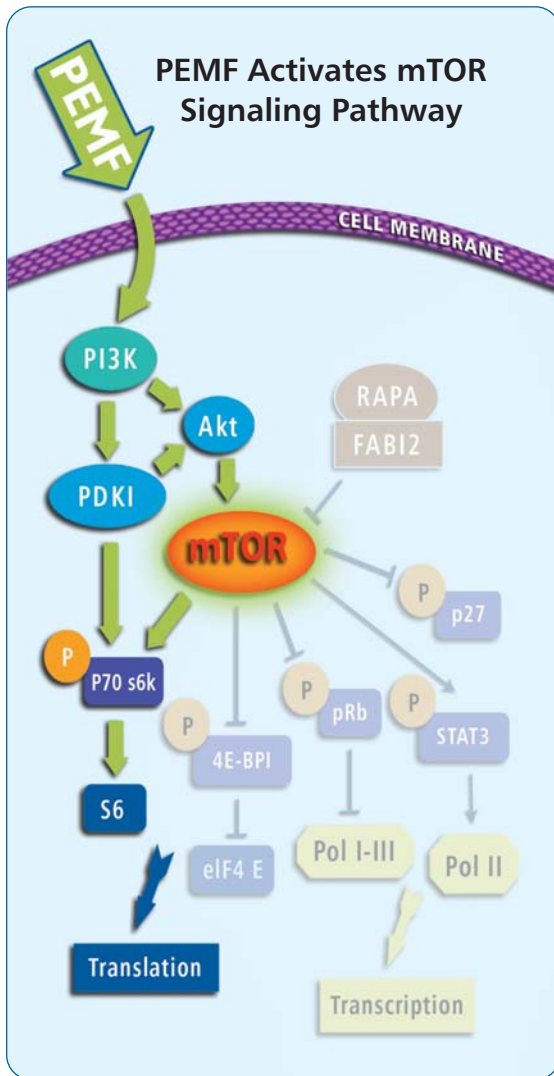


# Cell Signaling Events Induced by PEMF Follow Known Pathways for Bone Formation

Patterson T, Sakai Y, Grabiner M, Ibiwoye M, Midura R, Zborowski M, Wolfman A:  
Exposure of Murine Cells to Pulsed Electromagnetic Fields Rapidly Activates the mTOR Signaling Pathway.  
*Bioelectromagnetics* 2006; Vol. 27: 535-544.

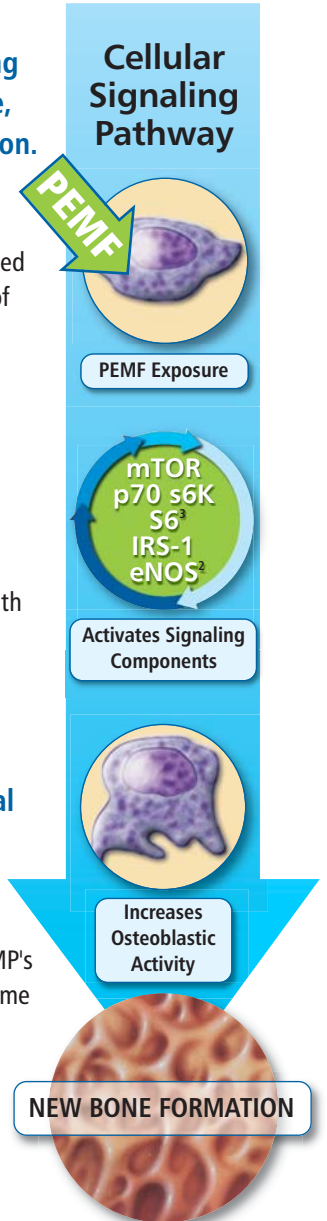


**PEMF activates mTOR, a critical component of a growth factor signaling pathway, early in the cellular response, resulting in cell growth and proliferation.**

- Exposure of MC3T3-E1 cells to PEMF resulted in a time-dependent increase in p-mTOR (Ser 2448), with a 75% increase detected within 10 minutes, peaking at 1 hr post onset of exposure and returning to baseline in 3 hours.
- Patterson, et al., showed that mTOR, its immediate downstream target (p70 S6 kinase) and the p70 S6 kinase downstream target (the ribosomal protein S6) were all phosphorylated by PEMF exposure in MC3T3-E1 cells.
- PEMF exposure is activating mTOR through a PI3-kinase-dependent pathway. The rapidity with which the mTOR pathway is activated by PEMF exposure, in both osteoblasts and fibroblasts, suggests that it is an early event in the cellular response.

**PEMF and BMP-4 activate similar signal transduction pathways.**

- Recently, Kozawa et al., 2001, reported that BMP-4 also leads to phosphorylation of p70 S6 kinase, raising the possibility that PEMF and BMPs affect osteoblast function by activation of the same signal transduction pathway(s).<sup>1</sup>



1. 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.  
2. Schnoke M and Midura R. 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.  
3. Patterson et al. Exposure of Murine Cells to Pulsed Electromagnetic Fields Rapidly Activates the mTOR Signaling Pathway. *Bioelectromagnetics* 2006; Vol. 27: 535-544.