Immunology

Innate, Adaptive, MHC

Lecture 7

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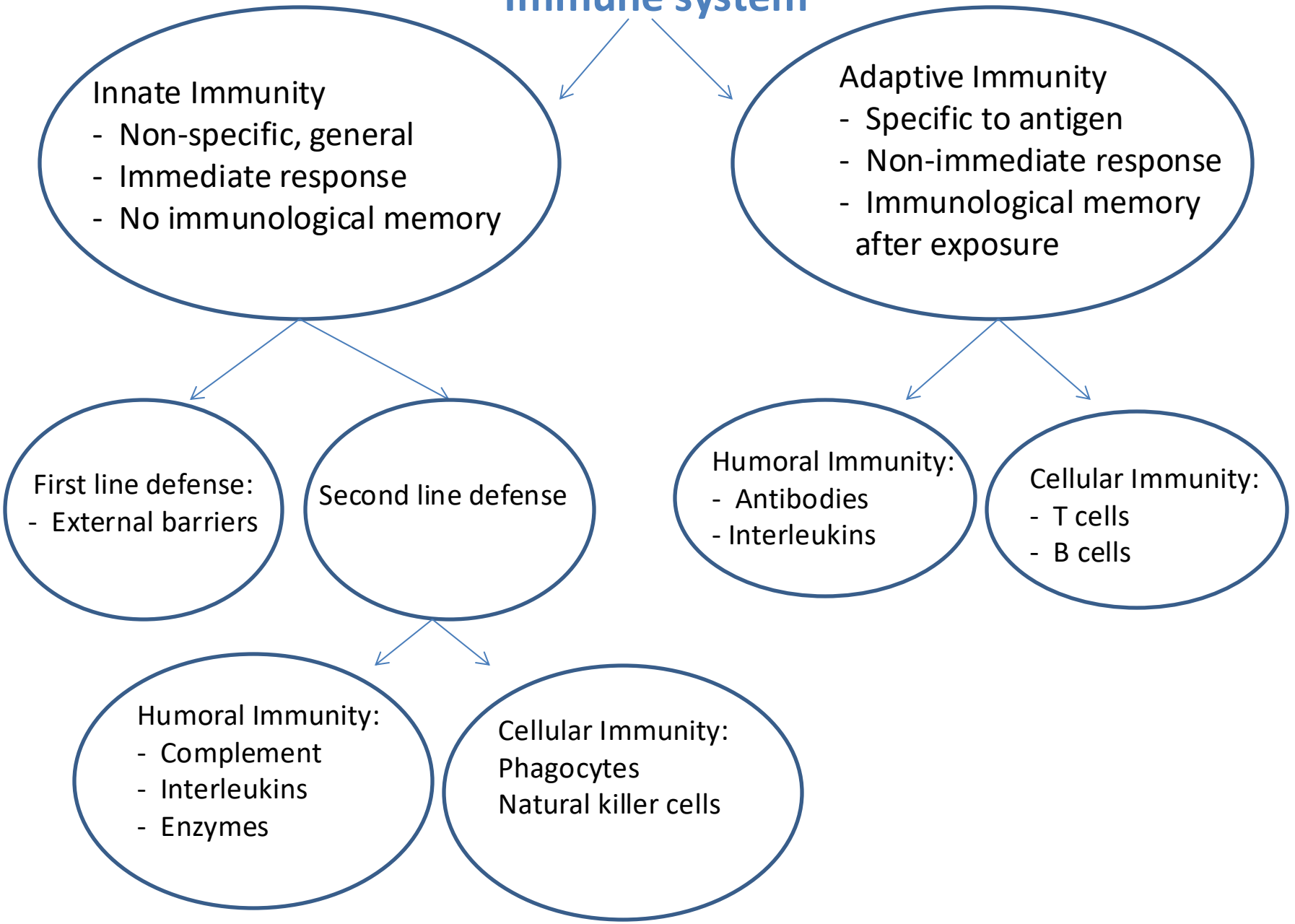
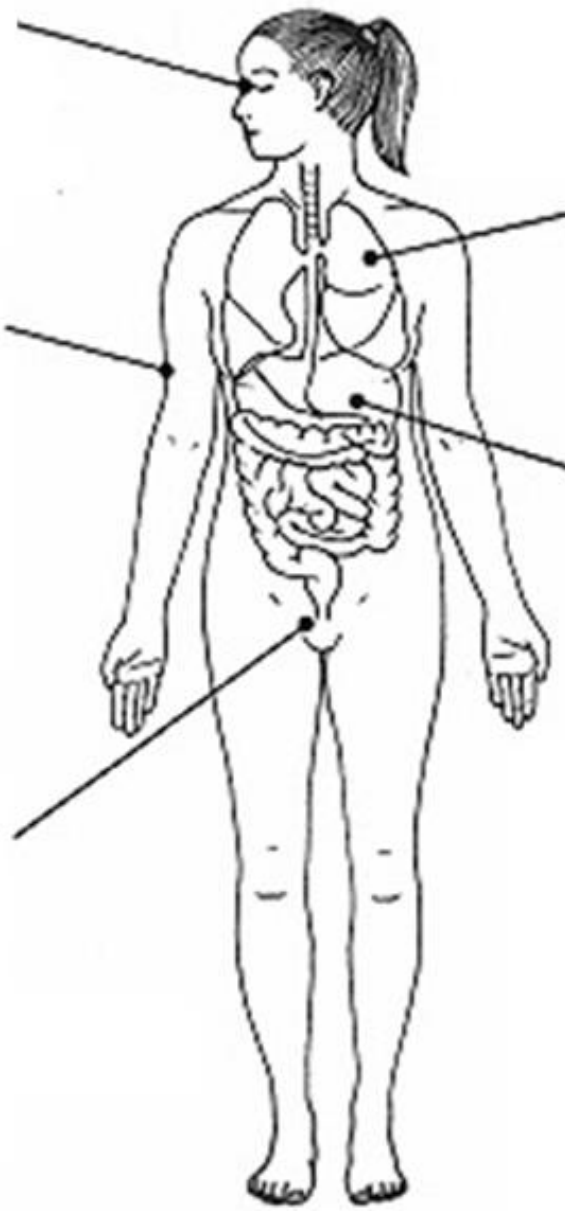
Introduction

Immune system



Innate immunity



Eye
Blinking
Tears
Lysozyme

Skin
Structural Barrier
sweat sebum
Lactic acid
Propionic acid
Lysozyme
Normal Flora

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

Respiratory Tract
Coughing Sneezing
Mucus
Cilliary action
Phagocytes
Lysozyme

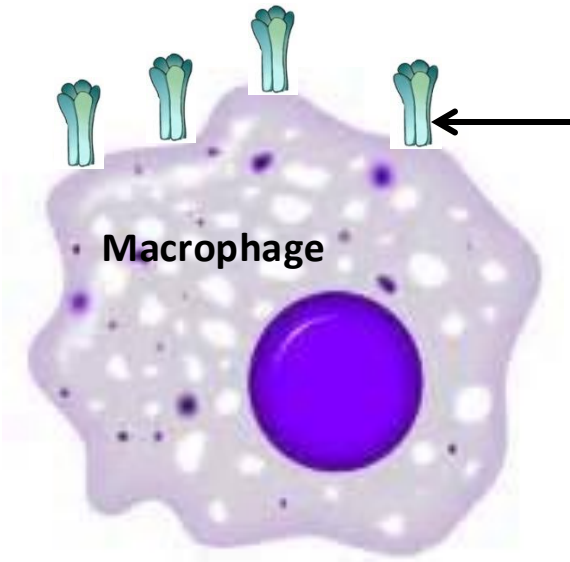
GI tract
Stomach acidity
Normal Flora
Peristaltis
Antimicrobial
compounds

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

Innate immunity

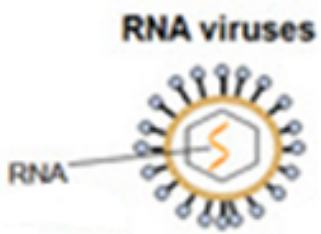
Stages Phagocytosis:

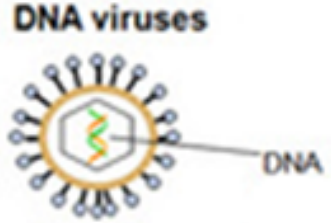
1. Recognition and attachment of microbes by phagocytes

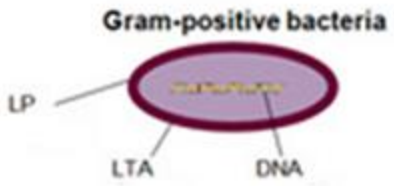


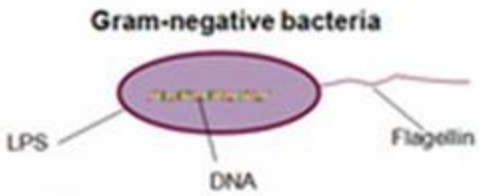
Toll like receptor (TLR)

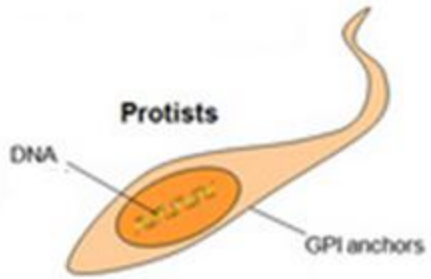
TLR recogizes pathogen associated molecular pattern

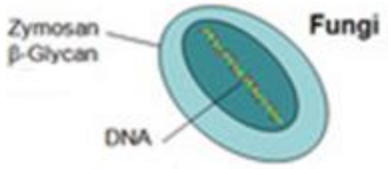












Adaptive Immunity

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

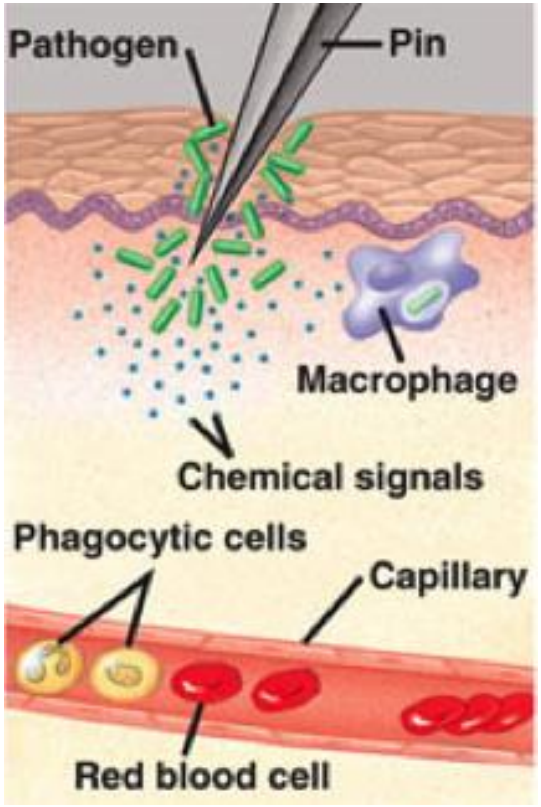
Complement

Defensins

Lysozymes

Vasodilatation

Mast cells



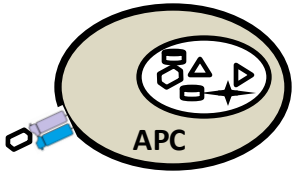
Antigens

Chemical signals

Neutrophils

Macrophages

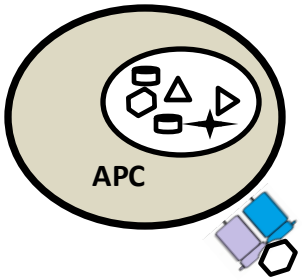
Dendritic cells

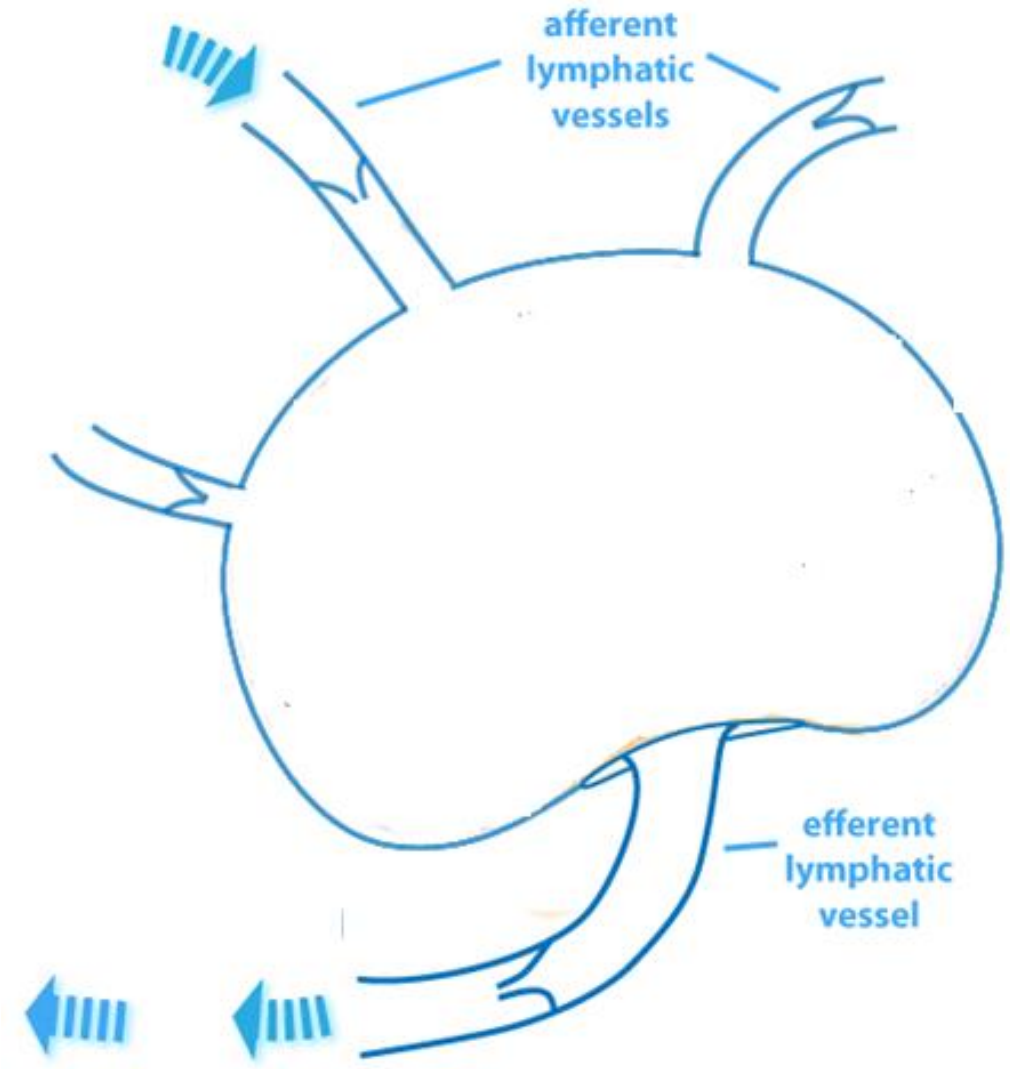


The initial step in triggering adaptive immunity

To the secondary lymphoid organs

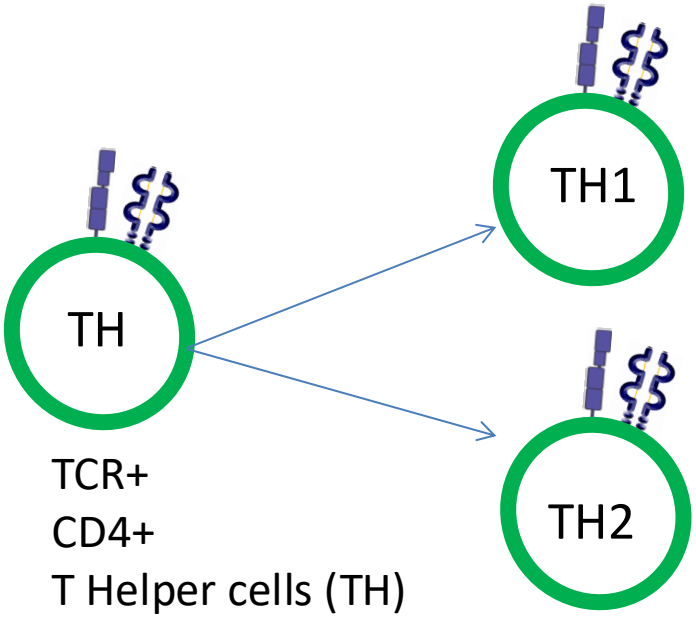
Adaptive Immunity



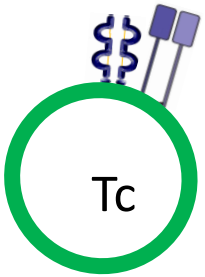


What will happen inside the lymph node?

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)

TH2

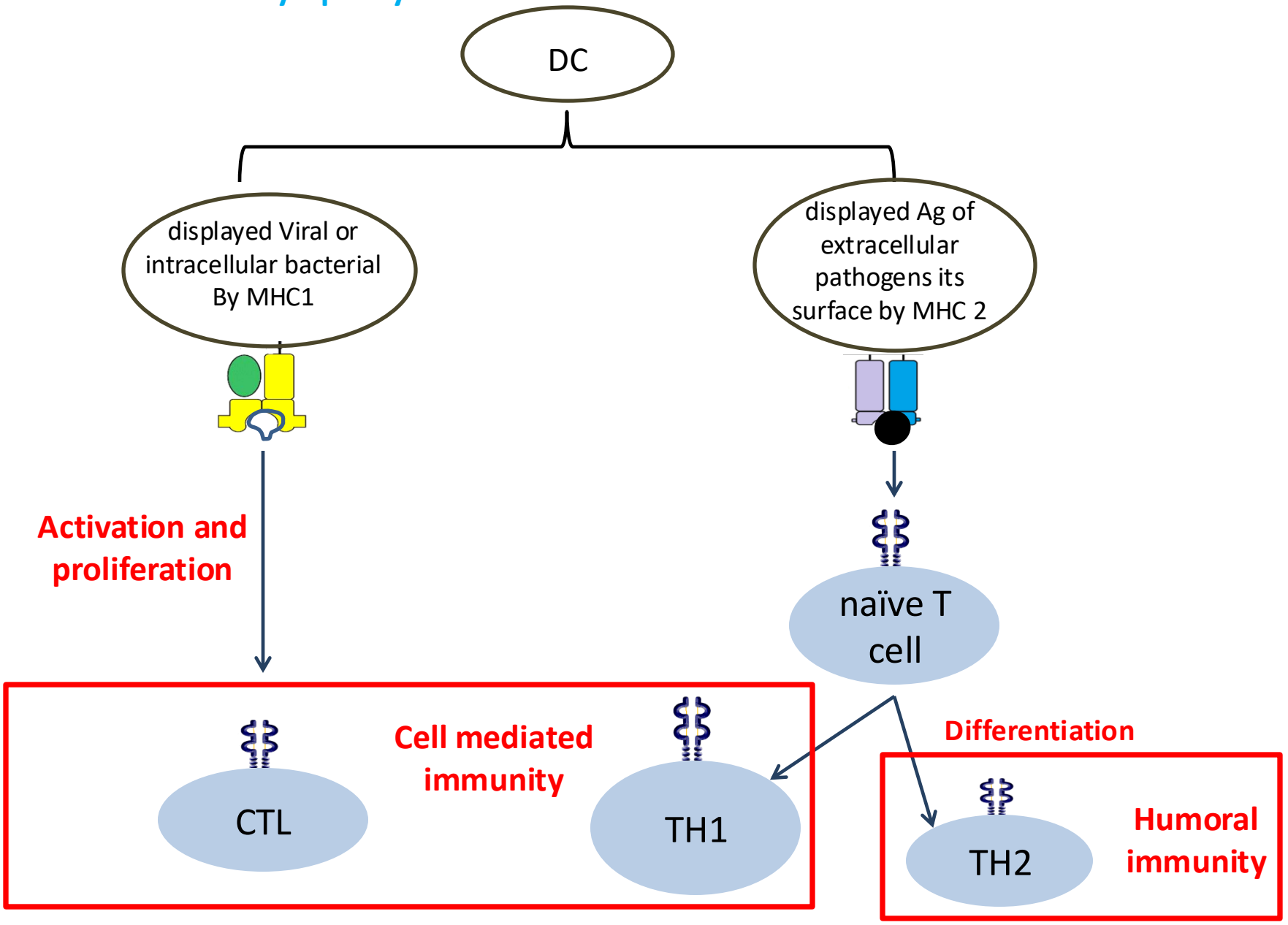
Activation of B lymphocytes

Cell mediated immunity

Humoral immunity

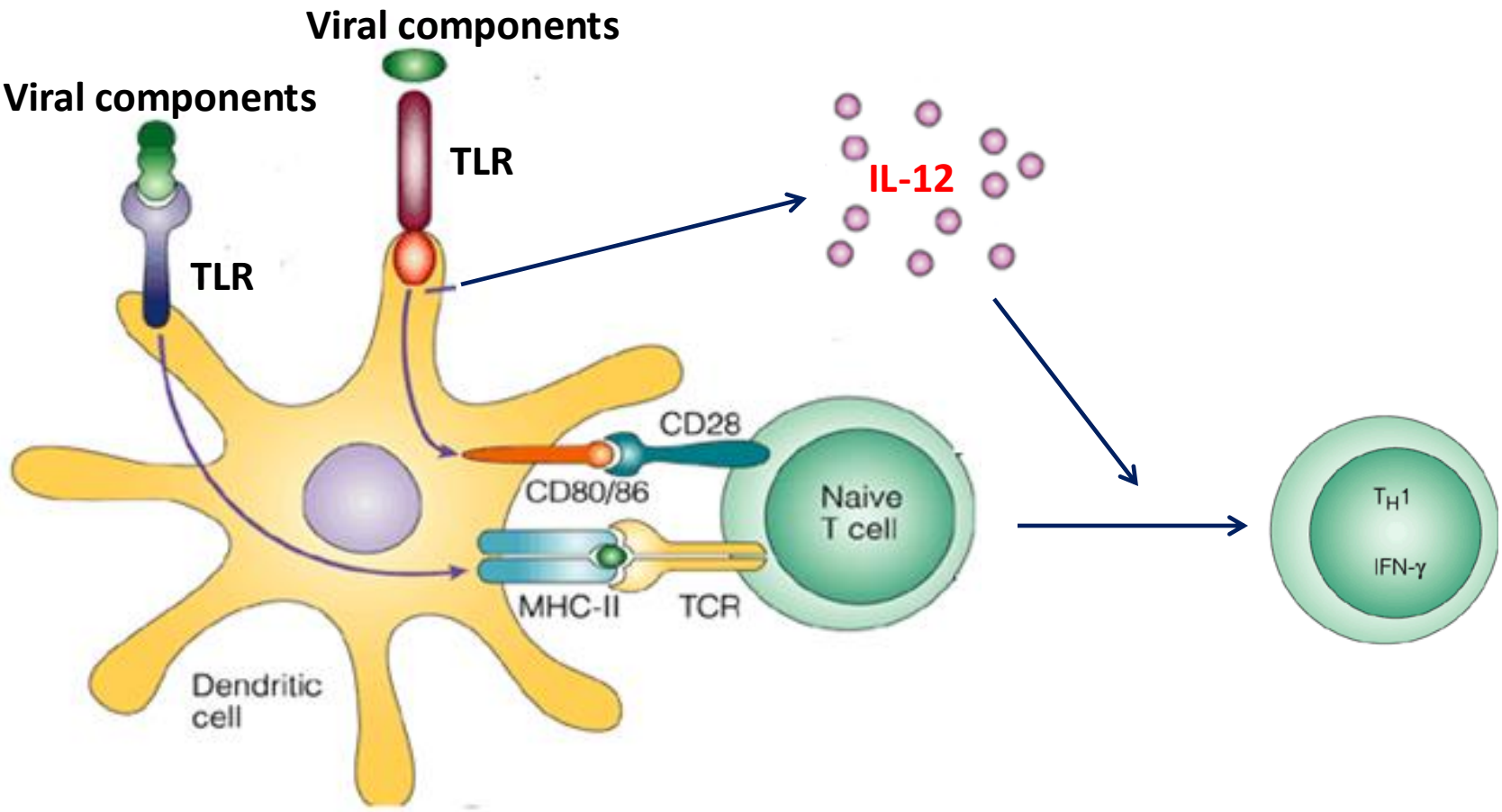
Adaptive Immunity

Activation of naïve T lymphocytes



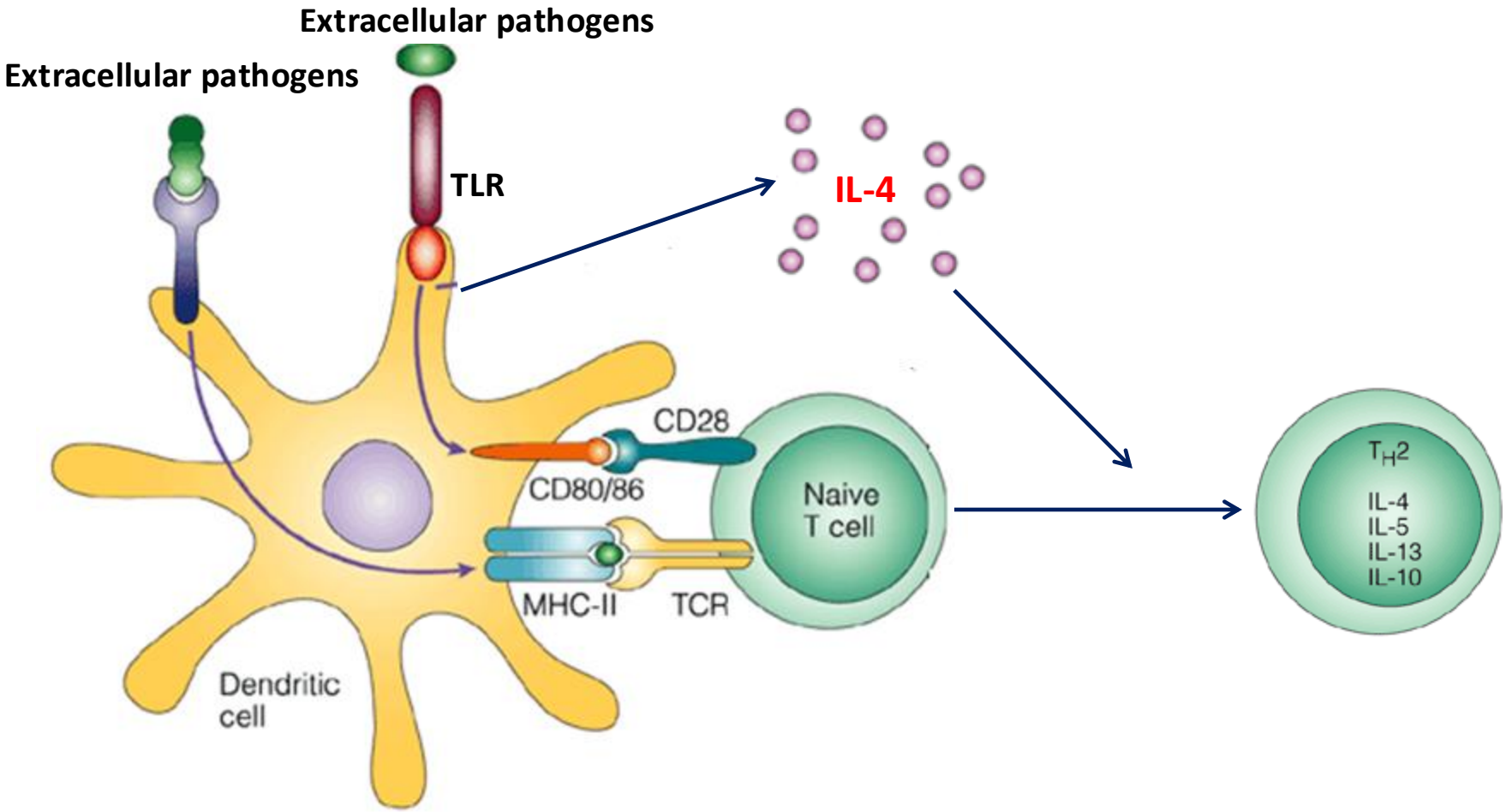
Adaptive Immunity

What determines the naïve T cell differentiation into Th1?



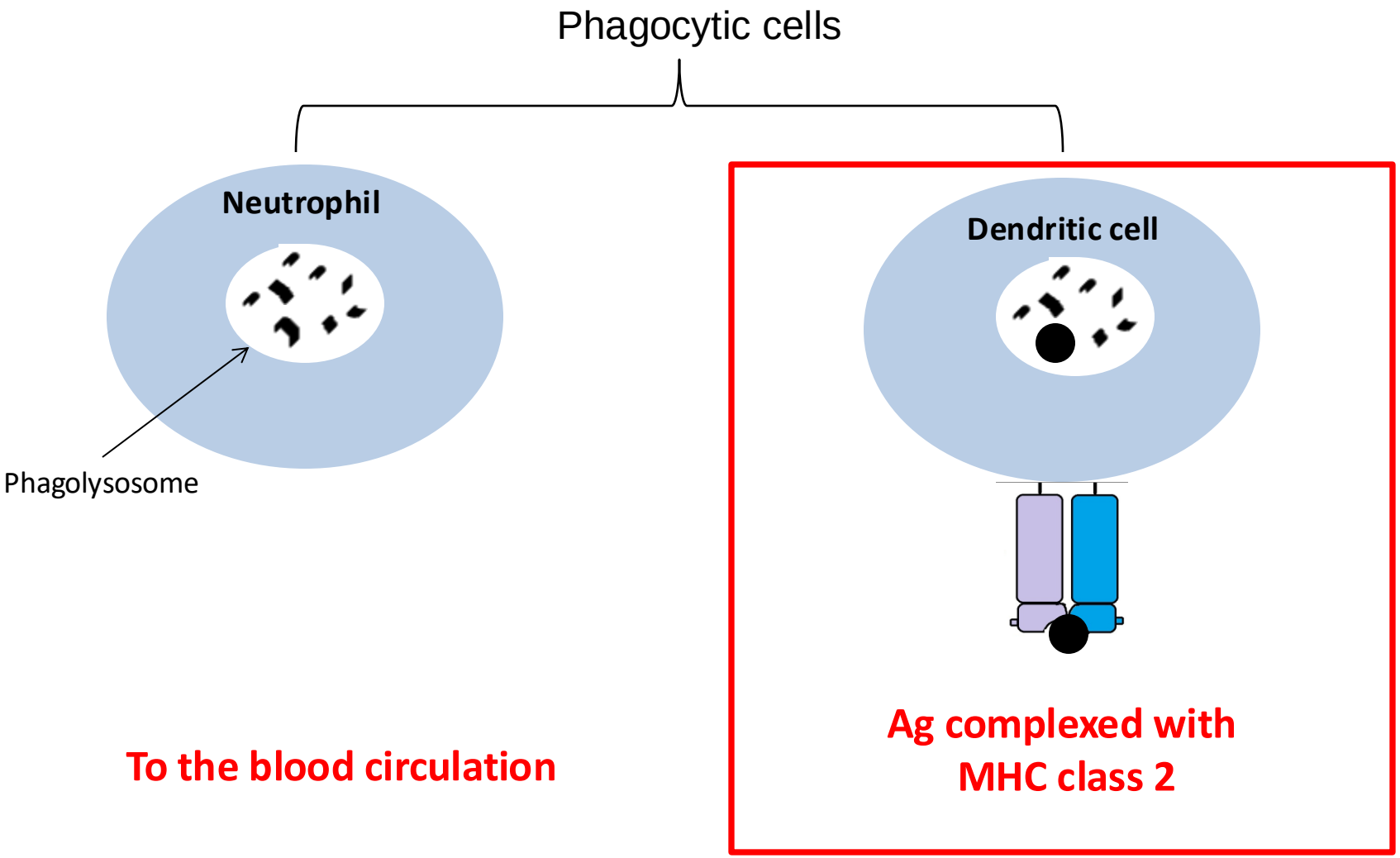
Adaptive Immunity

What determines the naïve T cell differentiation into Th2?



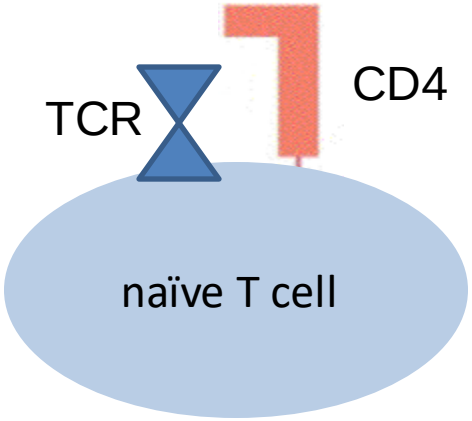
Humoral Arm of Adaptive Immunity

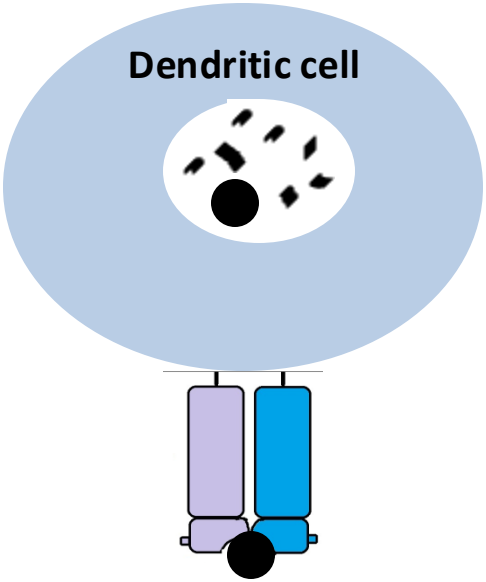
Humoral Immunity

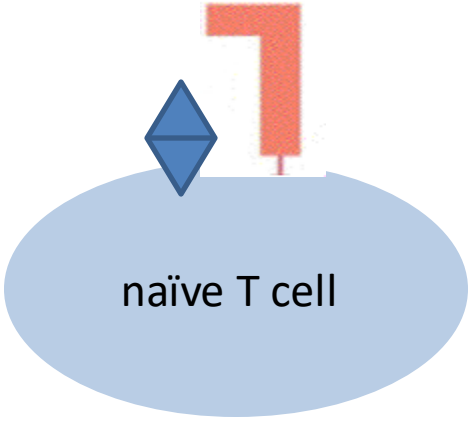


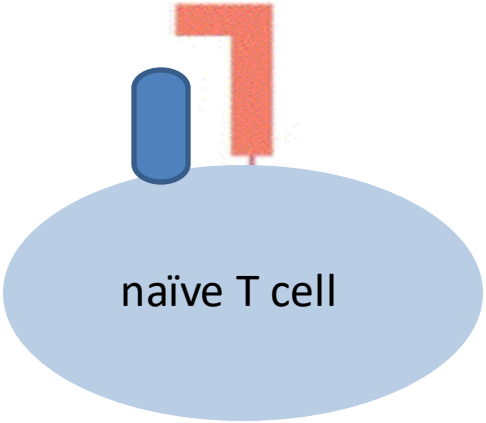
Humoral Immunity

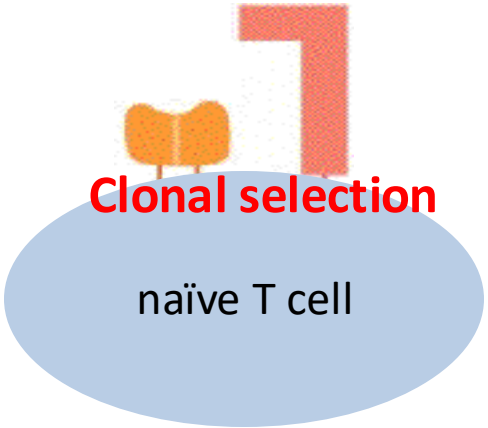
In the lymph node, dendritic cell Start presenting Ag to naïve T cells until Finding one T cell with specific TCR For the displayed Ag





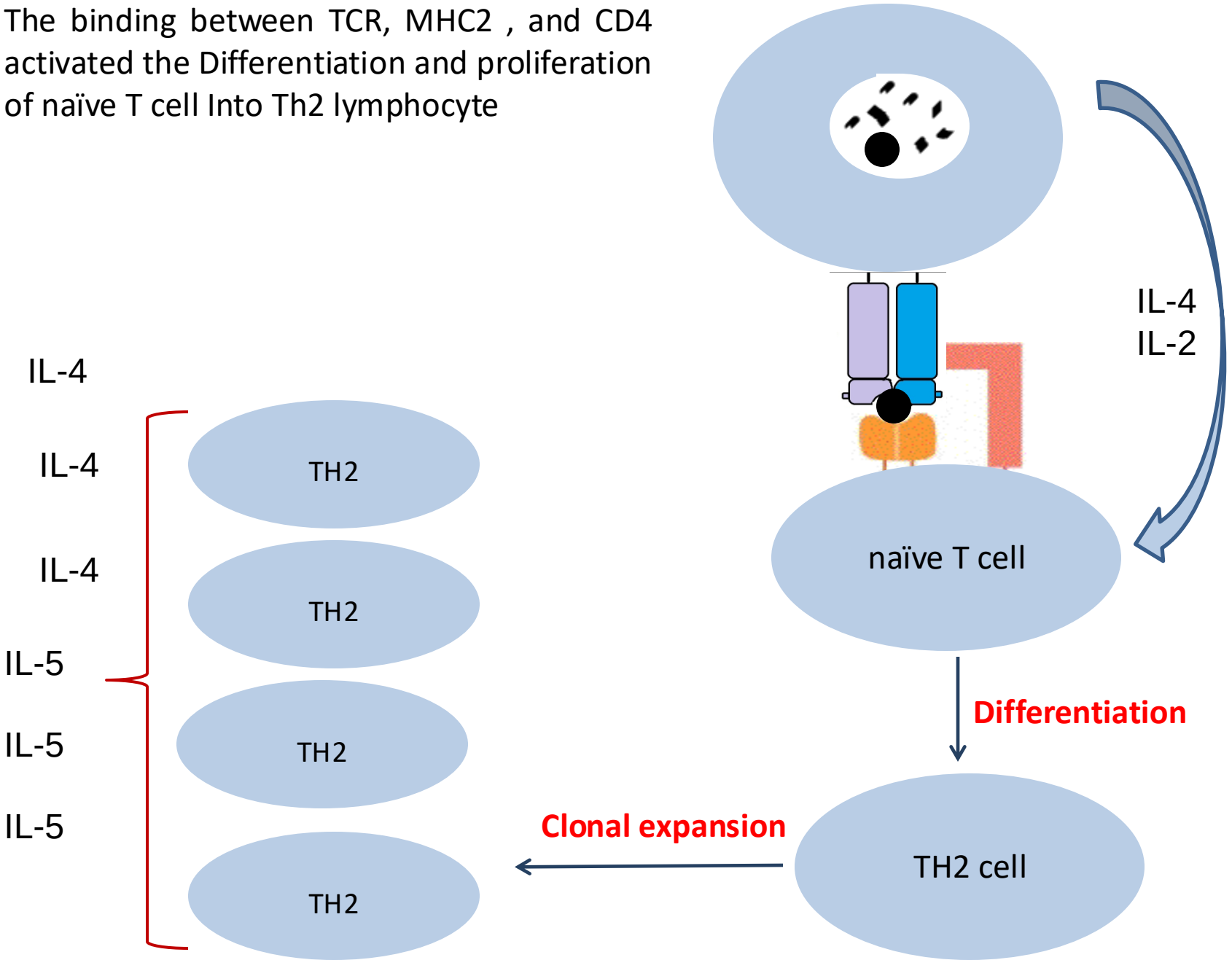




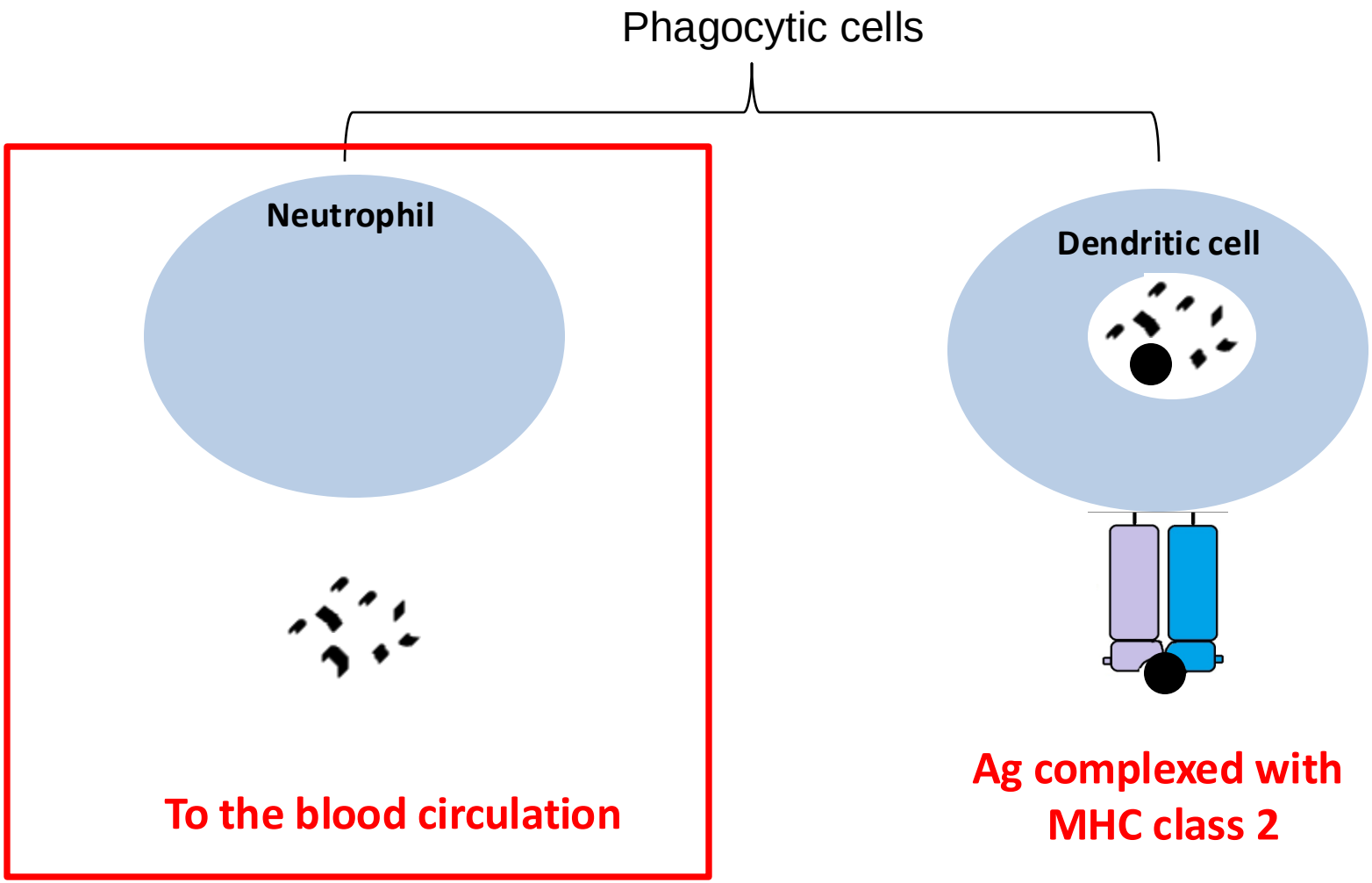


Humoral Immunity

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

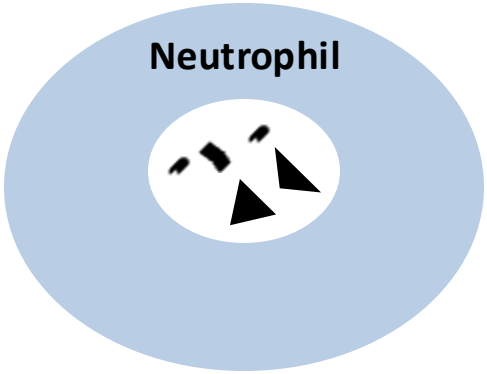


Humoral Immunity

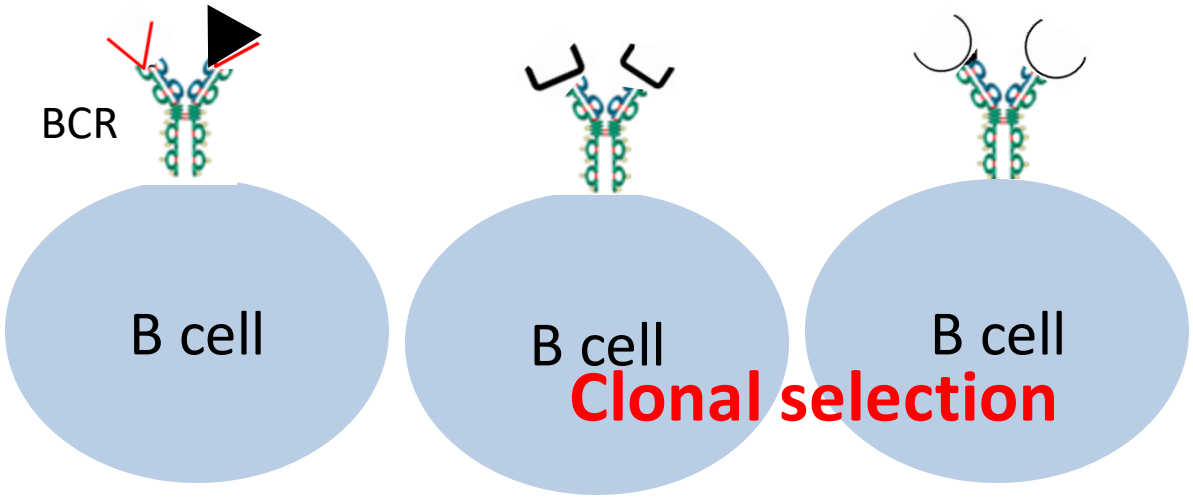


Humoral Immunity

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

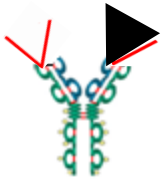


Reaching lymph node via lymph

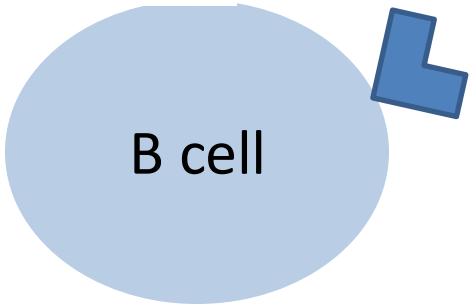


Humoral Immunity

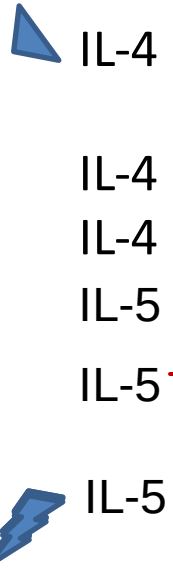
Antigen binding to the BCR will activate the IL-4R gene expression

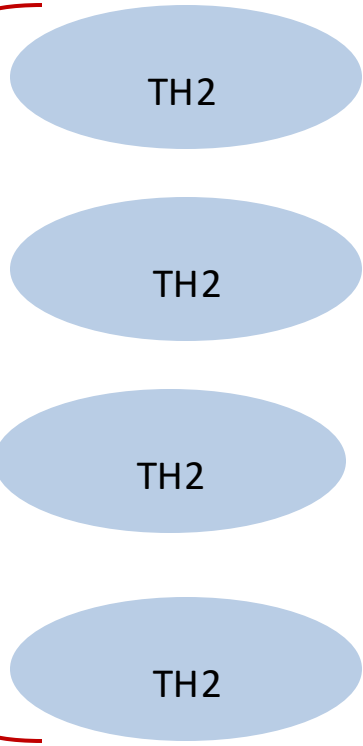


IL-4R

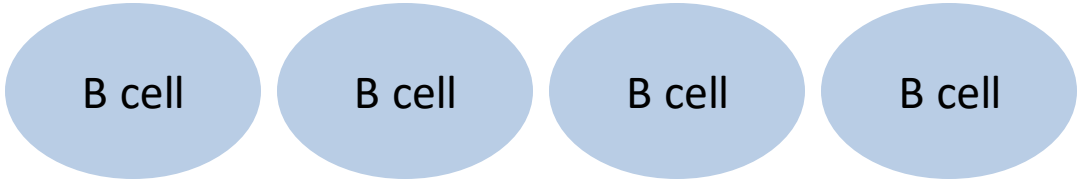


IL-4 will activate B cell proliferation

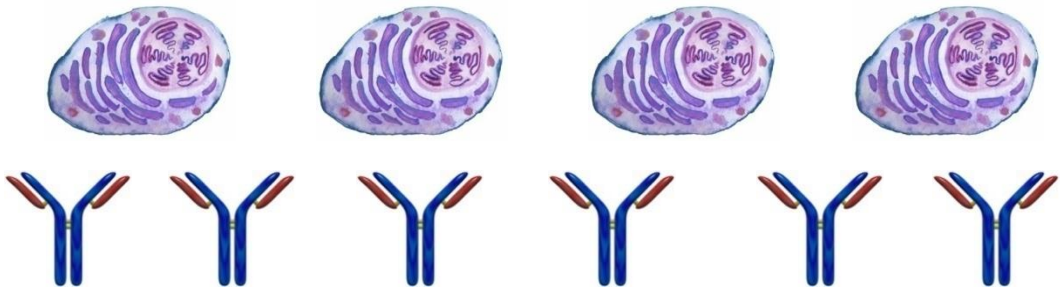




Clonal expansion

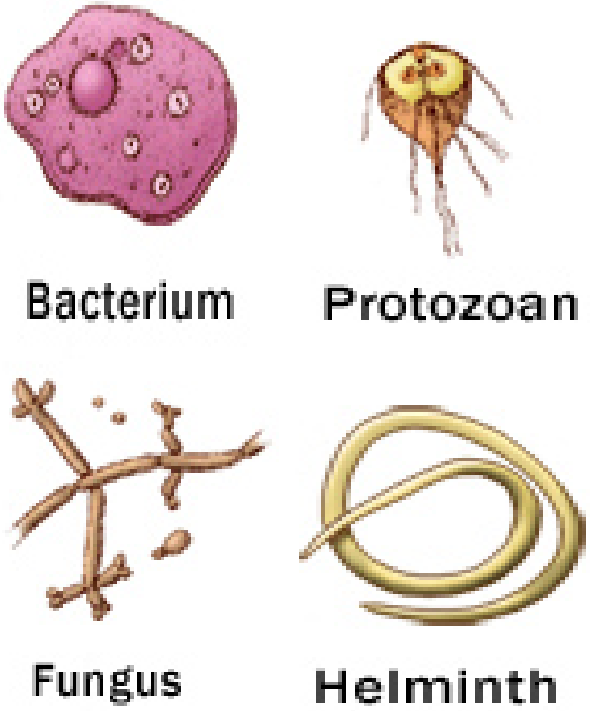


IL-5 will activate B cell differentiation into plasma cells



Cellular immunity vs. Humoral immunity

Extracellular pathogens

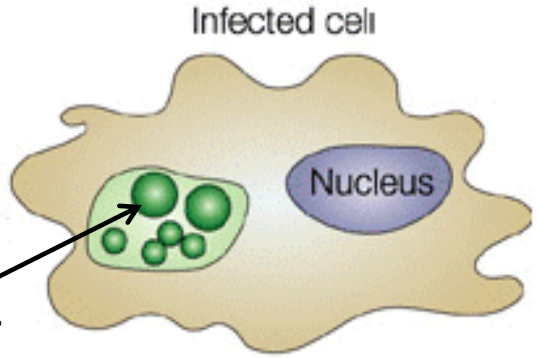


The body can defend itself against the extracellular pathogens by **complement, antibodies**

↓

Humoral immunity

Intracellular pathogens



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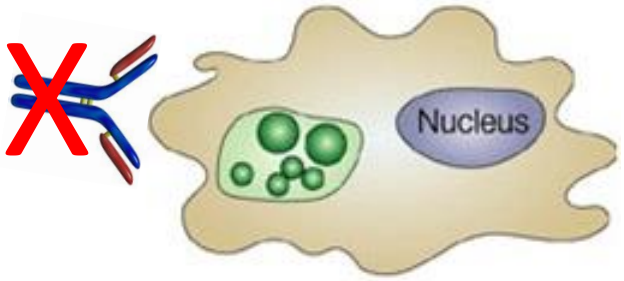
Complement & antibodies are ineffective in fighting intracellular pathogens



↓

Cellular immunity is activated

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

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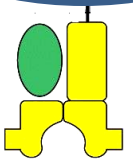
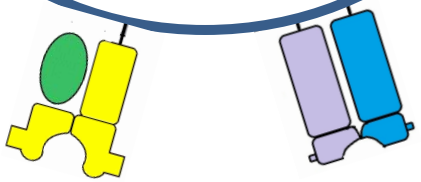
dependent the secretion by T cells of cytokines that enhance the ability of phagocytes to eliminate the phagocytized pathogens

All nucleated ells can express MHC1

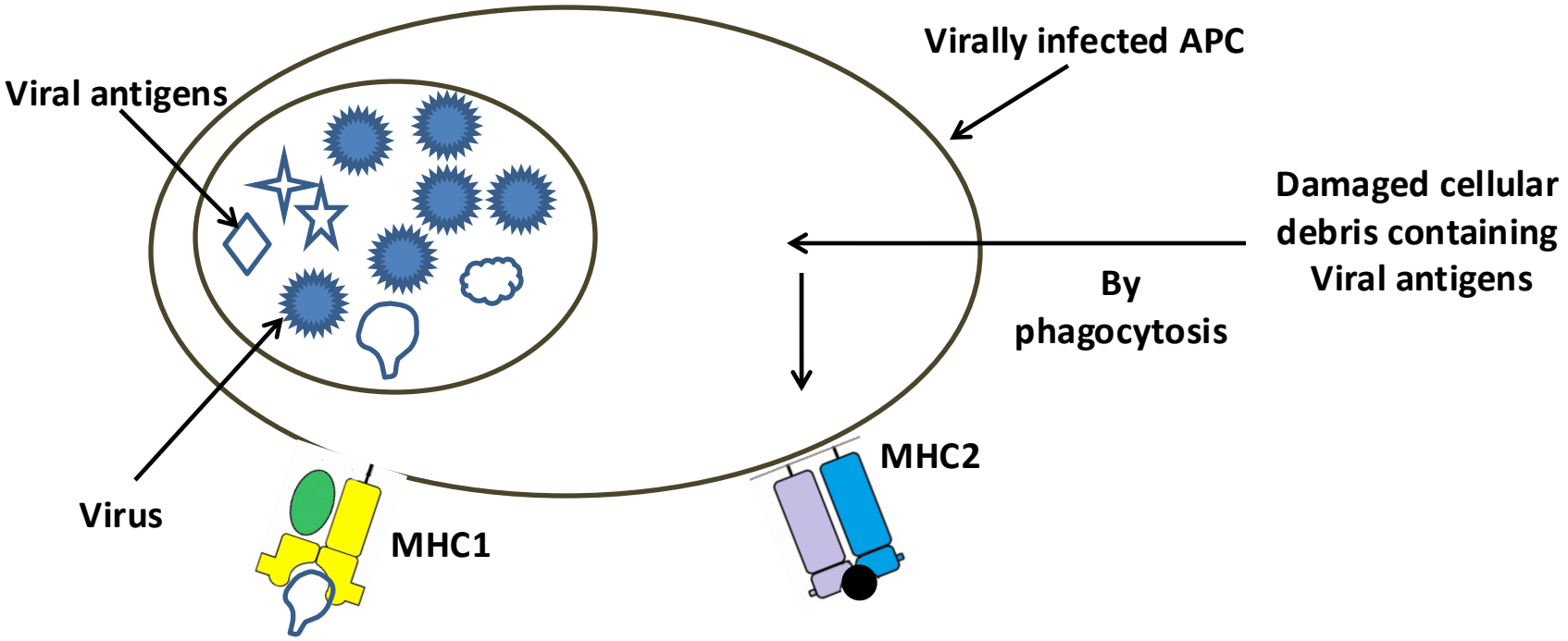


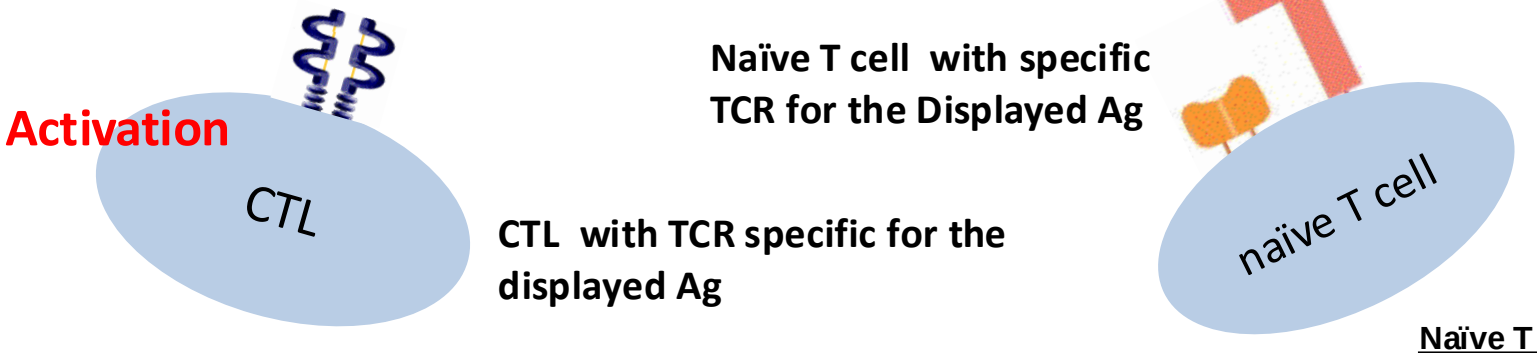
APC can express both MHC1 & MHC2



Cellular immunity

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

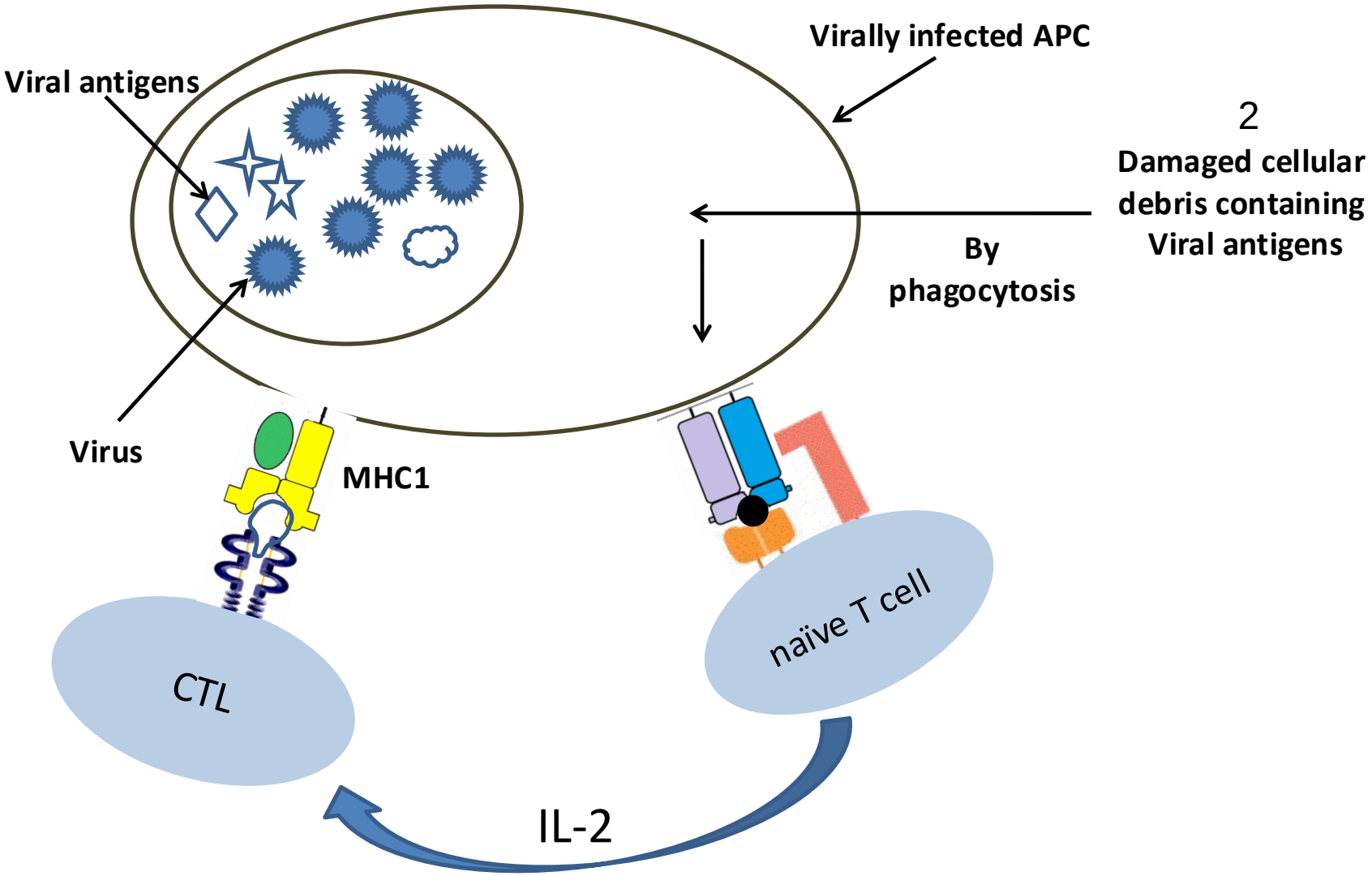




Naïve T cell matures into TH1

Cellular immunity

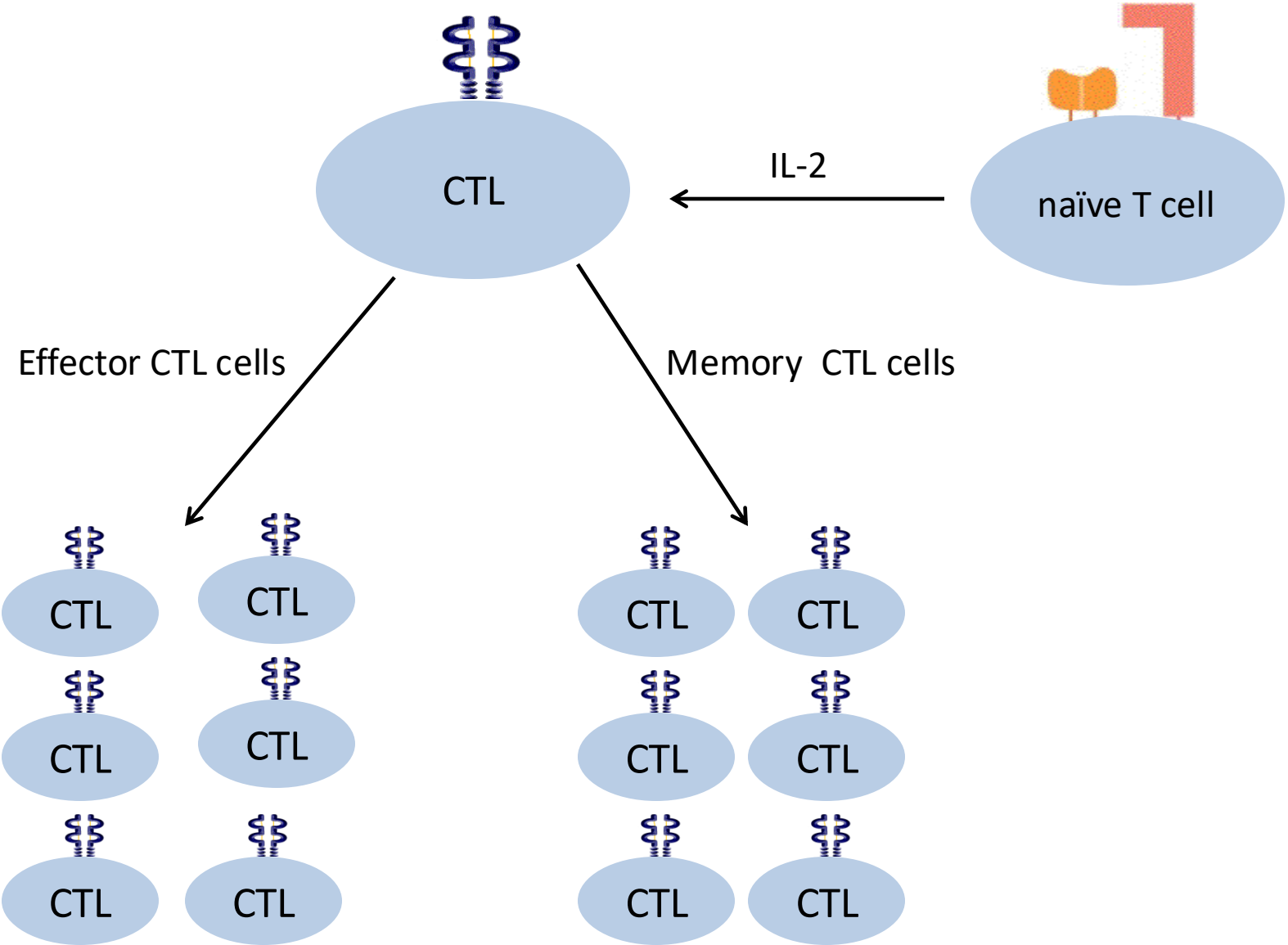
CD8⁺ cytotoxic T lymphocytes (CTLs) mediated cell lysis



Proliferation and differentiation

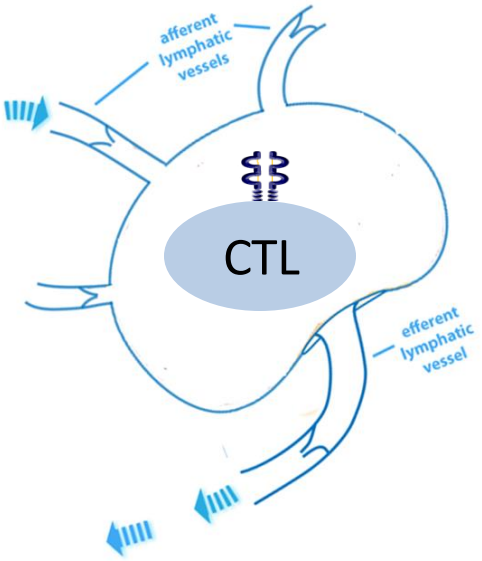
Cellular immunity

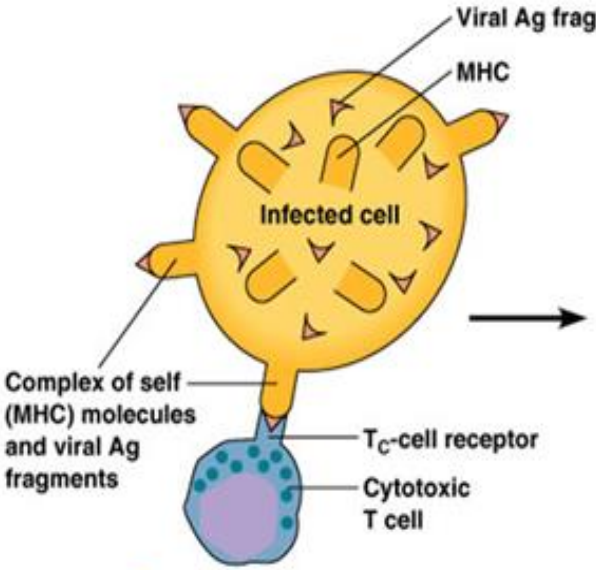
CD8$^+$ cytotoxic T lymphocytes (CTLs) mediated cell lysis

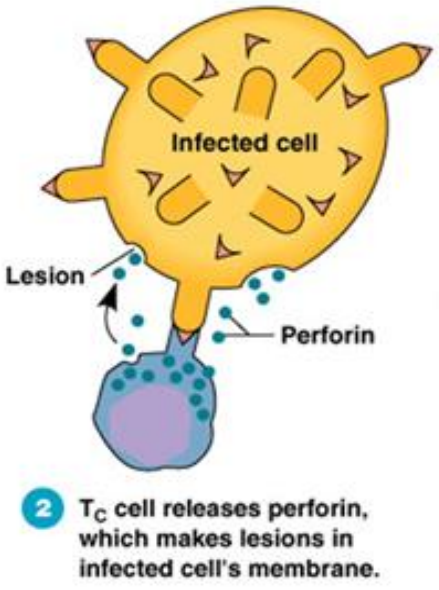


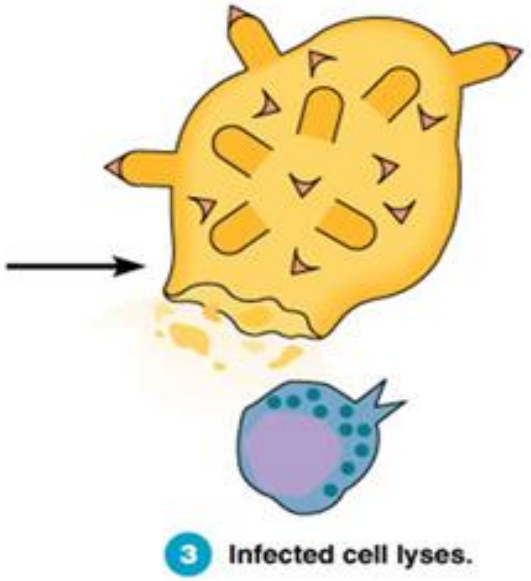
Cellular immunity

CTLs mediate cell lysis of virally infected cells









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)

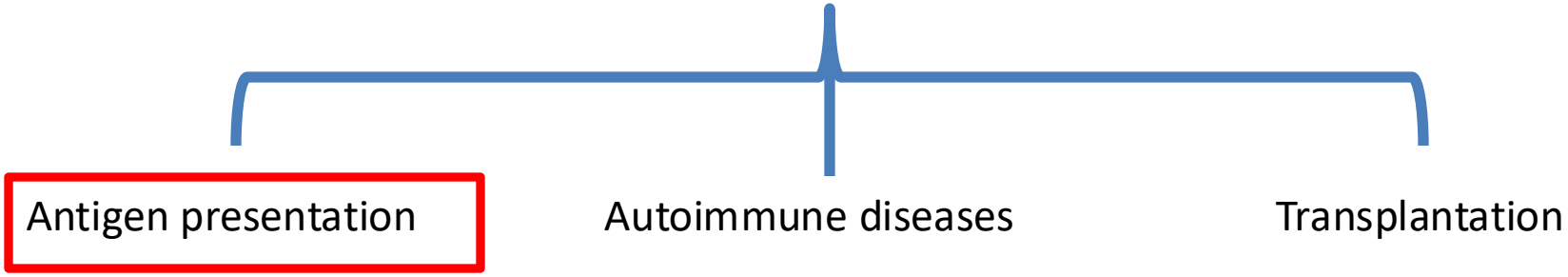
Major Histocompatibility Complex

Introduction

Definition of the MHC

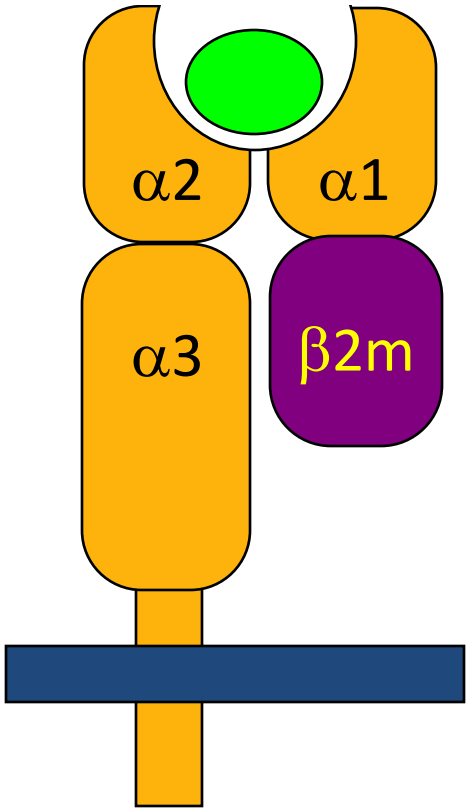
Is a set of cell surface molecules encoded by a large gene family which controls a major part of the immune system in all vertebrates

MHC molecules play a major role in three lines



Class I MHC Molecule

Overall structure of MHC class I molecules



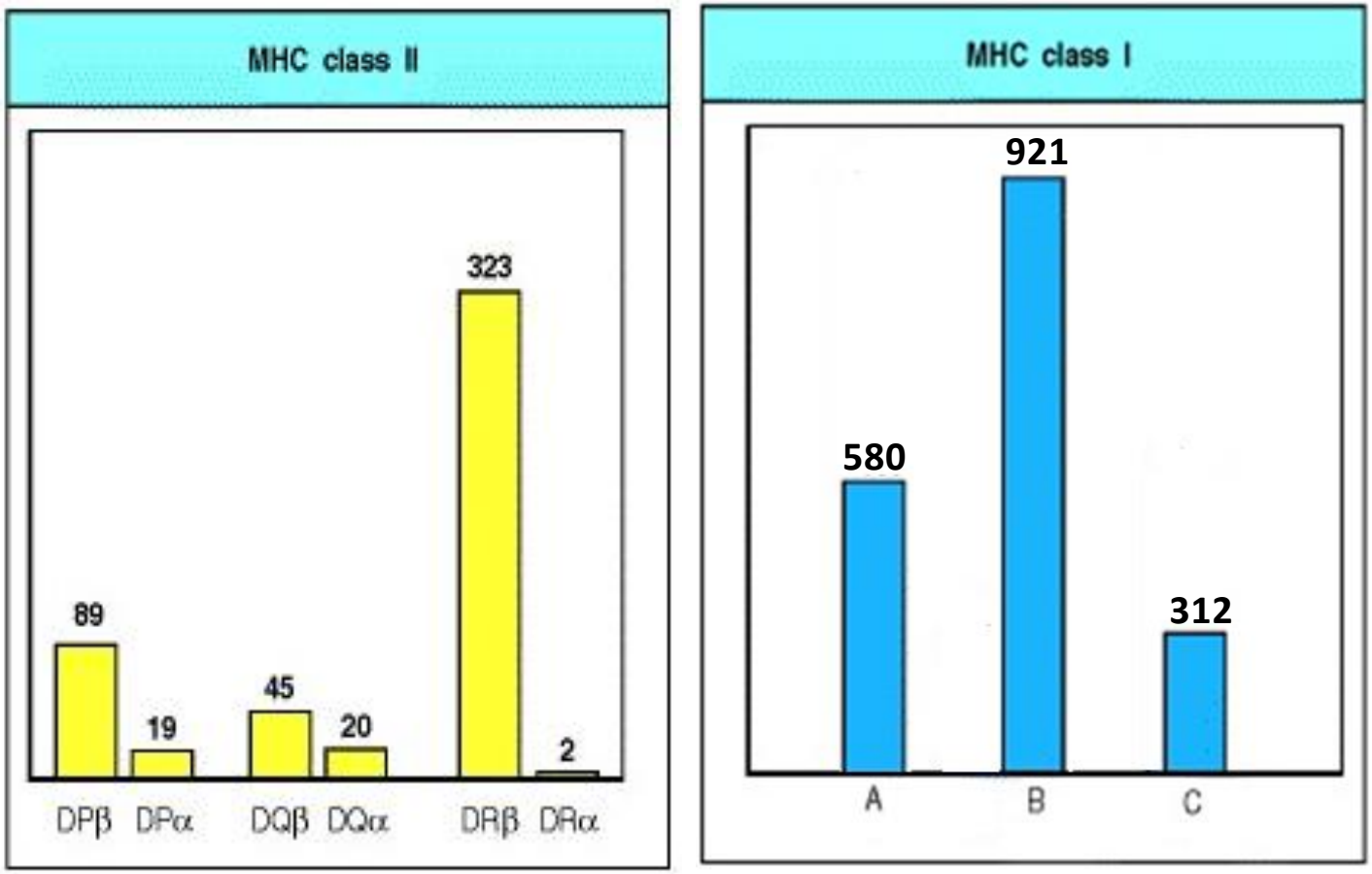
MHC-encoded α-chain of 43kDa

α-chain anchored to the cell membrane

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

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

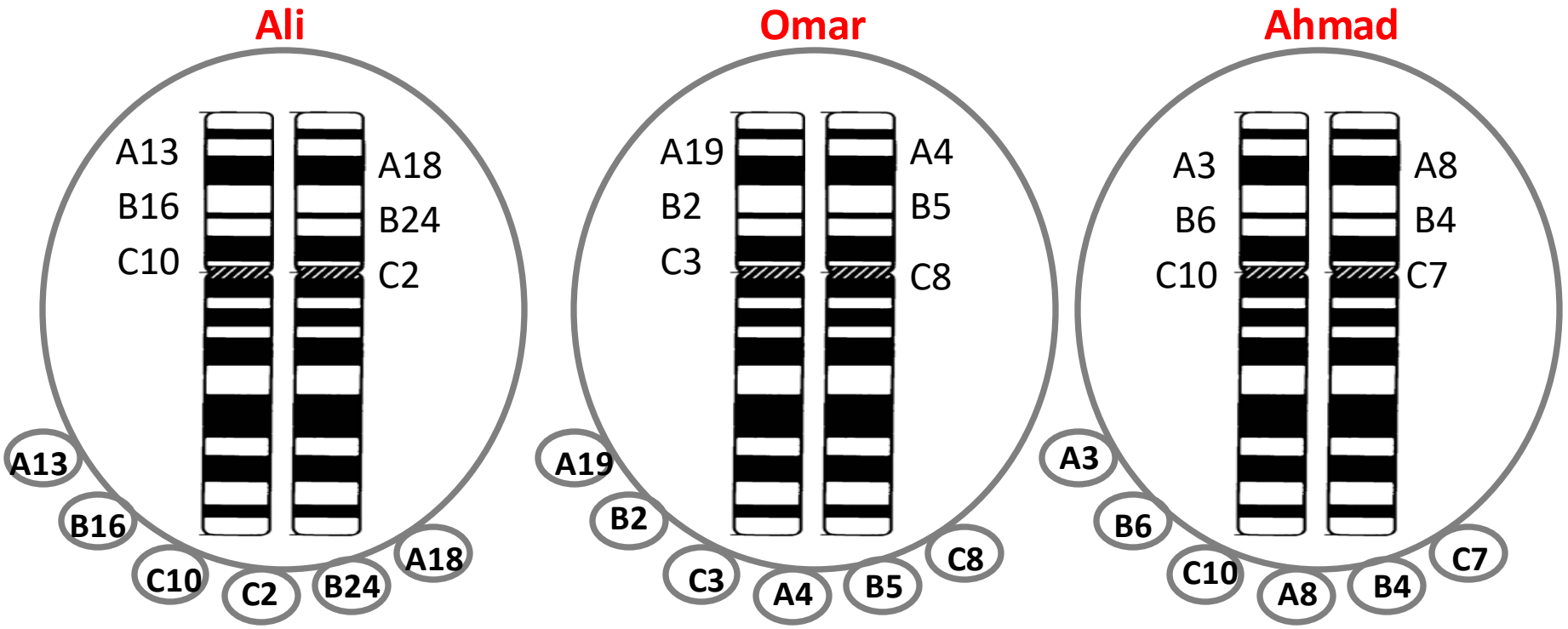
Human MHC Class 1 and 2 genes are highly polymorphic



- 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

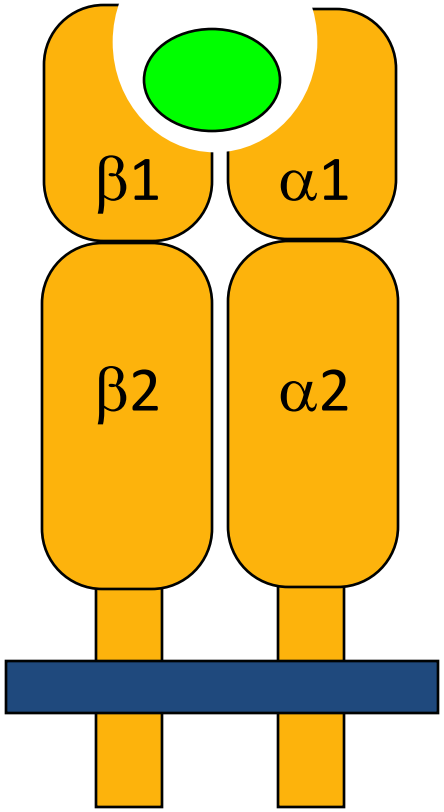
MHC-I

Inheritance of MHC-I



MHC-II

Overall structure of MHC class II molecules



MHC-encoded, α-chain and a β-chain

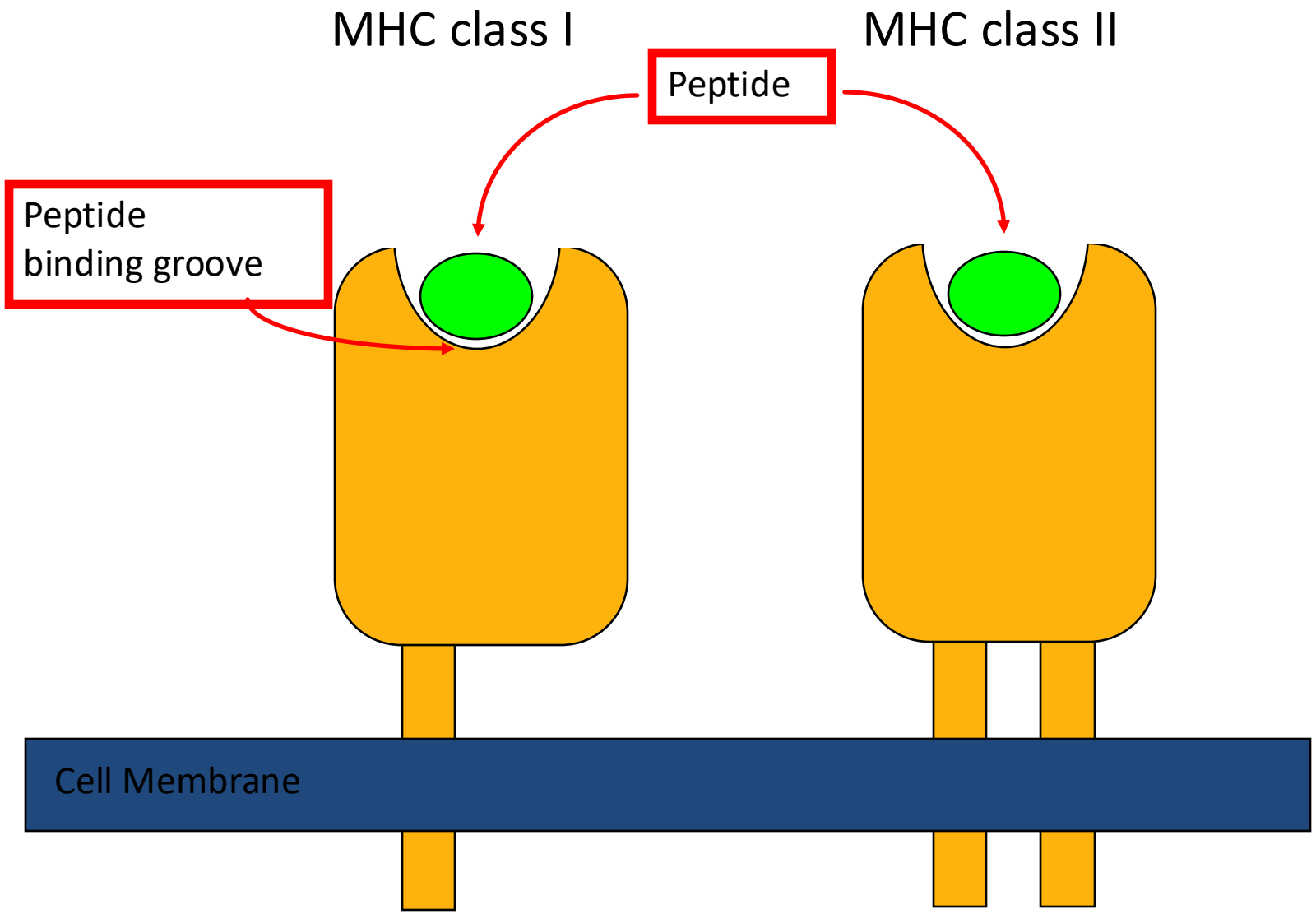
α and β chains anchored to the cell membrane

No β-2 microglobulin

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

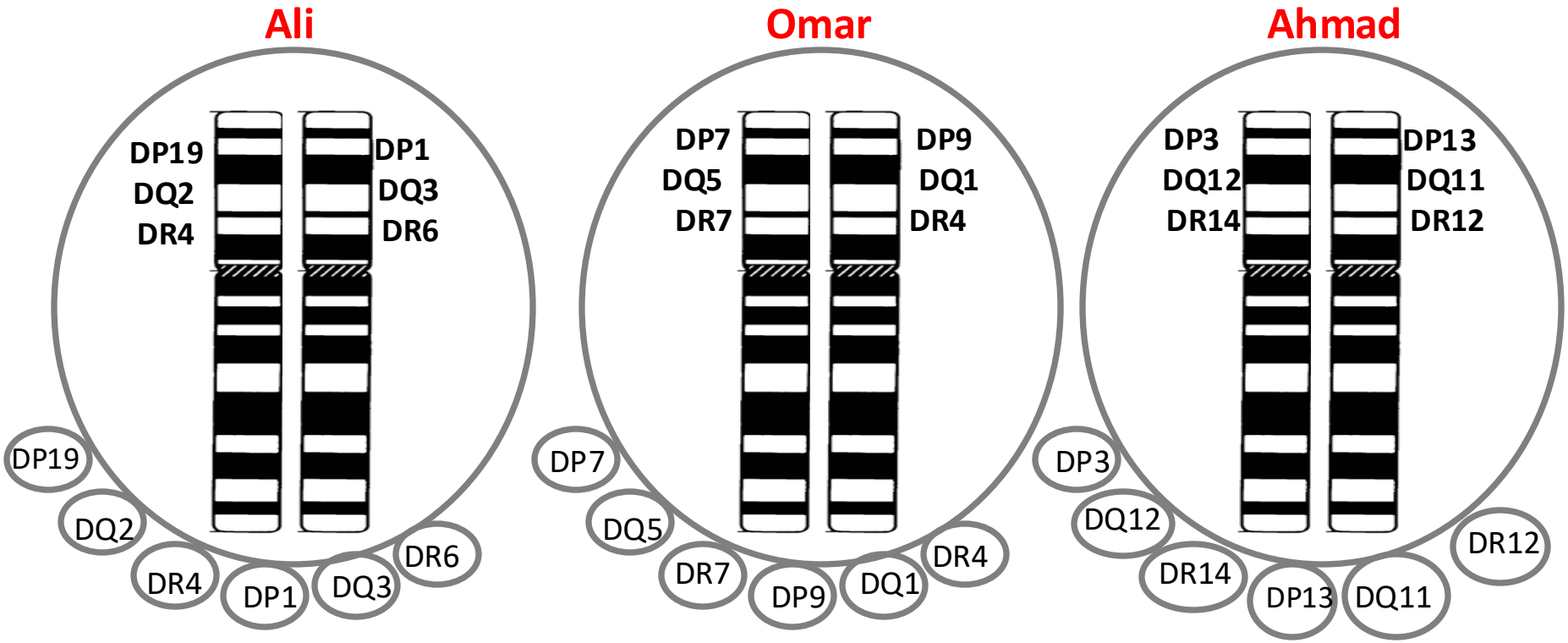
MHC-II

MHC-I vs. MHC- II



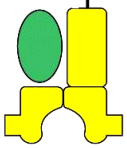
MHC-II

Inheritance of MHC-II

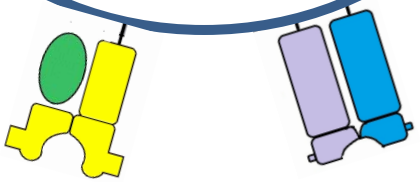


Expression of MHC molecules

All nucleated ells express MHC1



APC can express both MHC1 & MHC2

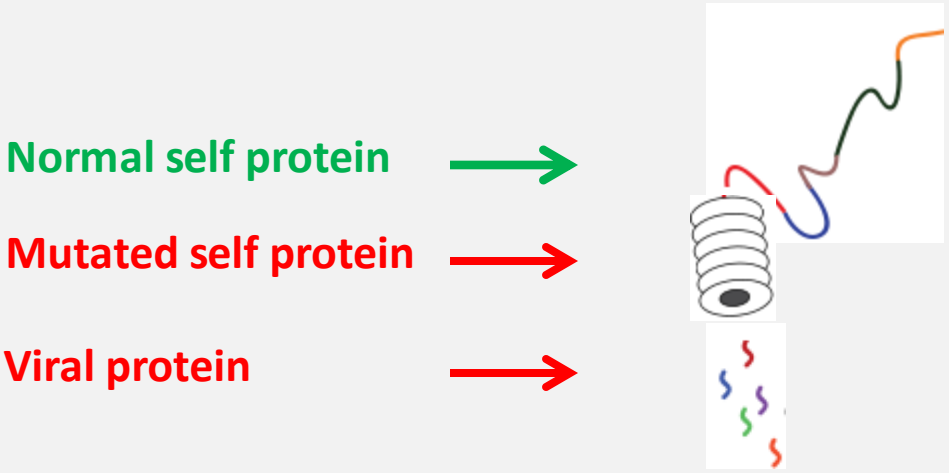


Functions of MHC-I molecules

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)

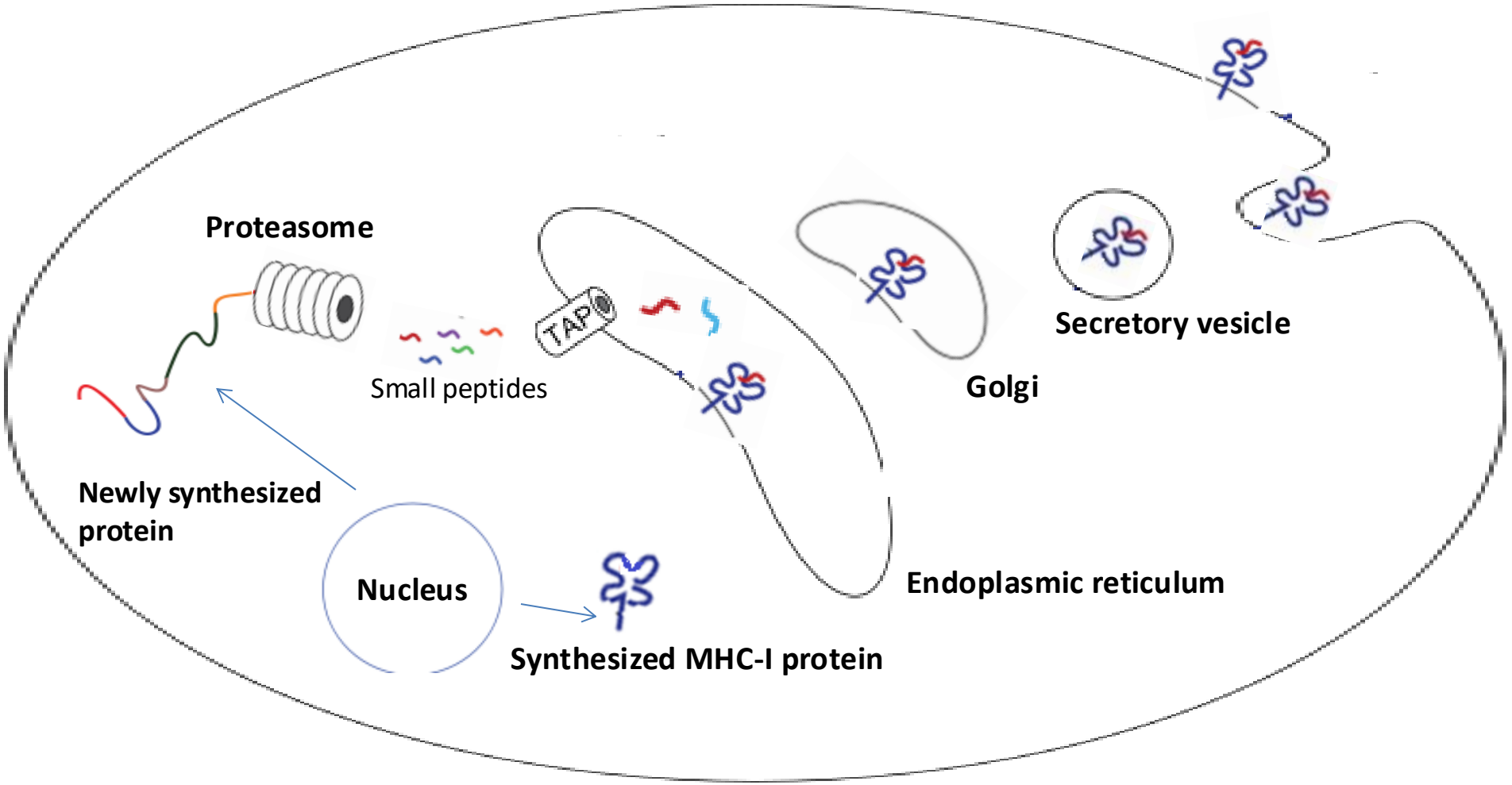
A small amount of these proteins are directed to the proteosome in which these proteins are degraded into short peptides in order to be complexed with the MHC-I molecules. Then these proteins with MHC-I are expressed on the surface of the cell to be presented to the cytotoxic T-cells (CTLs)



Functions of MHC-I molecules

MHC-I molecules

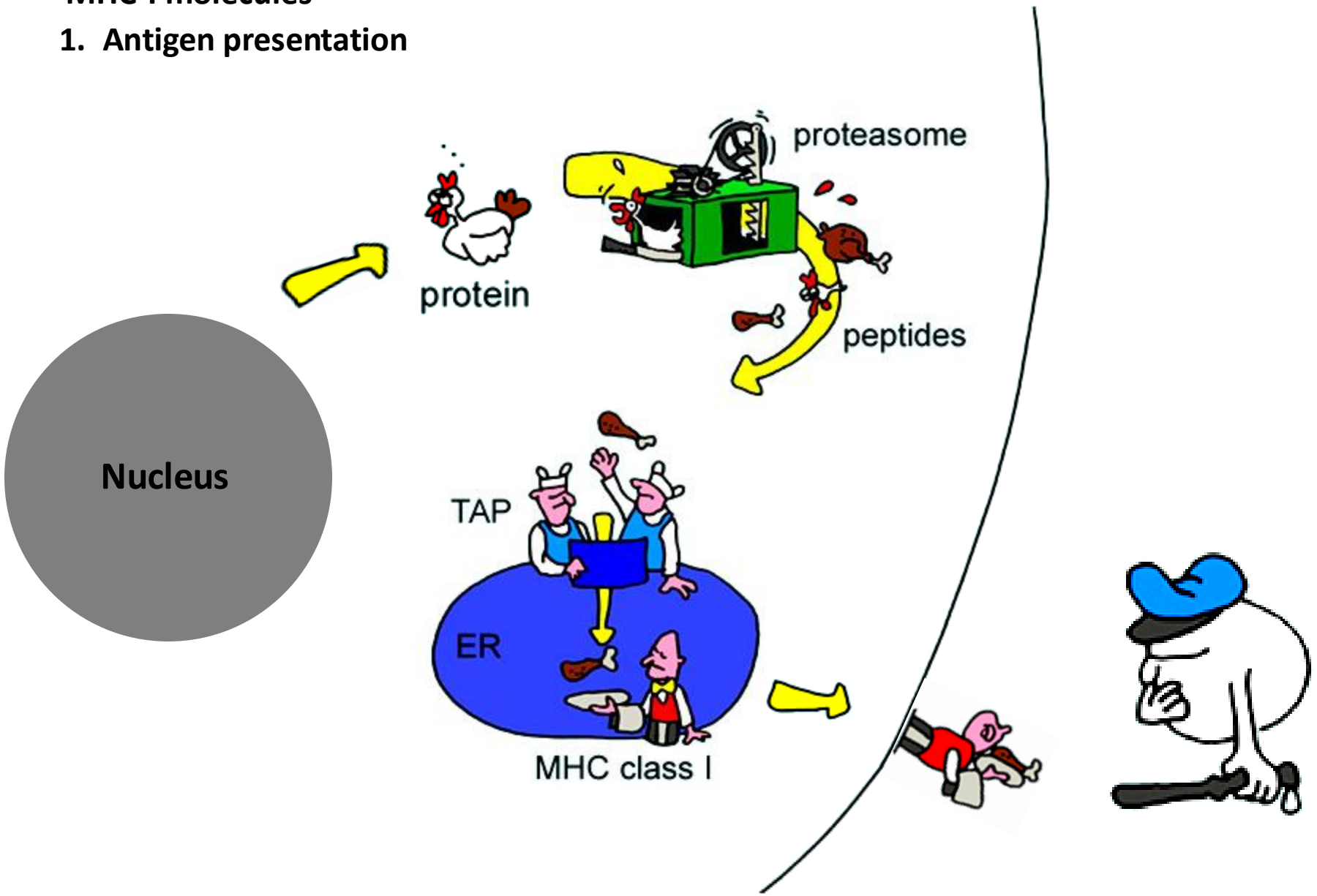
1. Antigen presentation



Functions of MHC-I molecules

MHC-I molecules

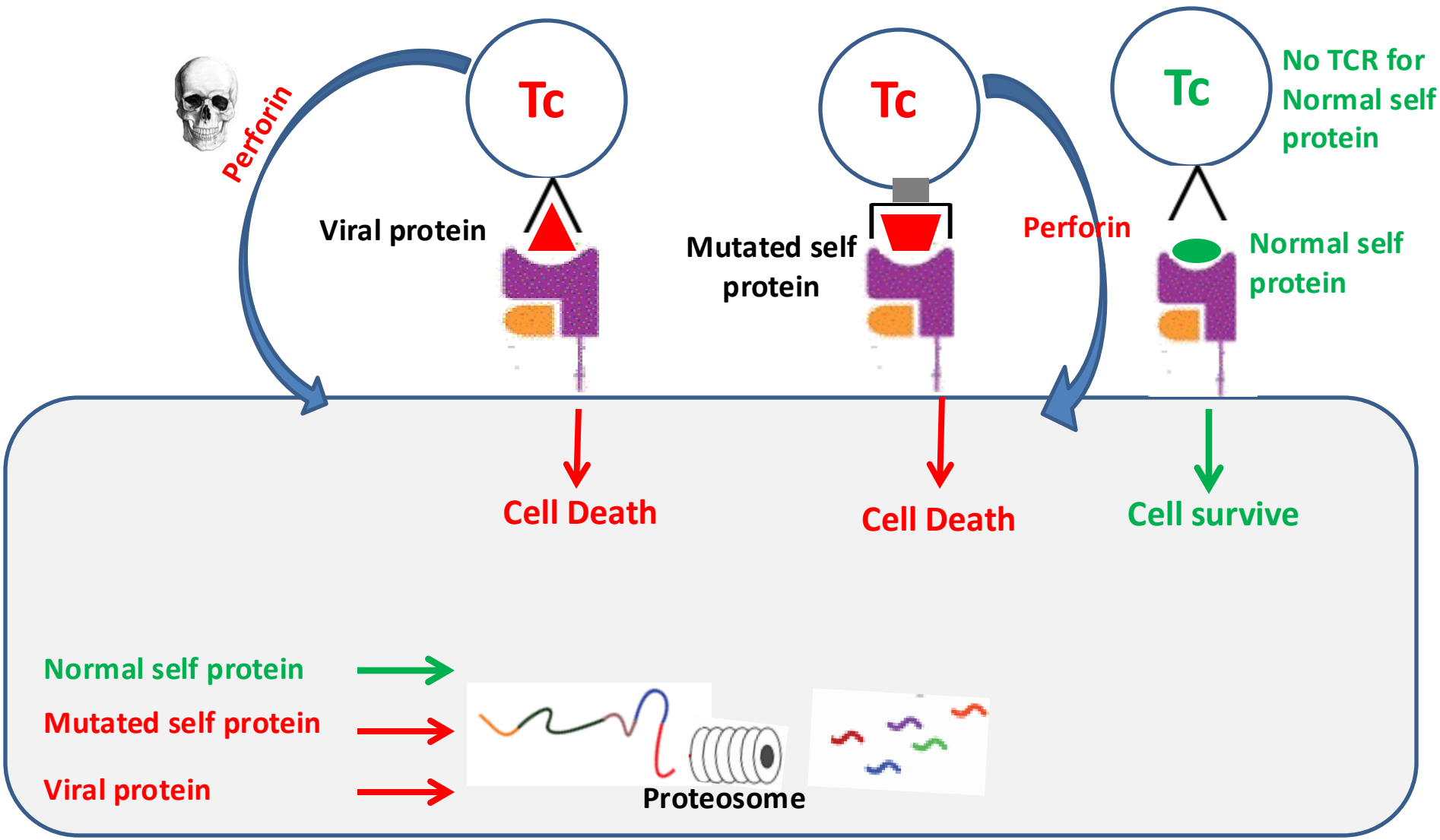
1. **Antigen presentation**



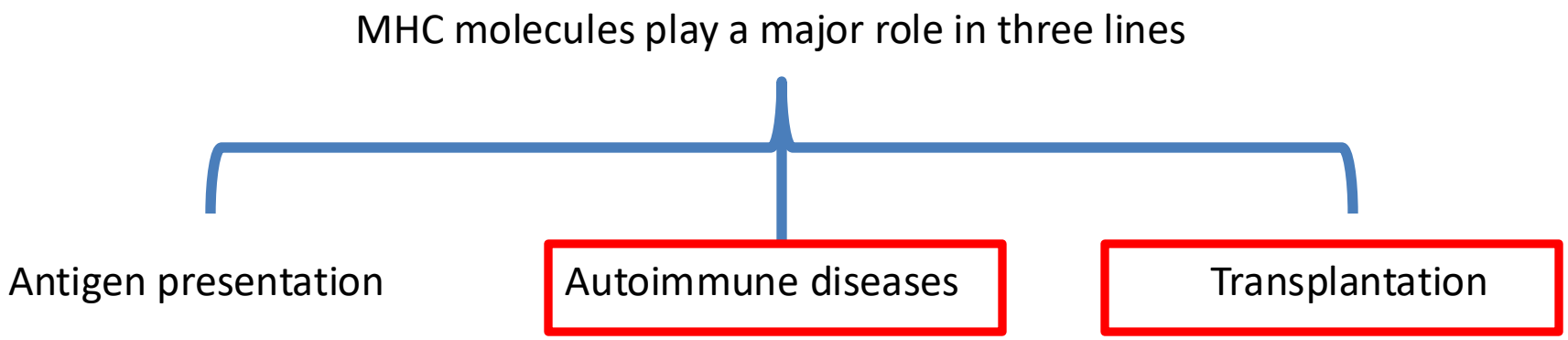
Functions of MHC-I molecules

MHC-I molecules

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

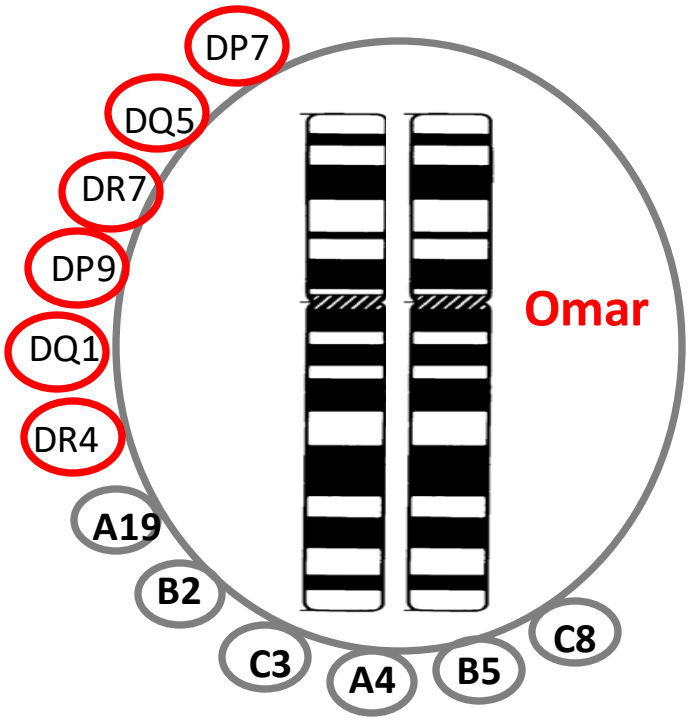


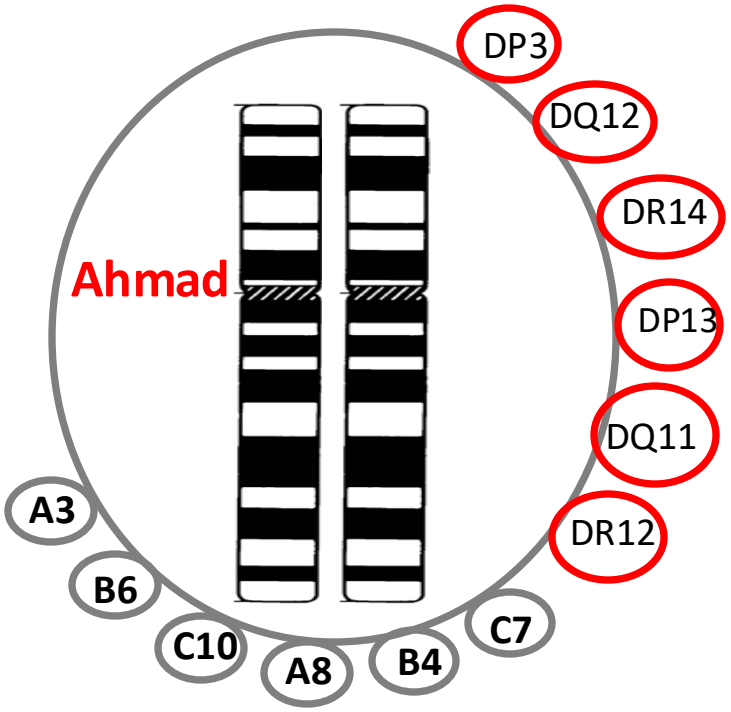
Biological Importance of MHC

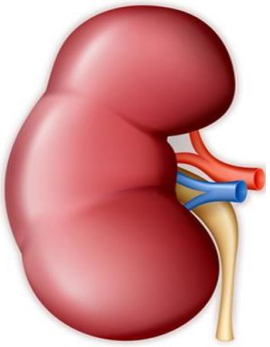


Functions of MHC molecules

2- Transplantation







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

Rejected

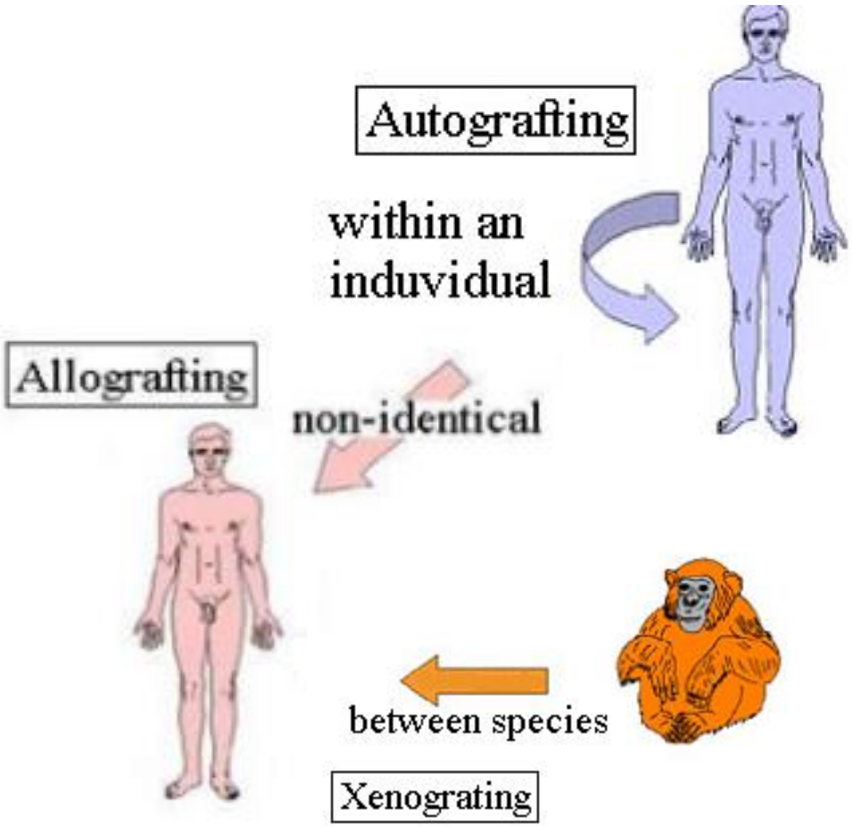
Functions of MHC molecules

2- Transplantation

Methods of Transplantation:

May take place between:

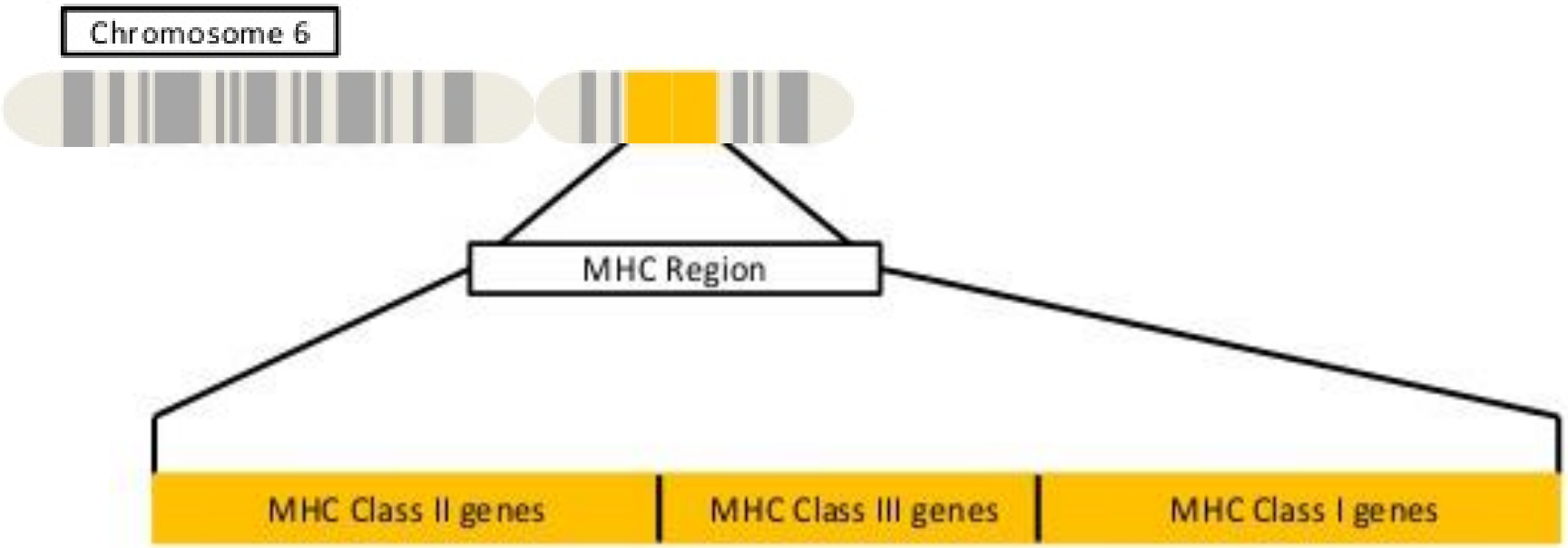
- different parts of the same organism (autografting)
- different organisms of the sam species (allografting)
- different species (xenografting



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

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