*Adaptive Immunity: Lec :*

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Adaptive immunity contrasts with innate immunity in the dynamic of the underlying cellular and molecular responses:

1. adaptive immunity is slower

2. reliant on complex interactions between antigen -presenting cells and T- and B-lymphocytes.

3. specificity of the responses

4. The ability of adaptive immune responses to improve during exposure to antigen on subsequent infection events (memory).

***Lymphocytes are the main cells of adaptive immune response:*** I.T-lymphocytes or T-cells: Derived from the thymus and play a role in cell-mediated immunity.

Different types of T-cells include:

1.Helper inducer T-cells (TH-cells) or CD4:They aid in the immune response of the B-cells to differentiate into plasma cells and produce antibodies.

2. Cytotoxic T-cells or CD8: Stimulates cytotoxic and microbicidal activity of the immune cells.

3.T suppressor cell :down regulate or suppress immune response.

II.B-lymphocytes or B-cells: Derived from liver, spleen and bone marrow. They are precursors for plasma cells and play a role in humoral immunity.

adaptive immunity initiates with antigen presenting cells (macrophage,B cells and dendritic cells) recognizing pathogen in the sites of infection and subsequently migrating in to the regional draining lymph nodes to present the processed antigen peptides i n the context of major histocompatibility complex (MHC) molecules to naive T lymphocytes and induce their activation and differentiation in to effector cell s (helper or cytotoxic cells).

***Cellular immunity to dental plaque***

The cell-mediated response in periodontal diseases: It is so called because it involves contact between cytotoxic T-cells and antigen to be destroyed. These reactions are effective against persistent antigens, which are resistant to degradation, intracellular antigen and the cells infected with virus.

***The humoral response to plaque***:

Plaque bacteria and their soluble products such as enzymes and toxins carry out activation of the humoral response. The lymphocytes, which recognize each individual antigen, are activated, and differentiate into plasma cells, which secrete antibody .Most of the lymphocytes and plasma cells remain in the lymph nodes and secrete antibodies into the blood stream. The antibody predominantly is IgG, which can opsonize and activate the complement. Small amounts of IgM is also seen which is more of an activator of the complement and less of an effective opsonin. These antibodies pass into the gingival inflammatory exudates and then out into the gingival crevice in the crevicular fluid.

Possible mechanisms of action of antibodies in periodontitis:

*I. Binding to bacteria, Thus:*

a. Opsonizing for phagocytosis

b. Activating neutrophil enzyme secretion

c. Coating bacteria and inhibiting attachment

d. Activating complement and thus enhancing opsonization

e. Directly inhibiting bacterial metabolism.

*II. Binding to soluble factors; Thus:*

a. Neutralizing toxins.

b. Inhibiting enzymes.

In adult periodontitis T helper- cells increase and T Suppressor -cells decrease with increased gingival inflammation.

A dynamic interaction between Th 1 an d Th 2 cells may provide an explanation for fluctuations in disease activity and progression of periodontal disease . It has been hypothesized that a strong innate response results in interleukin -12)I L-12) synthesis (e.g. , by tissue macrophages), leading to a Th1 response providing protective cell -mediated immunity that would be manifested as a “stable” periodontal lesion . Th 1 cells secrete interferon (IFNγ), which activates cell –mediated immunity (macrophages, natural killer (NK) cell s, and CD8 Cytotoxic T-cells) against pathogenic microorganisms. Activation of macrophages promotes phagocytosis and killing of microbial pathogens, where as NK cells and CD8 T-cells are cytotoxic T-cell s that kill infected host cells.

Conversely , a poor innate response would lead to reduced IL-12, which would permit the development of Th 2 responses, leading to activation of B-cell s that in turn would mediate a destructive lesion possibly through enhanced B-cell –derived I L-1β. Th2 cells regulate humoral (antibody -mediated) immunity and mast cell activity through the secretion of the cytokines I L-4 and I L-5 . Thus predominance of Th 2 cells leads to a B-cell response. The B-cell response may be protective, for example, by the production of specific antibodies that would serve to clear tissue infections through interaction with the complement system and by enhancing neutrophil phagocytosis. However, B-cell s are also a source of proinflammatory cytokines that contribute to tissue destruction .

**OSTEO-IMMUNOLOGY IN PERIODONTAL DISEASES**

As the advancing inflammatory front approaches the alveolar bone, osteoclastic bone resorption commences.

This is a protective mechanism to prevent bacterial invasion of the bone, but it ultimately leads to tooth mobility and even tooth loss. Resorption of alveolar bone occurs simultaneously with breakdown of periodontal ligament (PDL) in the inflamed periodontal tissues. There are two critical factors that determine whether bone loss occurs:

first ,the concentration of inflammatory mediators in the gingival tissues must be sufficient to activate pathways that lead to bone resorption ,

second, the inflammatory mediators must penetrate to within a critical distance of the alveolar bone.

Histologic studies have confirmed that the bone resorbs so that there is always a width of non-infiltrated connective tissue of about 0.5 to 1.0 mm overlying the bone.

It has also been demonstrated that bone resorption ceases when there is at least a 2.5-mm distance between the site of bacteria in the pocket and the bone.

Osteoclast s are stimulated by pro inflammatory cytokines and other mediators of inflammation to resorb the alveolar bone from the advancing inflammatory front . Osteoclasts are multinucleated cells formed from osteoclast progenitor cells/macrophages, and osteoclastic bone resorption is activated by a variety of mediators such as I L-1β, TNF-α, I L-6, and PGE2 . the key system for controlling bone turnover is the receptor activator of nuclear factor-κB (RANK)/RANK ligand (RANKL)/osteoprotegerin (OPG) system.

RANKL is produced as a membrane‐bound or secreted ligand by osteoblasts, fibroblasts, or activated T‐ and B‐cells.

By activating its cognate RANK receptor on the surface of pre‐osteoclasts, it triggers their fusion and differentiation into mature osteoclasts, thus activating bone resorption. The action of RANKL can be blocked by its soluble decoy receptor osteoprotegerin (OPG), which is a member of the TNF receptor superfamily, by binding to RANKL, OPG prevents its further interaction with RANK, and subsequently all the down‐stream molecular events that lead to osteoclast differentiation and bone resorption.

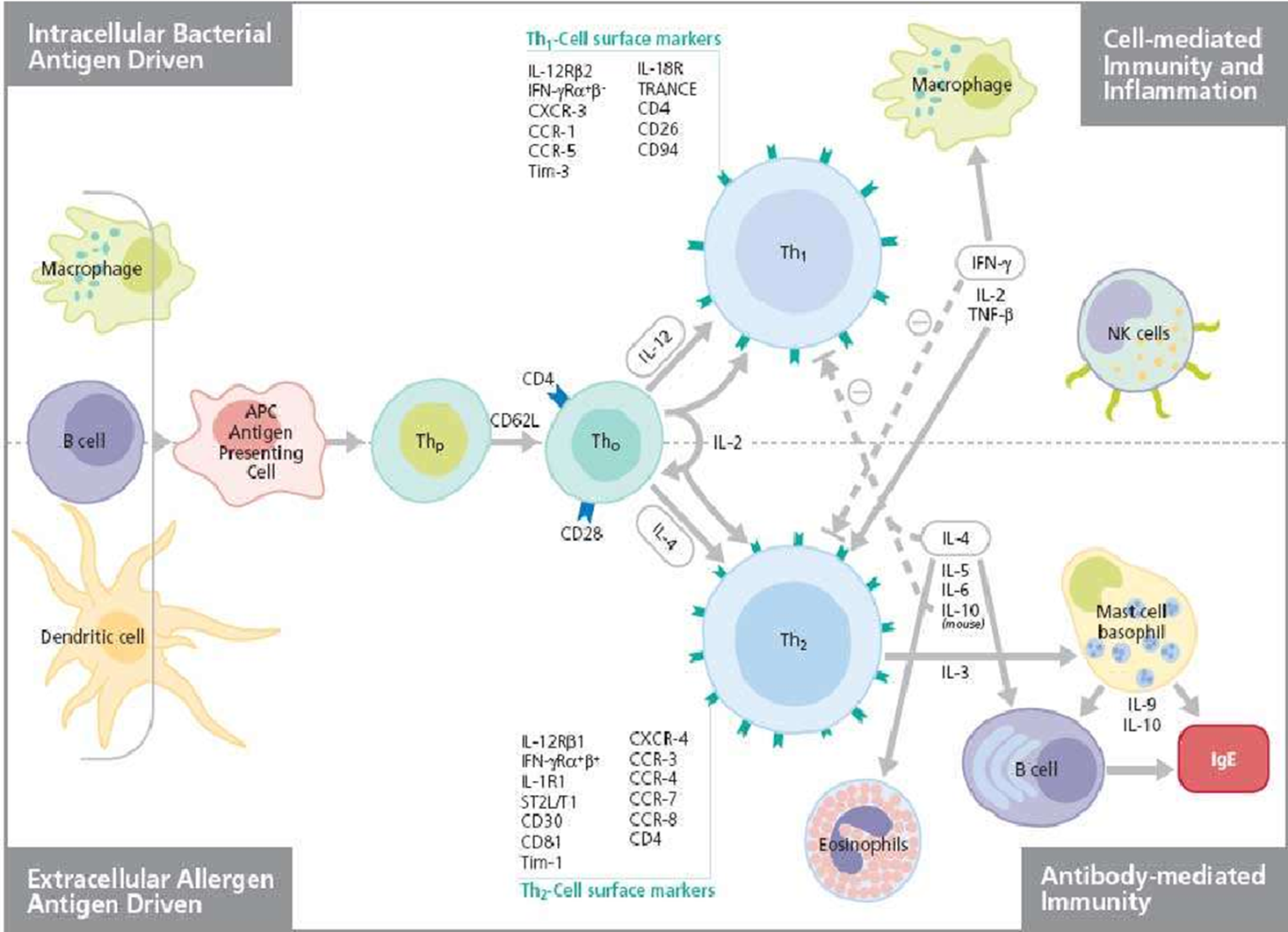
The production of RANKL and OPG by various cells types is controlled by systemic and local stimuli, including hormones, inflammatory mediators and bacterial products

Therapeutic Strategies for Disrupting Host-Cell Signalling in the Treatment of Periodontal Diseases

A variety of treatment strategies have been developed to target the host response to LPS-mediated tissue destruction . MMP inhibitors, such as low dose formulations of doxycycline, have been used in combination with scaling and root planning or surgical therapy .

In addition , high -risk patient populations, such as those with diabetes, have benefited from systemic administration of MMP inhibitors.

Encouraging results have also been shown using soluble antagonists of TNF and I L-1 delivered locally to the periodontal tissues in non human primates.



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