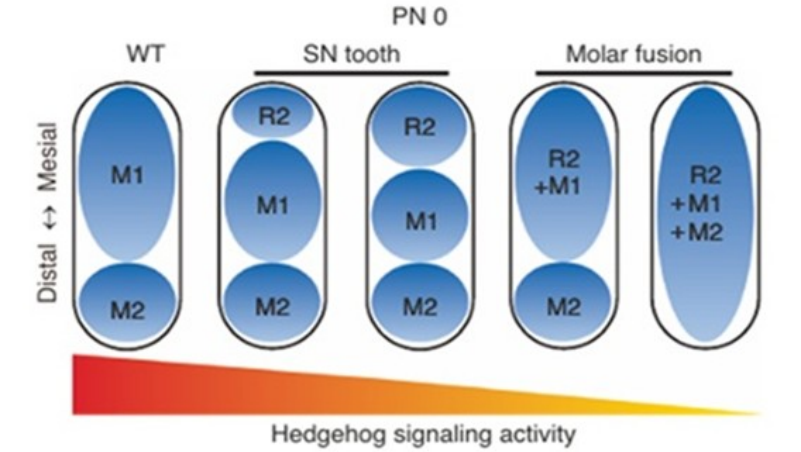
Codes in the Cilia: New Study Maps How Cilk1 and Hedgehog Levels Sculpt Tooth Architecture

Researchers demonstrated that declining Hedgehog signaling from Cilk1 loss produces stepwise changes in tooth formation and morphology



A hypothetical model illustrating how reduced Hedgehog signaling alters interactions between the rudimentary tooth bud (R2) and the first molar (M1), leading to supernumerary (SN) tooth or molar fusion formation.

CHENGDU, CHENGDU, CHINA, January 9, 2026 /EINPresswire.com/ -- Cilk1 deficiency disrupts normal tooth development by altering primary cilia function and weakening Hedgehog signaling. This reduction triggers extra diastemal teeth, enlarges them under further signaling loss, and can ultimately cause molar fusion. Researchers propose a progressive model linking Hedgehog signaling levels to sequential changes in tooth patterning. The study highlights a previously unknown role for Cilk1 in shaping tooth morphology and improving understanding of developmental dental disorders in humans.

Changes in early tooth development can have surprisingly big effects on a person's smile. Missing teeth, extra teeth, unusually small or large teeth, or teeth that fuse together can cause problems in appearance, chewing , and long-term oral and general health issues. Because these problems arise from intricate signaling networks that operate during tooth development, the underlying biological causes can be difficult to pinpoint, making diagnosis and prevention challenging. Scientists have uncovered many of the networks involved, but it remains challenging to fully explain how the body decides how many teeth to form—or where each tooth should go.

To help close this gap, researchers from Jeonbuk National University in Jeonju and Yonsei University in Seoul, South Korea, have identified an unexpected driver of tooth-pattern abnormalities: malfunctioning primary cilia. These tiny, antenna-like structures help cells process

developmental signals. The team found that when the ciliary kinase Cilk1 is disrupted, Hedgehog signaling becomes imbalanced, triggering a chain of changes in tooth number, size, and structure.

The research was led by Dr. Sung-Won Cho from the Department of Oral Biology, Yonsei University College of Dentistry, South Korea. The findings were made available online on 1 December 2025 and published in Volume 17, Issue 71, of the journal International Journal of Oral Science.

Using mouse models, the team examined a small embryonic tooth bud known as R2, which normally forms and then regresses. When Cilk1 was selectively removed from the dental mesenchyme, R2 failed to regress and instead continued to grow into an extra premolar-like molar. As Hedgehog signaling was reduced even further, the effects became more dramatic: the extra tooth could grow larger than the first molar, and in severe cases, adjacent molars fused into a single oversized tooth.

“This discovery highlights that even subtle disruptions in cilia-mediated signaling can completely rewrite the tooth pattern blueprint,” said Dr. Cho.

Molecular analyses revealed that losing Cilk1 reduces levels of Gli1, a key transcription factor, weakening Hedgehog activity and disrupting the balance between growth and regression at the R2 site.

“We believe this signaling switch acts like a volume dial for tooth development,” Dr. Cho added. “A slight reduction produces one effect; a stronger reduction produces another — from extra teeth to fused molars.”

The findings suggest that congenital conditions such as hyperdontia and regional tooth fusion may stem from ciliary dysfunction, not just mutations in tooth-specific genes. This insight may support earlier diagnosis for children with ciliopathies, whose unusual patterns of tooth development often go unexplained. It also highlights tooth development as a dynamic process—one shaped by interactions between neighboring tooth germs.

Beyond its clinical implications, the study offers a developmental framework that could eventually guide advances in regenerative dentistry. By precisely adjusting Hedgehog signaling, researchers may one day be able to reactivate dormant tooth germs in patients missing teeth and fine-tune the size of the regenerated tooth.

Overall, this study provides a new biological roadmap for understanding how tooth number and structure are determined. By identifying cilia-mediated Hedgehog signaling as a key regulator, the work paves the way for more accurate diagnosis and future therapeutic strategies aimed at preserving and restoring natural dentition.

Reference
Title of original paper: Progressive tooth pattern changes in Cilk1-deficient mice depending on Hedgehog signaling
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About Dr. Hyuk Wan Ko from Department of Biochemistry, Yonsei University
Dr. Hyuk Wan Ko is a Professor in the Department of Biochemistry at Yonsei University, Seoul, South Korea. His research investigates the molecular mechanisms of primary cilia and Hedgehog signaling, utilizing advanced mouse genetic models to decode the complexities of mammalian development and the pathogenesis of human ciliopathies. Dr. Ko's laboratory focuses on how these cellular organelles act as essential regulators of organ morphology, with a particular emphasis on the complex patterning of the craniofacial region.

About Dr. Eui-Sic Cho from Institute of Oral Biosciences, Jeonbuk National University School of Dentistry
Dr. Eui-Sic Cho serves as a professor at the Laboratory for Craniofacial Biology, Jeonbuk National University School of Dentistry, Jeonju, South Korea. He specializes in molecular signaling pathways that regulate odontogenesis. His work focuses on how disruptions in cilia-associated kinases affect gene expression during tooth development, aiming to better understand and potentially correct patterning abnormalities that lead to supernumerary or fused teeth.

About Dr. Sung-Won Cho from Department of Oral Biology, Yonsei University College of Dentistry
Dr. Sung-Won Cho is affiliated with the Department of Oral Biology, Yonsei University College of Dentistry, Seoul, South Korea. His research interests include craniofacial development and pattern formation. In the recent study on Cilk1-deficiency and tooth patterning, Dr. Cho contributed to the analysis of tooth development and histological and molecular assessments of molar formation, helping establish how ciliary dysfunction impacts tooth morphology.

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