

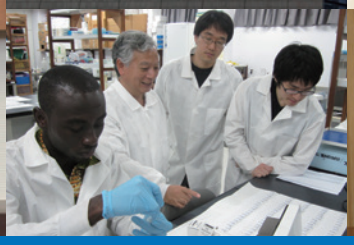


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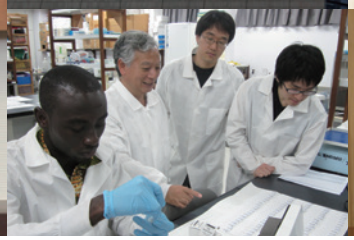
Tokyo Medical and Dental University (TMDU)

A WORLD LEADER IN BASIC AND CLINICAL LIFE SCIENCE RESEARCH AND EDUCATION






Tokyo Medical and Dental University (TMDU)

A WORLD LEADER IN BASIC AND CLINICAL LIFE SCIENCE RESEARCH AND EDUCATION

Tokyo Medical and Dental University (TMDU) is proud to have been founded, in 1928, as the first national dental school in Japan. Today, TMDU is unique among medical and dental universities in having two graduate schools — one in medical and dental sciences and the other in health care sciences — and two research institutes, the Institute of Biomaterials and Bioengineering and the Medical Research Institute. Approximately 3,000 students are enrolled at TMDU and are nearly evenly split between graduate and undergraduate programs. An array of over 200 life science degree programs attracts top students from Japan and overseas. Undergraduates at TMDU study medicine, dentistry, health care sciences or oral health care sciences. They begin their career at the College of Liberal Arts and Sciences to ensure a well-rounded education. They then concentrate on a curriculum that is increasingly integrated between medical and dental sciences and utilizes an inter-professional educational approach, just as the graduate programs have traditionally enjoyed. This prepares students for the increasingly interconnected worlds of scientific research and health care. In addition, the Faculty of Medicine and the Faculty of Dentistry each have a university hospital, which further facilitate the school's educational efforts, basic and clinical research activities, and community service.

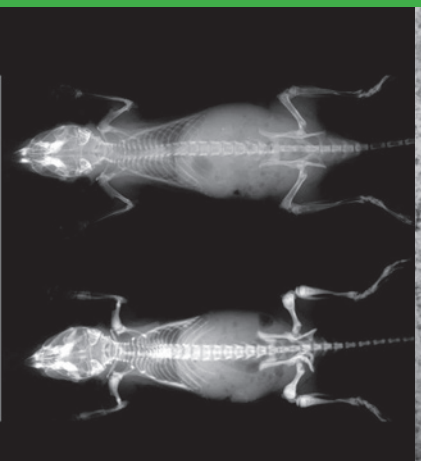
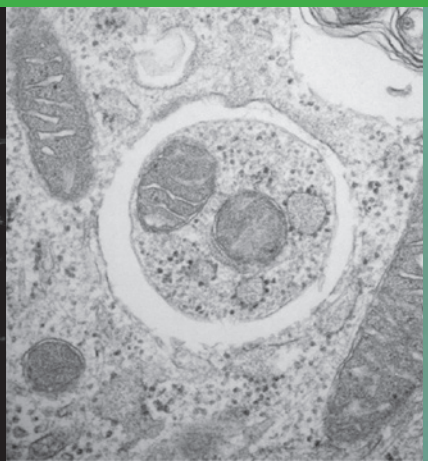
TMDU strives to produce scientists who expend every possible effort in seeking the truth, and who have the courage and ability to explore new areas, the tolerance and humility to respect diversity and accept new ideas, and the intellectual curiosity borne from a broad education. To encapsulate these goals, TMDU's mission statement is "Cultivating Professionals with Knowledge and Humanity". "Knowledge" refers to learning and techniques, and "Humanity" encompasses education and sensitivity. Medicine is driven by knowledge; humanity facilitates its implementation.

In line with our objectives of developing first-rate basic and clinical research and providing top-quality medical and dental clinical care, we have established three overseas research/education centers. The TMDU–University of Ghana Research Center for Infectious Diseases in Ghana, opened in 2009. In 2010, we opened the Latin American Collaborative Research Center for Colorectal Cancer in Chile and the Chulalongkorn University-TMDU Research and Education Collaboration Center in Thailand.

We currently have over 200 international students, who are almost exclusively enrolled in graduate studies and who primarily hail from Asia. Also, through our new tenure-track placement initiative, TMDU is recruiting outstanding young scientists from around the world for assistant professorship positions focused on medical science research.

On the domestic front, TMDU has successfully obtained many research grants, including the highly competitive Global Center of Excellence (GCOE) program for molecular science in tooth and bone diseases. This program will nurture the next generation of young researchers who will work globally on molecular science — a research field of critical importance for the future welfare of humankind and of particular importance in Japan, the world's most rapidly aging society.

To better utilize all the results produced through research activities — both within TMDU and through collaboration with industry/government — for the betterment of society, TMDU has established an organization for research and industry liaison promotion. This organization coordinates all the divisions related to research under the leadership of the trustee in charge of research. Within this framework, TMDU is establishing a center for collecting and maintaining high-quality bioresources and promoting the application of cutting-edge

medical technologies. TMDU is also playing a central role in medU-net, a networking initiative created by medical schools and aimed at accelerating industry-government-academia cooperation.

Three focal areas of research at TMDU are currently yielding important results.

Osteoimmunology

Research in the field of osteoimmunology investigates the interactions and shared mechanisms between the bone and immune systems. Under Hiroshi Takayanagi's leadership, we have focused our research on the mechanism of bone destruction in rheumatoid arthritis, especially the regulation by T cells of the osteoclast differentiation factor, RANKL. In addition to basic research on Th17 development and innate immune signaling, we have extensively studied the intracellular signaling pathways required for osteoclast development, revealing NFATc1 to be a master transcription factor. Mounting evidence suggests that immune cells, including hematopoietic stem cells and memory cells, interact with bone cells in the bone marrow to cooperatively regulate the osteoimmune system. Our lab has exquisitely demonstrated the bone function of immune molecules as well as the immune function of bone molecules by using genome-wide screening techniques and gene targeting strategies. Our studies will provide the molecular basis for novel therapeutic strategies for various immune and bone diseases including autoimmune diseases, osteoporosis and periodontal diseases.

Molecular mechanism and physiological roles of autophagy

Whole organisms and even individual cells can maintain their function and vitality by recycling their own constituents, such as proteins and organelles, and adapting to various internal and external changes. Macroautophagy, or autophagy in common parlance, is one of the major degradation pathways of a cell. During autophagy, intracellular components are sequestered by autophagosomes and then degraded upon fusion with lysosomes. Using autophagosome-indicator mice and various autophagy-deficient mice, with Noboru Mizushima at the helm, we have identified physiological functions of autophagy such as maintenance of the amino acid pool during starvation, promotion of preimplantation development as the amino acid supplying system, and quality control of cytoplasmic proteins organelles to prevent neurodegeneration and tumorigenesis. We are also investigating how autophagy is regulated and how autophagosome formation is achieved at the molecular level. We have identified a number of mammalian autophagy factors and reported that mTORC1 directly regulates an autophagy protein complex, and most autophagy factors function at a special site on or close to the endoplasmic reticulum in a hierarchical order.

Systems Approach for Musculoskeletal Development and Diseases

Compared with microarray analysis, *in situ* hybridization data provides more detailed information on the spatial regulation of gene expression and allows the identification of discrete clusters of transcribed genes. To provide new insight into the spatio-temporal distribution of individual genes implicated in whole body, under Hiroshi Asahara's direction, we created a whole-mount *in situ* hybridization (WISH) database, termed EMBRYS, containing expression data of 1,520 transcription factors and cofactors expressed in E9.5, E10.s5, and E11.5 mouse embryos, which are at a highly dynamic stage of tissue and organ development. Combined with cell-based high-throughput transfection screening, we identified the critical molecular network for myogenesis: an RP58 mediated regulatory loop for muscle development. ■

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