The Periodontal Ligament: Development, Anatomy and Function

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Abstract

This paper will explore the origin and development of the periodontal ligament (PDL), its anatomical structure and function. The developmental process and anatomy of the ligament is quite complex and some aspects are still unknown, for example the way that ligament lineages develop and are regulated have yet to be clarified. The ground substance will be discussed, as well as the vascular and neural supply, the fibres present, their orientation and the various cell types present in the ligament. There have been recent advances in PDL stem cell research. This area is rapidly growing and can have a huge impact from harnessing these cells to utilise in an array of medical uses. The ligament has several essential functions, which can be highlighted by any deviations from the healthy norm. This can result in retardation of the ligament structure and functional capability. For instance, trauma can result in dental ankylosis, which may disrupt the vital eruptive function of the ligament.

Key words: Periodontal ligament, Oral biology, Development, Structure, Anatomy, Function

Introduction

The periodontal ligament is a unique specialised connective tissue between the cementum covering the tooth root and the alveolar bone. It is derived from the dental follicle region, which originates from the cranial neural crest cells [1]. The ligament has an array of oriented fibres and is vascular. It is also highly cellular, for example it contains PDL fibroblasts, osteoblasts and cementoblasts [2]. The ligament is crucial as it protects, supports and provides sensory input for the masticatory system. It also maintains homeostasis and repairs tissue destruction caused by periodontal disease or mechanical trauma [3].

Origin and development

The PDL is produced mainly from fibroblasts before dental eruption, which originate in the dental follicle and start to differentiate during root development [4]. The dental follicle is a condensation of the ectomesenchymal tissue - its cells differentiate into cementoblasts during their apical development and form the cementum lining the surface of the root [5].

Firstly, collagen fibres become embedded in the cementum and Sharpey's fibres are laid down coronally within the PDL region. The initial orientation is nearly parallel to the root surface. Fibres are formed and deposited from the developing cementoenamel junction (CEJ) to the tooth's apex. The fibres that are deposited apical to the CEJ form the ligament. Fibres insert themselves within the cementum matrix from the CEJ and continue in a coronal direction, after a third of root formations. This process closely follows the outline of the newly formed crown. At this stage, none of the collagen fibres insert into the alveolar bone.

Loosely arranged fibres continue to deposit and insert along the developing root surface. Opposite to this surface, the fibres also insert along the lining of the bony socket wall and cross the ligament space in a similar way to the root side fibres. The root and bone side fibres will eventually come together in the middle of the ligament space to form the immediate plexus. Initially, the fibres are positioned parallel to the surface of the root, but this orientation dramatically changes as the teeth erupt [6] and may be a result of the positional relationship of the erupting tooth to the teeth adjacent [7].

During eruption, the dentogingival fibres align themselves from the CEJ in the occlusal direction, which then terminate in the gingiva connective tissue. The transseptal fibres extend over the alveolar crest in an oblique direction towards the surface of the adjacent developing tooth root. The fibres of the cervical-most one-third of the root surface run obliquely in the apico-occlusal direction from cementum to bone. They become more defined, although there is still no direct connection from the root and bone fibres in the mid-third of the root. The root is still to be made in the apical portion, therefore fibre arrangement is poorly developed.

When there is full eruption and occlusal contact, the ligament fibres take on their final arrangement. The dentogingival, transseptal and alveolar crest fibres all originate at the CEJ. The fibres are arranged horizontally within the coronal-third of the surface of the root. In the mid-third of the root, the fibres run obliquely from the occlusal surface to the alveolar bone. The apical-third maintain an oblique configuration, but the fibres run apically from the cementum surface to the alveolar bone [6,7].

Ligament formation in the teeth with and without primary predecessors differs in structure. Grant et al. [5] found that the way that ligament is formed in deciduous teeth differs from succedaneous teeth. Both classes of teeth follow the same stages, therefore they are not unique. However, the timing of development is delayed for secondary teeth. The succedaneous premolar only shows a few fibre extrusions from the cementum during the pre-eruptive stage. No fibres are apparent from bone. Most of the PDL space is filled with loose collagenous elements. The permanent molar has well defined predentogingival and alveodental fibres, which extend between bone and cementum. Upon eruption, the succedaneous tooth only shows organised dentogingival, alveolar crest and horizontal fibres, leaving the rest of the ligament in developing stages. During initial occlusal contact, the succedaneous premolar shows organised and continuous alveodental fibres for the coronal two-thirds of the root. The principal fibre formation is still progressing in the apical one-

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third. The molar exhibits continuous PDL fibres. During full occlusion function, the molar and premolar show classically aligned and thickened ligament fibres. Therefore, although the developmental timing differs, after eruption and a period of occlusion, the fibres in primary and secondary teeth thicken and become indistinguishable from each other.

Blood Vessels and Nerves of The Periodontal Ligament

Interstitial spaces

Interstitial spaces are areas of loose connective tissue between each bundle of the principal fibres, which make up the structural and functional bulk of the ligament. The regularity of these spaces clearly relates to the vascular and neural needs of the functioning PDL. They may be designed to carry these vascular and neural structures both by encircling the tooth at regular intervals and connecting with the vessels that run longitudinal to the root. The network of fine collagenous fibre bundles that surround these interstitial spaces are arranged at angles to the surface of the spaces, therefore they provide support for the maintenance of these spaces as they are compressed during mastication or tension [8].

Vascular supply

The PDL is very well vascularised considering it is a connective tissue, reflecting the high turnover rate of its cellular and extracellular elements. The principal blood supply is from the superior and inferior alveolar arteries. The arteries supplying the ligament are derived from a series of perforation arteries that pass through the alveolar bone. These vessels anastomose freely within the ligament, occupying the interstitial spaces. This distribution pattern has clinical importance in healing of extraction wounds. New tissue invades from the perforations and the formation of a blood clot occupying the socket is more rapid in its gingival and apical areas. Many arteriovenous anastomoses occur within the PDL. Venous drainage is achieved by axially directed vessels that drain into a system of networks. This system is in the apical portion of the ligament that consists of large diameter venules. Lymphatic vessels tend to follow the venous drainage [9].

Innervation

The innervation of the PDL arises from the trigeminal nerve, through its superior or inferior alveolar branches. The nerve fibres within the ligament are generally found in the outer section of the ligament space, nearer to the alveolar bone. A plexus of nerve fibres develop from those that enter the ligament in the apical region and those which perforate the lateral wall of the alveolus. Single nerve fibres, both myelinated and unmyelinated, can be seen branching off from the main nerve bundles and running towards the cementum in the inner part of the ligament. They often supply mechanoreceptors within the inner third of the ligament [9]. Maeda et al. [10] used PGP 9.5 antibody staining to find that the apical region of the ligament was richly supplied with nerve terminals. Sympathetic nerves have been identified in the ligament, but there is no evidence of a parasympathetic innervation.

Ground Substance of The Periodontal Ligament

All components of the PDL ground substance may be secreted by fibroblasts. Its composition varies according to the developmental state of the tissue and location [11]. The ligament is predominantly tissue rich in ground substance, even though it appears to be rich in collagen. Berkovitz et al. [12] found that even the collagen fibre bundles of rats consist of two-thirds of ground substance by volume.

The ground substance has similarity to most other connective tissues. It consists mainly of non-collagenous extracellular matrix proteins: alkaline phosphatase, hyaluronate glycosaminoglycans, proteoglycans and glycoproteins. They may be involved in the ligaments macromolecular organisation [13,14]. Dermatan sulphate is the principle glycosaminoglycan. Glycosaminoglycans exist as anionic polysaccharides, which form proteoglycans when covalently attached to a protein core. Proteoglycans are able to interact with fibrillar components, for example collagen, which shows that they may retain the organisation of connective tissue [15]. Fibronectin and tenascin are important identified glycoproteins. Fibronectin is uniformly distributed throughout the ligament in erupting and erupted teeth, whereas tenascin is not normally localised but is concentrated adjacent to the alveolar bone and cementum [16]. Their functions are yet to await clarification. The ligament ground substance is approximately 70% water and has significant ability of the tooth to withstand stress loads. When injury and inflammation arise, the tissue fluids within the ground substance matrix increase [14].

Periodontal Ligament Fibres

Principal fibres

Most of the PDL composition comes from principal fibres, which are oriented bundles of collagen fibres. They are placed at inclinations that are important to their functions. The principal fibres have two groups, which are named according to their location with respect to the teeth. They are the gingival fibre and dentoalveolar fibre groups [17]. Each individual collagen fibre is roughly 55 nm in diameter, which is small in comparison with the 100-250 nm length of collagen fibres in tendons. This difference could suggest the short half-life of PDL collagen, resulting in less time to assemble fibrils. The larger the diameter, the more it is certified as an older fibre, and the smaller diameters are liable to be due to high rate of collagen turnover [18]. PDL fibres are usually wavy in nature, enroute from the cementum to bone, to permit for tooth movement [19]. In a study by Pini et al. [20] bovine ligament was used to ascertain stress-strain responses under tactile and compressive loading conditions. It was found that there was no functional link between the thickness of individual fibres and mechanical response.

The ligament collagen bundle fibre composition is primarily interstitial collagens I and III, which then arrange as banded fibrils [7]. Collagen V is also involved with these fibrils and is located in the interstitial spaces between the bundles or within the centre of the fibrils. Other minor collagens involved in the fibrous meshwork of the PDL are collagens IV, V, VI and XII, which are important to maintain the normal architectural structure of the PDL and in the regeneration of ligament function during remodelling from tooth movement [9].

Sharpey's fibres

Sharpey's fibres are extensions of the principal fibres of the ligament into the tooth cementum and bone. Once they insert themselves into the alveolus wall or the cementum, they calcify and become associated with non-collagenous proteins in cementum and bone [21]. The fibres are commonly longer on the appositional side of the ligament, which is where tension is formed. This may show interstitial fibre growth where the bundles are integrated into the surrounding bone [9]. Also, Sharpey's fibres are coupled with high levels of osteopontin and bone sialoprotein. This could give useful physical properties to the hard and soft tissue interface. When bone remodelling occurs in the alveolar bone, this severs the fibres as the old bone is replaced by new bone. Therefore, the link between Sharpey's fibres and non-collagenous proteins would permit constant embedding of periodontal ligament into the alveolar wall [21].

Orientation

The orientation of ligament fibre bundles is relative to their location, therefore they are classified accordingly with their own functions. The dentoalveolar fibre group consist of five oriented principal fibre groups which insert into the dentoalveolar group and function to resist forces and movement: alveolar crest, horizontal, oblique, apical and interradicular. The gingival fibre groups are principal ligament fibres in the gingiva and consist of four groups: transseptal, dentogingival, alveologingival, circumferential. They act to resist tooth separation and gingival displacement [22].

The alveolar crest fibres run in an apically inclined direction, from the cementum of the tooth just beneath the junctional epithelium towards the alveolar crest. They act to prevent extrusion of teeth and resist lateral tooth movements. Horizontal fibres run perpendicularly to the long axis of the tooth, from cementum to alveolar bone, covering the apical two-thirds of the root. Oblique fibres are the most abundant fibre group in the PDL, extending from the cementum in a coronal direction obliquely to the alveolar bone. They resist vertical and intrusive forces, thus bear a large part of the vertical masticatory stresses and transfer them into tension on the alveolar bone. Apical fibres radiate in an irregular manner from the cementum to alveolar bone at the apical region of the socket and form only after the root is completely formed.

The ligament fibre bundles do not all insert into the alveolar bone. Interradicular fibres fan out from cementum to tooth in furcation areas of multi-rooted teeth. Dentogingival fibres are the most numerous and run from the cervical cementum into the lamina propria of the free and attached gingiva. Alveologingival group fibres radiate from the bone of the alveolar crest into the lamina propria. Circumferential fibres encircle the neck of each tooth to form a band within the marginal gingiva. Transseptal fibres run from the cementum of one tooth and insert into that of the adjacent tooth by crossing the interdental septum [23].

These classification systems have been challenged, particularly for animals that have continually growing teeth [18]. The PDL collagen fibres are generally organised closely aligned with *in vitro* load characteristics, which may show that the ligament morphology is changed by applied forces [24]. This indicates an intimate association between the ligament morphology and its ability to buffer or resist applied loads.

Elastic fibres

Three types of elastic fibres exist: elastin, oxytalan and elaunin. Only oxytalan fibres are found in the human PDL, but the gingival ligament also has fibre bundles which may be linked to elaunin fibres. Oxytalan fibres were described initially by Fullmer [25]. They are pure bundles of microfibrils, which resemble pre-elastic fibres and run in a vertical direction from the surface of the cementum, which forms a meshwork that covers the tooth root [25]. They have no definitive function and cellular origin as of yet, but may regulate blood flow and facilitate fibroblast migration and attachment [26]. Due to their elasticity, they can respond to variations in tension .

Cells of the periodontal ligament

A healthy, functioning periodontal ligament consist of numerous cell types, which involve fibroblasts, cementoblasts, progenitor cells, bone-associated cells, epithelial cell rests of Malassez and connective tissue cells [9]. They all act together to sense applied physical forces and respond to them by maintaining PDL width and preserving cell viability [21]. They are also capable of synthesising and releasing bioactive molecules, for instance cytokines, growth factors and cell adhesion molecules. Platelet-derived growth factor stimulates collagen synthesis, whereas transforming growth factor only has slight chemotactic effects and inhibited mitogenic responses [27].

Fibroblasts

Fibroblasts are the main component cell type in the PDL. In rodents, they make up 35% of the volume space of the ligament, approximately 20% in sheep and 25-30% in humans. The fibroblasts are interconnected by gap junctions and adherence-type junctions [28]. Fibroblasts are responsible for forming and remodelling the PDL fibres. They break down collagen in a controlled manner, intracellularly through phagocytosis. Fibroblasts migrate in the PDL of continuously erupting teeth, during wound healing and in teeth with restricted eruption during usual function. They also have many cytoplasmic microfilament systems, which are indispensable to be able to contract and move. Bellows et al. [22] showed that ligament fibroblasts *in vitro* contract strongly and can orient their extracellular matrix, depending on the level of α-smooth muscle actin. It is not well known how fibroblasts direct the way they migrate and contact, and what signals are necessary [29]. Choe et al. [30] have found that human ligament fibroblasts show *in vitro* phenotypic features consistent with cells that are like osteoblasts, suggesting that they are able to differentiate into osteoblasts and/or cementoblasts.

Epithelial cell rests of Malassez

These cells originate from Hertwig's epithelial root sheath and occur in close proximity to the cementum as clusters or strands. The fact that the epithelial cells are in connective tissue is a unique characteristic [31]. They have characteristics of typical epithelial cells. They are connected by desmosomes and a basal lamina surrounds them. With age, they tend to decrease along every part of the root, in humans and other mammals [32]. They may maintain normal PDL width and do not prevent ankylosis and root resorption [33].

Osteoblasts and osteoclasts

Osteoblasts are bone-forming cells located along the alveolar bone surface, which differentiate locally from mesenchymal cells when needed. They are only prominent when there is active bone formation. Bone is constantly being turned over. Therefore, the osteoblasts will form new bone in that area of alveolar bone being remodelled [34].

Osteoclasts originate from monocytes within the blood vascular system and are found in areas where bone and cementum are being reabsorbed. They are actively involved in the resorption process in instances of tooth movement and periodontal disease. When they resorb bone, the surface of the alveolar bone has Howship's lacunae, resorption concavities, in which the osteoclasts lie in to form as multi-nucleated cells [35].

Cementoblasts and cementoclasts

Cementum is a mineralised tissue that lines the tooth root surface. It is required to form functional PDL attachment during attachment. It is also thought to have a vital function in the reparative process during tissue regeneration after disease [36]. Cho and Garant [37] specified that cementoblasts originate from the ectomesenchymal cells of the dental follicle and appear along the surface of the cementum. Substantial evidence shows that they take part in the development of cellular cementum, which is found in the apical two-thirds of the root. They are also able to separate from the cementum surface and contribute to early PDL fibroblasts [37]. Cementum is resorbed, for example due to changes in tooth movement or occlusion, which results in the activity of new cementoblasts in the repair of resorbed cementum or root dentine [38,39].

Cementoclasts have an important responsibility in permanent teeth being resorbed pathologically. They are created under pathological conditions and cause permanent teeth resorption. For example, permanent tooth roots externally resorb due to stress, re-implanted teeth or induced by proliferation of tumorous lesions [40].

Defence cells

Macrophages are derived from blood monocytes and make up approximately 4% of the PDL population. They phagocytose particulate matter and invading organisms and synthesise a range of molecules with important functions, such as interferon, prostaglandins and factors that enhance the growth of fibroblasts and endothelial cells. Mast cells are often associated with blood vessels and have numerous functions, for instance they produce histamine, heparin and factors associated with anaphylaxis. Eosinophils are only occasionally seen in the normal ligament. They are capable of phagocytosis and possess granules that consist of one or more crystalloid structures [12].

Heterogeneous mesenchymal cell populations

The ligament cells contain heterogeneous mesenchymal cell populations, which are able to differentiate into cells that produce neighbouring mineralised tissues and ample extracellular matrix. This matrix is vital, as it controls the differentiation of periodontal ligament cells, as well as being essential for the homeostasis of the ligament tissue. The act of differentiation involves mechanotransduction, which links the matrix to the cytoskeleton [41].

Progenitor cells and periodontal ligament stem cells

Stem cell research has greatly expanded, although its therapeutic applications are transitioning at a slower rate. Globally, the future of advancing stem cell therapy is promising in tissue regeneration and disease management. It permits healing of defective tissues or functions by transplantating autologus cells. Seo et al. [42] found a group of cells within the PDL which showed specific mesenchymal stem cell traits. This includes clonogenicity, expression of stem cell markers and the ability to differentiate down a variety of cell lineages. This resulted in a large amount of research being conducted into PDL stem cells.

Progenitor cells are undifferentiated mesenchymal cells, which can potentially produce cementum or ligament-like tissue regeneration *in vivo*. Human ligament from the root surface contain these stem cells, which can be transplanted and increased *in vitro*, as a potential therapeutic approach to recreate tissues devastated by periodontal diseases [42]. Park et al. [43] found that after they isolated human PDL stem cells from inflamed ligament tissue, they sustained the reformative ability for cementum and ligament-associated tissues. Khoshhal et al. [44] found that mesenchymal stem cells of the periodontal ligament can be successfully isolated from primary and deciduous teeth.

Periodontal disease is common and has a major effect on worldwide public health. The ability of PDL tissue to regenerate is challenging for periodontal therapy [45]. It has been established that ligament cells can be the accessible pool of adult stem cells to regenerate periodontal tissues. Collagen sponge scaffolds seeded with PDL cells were successfully tested for the regeneration of periodontal fenestration defects in beagle dogs [46].

Ligament-derived stem cells that have primitive neural crest stem cell features were first reported by Techawattanawisal et al. [47]. This suggests that ligament-derived cells can also be used to treat neurological diseases, but more research is needed for confirmation of its clinical use [48]. Being able to harvest stem cells followed by expanding, differentiating, seeding onto a scaffold and then to re-transplant them is highly probable to develop into a clinical reality.

Functions

Eruptive

Ligament fibroblasts play a key role in tooth eruption. It has been suggested that they actively move during tooth eruption, to pull the tooth out of its socket simultaneously. The changes in shape and the way that PDL fibroblasts are oriented are stimulated by a shift from impeded to unimpeded eruption [49].

The importance of the eruptive function can be emphasised by pathologies of the PDL. Traumatic injuries to the teeth, most commonly by subluxation, also result in local injury or a defective PDL, followed by ossification during the healing process, which may lead to ankylosis. Hellsing et al. [50] were able to induce ankylosis by injuring the tooth root and ligament tissues mechanically, luxating the tooth to the point that it was mobile in all directions whilst still remaining within its socket [51].

Homeostasis

Homeostasis between ligament fibroblasts and bone cells that line the interior of the alveolus is one way that the periodontal width is maintained. Therefore, as PDL cells can inhibit osteogenesis, they can prevent ankylosis. However, ankylosis may result if this homeostasis is interfered with. Wesselink and Beertsen [52] administered the drug 1-hydroxyethylidene-1, 1-bisphosphonate to experimental rats. This drug can inhibit bone resorption, increase bone matrix formation and have a cytotoxic effect on ligament fibroblasts. The result was a decrease in ligament width, with ankylosis evident after 30 days.

The width of healthy PDL varies from 0.15-0.38 nm and shows a progressive decrease in thickness with age [14]. Zheng et al. [53] conducted the first study that was able to imitate the developmental microenvironment of PDL stem cells *in vitro*. They found that ligament stem cells obtained from aged donors showed decreased proliferation and differentiation capacity, in comparison to those from young donors. Therefore, regenerative potential to produce cementum/PDL-like structures may be negatively regulated by ageing. Inflammation can be associated with widening the ligament width by disturbing its homeostasis, for example in periodontitis [54]. Mesenchymal stem cells derived from an inflamed ligament have markedly dysfunctional immunomodulatory properties, which may contribute to an imbalanced immune response, acceleration of osteoclastogenesis and inflammatory alveolar bone loss in periodontitis [55].

Sensory

Mechanoreceptors exist within the ligament, which respond to force application. Periodontal mechanoreception is very sensitive and important in reflex mechanisms, with detection of forces of only a few grams applied to a tooth and objects of 10-100 μm between the teeth being possible [17]. It has also been suggested that the periodontal sensory innervation may interact with immunocompetent cells to assist their migration to inflamed areas of the ligament, for example to take part in the remodelling process during orthodontic tooth movement [56].

The PDL functions to provide unconscious sensory feedback during mastication. Humans can detect small particles between the occlusal surfaces of teeth. Teeth can also be very good at judging material properties. Proprioceptive sensors in the ligament give sensory information as to how fast and hard to bite [57]. Lund and Lamarre [58] found that after they anaesthetised patients' teeth, there was a 40% decrease in the force of bite applied, which shows that ligament proprioceptors are important in controlling the masticatory force and supporting the ligament sensory feedback role.

Periodontal disease

PDL fibroblasts produce the collagen and ground substance, which are subject to dynamic turnover. Evidence shows that fibroblasts may also contribute to lysis or dissolution of collagen fibres. There is high rate of collagen turnover in the ligament, therefore if disease interferes with fibroblast function, it will result in a rapid loss of the tooth supporting tissue. For example, periodontal diseases involve an inflammatory response, which in turn causes an increase in the expression of matrix metalloproteinases (MMPs), which aggressively destroy collagen [59]. MMPs have an important role in inflammation and regulating the immune response. They can increase or decrease the bioavailability of signalling molecules by varied methods, which can result in extensive loss of periodontal tissue and continual inflammation [60].

Bone remodelling

All structures of the periodontium, including the principal fibres, are constantly undergoing remodelling. When bone remodelling occurs in the alveolar bone, this severs the fibres as the old bone is replaced by new bone. The osteoblasts maintain the bone of the socket by producing new bone following bone resorption [34]. The PDL responds to physiological tooth movement, occlusal forces, repair of injuries and regeneration following periodontal therapy. Pressure stimulates bone resorption, whereas tension on the ligament fibres tends to stimulate bone and cementum formation. Severe pressure produces rapid bone resorption. It may also resort in resorption of the more resistant cementum and destroy areas of the ligament [61].

Nutrition

The nutritive function is served by the presence of blood vessels in the ligament. They provide nutrition to the cells of periodontium through the blood vessels of the principal fibre groups, because they contain various anabolites and other substances, which are required by the ligament cells. Compression of the blood vessels, due to heavy forces applied on the tooth, leads to cell necrosis. Blood vessels also remove catabolites. The PDL protects the blood vessels and nerves from injury by mechanical forces. It also attaches the tooth to the bone in the socket, and the absorption of occlusal forces protects the vessels, nerves and bone from injury [62].

Tooth support mechanism

A primary role of the ligament is to act as a medium of force transfer during mastication. Matsuo et al. [63] found that blood vessels in the ligament may contribute to 'shock absorber' behaviour of the PDL, to cushion the alveolus from occlusal load. The ligament exhibits viscoelastic behaviour, where the fluid component of the tissue modifies the action of the fibres in withstanding transmitted loads. As increasing levels of force are applied to the tooth, the initial resistance is low. The resistance increases until at high levels of force, the additional displacement is very small [62].

Evidence from connective tissue elsewhere in the body, particularly from tendons, suggests that the ligament collagen crimps play a role in the preliminary stages of masticatory loading, which permits some movement prior to the tissue experiencing tension. Experiments involving relatively long-term changes in the mechanical demands placed on the PDL, for example pinning a tooth to completely prevent tooth movements, produced no major changes in the structure of the periodontal ligament. They also provide evidence that the ligament is not as affected by the mechanical demands placed upon it, compared to tissues elsewhere in the body. Recent biochemical analysis of the proteoglycans within the ligament shows that under different loading regimens, the degree of aggregation/disaggregation of the ground substance may have a role in tooth support [64].

Conclusion

There is abundant research on the areas associated with the development, structure and function of the PDL. There are still gaps for further research into aspects of the PDL, as mentioned in this paper, for instance the way that ligament lineages develop and are regulated has not been completely clarified. Further experimental evidence relating to ligament stem cells should be gathered because of the vast potential they have to offer as stem cell based therapies in various aspects of dental and medical care.

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