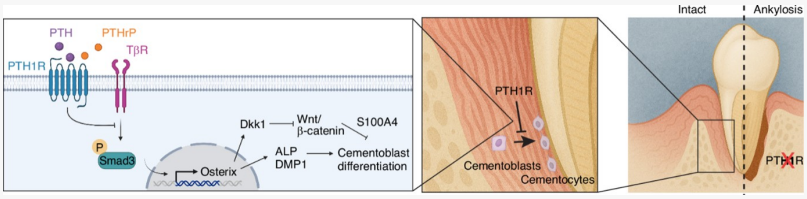
Tooth-Supporting Tissue Breakdown Linked to Key Receptor Loss in Mice

Researchers discovered that disrupted PTH1R signaling drives abnormal cementum growth and tooth-bone fusion in adult mice



Schematic showing how loss of PTH1R signaling disrupts Smad3 and Wnt pathways, driving abnormal cementum growth and pathological tooth-bone fusion.

CHENGDU, SICHUAN, CHINA, May 18, 2026 /EINPresswire.com/ -- A newly identified molecular pathway helps maintain the integrity of the bones in the skull and the face. Using mouse models, the study showed that loss of PTH1R signaling in periodontal cells triggers abnormal cementum overgrowth, severe periodontal ligament damage, and pathological tooth-bone fusion known as ankylosis. The findings uncover previously unknown mechanisms regulating adult periodontal tissue maintenance and may support future therapies for eruption disorders, ankylosis, and other periodontal diseases linked to abnormal mineralization.

Teeth remain securely attached to the jaw through a specialized support system known as the periodontium, which includes cementum, the periodontal ligament (PDL), and surrounding alveolar bone. These tissues work together to stabilize teeth while allowing them to withstand the constant mechanical forces generated during chewing and speaking. Disruption of this delicate balance can lead to ankylosis, a condition in which the tooth root becomes abnormally fused to surrounding bone, preventing normal movement and often resulting in severe dental complications. Although mutations affecting parathyroid hormone 1 receptor (PTH1R) signaling have been linked to tooth eruption disorders and root abnormalities, the precise role of this pathway in maintaining adult periodontal tissues has remained poorly understood.

Addressing this question, researchers investigated how PTH1R signaling regulates cementum homeostasis and periodontal integrity in adult mice. Using conditional genetic deletion of PTH1R in DMP1-Cre–targeted periodontal cells, the team combined microcomputed tomography imaging, histological analysis, immunohistochemistry, molecular signaling studies, and tissue quantification to examine changes in craniofacial structures and periodontal tissues. Their findings were published in Volume 14, Article number 46, of the journal Bone Research on April 27, 2026.

The research was led by Professor Xue Yuan from the Department of Otolaryngology-Head & Neck Surgery, Indiana University School of Medicine, Indianapolis, USA, along with Professor Teresita Bellido from the Department of Physiology and Cell Biology, University of Arkansas for Medical Sciences, USA.

The researchers found that mice lacking PTH1R signaling developed major abnormalities in the tissues surrounding molar teeth. Compared with healthy controls, mutant mice exhibited severe loss of the periodontal ligament, shortened tooth roots, reduced alveolar bone height, and extensive ankylosis. Interestingly, these defects were restricted mainly to molars, while incisor development remained largely unaffected. Detailed tissue analyses further revealed abnormal overgrowth of cementum, the mineralized layer covering the tooth root, together with severe disruption of collagen fiber organization within the periodontal ligament.

Further investigation showed that the ankylosed tissue originated from pathological cementum expansion rather than abnormal bone growth. Molecular analyses demonstrated that loss of PTH1R signaling triggered excessive activation of the Smad3-Osterix pathway, which promotes cementoblast differentiation and mineralization. At the same time, Dkk1 expression increased, suppressing protective Wnt signaling pathways that normally help maintain periodontal tissue balance. This combined dysregulation created a highly pro-mineralization environment that drove excessive cementum deposition and pathological tooth-bone fusion.

“Our findings identify PTH1R as a critical molecular safeguard that prevents excessive cementum formation and preserves periodontal ligament integrity,” explained Prof. Yuan. “When this signaling pathway is disrupted, the balance maintaining tooth attachment collapses, leading to pathological ankylosis and craniofacial abnormalities.”

The study may have important implications for understanding human tooth eruption disorders, infra-occluded teeth, periodontal degeneration, and ankylosis linked to PTH1R mutations. In the short term, the findings provide a clearer biological explanation for why some patients develop progressive root-bone fusion that limits orthodontic treatment and tooth retention. Over the longer term, the identified signaling pathways may support the development of targeted therapies capable of preserving periodontal tissues or preventing ankylosis progression.

“This work advances our understanding of how periodontal tissues maintain long-term stability throughout adult life,” said Prof. Bellido. “Targeting PTH1R-associated signaling networks may eventually help develop regenerative strategies for ankylosis, periodontal disease, and other craniofacial disorders involving abnormal mineralization.”

Overall, the study demonstrates that PTH1R signaling plays an essential role in maintaining periodontal homeostasis by restraining pathological cementogenesis and preserving periodontal ligament organization. By uncovering how disruption of Smad3-Osterix and Wnt signaling drives ankylosis, the research provides new insight into the molecular mechanisms underlying tooth

support and opens promising directions for future regenerative and therapeutic approaches.

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Reference
Title of original paper: Loss of PTH 1 receptor signaling in periodontal cells drives cementum dysfunction and molar ankylosis in mice
Journal: Bone Research
DOI: 10.1038/s41413-026-00533-5

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About Professor Xue Yuan
Professor Xue Yuan is an assistant professor in the Department of Otolaryngology-Head & Neck Surgery at Indiana University School of Medicine, USA. He joined the faculty in 2021 after completing postdoctoral training at Stanford University. Dr. Yuan earned his PhD from the State University of New York at Buffalo in 2015. His research focuses on oral epithelial stem cells, regenerative biology, wound repair, aging, and head and neck cancers. Supported by funding from the National Institute of Dental and Craniofacial Research, he leads projects investigating stem-cell regulation and tumorigenesis. He has authored over 60 publications with more than 1,875 citations globally.

About Professor Teresita Bellido
Prof. Teresita Bellido is Chair of the Department of Physiology and Cell Biology at the University of Arkansas for Medical Sciences. An internationally recognized leader in bone biology, her research focuses on osteocyte signaling, skeletal remodeling, hormonal regulation, and musculoskeletal disease mechanisms. She also holds appointments in endocrinology and orthopaedics and serves as Research Career Investigator at the Central Arkansas Veterans Healthcare System. She has received multiple NIH and Veterans Administration grants and previously served as president of the American Society for Bone and Mineral Research. Her scientific achievements and mentorship contributions have earned several prestigious international awards worldwide.

Funding Information

This research was supported by the National Institute of Dental and Craniofacial Research (R03DE033059 to X.Y.); the Veterans Administration (I01 BX002104 and IK6BX004596 to T.B.); the National Institutes of Arthritis and Musculoskeletal and Skin Diseases (R01-AR059357 to T.B.); the UAMS College of Medicine Sturgis Endowment Grant; and the Arkansas Research Alliance.

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