

The effect of Sclerostin-antibody on dental pathologies in Hyp mice

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Objective/Aim/Hypothesis:

X-linked hypophosphatemia (XLH) is the most common form of inherited rickets, affecting approximately 1 in 20,000 people. XLH is caused by an inactivating mutation in the phosphate regulating neutral endopeptidase on the X-chromosome (PHEX). This mutation leads to elevated fibroblast growth factor 23 (FGF23) levels, which subsequently impair phosphate reabsorption in the kidney and inhibit skeletal mineralization. Dental abnormalities are also common in patients with XLH and include tooth fractures, abscesses, and periodontal disorder. Our previous study demonstrated that sclerostin anti-body (Scl-Ab) improves phosphate metabolism and increases endochondral bone mass in Hyp mice (XLH murine model). This study aims to investigate the efficacy of Scl-Ab on the dentin-alveolar bone phenotype in Hyp mice.

Design/Approach/Methods:

Male hemizygous and female heterozygous Hyp mice and wild type littermates (37 male; 45 female) were used for this study. Mice were randomly assigned to biweekly subcutaneous injections of 25 mg/kg Scl-Ab or vehicle (saline) treatment starting at 12-weeks of age until sacrifice at 20 weeks of age. Left and right hemi-mandibles were collected at sacrifice. Left hemi-mandibles were analyzed with micro-computed tomography (μ CT) for assessing phenotypic changes in alveolar bone, dentin, and periodontal ligament (PDL) space. Right hemi-mandible were decalcified, paraffin embedded, stained with Hemotoxylin-Eosin (H&E), and compared for the presence of osteoid and osteocytic halos.

Results:

Consistent with our previous data in the femur, Scl-Ab treatment significantly increased bone volume over total volume (BV/TV) in the alveolar bone region ($p=0.001$ males; $p=0.002$ females). Gross comparison of H&E stained alveolar bone shows a decrease in osteoid and osteocytic halos. There was no Scl-Ab treatment effect on dentin thickness or the volume of the periodontal ligament space.

Conclusion:

The current study demonstrates that Scl-Ab treatments improve alveolar bone mass and mineralization in 20-week old Hyp mice. These findings suggest that Scl-Ab treatment may help to improve some of the alveolar bone phenotypes of XLH patients. While no significant dentin or PDL improvements were detected with μ CT analyses, future studies are needed to investigate further, such as PDL fiber-orientation and gene expression analysis.

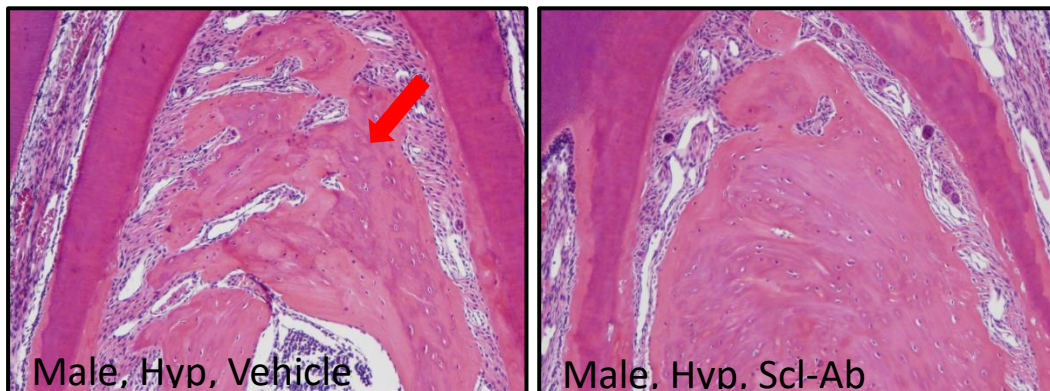


Figure 1. Representative images of H&E stained male Hyp vehicle and Scl-Ab treated mandibles. Region shown is of alveolar bone between the roots of the first molar. Vehicle treated animals have more osteoid (red arrow) present than Scl-Ab treated animals.