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The Periodontal Ligament: Development, Anatomy and Function

**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, which will be mentioned, 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. The recent advances in PDL stem cell research will also be discussed, which 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.

**Keywords:** Periodontal ligament, oral biology, development, structure, anatomy, function

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**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 (Miletich and Sharpe, 2004). It has an array of oriented fibres, is vascular and highly cellular, for example it contains PDL fibroblasts, osteoblasts and cementoblasts (Lekic *et al.*, 2001). The ligament is crucial as it protects, supports and provides sensory input for the masticatory system, maintains homeostasis and repairs tissue destruction caused by periodontal disease or mechanical trauma (Gronthos *et al*., 2006).

**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 (Ten Cate *et al.,* 1971). The dental follicle is a condensation of the ectomesenchymal tissue, and its cells differentiate into cementoblasts, during their apical development, and form the cementum lining the surface of the root (Grant and Bernik, 1972).

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 the root forms. 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 (Grant and Bernik, 1972) and may be a result of the positional relationship of the erupting tooth to the teeth adjacent (Bartold and Narayanan, 1998).

During eruption, the dentogingival fibres align themselves from the CEJ in the occlusal direction, and 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 (Grant and Bernik, 1972, Bartold and Narayanan, 1998).

Ligament formation in the teeth with and without primary predecessors differs in structure. Grant *et al..* (1972) found that the way that ligament is formed in deciduous teeth differs from succedaneous teeth. Both classes of teeth follow the same stages therefore 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, and 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-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 (Rygh, 1976).

*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 and venous drainage is achieved by axially directed vessels that drain into a system of networks in the apical portion of the ligament that consists of large diameter venules. Lymphatic vessels tend to follow the venous drainage (Beertsen *et al*., 1997).

*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 (Beertsen *et al.,* 1997). Maeda *et al..* (1994) 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 (Berkovitz *et al*., 2002). The ligament is predominantly tissue rich in ground substance, even though it appears to be rich in collagen. Berkovitz *et al..* (1981) 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 (Pearson, 1982, *Nanci et al.,* 2006). 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 (Purvis et al. 1984). 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 (Zhang *et al.,* 1993). 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 (Nanci *et al.,* 2006).

**Periodontal ligament fibres**

*Principal fibres*

Most of the PDL composition comes from principal fibres, which are oriented bundles of collagen fibres, placed at inclinations that are important to their functions, along the root surface. 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 (Avery and Chiego, 1999). Each individual collagen fibre is roughly 55nm in diameter, which is small in comparison with the 100-250nm 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 (Sloan and Carter, 1995, Nanci *et al.* 2006). PDL fibres are usually wavy in nature, enroute from the cementum to bone, to permit for tooth movement (Melcher and Eastoe, 1969). In a study by Pini *et al..* (2002), 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 (Bartold and Narayanan, 1998). 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 (Beersten, 1997).

*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 (McCulloch *et al.,* 2000). 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 (Beersten *et al.,* 2000). 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 (McCulloch *et al.,* 2000).

*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 (Melcher and Eastoe 1969, Avery and Chiego, 1999).

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 (Moss-Salentjin *et al.,* 1990).

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, whereas the 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 (Moss-Salentjin *et al.,* 1990).

These classification systems have been challenged, particularly for animals that have continually growing teeth (Sloan and Carter, 1995). 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 (Montes *et al.,* 1982). 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. 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 (Fullmer, 1958). They have no definitive function and cellular origin as of yet, but may regulate blood flow and facilitate fibroblast migration and attachment (Sims, 1975). Due to their elasticity, they can respond to variations in tension (Nanci *et al.,* 2006).

**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 (Beersten *et al.,* 1997). They all act together to sense applied physical forces and respond to them by maintaining PDL width and preserving cell viability (McCulloch *et al.,* 2000). 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 (Pierce *et al.,* 1989).

*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 (McCulloch *et al.,* 2000). The fibroblasts are interconnected by gap junctions and adherence-type junctions (Beertsen, 1980). 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 (Beersten, 1997). Bellows *et al..* (1981) 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 (Ogata *et al.,* 1994). Choe *et al..* (2012) 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 (Rincon *et al.,* 2005). 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 (Simpson, 1965). They may maintain normal PDL width, and do not prevent ankylosis and root resorption (Wesselink and Beertsen, 1993).

*Osteoblasts and osteoclasts*

Osteoblasts are bone-forming cells located along the alveolar bone surface, and 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 (Caetano-Lopes *et al.,* 2007).

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 (Wiebe *et al.,* 1996).

*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 (D’Errico *et al.,* 1999). Cho and Garant (1989) 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 (Bosshardt and Schroeder, 1992). They are also able to separate from the cementum surface and contribute to early PDL fibroblasts (Cho and Garant, 1989). 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 (Bosshardt and Selvig, 1997).

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 (Wise and King, 2008).

*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 (Berkovitz *et al.,* 2002).

*Progenitor cells and periodontal ligament 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 (Seo *et al.,* 2004). Park *et al..* (2011) found that after they isolated human PDL stem cells from inflamed ligament tissue**,** they sustained the reformative ability for cementum and ligament-associated tissues. Adult stem cell biology is continually advancing. Coura *et al..* (2008) provided evidence that the human PDL produces neural crest-like cells and showed itself as a viable alternative source for possible primitive precursors to be used in stem cell therapies. Recent studies have shown that SSEA-4+ human ligament cells may be a potential source of stem cells for regenerative medicine (Kawanabe *et al.,* 2010). However, the way that ligament lineages develop and are regulated has not been completely clarified (Techawattanawisal *et al.,* 2007). Periodontal disease is common and has a major affect on worldwide public health and the ability of PDL tissue to regenerate is challenging for periodontal therapy (Bartold *et al.,* 2000). It has been established that PDL cells can be the accessible pool of adult stem cells, to regenerate periodontal tissues. Ligament-derived stem cells that have primitive neural crest stem cell features were first reported by Techawattanawisal *et al..* (2007). 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 (Coura *et al.,* 2008). Congenital and acquired craniofacial deformities constitute global burdensome surgical problems. The outcome of current surgical therapies can be volatile and disappointing. 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 (Sanchez-Lara *et al.,* 2012).

**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. (Weinreb *et al..* 1997).

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..* (1993) 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 (Panzarini *et al.,* 2008).

*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 (1994) 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 0.15-0.38nm and shows a progressive decrease in thickness with age (Nanci *et al.,* 2006). Zheng *et al..* (2009) 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 (Auluck, 2007). 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 (Liu *et al.,* 2012).

*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 10-100μm between the teeth being possible (Avery and Chiego, 1999). 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 (Vandevska-Radunovic *et al.,* 1999).

The PDL functions to provide unconscious sensory feedback during mastication. Humans can detect small particles between the occlusal surfaces of teeth, and 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 (Hannam, 1982). Lund and Lamarre (1973) 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.

*Formative, resorptive, nutritive and protective*

These functions can be seen in developing and adult functioning teeth. Ligament cementoblasts can produce cementum of the tooth root at any time during the tooth life. The osteoblasts maintain the bone of the socket by producing new bone following bone resorption. PDL fibroblasts produce the collagen and ground substance, which are subject to dynamic turnover, especially during orthodontic treatment. 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, which aggressively destroy collagen (Everts *et al.,* 1996).

All structures of the periodontium, including the principal fibres, are constantly undergoing remodelling. The PDL formative function responds to physiological tooth movement, occlusal forces, repair of injuries and regeneration following periodontal therapy. The resorptive function accompanies the above. 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 (Cho and Garant, 2000).

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 (Wills *et al.,* 1978).

*Tooth support mechanism*

A primary role of the ligament is to act as a medium of force transfer during mastication. Matsuo and Takahashi (2002) 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 (Wills *et al.,* 1978).

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 (Annovazzi and Genna, 2010). 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, and provided evidence that the ligament is not as affected by the mechanical demands placed upon it, as 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 (Pilloni *et al.,* 2011).

**Conclusion**

There is abundant research on the areas associated with the development, structure and function of the PDL. This has come about as comparisons can be made in some aspects for a number of tissues, for example bone, cartilage and tendons, due to similarities in functions and structure. Furthermore, many experiments have been conveyed, mainly on rats but also dogs, to obtain a depth of knowledge on the ligament. We can acquire associations between humans and these animals, due to having some similarities in their tooth structures.

It can be summarised that the periodontal ligament is a unique specialised connective tissue, derived from the dental follicle region, which originates from the cranial neural crest cells, to form the extracellular components and cells of the ligament. The ligament cells maintain homeostasis and allow for the formative and resorptive function of the ligament, during and after development. There is also an important eruptive function, which can be inhibited by dental ankylosis. The PDL is essential because in the masticatory system, its removal results in resorption of the alveolar bone surrounding the tooth and loss of tooth function. It is also important because during mastication, the ligament allows sensory innervation and for a force exchange system between the tooth and alveolar bone, as it has the capacity to change position under occlusal loading and masticatory forces. Therefore, the ligament performs to its supportive structure. Furthermore, the PDL conveys blood vessels and provides nourishment for the periodontium.

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. I strongly feel that the recent advances in ligament stem cell research are crucial. There should be an emphasis on gathering further experimental evidence relating to ligament stem cells because of the vast potential they have to offer as stem cell based therapies in various aspects of dental and medical care, ranging from the treatment of craniofacial deformities to neurological disorders.

**References**

Auluck, A. (2007), *Widening of periodontal ligament space and mandibular resorption in patients with systemic sclerosis*, Dentomaxillofacial Radiology, 36(7), pp. 441-442.

Avery J, C.D. (1999), *Essentials of Oral Histology and Embryology: A Clinical Approach*, pp. 145-155.

Bartold M, N.A. (1998), *Biology of the Periodontal Tissues.* Chicago: Quintessence Publishing, pp. 151-172.

Bartold, P.M., Mcculloch, C.A., Narayanan, A.S. And Pitaru, S. (2000), *Tissue engineering: a new paradigm for periodontal regeneration based on molecular and cell biology,* Periodontology 2000, 24, pp. 253-269.

Beertsen, W. And Everts, V. (1980), *Junctions between fibroblasts in mouse periodontal ligament,* Journal of Periodontal Research, 15(6), pp. 655-668.

Beertsen, W., Mcculloch, C.A. And Sodek, J. (1997). The periodontal ligament: a unique, multifunctional connective tissue. *Periodontology 2000,* 13, pp. 20-40.

Bellows, C.G., Melcher, A.H. And Aubin, J.E. (1981), *Contraction and organization of collagen gels by cells cultured from periodontal ligament, gingiva and bone suggest functional differences between cell types,* Journal of Cell Science,50, pp. 299-314.

Berkovitz, B.K.B, Holland G.R, Moxham B.J (2002), *Oral anatomy, histology and embryology*, Edinburgh: Mosby/Elsevier, pp. 187-188.

Bosshardt, D.D. And Schroeder, H.E. (1992), *Initial formation of cellular intrinsic fiber cementum in developing human teeth. A light- and electron-microscopic study,* Cell and Tissue Research, 267(2), pp. 321-335.

Bosshardt, D.D. And Selvig, K.A. (1997), *Dental cementum: the dynamic tissue covering of the root*, Periodontology 2000*,* 13, pp. 41-75.

Caetano-Lopes, J., Canhao, H. And Fonseca, J.E. (2007), *Osteoblasts and bone formation,* Acta Reumatologica Portuguesa,32(2), pp. 103-110.

Cate, A.R.T., Mills, C. And Solomon, G. (1971), *The development of the periodontium. A transplantation and autoradiographic study,* The Anatomical Record*,* 170(3), pp. 365-379.

Cho, M.I. And Garant, P.R. (2000), *Development and general structure of the periodontium,* Periodontology 2000,24, pp. 9-27.

Cho, M.I. And Garant, P.R. (1989), *Radioautographic study of [3H]mannose utilization during cementoblast differentiation, formation of acellular cementum, and development of periodontal ligament principal fibers,* The Anatomical Record, 223(2), pp. 209-222.

Choe, Y., Yu, J.Y., Son, Y.O., Park, S.M., Kim, J.G., Shi, X. And Lee, J.C. (2012), *Continuously generated H2O2 stimulates the proliferation and osteoblastic differentiation of human periodontal ligament fibroblasts,* Journal of Cellular Biochemistry, 113(4), pp. 1426-1436.

Coura, G.S., Garcez, R.C., De Aguiar, C.B., Alvarez-Silva, M., Magini, R.S. And Trentin, A.G. (2008), *Human periodontal ligament: a niche of neural crest stem cells*, Journal of Periodontal Research*,* 43(5), pp. 531-536.

D'errico, J.A., Ouyang, H., Berry, J.E., Macneil, R.L., Strayhorn, C., Imperiale, M.J., Harris, N.L., Goldberg, H. And Somerman, M.J. (1999), *Immortalized cementoblasts and periodontal ligament cells in culture,* Bone*,* 25(1), pp. 39-47.

Everts, V., Van Der Zee, E., Creemers, L. And Beertsen, W. (1996), *Phagocytosis and intracellular digestion of collagen, its role in turnover and remodeling,* The Histochemical Journal,28(4), pp. 229-245.

Fullmer, H.M. (1958), *Differential staining of connective tissue fibers in areas of stress*, Science (New York, N.Y.),127(3308), pp. 1240.

Grant, D. And Bernick, S. (1972), *Formation of the periodontal ligament*, Journal of Periodontology, 43(1), pp. 17-25.

Grant, D.A., Bernick, S., Levy, B.M. And Dreizen, S. (1972), *A comparative study of periodontal ligament development in teeth with and without predecessors in marmosets,* Journal of Periodontology,43(3), pp. 162-169.

Gronthos, S., Mrozik, K., Shi, S. And Bartold, P.M. (2006), *Ovine periodontal ligament stem cells: isolation, characterization, and differentiation potential,* Calcified Tissue International, 79(5), pp. 310-317.

Hannam Ag. (1982), ‘The innervations of the Periodontal ligament’, in Berkovitz B, Moxham B, Newman H. (eds.), *The Periodontal Ligament in Health and Disease*, London: Mosbey-Wolfe, pp. 173-196.

Hellsing, E., Alatli-Kut, I. And Hammarstrom, L. (1993), *Experimentally induced dentoalveolar ankylosis in rats,* International Endodontic Journal*,* 26(2), pp. 93-98.

Kawanabe, N., Murata, S., Murakami, K., Ishihara, Y., Hayano, S., Kurosaka, H., Kamioka, H., Takano-Yamamoto, T. And Yamashiro, T. (2010), *Isolation of multipotent stem cells in human periodontal ligament using stage-specific embryonic antigen-4,* Differentiation; research in biological diversity, 79(2), pp. 74-83.

Lekic, P., Rojas, J., Birek, C., Tenenbaum, H. And Mcculloch, C.A., 2001. *Phenotypic comparison of periodontal ligament cells in vivo and in vitro*, Journal of Periodontal Research,36(2), pp. 71-79.

Liu, D., Xu, J., Liu, O., Fan, Z., Liu, Y., Wang, F., Ding, G., Wei, F., Zhang, C. And Wang, S. (2012), *Mesenchymal stem cells derived from inflamed periodontal ligaments exhibit impaired immunomodulation*, Journal of Clinical Periodontology*,* 39(12), pp. 1174-1182.

Lund, J.P. And Lamarre, Y. (1973), *The importance of positive feedback from periodontal pressoreceptors during voluntary isometric contraction of jaw-closing muscles in man*, Journal de Biologie Buccale*,* 1(4), pp. 345-351.

Maeda, T., Sodeyama, T., Hara, K. And Takano, Y. (1994). *Evidence for the existence of intraepithelial nerve endings in the junctional epithelium of rat molars: an immunohistochemical study using protein gene product 9.5 (PGP 9.5) antibody*, Journal of Periodontal Research,29(6), pp. 377-385.

Matsuo, M. And Takahashi, K. (2002). *Scanning electron microscopic observation of microvasculature in periodontium,* Microscopy Research and Technique, 56(1), pp. 3-14.

Mcculloch, C.A., Lekic, P. And Mckee, M.D. (2000), *Role of physical forces in regulating the form and function of the periodontal ligament*, Periodontology 2000,24, pp. 56-72.

Melcher A, E.J. (1969), ‘The connective tissues of the periodontium’, in Melcher A, Bowen W (eds.), *Biology of the Periodontium*, New York: Academic Press, pp. 291-330.

Miletich, I. And Sharpe, P.T (2004), *Neural crest contribution to mammalian tooth formation*, Birth defects research.Part C, Embryo today: reviews*,* 72(2), pp. 200-212.

Montes, G.S. And Junqueira, L.C. (1982), *Biology of collagen*, Revue Canadienne de Biologie Experimentale, 41(2), pp. 143-156.

Moss-Salentijn L, H.M. (1990), *Dental and Oral Tissues*, Lea & Febiger: Philadelphia, pp. 161-315.

Nanci, A. And Bosshardt, D.D. (2006), *Structure of periodontal tissues in health and disease*, Periodontology 2000, 40, pp. 11-28.

Ogata, Y., Yokota, Y., Niisato, N., Furuyama, S. And Sugiya, H. (1994), *Presence of endogenous chemotactic factors for periodontal ligament cells in bovine cementum and bone*, Archives of Oral Biology, 39(6), pp. 529-533.

Panzarini, S.R., Pedrini, D., Poi, W.R., Sonoda, C.K., Brandini, D.A. And Monteiro De Castro, J.C. (2008), *Dental trauma involving root fracture and periodontal ligament injury: a 10-year retrospective study,* Brazilian Oral Research,22(3), pp. 229-234.

Park, J.C., Kim, J.M., Jung, I.H., Kim, J.C., Choi, S.H., Cho, K.S. And Kim, C.S. (2011), *Isolation and characterization of human periodontal ligament (PDL) stem cells (PDLSCs) from the inflamed PDL tissue: in vitro and in vivo evaluations*, Journal of Clinical Periodontology, 38(8), pp. 721-731.

Pearson C. H (1982), ‘The ground substance of the periodontal ligament’, in Edited by Berkovitz B. H. B., Moxham B. J. and Newman H. N. (ed.), *The Periodontal Ligament in Health and Disease,* Pergamon Press, Oxford, pp. 119-150.

Pierce, G.F., Mustoe, T.A., Lingelbach, J., Masakowski, V.R., Griffin, G.L., Senior, R.M. And Deuel, T.F. (1989), *Platelet-derived growth factor and transforming growth factor-beta enhance tissue repair activities by unique mechanisms,* The Journal of Cell Biology, 109(1), pp. 429-440.

Pilloni, A., Annibali, S., Dominici, F., Di Paolo, C., Papa, M., Cassini, M.A. And Polimeni, A. (2011*), Evaluation of the efficacy of an hyaluronic acid-based biogel on periodontal clinical parameters. A randomized-controlled clinical pilot study,* Annali di Stomatologia, 2(3-4), pp. 3-9.

Pini, M., Wiskott, H.W., Scherrer, S.S., Botsis, J. And Belser, U.C. (2002), *Mechanical characterization of bovine periodontal ligament,* Journal of Periodontal Research, 37(4), pp. 237-244.

Purvis, J.A., Embery, G. And Oliver, W.M. (1984), *Molecular size distribution of proteoglycans in human inflamed gingival tissue,* Archives of Oral Biology*,* 29(7), pp. 513-519.

Rincon, J.C., Xiao, Y., Young, W.G. And Bartold, P.M. (2005), *Production of osteopontin by cultured porcine epithelial cell rests of Malassez*, Journal of Periodontal Research, 40(5), pp. 417-426.

Rygh, P. (1976), *Ultrastructural changes in tension zones of rat molar periodontium incident to orthodontic tooth movement*, American Journal of Orthodontics, 70(3), pp. 269-281.

Sanches-Lara Pa., Zhao H., Bajpai R., Abdelhamid Ai., Warburton D. (2012), *Impact of stem cells in craniofacial regenerative medicine*, Front Physiolo*gy,* 3, pp. 188

Seo, B.M., Miura, M., Gronthos, S., Bartold, P.M., Batouli, S., Brahim, J., Young, M., Robey, P.G., Wang, C.Y. And Shi, S. (2004), *Investigation of multipotent postnatal stem cells from human periodontal ligament*, Lancet*,* 364(9429), pp. 149-155.

Simpson, H.E. (1965), *The Degeneration of the Rests of Malassez with Age as Observed by the Apoxestic Technique*, The Journal of Periodontology*,* 36, pp. 288-291.

Sims, M.R. (1975), *Oxytalan-vascular relationships observed in histologic examination of the periodontal ligaments of man and mouse,* Archives of Oral Biology, 20(11), pp. 713-716.

Sloan P, C.D. (1995), ‘Structural organization of the fibers of the periodontal ligament’, in: Berkovitz B, Moxham B, Newman H. (eds*.), The Periodontal Ligament in Health and Disease,* London: Mosbey-Wolfe, pp. 51-72.

Techawattanawisal, W., Nakahama, K., Komaki, M., Abe, M., Takagi, Y. And Morita, I. (2007), *Isolation of multipotent stem cells from adult rat periodontal ligament by neurosphere-forming culture system*, Biochemical and Biophysical Research Communications*,* 357(4), pp. 917-923.

Vandevska-Radunovic, V., Kvinnsland, S. And Jonsson, R. (1999), *Delayed recruitment of immunocompetent cells in denervated rat periodontal ligament following experimental tooth movement*, Journal of Dental Research*,* 78(6), pp. 1214-1220.

Wiebe, S.H., Hafezi, M., Sandhu, H.S., Sims, S.M. And Dixon, S.J. (1996), *Osteoclast activation in inflammatory periodontal diseases*, Oral diseases*,* 2(2), pp. 167-180.

Weinreb, M., Gal, D., Weinreb, M.M. And Pitaru, S. (1997), *Changes in the shape and orientation of periodontal ligament fibroblasts in the continuously erupting rat incisor following removal of the occlusal load*, Journal of Dental Research*,* 76(10), pp. 1660-1666.

Wesselink, P.R. And Beertsen, W. (1994), *Ankylosis of the mouse molar after systemic administration of 1-hydroxyethylidene-1,1-bisphosphonate (HEBP),* Journal of Clinical Periodontology, 21(7), pp. 465-471.

Wesselink, P.R. And Beertsen, W. (1993), *The prevalence and distribution of rests of Malassez in the mouse molar and their possible role in repair and maintenance of the periodontal ligament,* Archives of Oral Biology,38(5), pp. 399-403.

Wills, D.J., Picton, D.C. And Davies, W.I. (1978), *The intrusion of the tooth for different loading rates*, Journal of Biomechanics,11(10-12), pp. 429-434.

Wise, G.E. And King, G.J. (2008), *Mechanisms of tooth eruption and orthodontic tooth movement,* Journal of Dental Research*,* 87(5), pp. 414-434.

Zhang, X., Schuppan, D., Becker, J., Reichart, P. And Gelderblom, H.R. (1993), *Distribution of undulin, tenascin, and fibronectin in the human periodontal ligament and cementum: comparative immunoelectron microscopy with ultra-thin cryosections,* The journal of Histochemistry and Cytochemistry: official journal of the Histochemistry Society, 41(2), pp. 245-251.

Zheng, W., Wang, S., Ma, D., Tang, L., Duan, Y. And Jin, Y. (2009), *Loss of proliferation and differentiation capacity of aged human periodontal ligament stem cells and rejuvenation by exposure to the young extrinsic environment,* Tissue engineering.Part A*,* 15(9), pp. 2363-2371.