Transcriptomic Profiling of Pulsed Electromagnetic Field (PEMF)-Stimulated Biomimetic Bone Tissue Model Cultured in a Direct Perfusion Bioreactor

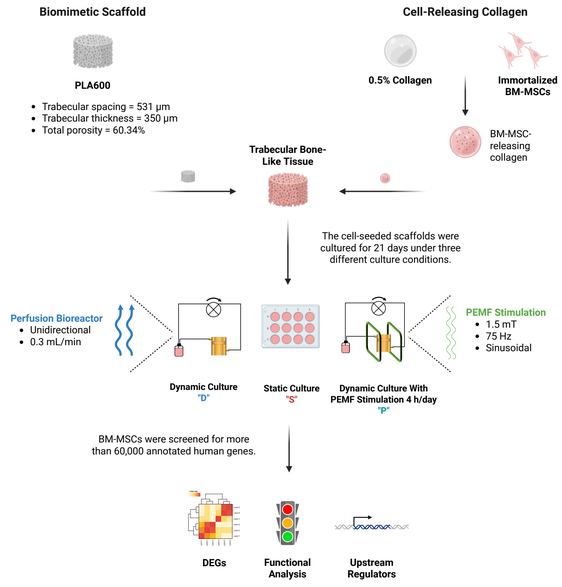
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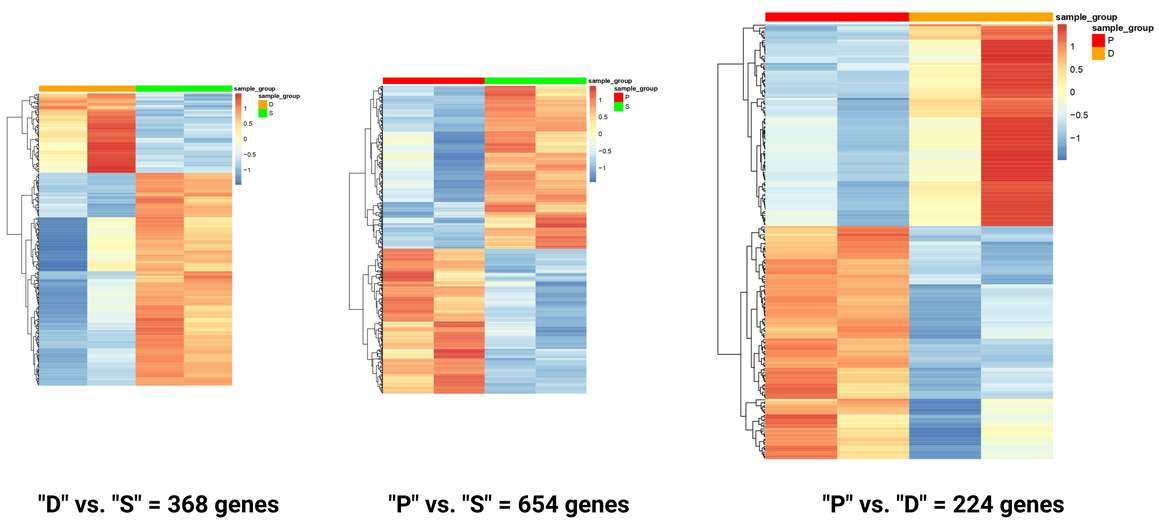
Background

- **The Problem:** While pulsed electromagnetic field (PEMF) is FDA-approved for treating nonunion fractures, its wide clinical application is hindered by a lack of standardized protocols and a poorly understood signaling pathways through which cells respond to these fields.
- **Our Approach:** We developed a biomimetic investigation platform using 3D-printed polylactic acid (PLA) scaffolds (resembling trabecular bone) and human mesenchymal stem cells (hMSCs).
- **Innovation:** A parallelized, automated perfusion bioreactor was used to provide physiological fluid flow-induced shear stress while simultaneously applying a custom-made PEMF stimulator (1.5 mT, 75 Hz).
- **Objective:** To identify the comprehensive transcriptomic profile of PEMF-driven signaling to move from empirical use toward precise, evidence-based clinical guidelines.

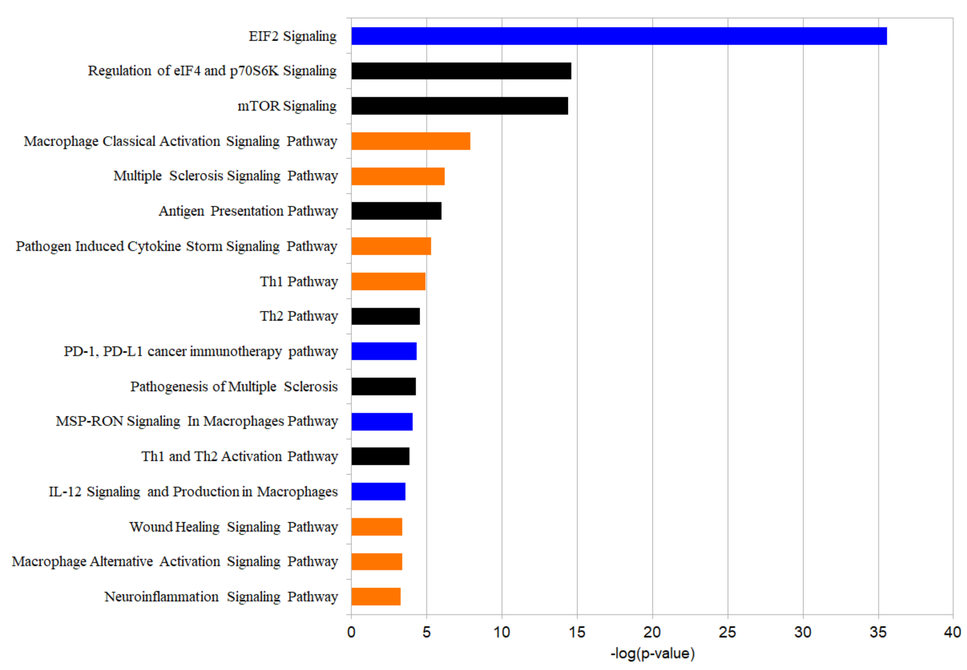
Methods



Heatmaps of DEGs



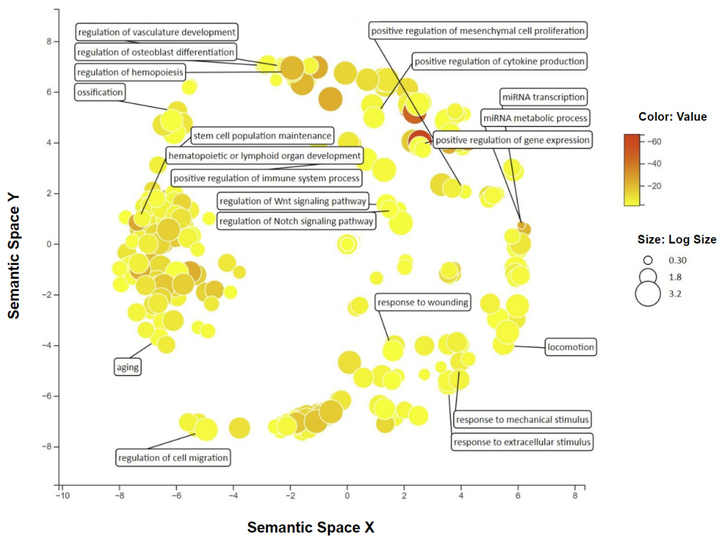
Functional Analysis of the DEGs



Bar plot representing selected enriched pathways from QIAGEN IPA of differentially expressed genes (DEGs) in the comparison of "P" vs. "D"

"D" represents bone-like, mechanical stimulation; and "P" represents bone-like, mechanical and biophysical stimulations.
Orange bars represent activated pathways; Blue bars represent deactivated pathways; and Black bars represent enriched pathways.

Pathway Enrichment Analysis of URs



Pathway enrichment analysis of the upstream regulators detected on QIAGEN IPA of the comparison of "P" vs. "D" using Revigo.

"D" represents bone-like, mechanical stimulation.; and "P" represents bone-like, mechanical and biophysical stimulations.

RNA-Seq analysis of BM-MSCs in our bioreactor platform revealed that PEMF acts as a "multi-modal orchestrator," simultaneously triggering three critical regenerative pillars:

1. **Immune/Pro-Healing Potential:** Modulation of pathways critical for the transition from inflammation to repair (Key pathways: mTOR signaling, Macrophage Classical Activation, and Wound Healing).
2. **Angiogenic Potential:** Recruitment of essential vascular growth factors (Key regulators: VEGFA, TGFβ-2, FGF-2, FGFR1).
3. **Osteogenic Potential:** Activation of the BMP/Smad and Wnt/β-catenin axes (Key regulators: BMP2/7, SMAD1/3, CTNNB1).

Conclusion

PEMF acts as a multi-modal driver of **immune**, **angiogenic**, and **osteogenic** pathways. Our **3R-compliant 3D platform** enables the precise isolation of these biophysical effects for clinical translation.

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