Masaki Noda

1. Topic in Research Achievements in the Year 2006

Loss of bone mass leads to high risk of fractures. Bone mass is determined based on the balance of two metabolic activities in bone, namely bone formation and bone resumption. Interaction between the cells responsible for these activities such as osteoblasts and osteoclasts, has been thought to play major role in determination of bone mass. The third category of the cells in bone is osteocytes. Osteocytes are the most abundant cells in bone. However, the functional relevance of these cells to bone mass determination has not yet been studied to the levels of investigations on the other two types of bone cells. Major bone matrix components are matrix proteins. Type I collagen consists of approximately 90% of protein components in bone. Thus, turn over of collagen would be the key events for proteinaceous metabolism in bone. MMP2 is one of major enzymes that degrades type I collagen. In search for molecular mechanisms underlying regulation of turn over of bone matrix, MMP2 knockout mice were studied. These mice indicated osteopenia in long bone and calvaria in young adult stage while they exhibited low bone mass in long bone in aged stage in association with high bone mass in calvaria at the same aged stage. In spite of these bone mass phenotypes, osteoclastic activities as well as osteoblastic activities were not largely altered. Analysis of bone matrix components exhibited increase in the number of empty lacunae in calvarial bone of aged mice. Accumulation of SOST in such lacunae suggested that loss of MMP2 resulted in loss of calaliculi. This would prevent SOST transportation from osteocytes to peristeme. Such mechanism at least in part would explain the increase in bone mass in calvaria of aged mice although long bones of these mice still exhibited low bone mineral density due to incomplete disruption of calaliculi. Where SOST would be still exported but transport of OMP1, a regulator of calcium deposition would be impaired. We also observed that another matrix molecule, osteopontin, could modulate high phosphate dependent alternation in bone metabolism, especially with respect to the function of osteoclasts in adult animals. Furthermore, we identified that one of master genes for osteoblastic differentiation, Runx2, would play an important role for the loss of bone due to unloading. These observations lead to the identification of multiple faces of mechanisms which determine bone mass and are contribute to the maintenance of bone structure and strength. Overall, regulation of bone mass by factors involved in matrix degradation and matrix signaling would determine state levels of bone mass.

2. Publications in the year 2006


3. Abstracts in the year 2006


