# Static Magnetic Fields in the Regulation of Bone Cell Function and Cell Differentiation

by

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# ABSTRACT

The prevalence of musculoskeletal disorders renders a better understanding of the cellular processes and therapies equipped to manage the condition and enhance patients' standard of living. Common treatments of musculoskeletal disorders involve the use of pharmacological agents, growth factors and life-styles changes. In addition, biophysical approaches (mechanical loading, electric fields and magnetic fields) have been explored for the treatment of bone-related fractures and disorders. Although investigated both *in vitro* and *in vivo*, the precise molecular mechanisms by which bone formation ensues is still unknown. Our hypothesis is that strong static magnetic fields (SSMFs) modulate key (molecular) markers of early bone cell differentiation and/or transcriptional factors for key cellular functions accelerating matrix deposition and mineralization. To test this hypothesis, studies examining the effects on key bone cell functions (proliferation, differentiation, and extracellular matrix synthesis) and early bone formation, using normal human osteoblasts (NHOst) and human mesenchymal stem (hMSCs) cells as *in vitro* cell systems were exposed to a SSMF in the order of 1 Tesla. In addition, studies targeting applications to tissue engineering were explored by exposing cell-scaffold constructs to various SSMF exposure regimes. Key findings from this thesis demonstrated that SSMFs can significantly modulate cell proliferative activities after 6 hr exposures. PCR (RT-PCR and qPCR) revealed modulation of key bone transcription factor, osterix, expressed in developing bone and necessary for both intramembraneous and endochondral ossification processes, after 6 hr treatments in both NHOst cells and hMSCs. Furthermore, significant enhancement of extracellular matrix synthesis in the form of calcium accumulation and collagen deposition was observed after 4 and 9 day SSMF treatments in NHOst cells. Conjunctional treatment with anabolic bone forming agents, bisphosphonates and BMP-2, revealed specific genetic modulation of early bone-related genes as well as accumulation of extracellular matrix components (collagen I and mineralized bone nodule formation). Specifically, SSMFs with BP treatment support more homogeneous mineralization activity. MicroCT assessment of polymeric scaffold-NHOst cell constructs exposed to SSMFs resulted in sites of early mineralization and HA accumulation after SSMF exposure. Those scaffolds exposed to SSMF treatment

showed mineral distributed both toward the center with larger patches of mineral in the peripheral regions.

To our knowledge this is the first study to link SSMF treatment with modulation of transcriptional factor, Sp7, in NHOst cells with the potential to engage in mineralization activity leading to new bone formation. hMSCs, cultured in the presence of osteogenic promoting agents with SSMF exposure, engaged in upregulation of Sp7 and OPN promoting progression down the osteogenic lineage. These experiments reveal distinct alterations of bone cell function and differentiation after treatment with SSMFs providing evidence that this specific biophysical stimulus can promote key osteoblast functions with potential application to bone tissue engineering and the development of novel therapies for the treatment of musculoskeletal disorders.