World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(REVIEW ARTICLE)

Check for updates

Dentin matrix protein-1 in oral biology research: Narrative review

Christian Khoswanto *

Department of Oral Biology Faculty of Dentistry, Airlangga University Surabaya, Indonesia.

World Journal of Advanced Research and Reviews, 2024, 23(03), 1176–1183

Publication history: Received on 29 July 2024; revised on 07 September 2024; accepted on 09 September 2024

Article DOI: https://doi.org/10.30574/wjarr.2024.23.3.2747

Abstract

Dentin matrix protein (DMP-1) is a matrix protein other than collagen that is present in dentin and bone mineralization. It could attach Ca^{2+} ions to control hydroxyapatite formation and promote odontoblast cellular proliferation into odontoblast-like cells. DMP-1 is a mineralized dentin structure protein that is also synthesized in nonmineralized tissues and essential to the development of mineralized tissue by initiating deposition and modulating mineral treatment. DMP-1, DMP-2, DSP, and DMP-4 are the four proteins that make up this group. DMP-1 demonstrated to affect an extensive array of capabilities, including stem cell and preosteoblast adhesion, proliferation, and development, as well as matrix mineralization. DMP-1 was discovered within the mineralizing globules, suggesting that it play a role in matrix-mediated hydroxyapatite nucleation. The preformed hydroxyapatite is exposed to the extracellular fluid by the crystals that are produced through the matrix vesicle membrane. Although the extracellular fluid generally contains enough Ca^{2+} and $PO4^{3-}$ to allow ongoing crystal multiplication and growth, fresh crystal formation requires some local circumstances in the matrix around the vesicles. DMP-1 and other signaling molecules may have an impact cells that are capable at the repair site of additional stimuli the host tissue's contribution, resulting in the development of a functionally active tissue and physically identical to physiologic dentin. The main objective of this research is to emphasize the critical functions of DMP-1 and give the most recent data regarding its use to dental science.

Conclusion: DMP-1 is vital in providing protection in osteogenesis, amelogenesis, dentinogenesis, and dental pulp regeneration. It demonstrates that DMP-1 plays an essential impact in odontoblast protection, ameloblasts, osteoblast, and osteocyte maturation.

Keywords: DMP-1; Dentinogenesis; Osteogenesis; Amelogenesis; Alveolar Bone

1. Introduction

Mineralized tissue structures, such as mineralized hard tissues include alveolar bone, enamel, and dentin. Crystalline hydroxyapatite is the predominant component made of inorganic of such two tissues, while Collagen is the most important component. For the synthesis of calcium and phosphate crystalline forms and the accumulation of calcium and phosphate morphologies into crystal hydroxyapatite, collagen I serves as a template that is both dynamic and instructional. Hydroxyapatite formation is quite complicated, and noncollagenous proteins (NCPs) are in charge of it. NCPs identified in bone and dentin are osteocalcin, dentin matrix proteins, bone sialoprotein, and osteopontin. Along with its highly acidic nature, DMP-1 is bone and dentin contains noncollagenous matrix protein mineralization matrices. It could attach Ca^{2+} ions to control hydroxyapatite formation and promote odontoblast cellular proliferation into odontoblast-like cells. DMP-1 is a mineralized dentin structure protein moreover synthesized in nonmineralized tissues and have a crucial effect in the development of mineralized tissue by initiating deposition and modulating mineral treatment.

* Corresponding author: Christian Khoswanto

Copyright © 2024 Author(s) retain the copyright of this article. This article is published under the terms of the Creative Commons Attribution Liscense 4.0.

DMPs are a kind of NCPs found in the proteins of dentin and bone. DMP-1, DMP-2, DSP and DMP-4 are the four proteins that make up this group. DMP-1 has proven to affect a number of features, including stem cell and preosteoblast adhesion, proliferation, and development, as well as matrix mineralization. These DMPs' multipurpose features make them appealing candidates for incorporation into a suitable substrate to make it possible to create bone tissue from stem cells. Whereas the DMPs were first discovered hydroxyapatite and calcium interaction coagulating proteins, they can also be employed as chemical messengers to control stem cell adhesion, attachment, and migration.[4] Undifferentiated osteoblasts have DMP-1 in their nuclei, which is then released into the extracellular matrix during the maturation process. During osteoblast differentiation, calcium ions released from the endoplasmic reticulum to the cytoplasm storage and inflow of material to the nucleus, facilitating DMP-1 transfer to the extracellular matrix.[5,6] The main objective of this research is to emphasize the critical functions of DMP-1 and give the most recent data regarding its use to dental science.

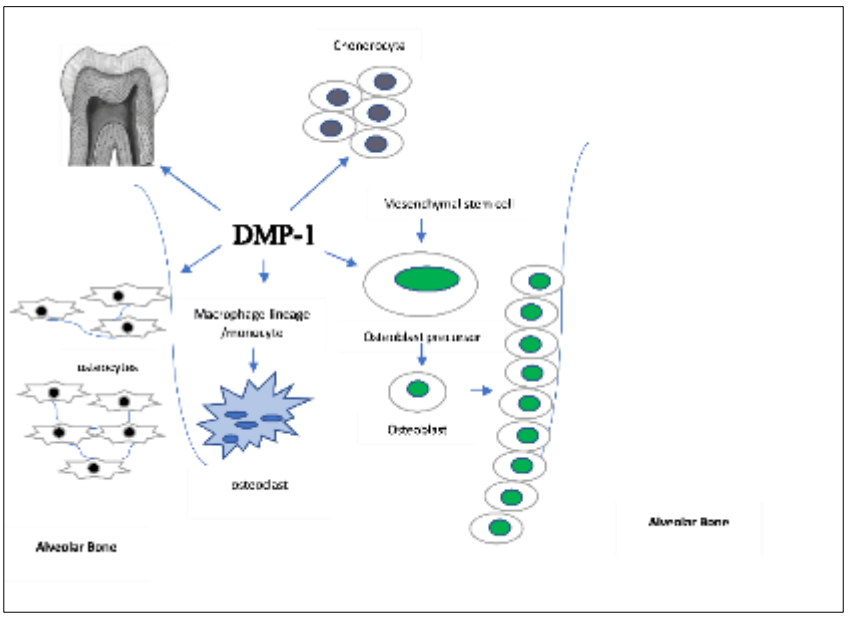

Figure 1 Dmp-1 Expression in Dental Tissue

2. Methods

On PubMed and Google Scholar, the scholarly literature on the subject of Dentin Matrix Protein-1 in Oral Biology research was analyzed. Articles that discussed or looked into the effects of Dentin Matrix Protein-1 in Oral biology on dentistry were looked for in search results. The cited papers from the journals were also evaluated for relevance and included if they met the requirements for inclusion. One of the requirements for admittance was having access to the entire material (Table 1).

Table 1 Research Method and Criteria for Choosing Studies

	Research Method and Criteria for Choosing Studies
A	Dentin Matrix Protein-1 in Oral Histology studies were looked for in the literature using PubMed and Google Scholar. Search techniques were applied using the combinations. ("name of Dentin Matrix Protein-1" + "Oral Biology ") of the phrases "DMP-1", "alveolar Bone", "dentinogenesis", "amelogenesis", and "dental pulp". According to the criteria for inclusion, the papers were evaluated between January 1, 1992, and December 31, 2023, in English.
B	Language: English; Publication period: January 1, 1992- July 31, 2024;. The publications comprised reviews, book chapters, original research papers, in vitro investigations, in vivo animal or human studies, clinical trials, and meta-analyses. Case studies, letters, editorials, studies that contained unnecessary or worthless data, pieces without entire texts, and articles written in languages other than English were all disqualified.

2.1. Role of DMP-1 in endothelial cells

Vasculature is a multistage procedure that existing vessels' Endothelial cells that have been stimulated move and multiply in the microvascular matrix to create capillary. Endothelial cells in the process of growing orient, form tunnels, and produce a basal layer, eventually resulting in functional new capillaries. The basic cell connection molecule in endothelial cells, vascular endothelial cadherin, is necessary for appropriate the advancement of the microvascular in the mouse embryo and the generation of new capillaries in the adult. Endothelial display a lower response to proliferating certain stimuli such as VEGF when VE-cadherin is engaged. [7,8]

DMP-1 induced endothelial cell physiological responses in the presence of VEGF include cellular proliferation, both of this is necessary for more complicated processes including the creation of in vivo investigations of the endothelial tube system in angiogenesis. Treatments of HUVECs with DMP-1 drastically attenuated all of these outcomes since DMP-1 does not impact with bFGF proliferation or angiogenesis allowing researcher think DMP-1 as a novel selective VEGF-induced angiogenesis inhibitor. Integrin-mediated endothelial cell matrix interactions are angiogenesis and tissue expansion both aided by this protein. DMP-1 has been linked to in vitro endothelial cell development implying that extracellular matrix proteins released have specialized activities that affect the dynamic equilibrium that controls vessel formation. The study also found that DMP-1 causes VE-cadherin upregulation and VEGFR-2 inactivation, which results in decreased in vivo healing process and tumor associated proliferation mediated by VEGF. [9-10]

2.2. Role of DMP-1 in dentinogenesis and amelogenesis

Ameloblasts and odontoblasts also express DMP-1. Dentinogenesis is a two-step procedure that starts with the production of organic predentin and finishes with mineralization at the calcification side. Predentin has a different composition than the matrix of dentin, indicating that some materials are introduced or just before the mineralization begin, while others are digested. Despite the fact that NCPs make amends 10 to 15 percent of the matrix material of dentin, their probable significance in the mineral formation has prompted extensive research. The primary dentin is described as prior to the completion of root development, the dentin is secreted. during tooth development and makes up the majority of the circumpulpal dentin. Prior to mineral development, dentinogenesis produces an extracellular organic scaffolding. This matrix material has a mineralization control capacity. A 10 to 30 mm layers predentin is found between the calcified tissue and the odontoblasts in the pulpal area. This is an organic matrix that is nonmineralized and acellular, generally originating from collagen and rich in proteoglycans and lipids. [11-13]

In the molecule called Dmp1-null mice, a rise in apoptotic odontoblasts and ameloblasts has been shown to cause hypophosphatemia, partial failure to dentin maturation, pulp hole, and root canal extension during postoperative morphogenesis. DMP-1 has also been demonstrated to control the activity of Dspp mRNA, which produces DSP and DPP. Recent research has shown that focused Dspp transgenic expression in null odontoblasts can successfully repair the Dmp1-deficient dentin phenotype without affecting homeostasis, implying direct participation of DMP-1 through Dspp, which is controlled by Dmp-1. Dmp-1 deletion has little impact on enamel development. The compound-deficient mice had no visible changes in their molar or incisor regions. The molecule called mice's proximal enamel region has the phenotypic severe, with little mineralized enamel remaining. Although kl/kl-deficient ameloblasts and Dmp1-null show an increase in apoptosis, ectopic calcification, is not caused by apoptotic processes in the ameloblasts. Mineralization spreads outside of segments into the surrounding matrix; extracellular DMP-1 was discovered within the mineralizing globules, suggesting that it play a role in matrix-mediated hydroxyapatite nucleation. The preformed hydroxyapatite is exposed to the extracellular fluid by the crystals that are produced through the matrix vesicle membrane. Although the extracellular fluid generally contains enough Ca^{2+} and $PO4^{3-}$ to allow ongoing crystal multiplication and growth, fresh crystal formation requires some local circumstances in the matrix around the vesicles. [14-16]

In conjunction with acidic noncollagenous proteins, such as strongly phosphorylated proteins with calcium-binding capabilities, the collagen structure that was attached to the membrane surfaces could function provides a link between the crystal and the extravesicular matrix. There are a lot of acidic domains in DMP-1 that become negatively charged following phosphorylation. The N-telopeptide found at the border of the collagen fibril's gap area, has a particular binding capacity for DMP-1. As a result, It is considered to serve a significant purpose in the mineralization tissue development by initiating and modifying mineral phase deposition. For structure mineralization, synergistic interactions between DMP-1 and collagen fibers may be necessary after the mineral particle deposits at the collagen surface bound with DMP-1.[17-19]

2.3. Role of DMP1 in alveolar Bone

During bone formation, Intracellular and external expression of dentin matrix proteins are also possible. Each of these molecules has a different function depending on their localization patterns. Such understanding might be important in the development of bone tissue engineering strategies. Three variants of DMP-1 have been discovered within the ECM of alveolar bone: 1. COOH-terminal subunit, 2. NH2-terminal segment, and 3. DMP1-PG. It's plausible to assume that these variations possess various in osteogenesis, several functions and roles are played, based on their clear biochemical distinctions. The COOH fragment enhances mineralization functioning as facilities for the hydroxyapatite, according to in vitro mineralization experiments.[20]

DMP-1 expressed in various parts at low levels and in significant amounts tissues that are experiencing contribute including dentin and bone, according to several studies. DMP-1 expression in 3 month old mouse bone sections, with high levels of DMP-1 expression in the bone and osteoblasts. The DMP-1 protein is recognized as two processed fragments in the ECM : the N fragment at 37 KDa and the C fragment at 57 KDa.[21-23] 57 KDa from DMP-1 is the physiologically active of the two segments. This segment alone was found to DMP-1's full length function should be reinstated in knockout mice models. In addition, the two pieces of DMP1 have different distributions in intracellular and extracellular compartments. DMP-1's C fragment is largely found in the ECM's mineralizing sites of bone and dentin. The C segment collects in the mesenchymal cells' nucleus. DMP-1's N segment, on the other hand, is found in predentin, a non-mineralizing tissue, as well as cartilage and bone in the ECM. It was mostly found in the plasma membrane and cytosol within the cell. The fact that both pieces of DMP-1 have such a wide distribution suggests that they may have different biological functions in the intracellular and extracellular domains. DMP-1 deficiency causes abnormal mineralization of bone and dentin, resulting in hypophosphatemic rickets and osteomalacia, especially in the phenotypic. DMP-1 modulates the hormone FGF23 and is involved in osteoblast development and mineralization, according to recent research. Both of these features will be highlighted in the following sections.[24-26] DMP-1 is a nucleating protein found in bone extracellular matrix. Overexpression of DMP-1 also enhanced mineralization and changed the biomechanical characteristics of cortical bone substantially.[27]

2.4. Role of DMP-1 in Pulp Tissue

Tissue regeneration is possible in dental pulp, leading to the synthesis of reparative dentin. After direct pulp capping, dental pulp tissue creates a hard structure known as the dentin bridge, which has been well documented. The original odontoblasts and pulpal cells at the exposure site die and are gradually replaced by newly differentiated odontoblast during reparative dentinogenesis.[28]

Mesenchymal cells exist in the adult dental pulp, which are capable to develop and generate in reaction to reparative dentin to proper stimuli. It's still unclear where these freshly developed odontoblast-like cells came from. Clonogenic cells can be found in dental pulp, intensely proliferative, and potential of tissue regeneration, traits that effectively identify as stem cells, according to research. The significant failure rates of pulp capping treatments due to flaws in the dentin created at the pulp exposed site of exposure utilizing accessible pulp capping is one of the issues that dental clinicians manage. DMP-1's application as a pulp capping agent has the potential to be beneficial to accelerate the transformation of primordial pulp cells by cytodifferentiation, additionally the creation of reparative dentin, was investigated in a recent rat study.[13,29] When embryonic pulp cells come into contact with a DMP1-treated membrane, DMP-1 may cause them to cytodifferentiate. Inflammation generated by pulp exposure boosted cell mobility and blood flow in the region, which aided in the recruitment more undifferentiated cells to touch with the DMP-1 impregnated membrane. As a result, DMP-1 and other signaling molecules may have an impact cells that are capable at the repair site of additional stimuli the host tissue's contribution, resulting in the development of a functionally active tissue and physically identical to physiologic dentin. Growth differentiation factor supplied via electroporation based gene delivery produced similar results.[30]

3. Discussion

DMP-1 is a particularly appealing protein to use as a native protein in its whole form or in its processed forms in tissue engineering applications because of its multifunctionality. DMP-1 has been utilized as a signaling molecule in biomimetic collagen structures to achieve this goal and repair soft tissues like the tooth pulp tissue.[31] They are proteins that can perform a variety of tasks, including signaling and interacting with calcium and HA, because they lack a fixed structure. The primary structure reveals that it is an acidic, serine-rich protein with numerous serine phosphorylation sites and an integrin-binding peptide.[32]

DMP-1 is mostly found in the pulp's peritubular region and is involved in the development of odontoblasts as well as dentin mineralization. Recent research has demonstrated that Dmp-1 knockout rats exhibit hypomineralization of the

dentin with expanded predentin and reduced dentin layer, which is brought on by a defect in the conversion of predentin to dentin. In Dmp-1 KO models, the dentin tubules are also less organized and have fewer branches than in control models of the same age. Additionally, a prior investigation revealed that DMP-1 could control crystal size and coordinate crystal orientation in dentin. For the purpose of repairing carious dentin, synthetic peptides including the type I collagen binding domain and the nucleating domains of DMP-1 were created. The collagen-binding domain served to anchor the peptides to the type I collagen's N-telopeptide region, and the nucleating domain promoted calcium binding and the subsequent conversion to crystalline hydroxyapatite. These peptides can be inserted into any collagen-based scaffold because they are non-toxic, simple to make, and safe.[31,33]

DMP-1 which is also acidic and exhibits a random-coil shape, promotes the production of hydroxyapatite when coupled to collagen and inhibits the crystal formation when free in solution. Due to its ability to bind calcium ions, the protein is directly implicated in the creation of apatite. In the presence of calcium ions, the 56K fragment of human DMP-1 forms dimers and tetramers. The monomeric form grew more compact under these circumstances. The 44K fragment compressed in the presence of calcium ions but did not dimerize. This shows that both DMP-1 segments are altered by calcium ions, although the 56K fragment may be responsible for DMP-1 oligomerization. It follows that DMP-1 may condense calcium ions during the biomineralization of bone and dentin.[34,35]

Circular dichroism demonstrated that a mixture of the acidic-containing oligomers from the C- and N-terminal domains increased its beta-sheet structures upon binding Ca+2, and based on FTIR and circular dichroism, a related chimeric protein made up of the acidic oligomer from the C-terminal domain and silk fibroin also increased its alpha-helix and beta-sheet structures in the presence of Ca+2. The full-length protein and its fragments were bound to HA, and we were interested in the conformational changes that occurred as a result. Because HA scatters light considerably, circular dichroism could not be used because of this. The 57K and 37K fragments' structures remained mostly unaltered while the full-length protein underwent conformational modifications upon binding to HA. Even while the PG fragment interacts with Ca+2, it does not also go through this conformational shift. These conformational alterations are in line with the theory that the flexible 57K and 37K pieces bind to the HA nucleus and promote HA crystal development and proliferation, which improves mineralization.[32,36]

In contrast to osteoblast maturation and matrix production, which is marked by increases in gene expression and cell metabolic activity, osteocyte maturation is marked by a sharp decline in gene expression and metabolic activity. According to recent research, DMP-1 is the best molecule for regulating osteocyte maturation. The following facts provide support for this assertion, DMP-1 is highly expressed in osteocytes while osteoblasts express it at a very low level, Dmp-1 null mice exhibit significant pathological changes in the osteocyte canalicular system, many genes expressed in normal osteoblasts either remained active in Dmp1 null osteocytes or were ectopically produced. The dentin matrix proteins are a subset of the noncollagenous proteins, which are crucial for the biomineralization process. By forming a brief amorphous precursor phase that eventually causes the nanocrystals to transition into a crystalline phase, these proteins can aid in the orientation and strengthening of the crystals.[37,38]

Biomineralization patterns from DMP-1 have been used to create synthetic peptides that can convert amorphous calcium phosphate (ACP) to crystalline hydroxyapatite (HAP), which is useful for bone regeneration. For bone tissue engineering applications, nucleation of crystalline HAP with a calcium to phosphorus ratio of 1.6, similar to that of native bone, is essential necessary to produce synthetic tissues of high quality that can sustain the mechanical loading that bones are often subjected to. In this sense, the capacity of peptides derived from DMP-1 to trigger the conversion of ACP to crystalline HAP is a useful tool in recent research for a signaling molecule to be integrated into the biomimetic framework. Integrating the osteogenic signaling part of DMP-1 may be important to induce osteogenic differentiation of adult stem cells because DMP-1 can drive MSCs to differentiate into functional osteoblasts. Recent research has also shown the signaling abilities of DMP-1, which, like its nucleating abilities, will eventually find uses in tissue engineering. The functional domains of DMP-1 can be combined in a variety of ways, creating potent tools that can be integrated into scaffolds to trigger reactions for the regeneration of mineralized tissue, depending on the intended usage.[39-42]

4. Conclusion and future outlook

DMP-1 plays a crucial protective role in osteogenesis, amelogenesis, dentinogenesis, and dental pulp regeneration. It demonstrates that DMP-1 plays an essential impact in odontoblast protection, ameloblasts, osteoblast, and osteocyte maturation. In the future, DMP-1 will play a variety of functions in dentistry, particularly oral histology and oral biology, to help with early detection and treatment in dentistry.

Compliance with ethical standards

Author's contributions

CK conceived and designed the study, conducted research, provided research materials, and collected and organized data. The author has critically reviewed and approved the final draft and responsible for the content and similarity index of the manuscript.

Funding

The authors declare that they have no known competing financial interests or personal ties that could have influenced the study presented in this paper.

References

[1] George A, Sabsay B, Simonian PA, Veis A. Characterization of a novel dentin matrix acidic phosphoprotein. J Biol Chem. 1993;268:12624-12630.

[2] Terasawa M, Shimokawa R, Terashima T, Ohya K, Takagi Y, Shimokawa H. Expression of dentin matrix protein 1 (DMP1) in nonmineralized tissues. J Bone Miner Metab. 2004;22:430-438.

[3] Young MF, Kerr JM, Ibaraki K, Heegaard AM, Robey PG. Structure, expression, and regulation of the major noncollagenous matrix proteins of bone. Clin Orthop Relat Res. 1992; 281:275–294.

[4] Hao J, Ramachandran A, George A. Temporal and spatial localization of the dentin matrix proteins during dentin biomineralization. J Histochem Cytochem. 2009; 57:227–237.

[5] Qin C, Huang B, Wygant JN, McIntyre BW, McDonald CH, Cook RG, Butler WT. A chondroitin sulfate chain attached to the bone dentin matrix protein 1 NH2-terminal fragment. J Biol Chem. 2006; 281:8034–8040.

[6] Narayanan K, Gajjeraman S, Ramachandran A, Hao J, George A. Dentin matrix protein 1 regulates dentin sialophosphoprotein gene transcription during early odontoblast differentiation. J Biol Chem. 2006; 281:19064–19071.

[7] Lampugnani MG, Resnati M, Raiteri M, et al. A novel endothelial-specific membrane protein is a marker of cell-cell contacts. J Cell Biol. 1992;118(6):1511-1522.

[8] Carmeliet P, Lampugnani MG, Moons L, et al. Targeted deficiency or cytosolic truncation of the VE-cadherin gene in mice impairs VEGF-mediated endothelial survival and angiogenesis. Cell. 1999;98(2):147-157.

[9] Brooks PC, Clark RA, Cheresh DA. Requirement of vascular integrin alpha v beta 3 for angiogenesis. Science. 1994;264(51):569-571.

[10] Pirotte S, Lamour V, Lambert V. et al. Dentin matrix protein 1 induces membrane expression of VE-cadherin on endothelial cells and inhibits VEGF-induced angiogenesis by blocking VEGFR-2 phosphorylation. Blood. 2011;117(8):2515-2526.

[11] Butler WT, Ritchie H. The nature and functional significance of dentin extracellular matrix proteins. Int J Dev Biol 1995; 39: 169–179.

[12] Smith AJ, Tobias RS, Cassidy N, Begue-Kirn C, Ruch JV, Lesot H. Influence of substrate nature and immobilization of implanted dentin matrix components during induction of reparative dentinogenesis. Connect Tissue Res 1995; 321: 291–296.

[13] Almushayt A, Narayanan K, Zaki AE, George A. Dentin matrix protein 1 induces cytodifferentiation of dental pulp stem cells into odontoblasts. Gene Therapy. 2006. 13, 611–620.

[14] Rangiani A, Cao ZG, Liu Y. et al Dentin matrix protein 1 and phosphate homeostasis are critical for postnatal pulp, dentin and enamel formation. International Journal of Oral Science. 2012. 4, 189–195.

[15] He G, George A. Dentin matrix protein 1 immobilized on type I collagen fibrils facilitates apatite deposition in vitro. J Biol Chem. 2004. 279:11649–11656.

[16] Anderson HC. Matrix vesicles and calcification. Curr Rheum Rep. 2003. 5:222–226.

[17] Butler WT, Ritchie H. The nature and functional significance of dentin extracellular matrix proteins. Int J Dev Biol. 1995. 39:169–179.

[18] Papagerakis P, Berdal A, Mesbah M, et al. Investigation of osteocalcin, osteonectin, and dentin sialophosphoprotein in developing human teeth. Bone. 2002. 30:377–385.

[19] He G, Dahl T, Veis A, George A. Dentin matrix protein 1 initiates hydroxyapatite formation in vitro. Connect Tissue Res. 2003. 44:240–245.

[20] Ravindran S, George A. Dentin Matrix Proteins in Bone Tissue Engineering Adv Exp Med Biol. 2015 ; 881: 129–142.

[21] Hao J, Zou B, Narayanan K, George A. Differential expression patterns of the dentin matrix proteins during mineralized tissue formation. Bone. 2004; 34:921–932.

[22] Huang CC, Ravindran S, Yin Z, George A. 3-D self-assembling leucine zipper hydrogel with tunable properties for tissue engineering. Biomaterials. 2014; 35:5316–5326.

[23] Qin C, Brunn JC, Cook RG, Orkiszewski RS, Malone JP, Veis A, Butler WT. Evidence for the proteolytic processing of dentin matrix protein 1. Identification and characterization of processed fragments and cleavage sites. J Biol Chem. 2003; 278:34700–34708.

[24] Lu Y, Yuan B, Qin C, Cao Z, Xie Y, Dallas SL, McKee MD, Drezner MK, Bonewald LF, Feng JQ. The biological function of DMP-1 in osteocyte maturation is mediated by its 57-kDa C-terminal fragment. J Bone Miner Res. 2011; 26:331–340.

[25] Maciejewska I, Qin D, Huang B, Sun Y, Mues G, Svoboda K, Bonewald L, Butler WT, Feng JQ, Qin C. Distinct compartmentalization of dentin matrix protein 1 fragments in mineralized tissues and cells. Cells Tissues Organs. 2009; 189:186–191.

[26] Feng JQ, Ward LM, Liu S, Lu Y, Xie Y, Yuan B, Yu X, Rauch F, Davis SI, Zhang S, Rios H, Drezner MK, Quarles LD, Bonewald LF, White KE. Loss of DMP1 causes rickets and osteomalacia and identifies a role for osteocytes in mineral metabolism. Nat Genet. 2006; 38:1310–1315.

[27] Bhatia A, Albazzaz M, Espinoza Orias AA, Inoue N, Miller LM, Acerbo A, George A, Sumner DR. Overexpression of DMP1 accelerates mineralization and alters cortical bone biomechanical properties in vivo. J Mech Behav Biomed Mater. 2012; 5:1–8.

[28] Goldberg, M.; Smith, A.J. Cells and extracellular matrices of dentin and pulp: A biological basis for repair and tissue engineering. Crit. Rev. Oral Biol. Med. 2004, 15, 13–27.

[29] Gronthos S, Mankani M, Brahim J, Robey PG, Shi S. Postnatal human dental pulp stem cells (DPSCs) in vitro and in vivo. Proc. Nat. Acad. Sci. 2000; 25: 13625–13630.

[30] Nakashima M, Mizunuma K, Murakami T, Akamine A. Induction of dental pulp stem cell differentiation into odontoblasts by electroporation-mediated gene delivery of growth/ differentiation factor. Gene Therapy 2002; 9: 814–818.

[31] Alsanea R, Ravindran S, Fayad MI, Johnson BR, Wenckus CS, Hao J, George A. Biomimetic approach to perforation repair using dental pulp stem cells and dentin matrix protein 1. J Endod. 2011; 37:1092–1097.

[32] Huang J, Wong C, George A, Kaplan DL. The effect of genetically engineered spider silk-dentin matrix protein 1 chimeric protein on hydroxyapatite nucleation. Biomaterials. 2007; 28:2358-2367.

[33] Lu Y, Ye L, Yu S, Zhang S, Xie Y, McKee MD, et al. Rescue of odontogenesis in Dmp1-deficient mice by targeted re-expression of DMP1 reveals roles for DMP1 in early odontogenesis and dentin apposition in vivo. Dev Biol. 2007; 303:191–201.

[34] Tartaix PH, Doulaverakis M, George A, et al. In vitro effects of dentin matrix protein-1 on hydroxyapatite formation provide insights into in vivo functions. J Biol Chem. 2004; 279:1811.

[35] Porębska A, Rożycka M, Hołubowicz R, et al. Functional derivatives of human dentin matrix protein 1 modulate morphology of calcium carbonate crystals. The FASEB Journal. 2020; 34:6147–6165.

[36] He G, Gajjeraman S, Schultz D, Cookson D, Qin C, Butler WT, et al. Spatially and temporally controlled biomineralization is facilitated by interaction between self-assembled dentin matrix protein 1 and calcium phosphate nuclei in solution. Biochemistry. 2005. 44:16140-16148.

[37] Lu Y, Yuan B, Qin C, Cao Z, et al. The Biological Function of DMP-1 in Osteocyte Maturation is Mediated by Its 57-kDa C terminal Fragment. J of Bone and Mineral Research. 2011; 26: 331–340.

[38] Ravindran S and George A. Dentin Matrix Proteins in Bone Tissue Engineering. Adv Exp Med Biol. 2015; 881: 129–142.

[39] Tsuji T, Onuma K, Yamamoto A, Iijima M, Shiba K. Direct transformation from amorphous to crystalline calcium phosphate facilitated by motif programmed artificial proteins. Proc Natl Acad Sci U S A. 2008; 105:16866–16870.

[40] Khoswanto C. Hypoxia Inducible Factor 1α as Key Factor in Wound Healing Post Tooth Extraction: an Overview. J Inter Dent Med Res 2020;13(3) :1191-1197.

[41] Huang CC, Ravindran S, Yin Z, George A. 3-D self-assembling leucine zipper hydrogel with tunable properties for tissue engineering. Biomaterials. 2014; 35:5316–5326.

[42] Khoswanto C, Dewi IK, The role of Wnt signaling on Tooth Extraction Wound Healing: Narrative review, The Saudi Dental Journal. 2024; Volume 36, Issue 4:516-520