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Perspective

Role of Cytokines in Health

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DESCRIPTION

The immune system is complex. Different types of immune cells and proteins perform different tasks. Cytokines are one of the proteins. To understand inflammation, we need to understand the role that cytokines play. Cells release cytokines into the bloodstream or directly into tissues. Cytokines localize to immune cells and target and bind to their receptors. This interaction provokes or stimulates a specific response of the target cell. Cytokines are small, low molecular weight, non-structural proteins that have complex regulatory effects on inflammation and immunity. Hematopoietic cells, lymphoid cells, and various pro-inflammatory and anti-inflammatory cells are involved in the development of immune and inflammatory responses, and it has long been thought that cytokines mediate the complex interactions of these cells. Cytokines are intercellular messengers of the immune system that integrate the functions of multiple cell types in different body compartments into a coherent immune response. They have evolved over the years to include interferon, interleukins, chemokine's, mesenchymal growth factors, tumor necrosis factor family, and adipokines.

Cytokines are produced and elicit a response from every cell except red blood cells. In response to various stimuli, cytokines are secreted by various cells, including white blood cells. Pleiotropism is the hallmark of a cytokine and there are failures and successes of cytokines and related agents as therapeutic agents. The membrane of the target cell has specific receptors for signal transduction and regulatory function. In addition to innate and adaptive immunity, cytokines play important roles in many different functions, including immune cell differentiation, inflammation, angiogenesis, tumorigenesis, neurobiology, and viral etiology. In addition to inflammation, immunity, and infection, cytokines are now expanding their domain to atherosclerosis and cancer. Therefore, cytokines are useful biomarkers for health and disease and serve as diagnostic, prognostic, and therapeutic tools.

The history of cytokine development has shown them as soluble factors produced by one cell and acting on another, establishing recognition of cytokine activity. It soon became clear that the production of these factors could be regulated by activation by antigen or non-specific mitogen. A standardized nomenclature was also developed to designate cytokines as interleukins in relation to their role among leukocytes was also developed, and the first to be named were IL-1 and IL-2. Leukemic monocyte lines were selected for the development of interleukin-1 and T-cell lymphoma for the production of IL2. Today, they are recognized as integral membrane proteins, and some cytokines may not be released from cells. Advances in knowledge have highlighted the complexity and biphasic nature of cytokines. The same molecule can have both beneficial and detrimental effects. For example, interferon gamma which is essential for defense against some intracellular microorganisms such as *Mycobacterium tuberculosis* is also an important cytokine in the pathogenesis of some autoimmune diseases. IL2 is required for the production of cytotoxic T cells (CTLs) and forms the basis of several vaccines, but the same cytokines cause graft-versus-host disease and limit the success of bone marrow transplants.

The cytokines exert various biological effects through receptors present on the membranes of responsive target cells. These receptors have an extracellular domain, a cytoplasmic domain and a single membrane spanning domain. There is the presence of conserved amino acid sequence motifs on the extracellular domain and these motifs include four conserved cysteine residues. There is also the presence of two polypeptide chains. One is the cytokine specific α subunit and other is a signal transducing β subunit.

The nature of the target cell to which the cytokines bind is determined by the presence of specific membrane receptors. Cytokines and their receptors exhibit very high affinity for each other and possess dissociation constants ranging from 10-10 to 10-12M and for this reason of high affinity, biological effects are produced by cytokines in Pico molar concentrations. They exhibit autocrine, paracrine, and endocrine actions and mediate cellular intercommunication. The intensity or duration of immune response is regulated by either stimulating or inhibiting the activation, proliferation and differentiation of various cells and thus regulating the secretion of antibodies or other cytokines.

The physiological responses of cytokines on binding to receptors include development of cellular and humoral immune response, induction of inflammatory response, regulation of haematopoiesis, control of cellular proliferation and differentiation and induction of wound healing. Other than this, the cytokines often induce the synthesis of other cytokines resulting in a cascade of activity in which the latter cytokines influence the activity of the former cytokines which secreted it. Finally, they function for a very limited period of time due to their short half-life in the blood stream and extracellular fluids Pro-inflammatory cytokines play a role in the development of inflammatory and neuropathic pain.

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