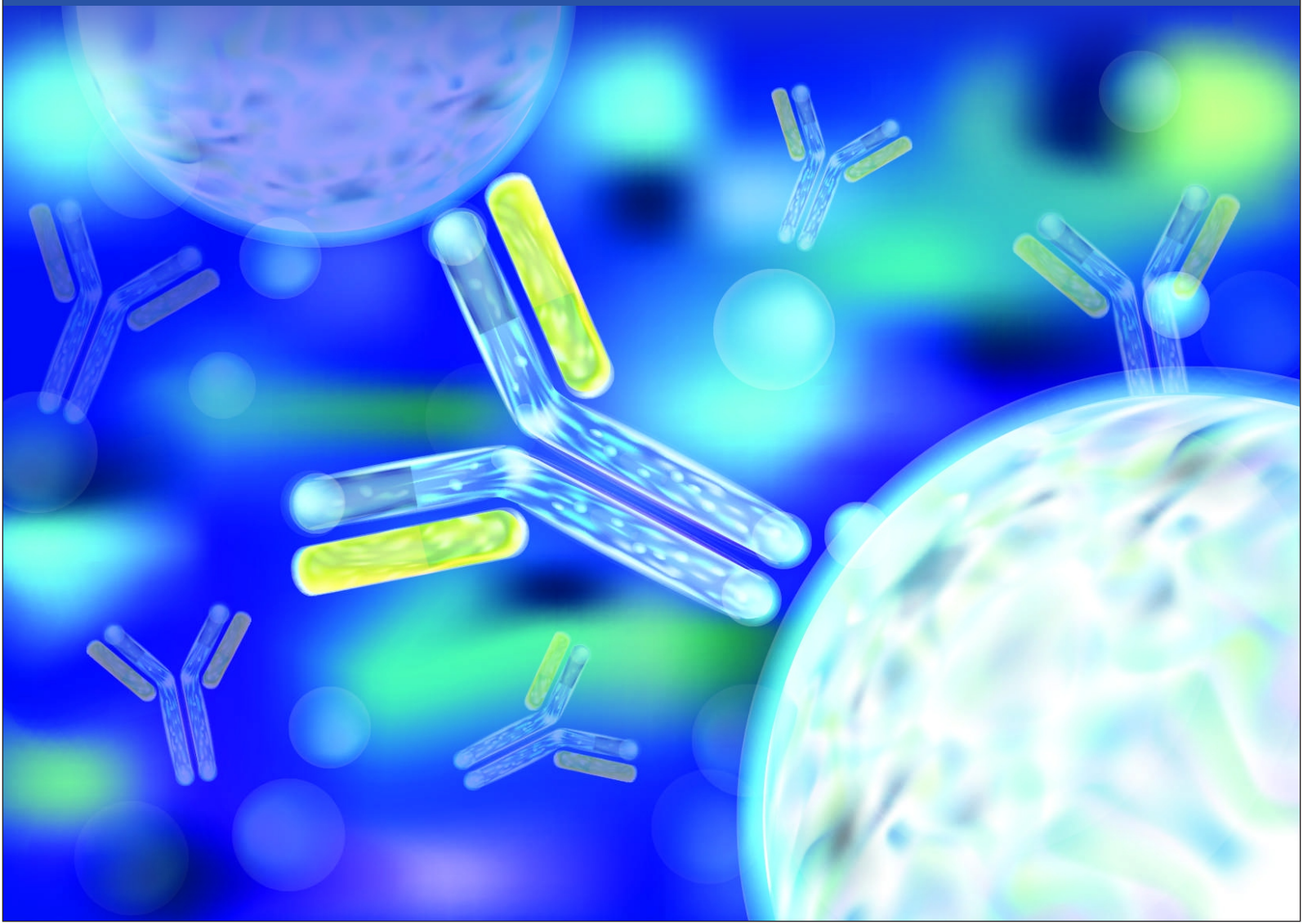
FUNDAMENTALS OF IMMUNOLOGY

Surendra Naha
Dr. Himani Kulshrestha



Fundamentals of Immunology

Surendra Naha
Dr. Himani Kulshrestha

Fundamentals of Immunology

Surendra Naha
Dr. Himani Kulshrestha

Dominant
Publishers & Distributors Pvt Ltd
New Delhi, INDIA

Knowledge is Our Business

FUNDAMENTALS OF IMMUNOLOGY
By Surendra Naha, Dr. Himani Kulshrestha

This edition published by Dominant Publishers And Distributors (P) Ltd
4378/4-B, Murarilal Street, Ansari Road, Daryaganj,
New Delhi-110002.

ISBN: 978-93-80642-87-1

Edition: 2022 (Revised)

Dominant
Publishers & Distributors Pvt Ltd

Registered Office: 4378/4-B, Murari Lal Street, Ansari Road,
Daryaganj, New Delhi - 110002.
Ph. +91-11-23281685, 41043100, Fax: +91-11-23270680

Production Office: "Dominant House", G - 316, Sector - 63, Noida,
National Capital Region - 201301.
Ph. 0120-4270027, 4273334

e-mail: dominantbooks@gmail.com
info@dominantbooks.com

w w w . d o m i n a n t b o o k s . c o m

CONTENTS

Chapter 1 Historical Perspectives on Immunology: Tracing Immune Knowledge's Evolution 1

— Dr.HimaniKulshrestha

Chapter 2 Cells of the Immune System: Health and Defence Guardians 8

— Dr.Ramakant

Chapter 3 The Innate Immune Response: First Line of Defences 15

— Dr.Ramakant

Chapter 4 Antigens and Antibodies: Understanding the Dynamics of Immune System 23

— Dr.Kirti Singh

Chapter 5 The Adaptive Immune Response: Molecular Defences Mechanism 29

— Dr.Kirti Singh

Chapter 6 B Cells and Antibody Production: Types and Functions 37

— Dr.Ramakant

Chapter 7 T Cells and Cellular Immunity: Understanding the Role of Immune Cells 44

— Dr.Ramakant

Chapter 8 Immunoglobulin Structure and Function: A Brief Overview 50

— Dr.SnehaVerma

Chapter 9 Antigen Processing and Presentation: Cellular Mechanisms 58

— Dr. Sneha Verma

Chapter 10 Immune Responses to Pathogens: A Comprehensive Exploration 64

— Dr.Ramakant

Chapter 11 Autoimmunity and Hypersensitivity: Immune System Disorders 69

— Dr.Ramakant

CHAPTER 1

HISTORICAL PERSPECTIVES ON IMMUNOLOGY: TRACING IMMUNE KNOWLEDGE'S EVOLUTION

Dr.HimaniKulshrestha, Assistant Professor
Department of Science, Maharishi University of Information Technology, Uttar Pradesh, India
Email Id- himani.kulshrestha@muit.in

ABSTRACT:

The Chapter Historical Perspectives on Immunology delves into the rich history of immunology, tracing the evolution of our understanding of the immune system from ancient times to modern discoveries. It highlights key figures, breakthroughs, and the impact of historical events on the development of immunological knowledge. The historiography of immunology since 1999 is reviewed, in part as a response to claims by historians such as Thomas Söderqvist the field was still immature at the time. First addressed are the difficulties, past and present, surrounding the disciplinary definition of immunology, which is followed by a commentary on the recent scholarship devoted to the concept of the immune self. The new literature on broad immunological topics is examined and assessed, and specific charges leveled against the paucity of certain types of histories, biographical and institutional histories, are evaluated. In conclusion, there are compelling indications that the history of immunology has moved past the initial tentative stages identified in the earlier reviews to become a bustling, pluripotent discipline, much like the subject of its scrutiny, and that it continues to develop in many new and exciting directions

KEYWORDS:

Antibodies, Antigens, Immune System, Immunization, Smallpox

INTRODUCTION

The introduction to the Chapter Historical Perspectives on Immunology serves as a gateway into the fascinating journey through time, unraveling the intricate tapestry of humanity's quest to comprehend the immune system. This introductory section sets the stage for the exploration of significant historical milestones and the individuals who shaped our understanding of immunology. It emphasizes the pivotal role of historical events and discoveries in laying the foundation for modern immunological science. From early observations of infectious diseases to the development of vaccines and the evolution of immunotherapy, this Chapter provides a captivating narrative that showcases the enduring human curiosity to conquer the mysteries of the immune system. Two decades ago, in the summer of 1992, the Naples Zoological Station’s summer school in the history of the life sciences, a roughly biennial event since the mid1970s, chose to focus on the history of immunology.

Whether the meeting achieved its stated purpose of facilitating dialogue and exchange between immunologists and historians appears to have been a matter of some contention among the attendees. But for the historians in attendance, the meeting seems to have served as a wake-up call, alerting them to the paucity of serious historical scholarship on the discipline of immunology. Within a few months these scholars organized a second symposium in Boston this time, primarily for the humanists [1], [2]. Where the aim was to foster the development of a history of immunology that would generate its own questions,

The proceedings of this second meeting were published shortly thereafter in a special issue of the Journal of the History of Biology which was subtitled Immunology as a historical object. A third meeting followed in 1995, the outcome of which appeared yet again in the Journal of the History of Biology, this time as a special section in the fall 1997 issue. Meanwhile, not to be outdone by their humanist colleagues, many of the scientists who had attended the 1992 meeting published their own version of the history of immunology. However, despite this flurry of activity within a relatively short span of time, the historian Thomas Söderqvist, a prominent presence at these meetings, opined in the title of his 1999 essay that The historiography of immunology is still in its infancy [3], [4].

By invoking Söderqvist and Stillwell's claim I might be justifiably charged with creating a straw man to combat, because any field of study by virtue of its very existence is open to historical analysis. Regardless, I believe their review provides a good starting point for a new review of the history and historiography of immunology, not only because of the comprehensiveness of its coverage until that time the article reviewed a dozen books on different aspects of the history of immunology published between 1991 and 1998 – but also because the criteria by which the authors assessed these books offer useful guidelines for assessing the progress of the field since then. Most of the work on the history of immunology until that time, their review charged, offered perspectives that were rather narrow and internalist, or else quite conventional, approaching their subject matter as intellectual history. While I hesitate to dismiss either internalist analyses or intellectual histories as narrow or conventional I prefer to characterize them as focused and rigorous – there is no doubt that Söderqvist and Stillwell's suggestions for broadening the scholarship on the development of immunology to include institutional histories, biographies and studies on sociopolitical contexts would only enrich the history and historiography of the field. An evaluation of whether the historiography of immunology has widened its scope to include such methods and narratives is one of the major aims of this review[5], [6].

The idea of immunity, which means being exempt from something, was first mentioned by Thucydides, a historian who wrote about the Peloponnesian War. In 430 BC, he wrote about a disease that spread in Athens. Only people who had already gotten sick and recovered could take care of the sick people, and they wouldn't get sick again. In the 15th century, Chinese and Turks tried to make people immune to diseases by purposefully infecting them with a method called variolation. In this way, people would either breathe in or put dried crusts from smallpox sores into small cuts in the skin. Advertisements are messages or announcements that are intended to promote or sell a product, service, or idea. They can be found in various forms, such as commercials on TV, radio, or the internet, as well as billboards or posters. The purpose of advertisements is to attract people's attention and persuade them to buy or support what is being advertised. They often use catchy slogans, visual images, or persuasive language to make the product or idea seem desirable or appealing.

In 1718, Lady Mary Wortley Montague, who was married to a British Ambassador, tried variolation on her own children and saw that it had a good result. In 1798, Edward Jenner, a doctor from England, made a big improvement to the way things were done. He put the liquid from a cowpox blister into the milk maids and other people who had smallpox and kept them safe. He purposefully made an 8-year-old child sick by giving them liquid from a pimple caused by cowpox, and then by giving them smallpox. The child didn't get smallpox. Louis Pasteur made a big breakthrough in the study of immunology. He grew harmful bacteria that cause cholera and showed that when chickens were injected with these grown bacteria, they also got cholera. Surprisingly, when he put the old cholera bacteria into the chickens, they got sick, but then they got better.

When these chickens were given a shot of fresh cholera germs, they did not get sick with the disease at all. Pasteur suggested the idea that the pathogen's strength becomes weaker as it ages. Advertisements are messages that companies or individuals create to promote their products or services. They can be found in various forms such as commercials on television or radio, print ads in newspapers or magazines, billboards on the street, or online ads on websites or social media platforms. The purpose of advertisements is to grab people's attention and persuade them to buy a particular product or service. They often use catchy slogans, appealing visuals, and persuasive language to convince consumers to make a purchase.

Therefore, giving a weaker version of the virus may help prevent the disease. He named the weakened versions of germs as vaccines because of Jenner's work with cowpox vaccination. Pasteur used what he learned to study other diseases by making the harmful strains weaker. In 1881, Pasteur gave a shot to a group of sheep with a weaker form of the anthrax bacteria that was killed by heat. Then he tested the vaccinated sheep and some unvaccinated sheep by exposing them to a strong strain of the Bacillus virus. He observed that all the sheep that got vaccinated stayed alive. This experiment was a very important step forward in the study of the immune system. In 1885, Pasteur gave his first shot to a boy who got bit by a mad dog. The boy didn't get sick and later worked at the Pasteur Institute. Bacillus Anthracis is a type of bacteria that causes the disease anthrax. Kitasato discovered a substance called antitoxin that could neutralize toxins produced by bacteria. This discovery showed that the body's immune system could be strengthened by introducing specific substances to fight against harmful bacteria. Kitasato was the first person to explain how immunity works. In 1901, von Behring won the Nobel Prize in medicine. He showed that the liquid part of blood from animals that had been given a vaccine for diphtheria could pass on immunity to animals that had not been vaccinated. The part of the immune serum that is active can stop the poison from bacteria, so it was called antitoxin. The progress made in the 1900s was very important.

DISCUSSION

Immunology is a relatively new branch of the medical sciences. It started as a branch of microbiology, which led to the study of infectious diseases and then the body’s response to them.

History of immunology

Two hundred years later, in 1798, Edward Jenner gave the concept of immunity in response to contagion. His coworker had a cowpox infection (cow means Vacca), and consequently, she was resistant to smallpox. He noticed that cowpox infection incited immunity against smallpox. This discovery started the process of vaccination [7], [8].Lister introduces the concept of aseptic surgery.

Julius Bordet was a young Belgium student who showed that bacteriolysis and lysis of RBC need two factors:

1. A specific factorSensitizer.
2. A non-specific factorAlexine.
3. Louis Pasteur gave the concept of attenuation, explaining that exposure to adverse conditions can change the virulence of pathogens. He also prepared the first vaccine against cholera, anthrax, and rabies.

In 1881, he did a famous experiment on two groups of sheep where he injected the first group, group-A, with heated anthrax bacilli and presumed that these sheep developed immunity against anthrax. Group B was not exposed to heated anthrax bacilli in the second group. Afterward, he exposed both groups to live anthrax bacilli. The immunized group-A survived because of this exposure, while the non-immunized group B died[9], [10].

1. Klebs and Loeffler isolated diphtheria bacillus.
2. Metchnikoff, a Russian zoologist, gave the idea of cellular immunity by showing the phagocytosis of fungus spores by white blood cells in the frog.
3. Robert Koch's phenomena. He showed that animals could be immunized by exposure to Tubercle bacilli and when exposed to Tuberculous bacilli, the animal showed a different reaction in the form of thickening the skin at the site of injection, which appears in 24-48 hours.
4. Julius Bordet ultimately discovered complement and got the Noble Prize.
5. Kraus discovered precipitation by mixing a patient's serum and filtrate of typhoid bacilli.
6. Landsteiner dominated for 40 years in the field of immunology. He discovered blood group antigens and antibodies. He also introduced the concept of incomplete antigen. He was also awarded the Nobel Prize.
7. Sir Almoth found that antibodies can help in phagocytosis and settled the controversy of humoral and cellular immunity.

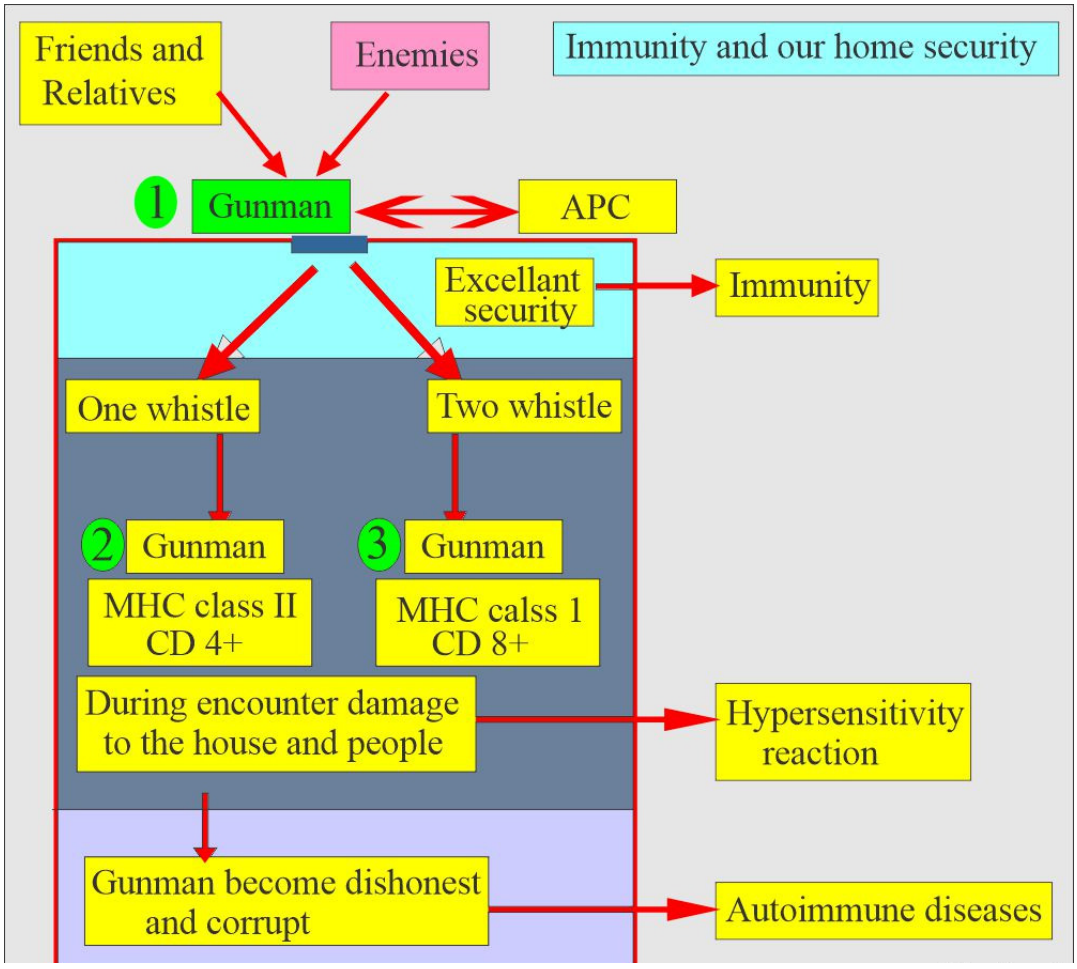


Figure 1: A showing comparison of the immune system and our home security [Labpedia. Net].

Immunology word first time appears in Medicus Index

Land Steiner published a book on the specificity of serologic reactions. He got the Nobel prize for his work on human blood groups.The first book was published on the chemistry of antigens and antibodies.Lady Mary Wortley Montagu was the wife of a British Ambassador in Turkey; she contracted smallpox and later advocated for smallpox vaccination.

Interesting Stories of Immunology

Ancient Chinese were injecting vesicle fluid of a smallpox patient to healthy people for developing immunity.Greek King Pontus took poison in a small amount and then increased the dose until he could tolerate higher doses. This process is called Methriditisim.Lady Mary Wortley Montagu, in 1721, was the wife of the British ambassador in Turkey. She also tried the process of variolation.Portuguese army officers used the ants for the poison to detoxify the poison, and later on found that ants contain the formal, which converts the toxin to toxoid.

Immunity

Immunity is our natural defense mechanism, comparable to our real-life defense mechanisms. The following diagram shows a diagrammatic comparison between a real-life defense system and our natural defense system. This figure 1 shown A showing comparison of the immune system and our home security.This diagram shows if the walls are high and thick, the security guards are strong, and the house will have complete protection. Security guard 1, at the entry (Antigen-presenting cell, APC), can recognize friends and get rid of weak enemies. If he comes across a strong enemy who can enter the house, he can get help from security guard 2 ($CD4^+$ cells/B-L) or guard no 3 ($CD8^+$ T-L/B-L). During the encounter, if some damage in the house occurs, that is just like a hypersensitivity reaction[11], [12]**.**If the security guard becomes dishonest and corrupt, it starts damaging the house like autoimmune diseases, where the immune system is defective. The above example shows that nature is present everywhere and has a similar system at a micro-level in our body and macro-level in our surroundings.

Definition of Immunology

This is defined as the study of molecules, cells, organs, and the system responsible for the recognition and disposal of non-self-substances.The function of the immune system is to recognize the non-self from the self to defend the body from the non-self.

Immunology has the following three main sections:

1. **Immunity** is the adaptive response to foreign substances (Ag), which may be an infection.
2. **Immunochemistry** is the study of the nature of antigens and antibodies.
3. **Immunobiology** is the study of the activity of immune cells.

Immunology is one of the most developing medical sciences. The following are some of its recent advances:

1. Immunopathology.
2. Tumor immunology.
3. Immunopharmacology.
4. Transplantation immunology.
5. Immunological disorders.

The immune system is the defensive system of our body and has two types: specific and non-specific.

Non-Specific Immunity

This immunity protects us from various pathogens and is the first line of defense. Non-specific immunity takes place through the following means:

1. Physical.
2. Chemical.
3. Cellular.
4. Physiological.

Specific Immunity

This immunity protects us from various specific pathogens and has a specific response for a particular antigen. Specific immunity takes place through the following means:

1. **Humoral:**Takes place through the activation of B-Lymphocytes.
2. **Cellular:**Takes place through the activation of T-Lymphocytes.

Let us look at an example of specific immunity. The following figure shows a child infected with smallpox and later recovering. During this process, the immune system recognized (R) smallpox, produced specific (S) antibodies, and kept memory (M) of the antigen; this RSM process is the backbone of the immune system. Afterward, whenever smallpox infects this child again, the specific immunity will notice that it is the same antigen and produce an exaggerated immune response, not allowing the infection; but exposure to other viruses (antigens) will not show such specific immunity but will instead result in repeating the RSM process.

Primary Immune Response

The immune system shows a primary immune response to the first encounter with a foreign substance (Antigen, Ag). This process consists of the following four phases:

1. **Phase-I:** This is the initial lag period of 7-10 days, during which no anti-foreign (Antibody, Ab) substance appears in the blood.
2. **Phase-II:**Primary Ab-IgM appears during this phase.
3. **Phase-III:** Ag and Ab-reaction take place.
4. **Phase-IV:** Ag disappears, resulting in excess of Ab

There is a lag period of 7-10 days before the anti-foreign substance (Antibody, Ab) appears in the blood. In the primary immune response, the IgM type of antibody always appears first, followed by the appearance of IgG. Afterward, the peak level of Ab is achieved; antigen and antibody reaction start, which clears off the antigens from circulation.

Secondary Response Immune

When the same antigen is re-exposed to the immune system, now because of specificity, recognition, and memory, there will be no lag period, and immediately formation of Ab (IgM & IgG) takes place due to the presence of memory cells, and antigen is cleared from the circulation.

CONCLUSION

In conclusion, the Chapter on Historical Perspectives on Immunology serves as a valuable retrospective journey into the annals of scientific discovery. It has provided a comprehensive overview of the key historical events, notable figures, and pivotal breakthroughs that have shaped our understanding of the immune system. Through this exploration, we have witnessed the evolution of immunology from ancient observations of disease to the sophisticated knowledge and technologies of the present day. As we reflect on the contributions of individuals like Edward Jenner, Louis Pasteur, Robert Koch, and Emil von Behring, we gain a deeper appreciation for their dedication and ingenuity in advancing the field of immunology. Their discoveries, often made under challenging circumstances, have had a profound impact on public health and have saved countless lives.Moreover, this Chapter underscores the enduring importance of immunology in our world today. From the development of vaccines to the treatment of autoimmune diseases and cancer, our understanding of the immune system continues to drive innovation and improve the well-being of individuals and communities worldwide. In closing, Historical Perspectives on Immunology serves as a reminder that scientific progress is built upon the foundation of past knowledge and that the pursuit of understanding the immune system remains as relevant and exciting as ever.

REFERENCES:

[1] B. Glasmacher *et al.*, New Cryopreservation Strategies : A View from Biothermal and Biomedical Process Technology, in *7th International Conference of Boar Semen Preservation, Bonn*, 2011.

[2] L. H. Rossi and D. A. Basketter, REACH and Immunotoxicology, in *Encyclopedia of Immunotoxicology*, 2014. doi: 10.1007/978-3-642-27786-3_1584-1.

[3] Chapter 15 New methods in immunotoxicology, *Immunotoxicol. Drugs Chem. an Exp. Clin. Approach*, 2004, doi: 10.1016/S1873-9822(04)80016-9.

[4] S. De Guise, M. Goedken, B. Morsey, J. Maratea, I. Sidor, and C. Perkins, Development of new methods to assess invertebrate immunology and immunotoxicology in aquaculture: Oysters and lobsters as examples, *International Journal of Environment and Pollution*. 2008. doi: 10.1504/IJEP.2008.020568.

[5] V. Galbiati, M. Mitjans, and E. Corsini, Present and future of in vitro immunotoxicology in drug development, *Journal of Immunotoxicology*. 2010. doi: 10.3109/1547691X.2010.509848.

[6] J. Descotes, *Introduction To Immunotoxicology*. 1998. doi: 10.1201/9781482295221.

[7] M. J. Derelanko, *The toxicologist's pocket handbook, third edition*. 2017. doi: 10.1201/b22047.

[8] J. M. R. Saint-Remy, Epitope mapping: A new method for biological evaluation and immunotoxicology, in *Toxicology*, 1997. doi: 10.1016/S0300-483X(96)03599-8.

[9] J. H. Dean, Issues with introducing new immunotoxicology methods into the safety assessment of pharmaceuticals, in *Toxicology*, 1997. doi: 10.1016/S0300-483X(96)03601-3.

[10] P. Kačmár, J. Pistl, and I. Mikula, Immunotoxicology and veterinary medicine, *Acta Vet. Brno*, 1999, doi: 10.2754/avb199968010057.

CHAPTER 2

CELLS OF THE IMMUNE SYSTEM: HEALTH AND DEFENCE GUARDIANS

Dr.Ramakant, Assistant Professor
Department of Science, Maharishi University of Information Technology, Uttar Pradesh, India
Email Id- ramakant@muit.in

ABSTRACT:

The Cells of the Immune System Chapter provides an in-depth analysis of the many cellular elements that make up the immune system. It explores the origins, characteristics, and interactions of immune cells, emphasizing their crucial function in protecting the body from infections and preserving homeostasis. This Chapter offers insights into the intricate biology of immune cells, their formation, and their coordinated responses to pathogens, immune system threats, and external invaders, from macrophages and neutrophils to T cells and B cells. This Chapter explores the numerous kinds of immune cells, highlighting their particular functions within both innate and adaptive immunity. It starts with a fundamental knowledge of immune cell formation, differentiation, and maturation. Every aspect of immune cell biology is meticulously dissected, from the voracious phagocytosis of neutrophils and macrophages to the complex antigen recognition and antibody production by B cells, the regulatory influence of T cells, and the necessity of antigen-presenting cells (APCs) like dendritic cells. Additionally, it studies the consequences of immune cell malfunction in a variety of clinical circumstances, providing insights into autoimmune disorders, illnesses of the immune system, and the function of immune cells in the detection and treatment of cancer.

KEYWORDS:

Adaptive Immunity, Antigen-Presenting Cells, B Cells, Cytokines, Dendritic Cells.

INTRODUCTION

The beginning of the Chapter Cells of the Immune System serves as the starting point for our investigation into the complex and diverse world of immune cells. This Chapter takes us on a trip that focuses on the immune system's cellular underpinnings, where a variety of specialized and closely coordinated cells act as the first line of defense against dangers to our body's health. These immune cells, each with a specific set of skills, tasks to perform, and functions, make up the immune system, a magnificent protection mechanism. Understanding the origins and purposes of these cellsfrom their development in the bone marrow to their distribution throughout the body in response to different threatsbegins with this Chapter. We will learn the intricate processes of immune cell development and differentiation, the amazing capacities of phagocytic cells like neutrophils and macrophages to engulf and neutralize invaders, the sentinel function of antigen-presenting cells like dendritic cells, and the crucial roles of lymphocytes, including B cells and T cells, in directing immune responses as we set out on this journey [1], [2].

We will also look at how these immune cells cooperate and interact with one another through signaling molecules like cytokines, engaging in a complex dance to defend the body against infections, preserve tissue integrity, and even identify and destroy malignant cells. Understanding the subtleties of immune cell biology is crucial for learning the foundations of immunology as well as for obtaining understanding of a variety of disease states, such as

cancer, autoimmune diseases, and immunodeficiencies. We will explore the complexities of immune cell biology in this Chapter, shedding light on the interesting functions that these cellular sentinels play in defending our health and wellbeing. As we go along, we'll learn to appreciate the immune system's amazing intricacy, elegance, and biological components [3], [4]. The thymus gland is a two-lobed gland that is placed above the heart, behind the sternum, and between the lungs. The thymus is only active throughout puberty before gradually shrinking and being replaced by fat and connective tissue. The thymus gland is in charge of manufacturing the hormone thymosin, which aids in the development of T lymphocytes. T cells grow in the thymus, acquire distinct antigen receptors, and develop into helper T cells and cytotoxic T cells. On the T cell surface, many proteins are expressed. By puberty, the thymus will have produced all of the T cells required. After maturing in the thymus and bone marrow, T and B lymphocytes migrate to the lymph nodes and spleen, where they remain until the immune system is activated. Lymph nodes are found all across the body. The spleen is situated in the upper left quadrant of the abdomen, behind the stomach and behind the diaphragm. The spleen's primary role is to filter blood. Damaged red blood cells, on the other hand, are broken down by macrophages large white blood cells specialized in engulfing and digesting cellular debris, pathogens, and other foreign substances in the body in the spleen. The spleen is a storage location for platelets and white blood cells. The spleen helps the immune system by detecting bacteria that could cause infection. In addition to the lymph nodes and spleen, mucosal associated lymphoid tissues (MALTs) and gut associated lymphoid tissues (GALTs) play important roles in the immune system despite being classified as lymphatic tissues. MALTs are lymphoid tissues located in mucosal areas of the body such as the intestines, eyes, nose, skin, and mouth. They contain lymphocytes and macrophages, which fight the body against diseases that enter from outside the body. GALTs are lymphoid tissues located in the gastrointestinal tract's mucosa and submucosa, tonsils, appendix, and Peyer's patches in the small intestine.

As part of the innate and adaptive immune systems, many cells collaborate. More information on innate and adaptive immune responses can be found in the module Innate vs. Adaptive Immune Response. Immune cells are often known as white blood cells or leukocytes. Granulocytes are a type of leukocyte with enzyme-containing granules in their cytoplasm. Granulocytes include neutrophils, basophils, and eosinophils. Neutrophils are considered the innate immune system's earliest responders. Neutrophils and macrophages move through the blood and live in tissues, looking for abnormalities. Both cells have the ability to eat bacteria as well as communicate with other immune cells if a problem emerges. Adaptive immune system cells perform an immunological function in response to a stimulus. Effector cells include natural killer T lymphocytes and B lymphocytes. T lymphocytes, for example, eliminate infections through a cell-mediated response. Activated B cells release antibodies that help the immune system mount an attack. Cancer is destroyed with the use of effector cells. Antigen-presenting cells (APCs), such as dendritic cells, regulatory T cells, tumor-associated macrophages, and myeloid-derived suppressor cells, are non-effector cells. Non-effector cells are unable to kill tumours on their own. Non-effector cells obstruct effector cell immunological function. Non-effector cells help tumours to proliferate in cancer.

DISCUSSION

The immune system is made up of several components that cooperate to protect the body against intruders. The thymus and bone marrow are the two main immune system components. All of the body's blood cells, including T and B lymphocytes, originate in the bone marrow, making it a vital component of the immune system. T cells go to the thymus, whereas B lymphocytes continue to develop in the bone marrow. A bilobed gland, the thymus

is situated above the heart, behind the sternum, and between the lungs. The thymus is only functional until adolescence, after which it gradually decreases and is replaced by connective tissue and fat. The thymus is in charge of producing the hormone thymosin, which promotes the development of T lymphocytes. T cells proliferate, pick up various antigen receptors, and develop into helper T cells and cytotoxic T cells while in the thymus. On the surface of T cells, several proteins are expressed, including CD4, CD8, and others. By the time a person reaches adolescence, the thymus has created all the T cells they need [5], [6].

The lymph nodes and spleen are where T and B cells linger until the immune system is activated after maturing in the thymus and bone marrow. All across the body, there are lymph nodes. The spleen is beneath the diaphragm and behind the stomach in the upper left region of the abdomen. The spleen's primary role is to filter blood. Healthy red blood cells travel through the spleen with no difficulty, but damaged red blood cells are broken down in the spleen by macrophages, which are huge white blood cells that have been specifically designed to absorb and digest cellular waste, infections, and other foreign substances in the body. White blood cells and platelets are kept in the spleen as a storage organ. By locating potential infection-causing germs, the spleen supports the immune system [7], [8].

Although they are regarded as being a component of the lymphatic system, mucosal associated lymphoid tissues (MALTs) and gut associated lymphoid tissues (GALTs) also play an important function in the immune system alongside the lymph nodes and spleen. MALTs are lymphoid tissues that may be found in bodily regions with mucosa, including the intestines, eyes, nose, skin, and mouth. They have lymphocytes and macrophages that protect the body from infections trying to enter from the outside. GALTs are lymphoid tissues that may be found in Peyer's patches in the small intestine, tonsils, the appendix, and the mucosa and submucosa of the gastrointestinal tract.

Adaptive T cells

Both the innate and adaptive immune systems include many cells cooperating. For further details on innate and adaptive immune response, go to the module Innate vs. Adaptive Immune Response. White blood cells or leukocytes are other names for immune cells. Leukocytes known as granulocytes have enzyme-containing granules in their cytoplasm. Types of granulocytes include neutrophils, basophils, and eosinophils. The innate immune system's neutrophils are regarded as the first defense. The blood is carried by neutrophils and macrophages, which remain in tissues and keep an eye out for any concerns. Both cells have the ability to eat germs and, in the event of a problem, to interact with other immune cells. Immune effector cells, or cells of the adaptive immune system, perform an immunological function in response to a stimulus. Effector cells include B lymphocytes and natural killer T lymphocytes. For instance, pathogens are eliminated by activated T lymphocytes in a cell-mediated response. B cells that have been activated release immune-supporting antibodies. Effector cells are a part of the cancer's demise [7], [8]. Antigen-presenting cells (APCs), such as regulatory T cells, tumor-associated macrophages, and myeloid-derived suppressor cells, are non-effector cells. Non-effector cells are unable to kill tumors on their own. Effector cells' immunological response is blocked by non-effector cells. Non-effector cells promote tumor growth in cancer. The immune system is a remarkable defense network within the human body, designed to protect against a wide array of threats, including pathogens such as bacteria, viruses, and fungi, as well as malignant cells. At the heart of this complex defense system are specialized immune cells, each with unique functions and properties. This discussion aims to provide a comprehensive understanding of the various immune cell types, their development, functions, interactions, and implications in health and disease.

Types of Immune Cells

Phagocytic Cells

1. Neutrophils.
2. Macrophages.
3. Dendritic Cells.

Lymphocytes

1. B Cells.
2. T Cells.

a. Helper T Cells (Th).
b. Cytotoxic T Cells (Tc).
c. Regulatory T Cells (Treg).
d. Natural Killer (NK) Cells.

Development of Immune Cells

1. Hematopoiesis
2. Differentiation and Maturation
3. Bone Marrow and Thymus

Functions of Immune Cells

1. Phagocytic Cells.
2. Engulfment of Pathogens.
3. Antigen Presentation.

1. Types of Immune Cells

Phagocytic Cells

Phagocytic cells are the first line of defense against invading pathogens. They engulf and digest foreign particles, thereby eliminating potential threats. The key phagocytic cells include neutrophils, macrophages, and dendritic cells.

Neutrophils

Neutrophils are the most abundant white blood cells in circulation and play a critical role in the innate immune response. They are rapid responders to infections, migrating to sites of inflammation and infection. Neutrophils use various mechanisms to destroy pathogens, including phagocytosis and the release of toxic substances.

Macrophages

Macrophages are versatile immune cells found in tissues throughout the body. They serve as scavengers, engulfing and digesting pathogens, dead cells, and cellular debris. Macrophages also play a crucial role in antigen presentation, helping initiate adaptive immune responses.

Dendritic Cells

Dendritic cells act as antigen-presenting cells (APCs). They capture antigens, process them, and then present antigen fragments to T cells, initiating adaptive immune responses. Dendritic cells bridge the gap between the innate and adaptive immune systems, making them essential in immune surveillance.

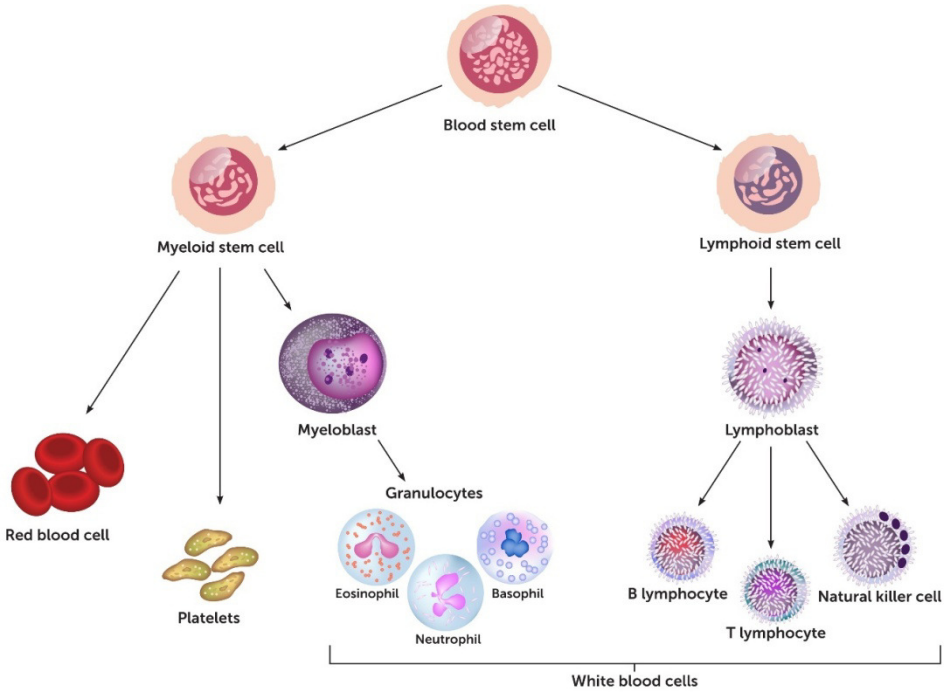


Figure 1: Representing the overview about the different types of cell presence in the immune system [Healio].

Lymphocytes: Lymphocytes are the primary cells of the adaptive immune system, and they include B cells, T cells, and natural killer (NK) cells.

B Cells: B cells are responsible for antibody production. When activated by encountering antigens, they differentiate into plasma cells that secrete antibodies (Figure 1). Antibodies play a crucial role in neutralizing pathogens and tagging them for destruction by other immune cells.

T Cells:T cells are central to cell-mediated immunity, with various subsets performing distinct functions:

a. **Helper T Cells (Th):** They assist other immune cells by releasing cytokines and coordinating immune responses. Different subsets of helper T cells regulate specific immune reactions.
b. **Cytotoxic T Cells (Tc):** Cytotoxic T cells are responsible for killing infected or abnormal host cells, such as those infected with viruses or cancer cells.
c. **Regulatory T Cells (Treg):** Regulatory T cells help maintain immune system balance by suppressing excessive immune responses, preventing autoimmunity.
d. **Natural Killer (NK) Cells:** NK cells are part of the innate immune system but have properties of both innate and adaptive immunity. They can detect and destroy infected or cancerous cells without prior sensitization.

2. Development of Immune Cells

The development of immune cells, known as hematopoiesis, is a complex process that occurs primarily in the bone marrow and the thymus gland.

a. **Hematopoiesis**:Hematopoiesis is the formation of blood cells, including immune cells. It occurs in the bone marrow, where hematopoietic stem cells give rise to various blood cell lineages, including erythrocytes, platelets, and white blood cells. Differentiation and maturation processes yield specialized immune cells.

b. **Bone Marrow and Thymus:**The bone marrow is a primary site for the development of immune cells, including B cells. T cells, on the other hand, undergo a critical maturation process in the thymus gland. The thymus is particularly essential for the selection of T cells with functional receptors and the elimination of self-reactive T cells [9], [10].

3. Functions of Immune Cells

a. **Phagocytic Cells:**Phagocytic cells, including neutrophils, macrophages, and dendritic cells, play pivotal roles in immune defense:
b. **Engulfment of Pathogens:** These cells recognize, engulf, and digest pathogens through phagocytosis, a process that helps eliminate infectious agents.
c. **Antigen Presentation**: Macrophages and dendritic cells serve as antigen-presenting cells (APCs), which means they process antigens from pathogens and present them to T cells, initiating adaptive immune responses.

CONCLUSION

In conclusion, the world of immune cells is a remarkable tapestry of specialized defenders, each with a unique role in maintaining health and combating disease. From the rapid response of neutrophils to the sophisticated antigen recognition of T cells and the antibody production of B cells, immune cells orchestrate a complex and highly coordinated defense system. This discussion has provided an in-depth exploration of immune cell types, their development, functions, interactions, and clinical relevance. Immune cells are not only essential in protecting the body from pathogens but also hold the key to understanding and treating various diseases, including cancer, autoimmune disorders, and immunodeficiency conditions. As research in immunology continues to advance, we can expect even more groundbreaking discoveries and innovative therapies on the horizon. The ongoing quest to unravel the mysteries of immune cells and harness their potential for medical interventions remains a promising frontier in science and healthcare. In a world where infectious diseases, cancer, and immune-related disorders continue to challenge our well-being, the study of immune cells and the immune system as a whole stand as a beacon of hope, offering solutions and strategies to safeguard human health and improve the quality of life for individuals around the globe.

REFERENCES:

[1] R. Bugianesi *et al.*, High-performance liquid chromatography with coulometric electrode array detector for the determination of quercetin levels in cells of the immune system, *Anal. Biochem.*, 2000, doi: 10.1006/abio.2000.4697.

[2] F. Cavallo, C. De Giovanni, P. Nanni, G. Forni, and P. L. Lollini, 2011: The immune hallmarks of cancer, in *Cancer Immunology, Immunotherapy*, 2011. doi: 10.1007/s00262-010-0968-0.

[3] J. S. Miller, The biology of natural killer cells in cancer, infection, and pregnancy, *Experimental Hematology*. 2001. doi: 10.1016/S0301-472X(01)00696-8.

[4] G. J. Clark *et al.*, The role of dendritic cells in the innate immune system, *Microbes and Infection*. 2000. doi: 10.1016/S1286-4579(00)00302-6.

[5] S. C. Byram, M. J. Carson, C. A. DeBoy, C. J. Serpe, V. M. Sanders, and K. J. Jones, CD4-Positive T Cell-Mediated Neuroprotection Requires Dual Compartment Antigen Presentation, *J. Neurosci.*, 2004, doi: 10.1523/JNEUROSCI.5276-03.2004.

[6] L. R. Watkins and S. F. Maier, The pain of being sick: Implications of immune-to-brain communication for understanding pain, *Annu. Rev. Psychol.*, 2000, doi: 10.1146/annurev.psych.51.1.29.

[7] P. M. Elias and M. Steinhoff, 'Outside-to-inside' (and now back to 'outside') pathogenic mechanisms in atopic dermatitis, *Journal of Investigative Dermatology*. 2008. doi: 10.1038/jid.2008.88.

[8] M. Krause, H. Foks, and K. Gobis, Pharmacological potential and synthetic approaches of imidazo[4,5-b]pyridine and imidazo[4,5-c]pyridine derivatives, *Molecules*. 2017. doi: 10.3390/molecules22030399.

[9] N. Baumgarth and M. Roederer, A practical approach to multicolor flow cytometry for immunophenotyping, *J. Immunol. Methods*, 2000, doi: 10.1016/S0022-1759(00)00229-5.

[10] M. Vicente-Manzanares and F. Sanchez-Madrid, Cell polarization: A comparative cell biology and immunological view, *Dev. Immunol.*, 2000, doi: 10.1155/2000/70801.

CHAPTER 3

THE INNATE IMMUNE RESPONSE: FIRST LINE OF DEFENCES

Dr.Ramakant, Assistant Professor
Department of Science, Maharishi University of Information Technology, Uttar Pradesh, India
Email Id- ramakant@muit.in

ABSTRACT:

The Chapter on The Innate Immune Response provides an in-depth exploration of the fundamental and immediate defense mechanisms that the human body employs to combat invading pathogens. It illuminates the intricate processes and cellular components involved in innate immunity, emphasizing its critical role as the first line of defense against a diverse array of microorganisms. From physical barriers to phagocytic cells and the release of inflammatory mediators, this Chapter elucidates the innate immune response's rapid and non-specific nature, highlighting its pivotal role in maintaining health and facilitating subsequent adaptive immune responses.The body's natural immune response is its first line of defense against germs. This fast and general defense system is very important for immediate protection. Important parts include things that physically block germs, substances that fight against germs, and special cells that help protect the body from germs. When the body recognizes a harmful germ, the immune system starts a process called inflammation, which helps to fight off the germ. It also causes cells called phagocytes to engulf and destroy the germ. Finally, the immune system releases special proteins called cytokines to communicate with other parts of the body and help coordinate the immune response. These responses try to stop or kill invaders, reducing how far infections spread. The innate immune system doesn't have the same specificity as the adaptive immune system, but it is very important in protecting the body before the adaptive immune system kicks in. It is extremely important to know about our natural defense system in order to fight infections and create treatments.

KEYWORDS:

Antimicrobial Peptides, Complement System, Cytokines, Inflammation, Innate Immunity.

INTRODUCTION

The introduction to the Chapter on The Innate Immune Response provides a foundational understanding of the body's immediate defense mechanisms against pathogens. Innate immunity serves as the first line of defense, acting swiftly to recognize and combat a wide range of invading microorganisms. This introduction sets the stage for a comprehensive exploration of the components and processes that make up the innate immune response. Innate immunity is an ancient and evolutionarily conserved system that provides crucial protection against infections. Unlike adaptive immunity, which is highly specific and requires time to develop, innate immunity is rapid and non-specific. It serves as a critical initial barrier that buys time for the adaptive immune response to kick in. This Chapter delves into the various aspects of innate immunity, including the physical barriers provided by the skin and mucous membranes, the roles of phagocytic cells such as neutrophils and macrophages, the recognition of pathogen-associated molecular patterns (PAMPs) by pattern recognition receptors (PRRs) like Toll-like receptors (TLRs), and the activation of the complement system. It also explores the release of cytokines and the inflammatory response as essential components of innate immunity [1], [2].

Understanding the innate immune response is fundamental not only for comprehending the body's defense mechanisms but also for gaining insights into how the immune system recognizes and responds to infections. Moreover, innate immunity plays a crucial role in shaping the subsequent adaptive immune response, highlighting its significance in maintaining health and combating diseases. As we delve into the intricacies of the innate immune response in this Chapter, we will uncover the remarkable and highly orchestrated processes that allow the body to rapidly and effectively confront a wide array of microbial threats. This foundation of innate immunity is the cornerstone upon which the more specialized and specific adaptive immune responses are built [3], [4]. Every day, humans come into contact with many harmful germs through touching, eating, and breathing them in. Our ability to stay away from getting sick depends on the adaptive immune system, which remembers previous fights against specific germs and kills them when they come back. When the body encounters a new germ, the immune system takes time to learn how to fight it. This is because certain types of cells need to become active and increase in number. It can take about a week before the immune response starts working well. On the other hand, just one tiny bacterium that can duplicate itself in one hour can create nearly 20 million offspring, a full-scale infection, in only one day. So, when we first come into contact with a new germ, our body's natural defense system helps to keep us safe. The body's natural immune responses aren't geared towards a specific infection like the body's learned immune responses are. They rely on a group of proteins and cells that can identify certain aspects of harmful germs and quickly become active to help eliminate them. The adaptive immune system evolved less than 500 million years ago and is only found in animals with backbones. On the other hand, innate immune responses are seen in animals with and without backbones, as well as in plants. The basic mechanisms that control these responses are similar among different organisms. The inside skin surfaces are also protected by a slimy layer called mucus. This layer shields the surfaces from germs, physical harm, and harmful chemicals. Amphibians and fish also have this slimy layer on their skin. The slippery gooey substance that covers something is mostly made of a slippery protein and other sticky proteins. It helps stop bad stuff from sticking to the protective layer. It also helps them leave by moving tiny hairs on the surface of the cell.

DISCUSSION

This type of immunity is present in an organism by birth. This is activated immediately when the pathogen attacks. Innate immunity includes certain barriers and defence mechanisms that keep foreign particles out of the body.This immunity helps us by providing the natural resistance components including salivary enzymes, natural killer cells, intact skin and neutrophils, etc. which produce an initial response against the infections at birth prior to exposure to a pathogen or antigens. It is a long-term immunity in which our body produces the antibodies on its own. Our body has few natural barriers to prevent the entry of pathogens [5], [6].These include the skin, body hair, cilia, eyelashes, the respiratory tract, and the gastrointestinal tract. These form the first line of defence.The skin does more than providing us with fair or dark complexions. Our skin acts as a physical barrier to the entry of pathogens. The mucus coating in our nose and ear is a protective barrier which traps the pathogen before it gets inside [5], [6].

Physiological barriers

We know that our stomach uses hydrochloric acid to break down the food molecules. Due to such a strongly acidic environment, most of the germs that enter our body along with the food are killed before the further process is carried on. Saliva in our mouth and tears in our eyes also have the antibiotic property that does not allow the growth of pathogens even though they are exposed all day [7], [8].

Cellular barriers

In spite of the physical and physiological barriers, certain pathogens manage to enter our body. The cells involved in this barrier are leukocytes (WBC), neutrophils, lymphocytes, basophil, eosinophil, and monocytes. All these cells are all present in the blood and tissues [9], [10].

Cytokine barriers

The cells in our body are smarter than we give them credit for. For instance, in case a cell in our body experiences a virus invasion, it automatically secretes proteins called interferons which forms a coating around the infected cell and prevents the cells around it from further infections.

Cells Involved in Innate Immunity

a. **Phagocytes**: These circulate through the body and look for any foreign substance. They engulf and destroy it defending the body against that pathogen.

b. **Macrophages**: These have the ability to move across the walls of the circulatory system. They release certain signals as cytokines to recruit other cells at the site of infections.

c. **Mast Cells**: These are important for healing wounds and defence against infections.

d. **Neutrophils**: These contain granules that are toxic in nature and kill any pathogen that comes in contact.

e. **Eosinophils**: These contain highly toxic proteins that kill any bacteria or parasite in contact.

f. **Basophils**: These attack multicellular parasites. Like the mast cells, these release histamine.

g. **Natural Killer Cells**: These stop the spread of infections by destroying the infected host cells.

h. **Dendritic Cells**: These are located in the tissues that are the points for initial infections. These cells sense the infection and send the message to the rest of the immune system by antigen presentation.

Microorganisms do breach the epithelial barriers on occasion. The innate and adaptive immune systems must then recognize and destroy them without damaging the host. As a result, immune systems must be able to discriminate between self and nonself. We look at how the adaptive immune system does this. The innate immune system is based on the detection of specific types of chemicals that are shared by numerous infections but not present in the host. These pathogen-associated compounds also known as pathogen-associated immunostimulants activate two forms of innate immune responses inflammation and phagocytosis by cells such as neutrophils and macrophages. Both of these reactions can occur fast, even if the host has never been exposed to the virus in question. Pathogen-associated immunostimulants come in a variety of forms. Procaryotic translation initiation differs from eucaryotic translation initiation in that formylated methionine is typically employed as the initial amino acid rather than ordinary methionine. As a result, any peptide with formylmethionine at its N-terminus must be of bacterial origin. Formylmethionine-containing peptides are highly strong chemoattractants for neutrophils, which swiftly migrate to the source of such peptides and consume the bacteria that produce them.

Furthermore, many bacteria have an outer surface made of chemicals that do not exist in their multicellular hosts, and these compounds act as immunostimulants. Bacterial peptidoglycan cell walls and flagella, as well as lipopolysaccharide (LPS) on Gram-negative bacteria and teichoic acids on Gram-positive bacteria, are among them. They also contain compounds found in fungi's cell walls such as zymosan, glucan, and chitin. Many parasites, including Plasmodium, have unique membrane components that act as immunostimulants, such as glycosylphosphatidylinositol. Short bacterial DNA sequences can potentially behave as immunostimulants. A CpG motif is to blame, which is made up of the unmethylated dinucleotide CpG flanked by two 5′ purine residues and two 3′ pyrimidines. This short sequence is at least twenty times less common in vertebrate DNA than in bacterial DNA, and it has the ability to activate macrophages, induce an inflammatory response, and enhance B cell antibody production. Pathogen-associated immunostimulants of diverse kinds frequently exist in recurring patterns on the pathogen surface. They are identified by a variety of specialised receptors in the host, known as pattern recognition receptors. Soluble receptors in the blood components of the complement system and membrane-bound receptors on the surface of host cells members of the Toll-like receptor family are examples of these receptors.

The cell-surface receptors have two functions: they initiate pathogen phagocytosis and they induce a gene expression program in the host cell to stimulate innate immune responses. Soluble receptors also contribute in phagocytosis and, in rare situations, direct pathogen death. The complement system is made up of around 20 interacting soluble proteins that are mostly produced by the liver and circulate in the blood and extracellular fluid. Most are dormant until activated by an illness. They were first identified by their ability to enhance and complement the action of antibodies, but some complement components are also pattern recognition receptors that can be directly activated by pathogen-associated immunostimulants. The early complement components are the first to be activated. There are three sets of them, each corresponding to a different complement activation pathway: the classical pathway, the lectin pathway, and the alternative pathway. All three routes' early components operate locally to activate C3, the critical component of complement. Individuals with a C3 deficiency are prone to bacterial infections. The early components and C3 are all proenzymes that are sequentially activated by proteolytic cleavage. Each proenzyme cleavage in the series activates the next component, which produces a serine protease, which cleaves the next proenzyme in the series, and so on. Because each activated enzyme cleaves several molecules of the next proenzyme in the chain, activation of the early components is a proteolytic cascade.

Many of these cleavages release a physiologically active short peptide fragment as well as a bigger membrane-binding fragment. The big fragment's adherence to a cell membrane, generally the surface of a pathogen, aids in the execution of the following reaction in the chain. Complement activation is thus generally restricted to the cell surface where it began. C3b, a bigger portion of C3, attaches covalently to the pathogen's surface. Once in situ, it not only serves as a protease, catalyzing the subsequent steps in the complement cascade, but it is also recognized by special receptors on phagocytic cells, enhancing their ability to phagocytose the pathogen. C3a, as well as portions of C4 and C5, work independently as diffusible signals to stimulate an inflammatory response by attracting phagocytes and lymphocytes to the site of infection. The classical pathway is activated by IgG or IgM antibody molecules attached to the surface of a microorganism. Mannan-binding lectin is a serum protein that forms clusters of six carbohydrate-binding heads around a central collagen-like stalk and initiates the second pathway of complement activation.

This assembly binds exclusively to mannose and fucoseresidues in bacterial cell walls that have the proper spacing and orientation to line up perfectly with the six carbohydrate-binding sites, demonstrating a pattern recognition receptor in action. The recruitment and activation of early complement components is caused by these initial binding events in the classical and lectin pathways. C3 is spontaneously activated at low levels in the alternative pathway, and the resulting C3b covalently bonds to both host cells and pathogens. Host cells produce a number of proteins that inhibit the complement response on their cell surfaces. Pathogens are targeted for elimination because they lack these proteins. Through a positive feedback loop, activation of the classical or lectin routes also activates the alternative pathway, amplifying their effects.

Membrane-immobilized C3b, which can be produced by any of the three pathways, initiates a series of processes that leads to the assembly of the late components to form membrane assault complexes. These complexes assemble around the region of C3 activation in the pathogen membrane and have a distinct look in negatively stained electron micrographs, where they are seen to produce aqueous pores through the membrane. As a result of this, and because they disrupt the structure of the bilayer in their vicinity, they cause the membrane to leak and, in some situations, cause the microbial cell to lyse, similar to defensins. Because of the complement cascade's self-amplifying, inflammatory, and destructive qualities, it is critical that important activated components be swiftly inactivated after they are created to ensure that the attack does not spread to surrounding host cells. Deactivation can be accomplished in at least two methods. First, particular inhibitor proteins in the blood or on the surface of host cells stop the cascade by attaching to or cleaving specific components that have been triggered by proteolytic cleavage. Second, many of the activated cascade components are unstable; unless they instantly attach to either an appropriate cascade component or a neighbouring membrane, they swiftly become inactive.

The Toll-like receptor (TLR) family contains several of the mammalian cell-surface pattern recognition receptors that are responsible for initiating host cell gene expression in response to pathogens. Toll in Drosophila is a transmembrane protein with a large extracellular domain made up of leucine-rich repeats. It was shown to be a protein involved in the formation of dorso-ventral polarity in developing fly embryos. However, it is also implicated in the adult fly's resistance to fungal infections. When a fly is exposed to a pathogenic fungus, the intracellular signal transduction pathway activated downstream of Toll leads to the translocation of the NF-B protein into the nucleus, where it activates the transcription of various genes, including those encoding antifungal defensins. Another Toll family member in Drosophila is activated by pathogenic bacteria, resulting in the synthesis of an antibacterial defensin. Humans have at least ten TLRs, several of which have been shown to play important roles in innate immune recognition of pathogen-associated immunostimulants such as lipopolysaccharide, peptidoglycan, zymosan, bacterial flagella, and CpG DNA. TLR activation in mammals induces the expression of molecules that both trigger an inflammatory response and aid in the induction of adaptive immune responses. TLRs are abundant on the surfaces of macrophages and neutrophils, as well as the epithelial cells that line the lungs and stomach. They serve as an alarm system, alerting both the innate and adaptive immune systems to the presence of an infection.

Lipopolysaccharide (LPS) activates a macrophage. In the blood, LPS is bound by LPS-binding protein (LBP), and the complex binds to the GPI-anchored receptor CD14 on the surface of macrophages. Toll and TLR-related molecules appear to be important in innate immunity in all multicellular organisms. Plants require proteins with leucine-rich repeats and

domains analogous to the cytosolic component of TLRs to resist fungal, bacterial, and viral invaders. Thus, at least two components of the innate immune system defensins and TLRs appear to be very ancient in evolutionary terms, possibly predating the split between animals and plants over a billion years ago. Their survival throughout evolution demonstrates the relevance of these innate mechanisms in microbial pathogen defence.

Invertebrates and vertebrates alike, the detection of a microbial intruder is frequently followed by its engulfment by a phagocytic cell. Plants, on the other hand, lack this form of innate immune response. Macrophages are found throughout the body in vertebrates and are particularly plentiful in places where infections are prone to occur, such as the lungs and gut. They are also abundant in connective tissues, the liver, and the spleen. These long-lived cells patrol the body's tissues and are the first to encounter invading germs. The neutrophils, the second major family of phagocytic cells in vertebrates, are short-lived cells that are plentiful in blood but not in normal, healthy tissues. They are quickly drawn to infection sites by activated macrophages as well as substances such as formyl methionine-containing peptides produced by the microorganisms.Macrophages and neutrophils have a number of cell-surface receptors that allow them to identify and engulf pathogens. TLRs, for example, are pattern recognition receptors. They also have cell-surface receptors for both the Fc portion of antibodies produced by the adaptive immune system and the C3b component of complement. Ligand binding to any of these receptors causes actin polymerization at the point of pathogen attachment, allowing the plasma membrane of the phagocyte to surround and engulf the pathogen in a huge membrane-enclosed phagosome.

Once the pathogen has been phagocytosed, the macrophage or neutrophil unleashes a lethal arsenal of weapons. The phagosome becomes acidic and unites with lysosomes, which contain lysozyme and acid hydrolases capable of degrading bacterial cell walls and proteins. Defensins, which account for around 15% of total protein in neutrophils, are also found in lysosomes. Furthermore, phagocytes form a NADPH oxidase complex on the phagosome membrane, which catalyzes the formation of a number of highly toxic oxygen-derived compounds such as superoxide (O2 -), hypochlorite (HOCl, the active ingredient in bleach), hydrogen peroxide, hydroxyl radicals, and nitric oxide (NO). The formation of these hazardous chemicals is accompanied by a brief surge in cell oxygen consumption known as the respiratory burst. Whereas macrophages will normally live and continue to patrol tissues for other infections, neutrophils will usually perish. Neutrophils that have died or are dying are a substantial component of the pus that develops in acutely infected wounds. The unique greenish colour of pus is caused by an excess of the copper-containing enzyme myeloperoxidase in neutrophils, which is one of the components active in the respiratory burst.If a pathogen is too large to be phagocytosed for example, if it is a huge parasite like a worm, a population of macrophages, neutrophils, or eosinophils will congregate around the invader. They will exocytose their defensins and other lysosomal products, as well as the toxic chemicals of the respiratory burst. This onslaught is usually enough to kill the infection.

Many pathogens have devised techniques to evade being consumed by phagocytes. Some Gram-positive bacteria encase themselves with an extremely thick, slimy polysaccharide coat, or capsule, that complement and phagocyte receptors cannot recognize. Other pathogens are phagocytosed but not destroyed; for example, Mycobacterium tuberculosis hinders phagosome development and hence persists. Some pathogens completely escape the phagosome, while others secrete enzymes that detoxify the products of the respiratory burst. These first lines of defence are insufficient for such cunning infections, and adaptive immune responses are necessary to confine them.

When a pathogen enters a tissue, it almost invariably causes an inflammatory reaction. Pain, redness, heat, and swelling at the site of infection characterize this response, which is mediated by alterations in local blood vessels. Blood arteries dilate and become permeable to fluid and proteins, causing local edema and an accumulation of blood proteins that aid in defence, such as complement cascade components. Simultaneously, endothelial cells lining local blood arteries are induced to express cell adhesion proteins, which aid in the attachment and proliferation of white blood cells such as neutrophils, lymphocytes, and monocytes. A number of signalling molecules are involved in the inflammatory response. When TLRs are activated, they produce both lipid signalling molecules like prostaglandins and protein or peptide signalling molecules like cytokines, all of which contribute to the inflammatory response. Proteolytic release of complement fragments also plays a role. Chemoattractant are created by some of the cytokines produced by activated macrophages. Some of these attract neutrophils, which are the first cells to be drawn to the site of a new infection in considerable numbers. Others attract monocytes and dendritic cells later on. Dendritic cells collect antigens from invading pathogens and transport them to neighbouring lymph nodes, where they offer the antigens to lymphocytes to mobilize adaptive immune system forces. Other cytokines cause fever, or an increase in body temperature. Fever, on the whole, helps the immune system fight illness because most bacterial and viral pathogens grow better at lower temperatures, but adaptive immune responses are more potent at higher temperatures.Some proinflammatorysignalling molecules drive endothelial cells to express proteins that cause blood clotting in tiny arteries in the immediate vicinity. This response can help prevent the pathogen from entering the bloodstream and spreading the illness to other parts of the body by occluding the vessels and cutting off blood flow.However, the same inflammatory responses that are so successful in controlling local infections can be deadly when they occur in a disseminated infection in the bloodstream, a condition known as sepsis. The systemic release of proinflammatorysignalling molecules into the blood induces blood vessel dilatation, plasma volume loss, and widespread blood clotting, resulting in septic shock, a potentially lethal illness.

CONCLUSION

In conclusion, the innate immune response is a vital and immediate defense mechanism that plays a fundamental role in safeguarding the body against a diverse array of pathogens. This Chapter has provided a comprehensive exploration of the innate immune system, shedding light on its mechanisms, components, and significance in maintaining health. The innate immune response serves as the body's first line of defense, acting rapidly to recognize and combat invading microorganisms. It operates through a variety of mechanisms, including physical barriers like the skin and mucous membranes, the actions of phagocytic cells such as neutrophils and macrophages, the recognition of pathogen-associated molecular patterns (PAMPs) by pattern recognition receptors (PRRs) like Toll-like receptors (TLRs), and the activation of the complement system. In addition, the release of cytokines and the initiation of inflammation are crucial components of innate immunity. One of the distinguishing features of innate immunity is its non-specific nature. It does not rely on prior exposure to specific pathogens, and its responses are largely hardwired into our genetic code.

This inherent responsiveness allows innate immunity to provide immediate protection against a broad range of microbial threats. Furthermore, the innate immune response acts as a bridge to the adaptive immune system, helping shape and facilitate the development of specific adaptive immune responses. It provides the necessary signals and cues to activate and guide adaptive immune cells, such as T cells and B cells, in mounting targeted defenses against pathogens. Understanding the innate immune response is not only essential for

comprehending the body's defense mechanisms but also for gaining insights into how the immune system recognizes and responds to infections. Moreover, it has significant implications in the fields of immunology and medical science. As research in immunology continues to advance, the knowledge gained from studying innate immunity is increasingly harnessed in the development of therapeutic strategies. These strategies range from the development of vaccines that stimulate innate immune responses to the design of therapies that modulate inflammation or enhance the body's natural defense mechanisms against infections and diseases. In summary, the innate immune response represents an ancient and highly effective system that plays a critical role in maintaining health and combating diseases. It is a testament to the body's remarkable ability to defend itself against a constantly evolving landscape of microbial challenges. As our understanding of innate immunity deepens, we can expect further breakthroughs in the prevention and treatment of infectious diseases, autoimmune disorders, and other conditions that involve the immune system. The innate immune response stands as a foundational pillar in the ongoing quest to safeguard human health and well-being.

REFERENCES:

[1] S. Rivest, Regulation of innate immune responses in the brain, *Nature Reviews Immunology*. 2009. doi: 10.1038/nri2565.

[2] V. Nizet and R. S. Johnson, Interdependence of hypoxic and innate immune responses, *Nature Reviews Immunology*. 2009. doi: 10.1038/nri2607.

[3] D. Kuttenkeuler *et al.*, A large-scale RNAi screen identifies Deaf1 as a regulator of innate immune responses in Drosophila, *J. Innate Immun.*, 2010, doi: 10.1159/000248649.

[4] R. L. Modlin, The innate immune response in leprosy, *Current Opinion in Immunology*. 2010. doi: 10.1016/j.coi.2009.12.001.

[5] R. Jiang *et al.*, Three pairs of protease-serpin complexes cooperatively regulate the insect innate immune responses, *J. Biol. Chem.*, 2009, doi: 10.1074/jbc.M109.071001.

[6] H. M. Lee, J. M. Yuk, D. M. Shin, and E. K. Jo, Dectin-1 is inducible and plays an essential role for mycobacteria-induced innate immune responses in airway epithelial cells, *J. Clin. Immunol.*, 2009, doi: 10.1007/s10875-009-9319-3.

[7] J. L. Caplan, X. Zhu, P. Mamillapalli, R. Marathe, R. Anandalakshmi, and S. P. Dinesh-Kumar, Induced ER Chaperones Regulate a Receptor-like Kinase to Mediate Antiviral Innate Immune Response in Plants, *Cell Host Microbe*, 2009, doi: 10.1016/j.chom.2009.10.005.

[8] N. B. Butchi, M. Du, and K. E. Peterson, Interactions between TLR7 and TLR9 agonists and receptors regulate innate immune responses by astrocytes and microglia, *Glia*, 2010, doi: 10.1002/glia.20952.

[9] V. M. Bruno, S. Hannemann, M. Lara-Tejero, R. A. Flavell, S. H. Kleinstein, and J. E. Galán, Salmonella typhimurium type III secretion effectors stimulate innate immune responses in cultured epithelial cells, *PLoS Pathog.*, 2009, doi: 10.1371/journal.ppat.1000538.

[10] C. A. Colton, Heterogeneity of microglial activation in the innate immune response in the brain, *Journal of Neuroimmune Pharmacology*. 2009. doi: 10.1007/s11481-009-9164-4.

CHAPTER 4

ANTIGENS AND ANTIBODIES: UNDERSTANDING THE DYNAMICS OF IMMUNE SYSTEM

Dr.Kirti Singh, Assistant Professor
Department of Science, Maharishi University of Information Technology, Uttar Pradesh, India
Email Id- kirti.singh@muit.in

ABSTRACT:

Antigens are chemicals or structures that excite the immune system and cause it to respond. They can be present on the surfaces of pathogens such as bacteria and viruses, as well as within the body's own cells in situations of autoimmunity. Immune cells create antibodies, also known as immunoglobulins, in response to antigens. Antibodies have extremely specialized binding sites that allow them to detect and neutralize antigens. Opsonization marking pathogens for destruction, complement protein activation, and antibody-dependent cellular cytotoxicity immune cells targeting and eliminating antigen-bound cells are all part of this immune response. Antigens and antibodies are critical components of the body's immune system and vaccine defence. The Chapter on Antigens and Antibodies is a comprehensive exploration of the fundamental components of the immune system that underpin immune recognition and response. Antigens, which are substances capable of eliciting an immune response, and antibodies, the specialized proteins produced by the immune system in response to antigens, are central to our understanding of immunology. This Chapter delves into the molecular intricacies of antigens and the remarkable versatility and specificity of antibodies. It highlights their roles in immunity, immune memory, and the development of vaccines, shedding light on their clinical relevance in diagnostics and therapeutics**.**

KEYWORDS:

Adaptive Immunity, Allergies, Antibodies, Antigens, Autoimmune Diseases.

INTRODUCTION

The Chapter on Antigens and Antibodies embarks on a journey into the fascinating world of the immune system, focusing on two fundamental entities: antigens and antibodies. These components lie at the heart of immune recognition and response, serving as the building blocks upon which the body's defense mechanisms are constructed. Antigens, as the initiators of immune responses, are substances that trigger the immune system's attention. They can be molecules from pathogens like bacteria, viruses, and fungi, or even components of our own cells that become altered or abnormal. Understanding antigens is pivotal since they are the targets of immune surveillance, acting as the identifiers that dictate what is foreign and potentially harmful to the body [1], [2].Antibodies, on the other hand, are the immune system's specialized warriors. These remarkable proteins, produced by B cells, play an indispensable role in defending the body against antigens. Antibodies exhibit extraordinary versatility and specificity in recognizing and neutralizing antigens. Their ability to bind to antigens with remarkable precision not only helps eliminate pathogens but also marks them for destruction by other immune cells. This Chapter will delve into the molecular intricacies of antigens, examining the various forms they can take and the diversity of substances that can act as antigens. Furthermore, we will explore the structure and functions of antibodies, highlighting their roles in neutralization, opsonization, and the activation of complement proteins [3], [4].Antigens and antibodies are pivotal in the development of vaccines, a

cornerstone of modern medicine. Vaccines harness the immune system's memory and specificity, allowing it to recognize and respond swiftly and effectively to previously encountered antigens. The principles of antigen-antibody interactions underpin diagnostic tests, enabling the detection of infections, allergies, and autoimmune diseases. As we delve deeper into the world of antigens and antibodies, we will uncover their clinical relevance in fields ranging from immunology to diagnostics and therapeutics. These fundamental elements of the immune system not only contribute to our understanding of immune responses but also hold the key to innovative approaches for preventing and treating diseases [5], [6].

Antibodies are produced by B cells, a type of white blood cell. There are many distinct types of B cells in our bodies, and each one produces a different type of antibody. These antibodies are all the same and are known as monoclonal antibodies. It's like having an army of warriors all trained to battle a single adversary. Isn't it incredible? Antibodies are unusual proteins with a distinct four-chain structure. Two of these chains are lengthy and are referred to as heavy chains, while the other two are short and are referred to as light chains. Because they are spherical and contain sugars linked to them, these proteins are also known as globular glycoproteins. The beautiful thing about antibodies is that they have a constant portion and a changing part depending on what they need to combat. The variable region is the component that varies and binds to the specific bad object that needs to be killed. The constant region, on the other hand, remains constant and aids the antibody's attachment to cells such as B cells. The antigen-binding site is located near the end of the variable region and is the section of the antibody that really binds to the antigen. Finally, disulfide bridges, which act like super-strong glue, hold the four chains together.

The structure of an antibody is fundamental to its function, and the antigen-binding site is the most important portion. This site has a distinct and highly specific three-dimensional structure that allows it to bind only to complimentary antigens. Because antibodies are proteins, they may form very specialized structures that allow them to attach to certain antigens. This specificity is what distinguishes antibodies; they can be tailored to precisely target individual cells and pathogens, providing a robust and adaptive defence against a wide range of dangers. The distinctive 'Y' form is also significant. As you shall see later, the presence of two binding sites rather than one permits antibodies to bind to two distinct antigens at the same time. This is significant because it permits antibodies to efficiently 'clump' bacteria and other particles together.

Antibodies bind to antigens via specific binding sites found at the variable region's ends. Each binding site is made up of a specific sequence of amino acids that form a 3-D shape. This shape works well with a certain antigen. When an antibody and an antigen bind together, they produce an antigen-antibody complex. Antibodies act in an indirect manner by preparing antigens for destruction by phagocytes, which are specialized white blood cells that ingest and destroy infections. Antibodies' principal function is to tag antigens, making it easier for the immune system to recognize and eliminate them. Antibodies accomplish this in two key ways:

a. Antibodies bind to the antigen's surface, making it more visible to phagocytes. Opsonization is a process that makes it easier for phagocytes to engulf and eliminate antigens.

b. Antibodies can also activate the complement system, which is a group of proteins that work together to destroy infections. When antibodies bind to antigens, they activate the complement system, which results in a series of chemical events that kill the pathogen.

In general, antibodies serve an important function in the immune system by marking antigens for destruction and assisting in the activation of the body's defences. When antibodies bind to several antigens, they cluster together, creating agglutination. This method is particularly beneficial when dealing with organisms with numerous antigens on their surface. Antibodies can help phagocytes engulf and destroy infections by clumping these antigens together. Because antibodies have two binding sites, they can bind to two separate diseases or antigens on the same pathogen at the same time. This permits them to aggregate viruses into larger clumps, making it easier for the immune system to recognize and eliminate them. Overall, agglutination is a crucial technique that antibodies use to fight infections, and it demonstrates the immune system's amazing specificity and versatility.

DISCUSSION

Antigens, or immunogens, are substances or toxins in your blood that trigger your body to fight them. Antigens are usually bacteria or viruses, but they can be other substances from outside your body that threaten your health. This battle is called an immune response. The presence of antigens rouses your body's illness-fighting white blood cells, called lymphocytes. This presence of antigens causes white blood cells to make cells called antibodies to fight against the antigens.There are two main types of antigens, heteroantigens and autoantigens. Heteroantigens are substances that are foreign to your body and involve substances made by or found within:

a. Viruses.
b. Bacteria.
c. Protozoa.
d. Blood and red blood cells from other people.
e. Snake venom.
f. Allergens such as pollen.
g. Certain proteins in foods.

Autoantigens, or self-antigens, are made by your body to fight your cells and are usually a sign of an illness such as an autoimmune condition.Antibodies are also called immunoglobulins or Ig. They are Y-shaped proteins made by your immune system's B lymphocytes or B cells.B cells attack and eliminate viruses and other toxins outside the cell.

They do this by making specific antibodies for a single type of antigen.These tailored antibodies lock on to their specific antigens and tag them for attack. Antibodies also block these antigens, keeping them away from your healthy cells. Ultimately, antibodies kill these antigens, stopping infection.The main types of antibodies include:

a. IgG. These are the most abundant types of antibodies in your plasma. They detoxify harmful substances and provide long-term protection.
b. IgM. These are the first antibodies made by B cells in response to antigens.
c. IgA. These antibodies collect antigens and remove them from your body in your mucus or other body fluids.
d. IgE. These antibodies trigger allergies and protect against parasites. Small amounts are in your skin, lungs, and mucosal membranes.
e. IgD. These antibodies bind to B cells and signal them to release IgM antibodies.

Each antibody guards against its target antigen, and many types of antibodies are found throughout your body. They play a vital role in your body's defense against illness and disease.

Traditional vaccines

Vaccines include weakened or inactive parts of antigens from viral infections like the flu. These inactive antigens trigger your B cells to make targeted antibodies to fight that specific infection. Newer vaccines include the genetic blueprints for making antigens instead of using actual antigen components, but they work much in the same way [7], [8].Vaccines boost the number of antibodies in your body against a specific antigen. When a vaccine enters your body, your B-cells respond as if a naturally occurring antigen has attacked your body. The B-cells respond to the vaccine by reproducing themselves to form an army of cells that are programmed to react to the antigens in the vaccine.

The antibodies created by the vaccine lie dormant in your body until you contract an infection from that antigen, and then they are called to action. If you contract an infection, antibodies called memory B cells quickly reproduce and make the specific antibodies you need to destroy that antigen. The memory B-cells' response is called a secondary immune response, and it's much faster and more effective than the reaction your body would have to the infection if you had not been vaccinated.

Structure of Antibody

As mentioned above, an antibody is a protein molecule in the shape of Y. It has four polypeptide chains. Two are the light chains that are identical and short and the other two are identical and longer and are called the heavy chains. The light chains are represented as L and the heavy chains are represented as H. So, while representing an antibody, it is represented as H2 L2. Both the heavy chains and light chains are held together by disulfide bonds. Both these chains also have two regions called the distinct region and the variable region. It is the variable region of the antibody that sees the action happening. Here the lock and key mechanism occur along with the antigen that has adhered to the antibody [9], [10].

Antigens and Antibodies. Their role in Vaccinations

Antigens and antibodies have a significant role to play in vaccines. They are present in vaccines so that they can stimulate the B lymphocytes present in the immune system. Once these lymphocytes are stimulated, they respond and produce plasma cells which secrete the specific antibodies for that specific disease. There are some B cells that become memory cells which help in recognizing any future exposure to the disease. So, ultimately, this helps in the faster production of antibodies. These antibodies work efficiently and bind themselves to the antigens and thereby eliminate the disease.

CONCLUSION

In conclusion, the Chapter on Antigens and Antibodies has illuminated the intricate and indispensable roles that these fundamental components play within the immune system. Antigens, the initiators of immune responses, serve as the identifiers of foreign and potentially harmful substances, while antibodies, the immune system's specialized warriors, are the frontline defenders against these antigens. Throughout this exploration, we have delved into the molecular intricacies of antigens, understanding their diversity and significance. Antigens can encompass a wide range of substances, including those originating from pathogens, allergens, and even components of our own cells when they become altered or abnormal. Recognizing and responding to antigens are central to the immune system's ability to maintain health and combat diseases. Antibodies, the versatile proteins produced by B cells, have been showcased for their remarkable specificity and adaptability.

Their ability to recognize and bind to antigens with precision not only neutralizes pathogens but also plays a pivotal role in opsonization and the activation of complement proteins, further enhancing the immune response. The importance of antigens and antibodies extends beyond their roles in immune responses. They are the foundation of vaccine development, a groundbreaking medical achievement that harnesses the immune system's memory and specificity to prevent diseases. Additionally, the principles of antigen-antibody interactions form the basis of diagnostic tests, enabling the detection of infections, allergies, autoimmune diseases, and other medical conditions.

Antigens and antibodies are not static entities; they are central players in the dynamic interplay of the immune system. As research in immunology continues to advance, our understanding of these components deepens, leading to innovative approaches in diagnostics and therapeutics. From monoclonal antibody therapies to the development of vaccines against emerging pathogens, the clinical relevance of antigens and antibodies continues to expand. In summary, antigens and antibodies are not just biological entities; they are the keys to unlocking the secrets of immunity, health, and disease.

They provide insights into the intricacies of the immune response, offer diagnostic tools to detect diseases, and serve as the foundation for therapeutic interventions. As we continue to explore and harness the potential of antigens and antibodies, we unlock new possibilities for improving healthcare, advancing medical research, and safeguarding human well-being in an ever-evolving world of pathogens and challenges.

REFERENCES:

[1] P. Arenkov, A. Kukhtin, A. Gemmell, S. Voloshchuk, V. Chupeeva, and A. Mirzabekov, “Protein microchips: Use for immunoassay and enzymatic reactions,” *Anal. Biochem.*, 2000, doi: 10.1006/abio.1999.4363.

[2] M. Katayama, T. Sato, and J. Kuromitsu, “Capture molecules preconditioned for kinetic analysis of high-affinity antigen-antibody complex in Biacore A100,” *Anal. Biochem.*, 2012, doi: 10.1016/j.ab.2012.02.006.

[3] Y. J. Chang *et al.*, “Donor-specific anti-human leukocyte antigen antibodies were associated with primary graft failure after unmanipulated haploidentical blood and marrow transplantation: A prospective study with randomly assigned training and validation sets,” *J. Hematol. Oncol.*, 2015, doi: 10.1186/s13045-015-0182-9.

[4] S. Brust, H. Duttmann, J. Feldner, L. Gürtler, R. Thorstensson, and F. Simon, “Shortening of the diagnostic window with a new combined HIV p24 antigen and anti-HIV-1/2/O screening test,” *J. Virol. Methods*, 2000, doi: 10.1016/S0166-0934(00)00229-9.

[5] G. A. Canziani, S. Klakamp, and D. G. Myszka, “Kinetic screening of antibodies from crude hybridoma samples using Biacore,” *Anal. Biochem.*, 2004, doi: 10.1016/j.ab.2003.11.004.

[6] Y. Ogura *et al.*, “Haemophilus parainfluenzae antigen and antibody in children with IgA nephropathy and Henoch-Schonlein nephritis,” *Am. J. Kidney Dis.*, 2000, doi: 10.1053/ajkd.2000.8264.

[7] C. L. Lau *et al.*, "Seroprevalence and Spatial Epidemiology of Lymphatic Filariasis in American Samoa after Successful Mass Drug Administration," *PLoS Negl. Trop. Dis.*, 2014, doi: 10.1371/journal.pntd.0003297.

[8] A. Cardinale, I. Filesi, and S. Biocca, "Aggresome formation by anti-Ras intracellular scFv fragments. The fate of the antigen-antibody complex," *Eur. J. Biochem.*, 2001, doi: 10.1046/j.1432-1327.2001.01876.x.

[9] K. A. Gustaw *et al.*, "Antigen-antibody dissociation in Alzheimer disease: A novel approach to diagnosis," *J. Neurochem.*, 2008, doi: 10.1111/j.1471-4159.2008.05477.x.

[10] D. Spector *et al.*, "Antigen and antibody testing for the diagnosis of blastomycosis in dogs," *J. Vet. Intern. Med.*, 2008, doi: 10.1111/j.1939-1676.2008.0107.x.

CHAPTER 5

THE ADAPTIVE IMMUNE RESPONSE: MOLECULAR DEFENCES MECHANISM

Dr.Kirti Singh, Assistant Professor
Department of Science, Maharishi University of Information Technology, Uttar Pradesh, India
Email Id- kirti.singh@muit.in

ABSTRACT:

The Chapter on The Adaptive Immune Response offers a comprehensive exploration of the remarkable and highly specialized defense mechanisms that constitute the adaptive arm of the immune system. The body's natural and learned defense systems against disease. Innate immune responses happen when harmful germs invade our bodies and protect all living things with more than one cell from getting sick. In animals with backbones, germs, along with the natural defenses they trigger, encourage a more specialized form of protection. The adaptive immune response, characterized by specificity, memory, and the ability to distinguish between self and non-self, plays a pivotal role in defending the body against pathogens, preventing reinfection, and maintaining immune health. This Chapter delves into the development and functions of lymphocytes, including B cells and T cells, the generation of immune memory, and the orchestrated response to antigens. It also explores the clinical implications of adaptive immunity, from vaccination to the treatment of autoimmune diseases and cancer immunotherapy.

KEYWORDS:

Antibodies, Antigen Recognition, B Cells, Cell-Mediated Immunity, Clonal Selection.

INTRODUCTION

The adaptive, or acquired, immune response takes days or even weeks to become establishedmuch longer than the innate response; however, adaptive immunity is more specific to pathogens and has memory. Adaptive immunity is an immunity that occurs after exposure to an antigen either from a pathogen or a vaccination. This part of the immune system is activated when the innate immune response is insufficient to control an infection. In fact, without information from the innate immune system, the adaptive response could not be mobilized. There are two types of adaptive responses: the cell-mediated immune response, which is carried out by T cells, and the humoral immune response, which is controlled by activated B cells and antibodies. Activated T cells and B cells that are specific to molecular structures on the pathogen proliferate and attack the invading pathogen. Their attack can kill pathogens directly or secrete antibodies that enhance the phagocytosis of pathogens and disrupt the infection. Adaptive immunity also involves a memory to provide the host with long-term protection from reinfection with the same type of pathogen; on re-exposure, this memory will facilitate an efficient and quick response.

Our ability to adapt and fight off infections keeps us from dying. A baby born with a very weak immune system will die if it is not kept away from germs, like bacteria, viruses, fungi, and parasites. Yes, all organisms made up of many cells have to protect themselves from harmful invaders called pathogens. Insects and other creatures without backbones have straightforward ways to defend themselves. They use barriers, chemicals that are harmful, and cells that eat and eliminate harmful microorganisms and larger parasites. Animals with backbones also rely on natural immune responses as a first line of defense, but they can also

have more advanced defenses called adaptive immune responses. The natural responses in our body signal the immune responses to start working, and they both work together to get rid of the harmful germs. Unlike the automatic immune responses, the adaptable responses are very specific to the specific germ that caused them. They can also keep you protected for a long time. When someone gets better from measles, their body's immune system remembers how to fight against measles in the future. But they are not protected from other viruses like mumps or chickenpox. In this Chapter, we mainly talk about how our bodies adapt to fight diseases. When we say immune responses, we generally mean the adaptive ones.

The job of the adaptive immune system is to get rid of harmful germs and the harmful substances they make. It is important to only respond with destructive actions to foreign molecules and not to the molecules of the host itself. Being able to tell apart things that are not part of our body from things that are is an important part of our immune system. Sometimes, the system doesn't recognize the difference and harms the host's own molecules. These types of immune diseases can cause death. Yes, there are many foreign molecules that can enter the body without causing harm. It would be unnecessary and possibly risky to activate the immune system against them. Allergy conditions like hay fever and asthma are when the immune system reacts badly to seemingly harmless things from outside the body. Normally, we try not to give improper responses because our body's natural defenses innate immune system only activates our specific defenses when it recognizes certain molecules from harmful germs, which are called pathogen-associated immunostimulants. Additionally, the natural defense system of our body can differentiate between different types of harmful substances and call upon the most efficient way to fight them off.

Any substance that can cause our immune system to respond is called an antigen or a generator of antibodies. We have learned a lot about these responses by doing experiments on animals, usually mice. In these experiments, scientists trick the animal's immune system into reacting to a harmless foreign substance, like a different protein. The trick is to inject a harmless molecule along with immune boosters usually from bacteria called adjuvants, which activate the body's natural defense system. This process is called getting a shot to protect against diseases. If given like this, almost any large molecule, as long as it is not native to the person receiving it, can cause an immune response that is directed specifically towards that molecule. Surprisingly, our immune system can tell the difference between similar things, like two proteins that are almost the same or two versions of the same molecule that look alike.

The body's defense system, consisting of white blood cells called lymphocytes, is responsible for adaptive immune responses. There are two main types of responses in our immune system antibody responses and cell-mediated immune responses. These responses are carried out by different types of lymphocytes, known as B cells and T cells. When the body fights off germs or infections, B cells are told to make special proteins called antibodies. These antibodies help to protect the body and fight off the germs or infections. The antibodies move around in the blood and other body fluids. They attach to the foreign antigen that caused them to be created. When an antibody binds to viruses or toxins, it stops them from attaching to our cells and causing harm. When antibodies bind to pathogens, it helps the immune system's cells to destroy them more easily. These cells can then consume the pathogens to eliminate them.

Activated T cells react directly against a foreign antigen presented to them on the surface of a host cell in cell-mediated immune responses, the second type of adaptive immune response. The T cell, for example, may destroy a virus-infected host cell with viral antigens on its surface, so removing the virus before it has a chance to proliferate. In other circumstances, the T cell generates signal molecules that stimulate macrophages to eliminate the

phagocytosed invading microorganisms.This Chapter begins by examining the general features of lymphocytes. The functional and structural characteristics of antibodies that allow them to recognize and neutralize extracellular bacteria and the poisons they produce are then discussed. Following that, we'll look at how B cells can generate an almost infinite number of distinct antibody molecules. Finally, we look at T cells' unique characteristics and the cell-mediated immune responses they are responsible for. Surprisingly, T cells can detect germs hidden inside host cells and either destroy or assist other cells in eliminating the microbes.

DISCUSSION

Unlike NK cells of the innate immune system, B cells (B lymphocytes) are a type of white blood cell that gives rise to antibodies, whereas T cells (T lymphocytes) are a type of white blood cell that plays an important role in the immune response. T cells are a key component in the cell-mediated responsethe specific immune response that utilizes T cells to neutralize cells that have been infected with viruses and certain bacteria. There are three types of T cells: cytotoxic, helper, and suppressor T cells. Cytotoxic T cells destroy virus-infected cells in the cell-mediated immune response, and helper T cells play a part in activating both the antibody and the cell-mediated immune responses. Suppressor T cells deactivate T cells and B cells when needed, and thus prevent the immune response from becoming too intense [1], [2].

Antigen-presenting Cells

An antigen is a foreign or non-self macromolecule that reacts with cells of the immune system. Not all antigens will provoke a response. For instance, individuals produce innumerable self antigens and are constantly exposed to harmless foreign antigens, such as food proteins, pollen, or dust components. The suppression of immune responses to harmless macromolecules is highly regulated and typically prevents processes that could be damaging to the host, known as tolerance. The innate immune system contains cells that detect potentially harmful antigens, and then inform the adaptive immune response about the presence of these antigens. An antigen-presenting cell (APC) is an immune cell that detects, engulfs, and informs the adaptive immune response about an infection.

When a pathogen is detected, these APCs will phagocytose the pathogen and digest it to form many different fragments of the antigen. Antigen fragments will then be transported to the surface of the APC, where they will serve as an indicator to other immune cells. Dendritic cells are immune cells that process antigen material; they are present in the skin and the lining of the nose, lungs, stomach, and intestines. Sometimes a dendritic cell presents on the surface of other cells to induce an immune response, thus functioning as an antigen-presenting cell. Macrophages also function as APCs. Before activation and differentiation, B cells can also function as APCs [3], [4].

After phagocytosis by APCs, the phagocytic vesicle fuses with an intracellular lysosome forming phagolysosome. Within the phagolysosome, the components are broken down into fragments; the fragments are then loaded onto MHC class I or MHC class II molecules and are transported to the cell surface for antigen presentation. Note that T lymphocytes cannot properly respond to the antigen unless it is processed and embedded in an MHC II molecule. APCs express MHC on their surfaces, and when combined with a foreign antigen, these complexes signal a non-self-invader. Once the fragment of antigen is embedded in the MHC II molecule, the immune cell can respond. Helper T- cells are one of the main lymphocytes that respond to antigen-presenting cells. Recall that all other nucleated cells of the body expressed MHC I molecules, which signal healthy or normal

T and B Lymphocytes

T cells encompass a heterogeneous population of cells with extremely diverse functions. Some T cells respond to APCs of the innate immune system, and indirectly induce immune responses by releasing cytokines. Other T cells stimulate B cells to prepare their own response. Another population of T cells detects APC signals and directly kills the infected cells. Other T cells are involved in suppressing inappropriate immune reactions to harmless or self-antigens. T and B cells exhibit a common theme of recognition/binding of specific antigens via a complementary receptor, followed by activation and self-amplification/maturation to specifically bind to the particular antigen of the infecting pathogen. T and B lymphocytes are also similar in that each cell only expresses one type of antigen receptor.

Any individual may possess a population of T and B cells that together express a near limitless variety of antigen receptors that are capable of recognizing virtually any infecting pathogen. T and B cells are activated when they recognize small components of antigens, called epitopes, presented by APCs, note that recognition occurs at a specific epitope rather than on the entire antigen; for this reason, epitopes are known as antigenic determinants. In the absence of information from APCs, T and B cells remain inactive, or naïve, and are unable to prepare an immune response. The requirement for information from the APCs of innate immunity to trigger B cell or T cell activation illustrates the essential nature of the innate immune response to the functioning of the entire immune system [5], [6].

Naïve T cells can express one of two different molecules, CD4 or CD8, on their surface, and are accordingly classified as $CD4^+$ or $CD8^+$ cells. These molecules are important because they regulate how a T cell will interact with and respond to an APC. Naïve $CD4^+$ cells bind APCs via their antigen-embedded MHC II molecules and are stimulated to become helper T (T_H) lymphocytes, cells that go on to stimulate B cells (or cytotoxic T cells) directly or secrete cytokines to inform more and various target cells about the pathogenic threat. In contrast, $CD8^+$ cells engage antigen-embedded MHC I molecules on APCs and are stimulated to become cytotoxic T lymphocytes (CTLs)**,** which directly kill infected cells by apoptosis and emit cytokines to amplify the immune response. The two populations of T cells have different mechanisms of immune protection, but both bind MHC molecules via their antigen receptors called T cell receptors (TCRs). The CD4 or CD8 surface molecules differentiate whether the TCR will engage an MHC II or an MHC I molecule. Because they assist in binding specificity, the CD4 and CD8 molecules are described as coreceptors[7], [8].

Helper T Lymphocytes

The T_H lymphocytes function indirectly to identify potential pathogens for other cells of the immune system. These cells are important for extracellular infections, such as those caused by certain bacteria, helminths, and protozoa. T_H lymphocytes recognize specific antigens displayed in the MHC II complexes of APCs. There are two major populations of T_H cells: T_H1 and T_H2. T_H1 cells secrete cytokines to enhance the activities of macrophages and other T cells. T_H1 cells activate the action of cyotoxic T cells, as well as macrophages. T_H2 cells stimulate naïve B cells to destroy foreign invaders via antibody secretion. Whether a T_H1 or a T_H2 immune response develops depends on the specific types of cytokines secreted by cells of the innate immune system, which in turn depends on the nature of the invading pathogen.

The T_H1-mediated response involves macrophages and is associated with inflammation. Recall the frontline defenses of macrophages involved in the innate immune response. Some intracellular bacteria, such as *Mycobacterium tuberculosis*, have evolved to multiply in macrophages after they have been engulfed. These pathogens evade attempts by macrophages

to destroy and digest the pathogen. When *M. tuberculosis* infection occurs, macrophages can stimulate naïve T cells to become T_H1 cells. These stimulated T cells secrete specific cytokines that send feedback to the macrophage to stimulate its digestive capabilities and allow it to destroy the colonizing *M. tuberculosis*. In the same manner, T_H1-activated macrophages also become better suited to ingest and kill tumor cells. In summary; T_H1 responses are directed toward intracellular invaders while T_H2 responses are aimed at those that are extracellular.

B Lymphocytes

When stimulated by the T_H2 pathway, naïve B cells differentiate into antibody-secreting plasma cells. A plasma cell is an immune cell that secrets antibodies; these cells arise from B cells that were stimulated by antigens. Similar to T cells, naïve B cells initially are coated in thousands of B cell receptors (BCRs), which are membrane-bound forms of Ig. The B cell receptor has two heavy chains and two light chains connected by disulfide linkages. Each chain has a constant and a variable region; the latter is involved in antigen binding. Two other membrane proteins, Ig alpha and Ig beta, are involved in signaling. The receptors of any particular B cell, as shown in are all the same, but the hundreds of millions of different B cells in an individual have distinct recognition domains that contribute to extensive diversity in the types of molecular structures to which they can bind. In this state, B cells function as APCs. They bind and engulf foreign antigens via their BCRs and then display processed antigens in the context of MHC II molecules to T_H2 cells. When a T_H2 cell detects that a B cell is bound to a relevant antigen, it secretes specific cytokines that induce the B cell to proliferate rapidly, which makes thousands of identical copies of it, and then it synthesizes and secretes antibodies with the same antigen recognition pattern as the BCRs. The activation of B cells corresponding to one specific BCR variant and the dramatic proliferation of that variant is known as clonal selection.

This phenomenon drastically, but briefly, changes the proportions of BCR variants expressed by the immune system, and shifts the balance toward BCRs specific to the infecting pathogen.T and B cells differ in one fundamental way: whereas T cells bind antigens that have been digested and embedded in MHC molecules by APCs, B cells function as APCs that bind intact antigens that have not been processed. Although T and B cells both react with molecules that are termed antigens, these lymphocytes actually respond to very different types of molecules. B cells must be able to bind intact antigens because they secrete antibodies that must recognize the pathogen directly, rather than digested remnants of the pathogen. Bacterial carbohydrate and lipid molecules can activate B cells independently from the T cells [9], [10]. CTLs, a subclass of T cells, function to clear infections directly. The cell-mediated part of the adaptive immune system consists of CTLs that attack and destroy infected cells. CTLs are particularly important in protecting against viral infections; this is because viruses replicate within cells where they are shielded from extracellular contact with circulating antibodies. When APCs phagocytize pathogens and present MHC I-embedded antigens to naïve $CD8^+$ T cells that express complementary TCRs, the $CD8^+$ T cells become activated to proliferate according to clonal selection. These resulting CTLs then identify non-APCs displaying the same MHC I-embedded antigens for example, viral proteins for example, the CTLs identify infected host cells.

Intracellularly, infected cells typically die after the infecting pathogen replicates to a sufficient concentration and lyses the cell, as many viruses do. CTLs attempt to identify and destroy infected cells before the pathogen can replicate and escape, thereby halting the progression of intracellular infections. CTLs also support NK lymphocytes to destroy early cancers. Cytokines secreted by the T_H1 response that stimulates macrophages also stimulate

CTLs and enhance their ability to identify and destroy infected cells and tumors. CTLs sense MHC I-embedded antigens by directly interacting with infected cells via their TCRs. Binding of TCRs with antigens activates CTLs to release perforin and granzyme, degradative enzymes that will induce apoptosis of the infected cell. Recall that this is a similar destruction mechanism to that used by NK cells. In this process, the CTL does not become infected and is not harmed by the secretion of perforin and granzymes. In fact, the functions of NK cells and CTLs are complementary and maximize the removal of infected cells, as illustrated in Figure 1. If the NK cell cannot identify the missing self pattern of down-regulated MHC I molecules, then the CTL can identify it by the complex of MHC I with foreign antigens, which signals altered self. Similarly, if the CTL cannot detect antigen-embedded MHC I because the receptors are depleted from the cell surface, NK cells will destroy the cell instead. CTLs also emit cytokines, such as interferons, that alter surface protein expression in other infected cells, such that the infected cells can be easily identified and destroyed. Moreover, these interferons can also prevent virally infected cells from releasing virus particles.

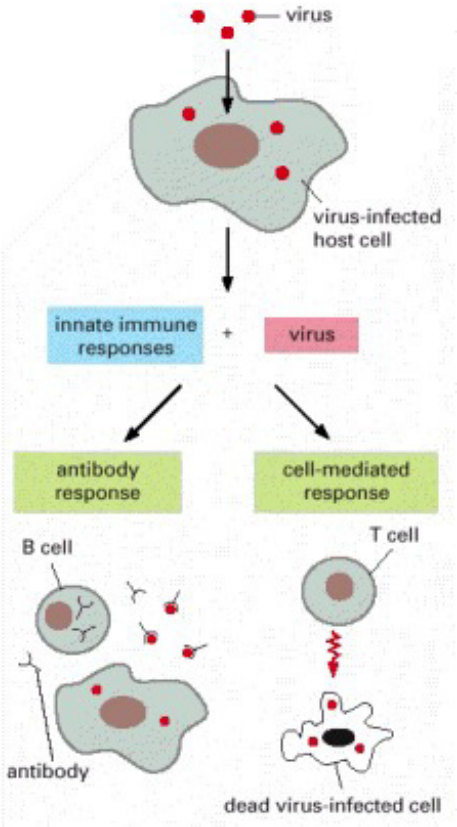


Figure 1: Representing the two main class of adaptive immune system [NCBI].

Mucosal Surfaces and Immune Tolerance

The innate and adaptive immune responses discussed thus far comprise the systemic immune system affecting the whole body, which is distinct from the mucosal immune system. Mucosal immunity is formed by mucosa-associated lymphoid tissue, which functions independently of the systemic immune system, and which has its own innate and adaptive components. Mucosa-associated lymphoid tissue (MALT), is a collection of lymphatic tissue that combines with epithelial tissue lining the mucosa throughout the body. This tissue functions as the immune barrier and response in areas of the body with direct contact to the external environment.

The systemic and mucosal immune systems use many of the same cell types. Foreign particles that make their way to MALT are taken up by absorptive epithelial cells called M cells and delivered to APCs located directly below the mucosal tissue. M cells function in the transport described, and are located in the Peyer's patch, a lymphoid nodule. APCs of the mucosal immune system are primarily dendritic cells, with B cells and macrophages having minor roles. Processed antigens displayed on APCs are detected by T cells in the MALT and at various mucosal induction sites, such as the tonsils, adenoids, appendix, or the mesenteric lymph nodes of the intestine. Activated T cells then migrate through the lymphatic system and into the circulatory system to mucosal sites of infection.

Immunological Memory

The adaptive immune system possesses a memory component that allows for an efficient and dramatic response upon reinvasion of the same pathogen. Memory is handled by the adaptive immune system with little reliance on cues from the innate response. During the adaptive immune response to a pathogen that has not been encountered before, called a primary response, plasma cells secreting antibodies and differentiated T cells increase, then plateau over time. As B and T cells mature into effector cells, a subset of the naïve populations differentiates into B and T memory cells with the same antigen specificities. A memory cell is an antigen-specific B or T lymphocyte that does not differentiate into effector cells during the primary immune response, but that can immediately become effector cells upon re-exposure to the same pathogen. During the primary immune response, memory cells do not respond to antigens and do not contribute to host defenses. As the infection is cleared and pathogenic stimuli subside, the effectors are no longer needed, and they undergo apoptosis. In contrast, the memory cells persist in the circulation.

Vaccinologist

Vaccination involves the delivery, usually by injection as shown of noninfectious antigen derived from known pathogens. Other components, called adjuvants, are delivered in parallel to help stimulate the immune response. Immunological memory is the reason vaccines work. Ideally, the effect of vaccination is to elicit immunological memory, and thus resistance to specific pathogens without the individual having to experience an infection.Vaccinologists are involved in the process of vaccine development from the initial idea to the availability of the completed vaccine. This process can take decades, can cost millions of dollars, and can involve many obstacles along the way.

For instance, injected vaccines stimulate the systemic immune system, eliciting humoral and cell-mediated immunity, but have little effect on the mucosal response, which presents a challenge because many pathogens are deposited and replicate in mucosal compartments, and the injection does not provide the most efficient immune memory for these disease agents. For this reason, vaccinologists are actively involved in developing new vaccines that are applied via intranasal, aerosol, oral, or transcutaneous absorbed through the skin delivery methods. Importantly, mucosal-administered vaccines elicit both mucosal and systemic immunity and produce the same level of disease resistance as injected vaccines.

CONCLUSION

The adaptive immune response is a slower-acting, longer-lasting, and more specific response than the innate response. However, the adaptive response requires information from the innate immune system to function. APCs display antigens via MHC molecules to complementary naïve T cells. In response, the T cells differentiate and proliferate, becoming T_H cells or CTLs.

T_H cells stimulate B cells that have engulfed and presented pathogen-derived antigens. B cells differentiate into plasma cells that secrete antibodies, whereas CTLs induce apoptosis in intracellularly infected or cancerous cells. Memory cells persist after a primary exposure to a pathogen. If re-exposure occurs, memory cells differentiate into effector cells without input from the innate immune system. The mucosal immune system is largely independent from the systemic immune system but functions in a parallel fashion to protect the extensive mucosal surfaces of the body.

REFERENCES:

[1] M. Bateni, A. Baraani, A. Ghorbani, and A. Rezaei, An ais-inspired architecture for alert correlation, *Int. J. Innov. Comput. Inf. Control*, 2013.

[2] P. Lusso, Chemokines and viruses: The dearest enemies, *Virology*, 2000, doi: 10.1006/viro.2000.0443.

[3] B. P. M. Verhaegh, M. J. Pierik, D. Goudkade, Y. S. M. T. Cuijpers, A. A. M. Masclee, and D. M. A. E. Jonkers, Early Life Exposure, Lifestyle, and Comorbidity as Risk Factors for Microscopic Colitis: A Case-Control Study, *Inflamm. Bowel Dis.*, 2017, doi: 10.1097/MIB.0000000000001103.

[4] F. M. Menzies, M. C. Shepherd, R. J. Nibbs, and S. M. Nelson, The role of mast cells and their mediators in reproduction, pregnancy and labour, *Hum. Reprod. Update*, 2011, doi: 10.1093/humupd/dmq053.

[5] H. Agaisse, An Adaptive Immune Response in Drosophila?, *Cell Host and Microbe*. 2007. doi: 10.1016/j.chom.2007.04.003.

[6] L. A. Zenewicz and H. Shen, Innate and adaptive immune responses to Listeria monocytogenes: a short overview, *Microbes and Infection*. 2007. doi: 10.1016/j.micinf.2007.05.008.

[7] M. R. Foote, B. J. Nonnecke, D. C. Beitz, and W. R. Waters, High growth rate fails to enhance adaptive immune responses of neonatal calves and is associated with reduced lymphocyte viability, *J. Dairy Sci.*, 2007, doi: 10.3168/jds.S0022-0302(07)72641-3.

[8] M. J. Cameron, J. F. Bermejo-Martin, A. Danesh, M. P. Muller, and D. J. Kelvin, Human immunopathogenesis of severe acute respiratory syndrome (SARS), *Virus Res.*, 2008, doi: 10.1016/j.virusres.2007.02.014.

[9] J. R. Schoenborn and C. B. Wilson, Regulation of Interferon-γ During Innate and Adaptive Immune Responses, *Advances in Immunology*. 2007. doi: 10.1016/S0065-2776(07)96002-2.

[10] E. J. Giamarellos-Bourboulis *et al.*, Altered innate and adaptive immune responses in patients with hidradenitis suppurativa, *Br. J. Dermatol.*, 2007, doi: 10.1111/j.1365-2133.2006.07556.x.

CHAPTER 6

B CELLS AND ANTIBODY PRODUCTION: TYPES AND FUNCTIONS

Dr.Ramakant, Assistant Professor
Department of Science, Maharishi University of Information Technology, Uttar Pradesh, India
Email Id- ramakant@muit.in

ABSTRACT:

The Chapter on B Cells and Antibody Production offers a comprehensive exploration of the specialized immune cells known as B cells and their pivotal role in the production of antibodies, essential components of the adaptive immune response. This Chapter delves into the development, activation, and functions of B cells, as well as the intricacies of antibody generation. It explores the remarkable diversity of antibodies, their mechanisms of action, and their significance in immune defense, immunological memory, diagnostics, and therapeutics.B cells, which originate in the bone marrow, are in charge of producing five types of antibodies, each with its unique purpose. B cells have their own tolerance mechanisms, however in peripheral tolerance, B cells that exit the bone marrow remain dormant due to T cell tolerance. Some B cells do not require T cell cytokines to produce antibody, and they do it by crosslinking their surface immunoglobulin with repeating carbohydrate residues found in many bacterial cell walls. Others necessitate the activation of T lymphocytes.

KEYWORDS:

Adaptive Immunity, Affinity Maturation, Antibody Diversity, B Cell Activation, Clonal Expansion.

INTRODUCTION

The Chapter on B Cells and Antibody Production delves into the intricate and highly specialized world of B cells, key players in the adaptive immune system, and the remarkable process of antibody production. This introduction serves as a gateway to understanding the central roles that B cells and antibodies play in the body's immune defense mechanisms. B cells are lymphocytes that play a crucial role in humoral immunity. Their journey begins in the bone marrow, where they undergo development and maturation, leading to the formation of a diverse repertoire of B cell receptors (BCRs). These BCRs are the key to B cells' ability to recognize and respond to a vast array of antigens.The hallmark of B cells is their capacity to generate antibodies, also known as immunoglobulins (Igs). These Y-shaped proteins possess an astonishing level of specificity, enabling them to bind to antigens with incredible precision. Antibodies act as the immune system's sentinels, patrolling the body to identify and neutralize harmful pathogens. This Chapter will explore the life cycle of B cells, from their development and activation to the processes of clonal expansion and antibody production. One of the remarkable features of B cells is their ability to undergo affinity maturation and somatic hypermutation, processes that enhance the specificity and effectiveness of the antibodies they produce [1], [2].

Furthermore, we will delve into the formation of memory B cells, a critical aspect of immunological memory. These long-lived cells remember encountered antigens, facilitating rapid and targeted immune responses upon re-exposure, a cornerstone of effective vaccines. The clinical relevance of B cells and antibody production is immense. Antibodies are utilized in diagnostics, enabling the detection of infections and other medical conditions. They also

serve as the basis for monoclonal antibody therapies, which have revolutionized the treatment of various diseases, including cancer and autoimmune disorders. As we journey through this Chapter, we will uncover the elegance and complexity of B cells and antibody production. Their roles extend beyond immunity to diagnostics, therapeutics, and the development of novel medical interventions. They stand as guardians of health, defending the body against pathogens and leaving an indelible mark on the landscape of immunology and medical science.Antibodies were the first component of the adaptive immune response to be identified by immune system researchers. Individuals who survived a bacterial infection were already immune to re-infection with the same germ. Early microbiologists examined germs under a microscope after mixing serum from an immunological patient with a fresh culture of the same species of bacterium. Agglutination is the mechanism by which bacteria clump together. The agglutination did not occur when a different bacterial species was utilized. As a result, there was something in immune persons' serum that could particularly attach to and agglutinate germs.

Scientists have discovered that the cause of the agglutination is an antibody molecule, commonly known as an immunoglobulin. What exactly is an antibody? An antibody protein is essentially a B cell receptor that has been released. The B cell receptor is also known as surface immunoglobulin. Surprisingly, both secreted antibodies and surface immunoglobulins are encoded by the same genes. A little change in how these proteins is generated distinguishes a naive B cell with antibody on its surface from an antibody-secreting plasma cell with no antibodies on its surface. Plasma cell antibodies have the same antigen-binding location and specificity as their B cell ancestors. Human antibodies are classified into five types: IgM, IgD, IgG, IgA, and IgE. Each of these has a distinct function in the immune response, so researchers can learn about the wide range of antibody functions that are crucial to various adaptive immune responses by studying them. B cells do not identify antigen in the same complicated way as T cells do. B cells can identify native, unprocessed antigen without the involvement of MHC molecules or antigen-presenting cells.

B cells develop in the bone marrow. During the maturation process, up to 100 trillion distinct clones of B cells are produced, equivalent to the diversity of antigen receptors seen in T cells. B cell differentiation and tolerance development are not as well understood as T cell differentiation and tolerance development. Central tolerance is the destruction or inactivation of B lymphocytes in the bone marrow that detect self-antigens, and its significance is crucial and well documented. Immature B lymphocytes that attach tightly to self-antigens produced on tissues are signalled to commit suicide by apoptosis, removing them from the population, during the clonal deletion process. However, in the process of clonal anergy, B cells exposed to soluble antigen in the bone marrow are not physically destroyed, but instead become inactive. T cell tolerance results in another process known as peripheral tolerance. In peripheral tolerance, mature, functioning B lymphocytes exit the bone marrow but are not yet exposed to self-antigen. Most protein antigens require signals from helper T cells (Th2) before antibody production may begin. When a B cell adheres to a self-antigen but receives no signals to manufacture antibodies from a nearby Th2 cell, the cell is signalled to undergo apoptosis and is killed. This is just another illustration of T cells' control over the adaptive immune response.

B cells develop into plasma cells after being stimulated by antigen binding. Plasma cells frequently leave secondary lymphoid organs, where the response is created, and move back to bone marrow, where the differentiation process began. They perish after a certain length of secreting antibodies since the majority of their energy is spent to generating antibodies rather than maintaining themselves. As a result, plasma cells are considered terminally

differentiated. The memory B cell, which emerges from the clonal proliferation of an activated B cell, is the final B cell of importance. Memory B cells work similarly to memory T cells. They result in a stronger and faster secondary response than the main response, as seen below. Antibodies are glycoproteins made up of two types of polypeptide chains with carbohydrates attached. The antibody is made up of two polypeptides: the heavy chain and the light chain. The main variations between antibody classes are in their heavy chains, but as you will see, the light chains play a crucial function, forming part of the antigen-binding site on the antibody molecules. There are two identical heavy chains and two identical light chains in all antibody molecules. Some antibodies have more than one unit of this four-chain structure. The Fc region of an antibody is generated by the joining of two heavy chains, which are normally linked by disulfide bonds. The Fc component of the antibody is significant because many immune system effector cells contain Fc receptors. These receptor-containing cells can then bind to antibody-coated pathogens, dramatically improving the specificity of the effector cells. Two identical antigen-binding sites are located at the other end of the molecule. B cells and T cells both undergo clonal selection and growth. Only B lymphocytes with the proper antigen specificity are chosen and grown. Eventually, the plasma cells release antibodies with the same antigenic specificity as those seen on the surfaces of the chosen B cells. Notice how both plasma cells and memory B cells are created at the same time. We have covered primary and secondary responses in relation to T cells. This section will look at B cell responses and antibody synthesis. Because antibodies can be acquired simply from blood samples, they are simple to track and graph. The major response to an antigen representing a disease is delayed by many days, as seen in the image. This is the amount of time required for B cell clones to grow and develop into plasma cells. Although the amount of antibody produced is minimal, it is sufficient for immunological protection. There is no time delay the second time a person encounters the same antigen, and the amount of antibody produced is substantially higher. As a result, the secondary antibody response swiftly overwhelms the pathogens, and in most cases, no symptoms are detected. When a new antigen is employed, a distinct initial response is elicited, with low antibody levels and a temporal lag.

Immunity to pathogens, as well as the ability to control pathogen growth so that damage to body tissues is limited, can be acquired through either active development of an immune response in the infected individual or passive transfer of immune components from an immune individual to a nonimmune one. There are examples of both active and passive immunity in nature and in medicine. Active immunity is resistance to infections gained during an individual's adaptive immune response. This Chapter focuses on naturally acquired active immunity, or the response to a pathogen. Vaccines are used to induce artificially acquired active immunity. A vaccination is a pathogen or its components that, when delivered to a healthy person, causes the establishment of immunological memory a reduced initial immune response without causing any symptoms. Thus, by using vaccines, one can prevent the disease-causing harm caused by the pathogen's first encounter while reaping the benefits of immunological memory protection. Vaccines were one of the most significant medical achievements of the twentieth century, leading to the abolition of smallpox and the control of many infectious illnesses such as polio, measles, and whooping cough.

Passive immunity occurs when antibodies are transferred to an individual without forcing them to generate their own active immune response. During fetal development, naturally acquired passive immunity is observed. IgG is passed from the maternal blood to the fetus via the placenta, protecting the fetus and the infant for the first few months of life. As previously established, a newborn benefit from the IgA antibodies obtained during breastfeeding. The fetus and infant thereby benefit from the mother's immunological recall of pathogens to

which she has been exposed. In medicine, artificially acquired passive immunity is typically achieved through the administration of immunoglobulins derived from animals that have already been exposed to a specific disease. This is a quick-acting means of temporarily shielding someone who has been exposed to a virus. The disadvantage of both types of passive immunity is the lack of immunological memory building. Once the antibodies are delivered, they are only potent for a short period of time before degrading.

DISCUSSION

B-cells are a type of white blood cell that makes infection-fighting proteins called antibodies. B-cells are an important part of your immune system, your body's defense against harmful pathogens that enter your body and make you sick. B-cells and T-cells are a specific type of white blood cell called lymphocytes. Lymphocytes fight harmful invaders and abnormal cells, like cancer cells. T-cells protect you by destroying pathogens and sending signals that help coordinate your immune system's response to threats. B-cells make antibodies in response to antigens. Antigens are markers that allow your immune system to identify substances in your body, including harmful ones like viruses and bacteria.[3], [4]

B-cells are also called B lymphocytes.

What are the different types of B-cells?

There are two main types of B-cells: plasma cells and memory cells. Both types help protect you from infection and disease.

a. **Plasma cells**: Plasma cells release antibodies in response to antigens. Once a B-cell becomes a mature plasma cell, it can release up to 2,000 antibodies per second. Plasma cells are also called plasmacytes or effector cells. They have a shorter lifespan than memory cells.
b. **Memory cells**: Memory cells remember particular antigens so, if they appear in your body in the future, your immune system can mount a defense quickly. While plasma cells fight bodily invaders by producing antibodies, memory cells help your immune system fight in the future. For example, most vaccines work because they expose your immune system to antigens that your memory cells remember. If an invader appears, your body can mount an attack quickly.

Why are B-cells important?

B-cells are an important part of your adaptive immune system. Your immune system includes your innate immune system and your adaptive immune system. While your innate immune system is your first defense against any threat, your adaptive immune system is specialized to recognize and fight particular types of threats. B-cells produce antibodies that destroy antigens or the pathogen associated with a particular antigen. B-cells can also remember specific antigens so your immune system can launch an effective defense if the pathogen ever enters your body again [5], [6].

How do B-cells work in the immune system?

B-cells work with other cells in your immune system to fight harmful invaders that can make you sick and abnormal cells, like cancer cells. Once B-cells are activated, they become plasma cells that produce antibodies in response to an antigen. Or they become memory cells that remember the antigen so your immune system can quickly identify and fight it in the future.Generally, the following steps occur when your immune system needs B-cells to fight invaders:

a. An antigen-presenting cell (APC) attaches to the antigen, breaking it down into smaller pieces. The APC attaches the antigen pieces to a molecule called the major histocompatibility-II complex, or MHC-II.
b. Helper T-cells (a type of T-cell) bind to the MHC-II complex. This binding activates helper T-cells. Activated helper T-cells are important because they spur B-cells into action.
c. An activated T-cell attaches to a B-cell, causing it to make copies, or clones, of itself. Some of the B-cells become plasma cells capable of producing antibodies. Other B-cells become memory cells that get stored in your body.
d. Plasma cells make millions of antibodies over the next several days. All antibodies are customized to destroy only the specific pathogen that produced the antigen.
e. These antibodies bind to antigens or the part of the pathogen that contains the antigen marker. These antibodies prevent pathogens from causing further harm to your body [7], [8].

Where is B-cells located?

B-cells exist in different places depending on their stage of development. In fetuses, the liver makes B-cells. Once you're born, B-cells develop in the spongy tissue inside your bone called bone marrow. They start as hematopoietic stem cells and eventually become B-cells during a process called hematopoiesis. Once they're fully mature, your B-cells travel to important parts of your lymphatic system, including your spleen and lymph nodes[9], [10].

Autoimmune diseases

Sometimes, B-cells make antibodies in response to antigens associated with your body's healthy cells. When this happens, the antibodies attack your healthy cells like a dangerous pathogen. This is what happens with autoimmune diseases, including:

a. Lupus.
b. Multiple sclerosis.
c. Rheumatoid arthritis.
d. Type 1 diabetes

Cancers

Several cancers are associated with abnormal B-cell development, including:

a. Acute lymphocytic leukemia.
b. Chronic lymphocytic leukemia.
c. Hodgkin lymphoma.
d. Non-Hodgkin lymphoma.
e. B-cell lymphoma.
f. Multiple myeloma.
g. Waldenström'smacroglobulinemia.

What is the normal range of B-cells?

The normal range of lymphocytes in adults is between 1,000 and 4,800 lymphocytes in every microliter of blood. Approximately 10% to 20% of your lymphocytes are B-cells.Having consistently high or low B-cells may mean you have a disease or condition. Your healthcare provider will need to perform tests to be sure.

What are the common tests to check the health of my B-cells?

A standard test called a complete blood count (CBC) allows your healthcare provider to identify how many lymphocytes you have. It doesn't provide specific information about specific types of lymphocytes, B-cells and T-cells.If they suspect you have a condition related to abnormal B-cells, your provider may order other tests that provide information on specific types of lymphocytes, like a lymphocyte profile (T- and B-cell counts) or a B-cell leukemia/lymphoma panel.

How can I increase my B-cells naturally?

There aren't widely agreed upon natural remedies for boosting B-cells. Still, there are steps you can take to protect the B-cells you have by keeping your immune system healthy. Many of these recommendations may seem like common sense wellness strategies, but they prevent your body from exhausting essential immune system resources, including your B-cells [5], [6].You can keep your immune system healthy by:

a. Getting all recommended vaccines.
b. Eating a well-balanced diet.
c. Managing your stress levels.
d. Avoiding alcohol or drinking in moderation.
e. Not smoking or vaping and quitting if you do.
f. Sleeping at least seven to eight hours each night.
g. Engaging in moderate exercise for at least 150 minutes a week.
h. Washing your hands frequently with soap and water or using hand sanitizer.

CONCLUSION

In conclusion, the Chapter on B Cells and Antibody Production has provided a comprehensive exploration of the remarkable roles that B cells and antibodies play within the immune system. These components, central to the adaptive immune response, are essential in defending the body against a diverse array of pathogens, facilitating immunological memory, and contributing to diagnostics and therapeutics cells, with their intricate journey from bone marrow development to activation and clonal expansion, are the architects of humoral immunity. They possess the extraordinary ability to generate a diverse repertoire of B cell receptors (BCRs), allowing them to recognize and respond to a wide variety of antigens. This diversity is further honed through processes like affinity maturation and somatic hypermutation, ensuring the production of highly specific antibodies. Antibodies, the immune system's versatile sentinels, are pivotal in immune defense. They are exquisitely designed to bind to antigens with precision, neutralizing pathogens and marking them for destruction. The formation of memory B cells ensures that the immune system retains a long-lasting memory of encountered antigens, leading to faster and more effective immune responses upon re-exposure.

The clinical implications of B cells and antibody production are vast. Antibodies are the foundation of diagnostic tests, allowing for the detection of infections, allergies, and autoimmune diseases. They have also ushered in a new era of medicine through monoclonal antibody therapies, which have transformed the treatment landscape for cancer, autoimmune disorders, and infectious diseases. As we conclude this Chapter, we recognize that B cells and antibody production are not merely biological processes; they represent the immune system's artistry in recognizing and combating the ever-evolving landscape of pathogens and challenges. Their significance extends far beyond immunology, influencing diagnostics, therapeutics, and the ongoing quest to safeguard human health and well-being. In an age

where science continues to unlock the potential of B cells and antibodies, we can anticipate further innovations in diagnostics and therapies. The story of these immune sentinels is one of resilience, specificity, and adaptability, offering endless possibilities for improving healthcare and advancing medical research in our pursuit of a healthier world.

REFERENCES:

[1] W. Ise *et al.*, Primary response of naive CD4+ T cells to amino acid-substituted analogs of an antigenic peptide can show distinct activation patterns: Th1- and Th2-type cytokine secretion, and helper activity for antibody production without apparent cytokine secretion, *FEBS Lett.*, 2000, doi: 10.1016/S0014-5793(99)01716-0.

[2] M. Itoh *et al.*, Production of IL-10 and IL-12 in CD40 and interleukin 4-activated mononuclear cells from patients with Graves' disease, *Cytokine*, 2000, doi: 10.1006/cyto.1999.0659.

[3] N. Müller, M. Riedel, M. Ackenheil, and M. J. Schwarz, Cellular and humoral immune system in schizophrenia: A conceptual re-evaluation, *World Journal of Biological Psychiatry*. 2000. doi: 10.3109/15622970009150588.

[4] T. Nakamura *et al.*, In vitro IgE inhibition in B cells by anti-CD23 monoclonal antibodies is functionally dependent on the immunoglobulin Fc domain, *Int. J. Immunopharmacol.*, 2000, doi: 10.1016/S0192-0561(99)00068-5.

[5] H. Kitamura *et al.*, α-galactosylceramide induces early B-cell activation through IL-4 production by NKT cells, *Cell. Immunol.*, 2000, doi: 10.1006/cimm.1999.1602.

[6] Q. H. Song, T. Kobayashi, L. M. Xiu, T. Hong, and J. C. Cyong, Effects of Astragali root and Hedysari root on the murine B and T cell differentiation, *J. Ethnopharmacol.*, 2000, doi: 10.1016/S0378-8741(00)00273-7.

[7] E. Paul, A. Nelde, A. Verschoor, and M. C. Carroll, Follicular exclusion of autoreactive B cells requires FcγRIIb, *Int. Immunol.*, 2007, doi: 10.1093/intimm/dxm002.

[8] R. Magliozzi *et al.*, Meningeal B-cell follicles in secondary progressive multiple sclerosis associate with early onset of disease and severe cortical pathology, *Brain*, 2007, doi: 10.1093/brain/awm038.

[9] S. Mahajan *et al.*, The role of ICOS in the development of CD4 T cell help and the reactivation of memory T cells, *Eur. J. Immunol.*, 2007, doi: 10.1002/eji.200636661.

[10] C. G. Carola Vinuesa, Br ief Definitive Repor t, *J. Exp. Med*, 2010.

CHAPTER 7

T CELLS AND CELLULAR IMMUNITY: UNDERSTANDING THE ROLE OF IMMUNE CELLS

Dr.Ramakant, Assistant Professor
Department of Science, Maharishi University of Information Technology, Uttar Pradesh, India
Email Id- ramakant@muit.in

ABSTRACT:

The Chapter on T Cells and Cellular Immunity offers an in-depth exploration of T cells, a diverse group of immune cells that play a central role in cell-mediated immunity. This Chapter delves into the development, activation, and functions of T cells, including cytotoxic T cells and helper T cells. It also examines their critical role in immune surveillance, the clearance of infected or abnormal host cells, and the coordination of immune responses. Additionally, it explores the clinical significance of T cells in infectious diseases, cancer immunotherapy, and autoimmune disorders.After they finish growing in the thymus, T cells go into the bloodstream and are carried around by the blood. When they reach a lymph node, they leave the blood and move through the lymph tissue. They go back into the bloodstream and continue to travel between the blood and lymph tissue until they find their specific antigen. Immature T cells that have not yet come across the things that can make them sick are called naive T cells. We will call these cells armed effector T cells because they act quickly when they come across their specific target on other cells. The cells that are affected by armed effector T cells will be called their target cells.

KEYWORDS:

Adaptive Immunity, Cytokines, Cytotoxic T Cells, Helper T Cells. Immunological Memory.

INTRODUCTION

T cells regulate the activities cells participating in immune responses. They provide help for antibody production by B cells, and they are also the effectors of antigen-specific cell-mediated immunity (CMI). CMI is important in the elimination of intracellular infections and aberrantly differentiating cells. CMI also destroys allogeneic cells. In addition, it is involved in cellular autoimmune responses, as well as type IV allergic reactions to drugs and contact dermatitis. Furthermore, T cells activate innate immune cells such as phagocytic cells to become more effective at killing other types of pathogens such as fungi. The Chapter on T Cells and Cellular Immunity invites us to delve into the intricate and highly specialized world of T cells, an essential component of the adaptive immune system, and their pivotal role in cell-mediated immunity. These immune sentinels are central players in the body's defense against a wide array of threats, from infections to cancer and autoimmune diseases. T cells are a diverse group of immune cells that undergo a rigorous process of development and maturation in the thymus, thus earning their name. They emerge from this process armed with unique receptors known as T cell receptors (TCRs), which enable them to recognize specific antigens [1], [2]. One of the remarkable features of T cells is their versatility.

They come in various forms, with two major subsets being cytotoxic T cells (CD8+ T cells) and helper T cells (CD4+ T cells). Cytotoxic T cells are known for their ability to seek out and destroy infected or abnormal host cells, contributing to immune surveillance and the elimination of threats within the body. Helper T cells, on the other hand, serve as coordinators of the immune response, orchestrating and directing the activities of other

immune cells.Cell-mediated immunity, the hallmark of T cell function, involves T cells recognizing and responding to antigens presented on the surface of host cells through the major histocompatibility complex (MHC). This mechanism allows T cells to distinguish between healthy and infected or abnormal cells, contributing to the clearance of threats while sparing normal tissue. Throughout this Chapter, we will explore the life cycle of T cells, from their development and activation to the critical role they play in immune surveillance and response. The generation of immunological memory by memory T cells enables the immune system to mount swift and targeted defenses upon re-exposure to familiar antigens [3], [4].

The clinical significance of T cells in infectious diseases, cancer immunotherapy, and autoimmune disorders cannot be overstated. Advances in immunology have led to the development of groundbreaking therapies that harness the power of T cells to target and eliminate cancer cells or modulate immune responses in autoimmune conditions. As we embark on this exploration of T cells and cellular immunity, we will uncover the elegance and complexity of these immune sentinels. Their roles extend far beyond immunology, influencing diagnostics, therapeutics, and the ongoing quest to safeguard human health and well-being in a world teeming with challenges and opportunities. T cell receptors (TCRs), in contrast to immunoglobulins, exist only as multimeric membrane-bound complexes and are not secreted intact in soluble form. Also unlike immunoglobulins, TCRs recognize fragments (peptides) of protein or glycoprotein antigens in complexes with major histocompatibility molecules on the surfaces of antigen-presenting cells or on targets of cytotoxicity. Note the distinction between the processed antigen (peptide) eliciting a response and the major histocompatibility complex (MHC) antigen with which it becomes associated to stimulate peptide-specific T cells [5], [6].

DISCUSSION

The most common context of T cells is within infectious diseases, but they are used for other aspects of adaptive immunity too. This includes responses to allergens and tumors. They maintain immune homeostasis in humans over decades but can also be responsible for inflammatory or autoimmune diseases. The role of T cells is slightly modified throughout the human lifetime. In infancy, naïve T cells are critical for developing immunity towards common pathogens or antigens. During this time, long-term reserves of memory T cells are established and can be maintained through adulthood. In adulthood, when fewer novel antigens are encountered, they function mainly to maintain homeostasis and immunoregulation of repeat or chronically encountered antigens. There is also some focus on surveillance for tumors during this stage in life.

T cell activation and mechanism

T cells originate in the bone marrow but are matured in the thymus. However, they are not activated until they find their specific antigen. They bind to this antigen on the surface of antigen-presenting cells (APCs). Typically, several types of T cells are involved in this, mainly CD4 helper T cells and CD8 cytotoxic T cells, and together they form the MHC complex.The activation of T cells is not always as binding to the MHC. Both helper T cells and cytotoxic T cells need secondary signals to become fully activated and be effective towards the threat. These are provided by several molecules, such as CD28 which activate helper T cells. In general, there are three types of T cells: cytotoxic, helper, and regulatory. All of these must react to foreign antigens strongly to be effective for immunity. T cells with a strong reaction are also given survival signals by several molecules, such as ICOS and OX40. These are only expressed on the T cell surface following binding with the antigen, to ensure it is only active after response to a pathogen. After activation, communication occurs

in the form of cytokines. The cytokines decide what form of responder the cells turn into. Helper T cells become Th1, Th2, or IL-17 types. Each of these types has its own role in the continued development of further immune responses [7], [8]. In this Chapter, we will learn about how specific cells in our immune system called naive T cells become activated when they first encounter a certain molecule on the surface of another immune cell called an activated antigen-presenting cell. This activation process helps these T cells become effector T cells that can fight off infections. The most important cells that show antigens to our immune system are called dendritic cells. They are very specialized and their main job is to eat and show antigens.

Dendritic cells in our body's tissues eat up harmful substances when there is an infection and become active as part of our natural defense against diseases. This causes them to move to nearby lymph nodes and develop into cells that are very good at showing antigens to circulating T cells. These fully developed dendritic cells have special molecules on their surface called co-stimulatory molecules. These molecules work together with antigens to activate T cells that haven't been exposed to the antigen before. Macrophages are cells that can fight off infections. They can also be activated to show other molecules that help the immune system. This allows them to work like cells that present antigens, even though they are not as good as dendritic cells at activating new T cells. B cells can sometimes act as cells that show antigens to other cells. After the immune system starts fighting off an infection, special cells called T cells also attack macrophages and B cells that have captured the same harmful substance. Dendritic cells, macrophages, and B cells are cells that are really good at showing antigens to other cells.

Effector T cells, , can be grouped into three categories based on their functions. They recognize peptide antigens that come from different kinds of germs. Peptides from harmful germs that grow inside cells are taken to the outer part of the cell by certain molecules called MHC class I. These peptides are then shown to CD8 T cells. These cells change into cytotoxic T cells that attack infected cells. Peptide antigens from germs growing inside small compartments in cells, and ones coming from germs and toxins that were eaten, are taken to the outside of cells by special molecules called MHC class II. They are then shown to CD4 T cells. These can change into two types of active T cells, known as TH1 and TH2. When there are many harmful microbes in our immune cells called macrophage and dendritic cells, it tends to cause the development of TH1 cells. On the other hand, when the harmful substances are outside the cells, it tends to make TH2 cells. TH1 cells help macrophages kill microbes and stimulate B cells to produce IgG antibodies that can coat and target pathogens for destruction by phagocytic cells. TH2 cells start the immune response by activating certain cells to make antibodies called IgM. These TH2 cells can later cause the body to make different types of antibodies, like IgA and IgE. They can also make certain types of IgG that can neutralize things or help with opsonization, but not very strongly. Please explain the following diagram.

When new T cells are exposed to a foreign invader, they become active and start to multiply and change into different types of cells. This is called the initial immune response. At the same time as producing a type of defense cells, this response also creates a memory that helps protect the body from future attacks by the same germ. We know less about how memory T cells are made compared to effector T cells. Memory T cells are different from naive T cells in a few ways, but they are like naive T cells in that they are inactive and need to be activated by antigen-presenting cells in order to become effector T cells again. Armed effector T cells are different from their naive precursors in many ways. These differences help them to respond faster and more effectively when they come across a specific antigen on target cells.

In the last two parts of this Chapter, we will explain how T cells and macrophages work together to fight off infections. T cells are a type of immune cell that can kill harmful cells, and macrophages are another type of immune cell that can be activated by T cells to help eliminate infections. We will discuss how B cells are activated by helper T cells when we talk about the immune response with antibodies[7], [9].

T Cell Production and Maturation

T cells, like all other white blood cells involved in innate and adaptive immunity, are formed from multipotent hematopoietic stem cells (HSCs) in the bone marrow. However, unlike the white blood cells of innate immunity, eventual T cells differentiate first into lymphoid stem cells that then become small, immature lymphocytes, sometimes called lymphoblasts**.** The first steps of differentiation occur in the red marrow of bones after which immature T lymphocytes enter the bloodstream and travel to the thymus for the final steps of maturation. Once in the thymus, the immature T lymphocytes are referred to as thymocytes.The maturation of thymocytes within the thymus can be divided into tree critical steps of positive and negative selection, collectively referred to as thymic selection. The first step of thymic selection occurs in the cortex of the thymus and involves the development of a functional T-cell receptor (TCR) that is required for activation by APCs. Thymocytes with defective TCRs are removed by negative selection through the induction of apoptosis. The second step of thymic selection also occurs in the cortex and involves the positive selection of thymocytes that will interact appropriately with MHC molecules. Thymocytes that can interact appropriately with MHC molecules receive a positive stimulation that moves them further through the process of maturation, whereas thymocytes that do not interact appropriately are not stimulated and are eliminated by apoptosis. The third and final step of thymic selection occurs in both the cortex and medulla and involves negative selection to remove self-reacting thymocytes, those that react to self-antigens, by apoptosis. This final step is sometimes referred to as central tolerance because it prevents self-reacting T cells from reaching the bloodstream and potentially causing autoimmune disease, which occurs when the immune system attacks healthy self cells.

Despite central tolerance, some self-reactive T cells generally escape the thymus and enter the peripheral bloodstream. Therefore, a second line of defense called peripheral tolerance is needed to protect against autoimmune disease. Peripheral tolerance involves mechanisms of **anergy** and inhibition of self-reactive T cells by regulatory T cells. Anergy refers to a state of non- responsiveness to antigen stimulation. In the case of self-reactive T cells that escape the thymus, lack of an essential co-stimulatory signal required for activation causes anergy and prevents autoimmune activation. Regulatory T cells participate in peripheral tolerance by inhibiting the activation and function of self-reactive T cells and by secreting anti-inflammatory cytokines [1].It is not completely understood what events specifically direct maturation of thymocytes into regulatory T cells. Current theories suggest the critical events may occur during the third step of thymic selection, when most self-reactive T cells are eliminated. Regulatory T cells may receive a unique signal that is below the threshold required to target them for negative selection and apoptosis. Consequently, these cells continue to mature and then exit the thymus, armed to inhibit the activation of self-reactive T cells.

It has been estimated that the three steps of thymic selection eliminate 98% of thymocytes. The remaining 2% that exit the thymus migrate through the bloodstream and lymphatic system to sites of secondary lymphoid organs/tissues, such as the lymph nodes, spleen, and tonsils, where they await activation through the presentation of specific antigens by APCs. Until they are activated, they are known as mature naïve T cells. T cells can be

categorized into three distinct classes: helperT cells**,** regulatory T cells, and cytotoxic T cells. These classes are differentiated based on their expression of certain surface molecules, their mode of activation, and their functional roles in adaptive immunity.All T cells produce cluster of differentiation (CD)molecules, cell surface glycoproteins that can be used to identify and distinguish between the various types of white blood cells. Although T cells can produce a variety of CD molecules, CD4 and CD8 are the two most important used for differentiation of the classes. Helper T cells and regulatory T cells are characterized by the expression of CD4 on their surface, whereas cytotoxic T cells are characterized by the expression of CD8. Classes of T cells can also be distinguished by the specific MHC molecules and APCs with which they interact for activation. Helper T cells and regulatory T cells can only be activated by APCs presenting antigens associated with MHC II**.** In contrast, cytotoxic T cells recognize antigens presented in association with MHC I, either by APCs or by nucleated cells infected with an intracellular pathogen.

The different classes of T cells also play different functional roles in the immune system. Helper T cells serve as the central orchestrators that help activate and direct functions of humoral and cellular immunity. In addition, helper T cells enhance the pathogen-killing functions of macrophages and NK cells of innate immunity. In contrast, the primary role of regulatory T cells is to prevent undesirable and potentially damaging immune responses. Their role in peripheral tolerance, for example, protects against autoimmune disorders, as discussed earlier. Finally, cytotoxic T cells are the primary effector cells for cellular immunity. They recognize and target cells that have been infected by intracellular pathogens, destroying infected cells along with the pathogens inside.

CONCLUSION

In conclusion, the Chapter on T Cells and Cellular Immunity has provided a comprehensive understanding of the pivotal roles that T cells play within the immune system. These remarkable immune sentinels, with their versatility and specificity, are central to cell-mediated immunity, ensuring the body's defense against a multitude of threats, from infections to cancer and autoimmune disorders. T cells come in various forms, including cytotoxic T cells and helper T cells. This diversity allows for a finely tuned immune response that can effectively target and eliminate specific threats while sparing normal tissue. Cytotoxic T cells serve as the body's hitmen, directly destroying infected or abnormal host cells, while helper T cells coordinate immune responses, ensuring a harmonized defense strategy. The recognition of antigens presented on the surface of host cells through the major histocompatibility complex (MHC) is a key function of T cells. This recognition process allows T cells to differentiate between healthy and infected or abnormal cells, contributing to immune surveillance. Activation of T cells upon antigen recognition initiates immune responses that are crucial for clearing threats.

T cells are instrumental in the formation of immunological memory. Upon encountering a specific antigen, they generate memory T cells that remember the threat. This memory facilitates faster and more effective immune responses upon re-exposure, providing long-lasting immunity. Memory T cells are a cornerstone of effective vaccines. The clinical implications of T cells are profound. They play essential roles in clearing infections, providing immunity, and contributing to the development of cancer immunotherapies. Additionally, T cells are involved in autoimmune diseases, where their misdirected responses target the body's own tissues. Understanding and modulating T cell responses are critical in managing these conditions. The field of T cells and cellular immunity continues to evolve. Ongoing research explores ways to enhance T cell responses in cancer immunotherapy, develop personalized therapies, and gain deeper insights into autoimmune diseases. Precision

medicine approaches aim to tailor treatments to individual patients, harnessing the power of T cells and immune responses[10].As we conclude this Chapter, we recognize that T cells are not just immune cells; they are architects of defense, conductors of immune orchestras, and guardians of health. Their roles extend far beyond immunology, influencing diagnostics, therapeutics, and the ongoing quest to safeguard human health and well-being in a world teeming with challenges and opportunities. In an era of scientific advancement, the study of T cells and cellular immunity promises to unlock new frontiers in healthcare, providing innovative solutions to diseases and advancing our understanding of the immune system's intricacies.

REFERENCES:

[1] A. Sobarzo *et al.*, Correspondence of neutralizing humoral immunity and CD4 T cell responses in long recovered sudan virus survivors, *Viruses*, 2016, doi: 10.3390/v8050133.

[2] J. D. Mena-Romo *et al.*, CMV-specific T-cell immunity in solid organ transplant recipients at low risk of CMV infection. Chronology and applicability in preemptive therapy, *J. Infect.*, 2017, doi: 10.1016/j.jinf.2017.05.020.

[3] N. Esteve, A. Ferrer, C. Mora, G. Gómez, H. Ribera, and P. Garrido, ¿Influye la anestesia en los resultados de la cirugía oncológica?, *Rev. la Soc. Española del Dolor*, 2014, doi: 10.4321/s1134-80462014000300007.

[4] A. K. Storset, G. Berntsen, and H. J. S. Larsen, Kinetics of IL-2 receptor expression on lymphocyte subsets from goats infected with Mycobacterium avium subsp. paratuberculosis after specific in vitro stimulation, *Vet. Immunol. Immunopathol.*, 2000, doi: 10.1016/S0165-2427(00)00227-0.

[5] M. P. Everson, K. Shi, P. Aldrige, A. A. Bartolucci, and W. D. Blackburn, Is there immune dysregulation in symptomatic Gulf War veterans?, *Z. Rheumatol.*, 2000, doi: 10.1007/s003930070007.

[6] C. R. Gabaglia, M. T. Valle, D. Fenoglio, M. A. Barcinski, and F. Manca, CD4+ T cell response to Leishmania spp. in non-infected individuals, *Hum. Immunol.*, 2000, doi: 10.1016/S0198-8859(00)00119-1.

[7] J. S. Jenson, A. Childerstone, H. H. Takamatsu, L. K. Dixon, and R. M. E. Parkhouse, The cellular immune recognition of proteins expressed by an African swine fever virus random genomic library, *J. Immunol. Methods*, 2000, doi: 10.1016/S0022-1759(00)00222-2.

[8] J. M. Sharma, I. J. Kim, S. Rautenschlein, and H. Y. Yeh, Infectious bursal disease virus of chickens: Pathogenesis and immunosuppression, *Dev. Comp. Immunol.*, 2000, doi: 10.1016/S0145-305X(99)00074-9.

[9] C. M. Hogan and S. M. Hammer, Host determinants in HIV infection and disease part 1: Cellular and humoral immune responses, *Annals of Internal Medicine*. 2001. doi: 10.7326/0003-4819-134-9_part_1-200105010-00013.

[10] R. Elgueta, M. J. Benson, V. C. De Vries, A. Wasiuk, Y. Guo, and R. J. Noelle, Molecular mechanism and function of CD40/CD40L engagement in the immune system, *Immunological Reviews*. 2009. doi: 10.1111/j.1600-065X.2009.00782.x.

CHAPTER 8

IMMUNOGLOBULIN STRUCTURE AND FUNCTION: A BRIEF OVERVIEW

Dr.SnehaVerma, Assistant Professor
Department of Science, Maharishi University of Information Technology, Uttar Pradesh, India
Email Id- sneha.verma@muit.in

ABSTRACT:

The Chapter on Immunoglobulin Structure and Function offers an in-depth exploration of immunoglobulins (Igs), also known as antibodies, elucidating their remarkable molecular structure and the diverse functions they perform within the immune system. This Chapter delves into the different classes and isotypes of Igs, their antigen-binding regions, effector functions, and the role they play in humoral immunity. The variable domains are made through a complicated process of rearranging genes. Afterwards, they can go through changes when exposed to a foreign substance, which helps improve their ability to recognize and bind to that substance. Each V domain can be divided into three parts with varying sequences called CDRs and four parts with consistent sequences called FRs. The three CDRs (complementarity determining regions) of the H chain are combined with the three CDRs of the L chain to create the antigen binding site, as traditionally described. There are five main groups of heavy chain C domains. Each class describes different types of antibodies called IgM, IgG, IgA, IgD, and IgE. IgG is a type of protein that can be divided into four subclasses: IgG1, IgG2, IgG3, and IgG4. Each subclass has its own characteristics. Similarly, IgA is another type of protein that can be divided into IgA1 and IgA2. The parts of the H chain that always stay the same can be changed to make the effector function different but still keep the ability to recognize the same antigen. Additionally, it explores the clinical applications of Igs in diagnostics, therapeutics, and the development of innovative medical interventions.

KEYWORDS:

Affinity, Antibody Diversity, Antigen-Binding Region, Complement Activation, Constant Variable Regions.

INTRODUCTION

The Chapter on Immunoglobulin Structure and Function opens the door to the captivating world of immunoglobulins (Igs), commonly known as antibodies. These molecular marvels are the cornerstone of humoral immunity, performing a diverse array of functions within the immune system to protect the body against pathogens. Immunoglobulins (Igs) are proteins produced by B cells, and they come in different classes and isotypes. Their primary function is to recognize and bind to antigens, which can be anything from the surface proteins of invading pathogens to allergens and cancer cells. This antigen-binding ability is crucial for the immune system's ability to distinguish between self and non-self and to mount targeted immune responses. One of the remarkable features of immunoglobulins is their structural diversity. Each Ig molecule is composed of constant and variable regions, with the latter being responsible for antigen recognition. The variability in the variable regions allows for the vast range of antigens that the immune system can recognize, making antibodies highly specific and adaptable [1], [2]. Beyond their antigen-binding capacity, immunoglobulins possess effector functions that contribute to immune defense. These functions include neutralization of pathogens, opsonization to facilitate phagocytosis, complement activation to destroy pathogens, and interaction with Fc receptors on immune cells, which modulates

immune responses. The clinical significance of immunoglobulins is immense. They serve as the basis for diagnostics, allowing for the detection of infections, allergies, autoimmune diseases, and more. Additionally, the development of monoclonal antibodies has revolutionized medicine, leading to groundbreaking therapies for cancer, autoimmune disorders, and infectious diseases. As we journey through this Chapter, we will explore the intricacies of immunoglobulin structure and function, uncovering their role in humoral immunity and their clinical applications. Immunoglobulins are not merely molecules; they are the architects of immune defense, playing a pivotal role in maintaining health and combating diseases.

DISCUSSION

Immunoglobulins are glycoprotein molecules that are produced by plasma cells in response to an immunogen and which function as antibodies. The immunoglobulins derive their name from the finding that they migrate with globular proteins when antibody-containing serum is placed in an electrical field.

Antigen binding: Immunoglobulins bind specifically to one or a few closely related antigens. Each immunoglobulin actually binds to a specific antigenic determinant. Antigen binding by antibodies is the primary function of antibodies and can result in protection of the host. The valency of antibody refers to the number of antigenic determinants that an individual antibody molecule can bind. The valency of all antibodies is at least two and, in some instances, more.

Effector Functions: Frequently the binding of an antibody to an antigen has no direct biological effect. Rather, the significant biological effects are a consequence of secondary effector functions of antibodies. The immunoglobulins mediate a variety of these effector functions. Usually, the ability to carry out a particular effector function requires that the antibody bind to its antigen. Not every immunoglobulin will mediate all effector functions. Such effector functions include:

1. Fixation of complement: This results in lysis of cells and release of biologically active molecules.

2. Binding to various cell types: Phagocytic cells, lymphocytes, platelets, mast cells, and basophils have receptors that bind immunoglobulins. This binding can activate the cells to perform some function. Some immunoglobulins also bind to receptors on placental trophoblasts, which results in transfer of the immunoglobulin across the placenta. As a result, the transferred maternal antibodies provide immunity to the fetus and newborn The basic structure of the immunoglobulins. Although different immunoglobulins can differ structurally, they all are built from the same basic units [3].

Heavy and Light Chains

All immunoglobulins have a four-chain structure as their basic unit. They are composed of two identical light chains (23kD) and two identical heavy chains (50-70kD)

Disulfide bonds

a. **Inter-chain disulfide bonds** - The heavy and light chains and the two heavy chains are held together by inter-chain disulfide bonds and by non-covalent interactions The number of inter-chain disulfide bonds varies among different immunoglobulin molecules.

b. **Intra-chain disulfide binds** - Within each of the polypeptide chains there are also intra-chain disulfide bonds.

Variable (V) and Constant (C) Regions

When the amino acid sequences of many different heavy chains and light chains were compared, it became clear that both the heavy and light chain could be divided into two regions based on variability in the amino acid sequences. These are the:

a. **Light Chain**: VL (110 amino acids) and CL (110 amino acids).

b. **Heavy Chain:** VH (110 amino acids) and CH (330-440 amino acids).

Hinge Region

This is the region at which the arms of the antibody molecule form a Y. It is called the hinge region because there is some flexibility in the molecule at this point.

Oligosaccharides

Carbohydrates are attached to the CH2 domain in most immunoglobulins. However, in some cases carbohydrates may also be attached at other locations.

Structure of the Variable Region

Hypervariable (HVR) or complementarity determining regions (CDR)

Comparisons of the amino acid sequences of the variable regions of immunoglobulins show that most of the variability resides in three regions called the hypervariable regions or the complementarity determining region. Antibodies with different specificities have different complementarity determining regions while antibodies of the exact same specificity have identical complementarity determining regions. Complementarity determining regions are found in both the H and the L chains [4], [5].

Framework regions

The regions between the complementarity determining regions in the variable region are called the framework regions. Based on similarities and differences in the framework regions the immunoglobulin heavy and light chain variable regions can be divided into groups and subgroups. These represent the products of different variable region genes. Immunoglobulin fragments produced by proteolytic digestion have proven very useful in elucidating structure/function relationships in immunoglobulins.

Fab

Digestion with papain breaks the immunoglobulin molecule in the hinge region before the H-H inter-chain disulfide bond. This results in the formation of two identical fragments that contain the light chain and the VH and CH1 domains of the heavy chain. Antigen binding - These fragments were called the Fab fragments because they contained the antigen binding sites of the antibody.

Each Fab fragment is monovalent whereas the original molecule was divalent. The combining site of the antibody is created by both VH and VL. An antibody is able to bind a particular antigenic determinant because it has a particular combination of VH and VL. Different combinations of a VH and VL result in antibodies that can bind a different antigenic determinant.

Fc

Digestion with papain also produces a fragment that contains the remainder of the two heavy chains each containing a CH2 and CH3 domain. This fragment was called Fc because it was easily crystallized. Effector functions. The effector functions of immunoglobulins are mediated by this part of the molecule. Different functions are mediated by the different domains in this fragment. Normally the ability of an antibody to carry out an effector function requires the prior binding of an antigen; however, there are exceptions to this rule [6], [7].

F(ab')2

Treatment of immunoglobulins with pepsin results in cleavage of the heavy chain after the H-H inter-chain disulfide bonds resulting in a fragment that contains both antigen binding sites. This fragment was called F(ab')2 because it is divalent. The Fc region of the molecule is digested into small peptides by pepsin. The F(ab')2 binds antigen but it does not mediate the effector functions of antibodies.

Immunoglobulin classes

The immunoglobulins can be divided into five different classes, based on differences in the amino acid sequences in the constant region of the heavy chains. All immunoglobulins within a given class will have very similar heavy chain constant regions. These differences can be detected by sequence studies or more commonly by serological means by the use of antibodies directed to these differences.

- **a.** IgG.
- **b.** IgM.
- **c.** IgA.
- **d.** IgD.
- **e.** IgE.

Immunoglobulin Subclasses

The classes of immunoglobulins can be divided into subclasses based on small differences in the amino acid sequences in the constant region of the heavy chains. All immunoglobulins within a subclass will have very similar heavy chain constant region amino acid sequences. Again, these differences are most commonly detected by serological means.

IgG Subclasses

- **a.** IgG1 - Gamma 1 heavy chains.
- **b.** IgG2 - Gamma 2 heavy chains.
- **c.** IgG3 - Gamma 3 heavy chains.
- **d.** IgG4 - Gamma 4 heavy chains.

IgA Subclasses

- **a.** IgA1 - Alpha 1 heavy chains.
- **b.** IgA2 - Alpha 2 heavy chains.

Immunoglobulin Types

Immunoglobulins can also be classified by the type of light chain that they have. Light chain types are based on differences in the amino acid sequence in the constant region of the light chain. These differences are detected by serological means.

a. Kappa light chains.

b. Lambda light chains.

Immunoglobulin Subtypes
The light chains can also be divided into subtypes based on differences in the amino acid sequences in the constant region of the light chain.

Lambda subtypes

a. Lambda 1.

b. Lambda 2.

c. Lambda 3.

d. Lambda 4.

IgG

Immunoglobulins are named based on the class, or subclass of the heavy chain and type or subtype of light chain. Unless it is stated precisely, you should assume that all subclass, types and subtypes are present. IgG means that all subclasses and types are present.Immunoglobulins considered as a population of molecules are normally very heterogeneous because they are composed of different classes and subclasses each of which has different types and subtypes of light chains. In addition, different immunoglobulin molecules can have different antigen binding properties because of different VH and VL regions. IgG is the most versatile immunoglobulin because it is capable of carrying out all of the functions of immunoglobulin molecules. IgG is the major Ig in serum - 75% of serum Ig is IgG IgG is the major Ig in extra vascular spaces Placental transfer - IgG is the only class of Ig that crosses the placenta. Transfer is mediated by a receptor on placental cells for the Fc region of IgG. Not all subclasses cross equally well; IgG2 does not cross well. Fixes complement - Not all subclasses fix equally well; IgG4 does not fix complement Binding to cells - Macrophages, monocytes, PMNs and some lymphocytes have Fc receptors for the Fc region of IgG. Not all subclasses bind equally well; IgG2 and IgG4 do not bind to Fc receptors. A consequence of binding to the Fc receptors on PMNs, monocytes and macrophages is that the cell can now internalize the antigen better. The antibody has prepared the antigen for eating by the phagocytic cells. The term opsonin is used to describe substances that enhance phagocytosis. IgG is a good opsonin. Binding of IgG to Fc receptors on other types of cells results in the activation of other functions[5],[8].

IgM
IgM is IgM normally exists as a pentamer (19S immunoglobulin) but it can also exist as a monomer. In the pentameric form all heavy chains are identical and all light chains are identical. Thus, the valence is theoretically 10. IgM has an extra domain on the mu chain (CH4) and it has another protein covalently bound via a S-S bond called the J chain. This chain functions in polymerization of the molecule into a pentamer.IgM is the third most common serum Ig.IgM is the first Ig to be made by the fetus and the first Ig to be made by a virgin B cells when it is stimulated by antigen.As a consequence of its pentameric structure,

IgM is a good complement fixing Ig. Thus, IgM antibodies are very efficient in leading to the lysis of microorganisms.As a consequence of its structure, IgM is also a good agglutinating Ig. Thus, IgM antibodies are very good in clumping microorganisms for eventual elimination from the body.IgM binds to some cells via Fc receptors.B cell surface IgSurface IgM exists as a monomer and lacks J chain but it has an extra 20 amino acids at the C-terminus to anchor it into the membrane. Cell surface IgM functions as a receptor for antigen on B cells. Surface IgM is noncovalently associated with two additional proteins in the membrane of the B cell called Ig-alpha and Ig-beta. These additional proteins act as signal transducing molecules since the cytoplasmic tail of the Ig molecule itself is too short to transduce a signal. Contact between surface immunoglobulin and an antigen is required before a signal can be transduced by the Ig-alpha and Ig-beta chains. In the case of T-independent antigens, contact between the antigen and surface immunoglobulin is sufficient to activate B cells to differentiate into antibody secreting plasma cells. However, for T-dependent antigens, a second signal provided by helper T cells is required before B cells are activated [9], [10].

IgA

Serum IgA is a monomer but IgA found in secretions is a dimer.When IgA exits as a dimer, a J chain is associated with it.When IgA is found in secretions is also has another protein associated with it called the secretory piece or T piece; sIgA is sometimes referred to as 11S immunoglobulin. Unlike the remainder of the IgA which is made in the plasma cell, the secretory piece is made in epithelial cells and is added to the IgA as it passes into the secretions. The secretory piece helps IgA to be transported across mucosa and also protects it from degradation in the secretions.IgA is the 2nd most common serum Ig.IgA is the major class of Ig in secretions - tears, saliva, colostrum, mucus. Since it is found in secretions secretory IgA is important in local immunity.Normally IgA does not fix complement, unless aggregated.IgA can binding to some cells - PMN's and some lymphocytes.

IgD

Structure

IgD exists only as a monomer.IgD is found in low levels in serum; its role in serum uncertain.IgD is primarily found on B cell surfaces where it functions as a receptor for antigen. IgD on the surface of B cells has extra amino acids at C-terminal end for anchoring to the membrane. It also associates with the Ig-alpha and Ig-beta chains.IgD does not bind complement.

IgE

IgE exists as a monomer and has an extra domain in the constant region.IgE is the least common serum Ig since it binds very tightly to Fc receptors on basophils and mast cells even before interacting with antigen.Involved in allergic reactions. As a consequence of its binding to basophils an mast cells, IgE is involved in allergic reactions. Binding of the allergen to the IgE on the cells results in the release of various pharmacological mediators that result in allergic symptoms.IgE also plays a role in parasitic helminth diseases. Since serum IgE levels rise in parasitic diseases, measuring IgE levels is helpful in diagnosing parasitic infections. Eosinophils have Fc receptors for IgE and binding of eosinophils to IgE-coated helminths results in killing of the parasite.IgE does not fix complement.

CONCLUSION

In conclusion, the Chapter on Immunoglobulin Structure and Function has provided a comprehensive exploration of the remarkable world of immunoglobulins (Igs), also known as antibodies. These versatile proteins are the linchpin of humoral immunity, performing a

multitude of functions within the immune system and making a significant impact on clinical diagnostics and therapeutics. Immunoglobulins exhibit an extraordinary level of structural diversity. Each Ig molecule consists of constant and variable regions, with the variable regions responsible for antigen recognition. The variability in these regions allows for the specific and adaptable binding of antibodies to a wide array of antigens, ensuring a highly tailored immune response. Immunoglobulins extend their influence beyond antigen recognition. They possess multiple effector functions, including neutralization of pathogens, opsonization to enhance phagocytosis, complement activation for pathogen destruction, and interaction with Fc receptors on immune cells, which modulates immune responses. This functional diversity is crucial in mounting effective immune defenses. The clinical significance of immunoglobulins is far-reaching. They are the foundation of diagnostic tests, enabling the detection of infections, allergies, autoimmune diseases, and more.

Additionally, the development of monoclonal antibodies has transformed medicine, leading to revolutionary therapies for cancer, autoimmune disorders, and infectious diseases. Monoclonal antibodies offer precision and specificity in targeting disease-associated molecules, making them a powerful tool in modern healthcare.As we conclude this Chapter, we recognize that immunoglobulins are not just molecules; they are the architects of immune defense and the keys to understanding and combating diseases. Their roles extend far beyond immunology, influencing diagnostics, therapeutics, and the ongoing quest to safeguard human health and well-being in an ever-evolving landscape of pathogens and challenges. In an era where scientific advancements continue to unlock the potential of immunoglobulins, we can anticipate further innovations in diagnostics, therapeutics, and medical research, offering new possibilities for improving healthcare and addressing some of the most pressing medical challenges of our time.

REFERENCES:

[1] H. W. Schroeder and L. Cavacini, Structure and function of immunoglobulins, *J. Allergy Clin. Immunol.*, 2010, doi: 10.1016/j.jaci.2009.09.046.

[2] D. Houde, Y. Peng, S. A. Berkowitz, and J. R. Engen, Post-translational modifications differentially affect IgG1 conformation and receptor binding, *Mol. Cell. Proteomics*, 2010, doi: 10.1074/mcp.M900540-MCP200.

[3] A. Kebir *et al.*, CD146 short isoform increases the proangiogenic potential of endothelial progenitor cells in vitro and in vivo, *Circ. Res.*, 2010, doi: 10.1161/CIRCRESAHA.109.213827.

[4] W. Y. Lee *et al.*, The role of cis dimerization of signal regulatory protein α (SIRPα) in binding to CD47, *J. Biol. Chem.*, 2010, doi: 10.1074/jbc.M110.180018.

[5] S. Lisi, M. Sisto, D. D. Lofrumento, S. D'Amore, and M. D'Amore, Advances in the understanding of the Fc gamma receptors-mediated autoantibodies uptake, *Clinical and Experimental Medicine*. 2011. doi: 10.1007/s10238-010-0098-1.

[6] T. Zenz, S. Fröhling, D. Mertens, H. Döhner, and S. Stilgenbauer, Moving from prognostic to predictive factors in chronic lymphocytic leukaemia (CLL), *Best Practice and Research: Clinical Haematology*. 2010. doi: 10.1016/j.beha.2009.12.003.

[7] J. Van Bergen and F. Koning, The tortoise and the hare: Slowly evolving T-cell responses take hastily evolving KIR, *Immunology*. 2010. doi: 10.1111/j.1365-2567.2010.03337.x.

[8] L. G. Pell *et al.*, The Solution Structure of the C-Terminal Ig-like Domain of the Bacteriophage λ Tail Tube Protein, *J. Mol. Biol.*, 2010, doi: 10.1016/j.jmb.2010.08.044.

[9] H. Almehdar, E. El-Fakharany, V. Uversky, and E. Redwan, Disorder in Milk Proteins: Structure, Functional Disorder, and Biocidal Potentials of Lactoperoxidase, *Curr. Protein Pept. Sci.*, 2015, doi: 10.2174/1389203716666150316114956.

[10] A. M. Davies and B. J. Sutton, Human IgG4: A structural perspective, *Immunological Reviews*. 2015. doi: 10.1111/imr.12349.

CHAPTER 9

ANTIGEN PROCESSING AND PRESENTATION: CELLULAR MECHANISMS

Dr. Sneha Verma, Assistant Professor
Department of Science, Maharishi University of Information Technology, Uttar Pradesh, India
Email Id- sneha.verma@muit.in

ABSTRACT:

The Chapter on Antigen Processing and Presentation provides an in-depth exploration of the intricate mechanisms by which the immune system processes and presents antigens to activate immune responses. This Chapter delves into the processes of antigen uptake, degradation, and presentation through major histocompatibility complex (MHC) molecules. It explores the roles of antigen-presenting cells (APCs) and their interactions with T cells, elucidating the crucial steps in initiating adaptive immune responses. MHC class I molecules are on all cells with a nucleus, not just certain types of cells. They usually show antigens from inside the cell, like viruses.MHC class II molecules are only on certain cells and usually show antigens from outside the cell, like bacteria.Additionally, it examines the clinical implications of antigen processing and presentation in vaccine development, immunotherapies, and autoimmune disease.

KEYWORDS:

Adaptive Immunity, Antigen-Presenting Cells (APCs), Cytotoxic T Cells, Helper T Cells, Major Histocompatibility Complex.

INTRODUCTION

The Chapter on Antigen Processing and Presentation opens the door to the intricate processes that lie at the heart of adaptive immunity. It is within this Chapter that we uncover the remarkable mechanisms by which the immune system captures, processes, and presents antigens, setting in motion the cascade of events that initiate immune responses. Antigen processing and presentation are essential steps in the body's ability to recognize and respond to foreign invaders, be they bacteria, viruses, or even abnormal host cells. This process is orchestrated by a cast of specialized cells known as antigen-presenting cells (APCs), which include dendritic cells, macrophages, and B cells. The journey of antigen processing begins with the uptake of antigens via various mechanisms, such as endocytosis. Once internalized, these antigens are subjected to a complex series of biochemical reactions within the APCs. The goal is to break down the antigens into smaller peptide fragments that can be presented on the cell's surface [1], [2].

The presentation of these peptide antigens occurs through the major histocompatibility complex (MHC) molecules. MHC molecules are the platform upon which peptide antigens are displayed, effectively presenting them to immune cells, particularly T cells, which are the conductors of the adaptive immune response. Crucially, this Chapter will explore the interaction between APCs, MHC molecules, and T cells, elucidating how these interactions are pivotal in immune response initiation. Helper T cells recognize antigens presented by MHC class II molecules on APCs and play a central role in orchestrating the immune response, while cytotoxic T cells are activated by antigens presented on MHC class I molecules and are responsible for targeting and eliminating infected or abnormal cells.

Beyond the fundamental understanding of antigen processing and presentation, this Chapter will delve into the clinical implications of these processes. The principles of antigen presentation underpin vaccine development, as vaccines aim to train the immune system to recognize specific antigens. Additionally, the study of antigen processing and presentation is relevant in immunotherapies for cancer and autoimmune diseases[3], [4].

The MHC molecules bring antigens to the surface of APCs. The MHC has many genes and variations, which allows us to recognize many different antigens that we might come across. There are different types of MHC, and each type has a different job.This makes sense because if there is a virus inside a cell, the immune system has to be able to react to it. This is also why it's hard for the body's defense system to find pathogens inside human red blood cells, like in malaria, because these cells don't have a nucleus.While this is usually the case, in cross-presentation, outside substances can be shown by certain cells, and in autophagy, inside substances can be shown by certain cells.Before a foreign substance enters the body, it must first go through a series of steps called processing in order to be shown to the immune system. Processing changes proteins into substances that can cause an immune response called antigenic peptides.MHC Class I molecules are special proteins found on the surface of most cells in the body. They help the immune system identify and destroy harmful invaders like viruses or cancer cells.

Inside the cell, small proteins for presentation to the immune system are made by certain enzymes and a specific structure called the proteasome. They are then moved into another part of the cell called the endoplasmic reticulum via a molecule called TAP. In the endoplasmic reticulum, they undergo further changes.Then, they come together with MHC I molecules and go to the outer layer of the cell where they are ready to be shown.The first step in the process of presenting exogenous antigens for MHC class II is when the antigen is taken into the cell through endocytosis. Once inside the cell, they are enclosed in endosomes that become acidic and activate enzymes, called proteases, which break down the antigen.MHC class II molecules move into small containers inside the cell called endocytic vesicles. Inside these vesicles, the MHC class II molecules attach to pieces of a foreign substance called peptide antigen. Afterward, the vesicles carrying the MHC class II molecules with the attached peptide antigen move to the cell surface.Antigen Presentation is the process by which the immune system presents and shows a foreign substance called an antigen to the immune cells.

T cells have a receptor called TCR that can recognize antigens displayed on MHCs. These target a specific antigen.T Cell Receptors are proteins on the surface of our immune cells called T cells. These receptors help T cells recognize and respond to foreign substances, like viruses or bacteria, that could cause harm to our bodies.Each T cell has many TCRs, each with a unique ability to recognize different things. This helps our immune system recognize many different things.This variety in TCRs is created through a process called V(D)J recombination while the body is growing in the thymus. TCR chains have a part that can change where gene pieces are mixed up on their own. Proteins called RAG1 and RAG2 cut the chains apart and then put them back together again.The TCRs can become even more varied by adding or removing parts of DNA at certain points. This creates a huge number of unique TCRs, up to 1015 different ones.TCRs recognize not just one type of substance, but also a specific protein found on the surface of cells. T cells can only identify an antigen if a certain kind of antigen with a specific MHC molecule is there. This is known as MHC restriction. Co-receptors are molecules that work together with receptors on the surface of cells to allow certain processes to occur.In addition to the TCR, another molecule called a co-receptor is needed for T cells to recognize antigens.

These are either a CD4 or CD8 molecule: n These can be either a CD4 or CD8 molecule.CD4 is on T helper cells and only attaches to antigen-MHC II combinations.CD8 is found on cytotoxic T cells and only sticks to antigen-MHC I combinations.This results in very different outcomes. When antigens are shown with MHC II, it makes T helper cells active. When antigens are shown with MHC I, it activates cytotoxic T cells. Cytotoxic T cells are responsible for killing the cells they identify. On the other hand, T helper cells can have various effects on the cells they interact with, such as activating B cells to produce antibodies or activating macrophages to eliminate harmful pathogens inside them.

DISCUSSION

MHC class I molecules are expressed by all nucleated cells. MHC class I molecules are assembled in the endoplasmic reticulum (ER) and consist of two types of chain – a polymorphic heavy chain and a chain called β2-microglobulin. The heavy chain is stabilised by the chaperone calnexin, prior to association with the β2-microglobulin. Without peptides, these molecules are stabilised by chaperone proteins: calreticulin, Erp57, protein disulfide isomerase (PDI) and tapasin. The complex of TAP, tapasin, MHC class I, ERp57 and calreticulin is called the peptide-loading complex (PLC). Tapasin interacts with the transport protein TAP (transporter associated with antigen presentation) which translocates peptides from the cytoplasm into the ER. Prior to entering the ER, peptides are derived from the degradation of proteins, which can be of viral- or self-origin. Degradation of proteins is mediated by cytosolic- and nuclear proteasomes, and the resulting peptides are translocated into the ER by means of TAP. TAP translocates peptides of 8 –16 amino acids and they may require additional trimming in the ER before binding to MHC class I molecules. This is possibly due to the presence of ER aminopeptidase (ERAAP) associated with antigen processing [5], [6].

It should be noted that 30–70% of proteins are immediately degraded after synthesis (they are called DRiPs – defective ribosomal products, and they are the result of defective transcription or translation). This process allows viral peptides to be presented very quickly – for example, influenza virus can be recognised by T cells approximately 1.5 hours post-infection. When peptides bind to MHC class I molecules, the chaperones are released and peptide–MHC class I complexes leave the ER for presentation at the cell surface. In some cases, peptides fail to associate with MHC class I and they have to be returned to the cytosol for degradation. Some MHC class I molecules never bind peptides and they are also degraded by the ER-associated protein degradation (ERAD) system [7], [8].There are different proteasomes that generate peptides for MHC class-I presentation: 26S proteasome, which is expressed by most cells; the immunoproteasome, which is expressed by many immune cells; and the thymic-specific proteasome expressed by thymic epithelial cells.

Antigen presentation

On the surface of a single cell, MHC class I molecules provide a readout of the expression level of up to 10,000 proteins. This array is interpreted by cytotoxic T lymphocytes and Natural Killer cells, allowing them to monitor the events inside the cell and detect infection and tumorigenesis.MHC class I complexes at the cell surface may dissociate as time passes and the heavy chain can be internalised. When MHC class I molecules are internalised into the endosome, they enter the MHC class-II presentation pathway. Some of the MHC class I molecules can be recycled and present endosomal peptides as a part of a process which is called cross-presentation.The usual process of antigen presentation through the MHC I molecule is based on an interaction between the T-cell receptor and a peptide bound to the MHC class I molecule.

There is also an interaction between the CD8+ molecule on the surface of the T cell and non-peptide binding regions on the MHC class I molecule. Thus, peptide presented in complex with MHC class I can only be recognised by CD8+ T cells. This interaction is a part of so-called 'three-signal activation model', and actually represents the first signal. The next signal is the interaction between CD80/86 on the APC and CD28 on the surface of the T cell, followed by a third signal the production of cytokines by the APC which fully activates the T cell to provide a specific response [5], [6].

MHC class I polymorphism

Human MHC class I molecules are encoded by a series of genes – HLA-A, HLA-B and HLA-C HLA stands for 'Human Leukocyte Antigen', which is the human equivalent of MHC molecules found in most vertebrates. These genes are highly polymorphic, which means that each individual has his/her own HLA allele set. The consequences of these polymorphisms are differential susceptibilities to infection and autoimmune diseases that may result from the high diversity of peptides that can bind to MHC class I in different individuals. Also, MHC class I polymorphisms make it virtually impossible to have a perfect tissue match between donor and recipient, and thus are responsible for graft rejection. This figure 1 shown MHC I.

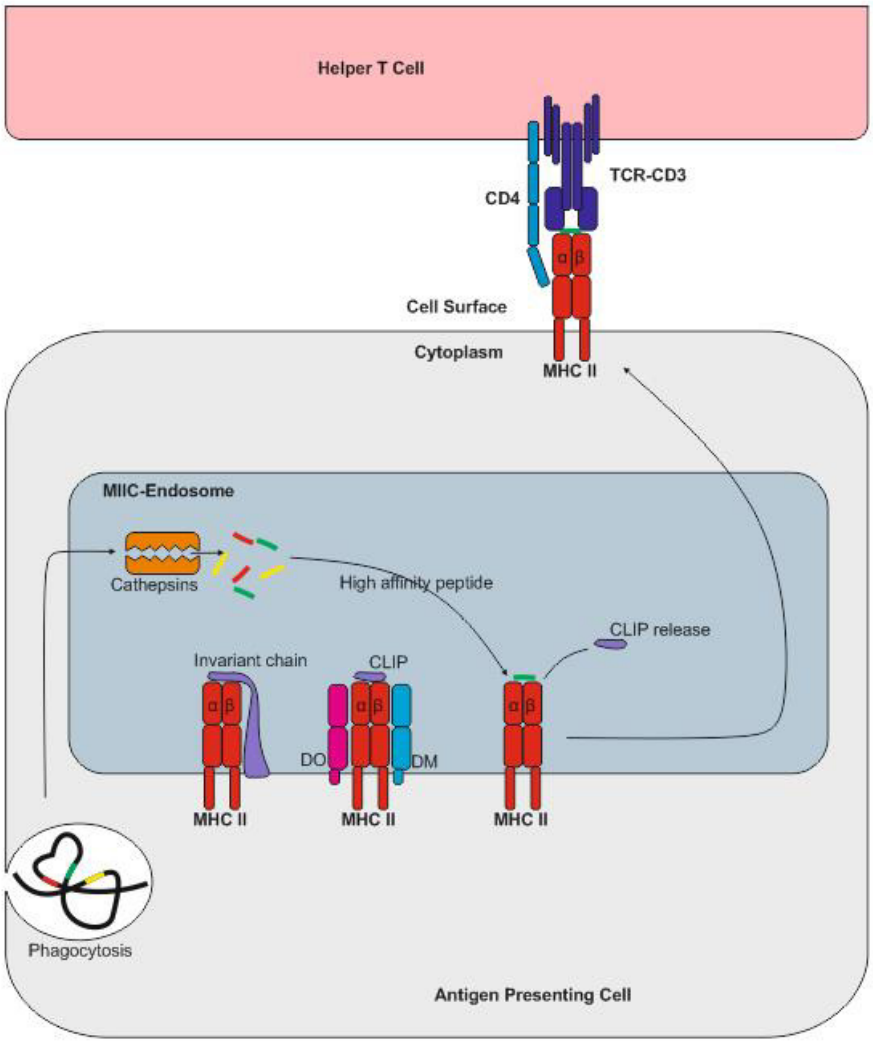


Figure 1: Representing the overview about antigen presentation by the MHC Class I [British Society for Immunology].

MHC class II presentation

MHC class II molecules are expressed by APCs, such as dendritic cells (DC), macrophages and B cells (and, under IFNγ stimuli, by mesenchymal stromal cells, fibroblasts and endothelial cells, as well as by epithelial cells and enteric glial cells). MHC class II molecules bind to peptides that are derived from proteins degraded in the endocytic pathway. MHC class II complexes consists of α- and β-chains that are assembled in the ER and are stabilised by invariant chain (Ii). The complex of MHC class II and Ii is transported through the Golgi into a compartment which is termed the MHC class II compartment (MIIC). Due to acidic pH, proteases cathepsin S and cathepsin L are activated and digest Ii, leaving a residual class II-associated Ii peptide (CLIP) in the peptide-binding groove of the MHC class II. Later, the CLIP is exchanged for an antigenic peptide derived from a protein degraded in the endosomal pathway. This process requires the chaperone HLA-DM, and, in the case of B cells, the HLA-DO molecule. MHC class II molecules loaded with foreign peptide are then transported to the cell membrane to present their cargo to CD4+ T cells. Thereafter, the process of antigen presentation by means of MHC class II molecules basically follows the same pattern as for MHC class I presentation. As opposed to MHC class I, MHC class II molecules do not dissociate at the plasma membrane. The mechanisms that control MHC class II degradation have not been established yet, but MHC class II molecules can be ubiquitinised and then internalized in an endocytic pathway [9], [10].

CONCLUSION

In conclusion, the Chapter on Antigen Processing and Presentation has unraveled the intricate processes that underpin the body's ability to recognize and respond to foreign antigens, setting the stage for adaptive immune responses. These processes are fundamental to understanding the initiation of immune reactions and have far-reaching implications in both health and disease. Antigen processing and presentation rely heavily on specialized immune cells known as antigen-presenting cells (APCs), including dendritic cells, macrophages, and B cells. These cells play a central role in capturing, processing, and presenting antigens to initiate immune responses. Their ability to recognize and internalize antigens is pivotal in immune surveillance. The presentation of peptide antigens on the cell surface occurs through the major histocompatibility complex (MHC) molecules. MHC class I molecules present antigens to cytotoxic T cells, while MHC class II molecules present antigens to helper T cells. This interaction between MHC molecules and T cells forms the foundation of adaptive immunity. The recognition of antigens by T cells is a crucial step in the activation of adaptive immune responses.

Helper T cells play a pivotal role in orchestrating immune reactions, while cytotoxic T cells are responsible for eliminating infected or abnormal host cells. This coordination is essential for an effective immune defense. The understanding of antigen processing and presentation has profound clinical implications. It is central to vaccine development, where vaccines aim to train the immune system to recognize specific antigens and establish immunological memory. Furthermore, the study of these processes informs the development of immunotherapies for cancer and autoimmune diseases, where modulating immune responses is a therapeutic strategy. In summary, antigen processing and presentation are the gatekeepers of adaptive immunity. They are the initial steps in the body's ability to distinguish between self and non-self and to mount targeted immune responses against pathogens, infected cells, and other foreign invaders. As we continue to explore and manipulate these processes, we unlock new avenues for vaccine development, immunotherapy, and the advancement of medical science, ultimately contributing to the betterment of human health and the management of diseases.

REFERENCES:

[1] J. M. Vyas, A. G. Van Der Veen, and H. L. Ploegh, The known unknowns of antigen processing and presentation, *Nature Reviews Immunology*. 2008. doi: 10.1038/nri2368.

[2] U. Gazi and L. Martinez-Pomares, Influence of the mannose receptor in host immune responses, *Immunobiology*. 2009. doi: 10.1016/j.imbio.2008.11.004.

[3] A. M. Knight, Regulated release of B cell-derived exosomes: Do differences in exosome release provide insight into different APC function for B cells and DC?, *European Journal of Immunology*. 2008. doi: 10.1002/eji.200838374.

[4] Biorad, Macrophage polarization mini review, *New Sci.*, 2012.

[5] H. K. Seong, A. Visser, C. Cruijsen, A. W. M. Van Der Velden, and M. Boes, Recruitment of Rab27a to phagosomes controls microbial antigen cross-presentation by dendritic cells, *Infect. Immun.*, 2008, doi: 10.1128/IAI.01044-08.

[6] B. Bogunovic, M. Stojakovic, L. Chen, and M. Maric, An unexpected functional link between lysosomal thiol reductase and mitochondrial manganese superoxide dismutase, *J. Biol. Chem.*, 2008, doi: 10.1074/jbc.M708998200.

[7] S. Gupta *et al.*, Anchor side chains of short peptide fragments trigger ligand-exchange of Class II MHC molecules, *PLoS One*, 2008, doi: 10.1371/journal.pone.0001814.

[8] M. M. Mendelson *et al.*, Epigenome-wide association study of soluble tumor necrosis factor receptor 2 levels in the framingham heart study, *Front. Pharmacol.*, 2018, doi: 10.3389/fphar.2018.00207.

[9] M. Boes, A. J. Stoppelenburg, and F. C. M. Sillé, Endosomal processing for antigen presentation mediated by CD1 and Class i major histocompatibility complex: Roads to display or destruction, *Immunology*. 2009. doi: 10.1111/j.1365-2567.2009.03078.x.

[10] C. Stoeckle and E. Tolosa, Antigen processing and presentation in multiple sclerosis, *Results Probl. Cell Differ.*, 2010, doi: 10.1007/400_2009_22.

CHAPTER 10

IMMUNE RESPONSES TO PATHOGENS: A COMPREHENSIVE EXPLORATION

Dr.Ramakant, Assistant Professor
Department of Science, Maharishi University of Information Technology, Uttar Pradesh, India
Email Id- ramakant@muit.in

ABSTRACT:

The Chapter on Immune Responses to Pathogens provides a comprehensive exploration of the intricate and dynamic interactions between the immune system and various pathogens, including bacteria, viruses, fungi, and parasites. This Chapter delves into the mechanisms of innate and adaptive immune responses, elucidating how the immune system recognizes, combats, and establishes immunological memory against these invaders. It explores the roles of immune cells, cytokines, antibodies, and the clinical implications of understanding and modulating immune responses in infectious diseases, vaccine development, and immunotherapies.Worm parasites like helminths are believed to be the main cause of the development of the mucosal immune response, IgE-mediated allergies and asthma, and eosinophils. These parasites used to be very common among people. When worms enter a person's body, often through food that has germs on it, they live in the digestive system. Eosinophils are drawn to the specific location by signals from T cells. When they reach the site, they release their contents. When mast cells release their stored substances, it causes fluid to leak out and makes it easier for the parasite to be flushed out from the body along with its babies. Moreover, if IgE marks the parasite, the eosinophils can attach to it through their Fc receptor.

KEYWORDS:

Adaptive Immunity, Antigen Recognition, Cytokines, Immune Cells, Immunological Memory.

INTRODUCTION

Immune responses to pathogens are the body's intricate and highly coordinated defense mechanisms designed to protect us from infections caused by various microorganisms, including bacteria, viruses, fungi, and parasites. These responses are essential for maintaining our health and well-being by recognizing and eliminating harmful invaders while preserving the integrity of our own cells and tissues. This is the first line of defense and provides immediate, nonspecific protection against pathogens. It includes physical barriers like the skin and mucous membranes, as well as cellular components like neutrophils and macrophages that engulf and destroy invaders. Innate immunity also triggers inflammation, a vital response that recruits immune cells and enhances the immune reaction. This arm of the immune system is highly specific and develops over time as it encounters pathogens. It involves two main types of responses T lymphocytes play a central role in this response. They can directly attack infected cells or help coordinate the immune response by releasing signaling molecules called cytokines.

B lymphocytes are responsible for producing antibodies, which can neutralize pathogens or mark them for destruction by other immune cells. The process of immune responses to pathogens typically involves the following steps Recognition Immune cells recognize pathogens through molecular patterns unique to them, called pathogen-associated molecular

patterns (PAMPs). These patterns are detected by pattern recognition receptors (PRRs) on immune cells [1], [2].Activation: Upon recognition, immune cells become activated and initiate a series of responses aimed at eliminating the pathogen. This may include the release of cytokines, the recruitment of additional immune cells, and the activation of cell-mediated and humoral immune pathways. Immune effectors, such as cytotoxic T cells and antibodies, target and neutralize the pathogens. Cytotoxic T cells can directly kill infected cells, while antibodies can block the entry of pathogens into host cells or mark them for destruction by other immune cells.

After the pathogen is eliminated, the immune system returns to a state of readiness. Importantly, the adaptive immune system forms immunological memory, which enables a faster and more effective response upon re-exposure to the same pathogen. This is the basis for vaccination [3], [4].The balance between effective pathogen clearance and prevention of autoimmunity an immune response against one's own cells is crucial for maintaining health. Dysregulation of the immune system can lead to various diseases, including autoimmune disorders, allergies, and immunodeficiency diseases. In conclusion, immune responses to pathogens are a remarkable and highly complex set of biological processes that are vital for our survival. Understanding how the immune system recognizes and combats invaders is fundamental in the fields of immunology and medicine, as it helps us develop strategies to prevent and treat infectious diseases and other immune-related conditions.

DISCUSSION

Now that you understand the development of mature, naïve B cells and T cells, and some of their major functions, how do all of these various cells, proteins, and cytokines come together to actually resolve an infection? Ideally, the immune response will rid the body of a pathogen entirely. The adaptive immune response, with its rapid clonal expansion, is well suited to this purpose. Think of a primary infection as a race between the pathogen and the immune system. The pathogen bypasses barrier defenses and starts multiplying in the host’s body. During the first 4 to 5 days, the innate immune response will partially control, but not stop, pathogen growth. As the adaptive immune response gears up, however, it will begin to clear the pathogen from the body, while at the same time becoming stronger and stronger. When following antibody responses in patients with a particular disease such as a virus, this clearance is referred to as seroconversion. Seroconversion is the reciprocal relationship between virus levels in the blood and antibody levels. As the antibody levels rise, the virus levels decline, and this is a sign that the immune response is being at least partially effective partially, because in many diseases, seroconversion does not necessarily mean a patient is getting well.An excellent example of this is seroconversion during HIV disease. Notice that antibodies are made early in this disease, and the increase in anti-HIV antibodies correlates with a decrease in detectable virus in the blood. Although these antibodies are an important marker for diagnosing the disease, they are not sufficient to completely clear the virus. Several years later, the vast majority of these individuals, if untreated, will lose their entire adaptive immune response, including the ability to make antibodies, during the final stages of AIDS [5], [6].

The Mucosal Immune Response

Mucosal tissues are major barriers to the entry of pathogens into the body. The IgA (and sometimes IgM) antibodies in mucus and other secretions can bind to the pathogen, and in the cases of many viruses and bacteria, neutralize them. Neutralization is the process of coating a pathogen with antibodies, making it physically impossible for the pathogen to bind to receptors. Neutralization, which occurs in the blood, lymph, and other body fluids and

secretions, protects the body constantly. Neutralizing antibodies are the basis for the disease protection offered by vaccines. Vaccinations for diseases that commonly enter the body via mucous membranes, such as influenza, are usually formulated to enhance IgA production.

Defenses against Bacteria and Fungi

The body fights bacterial pathogens with a wide variety of immunological mechanisms, essentially trying to find one that is effective. Bacteria such as *Mycobacterium leprae*, the cause of leprosy, are resistant to lysosomal enzymes and can persist in macrophage organelles or escape into the cytosol. In such situations, infected macrophages receiving cytokine signals from Th1 cells turn on special metabolic pathways. Macrophage oxidative metabolism is hostile to intracellular bacteria, often relying on the production of nitric oxide to kill the bacteria inside the macrophage. Fungal infections, such as those from *Aspergillus*, *Candida*, and *Pneumocystis*, are largely opportunistic infections that take advantage of suppressed immune responses. Most of the same immune mechanisms effective against bacteria have similar effects on fungi, both of which have characteristic cell wall structures that protect their cells [7], [8].

Defenses against Parasites

Worm parasites such as helminths are seen as the primary reason why the mucosal immune response, IgE-mediated allergy and asthma, and eosinophils evolved. These parasites were at one time very common in human society. When infecting a human, often via contaminated food, some worms take up residence in the gastrointestinal tract. Eosinophils are attracted to the site by T cell cytokines, which release their granule contents upon their arrival. Mast cell degranulation also occurs, and the fluid leakage caused by the increase in local vascular permeability is thought to have a flushing action on the parasite, expelling its larvae from the body. Furthermore, if IgE labels the parasite, the eosinophils can bind to it by its Fc receptor.

Defenses against Viruses

The primary mechanisms against viruses are NK cells, interferons, and cytotoxic T cells. Antibodies are effective against viruses mostly during protection, where an immune individual can neutralize them based on a previous exposure. Antibodies have no effect on viruses or other intracellular pathogens once they enter the cell, since antibodies are not able to penetrate the plasma membrane of the cell. Many cells respond to viral infections by downregulating their expression of MHC class I molecules. This is to the advantage of the virus, because without class I expression, cytotoxic T cells have no activity. NK cells, however, can recognize virally infected class I-negative cells and destroy them. Thus, NK and cytotoxic T cells have complementary activities against virally infected cells [5].

Interferons have activity in slowing viral replication and are used in the treatment of certain viral diseases, such as hepatitis B and C, but their ability to eliminate the virus completely is limited. The cytotoxic T cell response, though, is key, as it eventually overwhelms the virus and kills infected cells before the virus can complete its replicative cycle. Clonal expansion and the ability of cytotoxic T cells to kill more than one target cell make these cells especially effective against viruses. In fact, without cytotoxic T cells, it is likely that humans would all die at some point from a viral infection if no vaccine were available.

Evasion of the Immune System by Pathogens

It is important to keep in mind that although the immune system has evolved to be able to control many pathogens, pathogens themselves have evolved ways to evade the immune response. An example already mentioned is in *Mycobactrium tuberculosis*, which has

evolved a complex cell wall that is resistant to the digestive enzymes of the macrophages that ingest them, and thus persists in the host, causing the chronic disease tuberculosis. This section briefly summarizes other ways in which pathogens can outwit immune responses. But keep in mind, although it seems as if pathogens have a will of their own, they do not. All of these evasive strategies arose strictly by evolution, driven by selection. Bacteria sometimes evade immune responses because they exist in multiple strains, such as different groups of Staphylococcus aureus. S. aureus is commonly found in minor skin infections, such as boils, and some healthy people harbor it in their nose. One small group of strains of this bacterium, however, called methicillin-resistant Staphylococcus aureus, has become resistant to multiple antibiotics and is essentially untreatable.

Different bacterial strains differ in the antigens on their surfaces. The immune response against one strain does not affect the other; thus, the species survives. Another method of immune evasion is mutation. Because viruses' surface molecules mutate continuously, viruses like influenza change enough each year that the flu vaccine for one year may not protect against the flu common to the next. New vaccine formulations must be derived for each flu season [9].Genetic recombinationthe combining of gene segments from two different pathogensis an efficient form of immune evasion. For example, the influenza virus contains gene segments that can recombine when two different viruses infect the same cell. Recombination between human and pig influenza viruses led to the 2010 H1N1 swine flu outbreak. Pathogens can produce immunosuppressive molecules that impair immune function, and there are several different types. Viruses are especially good at evading the immune response in this way, and many types of viruses have been shown to suppress the host immune response in ways much more subtle than the wholesale destruction caused by HI.

CONCLUSION

In conclusion, immune responses to pathogens represent a marvel of biological defense mechanisms that safeguard our health and well-being. These responses involve a coordinated effort between the innate and adaptive arms of the immune system, working together to recognize, combat, and remember specific pathogens. Here are some key takeaways. The immune system comprises innate immunity, providing immediate, nonspecific defense, and adaptive immunity, offering specific, memory-based protection. These two components work in concert to combat infections. Recognition and Activation: Immune responses begin with the recognition of pathogen-associated molecular patterns (PAMPs) by pattern recognition receptors (PRRs) on immune cells. Upon recognition, immune cells become activated, initiating a cascade of events to combat the invading pathogens. Effector Responses: Immune effectors, such as antibodies, cytotoxic T cells, and various immune molecules, work to neutralize and eliminate pathogens. These responses are highly specific and can target a wide range of infectious agents. Resolution and Memory: After the pathogen is cleared, the immune system returns to a state of readiness. The adaptive immune system forms immunological memory, ensuring a quicker and more effective response upon subsequent encounters with the same pathogen, which is the basis for vaccines.

The immune system must maintain a delicate balance between attacking pathogens and avoiding self-harm. Dysregulation can lead to autoimmune diseases, allergies, or immunodeficiencies, highlighting the importance of immune system control and regulation.Understanding immune responses to pathogens is crucial for developing vaccines, treatments for infectious diseases, and therapies for immune-related disorders. Immunology research continues to advance our knowledge in these areas. In summary, immune responses to pathogens are a testament to the incredible complexity and sophistication of the human

immune system. They play a central role in protecting us from a wide range of infectious threats and are instrumental in maintaining our overall health and longevity. The ongoing study of these responses holds great promise for improving medical interventions and advancing our understanding of human health and disease.

REFERENCES:

[1] T. B. H. Geijtenbeek and S. I. Gringhuis, "Signalling through C-type lectin receptors: Shaping immune responses," *Nature Reviews Immunology*. 2009. doi: 10.1038/nri2569.

[2] E. N. N'Diaye *et al.*, "TREM-2 (triggering receptor expressed on myeloid cells 2) is a phagocytic receptor for bacteria," *J. Cell Biol.*, 2009, doi: 10.1083/jcb.200808080.

[3] G. E. Gudesblat, P. S. Torres, and A. A. Vojnov, "Stomata and pathogens: Warfare at the gates," *Plant Signal. Behav.*, 2009, doi: 10.4161/psb.4.12.10062.

[4] J. F. Hillyer, "Transcription in mosquito hemocytes in response to pathogen exposure," *Journal of Biology*. 2009. doi: 10.1186/jbiol151.

[5] V. Citovsky, A. Zaltsman, S. V. Kozlovsky, Y. Gafni, and A. Krichevsky, "Proteasomal degradation in plant-pathogen interactions," *Seminars in Cell and Developmental Biology*. 2009. doi: 10.1016/j.semcdb.2009.05.012.

[6] T. B H Geijtenbeek, "Dendritic Cell Immunotherapy, the Next Step in Cancer Treatment," *Multidiscip. Cancer Investig.*, 2017, doi: 10.21859/mci-01025.

[7] J. R. Powell, D. H. Kim, and F. M. Ausubel, "The G protein-coupled receptor FSHR-1 is required for the caenorhabditis elegans innate immune response," *Proceedings of the National Academy of Sciences of the United States of America*. 2009. doi: 10.1073/pnas.0813048106.

[8] T. B. H. Geijtenbeek, J. den Dunnen, and S. I. Gringhuis, "Pathogen recognition by DC-SIGN shapes adaptive immunity," *Future Microbiology*. 2009. doi: 10.2217/fmb.09.51.

[9] L. F. Lu and A. Rudensky, "Molecular orchestration of differentiation and function of regulatory T cells," *Genes and Development*. 2009. doi: 10.1101/gad.1791009.

CHAPTER 11

AUTOIMMUNITY AND HYPERSENSITIVITY: IMMUNE SYSTEM DISORDERS

Dr.Ramakant, Assistant Professor
Department of Science, Maharishi University of Information Technology, Uttar Pradesh, India
Email Id- ramakant@muit.in

ABSTRACT:
Autoimmunity and hypersensitivity are two distinct but closely related aspects of the immune system's function that can lead to various immune-related disorders. Autoimmunity involves the misdirection of the immune response against the body's own tissues and cells, resulting in autoimmune diseases. Hypersensitivity, on the other hand, refers to exaggerated or inappropriate immune reactions against harmless substances, leading to allergies and other hypersensitivity disorders. This abstract provides an overview of these phenomena, their underlying mechanisms, and their clinical implications. Understanding autoimmunity and hypersensitivity is vital for diagnosing, managing, and developing treatments for a wide range of immune-mediated conditions.

KEYWORDS:

Autoimmunity, Antigen, Hypersensitivity, Immune Tolerance, Type II Hypersensitivity.

INTRODUCTION

A functioning immune system is essential for survival, but even the sophisticated cellular and molecular defenses of the mammalian immune response can be defeated by pathogens at virtually every step. In the competition between immune protection and pathogen evasion, pathogens have the advantage of more rapid evolution because of their shorter generation time and other characteristics. For instance, *Streptococcus pneumoniae* bacterium that cause pneumonia and meningitis surrounds itself with a capsule that inhibits phagocytes from engulfing it and displaying antigens to the adaptive immune system. *Staphylococcus aureus* bacterium that can cause skin infections, abscesses, and meningitis synthesizes a toxin called leucocidin that kills phagocytes after they engulf the bacterium. Other pathogens can also hinder the adaptive immune system. HIV infects TH cells via their CD4 surface molecules, gradually depleting the number of TH cells in the body; this inhibits the adaptive immune system's capacity to generate sufficient responses to infection or tumors. As a result, HIV-infected individuals often suffer from infections that would not cause illness in people with healthy immune systems but which can cause devastating illness to immune-compromised individuals. Maladaptive responses of immune cells and molecules themselves can also disrupt the proper functioning of the entire system, leading to host cell damage that could become fatal [1], [2].

Autoimmune disease happens when the body's immune system mistakenly attacks its own healthy cells and tissues. When our body's defenses react to a foreign substance, the usual result is getting rid of that substance from our body. Cells infected with viruses are destroyed by a type of cell called cytotoxic T cells. On the other hand, immune complexes of antibody and antigen are used to clear soluble antigens. These complexes are taken up by cells called macrophages in the mononuclear phagocytic system. When the immune system starts to fight against its own cells, it can't completely get rid of the harmful substances. This causes a continuous response from the immune system. This means that the immune system can cause long-term inflammation in tissues, which can be deadly.

The causes of tissue damage in autoimmune diseases are very similar to those in protective immunity and hypersensitivity diseases. Certain frequent autoimmune illnesses. The body's immune system fights off germs and other invaders by using special cells called T cells. When the T cells recognize a specific target, they start a response to get rid of it. It is thought that the same process happens when the immune system mistakenly attacks the body's own healthy cells, which is called autoimmunity. When the body's immune cells called T-cells respond to substances in the body that are not supposed to be there, they can cause harm to the tissues either by attacking them directly or by causing problems indirectly. Cytotoxic T-cells and TH1 cells can harm tissues, while T-cells helping self-reactive B cells can cause harmful autoantibody responses. Autoimmune responses happen because B-cells and T-cells can recognize any germ due to their wide range of receptors.

Even though these collections of receptors remove most of the ones that strongly bind to substances in the body that may cause harm, they still contain some receptors that weakly react to certain substances in the body. We don't know what causes autoimmunity, but things in the environment and our genes, especially our MHC genotype, are definitely important. Simple words: Temporary immune reactions are normal, but they only become a concern when they continue and harm the body's tissues in the long term. In this part, we will study how our body's immune system makes mistakes and attacks our own tissues, causing harm. In the last part of this Chapter, we will study how self-tolerance is lost and how autoimmune responses start.

Early in the study of immunity, it was discovered that the potent effector mechanisms engaged in host defence could induce severe tissue damage if turned against the host; Ehrlich dubbed this nightmare autotoxicus. Healthy people do not produce prolonged adaptive immune responses to their own antigens, and while temporary responses to damaged self-tissues can occur, they seldom result in additional tissue damage. Although self-tolerance is the general rule, certain people experience chronic immune reactions to their own tissues, resulting in the severe tissue damage predicted by Ehrlich.Autoimmune illness can be experimentally generated in certain genetically vulnerable strains of experimental animals by injecting'self' tissues from a genetically identical animal mixed with powerful adjuvants including bacteria. This demonstrates that autoimmunity may be induced by eliciting a specific, adaptive immune response to self-antigens, and it serves as the foundation for our understanding of how autoimmune disease develops. Autoimmunity typically develops spontaneously in people; that is, we do not know what circumstances trigger the immune response to self that leads to the autoimmune illness. As we will see in the final section of this Chapter, there is evidence that some autoimmune illnesses, such as rheumatic fever, may be induced by infectious organisms. However, there is evidence, notably from animal models of autoimmunity, that many autoimmune illnesses are caused by internal immune system dysregulation rather than by pathogenic pathogens.

Disease classification is an ambiguous science, particularly in the absence of a thorough understanding of the underlying mechanisms. The difficulty in categorizing autoimmune disorders is a good example of this. It is useful to distinguish between two types of autoimmune disease: those in which autoimmunity is expressed only in specific organs of the body, known as 'organ-specific' autoimmune diseases, and those in which many tissues of the body are affected, known as'systemic' autoimmune diseases. Hashimoto's thyroiditis and Graves' disease, both of which affect the thyroid gland, are examples of organ-specific autoimmune disorders, as is type I insulin-dependent diabetes mellitus (IDDM), which affects the pancreatic islets. Systemic autoimmune diseases, such as systemic lupus erythematosus (SLE) and primary Sjögren's syndrome, can affect tissues as diverse as the skin, kidneys, and

brain. Insulin-Dependent Diabetes Mellitus and Systemic Lupus Erythematosus, Case Studies in Immunology, details in the Preface. The autoantigens identified in these two types of illness are organ-specific and systemic, respectively. Graves' illness is distinguished by antibodies to the thyroid-stimulating hormone (TSH) receptor in the thyroid gland, Hashimoto's thyroiditis by antibodies to thyroid peroxidase, and type I diabetes by anti-insulin antibodies. SLE, on the other hand, is distinguished by the presence of antibodies to antigens that are present in every cell of the body, such as anti-chromatin antibodies and antibodies to proteins of the pre-mRNA splicing machinerythe spliceosome complexwithin the cell.

Organ-specific and systemic autoimmune disorders are expected to have slightly different etiologies, providing a scientific basis for their classification into two major categories. Observations of distinct autoimmune illnesses clustering among people and families also support the validity of this classification. Organ-specific autoimmune disorders may coexist in a variety of combinations; for example, autoimmune thyroid disease and the autoimmune depigmenting disease vitiligo are frequently observed in the same person. Similarly, SLE and primary Sjögren's syndrome can coexist in the same person or among different members of the same family.These autoimmune disease clusters give the most useful classification into several subtypes, each of which may have a unique mechanism. The rigorous categorization of diseases into 'organ-specific' and'systemic' categories is considered to fail to some extent. This classification does not apply to all autoimmune disorders. Autoimmune hemolytic anemia, for example, can exist as a single entity and may be characterized as an organ-specific disease. In other cases, it may occur alongside SLE as part of a systemic autoimmune disease.

Family studies, particularly twin studies, provide the greatest evidence in humans for susceptibility genes for autoimmunity. Comparing the incidence of disease in monozygotic and dizygotic twins is a semiquantitative technique for determining whether proportion of susceptibility to a given disease is due to hereditary factors. If a condition is shared by all twins, it could be due to common genetic or environmental factors. This is because both monozygotic and dizygotic twins are typically raised in the same environment. However, if the high concordance is limited to monozygotic twins rather than dizygotic twins, genetic factors are likely to be more relevant than environmental factors.Several human disorders involving autoimmunity have been studied using twins, including type I IDDM, rheumatoid arthritis, multiple sclerosis, and SLE. In each scenario, approximately 20% of pairs of monozygotic twins have illness concordance, compared to less than 5% of pairs of dizygotic twins. A similar strategy is to compare the prevalence of an illness, such as diabetes, in siblings of diabetic patients to the prevalence of that disease in the general population. The ratio of these two frequencies indicates the disease's heredity, while shared environmental factors within families may also be at least partially responsible for an elevated frequency.

The findings of twin and family studies indicate that both hereditary and environmental factors play an essential role in the development of autoimmune disease. In addition to human evidence, certain inbred mouse strains show almost uniform vulnerability to specific spontaneous or experimentally caused autoimmune disorders, whereas others do not. These discoveries prompted an extensive search for genes that influence vulnerability to autoimmune illness.So far, MHC genotype has been most consistently connected with vulnerability to autoimmune illness. Susceptibility to most of these disorders is highly associated to MHC class II alleles, however in other cases there are strong connections with specific MHC class I alleles.The relationship between MHC genotype and disease is first investigated by comparing the frequency of various alleles in patients to their frequency in

the general population. This method initially indicated a correlation with HLA-DR3 and HLA-DR4 alleles detected by serotyping in IDDM. Such investigations also revealed that the MHC class II allele HLA-DR2 has a dominant protective effect; those who carry HLA-DR2, even when combined with one of the susceptibility alleles, are less likely to develop diabetes. Another method for evaluating if MHC genes have a role in autoimmune disease is to analyze the families of afflicted patients; it has been demonstrated that two siblings with the same autoimmune disease are far more likely than predicted to share the same MHC haplotypes (Disease connections that were originally established through HLA serotyping using antibodies have been defined more precisely as HLA genotyping has grown more precise through the sequencing of HLA alleles.

The correlation between IDDM and the DR3 and DR4 alleles, for example, is now understood to be attributable to their close genetic linkage to DQ alleles that confer disease vulnerability. Indeed, variations at a specific place in the DQ amino acid sequence are most closely connected with illness risk. The most abundant DQ amino acid sequence contains an aspartic acid at position 57 that can build a salt bridge over the end of the DQ molecule's peptide binding cleft. Diabetic patients in Caucasoid ethnicities, on the other hand, contain valine, serine, or alanine at that location and consequently produce DQ molecules that lack this salt bridge.

The homologous MHC class II molecule, known as I-Ag7, also contains a serine at that position in the nonobese diabetic (NOD) mouse strain, which develops spontaneous diabetes. The link between MHC genotype and autoimmune disease is not surprising, because autoimmune reactions include T cells, and T cells' ability to respond to a specific antigen is determined by MHC genotype. Thus, the relationships can be explained by a simple model in which susceptibility to an autoimmune disease is dictated by changes in the ability of distinct allelic variants of MHC molecules to present autoreactive T cells with autoantigenic peptides. This is consistent with what we know about T-cell involvement in specific illnesses. Diabetes, for example, has been linked to both MHC class I and MHC class II alleles, which is consistent with the discovery that CD8 and CD4 T cells, which respond to antigens presented by MHC class I and MHC class II molecules, respectively, trigger the autoimmune response.

An alternate hypothesis for the link between MHC genotype and autoimmune disease susceptibility highlights the role of MHC alleles in determining the T-cell receptor repertoire. According to this concept, self-peptides coupled with specific MHC molecules may induce the positive selection of developing thymocytes specialized for certain autoantigens. Such autoantigenic peptides may be expressed at insufficient levels or bind to self MHC molecules insufficiently to drive negative selection in the thymus, but exist at sufficient levels or bind strongly enough to induce positive selection. This notion is reinforced by the fact that I-Ag7, the disease-associated MHC class II molecule in diabetic NOD mice, binds numerous peptides extremely poorly and may thus be less effective in driving intrathymic negative selection of T cells that bind self-peptides.

However, MHC genotype alone does not determine disease susceptibility. Identical twins who share all of their genes are considerably more likely than MHC-identical siblings to acquire the same autoimmune disease, suggesting that genetic factors other than the MHC influence whether an individual gets disease. Recent research on the genetics of autoimmune diabetes in humans and mice has revealed that, in addition to the MHC, there are several independently segregating disease susceptibility loci.There is additional evidence that differences in the concentration of a potential autoantigen within the thymus can influence disease progression.

The degree of transcription of the insulin gene displays genetic diversity across individuals in the case of human insulin, which can act as an autoantigen in type I IDDM; this is connected with a polymorphic minisatellite sequence situated upstream of the gene. Gene variants that are transcribed at a high level in the thymus are related with illness susceptibility, whereas variants that are transcribed at a low level are associated with disease susceptibility. This is because excessive levels of insulin expression in the thymus may result in the loss of T lymphocytes specialized for insulin peptides.

The existence of autoantibodies to ubiquitous and abundant intracellular antigens, such as chromatin, is the most significant serological anomaly in SLE. How is tolerance to such widespread self-antigens broken? In humans and animals, a variety of genes have been linked in the genesis of SLE. These can be divided into three groups based on their physiological function.

The first group consists of genes whose products are involved in the body's mechanisms for disposing of dead and dying cells, which could serve as a source of autoantigens. Four genes in this group have been genetically knocked out in mice to create animal models of SLE. One of these genes encodes the complement protein C1q, which is involved in the efficient clearance of immune complexes and apoptotic cells along with other complement proteins.

A second gene in this category encodes a component of serum amyloid P that binds to chromatin and may disguise it from the immune system. Its loss causes the formation of antibodies against chromatin as well as the development of glomerulonephritis due to the deposition of immunological complexes of these antibodies in the kidney.

Third, the absence of DNase I, an enzyme that digests extracellular chromatin, causes the formation of anti-chromatin antibodies as well as glomerulonephritis. Fourth, a similar phenotype has been observed in animals lacking the secretory region of the immunoglobulin chain, and therefore lacking secreted IgM, which may play a significant role in the clearance of effete cells. The bulk of spontaneous SLE cases, however, are likely to be impacted by significantly more complex genetic variables than these single-gene abnormalities.

DISCUSSION

Immunodeficiency

Failures, insufficiencies, or delays at any level of the immune response can allow pathogens or tumor cells to gain a foothold and replicate or proliferate to high enough levels that the immune system becomes overwhelmed. Immunodeficiency is the failure, insufficiency, or delay in the response of the immune system, which may be acquired or inherited. Immunodeficiency can be acquired as a result of infection with certain pathogens such as HIV, chemical exposureincluding certain medical treatments, malnutrition, or possibly by extreme stress. For instance, radiation exposure can destroy populations of lymphocytes and elevate an individual’s susceptibility to infections and cancer.

Dozens of genetic disorders result in immunodeficiencies, including Severe Combined Immunodeficiency (SCID), Bare lymphocyte syndrome, and MHC II deficiencies. Rarely, primary immunodeficiencies that are present from birth may occur. Neutropenia is one form in which the immune system produces a below-average number of neutrophils, the body’s most abundant phagocytes. As a result, bacterial infections may go unrestricted in the blood, causing serious complications [3], [4].

Hypersensitivities

Maladaptive immune responses toward harmless foreign substances or self-antigens that occur after tissue sensitization are termed hypersensitivities. The types of hypersensitivities include immediate, delayed, and autoimmunity. A large proportion of the population is affected by one or more types of hypersensitivity [5].

Allergies

The immune reaction that results from immediate hypersensitivities in which an antibody-mediated immune response occurs within minutes of exposure to a harmless antigen is called an allergy. In the United States, 20 percent of the population exhibits symptoms of allergy or asthma, whereas 55 percent test positive against one or more allergens. Upon initial exposure to a potential allergen, an allergic individual synthesizes antibodies of the IgE class via the typical process of APCs presenting processed antigen to T_H cells that stimulate B cells to produce IgE.

This class of antibodies also mediates the immune response to parasitic worms. The constant domain of the IgE molecules interact with mast cells embedded in connective tissues. This process primes, or sensitizes, the tissue. Upon subsequent exposure to the same allergen, IgE molecules on mast cells bind the antigen via their variable domains and stimulate the mast cell to release the modified amino acids histamine and serotonin; these chemical mediators then recruit eosinophils which mediate allergic responses.

The effects of an allergic reaction range from mild symptoms like sneezing and itchy, watery eyes to more severe or even life-threatening reactions involving intensely itchy welts or hives, airway contraction with severe respiratory distress, and plummeting blood pressure. This extreme reaction is known as anaphylactic shock. If not treated with epinephrine to counter the blood pressure and breathing effects, this condition can be fatal. Delayed hypersensitivity is a cell-mediated immune response that takes approximately one to two days after secondary exposure for a maximal reaction to be observed. This type of hypersensitivity involves the T_H1 cytokine-mediated inflammatory response and may manifest as local tissue lesions or contact dermatitis rash or skin irritation.

Delayed hypersensitivity occurs in some individuals in response to contact with certain types of jewelry or cosmetics. Delayed hypersensitivity facilitates the immune response to poison ivy and is also the reason why the skin test for tuberculosis results in a small region of inflammation on individuals who were previously exposed to *Mycobacterium tuberculosis*. That is also why cortisone is used to treat such responses: it will inhibit cytokine production [6], [7].

Autoimmunity

Autoimmunity is a type of hypersensitivity to self-antigens that affects approximately five percent of the population. Most types of autoimmunity involve the humoral immune response. Antibodies that inappropriately mark self-components as foreign are termed autoantibodies. In patients with the autoimmune disease myasthenia gravis, muscle cell receptors that induce contraction in response to acetylcholine are targeted by antibodies. The result is muscle weakness that may include marked difficultly with fine and/or gross motor functions. In systemic lupus erythematosus, a diffuse autoantibody response to the individual's own DNA and proteins results in various systemic diseases. Systemic lupus erythematosus may affect the heart, joints, lungs, skin, kidneys, central nervous system, or other tissues, causing tissue damage via antibody binding, complement recruitment, lysis, and

inflammation [5], [8]. Autoimmunity can develop with time, and its causes may be rooted in molecular mimicry. Antibodies and TCRs may bind self-antigens that are structurally similar to pathogen antigens, which the immune receptors first raised. As an example, infection with *Streptococcus pyogenes* bacterium that causes strep throat may generate antibodies or T cells that react with heart muscle, which has a similar structure to the surface of *S. pyogenes*. These antibodies can damage heart muscle with autoimmune attacks, leading to rheumatic fever. Insulin-dependent (Type 1) diabetes mellitus arises from a destructive inflammatory T_H1 response against insulin-producing cells of the pancreas. Patients with this autoimmunity must be injected with insulin that originates from other sources [4], [9].

CONCLUSION

In conclusion, autoimmunity and hypersensitivity are two distinct but closely related aspects of the immune system's function that can have significant implications for health and disease. Autoimmunity occurs when the immune system mistakenly targets and attacks the body's own cells and tissues. This can lead to a wide range of autoimmune diseases, such as rheumatoid arthritis, multiple sclerosis, and lupus. The exact causes of autoimmunity are complex and multifactorial, involving genetic, environmental, and immunological factors.

Hypersensitivity, on the other hand, refers to an exaggerated or inappropriate immune response to a normally harmless substance, known as an allergen. There are four types of hypersensitivity reactions, with varying degrees of severity and mechanisms involved. These reactions can manifest as allergies, asthma, or even life-threatening anaphylactic shock. Both autoimmunity and hypersensitivity underscore the importance of immune system regulation and tolerance. Failure in the mechanisms responsible for distinguishing self from non-self or maintaining immune homeostasis can result in autoimmune diseases or hypersensitivity reactions.

Managing autoimmunity and hypersensitivity typically involves a combination of approaches, including immunosuppressive medications, lifestyle modifications, and allergen avoidance for hypersensitivity. Early diagnosis and appropriate management are crucial for improving the quality of life and preventing complications associated with these conditions. Ongoing research in immunology and autoimmune diseases is providing valuable insights into the underlying mechanisms and potential therapeutic strategies to better control and treat these conditions. Understanding the intricate workings of the immune system is essential for advancing our knowledge and improving the management of autoimmunity and hypersensitivity disorders.

REFERENCES:

[1] K. P. Mishra, Lead exposure and its impact on immune system: A review, *Toxicology in Vitro*. 2009. doi: 10.1016/j.tiv.2009.06.014.

[2] R. J. Brown *et al.*, Minocycline-induced drug hypersensitivity syndrome followed by multiple autoimmune sequelae, *Arch. Dermatol.*, 2009, doi: 10.1001/archdermatol.2008.521.

[3] J. B. Hodgin, J. Whelan, G. S. Markowitz, and M. B. Stokes, Giant Cell Tubulitis With Immune Complex Deposits in a Patient With Lupus Nephritis, *Am. J. Kidney Dis.*, 2009, doi: 10.1053/j.ajkd.2008.09.015.

[4] N. Aota and T. Shiohara, Viral connection between drug rashes and autoimmune diseases: How autoimmune responses are generated after resolution of drug rashes, *Autoimmunity Reviews*. 2009. doi: 10.1016/j.autrev.2009.02.029.

[5] P. H.D., S. C.F., T. S.S., and G. M.E., Mold and human health: Separating the wheat from the chaff, *Clinical Reviews in Allergy and Immunology*. 2010.

[6] S. N.B., Pediatric psoriasis: An update, *Therapeutics and Clinical Risk Management*. 2009.

[7] J. V. Castell and I. Miñana, Idiosyncratic Drug-Induced Liver Injury: Facts and Perspectives, in *The Epigenetics of Autoimmune Diseases*, 2009. doi: 10.1002/9780470743553.ch11.

[8] B. J.S., Proton pump inhibitor induced acute interstitial nephritis-remaining mindful of the medication reconciliation, *Journal of General Internal Medicine*. 2015.

[9] A. Mustafa *et al.*, Gestational exposure to 2,3,7,8-Tetrachlorodibenzo-p-dioxin disrupts B-cell lymphopoiesis and exacerbates autoimmune disease in 24-week-old SNF1 mice, *Toxicol. Sci.*, 2009, doi: 10.1093/toxsci/kfp177.