

A brief overview on antigens: Properties, classes and mode of action

Abstract

This review therefore seeks to address the gaps and provide an in-depth review of antigens, their properties, classes, types, mode of action, the factors affecting antigenicity as well as its applications. The concept of antigens arose from the fact that our body can distinguish between the components of the body and foreign particle. The immunogenicity of the antigen increases with the increase in the degree of foreignness. In the case of biological antigens, the foreignness increases with the increase in the phylogenetic gap between the two species. However, there are some exceptions in that some proteins occurring within the host might also induce an immune response, as in the case of auto antigens. Auto antigens are proteins or protein complexes of the host that are attacked by the host's immune system, resulting in autoimmune diseases. Auto antigens can be deadly to the host as the body's own cells should not be targeted by the immune system. Though antigens could be pathogens, foreign substances, proteins and peptides, they help to trigger immune responses which is essential for the body's defense against harmful invaders. The knowledge of antigens is fundamental in Immunology, vaccine development and disease diagnosis. Further research is also required to discover more about antigens and their roles in medicine and health.

Keywords: autoimmune diseases, Immunology, antigens, foreign particle

1. INTRODUCTION

An antigen is a molecule that initiates the production of an antibody and causes an immune response. In simple words, antigens could be anything that doesn't belong to the body and are foreign but has the ability to induce an immune response in the form of production of antibodies against them [1]. The concept of antigens arose from the fact that our body can distinguish between the components of the body and foreign particles [2]. In response to these antigens, the body induces the production of antibodies that act against the said antigens. In humans most antigens are proteins, polypeptides or polysaccharides: however, lipid and nucleic acids can also act as antigens when combined with proteins or polysaccharides [3]. Antigens have several properties which enables them to stimulate immune responses in the body. These properties include a specific chemical structure, molecular size, molecular rigidity and complexity, a certain number of antigenic determinants and cross reactivity [4]. The molecular structure of antigens is characterized by its ability to bind to the antigen-binding site of an antibody. Antigens can also be grouped into different types based on different factors. Some of the common

classifications are based on the origin of the antigen and its immunogenicity [5]. Antigenicity and Specificity are major components of an antigen as they describe the ability of a foreign material which is an antigen to bind to, or interact with, the products [6].

There has been an insufficiency in detailed reviews that have been published on Antigens which could help to provide knowledge about the concept and properties of antigens. This review therefore seeks to address the gaps and provide an in-depth review of antigens, their properties, classes, types, mode of action, the factors affecting antigenicity as well as its applications.

2. OVERVIEW OF ANTIGENS

According to Abbas *et al.* [7], an antigen is a molecule, moiety, foreign particulate matter, or an allergen such as pollen, that can bind to a specific antibody or T-cell receptor and its presence in the body may trigger an immune response. Antigens can be proteins, peptides (amino acid chains), polysaccharides (chains of simple sugars), lipids or nucleic acids. They could also exist on normal cells, cancer cells, parasites, viruses, fungi and bacteria.

Ullah [8] defined Antigens as molecules or molecular structures that are foreign to the body and generally induces an immune reaction in the form of the production of antibodies against them. He stated that all antigens might not induce an immune response. The antigens that induce an immune response are termed immunogens. Also, the ability of antigens to elicit an immune response depends on the presence of specific regions on the antigens called antigenic determinants. The determinants bind to receptor molecules with the complementary structure on immune cells to elicit an immune response. In addition, the concept of antigens arose from the fact that our body can distinguish between the components of the body and foreign particles (self and non-self). In response to these foreign particles (antigens), the body induces an immune response such as the production of antibodies that can act against the said antigens.

Janeway *et al.* [9] also reported that antigens can be recognized by antigen receptors, including antibodies and T-cell receptors. Diverse antigen receptors are made by cells of the immune system so that each cell has a specificity for a single antigen. Upon exposure to an antigen, only the cells that recognize the antigens are activated and expanded, a process known as 'clonal selection'. In most cases, antibodies are antigen-specific, meaning that an antibody can only react to and bind to one specific antigen. In some cases, however, antibodies may cross-react to bind more than one antigen. The reaction between an antigen and an antibody is called an antigen-antibody reaction.

Gallucci *et al.* [10] further stated that antigens can originate either from within the body ('self-antigens') or from the external environment (non-self). The immune system identifies and attacks 'non-self' external antigens. Antibodies usually do not react with self-antigens and the disease in which antibodies react with self-antigens and damage the body's own cells are called autoimmune diseases. Also, vaccines are examples of antigens in an immunogenic form, which are intentionally administered to a recipient to

induce the memory function of the adaptive immune system towards antigens of the pathogen invading that recipient.

2.1 Properties of Antigens

2.1.1 Foreign Nature

According to Sakpota [11], all antigens that induce an immune response in the host are foreign to the body of the recipient. The host body recognizes the antigen to be different from the normal body components. The immunogenicity of the antigen increases with the increase in the degree of foreignness. In the case of biological antigens, the foreignness increases with the increase in the phylogenetic gap between the two species. However, there are some exceptions in that some proteins occurring within the host might also induce an immune response, as in the case of auto antigens. Similarly, proteins and other molecules from other species might also not induce an immune response, if they lack antigenic determinants or epitopes.

2.1.2 Chemical Structure

Antigens are usually proteins, followed by polysaccharides. However, other molecules like lipids and nucleic acids can also act as antigens when complex with proteins and polysaccharides. In the case of proteins, an antigen should contain immunogenic regions with at least 30% of amino acids like lysine, glutamine, arginine, glutamic acids, asparagine and aspartic acid, along with a high number of hydrophilic or charged groups. The level of immunogenicity also increases with the heterogeneity of the molecules. Homopolymers are usually less immunogenic than heteropolymers [12].

2.1.3 Molecular size

The molecular size of an antigens is also crucial in the immunogenicity of the molecules. An antigen should have a minimum size of greater than 5000 Da before they can be considered immunogenic however, low molecular weight substances can demonstrate immunogenicity when coupled with large-sized carriers and these substances are termed as Haptens [13].

2.1.4 Molecular rigidity and complexity

The rigidity and complexity of molecules are essential factors that determine immunogenicity. In general, rigid molecules are good antigens as they can raise antibodies to certain structures when compared to the less rigid ones. The complexity of the structure is also an essential factor as a peptide antigen with a repeating unit of a single amino acid is less immunogenic than a molecule with two or more repeating amino acids units [14].

2.1.5 Antigenic determinants and cross-reactivity

Antigenic determinants are regions in an antigen molecule that is involved in the reaction with antibodies. Antigens with two or more antigenic determinants can induce an antibody reaction. Thus, a smaller antigen usually doesn't induce antibody production as it is not possible for a small molecule to have more than one antigenic determinant [15].

Cross-reactivity of antigens is also an essential factor where antibodies induced by a different antigen can interact with another antigen. The complexity of the structure is also an essential factor as a peptide antigen with a repeating unit of a single amino acid is less immunogenic than a molecule with two or more repeating amino acids units [16].

3. STRUCTURE OF ANTIGENS

The structure of antigens can be described using the 'lock and key' metaphor. The antigen can be seen as a string of keys (epitopes) each of which matches a different lock (antibody). The epitope is the distinct surface feature of the antigen. Antigenic molecules, normally "large" biological polymers, usually present surface features that can act as points of interaction for specific antibodies. Any such feature constitutes an epitope. Most antigens have the potential to be bound by multiple antibodies, each of which is specific to one of the antigen's epitopes [17].

Saylor et al. [18] reported that the molecular structure of an antigen is characterized by its ability to bind to the antigen-binding site of an antibody. Antibodies differentiate between different antigens on the basis of the specific molecular structures present on the surface of the antigen. Most antigens are proteins or polysaccharides such as coats, capsules, flagella, toxins, and fimbriae of bacteria, viruses, or other microorganisms. Besides, secretions and other chemicals of the same nature can also act as antigens. Lipids and nucleic acids of these microorganisms are only antigenic when these are combined with proteins or polysaccharides. The structure of antigens might be different depending on the nature of the antigen, their size, and immunogenicity. All immunogenic antigens have a specific structural component called epitope or antigenic determinant. The number of epitopes differs in different antigens and determines the number of antibodies a single antigen can bound to. The structural components of interaction in antigens are different, which determines the classes of antibodies they bind to. The region on antibodies that interacts with antigens is called a paratope.

4. EXAMPLES OF ANTIGENS

4.1 Blood group antigens

The report of Dean [19] stated that Blood group antigens are proteins or sugars present on the surface of different components in the red blood cell membrane. The antigens in the ABO blood group are the sugar that is produced by a series of reactions that catalyzes the transfer of sugar units. The type of sugar in the red blood cell is determined by the type of enzyme involved, which in turn is determined by the

person's DNA. The antigens of the Rh blood group are proteins that are also determined by the host's DNA. The RhD gene encodes the D antigen, which occurs as a large protein on the red blood cell. These antigens can be distinguished by antigen-antibody reactions that help determine different blood groups in humans.

4.2 Bacterial Capsule

Nossal & Ada [20] stated that a bacterial capsule is a polysaccharide layer occurring outside the cell envelope that induces an immunogenic reaction in the host. The capsule is a well-organized layer that cannot be removed easily and thus is considered a possible cause of bacterial pathogenicity. In some bacteria, the capsule can also be involved in evading phagocytosis as a capsule-specific antibody is required to cause phagocytosis. Bacterial capsules are also used as antigens used in vaccines where the polysaccharide component of the capsule is conjugated with protein carriers. The exact structure, function, and involvement of capsules in bacteria differ in different bacterial species.

5 CLASSES OF ANTIGENS

Ullah [8] reported that Antigens can be classified into different types based on factors. Some of the common classifications are based on the origin of the antigen and its immunogenicity.

5.2 Types of antigen based on their origin

Antigens can be classified into two groups on the basis of their origin

5.2.1 Exogenous antigen

Exogenous antigens are the antigens that originate outside the body of the host and, thus, are foreign to their host. These antigens might enter the body through inhalation, ingestion, or injection and then circulate throughout the body via bodily fluids. The uptake of exogenous antigen is primarily mediated by phagocytosis via Antigen Presenting Cells (APCs) like macrophages and dendritic cells. Many antigens like intracellular viruses might begin as exogenous antigens and later become endogenous [21].

5.2.2 Endogenous antigen

Endogenous antigens are antigens that originate within the body of the host during metabolism or as a result of intracellular viral or bacterial infection. Endogenous antigens are usually the cells of the body or fragments, compounds, or antigenic products of metabolism. They are usually processed in the macrophages and are later detected by cytotoxic T-cells of the immune system. Endogenous antigens include antigens that are xenogeneic or heterologous, autologous, and idiotype or allogenic. They could also result in autoimmune diseases as the host immune system detects its own cells and particles as immunogenic [22].

5.2.3 Auto antigens

Auto antigens are proteins or protein complexes of the host that are attacked by the host's immune system, resulting in autoimmune diseases. Auto antigens can be deadly to the host as the body's own cells should not be targeted by the immune system. The immunological tolerance to such antigens is lost as a result of genetic and environmental factors [23].

5.2.4 Tumor antigens

The report of Schumacher & Schreiber [24] revealed that tumor antigens also known as neoantigens are presented by Major Histocompatibility Complex (MHC) 1 and 11 on the surface of tumor cells. The antigens are produced as a result of a tumor specific mutation during the malignant transformation of normal cells. These antigens usually do not induce an immune response as the tumor cells develop ways to evade antigen presentation and immune defense.

5.2.5 Native Antigens

Native antigens are antigens that are not processed by any antigen-presenting cells (APC), and thus immune cells like T-cells cannot bind to these antigens. However, B-cells can be activated such antigens even without any processing [25].

5.3 Types of antigens on the basis of immune response

According to [26], Antigens can be classified into two distinct groups on the basis of immune response:

5.3.1 Complete Antigens/ Immunogens:

Complete antigens or immunogens are antigens that elicit a specific immune response. These antigens can induce an immune response by themselves without any carrier particles. These are usually proteins, peptides or polysaccharides with high molecular weight (greater than 10,000 Da).

5.3.2 Incomplete Antigens/Haptens

Incomplete antigens or haptens are antigens that cannot generate an immune response by themselves. These are usually non-protein substances that require a carrier molecule to form a complete antigen. Haptens have a lower molecular weight (usually less than 10,000 Da) and fewer antigenic determinant sites. The carrier molecule bonded to the hapten is considered a non-antigenic component and is a protein or a polysaccharide molecule.

5.4 Antigenicity and Specificity

According to the report of Dowds *et al.* [27], Antigenicity is the capacity of a chemical structure (either an antigen or hapten) to bind specifically with a group of certain products that have adaptive immunity such as T cell receptors or antibodies also known as B cell receptors. Antigenicity was more commonly used in the past to refer to what is known as Immunogenicity, and the two terms are still often used interchangeably. However, strictly speaking, Immunogenicity refers to the ability of an antigen to induce an adaptive immune response. Thus, an antigen might bind specifically to a T or B cell receptor, but not induce an adaptive immune response. If the antigen does induce a response, it is an immunogenic antigen, which is referred to as an immunogens.

Specificity, as reported by Abbas & Lichtman [7], is the ability of the host cells to recognize an antigen specifically as a unique molecular entity and distinguish it from another with exquisite precision. Antigen specificity is due primarily to the side-chain conformations of the antigen. It is measurable and need not to be linear or of a rate-limited step for equation. Both T cells and B cells are cellular components of adaptive immunity.

5.5 Factors affecting antigenicity

The report of Kuriakose *et al.* [28-29] stated that the factors affecting antigenicity. They include:

1. **Foreignness:** An antigen must be foreign as the immune system normally discriminates between self and non-self and cannot generate an immune response for self-antigens. Therefore, only foreign molecules are antigenic.
2. **Size:** There is no absolute size above which a substance will be antigenic. However, in general, the larger molecule the more antigenic it is likely to be.

3. **Chemical composition:** The more complex the substance is chemically, the more antigenic it will be. The antigenic determinants are created by the primary sequence residues in the polymer and/or by the secondary, tertiary or quaternary structure of the molecule.
4. **Physical Form:** In general, particulate antigens are more immunogenic than soluble ones and denatured antigens more immunogenic than the native form.
5. **Degradability:** Antigens that are easily phagocytosed are generally more immunogenic. This is because for most antigens, the development of an immune response requires that the antigen be phagocytosed, processed and presented to helper T cells by an antigen presenting cell.

6. Applications of antigens

Gayed [30] reported the applications of antigens. They include:

- Antigens are used for the differentiation of bacterial species as due to the specificity of antigens.
- Antigens can also be used for diagnostic purposes to detect the presence of antibodies in a sample.
- Antigens are essential components of antigen-antibody complexes, which have forensic application in the identification of human blood and other samples.
- These are also used in immunoassays for the quantification of various chemical and biological substances.
- Auto antigens are responsible for autoimmune diseases, which in some cases can be lethal.
- Inactivated enzymes are used in vaccines as a form of passive immunity to prevent and cure different diseases.

7. CONCLUSION

Antigens play a crucial role in the body's immune system. They serve as key agents that stimulate the production of antibodies. Though antigens could be pathogens, foreign substances, proteins and peptides, they help to trigger immune responses which is essential for the body's defense against harmful invaders. The knowledge of antigens is fundamental in Immunology, vaccine development and disease diagnosis. Further research is also required to discover more about antigens and their roles in medicine and health.

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