Cell Signaling

1. Staffs and Students (April, 2009)

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2. Purpose of Education

Organized signal networks in the body are crucial for the higher physiological functions and the tissue organization. To understand the regulation of signal events, we take on cell signaling course including the molecular mechanism of both the "intra" cellular and the "inter" cellular signal transduction. Especially, the course will be focused on the molecular networks of signal transduction in osteoclasts and osteoblasts, but also on the osteoimmunology, which is a new integrated field of bone homeostasis and immunology. Besides, to promote the practical and clinical understanding, the course will deal with the molecular mechanism of osteoporosis and inflammatory bone destructed diseases, such as periodontal disease and rheumatoid arthritis, in parallel with the basic molecular biology.

3. Research Subjects

1) Function and transcriptional regulation of NFATc1, a master regulator of osteoclast differentiation
2) Transcriptome and Proteome of cytokine-induced genes
3) Regulation of bone homeostasis by immunoglobulin receptors
4) Identification of bone-derived systemic regulatory factors (osteokines)
5) Mechanism of sensing and adapting to mechanical stress
6) Functional analysis of genes by gene manipulations, RNAi and gene-disrupted mice
7) Development of clinical application by experimental animal disease models

4. Publications

【Original Article】

1. Nishikawa, K., Nakashima, T., Takeda, S., Isogai, M., Hamada, M., Kimura, A., Kodama, T., Yamaguchi, A., Owen, MJ., Takahashi, S. and Takayanagi, H.: Maf promotes osteoblast differentiation in mice by mediating the age-related switch in mesenchymal cell differentiation. **J Clin Invest**. 120(10), 3455-3465, 2010
2. Okamoto, K., Iwai, Y., Oh-hora, M., Yamamoto, M., Morio, T., Aoki, K., Ohya, K., Jetten, AM., Akira, S., Muta, T. and Takayanagi, H.: IκBζ regulates TH17 development by cooperating with ROR nuclear receptors. **Nature**. 464(7293), 1381-1385, 2010
3. Hayashi, M., Nakashima, T., Kodama, T., Makrigiannis, AP., Toyama-Sorimachi, N. and Takayanagi, H.: Ly49Q, an ITIM-bearing NK receptor positively regulates osteoclast differentiation. **Biochem Biophys Res Commun**. 393(3), 432-438, 2010
4. Nishikawa, K., Nakashima, T., Hayashi, M., Fukunaga, T., Kato, S., Kodama, T., Takahashi, S., Calame, K. and Takayanagi, H.: Blimp1-mediated repression of negative regulators is required for osteoclast differentiation. **Proc Natl Acad Sci USA**. 107(7), 3117-3122, 2010
5. Kayamori, K., Sakamoto, K., Nakashima, T., Takayanagi, H., Morita, K., Nguyen, S.T., Omura, K., Miki, Y., Akashi, T., Ogata, E. and Yamaguchi, A.: Roles of IL-6 and PTHrP in osteoclast formation associated with oral cancers: The significance of IL-6 synthesized by stromal cells in response to cancer cells. **Am J Pathol**. 176(2), 968-980, 2010

【Review Article】

1. Takayanagi, H.: New immune connections in osteoclast formation. **Ann N Y Acad Sci**. 1192, 117-123, 2010
2. Takayanagi, H.: The unexpected link between osteoclasts and the immune system. **Adv Exp Med Biol**. 658, 61-68,

2010

【Books】

1. Joseph Lorenzo, Yongwon Choi, Mark Horowitz, Hiroshi Takayanagi (Editors): **Osteoimmunology: Interactions of the Immune and Skeletal Systems**, 2010
2. Joseph Lonrenzo, Yongwon Choi, Mark Horowitz,and Hiroshi Takayanagi. Overview: The Developing Field of Osteoimmunology. Joseph Lorenzo, Yongwon Choi, Mark Horowitz, Hiroshi Takayanagi (Editors) **Osteoimmunology: Interactions of the Immune and Skeletal Systems**, p1-5, 2010
3. Roberta Faccio, Yongwon Choi, Steven L. Teitelbaum, and Hiroshi Takayanagi. Osteoimmunology: Interactions of the Immune and Skeletal Systems. Joseph Lorenzo, Yongwon Choi, Mark Horowitz, Hiroshi Takayanagi: **Osteoimmunology: Interactions of the Immune and Skeletal Systems**, p141-185, 2010

【Presentation】

1. Hiroshi Takayanagi: RANKL and Osteoimmunoloty ENS de Lyon – Todai Workshop, Mineralised Tissues Session 2010. 11.10, Lyon, France
2. Hiroshi Takayanagi: REF Oscar S. Gluck, MD, Memorial Lectureship – Osteoimmunology: Crosstalk Between the Immune and Bone Systems: Biologic and Clinical Implications ACR/ARHR Annual Scientific Meeting,Special Sessions – ACR REF 2010. 11.8, Atlanta, USA
3. Hiroshi Takayanagi : Positive and negative regulators of osteoclast differentiation ASBMR 2010 Annual Meeting 2010.10.15, Toronto, Canada
4. Hiroshi Takayanagi : Mouse genetics in osteoimmunology EMBO 2010: Anatomy and embryology of the mouse 2010.9.15, Split, Croatia
5. Hiroshi Takayanagi : Overview of osteoimmunology – Workshop:Osteoimmunoloty - Chair 14th International Congress of Immunology 2010.8.26, Kobe, Japan
6. Hiroshi Takayanagi : RANKL and Osteoimmunology - Lunch Time Lecture 14th International Congress of Immunology 2010.8.25, Kobe, Japan
7. Hiroshi Takayanagi : Bone destruction in arthritis - APLAR Session: Osteoimmunology 14th Congress of Asia Pacific League of Associations for Rheumatology 2010.7.15, Hong Kong, China.
8. Hiroshi Takayanagi : Ostoimmunology - APLAR Basic Science Review Course 14th Congress of Asia Pacific League of Associations for Rheumatology 2010.7.11, Hong Kong, China.
9. Hiroshi Takayanagi : Adaptive immune responses and bone 3rd International Conference on Osteoimmunology, 2010.6.24, Santorini, Greece
10. Hiroshi Takayanagi : The role of TH17 cells and IL-17 in bone remodeling. Annual European Congress of Rheumatology (EULAR 2010), 2010.6.19, Rome, Italy
11. Hiroshi Takayanagi : Osteoimmunology – interaction between bone and the immune system, Raine Visiting Professorship Lecture Series at University of Western Australia, 2010.5.05, Perth, West Australia.
12. Hiroshi Takayanagi : Bone destruction in arthritis and osteoimmunology -Osteoimmunology:the impact on diseases-, The Forth Margaret River Region Forum: Pathways toward Molecular and Cellular Therapy, 2010.4.29, Margaret River, West Australia.
13. Masatsugu Oh-hora, Hiroshi Takayanagi, Anjana Rao. Different Ca^{2+} sensitivity of the development of T-lineage cells Keystone Symposia Colorado USA, 2010 February 27 – March 4
14. Mikihito Hayashi, Tomoki Nakashima, Noriko Toyama-Sorimachi, Hiroshi Takayanagi. Ly49Q, an ITIM-bearing NK receptor, positively regulates osteoclast differentiation. 3rd International Conference on Osteoimmunology: Interactions of the Immune and Skeltal Systems. Fira, Santorini, Greece, 2010 June 20 – 25
15. Takako Negishi-Koga, Hans-Jurgen Gober, Toshiyuki Takai, Hiroshi Takayanagi. The regulation of osteoclastgenesis by Fcg receptors. 3rd International Conference on Osteoimmunology: Interactions of the Immune and Skeltal Systems. Fira, Santorini, Greece, 2010 June 20 – 25
16. Kazuo Okamoto, Masatsugu Oh-hora, Masahiro Yamamoto, Sizuo Akira, Tatsushi Muta, Hiroshi Takayanagi. Title: An essential role of IkBz in the development of osteoclastogenic helper T cells – Th17 cells. 3rd International Conference on Osteoimmunology: Interactions of the Immune and Skeltal Systems. Fira, Santorini, Greece, 2010 June 20 – 25
17. Kaori Takechi, Takako Negishi-Koga, Takahiro Maeda, Pier Paolo Pandolfi, Keiji Moriyama, Hiroshi Takayanagi. Transcriptional repressor, LRF regulates NFATc1 expression in osteoclastogenesis 3rd International Conference on

Osteoimmunology: Interactions of the Immune and Skeltal Systems. Fira, Santorini, Greece, 2010 June 20 – 25

18. Kazuo Okamoto, Masatsugu Oh-hora, Masahiro Yamamoto, Sizuo Akira, Tatsushi Muta, Hiroshi Takayanagi. An essential role of IkBz in Th17 development. The second International Conference on Regulatory T Cells and Th17 Cells and Clinical Application in Human Disease. Shanghai, China, 2010 July 17
19. Masatsugu Oh-hora, Noriko Komatsu, Anjana Rao, Hiroshi Takayanagi. Lineage-specific requirement of store-operated calcium entry in T-lineage development. 14th International Congress of Immunology Kobe, Japan, 2010 August 22 - 25
20. Kazuo Okamoto, Yoshiko Iwai, Masatsugu Oh-hora, Masahiro Yamamoto, T omohiro Morio, Anton M Jetten, Sizuo Akira, Tatsushi Muta, Hiroshi Takayanagi. IκBζ is required for the transcriptional program in Th17 development. 14th International Congress of Immunology Kobe, Japan, 2010 August 22 - 25