Molecular and cellular biology of alveolar bone.

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Leider kein Abstract erhältlich

Molecular mechanisms controlling bone formation during fracture healing and distraction osteogenesis.

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Abstract

Fracture healing and distraction osteogenesis have important applications in orthopedic, maxillofacial, and periodontal treatment. In this review, the cellular and molecular mechanisms that regulate fracture repair are contrasted with bone regeneration that occurs during distraction osteogenesis. While both processes have many common features, unique differences are observed in the temporal appearance and expression of specific molecular factors that regulate each. The relative importance of inflammatory cytokines in normal and diabetic healing, the transforming growth factor beta superfamily of bone morphogenetic mediators, and the process of angiogenesis are discussed as they relate to bone repair. A complete summary of biological activities and functions of various bioactive factors may be
**Perspectives for tissue regeneration using biologically active factors**

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zm 10/2001, Seite 38

Summary

Numerous preclinical and the first clinical studies have demonstrated the potential of polypeptide growth and differentiation factors (BMPs) for tissue engineering. This review focuses on the use of such biologically active factors for the stimulation of new dentin formation, periodontal regeneration, oral implant integration, sinus augmentation and mandibular reconstruction. It is anticipated that in the near future the application of these potent growth proteins will become part of our regenerative strategies for oral- and maxillofacial reconstruction.

[http://www.zm-online.de/m5a.htm?/zm/10_01/pages2/titel5.htm](http://www.zm-online.de/m5a.htm?/zm/10_01/pages2/titel5.htm)

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**Bone Morphogenetic Protein-7 Enhances Cementoblast Function, In Vitro.**

Hakki SS, Foster BL, Nagatomo KJ, Bozkurt SB, Hakki EE, Somerman MJ, Nohutcu RM.


Abstract

Background and Aims: Bone Morphogenetic Protein-7 (BMP-7) is a potent bone-inducing factor and has been shown to promote periodontal regeneration in vivo and in vitro, however, the specific effect of BMP-7 on cementoblasts, has not been defined. We aimed to investigate the effects of BMP-7 on cementoblasts, cells responsible for tooth root cementum formation. We hypothesized that BMP-7 would regulate mineralized tissue-associated genes in cementoblasts, as well as influence the expression profile of genes associated with cementoblast extracellular matrix (ECM) and with cell adhesion molecules (CAM). Methods: A murine immortalized cementoblasts (OCCM.30) were cultured with and without 50 ng/ml BMP-7. After 72 hours, total RNA was isolated and mRNA levels for bone/cementum markers, including bone sialoprotein (BSP), osteocalcin (OCN), osteopontin (OPN), and runt related transcription factor-2 (Runx2), were investigated by real-time quantitative RT-PCR (Q-PCR). In vitro mineral nodule formation was assayed on day 8 using von Kossa staining. A pathway specific gene expression array was used to determine BMP-7 responsive ECM and CAM genes in cementoblasts. Results: Mineralized tissue markers were strongly regulated by BMP-7, with an almost 3-fold increase in BSP and OCN transcripts, and significant increases in OPN and Runx2 mRNA expressions. BMP-7 treatment markedly stimulated cementoblast-mediated biomineralization, in vitro when compared to untreated cells at day 8. BMP-7 treatment altered the OCCM.30 expression profile for ECM and CAM functional gene groups. BMP-7 tended to increase expression of collagens and MMPs, mildly decreased TIMPs, and had mixed regulatory effects on integrins. Using Q-PCR, selected
array results were confirmed, including a significant BMP-7 induced increase in MMP-3 and decrease in TIMP-2 mRNA expression. Conclusion: These results support the promising applications of BMP-7 in therapies aimed at regenerating periodontal tissues lost as a consequence of disease.

The management of inflammation in periodontal disease.

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Abstract

It has become clear in recent years that periodontitis is an inflammatory disease initiated by oral microbial biofilm. This distinction implies that it is the host response to the biofilm that destroys the periodontium in the pathogenesis of the disease. As our understanding of pathways of inflammation has matured, a better understanding of the molecular basis of resolution of inflammation has emerged. Resolution of inflammation is an active, agonist-mediated, well-orchestrated return of tissue homeostasis. There is an important distinction between anti-inflammation and resolution; anti-inflammation is pharmacologic intervention in inflammatory pathways, whereas resolution is biologic pathways restoring homeostasis. A growing body of research suggests that chronic inflammatory periodontal disease involves a failure of resolution pathways to restore homeostasis. This article reviews the resolution of inflammation in the context of periodontal disease and the potential for the modification of resolution pathways for the prevention and treatment of periodontal diseases. Proof-of-concept studies in the 1980s demonstrated that pharmacologic anti-inflammation prevented and slowed the progression of periodontal diseases in animals and man. However, the side-effect profile of such therapies precluded the use of non-steroidal anti-inflammatory drugs or other enzyme inhibitors or receptor antagonists in periodontal therapy. The isolation and characterization of resolving agonist molecules has opened a new area of research using endogenous lipid mediators of resolution as potential therapeutic agents for the management of inflammatory periodontitis. Work in animal models of periodontitis has revealed the potential of this therapeutic approach for its prevention and treatment and forced the reconsideration of our understanding of the pathogenesis of human periodontal diseases.

⇒ http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2563957/?tool=pubmed
A role for alpha11beta1 integrin in the human periodontal ligament.


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Abstract

We previously demonstrated a role for alpha11beta1 integrin in periodontal ligament (PDL)-driven tooth eruption in the mouse. To explore a possible role for alpha11beta1 in the human periodontium, we have characterized the expression and function of alpha11 in human PDL tissue, in human PDL fibroblasts (hPDLF), and in human gingival fibroblasts (hGF). alpha11 expression was detected in PDL tissue, in hPDLF, and in hGF cells. Platelet-derived growth factor-BB and insulin-like growth factor II stimulated contraction of collagen lattices by both types of fibroblasts. alpha2 integrin blocking antibodies and the use of alpha11 siRNA demonstrated a role for both alpha2beta1 and alpha11beta1 in collagen lattice remodeling. Analysis of the proximal ITGA11 promoter from persons with chronic periodontal disease failed to reveal any polymorphism. Analysis of our data shows that alpha11beta1 is a major collagen receptor on cultured human PDL cells and implies that it is also functionally important in the PDL in vivo.

Defining a visual marker of osteoprogenitor cells within the periodontium.

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Abstract

BACKGROUND AND OBJECTIVE: Cells with osteoprogenitor potential are present within periodontal tissues during development and in postnatal life. To identify an osteoprogenitor population, this study utilized a transgenic model in which an alpha-smooth muscle actin (alphaSMA) promoter directed green fluorescent protein (GFP) expression.

MATERIAL AND METHODS: Observation of GFP expression was complemented with analysis of osteogenic differentiation by determining the expression of RNA of bone markers, by histochemical staining for alkaline phosphatase and by the detection of mineralized nodules using xylene orange. Flow cytometry was utilized to determine the proliferative potential and cell-surface phenotype of cultured alphaSMA-positive cells.

RESULTS: alphaSMA-GFP expression was detected within the dental follicle and in the apical region of the root (i.e. areas rich in vascularization) but not in mature bone. alphaSMA-GFP expression was observed during the early stages of primary cultures derived from the dental follicle and periodontal ligament and was diminished in areas undergoing mineralization. Intense alkaline phosphatase activity and the presence of mineralized
nodules was observed 2 wk after osteogenic induction. Consequently, the expression of bone sialoprotein, osteocalcin and dentin matrix protein-1 was increased. Flow cytometry revealed that in vitro expansion enriched for an alphaSMA-GFP-positive population in which 55-65% of cells expressed the cell-surface markers Thy1(+) and Sca1(+). The alphaSMA-GFP-positive population exhibited high proliferative and osteogenic potentials when compared with an alphaSMA-GFP-negative population.

CONCLUSION: Our data indicate that the alphaSMA promoter can be used to identify a population of osteoprogenitor cells residing within the dental follicle and periodontal ligament that can differentiate into mature osteoblasts.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2871067/?tool=pubmed

Stimulation of osteoblasts with Emdogain increases the expression of specific mineralization markers.

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Abstract

OBJECTIVE: The purpose of this study was to determine the effects of enamel matrix derivative on mRNA expression of markers related to periodontal healing.

STUDY DESIGN: Murine osteoprogenitor cells (MC3T3-E1) were grown for 12 and 16 days in mineralization media and stimulated with 100 microg/mL Emdogain (EMD). Cell cultures treated with 2% and 10% fetal calf serum (FCS) served as control. The mRNA expression of bone sialoprotein (BSP), osteopontin (OPN), and runt-related protein 2 (Runx2) was analyzed by real-time polymerase chain reaction. One-way analysis of variance was used for statistical analysis.

RESULTS: Stimulation with EMD significantly (P < .01) enhanced mRNA expression of BSP up to 13.9-fold and of OPN up to 3.2-fold at day 16 compared with the 2% FCS control. The expression of mRNA for transcription factor Runx2 was not significantly changed.

CONCLUSION: The beneficial effects seen in periodontal regeneration after treatment with EMD may be related to an increase of the mineralization markers BSP and OPN at mRNA level.
Root cementum may modulate gene expression during periodontal regeneration: a preliminary study in humans.

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Abstract

BACKGROUND: Previous data demonstrated that root cementum may affect periodontal regeneration. As such, this study aimed to explore further possible mechanisms involved in this process by investigating in humans whether root cementum modulates gene expression in the regenerating tissue formed under membrane-protected intrabony defects.

METHODS: Thirty subjects with deep intrabony defects (> or =5 mm; 2- or 3-wall) were selected and assigned to the control or test group. The control group received scaling and root planing with the removal of granulation tissue and root cementum; the test group underwent removal of granulation tissue and soft microbial deposits by cleaning the root surface with a microbrush and saline solution, aiming at cementum preservation. Guided tissue regeneration (GTR) was applied to both groups. Twenty-one days later, the newly formed tissue under the membrane was assessed for the expression of the following genes: alkaline phosphatase (ALP), osteopontin (OPN), osteocalcin (OCN), platelet-derived growth factor-alpha (PDGFA), bone sialoprotein (BSP), and basic fibroblast growth factor (bFGF).

RESULTS: Data analysis demonstrated that mRNA levels for PDGFA, BSP, and bFGF were higher in the sites where root cementum was kept in place compared to the sites where root cementum was removed completely as part of the periodontal therapy (P <0.05); in contrast, OCN levels were lower (P <0.05). No difference for ALP or OPN was observed between the control and test groups (P >0.05).

CONCLUSION: Root cementum may modulate the expression of growth and mineral-associated factors during periodontal regeneration.

Guided tissue regeneration may modulate gene expression in periodontal intrabony defects: a human study.

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Abstract

BACKGROUND AND OBJECTIVE: Guided tissue regeneration has been shown to lead to periodontal regeneration, however, the mechanisms involved remain to be clarified. The present study was carried out to assess the expression of genes involved in the healing
process of periodontal tissues in membrane-protected vs. nonprotected intrabony defects in humans.

MATERIAL AND METHODS: Thirty patients with deep intrabony defects (> or = 5 mm, two or three walls) around teeth that were scheduled for extraction were selected and randomly assigned to receive one of the following treatments: flap surgery alone (control group) or flap surgery plus guided tissue regeneration (expanded polytetrafluorethylene (e-PTFE) membrane) (test group). Twenty-one days later, the newly formed tissue was harvested and quantitatively assessed using the polymerase chain reaction assay for the expression of the following genes: alkaline phosphatase, receptor activator of nuclear factor-kappa B ligand, osteoprotegerin, osteopontin, osteocalcin, bone sialoprotein, basic fibroblast growth factor, interleukin-1, interleukin-4, interleukin-6, matrix metalloproteinase-2 and matrix metalloproteinase-9.

RESULTS: Data analysis demonstrated that mRNA levels for alkaline phosphatase, receptor activator of nuclear factor-kappa B ligand, osteoprotegerin, osteopontin, bone sialoprotein, basic fibroblast growth factor, interleukin-1, interleukin-6, matrix metalloproteinase-2 and matrix metalloproteinase -9 were higher in the sites where guided tissue regeneration was applied compared with the control sites (p < 0.05), whereas osteocalcin mRNA levels were lower (p < 0.05). No difference was observed in interleukin-4 mRNA levels between control and test groups.

CONCLUSION: Within the limits of this study, it can be concluded that genes are differentially expressed in membrane barrier-led periodontal healing when compared with flap surgery alone, and this may account for the clinical outcome achieved by guided tissue regeneration.

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