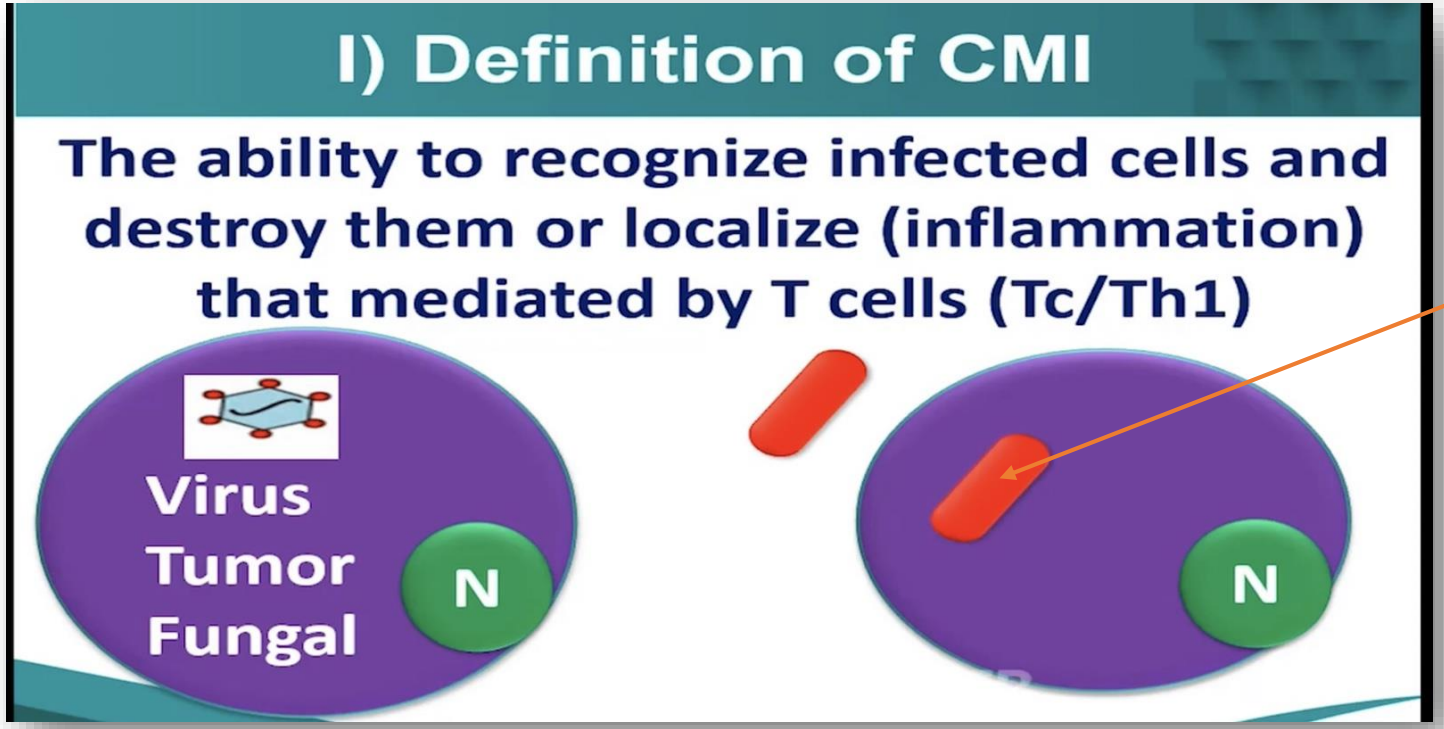
Lecture # 8

Cell Mediated Immunity (CMI)

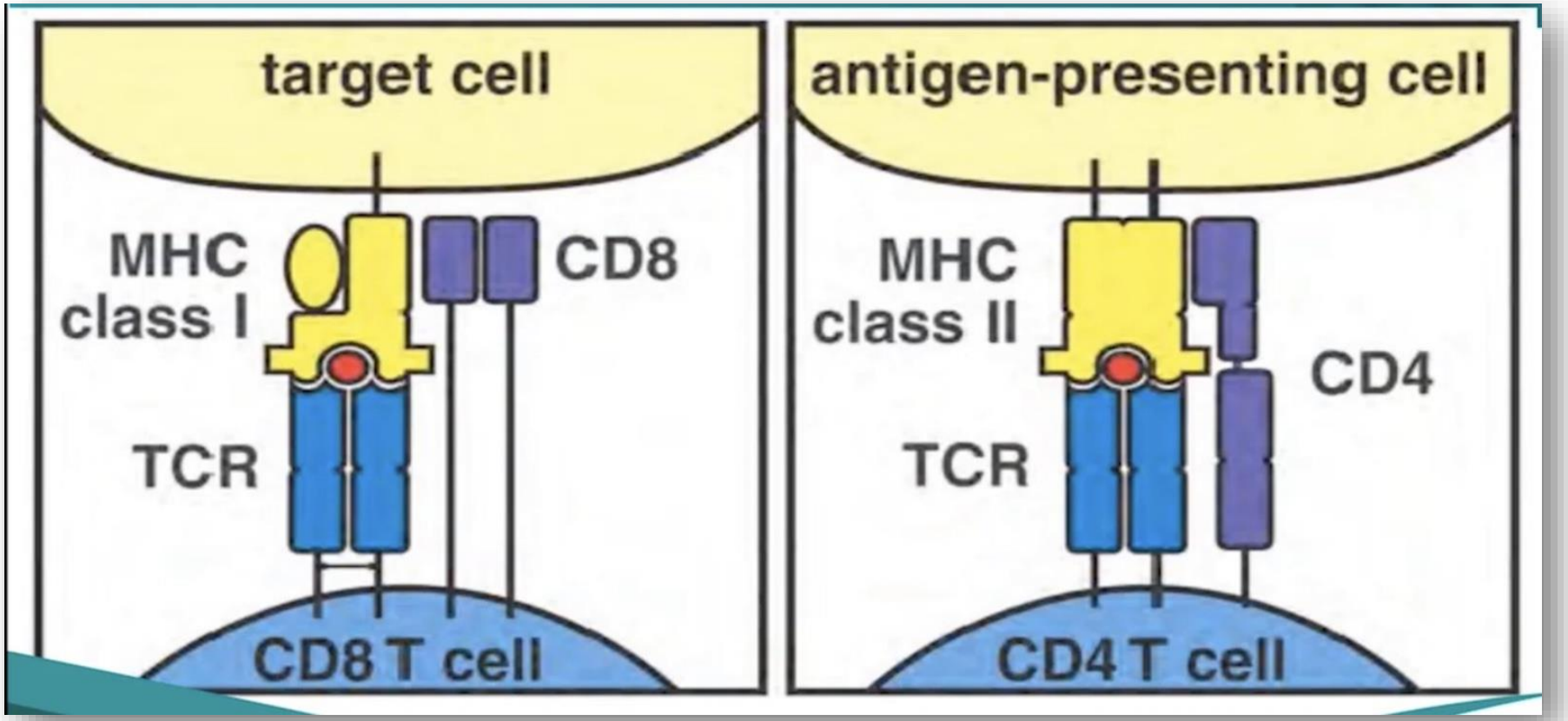
At the end of this lecture, student will be able to understand the following:

1- Definition of CMI
2- Steps of CMI
3- Superantigen

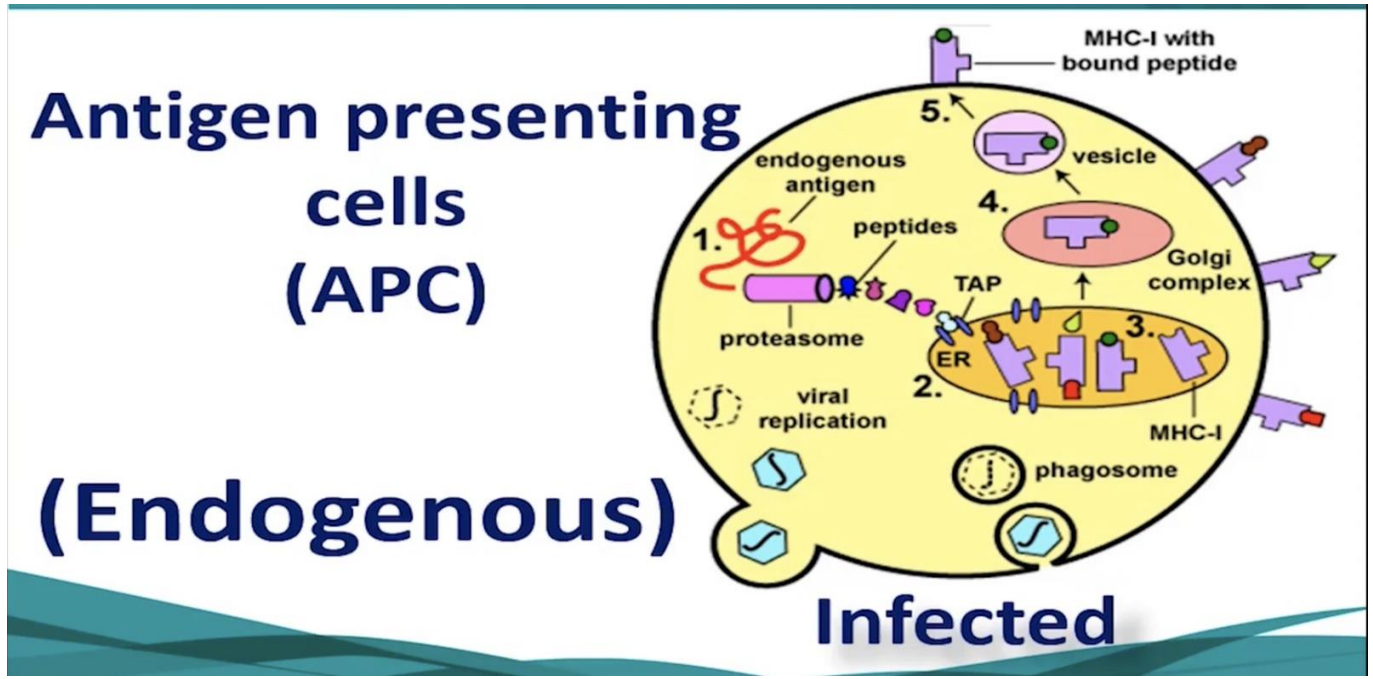


Facultative intracellular bacteria like T.B

Try to draw a diagram to show by which CD4 and CD8 cells are bind.



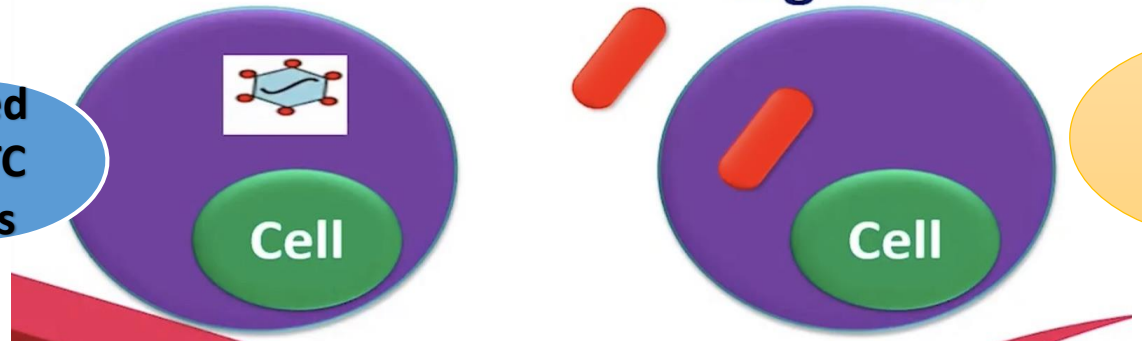
This is one of APCs called macrophages Infected by a virus (endogenous peptide on MHC class I. Macrophages can be infected by bacteria like T.B which resist intracellular killing mechanisms of MO, but can present exogenous peptide of T.B in association with MHC class I



III) Steps of CMI

A) Infected cells (virus/tumor)

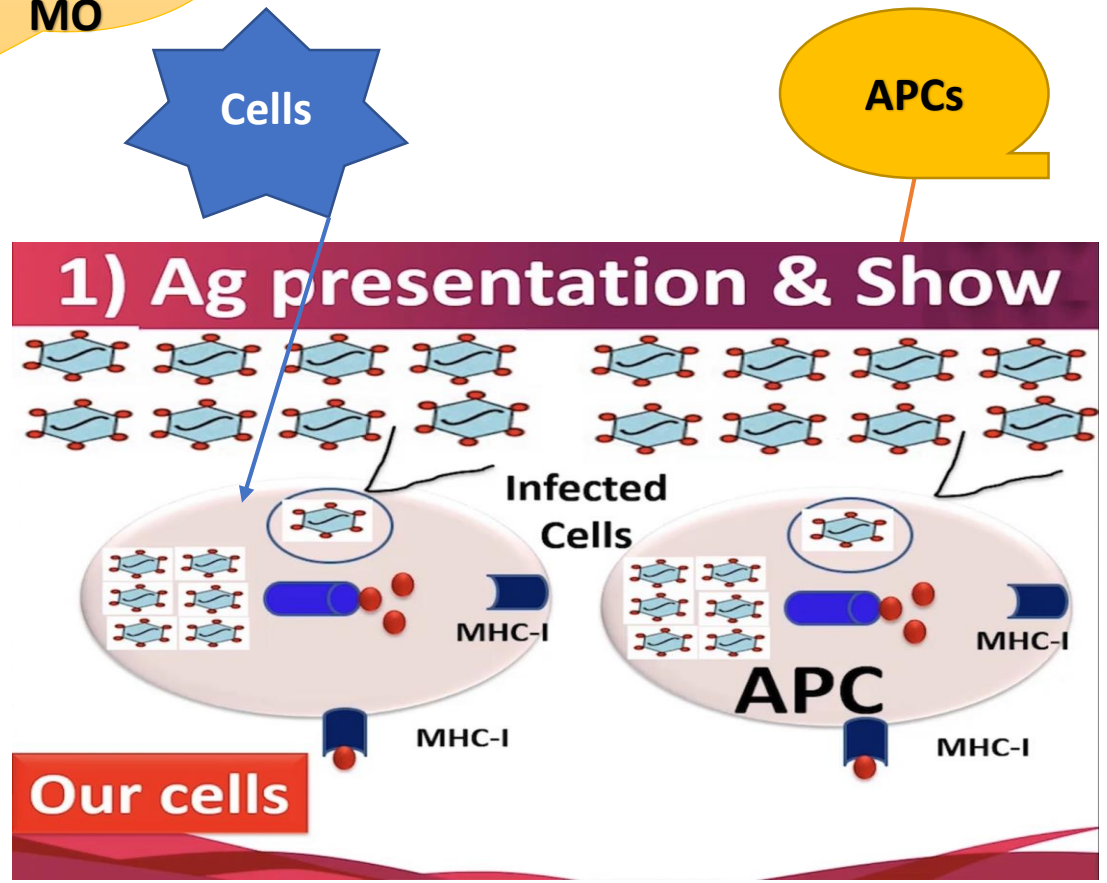
B) Facultative intracellular organism



A) Infected cells (virus/tumor)

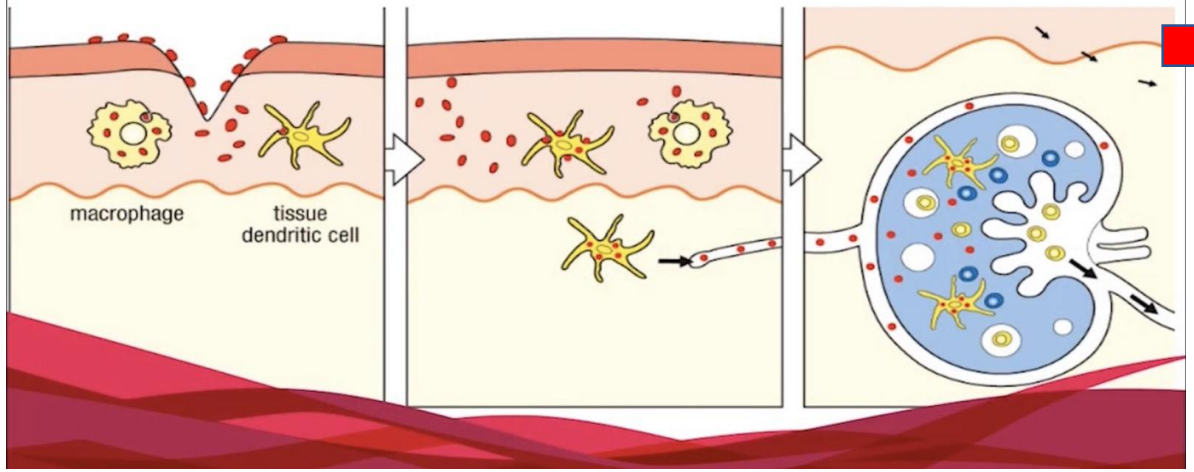
Naïve T cells → Effector T cells

1. Ag presentation
2. Activation & proliferation
3. Differentiation (Effector)
4. Killing by Tc cells



2) Activation & Proliferation

APC migrates into lymph nodes to meets the specific Tc cells (Activation)



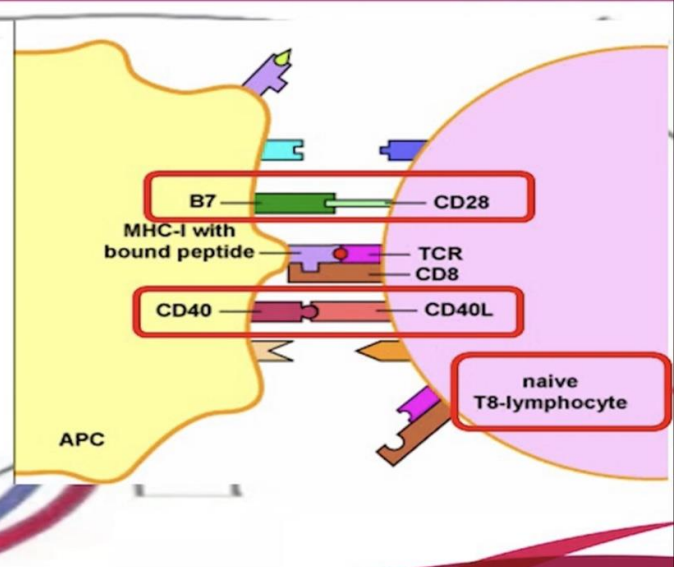
2) Activation of Tc cells

1st signal

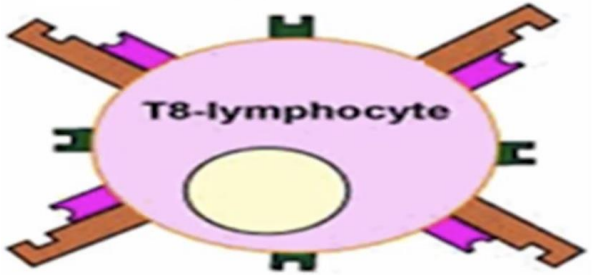
MHCI & TCR-CD8

2nd signal

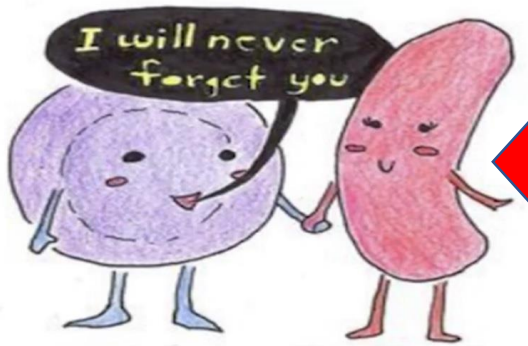
- **B7 & CD28**
- **CD40 & CD40L**



3) Differentiation of Tc cells

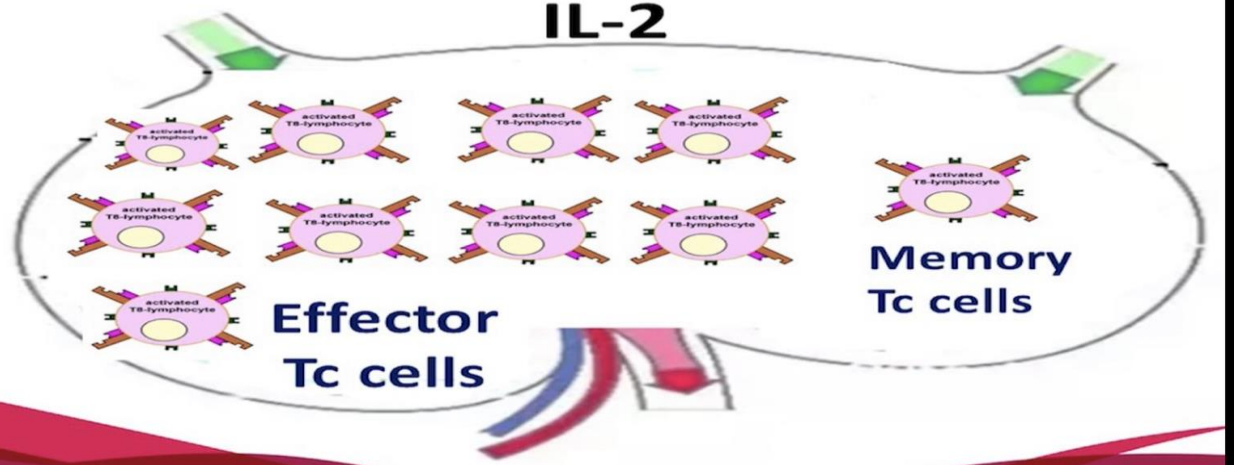


Effector cell (Sensitized cell)



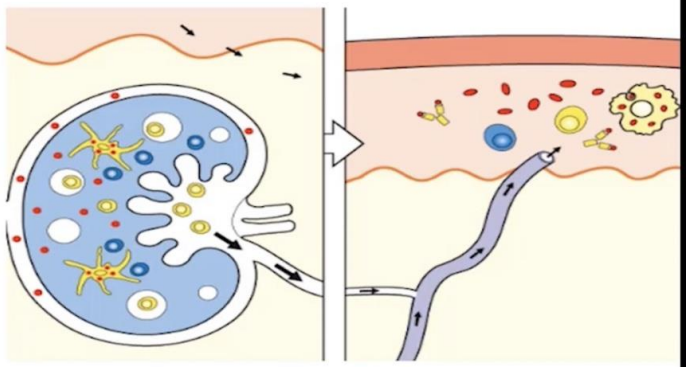
Memory cell

3) Proliferation & Differentiation of Tc



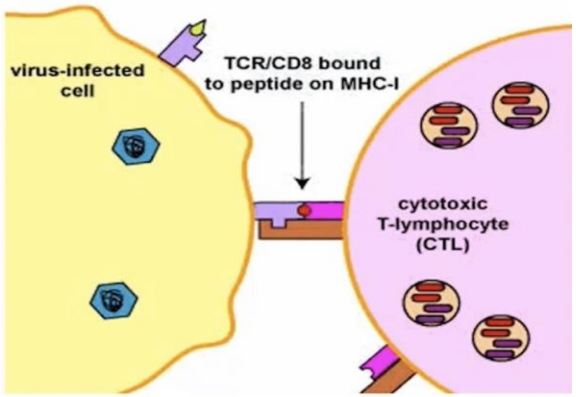
4) Killing by Tc cells (Perforin-Granzyme)

Effectors CD8 leave the lymph nodes to search for an infected cells (MHC I)



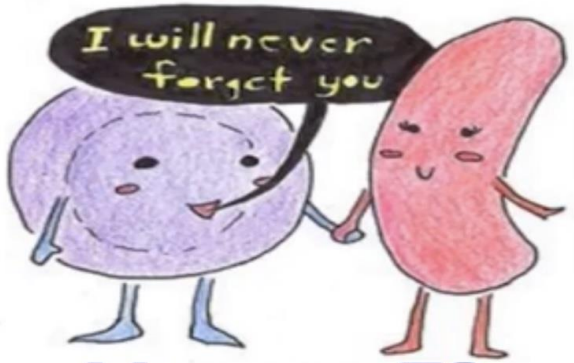
4) Killing by Tc cells (Perforin-Granzyme)

Effector CD8 kills by 1st signal



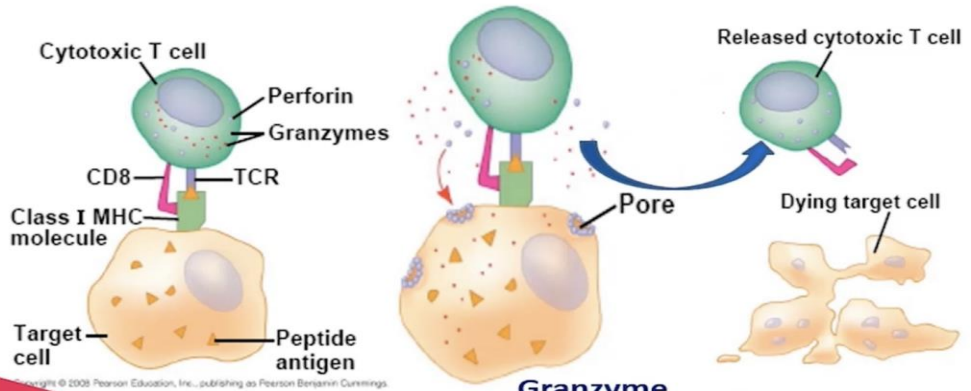
A) Infected cells (virus/tumor)

- Re-exposure to the same Ag
- kills by 1st signal



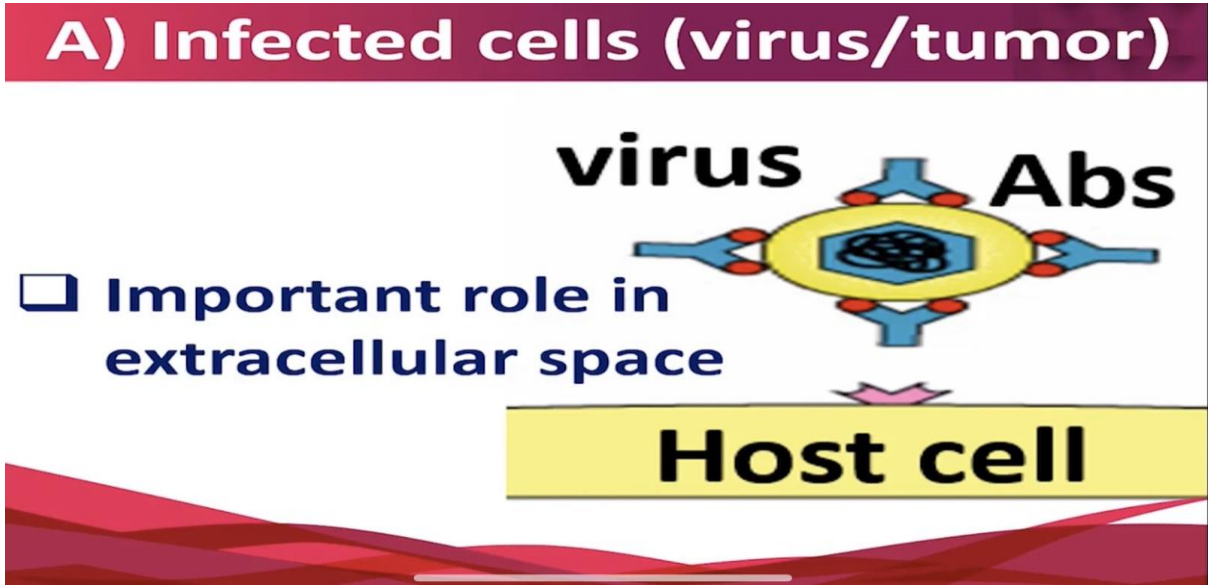
Memory T8 cells

4) Killing by Tc cells (Perforin-Granzyme)



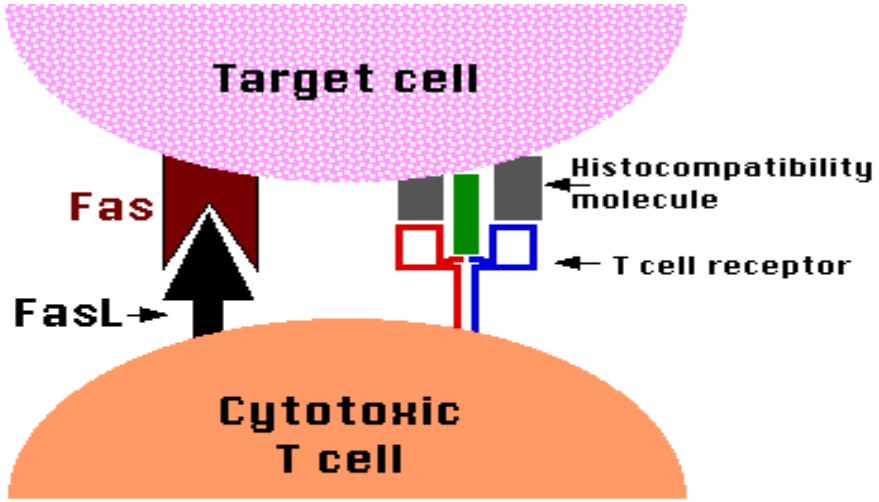
Inactive Caspases → Active caspases

Are antibodies have role in CMI?



Comparison between Naïve CD8 and effector CD 8 cells

Naïve CD8 cells	Effector CD8 cells
For activation	For killing
Slow	Fast
Triggered by 1st & 2nd signals	Triggered by 1st
Deal with APC only	Deal with somatic cells (Infected cells)



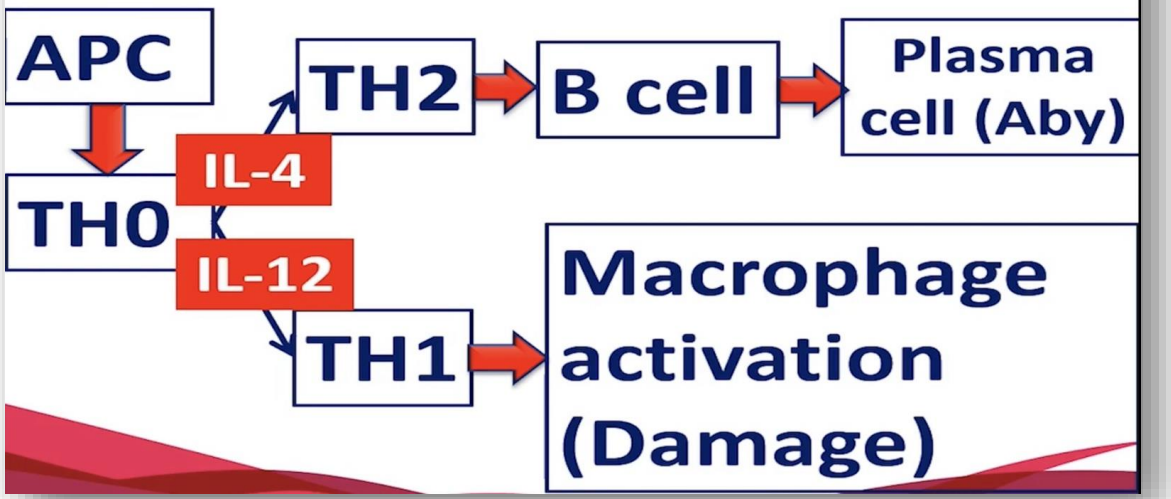
One method by which cytotoxic T cells induce their targets (e.g., virus-infected cells) to commit suicide (apoptosis)

B) Facultative intracellular organism

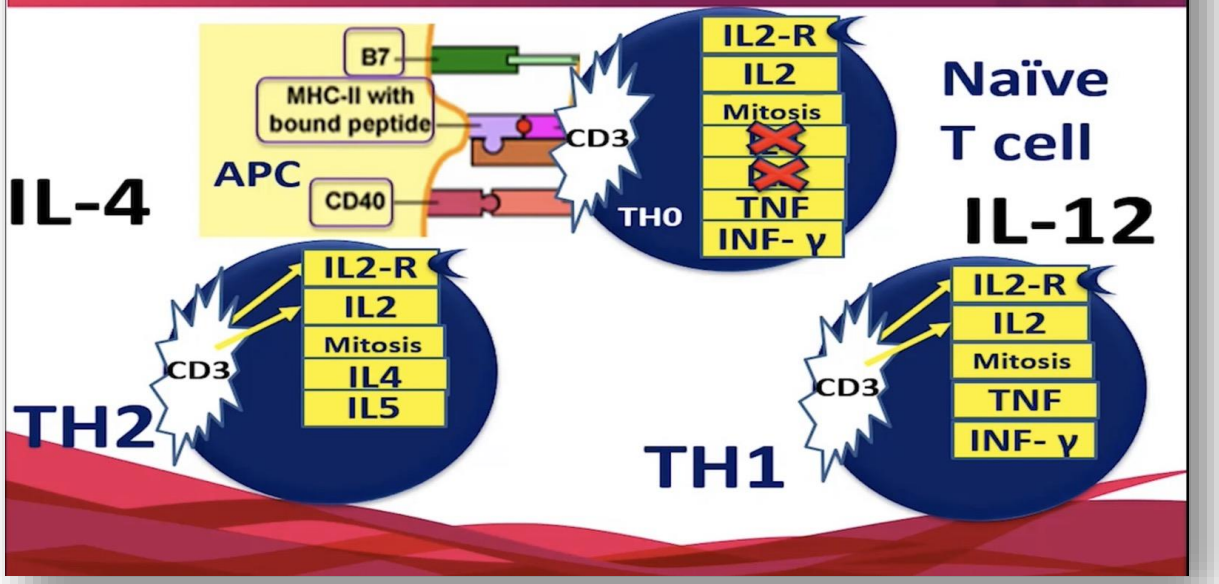
Naïve T cells → Effector T cells

1. Ag presentation
2. Activation & proliferation
3. Granuloma formation

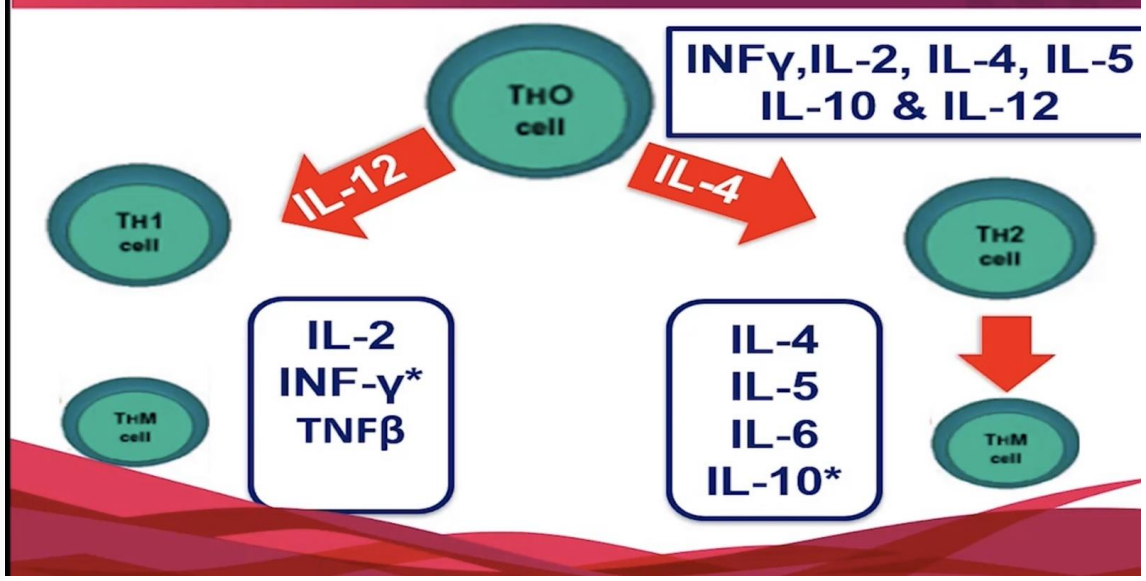
T-helper cell



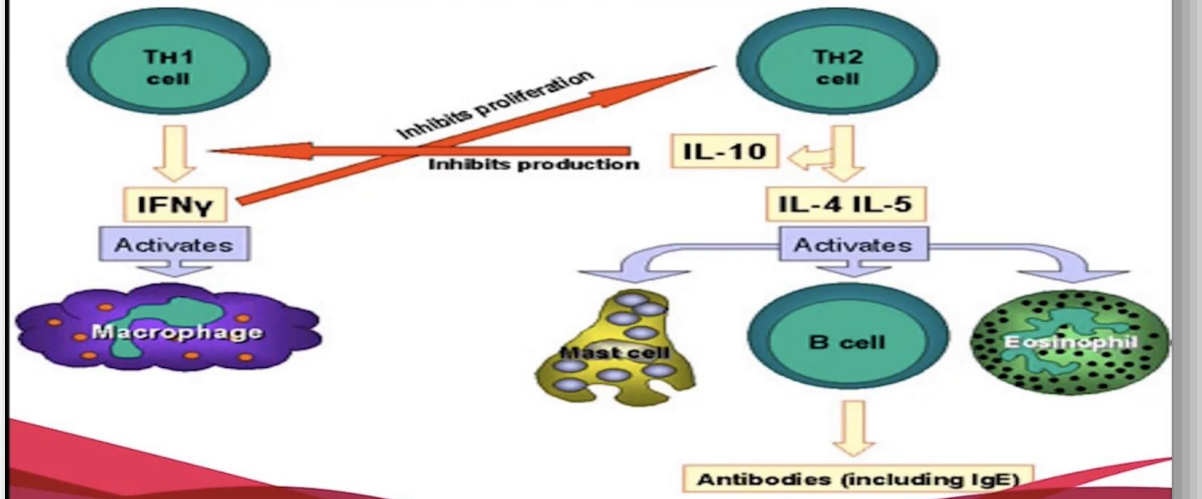
T-helper cell



B) Facultative intracellular organism



B) Facultative intracellular organism

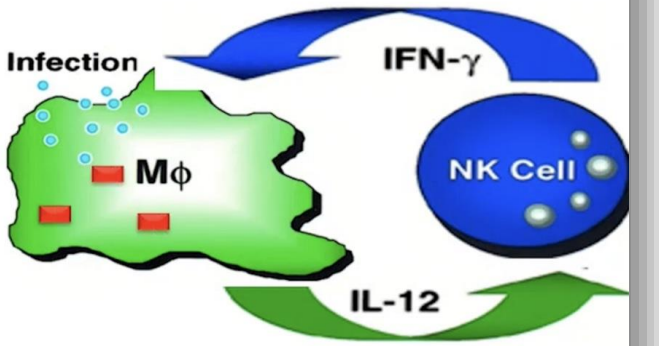


1) Ag presentation

Macrophage Secrete IL-12

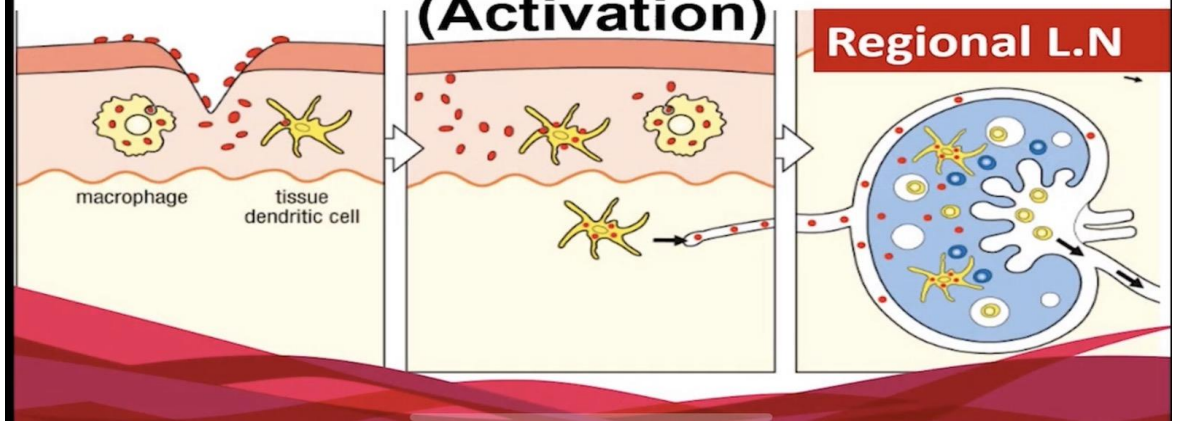
NK cells

INF- γ



2) Activation &proliferation

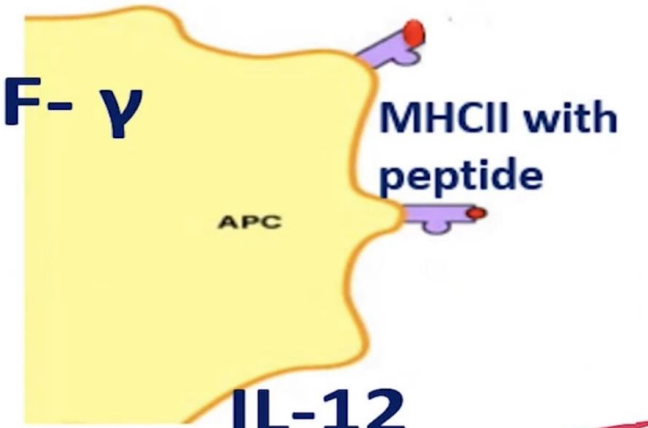
APC migrates into lymph nodes to meets the specific TH cells (Activation)



1) Ag presentation

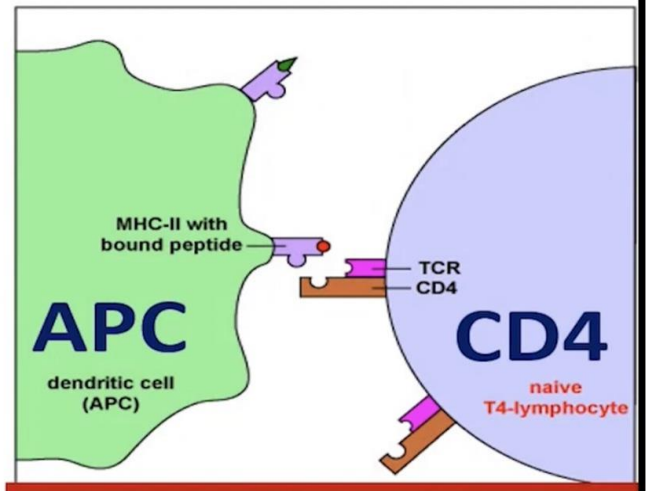
Ag Presentation (APC) (Exogenous)

INF- γ



2) Activation &proliferation

APC The only cells that can activate Naïve T helper cells



APC get Suitable TCR

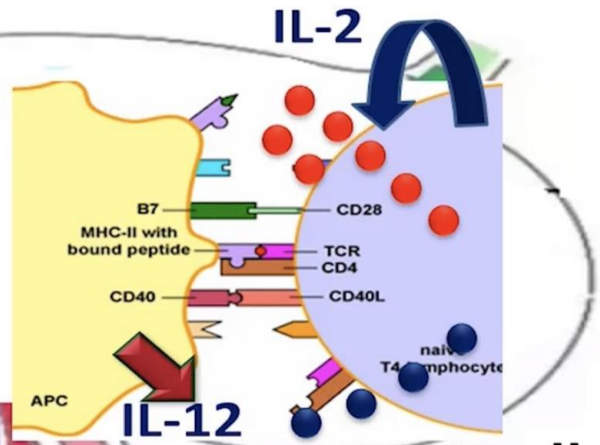
2) Activation &proliferation

1st signal

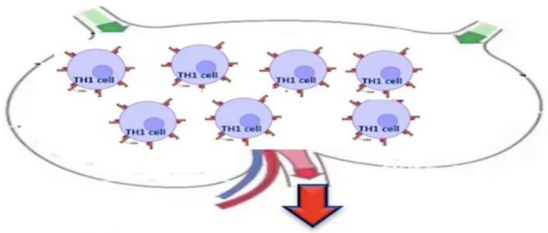
MHCII & TCR-CD4

2nd signal

- B7 & CD28
- CD40 & CD40L

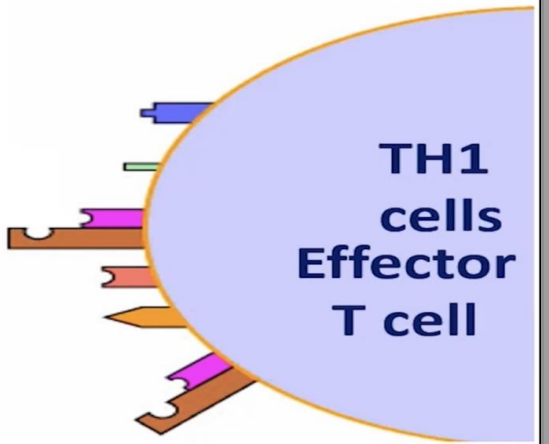


3) Granuloma formation



Effector TH1 cells enter circulation

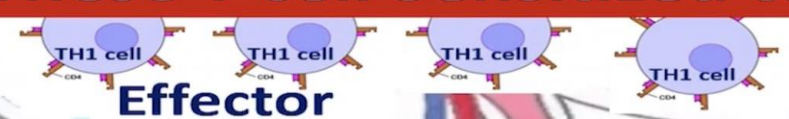
Travel to the site of infection



2) Activation &proliferation

Clonal expansion IL-2

These T cell Sensitized to TB

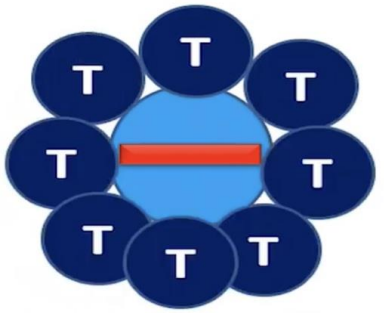


Effector cells

Enlarged L.N

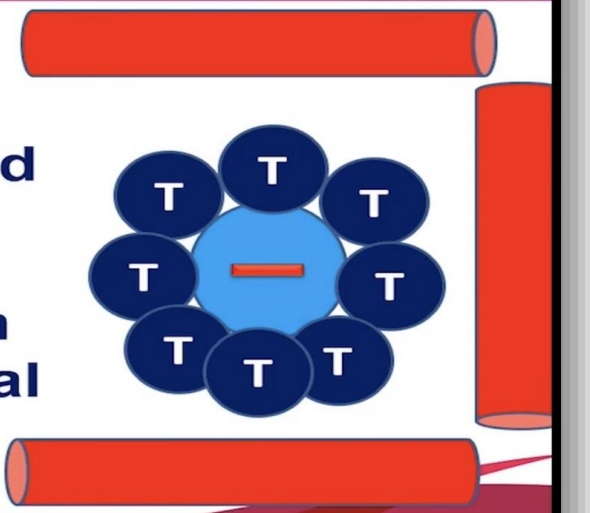
3) Granuloma formation

- Sensitized T cell
- Proliferation of lymphocytes (IL-2)



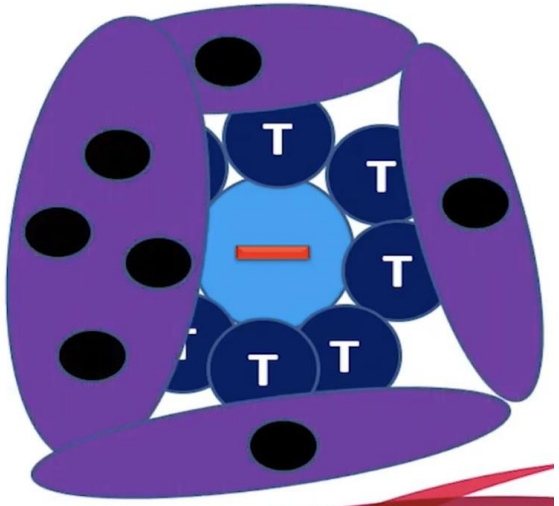
3) Granuloma formation

- TH cells produced TNF
- TNF act on Microcirculation (Activate endothelial cells)



3) Granuloma formation

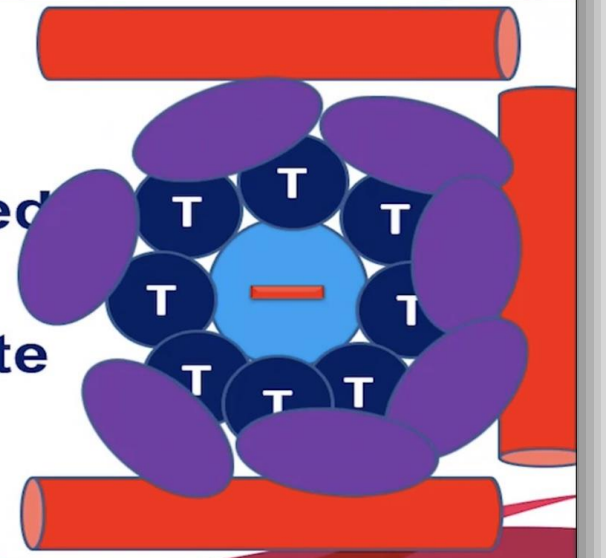
- Under the influence of INF-γ
- Each epithelioid cell fused with other (Giant cell)



3) Granuloma formation

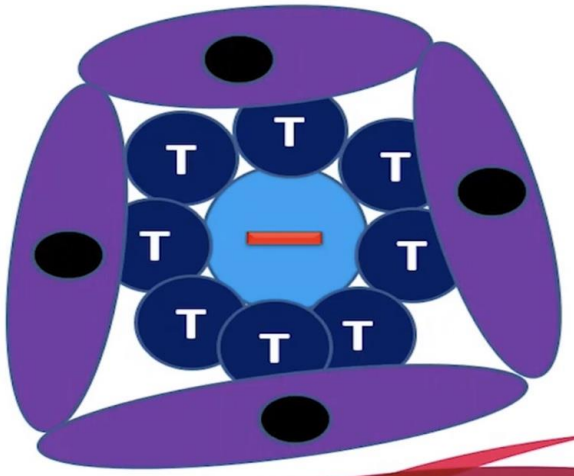
- TH cells produced INF-γ

(Attract and activate Monocytes (macrophage)



3) Granuloma formation

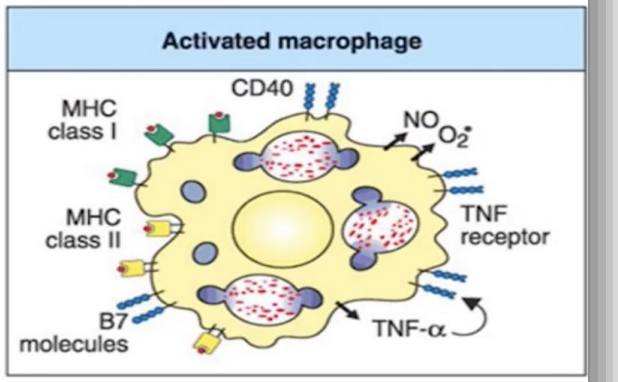
- Macrophages change into Epithelioid cells INF- γ



3) Granuloma formation

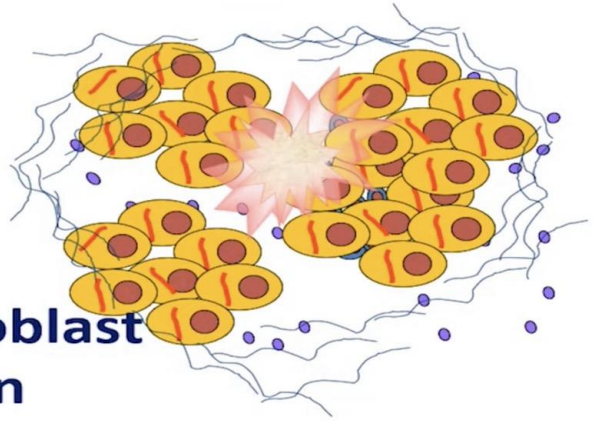
- INF- γ activate macrophage
  - Oxygen free radicals
  - Nitric oxide

Tissue damage (Type IV)



3) Granuloma formation

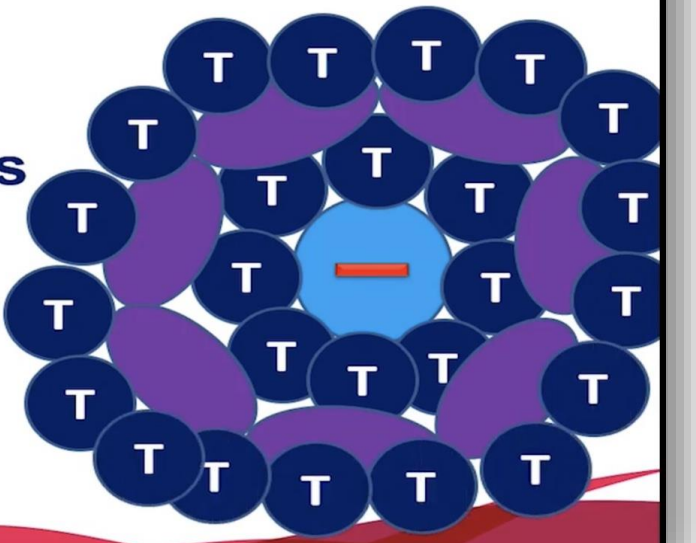
- Platelet derived growth factor (PDGF)



- Fibrocyte into Fibroblast produced collagen (fibrotic reaction)

3) Granuloma formation

- Epithelioid cells attract lymphocytes (Granuloma)



Granuloma formation is a kind of immune response to localize intracellular pathogens that can not be killed but if several lesions develop at one organ like lung can damage that organ.

Brucellosis cause granulomatous lesions in bone marrow. Explain how Brucella cause garnuloma

Imagine what will be occurred when TH2 cells deal with a facultative intracellular instead of THI?

- No macrophage activation
- No granuloma formation

(No Localization of infection)

In the lepromatous leprosy

Wrong decision occurred by selection TH2

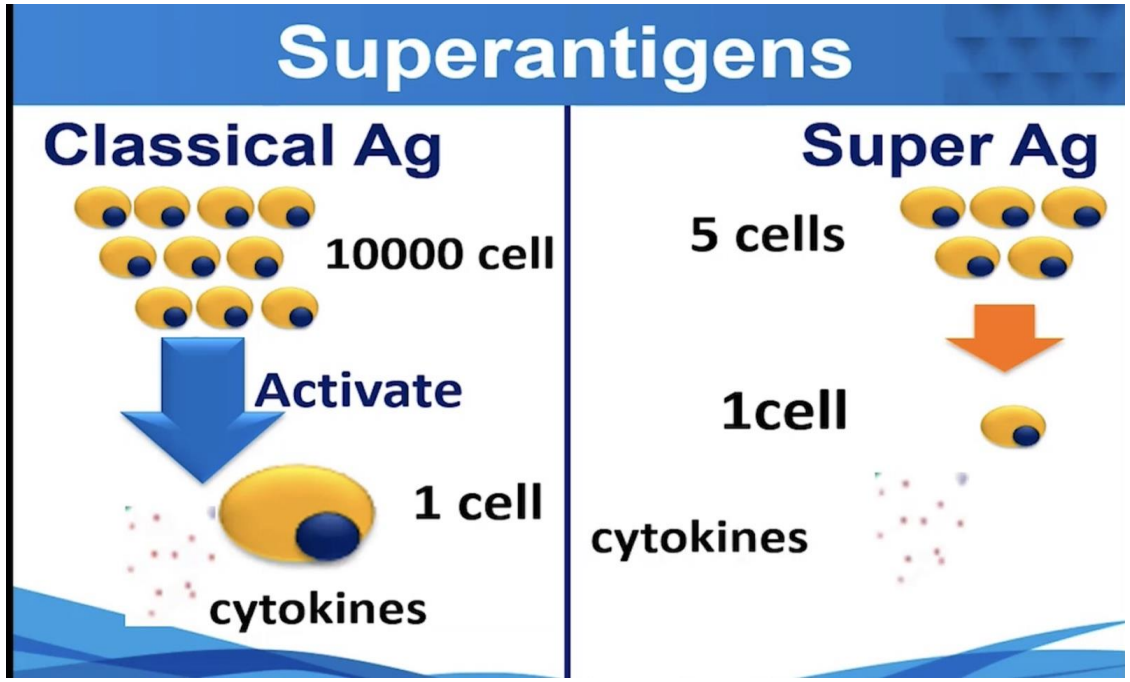
- No macrophage activation
- No granuloma formation

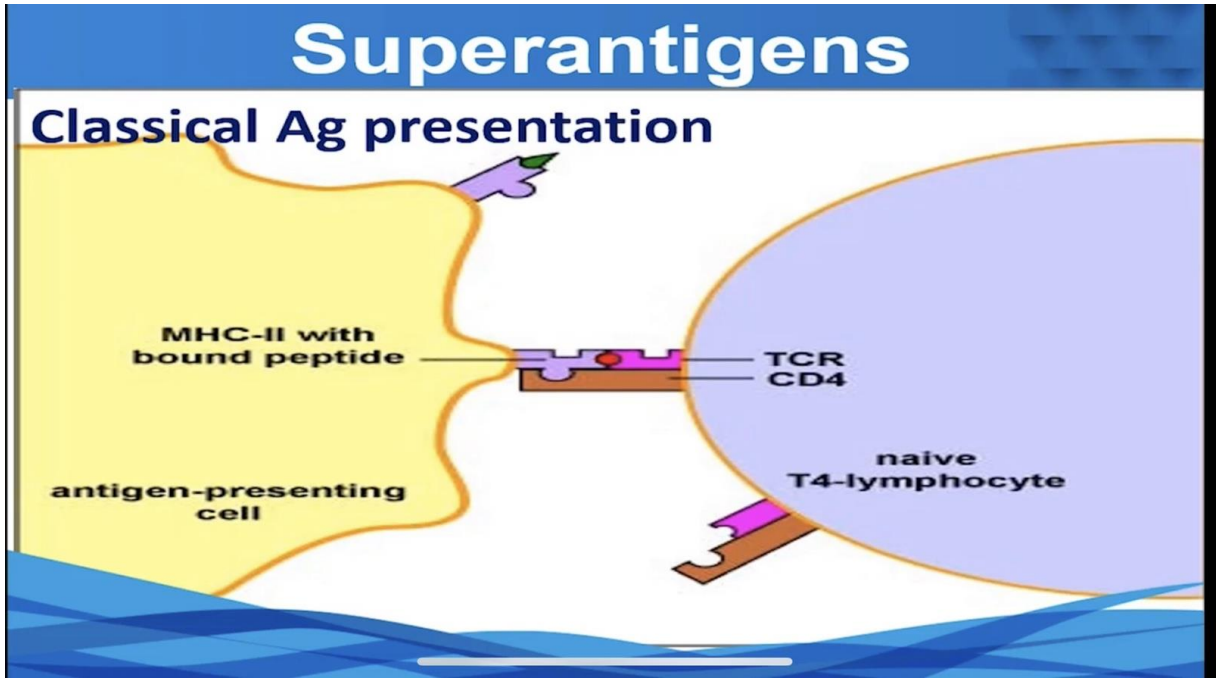
(No Localization of infection)

lepromatous leprosy

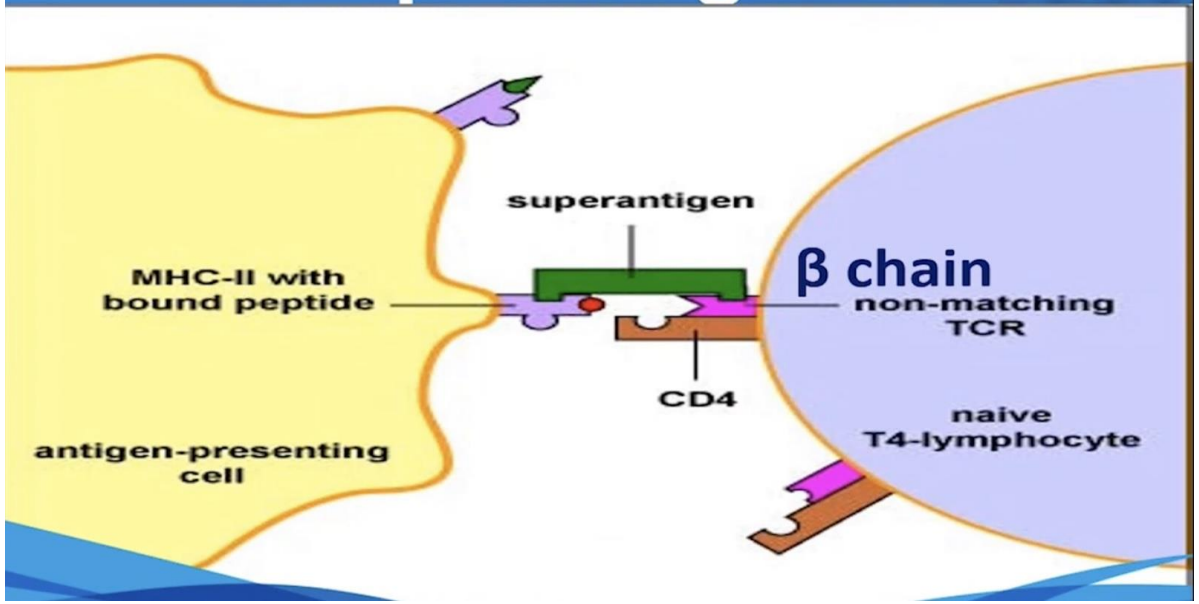
Any cell infected by intracellular organism must possess MHC I molecules in order to be able to show the peptide of intracellular organism to TC cell to kill the infected cell.

What will be happened when RBCs are infected by viruses?

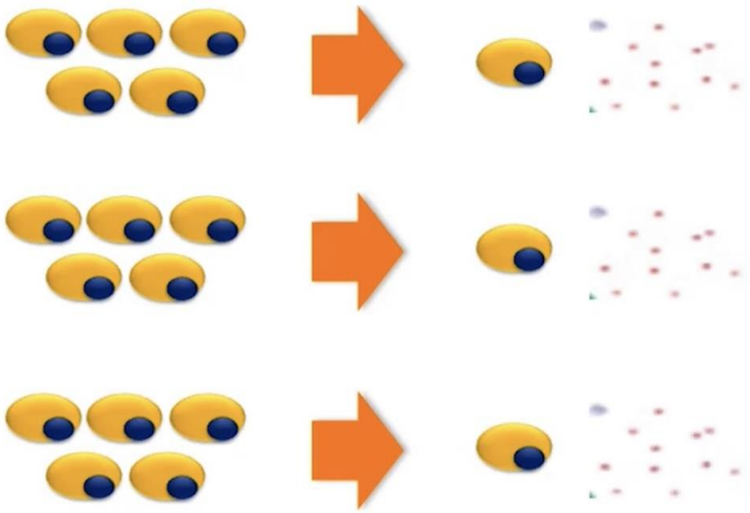




Superantigens



Superantigens



A high levels of cytokines IL-1 & TNF-α

Superantigens

- A high levels of cytokines IL-1 & TNF-α
- Fever | Diarrhea | Drop in blood pressure
- Shock
- Toxic shock syndrome

Predict

Predict what happened if person infected with organism release superantigen followed by ordinary Ag?

Superantigen

↓

Large amount of cytokines

↓

Immune system exhausted

Ordinary Ag

↓

It can not get immune response

↓

It's a plan from organism to deviate the immune system and make a disease

Which of the following immune cells are most effective at destroying intracellular pathogens?

- T helper cells
- B cells
- Antibodies
- T cytotoxic cells

Lepromine test is negative in lepromatous leprosy due to

- Absence of cell mediated immunity
- Absence of TH1 cells
- The main cells in this case are TH2
- TH2 produce IL-10, suppress CMI

Which of the following immune cells are most effective as localize the infection in facultative organism?

- T helper2 cells
- T cytotoxic cells
- T helper 1 cells
- Naïve T helper cells

CD28 molecule is

- Present on all T cells
- It binds to B7
- Necessary for T cell activation
- It is a primary signal

The function of CD3 that present in all T cells is

- Primary signal bet. TCR & MHCI
- Transmission signals from TCR to inside cells
- Activation bet. APC & T helper cell
- Activation between B cells & T heper cells

Increasing the production of toxic oxygen radicals, nitric oxide, and hydrolytic lysosomal enzymes; These are all benefits from the activation of ---------- by TH1 cells

- Macrophages
- NK cells
- TH2 cells
- T cytotoxic cells

Superantigens are bind

- outer portion of T helper cells &(APCs)
- inside specific MHC II antigens on APCs
- APC & TH1 cells
- APC & T cytotoxic cells

Naïve T helper cells converted into TH1 cells by

- IL-4
- IL-5
- IL-12
- IL-10