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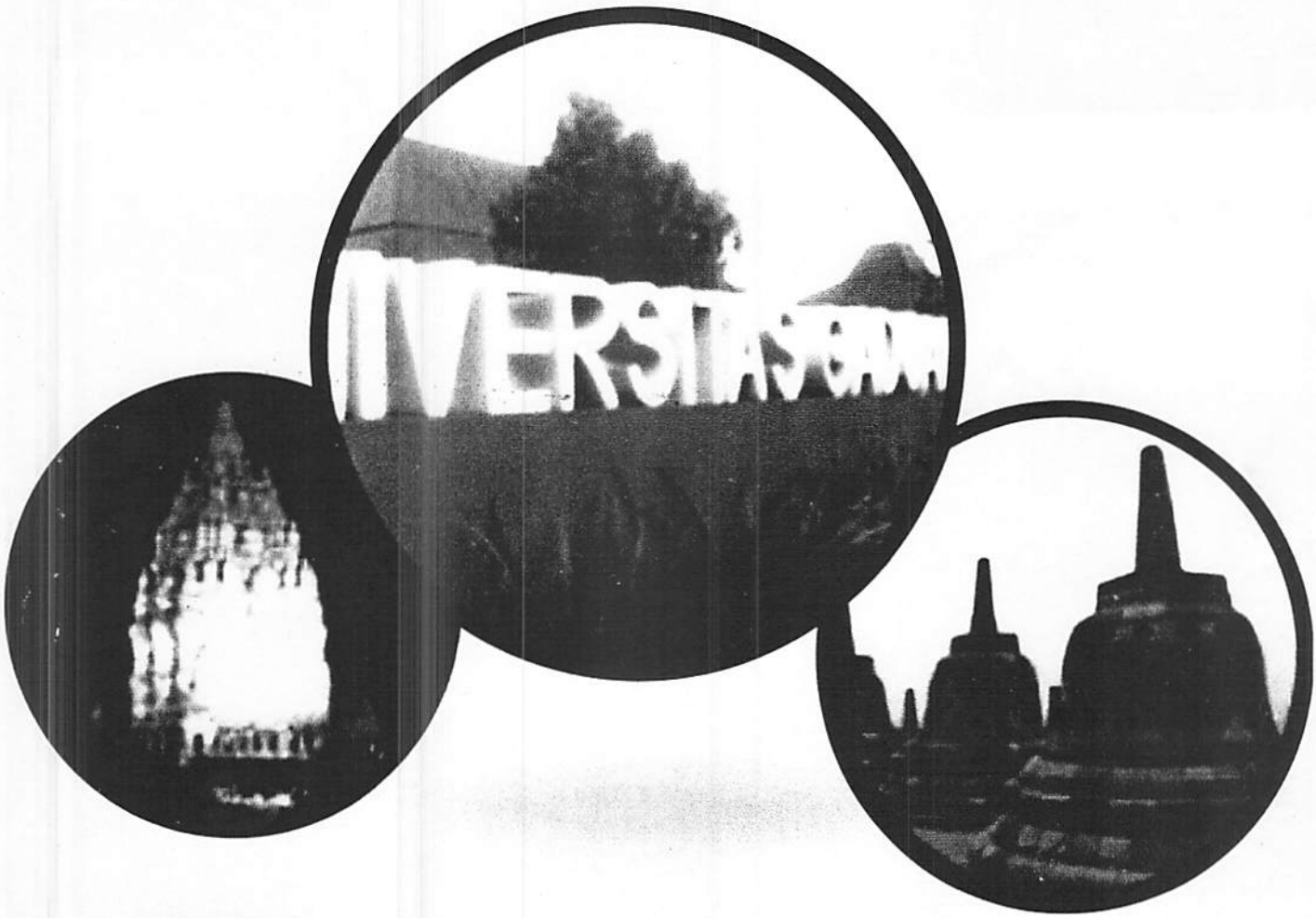
To Commemorate The 64th Anniversary of The Faculty of Dentistry
Universitas Gadjah Mada, Yogyakarta, Indonesia

The 2nd International Joint Symposium on Oral and Dental Sciences

In Conjunction with Dental Specialists Seminar

March 1-3, 2012
Hotel Inna Garuda Yogyakarta, Indonesia



Proceeding Book

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ACTIVATION OF INNATE IMMUNITY THROUGH TOLL-LIKE RECEPTOR-2 BY LIPOTEICHOIC ACID BACTERIA *ENTEROCOCCUS FAECALIS*

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Abstract

A persistent infection after root canal preparation is the main etiology in root canal treatment failure. Cleanup the complete of root canal preparation is difficult to achieve because of the complexity of root canal anatomy. The bacteria *Enterococcus faecalis (E. faecalis)* is the largest species found in root canal treatment failure. Prevalence in the re-treatment amounting to 89.6% and 67.5% for primary infection. Lipoteichoic acid (LTA) is a molecule found in Gram-positive bacterial cell surface that is functionally an important factor for growth and survival of bacteria. TLR-2 is a receptor expressed on the cell surface that recognize foreign substances such as bacteria. The conclusion of this paper is the destruction of microbes that cause infections is of paramount importance to prevent re-infection. *E. faecalis* is a bacteria that is resistant to root canal treatment procedures so that it can be a cause of failure of root canal treatment through the mechanisms of innate immunity activation of TLR-2 by LTA bacterium *E.faecalis.*

Key words: persistent infection, *Enterococcus faecalis*, Toll-like receptors.

INTRODUCTION

Bacteria and their products are considered as the main cause of pulp necrosis and periapical lesions. Destruction of microbes that cause infections is of paramount importance in routine root canal treatment. Instrumentation and root canal irrigation with anti-microbial activity is not always achievable in clinical practice because of the complexity of root canal anatomy.

A persistent infection after root canal preparation is a major etiological factor in the failure of root canal treatment [1]. Pinheiro [2] proved that the root canal treatment failure was found bacteria *Enterococcus faecalis (E. faecalis)* as the most species. Prevalence in the re-treatment amounting to 89,6% and 67,5% for primary infection.

E. faecalis is a cocci facultative anaerobic Gram-positive bacteria, resistant to alkaline pH of 9.0 to 10.0. Lipoteichoic acid (LTA) is one of a group amphipatic molecule found on the cell surface of Gram-positive bacteria. LTA is functionally an important factor for cell growth and survival of bacteria.[3] LTA is a virulence factor of Gram-positive bacteria, can stimulate murin macrophage, producing TNFα and can stimulate TLR2. Toll-like receptors (TLRs) are a class of proteins that play a role very important in the innate immune system. TLRs may recognize by activating non-specific immune cell responses. TLRs are the development of "pattern recognition receptors" that plays an important role in innate immune responses to microbes. Activation of TLRs by microbial products plays an important role for the induction of many genes that function in inflammation and immune responses.

DISCUSSION

Microorganism in the root canals

Craig 4 says that the normally dental pulp and periapical tissues in a sterile condition. Endodontics infection occurs when microorganisms invasion and multiplication in the pulpchamber or periapical tissues.

Gram-positive bacteria *Enterococcus faecalis*

Enterococcus faecalis is the species most frequently isolated or detected within the scope of oral infections, including periodontitis marginalis, infection of root canals and periapical abscesses. Pinheiro[2] evaluated the teeth with failed endodontic treatment which was obtained 80% of Gram-positive bacteria, and as much as 58% are facultative anaerobic microorganisms such as *Enterococcus.*

Enterococcus faecalis is a bacteria that most often found in periapical lesions and causes 85-90% of *Enterococcus* infections.[5] Although present in small amounts of the total flora of necrotic teeth that have not been treated, *Enterococcus faecalis* is often found in the root canal was done filling the root canal with symptoms of chronic apical periodontitis.[6]

Lipoteichoic acid (LTA)

Lipoteichoic acid (LTA) is the main constituent of the outer envelope of Gram-positive bacteria. Teichoic Acid of LTA contribute to the structural integrity of Gram-positive bacteria, but also important in the pathogenesis and implicated in the processes of adhesion to the host in affecting immune surveillance[7]

Next is a picture of the cell wall of Gram-positive bacteria containing LTA components taken from http://www.kcom.edu/faculty/ chamberlain / LECTS / Bacteria.htm.

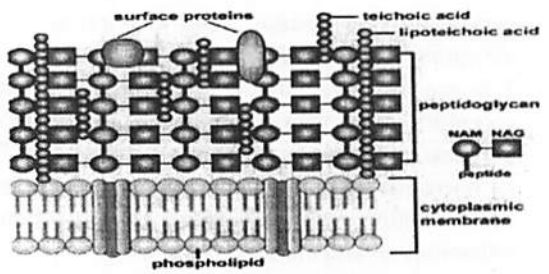


Figure 1 : Gram positive bacterial cell wall

Innate immunity

The ability of multicellular microorganisms to defend themselves against invading pathogens such as bacteria and fungi depend on the ability of the immune response. Vertebrates have not only innate imunity but also capable to induce defense mechanisms to establish adaptive immunity[8]

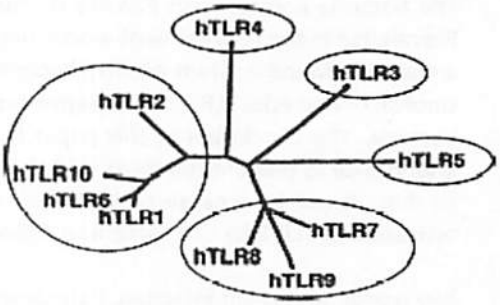
Signaling the presence of infection (Toll-like Receptors signaling pathways)

The introduction of PAMPs by PRRS will activate proinflammatory pathways and can activate the adaptive immune (APC). Makrophag, dendritic cells and epithelial cells have a transmembrane receptors that recognize different types of PAMPs. This is known as the Tool-like receptors (TLRs). Mammals have 12 different TLRs.

Toll-like Receptors (TLRs).

Structure

TLRs are an evolutionarily conserved family of pattern recognition receptors expressed on several cell types that play an important role in the innate immune response against microbes. There are 12



mammalian TLR genes and 11 were expressed in humans.9 TLRs include a family of type I transmembrane receptors that characterize the leucine rich repeats (LRRs) in the extracellular and the intracellular TIR domain (Toll/IL-1 receptor) which is homologous to the intracellular domain of IL-1 receptor family.[10]

Figure 2: Grouping of TLR

Diversity of TLR

TLRs are grouped into two classes based on sub-cellular localization, signaling mechanisms and how the introduction of the ligand. The first is: TLR-1, TLR-2, TLR-4, TLR-5 and TLR-6 are expressed on the plasma membrane and detect cell wall components of bacteria and fungi. The second is: TLR-3, TLR-7 and TLR-9 is expressed in the endosomal and recognize viral nucleic acids.[11]

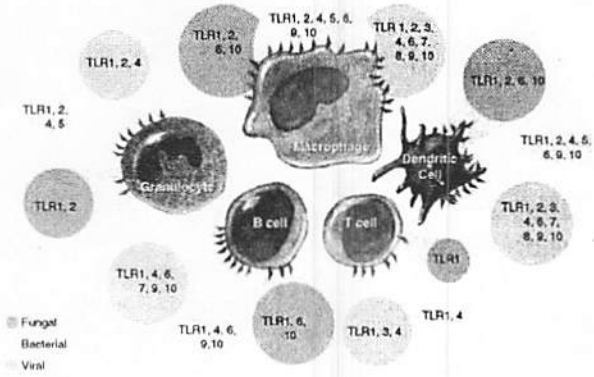


Figure 3: Diversity of TLRs

Toll-like receptor-2 (TLR-2)

Toll-like receptor 2 is commonly known as TLR-2, is a protein found in human. TLR-2 play in the immune system, is a membrane protein. a receptor expressed on the surface of certain cells and recognize foreign substances as well as find a suitable signal to the immune system cells. [10]

There are two possible mechanisms that could explain why the TLR-2 can recognize a wide spectrum of microbial components. The first explanation is a TLR-2 form dimers heterophillik with other TLRs such as TLR-1 and TLR-6 are structurally has a relationship with TLR2. Macrophage of TLR-6-deficient mice showed no production of inflammatory cytokines in response to mycoplasma-derived diacyl lipopeptides, although these cells showed normal production of inflammatory cytokines in response to triacyl lipopeptides from Gram-negative bacteria. As a difference, macrophage of TLR-1-deficient mice showed normal response to the mycoplasma-derived diacyl lipopeptides but it has an unpaired response to triacyl lipopeptides. So that the TLR-1 and TLR-6 are functionally associated with TLR-2 and differentiate between the diacyl and triacyl lipopeptides. Therefore the involvement of TLR-1 on the introduction of the outer surface lipoproteins of Borrelia burgdorferi can be shown. As a second explanation is the involvement of the introduction of the fungus by the components of the TLR-2, showing functionally collaborate with the receptor as dectin-1, a lectin family receptor for the fungal cell wall component β-glucan. Thus, TLR-2 is widely recognize microbial products through functional cooperation with several proteins that are structurally relation [7,9]

As the membrane surface receptors, TLR-2 recognizes bacteria, fungi, viruses and certain endogenous substances. In general the results (internalization, phagositosis) quick to recognize and bind to the molecule by endosom or phagosom in cellular activation. Thus, the element of innate immunity as macrophages, PMN and dendritic cells recognize the function of non-specific immune defense. B1a and MZ B cells are formed on the first antibodies and specific antibody formation will begin the process. Cytokines participate including tumor necrosis factor-alpha (TNFα) and various interleukins (IL-1α, IL-1β, IL-6, IL-8 and IL-12). Before TLRs know, some of the substance as a mean and to classify modulin.

A special properties found in 2006 that the discovery of the expression of TLR-2 on Tregs (a type of T cells) which can control the proliferation of TCR. Plays an important role for beginning phase of inflammation and the formation of specific antibodies [12]

CONCLUSION

Destruction of microbes that cause infections is of paramount importance to prevent re-infection. E. faecalis is a bacteria that is resistant to root canal treatment procedures so that it can be a cause of failure of root canal treatment through the mechanism of innate immunity activation of TLR-2 by Lipoteichoic acid (LTA) bacteria E. faecalis

REFERENCES

(1). Johnson EM, Flannagan SE and Sedgley CM. 2006. Coaggregation Interaction Between Oral and Endodontic Enterococcus faecalis and Bacterial Species Isolated From Persistent Apical Periodontitis. JOE 32 (10) : 946-950.

(2). Pinheiro ET, Gomes BP, Ferraz CC and Souza EL. 2003. Microorganism from canals of root filled teeth with periapical lesions. Int Endod J. 36(1) :1-11.

(3). Grundling A and Schneewind O. 2007. Synthesis of glycerol phosphate lipoteichoic acid in Staphylococcus aureus. Proc Natl Acad Sci USA 104 : 847-883.

(4). Craig B. 2004. Microbiologic Aspects of Endodontic Infections. CDA J. 32 : 6-11.

(5). Nakajo K, Nakazawa F, Iwaku M and Hoshino E. 2004. Alkali Resistant Bacteria in Root Canal System, Oral Microbiol Immunol. 19 : 390-394.

(6). Kayaoglu G and Orstavik D. 2004. Virulence Factors of Enterococcus faecalis :Relationship to Endodontic Disease, Crit Rev Oral Biol Med. 15 : 308-20.

(7). Carpenter S and O Neill LAJ, 2007, How important are Toll-like receptors for antimicrobial responses? Cell Microbial. 9 (8): 189-191.

(8). Abbas AK, Andrew HL, Pillai S. 2010. Cellular and Molecular Immunology, 6 th ed, Saunders Elseviers Inc. p.19-46.

(9). Baik JE, Han JY and Kum KY. 2008. Lipoteichoic acid partially constributes tothe inflamatory responses to Enterococcus faecalis. J. Endod. 34 (8) : 975-82

(10). Akira S. 2006. "TLR Signaling". Cell Death Differ. 13 (5): 816-25.

(11). Kaisho T and Akira S. 2006. Toll-like receptors function and signaling. J AllergyClin Immunol. 117 :976-987.

(12). Janssens S, Bayaert R. 2003. Role of Toll-like receptors in pathogen recognition"Clin Microbiol Rev. 16 (4) : 637-646.