PiT2 deficiency results in skeletal phenotype associated with alteration of bone marrow adipose tissue

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A growing interest in the bone marrow adipose tissue (BMAT) and its intimate relationship with skeletal health has emerged during the past 10 years. We recently investigated the skeletal phenotype of PiT2 knock-out (PiT2KO) mice to determine the role of this sodium-phosphate co-transporter during skeletogenesis. We showed that PiT2KO mice exhibit reduced bone volume, impaired mineralization and altered biomechanical parameters. In addition, plasma chemistry analyses showed an increased circulating alkaline phosphatase compared to control mice. Despite the profound skeletal phenotype, we demonstrated that the skeletal effects of PiT2 deficiency are indirect. We now hypothesize that, in PiT2KO mice, the dialogue between bone and BMAT is altered and impact on skeletal health.

To characterize the BMAT phenotype, perilipin immunostaining was performed on mouse tibial sections at post-natal day 16 (n=8 PiT2WT, n=7 PiT2KO). In the PiT2KO, we showed a 3-fold increase in the number of perilipin-positive adipocytes in both the proximal and the distal MAT ($p<0,0036$ and $p<0,0076$, respectively). Despite this BMAT increase, plasma level of adiponectin was unchanged, suggesting that the metabolic activity of the PiT2-deficient adipocytes from the bone marrow was different from the one observed in some clinical conditions where BMAT is also increased. We are now evaluating the reciprocal relationship between osteoblasts and adipocytes by analysing the effect of PiT2 deficiency on mesenchymal stem cells differentiation.

Altogether, these results indicate that PiT2 could be a new player in the communication between bone and adipose tissues and reveal the PiT2KO mice as a new model to better understand the regulation of BMAT and its role on the physiology of the bone.