

REVIEW ARTICLE



Prevotella intermedia – An overview and its role in periodontitis

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Abstract

Periodontal disease, the most common of oral cavity diseases is the most common cause of tooth loss. On further analysis, it has been found that the bacterial plaque, its pathologic by-products and the host immune system plays a key role. However later, the role of micro-organisms as an etiology in periodontal diseases has gained more importance. The presence of specific bacteria in sub-gingival plaque has been extensively documented and found associated with severity of attachment loss. Recently, it is proposed that the environment and the genetics of the microbe and the host add up for the progression of periodontal disease. Hence, this topic focuses on periodontally important bacteria “*Prevotella intermedia*” and its role in periodontitis.

Scientific classification

Kingdom	Bacteria
Phylum	Bacteroides
Class	Bacteriodia
Order	Bacteriales
Family	Prevotellaceae
Genus	<i>Prevotella</i>
Species	<i>Intermedia</i>

Introduction

There are over 500 different types of bacterial species present in the oral cavity.^[1] Among these bacterial colonies, the soft tissues usually represent as mono species whereas the oral biofilm attached to the tooth surface often exist as complex multispecies colonies.

These multispecies colony biofilm are Gram-positive, Gram-negative, aerobic, facultative, and anaerobic micro-organisms arranged in a sequential pattern. This sequence is a result of early colonizer adhesion to host-derived glycoproteins, mucins, and other proteins that coat the surface of tooth.^[2]

Further, plaque biofilm develop by physical interaction of bacterial colonies (monospecies or multispecies) through co-aggregation and co-adhesion.^[3] Lectin-like receptors are associated with co-aggregation and pilli in cell-cell interactions. During maturation, Gram-positive, facultative flora shifts to Gram-negative, anaerobic species.

In sub-gingival plaque, periodontal pathogens are usually present as clusters. Despite the polymicrobial infectivity seen in periodontal disease attempts made to apply Koch’s postulates to certain bacteria have been entangled as these pathogens cannot grown in a pure culture, they can occur in an asymptomatic carrier state, and they may exhibit a limited host range.^[4] Following Socransky’s modifications of microbial action in periodontitis, three bacteria have been found to cause periodontitis: *Porphyromonas gingivalis*, *A. actinomycetocomitans*, and *T. forsythus*.^[5]

Pathogenic Potential of Periodontal Pathogens**Adherence, colonization, and growth**

Adhesion is necessary for colonization of sub gingival bacteria, either by co-aggregation and co-adhesion. During the growth

of biofilm, there are alternating zones of high and low bacterial colonies with aqueous channels for the transport of nutrients for the microbial growth and metabolic waste removal.^[6]

As subgingival microbial complex increases, there is an apical migration of the subgingival epithelium resulting in destruction of the attachment apparatus adjacent to the tooth. The outcome of which is subgingival biomass expansion.^[7]

Tissue penetration and invasion

The indication of the pathogenesis is the microbial invasion to its surrounding tissues. Recent studies have proved the invasion of microbes into the radicular dentin justifying the fact that tooth acts as a reservoir of bacterial colonies.

The host response

Periodontal tissue destruction is mainly a result of an indirectly acting host cell tissue degradative process wherein the host's protective mechanism counters its destructive potential. Cytokines (IL-1, IL-6, and IL-8) are mainly involved in the periodontal destruction. These cytokines individually or combines with TNF- α and PGE₂ as a series of reaction produce MMP that causes extracellular matrix degradation ending up in bone resorption. Higher levels of cytokines are found in periodontal pathologies.^[8]

Innate host response

Innate immunity has an important part in the response to microbial colonization. Here, secretory IgA and antimicrobial factors (lysozyme, lactoferrin, peroxidases, etc.^[9]) neutralizes microbial components. Their aim is to lessen the effect of the biofilm microbial complex and function synergistically.

In sub-gingival plaque, the microbes are more complex and more protected. Hence, the immune response also changes. As salivary component has no access here, the crevicular fluid in the gingival sulcus or pocket contains factors such as antibodies and neutrophil-derived components capable of resisting bacterial progression.^[6]

Prevotella

Prevotella lately was placed under Bacteriodes melaninogenicus and later was reclassified and subdivided into *Prevotella melaninogenica* and *Prevotella intermedia*.^[10]

Prevotella species are Gram-negative, non-motile, singular cells, and obligate anaerobes.^[11]

Morphology

Prevotella species are usually bacillus to utmost coccoid bacteria.^[11] They are pleomorphic and do not form endospores. *P. melaninogenica* and *P. asaccharolytic* form gram negative rods, dark brown colored as it is derived from heme.^[11] They thrive on tissues with decreased oxidation-reduction potentials.^[11]

Growth favors a slightly basic pH with a temperature between 34 and 36°C.

Physiology

Prevotella is obligate anaerobes with a fermentive form of metabolism.^[11] Some species, such as *P. melaninogenica*, depend on Vitamin-K and heme for its action.^[11] Species of *Prevotella* having affiliated with β -lactamase activity are resistance to some β -lactam antibiotics.^[11]

Associations

P. intermedia are found in commensal Actinomyces, Streptococci, and Veillonella.^[12] Because of its cell-cell recognition, together they undergo genetic and metabolite exchange.^[12] *P. intermedia* has a signaling molecule, autoinducer-2, that promote communication between oral bacteria.^[12] *Prevotella* communicates with *Peptostreptococcus* species, increasing the virulence factor of microbes thereby causing dentoalveolar infections.^[12]

Molecular Biology

Broad Institute classified 11 *Prevotella* genomes (*Prevotella* Group, 2012).

S. No.	<i>Prevotella</i> genomes	Size (mb)	GC content (%)	No. of genes
1	<i>Prevotella buccae</i> (Oral taxon 560D17)	3.36	50.95	2617
2	<i>Prevotella melaninogenica</i> (Oral taxon 469D18)	3.29	40.86	2461
3	<i>Prevotella</i> sp. F0039	2.48	37.50	1976
4	<i>Prevotella</i> sp. (Oral taxon 317F0108)	4.1	47.05	2926
5	<i>Prevotella oris</i> C735	3.35	43.91	2742
6	<i>Prevotella</i> sp. F0323	2.59	45.49	2014
7	<i>Prevotella histicola</i> F0411	2.99	41.18	2479
8	<i>Prevotella oulorum</i> F0390	2.81	46.78	2488
9	<i>Prevotella</i> sp. C561	4.03	41.83	3402
10	<i>Prevotella maculosa</i> F0099	3.15	47.71	2574
11	<i>Prevotella micans</i> F0438	2.49	45.51	2064

Invasion and Virulence of *Prevotella intermedia*

The invasion and the ability of the pathogens to survive inside the host cells evading the immune system determine the virulence of the *Prevotella* and other pathogens such as *A. actinomycetemcomitans* and *P. gingivalis* causing periodontitis.^[13] The presence of fimbria, hemolysins, adhesions, and hemagglutinins determines the virulence of *Prevotella*.^[14]

Incidence of *Prevotella intermedia* in Healthy and Diseased Periodontium

Prevotella and *Porphyromonas* are usually the common cause of periodontal and endodontic infections.^[15]

<i>Porphyromonas gingivalis</i>	Active periodontal disease area, periodontal and attachment loss ^[16]
<i>Prevotella intermedia</i> -healthy	Pregnancy gingivitis ^[17]
<i>Prevotella intermedia</i> -diseased	Periapical abscess, ANUG, and HIV associated periodontal lesions ^[15]
<i>Prevotella nigrescens</i>	Healthy gingiva and endodontic infection, ^[18] non oral abscesses
<i>Prevotella melaninogenica</i>	Periodontal diseases, endodontic infections, nasopharynx, chronic otitis media, and middle ear effusion

The pathogens produce immunoglobulin degrading and tissue degrading enzymes.^[19] The hydrolysis and depolymerization enzyme reaction of *P. intermedia* has more inclination toward the pathogenic periodontal breakdown. Comparatively, enzymes of *P. intermedia* such as acid phosphatase, esterase, and f-fucosidase are found to be higher in healthy individuals.

Tatami reported *P. intermedia*'s enzyme activity of DNase, hyaluronidase, chondroitin sulfate is higher in cellulitis and dentoalveolar abscess than in saliva and dental plaque.^[20]

Interpain-A(inpa) and *Prevotella intermedia*

Interpain-A, a protein secreted by *Prevotella*, is made of 868 amino acid residues. INPA degrades c3 complement of complementary pathway that helps *P. intermedia* to modulate the host innate immunity simplifies it's sustain in the host tissues.^[21]

Pathophysiology

Pathogenesis of *Prevotella* is mainly due to its ability to produce β -lactamase enzyme, making it less susceptible to the penicillins.^[22] These pathogens besides being normal commensals, they act synergistically with its aerobic and anaerobic analogues causing opportunistic infections.^[23]

Prevotella intermedia in Pregnancy

As there is a surge in the female sex hormone levels during pregnancy, Gram-negative anaerobes use these hormones instead of Vitamin-K for its growth boosting chances of gingivitis referred as pregnancy gingivitis.^[24] This is more common during the 2nd trimester, 4–6 weeks postpartum^[25] and during puberty and use of oral contraceptives.^[24]

Chairside Evaluation of *P. intermedia*

Microbiological test kits

The microbiological test includes Microscopical examination; Cell Culture, Omnigene, Affirm DP, and Evalusite. The three methods of analyzing number of *Prevotella* are

Phylogenetic analysis	16S rRNA gene
Restriction enzyme analysis	SDS-PAGE protein electrophoresis, 16S rDNA PCR-RFLP, ribotyping ^[26]
Restriction fragment length analysis	Gene Bank or RDP-11 data bases

Omnigene

These are DNA probe systems where a subgingival plaque sample collected in a paper point is placed in the container and dispatched to the company for evaluation. Different probes are available for the detection of *A. actinomycetemcomitans*, *P. gingivalis*, *P. intermedia*, *Fusobacterium nucleatum*, *Campylobacter rectus*, *Treponema Denticola*, and *Eikenella corrodens*.^[27]

Evalusite

Evalusite is a membrane-based enzyme immunoassay kit. A subgingival plaque sample collected in paper points is placed in a sample tube containing an eluent. This method employs a sandwich-type ELISA wherein a pink spot is displayed in the presence of test organism.^[27]

This method detects three periodontal pathogens: *A. actinomycetemcomitans*, *P. gingivalis*, and *P. intermedia*.

Perioscan

Perioscan is a diagnostic test kit that employs BANA-hydrolysis reaction, to identify bacterial trypsin-like proteases present in the dental plaque. This method helps in identifying strains of *P. gingivalis*, *P. intermedia*, *T. forsythia*, *T. denticola*, and *Capnocytophaga*.

Subgingival plaque collected is placed 1st on a BANA-containing strip, then folded and placed on a 2nd "Fast –Black" dye reagent containing strip. This is placed inside an oven for 15 min at 55°C and appearance of a color between blue to black appears is counted positive for the above mentioned species.^[27]

Conclusion

It is rationale that the multifactorial bacterial complex present in the biofilm amid disease phase act synergistically provoking pathogenesis. Oral microbial flora plays a key role in maintaining the ecosystem of oral cavity. It is, therefore, necessary for clinicians to be mindful in treating the disease aiming to maintain a stable ecosystem than eradicating it.

Collectively, *Prevotella* being secondary colonizers abounded with its virulence factors invade the periodontal tissues and modulate the host immune response causing various periodontal diseases. In addition, *Prevotella* acts synergistically with the normal commensal of oral cavity proving periodontal diseases are a result of polymicrobial complex.

A thumbnail of this article is that clinicians should have a complete knowledge of the various microbial and host components, their pathologic effects are necessary to ideally treat a patient presenting with periodontal infection.

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