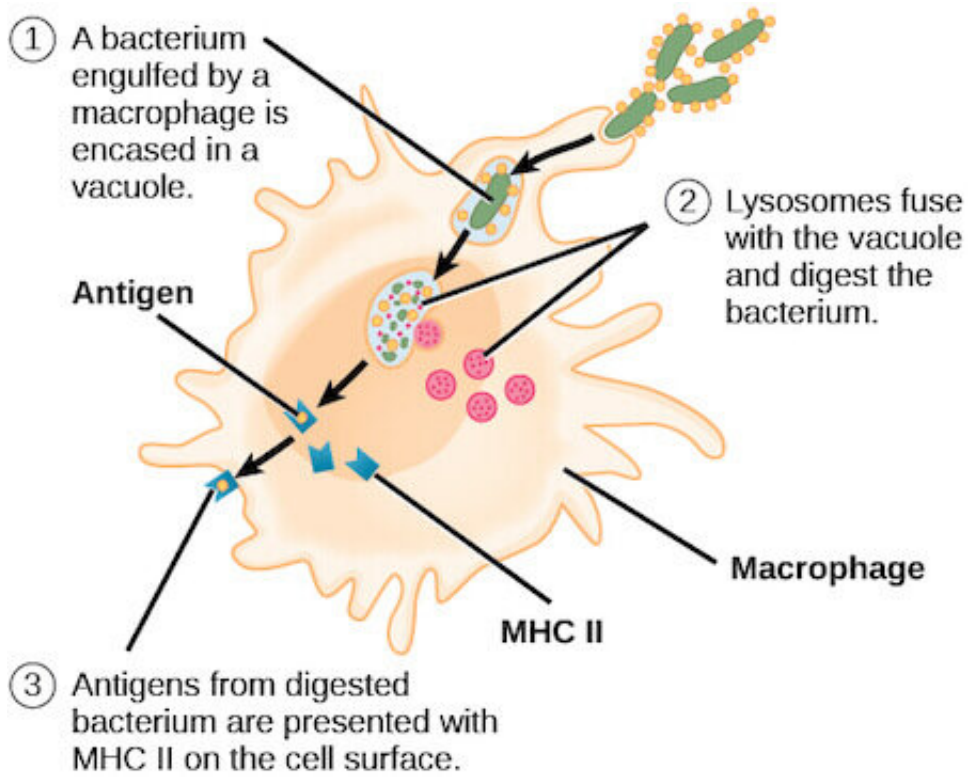
Understanding immunological memory

May 11 2023, by Adenike Shittu



Antigen-presenting cells engulf pathogens and use MHC II molecules to display antigens on their cell surfaces. Credit: Wikimedia Commons

Humans encounter innumerable pathogenic bacteria, viruses and other microbes in their day-to-day activities. While infections from some pathogens can be easily cleared by the innate immune system, others can evade this first line of defense and require the highly specific responses of the adaptive immune system. Vaccines are also able to activate the adaptive immune system to create "memory" conferring long-lasting

immunity specific to the pathogen. However, research demonstrates that protective immunity developed naturally and through vaccination may weaken over time.

These complexities make advancing scientific knowledge of mechanisms involved in generating and maintaining long-lasting, protective immunity through natural infection or vaccination extraordinarily complicated. Herein, we discuss what is known about how immunological memory is developed, current challenges in the field and proposed advancements to enhance long-lasting immunity to pathogenic infections.

What is immunological memory?

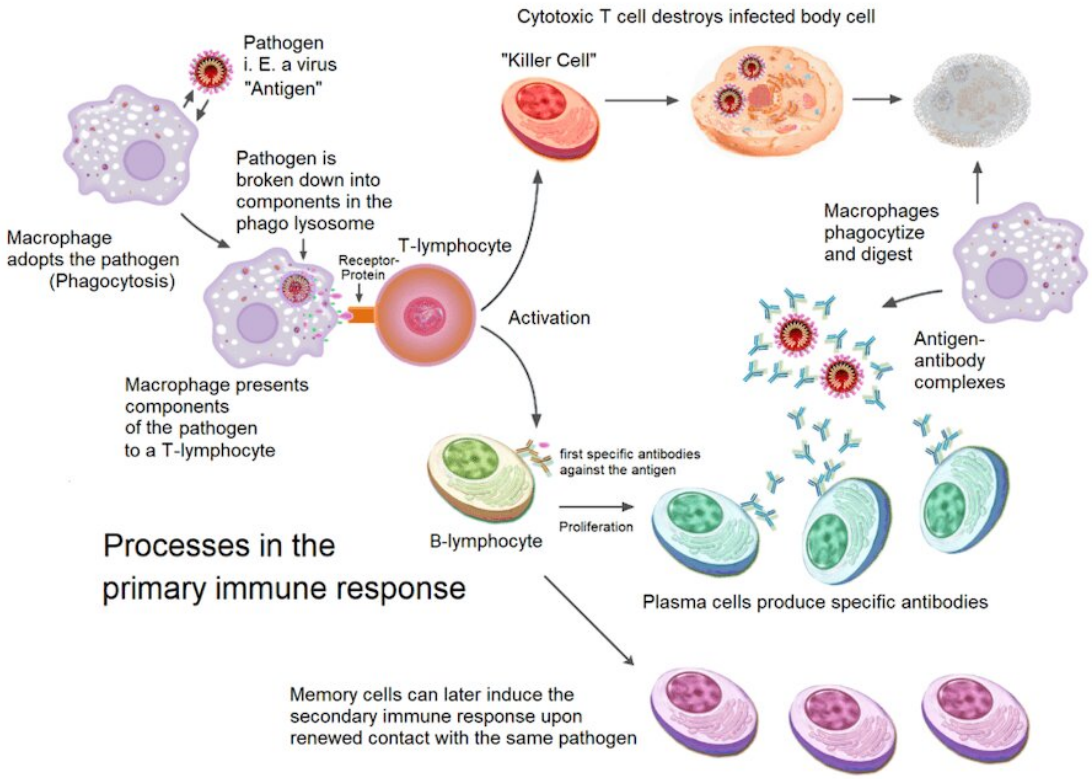
Immunological memory is the adaptive ability of the immune system to recognize pathogens encountered previously and respond effectively upon re-exposure. When a pathogen or its cognate antigens enter the body for the first time, either through natural infection or vaccination, a cascade of immune system responses is generated against that pathogen.

During this initial encounter, some immune cells develop a "memory" of the invader. If the immune system reencounters the same pathogen, a stronger and faster response will be mounted, allowing the body to ensure effective pathogen clearance, without severe illness or development of disease.

How is immunological memory established?

Immunological memory is developed by cells of the adaptive immune system that produce a highly sophisticated and specific immune response to destroy invading cells. This specificity is crucial to ensure that only antigen molecules that are foreign to the host, and not those that are host-

specific, are targeted. T and B lymphocytes (specialized white blood cells) are the primary players in this process, effectively attacking and killing pathogen-infected cells and producing antibodies, respectively.



The primary immune response includes T and B cell activation, differentiation and proliferation. Credit: Wikimedia Commons

Upon entry to the host's tissues and/or bloodstream, a pathogen is recognized as non-self by antigen-presenting cells (APCs), a group of immune cells that detect and engulf pathogens. Later, APCs display antigens that correspond to the encountered pathogen on their surfaces

and present them to T cells, causing subsequent T cell activation, differentiation and expansion.

During the first encounter with a pathogen, naïve T cells (i.e., those that have never encountered an antigen) differentiate to effector T cells, which are able to mount an efficient and immediate immune response against the pathogen. Some effector T cells (cytotoxic T cells) directly kill infected cells, while others, known as helper T cells, help immune cells mount a response, including stimulating B cells to secrete antibodies against pathogens and generate memory B cells. Upon pathogen clearance, most of these differentiated effectors T cells die, while the surviving cells become long-lived memory T cells.

Memory T cells

Memory T cells are antigen-experienced cells that have been trained to recognize specific antigens. They circulate in the blood and persist in secondary lymphoid organs, like the spleen and lymph nodes, where they keep watch for another encounter with that particular pathogen. Within a few hours of secondary encounter with a specific pathogen, memory T cells generate a more effective and rapid immune response against the pathogen. In contrast, it takes naïve T cells days after the first pathogen encounter to generate immune response.

Memory B cells

Memory B cells are specialized B cells that can recognize the same pathogen that triggered their formation and produce specific antibodies against it. They reside mainly in secondary lymphoid organs, where they can rapidly respond to pathogen re-exposure by producing large amounts of antibodies, which subsequently bind corresponding antigens and neutralize the associated pathogen. Memory B cells also undergo a

process called affinity maturation, where their antibodies acquire increased specificity and affinity for the pathogen, leading to a more potent and effective immune response. In the first pathogen encounter, it takes 2 weeks for detectable antibodies to be generated; however, during a memory response, sufficient quantities of antibodies are produced in only 2–4 days. Because these antibodies are generated by the cells that were most effective during the initial infection, they are also highly efficient.

Current challenges in immunological memory research

1. Heterogeneity of memory cell subtypes

Immunological memory is essential for maintaining long-lasting, protective immunity against infectious diseases. However, there are several outstanding challenges in immunological memory research, which limit our understanding of this complex process. Among them is the heterogeneity and different subtypes of cells involved in immunological memory.

Specifically, memory T cells can be further classified as central memory T cells, effector memory T cells, stem-cell like memory T cells and tissue-resident memory cells based on their distinct locations, properties, responses and functions. All memory T cells are important in establishing immunological memory, however, the functions and specific roles of each of these memory T cell subtypes are not fully understood. In addition, effector memory cells are found at low concentration in the circulating blood, and resident memory cells are tissue-specific, making it difficult to obtain these cells at numbers sufficient for experimental study.

2. Plasticity of memory cells

Another major challenge to studying immunological memory is the potential of a host's pathogen-specific memory response to wane over time. This plasticity allows the immune system to modify its memory response as it encounters various pathogens—each with a unique antigenic fingerprint—enabling effective protection against known and emerging pathogens. However, such flexibility also makes it difficult to predict how long protective immunity established by memory cells will last—a variable that is of key significance when it comes to developing effective vaccines.

The strength and duration of vaccine-induced immunological memory can be influenced by many variables, including host and environmental factors (e.g., level of exposure to infection/antigen doses, age and genetics), as well as the nature of the pathogen itself. For example, pathogens with genes that are considered stable (i.e., those that do not mutate frequently), such as the causative agents of measles and chicken pox, require a series of vaccinations with a defined number of doses to provide long-lasting immunity.

The case is different for microorganisms that cause diseases like cholera and frequently mutating influenza viruses, because such acquired mutations may make the pathogen unrecognizable to existing memory T and B cells. If these cells are not able to recognize their cognate antigens, they will not mount a response against it, making it is a challenge to get an immunological response to last a couple years after vaccination for these pathogens.

3. Immunocompetency

Immunocompromised individuals—those with weakened immune

systems, HIV, cancer or patients who have had organ transplantation—generate weaker or shorter-lived immune responses to infections and vaccination compared to those who are not immunocompromised. Understanding the defects in the immune responses and development of immunological memory of immunocompromised individuals is critical to identifying mechanisms that are essential in generating effective immune responses. In addition, characterizing genetic variations associated with immunocompromised individuals would help in the classification of genetic factors that can be utilized in the development of better vaccination strategies and therapeutic interventions to infectious diseases and other immune related diseases.

4. Exhaustion of the immune system

Finally, although vaccines are known to induce effective and long-lasting protective immunity to specific pathogens, the long-term effects of vaccinations on immune memory are not fully understood. Repeated antigen exposure through vaccines can cause exhaustion of the immune system and may induce the immune system to become less responsive or even suppress certain related immune functions altogether. Further studies are needed to evaluate the potential risks and benefits of repeated vaccination.

Proposed advances to enhance long-lasting immunity

Immunological memory is a critical component of the adaptive immune response, and if there is one thing that immunologists agree on, it is that the concept of immunological memory needs to be further explored. Additional studies to characterize the immune receptors, signaling molecules, transcriptional and epigenetic regulators that are essential for maintenance and generation of immunological memory are needed if we

are to understand the inner workings of this complex immunological system.

Coupling this knowledge with an understanding of the crosstalk between immunity developed from infection or vaccination will bolster efforts to maintain long-lasting immunity against common and emerging infectious diseases.

Provided by American Society for Microbiology

Citation: Understanding immunological memory (2023, May 11) retrieved 9 May 2024 from https://medicalxpress.com/news/2023-05-immunological-memory.html