

Nobuhiro Kamiya, M.D., Ph.D.

Staff Scientist of the Sarah M. and Charles E. Seay Center for Musculoskeletal Research

Director of Tissue Bank Core

Texas Scottish Rite Hospital for Children

Assistant Professor

Department of Orthopaedic Surgery

The University of Texas Southwestern Medical Center

2222 Welborn Street, Dallas, Texas 75219

Phone: (214) 559-8455

Fax: (214) 559-7872

Email: Nobby.Kamiya@tsrh.org

Education

Medical Degree, Gifu University School of Medicine, Japan

Ph.D., Gifu University Graduate School of Medicine, Japan

Orthopaedic Residency, University of Gifu

Research Interest*1. Effects of BMP signaling on bone mass*

Recently, the FDA approved BMP2 and BMP7 for clinical use. However, data supporting their clinical effectiveness is mixed. This may be due in part to a lack in understanding of the variable effects BMPs have on different cell types in the skeleton including chondrocytes, osteoblasts and osteocytes. My recent study suggests that BMP signaling in osteoblasts reduce bone mass by enhancing osteoclastogenesis through the OPG-RANKL signaling pathway. Thus, it is critical to understand the effects of BMP signaling on both osteoblasts and osteoclasts, which can determine the final outcome of bone mass.

2. Relationship between BMP signaling and Wnt signaling

Wnt signaling is also crucial for regulating bone formation and bone mass. The interaction between BMP and Wnt signaling is not well described in bone *in vivo*, as changes in BMP signaling have not been studied in Wnt signaling mutants and vice versa. We recently discovered that sclerostin is a downstream target of the BMP type I receptor BMPRII as a Wnt inhibitor and bone mass mediator, suggesting that BMP signaling negatively regulates Wnt signaling by upregulating sclerostin in osteoblasts *in vivo*.

3. Effects of BMP signaling on fracture healing

Treatment of fractured bones with BMPs (BMP2 or BMP7) has been clinically used in these five years, but BMPs do not always accelerate the healing process. It is very interesting to

precisely address the effects of BMP signaling on endochondral bone formation, intramembranous bone formation, bone resorption, and vascularization for better usage of BMPs on fracture healing.

4. Effects of BMP signaling on mechanical stress

It is totally unknown how BMP signaling in endogenous bone responds to mechanical stress. Loss of BMP signaling in osteoblasts increases bone mass with a variety of degree by bone-site. Wnt signaling is also altered under this condition, consistent with the evidence that mechanical stress induces Wnt signaling. It is very intriguing to address the mechanism by which BMP signaling responds to mechanical stress. This information may also be helpful for potential application of BMPs on osteoporotic bones to prevent bone fracture.

5. Alteration of BMP signaling in bone diseases and future clinical application of BMPs

BMP signaling is important for bone development and remodeling. However, alterations of BMP signaling in bone diseases including osteoporosis, osteoarthritis, and scoliosis are poorly understood, partly because most often the causative genes for these disorders are unknown. In addition, results from our tissue-specific and age-specific conditional knockout specimens suggest that BMP signaling has diverse functions on bone biology in a cell-type, bone-site, and age-dependent manner. Although BMP2 and BMP7 are approved for clinical use, precise conditions of the usage are further desired with respect to: 1) target cell type and bone-site, 2) timing of usage by age or by progression, 3) period of usage to avoid a side effect. Taken together, I think it is very meaningful to elucidate changing of BMP signaling in bone diseases and establish proper conditions of BMPs usage. One of our future directions is to establish a condition of BMPs treatment for each disease.

Selected peer-reviewed publications

1. Ogino, N., Tatsuoka, Y., Matsuoka, R., Nakamura, K., Nakamura, H., Tanaka, C., **Kamiya, N.**, Matsuoka, Y. Cerebral infarction after deflation of a pneumatic tourniquet during total knee replacement. *Anesthesiology*, 90, 297-298, 1999.
2. Fujibayashi, S., Shikata, J., **Kamiya, N.**, Tanaka, C. Missing anterior cervical plate and screws, A case report. *Spine*, 25, 2258-2261, 2000.
3. **Kamiya, N.**, Watanabe, H., Habuchi, H., Takagi, H., Shinomura, T., Shimizu, K., Kimata, K. Versican/Pg-M Regulates Chondrogenesis as an Extracellular Matrix Molecule Crucial for Mesenchymal Condensation. *J Biol Chem*. 281 (4), 2390-400, 2006.
4. Matsumoto, K., **Kamiya, N.**, Suwan, K., Atsumi, F., Shimizu, K., Shinomura, T., Yamada, Y., Kimata, K., Watanabe, H. Identification and characterization of versican/Pg-M aggregates in cartilage. *J Biol Chem*. 281 (26), 18257-63, 2006.

5. Nagayama, M., Iwamoto, M., Hargett, A., **Kamiya, N.**, Tamamura, Y., Young, B., Morrison, T., Takeuchi, H., Pacifici, M., Enomoto-Iwamoto, M., Koyama, E. Wnt/beta-catenin signaling regulates cranial base development and growth. *J Dent Res.* 87(3), 244-9, 2008.

6. **Kamiya, N.**, Ye, L., Kobayashi, T., Lucas, D. J., Mochida, Y., Yamauchi, M., Kronenberg, H. M., Feng, J. Q., Mishina, Y. Disruption of BMP signaling in osteoblasts through type IA receptor (BMPRIA) increases bone mass. *J Bone Miner Res.* 23(12): 2007-17, 2008.

7. **Kamiya, N.**, Ye, L., Kobayashi, T., Mochida, Y., Yamauchi, M., Kronenberg, H. M., Feng, J. Q., Mishina, Y. BMP signaling negatively regulates bone mass through sclerostin by inhibiting the canonical Wnt pathway. *Development.* 135(22): 3801-11, 2008

8. Yu, P. B., Deng, D. Y., Lai, C. S., Hong, C. C., Cuny, G. D., Bouxsein, M. L., Hong, D. W., McManus, P. M., Katagiri, T., Sachidanandan, C., **Kamiya, N.**, Fukuda, T., Mishina, Y., Peterson, R. T., Bloch, K. D. BMP type I receptor inhibition reduces heterotropic ossification. *Nat Med.* 14(12): 1363-9, 2008

9. Konno, Y., Kodama, S., Moore, R., **Kamiya, N.**, Negishi, M. Nuclear xenobiotic receptor PXR locks co-repressor SMRT onto the CYP24A1 promoter to attenuate vitamin D3 activation. *Mol Pharmacol.* 75(2): 1265-71, 2009

10. **Kamiya, N.**, Kobayashi, T., Mochida, Y., Yu, P. B., Yamauchi, M., Kronenberg, H. M., Mishina, Y. Wnt inhibitors Dkk1 and Sost are downstream targets of BMP signaling through the Type IA receptor (BMPRIA) in osteoblasts. *J Bone Miner Res.* 25(2):200-210. 2010.

Honors

- 2003 Kanehara-Ichiro Foundation Award
- 2003 Gordon Research Conference Fellowship Award
- 2004 Lilly Foundation Award
- 2006 ASBMR Young Investigator Award
- 2006 The Fellows Award for Research Excellence, NIH
- 2007 The Japanese Society of Cartilage Metabolism Award
- 2007 The Japanese Society for Bone and Mineral Research Abstract Award
- 2007 The Fellows Award for Research Excellence, NIH
- 2007 ASBMR Travel Award
- 2008 Young Investigator Award, 7th International Conferences on BMPs