

Synthetic Peptide CK2.3 Enhances Bone Mineral Density in Senile Mice

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ABSTRACT

Background: Osteoporosis is a silent disease caused by low bone mineral density that results in bone fractures in 1 out of 2 women and 1 in 4 men over the age of 50. Although several treatments for osteopenia and osteoporosis are available, they have severe side effects and new treatments are desperately needed. Current treatments usually target osteoclasts and inhibit their activity or differentiation. Treatments that decrease osteoclast differentiation and activity but enhance osteogenesis and osteoblast activity are not available. We recently developed a peptide, CK2.3, that induces bone formation and increases bone mineral density as demonstrated by injection over the calvaria of 6 to 9-day-old mice and tail vein injection of 8-week-old mice. CK2.3 also decreased osteoclast formation and activity. However, these studies raise questions: does CK2.3 induce similar results in old mice and if so, what is the effective CK2.3 concentration and, is the bone mineral density of vertebrae of the spinal column increased as well?

Methods: CK2.3 was systematically injected into the tail vein of female 6-month old mice with various concentrations of CK2.3: 0.76 µg/kg, 2.3 µg/kg, or 6.9 µg/kg per mice. Mice were sacrificed one week, two weeks, and four weeks after the first injection. Their spines and femurs were collected and analyzed for bone formation.

Introduction:

Bone remodeling is a dynamic process and the balance between osteoclast and osteoblast activity is key to the normal bone remodeling. Changes in this balance may cause many bone diseases, including osteoporosis. Age-related or senile osteoporosis is the most common type of osteoporosis especially in the elderly. Bone fractures are often the secondary complication in patients with hip fractures posing a serious threat to the patients. The mortality rate ranges from 10% to 40% during the first year after the fracture [1]. Osteoporosis affects more than 10 million adults in the United States [2]. Treatment of osteoporosis-related fractures is costly [3]. Current treatments for osteoporosis include bisphosphonates or hormone therapy; however these treatments exhibit some serious side effects including jaw pain, esophageal cancer, and stroke [4,5].

Therefore, a new treatment for osteoporosis with less severe side effects is needed to improve the quality of life for patients.

Discussion:

Osteoporosis is a bone disease that affects an estimated 10 million adults in the US [2]. Typically, treatments for osteoporosis include bisphosphonates and hormone therapy. However, these drugs often have detrimental side effects [4,5]. Other treatments, such as rhBMP2 therapy, focus on bone fracture healing by enhancing osteoblastogenesis [6]. Nevertheless, rhBMP2 also has limitations including its direct and indirect enhancement of osteoclastogenesis and bone resorption [8-11]. Our research led us to discover CK2 as a regulatory protein of BMP2 signaling pathway [13]. The blocking of the binding of CK2 at one of the three potential binding sites on BMPRIa resulted in enhancing bone mineralization in vitro and in vivo and suppressing osteoclastogenesis and bone resorption in vitro [14]. In this study, we used 6-month-old female mice. It was reported that female mice had lower total body BMD and bone volume to tissue volume ratio (BV/TV) than male mice at 4 to 20-month-old [25]. In addition, their study reported that both male and female mice were reported to have a decrease in total bone BMD and BV/TV. Furthermore, it shows that women over the age of 50 have 4 times higher rate of osteoporosis and 2 times higher rate of osteopenia than men [26]. Thus, for this study female mice were chosen.

Conclusion: For the first time, this study showed the increase of lumbar spine BMD by CK2.3. Moreover, it showed that enhancement of femur BMD was accompanied by increased femur stiffness only at medium concentration of CK2.3 four weeks after the first injection indicating the maintenance of bone's structural integrity by CK2.3

Keywords: Casein kinase II; Bone morphogenetic protein; Osteoporosis; Osteoblastogenesis; Osteoclastogenesis.