# Abstracts of the ECTS 2023 Congress featuring BRS Annual Meeting

## ECTS 2023 Congress

50th European Calcified Tissue Society Congress

15 – 18 April 2023

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Each abstract was scored blind.

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HYPODD patients treated with cholecalciferol (C-cohort) or with placebo (P-cohort) were evaluated at enrollment and 2 months after for changes in the cardiovascular risk profiles. It resulted in the correction of vitamin D deficiency in all patients in the C-cohort (42.6 vs 78.1 nmol/l, p<0.05). Also, a significant reduction in the serum levels of intact parathormone (4.75 vs 4.39 pmol/l, p<0.05), total cholesterol (4.67 vs 4.23 mmol/l, p<0.05), and low-density lipoprotein (LDL) cholesterol (2.72 vs 2.02 nmol/l, p<0.05) were observed at the same timings (p<0.05). No significant change in any biochemical parameter measured was observed in the patients receiving placebo treatment. The miR-21circulating levels were measured in four C-cohort patients and five P-cohort patients. In vitro, the miR-21 levels were measured in HEK-293 cells treated with calcitriol or with ethanol vehicle control. Cholecalciferol treatment increased 25OHD levels and reduced parathormone, total cholesterol, and low-density lipoprotein cholesterol levels in C-cohort patients, whereas no significant changes in these parameters were observed in P-cohort patients. The miR-21 circulating levels did not change in the C- or the P-cohort patients upon treatment. Calcitriol treatment did not affect miR-21 levels in HEK-293 cells.

In conclusion, hypovitaminosis D correction ameliorated the cardiovascular risk profiles in hypertensive patients treated with cholecalciferol but did not influence the miR-21 expression.

**P141**

## Region-specific differences of marrow adipogenesis in mesenchymal stromal (stem) cells of human acetabulum and femur: involvement of fatty acid oxidation

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**Abstract Text**

Aging and disease-induced adipogenesis in skeletal system has been described as detrimental process for bone tissue metabolism. Dynamic of adipogenic program is controlled by microenvironmental factors and activity of bone marrow (BM) mesenchymal stromal (stem) cells (MSC)s. As different skeletal locations are not affected by extrinsic factors in same manner, we assumed that marrow adipogenic program can be distinct in acetabular (aMSCs) and femoral MSCs (fMSCs).

Here, we compared expanded aMSCs and fMSCs from matched patients undergoing hip arthroplasty (n=6, Ethical approval I-97/11). Cellular and molecular assays were performed to investigate differences in MSC features. Statistical significance was estimated by ANOVA.

Results showed that adipogenic stimuli triggered stronger adipogenesis in fMSCs when compared to acetabular counterparts (p=0.036). Tissue non-specific alkaline phosphatase (TNAP) activity and protein expression was higher in fMSCs than in aMSCs, along with significantly higher TNAP levels detected in mitochondrial-enriched fraction proteins in fMSCs. Stronger expression of mitochondrial electron transport chain (ETC) proteins, supercomplexes I and V was found in fMSCs than in aMSCs. This coincided with increased β-galactosidase and total intracellular reactive oxygen species (ROS) production in fMSCs. Lipid droplet accumulation was followed by upregulated tissue beta-galactosidase and TNAP activities, expression of glyceraldehyde 3-phosphate dehydrogenase

(GAPDH), in parallel with stimulated ROS and mitochondrial superoxide production in both MSCs. Presence of fatty acid oxidation (FAO) inhibitor etomoxir increased gene expression of fatty acid binding protein (*Fabp)4*, while decreased protein and gene expression of GAPDH in both populations. Although etomoxir supported adipogenic differentiation and β-galactosidase activity in aMSCs only, TNAP activity and ROS content stayed unaltered.

These results indicate that mitochondrial pathways required for energy production, ETC and FAO are bone-specific, and differently affect marrow adipogenesis in acetabular and femoral regions. Further elucidation of marrow adipogenesis can contribute to development of pharmacologic strategies to support skeletal and metabolic health.

**P143**

**Acute hyperglycemia increases osteokine expression in osteoblasts, while long-term exposure has an opposing effect**

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**Abstract Text**

**Background:** Impaired glucose metabolism negatively affects bone strength and quality. Elevated glucose levels may directly affect osteoblasts and impair their function. Osteoblasts communicate with other organs via hormone-like proteins, i.e. osteokines, such as osteocalcin (*Ocn*), sclerostin (*Sost*), and matrix extracellular glycophosphoprotein (*Mepe*). However, the effect of elevated glucose on osteokines is not known.

**Purpose:** To study how high extracellular glucose (hyperglycemia, HG) affects mature osteoblasts *in vitro*.

**Methods:** Primary rat bone marrow stromal cells were differentiated into osteoblasts for 10 days and exposed to HG (25mM) acutely for the last 24 or 72 hours prior to RNA collection. Cultures at normoglycemia (5.5mM) served as control. Long-term exposure was evaluated by differentiating osteoblasts in HG for 10 days. Global changes in transcriptome were assessed by mRNA sequencing (RNA-seq). Expression of selected osteokines were verified by qPCR. Cell numbers were assessed by measuring confluence after calcein staining.

**Results:** RNA-seq revealed 1927 (134 after adjusting for multiple comparison) differentially expressed genes after 24h HG exposure. Pathway analysis revealed significant changes in genes related to e.g. bone metabolism and advanced glycation end-product signaling. Several osteokines such as *Sost*, *Mepe*, and *Ocn* were upregulated in response to 24h HG in RNA-seq and by qPCR ($p<0.05$). Interestingly, 72h HG resulted in more modest global changes, only 757 (3 after adjusting) differentially expressed genes and no enriched pathways were identified. No changes in osteokines were observed. In contrast, long-term 10-day HG exposure resulted in opposing outcome on osteokines. In qPCR analysis, long-term HG significantly decreased the expression of *Ocn*, *Sost*, and *Mepe* ($p<0.05$). Cell numbers were also decreased ($p<0.05$).

**Conclusions:** Short-term HG affects osteoblast activity by increasing the expression of e.g. *Ocn, Sost*, and *Mepe*. Osteoblasts seem to adapt to HG during 72h exposure. Long-term HG significantly decreases osteokine expression and osteoblast numbers suggesting impaired osteoblast function.