

【Grant-in-Aid for Young Scientists(S)】

Biological Sciences (Medicine, dentistry, and pharmacy II)



Title of Project : Molecular elucidation of the interrelationship between bone and other tissues: bone-brain axis and gut-bone axis

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Research Area : Medicine, dentistry, and pharmacy

Keyword : Bone, Central Nervous System

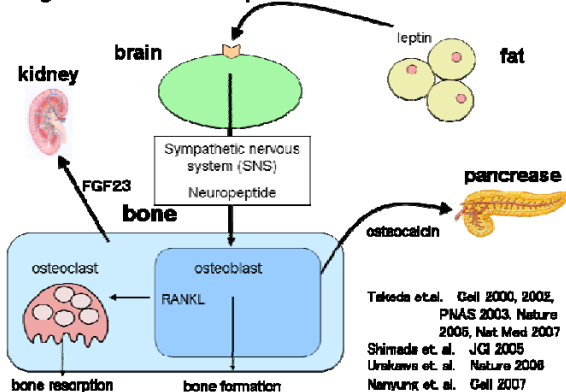
【Purpose and Background of the Research】

Osteoporosis is caused by imbalance between bone formation by osteoblasts and bone resorption by osteoclasts. It has been widely assumed that bone metabolism is controlled mostly by the local environment. In addition, alteration of bone metabolism is believed not to affect the metabolism of other tissues, i.e., bone establishes an independent domain from the rest of the body. However, the discovery of neuronal control of bone mass by leptin has shed light on a novel pathway controlling bone metabolism, namely “central control of bone remodelling”. Furthermore, the recent discovery that osteocalcin modified by OST-PTP regulates glucose metabolism opened a new research field beyond classical skeletal biology. Although in most cases these pathways are still far from being fully defined, the identification of a network between bone and other organs has already attracted much attention from basic and clinical scientists. In this study, we try to elucidate a molecular mechanism of the novel interrelationship between bone and other tissues: bone-brain axis and gut-bone axis.

【Research Methods】

For the homeostasis, one needs a feedback system. Thus, in the case of central control of bone remodelling, there must be a feedback

Figure1: Interrelationship between bone and other tissues



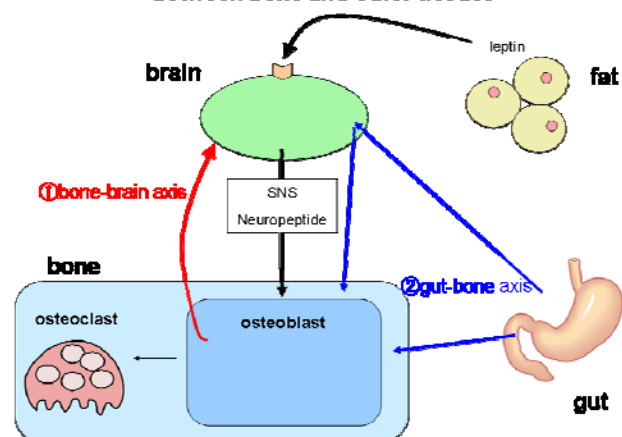
system from bone to brain. We are currently investigating such pathway(s), especially focusing on cytokines and neuronal pathways that emanate from bone, by using various mutant mouse models.

We also try to uncover the pathogenesis of osteoporosis secondary to the resection of the gastrointestinal tract, mainly focusing on secreted molecules from GI tract that may affect bone remodelling.

【Expected Research Achievements and Scientific Significance】

This study should further advance our understanding of the interrelationship between bone and other tissues, which would also lead to the identification of a new drug target for the treatment of osteoporosis.

Figure 2: Proposed Interrelationship between bone and other tissues



【Publications Relevant to the Project】

- Takeda, S. et. al. Leptin regulates bone formation via the sympathetic nervous system. *Cell* 2002; 111: 305-17
- Eleftheriou, F., Takeda, S. et. al. Leptin regulation of bone resorption by the sympathetic nervous system and CART. *Nature* 2005; 434: 514-20.
- Sato, S., Takeda, S. et. al. Central control of bone remodeling by neuromedin U. *Nat Med* 2007; 13: 1234-40

【Term of Project】

FY2009-2013

【Budget Allocation】

80,400 Thousand Yen

【Homepage Address and Other Contact Information】

<http://www.keio-emn.jp/donation/index.html>