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Connective Tissue Biology

Bisphosphonate modulates proliferation and differentiation of rat periodontal ligament cells during wound healing

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Abstract

Background

Periodontal ligament (PL) width is precisely maintained throughout the lifetime of adult mammals, but the biological mechanisms that regulate the spatial locations of the cell populations for bone, cementum, and PL are unknown.

Methods

As bisphosphonates induce ankylosis in mouse molar teeth, we used ethane-1-hydroxy-1, 1-bisphosphonate - (HEBP, Etidronate; Didronel) in combination with a periodontal window wound model to identify those cell populations involved in the regulation of PL width during the reformation of cellular domains after wounding. Four groups of Wistar rats were wounded by drilling through the alveolar bone and extirpation of the PL. Rats were administered HEBP for 1 week and then sacrificed or allowed to recover for an additional week prior to sacrifice. Control rats were sacrificed after 1 or 2 weeks. One hour prior to sacrifice, rats were injected with ³H-thymidine to label proliferating cells. Tissue sections were immunohistochemically stained for osteopontin (OPN) or bone sialoprotein (BSP) or were prepared for in situ hybridization (BSP) to identify extra- and intracellular expression of these non-collagenous bone proteins associated with periodontal healing.

Results

HEBP treatment for 1 week induced a twofold increase in the thickness of the alveolar bone matrix in which weak immuno-staining for OPN and BSP mRNA signal was seen. During the recovery phase the increased bone width was reduced but was still considerably thicker than in control ($P < 0.001$). OPN staining as well as the BSP mRNA signal were much more intense than at 1 week. HEBP induced a $> 40\%$ reduction of PL width which returned to normal dimensions following the recovery phase. HEBP also modulated PL cell proliferation and differentiation: PL cell counts and labelling indices were reduced fivefold after 1 week of HEBP but returned to control values after the recovery phase. In controls, PL cells did not express OPN and BSP, but after HEBP treatment, and particularly after the recovery phase, PL cells expressed both of these markers intensely. In contrast, gingival and pulp connective tissues that were contiguous with the PL were not stained for OPN and did not express BSP mRNA after HEBP treatment.

Conclusions

While wounding induced transient increases of proliferation which were followed by repopulation of the extirpated tissue, the effects of HEBP on cell differentiation were independent of wounding. HEBP modulates the differentiation of PL cells and recruits cells that contribute to alveolar bone formation and loss of PL width homeostasis. Conceivably, bisphosphonates could be used therapeutically to selectively alter the differentiation of PL cells and promote the formation of alveolar bone and cementum. Anat. Rec. 247:329-340, 1997. © 1997 Wiley-Liss, Inc.

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