conferenceseries.com

Tsuyoshi Miyazaki et al., J Gerontol Geriat Res 2016, 5:5(Suppl)
http://dx.doi.org/10.4172/2167-7182.C1.010

4th International Conference on
Geriatrics & Gerontological Nursing
October 3-4, 2016 | London, UK

OSTEOCYTE-SPECIFIC *CAS* KNOCKOUT MICE EXHIBIT DECREASED BONE MASS THROUGH INCREASED OSTEOCLASTIC BONE RESORPTION

Tsuyoshi Miyazaki[a], **Fumiaki Tokimura**[a], **Seiichi Azuma**[b], **Ichiro Harada**[c] and **Yasuhiro Sawada**[d]
[a]Tokyo Metropolitan Geriatric Hospital and Institute of Gerontology, Japan
[b]Saitama Red Cross Hospital, Japan
[c]Locomotive Syndrome Research Institute, Japan
[d]National Rehabilitation Center for Persons with Disabilities, Japan

The skeleton is a metabolically active organ that undergoes continuous remodeling throughout life. Osteoporosis, which is fostered by advancing age, is the most common clinical disorder affecting bones. Although it has been postulated that osteocytes play an important role in sensing mechanical load in bone tissues, detailed molecular mechanisms of how osteocytes regulate bone metabolism remain largely unclear. The adaptor molecule p130Cas (Crk-associated substrate, hereafter referred to as Cas), which is phosphorylated at focal adhesions upon extracellular matrix engagement, is involved in various cellular processes including migration, survival, transformation, and invasion. In addition, we reported that Cas binds to the cytoskeletons in a stretch-dependent manner. This suggests that Cas can function as an initiator of intracellular signaling cascades through force-dependent changes in the cytoskeleton network. To investigate the role of Cas in bone metabolism, we generated osteocyte-specific *Cas* conditional knockout (cKO) mice by mating $Cas^{flox/flox}$ mice with *Dentin matrix protein 1 (Dmp1)-Cre* transgenic mice, in which the Cre recombinase gene was specifically expressed in osteocytes. The resulting $Dmp1\text{-}Cre^{+/-};Cas^{flox/flox}$ mice (referred to herein as *Cas* cKO mice) exhibited a significant decrease in bone volume, as determined by μCT analysis. Histomorphometric analysis of *Cas* cKO mice revealed a significant increase in the eroded surface/bone surface ratio, osteoclast surface, and osteoclast number. Furthermore, the expression levels of *RANKL* genes were significantly increased in the osteocyte fractions derived from *Cas* cKO mice. Collectively, these findings suggest that the bone loss in *Cas* cKO mice was caused by increased osteoclatstic bone resorption.

Biography

Tsuyoshi Miyazaki has completed his MD at the age of 24 years and his PhD at the age of 31 years from University of Tokyo and postdoctoral studies from Yale University School of Medicine. He is the director of Department of Orthopaedic Surgery, Tokyo Metropolitan Geriatric Hospital and Institute of Gerontology. He has published more than 30 papers in reputed journals.

miyazak14@tmig.or.jp

Notes: