Immune response

Lec.11.

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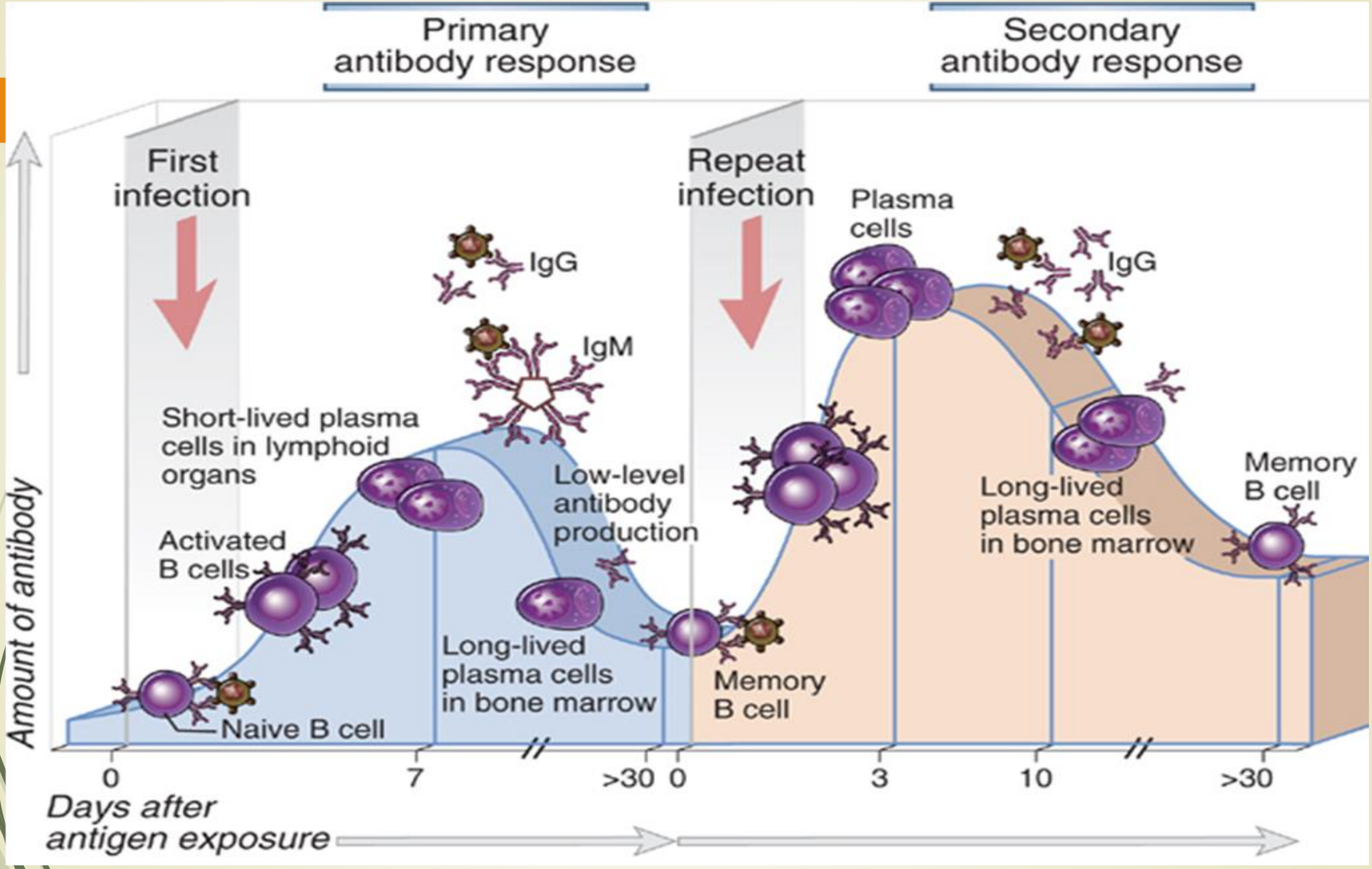
Introduction

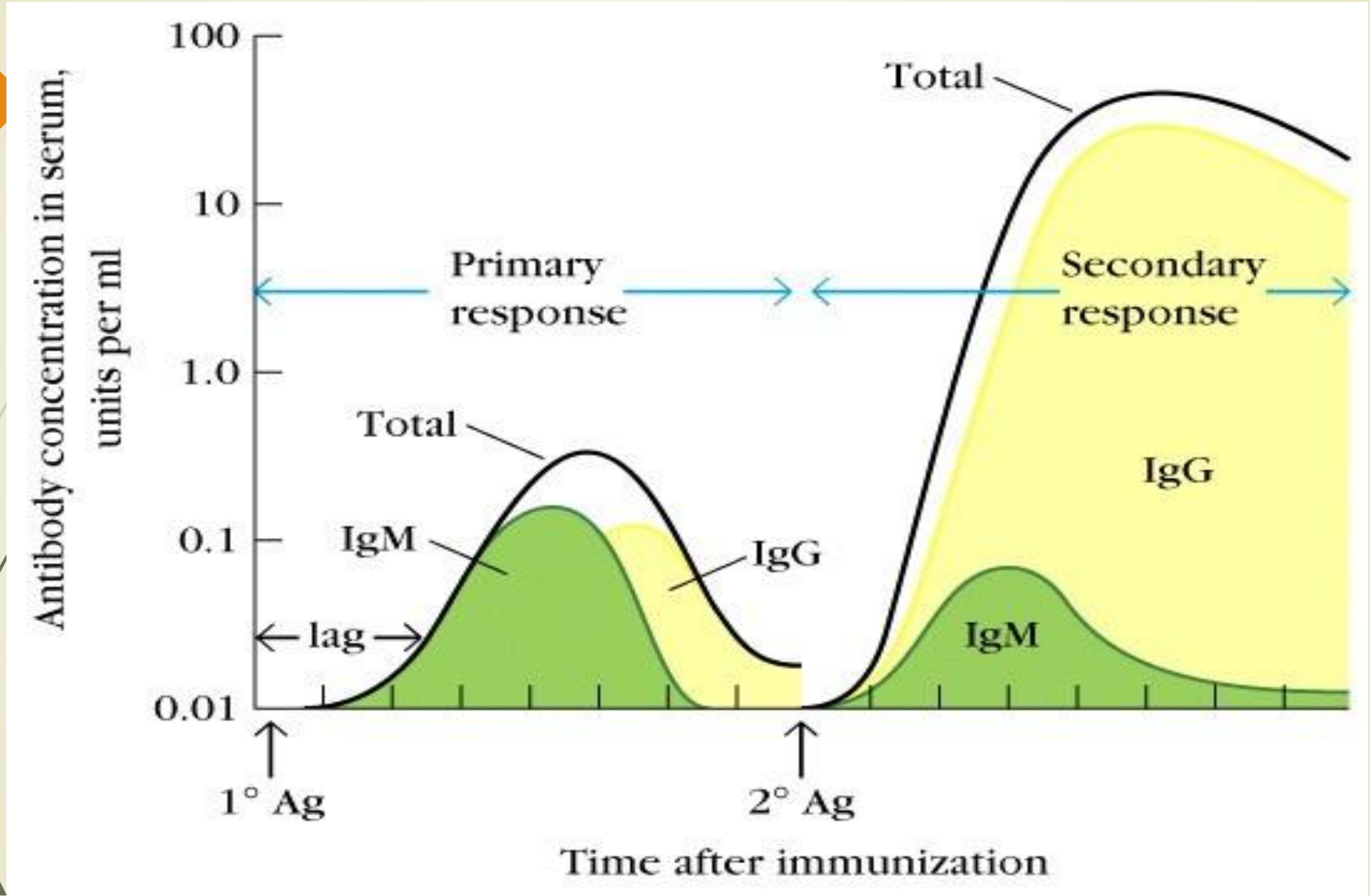
- An immune response is a reaction which occurs within an organism for the purpose of defending against foreign invaders. These invaders include a wide variety of different microorganisms including viruses, bacteria, parasites, and fungi which could cause serious problems to the health of the host organism if not cleared from the body.
- There are two distinct aspects of the immune response, **the innate and the adaptive,** which work together to protect against pathogens.
- **The innate branch**—the body's first reaction to an invader—is known to be **a non-specific** and quick response to any sort of pathogen.
- Components of the innate immune response include **physical barriers like the skin and mucous membranes, immune cells such as neutrophils, macrophages, and monocytes, and soluble factors including cytokines and complement.**

Introduction

- On the other hand, **the adaptive branch** is the body's immune response which is catered against specific antigens and thus, it takes longer to activate the components involved. The adaptive branch **include cells such as dendritic cells, T cell, and B cells as well as antibodies**, which directly interact with antigen and are a very important component for a strong response against an invader.
- The first contact that an organism has with a particular antigen will result in the production of **effector T and B cells** which are activated cells that defend against the pathogen.
- The production of these effector cells as a result of **the first time exposure is called a primary immune response. Memory T and memory B cells are also produced.**
- re-exposed to the same pathogen, **a secondary immune response** will be able to respond in both **a fast and strong manner because of the memory cells from the first exposure**.
- **Vaccines** introduce a weakened, killed, or fragmented microorganism in order to **evoke a primary immune response**. This is so that in the case that an exposure to the real pathogen occurs, the body can rely on the secondary immune response to quickly defend against it.

Primary Immune Response	Secondary Immune Response
After initial exposure to a foreign antigen, there is a lag phase where B cells are differentiating into plasma cells, but not yet producing antibodies. Antibody generation can take anything from 2 days to several months.	If a previously encountered antigen enters the body again, a few days up to several years later, a secondary immune response develops. This time, the lag phase is greatly reduced, to about 3-4 days.
Low quantities of antibodies are normally secreted.	High levels of antibodies are produced.
After a while, the amount of antibody decreases to minimal levels.	Antibody levels remain elevated for longer.
Antibodies are mostly IgM, but some IgG antibodies are produced.	IgGs are the main antibody secreted, with some small amounts of IgM sometimes.


Primary antibody response
Secondary antibody response
First infection
Repeat infection
IgG
IgM
Plasma cells
IgG
Short-lived plasma cells in lymphoid organs
Low-level antibody production
Activated B cells
Long-lived plasma cells in bone marrow
Memory B cell
Long-lived plasma cells in bone marrow
Memory B cell
Naive B cell
Amount of antibody
0
7
>30
0
3
10
>30
Days after antigen exposure


100
10
1.0
0.1
0.01
Antibody concentration in serum, units per ml
Total
Primary response
Secondary response
Total
IgG
IgM
IgG
lag
IgM
1° Ag
2° Ag
Time after immunization

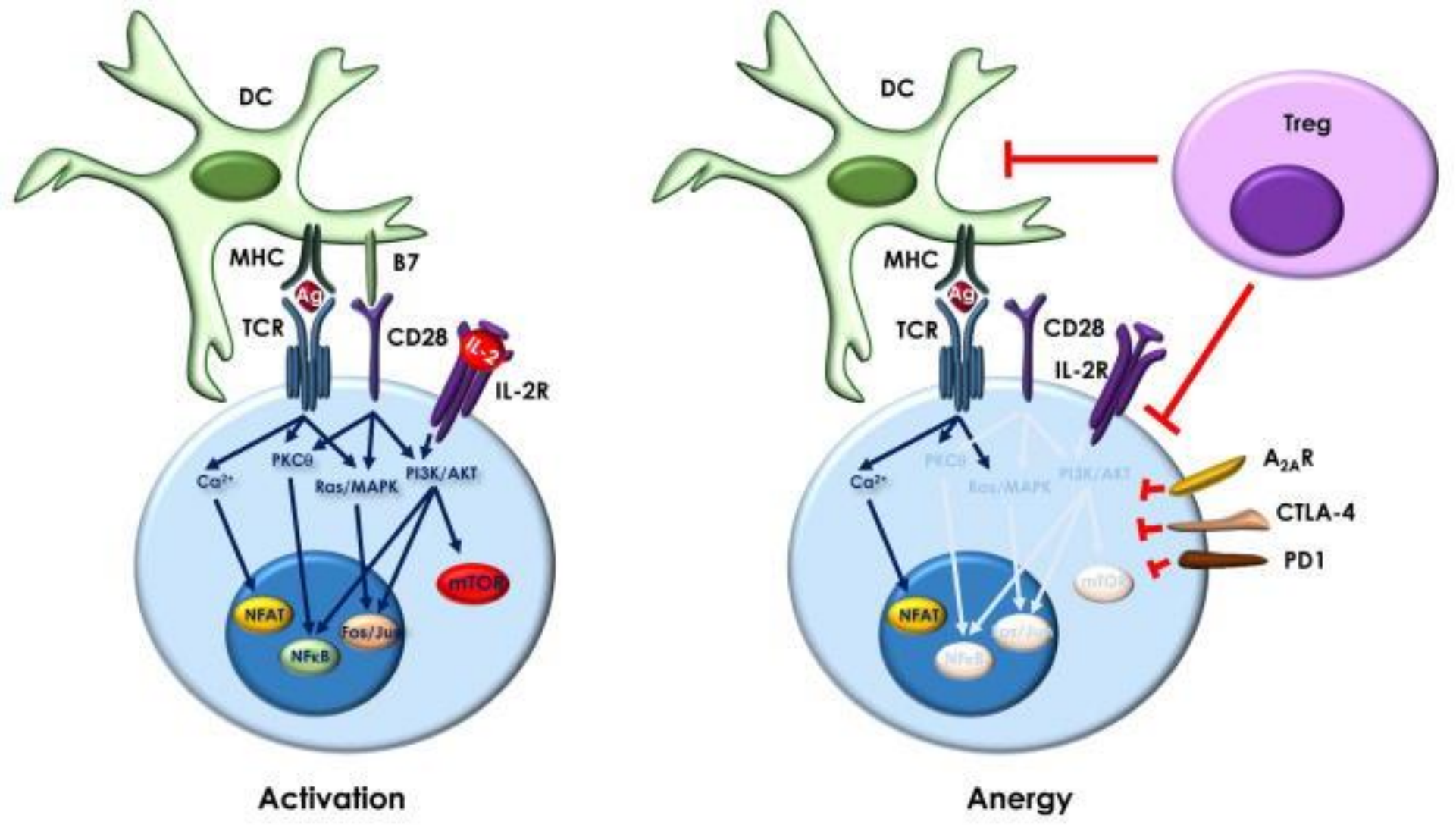
Innate immune response

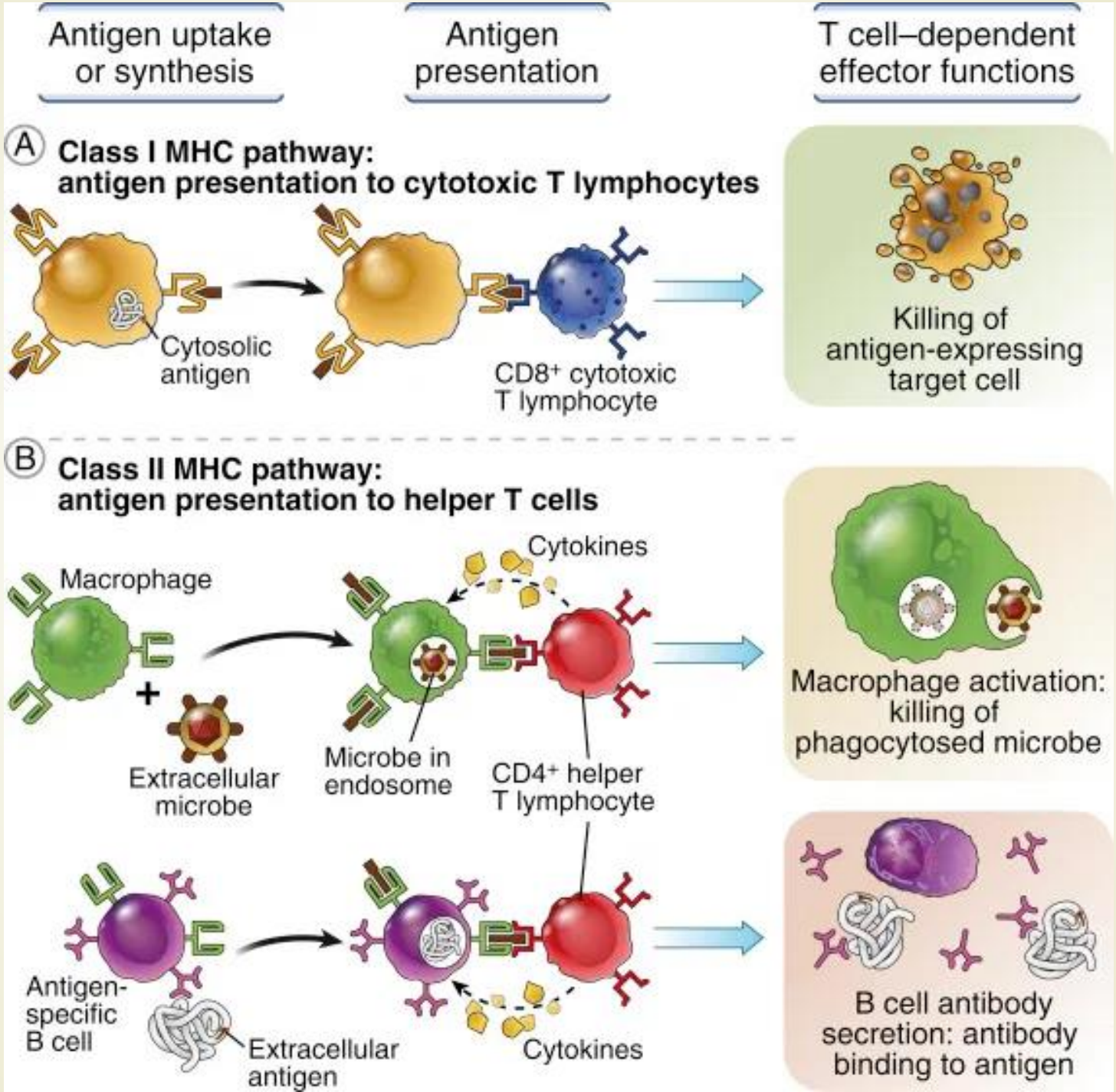
- Pathogens are recognized and detected via **pattern recognition receptors (PRR)**. These receptors are structures on the surface of **macrophages** which are capable of binding foreign invaders and thus **initiating cell signaling** within the immune cell. Specifically, **the PRRs identify pathogen-associated molecular patterns (PAMPs)** which are integral structural components of pathogens. Examples of PAMPs include the **peptidoglycan cell wall or lipopolysaccharides (LPS),** both of which are essential components of bacteria and are therefore evolutionarily conserved across many different bacterial species.
- **The signaling pathway** which allows for the **transcription factor NF-κB** to enter the nucleus of the macrophage and initiate the transcription and eventual secretion of various cytokines such as **IL-8, IL-1,** and **TNFa.** Release of these cytokines is necessary for the entry of **neutrophils** from the blood vessels to the infected tissue. Once neutrophils enter the tissue, like macrophages, they are able to phagocytize and kill any pathogens or microbes.
- **Complement, classical pathway** is triggered when IgG or IgM is bound to its target antigen on either the pathogen cell membrane or an antigen-bound antibody.
- **The alternative pathway** is activated by foreign surfaces such as viruses, fungi, bacteria, parasites, etc., and is capable of auto activation due to "**tickover"** of C3. The **lectin pathway** is triggered when mannose binding lectin (MBL).
- Though the pathways are activated differently, the overall role of the complement system is to **opsonize pathogens and induce a series of inflammatory responses that help to combat infection.**

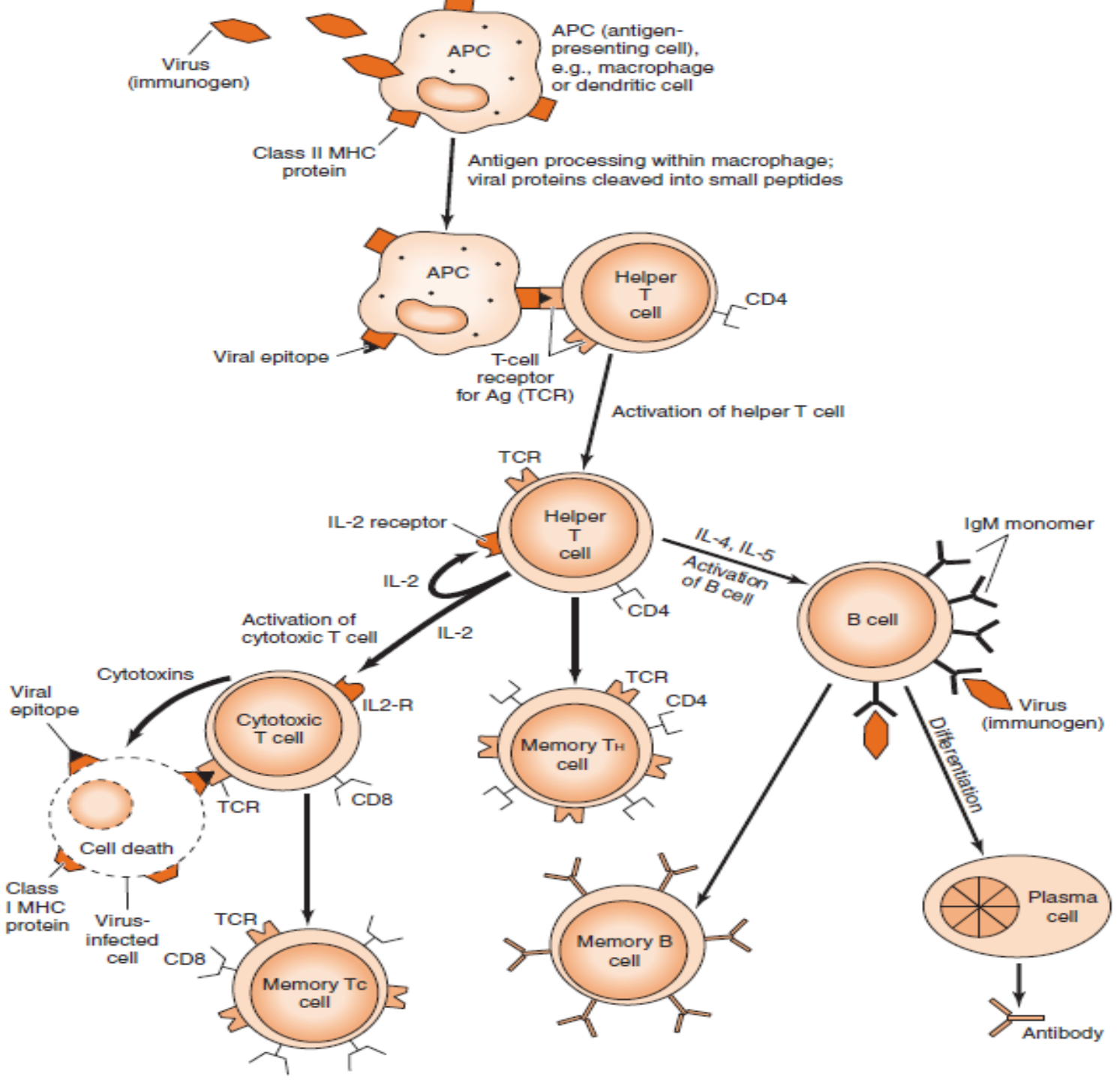
Adaptive immune response

- The cells of the adaptive immune system are extremely specific because during early developmental stages the **B and T cells develop antigen receptors that are specific to only certain antigens**.
- **Activation of naïve helper T cells** occurs when **antigen-presenting cells (APCs)** present foreign antigen via **MHC class II molecules on their cell surface**. These **APCs include dendritic cells, B cells, and macrophages** which are specially equipped not only with MHC class II but also with **co-stimulatory ligands** which are recognized by co-stimulatory receptors on helper T cells. Without the co-stimulatory molecules, the adaptive immune response would be inefficient and T cells would become **anergic.**
- Once **helper T cells are activated, they are able to activate naïve B cells in the lymph node**. However, B cell activation is a two-step process. **Firstly, B cell receptors**, which are just Immunoglobulin M (IgM) and Immunoglobulin D (IgD) antibodies specific to the particular B cell, must bind to the antigen which then results in internal processing so that it is presented on the MHC class II molecules of the B cell. Once this happens a T helper cell which is able to identify the antigen bound to the MHC interacts with its co-stimulatory molecule and activates the B cell. As a result, **the B cell becomes a plasma cell which secretes antibodies that act as an opsonin against invaders.**
- the adaptive immune response is also known for **immunological memory**. After encountering an antigen, the immune system produces **memory T and B cells** which allow for a speedier, more robust immune response in the case that the organism ever encounters the same antigen again.

Activated and anergy T cell




Antigen uptake or synthesis
Antigen presentation
T cell–dependent effector functions
A
Class I MHC pathway:
antigen presentation to cytotoxic T lymphocytes
Cytosolic antigen
CD8+ cytotoxic T lymphocyte
Killing of antigen-expressing target cell
B
Class II MHC pathway:
antigen presentation to helper T cells
Macrophage
Cytokines
Extracellular microbe
Microbe in endosome
CD4+ helper T lymphocyte
Macrophage activation: killing of phagocytosed microbe
Antigen-specific B cell
Extracellular antigen
Cytokines
B cell antibody secretion: antibody binding to antigen


Virus
(immunogen)
APC
APC (antigen-presenting cell), e.g., macrophage or dendritic cell
Class II MHC protein
Antigen processing within macrophage; viral proteins cleaved into small peptides
APC
Helper T cell
CD4
Viral epitope
T-cell receptor for Ag (TCR)
Activation of helper T cell
TCR
IL-2 receptor
Helper T cell
IL-4, IL-5
Activation of B cell
IgM monomer
IL-2
CD4
B cell
Activation of cytotoxic T cell
IL-2
Cytotoxins
Viral epitope
Cytotoxic T cell
IL2-R
TCR
CD8
Memory TH cell
TCR
CD4
Virus (immunogen)
Differentiation
Cell death
Class I MHC protein
Virus-infected cell
TCR
CD8
Memory Tc cell
Memory B cell
Plasma cell
Antibody

Thank you