Asian Journal of Immunology

Volume 7, Issue 1, Page 201-208, 2024; Article no.AJI.123549

An Overview of Antigen Properties, Classifications and Mechanisms of Action

Agbiji, N.N. [a*] and Ekong, M.O [a]

[a] Department of Microbiology, Faculty of Biological Sciences, University of Cross River State, (UNICROSS), Nigeria.

Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Article Information

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/123549

Review Article

Received: 18/07/2024
Accepted: 21/09/2024
Published: 29/10/2024

ABSTRACT

The goal of this review is to fill in the gaps by offering a thorough analysis of antigens, including their characteristics, classes, types, and mode of action, as well as the variables influencing antigenicity and its uses. The idea of antigens originated from the body's ability to discriminate between foreign particles and its own constituent parts. As the level of alienation rises, so does the antigen's immunogenicity. When it comes to biological antigens, the degree of alienation rises as the evolutionary distance between the two species widens. There are, however, certain exceptions, such as auto antigens, which are proteins that naturally reside in the host and may also trigger an immune response. Protein complexes or host proteins are targeted by auto antigens, resulting in autoimmune diseases.

Auto antigens can be fatal to the host because the immune system shouldn't attack the body's own cells. Although infections, foreign substances, proteins, and peptides can all be considered antigens, their role in inducing immune responses is crucial for the body's defense against

**Corresponding author: E-mail: nneka.ndifon@gmail.com;*

Cite as: *N.N., Agbiji, and Ekong, M.O. 2024. "An Overview of Antigen Properties, Classifications and Mechanisms of Action". Asian Journal of Immunology 7 (1):201-8. https://journalaji.com/index.php/AJI/article/view/144.*

dangerous intruders. Understanding antigens is essential for immunology, in the developing of vaccinations, and the diagnosis of disease since some antigens have been suggested as the best targets for immunotherapy in clinical settings, have significant uses in medical diagnostics, and can be employed in the creation of vaccines to treat cancer. To discover more about antigens and how they function in medicine and health, further research is also required.

Keywords: Autoimmune diseases; Immunology; antigens; foreign particle.

1. INTRODUCTION

A molecule known as an antigen is what starts the synthesis of antibodies and also triggers an immunological reaction. To put it simply, an antigen is anything outside of the body that has the potential to trigger the development of antibodies against it in the immune system [1]. The ability of our body to discriminate between foreign particles and its own constituent parts gave rise to the idea of antigens [2]. The body produces antibodies in reaction to these antigens, which work to neutralize the antigens. Proteins, polypeptides, or polysaccharides make up the bulk of human antigens but, when paired with proteins or polysaccharides, lipids and nucleic acids can also function as antigens [3]. Antigens can trigger the body's immune system due to a variety of characteristics. These characteristics include cross reactivity, a particular number of antigenic determinants, molecular stiffness and complexity, and a particular chemical structure [4]. The capacity of an antigen to attach to an antibody's antigen-binding location is a characteristic of its molecular structure. Additionally, Antigens are categorized into many classes according to various criteria. Based on the antigen's immunogenicity and place of origin, some common classifications exist [5]. Two important aspects of an antigen are its specificity and antigenicity, which indicate how well a foreign substance acts as an antigen by binding to or interacting with its target 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], a foreign component or molecule, particle matter, or allergen, like pollen, is defined as an antigen if it has the ability to attach to a particular T-cell receptor or antibody and cause an immune response in the body. Proteins, peptides (chains of amino acids), polysaccharides—simple sugar chains, lipids, and nucleic acids are instances of antigens. They might also be present on bacteria, fungi, viruses, parasites, cancer cells, and healthy cells.

Ullah [8] defined Antigens as foreign molecules or chemical structures that typically cause the body to mount an immunological response by producing antibodies against them. He stated that not every antigen will trigger an immunological reaction. However, Antigens known as immunogens elicit an immunological response. Furthermore, the existence of particular areas on antigens known as antigenic determinants affects the antigens' capacity to trigger an immune response. To trigger an immunological response, the determinants attach to receptor molecules on immune cells that have a complementary shape. The idea of antigens also originated from the body's ability to discriminate between foreign particles and its own constituent parts (self and non-self). The body mounts an immunological defense against these foreign objects, or antigens by means of antibody production that are effective against them.

Antigen receptors, such as T-cell receptors and antibodies, are able to identify antigens, according to Janeway et al. [9]. Immune system cells produce a variety of antigen receptors, giving each cell a unique affinity for a particular antigen. The process of "clonal selection" occurs when an antigen is encountered; only cells that are able to identify the antigens become activated and proliferate. Antibodies are often antigen-specific, which means that they can only attach to and respond with a single type of antigen. However, antibodies have the ability to cross-react and bind several antigens in some situations. An antigen-antibody response is the result of an interaction between an antibody and an antigen.

Gallucci et al. [10] further stated that antigens can come from the outside world (non-self) or from inside the body (self-antigens). The immune system is conscious of this and targets foreign antigens that are "non-self." Antibodies typically do not respond with self-antigens; therefore, autoimmune disorders are defined as conditions in which the bodies own cells are harmed by the antibodies' reaction with self-antigens. Vaccines are another example of an immunogenic antigen—antigens that are purposefully given to a patient in order to trigger the adaptive immune system's memory function against the pathogen's antigens.

2.1 Properties of Antigens

2.1.1 Foreign nature

Sakpota [11] reported that that any antigen that triggers an immunological reaction from the host is alien to the recipient's body. The antigen is acknowledged by the host body as being distinct from the regular parts of the body. As the degree of foreignness increases, so does the antigen's immunogenicity. When it comes to biological antigens, the degree of alienation rises as the 0evolutionary separation between the two species widens. There are, however, certain exceptions, such as auto antigens, which are proteins that naturally reside in the host and may also elicit an immunological reaction. Likewise, if molecules such as proteins are from different species and do not include antigenic determinants or epitopes, they may also fail to cause an immunological reaction.

2.1.2 Chemical structure

Proteins are typically the first type of antigen, then polysaccharides. However when they combine with proteins and polysaccharides, other substances like lipids and nucleic acids can also function as antigens. When it comes to proteins, an antigen should have a high concentration of hydrophilic or charged groups coupled with immunogenic areas that include at least 30% of amino acids such as lysine, glutamine, arginine, glutamic acids, asparagine, and aspartic acid. As the molecules become more heterogeneous, so does the degree of immunogenicity. Generally speaking, homopolymers are less immunogenic than heteropolymers [12].

2.1.3 Molecular size

An antigen's molecular size has a significant impact on how immunogenic it is. Before an antigen may be considered immunogenic, its size must be more than 5000 Da. However, compounds with low molecular weights, known as haptens, can exhibit immunogenicity when combined with large-sized carriers [13].

2.1.4 Complexity and stiffness of molecules

One of the primary determinants of immunogenicity are the intricacy and stiffness of molecules. Rigid molecules are often considered good antigens because, in contrast to less rigid ones, they can elicit antibodies to specific structures. A single amino acid in a peptide antigen acid repeating unit is less immunogenic than a protein with two or more repeating amino acid units, therefore structural complexity is also crucial [14].

2.1.5 Antigenic determinants and cross-reactivity

The part of an antigen molecule that interacts with antibodies is known as an antigenic determinant. An antibody response can be triggered by antigens that contain two or more factors that are antigenic. Because a small molecule cannot have more than one antigenic determinant, a smaller antigen typically does not cause the formation of antibodies [15].

In order for antibodies produced by one antigen to interact with another, antigen cross-reactivity is another essential element. A solitary amino acid peptide antigen repeating unit is less immunogenic than a protein with two or more amino acid repeats units, therefore structural complexity is also crucial [16].

3. STRUCTURE OF ANTIGENS

The "lock and key" metaphor is a good illustration used to explain the making of antigens. The antigen might be thought of as a sequence of keys, or epitopes, that correspond to distinct locks, or antibodies. The antigen's unique surface characteristic is called an epitope. Typically "large" biological polymers, antigenic molecules have surface characteristics that can serve as areas of engagement for particular antibodies. An epitope is any characteristic of this type. The majority of antigens have the capacity to bind many antibodies, each of which is particular to an epitope on the antigen [17].

Saylor et al. [18] reported that the capacity of an antigen to attach to the antigen-binding site of an

antibody provides information on the molecular structure of the antigen. Due to the diverse molecular structures on the surface of each antigen, antibodies are able to differentiate between different antigens. The majority of antigens are proteins or polysaccharides found in things like bacterial, viral, or other microbes' coats, capsules, flagella, poisons, and fimbriae. Furthermore, secretions and similar substances have the potential to function as antigens. These microbes, nucleic acids and lipids are only antigenic when combined with polysaccharides or proteins. Depending on the antigen's composition, size, and immunogenicity, their structures may differ. A determinant that is antigenic in nature, or an epitope, is a unique structural element shared by all immunogenic antigens. The quantity of epitopes varies amongst antigens and establishes the maximum number of antibodies that an antigen can bind to. The kinds of antibodies that antigens bind to are determined by the differences in the structural components of interaction. A paratope is the area of an antibody that interacts with antigens.

4. EXAMPLES OF ANTIGENS

4.1 Blood Group Antigens

The report of Dean [19] stated that antigens specific to blood groups are either sugars or proteins that are found upon the exterior of several membrane constituents of red blood cells. That sugar created by a variety of processes that catalyze the exchange of sugar units is known as the antigen within the ABO blood type. The kind of enzyme in question is influenced by an individual's DNA, determines the kind of sugar found in red blood cells. Proteins known as blood group antigens Rh are also influenced by the DNA of the host. The D antigen, a big protein found on red blood cells, is encoded by the RhD gene. Antigen-antibody responses that help identify various human blood types can be utilized to distinguish these antigens.

4.2 Bacterial Capsule

According to Nossal & Ada [20], a coating of polysaccharides called a bacterial capsule is what develops outside of the cell envelope and causes the host to become immunogenic. The capsule is thought to be a potential source of bacterial pathogenicity since it is a properly organized layer that is difficult to remove. Since phagocytosis requires the presence of a capsule-specific antibody, the capsule may possibly participate in some bacteria's ability to evade phagocytosis. In vaccinations, capsules of bacteria are usually employed as antigens since their polysaccharide component has been coupled with protein carriers. Varied bacterial species have different precise capsule compositions, roles, and activities.

5. CLASSES OF ANTIGENS

According to Ullah [8], antigens can be categorized into several kinds according to certain criteria. In light of the antigen's immunogenicity and place of origin, some common classifications exist.

5.1 Types of Antigen According to Origin

Antigens can be divided into two categories according to their origin

5.1.1 Exogenous antigen

Exogenous antigens are antigens which are foreign to their host and can enter the body by ingestion, inhalation, or injection; they can then move throughout the body through bodily fluids; the absorption of foreign antigen is principally carried out by Antigen Processing Cells (APCs) via phagocytosis, such as dendritic cells and macrophages. Many antigens, such as intracellular viruses, can begin as exogenous antigens and change into endogenous antigens later on [21].

5.1.2 Endogenous antigen

Endogenous antigens those who are produced by the host's own body as a byproduct of metabolism or as a result of an intracellular bacterial or viral infection. The body's cells, as well as any broken down substances or antigenic byproducts of metabolism, are considered endogenous antigens. Usually, they are broken down by macrophages and then identified by immune system cytotoxic T-cells. Antigens classified as endogenous include those that are autologous, idiotype or allogenic, and xenogeneic or heterologous. They may also result in autoimmune illnesses since the host immune system recognizes its own cells and particles as immunogenic [22].

5.1.3 Auto antigens

Auto antigens are proteins in the host or protein complexes that the immune system targets,

leading to autoimmune illnesses. Since the immune system shouldn't assault the cells throughout the body, auto antigens can be fatal to the host. Genetic and environmental factors lead to the loss of immunological tolerance to certain antigens [23].

5.1.4 Tumor antigens

According to Schumacher & Schreiber's findings [24], Major Histocompatibility Complex (MHC) 1 and 11 on the surface of tumor cells present tumor antigens, also referred to as neoantigens. When normal cells undergo the malignant transformation, a mutation unique to the tumor causes the production of antigens. Since the tumor cells learn how to avoid immune defense and antigen presentation, these antigens typically do not trigger an immunological response.

5.1.5 Native Antigens

Since no antigen-presenting cells (APC) process native antigens, immune cells like T-cells are unable to attach to them. However, even in the lack of processing, these antigens can activate B-cells [25].

5.2 Types of Antigens on the Basis of Immune Response

Based on the immunological response, antigens can be divided into two categories [26].

5.2.1 Complete antigens/ immunogens

Antigens that trigger a certain type of immune response are known as complete antigens or immunogens. Even in the absence of any carrier particles, these antigens are capable of evoking an immunological response. These are often high molecular weight proteins, peptides, or polysaccharides (more than 10,000 Da).

5.2.2 Incomplete antigens/haptens

Haptens, also known as incomplete antigens, are substances that, by themselves, are incapable of triggering an immune response. Usually non-protein molecules, these need a carrier molecule in order to create a whole antigen. Less antigenic determinant sites and a reduced molecular weight—typically less than 10,000 Da—are characteristics of haptens. A protein or a polysaccharide molecule forms the carrier molecule that is bound to the hapten and is regarded as a non-antigenic component.

5.3 Antigenicity and Specificity

The capacity of a chemical structure (either an antigen or hapten) to bind selectively with a subset of products that have adaptive immunity, such as T cell receptors or antibodies also referred to as B cell receptors, is known as antigenicity, according to the report of Dowds et al. [27]. The term "antigenicity" was formerly more frequently used to refer to "immunogenicity," and the two terms are still frequently used synonymously. On the other hand, immunogenicity technically refers to an antigen's capacity to evoke a flexible reaction immune response. Therefore, an antigen may attach to a T or B cell receptor selectively without triggering an adaptive immune response. An antigen is considered immunogenic if it elicits an immunological reaction; this type of antigen is known as an immunogen.

According to Abbas & Lichtman [7], specificity is the host cell's capacity to identify an antigen as a distinct molecular entity and discriminate it from another with extreme precision. The main cause of antigen specificity is the antigen's side-chain conformations. It is quantifiable and doesn't have to follow a linear or rate-limited step formula. Adaptive immunity comprises B and T cells as its biological constituents.

5.4 Factors Affecting Antigenicity

The report of Kuriakose et al. [28-29] mentioned the variables influencing antigenicity. Among them are:

1. Foreignness: Considering that the immune system typically distinguishes between self and non-self and is unable to mount an immunological defense against self-antigens, an antigen needs to be foreign. Only alien molecules are hence antigenic.
2. Size: A material is not necessarily allergenic over a certain size. But generally speaking, a molecule's likelihood of being antigenic increases with its size.
3. Chemical composition: A substance's antigenicity increases with its chemical complexity. The polymer's primary sequence residues and/or the molecule's secondary, tertiary, or quaternary structure combine to form the antigenic determinants.
4. Physical Form: Particulate antigens tend to elicit stronger immune responses than soluble ones, while denatured antigens

elicit stronger responses than their original form.

5. Degradability: Generally, immunogenic antigens those who are readily phagocytosed. This is due to the fact that the majority of antigens must be broken down and phagocytosed, and given to helper T cells by an antigen-presenting cell in order for an immune response to emerge.

5.5 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 have further uses as a diagnostic tool to find out whether a sample contains any antibodies.
- Antigens are necessary building blocks of complexes of antigen and antibody, which are used in forensic analyses to identify human blood as well as additional materials.
- These are also utilized in immunoassays to quantify different biological and chemical substances.
- Autoimmune disorders, some of which are fatal, are brought on by auto antigens.
- Vaccines employ inactivated enzymes as a passive immunity technique to treat and prevent a variety of illnesses.
- It has recently been suggested that peptides known as neoantigens, which are found on the surfaces of cancer cells, are the best targets for immunotherapy in clinical settings [31].
- Antigens play a significant role in medical diagnostics through the process of antigen-antibody responses. Antigens' existence in patient samples like blood, urine, or saliva can be determined using antibodies. Antigen-antibody reactions, for instance, are employed in the widely used diagnostic test known as ELISA which means Enzyme-Linked Immunosorbent Assay (ELISA) [32].

6. CONCLUSION

An essential part of the body's immune system is played by antigens. They have a crucial role in promoting the synthesis 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.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that generative AI technologies such as Quillbot have been used during editing of manuscripts. This explanation will include the name, version, model, and source of the generative AI technology and as well as all input prompts provided to the generative AI technology.

Details of the AI usage are given below:

1. Name: Quillbot for chrome
2. Version: v15.407.0
3. The input prompts provided to the generative AI technology is the work written. It assisted in paraphrasing the work to reduce plagiarism.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. National Human Genome Research Institute, US National Institutes of Health; 2020.
   Retrieved 13 October 2020.
2. Immune system and disorders. Medline Plus, US National Institute of Medicine; 28 September 2020.
   Retrieved 13 October 2020.
3. Antigen. Cleveland Clinic; 2023.
   Retrieved 23 May 2023.
4. Antigenic characterization. US Centers for Disease Control and Prevention; 15 October 2019.
   Retrieved 13 October 2020.
5. Parham P. The Immune System, 3rd Edition, p. G: 2, Garland Science, Taylor and Francis Group, LLC; 2019.
6. Kuby Immunology (6th Ed.). Macmillan. 2006;77.
   ISBN 978-1-4292-0211-4.

7. Abbas AK, Lichtman A, Pillai S. Antibodies and antigens. Cellular and molecular Immunology (9th Ed.). Philadelphia: Elsevier; 2018.
8. Ullah I. Antigens and Antibodies. Journal of immunology Research. 2022;24(1):121-126.
9. Jane way, JR, A, Travers P, Walport M, Shlomchik MJ. Auto immune responses are directed against self-antigens. Immunobiology: The immune system in health and disease (5th Ed.). Elsevier Espana; 2011.
10. Gallucci S, lolkema M, Matzinger P. Natural adjuvants endogenous activators of dendritic cells. Nature Medicine. 2019;5(11):249-1255.
11. Male DK, Roitt IM, Brostoff J. Immunology. Elsevier Health Sciences. 2016;10.
ISBN 978-0323033992.
12. Sakpota A. Antigen: Properties, Structure, Types, Examples. Microbes note. Edited By: Sagar Aryal; 2023.
13. Peter J, Delves SJ, Martin DR, Burton, Ivan M. Roitt's Essential Immunology, Thirteenth Edition. John Wiley & Sons, Ltd; 2017.
14. Judith A, Owen JP, Stranford SA. Kuby Immunology. Seventh Edition. W. H. Freeman and Company; 2013.
15. Kapingidza AB, Kowal K, Chruszcz M. Antigen-antibody complexes. Subcell Biochem. 2020;94:465-497.
DOI: 10.1007/978-3-030-41769-7_19
PMID: 32189312.
16. Available:https://microbiologyinfo.com/antigen-properties-types-and-determinants-of-antigenicity/
17. Saylor K, Gillam F, Lonnie T, Zhang C. Designs of antigen structure and composition for improved Protein-based vaccine Efficacy. Frontiers in Immunology; 2020.
DOI: 10.3389/fimmu. 2020.00283
18. Dean L. Blood Groups and Red Cell Antigens [Internet]. Bethesda (MD): National Center for Biotechnology Information (US). Chapter 2, Blood group antigens are surface markers on the red blood cell membrane; 2005.
Available:https://www.ncbi.nlm.nih.gov/books/NBK2264/
19. Nossal GJ, Ada GL. Antigens in immunity. XV. Ultra structural features of antigen capture in primary and secondary lymphoid follicles. The Journal of Experimental Medicine. 2014;277-90.
DOI: 10.1084/jem.127.2.277
20. Santambrogio Laura, Brenham Stella J, Engelhard Victor H. The antigen processing and presentation machinery in lymphatic endothelial cells. Frontiers in Immunology; 2019.
DOI: 10.3389/fimmu.2019.01033
21. Maurice Landy, Werner Braun. Properties of antigens in relation to responsiveness and non-responsiveness. Immunological Tolerance. Academic Press. 2019;1-52.
Available:https://doi.org/10.1016/B978-1-4832-2727-6.50008-7.
22. Wang Q, Douglass J, Hwang MS. Direct Detection and Quantification of Neoantigens. Cancer Immunology Research. 2019;7(11):1748–1754.
DOI: 10.1158/2326-6066.CIR-19-0107
PMC 6825591. PMID 31527070
23. Schumacher TN, Schreiber RD. Neoantigens in cancer immunotherapy. Science. 2015;348(6230):69-74.
24. Lindeman J. Origin of the terms 'antibody' and 'antigen'. Scandinavian Journal of Immunology. 2014;19(4):281–285.
DOI: 10.1111/j.1365-3083.1984.tb00931.x
PMID 6374880. S2CID 222200504
25. Dowds C, Marie, Kornell S, Richard S, Zeissig S. Lipid antigen in immunity. Biological Chemistry. 2014;395(1):61-81.
26. Abbas AK, Lichtman A, Pillai S. Antibodies and antigens. Cellular and Molecular Immunology (9th ed.). Philadelphia: Elsevier; 2018.
ISBN 9780323523240.
OCLC 1002110073.
27. Kuriakose A, Chirmule N, Nair P. Immunogenicity of Bio therapeutics: Causes and association with posttranslational Modifications, Journal of Immunology Research. 2016;20(16):1-18.
28. Kotsias F, Cebrian I, Alloatti A. Antigen processing and presentation. Int Rev Cell Mol Biol. 2019;348:69-121.
DOI: 10.1016/bs.ircmb.2019.07.005
Epub 2019 Aug 1. PMID: 31810556.
29. Gavin AL, Hoebe K, Duong B, Ota T, Martin C, Beutler B, Nemazee D. Adjuvant-enhanced antibody responses in the absence of toll-like receptor signaling. Science. December 2006;314(5807):1936–1938.
Bibcode: 2006Sci...314.1936G.
DOI: 10.1126/science.1135299
PMC 1868398. PMID 17185603.

30. Gayed PM. Toward a modern synthesis of immunity: Charles A. Janeway Jr. and the immunologist's dirty little secret. The Yale Journal of Biology and Medicine. 2011; 84(2):131–138.
PMC 3117407. PMID 21698045.
31. Qing H, Yuhang L, Yi Y, Yiqi D, Zhenyu D, Li Y, Yang S, Heng X. Development and Clinical Applications of Therapeutic Cancer Vaccines with Individualized and Shared Neoantigens. Vaccines. 2024;12(7):717.
Available:https://doi.org/10.3390/vaccines12070717
32. David J. Applications of antigen-antibody reactions in immunology and medical diagnostics. Drug Designing: Open Access; 2023.
DOI: 10.35248/2169-0138.23.12.231.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/123549