Identification of Runx2^{+} stem cells in the mandibular condylar cartilage

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Objectives: The mandibular condylar cartilage (MCC) is an essential component of the temporomandibular joint (TMJ). Within MCC, the polymorphic layer is pivotal to the vertical growth of the mandibular condyle as it houses populations of chondrocyte precursor cells. We previously showed that Runx2, an osteogenic transcription factor, is expressed in the polymorphic layer and required for maintaining postnatal MCC chondrogenesis. The study aimed to define the role of Runx2^{+} cells in the polymorphic layer in postnatal MCC chondrogenesis using in vivo clonal analysis.

Experimental Methods: We generated a *Runx2-P2A-iCreER* (*Runx2-creER*) allele using CRISP/Cas9. In vivo clonal analysis of Runx2^{+} cells was performed by *cre*-inducible biallelic *R26R-RGBow* (RGB) multicolor reporters using *Runx2-creER; R26R$^{RGB/RGB}$* mice. In this system, Runx2^{+} cells are genetically marked with one of the six color combinations of eGFP, mOrange2, and mKate2, which is passed to all daughter cells. These mice were pulsed at postnatal day 28 (P28) and chased to various time points to visualize Runx2^{+} cells and their descendants.

Results: A short chase revealed individual Runx2^{+} cells with all six color combinations in the MCC polymorphic layer. When chased to P56, clones with distinct colors were formed from the polymorphic to chondrocyte layer and organized in a mosaic pattern, indicating their stem cell potential. Upon a long chase, the clone number and size decreased, indicating the possible transient nature of Runx2^{+} stem cells. Interestingly, some clones were also formed in the superficial layer.

Conclusion: Runx2^{+} cells in the MCC polymorphic layer exhibit some characteristics of stem cells as they can self-renew and form clones, at least transiently. Runx2^{+} cells in the superficial layer may also contribute to continued chondrogenesis in the MCC. Our project reveals unique characteristics of chondroprogenitor cells in MCC, facilitating future studies to define the function of stem cells and their plasticity in TMJ.

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