

## LMP Knockout Mice Have Reduced Spine Trabecular Bone Density on Micro-computed Tomography Due to Decreased BMP Responsiveness.

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### Introduction

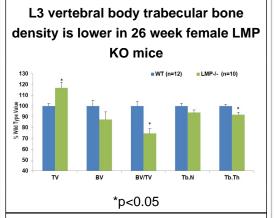
Bone morphogenetic protein(BMP)-2 has been shown to be a potent enhancer of spine fusion but its role in osteoporosis has not yet been defined. The number of vertebral compression fractures related to osteoporosis is expected to double by 2025.(1) BMP-2 responsiveness has recently been shown to be enhanced by an intracellular protein, Lim Mineralization Protein(LMP)-1. Because of BMP-2's critical role in development, attempted knockout of the BMP-2 gene is embryonically lethal. To model globally decreased BMP responsiveness, we generated an LMP knockout mouse and hypothesized it would have decreased bone mineral density.

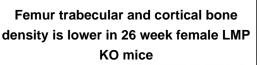
### Methods

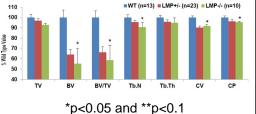
Global Pdlim7 (mouse equivalent of LMP) knockout mice were developed using gene trapping and breeding techniques. The mice were euthanized at 18 or 26 weeks for analysis. Trabecular bone morphology of the femur and spine were measured using micro-computed tomography.

### Results

The LMP KO mice weighed less and were shorter at 18 weeks, p=0.001. In the female KO mice, there was a decrease in the femur trabecular bone density (BV/TV) of 23% (p=0.06) at 18 weeks and 45% (p=0.007) at 26 weeks. This was mirrored in the vertebral body BV/TV ratio with a 25% decrease in the KOs at 26 weeks, p = 0.0005. The cortical bone volume of female KO mice was decreased by 6% (p=0.06) at 18 weeks and 8% (p=0.002) at 26 weeks. Marrow derived stromal cells from the LMP deficient mice formed significantly less mineralization.

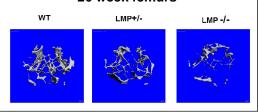


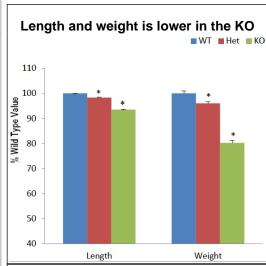




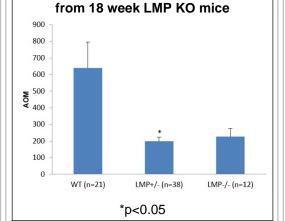
Femur trabecular and cortical bone density is lower in 18 week female LMP *KO* mice  $\frac{10^{-0}}{\sqrt{10^{-0}}} \frac{10^{-0}}{\sqrt{10^{-0}}} \frac{10^$ 

### Trabecular 3D cross sections of female 26 week femurs





# The area of mineralization is lower in cultured marrow stromal cells obtained



### Conclusions

We present here the development of the first LMP knockout mouse. We conclude that LMP is an important determinant of weight and length, female bone density and marrow stromal cell propensity for mineralization. We speculate that these mice will be useful in discovering and testing novel therapeutics to improve BMP-2 responsiveness and prevent vertebral fractures.

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#### Abbreviations

AOM=Area of mineralization, BMP=Bone morphogenetic protein, BV=Bone volume, Conn.D=Trabecular connectivity density, CP=Cortical porosity, CV=Cortical volume, het=heterozygous, KO=Knockout, LMP=Lim mineralization protein, Tb.N=Trabecular number, Tb. SP=Trabecular space, Tb.Th=Trabecular thickness, TV=Trabecular total volume, WT=Wild type