The potential role of Runx2 in idiopathic condylar resorption

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Objectives: Idiopathic condylar resorption (ICR) is a rare but clinically underdiagnosed condition characterized by progressive bone loss of the mandibular condyle, predominantly affecting young women between 10 and 20 years of age. ICR occasionally occurs post-orthognathic surgery or trauma; however, the etiology remains unknown. We previously reported that parathyroid hormone-related protein (PTHrP) is essential for mandibular condylar cartilage (MCC) formation and maintaining Runx2 expression in the MCC polymorphic layer. The study aims to define the impact of acute Runx2 loss in cartilage-forming chondrocytes of the mandibular condyle and the long bone.

Experimental Methods: We used a tamoxifen-inducible *Sox9-creER* and *Runx2* floxed alleles to specifically and acutely inactivate Runx2 in postnatal chondrocytes. *Sox9-creER; Runx2*$^{fl/fl}$*; R26R*^{tdTomato} (Runx2-cKO) and their Control mice were pulsed by a single dose of tamoxifen at postnatal day 28 (P28) and chased to P56 or 3 months of age. The gross morphology of the mandibular condyle and femur was evaluated using 3D-microCT digital overlay, and the cartilage was histologically evaluated by Safranin-O staining.

Results: The Runx2-cKO MCC, but not the Runx2-cKO femoral growth plate, showed a substantial loss of Safranin-O^{+} cartilaginous matrix. The 3D micro-CT analysis revealed that the Runx2-cKO condyle was significantly truncated compared to the Control, while the Runx2-cKO femur morphology was unchanged. These findings show that acute Runx2-deficiency in chondrocytes causes the truncation of the mandibular condyle without affecting the femur, recapitulating the clinical manifestation of ICR.

Conclusion: Runx2 in chondrocytes play essential roles in maintaining the postnatal mandibular condylar cartilage but not the long bone growth plate. As chondrocyte-specific acute Runx2 inactivation specifically causes pathological resorption of the mandibular condyle, this genetic model could be a promising tool for future preclinical research on ICR.

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