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Immune Responses in Periodontal Pathogenesis

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Innate immunity

The term innate immunity refers to the elements of the immune response that are determined by inherited factors (and therefore "innate")

Defenses against infection include a wide range of mechanical, chemical, and microbiologic barriers that prevent pathogens from invading the cells and tissues of the body.

- Saliva
- GCF,
- epithelial keratinocytes
- The commensal microbiota (e.g., in dental biofilm)
- If bacterial products enter the tissues, then the cellular and molecular elements of the innate immune response are activated.

Innate immune responses are orchestrated by a broad range of cytokines, chemokines, and cell surface receptors, and the stimulation of innate immunity leads to a state of inflammation.
If innate immune responses fail to eliminate infection, then the effector cells of adaptive immune responses (lymphocytes) are activated.

SALIVA

Saliva has an important role in the maintenance of oral and dental health. It is secreted from the three major salivary glands (i.e., parotid, submandibular, and sublingual),and numerous minor salivary glands. The action of shear forces associated with saliva flow is important for preventing the attachment of bacteria to the dentition and oral mucosal surfaces. Human saliva also contains numerous molecular components that contribute to host defenses against bacterial colonization and periodontal disease .

Epithelial Tissues

It Plays a key role in host defense because they are the main site of the initial interactions between plaque bacteria and the host, and they are also the site of the invasion of microbial pathogens. The keratinized epithelium provides protection for the underlying periodontal tissue in addition to acting as a barrier against bacteria and their products. The junctional epithelium has significant intercellular spaces, it is not keratinized, and it exhibits a higher cellular turnover rate. the junctional epithelium permeable, thereby allowing for the inward movement of microbes and their products and the outward movement of GCF and the cells and molecules of innate immunity. Epithelial cells also constitutively express antimicrobial peptides (e.g., hBDs, LL-37), and the synthesis and secretion of these molecules is up-regulated in response to periodontal bacteria. Neutrophils are also a source of antimicrobial peptides (i.e., α-defensins).

The α-defensins (e.g., human neutrophil peptides 1 through 4) are expressed by neutrophils and are commonly found in GCF. The hBDs (e.g., hBDs 1 through 3) are expressed in the **gingival epithelial cells, the salivary glands, and the tongue, as well as in immune cells** (e.g., macrophages, dendritic cells); some hBDs are constitutively expressed, and others are expressed only in response to cytokines and bacterial products (e.g., gingipains of P. gingivalis). Epithelial cells also secrete a range of cytokines in response to periodontal bacteria (e.g., P. gingivalis, A. actinomycetemcomitans, F. nucleatum, Prevotella intermedia), which signal immune responses. These include the proinflammatory cytokines IL-1β, TNF-α, and IL-6, as well as the chemokine IL-8 (CXCL8) and the monocyte chemoattractant protein-1 (MCP-1), which serve to signal neutrophil and monocyte migration from the vasculature into the periodontal tissue.

Gingival Crevicular Fluid GCF

It originates from the postcapillary venules of the gingival plexus. It has a flushing action in the gingival crevice, bring the blood components (e.g., neutrophils, antibodies, complement components) of the host defenses into the sulcus. The

flow of GCF increases in inflammation, and neutrophils are an especially important component of GCF in periodontal health and disease

ADAPTIVE IMMUNITY
It is slower and reliant on complex interactions between antigen presenting cells, T and B lymphocytes.
Key elements*:*

Antigen specificity of the responses that facilitate specific targeting of a diverged range of effector elements (cytotoxic T cells and antibodies).

ANTIGEN-PRESENTING CELLS
MHC is a locus on short arm of chromosome 6 (6p21.3) that encodes MHC classes I,II, III, which are involved in antigen uptake, processing and presentation. *MHC class I* molecules: present intracellular antigens to CD8+ T cells and NK cells. *MHC class II* molecules: present extracellular antigens to CD4+ T cells. *MHC class III* molecules include complement factors B, C2 and C4.

The three main professional APC's are

- Peripheral dendritic cell
- Monocyte
- Bcells these are specialized to present antigen to $CD4_+$ T cells which recognize antigen in association with MHC class II molecule. The professional APC expresses MHC classII molecule Externally derived antigens are processed by phagocytosis and resulting peptides molecules associate with MHC class II molecules on the cell surface . Molecules of MHC class I, II,III are among the most pleomorphic molecules in humans Pleomorphism refers to stable variations among individual with in species ,based on the occurrence of variant of certain certain genes .

Pleomorphism in MHC is particularly high near the specificity pockets (this means that the antigens bound by one person's MHC class I ,II molecules may not bind exactly the same peptides as those from different individual). The interaction between two cells permits high level of sophistication enabling the APC to present antigen to the Tcell With second signal ,which is called **co-stimulation.**

Co-stimulation reaffirms to the T cell that it has recognised an undesireable antigen .
Co-stimulation is mediated by a variety of transmembrane molecules of TNF superfamily.
Co-stimulation performs three function:

- Makes the cell resistant to apoptosis
- Upregulates the growth factor receptors on the Tcell
- Decrease the amount of time needed to trigger T cell

Macrophages increases the expression of co-stimulatory molecules if they are exposed to bacterial LPS .
B cells exposed to antigen to which they are specific respond by increasing the expressions of co-stimulatory molecule B7 -1 and B7 -2.

B Cells
B cells produces immunoglobulin. Human possess nine genetically distinct isotypes of immunoglobulin . To form secondary response isotypes B cell must enter a pathway of differentiation in which it undergo a process of isotype switching . The ability of B cells to respond to antigen depends on **B cell antigen receptor (BCR)** .BCR is formed partly by immunoglobulin molecules on B cell surface and partly by trandsductory elements on immunoglobulin superfamily . B cell must interact with Tcells to enter the memory pathway,so memory pathway is considered as T cell dependent pathway. B cells bind soluble antigen using BCR ,if enough antigen is bound ,they then are ingested and processed and the parts of antigen are presented to specific CD4+ Tcells using MHC class II molecules . After antigen presentation ,the T cells provide an activation signal to the B cell .Tcell activators are transmembranous molecules ,analogous to the co-stimulatory factors for T-cells .

T Cells
T cells develop in the bone marrow and thymus and migrate to the peripheral tissues to participate in adaptive immune responses. CD4+ helper T cells are the predominant phenotype in the stable periodontal lesion, and it is thought that

alterations in the balance of effector T-cell subsets within the CD4+ population may lead to progression toward a destructive, B-cell–dominated lesion. CD4+ T-cell subsets are defined by the expression of specific transcription factors, and their functional characteristics are associated with their cytokine secretion profile. Dynamic interaction between Th1 and Th2 cells may provide, in part, an explanation for fluctuations in disease activity and the progression of periodontal disease

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