

## Interaction between mineral and skeletal homeostasis in rats fed different calcium content diets with/without PTH (1-34)

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Aim of the study is to analyze how mineral and skeletal homeostases influence both the bone loss due to calcium-diet deprivation and the successive bone mass recovery after calcium-diet restoration, with/without concomitant PTH(1-34) administration. The present investigation, performed on 3-months-old Sprague-Dawley male rats, is the second step (concerning the normal-diet restoration) of a previous one (concerning the calcium-free diet)<sup>1</sup>, conducted to determine the factors mainly affecting amounts and deposition sites during bone mass recovery. Observations emerged allowed to: 1) define times and modalities of bone mass recovery; 2) identify the most involved bony architecture (trabecular or compact) in bone response to dietary regimen; 3) verify eventual effects of intermittent PTH(1-34) administration in modifying the process of bone recovery. Histomorphometric evaluations of static/dynamic bone parameters and immunohistochemical analysis for Sclerostin expression were conducted on vertebral bodies and femurs. Serum analysis for calcium, phosphorus, osteoprotegerin, bone alkaline phosphatase, CrossLaps and PTH(1-34) was also performed. Results evidenced the greater involvement of trabecular bone with respect to the cortical one, in answering to different calcium diet content, and the effect of PTH mostly in the recovery of trabecular bony architecture. Observations clearly show that the integration between mineral and skeletal homeostases occurs in determining bone response in different sites of the skeleton (axial or appendicular) with different architecture. As expected, Sclerostin expression resulted to be higher in animals fed calcium-deprived-diet with respect to the other animal groups. In conclusion, the main finding of the present study is to strengthen the importance of interplay between mineral and skeletal homeostases in modulating and guiding bone answers to mineral alterations and to underline that the more involved bony architecture is the trabecular one, the most susceptible to the dynamical balance of the two homeostases. Clinical strategies in recovery of any skeletal impairment (of metabolic or traumatic origin) must take into account: i) mostly the type of the bone architecture involved regardless of the amount of bone mass to recover and ii) the evidence that the main target of PTH(1-34) is the trabecular bone. Thus, therapeutic treatments cannot fail to consider these aspects to optimize the drug effect and speed up the recovery.

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### References

- [1] Ferretti et al. (2015). Mineral and Skeletal Homeostasis Influence the Manner of Bone Loss in Metabolic Osteoporosis due to Calcium-Deprived Diet in Different Sites of Rat Vertebra and Femur. *Biomed Res Int.* 2015:304178.

### Key words

Calcium diet content, mineral/skeletal homeostasis, trabecular bone, PTH(1-34), rat.