

PEMF Rapidly Modulates Osteoblast Intracellular Signaling Events with Similar Intensity to Parathyroid Hormone (PTH) and Insulin

Schnoke, M. and Midura, R. Pulsed Electromagnetic Fields Rapidly Modulate Intracellular Signaling Events in Osteoblastic Cells.



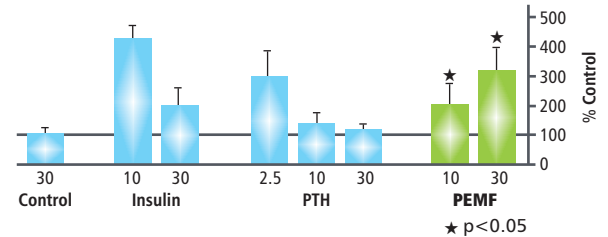
PEMF induces intracellular signaling responses similar to PTH and insulin.

- PEMF can induce intracellular signaling responses of comparable kinetic time frame and approximate intensity level to those induced by short term insulin or PTH exposure.
- PEMF induces rapid phosphorylation reactions of select intracellular signaling molecules in an osteoblast-like cell line, clearly indicating that bone cells recognize this physical stimulus in real time.
- This study supports the hypothesis that exposure of bone cells to PEMF induces immediate intracellular signal transduction events consistent with those associated with anabolic bone cell responses.

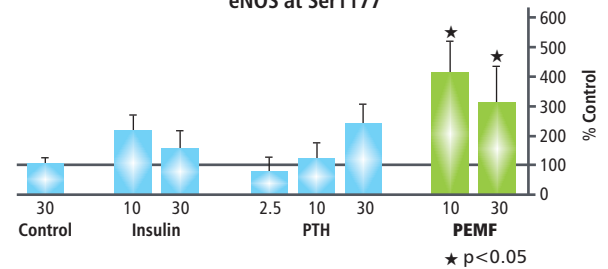
PEMF treatment induces immediate intracellular signaling events involving IRS-1, eNOS and S6

- IRS-1 activation is required for the anabolic function of PTH *in vivo*.³
- Endothelial nitric oxide synthase (eNOS) is thought to be the most highly expressed NO synthase in osteoblasts.⁴ Most notably, it has been reported that NO donors increase bone deposition in both male and female rats, and in postmenopausal women.⁵
- Consistent with prior findings,⁶ this study in the UMR model documents that short duration PEMF exposure induces a transient phosphorylation of S6 at the activating amino acids Ser235/236. S6 activation is currently considered to be a possible indicator of cellular anabolism.⁷

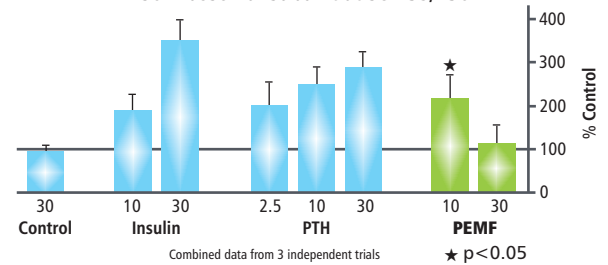
PEMF Treatment Induces Phosphorylation of IRS-1 at Ser307



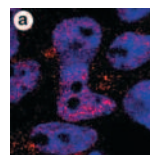
PEMF Treatment Induces Phosphorylation of eNOS at Ser1177



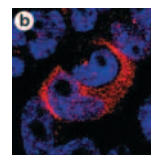
PEMF Treatment Induces Phosphorylation of the S6 Ribosomal Subunit at Ser235/236



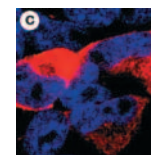
PEMF Induces Phosphorylation of S6 Translocation to the Cytoplasm



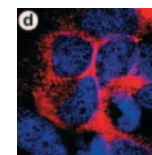
Untreated Cells



10 minute PEMF Exposure



30 minute PTH Exposure



30 minute Insulin Exposure

Evidence of S6 Activation

1. Schnoke, M. and Midura, R. J. Pulsed Electromagnetic Fields Rapidly Modulate Intracellular Signaling Events in Osteoblastic Cells: Comparison to Parathyroid Hormone and Insulin. *Journal of Orthopaedic Research*, July 2007; Vol. 25: 933-940.
 2. Kozawa O, Matsuno H, Uematsu T. 2001. Involvement of p70 S6 Kinase in Bone morphogenetic protein signaling: Vascular endothelial growth factor synthesis by bone morphogenetic Protein-4 in osteoblasts. *J Cell Biochem* 31:430-436.
 3. Dufrer A, Thomas G. 1999. Ribosomal S6 kinase signaling and the control of translation. *Exp Cell Res* 253:100-109.
 4. Yamaguchi M, Ogata N, Shinoda Y, et al. 2005. Insulin receptor substrate-1 is required for bone anabolic function of parathyroid hormone in mice. *Endocrinology* 146:2620-2628.
 5. Aguirre J, Buttery L, O'Shaughnessy M, et al. 2001. Endothelial nitric oxide synthase gene-deficient mice demonstrate marked retardation in postnatal bone formation, reduced bone volume, and defects in osteoblast maturation and activity. *Am J Pathol* 158:247-257.
 6. Patterson et al. Exposure of Murine Cells to Pulsed Electromagnetic Fields Rapidly Activates the mTOR Signaling Pathway. *Bioelectromagnetics* 2006; Vol. 27: 535-544.
 7. Wimalawansa SJ. 2000. Nitroglycerin therapy is as efficacious as standard estrogen replacement therapy (Premarin) in prevention of oophorectomy-induced bone loss: a human pilot clinical study. *J Bone Miner Res* 15: 2240-2244.