No. 1322

Sodium-Dependent Phosphate Transport System in the Kidney-Bone Axis －Phosphate Handling of Osteocytes－

Ken-ichi Miyamoto, Sawako Tatsumi

Molecular Nutrition, The University of Tokushima Graduate School, Tokushima, Japan.

Summary

Recent studies have shown that alterations in osteocytes metabolism occur in very early stages of chronic renal disease (CKD) and likely mediate altered bone and mineral metabolism in patients with even very mild degree of renal dysfunction. The fibroblast growth factor 23 (FGF23) and dentin matrix protein 1 (DMP1) genetic mutations cause phosphorous (Pi) metabolic disorders. FGF23 and DMP1 are made primarily in osteocytes. These are suggesting that the osteocyte plays the total systemic Pi regulation. In a previous study, we have established a transgenic mouse model, based on the diphtheria toxin (DT) receptor-mediated cell knockout (TRECK) system, in which inducible and specific ablation of osteocytes is achieved in vivo (Tatsumi S *et al*. Cell Metab 2007). Within 48 hours of DT administration, more than 70% the osteocytes were killed. "Osteocyte-ablated" mice exhibited excessive bone resorption, impaired mineralization and adipose tissue proliferation in marrow space, all of which are hallmarks of the ageing skeleton. To analysis the role of osteocyte in Pi homeostasis, we investigated renal Pi handling in the osteocyte-ablate mice. Plasma Pi and calcium concentration were not changed in the ablated mice. Plasma FGF23 levels were significantly decreased and plasma PTH levels were not changed in the ablated mice. Urinary Pi excretion was markedly increased and renal sodium dependent Pi cotransporter NaPi-IIa protein levels were significantly decreased in the ablated mice. Thus, the osteocyte-ablated mice show increased renal Pi excretion. In addition, dietary Pi manipulation was not affected Pi excretion in the osteocyte-ablated mice. We concluded that FGF23 and PTH independent system is involved in Pi homeostasis in the osteocyte-ablated mice.