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## Notum: A Novel Regulator of Bone and Its Implications in Osteoporosis

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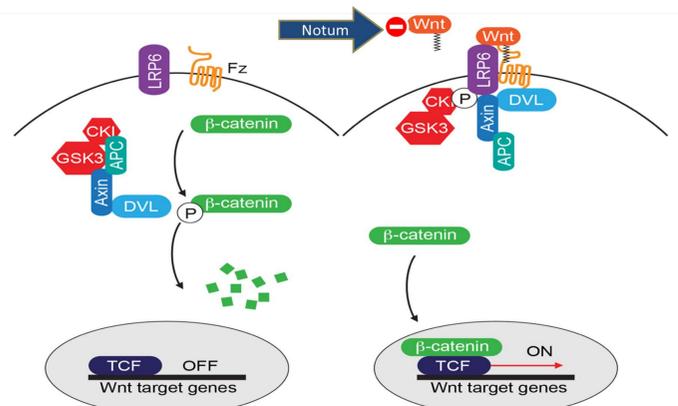


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# The Role of Notum in Bone's Response to Mechanical Loading and Aging

- Osteoporosis is a silent, dangerous pathology frequently undiagnosed until patients experience a major fracture.
- About 1 in 2 women and 1 in 4 men ages 50 and above will experience bone fractures due to osteoporosis.
- Fractures from osteoporosis may lead to a 20% increase in mortality.
- Notum is a lipase, primarily expressed in the liver, that inhibits the Wnt signaling pathway. The Wnt pathway is involved in growth, development, and healing.
- Recently, inhibition or absence of Notum led to increased endocortical bone formation and thickness via osteoblast activity in a mouse model.
- Potentially, modifying factors that affect Notum expression could promote anabolic bone growth.



## HYPOTHESIS

**Notum expression is affected by mechanical loading and aging.**



# Notum: A Novel Regulator of Bone and Its Implications in Osteoporosis

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## RESULTS

*Notum expression increases in aged bone*

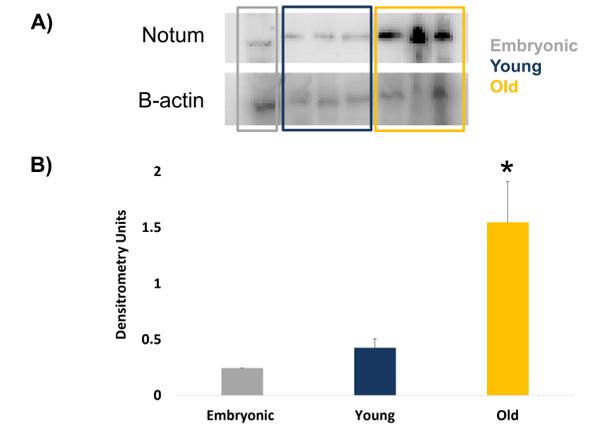


Figure 3. A) Whole bone samples were taken from different aged mice, protein extracted and evaluated by Western blot. "Embryo." (embryonic) sample age: embryonic week 12. "Young" samples: 1 week, 4 weeks, 8 weeks. "Old" samples: 15 weeks, 35 weeks, 55 weeks. B) The software program ImageJ was used to quantify Notum and B-actin levels (\*p<0.05).

## SUMMARY

- Mechanical loading decreases Notum protein expression in an osteocyte cell line, MLOY4.
- Mechanical loading has no effect on Notum expression in an osteoblast cell line, MC3T3-E1.
- Aging increases the expression of the Notum gene in a mouse model.

## FUTURE DIRECTIONS

- Continue trials on assessing mechanical loading affect on Notum expression in osteoblast cell line, MC3T3-E1.
- Future studies in inhibiting Notum expression in bone via a small molecule inhibitor and an siRNA will be conducted to investigate a potential novel approach to promoting anabolic bone growth.

## RESULTS

*Mechanical loading decreases Notum expression*

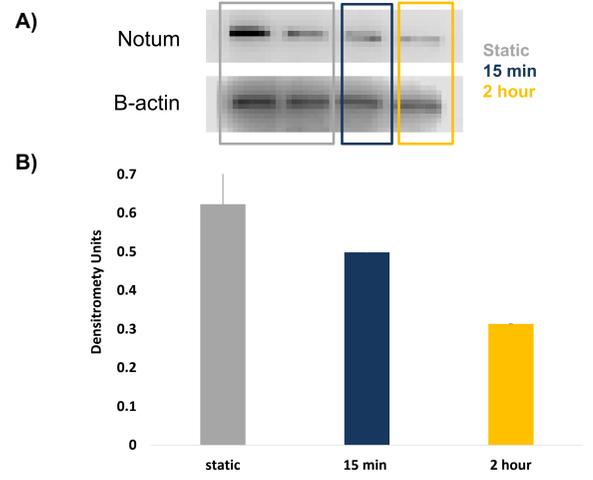


Figure 1. A) Cells from an osteocyte cell line, MLOY4, were cultured, harvested and subjected to mechanical loading mimicked via orbital shear stress for 15 minutes or 2 hours. Protein was then isolated and evaluated by Western blot. B) The software program ImageJ was used to quantify Notum and B-actin levels.

*Mechanical loading has no effect on Notum expression*

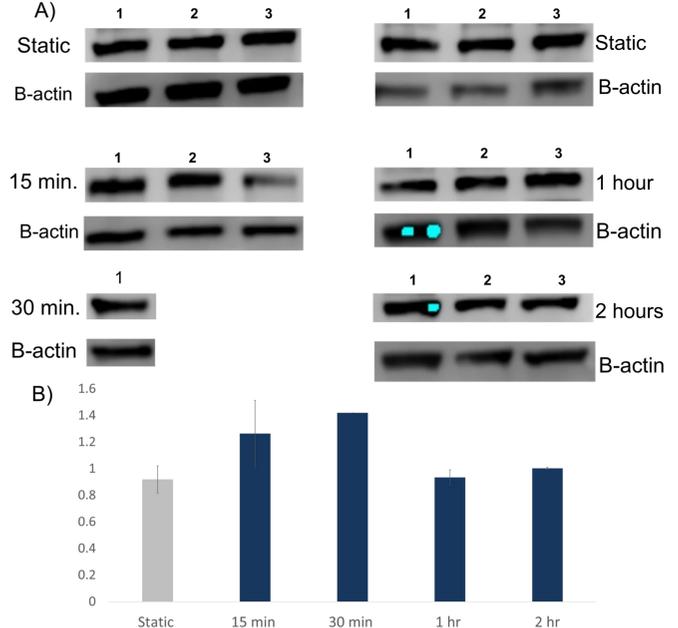


Figure 2. A) Cells from an osteoblast cell line, MC3T3-E1, were cultured, harvested and subjected to mechanical loading mimicked via orbital shear stress for 15 minutes, 30 minutes, 1 hour, and 2 hours. Protein was then isolated and evaluated via Western blot. B) The software program ImageJ was used to quantify Notum and B-actin levels.

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