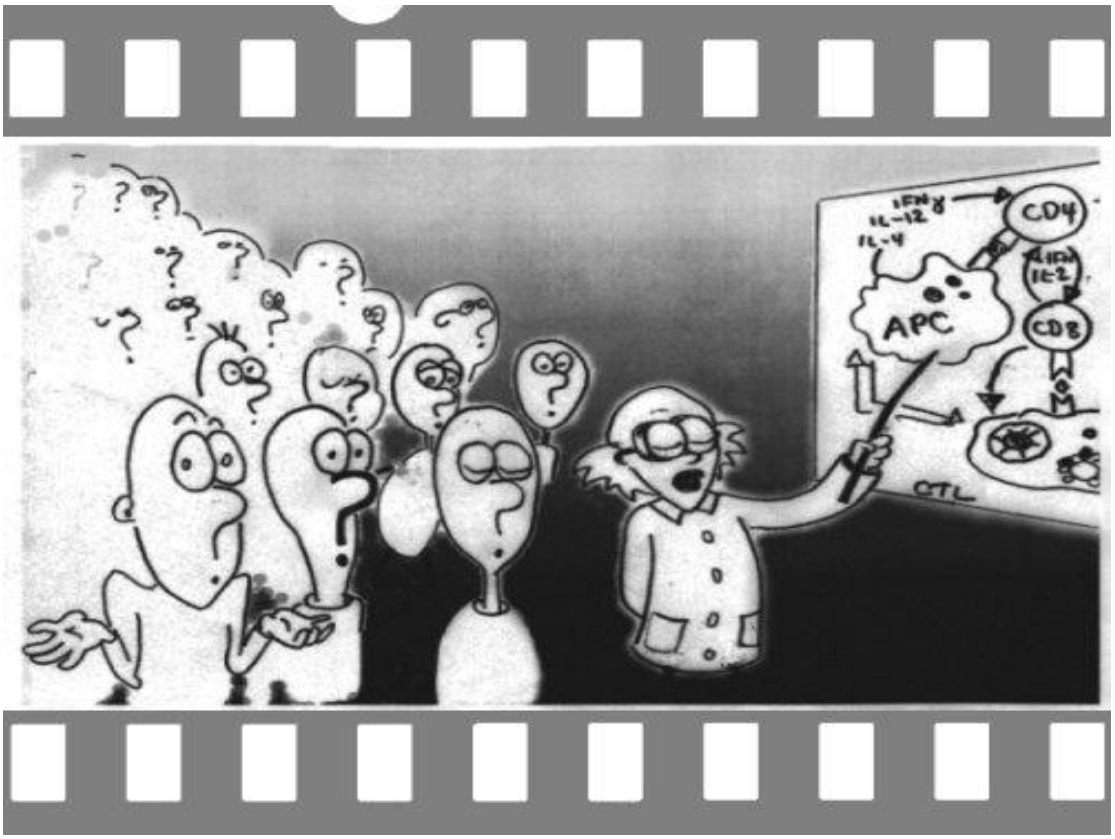
Immunology



Musculoskeletal Block (1)

Autoimmunity

Ibrahim[2]

Alshiddi | Alsadhan

⊖ **These are the notes said in the lecture but not found in the slides. Study them with the slides to be in the safe side.**

* Special thanks to Abdullah Aleisa.

- In central lymphoid organs, immune cells are programmed to differentiate between self and non-self antigens [they develop tolerance].

Tolerance can be:

1) Central tolerance
2) Peripheral tolerance
3) **Regulatory T cells**
4) **Clonal ignorance**

Central tolerance:

- Deletion of autoreactive cells early in central lymphoid organs.
- Deletion by **apoptosis**.

Peripheral tolerance:

- Deletion of autoreactive cells in peripheral lymphoid tissues.
- Occurs if autoreactive cells pass to the blood.
- Deletion by **apoptosis** or **anergy**.

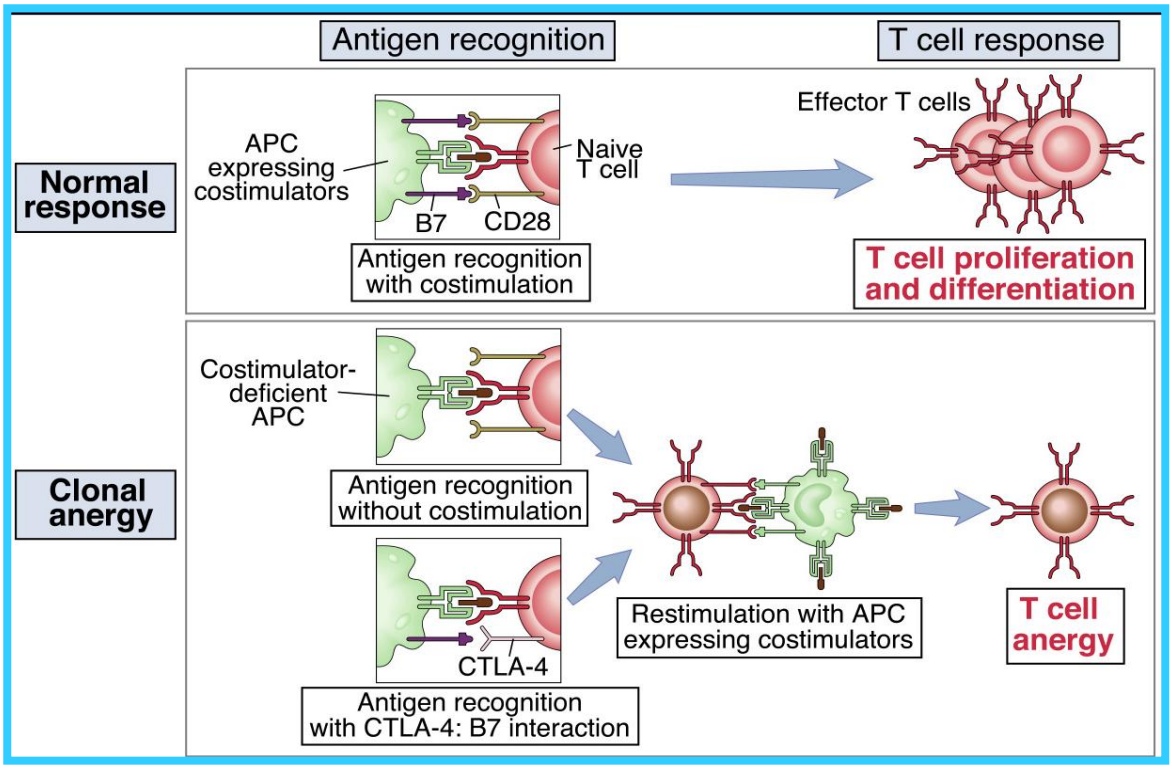
a) **Anergy "unresponsiveness"**: means that the immune cell will produce no reaction.

It happens by two mechanisms:

1. Absence of co-stimulation
2. Antigen recognition with CTLA-4, B7 interaction.

When B7 molecule on the surface APC interacts with CD-28 molecule on T-cell, immune reaction occur. [co-stimulation]

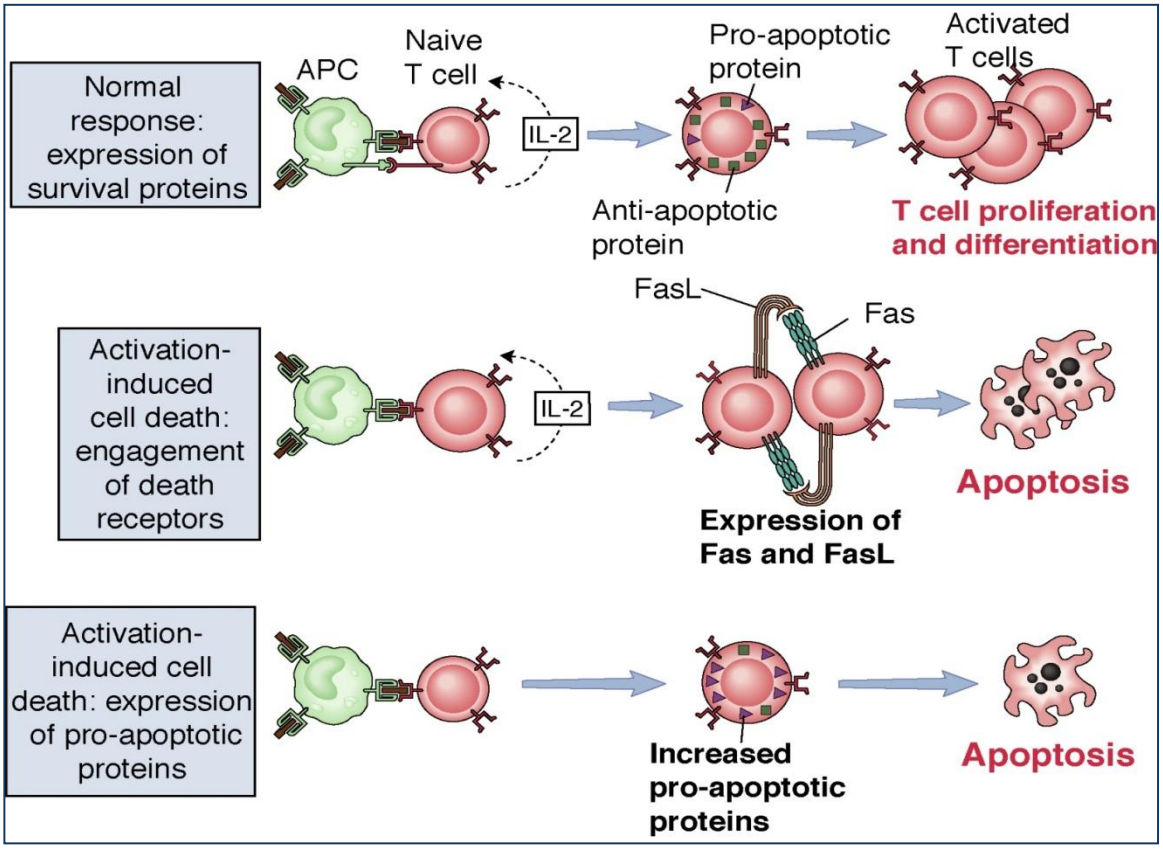
But, when B7 interacts with CTLA-4 molecule on T-cell, immune reaction will be inhibited and the cell becomes anergic.



b) **Apoptosis**: It happens by two mechanisms:

1. Engagement of death receptors (Fas): Fas receptor present on T-cell surface bind with FasL receptors on APC when there's a self antigen presented by APC. This binding triggers apoptosis of T-cell.

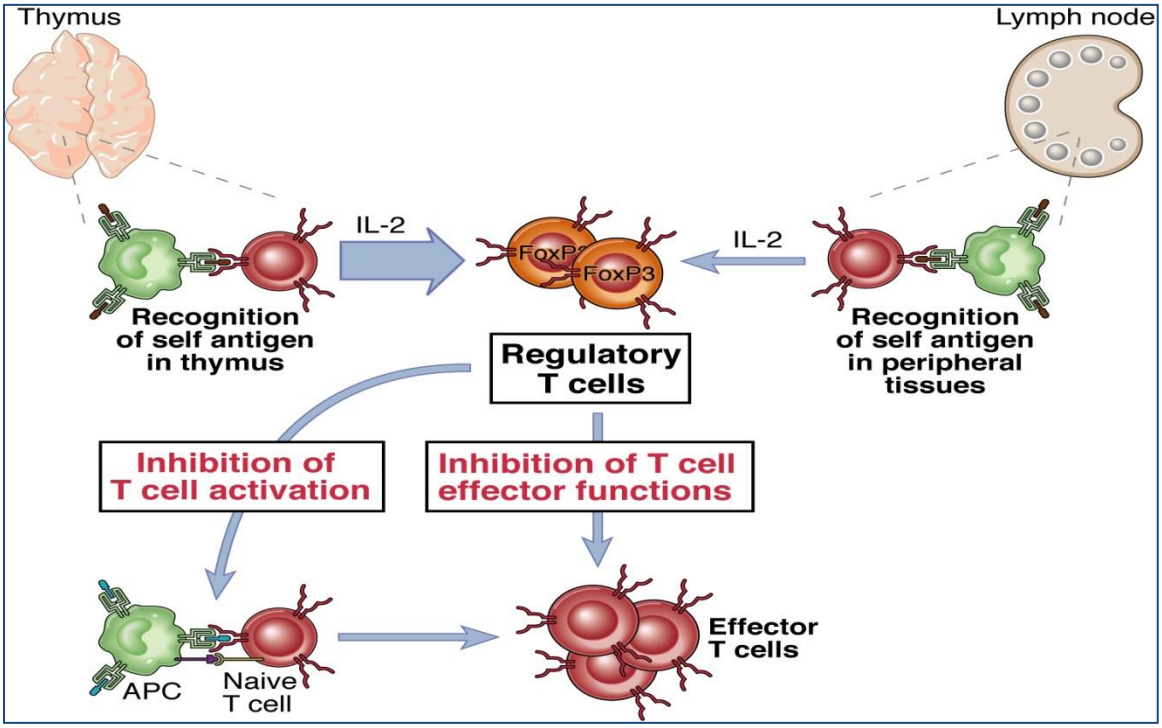
2. Expression of pro-apoptotic proteins.



⊖ Peripheral B cell Tolerance Mechanisms: when B-cells encounter self antigens, they become anergic. Then, they bind with T helper cells through Fas receptors leading to their apoptosis.

Regulatory T cells:

It's an extra mechanism to eliminate autoreactive cells.



Clonal ignorance:

Autoreactive cells are prevented from attacking self cells by **blood barrier.**

!Faliure of these mechanisms lead to autoimmune disease.

Autoimmunity patterns

[Immunopathogenesis of autoimmunity] :

1) Hidden antigens.
2) Molecular mimicry
3) Inappropriate MHC expression on non-APC cells.
4) Polyclonal B-cell activation

1st: Hidden antigens: [Sequestered Antigens]

- Some antigens are hidden, anatomically, from contact with immune cells.
- When these hidden antigens are exposed to immune cells, they're dealt with as non-self antigens and then attacked.
- See examples in the slides.
- When eye lens are attacked the disease is called

sympathetic ophthalmia

2nd: Molecular mimicry: [Cross-reacting Antigens]

Viruses and bacteria that have antigen resembling [look like] self antigen may trigger an autoimmune reaction.

3rd: Inappropriate MHC expression on non-APC cells:

- Class II MHC ordinarily expressed on APC's, but when class II MHC is expressed on other cells they may be attacked by the immune system.
- This abnormal expression may be due to local production of IFN-γ for any reason [e.g. viral infection]
- An example of this pattern may be Type I Diabetes

4th: Polyclonal B-cell activation:

Viruses and bacteria can induce nonspecific antibodies [IgM] production by B-cells.

ϴ Some hormones may induce or exacerbate autoimmunity. For example, estrogen may induce B-cell autoimmunity. This could explain why females are more prone to autoimmune diseases.