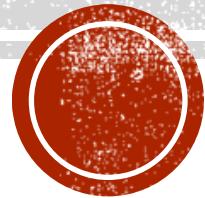
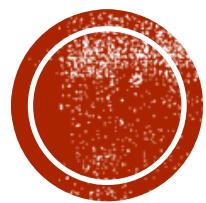


# **INTRODUCTION TO IMMUNOLOGY**

**M. H. Mwaba, (BSc, MSc, PhD)**

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# Introduction and general principles of immunology

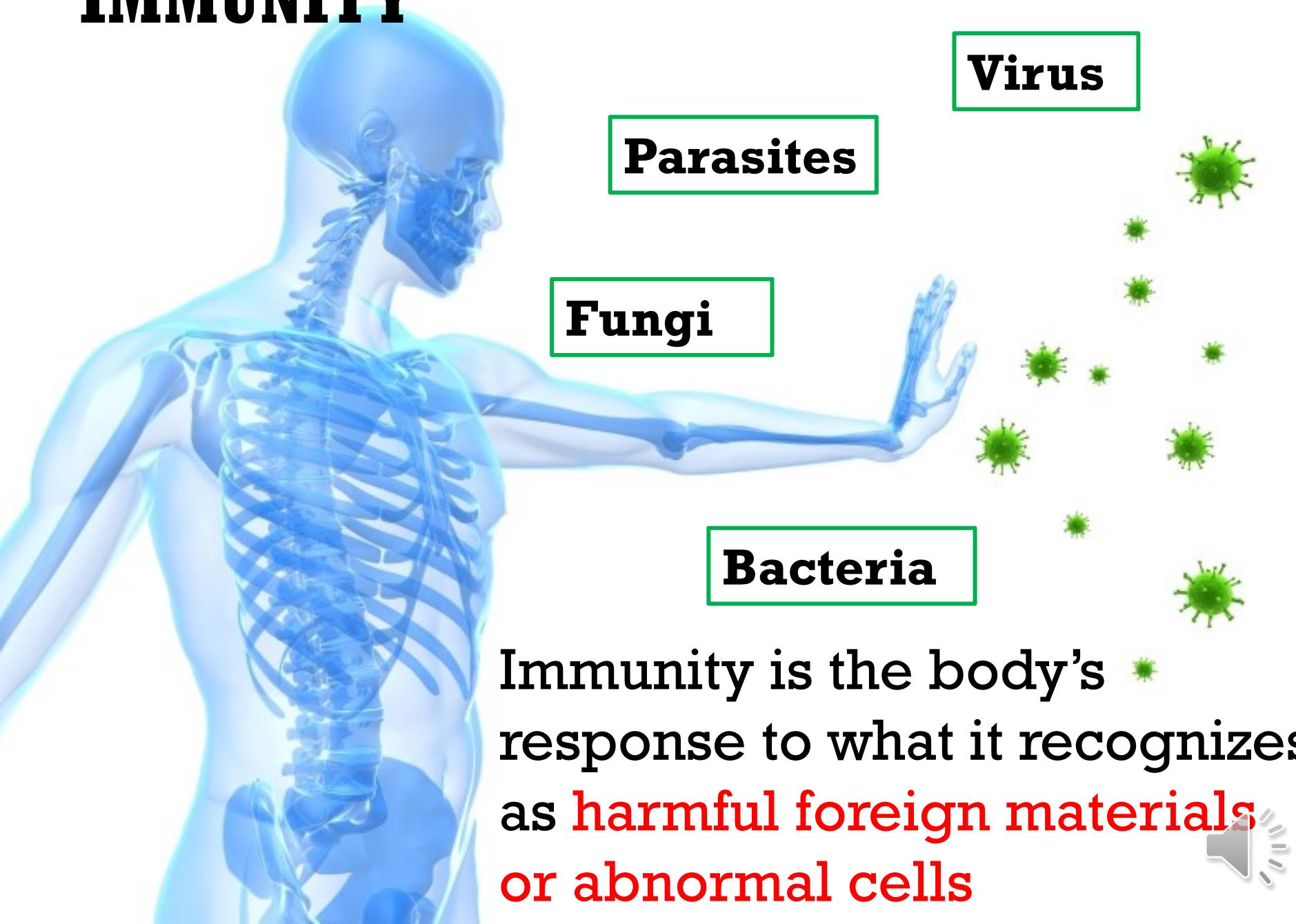


# OBJECTIVES

- **Trace the study of immunology** from a desire to vaccinate against infectious disease to far reaching applications in basic research, medicine, and other fields of study.
- **Examine and question prior assumptions related to immunology** and categorize features unique to the immune system.
- **Practice and apply some immunology-specific vocabulary**, while distinguishing cells, structures, and concepts important to the field of immunology.
- **Begin to integrate concepts from immunity into real-world issues** and medical applications.



# IMMUNITY



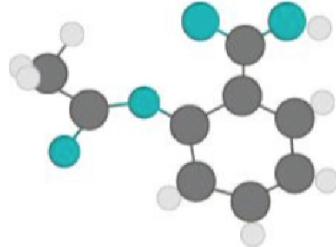
Immunity is the body's response to what it recognizes as **harmful foreign materials** or **abnormal cells**

# Importance of Immunology - Biosimilars

- **Biosimilars** (biopharmaceutical products of immunology) are growing and immensely contributing to revenue in the pharmaceutical industry.

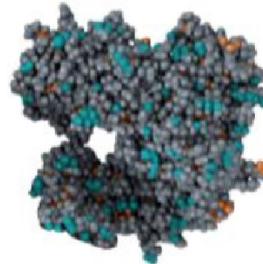
## Small molecule

Low molecular weight.  
Chemically synthesised.  
Well defined structure.



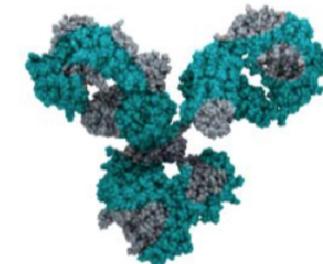
## Biological molecule

High molecular weight.  
Derived from living organisms.  
Large and complex structure.



## Monoclonal antibody

High molecular weight.  
Derived from living organisms.  
More complex structure.



Degree of complexity



# The Top Selling Prescription Drugs By Revenue (small molecule drugs and biosimilars)

7 of the 10 top selling drugs in the developed markets are biosimilars

10. Xarelto (rivaroxaban) - Cardiovascular diseases

9. Opdivo (nivolumab) – anti-PD-1

8. Eylea (aflibercept) - wet macular degeneration, macular oedema secondary to retinal vein occlusion

7. Avastin (bevacizumab) - lung, colorectal, kidney, cervical, ovarian cancer and relapsed glioblastoma

6. Herceptin (trastuzumab) - HER2-positive breast cancer



# The Top Selling Prescription Drugs By Revenue

**5. Enbrel (etanercept)** - rheumatoid arthritis, plaque psoriasis, and psoriatic arthritis

**4. Keytruda (pembrolizumab)** - anti-PD-1 therapy

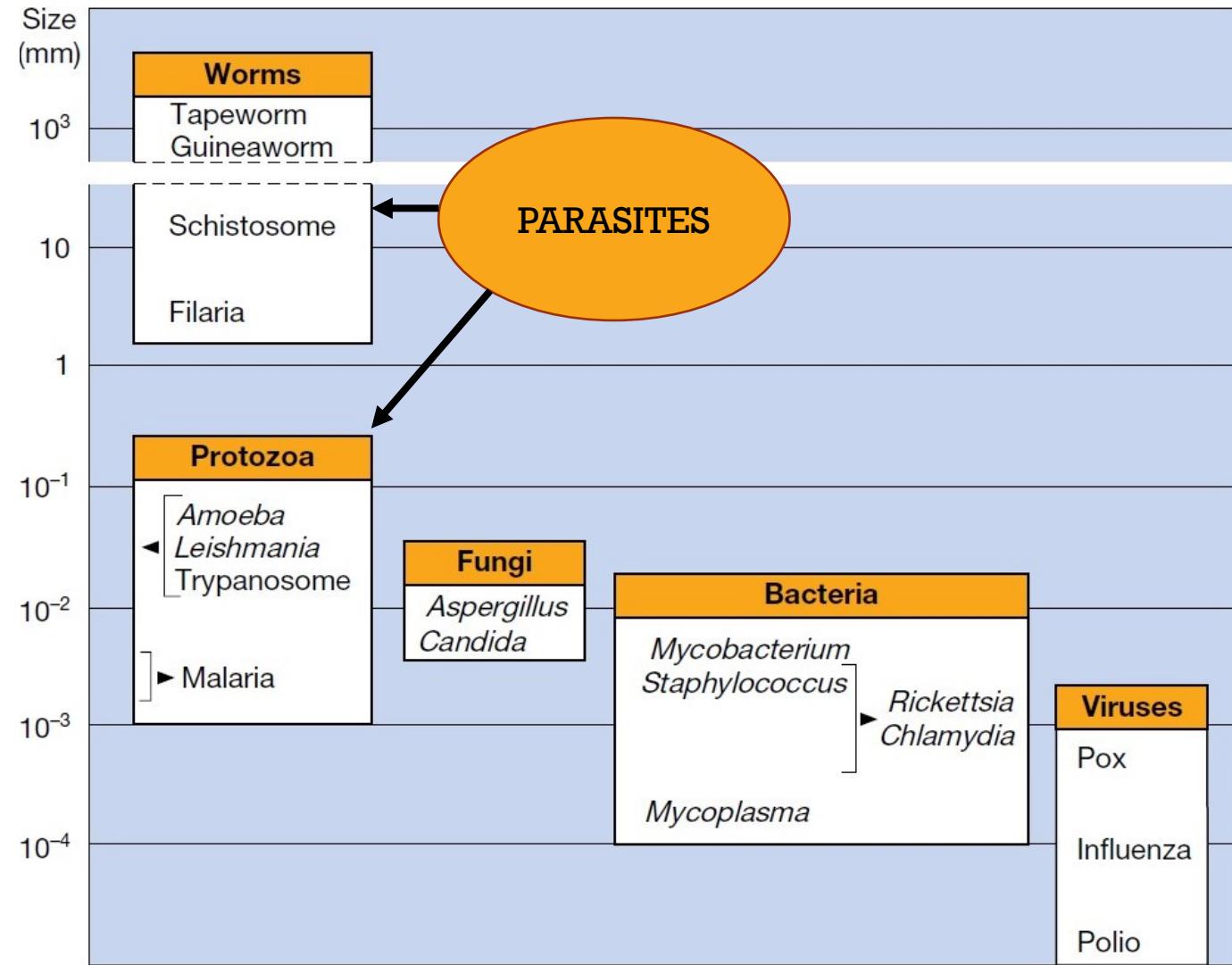
**3. Revlimid (lenalidomide)** - multiple myeloma, relapsed/refractory non-Hodgkin lymphoma, and diffuse large B-cell lymphoma

**2. Eliquis (apixaban)** - reduce stroke and systemic embolism risk

**1. Humira (adalimumab)** - autoimmune diseases, including rheumatoid arthritis, psoriatic arthritis, Crohn's disease, ankylosing spondylitis, and plaque psoriasis



# IMMUNITY – Types of pathogens



Pathogens vary in size with worms being the biggest and viruses the smallest



# IMMUNITY



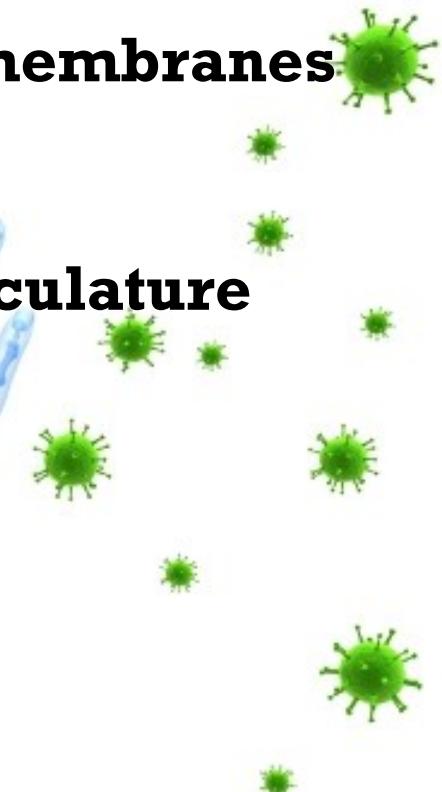
Consists of following activities:

- 1. Defense against invading pathogens** (viruses, bacteria, etc)
- 2. Removal of 'worn-out' cells** (e.g., old RBCs) & **tissue debris** (e.g., from injury or disease)
- 3. Identification & destruction of abnormal or mutant cells** (primary defense against cancer)
- 4. Rejection of 'foreign' cells** (e.g., organ transplant)
- 5. Inappropriate responses:**
  - i. Allergies
  - ii. Autoimmune diseases



# IMMUNITY



- Skin
  - Lining of mucus membranes
  - Secretions
  - Blood cells and vasculature
  - Liver
  - Bone marrow
  - Lymphatic system and lymphoid organs
  - Most tissues – have resident immune cells
- 
- A cluster of green, star-shaped virus particles with spikes, resembling coronaviruses, is shown floating around the hand area of the skeleton illustration.
- 
- A small grey speaker icon with sound waves is located in the bottom right corner of the slide.

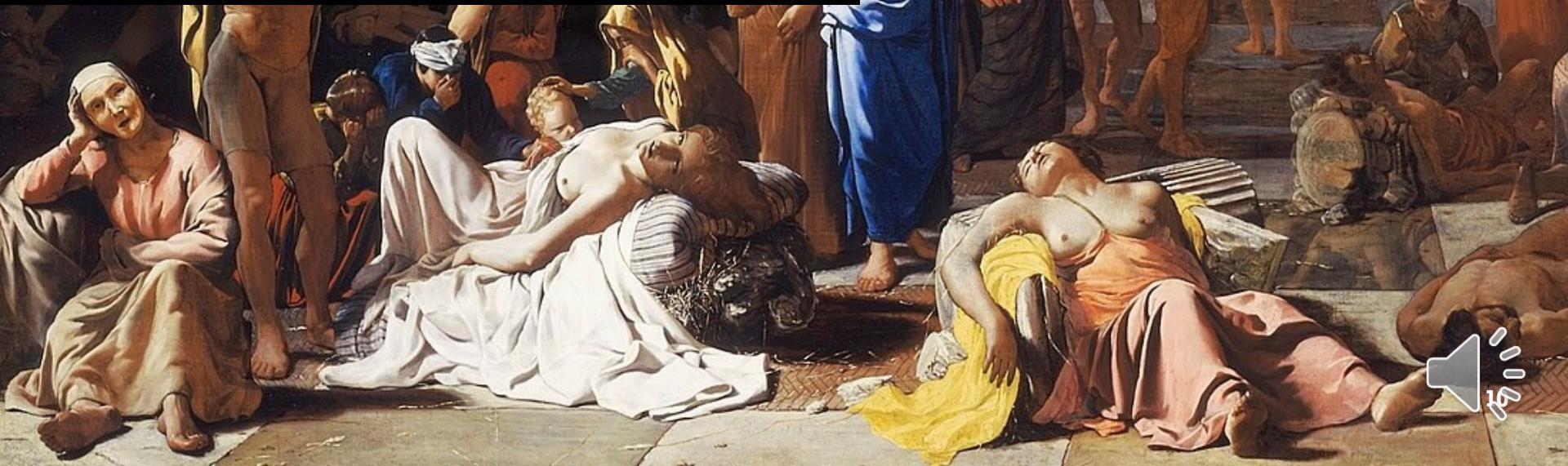
# HISTORY: Notable immunological discoveries

9



Thucydides is credited with the 1st documentation of immunological observation  
(Plague in Athens 430 BC)

Those who had recovered from the plague could nurse the sick because they would not contract the disease a second time.



# HISTORY OF IMMUNOLOGY

- 15th century Chinese and Turks attempted to deliberately induce immunity to prevent smallpox.
- Dr. Edward Jenner observed that Milkmaids who had contracted cowpox were observed to be immune to smallpox.
- Louis Pasteur induced immunity to cholera by injecting with attenuated cholera strains
- **Attenuation** – process of eliminating or reducing virulence of a pathogen.
- **Virulence** is the harmfulness of a pathogen

*Jenner inoculating with cowpox to protect against smallpox*

## Vaccination



# HISTORY OF IMMUNOLOGY

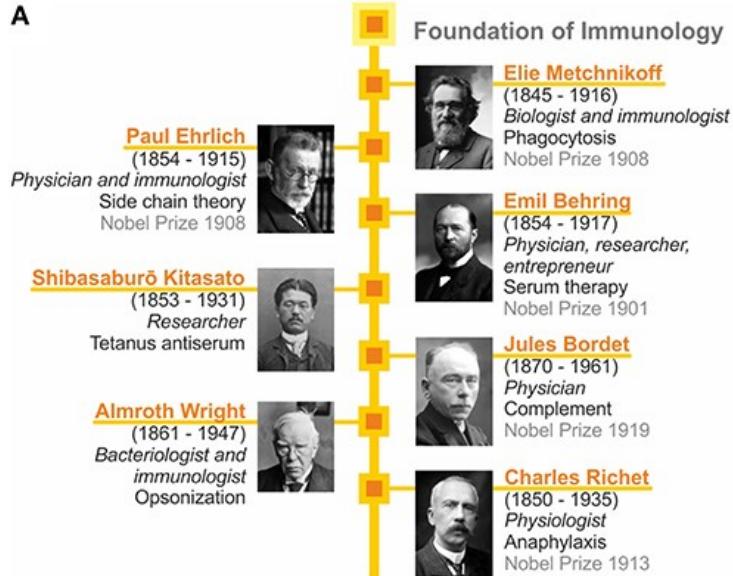
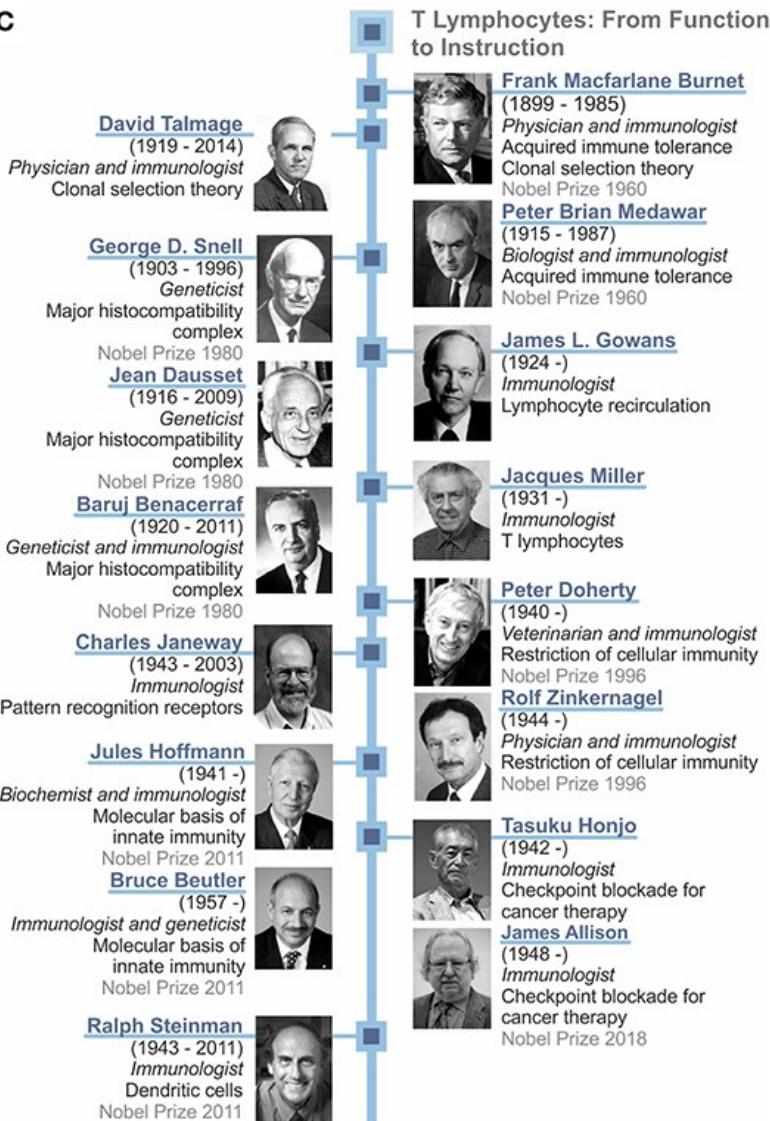
- 15th century Chinese and Turks attempted to deliberately induce immunity to prevent smallpox.
- Dr. Edward Jenner observed that Milkmaids who had contracted cowpox were observed to be immune to smallpox.
- **Vaccination exposes to safe forms of an infectious agent resulting in future acquired protection more dangerous infectious agent.**

## Vaccination



*Jenner inoculating with cowpox to protect against smallpox*



**A****B****C**

Since 1901 there have been **23 / 110** Nobel Prizes for immunology-related research.



## **OVERVIEW OF THE IMMUNE SYSTEM**

### **Cells and Organs of the immune system**

Cells of the immune system are generated in the **Primary Lymphoid Tissues**.

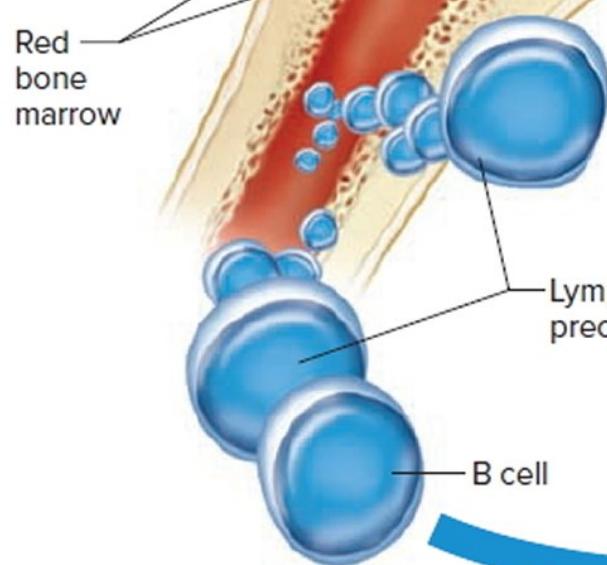
1. **Thymus** – where T lymphocyte immune system cells develop functionality.
  
2. **Bone marrow** – where all the cells of immune response generate.



# Thymus

- 1 Stem cells in red bone marrow give rise to lymphocyte precursors

Red bone marrow



Thymus

T cell

Blood transport

Lymphocyte precursors

B cell

- 3 Some lymphocyte precursors are processed within the bone marrow to become B cells

## Lymph Node

- 2 Some lymphocyte precursors are processed in the thymus to become T cells

Blood transport

T cell

B cell

Blood transport

Lymph node

- 4 Both T cells and B cells are transported through the blood to lymphatic organs, such as the lymph nodes and spleen



## **OVERVIEW OF THE IMMUNE SYSTEM**

### **Cells and Organs of the immune system**

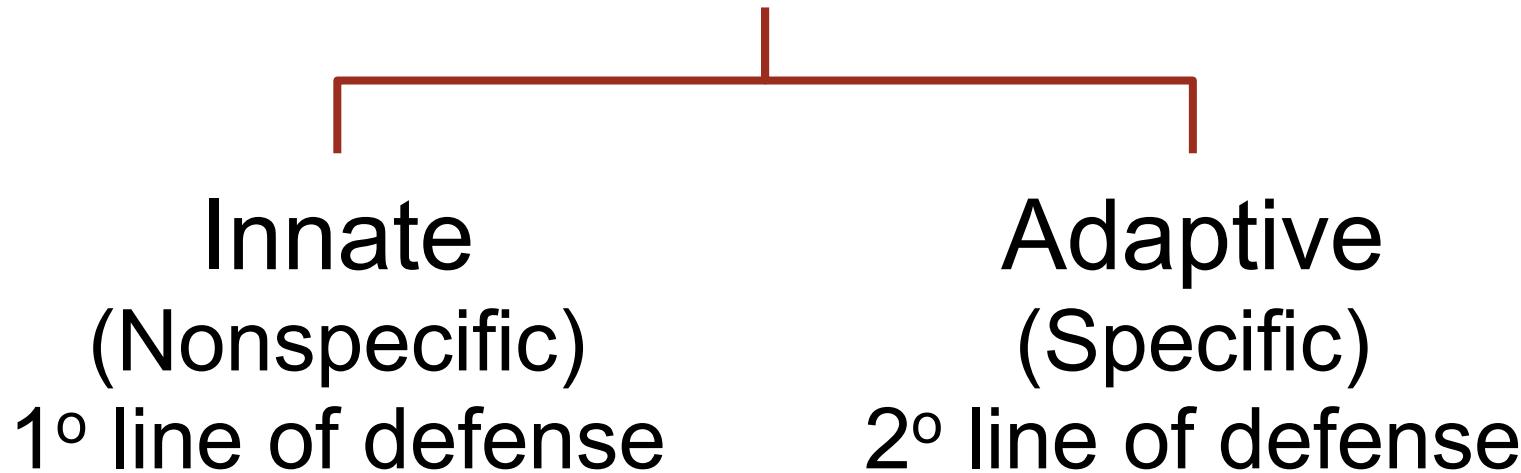
The adaptive immune responses are induced in the **Secondary Lymphoid Tissues**.

- 1. Mucosa Associated Lymphoid Tissue (MALT):** Pathogens at mucosal surfaces.  
i.e. Respiratory, Gastrointestinal, Urogenital tracts
- 2. Lymph nodes:** Pathogens in body tissues
- 3. Spleen:** Pathogens in blood circulation



# OVERVIEW OF THE IMMUNE SYSTEM

## Immune System



Immune response is divided into two main branches: innate and adaptive immune response.



# **INNATE IMMUNITY VS ADAPTIVE IMMUNITY**

## **Innate Immunity** (first line of defense)

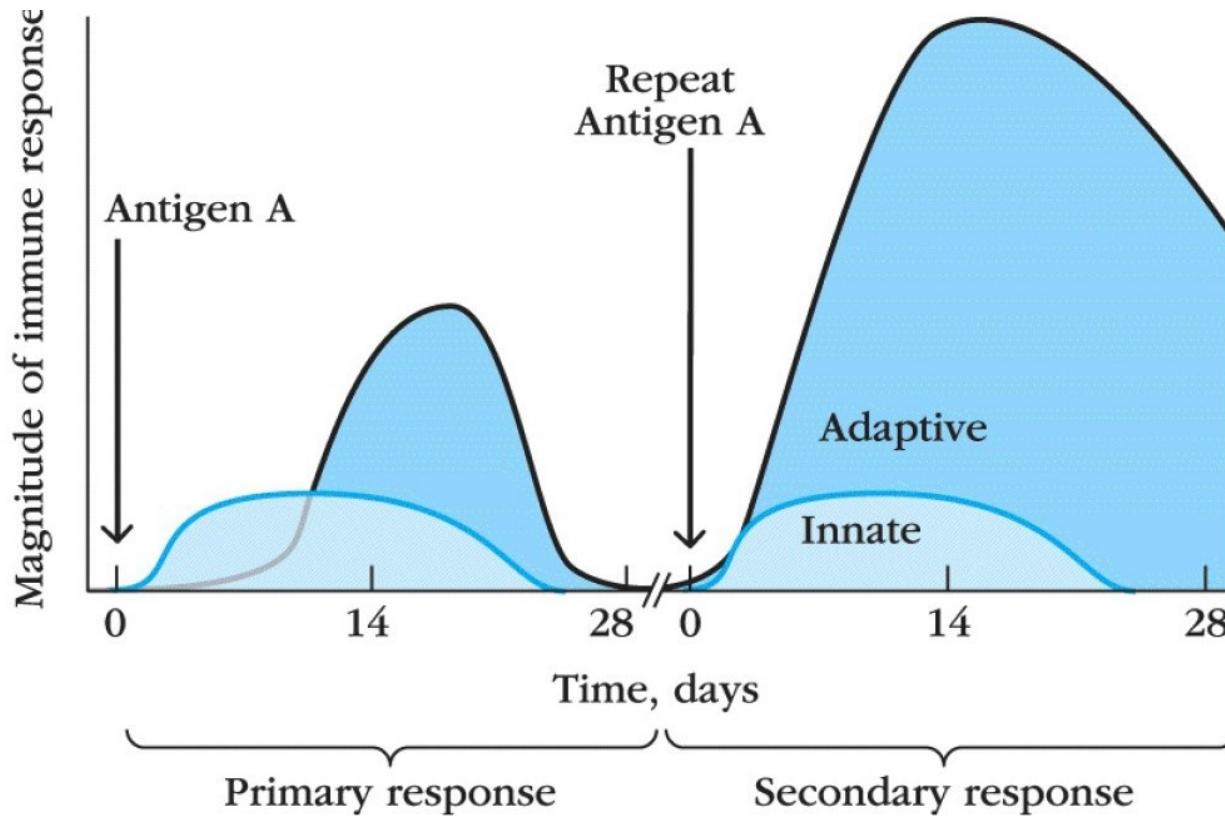
- No time lag
- Broad specificity for Pathogen associated molecular patterns (PAMPs)
- No memory
- Same intensity every time

## **Adaptive Immunity** (second line of defense)

- A lag period
- Antigen specific
- Development of memory
- Stronger and faster upon re-infection



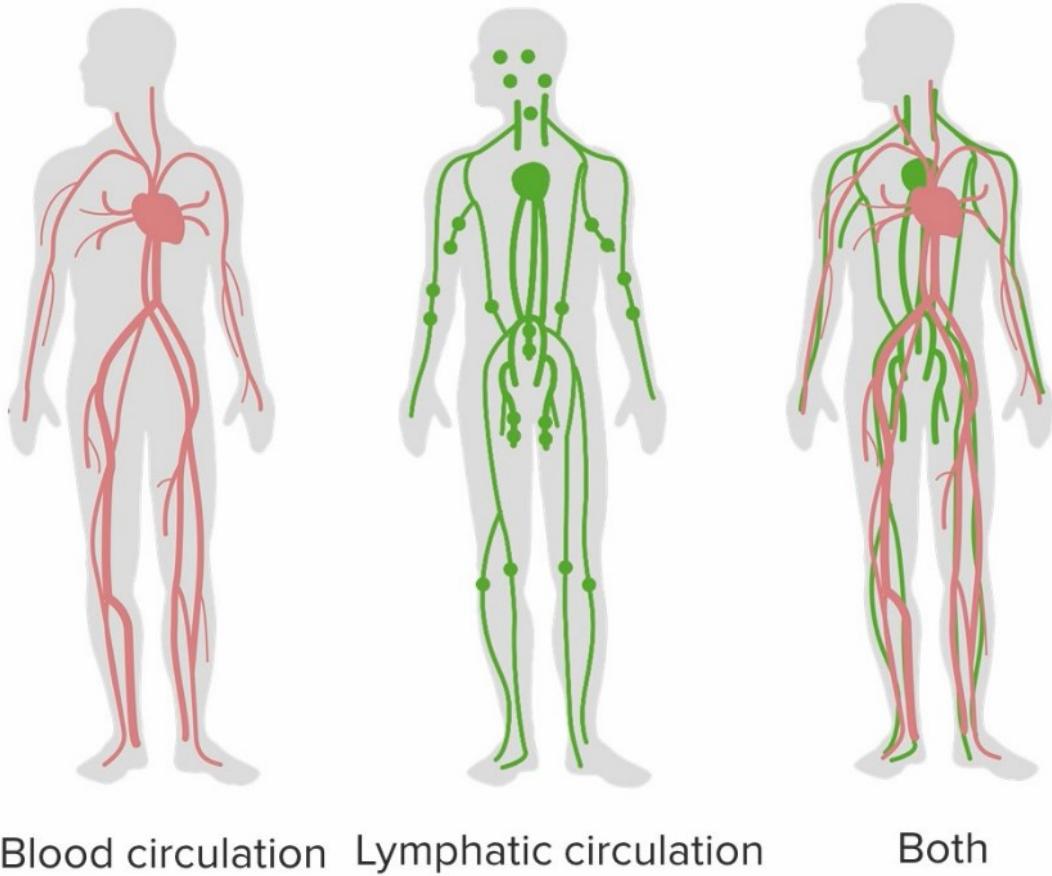
# INNATE IMMUNITY VS ADAPTIVE IMMUNITY



The initial response is called the primary response and is characterised by low adaptive immune response. Re-introduction of the same pathogen is followed by increased adaptive immunity. Innate immune response remains the same in both primary and secondary response.



# How pathogens are eliminated?



Immune cells move through both the **blood** and **lymphatic circulation** to access all sites of infection. They eliminate pathogen by;

1. Phagocytosis e.g. macrophages
2. Release molecule to kill the pathogen e.g. Natural Killer cells
3. Kill infected cell e.g. cytotoxic T cells



# **INNATE IMMUNITY is comprised of;**

## **A. EXTERNAL BARRIERS**

1. Skin forms a physical barrier
2. Mucus prevents colonisation
3. Commensal microorganisms occupy niche (competes with pathogens for nutrients and space)
4. Acid pH (stomach) resists pathogens
5. Enzymes (in tears/ saliva) attack pathogens



# **INNATE IMMUNITY is comprised of;**

## **B. INTERNAL BARRIERS**

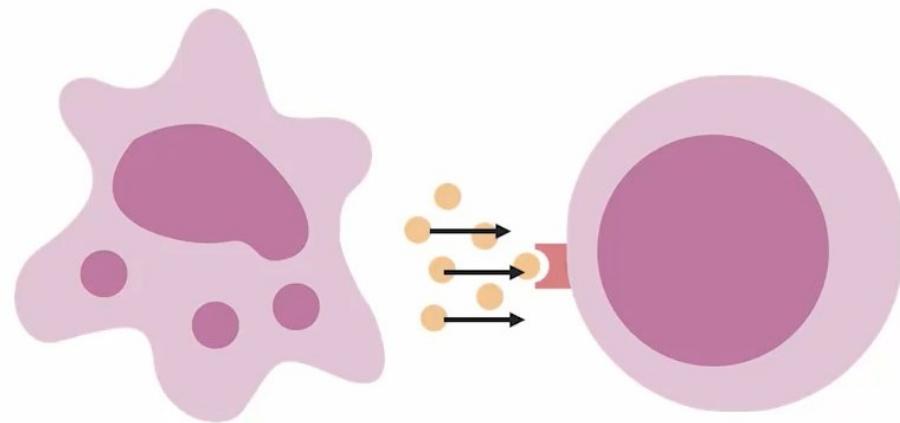
1. Phagocytic cells
2. Complement cells
3. Natural killer cells
4. Inflammatory response
5. Antimicrobial proteins



# How do immune cells communicate with each other?



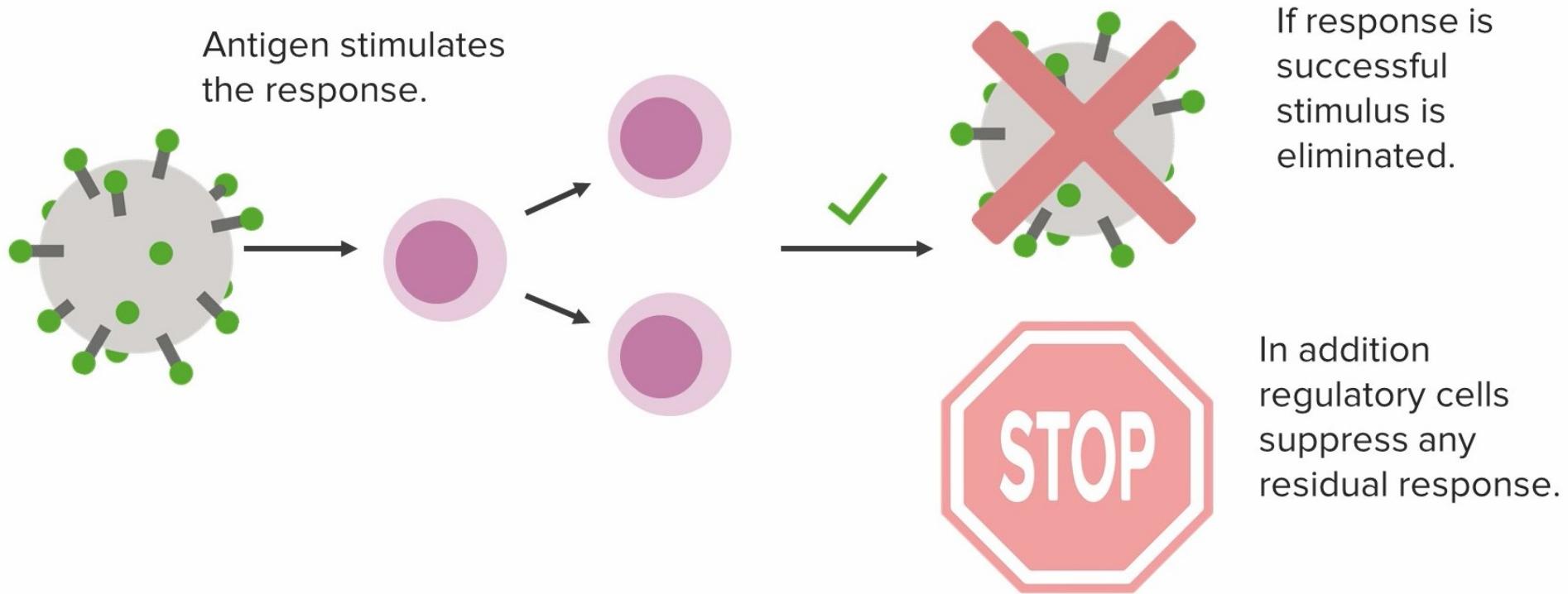
Cell – cell contact



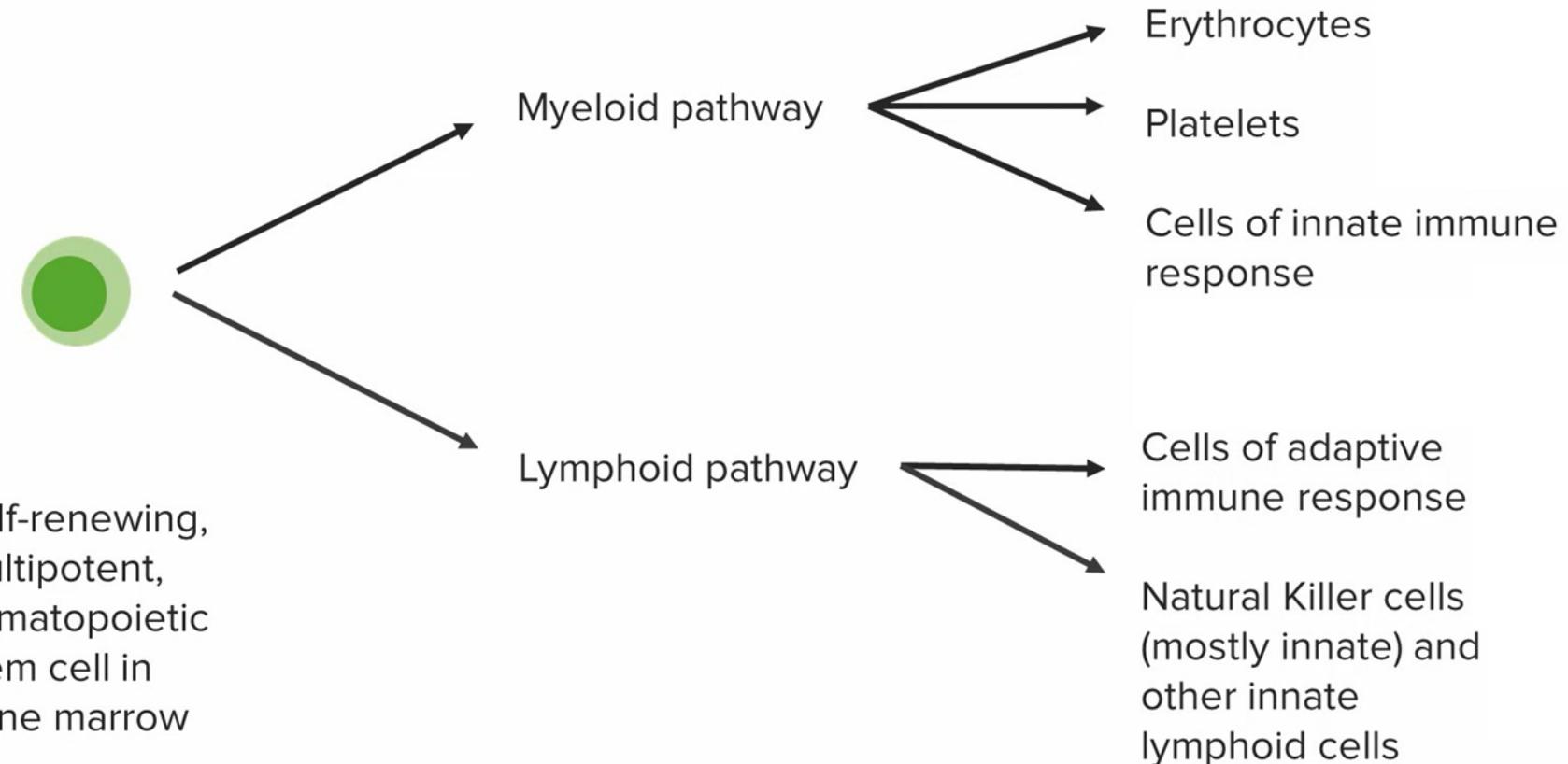
Secretion of molecules



# How is the immune response regulated?



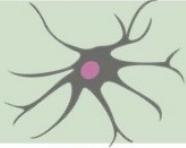
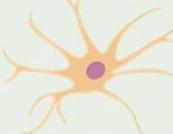
# HAEMATOPOIESIS



**Haematopoiesis:** is the production of all types of blood cells including formation, development, and differentiation of blood cells.



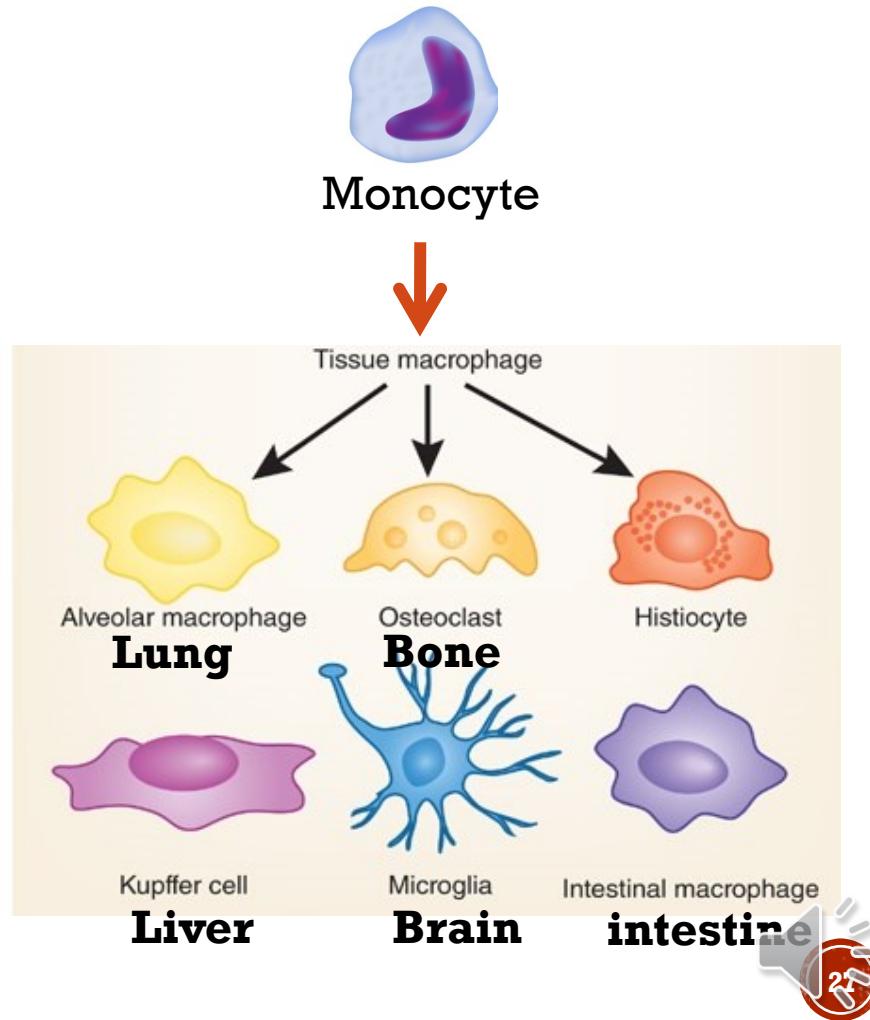
# Innate immune cells

Cell type		Main function
Neutrophil		Phagocytosis
Monocyte and macrophage		Phagocytosis
Dendritic cell		Activation of T-cells
Follicular dendritic cell		Activation of B-cells
Eosinophil, basophil and mast cell		Production of inflammatory mediators
Natural Killer (NK) cell and other innate lymphoid cells (ILCs)		NK cell killing of infected cells. Diverse functions of ILCs

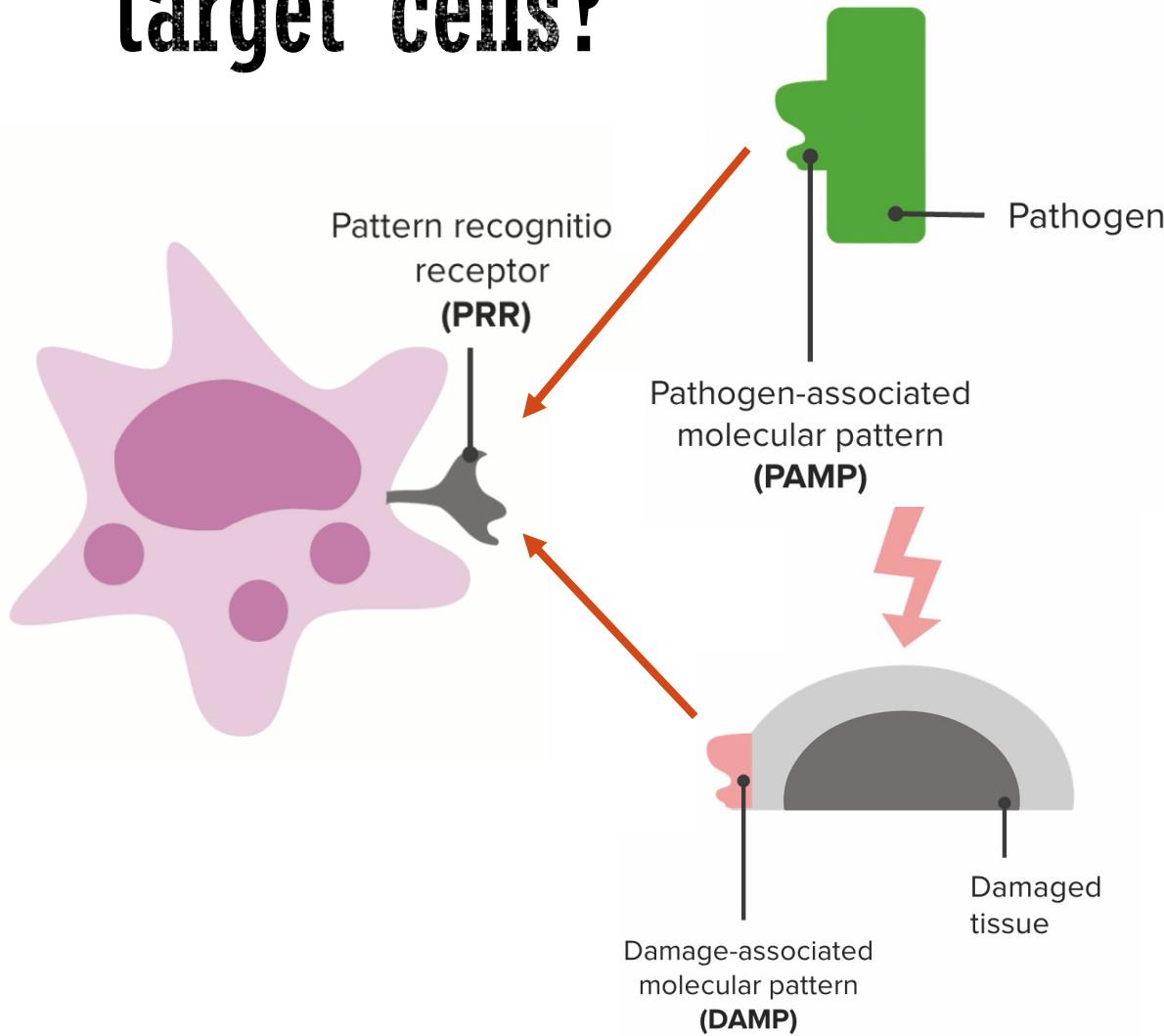


# PHAGOCYTIC CELLS

Mainly includes neutrophils, monocytes and macrophages. **Monocytes** present in the blood are short lived, but they leave the blood into the tissues to develop into long lived macrophages.



# How do Innate immune recognise target cells?



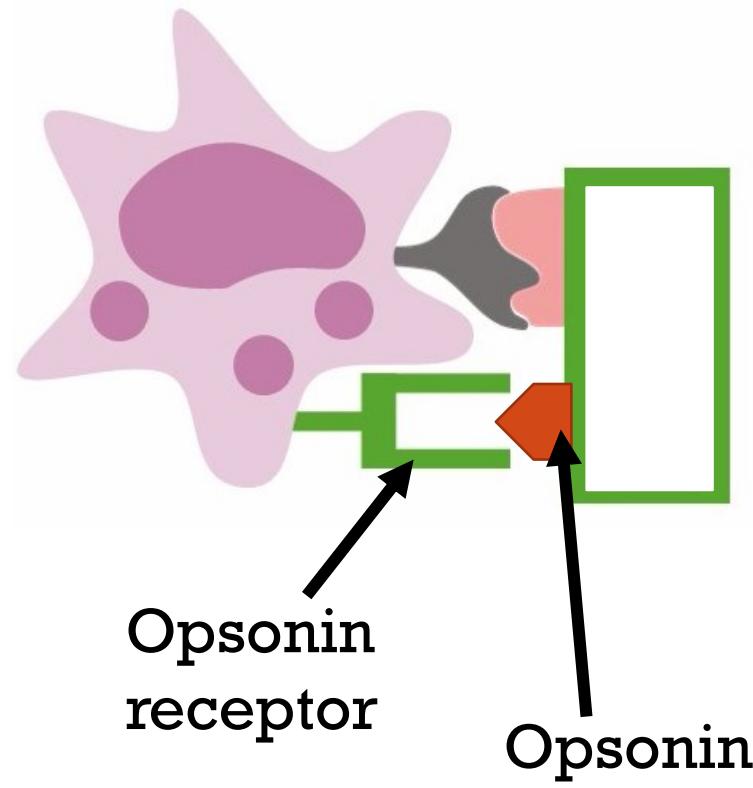
**PRRs** found on innate immune cells have broad specificity for **PAMPS** on the pathogen and **DAMPS** on damaged host cells



# How do Innate immune recognise target cells?

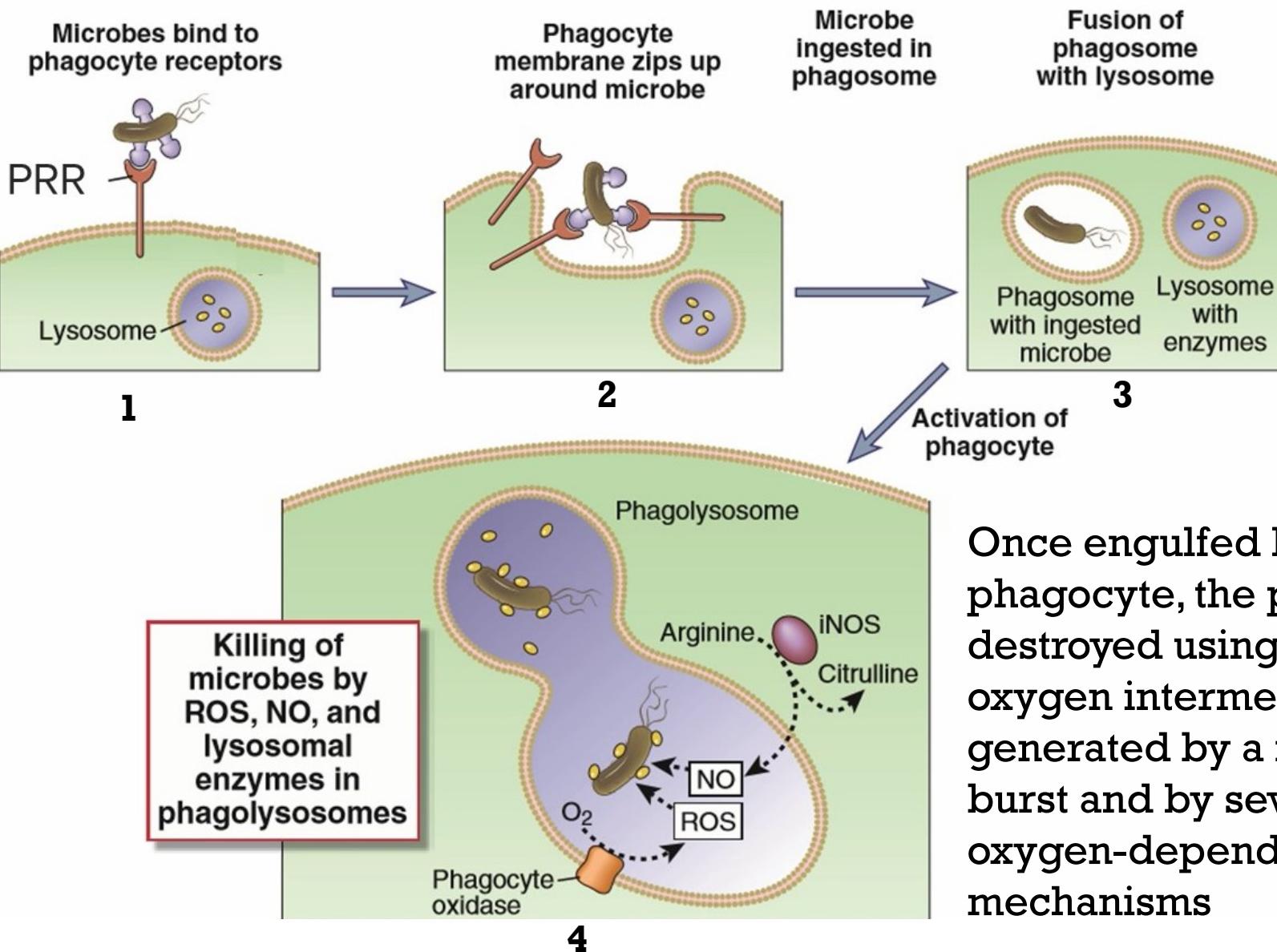
The phagocytic cells use PRRs to recognise PAMPs.

The pathogen can also become coated with substances called **opsonins** that are recognised by the opsonin receptors on the phagocytic cells



## PHAGOCYTIC CELLS

# MECHANISM OF PHAGOCYTOSIS



Once engulfed by the phagocyte, the pathogen is destroyed using reactive oxygen intermediates generated by a respiratory burst and by several non-oxygen-dependent killing mechanisms

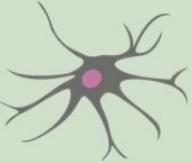


# Phagocytosis

- [https://youtu.be/I\\_xh-bkiv\\_c](https://youtu.be/I_xh-bkiv_c)
- <https://www.youtube.com/watch?v=ZUUfdP87Ssg>

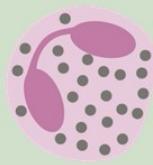
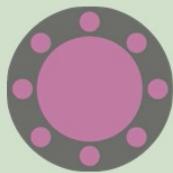


# Other Innate immune cells

Dendritic cells	Follicular dendritic cells
	
Derived from hematopoietic stem cells	Derived from mesenchymal stem cells
Present throughout the body	Only present in germinal centers of secondary lymphoid tissues
Initially phagocytic	Never phagocytic
Possess MHC class II and costimulatory (e.g. B7) molecules	Lack MHC class II and costimulatory molecules
Activate helper T-cells	Do not activate helper T-cells, but specialised to show antigen to B-cells



# Other Innate immune cells

Eosinophil	Basophil	Mast cell
		
Present in blood and tissues	Present in blood	Present in mucosal and connective tissues
Characteristically releases major basic protein	Releases histamine, prostaglandins and leukotrienes	Releases histamine, prostaglandins and leukotrienes



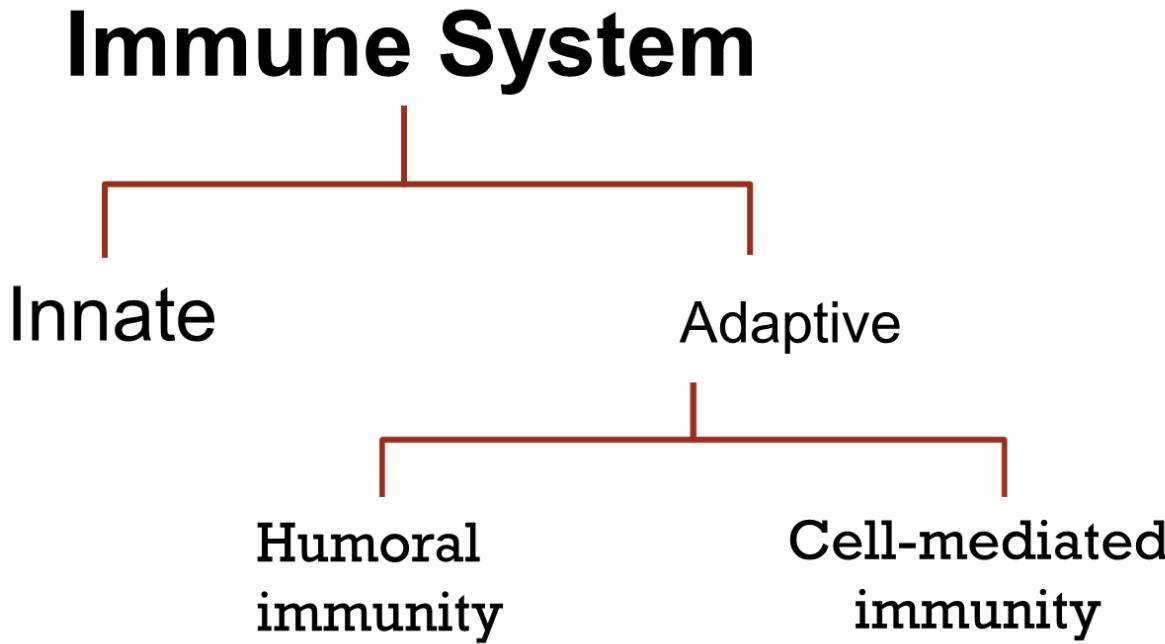
# Innate lymphoid cells

One type of Innate Lymphoid Cells (innate cells that develop through the lymphoid pathway of hematopoiesis), the Natural Killer cell, induces apoptotic cell death in infected cells using two pathways;

1. FasFasL pathway
2. Granzyme/Perforin pathway



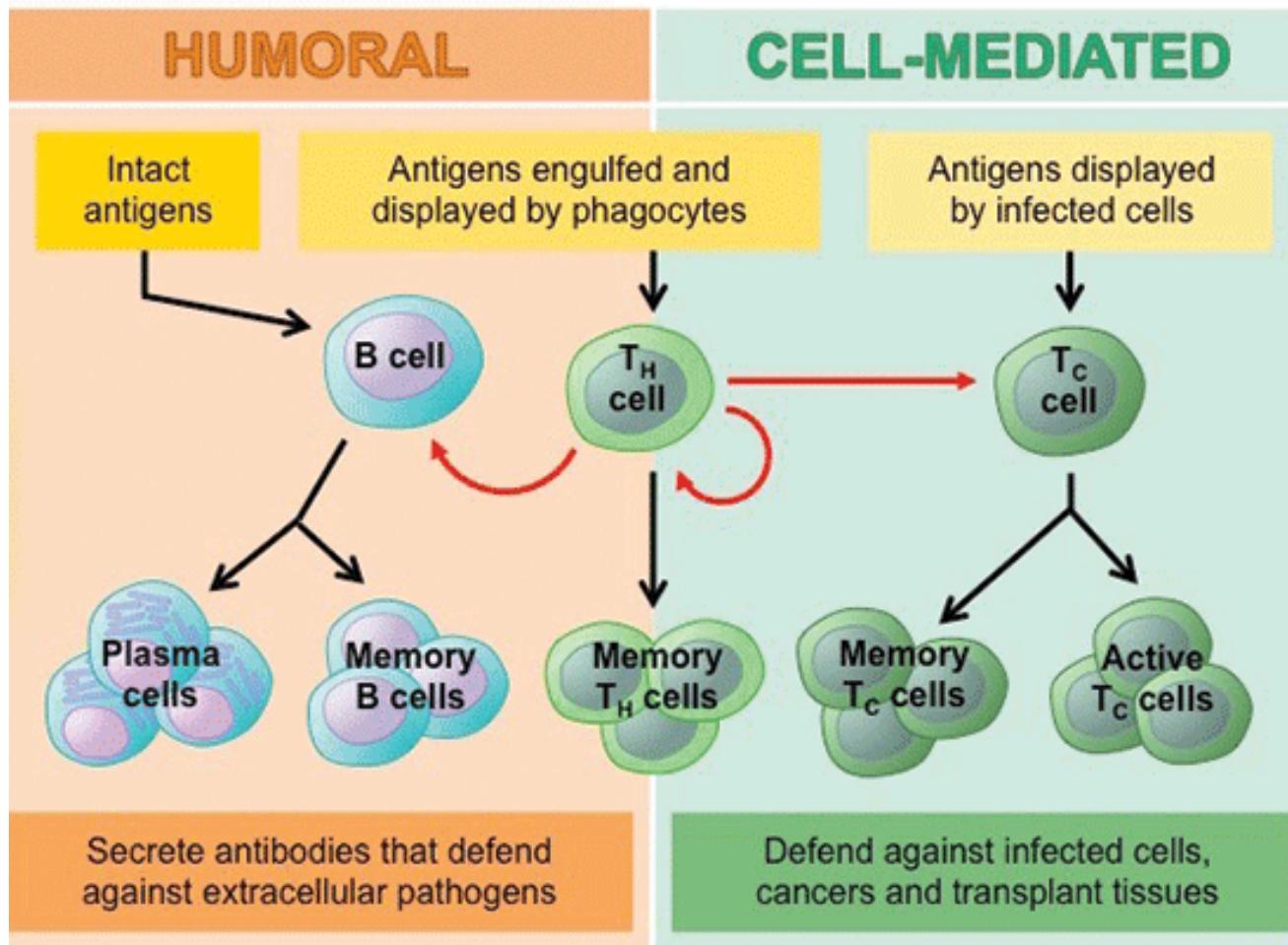
# OVERVIEW OF THE IMMUNE SYSTEM



The immune system is divided into the innate and adaptive immune response. The adaptive immunity is further divided into Humoral and cell-mediated immunity.



# ADAPTIVE IMMUNITY



Humoral immunity involves action by B cells against extracellular pathogens while Cell-mediated immunity involves defending the body against infected cells, cancers and foreign tissues.



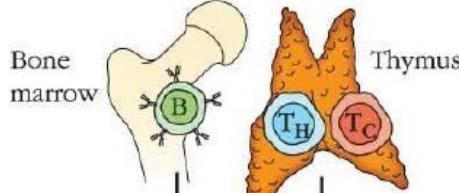
# ADAPTIVE IMMUNE CELLS

Cell type		Main function
Helper T-cell		Help activate macrophages, cytotoxic T-cells and B-cells
Regulatory T-cell		Suppress other cells of the immune response
Cytotoxic T-cell		Kill infected cells
B-cell and Plasma cell		Produce antibodies

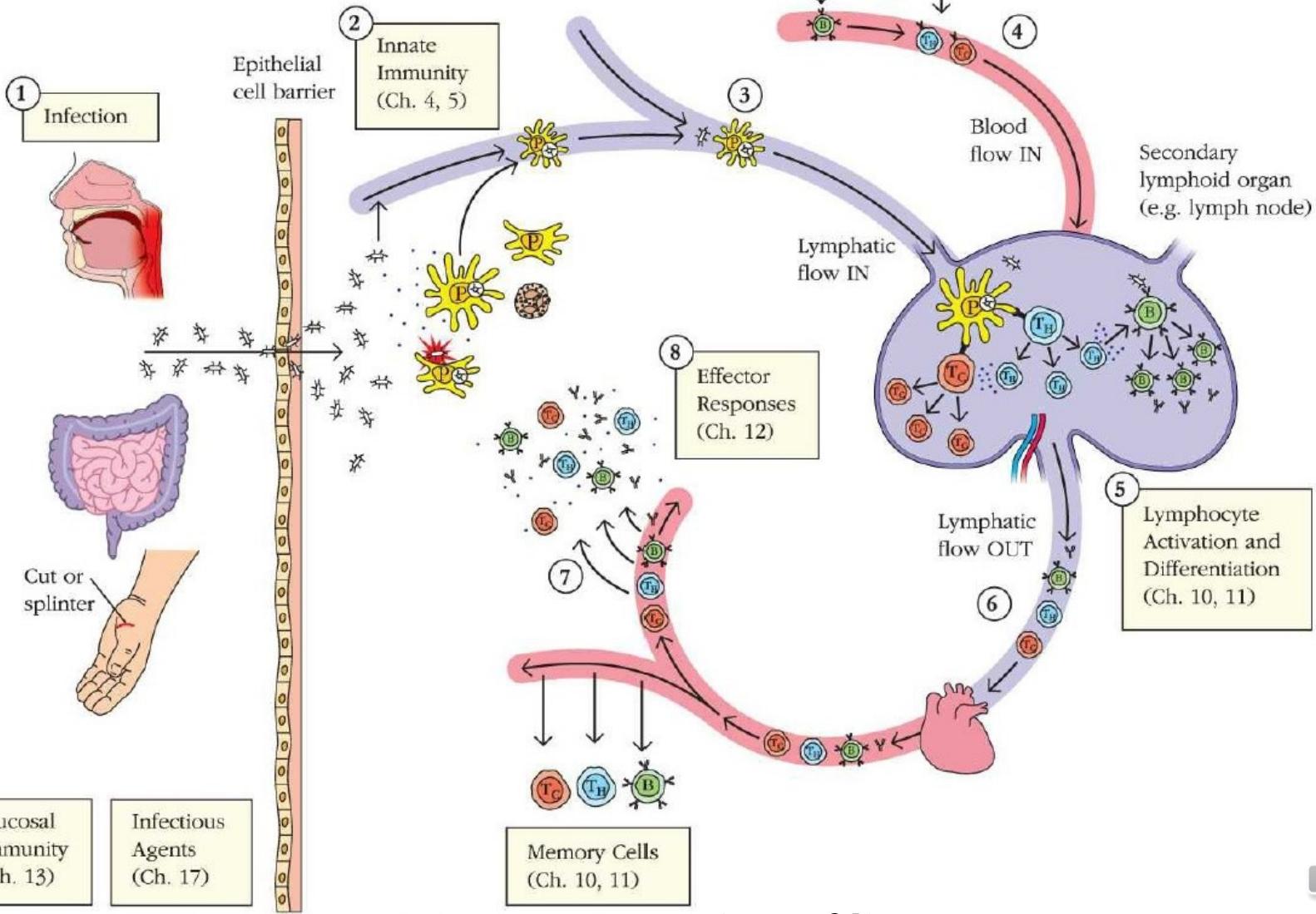


# SUMMARY

## Primary lymphoid organs



Lymphocyte Development  
(Ch. 6, 7, 8, 9)



# IMMUNE DISORDERS AND DEFICIENCIES

*Janeway's Immunology p32*

Antigen	Effect of response to antigen	
	Normal response	Deficient response
Infectious agent	Protective immunity	Recurrent infection
Innocuous substance	Allergy	No response
Grafted organ	Rejection	Acceptance
Self organ	Autoimmunity	Self tolerance
Tumor	Tumor immunity	Cancer

**Tolerance** is the strategy by which the immune system is able to discriminate between self and nonself, thereby, avoiding accidentally destroying host tissues



# IMMUNE DISORDERS AND DEFICIENCIES

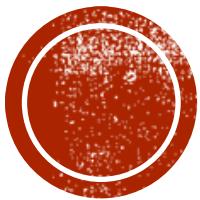
Allergy against innocuous substance, graft organ rejection and autoimmunity against self organs are normal body responses, however, they are not beneficial to the body's immunity.



# IMMUNE DISORDERS AND DEFICIENCIES

- **Immune deficiency**(Recurrent infection) : Insufficiency of the immune response to protect against infectious agents
- **Hypersensitivity (allergy)**: Overly zealous attacks on common benign but foreign antigens
- **Autoimmune disease**: Erroneous targeting of self-proteins or tissues by immune cells
- **Immune imbalance**: Dysregulation in the immune system that leads to aberrant activity of immune cells, especially enhanced inflammation and/or reduced immune inhibition





**END**

