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## HOW THE SEVERITY LEVEL OF ENERGY DEFICIT IN MICE MODEL AFFECTS THE BONE MARROW ADIPOSITY, BONE QUALITY AND BONE MARROW STROMAL CELLS DIFFERENTIATION?

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Severe energy deficit, induced in anorexia nervosa (AN) condition, was found to be associated with changes in bone parameters that depend on the duration and severity of the disease. It was demonstrated in many studies using mouse models that Bone Marrow Adiposity (BMA) is increased in response to caloric restriction, however weight loss is generally low when there is not a body weight gain in these studies. It was widely described that low Sirtuin Type 1 (Sirt1) expression level induces adipogenic differentiation at the expense of osteoblastic differentiation. However, at present, no study focused on the regulation of Sirt1 in Bone Marrow (BM). Further, no studies focused on the link between changes in severity of energy deficit (described here in % weight loss) and Sirt1, BMA and bone mass in osteoporosis related to AN. Previously in our lab the Separation Based Anorexia (SBA) model was established to induce AN consequence in mice. Therefore, the aims of this work were to (1) determine BMA and bone changes in mice models by recreating the phenotype of AN and inducing different weight loss levels (SBA 12%; 18% and 24%); (2) establish the expression of Sirt1 in Bone Marrow Stromal Cells (BMSCs) extracted from mice models and identify their differentiation capacity. After studying bone quality, results demonstrated decrease in Trabecular (Tb.Th.) and Cortical (C.Th.) Thickness, confirming results of our previous studies and others described in literature. However, an increase in BMA was not observed. Results of the gene expression profile after 48 hours of BMSC in a standard growth medium culture showed a decrease in Sirt1 mRNA expression in SBA 12%, 18% and 24% weight loss groups, accompanied by an increase in mRNA level of

adiponectin in cells from these three SBA groups. Additionally, an increase in early osteogenic markers (mRNA levels of SP7 and COL1) was found in SBA conditions. Surprisingly, downregulation of Sirt1 did not affect the PPAR $\gamma$  and RUNX2 mRNA expression, known to be transcriptional factors of adipogenic and osteogenic differentiation respectively. To better understand changes in BMSCs, their differentiation capacities after 5, 10 and 14 days, in the co-differentiation medium which allows both osteogenic and adipogenic differentiation is now being studied. Despite the decrease in Sirt1 expression in SBA groups, not all osteogenic and adipogenic markers were affected. These preliminary results suggest that (1) not all protocols of calorie restriction induce an increase in BMA and (2) increased BMA is not necessary to induce bone alteration and changes in BMSCs activities.