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# Introductory Chapter: Immunity and Immunomodulation

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## 1. Introduction

The mammalian immune system is comprised of two branches of immune system; innate and adaptive, which render tolerance towards host for protection from microbial infections. The innate immune system consists of functionally distinct mechanism that evolved to render protection against pathogens. The nonadaptive immune system senses pathogens through pattern recognition receptors which trigger the activation of antimicrobial defense system to stimulate and provoke the efficient immune response. The acquired immune system in response activates the nonadaptive immune effector mechanisms in an antigen-specific and dependent manner. Although the link between various immune components are not fully understood, recent progresses bring us closer to an integrated view of immune system and its function towards the host defense [1].

The infectious diseases are the leading cause for the greater rate of morbidity and mortality world-wide and are a major challenge for the biomedical sciences. The physical methods such as improved sanitary conditions, clean water supplies and vector control are by far the most effective measures, development of vaccines and therapeutics are panacea for their treatment. The development of vaccine and therapeutic interventions require the understanding of host immune system. Recently, significant progress has been made towards unraveling the mechanisms of microbial pathogenesis and host-microbe symbiosis. There are many challenges remain and most daunting is the development of effective vaccine. Indeed, it is not known how to elicit protective immunity against most pathogens in a safe and practical manner. To address and overcome the autoimmune response mounted by the host are required and to be explored by the basic science researchers.

The innate immune system is the phylogenically oldest component of the human immune system. The innate immune system is highly complex and consists of barriers to infection (epithelia of skin, gastrointestinal, respiratory, genitourinary tracts), antimicrobial peptides and proteins, humoral components (i.e., complement and opsonins) and cellular components (i.e., neutrophils, monocytes/macrophages, dendritic cells, and innate lymphoid cells). Innate immunity serves as the front line of host defense and plays an essential role in preventing infection while tolerating normal host flora. The defects in innate immunity are associated with invasive, life-threatening infection, and inappropriate activation of innate immune system may lead to auto-inflammatory states. The innate immune system directs the subsequent development of adaptive immune responses [2].

The human acquired immune system is responsible for the destruction of foreign particles once they have entered the body. During the first exposure to an invader (which could be a virus, a bacteria or any unwanted particle), the acquired immune system must “learn” how to attack and destroy the foreign particle. This

implies that adaptive system is not as active and efficient in the clearance of any pathogens as innate immune system [3].

Activation of acquired immune system: unlike the innate immune system, the acquired immune system needs to be exposed with a substance before its effective action. The acquired immune system is target specific and takes its own time to prepare to act against pathogens [3].

### **1.1 Role of cytokines in the immune response activation and immunomodulation**

Cytokines participate in many physiological processes including the regulation of immune and inflammatory responses. These effector molecules are produced transiently and locally and control the quantum of amplitude and duration of the response. The research outcomes have shown that meagre or suboptimal production of these informational molecules may significantly contribute to the pathophysiology of various diseases [4]. Particularly the cytokines released by CD4<sup>+</sup> T cells at the onset of an immune response are decisive for pathological or physiological consequences. IL-1, IL-4, IL-6, IL-10, IL-12, TNF-alpha and IFN-alpha, -beta, -gamma, etc., are known to contribute to the pathophysiology of autoimmune diseases, infectious diseases, and allograft rejection [4].

The inflammatory responses in the peripheral and central nervous systems play key roles in the development and persistence of many pathological pain states [5]. Cytokine a broader name which includes lymphokine; cytokines secreted by the lymphocytes, monokines are secreted by the cells of myeloid origin such as monocytes, chemokine shows chemotactic activities, and the interleukins are the cytokines made by one leukocyte which acts on other leukocytes. The cytokines may act on the cells that secrete them in an autocrine manner or on nearby cells following the paracrine fashion. The action in some instances on distant cells is termed as “endocrine action” [6].

### **1.2 Pro-inflammatory cytokines**

An inflammatory or pro-inflammatory cytokine is a type of signaling molecule that is excreted by the cells of immune cells such as helper T cells (Th) and macrophages, and some other cell types which are known to promote inflammation as a defense mechanism. The interleukin-1 (IL-1), IL-12, and IL-18, tumor necrosis factor (TNF), interferon gamma (IFN- $\gamma$ ), and granulocyte-macrophage colony stimulating (GM-CSF) factor and play an important role in mediating and regulating the nonadaptive immune response. The inflammatory cytokines are predominantly produced by and involved in the upregulation of inflammatory reactions to show resistance towards infectious pathogen [7, 8].

### **1.3 Anti-inflammatory cytokines**

The anti-inflammatory cytokines are a series of immunoregulatory molecules that control pro-inflammatory cytokines, production and their response. The cytokines act in concert with specific cytokine inhibitors and soluble cytokine receptors with an objective to regulate the human immune response. Their physiologic role in provoking inflammatory responses and pathologic role in systemic inflammatory states are increasingly recognized. The chief anti-inflammatory cytokines include interleukin (IL)-1 receptor antagonist, IL-4, IL-6, IL-10, IL-11, and IL-13. The specific cytokine receptors for IL-1, tumor necrosis factor- $\alpha$  and IL-18 also function as the inhibitors of the pro-inflammatory cytokines [9, 10].

## 1.4 Immunomodulation

Mesenchymal Stem Cells (MSCs) emerging as key players in regenerative medicine for the treatment of various inflammatory and infectious diseases. The MSCs are emerging an effective tool in developing therapeutic interventional approaches and further advancements. Several tissues have been identified as potential sources of MSCs including bone marrow, cord blood, dental pulp, umbilical cord, adipose tissue, peripheral blood, fetal liver, of which some are clinically recognized. MSCs activate the immune responses and inhibit proliferation, maturation and differentiation of T and B cells. The MSCs activated immune response induce the expression of regulatory T cells (Tregs) [11] which are very important in regulating the immune system and immune effectors of diseased cells.

The immune response activation and immunomodulation is an essential reading to all medical students, biologist, biochemist, and professionals involved in the field of immunology of infectious diseases and beyond. The book is a useful and ideal guide for novice researchers interested in learning research methods to unravel the knot of immune responses and their activation. The role of various cytokines in mounting the protective/immune response as well as during immunomodulation is the central theme of this book.

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