

Kisspeptin's Role in Bone Cell Differentiation & Growth

Jordan A. Matz, Julia M Hum, Ph.D. | College of Osteopathic Medicine | Marian University



ABSTRACT

Introduction: Kisspeptin together with its receptor, GPR54 (Kiss1R), are known for their function as the principal regulators of the onset of mammalian puberty. Given the characteristic growth spurt and bone development that occurs during puberty, recent studies have provided insights into the role kisspeptin has in the control of skeletal homeostasis as well as bone cell differentiation. **Objective:** The present study hypothesizes kisspeptin and/or its receptor are expressed by bone cells and provide a communication pathway to regulate growth and differentiation. The objective of this work is to establish the expression patterns of kisspeptin and Kiss1R across various bone cell lines, as well as changes in their respective expression patterns with aging and mechanical stress.

Methods: Osteoblast precursor cell line, MC3T3-E1, was cultured and cells were harvested to perform western blots to characterize the baseline expression patterns of kisspeptin and Kiss1R, respectively. **Ongoing studies:** Next, the role of kisspeptin and its receptor will be investigated in MC3T3-E1 cells placed under mechanical stress, via an orbital shaker. In addition, the expression pattern of kisspeptin and its receptor will be characterized in the long bones of young and aged mice. **Future studies:** Examine the utility of pharmacologically targeting a kisspeptin signaling pathway to promote anabolic bone growth.

BACKGROUND

Kisspeptin (KP-10):

- Human gene: *KISS1*
- Receptor: GPR54 (Kiss1R)
 - Via GPCR signaling pathway
- Most notable role:
 - Principal regulator: Onset of mammalian puberty
 - Via direct GnRH secretion initiation
 - Disruption in kisspeptin-GPR54 signaling system:
 - Hypogonadotropic hypogonadism
- Source in humans:
 - Majority neuronal cell bodies localized to:
 - Infundibular (arcuate) nucleus
 - Rostral pre-optic region

Previous Study:

- KP-10/GPR54 signaling induces osteoblast differentiation in C3H10T1/2 cell line (Son, *et al.*, 2018)
 - KP-10 induces osteogenesis by acting directly on bone

PRELIMINARY DATA

Figure 1: Kiss1R expression in osteoblasts

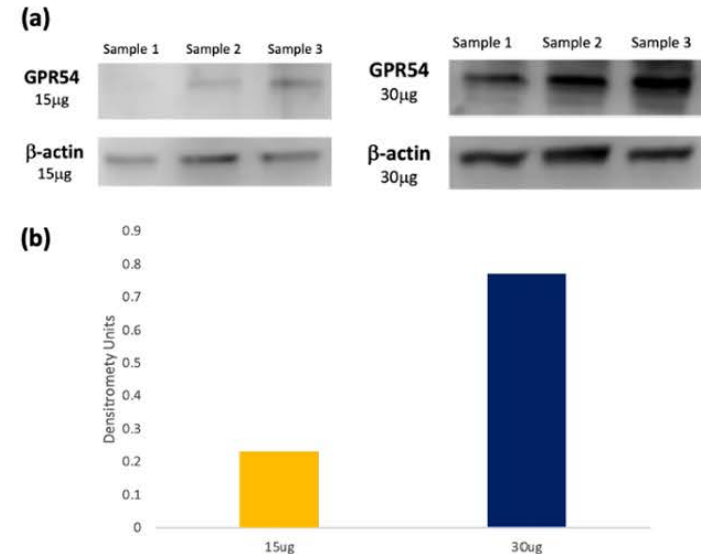


Figure 1. (a) Cells from the osteoblast-like cell line, MC3T3-E1, were cultured and harvested. Protein was extracted and evaluated by Western blot at a loading dose of 15- and 30-mg (n=3). (b) NIH software program, ImageJ, was used to quantify GPR54 and β -actin.

FUTURE ENDEAVORS

- Investigate whether GPR54 expression changes when introduced to mechanical stress in MC3T3-E1 cell line
- Examine utility of pharmacologically targeting the kisspeptin signaling pathway to promote anabolic bone growth
- Characterize Kisspeptin/GPR54 expression in other bone cell lines, such as the osteocyte precursor line, MLO-Y4.
- Induce expression of proteins normally activated during bone cell differentiation by treating GPR54-expressing bone cells with kisspeptin

