THE IMMUNE SYSTEM: A BRIDGE BETWEEN HEALTH AND DISEASE

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The immune system has evolved to provide protection against invasion by disease producing microorganisms. The human immune system is comprised of two distinct pathways that cooperate with one another on a cellular and molecular basis. These two pathways are the innate and the adaptive components of immunity. The innate pathway consists of cells and molecules that provide the body's first line of defense against infectious microorganisms. The adaptive pathway of the immune system consists of specialized cells called lymphocytes (B cells and T cells). Adaptive immune responses are more specific and develop greater activity upon subsequent exposure to the pathogen. Cells from both arms of the immune system utilize membrane receptors to recognize distinct components associated with microorganisms.

Innate Immunity

Epithelial cells and their products provide the first line of defense in innate immunity protecting the host from invasion of microbes from the external environment. However, if a microbe enters the tissues or circulation they initially encounter cellular components of innate immunity. A prominent group of innate immune cells are phagocytes. Mononuclear phagocytes include monocytes that circulate in the blood and macrophages that are found in virtually every organ. Polymorphonuclear leukocytes consist predominantly of neutrophils that circulate in the blood along with a small number of eosinophils and basophils. Other cells that participate in innate immunity include dendritic cells found in various lymphoid organs, Langerhans cells found in the skin and natural killer cells (NK cells) found in the blood. A family of plasma proteins called the complement system also plays a critical role in the early interaction of the host with invading pathogens. In addition to its role in providing the initial defense against infections, the innate immune responses enhance the subsequent adaptive immune responses against the infectious microorganism.

Cells of the innate immune system recognize structures that are shared by classes of microbial organisms. These structures are broadly classified as *Pathogen associated molecular patterns (PAMPS).* Receptors have evolved on phagocytic cells of the innate immune system to recognize these PAMPS and are called *Pattern Recognition Receptors (PRR).*

Adaptive Immunity

Cells of the adaptive immune pathway, lymphocytes, express receptors that recognize diverse molecules produced by microbes as well as noninfectious molecules. These molecules are referred to as antigens and the receptors on B cells and T cells that recognize and bind antigens are called B cell antigen receptors and T cell antigen receptors. These specific antigen receptors trigger effector functions that are designed to eliminate the invading pathogen. Thus binding of antigen to the B cell antigen receptor results in the production of antibodies that function to eliminate microorganisms from extracellular locations whereas activated T cells eliminate microbes that are living inside cells.

The adaptive immune pathway is characterized by diversity, specificity and memory. Diversity is provided by millions of different lymphocytes each expressing a unique antigen receptor. These receptors arise during development of these lymphocytes in a random manner and are available to respond to an antigen when an individual encounters that specific molecule. Specificity refers to the concept that each antigen receptor recognizes a precise component of the antigen molecule called an epitope. When a lymphocyte binds an antigen via its antigen receptor the receptor transduces an activating signal into the cell. This signal instructs the cell to replicate and one of the progeny cells differentiates into an effector cell while the other produces a clone of itself which is referred to as a memory cell. Each time the cell with the specific receptor for that antigen encounters the epitope it expands the pool of memory cells for that antigen and increases the speed and magnitude of the immune response. This is the mechanism by which vaccine development occurs. The specificity and diversity of the lymphocyte receptors results in a clonal distribution of receptors for antigen such that the total population of lymphocytes consists of many different clones.

Two classes of T lymphocytes exist. One class is referred to as cytolytic T cells and recognize foreign antigenic epitopes presented to it by a surface protein on host cells. This protein is called the Major Histocompatibility Class 1 protein and presents antigenic epitopes from pathogens that infect a cell. Cytolytic T cells play a prominent role in host defense against virally infected host cells. A second class of T cells is called helper T cells and they recognize foreign antigenic epitopes presented by Major Histocompatibility Class 2 protein. These molecules present antigenic peptides that 'professional antigen

presenting cells' take up from outside the cell, predominantly bacterial antigens. Helper T cells respond by producing molecules called cytokines which are the hormones of the immune system and act locally and distantly to regulate the function of cells derived from both the innate and adaptive arm of the immune system. For example, some antigens direct helper T cells to produce groups of cytokines that are pro-inflammatory and activate the function of macrophages, innate immune system cells, whereas other antigens may stimulate helper T cells to produce cytokines that facilitate the production of antibodies by B lymphocytes or accelerate an allergic reaction.

Immunologic Disease

Despite it complexity and many points of control, some individuals in the population develop diseases that are the result of immunologic 'hypersensitivity'. One example of immunologic hypersensitivity is the development of allergy which affects almost 20% of the population. Underlying allergic responses is the production of a class of antibody, IgE, to environmental antigens which are referred to as allergens. The IgE molecules bind to IgE Receptors on mast cells found in mucosal tissues and are crosslinked when they bind the allergens. Crosslinking of the receptors on mast cells results in the degranulation and release of chemical mediators, such as histamine, that cause the allergic symptoms. A second type of immunologic hypersensitivity is autoimmune disease in which tolerance to self antigens is lost and either an antibody-mediated or cell-mediated response to host cells or proteins develops. Finally, immunodeficiency syndromes, either congenital or acquired, result in susceptibility to a variety of pathogens depending on which component of the immune system is defective.

Conclusion

Thus the immune system is a finely balanced system designed to protect the individual against invasion and subsequent disease production by a myriad of infectious agents. It utilizes an early defense system of cells and molecules, innate immunity, to eliminate infectious microbes together with an adaptive immune system that has a fine specificity for foreign substances and responds more effectively with each subsequent exposure to a microbe to provide long-lasting immunity.