

GLANCE INTO PROTEINS PRESENT IN PERIODONTAL TISSUES-A REVIEW – PART II

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Abstract

Proteins are large biological molecules consisting of one or more long chains of amino acid residues. Proteins perform a vast array of functions within living organisms, including catalysing metabolic reactions, replicating DNA, responding to stimuli, and transporting molecules from one location to another. Periodontium is defined as the tissues that surrounds and supports the teeth, consists of four different tissues; gingiva, periodontal ligament, cementum and alveolar bone. Several proteins are present in periodontium which are involved in various functions such as cell matrix adhesion and signalling, regulate diffusion of nutrients, waste products, and soluble signalling molecules. Abnormalities in either protein function or structure have been associated with various inherited and non-inherited diseases. Periodontal disease is known to be a major cause of tooth loss which occurs due to functional and structural changes including proteins. Therefore a thorough knowledge of the proteins present in the periodontal tissues it is necessary to understand the normal biochemistry and pathology of the periodontal tissues. Hence this article reviews the list of various types of proteins present in the periodontium especially in the cementum and the alveolar bone.

Key Words: - Alveolar bone, Cementum, Periodontium, Proteins.

Introduction

Proteins are polymeric chains that are built from monomers called amino acids. All structural and functional properties of proteins derive from the chemical properties of the polypeptide chain. The term protein was coined by Jons J Berzelius in 1838, derived from a Greek word “*proteios*” which means “*of the first rank*”. Proteins perform an extensive variety of specific functions in the living cells. These include proteins acting as enzymes, hormones, immunoglobulins, membrane receptors, blood clotting factors, storage proteins genetic controlling, muscle contraction, respiration etc.¹

Periodontium is defined as the tissues that surround and support the teeth which include two soft tissues; gingiva and periodontal ligament and two hard tissues; cementum and alveolar bone. The different organs, tissues and cells that built the periodontium and the associated structures are complex entities that show distinctive functional and developmental characteristics.²

The periodontal tissues are made up numerous molecules, cells and tissues embedded in different layers of matrix structure.³ Periodontal proteins are involved in several functions such as cell matrix adhesion and signaling, regulate diffusion of nutrients and waste products They also known to impart tensile and compressive strengths to the tissues and in few tissues they provide the appropriate conditions for the nucleation and growth of mineral crystals.⁴

Periodontitis is a multi-factorial disease considered as a major cause of tooth loss which occurs due to pathological changes in the supporting tissues. Deviations in either protein structure or function have been associated with various genetic and non-genetic diseases.⁵ Therefore the knowledge of different proteins present in periodontium is

important to understand the physiology and pathology of the periodontal tissues. Hence this article reviews the list of various types of proteins present in cementum and alveolar bone of periodontium.

PROTEINS OF CEMENTUM

Cementum is a mesenchymal tissue that covers the root surface of the tooth. It enables attachment for the periodontal ligament to the root surface and hence an integral part of periodontium. Two main forms of cementum that have different structural and functional characteristics are acellular cementum, which offers attachment for the tooth, and cellular cementum, which has an adaptive role in response to tooth wear and movement and is associated with repair of periodontal tissues.

Biochemical composition of cementum

For better understanding of the proteins present in cementum it is obligatory to discuss about the biochemical composition of the same. The composition of cementum is similar to that of bone. Cementum contains 45% to 50% of inorganic content and 50% to 55% of organic contents. The inorganic content is made up of hydroxyapatite by weight and the remaining organic portion consists of collagen and non-collagenous matrix proteins.⁶ Organic matrix of cementum consists mainly of collagens. Similar to bone and periodontal ligament, the two typical fibril-forming collagens type I and III are also found in cementum. The organic portion of cementum also contains several non-fibrous proteins such as bone-sialoprotein, osteopontin, tenascin, fibronectin, osteonectin and proteoglycans.⁷

Bone-sialoprotein and **osteopontin** were originally called bone sialoproteins I and II. Both these proteins are highly glycosylated and phosphorylated with greater levels of acidic amino acids. Glutamic acid is predominant in Bone

sialoprotein and apatite in osteopontin. These proteins are involved in hydroxyapatite binding, cell attachment and activation of cell signaling pathways. Osteopontin also plays a role in bone resorption by inhibiting hydroxyapatite crystal growth and mediating attachment of osteoclasts.^{8,9}

Fibronectin is a chief glycoprotein present in gingival connective tissue. It is produced by hepatocytes and fibroblasts. It is considered as a principal protein of ECM as it binds the cells to the extracellular matrix essential for connective tissue turnover in the gingiva. Fibronectin is a large dimer of two similar 230-270 Kd polypeptide subunits which are connected by disulfide bonds at the C-terminus. Through these associations, fibronectin is involved in the cell attachment, migration, differentiation, and growth.¹⁰

Tenascin is a large glycoprotein molecule with a six-arm, star-shaped structure. The tenascin molecule entails of 6 disulfide-linked polypeptide chains that spread from the center like the tentacles of an octopus. Tenascin binds to fibronectin and to proteoglycans, particularly the cell surface proteoglycan syndecan. Tenascin is synthesized at specific times and locations during embryogenesis and is present in adult connective tissues, but with a more restricted distribution. Tenascin, also acknowledged as myotendinous antigen, glioma mesenchymal extracellular matrix antigen that has a minor distribution in adult extracellular matrices. Each chain comprises epidermal growth factor-like repeats, calcium binding regions and integrin-specific cell binding domains. Even though the distribution of tenascin is restricted in adults, it is seen in elevated but transitory levels during the development of various tissues wound healing and oncogenesis.¹¹

Osteonectin is a hard tissue counterpart of the cellular matrix protein existing in soft tissue tenascin. Its role is mainly to link collagen to the mineralized matrix of bone. Osteonectin is also known as SPARC which means "secreted protein, acidic, rich in cysteine", it is a 40 KDa glycoprotein that is predominantly bound to hydroxyapatite. SPARC can comprise as much as 25% of the non-collagenous proteins. It is a secreted calcium-binding glycoprotein, which interacts with a range of extracellular matrix molecules. SPARC has a high affinity calcium-binding site and several low affinity calcium-binding sites.¹²

Proteoglycans in various categories are observed in the organic composition of cementum. Versican, decorin, biglycan, syndecan are the different proteoglycans that are observed in cementum.¹³

Biglycan is a relatively small extracellular proteoglycan similar to decorin. It is also known as dermatan sulfate PG-S1, is a small proteoglycan of 200 kDa whose protein core is highly homologous to decorin. Although biglycan is strongly bound in the extracellular matrix, it has no demonstrable collagen binding activity.¹⁴

Syndecan is a transmembrane proteoglycan that binds extracellular matrix proteins. Syndecan is made up of stratified epithelium and is composed of only one short

chain of dermatan sulfate or chondroitin sulfate and is located over the entire cell surface. In simple epithelium, syndecan has 3 long heparan sulfate chains and 2 short chondroitin sulfate chains and is associated only with the basolateral border of cells. In oral tissues, syndecan has been reported to be developmentally regulated in mesenchyme during tooth organogenesis. The actions of syndecan in the adult periodontium are currently unknown, but it may function during wound healing as a requisite or obligate protein for cell adhesion and growth factor binding.¹⁵

Cementum attachment protein (CAP) is consistently found in acellular cementum. It is biochemically thought to be involved in communication pathways that are thought to play a role in the development of cementoblasts from their precursor cells. Apart from this CAP is also thought to provide attachment to the periodontal ligament fibers.¹⁶

PROTEINS OF ALVEOLAR BONE

The alveolar process is the portion of the maxilla and mandible that forms and supports the tooth sockets. It develops in conjunction with the development and eruption of the teeth and is resorbed gradually if the teeth are lost. Together with root cementum and the PDL it forms the attachment apparatus of the teeth which absorb and distribute forces generated by mastication and other tooth contacts. The parts of the alveolar bone are,

1. Alveolar bone proper; (Innermost) thin compact bone.
2. Supporting alveolar bone. It consists of,
 - I. Cortical plates (outermost), forms outer and inner plates (buccal and lingual) of alveoli.
 - II. Spongiosa (middle portion) fills the area between, the cortical plates and alveolar bone proper.

Bone is a hard mineralized tissue. The tissue chemistry of bone is clarified by consideration of some histological and ultra-structural concepts. The biochemical composition of alveolar bone consists of cells, organic and inorganic contents embedded in extracellular matrix.

Type I collagen makes up about 90% of the organic matrix. Type I collagen forms fiber bundles that provide basic structural integrity to bone. In addition to this type V, III & XII are also present. Type III collagen is present in relation to Sharpey's fibers. Type I, V & XII are produced by osteoblasts and type III is produced by fibroblasts. The remaining 10% consists of non-collagenous components.¹⁷

Numerous non-collagen proteins, such as osteocalcin, osteonectin, osteopontin, sialoproteins, proteoglycans, etc., represent approximately 8% of the organic matrix. Fibronectin and tenascin are two substrate adhesion molecules, have been identified on the periosteal and endosteal surfaces of alveolar bone. Decorin and biglycan are the predominant proteoglycan species of bone. The principal glycosamino-glycans recognized in human alveolar bone were chondroitin-4-sulfate (93.8% of the total

glycosaminoglycan extracted) followed by small concentrations of dermatan sulfate (3.1%), heparan sulfate (1.8%) and hyaluronic acid (1.3%). Non-collagenous components of alveolar bone have been categorized by Robey et al into proteoglycans and glycoproteins.

Proteoglycans have a core protein to which one or more heteropolysaccharides called **Glycosaminoglycans** are covalently linked. The glycosaminoglycans consist of repeating carbohydrate units that are sulfated, such as chondroitin sulfate, dermatan sulfate, keratan sulfate and heparin sulfate. Examples of proteoglycans include versican, decorin, biglycan, fibromodulin, osteoglycin and osteoadherin. These may be involved in growth factor regulation. The major proteoglycans in alveolar bone are expressed with chondroitin sulfate side chains, dermatan sulfate forms are expressed by undifferentiated bone cells.¹⁸

Versican is a chondroitin sulfate proteoglycan that takes a large solvent space in the interstitial spaces of the connective tissue matrix. Versican, a primary proteoglycan of loose connective tissue, is a large macromolecule. The protein core consists of epidermal growth factor-like and lectin-like amino acid sequences. At the amino terminal is a hyaluronic acid-binding region and at the carboxy-terminal a complement regulatory protein-like domain. The protein core contains 14 attachment sites in the central region for glycosaminoglycans. This molecule has been thought to be secreted by fibroblasts.¹⁹

Decorin and **biglycan** are the 2 important proteins found in alveolar bone. They bind to TGF- β and collagen and regulate fibrillogenesis. Decorin and biglycan are associated with the collagen matrix of bone. There also exist numerous bound PG's such as osteoadherin that have mineral binding properties. Other proteins found in bone include procollagen peptides such as thrombospondin, fibronectin and vitronectin that modulate cell attachment and regulate enzyme alkaline phosphatase for mineralization to occur.¹⁷ Glycoproteins in alveolar bone include osteonectin, thrombospondin, osteopontin and bone sialoprotein, osteocalcin.

Osteocalcin also recognized as bone gla protein was the first non collagenous bone protein to be characterized. It is a 5.8 KDa acidic protein that is altered by vitamin k-dependent carboxylating enzymes that convert two to three glutamic acids into γ -carboxyglutamic acids (gla groups). Osteocalcin is said to play a role in mineral maturation and bone resorption since it is regulated by vitamin D3 and PTH and acts as a chemo attractant to osteoclast precursors.²⁰

Bone morphogenic proteins are unique group of low molecular weight proteins belonging to transforming growth factor- (TGF- β) superfamily genes. Bone morphogenic proteins are osteoinductive substances which are released during bone repair that are required for healing. They are pleiotropic glycoproteins involved in differentiation, chemotaxis and mitosis of various cells both during

embryogenesis and development that continue post-foetally. Different bone morphogenic proteins have different functions. Human genome encodes about 20 types of bone morphogenic proteins. 34-38% is related to TGF- β superfamily. Bone morphogenic proteins are homodimeric proteins of approximately 30 KD with two identical strands linked by a cysteine binding group.²¹

Conclusion

Proteins are the class of macromolecules containing nitrogen that are essential for the survival of life. Proteins are present in different body tissues including periodontium. Each periodontal structure has its own diverse biochemical, architectural and cellular composition. The periodontal disease conditions thought to produce functional and structural changes in the molecular components including proteins of the periodontium. Hence the knowledge of different proteins present in periodontium is vital to understand the physiology and pathology of the periodontal tissues.

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