Immunology

Innate, Adaptive, MHC

Lecture 7

Dr. Mohammad Odaibat

Department of Microbiology and Pathology

Faculty of Medicine, Mutah University

اللي بشتغل بسرعة

1- macrophage

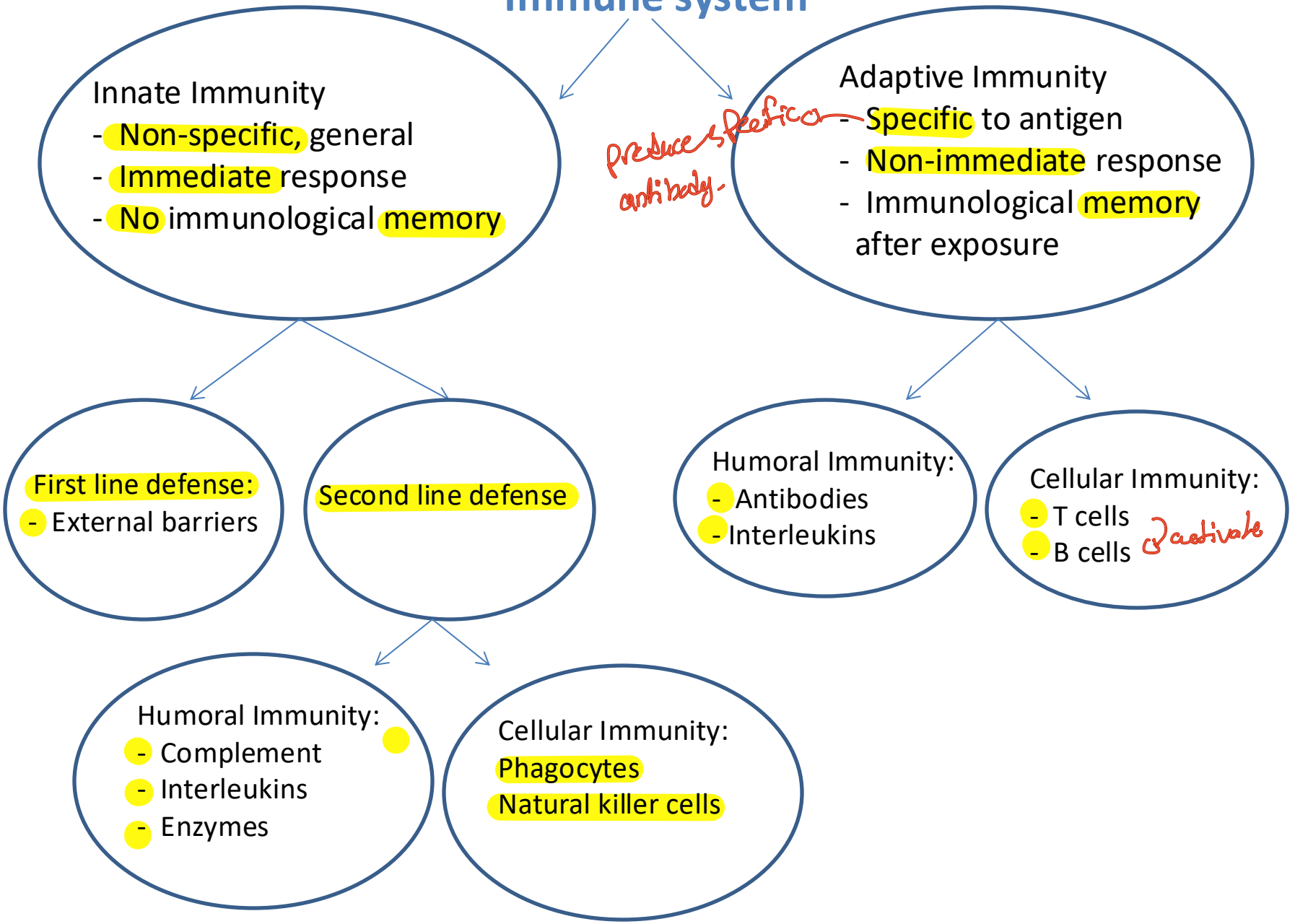
2 neutrophils

3- skin

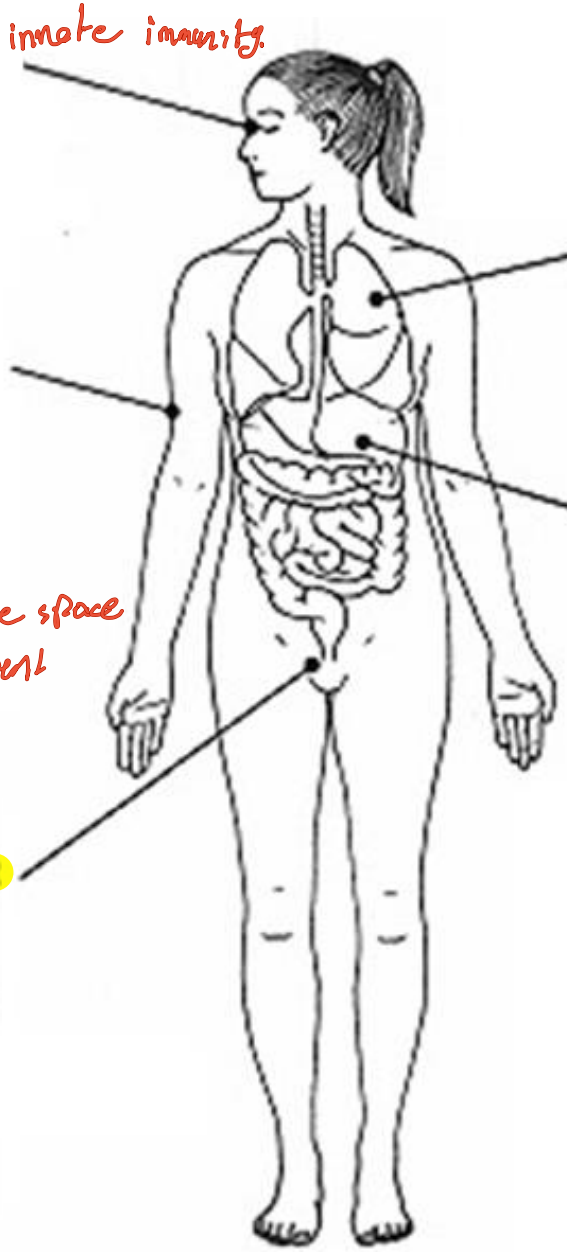
4- complement (classical, MBL

Introduction

Immune system



Innate immunity



innate immunity

Eye
- Blinking
- Tears
- Lysozyme

Skin
- Structural Barrier
- sweat sebum
- Lactic acid
- Propionic acid
- Lysozyme
- Normal Flora → close space between skin → prevent bacteria to grow

Respiratory Tract
- Coughing Sneezing
- Mucus
- Cilliary action
- Phagocytes
- Lysozyme

GI tract
- Stomach acidity
- Normal Flora
- Peristaltis
- Antimicrobial compounds

Urogenital Tract
- Lavaging action of urine
- Acidity of urine
- Lysozyme
- Vaginal lactic acid
- Normal flora

The pathogens like neutral pH => so we prevent growth it by acidity.

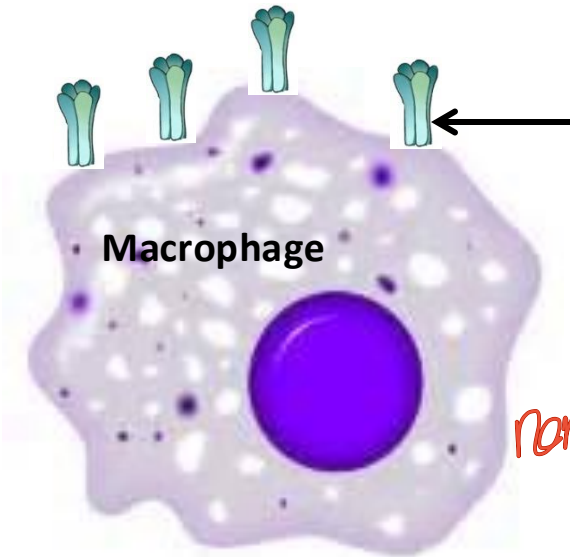
pH

- ✓ Skin about 5,5
- ✓ Stomach between 1-3
- ✓ Vagina between 4,4-4,6

Innate immunity

Stages Phagocytosis: interaction with pamp.

1. Recognition and attachment of microbes by phagocytes



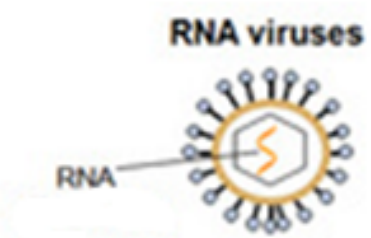
on phagocytosis surface.

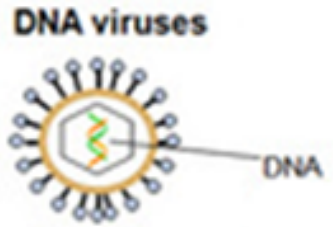
Toll like receptor (TLR)

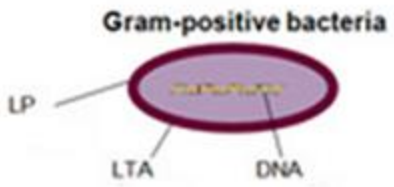
Great that

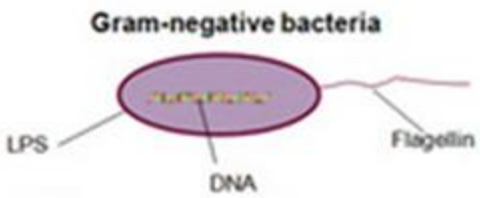
TLR recogizes pathogen associated molecular pattern

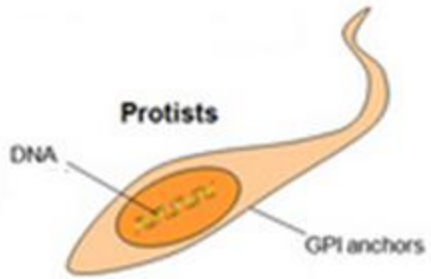
non specific

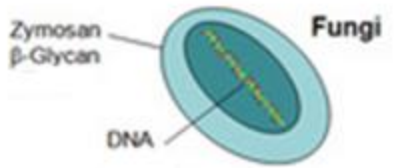












Adaptive Immunity

Objectives

- The **definition and the importance** of the adaptive immunity

- Understanding the **arms** of the adaptive immunity:
  - ✓Humoral immunity
  - ✓Cell-mediated immunity

- The **importance of T- helper** cells in communicating and activating immune cells

- **Function and mechanism of action of TH1 & TH2 cells**

- **Function and mechanism of action of T cytotoxic cells**

Introduction

Initiation of innate and acquired immunity

Inflammation

Innate immune response

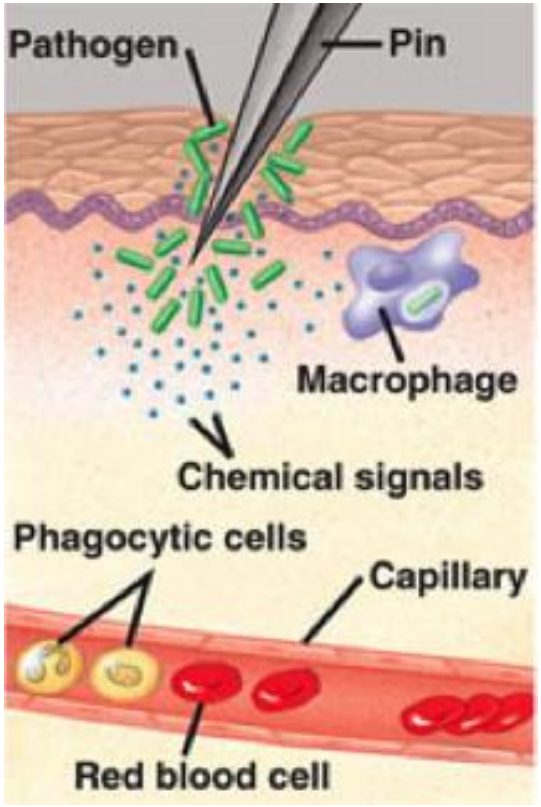
Complement

Defensins

Lysozymes

Vasodilatation

Mast cells



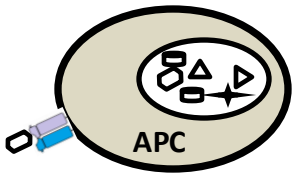
Antigens

Chemical signals

Neutrophils

Macrophages

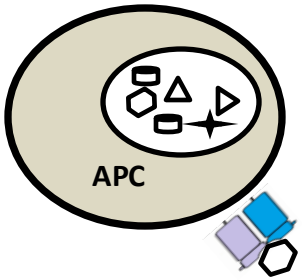
Dendritic cells

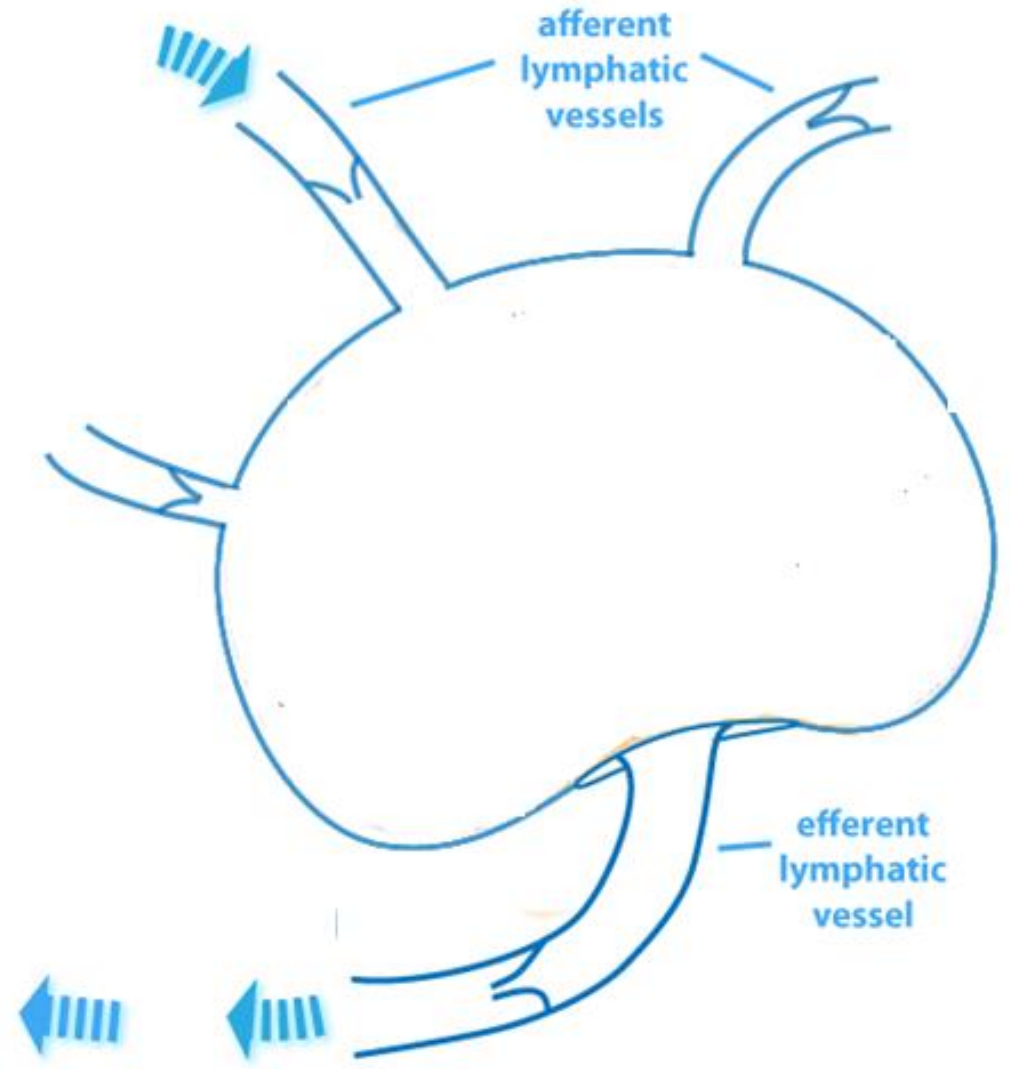


The initial step in triggering adaptive immunity

To the secondary lymphoid organs

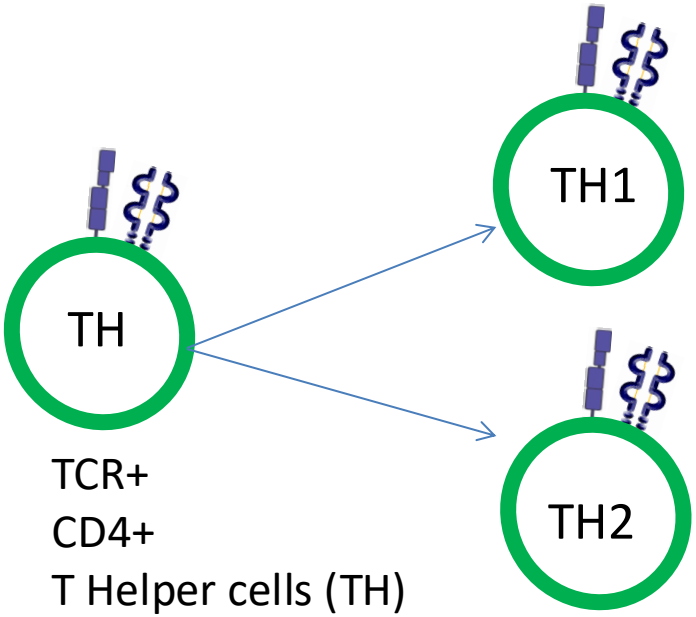
Adaptive Immunity



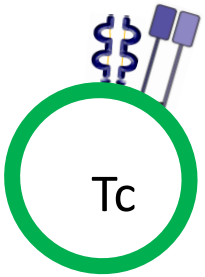


What will happen inside the lymph node?

T lymphocytes



TCR+
CD4+
T Helper cells (TH)
Recognized MHC2



TCR+
CD8+
T cytotoxic cells (Tc)
Recognized MHC1

What will happen inside the lymph node?

Activation of T lymphocytes

TH1

T cytotoxic lymphocytes (TCL)

Cell mediated immunity

Killing

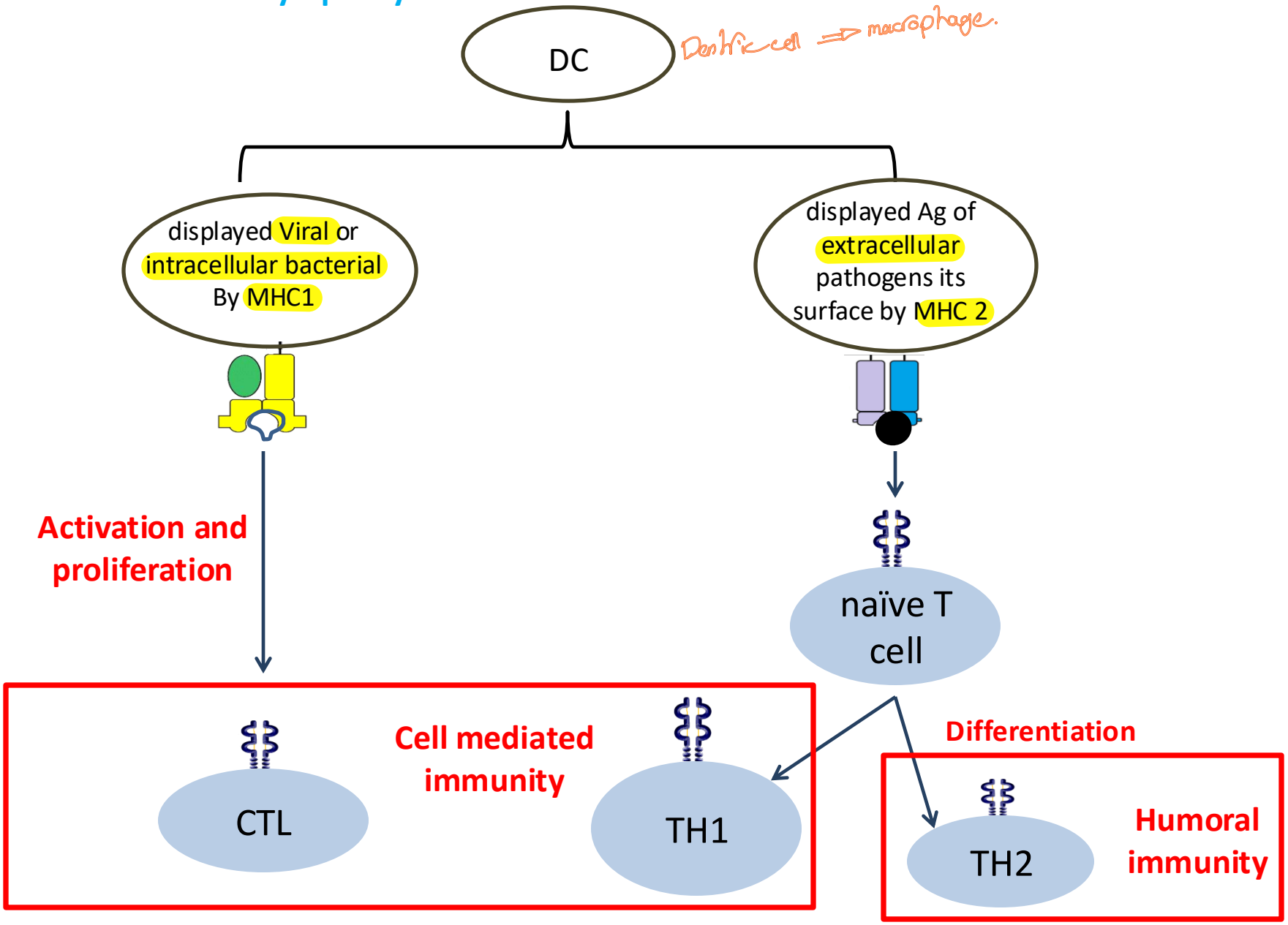
TH2

Activation of B lymphocytes

Humoral immunity

Adaptive Immunity

Activation of naïve T lymphocytes

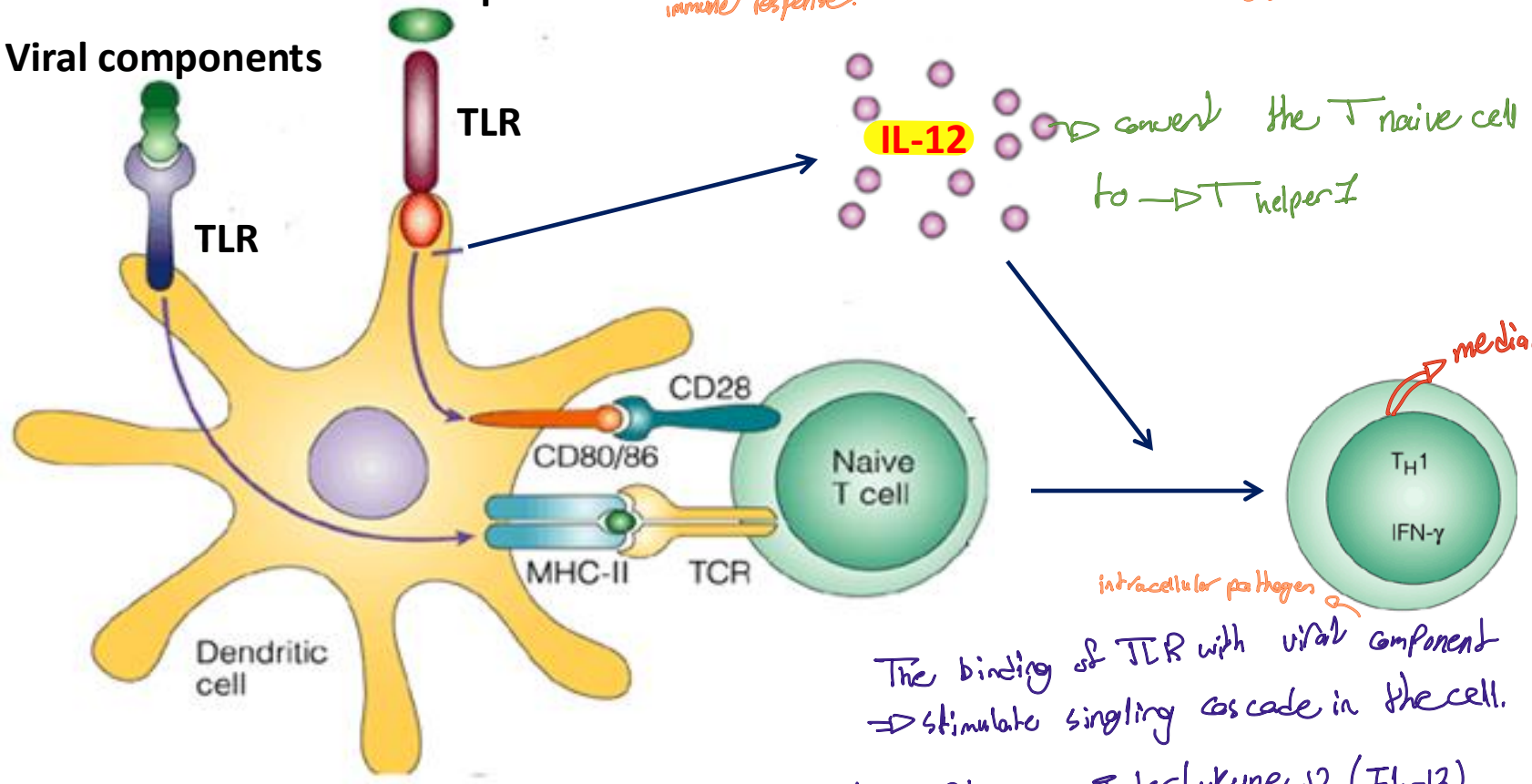


Adaptive Immunity

What determines the naïve T cell differentiation into Th1?

intracellular Pathogen

The cell determines what should it activate mediated or humeral immunity according on who TLR that activated.



The onset of immune response.

⇒ convert the T naive cell to ⇒ T helper I

mediated.

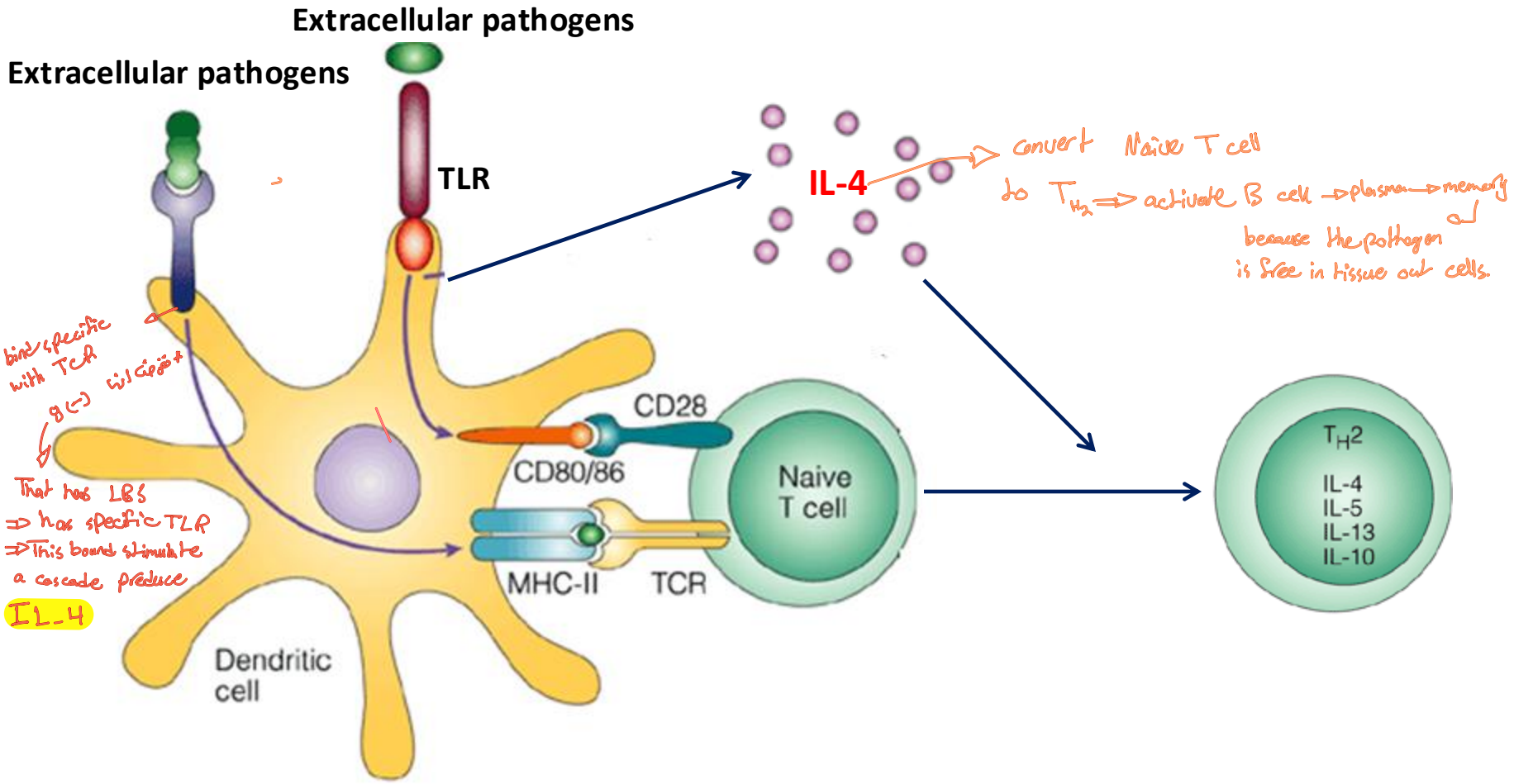
The binding of TLR with viral component ⇒ stimulate singling cascade in the cell.

to produce Interlukyne-12 (IL-12)

TLR :- Toll Like receptors :⇒ receptor on surface of macrophage recognize a PAMP

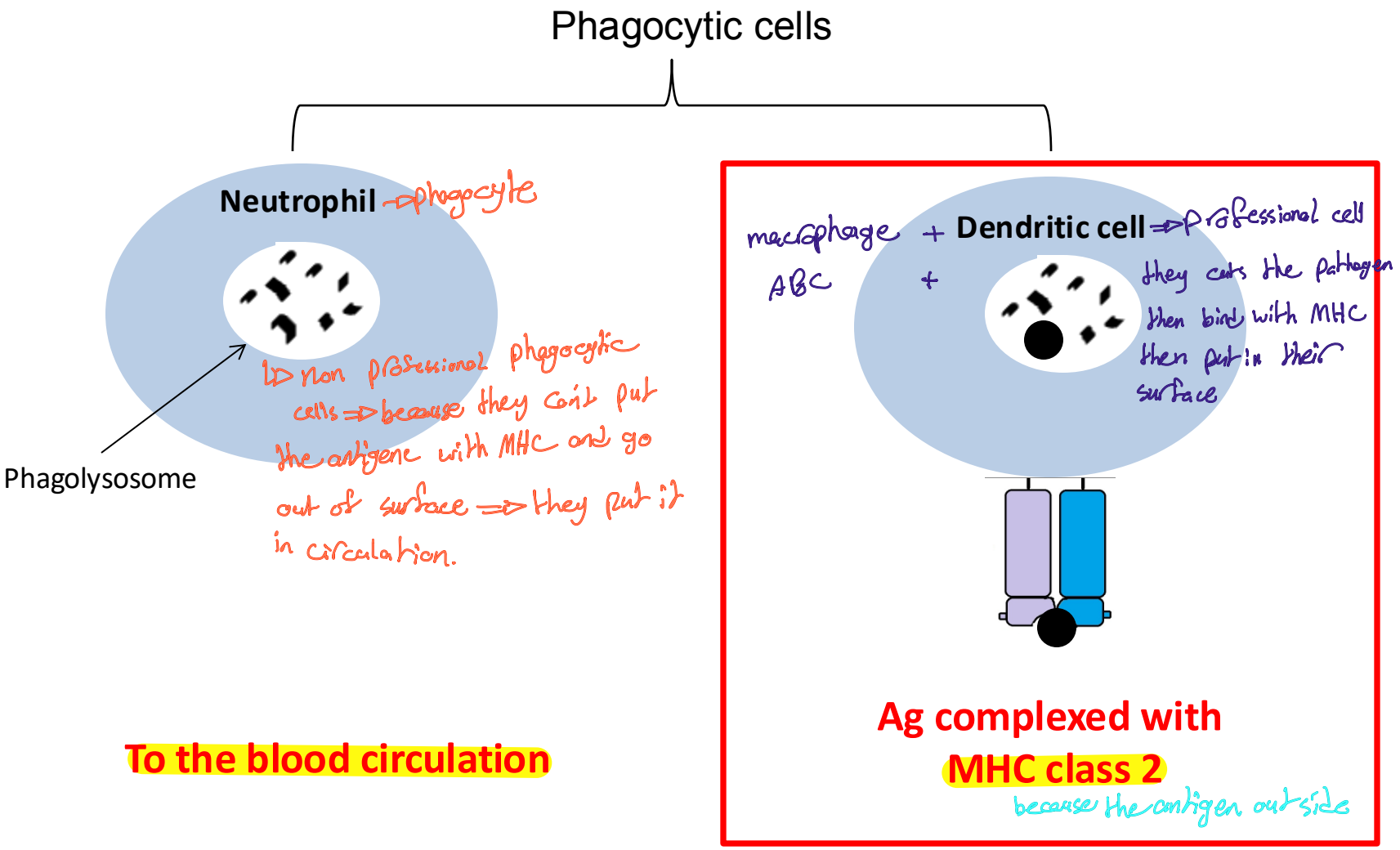
Adaptive Immunity

What determines the naïve T cell differentiation into Th2?



Humoral Arm of Adaptive Immunity

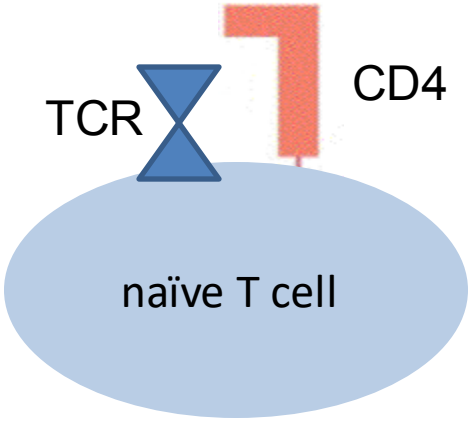
Humoral Immunity



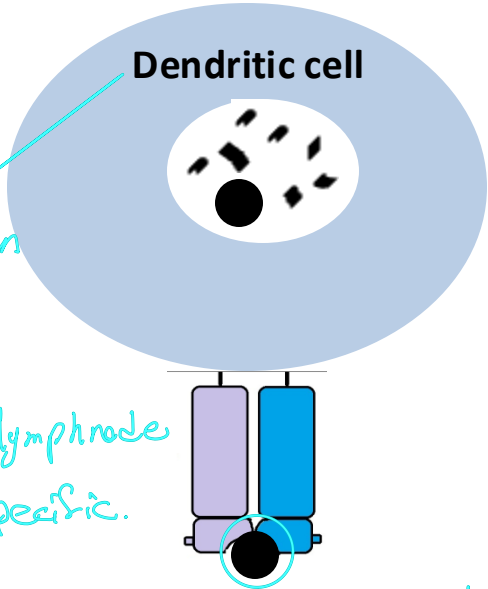
#The two step in neutrophils + Dentric cell
⇒ to activate the Bcell.

Humoral Immunity

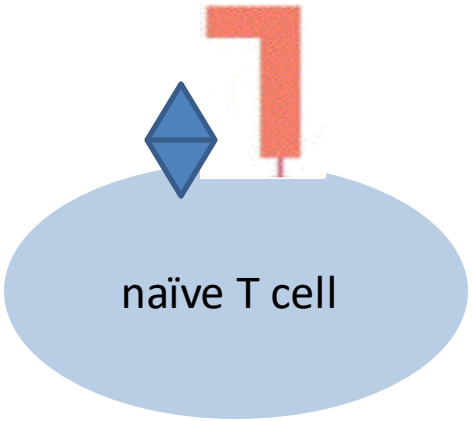
In the lymph node, dendritic cell Start presenting Ag to naïve T cells until Finding one T cell with specific TCR For the displayed Ag

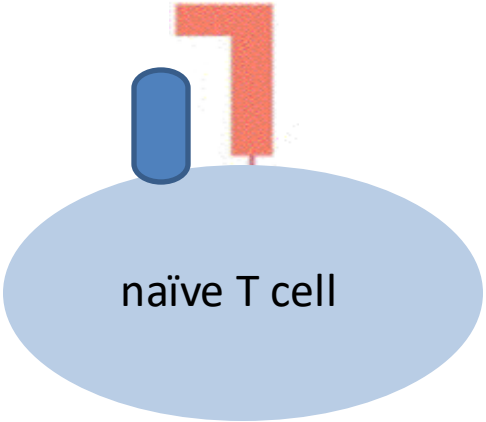


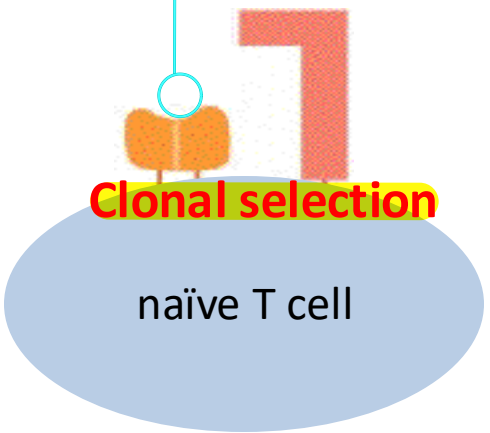
cut the pathogen and
every specific antigen
has specific MHC
⇒ out of surface.
⇒ go to the nearlier lymphnode
⇒ we find T cell has specific.
TCR



first step of triggering of adaptive immune responce. ⇒ humeral.

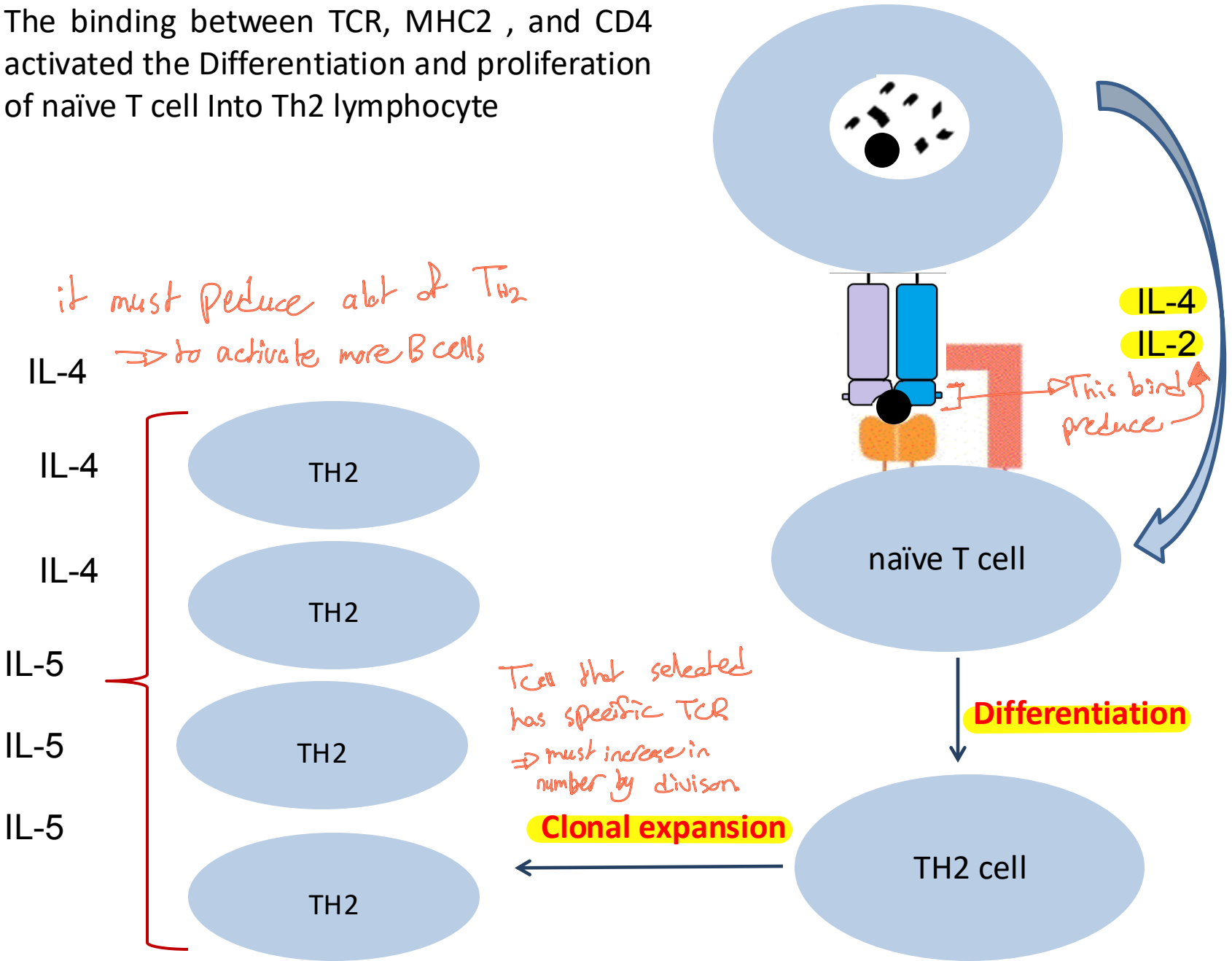




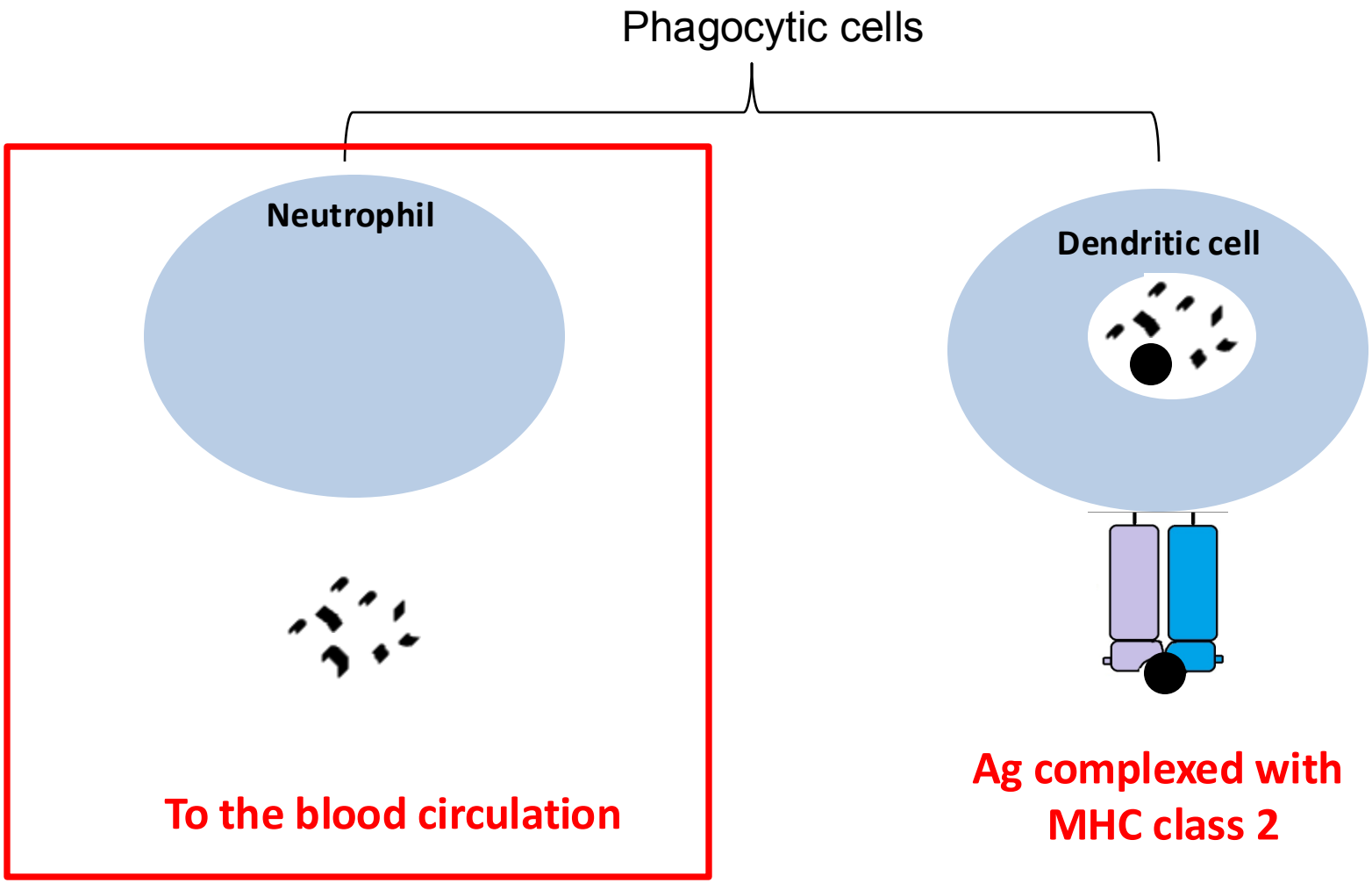


Humoral Immunity

The binding between TCR, MHC2 , and CD4 activated the Differentiation and proliferation of naïve T cell Into Th2 lymphocyte

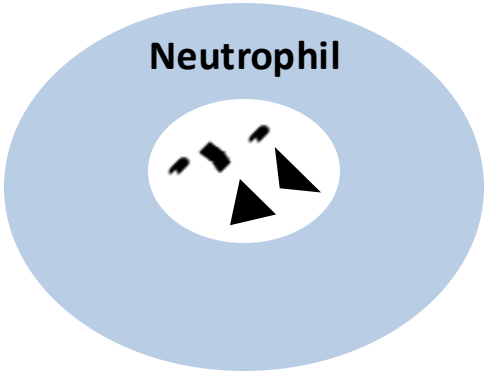


Humoral Immunity

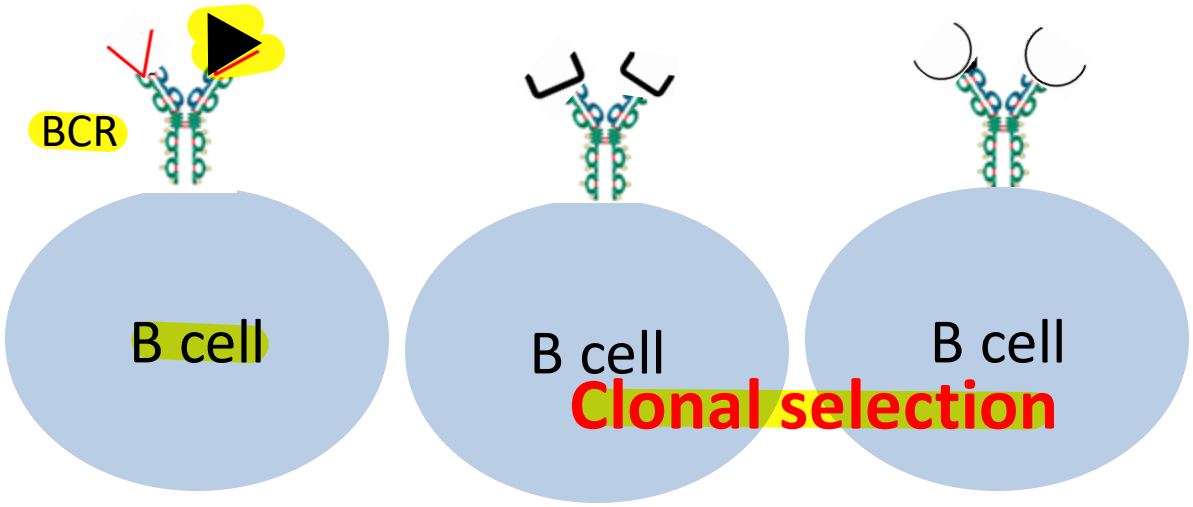


Humoral Immunity

The free antigens that were released from neutrophils will activate naïve B cells

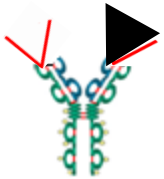


Reaching lymph node via lymph



Humoral Immunity

Antigen binding to the BCR will activate the IL-4R gene expression



IL-4R

B cell

IL-4

IL-4

IL-4

IL-5

IL-5

IL-5

TH2

TH2

TH2

TH2

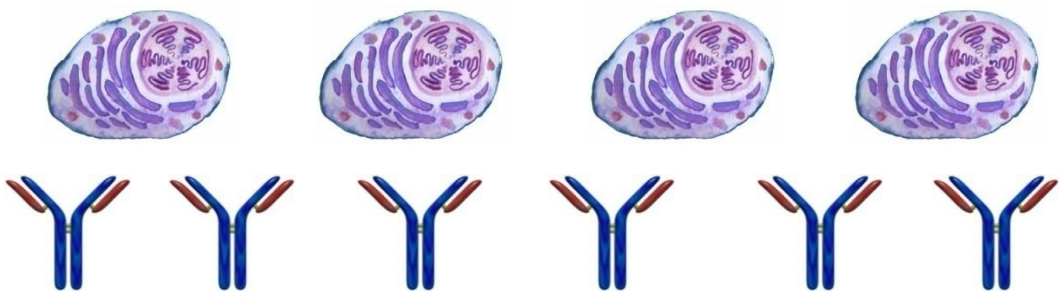
IL-4 will activate B cell proliferation

expansion.

Clonal expansion

B cell | B cell | B cell | B cell

IL-5 will activate B cell differentiation into plasma cells

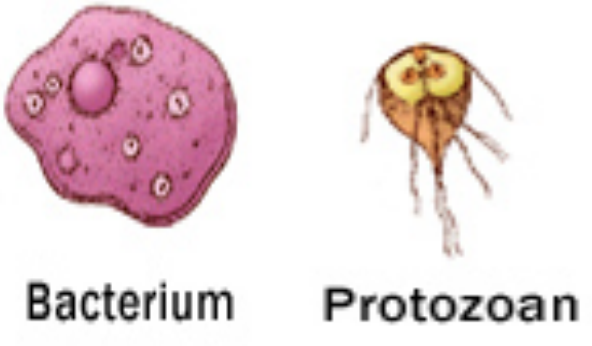


*ABC → Just work on T cell.

T cell do cooperation between macrophage and B cell

Cellular immunity vs. Humoral immunity

Extracellular pathogens ⇒ humeral



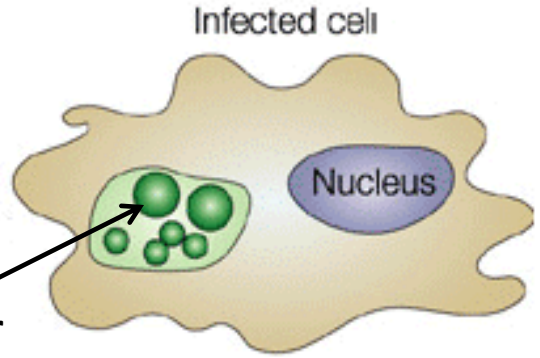
⇒ IgE
Besophiles.

The body can defend itself against the extracellular pathogens by **complement, antibodies**

↓

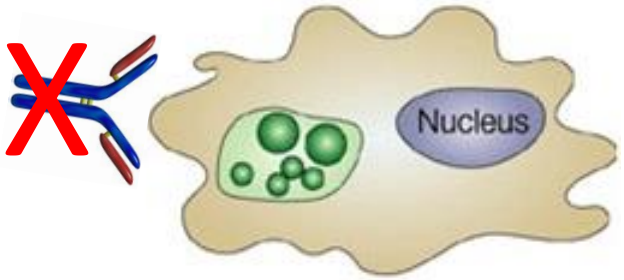
Humoral immunity

Intracellular pathogens



↓

Complement & antibodies are ineffective in fighting intracellular pathogens



↓

Cellular immunity is activated

or cell mediated.

Cellular Arm of Adaptive Immunity

Cellular immunity

Types

$CD8^+$ cytotoxic T lymphocytes (CTLs) mediated cell lysis

↓

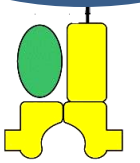
immunity independent of antibody and subsequent destruction of cells bearing the antigen

Macrophage activation by TH1 cells

↓

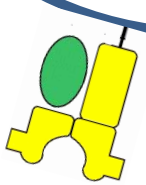
dependent the secretion by T cells of cytokines that enhance the ability of phagocytes to eliminate the phagocytized pathogens

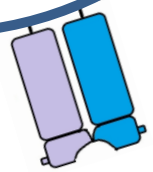
All nucleated ells can express MHC1



APC can express both MHC1 & MHC2

macrophage



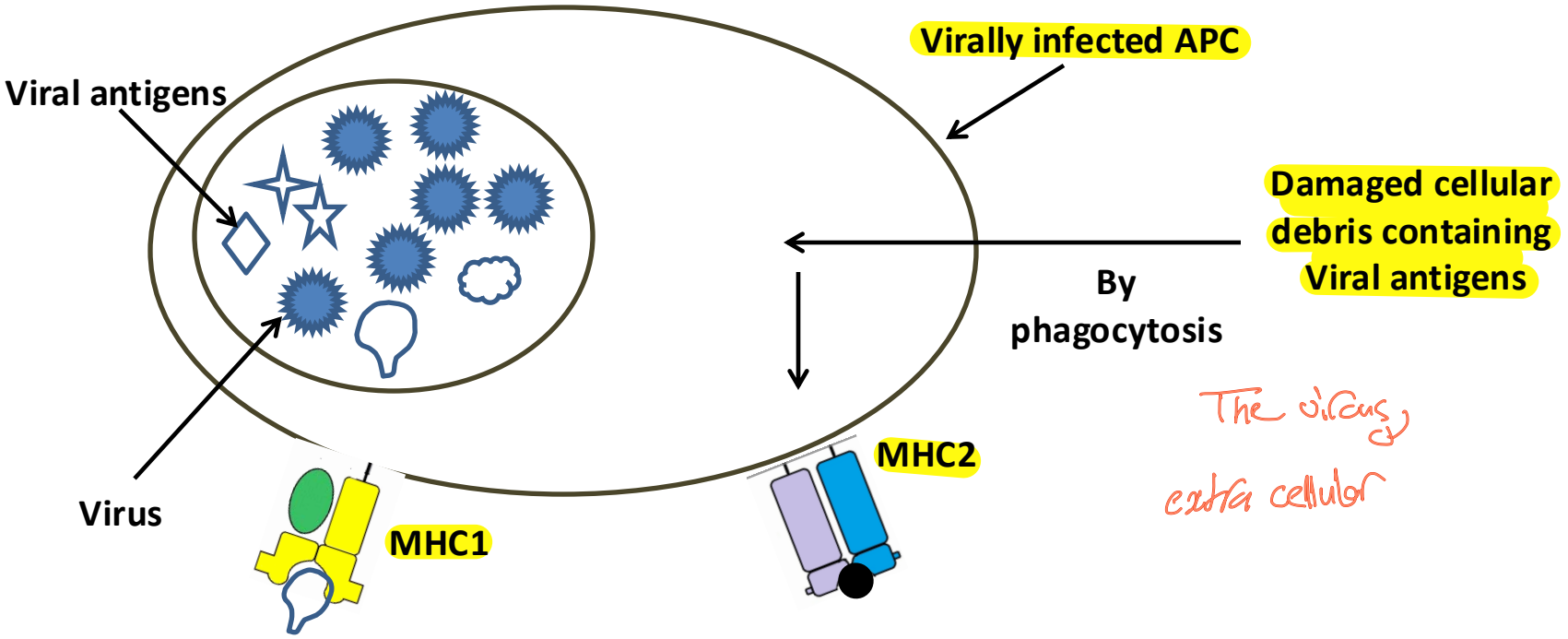


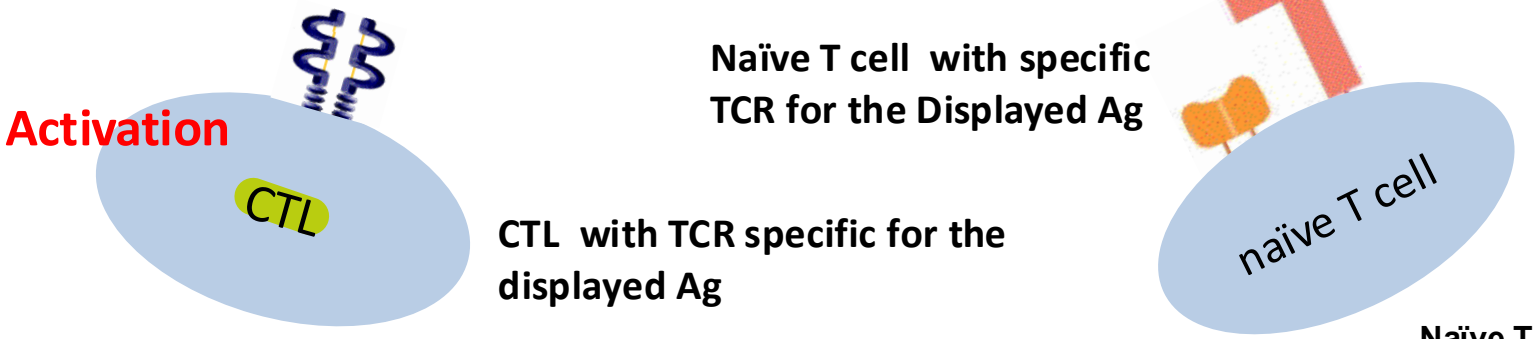
* phagocytosis → take the bacterga by their will

* virus → go inside the cell او حتى

Cellular immunity

CD8$^+$ cytotoxic T lymphocytes (CTLs) mediated cell lysis

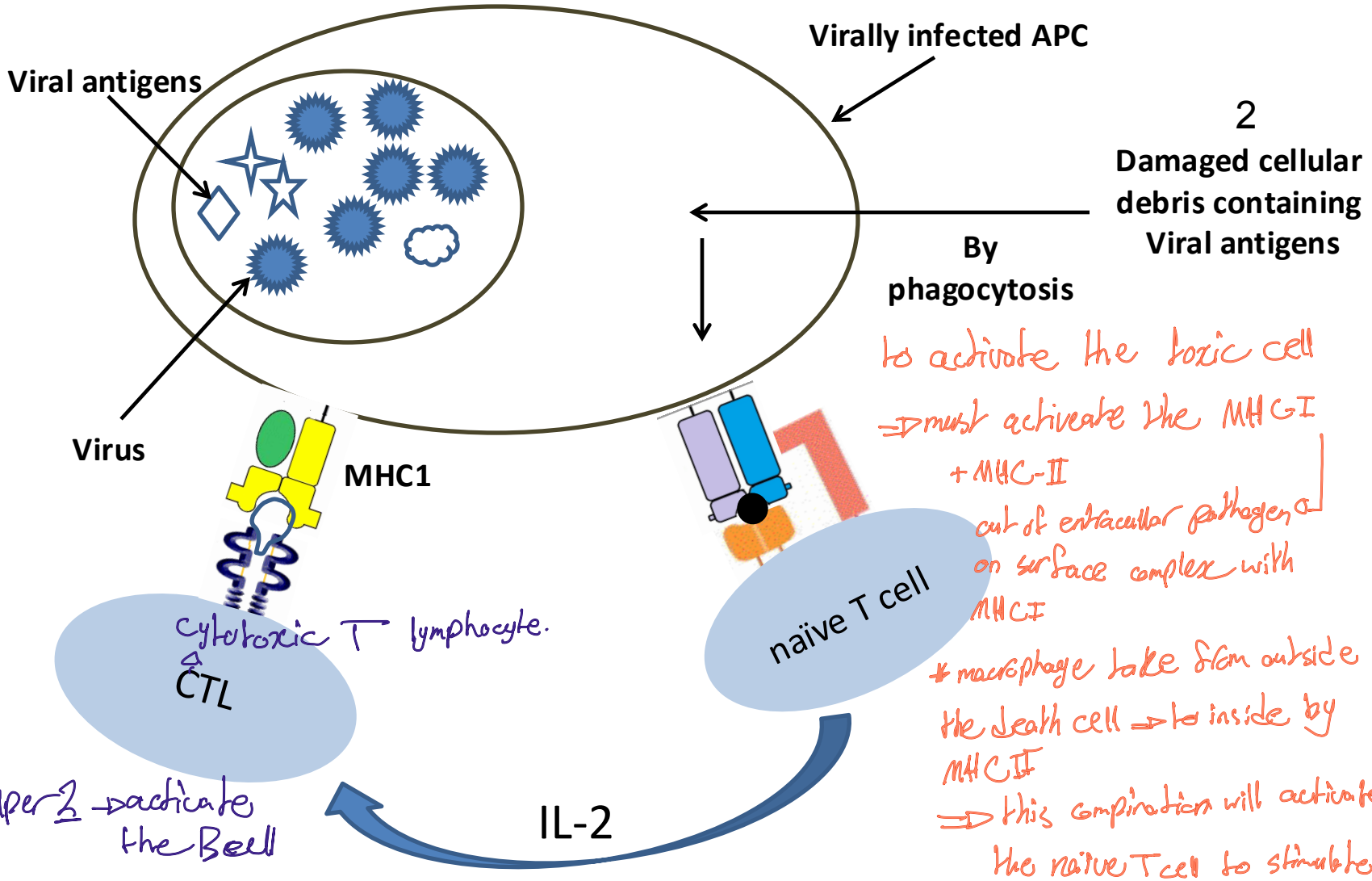




Naïve T cell matures into TH1

Cellular immunity

CD8⁺ cytotoxic T lymphocytes (CTLs) mediated cell lysis

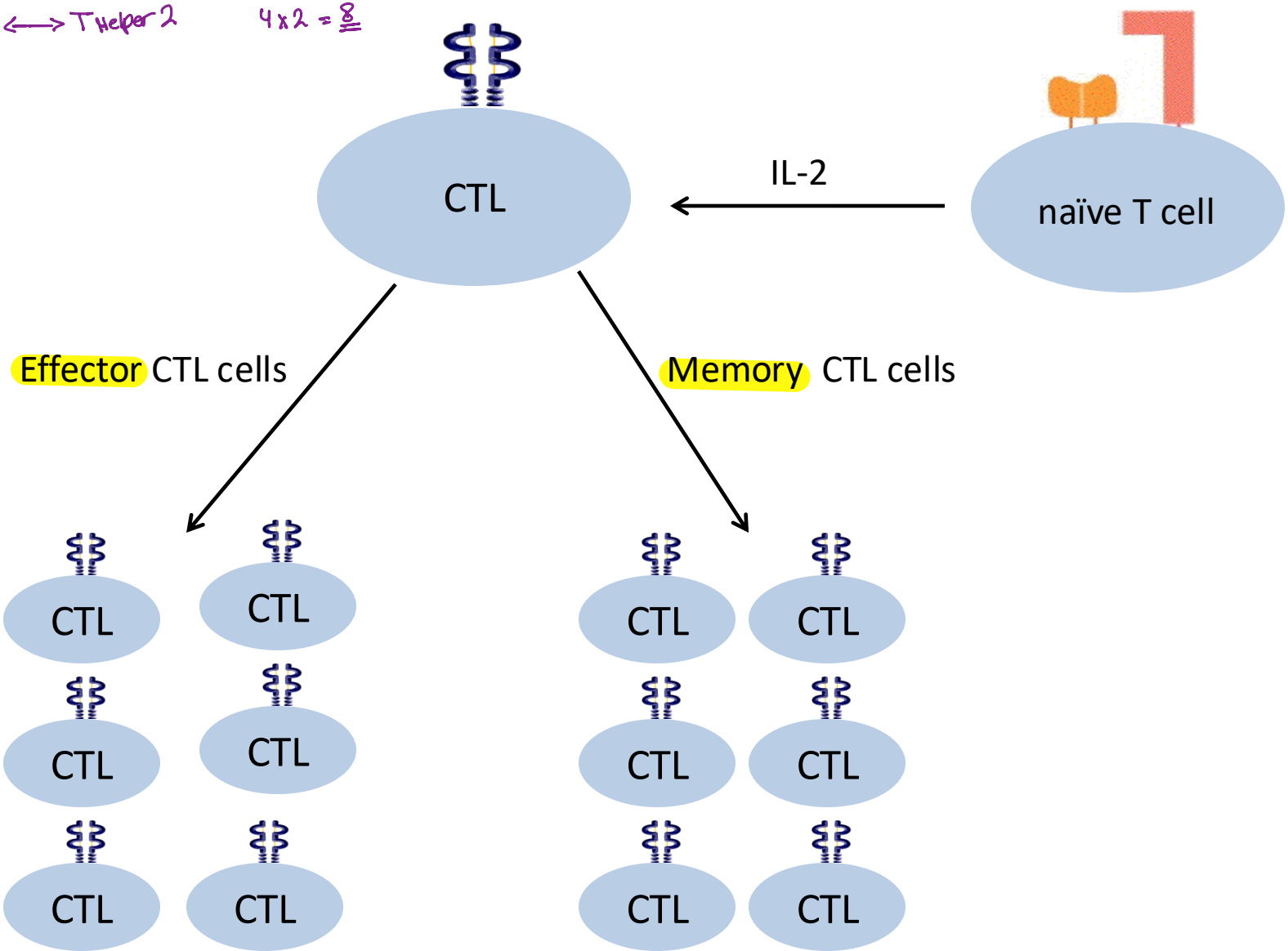


Cellular immunity

CD8⁺ cytotoxic T lymphocytes (CTLs) mediated cell lysis

CD 8⁺ ⟷ T Helper 1 8 x 1 = 8

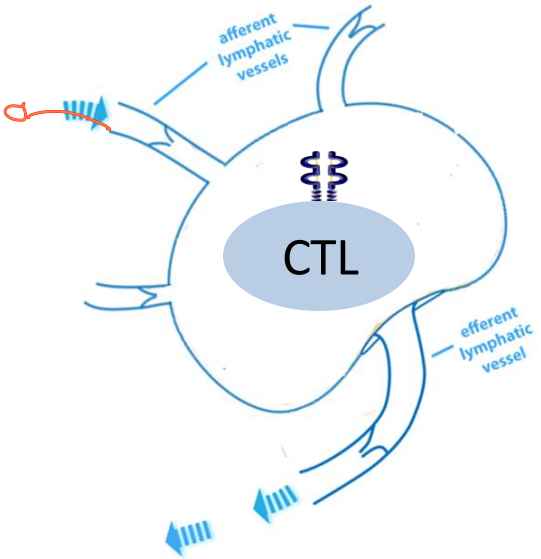
CD 4⁺ ⟷ T Helper 2 4 x 2 = 8

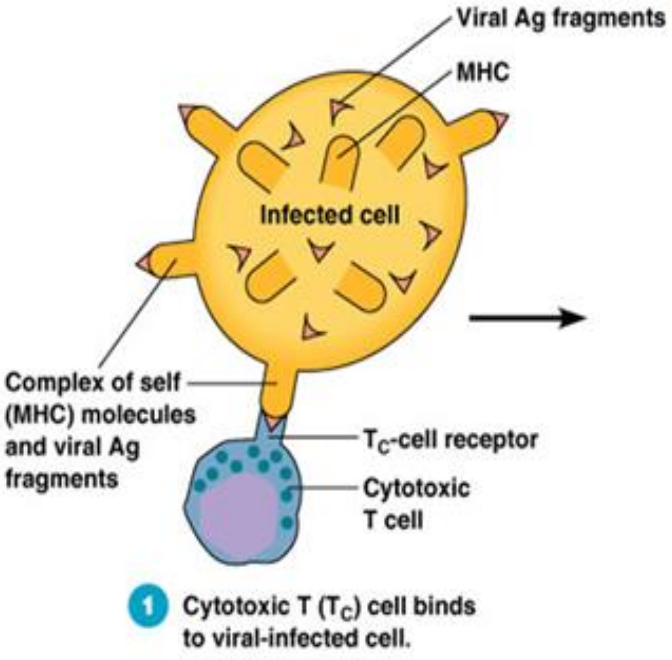


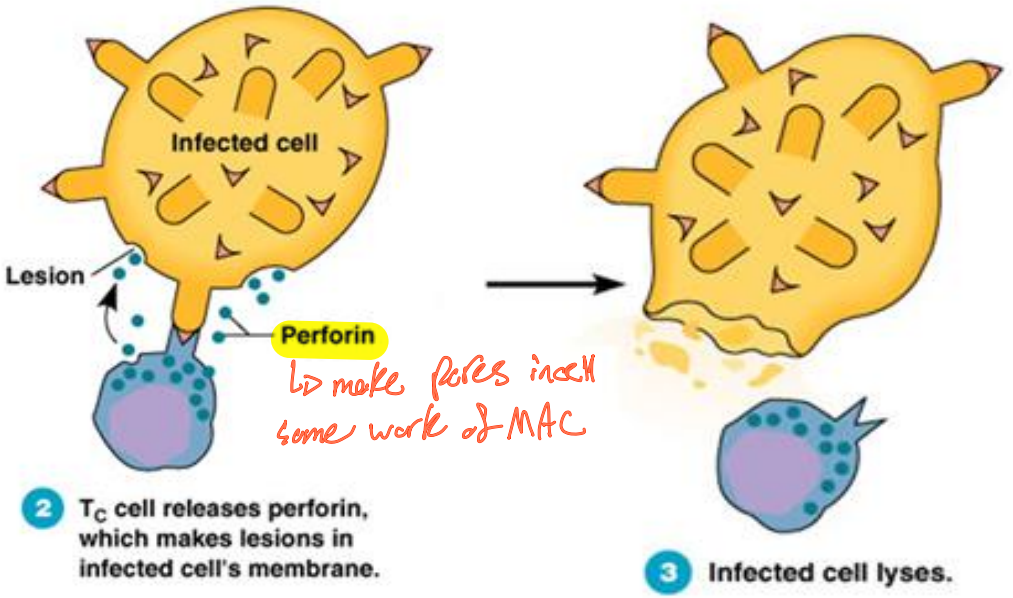
Cellular immunity

CTLs mediate cell lysis of virally infected cells

* activated CTL out from the lymph node and go to any cell that have in the surface the same antigen that on virus.







Innate vs. Adaptive Immunity

Innate immunity	Adaptive immunity
• general protection (not antigen-specific)	• highly specific for a particular pathogen (antigen-specific)
• early phase of host response to pathogens without requiring prior exposure	• late phase response of antigen-specific lymphocytes to antigens
• immediate maximal response	• lag time between exposure and maximal response
• does not alter on repeated exposure (no immunological memory)	• improves with each successive exposure (immunological memory)
* (rapid, non-specific, no memory)	* (slower, specific, diverse, memory)

Major Histocompatibility Complex

* In old book it was called Iuman Lukasite Antigen (HLA)

⇒ then they found that white blood cell (leukocyte) has antigen that determine the similarity between the tissue in human.

⇒ Then they found that this antigen and protein is present in all cells and has a specific function in the tissue match

⟹ so they called on it Major Histocompatibility complex. (MHC)

Introduction

Definition of the MHC

Is a set of cell surface molecules encoded by a large gene family which controls a major part of the immune system in all vertebrates

MHC I ⇒ for viral + intracellular pathogen

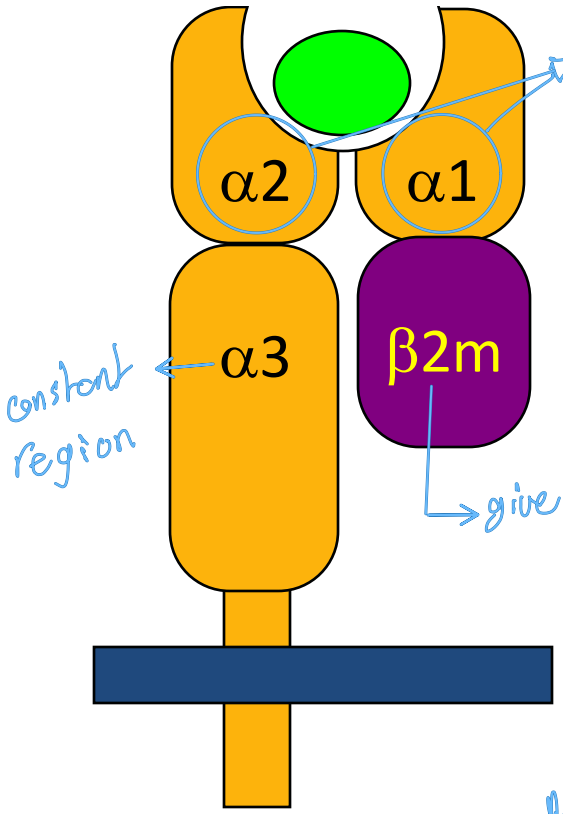
MHC II ⇒ for extracellular pathogen.

MHC molecules play a major role in three lines

- Antigen presentation
- Autoimmune diseases
- Transplantation
  - ↳ it was a different
  - ⇒ rejection

Class I MHC Molecule

Overall structure of MHC class I molecules



variable region. that connect with antigen

MHC-encoded α-chain of 43kDa

α-chain anchored to the cell membrane

constant region

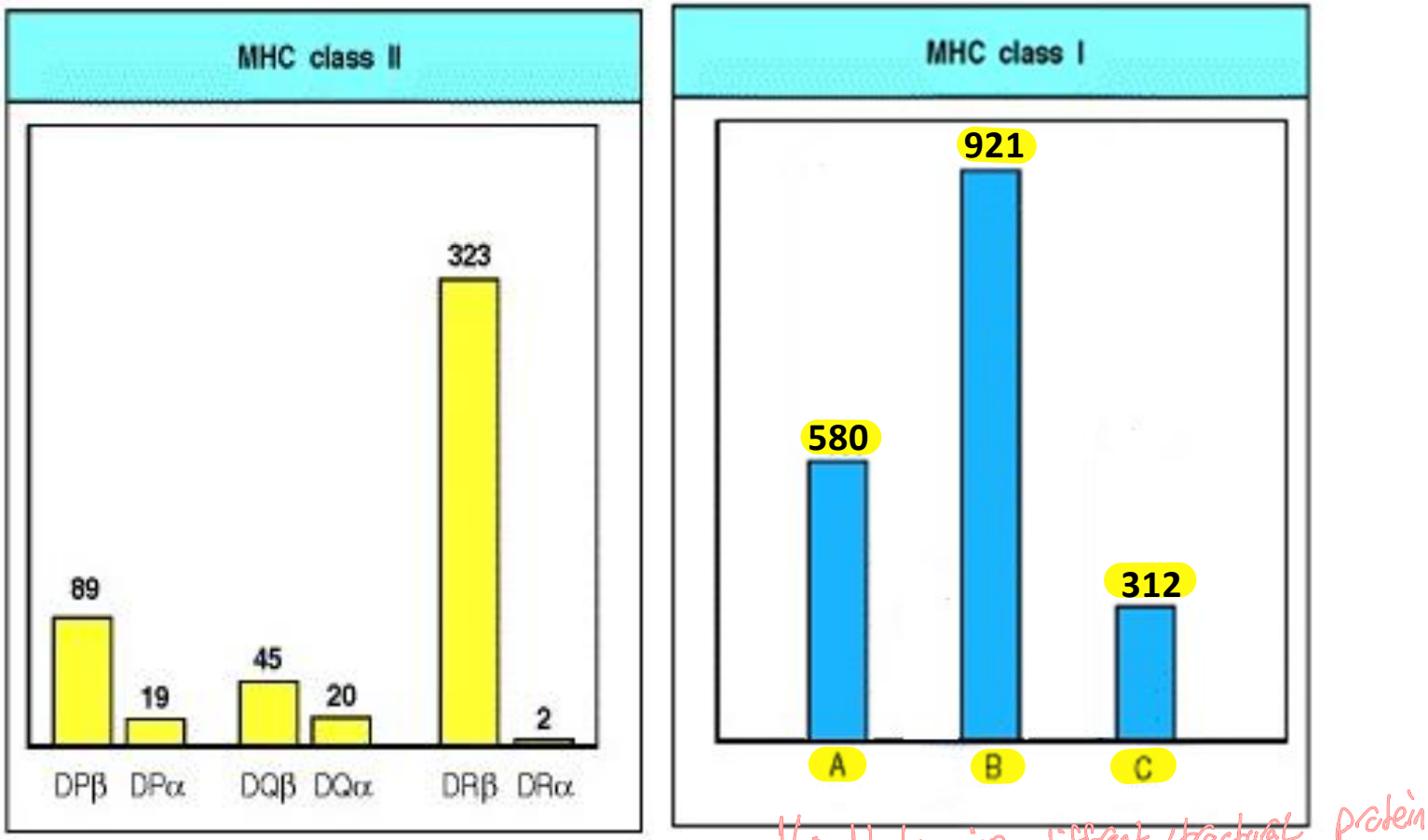
Peptide antigen binds in a groove formed From α1 and α2 domains

give stability for molecule.

β2-microglobulin, 12kDa, non-MHC encoded, non-transmembrane, non covalently bound to α-chain

* MHC I bind with membrane in one region.
* MHC II " " " two region

Human MHC Class 1 and 2 genes are highly polymorphic

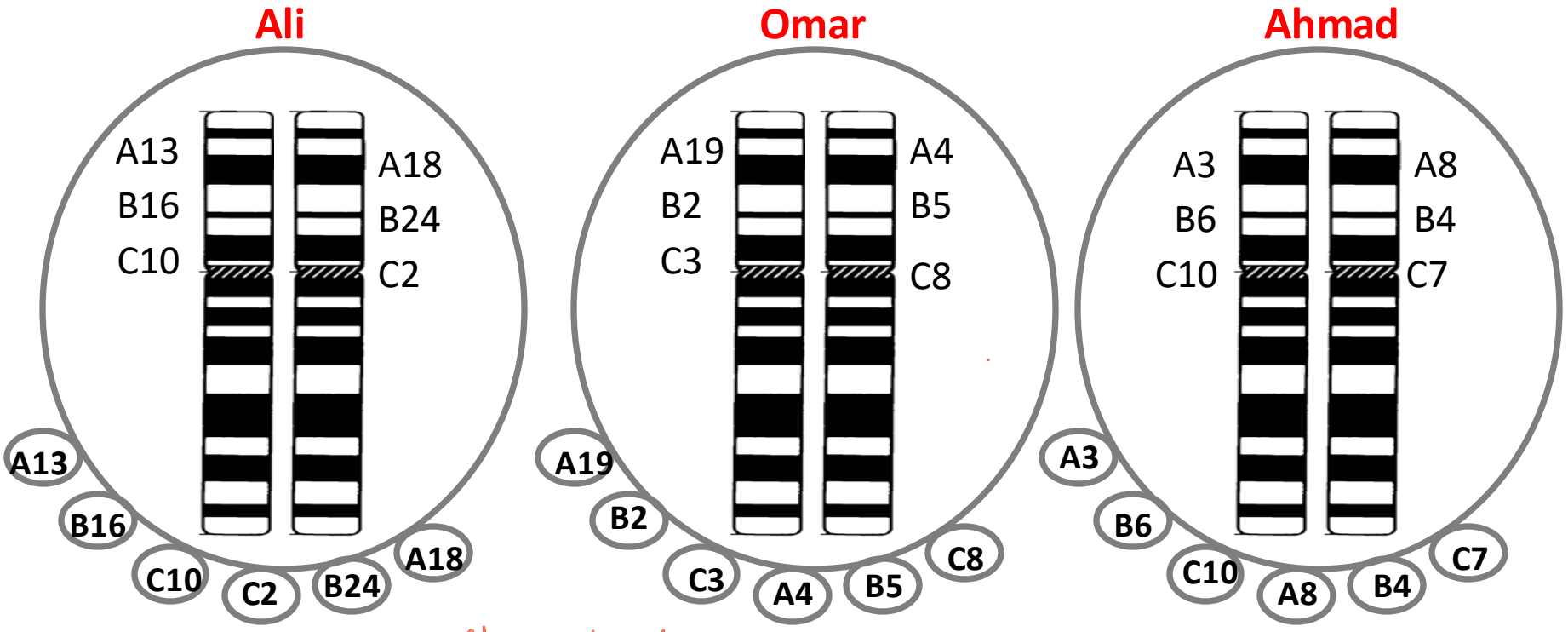


↳ that give different structural protein
⇒ to cover different antigene

- Each MHC locus has many alleles.
- The difference in the inheritance of MHC molecules among individuals is due to the presence of a big number of MHC alleles

MHC-I

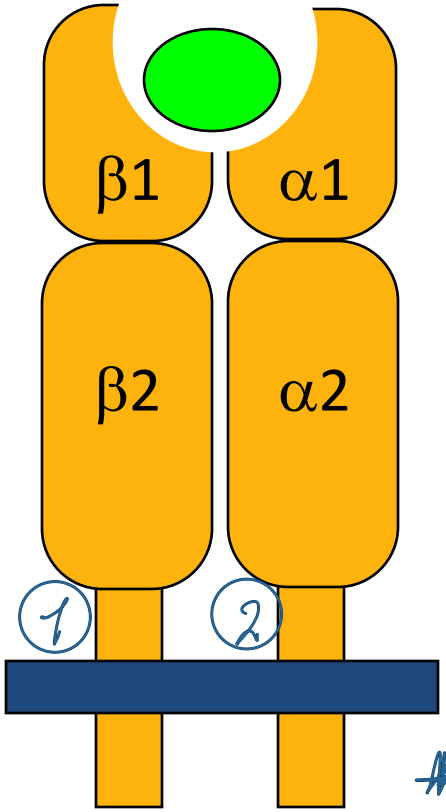
Inheritance of MHC-I



The diffrence between Ali and ahmed
⇒ The tissue will be diffrent
⇒ we can't transplantation
⇒ so we need first relative and make atest to ensure that they have the same MHC-I

MHC-II

Overall structure of MHC class II molecules



MHC-encoded, α-chain and a β-chain

α and β chains anchored to the cell membrane

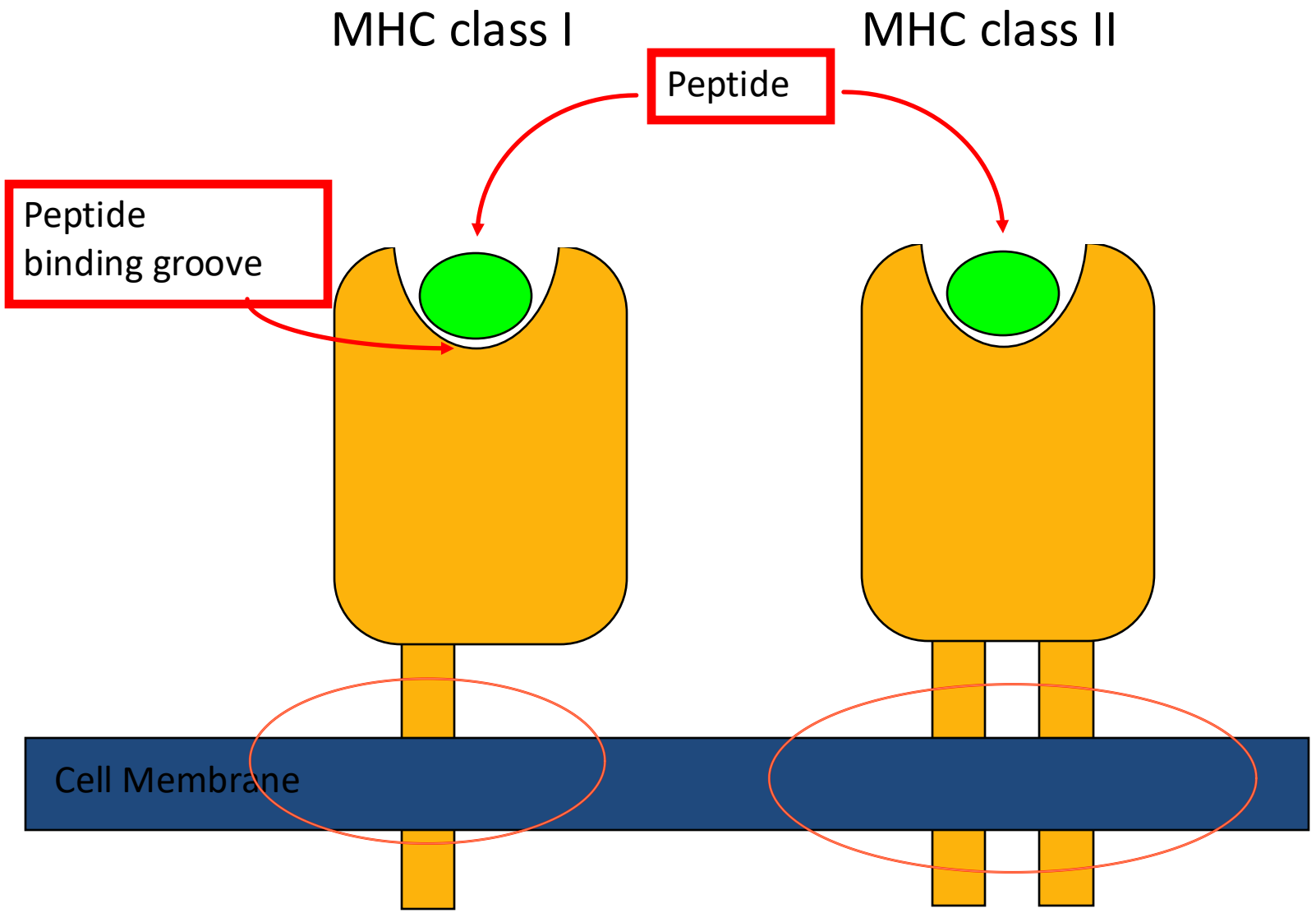
No β-2 microglobulin

Peptide antigen binds in a groove formed
From α1 and ß1 domains

it hasn't B2M

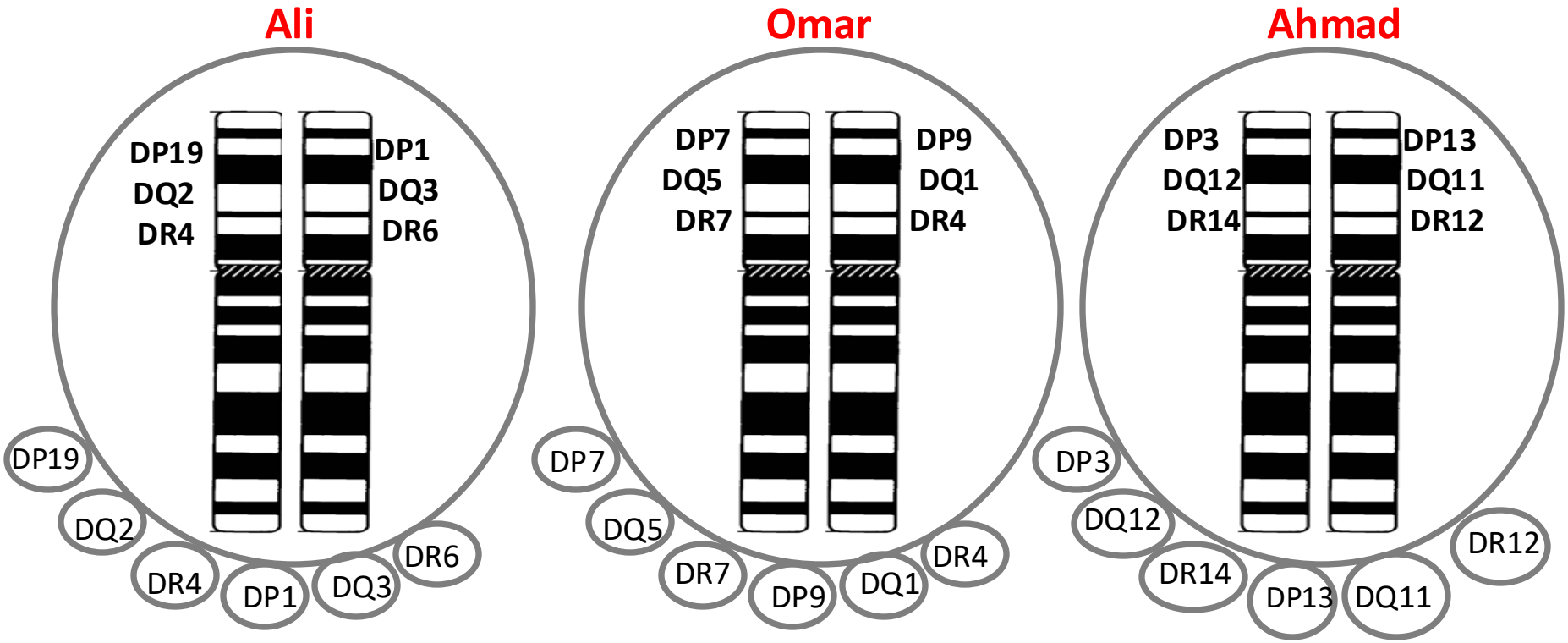
MHC-II

MHC-I vs. MHC- II



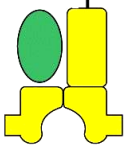
MHC-II

Inheritance of MHC-II

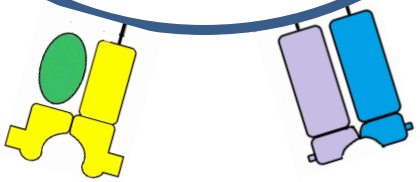


Expression of MHC molecules

All nucleated ells express MHC1



APC can express both MHC1 & MHC2

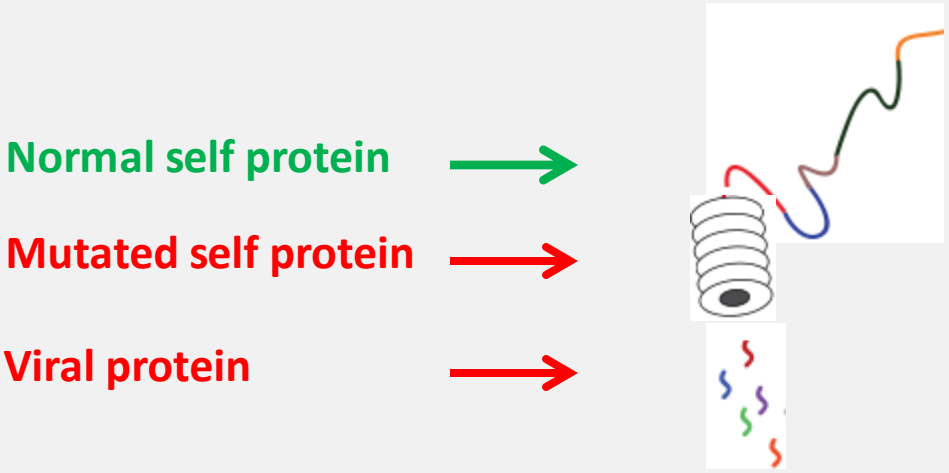


Functions of MHC-I molecules

Types of endogenous proteins synthesized in the human cells including:

1. The normally synthesized cellular proteins
2. The mutated cellular proteins
3. The viral proteins (antigens)

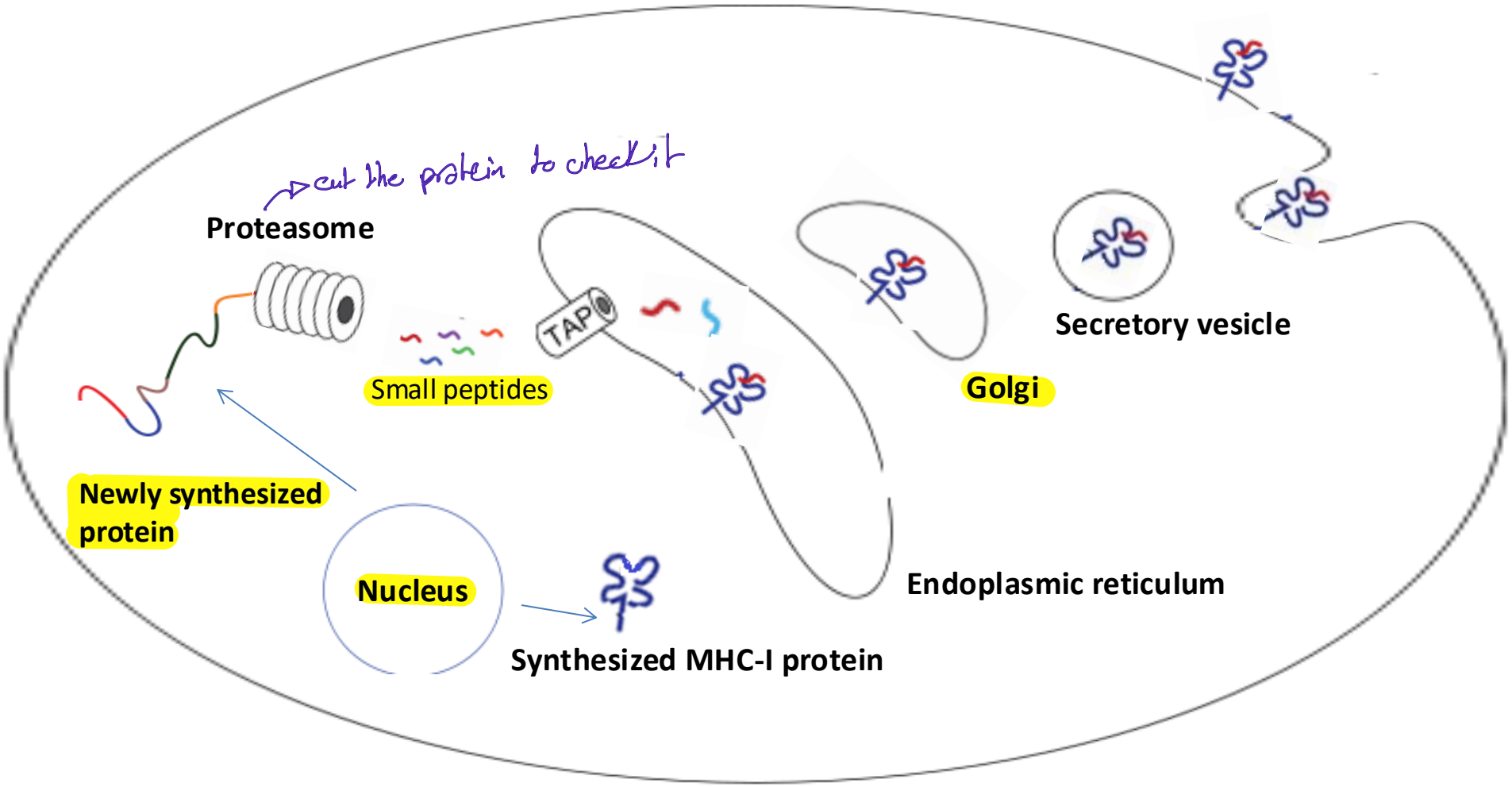
A small amount of these proteins are directed to the proteosome in which these proteins are degraded into short peptides in order to be complexed with the MHC-I molecules. Then these proteins with MHC-I are expressed on the surface of the cell to be presented to the cytotoxic T-cells (CTLs)



Functions of MHC-I molecules

MHC-I molecules

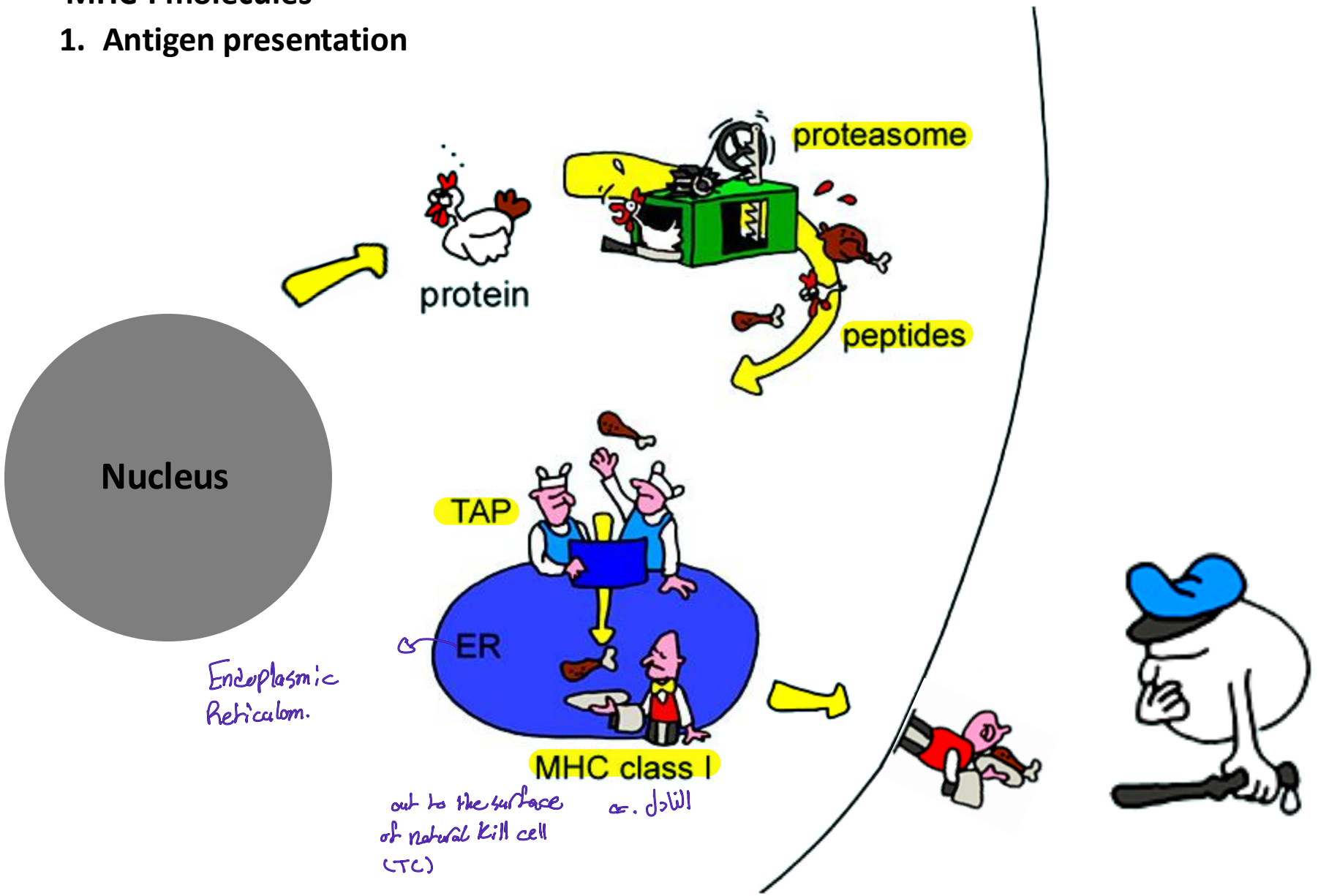
1. Antigen presentation



Functions of MHC-I molecules

MHC-I molecules

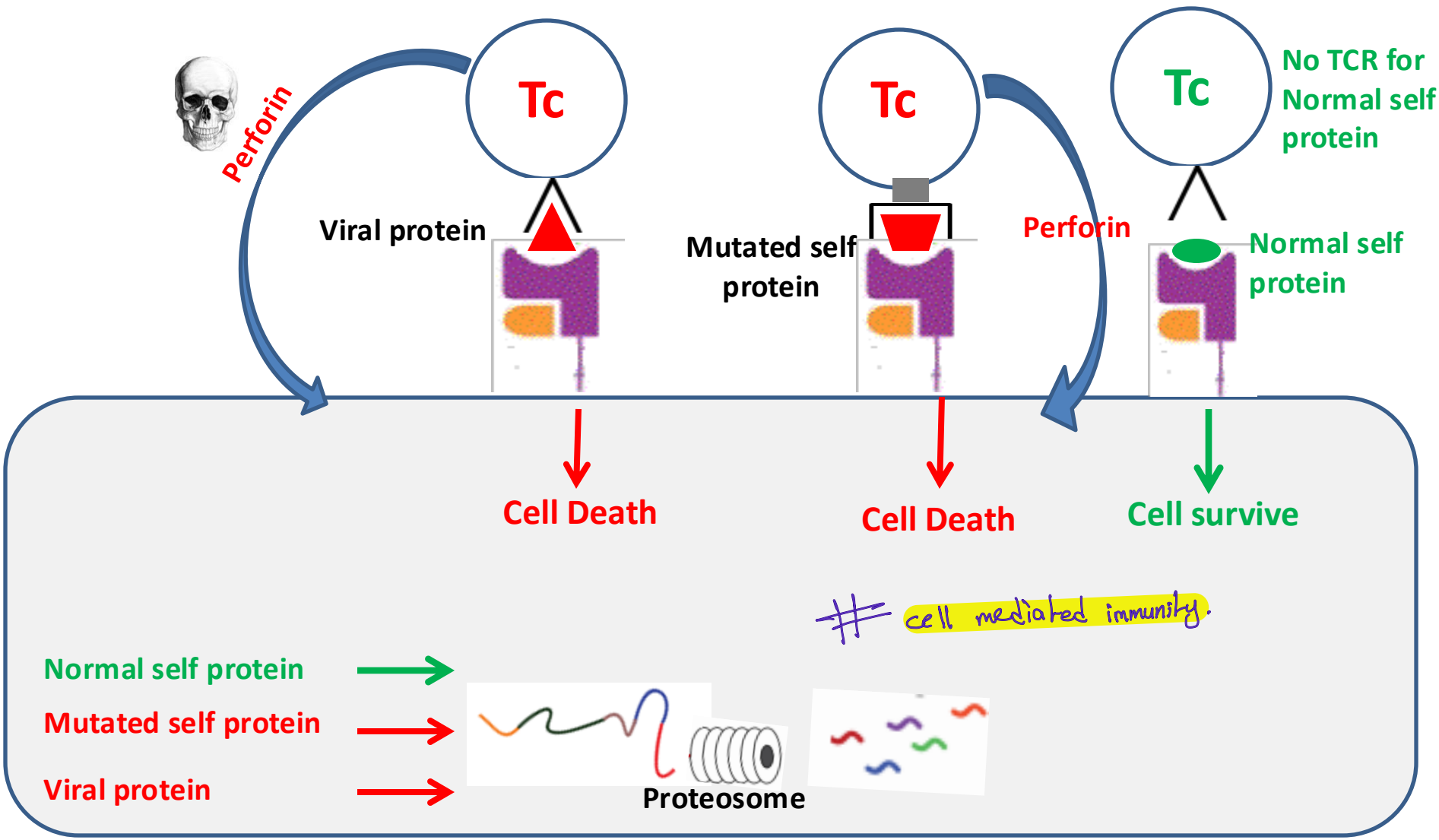
1. **Antigen presentation**



Functions of MHC-I molecules

MHC-I molecules

1. Antigen presentation to CTL to check the normal expression of cellular proteins



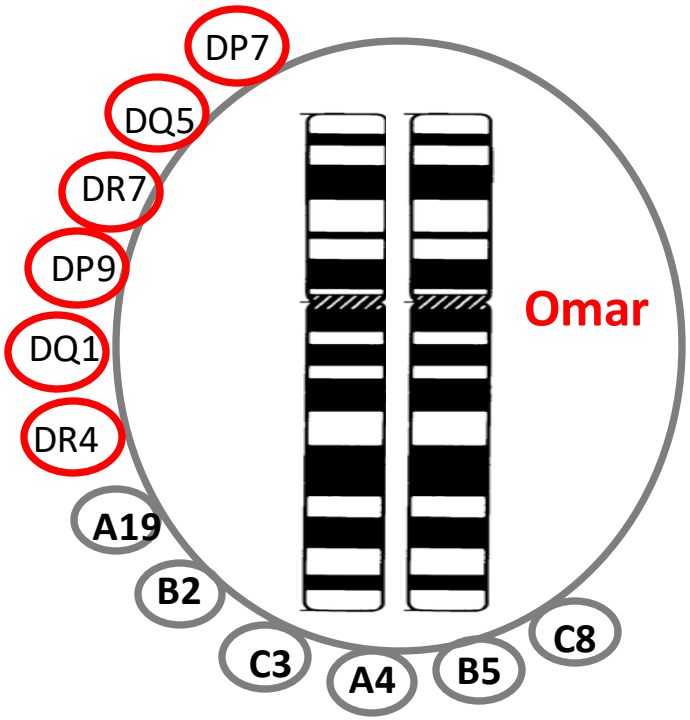
Biological Importance of MHC

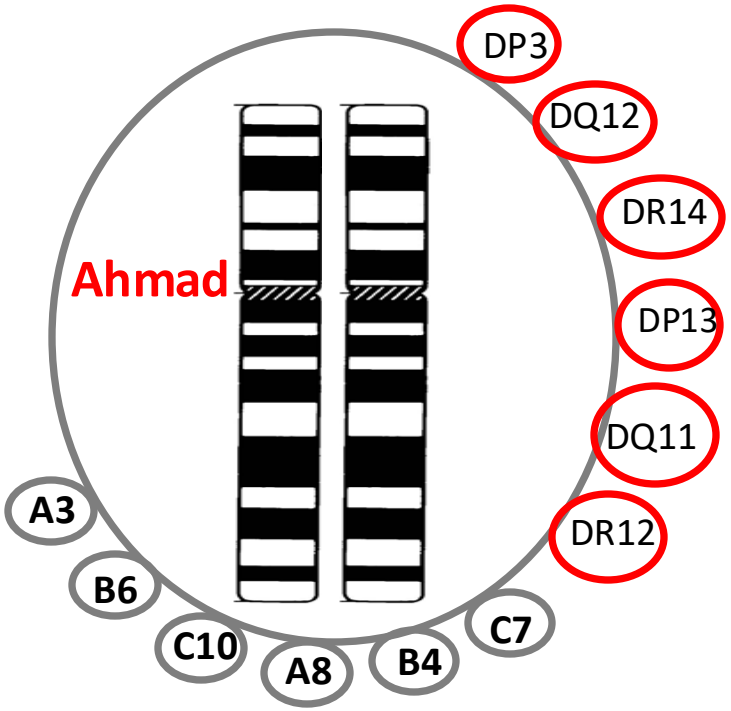
MHC molecules play a major role in three lines

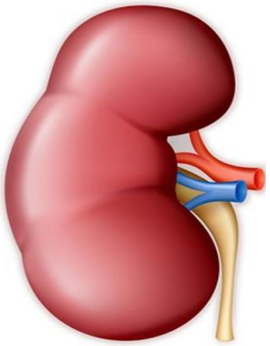
- Antigen presentation
- Autoimmune diseases
  - some MHC, Antigen, protein that have relationship with autoimmune disease
- Transplantation

Functions of MHC molecules

2- Transplantation







Kidney from Omar to Ahmad Will be rejected because of MHC molecules incompatibility

because of difference in MHC. → **Rejected**

Functions of MHC molecules

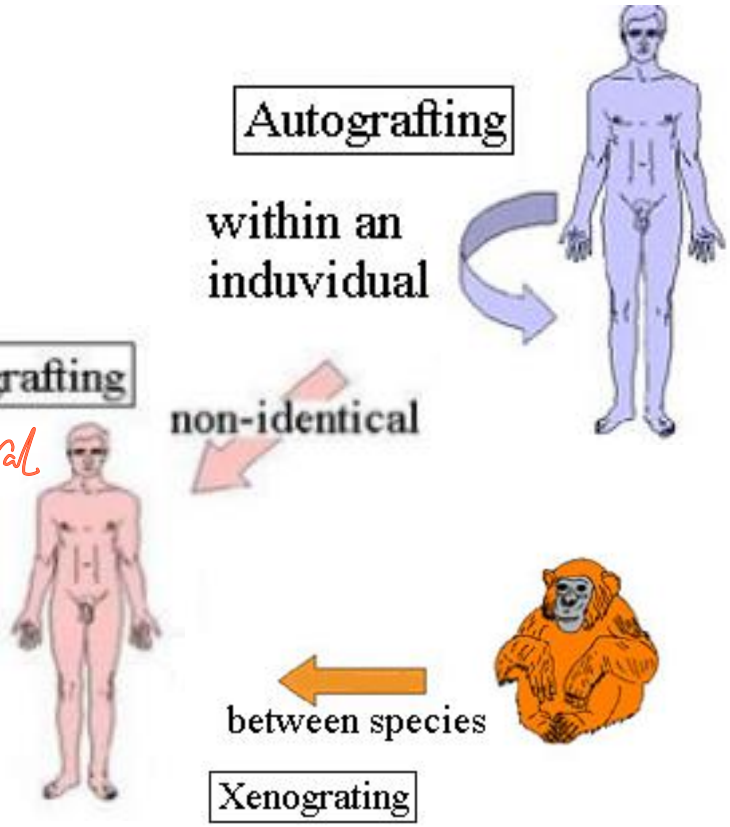
2- Transplantation

Methods of Transplantation:

May take place between:

- different parts of the same organism (autografting)
- different organisms of the sam species (allografting) → from human to human
- different species (xenografting

from animal to human.



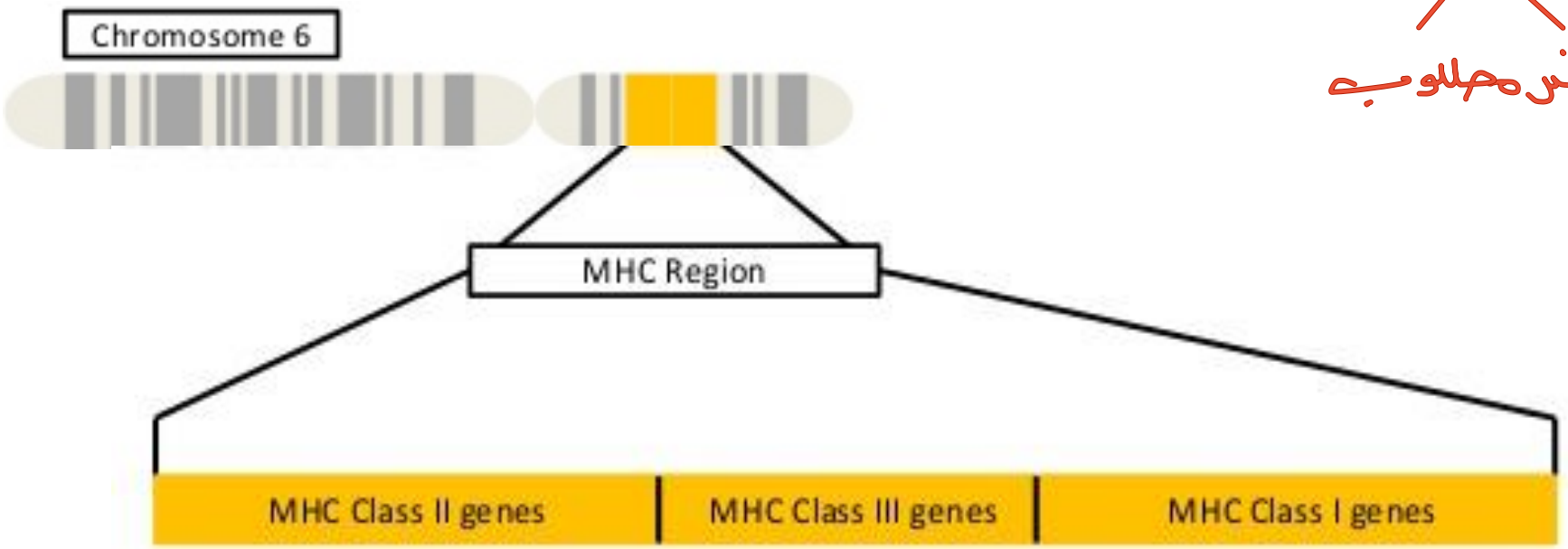
Matching and cross-matching

- Matching: finding a donor who shares the HLA antigens of the recipient, to minimize antigen differences
  - requires donor and recipient antigens to be identified
- Cross-matching: testing the SERUM of the recipient for antibodies against the donor antigens

has antibody against antigens

* we mix the serum from recepient with the doner antigens => if interaction happen => reject
if don't interaction happen => Accept.

MHC and associated diseases

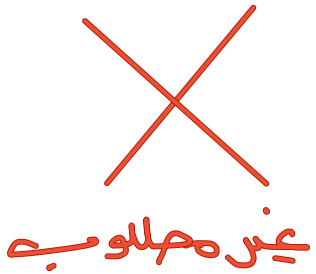


- Multiple Sclerosis
- Psoriasis
- Systemic Lupus
- Asthma
- Childhood Acute Lymphoblastic Leukemia (ALL)
- HIV-related disease
- Thyroid Carcinoma
- Nephropathy
- Kawasaki disease
- Celiac Disease

- Leprosy
- Multiple Sclerosis
- Lymphoid Leukemia
- Rh(D) isoimmunization
- Psoriasis
- Ankylosing spondylitis
- Hemophilia with synovitis
- Malaria
- Susceptibility or Resistance to HIV-1
- Type1 autoimmune hepatitis
- ANCA-positive autoimmune disease

Association of Human MHC Alleles and Risk for Diseases

Disease	Associated HLA Allele	Relative Risk**
Ankylosing Spondylitis*	B27	90
Hereditary Hemochromatosis	A3/B14	90
Insulin Dependent Diabetes*	DR4/DR3	20
Multiple Sclerosis*	DR2	5
Myasthenia Gravis*	DR3	10
Rheumatoid Arthritis*	DR4	10
Systemic Lupus Erythromatosis*	DR3	5
Narcolepsy	DR2	130



* Autoimmune Disease

**Percent of Patients with Allele Divided by Percent of Non-Affected Persons with this Allele