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

Mariah Castanon
Marian University - Indianapolis

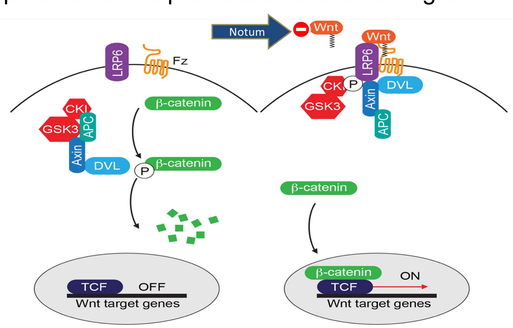
Vince Marshall OMS-3
Marian University - Indianapolis

Bryan Wacker OMS-3
Marian University - Indianapolis

Julia M. Hum Ph.D
Marian University - Indianapolis

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.

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Mariah Castanon, Vince Marshall, Bryan Wacker, & Julia M. Hum

Division of Biomedical Sciences
Marian University College of Osteopathic Medicine

RESULTS

Mechanical loading decreases Notum expression

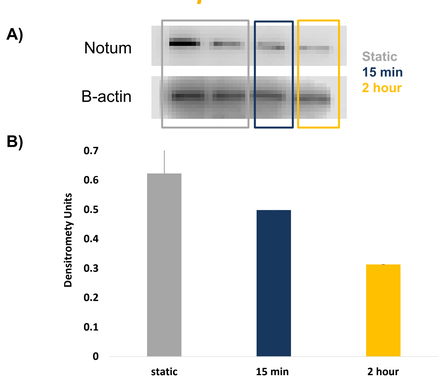

Figure 1. A) Cells from an osteocyte cell line, MLOY4, were cultured, harvested and subjected to mechanical loading mimicked via orbital shear stress for 15 minutes or 2 hours. Protein was then isolated and evaluated by Western blot. B) The software program ImageJ was used to quantify Notum and B-actin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

Mechanical loading has no effect on Notum expression

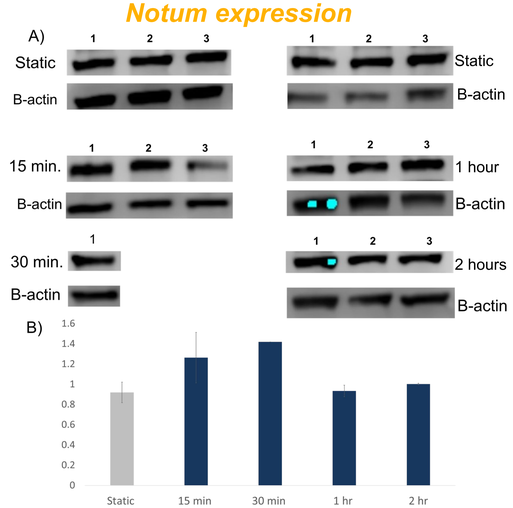

Figure 2. A) Cells from an osteoblast cell line, MC3T3-E1, were cultured, harvested and subjected to mechanical loading mimicked via orbital shear stress for 15 minutes, 30 minutes, 1 hour, and 2 hours. Protein was then isolated and evaluated via Western blot. B) The software program ImageJ was used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

RESULTS

Notum expression increases in aged bone

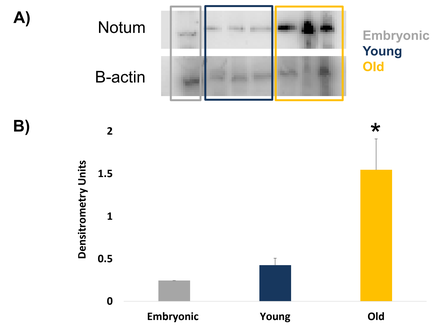

Figure 3. A) Whole bone samples were taken from different aged mice, protein extracted and evaluated by Western blot. "Embryo." (embryonic) sample age: embryonic week 12. "Young" samples: 1 week, 4 weeks, 8 weeks. "Old" samples: 15 weeks, 35 weeks, 55 weeks. B) The software program ImageJ was used to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

#HumLab
@DrJuliaHum