ECRONICON OPEN ACCESS

EC DENTAL SCIENCE
Conceptual Paper

Cytokine's and Growth Factors from Bone and Dentine Extracellular Matrix as Regulators of Bone Engineering

Anka Letic Gavrilovic and Ivana Gavrilovic*

Department of Periodontology, Dental Clinic, Zagarolo (RM), Italy

***Corresponding Author**: Ivana Gavrilovic, Department of Periodontology, Dental Clinic, Zagarolo (RM), Italy.

Received: February 26, 2020; **Published:** March 06, 2020

Keywords: *Tooth; Dentin; Cytokines; Cell Communication; Osteoconduction; Osteoinduction; Bone Engineering*

In this conceptual review, we have compiled many of the important research findings in genetics and molecular control of bone and tooth formation. We have reviewed a brief assessment of cytokine's role, important for control both of dentin and bone engineering.

During clinical work practitioners need natural or artificial bone equivalents. Presently on the market could be find countless types of heterogenous bone, but of dubious quality and *in situ* acceptability. The autogenous bone biomaterials would contribute to the best new bone augmentation. Recently, it is shown that dentin contains bone and cartilage-inducing factors that facilitate chondro-osteogenesis and modify the calcification process [1]. Nevertheless, dentine-pulp demonstrates strong regenerative potential which allows it to respond to disease and traumatic injury. Such activities are strongly influenced by cell-matrix interactions and modified by disease processes, including infection and inflammation. During embryological development of the dentin (tooth) and bone comparable organic deposition and mineralization procedures occurred. Odontoblasts, as a main tooth-dentin creating cells fabricate and assemble collagenous and NCP (non-collagenous matrix protein) during dentin generation. Dentin may be regarded as a mineralized connective tissue, same as bone. In its composition as well as its mode of formation, dentin exhibits several similarities with bone, but also specific differences. The dentin organic phase, the matrix, determines its morphology and is believed to be actively involved in the formation of the mineral phase [2]. The identification of many bioactive molecules within dentine organic matrix (Table) has allowed better understanding of regenerative and other tissue responses towards novel clinical therapies, such as bone engineering [3]. A fibrous mesh of collagen type I dominates the organic matrix. Also, minor amounts of other collagen types may be present. The non-collagenous proteins (NCPs), which constitute about 10% of the matrix, fall into several categories: phosphoproteins, Gla-proteins of the osteocalcin type as well as matrix Gla-protein, proteoglycans, different acidic glycoproteins, and serum proteins [4]. These NPCs matrix proteins may be mediators of cell-matrix interactions, matrix maturation, and final mineralization. Comparably, dentin and bone contains interchangeably organic and non-organic substrates. Organic residues of bone and dentin are almost identical. Both tissues are mineralized even they have different structural evolution. Regenerative capacities are significant and foremost for bone engineering. Dentin in form od DDM (demineralized dentin matrix) is lack of cells but predominant with cytokines and growth factors, necessary for intensive cell to cell communication, secretion and ending with mineralization [5,6].

Polypeptide growth factors, cytokines, are a class of natural biological bone mediators regulating the critical cellular events which are involved in healing, cell proliferation, chemotaxis, differentiation, and matrix synthesis. Cytokines generate theirs effects by binding to specific cell surface receptors, which transduce signals to the nucleus via complex signal transduction pathways. Examples of growth factors found in bone, dentin, cementum and similar healing tissues include factors listed in table. The *in situ* factors are able to induce new mineralization i.e., new osseointegration of the implanted material. Process still is not fully understood, but most researchers agree that

Collagens (I, III, V)
Non-collagenous proteins
Glycoproteins
Phosphorylated matrix proteins
Chondroitin sulfate
Proteoglycans
Gla proteins
Heparan sulfate (entactin, perlecan)
Dermatan,
Non-phosphorylated proteins
Matrix Gla1 proteins
Plasma proteins
Bone sialoprotein
Hormones
Osteocalcin
Osteonectin
Osteopontin,
Osteoprotegerin
Growth factors, cytokines
TGF-β (TGF-β1, TGF-β2, TGF-β3)
BMP (BMP-2, BMP-4, BMP-7)
IGF (IGF-1, IGF-2)
PDGF, VEGF4,
Neuropeptides (NGF)
RANKL
Sclerostin
Ephrins
Semaphorins
Molecules for adhesive interactions
Collagen I, III
Fibronectin and derived peptides
Keratin sulfate
Fibrinogen
Laminin and derived peptides
Vitronectin
Endothelin
Enzymes
Matrix Metaloproteinases (1, 2, 3,..)

Table: *Ingredients of DDM (demineralized dentin matrix) comparable to the bone organic matrix.*

the contact between the bioactive materials and cells in the bone is not static but dynamic. Bone and particularly dentin are very dynamic tissue with continuous remodeling due to extreme cell to cell communication and collaboration. Since these biomolecules are responsible for cell anchorage, attachment, spreading, adhesion, migration and all other events connected to the biointegration, implantable biomaterial, such as DDM should be capable of releasing these peptides in a controllable way, under strict local conditions, in order to maximize osteogenesis. The three main ingredients for bone regeneration are regulatory signals, responding stem cells, and extracellular matrix proteins (ECMs). The osteoinductive signals are the bone morphogenetic proteins (BMPs) (Table). BMPs are members of superfamily

which consist of almost 15 secreted signaling proteins. They are responsible for a broad range of biological and developmental effects and control processes during tissue development and repair. These factors affect mesenchymal cells recruitment (odontoblast, osteoblasts, osteocytes), theirs proliferation, differentiation and secretion of extracellular matrix components, followed by cascade of cellular events that are involved in the initiation of *in vivo* bone genesis. Recombinant human BMPs (rhBMPs) were shown to induce new bone formation *in vivo* and to heal a large segments of bone defects by fostering osteogenesis [7]. The two demineralized matrixes, dentins' and bone contains mainly collagen type I and matrix-binding proteins known as BMPs. Together with numerous molecules for adhesive interactions create interactive network between bone cells: osteoblasts, osteoclasts and osteocytes. Osteoclasts produce factors called clastokines that control osteoblasts' during the bone remodeling cycle. Osteocytes cemented inside of bone, with their dendritic processes, are very important, since they evaluate and register distribution and amount of mechanical forces which are normally applied to the bone. Extremely important for dynamic bone remodeling.

Conclusively, DDM graft is a matrix-based therapy with possible clinical applications of biologically active molecules, growth factors and cytokine. DDM can be used and recycled as natural autologous bone equivalent and scaffold for local bone engineering. Dentin is rich with regulatory molecules, growth factors and cytokines. Prerequisite for regulation of bone engineering, and therefore clinical applications.

Additionally, preparation the demineralized dentin matrix undergo the strong acid treatment resulted in antiseptic properties and decreased antigenicity. Bacteria-free DDM for that reason, is excellent biomaterial for clinical application, since has no risk of immunological reaction or any other disease. Having combination of bone and dentin (DDM and DBM) may accelerate bone formation and bone healing and open new prospects for reconstructive bone therapy.

Bibliography

1. Kim YK., *et al*. "Guided bone regeneration using autogenous teeth: case reports". *Journal of Korean Association of Oral Maxillofacial Surgery* 37.2 (2011): 142-147.

2. Kim YK., *et al*. "Development of a novel bone grafting material using autogenous teeth". *Oral Surgery Oral Medicine Oral Pathology Oral Radiology Endodontics* 109.4 (2010): 496-503.

3. AJ Smith., *et al*. "Dentine as a bioactive extracellular matrix". *Archives of Oral Biology* 57.2 (2012): 109-121.

4. In-Woong Um. "Demineralized dentin matrix scaffolds for alveolar bone engineering". *The Journal of Indian Prosthodontic Society* 17.2 (2017): 120-128.

5. Ike M and Urist MR. "Recycled dentin root matrix for a carrier of recombinant human bone morphogenetic protein". *Journal of Oral Implantology* 24.3 (1998): 124-132.

6. Kim YK., *et al*. "Tooth-derived bone graft material". *Journal of Korean Association Oral Maxillofacial Surgery* 39.3 (2013): 103-111.

7. Letic-Gavrilovic A., *et al*. "Genetic Potential of Interfacial Guided Osteogenesis in Implant Devices". *Dental Material Journal* 19.2 (2000): 99-132.

Volume 19 Issue 4 March 2020