylinder, without mounting a force sensor on the tip of the forceps.



Surgical robot system

We are developing a pneumatically driven surgical robot system. We are evaluating its performance with in vitro and in vivo experiments.



#### Assist device using pneumatic artificial rubber muscle

We are developing a soft, wearable gait-assistive suit. The gait-assistive suit is driven by pneumatic artificial rubber muscles (PARMs). The walking phase is detected from the pressure derivative in the PARMs, and the suit assists walking when the legs are swinging. Since the suit has no sensors on its attachment parts, users can easily wear, use, and remove the suit. In addition, the suit is available for underwater training with a weight-bearing effect, which is popular with elderly people and those undergoing rehabilitation.



#### Soft actuator made of silicone

We are developing a soft actuator made of silicone. The actuator consists of a soft silicone rubber tube covered with a metal spring. The spring acts to restrain expansion of the actuator in the radial direction during pressurization, and to generate pulling force during depressurization. Furthermore, the use of the spring facilitates the manufacture of the actuator. We are applying the actuator to drive robotic hands and forceps.



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# **Department of Bioelectronics**

Associate Professor Assistant Professor Akira Matsumoto Tatsuro Goda

o Tatsuro Goda Project Assistant Professor

Project Assistant Professor Yukichi Horiguchi



#### Nanobio engineering for medicine of the future

- **1. Bioelectronics for next-generation DNA sequencing**
- 2. Devices for early cancer diagnosis
- 3. Organic bioelectronics for point-of-care testing
- 4. Smart gel-based "Artificial Pancreas" to treat diabetes
- 5. Quantitative dental caries diagnosis by micro pH sensor
- 6. Detection of extracellular nano-particles for liquid biopsy
- 7. FET-based gas sensors for VOCs for healthcare
- 8. Design and synthesis of functional molecules

 Sakata T, Miyahara Y: DNA sequencing based on intrinsic molecular charges, Angew Chem Int Ed 45(14), 2225, 2006.

Professor Yuji Miyahara Tenure-track Assistant Professor

Specially Appointed Assistant Professor

Miyuki Tabata

Toshihiro Yoshizumi

- Matsumoto A, Sato N, Sakata T, Yoshida R, Kataoka K, Miyahara Y: Chemical-to-electricalsignal transduction synchronized with Smart Gel volume phase transition<sup>\*</sup>, Adv Mater 21(43), 4372, 2009.
- Goda T, Toya M, Matsumoto A, Miyahara Y: Poly(3,4-ethylenedioxythiophene) bearing phosphorylcholine groups for metal-free, antibody-free, and low-impedance biosensors specific for C-reactive protein, ACS Appl Mater Interfaces 7(49), 27440, 2015.
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By studying the interaction between biomolecules such as DNA, proteins and cells, and semiconductor materials and devices, our research focuses on detection of biomolecules and their functions. Our interdisciplinary research involves materials science, chemistry, device technology and medicine, and its output centers on the development of highly-sensitive biosensors while also providing bases for exploring the imminent future of medicine, including homecare and telemedicine.

#### Next-generation DNA-sequencing technologies

Changes in the charge density on a solid surface as a result of DNA-DNA hybridization is transduced into the potentiometric signal of a field-effect transistor (FET) device. A single-base change was detectable by coupling with primer extension reactions on the gate. This approach allowed for detection of single nucleotide polymorphism (SNP) and even DNA sequencing.

Reference electrode

Semiconductor-based DNA sequencing

# Conducting polymer-based biosensing and bioelectronics for ubiquitous testing

Conductive polymers possess electronic and ionic conductivities in biological environments. They are attractive materials for pointof-care applications because of their processability and mass productivity. By attaching bioreceptors to the polymers, they can be used for specific biosensing.



Functionalization of conducting polymers for biosensing

#### **Devices for early cancer diagnosis**

A gold electrode surface serving as an extended gate was chemically modified with self-assembled monolayers (SAM) of alkanethiol with different termini. Potentiometric signals for adsorption of proteins on the SAM layer can be detected and investigated quantitatively. Specific recognition of proteins is also possible using antibodies and other capturing molecules.

# Smart gel-based "artificial pancreas" for the treatment of diabetes

A new paradigm for developing an inexpensive and easy-to-access type of artificial pancreas can better address the well-recognized unmet medical needs in diabetes. These needs include long-term glycemic management, avoidance of hypoglycemia and improvement of patients' quality of life.



Schematics of smart gel-based "artificial pancreas"



#### **Division of Medical Devices**

# **Department of Biomedical Information**

#### Professor Yoshikazu Nakajima

#### Artificial intelligence and numerical computation for medicine

- 1. High-dimensional and multidisciplinary medical imaging
- 2. Artificial intelligence (AI) and brain-machine interface (BMI)
- 3. Intuitive surgical navigation with augmented reality
- 4. Surgical assistant devices using stiffness-tunable mechanism
- 5. Autonomously networking computer agents for medical applications
- 1. Nakajima Y. Tashiro T. Sugano N. Yonenobu K. Kovama T. Maeda Y. Tamura Y. Saito M. Tamura S. Mitsuishi M, Sugita N, Sakuma I, Ochi T, Matsumoto Y: Fluoroscopic bone fragment tracking for surgical navigations on femur fracture reduction by incorporating optical tracking of hip joint rotation center," IEEE Trans. on Biomedical Engineering 54(9), 1703-1706, 2007.
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The mission of Nakajima Laboratory is to bring the power of medical computation servers and surgical assistance systems into clinical settings. The methods developed by our group can provide artificial-intelligence (AI)-based integration of multi-modal medical data. These technologies provide intelligence that is useful to analyze, simulate, plan and assist surgeries. In addition, we have developed an internet-of-things (IoT) platform that can integrate such AI computers with sensors and surgical robots. These developments can truly lead the computerization of medicine. Our systems have been introduced into practical surgery routines in several hospitals. They have reported using our systems in more than 200 successful clinical cases.

#### High-dimensional and multidisciplinary integration of medical data

The combination of feature extraction and correspondence was applied to different medical modalities to provide high-dimensional and multidisciplinary data. We were able to integrate volumes of

data from CT, MR and PET images, pre- and intra-operative measurements, the patient's measurements and general numerical knowledge of the human body. These data were summarized to create a human body model that was statistically average in shape and variations, and that also could be reshaped. The human body model was analyzed by an AI computer and each part of it was labeled to link to numerous quantitative data and knowledge databases.





#### Autonomously organizing computer agents and an internet-of-things (IoT) platform for medical systems

Agents of various data and processors were unmewed on the network. The agents asked questions of one another, checked connection possibilities, introduced themselves to one another, and then sent data to one another. Each agent was embedded into a sensor, a database interface, or a search engine of the internet. When these agents connected autonomously, the networks per-

formed powerfully on data processing and analyzing compared with connection-fixed neural networks.



#### Artificial-intelligence (AI)-based medical data analysis and brain-machine interface (BMI)

Artificial intelligence (AI) was applied to process medical tasks. A deep-learning neural network labeled anatomical parts of organs on a patient's images and segmented them to each

organ to analyze quantitatively. As another approach to brain science, brain signal patterns were measured and analyzed with respect to external stimulation of vision and thoughts. These studies gave some hints for the design of AI algorithms. They were also applied to designing the interfaces connecting the brain and computers.



#### Surgical-assistance navigators and robots

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Augmented reality and laser projection mapping were applied to vis-

ualize quantitative surgical data intuitively. To achieve high accuracy, our device captured the organ's shape and tracked its deformation. After compensating for the deformation in data space, surgical plans were projected onto the organ surface directly with a laser projector. In addition, some compact surgical robots were developed and tested to achieve more accurate surgeries. The deformation tracking also worked for navigating these robots.







#### **Division of Medical Devices**

# **Department of Biomedical Devices and Instrumentation**

# Professor Kohji Mitsubayashi

Junior Associate Professor Assistant Professor Takahiro Arakawa Koji Toma

#### Advanced sensor technologies for biomedical and health sciences

- 1. Cavitas sensors: Detachable bioinformation monitoring systems for body cavities
- 2. Bio-sniffers & Sniff-cams: Biochemical "odor" sensors and imaging systems
- 3. Regeneratable immunosensors for medical treatment and environmental medicine
- 4. Organic Engine: A chemo-mechanical energy conversion system for artificial pancreas
- 1. litani K. Sato T. Naisierding M. Havakawa Y. Toma K. Arakawa T. Mitsubavashi K: Fluorometric sniff-cam (gas-imaging system) utilizing alcohol dehydrogenase for imaging concentration distribution of acetaldehyde in breath and transdermal vapor after drinking, Anal Chem 90, 2678-2685, 2018.
- 2. Chien PJ, Suzuki T, Tsujii M, Ming Y, Minami I, Toda K, Otsuka H, Toma K: Biochemical gas sensors (biosniffers) using forward and reverse reactions of secondary alcohol dehydrogenase for breath isopropanol and acetone as potential volatile biomarkers of diabetes mellitus, Anal Chem 89, 12261-12268, 2017.
- 3. Toma K, Miki D, Yoshimura N, Arakawa T, Yatsuda H, Mitsubayashi K: A gold nanoparticleassisted sensitive SAW (surface acoustic wave) immunosensor with a regeneratable surface for monitoring of dust mite allergens, Sensors Actuators B Chem 249, 685-690, 2017.

Our group pursues interdisciplinary research on biosensors and bio-Micro Electro Mechanical Systems (MEMS) by combining knowledge from a broad range of fields, such as electrochemistry, mechanical and electrical engineering, material science and information technology, to develop new and advanced medical and healthcare sensing devices.

#### Cavitas sensors for bioinformation monitoring

Cavitas sensors such as contact-lenses and mouthguard biosensors for biomonitoring are being developed using advanced polymer MEMS techniques.



Contact lens-type biosensor Mouthguard-type biosensor

#### **Biochemical sensors and imaging systems** for non-invasive health evaluation

A sensitive and selective "Bio-sniffer" and "Sniff-cam" are being developed utilizing drug-metabolizing enzymes from liver for noninvasive and simple medical screening and healthcare sciences.



#### Immunosensors for medical treatment and environmental medicine

Immunosensors relying on light or surface acoustic waves are being developed for rapid and repeated - semi-continuous measurement of antigens, such as mite allergens.





An Organic Engine that directly converts the chemical energy of biological components into mechanical energy is being developed for the artificial pancreas, resulting in an autonomous drug-release system





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# **Department of Medicinal Chemistry**

# Chemical biology aimed at drug discovery

- 1. Development of peptidomimetics and drug discovery templates
- 2. Development of bioprobes and chemical biology
- 3. Analysis of the interactions between receptors or enzymes and their ligands
- 4. Development of HIV inhibitors and AIDS vaccines
- 5. Development of genome and epigenome editing platforms for gene therapy
- Kobayakawa T, Matsuzaki Y, Hozumi K, Nomura W, Nomizu M, Tamamura H: Synthesis of a chloroalkene dipeptide isostere-containing peptidomimetic and its biological application, ACS Med Chem Lett 9(1), 6-10, 2018.

Assistant Professo

Takuya Kobayakawa

Professor Hirokazu Tamamura

Associate Professor

Wataru Nomura

- Ohashi N, Kobayashi R, Nomura W, Kobayakawa T, Czikora A, Herold BK, Lewin NE, Blumberg PM, Tamamura H: Synthesis and evaluation of dimeric derivatives of diacylglycerollactones as protein kinase C ligands, Bioconjugate Chem, 28(8), 2135-2144, 2017.
- Takano H, Narumi T, Nomura W, Tamamura H: Microwave-assisted synthesis of azacoumarin fluorophores and the fluorescence characterization, J Org Chem 82(5), 2739-2744, 2017.
  Nomura W, Aikawa H, Obsehi N, Urano E, Motifiet M, Evilipo M, Modeli K, Ospiki T, Narus A.
- 4. Nomura W, Aikawa H, Ohashi N, Urano E, Metifiot M, Fujino M, Maddali K, Ozaki T, Nozue A, Narumi T,Hashimoto C, Tanaka T, Pommier Y, Yamamoto N, Komano J, Murakami T, Tamamura H: Cell-permeable stapled peptides based on HIV-1 integrase inhibitors derived from HIV-1 gene product, ACS Chem Biol 8(10), 2235–2244, 2013.
- Tanaka T, Nomura W, Narumi T, Masuda A, Tamamura H: Bivalent ligands of CXCR4 with rigid linkers for elucidation of dimerization state in cells, J Am Chem Soc (Commun) 132(45), 15899–15901, 2010.

We are conducting research using chemical biology techniques. By targeting chemokine receptor CXCR, protein kinase C, secretase and the like, we are pursuing drug discovery research aimed at creating therapeutic drugs and gene therapy methods to treat cancer, Alzheimer-type dementia, rheumatoid arthritis and AIDS.





#### **Division of Biomolecular Chemistry**

# **Department of Chemical Bioscience**

#### Professor Takamitsu Hosoya

Associate Professor Suguru Yoshida Yo



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#### New chemistry for life sciences

- 1. Development of novel generation methods for benzyne species and their synthetic applications
- 2. Development of new methods for chemical modification of biomolecules by strained alkynes
- 3. Development of new methods for target identification of bioactive compounds by photoaffinity labeling based on azide chemistry
- 4. Development of efficient methods for connecting multiple molecules based on the characteristic features of azido groups
- 5. Design and synthesis of efficient substrates for bioluminescence reactions, and fluorescent probes for bioimaging and diagnosis of diseases
- 6. Development of PET (positron emission tomography) probe candidates for *in vivo* imaging to promote drug discovery

- Yoshida S, Kanno K, Kii I, Misawa Y, Hagiwara M, Hosoya T: Convergent synthesis of trifunctional molecules by three sequential azido-type-selective cycloadditions, Chem Commun, 54, 3705-3708, 2018.
- Yoshida S, Shimizu K, Uchida K, Hazama Y, Igawa K, Tomooka K, Hosoya T: Construction of condensed polycyclic aromatic frameworks through intramolecular cycloaddition reactions involving arynes bearing an internal alkyne moiety, Chem Eur J, 23, 15332-15335, 2017.
- Sakaguchi H, Uetake Y, Ohashi M, Niwa T, Ogoshi S, Hosoya T: Copper-catalyzed regioselective monodefluoroborylation of polyfluoroalkenes en route to diverse fluoroalkenes, J Am Chem Soc, 139, 12855-12862, 2017.
- Kanemoto K, Sugimura Y, Shimizu S, Yoshida S, Hosoya T: Convergent synthesis of trifunctional molecules by three sequential azido-type-selective cycloadditions, Chem Commun, 53, 10640-10643, 2017.
- Nishiyama Y, Hazama Y, Yoshida S, Hosoya T: Synthesis of unsymmetrical tertiary phosphine oxides via sequential substitution reaction of phosphonic acid dithioesters with Grignard reagents, Org Lett, 19, 3899-3902, 2017.

We aim to develop molecular probes and methodologies that can be used to elucidate and regulate biological phenomena, based on synthetic organic chemistry. In particular, we are focusing on the synthesis of functional compounds based on developing new reactions using highly distorted molecules, and developing molecular imaging probes that can be used *in vivo*.



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# **Department of Organic and Medicinal Chemistry**

#### Professor Hiroyuki Kagechika

Associate Professor As Tomoya Hirano Assistant Professor Te

Assistant Professor Shuichi Mori

ant Professor Technical Specialist Mari Yuasa Hiroyuki Masuno



## Drug discovery based on molecular structure and function

- 1. Medicinal chemistry of retinoids and nuclear receptors
- 2. Development of novel modulators of gene transcription or signaling pathways for clinical applications in intractable diseases
- 3. Development of novel fluorophores and fluorescent sensors
- 4. Aromatic architecture based on amide conformational properties

- Ando F, Mori S, Yui N, Morimoto T, Nomura N, Sohara E, Rai T, Sasaki S, Kondo Y, Kagechika H, Uchida S: AKAPs-PKA disruptors increase AQP2 activity independently of vasopressin in a model of nephrogenic diabetes insipidus, Nature Commun 9, 1411, 2018.
- Yokoo H, Ohsaki A, Kagechika H, Hirano T: Unique properties of 1,5-naphthyridin-2(1H)-one derivatives as environmental-polarity-sensitive fluorescent dyes, Eur J Org Chem 2018, 679-687.
- Mori S, Hirano T, Takaguchi A, Fujiwara T, Okazaki Y, Kagechika H: Selective reagent for detection of N- ε-monomethylation of a peptide lysine residue through SNAr reaction, Eur J Org Chem 2017, 3606-3611.
- Fujii S, Masuno H, Taoda H, Kano A, Wongmayura A, Nakabayashi M, Ito N, Shimizu M, Kawachi E, Hirano T, Endo Y, Tanatani A, Kagechika H: Boron cluster-based development of potent non-secosteroidal vitamin D receptor ligands: Direct observation of hydrophobic interaction between protein surface and carborane, J Am Chem Soc 133, 20933-20941, 2011.
  Kagechika H, Shudo K: Retinoids: Recent developments concerning structure and clinical utility, J Med Chem 48, 5875-5883, 2005.

Our group is working on the development of various functional molecules based on organic chemistry and its application in the field of drug discovery and material sciences. In particular, we focus on medicinal chemistry and chemical biology research to elucidate the functions and clinical utility of hydrophobic signaling molecules, such as steroid hormones and active vitamins.

#### **Medicinal chemistry of retinoids**

Retinoids – the natural and synthetic analogs of retinoic acid – regulate various biological phenomena. We are developing novel synthetic retinoid agonists and antagonists, and examining their clinical applications in the fields of cancer, autoimmune diseases, neurodegenerative diseases, and others. Among our compounds, Am80 (tamibarotene) was approved as a drug for relapsed acute promyelocytic leukemia (APL) in Japan, and the study of further clinical applications for Am80 is ongoing.



#### **Development of fluorescent molecules**

Fluorescent molecules applicable to biological research and medical diagnosis have been developed based on a fluorescent compound library derived from organic synthesis and natural compounds.



#### Medicinal chemistry of nuclear receptors

Nuclear receptors are ligand-inducible transcription factors, responsible for the biological activities of hydrophobic hormones. We are developing novel ligands for various nuclear receptors by using unique hydrophobic pharmacophores, such as carboranes (boron clusters).



Based on our finding that N-methylated aromatic amides and ureas exist in cis conformation, we have constructed aromatic foldamers with unique structures and functions.





# **Academia-Industry Alliance**

The IBB aims to help activate industries and the economy through the positive transfer of research products and technologies to companies to create new industries and support technological developments. The Medical Innovation Promotion Center (MIPC) and the Research Center for Industry Alliances of our university will be helpful for these activities. We also intend to employ superior technologies and original ideas from other research institutions and commercial fields to satisfy challenging clinical needs with fruitful joint research. The Incubation Laboratory, which exists within the aforementioned MIPC, is directed by a professor from our institute, so the research resources of the institute can be utilized effectively for the assessment of safety and efficacy of medical products, non-clinical testing under regulation schema, and applications to obtain the approval of the PMDA (Pharmaceuticals and Medical Devices Agency).



#### Practical applications of research on new medical devices and medications



# **Graduate Education**

The Institute of Biomaterials and Bioengineering at Tokyo Medical and Dental University heartily invites you to join the research projects underway in our departments as a graduate student (master's or doctor's course), or as a research student. Tokyo Medical and Dental University's graduate programs are composed of two courses, the Master's Course (two years) and the Doctor's Course (an additional three or four years).

#### Master's Course: Health Sciences and Biomedical Engineering, Graduate School of Medical and Dental Sciences

Admission to the Master's Course requires an entrance examination and prior agreement by the advisor responsible to the department whose research you want to join. Students who have completed the Master's Course are granted a master's degree (Master of Medical Science, Master of Dental Science, Master of Oral Health Care Science, Master of Engineering, Master of Science, or Master of Medical Laboratory Science).

#### Doctor's Course: Biomedical, Life and Health Sciences Engineering Track, Graduate School of Medical and Dental Sciences

Applicants who have obtained, or will obtain, a master's degree (or who are recognized as having academic

qualifications equal or superior to a master's degree), may apply to this three-year doctoral course. Students who have completed the Doctor's Course receive a doctoral degree (PhD in Science, PhD in Engineering, or PhD in Medical Laboratory Science).

#### Doctor's Course: Medical and Dental Sciences Track, Graduate School of Medical and Dental Sciences

Applicants who have graduated, or will graduate, from a faculty of medicine or dentistry, and those who have obtained, or will obtain, a master's degree (or who are recognized as having academic qualifications equal or superior to a master's degree), may apply to this four-year doctoral course. Students who have completed this course will receive a doctoral degree (PhD in Medical Science, PhD in Dental Science, or PhD).

#### **Research Student Program**

The research student program enables students to enter graduate school to study a specific subject or pursue research as "research students" with the permission of the graduate school. However, such students are not entitled to receive degrees. Most research students use this program to prepare for enrollment in regular courses at graduate schools.







# **Research Staff of IBB**

#### **Division of Biomedical Materials**

#### **Department of Metallic Biomaterials**

Professor Takao Hanawa, Associate Professor YusukeTsutsumi, Assistant Professor Hisashi Doi, Assistant Professor Maki Ashida, Assistant Professor Peng Chen, Assistant Professor Akira Umise, Technical Staff Shukan Okano, Technical Staff Michiko Nakaishi

#### **Department of Inorganic Biomaterials**

Professor Kimihiro Yamashita, Associate Professor Miho Nakamura, Assistant Professor Naohiro Horiuchi

#### **Department of Organic Biomaterials**

Professor Nobuhiko Yui, Associate Professor Atsushi Tamura, Assistant Professor Yoshinori Arisaka

#### **Division of Biofunctional Restoration**

#### **Department of Biofunction Research**

Professor Keiji Itaka, Assistant Professor Kosuke Nozaki

#### **Department of Material-based Medical Engineering**

Professor Akio Kishida, Associate Professor Tsuyoshi Kimura, Assistant Professor Yoshihide Hashimoto, Research Scientist Zhang Yongei

#### **Department of Biomechanics**

Professor Kenji Kawashima, Assistant Professor Takahiro Kanno, Assistant Professor Tetsuro Miyazaki, Assistant Professor Toshihiro Kawase

#### **Division of Medical Devices**

#### **Department of Bioelectronics**

Professor Yuji Miyahara, Associate Professor Akira Matsumoto, Assistant Professor Tatsuro Goda, Tenure-track Assistant Professor MiyukiTabata, Project Assistant Professor Yukichi Horiguchi, Specially Appointed Assistant Professor Toshihiro Yoshizumi

#### **Department of Biomedical Information**

Professor Yoshikazu Nakajima

#### **Department of Biomedical Devices and Instrumentation**

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#### **Department of Chemical Bioscience**

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#### **Department of Organic and Medicinal Chemistry**

Professor Hiroyuki Kagechika, Associate Professor Tomoya Hirano, Assistant Professor Shuichi Mori, Assistant Professor Mari Yuasa, Technical Specialist Hiroyuki Masuno

# **Campus and Access**



## TMDU Yushima and TMDU Surugadai Campuses

#### Exit stations:

JR Line Ochanomizu Station

Subway Marunouchi Line Ochanomizu Station

Subway Chiyoda Line Shin-Ochanomizu Station





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