The Effect of the Kalirin Gene on Osteoid Development

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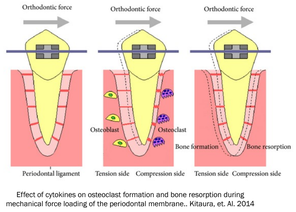
ABSTRACT

Lrp5 Gene Over-expression Leads to Decreased Tooth Movement. R. Holland*, C. Bain, A. Robling, A. Utreja. (Indiana University School of Dentistry) Lrp5 (Low-density lipoprotein receptor-related protein 5) is a co-receptor of the Wnt intracellular signaling system. The Wnt system is known to play an important role in bone biology. Increased activity of the Wnt system leads to an increase in bone mass. The aim of this study was to compare tooth movement in genetically modified Lrp5 knock-in mice to control mice. Thirty-six C57BL/6 wildtype mice were utilized. Eighteen possessed a A214V mutation and eighteen possessed a G171V mutation in the Lrp5 gene. Eighteen wild type C57BL/6 mice served as control. Experimental tooth movement was produced by attaching a 3mm closed-coil nickel-titanium spring from the first molar to the incisors. Tooth movement occurred for three weeks prior to sacrifice. For all but six mice, a microchromotagraphy scan was taken after sacrifice followed by a histologic analysis. The remaining six mice were Mice were injected with Calcin, Alizeren and Tetracycline at eight, four and two days pre-sacrifice respectively. These mice were processed in plastic and analyzed with fluorescent microscopy. Genetic knock-in mice showed higher percent bone volume (BV/TV), lower bone surface/volume ratio (BS/BV) and increased trabecular thickness (Tb.Th) compared to the control group. Cellular expression of the Sclerostin gene was higher per unit area in the genetic knock-in mice compared to the control mice. Fluorescent microscopy showed decrease in bone turnover in the genetic knock-in mice compared to the control. This study demonstrates that overexpression of the Lrp5 gene leads to an increased bone density, decreased bone turnover and a decreased rate of tooth movement in mice. Further study should be completed on the Wnt signaling pathway as this could lead to improvement of future orthodontic treatments.

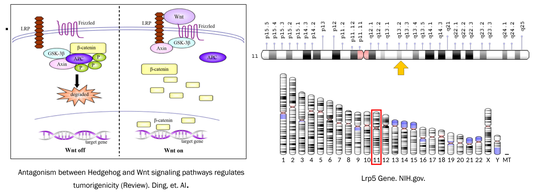
BACKGROUND



Effect of cytokines on osteoclast formation and bone resorption during mechanical force loading of the periodontal membrane., Kitaura, et. Al. 2014

Orthodontic tooth movement
occurs when bone resorption
occurs on the compression side of the socket while bone
formation occurs on the tension

The low-density lipoprotein receptor-related protein 5 (Lrp5) is a co-receptor of the Wnt signaling pathway. The Wnt pathway is known to play a role in bone formation.



Antagonism between Hedgehog and Wnt signaling pathways regulates tumorigenicity (Review). Ding, et. Al.

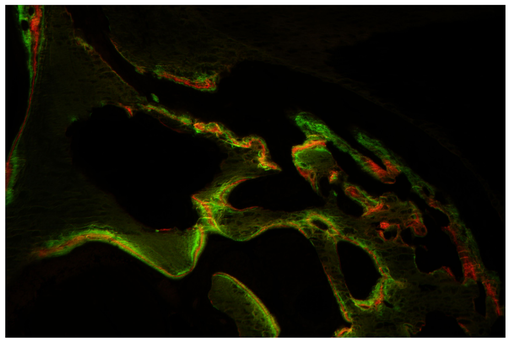
Lrp5 Gene. NIH.gov.

MATERIALS/METHODS

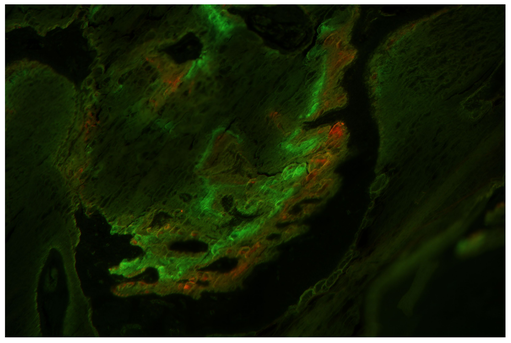
Mice: Experimental mice used for this study possess a genetic knock-in of the Lrp5 gene causing overexpression of the Lrp5 co-receptor. Two different genetic strains were included (A214V and G171V.) Eighteen A214V and eighteen G171V mice were utilized along with eighteen wild-type mice. Two mice from each group were were injected with Calcin, Alizeren and Tetracycline at eight, four and two days pre-sacrifice respectively.
Histology: Mice were sacrificed after 3 weeks of tooth movement. Mice with fluorescent labels were processed in plastic and imaged with fluorescent microscopy. The remaining mice were processed in paraffin and stained for SOST gene expression.
Microchromotography: All mice underwent microchromotography scan and scans were reconstructed and analyzed for a variety of bone paramters utilizing CTAN software.

PHOTOS

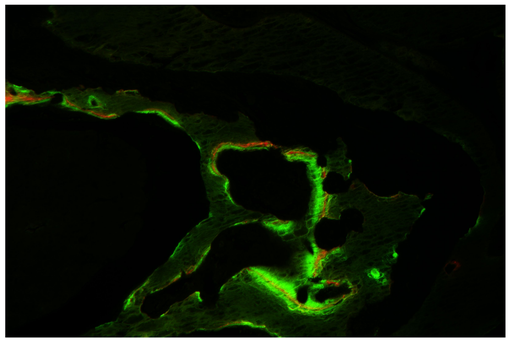
WT

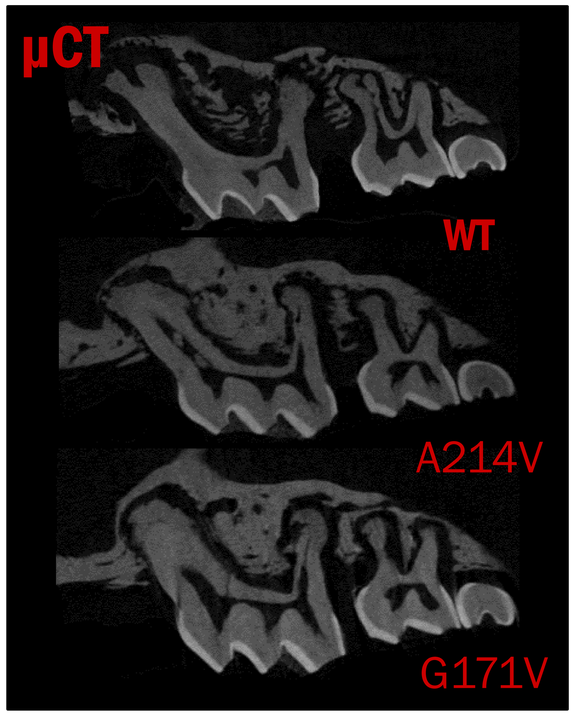


A214V

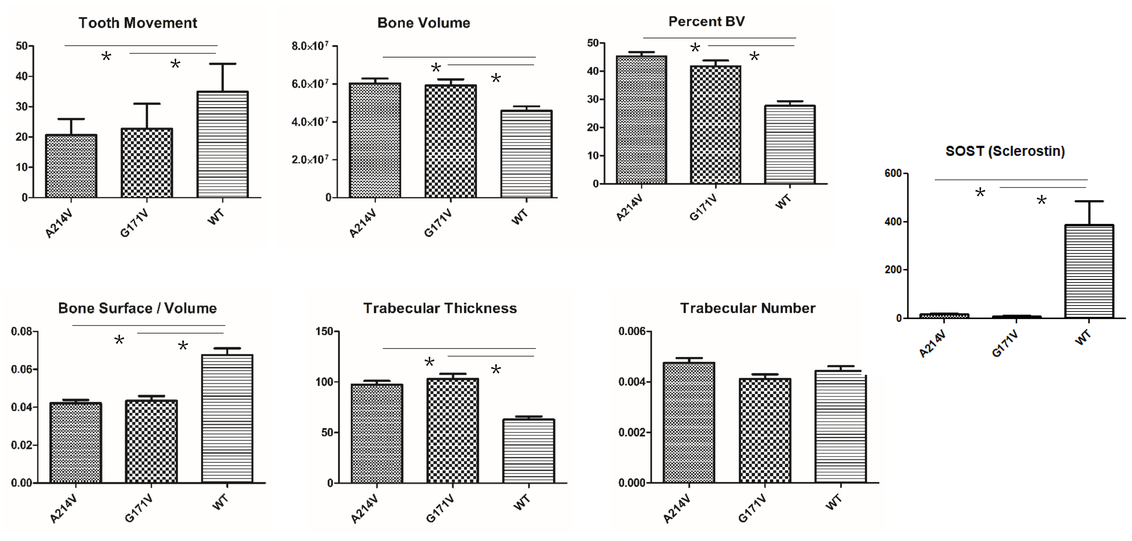


G171V





TABLES AND FIGURES



* P < 0.05

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