Journal of Applied Dental and Medical Sciences
NLM ID: 101671413 ISSN:2454-2288
Volume 4 Issue 3 July-September 2018

Review Article

Junctional Epithelium: A dynamic seal around the tooth

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ARTICLE INFO

Keywords:
Junctional epithelium, basal lamina, hemidesmosome, periodontitis

ABSTRACT

Junctional epithelium located at an interface of gingival sulcus and periodontal connective tissue, provides a dynamic seal around the teeth, protecting the delicate periodontal tissue from offending bacteria, which is critical for health of supportive periodontal tissue, and hence tooth as a whole. Its rapid turnover is important for maintaining tissue homeostasis. It plays a more active role in innate defense than what was thought earlier. In addition, it expresses some mediators of inflammation involved in immune response. Its unique structural and functional adaptability maintains the anti-microbial security. Detachment of JE from tooth surface is the hallmark of initiation of periodontal pocket, and hence periodontitis. This review article has made an attempt to put light on various aspects of this unique tissue.

INTRODUCTION

Junctional epithelium represents the epithelial component of the dento-gingival complex that lies in contact with the tooth surface, at the interface between the gingival sulcus and the periodontal ligament fibers[1].It forms an intimate seal around the tooth, the so called 'epithelial attachment', that serves as an effective barrier, protecting the delicate periodontal tissues from exterior[1]. It provides definite anti-microbial defense by the barrier action, as well as by secreting different anti-microbial peptides. Junctional epithelium shows a markedly high turnover rate, and plays an important role in tissue homeostasis[2,3,4]. Schroeder and Listgarten first clarified the ultra-structure of dento-gingival junction (using electron microscope) in a monograph named 'Fine structure of developing epithelial attachment of human teeth [3]. After that, various research works have been done on this and the knowledge has been reviewed in number of articles. The aim of this article is to discuss various structural and functional aspects of this tiny unique tissue, called junctional epithelium.

HISTORICAL ADVANCEMENT

There was little information available regarding the junction of tooth and epithelium in early twentieth century. G.V. Black (1915) opined that a 'sub-gingival space' extends up to Cemento-enamel Junction, under loosely fitting gingiva. It was Gottlieb, who first depicted the connection between tooth and gingiva (1921). He believed in existence of an organic union between tooth and gingiva, which he referred as 'epithelial attachment' (epithelansatz). This was accepted universally until

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Waerhaug (1952) challenged Gottlieb's idea and disagreed any organic union. He declared that gingiva is separated from tooth by a capillary space forming 'epithelial cuff'. The conflict between two schools of thought went on until Orbans, a disciple of Gottlieb, agreed to both and put forward the concept of 'epithelial attachment cuff'. Later Stern (1962) demonstrated in rat incisor that the dento-gingival junction consists of basal lamina and hemi-desmosomes. Four years later, with Anderson, he coined the term 'junctional epithelium'. Finally Schroeder and Listgarten (1971), with electron microscopic study, gave detailed description of the ultra-structure of junctional epithelium[5].

DEVELOPMENT

The Junctional Epithelium forms with the eruption of tooth crown into the oral cavity [6]. It arises from the Reduced Enamel Epithelium, forming a collar around the cervical part of the tooth along cemento-enamel junction; while it's free surface forms the floor of sulcus [4]. Its development takes place in the following way:

At the late bell stage, the crown an erupting tooth, is covered by reduced enamel epithelium, consisting of reduced amelo blasts and the remaining cell layers of enamel organ before the emergence of tooth into the oral cavity [6].When the crown is about to breach the oral mucosa, cell transformation process begins from cuspal/ incisal margin towards cemento-enamel junction [6,2,1].At the time of transformation, the reduced ameloblast changes their shape from short columnar to flattened cells, lying parallel to the enamel surface and the cells present externally regain mitotic activity after undergoing a structural change[2].These transformed ameloblast cells migrate coronally, exfoliating at the base of sulcus, and are being replaced by the external cells[2]. Within 1-2 years, reduced enamel epithelium gradually converts into multi-layered junctional epithelium [1,7,8,2]. The primary Junctional epithelium develops from cells of inner layers of reduced enamel epithelium ,but later on the external cells of the transformed amelo blast gradually replace them, forming secondary Junctional epithelium [2].

The junctional epithelium, that was originally derived from the reduced enamel epithelium, can be replaced by a junctional epithelium developed from basal cells originating from the gingival epithelium [9].This holds true, at least, for *de novo* formation of the junctional epithelium [10,11]. Even, basal cells other than those of gingival origin also can regenerate a junctional epithelium [12, 13, 14, 15].

According to the recent studies, the primary junctional epithelium develops more specifically from the reduced amelo blast associated proteins and amelot in which also has the capacity for regeneration of junctional epithelium [16,17,18].

MICROSCOPIC FEATURES

Junctional epithelium is a non-keratinized stratified squamous epithelium that surrounds the tooth like a collar with a wedge like cross-section [19]. Externally it is attached to the tooth surface, whereas internally it is being supported by the gingival connective tissue [20]. Again, periodontal ligament limits its apical extent, and coronally it is continuous with sulcular epithelium [20].

- Thickness: 15-30 cell layers at the coronal end, which tapers to 1-3 cells layers at the apical end.
- Length in average : 0.25mm-1.35mm

This non-keratinizing stratified squamous epithelium is made up of two strata: **basal layer** and the **supra-basal layer** [20].

- Basal layer – consisting of cuboidal cells, are arranged along the connective tissue interface [20].

- Supra-basal layer – multiple layers of flattened cells lying parallel to tooth surface [20].

Junctional epithelium is attached to gingival connective tissue by an external basal lamina, while it is attached to the tooth surface by internal basal lamina. The single layer of cell, lying in contact with tooth surface, is referred to as **DAT (Directly attached to tooth)** cells [20]. Recent studies indicate that they are capable of undergoing cell division [21]. The existence of a proliferating population of epithelial cells (DAT cells) in a supra-basal location, several layers away from the connective tissue, is a unique feature of the junctional epithelium. This possibly results from specific permissive or instructive signals provided by the internal basal lamina matrix on the tooth surface. Therefore, any structural/ molecular changes in the internal basal lamina can influence the DAT cells homeostasis and also, its antimicrobial defense or vice versa. The interaction between the IBL and cell surface macro-molecule is fundamental for cell motility, adhesion, synthetic capacity, tissue stability, regeneration and response to external signal [22]. DAT cells possess the capacity to form and renew the components of epithelial attachment [23,24].

The cells of junctional epithelium present following features:

1. These cells contain dense cytoplasm, abundant rough endoplasmic reticulum, Golgi complex, few tonofilaments, lysosomal bodies and numerous polyribosomes [2,4].
2. Cytokeratins (CK) are the intermediate filament proteins of cytoskeletal family and form the main structural proteins of these Junctional epithelial cells [25,26]. They express CK5,CK10, CK13, CK 14, CK16 and CK19 [2, 27,28,29,30]. The expression of CK19 being high, found in almost all the layers of junctional epithelium, have been regarded as the characteristic histological marker for Junctional epithelium [27,28,29,30].
3. The cells exhibit relatively loose intercellular junctions comprising of few desmosomes, adherens junctions and occasional gap junctions [31,32,9, 33-35]. The fluid-filled inter-cellular spaces are responsible for remarkable permeability [35].
4. Intercellular spaces are occupied by mononuclear leukocytes of varied nature. Different types of cells like the polymorpho nuclear leukocytes, lymphocytes, macrophages, antigen-presenting cells, Langerhans cells are seen to exist in and around the junctional epithelium cells [31, 36,1,37].
5. It is also being innervated by sensory nerve fibers [38,39].Therefore, it aids in neuro-sensory pain conduction, by releasing Neuropeptides, that helps in plasma extravasation and immigration of leucocytes with endocytic activities [40,41].

Junctional epithelium presents two basal-lamina: one facing the gingival connective tissue is the external basal lamina, while the other facing the tooth surface represents the internal basal lamina. External basal lamina contains the structures similar to that of typical basement membrane, with the lamina densa supporting the underlying connective tissue and lamina lucida lying in between the lamina densa and the basal keratinocytes [2,42].

Internal basal lamina lacks true basement membrane components like: collagen IV and VII, laminin 111, laminin 511, perlecan, heparan sulfate proteoglycan, fibronectin, nidogen [43,2]; while it contains cell-adhesion protein- laminin 332, laminin 5 [22,43,44,45]. Epithelium-tooth interface contains versican and type VIII collagen (usually absent in typical basement membrane); hence

now-a-days it is considered as a specialized extracellular matrix [46,47].

The gingiva (specifically junctional epithelium) is adherent to tooth through a structural complex, referred to as **epithelial attachment apparatus** [4]. This consists of[1]**hemidesmosomes** and [2] a basal lamina, i.e. **internal basal lamina**, to which the cells are attached through hemidesmosomes [48,13,49,1].

The hemidesmosome comprises of an attachment plaque, cytokeratin filaments and a sub-basal lamina dense plate[50]. They are believed to act as sites for signal transduction. The interaction between IBL and cell surface macro-molecule helps in cell motility, adhesion, synthetic capacity, tissue stability, regeneration and response to external signal [51].

The elements of attachments are produced and renewed by the adjacent DAT cells [24]. This attachment mechanism are shown to exist on dental calculus layer in a bacteria-free environment (Listgarten &Ellegaard, 1973) [50].

The connective tissue supportingjunctional epithelium is different from that of outer and sulcular epithelium both structurally and functionally [3]. It contains extensive blood vascular plexus, and varying amount of inflammatory cells, such as PMNs and T-cells, migrate into the gingival sulcus and oral fluid [3].

Junctional epithelium can be considered as "*Incompletely developed striated squamous epithelium. Alternatively, it can be viewed as a structure that evolves along a different pathway and produces the components of epithelial attachment instead of progressing further into a keratinized epithelium*" (Nanci & Bosshardt, 2006).

The special nature is attributed to the connective tissue supporting it. Thus it is functionally different as it provides instructive signals for the normal progression of stratified squamous epithelium which is absent in other parts of gingiva [52,53].

Function:

1. Barrier: junctional epithelium forms a dynamic seal around the tooth, protecting delicate periodontal tissues from external environment, and acts as a physical barrier [1].
2. Rapid turnover: junctional epithelium shows exceptionally high turnover rate, which not only maintains a structural integrity but also adopts itself as per need [54,33,55,21].
3. Anti-microbial function: junctional epithelium has no keratinized layer at its free surface, some special structural and functional characteristicscompensate for absence of this barrier, thereby help to maintain a potent anti-microbial mechanism, which is a unique property of J.E [2,31].

- **Antimicrobial mechanisms in junctional epithelium**

I. In the coronal part, rapid cell exfoliation occurs due tohighturn-over rate and funneling of cells towards the sulcus prevents bacterial colonization [51].

II. Laterally, the (external) basal lamina forms an effective barrier against invading microbes [51].

III. Active antimicrobial substances are produced in junctional epithelial cells. These include β-defensins, secretory leucocyte protease inhibitor (SLPI1), S100A8 and lysosomal enzymes [56-58,60].β-defensins are anti-microbial peptides which function as innate defense mechanism against the bacterial challenge [57,58]. SLPI-1 is responsible for the maintainance of tissue integrity while S100A8 & 9 form a heterodimeric complex, thus forming an antimicrobial peptide [61,62].

Junctional epithelium cells activated by the anti-microbial substances secrete variety of cytokines (like keratinocyte derived chemokine, macrophage inflammatory protein -2) that bring and activate neutrophils [63].

In addition, the junctional epithelial cells express follicular dendritic cell secretory protein and odontogenic ameloblast associated protein [64,16,65]. The genes encoding these proteins lie adjacent to the cluster of genes encoding for C-X-C chemokines. These interactions are suggestive of a close association between the expression of pro-inflammatory cytokines and the expression of products by the junctional epithelium as mentioned above [65].

IV. These cells also have an endocytic capacity equal to that of macrophages and neutrophils and this activity is protective in nature [66].

- **The role of the epithelial attachment in tooth resorption of primary teeth**

Bernice S et al suggested that during tooth resorption, the epithelial attachment proliferates apically, destroying the attachment fibers either by a lytic or pressure effect, causing degeneration and detachment of the principal fibers. The fibers below the epithelial attachment remain attached to the viable cementum. Then an inflammatory process accompanies the migrating epithelium.This process continues until the epithelium reaches the resorbing area of tooth structure aiding in the final exfoliation of the deciduous tooth [67].

- **The Role of junctional epithelium in formation of periodontal pocket**

The transformation of the junctional epithelium into pocket epithelium is regarded as a hallmark in the development of periodontitis. The initiation of formation of periodontal pocket may be either due to the detachment of DAT cells from the tooth surface orit may due to the development of an intra-epithelial split.

Progressive inflammation of gingiva causes destruction of collagen fibers just apical to junctional epithelium, and the area becomes occupied by inflammatory cells and edema. Consequently cells from apical end of junctional epithelium proliferate along root surface. When relative volume of cellular infiltrates reach 60%, the tissue loses cohesiveness, and coronal part of the junctional epithelium gets detached from tooth surface and gets converted to sulcular epithelium, and subsequently the base of the sulcus shifts apically. Thus gingival sulcus is transformed to periodontal pocket, with the commencement of periodontitis [68].

- **Regeneration of Junctional Epithelium**

Waerhaug (1981) studied healing of the junctional epithelium after the use of dental floss at premolars in 12-year-old humans. He observed that detachment of cells persisted for 24 hrs after flossing ceased. Then new attachment of junctional epithelial cells started 3 days after flossing ceased. Finally the cell populations on the experimental and control surfaces were again indistinguishable after two weeks [69].

In general, a new junctional epithelium after gingivectomy forms within 20 days [13,1].

- **Junctional epithelium in relation to implants**

The junctional epithelium around implants originate from epithelial cells of the oral mucosa.Structurally, the peri-implant epithelium closely resembles the junctional epithelium around teeth.Many molecules are involved in the defensive activity against the bacterial challenge which are being expressed in the peri-implant epithelium.

So, a functional adaptation occurs when oral epithelia forms an epithelial attachment around implants [70].

CONCLUSION

Junctional epithelium, as stated earlier, represents a dynamic seal around the tooth, at a strategically important interface of oral cavity (flushed with oral fluid containing innumerous pathogens) and delicate periodontal tissues. This is a specialized unique tissue, capable enough to act as a barrier against the bacterial challenge by adapting both structurally and functionally as per the requirement.The integrity of this tiny tissue carries extreme importance for the health of supportive periodontal structures, and virtually the tooth. Detachment of junctional epithelium from tooth surface initiates formation of periodontal pocket, and hence periodontitis. So further understanding of the structure and function of junctional epithelium would enable us to attain knowledge regarding its uniqueness and also develop new therapeutic strategies against the microbial infection and subsequent tissue destruction.

REFERENCES

1. Schroeder HE. Histopathology of the gingival sulcus. In: The borderland between caries and periodontal disease. Lehner T, editor. London: Academic Press, 1977, 43-78.
2. Schroedar HE. The Junctional Epithelium: origin, structure and significance. A review. Acta Med Dent Helv. 1996; 1:155-167
3. Schroedar HE, Listgarten MA. The gingival tissues: the architecture of periodontal protection. Periodontol.1997; 13:91-120
4. Frank DE, Carter WG. Laminin 5 deposition regulates keratinocyte polarization and persistent migration. J Cell Sci. 2004; 117: 1351-1363
5. History of periodontology. Carranza, Shikar-ke, Williams. Quintessence Publishing Co, Inc.
6. Ten Cate AR. Development of the periodontium In : Oral Histology. Development, structure and function. Ten Cate AR, editor. St. Louis: Mosby, 1998, 236-252
7. Glavind I, Zander HA. Dynamics of dental epithelium during tooth eruption. J Dent Res. 1970; 49:549-555
8. Listgarten MA. Normal development, structure, physiology and repair of gingival epithelium. Oral Sci Rev. 1972b; 1:3-67
9. Ten Cate AR. The role of epithelium in the development, structure and function of the tissues of tooth support. Oral Dis. 1996; 2:55-62
10. Salonen J. Sampling and preliminary analysis of the extra and intracellular material involved in the attachment of human oral epithelium in vitro. J Periodontal Res. 1986; 21: 279-287
11. Salonen JI, Kautsky MB, Dale BA. Changes in cell phenotype during regeneration of junctional epithelium of human gingival in vitro. J Periodontal Res. 1989; 24:370-377
12. Listgarten MA. Electron microscopic features of the newly formed epithelial attachment after gingival surgery. A preliminary repot. JPeriodontal Res. 1967; 2: 46-52
13. Listgarten M. Ultrastructure of the dento-gingival junction after gingivectomy. J Periodontal Res. 1972a; 7: 151-160.
14. Braga AM, Squier CA. Ultrastructure of regenerating junctional epithelium in the monkey. J Periodontal. 1980; 51: 386-392
15. Freeman E. Development of the dento-gingival junction of the free gingival graft. A histological study. J Periodontal Res. 1981; 16:140-146

16. Nishio C et al. Expression pattern of odontogenic ameloblast-associated and amelotin during formation and regeneration of the junctional epithelium. Eur. Cell Mater. 2010; 20:393-402
17. Mofatt, P. Et al. Cloning of rat amelotin and localization of the protein to the basal lamina of maturation stage ameloblast and junctional epithelium. Biochem J. 2006; 399:37-46
18. Mofatt P, Smith CE, St. – Arnaud R, Nanci A. Characterization of Apin, a secreted protein highly expressed in tooth –associated epithelia. J. Cell Biochem. 2008; 103:941-956.
19. University of Pittsburgh, School of Dental Medicine
20. Salonen JI, Kautsky MB, Dale BA. Changes in cell phenotype during regeneration of junctional epithelium of human gingiva in vitro. J. Periodontal Res. 1989; 24: 370-377
21. Salonen JI. Proliferative potential of the attached cells of human junctional epithelium. J Periodontal Res. 1994; 29: 41-45
22. Salonen J, Uitto VJ, Pan YM, Oda D. Proliferating oral epithelial cells in culture are capable of both extracellular and intracellular degradation of interstitial collagen. Matrix. 1991; 11:43-55
23. Stallard RE, Diab MA, Zander HA. The attaching substance between enamel and epithelium- a product of the epithelial cells.J Periodontal. 1965; 36:130-132
24. Osman M, Ruch JV. Secretion of basal lamina by trypsin-isolated embryonic mouse molar epithelia cultured in vitro. Dev Biol. 1980; 75: 467-470
25. Pitaru S, McCulloch CA, Narayan SA. Cellular origins and differentiation control mechanisms during periodontal development and wound healing. J Periodontal Res. 1994; 29(2):81-94
26. Moll R, Divo M, Langbein L. The human keratins: biology and pathology. Histochem Cell Biol 2008; 129(6):705-733
27. Pritlove-Carson S, Charles worth S, Morgan PR, Palmer PM. Cytokeratin phenotypes at the dento-gingival junction in relative to health and inflammation, in smokers and non-smokers. Oral Dis 1997; 3(1):19-24
28. Feghali-Assaly M, Sawaf M, Serres G, Forest N, Ouhayoun J. Cytokeratin profile of the junctional epithelium in partially erupted teeth. J Periodontal Res. 1994; 29(3):185-195
29. Sculean A, Berakdar M, Pahl S, Windisch P, Brecx M, Reich E, Donos N. Patterns of cytokeratin expression in monkey and human periodontium following regeneration and conventional periodontal surgery. J Periodontal Res. 2001; 36(4): 260-268
30. Jiang Q, Li D. Cytokeratin expression in human junctional epithelium, oral epithelium and sulcular epithelium. Zhonghua Kou Qiang Yi Xue Za Zhi= Zhonghua Kouqiang Yixue Zazhi= Chin J Stomatol. 2005; 40(4):298
31. Schroeder HE, Listgarten MA. The gingival tissues: the architecture of periodontal protection. Periodontology. 2000; 1997(13): 91-120
32. Luke D. The structure and function of dento-gingival junction and periodontal ligament. Br Dent J. 1992; 172:187-90
33. Skougaard MR. Cell renewal , with special reference to the gingival epithelium. Adv Oral Biol. 1970; 4: 261-88
34. Stern IB. Current concepts of the dentogingival junction: the epithelial and connective tissue attachments to the tooth. J Periodontal. 1981; 52: 465-76

35. DD Bossahardt, NP Lang. deptt of Periodontology and Fixed Prosthodontics, School of Dental Medicine, University Of Berne.'The Junctional Epithelium: from Health to Disease', J Dent Res. 2005; 84(1):9-20.
36. Schroeder HE. Transmigration and infiltration of leucocytes in human junctional epithelium. Helv Odontol Acta. 1973; 17: 6-18
37. Juhl M, Stoltz K, Reibel J. Distribution of Langerhans cells in clinically healthy human gingival epithelium with special emphasis on junctional epithelium. Scand J Dent Res. 1988; 96: 199-208
38. Byers MR, Holland GR. Trigeminal nerve endings in gingival, junctional epithelium and periodontal ligament of rat molars as demonstrated by autoradiography. Anat Rec. 1977; 188:509-523.
39. Byers MR, Mecifi KB, Kimberly CL. Numerous nerves with calcitonin gene-related peptide like immunoreactivity innervate junctional epithelium of rats. Brain Res. 1987; 419:311-314
40. Kondo T, Ayasaka N, Nagata E, Tanaka T. A light and electron microscopic anterograde WGA-HRP tracing study on the sensory innervation of junctional and sulcular epithelium in the rat molar . J Dent Res. 1992; 71: 60-65
41. Maeda T, Sodeyama T, Hara K, Takano Y. Evidence for the existence of intraepithelial nerve endings in the junctional epithelium of rat molars: an immune histochemical study using protein gene product 9.5 (PGP 9.5) antibody. J Periodontal Res. 1994; 29:377-385
42. Larjava H, Koivisto L, Hakkinen L, Heino J. Epithelial integrins with special reference to oral epithelia. J Dent Res 2011; 90:1367-76
43. Hormia M, Sahlberg C, Thesleff I, Airenne T. The epithelium –tooth interface_ a basal lamina rich in laminin-5 and lacking other known isoforms. J Dent Res. 1998; 77:1479-85 cell adhesion by type I hemidesmosomes in the absence of a true basal lamina. J Periodontal 2001; 72: 788-97
44. Hormia M, Owaribe K, Virtanen I. The dento-epithelial junction: cell adhesion by type I hemidesmosomes in the absence of a true basal lamina. J Periodontal 2001; 72: 788-97
45. Oksonen J, Sorokin LM, Virtanen Hormia M. The junctional epithelium around murine teeth differs from gingival epithelium in its basement membrane composition. J Dent Res 2001; 80:2093-7
46. Abiko Y, Nishimura M, Rahemtulla F, Mizoguchi I, Kak T. Immuno histo chemical localization of large chondroitin sulfateproteoglycan in porcine gingival epithelia. Eur J Morphol 2001; 39:9-104
47. Salonen J,Oda D, Funk SE, Sage H. Synthesis of type VIII collagen by epithelial cells of human gingival. J Periodontal Res 1991; 26:355-60
48. Listgarten MA. Electron microscopic study of the gingivo-dentaljunction of man. Am J Anat. 1966; 119:147-177
49. Schroeder He. Ultrastructure of the junctional epithelium of the human gingival. Helv Odontol Acta. 1969; 13: 65-83
50. Listgarten MA, Ellegaard B. Electron microscopic evidence of a cellular attachment between junctional epithelium and dental calculus . J Periodontal Res. 1973; 8: 143-150
51. Marja T. Pollanen, Jukka I. Salonen and Veli- Jukka Uitto. Structure and function of the tooth-epithelial interface in health and disease. Periodontology. 2003; 31:12-31

52. Karring T, Lang NP, Loe H. The role of gingival connective tissue in determining epithelial differentiation. J Periodontal Res. 1975; 10:1-11
53. Karring T, Ostergaard E, Loe H. Conservation of tissue specificity after heterotopic transplantation of gingival and alveolar mucosa. J Periodontal Res. 1971; 6: 282-293
54. Skougaard M. Turnover of the gingival epithelium in marmosets. Acta Odontol Scand. 1965; 23: 623-643
55. Demetriou NA, Ramfjord SP. Premitotic labeling and inflammation in the gingiva of Rhesus monkeys. J Periodontal. 1972; 43:606-613
56. Hayasi Y, Matsunaga T, Yamamoto G, Nishil K, Usui M, Yamamoto M, et al. Comprehensive analysis of gene expression in the junctional epithelium by laser microdissection and microarray analysis. J periodontal Res. 2010; 45: 618-25
57. Dinulos JG, Mentele L, Fredericks LP, Dale BA, Darmstadt Gl. Keratinocyte expression of human beta defensin 2 following bacterial infection : role In cutaneous host defense. Clin Diagn Lab Immunol. 2003; 10:161-6
58. Nishii K, Usui M, Yamamoto G, Yajima S, Tsukamoto Y, Tanaka J, et al. The distribution and expression of S100A8 and S100A9 in gingival epithelium of mice J Periodontal Res. 2013; 48:235-42
59. Lange D, Schroeder HE. Cytochemistry and ultrastructure of gingival sulcus cells . Helv Odontal Acta. 1971; 15(15): 65-86
60. Si-Tahar M, Merlin D, Sitaraman S, Madara JL. Constitutive and regulated secretion of secretory leucocyte proteinase inhibitor by human intestinal epithelial cells. Gastroenterology 2000; 118: 1061-71
61. Goyette J, Geczy CL. Inflammation associated S-100 proteins: new mechanisms that regulate function. Amino acids. 2011; 41:(8)1-42
62. Tsukamoto Y, Usui , Yamamoto G, Takagi Y, Tachikawa T, Yamamoto M, et al. Role of the junctional epithelium in periodontal innate defence and homeostasis. J Periodontal Res. 2012; 47: 750-7
63. Shinomura T, Nakamura S, Ito K, Shirasawa S, Hook M, Kimura JH Adsorption of follicular dendritic cell –secreted protein (FDC-SP) onto mineral deposits. Application of a new stable gene expression system. J Biol Chem. 2008; 283:33658-64
64. Dos Santos Neves J, Wazen RM, Kuroda S, Francis Zalzal S, Mofatt P, Nanci A. Odontogenic ameloblast associated and amelotin are novel basal lamina components .Histochem Cell Biol. 2012; 137:329-38
65. Marshall AJ, Du Q, Draves KE, Shikishima Y, Hayglass KT, Clark CA, FDC-SP,a novel secreted protein expressed by follicular dendritic cells . J Immunol. 2002; 169:2381-9
66. Moon IL, Cho, Philias R. Garant. Development and general structure of the periodontium. Periodontology. 2000; 24: 9-27
67. Bernice et al. The Role of the epithelial attachment in tooth resorption of primary teeth. Oral Surg.,Oral Med, Oral Pathol, 1951.
68. Carranza's Clinical Periodontology. Newman, Takei, Klokkevold, Carranza. Tenth edition. Saunders Elsevier
69. Waerhaug J. Healing of the dento-gingival junction following the use of dental floss. J Clin Periodontal. 1981; 8:241-246
70. Clinical Periodontology and Implant Dentistry. Jan Lindhe, Lang, Jarring. Fifth edition. Blackwell.