【Grant-in-Aid for Specially Promoted Research】

Biological Sciences

Title of Project : Promotion of osteoimmunology for understanding the new regulatory systems of vertebrate

Hiroshi Takayanagi
(The University of Tokyo, Graduate School of Medicine and Faculty of Medicine, Professor)

Research Project Number : 15H05703 Researcher Number : 20334229
Research Area : Medicine, Dentistry and Pharmacology
Keyword : Bone and Cartilage Metabolism, Joint disease, Immunology, Cytokine

【Purpose and Background of the Research】

Bone is not only a component of the skeletal-locomotor system, but also a "primary lymphoid organ" where bone marrow microenvironment supports and nurtures hematopoietic stem cells and various immune progenitor cells. Bone is intricately regulated by other various biological systems. Especially, the immune and bone systems are closely related through a number of shared regulatory molecules including cytokines. Bone destruction in rheumatoid arthritis (RA) is the most typical pathogenesis closely linked to their relationship. We have explored the interdisciplinary field "osteoimmunology" by investigating the shared mechanisms and crosstalks between the bone and the immune system. As seen in recent advances of anti-cytokine therapies for RA, the osteoimmunological insight is now of growing importance in clinical applications. In this project, we aim to deepen and extend the concept of osteoimmunology to various biological systems, by elucidating the crosstalks between the immune and bone systems in the various skeletal or immune diseases and revealing their physiological roles in the hematopoiesis in bone marrow.

【Research Methods】

[1] Understanding the pathogenesis and developing new therapeutic approaches for autoimmune diseases including RA: using proteome and transcriptome analyses, we aim to identify molecules essential for the immune cells and bone cells, to understand the pathogenesis of autoimmune diseases, and to provide a molecular basis for novel drug discovery in the field.
[2] Identifying new interactions between the bone and immune systems: we aim to reveal novel immune-bone interactions in various immune and skeletal diseases by analyzing the mouse diseases models and identify the novel molecules shared by the immune and bone systems.
[3] Revealing the cell network in the bone marrow microenvironment for hematopoiesis: by using the genetically modified mice and establishing the imaging system, we aim to elucidate the physiological significance of bone marrow cell subsets and mediators for hematopoiesis.

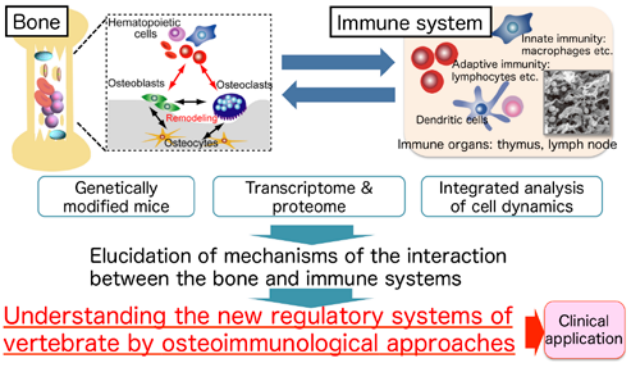

Figure: whole concept of the study

【Expected Research Achievements and Scientific Significance】

By fully uncovering the novel bone－immune relationships, we will provide not only a novel framework for advances in biological control system, but also a molecular basis for the pharmacological intervention into various diseases affecting the bone and immune systems.

【Publications Relevant to the Project】

Komatsu, N., Okamoto, K., Sawa, S., (5 authors) and Takayanagi, H., Pathogenic conversion of Foxp3^{+} T cells into T$_{H}$17 cells in autoimmune arthritis. ***Nature Med.*** 20: 62-68 (2014)
Hayashi, M., Nakashima, T., Taniguchi, M., Kodama, T., Kumanogoh, A., Takayanagi. H. Osteoprotection by Semaphorin 3A. ***Nature.*** 485: 69-74 (2012)

【Term of Project】 FY2015-2019

【Budget Allocation】 398, 300 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.osteoimmunology.com/