Unraveling the transcriptome profile of pulsed electromagnetic field stimulation in bone regeneration using an *in vitro* investigation platform

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INTRODUCTION: Perfusion bioreactors are currently a good tool for applications in regenerative medicine and bone tissue engineering [1]. In the realm of bone and cartilage regeneration, pulsed electromagnetic field (PEMF) stimulation has become widely utilized in clinical practice [2]. Numerous signaling pathways involved in its osteogenic, chondrogenic, and anti-inflammatory effects have been identified, but the majority of the pathways are yet unknown [3]. Using a novel *in vitro* investigation platform, this study aimed to identify the signaling pathways altered by PEMF by exposing3D bone-like models to physiological-like perfusion and PEMF stimulation.

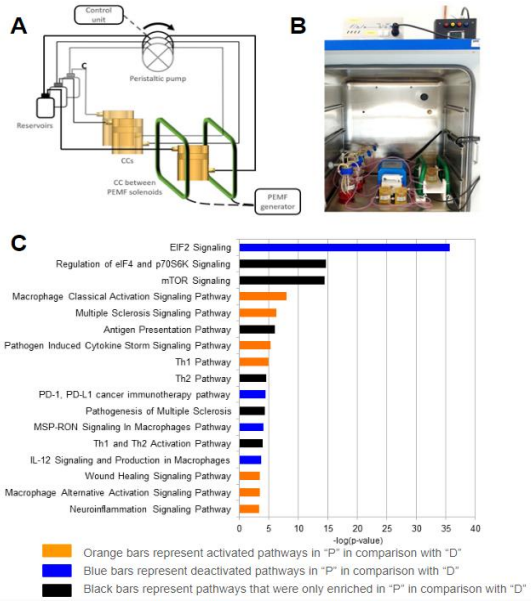

***Figure 1**: A - Schematic representation; B - the platform; C - selected pathways in the comparison of P vs. D*

EXPERIMENTAL: *Bioreactor* -An automated perfusion bioreactor with tunable perfusion (0.006-24 mL/min) and a PEMF generator (1.5 mT, 75 Hz) (Fig. 1A & 1B). *Scaffolds* - 3D-printed polylactic acid (PLA) scaffolds resembling trabecular bone microarchitecture. *Biological evaluations* - Scaffolds were seeded with human mesenchymal stem cells (hMSCs) and exposed to perfusion (0.3 mL/min) with ("P") and without ("D") PEMF stimulation (4 h/day) for 21 days in basal or osteogenic medium. Samples were evaluated in triplicates (n = 3). Static cultures served as control ("S"). RNA sequencing (RNA-Seq) and real-time qPCR were conducted to detect the signaling pathways elicited by PEMF.

RESULTS AND DISCUSSION: In the absence of biochemical, and according to RNA-Seq analysis PEMF stimulation in basal medium addresses the four stages of bone regeneration: inflammatory, fibrovascular, bone formation, and bone remodeling stages, even in the absence of a pathological state (Figure 1C).

CONCLUSIONS: The suggested *in vitro* research platform represents a novel tool for studying bone biology.

References

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