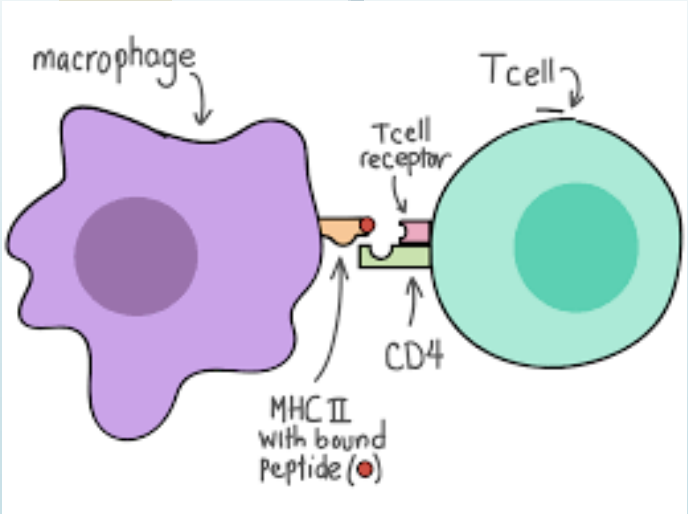
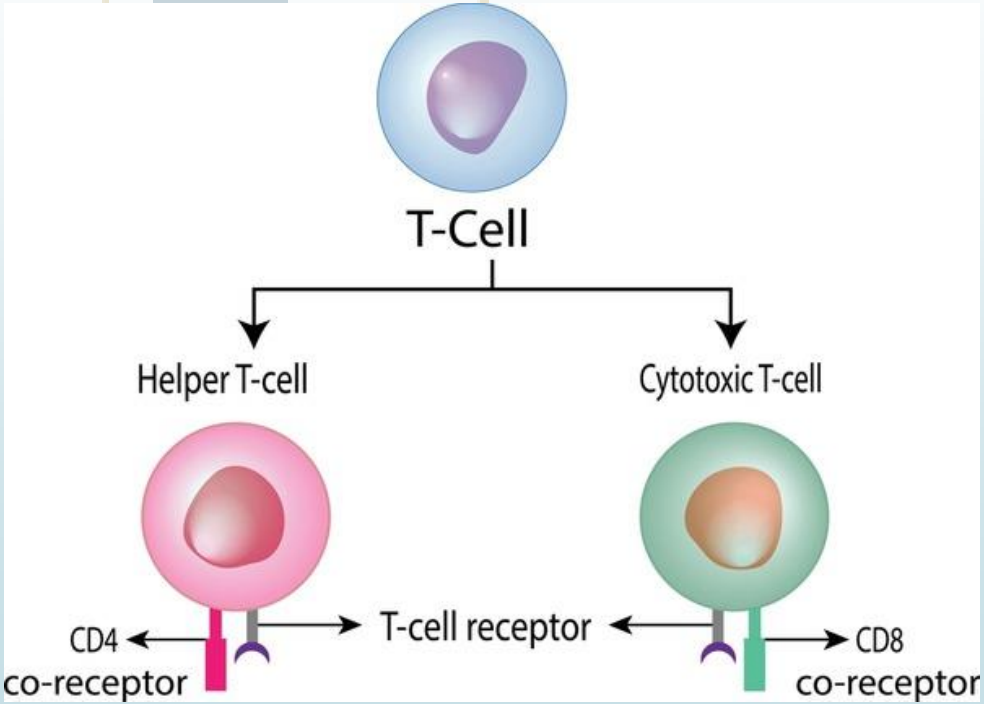
Document 7

Antigen Recognition by T-lymphocytes

- ***How does a TCR recognize an antigen?***



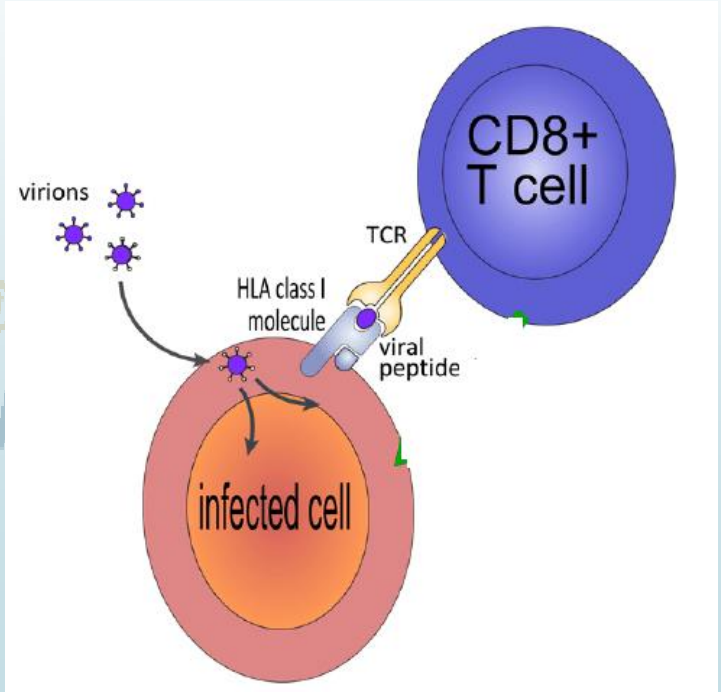
- TL have membrane receptors specific for antigens known as TCR.



- Unlike BL, TL cannot recognize free antigens.
- TL can recognize only processed antigen (fragmented into peptides within the host cell).
- TCR recognize only antigens that are displayed on the surface of "self cells".

- **The immune response induced by TL :**

  Specific Cell-mediated Immune Response.

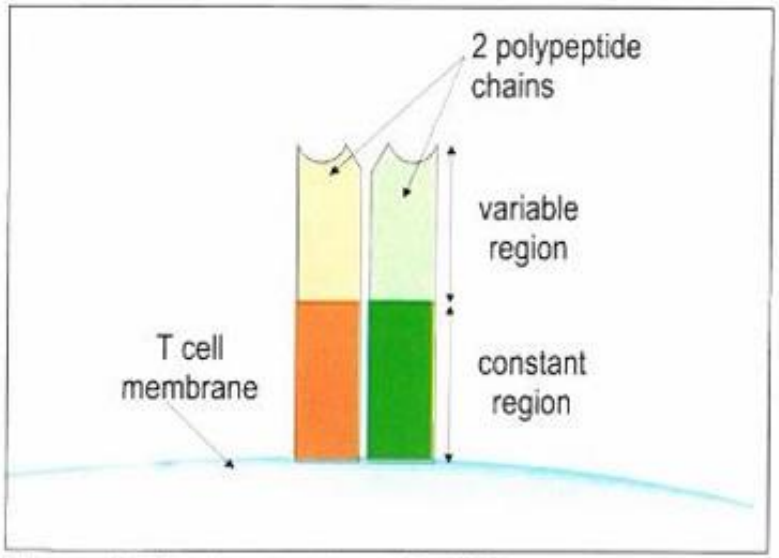


I. Structure of TCR

- Doc.a, p.127.
- Structure of TCR is similar to that of an antibody:

→It is made of a constant region which is identical for all the T-cells of the body, and a variable region that differ from one T-cell to another.

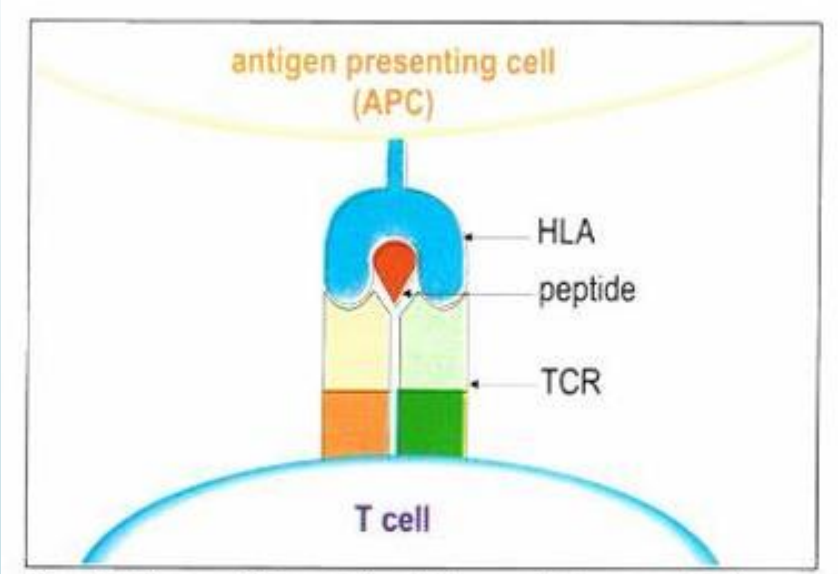
→ However, a TCR has two polypeptide chains that form together a single antigen binding site. Doc.a, p.127.



Doc.a *Molecular structure of a TCR.*

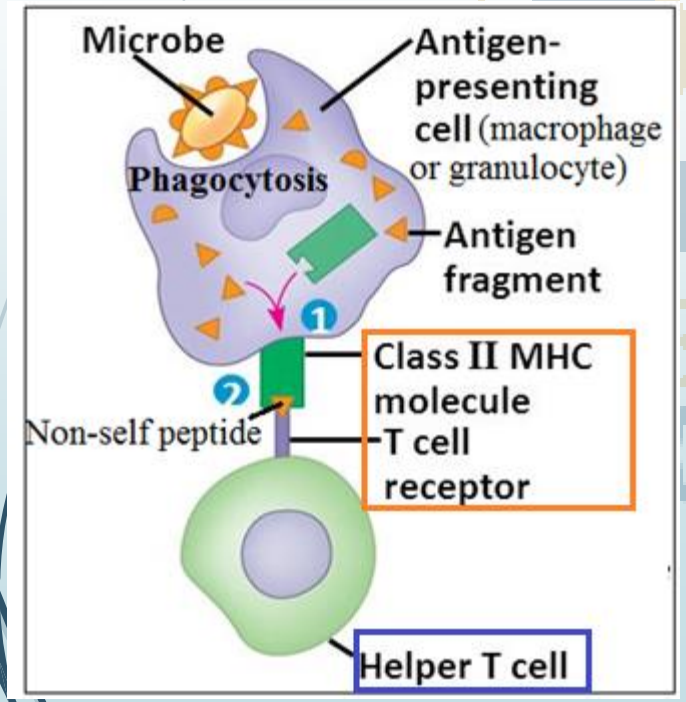
II. Double Recognition by TCR

- TCR should recognize and bind to self HLA molecule carrying non-self-peptide ⇨ This process is known as **double recognition**. Doc.b, p.127.

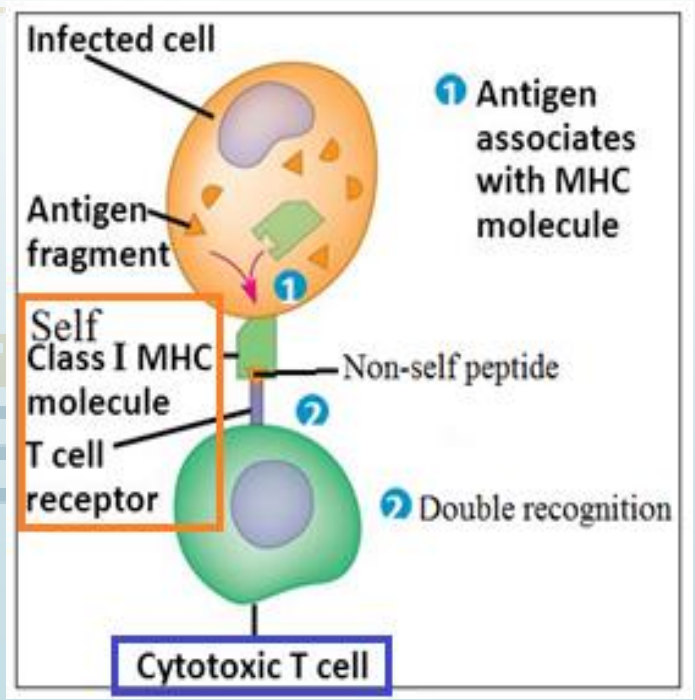


Doc.b *Recognition of the HLA-peptide complex by TCR.*

TCR of TH or T4 binds to HLA class 2 (II) carrying non-self-peptide.



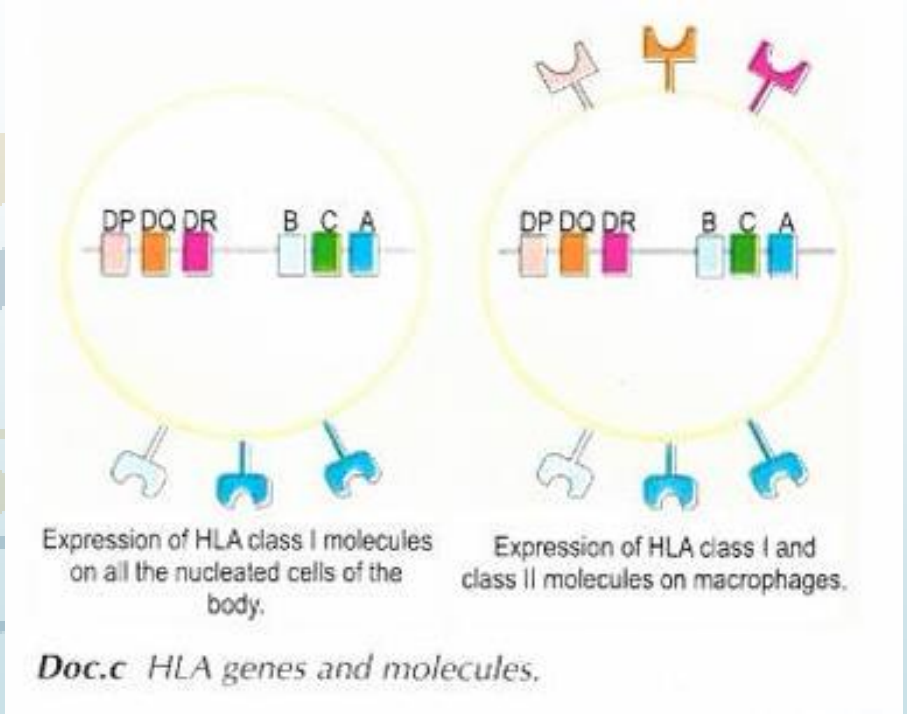
TCR of TC or T8 binds to HLA class 1 (I) carrying non-self-peptide.



III. Different Types of HLA molecules

- Doc.c, p.127.

- HLA genes (DP,DQ, DR, A,B and C) code for 2 classes of proteins that differ by their structure and role:
  → **Class I molecules:** coded by A,B and C genes. They are expressed by **all the nucleated cells of the body.**
  → **Class II molecules:** coded by DP, DQ and DR. **They are expressed** by some cells of the immune system mainly **macrophages.**



Doc.c HLA genes and molecules.

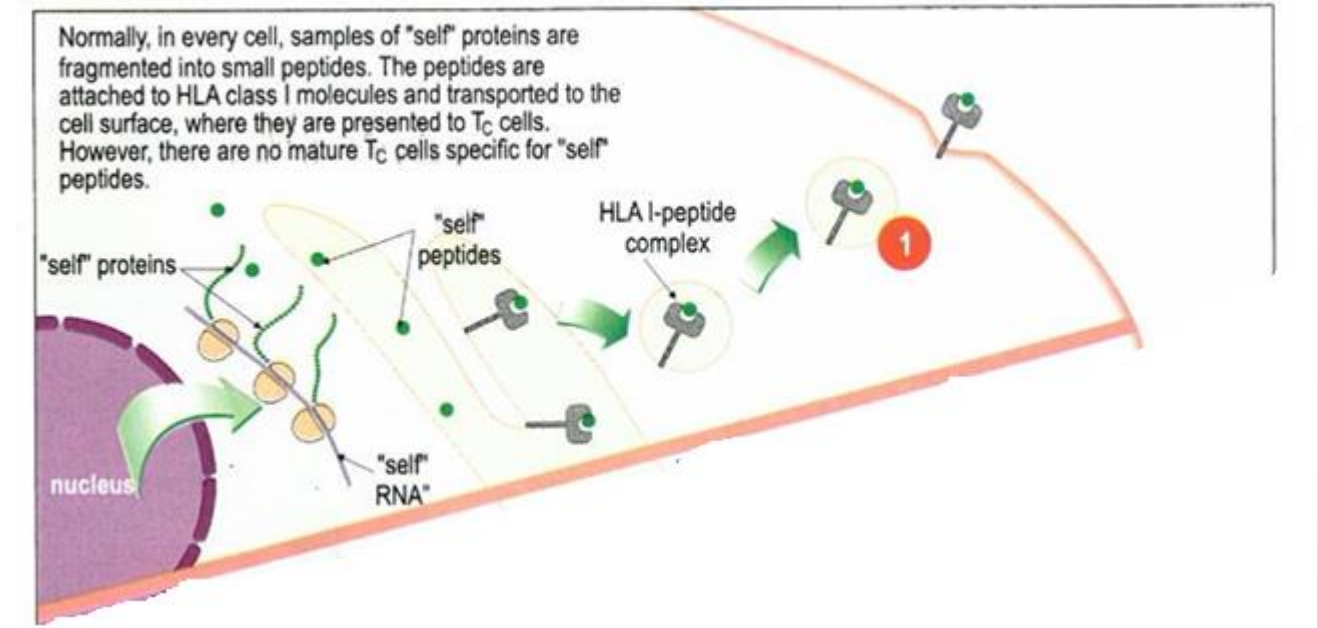
IV. Peptide Presentation to T lymphocytes

- Doc.d, p.128.

❶ Shows **normal protein synthesis in the cell:**

→ Self proteins are fragmented into self-peptides and presented by self HLA class I

⇨ ***It is not recognized by mature TC.***



❷ Peptide Presentation to TC.

- HLA class I molecules present peptides of proteins synthesized in the cell.

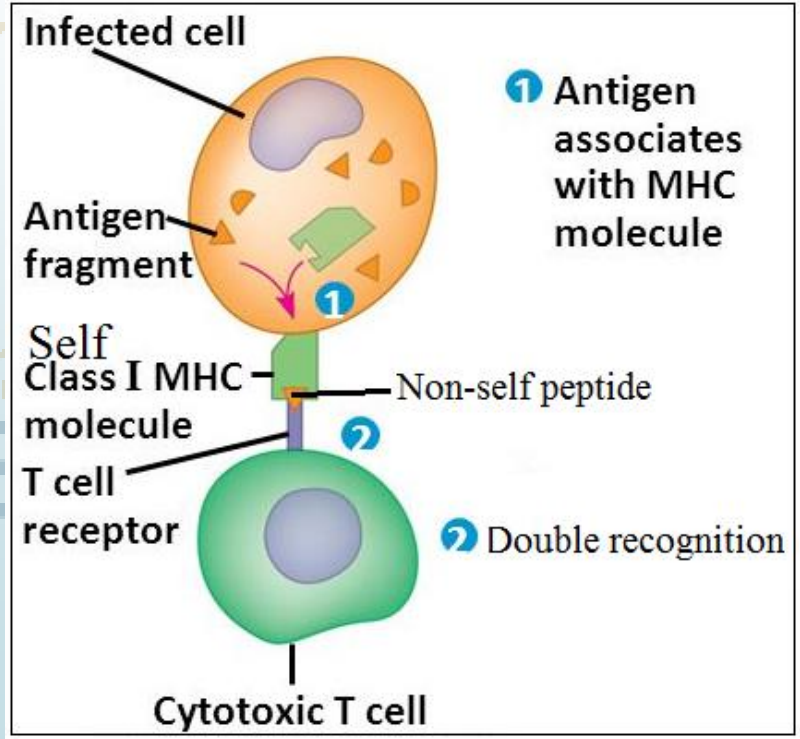
→ Self cell becomes modified self-cell or APC when infected by virus.

⇨ TCR of TC recognize self HLA I + non-self-peptide.

→ **There will be:**

1- Double recognition.

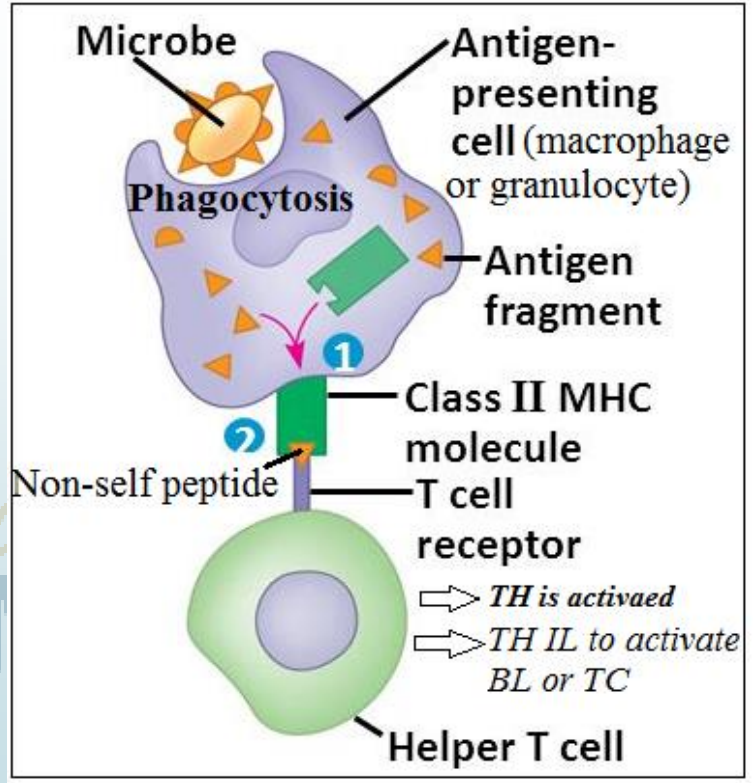
2- Attack of the infected cell by cytotoxicity.



❸ Peptide Presentation to TH

→ After phagocytosis, macrophages or granulocytes become APC.

⇨ TCR of TH recognize self HLA II + non-self-peptide.

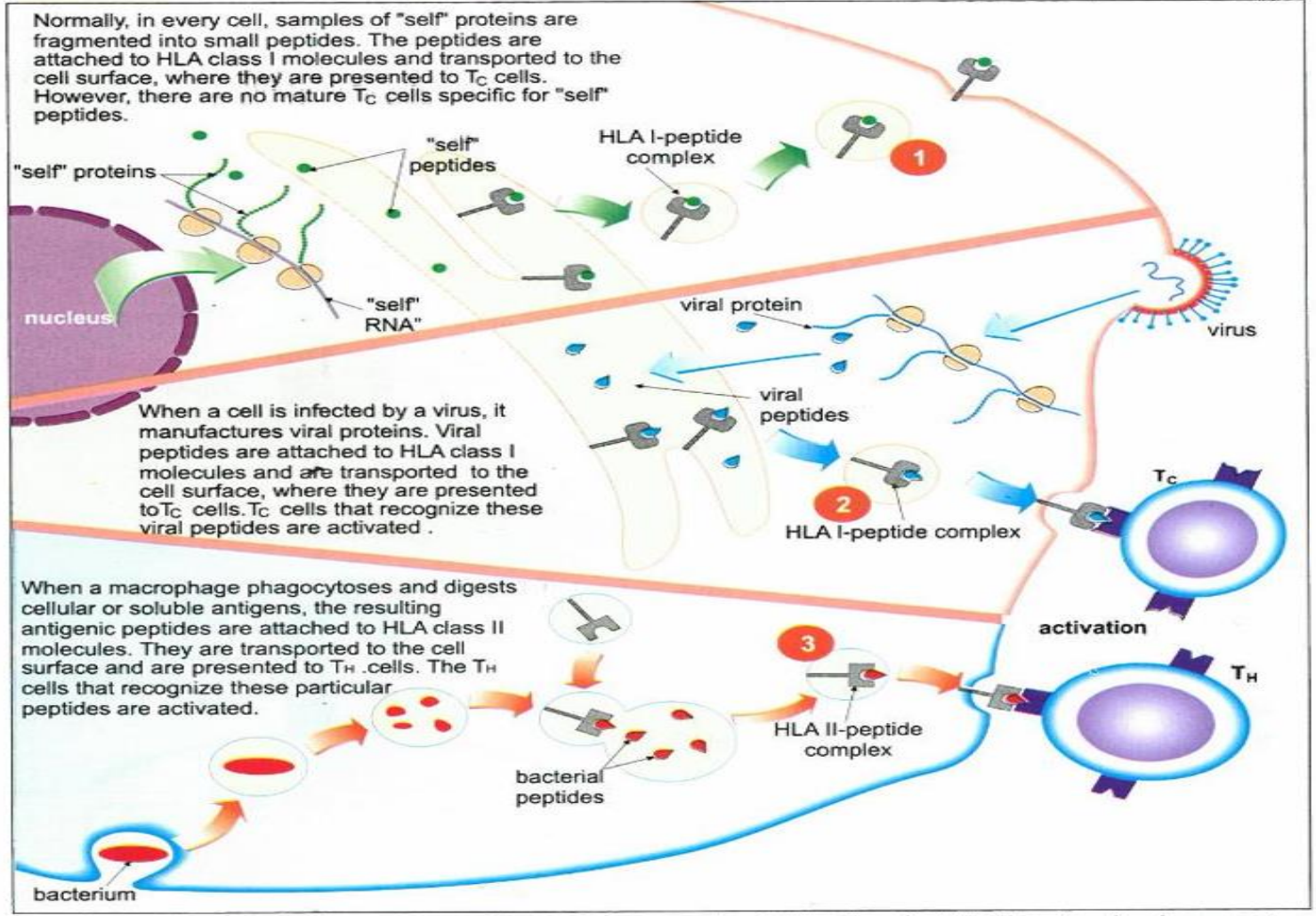


→ **There will be :**

1- Double Recognition

2- Activation of TH

3-Activated TH will release Interleukins (IL 2 or IL4) .



Doc.d *HLA class I molecules present peptides of proteins synthesized in the cell. HLA class II molecules present peptides of proteins digested in the cell.*

- Probing the Documents, p.128

Probing the documents

1. Establish a comparative table of an antibody and a TCR concerning their location, structure, antigen recognition and the number of antigen binding sites.
2. What does each of numbers 1, 2 and 3 stand for in ***doc.d*** : a "self", a "non-self" or a modified "self"? Justify your answer.
3. Explain the following statement: "B cells and antibodies recognize the "non-self", while T cells recognize the modified "self".

1- Antigen recognition by TCR is double (self HLA-non self peptide and TCR), while by antibodies is direct (epitope-antibody).

2- 1: Stands for the immunological self since it represents an association between an HLA molecule and a "self" peptide.

2: Stands for a modified self since the HLA molecule of class I is associated to viral (non-self) peptides that are synthesized and fragmented in the self.

3: stands also for a modified self since the HLA molecule of class II is associated to bacterial peptides (non-self) that are fragmented by the macrophage.

Probing the documents

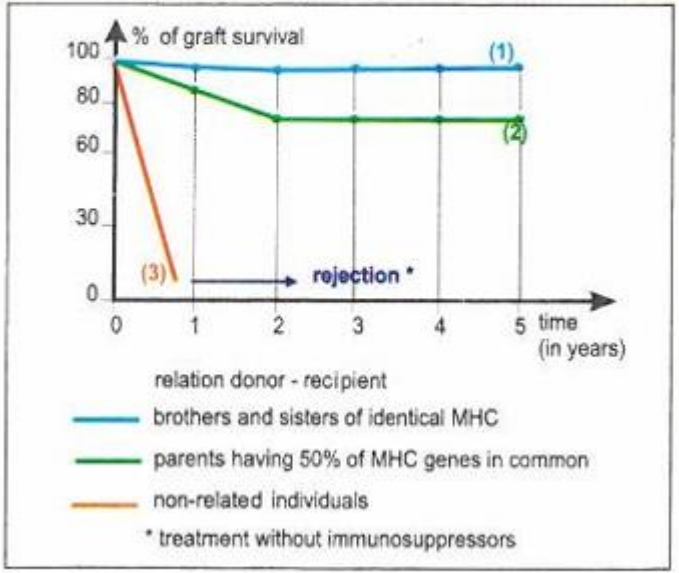
1. Establish a comparative table of an antibody and a TCR concerning their location, structure, antigen recognition and the number of antigen binding sites.
2. What does each of numbers 1, 2 and 3 stand for in ***doc.d*** : a "self", a "non-self" or a modified "self"? Justify your answer.
3. Explain the following statement: "B cells and antibodies recognize the "non-self", while T cells recognize the modified "self".

3- Antibodies recognize “non-self” because they are able to bind to a free soluble or cellular antigen. While T-cells recognize only antigenic (non-self) peptides presented by HLA (self-molecule) on the surface of a body cell, such as macrophage or an infected cell.

- **Selected Exercises (p.133-134):**

☐ *Exercise III*

The next document sums up the results of the percentage of graft survival in Man during five years.



After analyzing this document, deduce the tested hypothesis.

- Formulate the tested hupothesis.

Hypothesis: The success of graft depends on HLA similarity between the donor and the recipient which is the highest in case of identical twins.

Exercises of the National Book

- ***Exercise IV and VIII***

Exercise IV

In 1974, Zinkernagel demonstrated the double recognition of peptide-HLA complexes by TCR, based on the following experiment:

Mice of strain X were infected with CML virus (choriomeningitic leukemia virus), that causes a serious, but non-fatal, cerebral disease.

One week later, T cells from the infected mice were collected and put in culture in the presence of infected or non-infected mouse cells, derived either from strain X, or from a different strain referred to as Y strain. The following results were obtained:

Infected X cells	Lysis
Non-infected X	No lysis
Y infected cells	No lysis
Y non-infected cells	No lysis

Interpret these results.

-Solution

*Different strains have different MHC markers.

-Interpret the results

After adding T-cells obtained from mouse of strain X infected with CML virus into a culture containing infected X cells with the same virus, there was lysis of infected X-cells by T-cells. While, upon adding these T-cells into a culture containing non-infected X-cells or Y-cells (from mouse of strain Y), whether infected or not, there was no lysis by T-cells.

This means that, T-cells obtained from mice of strain X infected by CML virus destroy the cells of the same strain X infected by the same CML virus.

Exercise IV

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Infected X cells	Lysis
Non-infected X	No lysis
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Y non-infected cells	No lysis

Interpret these results.

-Explain the results obtained.

Analyze…..+ because there should be double recognition between TCR of T-cells and self MHC carrying non-self-peptide in order to cause cell lysis.

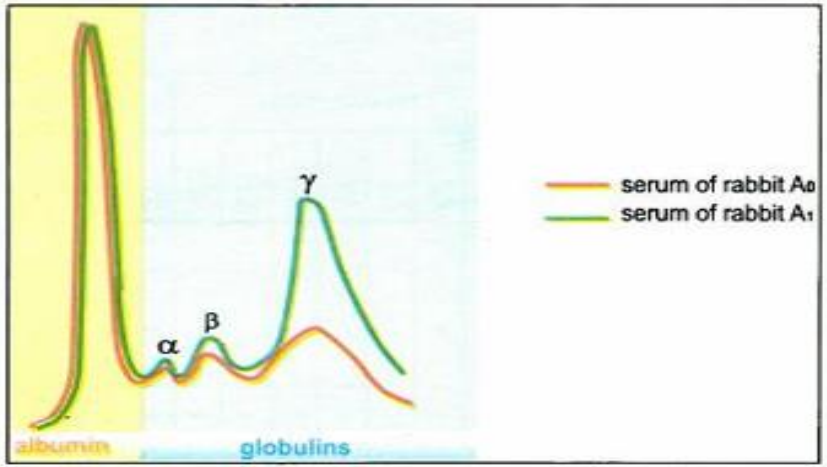
Exercise VIII

We can separate the proteins of a blood serum by electrophoresis. ***Document 1*** represents the curves relative to the electrophoresis of the serum of rabbit A0 and that of rabbit A1.

The peak of albumin is identical in both cases.

A0: control rabbit

A1: rabbit injected with tetanus toxoid 15 days ago.



Document 1

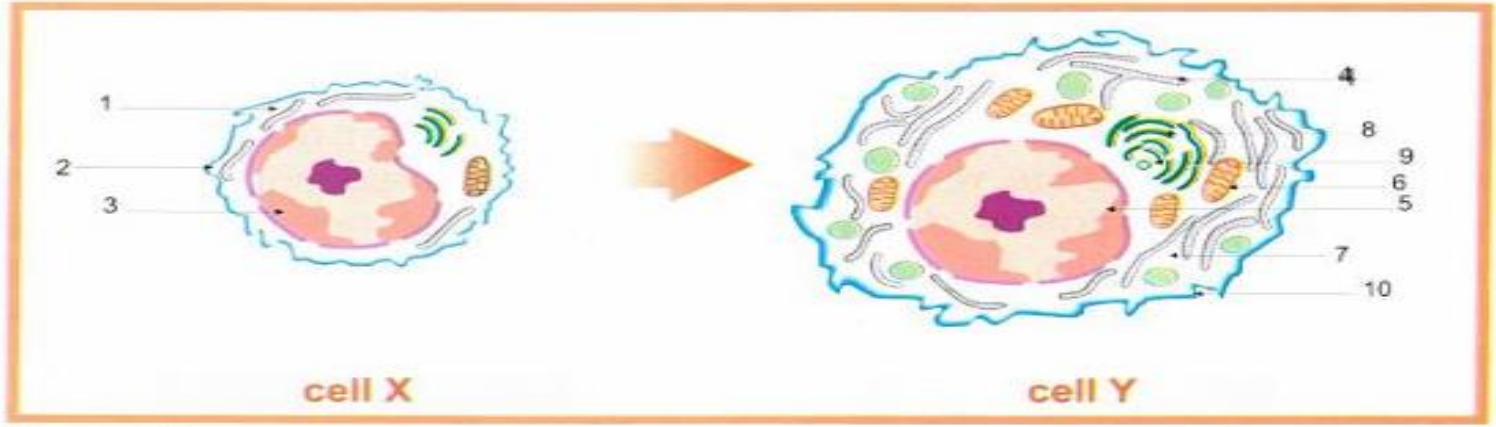
a- What do you conclude?

The serum of rabbit Ao contains different proteins (albumin, globulin). 15 days later, the rabbit A1 contains a greater amount of γ globulins or antibodies.

a- **Draw out a conclusion.**

Thus, γ represents anti-tetanus antibodies produced by rabbit A1 upon injecting it with tetanus toxoid.

In rabbit A1, at the level of the nodes neighboring the site of inoculation of the tetanus toxoid, we find a large number of cells represented in ***document 2***. Cell X is transformed into cell Y.



Document 2

b- Name the structures from 1 to 10 as well as cells X and Y without reproducing them.

c- Taking into consideration the comparison between both cells and the conclusion in part a, what would be the main function of cells Y?

In 1966, Claman, Miller and Mitchell used adult mice deprived, since birth, from their thymus through a surgical operation, and exposed (at the same age) to X rays that destroy the stem cells of the bone marrow. These mice were divided into 3 groups and received different treatments.

The results are illustrated in ***document 3***.

b- - Cell X: B lymphocyte: 1: cytoplasm 2: cell membrane 3: nucleus

- Cell Y: Plasma cell: 4: ribosome 5: nucleus 6: mitochondria 7: cytoplasm 8: golgi body 9: secretary vesicle 10: cell membrane

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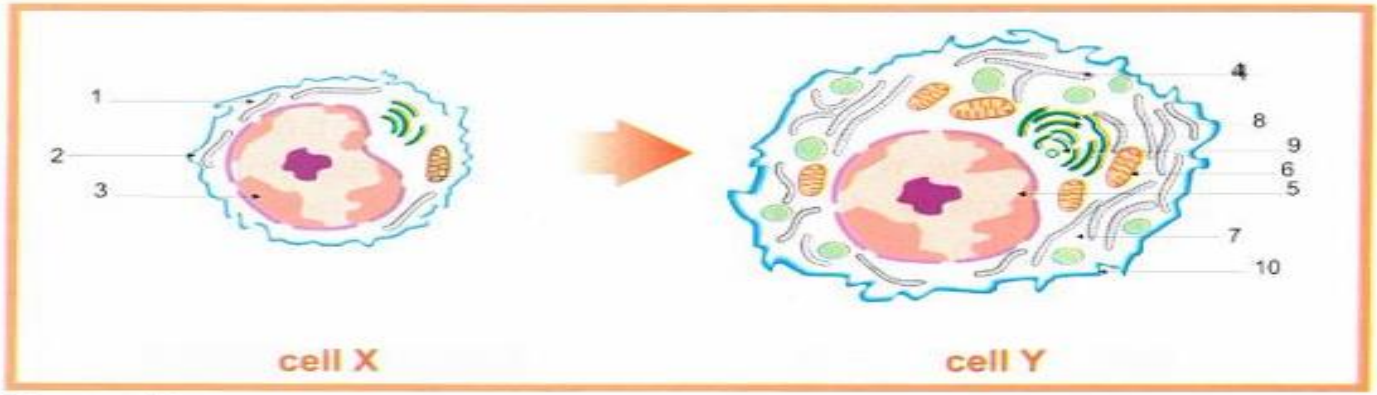

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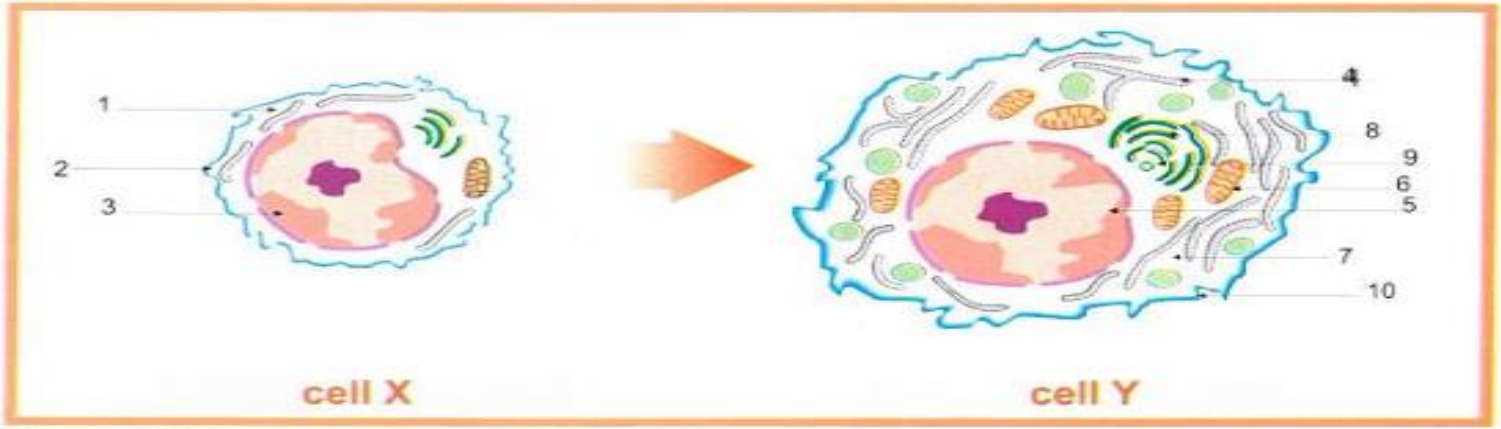
c- Cell Y is bigger in size than cell X, more developed and contains more differentiated structures (more ribosomes, more golgi body, more mitochondria and secretary vesicles). That is to synthesize anti-tetanus antibodies (to make translation and produce anti-tetanus antibodies that are proteins in nature).

In rabbit A1, at the level of the nodes neighboring the site of inoculation of the tetanus toxoid, we find a large number of cells represented in ***document 2***. Cell X is transformed into cell Y.



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The results are illustrated in ***document 3***.

Treatment	Group 1	Group 2	Group 3
Time t_1 intravenous injection	thymus cells	red bone marrow cells	thymus cells and red bone marrow cells
Time t_2 (a few days later) intravenous injection	sheep's red blood cells (SRBC)	sheep's red blood cells	sheep's red blood cells
Time t_3 (a few days later)	serum sample +SRBC	serum sample +SRBC	serum sample +SRBC
Time t_4 a few days after the contact between serum and SRBC	No agglutination	slight agglutination	important agglutination

Document 3

d- Referring to the acquired knowledge, explain the results shown in ***document 3***.

****agglutination = binding of the antibody to its specific antigen.***

If serum + antigen X → agglutination ⇨ presence of antibodies in the serum (anti- X).

If serum + antigen → no agglutination ⇨ absence of antibodies.

Treatment	Group 1	Group 2	Group 3
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Document 3

d- Referring to the acquired knowledge, explain the results shown in ***document 3***.

d- Explain: Analyze + because…

Group 1: analyze…., no agglutination took place due to the absence of bone marrow which is the site of production of B cell. In the absence of bone marrow, there will be no production of B-cells and thus no antibodies.

Treatment	Group 1	Group 2	Group 3
Time t_1 intravenous injection	thymus cells	red bone marrow cells	thymus cells and red bone marrow cells
Time t_2 (a few days later) intravenous injection	sheep's red blood cells (SRBC)	sheep's red blood cells	sheep's red blood cells
Time t_3 (a few days later)	serum sample +SRBC	serum sample +SRBC	serum sample +SRBC
Time t_4 a few days after the contact between serum and SRBC	No agglutination	slight agglutination	important agglutination

Document 3

d- Referring to the acquired knowledge, explain the results shown in ***document 3***.

Group 2: analyze…, slight agglutination due to the absence of thymus which is the site of maturation of T-cells. In the absence of mature TH cells there will be no activation of B-cells to differentiate into plasma cells and no antibody production which explains the slight agglutination.

Treatment	Group 1	Group 2	Group 3
Time t_1 intravenous injection	thymus cells	red bone marrow cells	thymus cells and red bone marrow cells
Time t_2 (a few days later) intravenous injection	sheep's red blood cells (SRBC)	sheep's red blood cells	sheep's red blood cells
Time t_3 (a few days later)	serum sample +SRBC	serum sample +SRBC	serum sample +SRBC
Time t_4 a few days after the contact between serum and SRBC	No agglutination	slight agglutination	important agglutination

Document 3

d- Referring to the acquired knowledge, explain the results shown in ***document 3***.

Group 3: analyze…, important agglutination due to the presence of thymus and bone marrow, which means the presence of mature B and T-cells. Mature TH cells will activate B cells (BL) where they will differentiate into plasma cells that release specific antibodies against SRBC causing important agglutination.