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Okayama University research: Role of commensal microbiota in bone remodeling

(Okayama, 26 December) **Researchers at Okayama University report in the journal *Molecules* that commensal microbiota — microorganisms present in the human body — may play a key role in human-bone remodeling by enhancing the activity of both cells breaking down bone tissue and cells synthesizing bone.**

Humans are host to several types of microorganisms like bacteria, fungi and viruses. Those residing in the human body without harming it are collectively called commensal microbiota. While it has been established that commensal microbiota play an important role in the body's energy management and the development of its immune system, recent findings have suggested that they affect the regulation of human bone formation too. Now, by performing comparative experiments on mice, Professor Manabu Morita, Yoko Uchida (D.D.S.) and colleagues from Okayama University confirmed the link between commensal microbiota and bone cell regulation. Specifically, they found that the presence of the microorganisms enhances the activity of both osteoclasts (cells that break down bone tissue) and osteoblasts (cells that synthesize bone).

Professor Morita and colleagues worked with two types of mouse: germ-free (GF) mice, free of any microorganisms, and specific-pathogen-free (SPF) mice, which are guaranteed to be free of certain pathogens but at the same time host to commensal microbiota.

The researchers investigated the activity of osteoclasts and osteoblasts in 8-week-old GF and SPF mice. They first looked at body weight and size. The SPF mice were found to have larger body size but lower bone mineral density in alveolar bones (the bones that contain the tooth sockets on the jaw bones), an observation attributed to the presence of commensal microbiota. In addition, by analyzing blood serum of the mice for substances that are associated with osteoclast activity, Professor Morita and colleagues were able to conclude that commensal microbiota cause greater development and activity of osteoclasts.

The scientists also discovered that the expression of osteocalcin messenger RNA— a maker of bone mineralization — is significantly higher in SPF mice, providing a further link between commensal microbiota and bone-remodeling processes.

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While the precise mechanism of commensal microbiota affecting the expression of osteoblast-specific genes such as osteocalcin needs to be further investigated in order to be completely understood, quoting Professor Morita and colleagues, "[these results] suggest that the commensal microbiota prevents excessive mineralization possibly by stimulating osteocalcin expression in osteoblasts, and enhances both osteoblast and osteoclast activity by regulating specific transcription factors."

Background

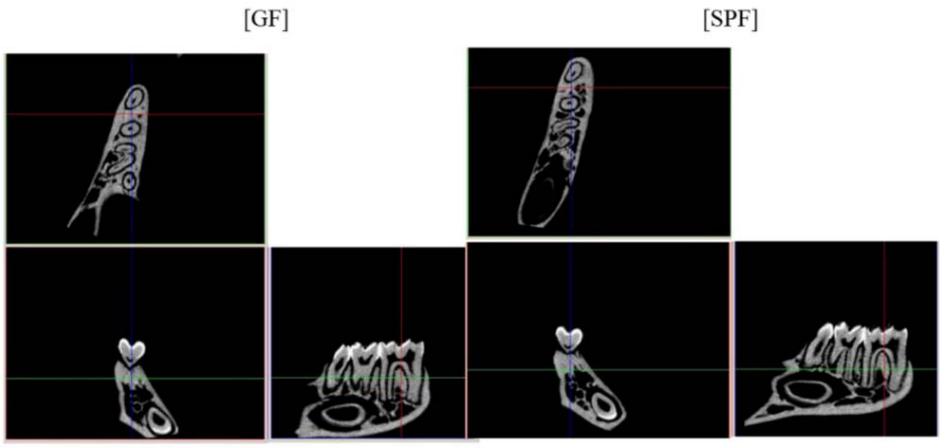
Commensal microbiota

The term microbiota refers to the collective of bacteria and other microorganisms in an animal's body. The term commensal is used when the presence of the microbiota is not harmful for the animal host. Professor Manabu Morita, Yoko Uchida (D.D.S.) and colleagues from Okayama University have now studied the influence of commensal microbiota on bone remodeling in mice. Their findings show that commensal microbiota have a regulatory effect on bone formation, as shown by differences in body weight and size between mice with and without commensal microbiota.

Osteocalcin. Bone density

Osteocalcin is a protein occurring in bone, produced by osteoblasts (bone-synthesizing cells). It is known to play a role in bone mineralization. As such, osteocalcin is often used as a biochemical marker for bone-formation activity. Professor Morita and colleagues were able to show that in specific-pathogen-free (SPF) mice, the expression of osteocalcin is related to the presence of commensal microbiota.

The study also involved measurements of bone density, or bone mineral density — the amount of bone mineral in bone tissue. While the SPF mice exhibited a larger body size, their bone density was found to be lower.



Caption

Microtomography images of a part of the alveolar bone in germ-free (GF) and specific-pathogen-free (SPF) mice.

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Reference

Yoko Uchida, Koichiro Irie, Daiki Fukuhara, Kota Kataoka, Takako Hattori, Mitsuaki Ono, Daisuke Ekuni, Satoshi Kubota, Manabu Morita. Commensal microbiota enhance both osteoclast and osteoblast activities. *Molecules*, 2018 Jun 23;23(7). pii: E1517.
DOI: 10.3390/molecules23071517.
https://www.mdpi.com/1420-3049/23/7/1517

Reference (Okayama University OU-MRU) : Professor Morita's team

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Okayama University is one of the largest comprehensive universities in Japan with roots going back to the Medical Training Place sponsored by the Lord of Okayama and established in 1870. Now with 1,300 faculty and 13,000 students, the University offers courses in specialties ranging from medicine and pharmacy to humanities and physical sciences.

Okayama University is located in the heart of Japan approximately 3 hours west of Tokyo by Shinkansen.

Website: http://www.okayama-u.ac.jp/index_e.html

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