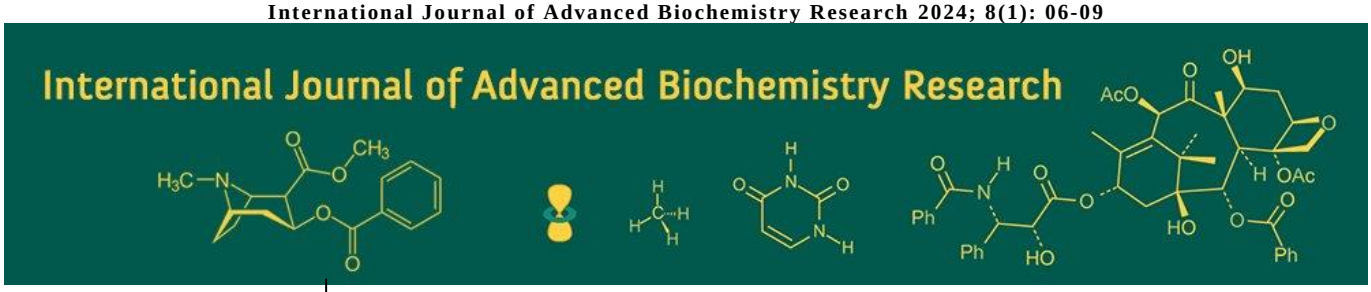

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Harnessing the power of adaptive immune response and crosstalk

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Abstract
Essentially, the immune system is a network of cells, tissues, and organs that are designed to protect the body from outside invaders. Infections are primarily caused by microbes, which include bacteria, parasites, and fungi. Viruses also cause infections, but they are too primitive to be classified as living organisms. Humans provide a perfect environment for a wide range of bacteria and viruses. As a matter of fact, the immune system should seek out and destroy them, if that doesn't work. Immunity is one of the most complex systems in the human body. Neither an organ nor a cell can be considered a part of it. There are many different types of cells and organs that make up the immune system. There are two main groups of these organs based on their function. Lymphocytes are trained to discriminate between self and non-self-antigens in the primary lymphoid organs by providing appropriate microenvironments. As the primary lymphoid organ in humans, the bone marrow produces B-cells, whereas the thymus produces t-cells.

Keywords: B-cells, t-cells, immune response, crosstalk

Introduction
Besides the spleen and lymph nodes, other lymphoid tissues form secondary lymphoid organs. As secondary lymphoid organs, secondary lymphocytes trap antigen and interact effectively with that antigen when it is present within tissues or vascular spaces. A functional whole is formed by the connections between these organs through blood vessels and lymphatic systems. There are several kinds of white blood cells, or leukocytes, present in the blood and lymph of the body and populating the lymph nodes. Bone marrow contains multipotent multilineage haematopoietic stem cells, mainly lymphoid and myeloid. In immunophenotyping applications, cluster of differentiation (CD) is a technique for identifying and evaluating cell surface molecules. Often cell types are mentioned as their marker CD names as shown below.

Type of cell	CD markers
Stem cells	CD34+, CD31-
All leukocyte groups	CD45+
Granulocyte	CD45+, CD15+, CD24+, CD114+,
CD182+[6] Monocyte	CD45+, CD14+, CD114+, CD11a, CD91+[7]
T lymphocte	CD45+, CD3+
T helper cell	CD45+, CD3+, CD4+
T regulatory cell	CD4, CD25, and Foxp3
B lymphocyte	CD45+, CD3+, CD8+
Thrombocyte	CD45+, CD19+ or CD45+, CD20+, CD24+
Natural Killer cell	CD16+, CD56+, CD3-, CD31, CD30

Activated immune cells begin to produce powerful chemicals once they receive the danger alarm. By utilizing these substances, cells can control their own behavior and growth, recruit other immune cells, and direct them to troubled regions. This system is similar to a vast army, consisting of surveillance, artillery, and communications. And like an army, there's the danger of friendly and often cell types are fire: To ensure that a body attacks an invader rather than itself, it needs to make sure to attack an invader rather than itself.

The body's immune system may attack itself while trying to fight off an outside enemy, resulting in diseases such as rheumatoid arthritis (the joints attack the body) and diabetes type 1 (the pancreas attacks the body).Immune system has a less specific component, the "Innate immunity" and, more specific component, the "Adaptive immunity"

When the host is exposed to a pathogen, innate immunity provides the best line of defense. In general, The innate immune system of a healthy individual is capable of eradicating the majority of microorganisms encountered within a few days.

A wide range of inmate immune mechanisms operate which do not improve with repeated exposure to Infection. The very first strategy is to keep the foreign assailants out of the host system or expel them out as fast as possible.

The external barriers: In addition to the expulsion of microorganisms through the skin, mucus secretion, ciliary action, lavaging by bactericidal fluids (e.g., tears), and microbial antagonism, microorganisms are kept at bay by the microbial antagonists that live in the body. Through lysozyme, soluble factors are used to destroy bacteria, which can then be degraded by phagocytosis within the cell.

The phagocytes: Polymorphonuclear neutrophils and macrophages are the main phagocytic cells. Pathogen associated molecular patterns (PAMPS) on microbe surfaces are recognized by the phagocytic cells using their pattern recognition receptors (PRRs). A phagocyte that engulfs an organism activates the engulfment process, which takes the organism inside the cell where it fused with the cytoplasmic granules. In addition, multiple oxygen-independent factors are released from the granules through the conversion of O2 into reactive oxygen intermediates, the synthesis of nitric oxide, and the breakdown of a variety of reactive oxygen intermediates. The monocytes, macrophages and dendritic cells contribute the reticuloendothelial system.

The complement system: A multicomponent system consisting of soluble zymogens, cell surface receptors. soluble as well as cell surface regulatory proteins. Zymogens on activation by immune complexes or specific molecular patterns get activated by antibody dependent and independent pathways. Activation generates peptides and molecular assemblies to facilitate extravasation, chemotaxis, opsonization, phagocytosis and direct lysis and killing of microbes. Complement cascade components are named as C1-C9 along with factor B, D and P. The initial trigger is different for different pathways. C3 is the most abundant and central component of the complement cascade. On activation C3 generates C3a and C3b. C3b becomes linked covalently to the microorganism. Activation of C5 yields a small peptide, C5a; C5b remains on the surface and assembles to form a membrane attack complex which is impermeable to solutes and can cause osmotic lysis. C5a is an effective chemotactic agent for neutrophils and increases capillary permeability greatly. In response to C3a and C5a acting on mast cells, further mediators are released, including histamine, leukotriene B, and tumor necrosis factor (TNF), affecting capillary permeability, adhesion, chemotaxis, and neutrophil activation. It is also possible for tissue macrophages to initiate inflammation, since they release neutrophil chemotactic and activating factors in response to exposure to bacterial toxins, C5a or iC3b-coated bacteria adhering to surface complement receptors. The effects of complement peptides are produced when they bind with complement receptors. A large number of complement regulatory proteins control the activation of the complement cascade on the system is pro-inflammatory cell exaggerated activation cancer self-tissue distribution.

Extracellular killing by C3b-bound eosinophils: Might be liable for the disappointment of numerous huge parasites to lay out a traction in likely has. In addition to lysozyme, peptide defensins and the complement system.

The synthesis of other humoral defense: Proteins is greatly enhanced during infection, such as C-reactive proteins and mannose binding proteins. These patterns are used to discriminate between surface carbohydrate groups belonging to microbial cells and those belonging to 'self'. Mannose-binding protein is a member of the collectin family along with conglutinim, surfactants SP-A and SP-D. When interferons interfere with viral replication, recovery from viral contamination can be affected.

Natural killer cells: Through a perforin/granzyme pathway and separate Fas-mediated pathway, large granular lymphocytes with natural killer (NK) activity can kill virally infected cells. By activating the caspase protease cascade, the caspase protease cascade fragments the nuclear DNA and causes programmed cell death (apoptosis).

The surface receptors of basophills and mast cells: When cross linked by complement or antibody opsonized antigens are degranulated to produce inflammation. Inflammation makes the blood vessels leaky and permit phagocytes cross the blood vessels to extravascular compartments to destroy the pathogens.

The adaptive immune system: Recognizes, remembers, and selectively eliminates certain foreign microorganisms and molecules (known as foreign antigens). In contrast to innate immune responses, adaptive immune responses are elicited by specific antigenic challenges whereas innate immune responses are not conserved among species. The four characteristic attributes of adaptive immunity can be categorized as follows. Specificity of antigens, diversity of immune responses, immune memory, and recognition of self and nonself are four of them. The specific cellular markers of adaptive immunity are T-Lymphocytes and B-lymphocytes which on recognition of antigens proliferate and get differentiated into different subsets.

B-Cells: On binding with an antigen undergo several cycles of proliferation and get differentiated into plasma cells which produce antibodies. Antibodies bind specifically with the epitopes on an antigen. A subset of B cell get differentiated as memory cells. Memory cells when triggered by a second exposure to the same antigen mount a much larger antibody response with affinity maturation and class switch. The immune response displayed on first exposure to an antigen is termed as Primary Immune response and that displayed on subsequent exposures to the same antigen is termed as Secondary Immune response. These are T- dependent antigens. Some antigens need T-cell cytokines for B-Cell proliferation and differentiation into plasma cells but not direct T-B cell cross linking and few other elicit a B-cell response with no T-cell dependency. These are T-cell independent B-cell responses, lacking memory, class switch and affinity maturation. The primary immune response by B-cells is characterized by a lag phase

and formation of IgM antibodies. Antigens mostly need direct T-B cell cross-linking to mount a specific and effective B-cell response with good memory, class switch and affinity maturation.

T-Cells: On activation differentiates into helper T-cells, memory T-cells and cytotoxic T-cells.

T-Helper (Th) cells: Help B-cells for generation of antibodies and enhance effecter functions of all the cells of the immune system, irrespective of whether they belong to innate or adaptive immune system. Th cells are sub populated as Th1 and Th2 cells. Th1 activates all different types of cells including B-cells and are responsible for delayed Type-Hypersensitivity (DTH) reactions. Th2 cells mainly help B-cells to generate antibodies of specific types.

Cytotoxic T-cells (Tc): Directly destroy the infected cells along with the release of inflammatory cytokines once they are sensitized and activated by antigens.

Another heterogenous population of T-cells: Is represented by regulatory T-cells (T-reg CD4, CD25, and $Foxp3^{+}$). The natural T-reg cells are present in thymus, contribute significantly in the phenomenon of self-tolerance. In the periphery there are inducible T-regs. Treg cells keep the adaptive immune response under control.

Discussion

To summarize, the innate immune system comprises of external barriers, chemical and physical barriers, cells of the reticuloendothelial system, eosinophills, basophills, mast cells, polymorphonuclear neutrophils, natural killer cells, interferons, cytokines from these different cell types, other soluble factors and most importantly the complement proteins. The T-and B-lymphocytes and the related cytokines are the specific components of the adaptive immune system. Of these cells, only the T and B-lymphocytes possess the attributes of diversity, specificity, memory, and self/nomself recognition, the hallmarks of an adaptive immune response. The rest of the cells function as accessory cells in adaptive immunity, activating lymphocytes, enhancing phagocytosis, or secreting immune-effector molecules to help remove the antigen from the body. However, adaptive immunity comes to play only when the microbe or the Invader survives the first line of defence by innate immunity.

The innate immune system responds to exogenous antigens and agents by pattern recognition through germ-line receptors with limited repertoires. It is possible for the immune system to respond swiftly to stimulants because it has available natural or innate immune cells that express their response receptors before exposure. There are two types of receptors involved in this process: scavenger receptors and Toll-like receptors (TLRs). Antigen-presenting cells may be activated by these receptors on monocytes/macrophages and dendritic cells. Cells of the adaptive immune system, such as natural killer (NK) cells, may also contain these proteins. There are several subpopulations of macrophages and dendritic cells. A diverse range of recognition response elements can be generated by adaptive immune cells bearing rearranged receptors on their surfaces.

Several cell types that share functional characteristics of these two branches of the immune response bridge these two branches. Among these cells are the B1 cells, the γδ T-cells, and perhaps natural killer T (NKT) cells. The immune system's traditional B and T cells have much less diversity than these cells that express Immunoglobulins or T-cell receptors. IgM antibodies are made by most B1 cells; these antibodies recognize oxidized LDL molecules, for instance. During ontogeny, these cells may have selected in response to apoptotic cells, and so they exist at birth. Consequently, they respond promptly to a mimic molecule, like the phosphatidylcholine produced by Streptococcus pneumoniae, as is characteristic of an innate immune cell. B1 cells are polyclonal in nature and secrete natural antibodies. γδ T-cells and NKT cells also recognize antigens of limited diversity. NKT cells recognize lipid antigens with their invariant T cell receptor in the context of CDI, a protein related to MHC class I. The former recognizes lipid antigens without the involvement of major histocompatibility complex (MHC) molecules.

Conclusion

Cross talks between the innate and adaptive immune system

Antigen Presentation: In the innate immune system, antigens are important for communicating with its adaptive immune partner. MHC molecules are proteins on cell membranes that are bound to antigens that T-cell receptors can recognize. These molecules are polymorphic (genetically diverse) glycoproteins found on cell membranes that function in the recognition event called "antigen presentation." This recognition event is known as "antigen presentation." It consists of a heavy chain linked to a small invariant protein called 2-microglobulin that is expressed by nearly all nucleated cells in vertebrates: MHC molecules from class I consist of nearly all nucleated cells. Antigen-presenting cells are the only cells that express Class II MHC molecules, which are made up of alpha and beta glycoprotein chains. The proliferation and differentiation of naive T cells into memory T cells and various effector T cells occurs after they encounter antigen coupled with the MHC molecule on a cell. MHC represents the most polymorphic cell surface molecules and hence, is responsible for graft rejection if donors and acceptors are not well matched. Dendritic cells, Macrophages and B-cells are professional antigen presenting cells involved in antigen processing capture, processing and presentation of epitopes to Th ($CD4^{+}$) cells in association with MHC II peptides. Whether an antigen will be associated with MHC I and MHC II is decided by the nature and cellular location of antigens. The intracellular antigens like viruses are processed by cytosolic proteasomes and can be presented on the cell-surface for recognition by T_c. (Cytotoxic $CD8^{+}$ T-cells) which destroy the viruses and the virally infected cells. Extracellular antigens however are processed and presented by professional antigen presenting cells and are presented to Th cells.

Cytokines produced either because of the first exposure of phagocytes to the antigen followed by their

activation, during maturation of dendritic cells or after their cross-talks with T-cells instruct each other for further expression of co-stimulator, chemo attractants and differentiation of T-and subsequently B-cells to effector cell populations. Innate immunity does not exist in isolation from adaptive immunity. Specific immunity is mediated by phagocytic cells that play a crucial role in nonspecific immune responses. The activity of these phagocytic cells has been shown to be enhanced by the presence of several soluble factors produced by a specific immune response. It

is believed that immune cells are drawn to an inflammatory response when soluble mediators are produced. As a result, Inflammatory responses are regulated by the immune response. Like antigen presenting cells and phagocyte there are intimate talks between the complement, essentially the key humoral component of the innate immune system with initiation, regulation, and effecter mechanisms of the T and B-cells. Through the carefully regulated interplay of adaptive and innate immunity, the two wings of the immune system work together to eliminate a foreign invader.

References

1. Delves PJ, Martin SJ, Burton DR, Roitt IM. 12th Edition. Essential immunology. Publisher: Wiley-Blackwell; c2011.
2. Abul K Abbas, Andrew H. Lichtman, Shiv Pillai. Celullar and Molecular Immunology, 7th Edition. Saunders 7 Edition; c2011.
3. Thomas J Kindt, Barbara A Osborne, Richard A Goldsby. Kuby Immunology. W.H. Freeman & Company; 6th Edition; c2006.
4. Khanna R. Immunology. Oxford University Press; c2011.
5. Godfrey S Getz. Bridging the innate and adaptive immune system. The Journal of Lipid Research. 46, 619-622.
6. Hansson GK, Libby P, Schonbeck U. Zhong-Qun Yan Innate and Adaptive Immunity in the Pathogenesis of Atherosclerosis. Circulation Research. 2002;91:281-291.
7. Shanker A, Buferne M, Verhulst SAM. Cooperative action of CD8 T lymphocytes and natural killer cells controls tumour growth under conditions of restricted T-cell receptor diversity. Immunology. 2010;129(1):41-54. DOI: 10.1111/j.1365-2567.2009.03150.x.
8. Shanker A, Menaka CT, Manoj K Mishra, Mikhail MD, Roman VU. Innate-Adaptive Immune Crosstalk. J Immunol Res. Published Online 2015 Nov 4. 2015;2015:982465.. DOI: 10.1155/2015/982465.
9. John A, Peter L, Goran K. Hansson. Adaptive immunity and atherosclerosis. Clinical Immunology. 2010;134(1):33-36.
10. Anna M. Lundberg, Gorran K Hansson. Innate immune signals in atherosclerosis. Clinical Immunology. 2010;134(1):5-24.