Annals of R.S.C.B., Vol. 24, Issue 1, 2020, pp. 416 - 421
Received 18April2020; accepted 23June2020

An Overview On Porphyromonas Gingivalis – An Important Periodontopathic Pathogen

ManonmaniPavithra R, Geetha Ari*, Sathish Rajendran, Jaideep Mahendra, AmbalavananNamasivayam

Meenakshi Academy of Higher Education and Research,
Faculty of Dentistry, Meenakshi AmmalDentalCollege and Hospital, Chennai, India.
drgeetha.perio@madch.edu.in[2*]

ABSTRACT

Porphyromonasgingivalis is a Gram-negative oral anaerobe that is involved in the pathogenesis of periodontitis and is a member of more than 500 bacterial species that live in the oral cavity. This anaerobic bacterium is a natural member of the oral microbiome, yet it can become highly destructive (termed pathobiont) and proliferate to high cell numbers in periodontal lesions: this is attributed to its arsenal of specialized virulence factors. The purpose of this review is to provide an overview of one of the main periodontal pathogens—*Porphyromonasgingivalis.* This bacterium, along with *Treponemadenticola* and *Tannerella forsythia*, constitute the "red complex," a prototype polybacterial pathogenic consortium in periodontitis. This review outlines *Porphyromonasgingivalis* structure, its metabolism, its ability to colonize the epithelial cells, and its influence upon the host immunity.

Key words: P.gingivalis, Periodontal pathogen, bacteria, Gram negative, periodontal disease, red complex bacteria, pathogenesis.

I.Introduction

*Porphyromonasgingivalis*is a Gram-negative periodontal pathogen that lives mostly in the human oral cavity's subgingival sulcus. Porphyromonas is derived from the Greek word porphyreos, which means purple, and the Greek noun monas, which means unit (Shah and Collins 1988). It was previously known as asaccharolytic black pigmenting rods, but Nisengard and Newman separated it into a distinct genus in 1994. It is a secondary coloniser of dental plaque, adhering to primary colonisers such as *Streptococcus gordonii* and *Prevotellaintermedia*. The purpose of this article is to discuss its structure, metabolism, ability to infiltrate epithelial cells, and impact on host immunity.[1]

II.Methods of Identification

For the culture of *P.gingivalis*, blood agar is the most common medium. They have smooth raised colonies that start out white to cream in colour before turning deep red to black due to protoheme concentration. The colour of young colonies is usually yellow to green. Other methods of identification include immunodiagnostic tests such as ELISA, immunofluorescence, DNA probes, and polymerase chain reactions (PCR).[2]

III.Virulence Factors

Virulence factors are described as an organism's elements or metabolites that are required at different phases of its life cycle and cause harm to the host. [3] Fimbriae, hemagglutinins, outer membrane proteins and vesicles, and gingipains are among the virulence factors of

Annals of R.S.C.B., Vol. 24, Issue 1, 2020, pp. 416 - 421
Received 18April2020; accepted 23June2020

P.gingivalis that are involved in colonisation and attachment; capsule, lipopolysaccharide, Ig and complement proteases, other antiphagocytic products, and fimbriae are among the virulence factors that are involved in evading(modulating) host responses; and those invloved in damaging host tissues and spreading includes proteinases, collagenases and fibrinolytic, keratinolytic and other hydrolytic enzymes.[4]

IV.Role of Adhesins

A variety of adhesins, including fimbriae, hemagglutinins, and proteinases, aid in the retention and proliferation of *Porphyromonasgingivalis* on a variety of surfaces. [5]*Porphyromonasgingivalis* produces a significant number of cysteine proteinases that are selective for arginine and lysine in both cell-associated and secretory forms. [6] These enzymes, known as gingipains, cleave protein and peptide substrates after arginine (gingipain R) and lysine (gingipain K) residues, and neither can be blocked by host proteinase inhibitors. An ELISA test was used to check for antibodies to the *Porphyromonasgingivalis*-specific virulence factor arginine gingipainB.Anti-RgpB antibody levels were found to be significantly greater in the periodontitis subset than in the non-periodontitis control subset. Anti-RgpB antibody levels in periodontitis serum were significantly higher than in non-periodontitis serum, suggesting that elevated anti-RgpBIgG levels could be utilised as a surrogate for chronic periodontitis in studies where periodontal status is of relevance but unclear. [7] *Porphyromonasgingivalis* has been linked to adult-onset periodontitis as a virulence factor due to its high quantities of cysteine proteinases with trypsin-like activity.Because*Porphyromonasgingivalis* enhances both bacterial adherence to and invasion of specific areas, *Porphyromonasgingivalis* fimbriae are a vital element in mediating this bacterial organism's contact with host tissues. In periodontal locations, *Porphyromonasgingivalis* fimbriae is likely to disrupt cellular signalling via extracellular matrix proteins/integrins. Fimbriae are also suggested to play a key role in this bacterial organism's invasion into host cells.[8]

V. Lipopolysaccharide of *Porphyromonasgingivalis*

Porphyromonasgingivalis lipopolysaccharide is a crucial component in the progression of periodontitis. [9] In periodontitis lesions, gingival fibroblasts, which make up the majority of gingival connective tissue, may interact directly with *Porphyromonasgingivalis* and its bacterial products, such as lipopolysaccharide. [10] It has been proposed that it serves as a key molecule that informs the host of a potential bacterial infection because of its ability to potently stimulate host inflammatory and innate defensive responses.LPS from *Porphyromonasgingivalis* causes periodontal tissue damage by inducing proinflammatory cytokines such IL-1, IL-6, and IL-8. In PDLSCs that were positive for STRO-1 and SSEA-4, *Porphyromonasgingivalis* LPS suppressed alkaline phosphatase activity, collagen type 1 Alpha 1, osteocalcin synthesis, and mineralization. LPS from *Porphyromonasgingivalis* also enhanced cell proliferation and generated interleukin-1, interleukin-6, and interleukin-8 (IL-1, IL-6, and IL-8).[11]

VI.Cysteine Proteases of *Porphyromonasgingivalis*

Annals of R.S.C.B., Vol. 24, Issue 1, 2020, pp. 416 - 421
Received 18April2020; accepted 23June2020

The cysteine proteases of *Porphyromonasgingivalis* are extracellular products of an important etiological agent in periodontal diseases.[12] Many of the in vitro actions of these enzymes are consistent with the observed deregulated inflammatory and immune features of the disease. They are significant targets of the immune responses of affected individuals and are viewed by some as potential molecular targets for therapeutic approaches to periodontal diseases.[13] These enzymes are involved in both the destruction of periodontal tissues and interrupting host-defense mechanisms through the degradation of immunoglobulins and complement factors leading eventually to disease progression.[14]

VII.*Porphyromonasgingivalis* and Complement System

It is an important host response to invading bacteria Activation of the complement leads to deposition on C3b on the bacterial surface and phagocytosis of the opsonized bacteria by host cells.[9]The entire complement pathway, including terminal components C5b-9 maybe activated on the cell surface which gives rise to generation and insertion of membrane attack complex into bacterial membrane and cell lysis*(Slaney J.M et al.,2008)*.[15] Signalling crosstalk between complement and Toll-like receptors(TLRs) serves to coordinate host immunity. *P.gingivalis* expresses C5 convertase-like enzymatic activity and exploits TLR-crosstalk to subvert host defences. This defective immune surveillance leads to remodelling of the periodontal microbiota to a dysbiotic state that causes inflammatory periodontitis *(Hajishengallis et al., 2012).*[16]

VIII.*Porphyromonasgingivalis* and Neutrophils

*P.gingivalis*has developed a variety of techniques to disrupt the gingival epithelium's structural and functional integrity (Andrain.E et al.,2006). [17] The triggering receptor expressed on myeloid cells I (TREM-1) is an immunoglobulin superfamily cell surface receptor that can increase proinflammatory cytokine production and control apoptosis. TREM-1 is primarily produced by PMNs, which are the initial line of defence against infection. The differential regulation of TREM-1 by *P.gingivalis*gingipains could represent a novel method by which *P.gingivalis* manipulates the host's innate immune response to aid in the establishment of chronic periodontal inflammation. (Bostanci.N and colleagues, 2013). [18]

IX.Survival strategies of *P.gingivalis*

An opportunist who can disrupt the inflammatory reaction's defence mechanism, rather than an aggressor of the inflammatory response. *P.gingivalis* survives and establishes itself in the periodontal pocket by employing this technique (Hajishengallis et al., 2011). Innate immunity is deregulated, which may limit adaptive immunity. It can both stimulate and inhibit interleukin (IL)-8 production by epithelial cells (Sandros et al., 2000; Asai et al., 2001; Kusumoto et al., 2004). (Darveau et al., 1998).In the periodontal tissues, incapacitates the initial line of defence. Furthermore, it limits cytotoxic T-cell activation and thereby bacterial clearance by blocking macrophage IL-2 production – Hajishengalis et al., 2007. Pulendran et al., 2001; Hajishengallis et al., 2007). Inhibits interferon (IFN) production by T cells, as well

as macrophage bacteriocidal action and so bacterial clearance. *P.gingivalis* inhibits complement system activation (Wang et al., 2010).[8]

X.Recent Research on *Porphyromonasgingivalis*

Because *P.gingivalis* and *Aggregatibacteractinomycetomcommitans* are the main causes of gingivitis, symbiosis among the bacterial communities in the mouth is beneficial (Wu Y.M et al., 2007). ¬[19] More research into fimbriae, specifically identifying strategies to avoid the growth of biofilm on teeth by inhibiting the synthesis of minor fimbriae (Lin.X et al., 2006). Current pathogen-killing techniques, such as ammonium nitrate, are effective. The precise method by which they cause cytotoxicity is uncertain (Xia D.S et al., 2006). Although *P.gingivalis* infection is linked to a typical periodontal ecopathology, the pathogen's susceptibility to person-to-person transmission maybe controlled by periodontal therapy(Asikainen et al., 2000) [20]

XI.Conclusion

In the development of chronic periodontitis, *P.gingivalis* is a key etiological factor. Secondary colonisers have been discovered to produce a variety of virulence factors that are involved in populating the subgingival plaque and influencing host cell immune responses. *P.gingivalis* can locally infect periodontal tissue to boost its chances of survival in the host. Alveolar bone resorption is caused by *Porphyromonasgingivalis*, and morphologic assessments are the most common way to detect it in periodontal research.Recent advances in the understanding of the pathomechanisms of *Porphyromonasgingivalis* may lead to the development of novel strategies for eradication of *Porphyromonasgingivalis* and treatment for periodontal diseases in the future.

References

1. How KY, Song KP, Chan KG. Porphyromonasgingivalis: an overview of periodontopathic pathogen below the gum line. Frontiers in microbiology. 2016 Feb 9;7:53.
2. Bostanci N, Belibasakis GN. Porphyromonasgingivalis: an invasive and evasive opportunistic oral pathogen. FEMS microbiology letters. 2012 Aug 1;333(1):1-9.
3. Pandit N, Changela R, Bali D, Tikoo P, Gugnani S. Porphyromonasgingivalis: Its virulence and vaccine. Journal of the International Clinical Dental Research Organization. 2015 Jan 1;7(1).
4. Mysak J, Podzimek S, Sommerova P, Lyuya-Mi Y, Bartova J, Janatova T, Prochazkova J, Duskova J. Porphyromonasgingivalis: major periodontopathic pathogen overview. Journal of immunology research. 2014 Oct;2014.
5. Jia L, Han N, Du J, Guo L, Luo Z, Liu Y. Pathogenesis of important virulence factors of Porphyromonasgingivalis via toll-like receptors. Frontiers in cellular and infection microbiology. 2019 Jul 18;9:262.
6. T. Kadowaki, K. Nakayama, K. Okamoto et al., "*Porphyromonasgingivalis* proteinases as virulence determinants in progression of periodontal diseases," *Journal of Biochemistry*, vol. 128, no. 2, pp. 153–159, 2000.

7. N. Kharlamova, N. Sherina, A. M. Quirke, K. Eriksson et al., "A6.8 Elevated antibody levels to porphyromonasgingivalis detected in rheumatoid arthritis patients with a specific anti-citrullinated protein/peptide antibody profile," *Annals of the Rheumatic Diseases*, vol. 73, supplement 1, pp. A73–A74, 2014.
8. A. Amano, "Molecular interaction of *Porphyromonasgingivalis* with host cells: implication for the microbial pathogenesis of periodontal disease," *Journal of Periodontology*, vol. 74, no. 1, pp. 90–96, 2003.
9. J. Potempa and J. Travis, "*Porphyromonasgingivalis* proteinases in periodontitis, a review," *ActaBiochimicaPolonica*, vol. 43, no. 3, pp. 455–466, 1996.
10. P.-L. Wang and K. Ohura, "*Porphyromonasgingivalis* lipopolysaccharide signaling in gingival fibroblasts—CD14 and toll-like receptors," *Critical Reviews in Oral Biology and Medicine*, vol. 13, no. 2, pp. 132–142, 2002.
11. H. Kato, Y. Taguchi, K. Tominaga, M. Umeda, and A. Tanaka, "*Porphyromonasgingivalis* LPS inhibits osteoblastic differentiation and promotes pro-inflammatory cytokine production in human periodontal ligament stem cells," *Archives of Oral Biology*, vol. 59, no. 2, pp. 167–175, 2014.
12. J. Travis, R. Pike, T. Imamura, and J. Potempa, "*Porphyromonasgingivalis* proteinases as virulence factors in the development of periodontitis," *Journal of Periodontal Research*, vol. 32, no. 1, part 2, pp. 120–125, 1997.
13. M. A. Curtis, J. Aduse-Opoku, and M. Rangarajan, "Cysteine proteases of *Porphyromonasgingivalis*," *Critical Reviews in Oral Biology and Medicine*, vol. 12, no. 3, pp. 192–216, 2001.
14. J. Polanowska and A. Polanowski, "The role of *Porphyromonasgingivalis* proteinases in periodontitis," *PostpyHigieny I MedycynyDoświadczalnej*, vol. 51, no. 2, pp. 149–169, 1997.
15. J. M. Slaney and M. A. Curtis, "Mechanisms of evasion of complement by *Porphyromonasgingivalis*," *Frontiers in Bioscience*, vol. 13, no. 1, pp. 188–196, 2008.
16. G. Hajishengallis and E. Harokopakis, "*Porphyromonasgingivalis* interactions with complement receptor 3 (CR3): innate immunity or immune evasion?" *Frontiers in Bioscience*, vol. 12, no. 12, pp. 4547–4557, 2007.
17. E. Andrian, D. Grenier, and M. Rouabhia, "*Porphyromonasgingivalis*-epithelial cell interactions in periodontitis," *Journal of Dental Research*, vol. 85, no. 5, pp. 392–403, 2006.
18. N. Bostanci, T. Thurnheer, J. Aduse-Opoku, M. A. Curtis, A. S. Zinkernagel, and G. N. Belibasakis, "*Porphyromonasgingivalis* regulates TREM-1 in human polymorphonuclear neutrophils via its gingipains," *PLoS ONE*, 2013.
19. N. Bostanci, T. Thurnheer, J. Aduse-Opoku, M. A. Curtis, A. S. Zinkernagel, and G. N. Belibasakis, "*Porphyromonasgingivalis* regulates TREM-1 in human polymorphonuclear neutrophils via its gingipains," *PLoS ONE*, 2013.

20. S. Asikainen and C. Chen, “Oral ecology and person-to-person transmission of *Actinobacillusactinomycetemcomitans* and *Porphyromonasgingivalis*,” *Periodontol ogy 2000*, vol. 20, no. 1, pp. 65–81, 2000.