【Grant-in-Aid for Scientific Research (S)】

Biological Sciences (Medicine, Dentistry, and Pharmacy)

Title of Project : Elucidation of the molecular mechanism of homeotic control of muscle and bone from the viewpoints of inter-organ crosstalk

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Research Project Number : 16H06392 Researcher Number : 30376727
Research Area : Orthopedic Surgery
Keyword : Bone and cartilage metabolism

【Purpose and Background of the Research】

Age-related decrease in muscle mass and muscle function, i.e. sarcopenia, has been to lead decrease in motor ability and eventually shorten the healthspan. However, its pathogenesis is unknown and new medical treatment is strongly awaited. In addition, detailed molecular mechanism of bone formation is largely unknown. Novel regulatory mechanism of metabolism by the functional communication between organs or tissues, i.e., inter-organ network, such as cardio-renal axis or adipo-vascular axis, draws great attention, indicating that a novel regulatory function can be discovered by the development of research project focusing inter-organ network. We previously demonstrated that hormones and neuropeptides, such as leptin and NMU, regulated bone remodeling through the central nervous system and proposed the concept "control of bone by organs other than bone". Moreover, we also demonstrated that sensory neurons are physiologically essential for the homeostasis of bone remodeling.

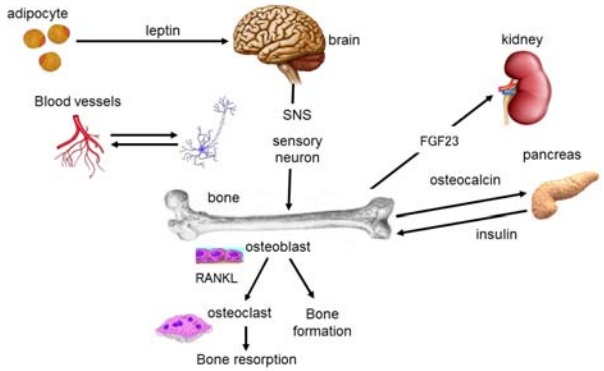
In this research project, we will study the role of neurons and blood vessels for the regulation of muscle and osteochndro progenitor cells and aimed to identify regulatory factors for these progenitors and apply them for novel therapeutics.

【Research Methods】

We will analyze neurons and blood vessels innervating muscles and bones in three dimensions by using newly developed techniques that make the tissues transparent. By using tissue-specific Sema3a receptor-deficient mice, we will also analyze the role of neurons and blood vessels for the regulation of muscle and osteochndro progenitor cells and aimed to identify regulatory factors for these progenitors and apply them for novel therapeutics.

【Expected Research Achievements and Scientific Significance】

This research project will further develop the concept "control of metabolism by inter-organ network" and enable us to address the molecular mechanism of neuron-dependent control of muscle and osteochondro stem cells. In addition, this project is expected to lead to develop novel therapeutics for the treatment of sarcopenia and osteoporosis.



Inter-organ metabolic crosstalk between bone and other organs

【Publications Relevant to the Project】

・Takeda, S., Elefteriou, F., Levasseur, R., Liu, X., Zhao, L., Parker, K.L., Armstrong, D., Ducy, P., and Karsenty, G. Leptin regulates bone formation via the sympathetic nervous system. Cell 111:305-17, 2002

・Fukuda, T., Takeda, S., Xu, R., Ochi, H., Sunamura, S., Sato, T., Shibata, S., Yoshida, Y., Gu, Z., Kimura, A., Ma, C., Xu, C., Bando, W., Fujita, K., Shinomiya, K., Hirai, T., Asou, Y., Enomoto, M., Okano, H., Okawa, A., and Itoh, H. Sema3A regulates bone-mass accrual through sensory innervations. Nature 497:490-3, 2013

【Term of Project】 FY2016-2020

【Budget Allocation】 150,300 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.med.tmd.ac.jp/medicine/list/basic/functional/cell_physiology.html