The mesenchymal cells derived from dental follicle contribute to periodontal regeneration

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Objectives: Periodontitis is a common disease that leads to destruction of periodontal tissue. During periodontal regeneration, it has been considered that mesenchymal progenitor cells in periodontal ligament (PDL) contribute to repair of periodontal attachment apparatus. Dental follicle (DF) contains the precursor cells of PDL and provides proper formation of attachment apparatus via parathyroid hormone-related protein (PTHrP) and its receptor, PPR. However, how these DF cells contribute to homeostasis of functional periodontal tissue in adulthood has not been elucidated. The objective of this study is to identify the fate of mesenchymal cells derived from PTHrP$^+$ DF cells during periodontal regeneration in surgically created periodontal defect in mice.

Experimental Methods:We utilized a tamoxifen-inducible *PTHrP-CreER* transgenic line that specifically marks DF cells and tdTomato reporter alleles to visualize their descendants. For these experiments, we pulsed tamoxifen (0.25 mg) to *PTHrP-CreER; R26R*-tdTomato at postnatal day 3. After 8 weeks, we surgically created bone defect (φ1.0 mm) in buccal plate of right mandibular and removed cementum of first molar mesial root. We chased the fate of tdTomato$^+$ periodontal cells derived from PTHrP$^+$ DF cells at various time points after surgery using fluorescence microscopy.

Results: At 8weeks, before creating periodontal defect, the descendants of PTHrP$^+$ DF cells were mostly located in PDL space, while some of them are in alveolar cryptal bone and acellular cementum. tdTomato$^+$ cells abundantly migrated from PDL space into periodontal defect at 7 days after surgery. After 14 days, tdTomato$^+$ cells differentiated into osteocalcin$^+$ alveolar bone osteoblasts in surgical defect. After 28 days, newly formed PDL and alveolar bone were observed and tomato$^+$ cells were in both PDL and alveolar bone.

Conclusion: Our data demonstrate that mesenchymal progenitor cells derived from PTHrP$^+$ DF cells contribute bone repair in surgically created periodontal defect and maintain homeostasis of functional periodontal tissue.

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