Annals of R.S.C.B., Vol. 24, Issue 1, 2020, pp. 559- 563
Received 18April2020; accepted 23June2020

A Review On B-Defensins In Periodontal Disease

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ABSTRACT

Gingival epithelium is known to produce the first line of defence in gingival tissues. This is attributed to the presence of defensins which are small cationic peptide. These defensins act by enhancing the innate immune response by increasing the secretion of both the pro and anti-inflammatory cytokines. This review article will focus on the role of β - defensins in periodontal disease.

Keywords*:*Antimicrobial peptides (AMP) , human β defensins (hBD), Toll like receptor (TLR).

I.Introduction

Antibacterial peptides are a class of amino acid-based compounds that have antimicrobial action throughout a broad spectrum. Defensins, cathelicidins, and saposins are the three types of defensins. Defensins are further divided into two types: α andβ defensins. The history, function, and clinical significance of defensins in periodontal disease will be detailed in this review paper.

Human defensins (hBD) are a family of tiny cysteine-rich cationic peptides that have been demonstrated to play a critical role in the immunological and inflammatory responses of immature dendritic cells, memory T-cells, and monocytes. hBD 1, 2, 3, and 4 are the four human defensins that have been identified. hBDs are found in a variety of epithelial cell types, including airway epithelial layers, kidney epithelial layers, corneal epithelial layers, and gingival epithelial layers. In the oral epithelium, hBD 1, 2, and 3 can be found. They have been found to have extensive antimicrobial activity against a wide range of pathogens and to play a key function in the innate immune response.

II. Other names of antimicrobial peptides[1]

Host defence peptides, Anionic antimicrobial peptides, Cationic amphipathic peptides, Cationic AMPs, α-helical antimicrobial peptides

III. History

Dubos isolated an antibacterial compound from a soil Bacillus strain in 1939, which led to the discovery of AMPs. This concentrate has been found to protect mice against Pneumococci infection. Hotchkiss and Dubos separated this concentration the following year and discovered an AMP called gramicidin. Despite certain reported risks associated with intraperitoneal administration, gramicidin has been found to be beneficial in the treatment of wounds and ulcers on the skin. Another AMP, tyrocidine, was shown to be consistently

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viable against Gram-negative and Gram-positive microbes in 1941. Regardless, human platelets were found to be poisonous to tyrocidine.Another AMP, purothionin, was isolated from a plant Triticumaestivum in the same year and found to be effective against pathogenic bacteria. The first antimicrobial peptide was isolated from animal defensin in 1956. Bombinin from epithelia and lactoferrin from dairy animals' milk were both depicted in the following years. It was also discovered that human leukocytes have AMPs in their lysosomes at the same period.[1]

IV. Where are ß-defensins seen?

Despite the fact that periodontal disease affects the junctional epithelium, these hBDs have been found in the oral sulcular epithelium. hBD-1, which is found in the gingival epithelium's spinous layer, is reported to be persistently secreted by gingival epithelial cells, with no difference in amount between gingival health and disease. hBD-2 has been discovered in the gingival epithelium's spinous layer, although hBD-3 has been discovered deep into the basal layer. The secretions of hBD-2 and 3 have been observed to gradually increase with the development of infection and inflammation in the periodontium.

V. Secretion of ß-defensins

Toll-like receptors (TLRs) are the first to identify both Gram-positive and Gram-negative bacteria. As a result, experiments were carried out by silencing TLR-2, with the results revealing a decrease in hBD-2 secretion, demonstrating the role of TLR in defensin secretion. 2 Other than this approach, *Actinobacillusactinomycetemcomitans* has also been shown to secrete hBDs when outer membrane proteins are activated via the MAPK pathway.[3]

VI. ß-defensins and periodontal pathogens

Periodontitis is an inflammatory condition of the teeth's supporting tissues caused by microbial interactions with the host. *Porphyromonasgingivalis* is a significant causal bacterium among the germs that cause periodontitis. In the oral cavity, hBDs are known to be the initial line of defence. These defensins work by breaking the bacterial cell membrane, allowing germs to pass through the cell wall. These defensins' antibacterial activity is salt-dependent, and salt-containing ions including Na+, Mg+, and Ca+ have been demonstrated to reduce their effectiveness. The hBD-3 has been demonstrated to be the least salt resistant among the hBDs.These hBDs can also disrupt the lipopolysaccharide layer of Gram-negative bacteria, in addition to disrupting cell membranes.

In an in-vitro study, typical commensal organisms in the oral cavity were found to elevate the hBD-2 and 3 that are stimulus dependent.[5]Fusobacteriumnucleatum, but not P.gingivalis, was found to increase hBD secretion in a study by Krisanaprakornkit et al. This was later related to a gene called Fusobacterium associated defensin inducer-1 found in F.nucleatum (FAD-1). Through the TLR-2 route, this FAD-1 has been demonstrated to promote hBD-2 secretion.[4] Furthermore, FAD-1 transfected P.gingivalis was found to promote hBD-2 secretion.[5]The secretion of hBD-3 varies amongst different strains of the same bacterium.For example, serotype c of *Actinobacillusactinomycetemcomitans*, which is commonly found in healthy

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people, has been shown to increase hBD-3 production, whereas serotype b, which is commonly found in aggressive periodontitis patients, has been shown to decrease it. [3]

Periodontitis-causing bacteria were unable to resist defensins, resulting in periodontal disease. P.gingivalis is one of these species, and it inhibits defensins, particularly hBD-3, by secreting different gingipains. Other species, such as *Treponemadenticola*, have been demonstrated to be resistant to defensins by reducing TNF release and blocking the TLR pathway.

VII. Activation of ß-defensins

The stimulation of hBD-1, which is released continuously by gingival epithelial cells, has been proposed as a theory. These defensins are inactive in healthy people, but they are thought to be active in periodontitis patients because they are generated via oxidoreduction of hBD-1 via the thioredoxin system. This is an oxidoreductive enzyme that is released when antigen-presenting T-cells come into contact with it. [6]

Furthermore, the periodontal pathogen F.nucleatum has been demonstrated to induce thioredoxin, increasing the active form of hBD-1.

VIII. Role of ß-defensins in innate immune response

The production of pro-inflammatory cytokines such as TNF- and IL-1 has been demonstrated to increase hBD-2 secretion. INF-, IL-17, and IL-22 are three different types of interferons. Anti-inflammatory cytokines like IL-4 and IL-10.[7]On the other hand, reduced their release. As a result, these chemokines and defensins have been discovered to be interdependent. Chemokines were found to have antibacterial properties, while defensinshave chemoattractant properties.[8]

IX. ß-defensins in periodontal disease

The levels of hBD-2 and 3 were found to increase in vitro in periodontal disease, although they reduced in an in vivo research. [9] There was no clear reason for the decrease in defensins during periodontal disease. However, numerous authors have proposed other theories.

According to the first hypothesis, a decrease in defensin secretion was responsible for the increasing change from innate to adaptive immune responses as disease progressed.[10] The second idea claims that periodontitis only occurs in people who have a genetic variation in a gene associated to ß-defensins.[11] Proteolytic enzymes released by the host and periodontal bacteria are essential to the new theory. These proteolytic enzymes have been shown to degrade ß-defensins secreted by gingival epithelial cells, lowering the amount of ß-defensin in the body.[12]

X. Clinical application of ß-defensins

Antimicrobial peptide-based therapeutic techniques are still in their early stages, and more study is needed before they may be used in clinical settings. They are utilised in nanotechnology-based drug delivery because of their broad spectrum of action, and they have proved to generate promising results in the future.[13] Antimicrobial coatings for dental

implants based on ß-defensins have also been created to prevent periimplantitis and are now being studied.[14]

XI. Conclusion

In gingival epithelium, ß-defensins have been found to provide a first line of defence. Furthermore, they have both proinflammatory and anti-inflammatory properties. The breakdown of these antimicrobial peptides may have contributed to their reduction in periodontal disease.

XII. References

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