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TITLE: Dentoalveolar Defects in the Hyp Mouse Model of X-linked Hypophosphatemia

AUTHORS (FIRST NAME INITIAL LAST NAME): H. Zhang, M. B. Chavez, T. Kolli, M. H. Tan, H. Fong, E. Y. Chu, Y. Li, X. Ren, K. Watanabe, D. Kim, B. L. Foster

AUTHORS/INSTITUTIONS: M.B. Chavez, T. Kolli, M.H. Tan, B.L. Foster, College of Dentistry, The Ohio State University, Columbus, Ohio, UNITED STATES; H. Zhang, School of Dentistry, University of Washington, Seattle, Washington, UNITED STATES; E.Y. Chu, NIAMS/NIH, Bethesda, Maryland, UNITED STATES; K. Watanabe, Orthodontics and Dentofacial Orthopedics, Tokushima University Graduate School, Tokushima, Tokushima, JAPAN; D. Kim, Orthodontics, Ohio State University, Columbus, Ohio, UNITED STATES; H. Fong, University of Washington, Seattle, Washington, UNITED STATES; Y. Li, Sichuan University, Chengdu, Washington, CHINA; X. Ren, Shanxi Medical University, Taiyuan, Washington, CHINA;

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ABSTRACT BODY:

Objectives: Mutations in PHEX cause X-linked hypophosphatemia (XLH), a form of hypophosphatemic rickets. Hyp (Phex mutant) mice recapitulate the XLH phenotype. Dental problems are prevalent in individuals with XLH, however dentoalveolar defects remain incompletely understood. We aimed to examine Hyp mouse dentoalveolar defects to define effects of XLH on dentin, cementum, and bone, and provide insights into biomineralization processes of these tissues.

Methods: Dentoalveolar tissues from Hyp and wild-type (WT) mice at 42 and 90 days postnatal (dpn) were analyzed by histology, radiography, scanning electron microscopy (SEM), high resolution microcomputed tomography (micro-CT), static and dynamic mechanical analysis, in situ hybridization, and immunohistochemistry.

Results: Phex mRNA was expressed by odontoblasts (dentin), osteocytes (bone), and cementocytes (cellular cementum). Dentin defects in Hyp molars were indicated histologically by wide predentin, thin dentin, and extensive interglobular dentin, as confirmed by micro-CT findings of reduced dentin volume and density (p<0.01 to 0.0001). Acellular cementum was thin and showed PDL detachment, and mechanical testing indicated reduced static and dynamic stiffness (>60%; p<0.01-0.001) in Hyp vs. WT periodontia. Hyp mandibles demonstrated expanded bone with accumulation of osteoid, and micro-CT confirmed 24% decreased bone volume fraction (BV/TV; p<0.001) and 25% decreased alveolar bone density (p<0.0001). Cellular cementum area significantly increased in Hyp vs. WT molars by 90 dpn (p<0.01). Hypomineralized cementoid increased 50-fold in Hyp vs. WT mice (p<0.001), and comprised 30-40% of total cellular cementum area. Histology and SEM revealed hypomineralized “halos” surrounding Hyp cementocyte/osteocyte lacunae. Altered Spp1 and Dmp1 mRNA expression was observed in both cementocytes and osteocytes, along with abnormal BSP, OPN, and DMP1 protein distribution in Hyp bone and cementum.

Conclusions: Novel findings were identified in Hyp mouse developmental defects, including cementocyte defects paralleling those found in osteocytes. This study provides insights into XLH and fundamental processes of cementum, bone, and dentin biology.
KEYWORDS: Dentin, Enamel, Cementum, Bone, Mineralization.

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