Osteoprogenitor Cell Differentiation into Bone is Accelerated by a Novel Delivery System of High-frequency Pulsed Electromagnetic Fields

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Purpose

The major limitation in the repair of craniofacial defects lies in the finite supply of autologous tissue (i.e., bone) available. Moreover, in many clinical scenarios, autologous tissue is simply not enough. These challenges require the investigation of novel strategies to regenerate bony tissue. To this end, we have demonstrated that the delivery of high-frequency pulsed electromagnetic fields (PEMFs) through a novel device accelerates osteogenic differentiation of murine osteoprogenitor cells.

Methods and Materials

Murine osteoprogenitor cells (C3H10T1/2) and cells harvested from the calvariae of 21-day old CD-1 mice were stimulated by the ActiPatch™ (BioElectronics, Frederick, MD) for 14 days (24 h/day).[1] The nominal carrier frequency delivered by the ActiPatch™ is 27.1 MHz. Markers of cellular proliferation and early, intermediate and terminal osteogenic differentiation were measured and compared to unstimulated controls.

Results

Alkaline phosphatase (ALP) activity, an early marker of osteogenic differentiation[2], was significantly elevated in PEMF-stimulated C3H10T1/2 cells and primary calvarial cells at multiple time points throughout the study **(Figure 1)**. In addition, stimulated C3H10T1/2 cells expressed increased mRNA transcript levels of osteocalcin, p38α, and BMP-2, -4, -6, -7, and -9. Stimulated C3H10T1/2 cells also displayed increased osteocalcin and osteopontin protein expression as assessed by immunohistochemical staining. Both C3H10T1/2 and primary calvarial cells that underwent PEMF stimulation displayed increased bone nodule formation at day 14 via Alizarin red S staining **(Figure 2)**. PEMF stimulation did not induce alterations of cellular proliferation patterns in either cell line.

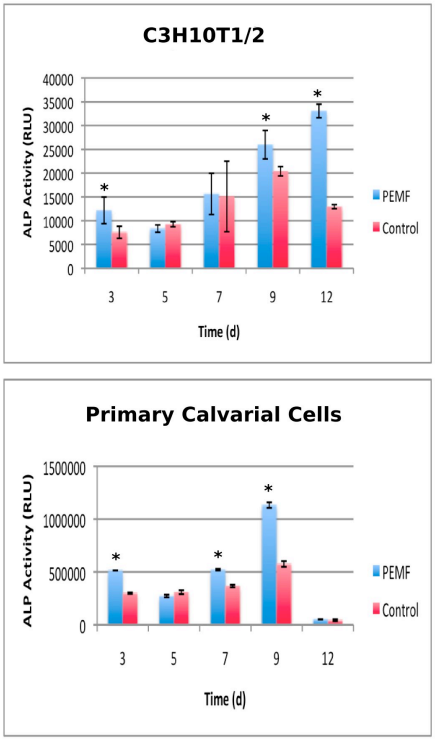

Figure 1. Alkaline phosphatase (ALP) activity in stimulated and unstimulated C3H10T1/2 and primary calvarial cells. ALP activity was measured at 3, 5, 7, 9, and 12 days after the initiation of PEMF stimulation. *p<0.05.

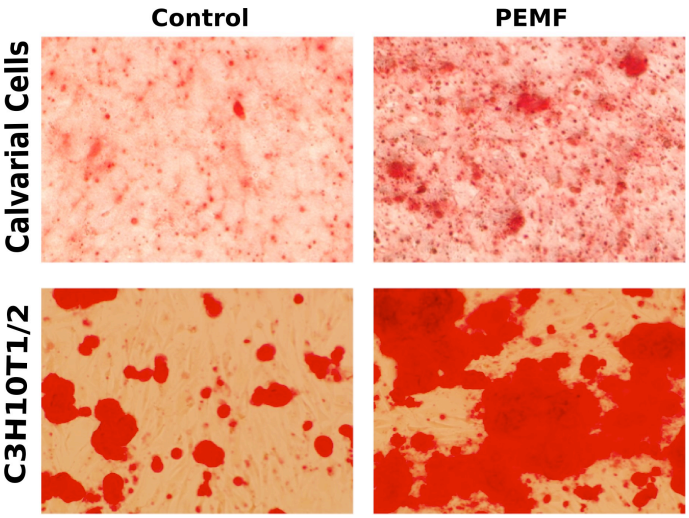

Figure 2. Alizarin red S staining of stimulated and unstimulated C3H10T1/2 and primary calvarial cells. Staining was performed 14 days after initiation of PEMF stimulation.

Conclusion

We have demonstrated that a novel delivery system of high-frequency PEMFs is capable of accelerating osteoprogenitor cell differentiation into bone. Our findings evoke future experiments to address the cell-specific response to this form of biophysical stimulation, the mechanism underlying high-frequency PEMF stimulation, and the potential role of this device for in vivo bone tissue engineering.

References

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Disclosure/Financial Support

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