PREVENTION OF GLUCOCORTICOID INDUCED OSTEONECROSIS WITH EITHER PARATHYROID HORMONE OR LLP2A-ALE

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Abstract
Aromatase osteonecrosis (ON) results from reduced bone vascularity. Glucocorticoids (GC) are a major risk factor for ON. GCs reduce vascular endothelial growth factor, vascular density, and bone mass in mice. LLP2A-Ale is a bone targeted therapy that directs mesenchymal stem cells to bone surfaces. LLP2A-Ale and PTH reduced GC-induced bone changes in mice (Mohan et al CTI 2017). The aim of this study was to determine if PTH or LLP2A-Ale co-treatment could prevent GC-induced ON and GC induced changes in bone blood flow.

Methods
5-week-old male BALB/c mice were randomized into groups receiving Placebo (PL), GC (0 mg/L dexamethasone in drinking water), GC+500 µg/kg LLP2A-Ale, GC+80 µg/kg LLP2A-Ale (SC, 1X2 wkly), or GC+48 µg/kg PTH (PTH1-34). Each, PL (n=10 for all GC groups). Mice were sacrificed on day 45. (A) MicroCT scans were obtained after sacrifice. (B) Whole femurs were decalcified and embedded in paraffin. Slices of the distal femoral epiphysis were stained with H&E. GC was identified in the DF epiphysis (DFE) using modified criteria. Microvessel density was calculated using the primary marker CD31 and PECAM1 expression was significantly lower in GC than PL and Ale or GC + PTH (p<0.05). MicroCT and histology revealed significantly lower GC-induced bone vascularity compared to PL and Ale or GC + PTH. Glucocorticoids (GC) are a major risk factor for ON. GCs reduce vascular endothelial growth factor, vascular density, and bone mass in mice. LLP2A-Ale is a bone targeted therapy that directs mesenchymal stem cells to bone surfaces. LLP2A-Ale and PTH reduced GC-induced bone changes in mice (Mohan et al CTI 2017). The aim of this study was to determine if PTH or LLP2A-Ale co-treatment could prevent GC-induced ON and GC induced changes in bone blood flow.

Results
MicroCT and histology revealed significantly lower GC-induced bone vascularity compared to PL and Ale or GC + PTH. Glucocorticoids (GC) are a major risk factor for ON. GCs reduce vascular endothelial growth factor, vascular density, and bone mass in mice. LLP2A-Ale is a bone targeted therapy that directs mesenchymal stem cells to bone surfaces. LLP2A-Ale and PTH reduced GC-induced bone changes in mice (Mohan et al CTI 2017). The aim of this study was to determine if PTH or LLP2A-Ale co-treatment could prevent GC-induced ON and GC induced changes in bone blood flow.

Discussion
MicroCT and histology revealed significantly lower GC-induced bone vascularity compared to PL and Ale or GC + PTH. Glucocorticoids (GC) are a major risk factor for ON. GCs reduce vascular endothelial growth factor, vascular density, and bone mass in mice. LLP2A-Ale is a bone targeted therapy that directs mesenchymal stem cells to bone surfaces. LLP2A-Ale and PTH reduced GC-induced bone changes in mice (Mohan et al CTI 2017). The aim of this study was to determine if PTH or LLP2A-Ale co-treatment could prevent GC-induced ON and GC induced changes in bone blood flow.

Acknowledgement
This work was supported by National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIH/NAMS); Grant numbers: R01AR043052; the California Institute of Regenerative Medicine (CIRM); and the endowment for the Center for Musculoskeletal Health and the Aging Endowment to NEL.