



ROLE OF FIBROBLAST IN PERIODONTAL HOMEOSTASIS: A NARRATIVE REVIEW

Periodontology

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ABSTRACT

The major cell type in the fibrous connective tissues of the periodontium is fibroblast. They play essential roles in the periodontium's development, physiology, defense, disease progression, and therapy of the various diseases that affect it. The primary residing cells in the periodontal tissues are called fibroblasts. They are essential for keeping the connective fibers that hold the tooth in place. Several extracellular compounds can be produced and secreted by fibroblasts. Collagen, elastin, proteoglycans, and glycoproteins are the main four kinds. The most prevalent proteins in our bodies are all types of collagen. In cell function, wound healing, and tissue integrity, fibroblasts' capacity to multiply, move, elongate, adhere, immobilize, and initiate matrix production is essential. They play an active role in host defense as well. Gingival fibroblasts release a variety of soluble mediators of inflammation after being stimulated by bacterial infections and their metabolites as well as by cytokines. Their origins, growth factor and regulatory cytokine synthesis in health and illness, and significance in soft tissue regeneration are all largely unexplored. Therefore, the purpose of this review is to describe the most recent research on the subject of periodontal fibroblasts in both healthy and diseased states, as well as following periodontal therapy.

KEYWORDS

Periodontal Ligament Fibroblast, Extracellular Matrix, Homeostasis, Remodeling

INTRODUCTION.

The periodontium, an organ of connective tissue and epithelium that connects the jawbones to the teeth, acts as a constantly evolving structure to support the teeth while they are functioning. Fibroblasts have critical functions in the growth, composition, and operation of the tooth supporting system. Extracellular matrices, such as collagen and elastin fibers and a substantial number of non fibrillar glycoproteins, are created and modified by fibroblasts. Additionally, these cells are contractile and motile, which contribute to the internal structure of the tissue, particularly when the periodontal ligament is developing. Since fibroblasts make up the majority of the periodontal connective tissues, they are crucial for regular turnover, repair, and regeneration. 'Fibroblasts are by far the most prevalent stromal cell type in soft connective tissues, such as healthy periodontal ligament or gingiva.' The primary cell type in the fibrous connective tissues of the periodontium is FIBROBLASTS.

They play significant roles in the periodontium's fibrous connective tissues' physiology, development, disease, and treatment. The fibroblast, which is in charge of the development and turnover of fibers and ground substance, is the main cell in the lamina propria of oral mucosa and the periodontal ligament. Thus, the fibroblast is essential for preserving tissue integrity. This review's objective is to highlight the most recent research on the topic of periodontal fibroblasts in health, disease, and its role in periodontal homeostasis.

Structure Of Fibroblast

The fibroblasts are cigar-shaped (fusiform) or star-shaped (stellate) under a light microscope, with lengthy processes that often run parallel to bundles of collagen fiber and are difficult to see under a light microscope. One or more pronounced nucleoli can be found in fibroblast nuclei. The fibroblasts are ultra structurally similar to active synthetic cells because they contain plenty of mitochondria, a big granular endoplasmic reticulum, a big golgi complex, and lots of membrane-bound vesicles. In adult mucosa, fibroblasts do not proliferate frequently, with the exception of when a wound is healing, when their numbers rise as a result of cell division in the nearby healthy tissues. The fibroblasts that make up the periodontal ligament are big cells with a considerable amount of organelles involved in protein synthesis and secretion in their cytoplasm. Their cytoskeleton is substantially developed. They also display adhesion molecules and gap junctions, two types of cell-cell interactions. They feature extensive processes that wrap around the fiber bundles and are oriented along the general direction of the bundles.

Features Of Fibroblasts.

- 1) Extracellular matrix synthesis and deposition³ and

- 2) Tissue turnover and remodelling in diverse healthy and pathological situations⁶
- 3) Homeostasis and tissue integrity⁴
- 4) Fibroblasts can contract and take part in the contraction of a wound, in which case they produce intracytoplasmic actin filaments.
- 5) Chemotaxis, phagocytosis of foreign particles, consumption of cross-linked collagen, and control of inflammasome responses locally⁵
- 6) Modulating interactions between cells, such as those with lymphocytes⁶ and the epithelium⁷, in nearby tissues and cells.
- 7) Regeneration of the Periodontium

Role Of Fibroblast In Maintaining Periodontal Integrity.

Aside from well-described structural and functional similarities (such as the production of collagen and fibronectin, vimentin intermediate filaments, and t3-actin), fibroblasts also differ significantly in terms of cytoskeletal proteins (such as the expression of -smooth muscle actin)⁸, surface markers (such as Clq receptors), and size⁹, which may indicate the existence of distinct cellular subsets. Both variations within a certain site (such as the gingiva) and variations between sites from various anatomical locations have been described.¹⁰

The management of fibroblast populations in steady-state and pathological situations has been argued to be crucial for a thorough understanding of the fundamental mechanisms underlying health and illness.¹¹ The periodontal ligament (PL) and healthy gingiva are mostly made up of fibroblasts, which play a significant role in the growth, maintenance, and regeneration of the tooth support system. With about 65% of the total cell population and 5.2% of the volume, fibroblasts make up the majority of the cells in healthy gingival connective tissue. 14.5% of the volume of inflammatory gingival connective tissue is made up of fibroblasts.¹² In periodontal tissues that are functioning correctly, cell turnover entails the creation of new cells through proliferation, which is then counterbalanced by apoptotic cell death. Numerous different types of more distinct, specialized cells, such as a high number of fibroblastic cells and a much smaller number of osteogenic or cementogenic cells, can be produced by progenitor cells. Fibroblasts are a steady-state renewal cell system as a result. By having the capacity to remodel tissues, repopulate wounds, affect other cell types' metabolisms, and develop new fibrous attachments, fibroblasts assist in maintaining periodontal homeostasis. Trauma and a number of common disorders can alter the make-up and integrity of these tissues. Notably, periodontitis frequently manifests as damaging, gradual alterations of the dento-gingival junction, alveolar bone, cementum, and periodontal ligament. Due to the irreversible death of connective tissue cells and matrix, this diverse group of disorders has

clinical and biological significance. These damaging processes include the resorption of alveolar bone and tooth roots as well as the loss of fibrous attachment, alterations that may result in tooth loss. Restoring fibrous attachments and lost bone is a key goal of periodontal therapy. To restore the shape and functionality of damaged tissues, integrated synthetic and remodelling processes are needed. There must also be the development of new cementum and bone, as well as the attachment of new connective tissue fibers to the tooth, in addition to the restoration of a new epithelial connection. Thus fibroblasts play the central role in the health, disease and treatment of the periodontium.

Products Synthesized By Fibroblasts.

Numerous extracellular compounds can be produced and secreted by fibroblasts.

Generally, there are four types:

Collagens, elastins, proteoglycans, and glycoproteins.

Collagen.

Many skeletal and soft connective tissues mostly consist of collagens. Collagen makes up about 30% of the body's total protein. The preservation of the tissues' structure and tone is carried out by these stiff proteins. Based on their molecular structure and makeup, at least 14 distinct collagens have been found so far. With such variability, it is clear that there are different structural groupings within the collagen family and that the structure of collagens is not uniform. Recognizing collagen as a structural protein that has one or more domains with a collagen triple helix conformation is important.¹³

collagens may be grouped according to a variety of structural features as:

- Collagens participating in quarter staggered fibrils,
- Fibril-associated collagens with interrupted triple helices (FACITS), Collagens forming sheets,
- Collagens forming beaded fibrils,
- Collagens forming anchoring fibrils, and
- Miscellaneous.

ELASTIN

Most vertebrate tissues, to varied degrees, include elastin, an extremely flexible and distensible protein that gives tissues the capacity to stretch, bend, and twist. In numerous disorders, including as atherosclerosis, emphysema, solar dermatosis, and ageing, elastin goes through a multitude of alterations. Elastin fibers are made up of an exterior microfibrillar component and an interior amorphous elastin component. Numerous crosslinks stabilize the molecule; some are similar to those in collagen and others, such as desmosine and isodesmosine, are specific to elastin. Tropoelastin, the precursor of elastin, assembles into elastin fiber extremely quickly extracellularly by effective crosslinking processes. It has been discovered that elastin has cell surface receptors (or binding proteins) that may be related to cell chemotaxis.¹⁴

PROTEOGLYCAN.

All connective tissues include enormous, highly anionic glycoproteins called proteoglycans. They can be found on cell surfaces and inside cell organelles, as well as inside the matrix, which really is home to them. Because of their high charge, they have been assigned a number of roles, including regulating collagen fiber synthesis, binding growth factors, promoting cell adhesion and proliferation, and hydrating tissues. A proteoglycan is a single protein core that has been covalently joined by one or more glycosaminoglycan side chains. Historically, proteoglycans were categorised according to the makeup of their glycosaminoglycans, with names like "little dermatan sulphate proteoglycans" or "large aggregating chondroitin sulphate proteoglycans."

Glycoproteins are classified as follows based on their location, namely:

- (I) Matrix organizers and tissue space fillers,
- (ii) Cell surface proteoglycans or
- (iii) Intracellular proteoglycans of the haemopoietic cells.¹⁴

Role Of Fibroblasts In Turnover & Remodelling.

The periodontal ligament undergoes turnover and remodelling, which implies the production and decomposition of matrix elements, particularly the collagenous fiber meshwork that spans the gap between the cementum and the bone. The periodontal ligament's

collagen fibers, as previously mentioned, are essential for the support of teeth and their attachment to bone. They come together to form a mesh of smaller fibers, each of which is made up of unbranched collagen fibrils that may cross over into other fiber strands. Even though there is no conclusive evidence in favour of or against this theory, research has revealed that remodelling of the ligament is mostly restricted to the mid-region of the periodontal ligament where fiber from the bone and fiber from the tooth interdigitate in an irregular pattern as "intermediate plexus".¹⁵

The periodontal ligament's fiber systems must be broken down and new fiber must be generated in order to adjust to changes in tooth position. Remodeling doesn't always take place at all sites simultaneously since the periodontal ligament is made up of a complicated meshwork rather than single strands of straight collagen fiber.

The mechanism appears to be flexible enough to allow adaptation changes by dissolving some small fragments of collagen fiber bundles or individual fibrils while maintaining others. The phagocytosis of collagen surely aids in this very targeted remodeling process. Collagen phagocytosis allows periodontal ligament fibroblasts to very precisely remove collagen fibrils at specific places, as opposed to the mass removal of collagen that is caused by extracellular matrix metalloproteinases.¹⁶

Fibroblast In Maintaining Tissue Integrity And Homeostasis

Mammalian teeth with limited eruption can change positions while still being firmly linked to the bone socket due to the cooperation of the cells, vascular components, and extracellular matrix proteins of the periodontal ligament. The flexibility of the periodontal ligament to adjust to rapidly changing applied force levels and the potential to maintain its width at constant proportions throughout the animal's lifetime are, in fact, some of its most intriguing characteristics. This maintenance of periodontal ligament width over the course of a mammal's lifetime is a crucial indicator of the homeostasis of the ligament and provides knowledge about the operation of biological systems that tightly control the metabolism and spatial distribution of the cell populations involved in the development of bone, cementum, and the periodontal ligament. The very constant retention of PL width throughout time is a crucial aspect of the PL. In this condition, bone cells are not typically seen in the area between the tooth and the alveolar bone surrounding it. As a result, there must be cellular signalling mechanisms that can precisely "measure" and maintain the width of the PDL. The disorder known as tooth ankylosis, in which the tooth root fuses to the bone, has been linked to the inability of homeostatic systems to maintain PL width.¹⁷

Cell To Cell Interactions

Fibroblast – Lymphocyte Interaction

Fibroblasts and endothelial cells, which ordinarily do not express MHC Class II antigen, have been observed to become HLA-DR positive at regions of inflammation, most likely as a result of interferon gamma (IFN- γ) action. In the setting of MHC Class II products, T-lymphocytes identify antigen supplied by a cell that takes it up and destroys it and exhibit the pertinent immunogenic fragments. MHC Class II antigens must therefore be expressed by an antigen-presenting cell (APC). Endothelial cells, astrocytes, keratinocytes, and fibroblasts, which are typically MHC Class II antigen negative, may have the capacity to serve as APCs after they are induced to express MHC Class II antigens by IFN. Human gingival fibroblasts (HGF) activated with IFN were tested for their APC capabilities.¹⁸

Physiological And Pathophysiological Roles Of Adhesive Interactions Between Lymphocytes And Fibroblasts.

Numerous investigations have shown that heterotypic cell adhesion is mediated by VLA integrins, CD44/HA, and LFA-1/ICAM-1 molecules, and that activated lymphocytes develop the ability to bind fibroblasts. Both juxtacrine control, which involves the interaction of a membrane-bound cytokine or an ECM-associated cytokine with its receptor expressed by a nearby target cell, and paracrine control, which involves the synthesis of soluble factors by one cell that affect the growth and functional activities of nearby cells expressing the receptor for this factor, are made possible by the close adhesion of these cell types. Additionally, a number of lines of research showed that cell adhesion molecules are crucial for both homotypic and heterotypic cell-cell interactions.

Additionally, interactions between lymphocytes and fibroblasts depend heavily on these molecules. An intriguing result of these interactions was that the cell adhesion molecules operate as signal transducers in addition to serving as "glue" between the cells when they interact with their individual ligands.¹⁸

Epithelial – Mesenchymal Interaction

There are numerous instances when the epithelium and connective tissue interact to influence one another as diverse organs develop in the embryo. One typical example of such a phenomenon is the growth of teeth. The development of the tooth bud is controlled by the connective tissue. According to research, the epithelium's distinctive characteristics are genetically defined. Monkey experiments have demonstrated that non-keratinized alveolar mucosa epithelium transplanted to the gingiva becomes keratinized. This suggests that the gingival connective tissue has the capacity to alter how the epithelium derived from the alveolar mucosa differentiates.¹⁹ This means that the specificity of the gingival epithelium is determined by genetic factors inherent in the connective tissue.¹⁹

The permissive requirements may be

- 1) Production of effector molecules that diffuse between cells
- 2) Influence of matrix synthesized by the instructive population
- 3) Direct contact between the interacting cells²⁰.

Cellular Responses To Mechanical Force Loading²¹

Research on tooth support conducted in vivo are helpful in understanding how the body reacts to mechanical loading. Despite the fact that the real mechanism of tooth support is much more complicated than can be described in vitro, it is obvious that this complexity can operate as a barrier to a deeper understanding of fundamental biological adaptations to force loading. Cells from the periodontal ligament are crucial for mounting adaptive responses to the mechanical loading of the tooth as well as for the regeneration and repair of the periodontium. The primary kind of fiber in the periodontal ligament is collagen, which demonstrates a close physical and molecular interaction with the supporting material and plays a substantial role in tooth support.

At their points of insertion into bone and cementum, collagen fiber bundles are visible, and the angle of implantation is connected to forces operating on the tooth. The enamel surface is generally parallel to the direction of the fibers. The fiber configuration looks to be constructed to withstand force coming from any angle. In vitro research has revealed that the biomechanical properties of periodontal ligament collagen are similar to those of collagen fibers in tendons. In contrast, extrusive forces produce significantly less displacement than intrusive forces, observations that are consistent with the idea that short apical and furcational fibers are parallel to the direction of displacement. Elongation and realignment of fibers have been observed in areas of presumed tension.²¹

CONCLUSION.

The fibroblast, which is in charge of the development and turnover of fibers and ground substance, is the main cell in the lamina propria of oral mucosa and the periodontal ligament.

Thus, the fibroblast is essential for preserving tissue integrity. By having the capacity to restructure tissues, repopulate wounds, affect other cell types' metabolisms, and form new fibrous attachments, fibroblasts help maintain periodontal homeostasis. The PDL's progenitor cell populations are more abundant next to blood vessels and in nearby endosteal spaces. PDL cells have a variety of cellular morphologies, hence it has been hypothesized that after injury, the various phenotypes that repopulate the spot would eventually determine the type and form of tissue. PDL fibroblasts are crucial in the responses of the tooth to mechanical force loading because they remodel and repair broken matrix elements. Fibroblasts could be referred to as "the architect, builder, and caretaker" of the periodontal tissues in light of the significant functions they play in maintaining the homeostasis of these tissues.

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