

# Immunology

## Teamwork 437

### Lecture (3): Cell Mediated Immunity

Color index:

**IMPORTANT**

Definition

Explanations + notes

Extra (or gray)

Objectives

- To describe antigen recognition by T cells.
- To describe the pathways involved in processing endogenous and exogenous antigens.
- To discuss self MHC restriction in Ag presentation to T cells.
- To describe the induction of cell mediated immunity (Chronic Inflammation).



Reference  
Kuby Immunology 7<sup>th</sup> Edition 2013  
Chapter 8 Pages 270-276  
Chapter 11 Pages 357-381

Note: there`s explanatory videos on some pictures

## Antigen Presenting cells

- Monocytes: Peripheral blood.
- Macrophages: Tissues.
- Dendritic cells (Langerhans cells): Lymphoid tissue, skin.
- B-cells: Lymphoid tissue, Blood.
- **Langerhans cells** are dendritic **cells** (antigen-presenting immune **cells**) of the skin and mucosa, and contain organelles called Birbeck granules.

## Cell Mediated Immunity (CMI)

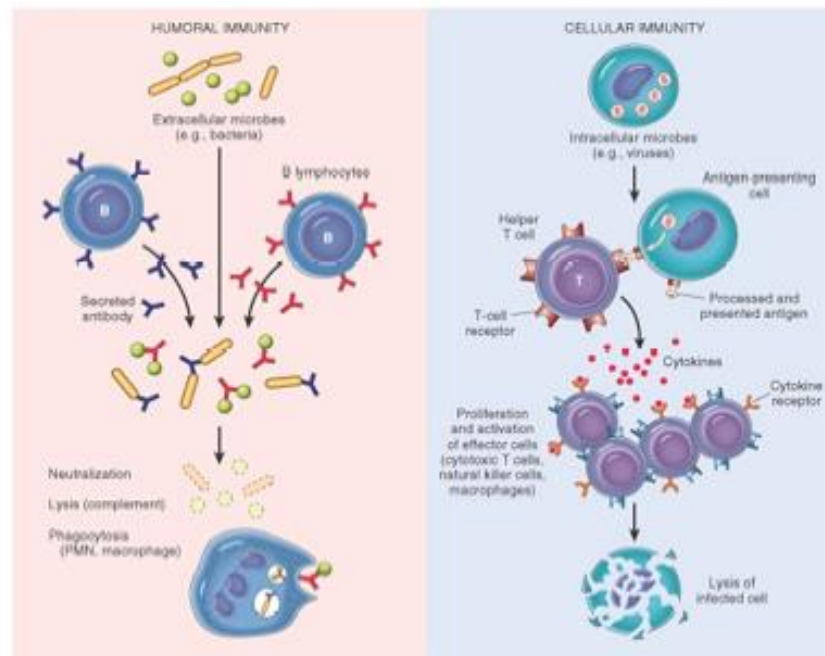
- T cells (lymphocytes) through their receptors bind to the surface of other cells (Antigen Presenting Cells) that display the processed antigen and trigger a response.
- Mononuclear cell inflammatory process usually associated with chronic inflammation.

**Antigen + MHC** → **T-lymphocytes** → **Immune responses**

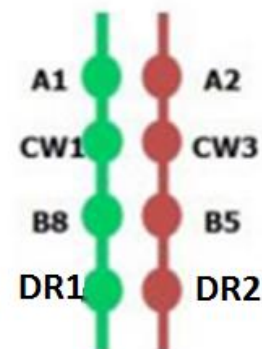
## Major Histocompatibility Complex (MHC)

- Major histocompatibility complex (MHC) proteins were discovered for the first time when tissue transplantation started.
- The success of tissue and organ transplantation depends upon the match of donor's and recipient's "**human leukocyte antigens**" (HLA) encoded by HLA genes.
- Genes for HLA proteins are clustered in the MHC complex located on **the short arm of chromosome 6**.
- Each individual has two "**haplotypes**" two sets of these genes one paternal and one maternal.
- A **haplotype** (haploid genotype) is a group of genes in an organism that are inherited together from a single parent.
- MHC Class I molecules are found on the surface of virtually all nucleated cells.
- MHC Class II molecules are normally present of the surface of antigen presenting cells such as:

1. **Macrophages**
2. **Dendritic cells**
3. **B cells**



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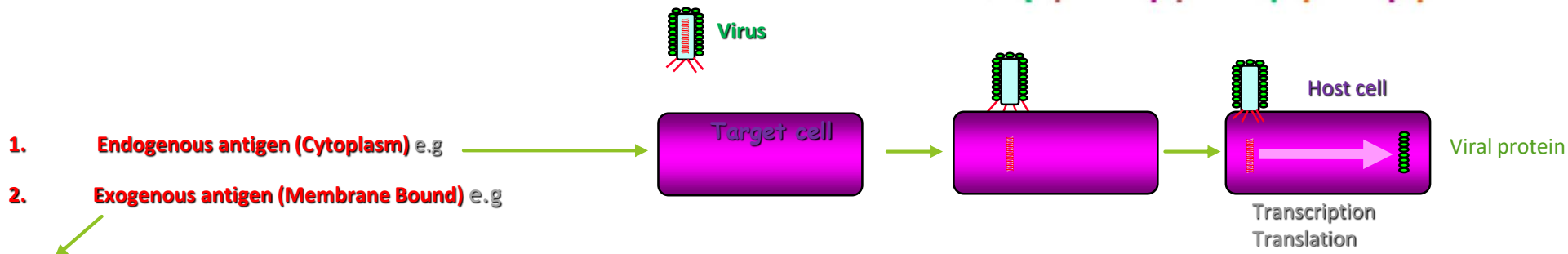
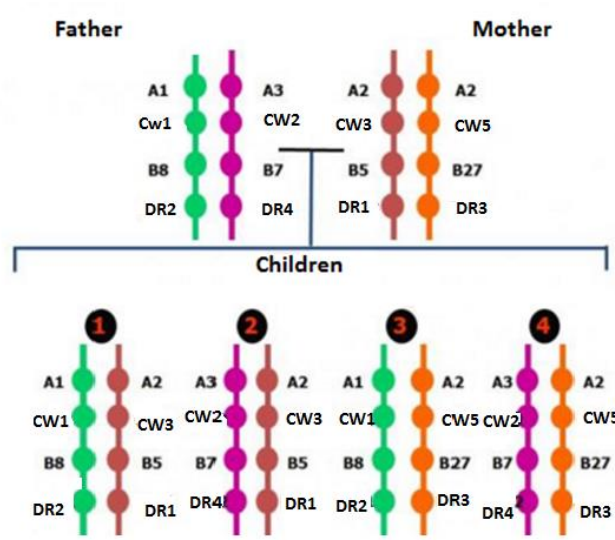
# Biologic Importance of MHC

## Antigen recognition

- T cytotoxic (CD8) cells kill virus infected cells in association with class I MHC proteins.
- T helper (CD4) cells recognize antigens in association with class II MHC proteins.
- This is called MHC restriction**

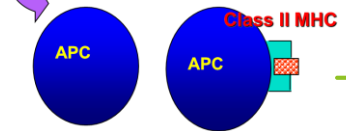
## Transplantation

- Success of organ transplant is determined by compatibility of the MHC genes.



- Endogenous antigen (Cytoplasm)** e.g
- Exogenous antigen (Membrane Bound)** e.g

(Exogenous antigen entered the body and encountered the APC)



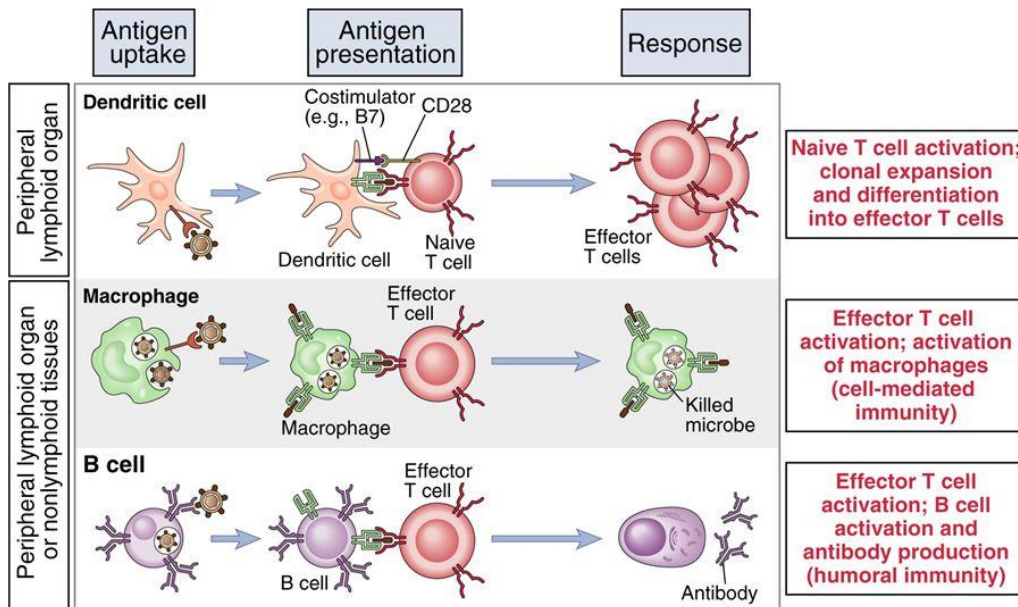
T-lymphocytes(CD4+ cells) → CMI (Cell Mediated Immunity)

- Antigen presenting cells
- Monocytes/Macrophages
  - Dendritic cells
  - Langerhans cells
  - B-cells

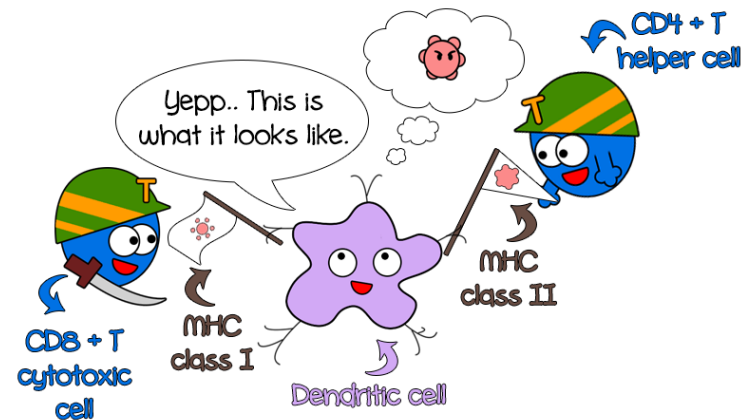
# Antigen Presenting Cells

Dendritic cells and macrophages digest invading microbes and then present the antigen of the microbe to lymphocytes in lymphoid organs.

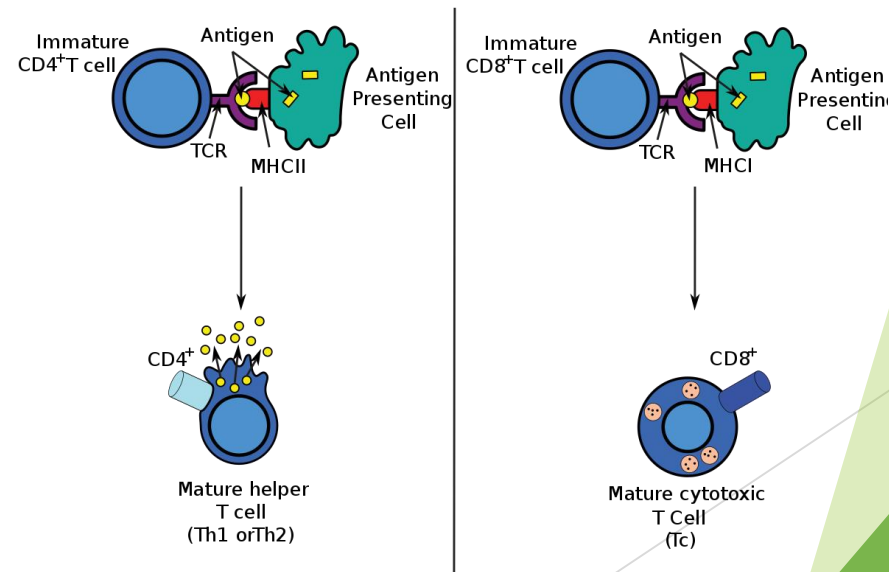
## Functions of Different Antigen Presenting Cells



Abbas & Lichtman, Cellular and Molecular Immunology, 5th ed. W. B. Saunders 2003

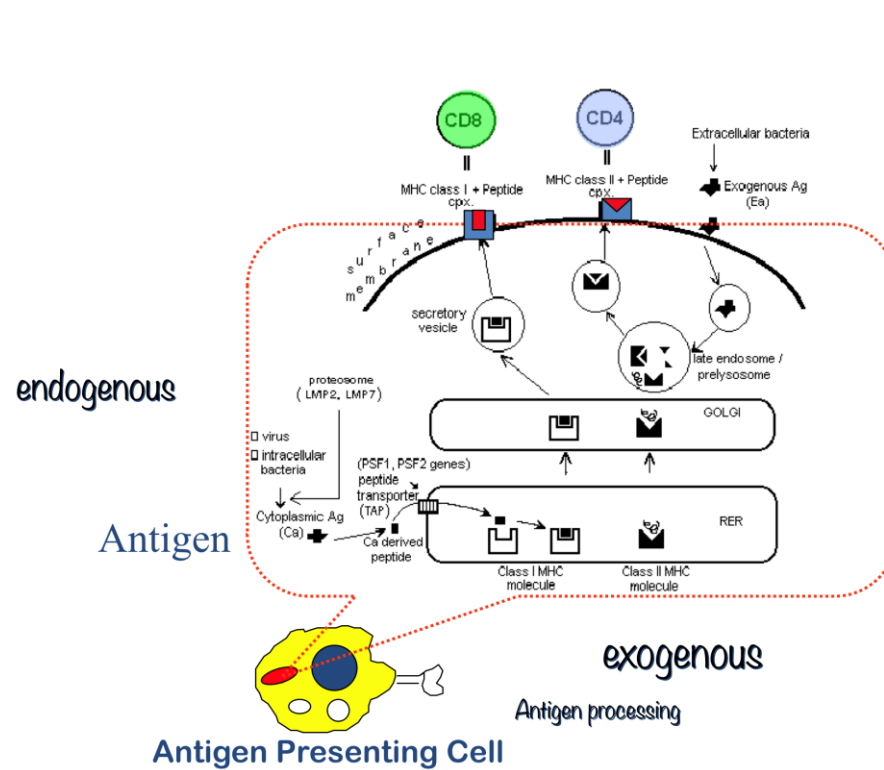
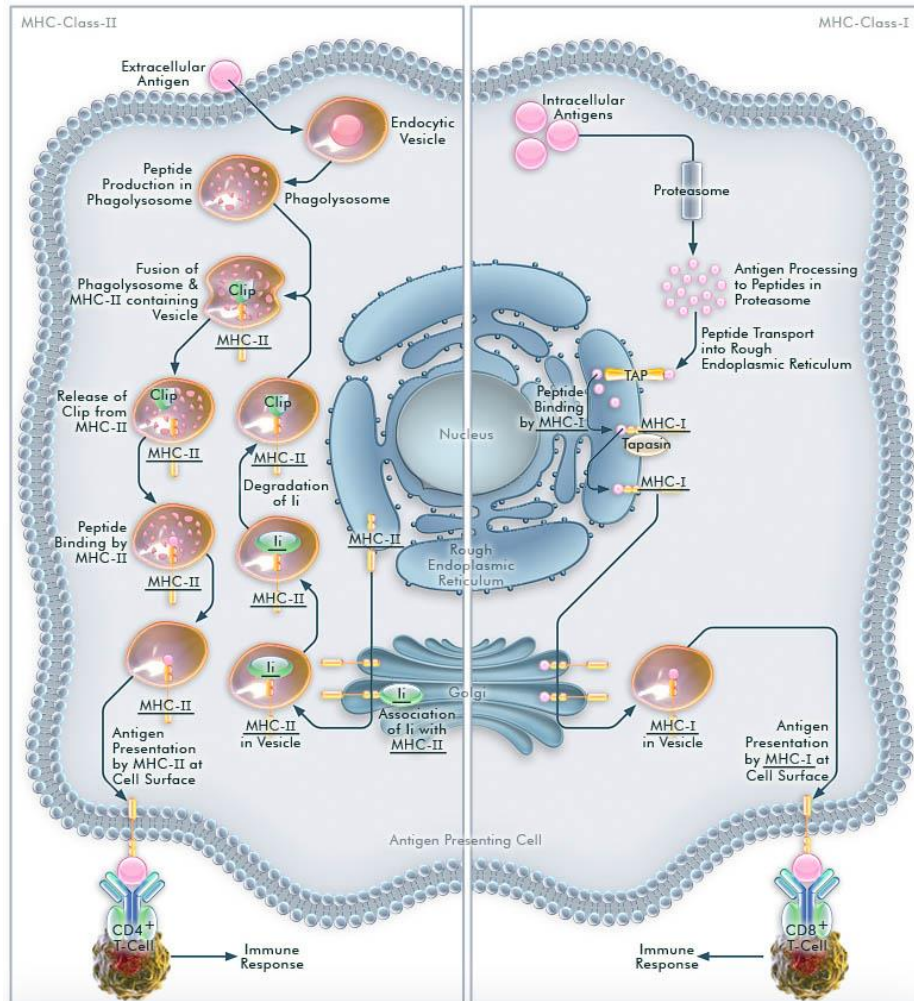


Antigen presentation by Immense Immunology Insight



# Endogenous & Exogenous antigen

This is the difference between endogenous and exogenous antigen:



# Two signals are required for the activation of T cells:

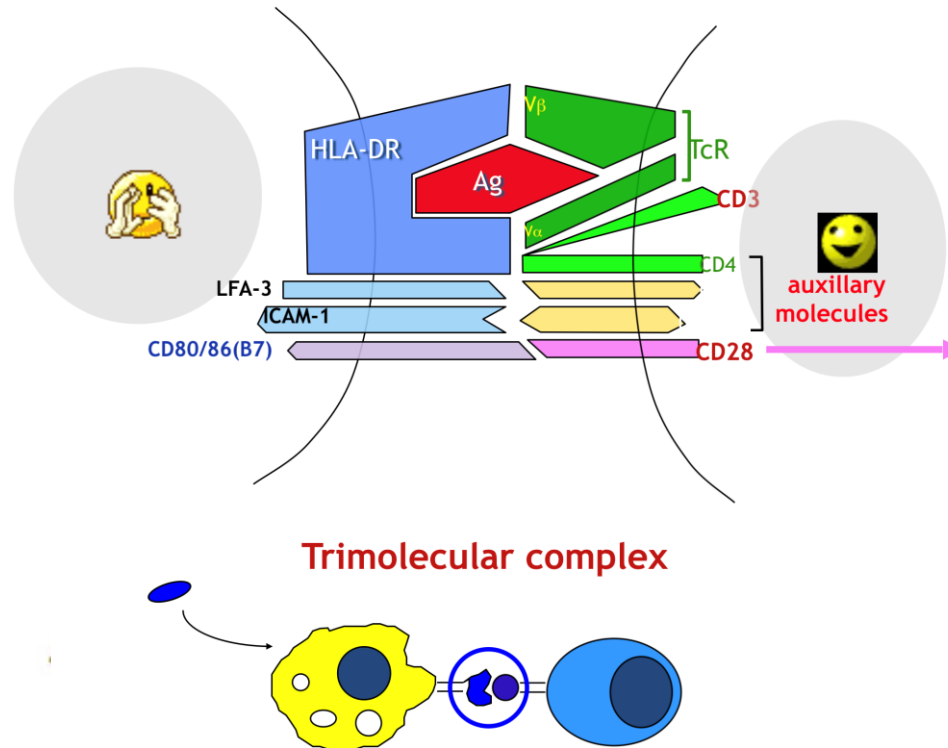
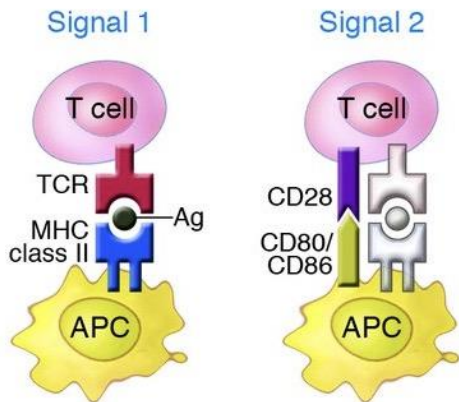
First signal:

Class II MHC + antigen - TCR  
IL-1, LFA-1 with ICAM

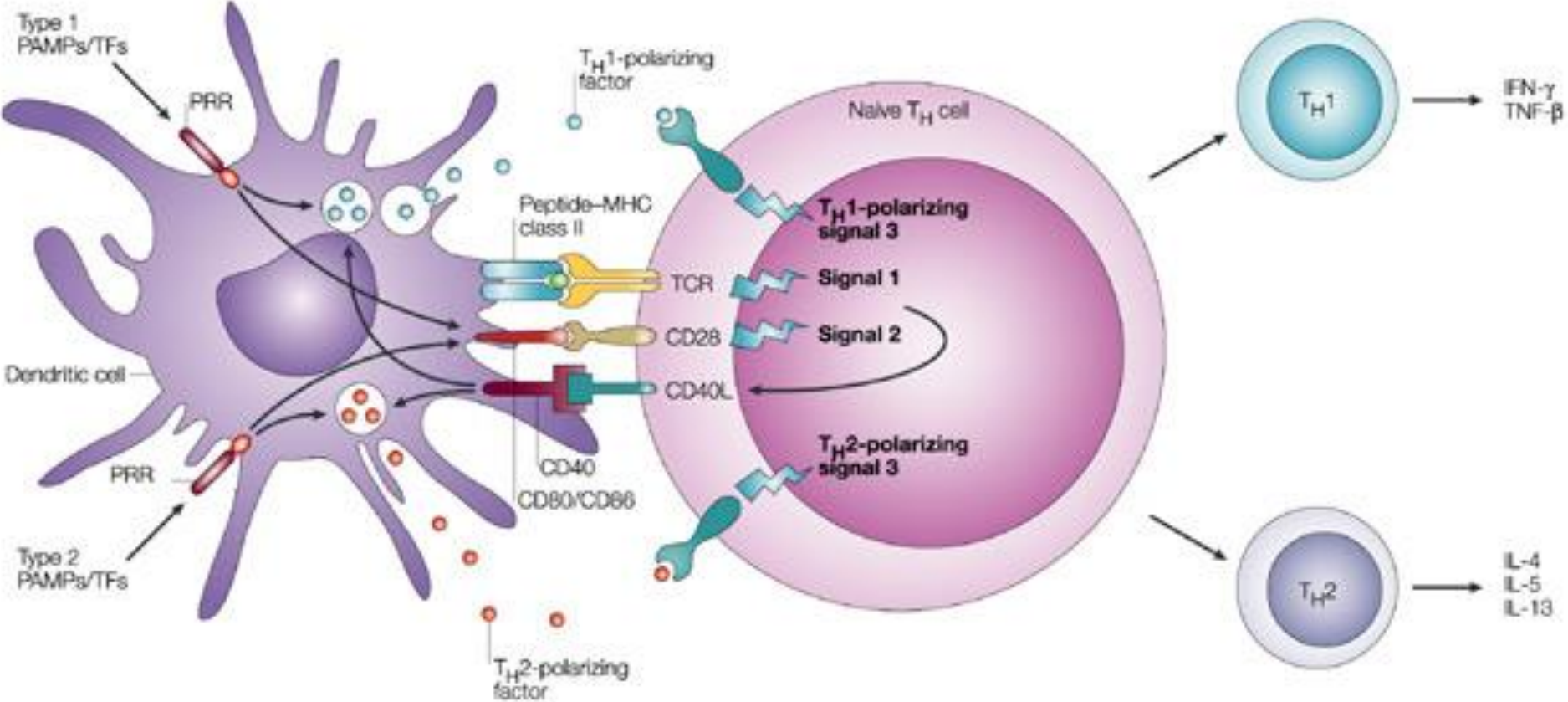
Second signal (Costimulatory signal)

B7 on APC interacts with  
CD28 on lymphocyte

Doctor's question:  
Is there any possibility for T-cells to activate without the second signal?  
Answer: Impossible



# Illustrative Diagram:



# T lymphocytes ("T cells"): CMI

## Subsets include:

- CD4+ helper T cells enhance CMI and production of antibodies by B cells
- CD8+ cytotoxic T lymphocytes (CTLs) that kill virus-infected and tumor cells

## Out come of T helper cell activation:

### Production of IL-2 and its receptor

Effector and regulatory cells are produced along with "memory" cells

IL-2 is also know as T cell growth factor

Proliferation of antigen specific T cells

IL-2 also stimulates CD8 cytotoxic cells

### Doctor's note:

- T-cells that enhance CMI are also called inflammatory T-cells (TH1).
- T-cells that enhance production of antibodies are also called inflammatory T-cells (TH2).
- IL2 is considered a cytokines and it's important in the regulation of the response action. It's also important in differentiation and maturation.
- Interferons are important in fighting viral disease

### Production of Interferons

Enhances anti-microbial activity of macrophages



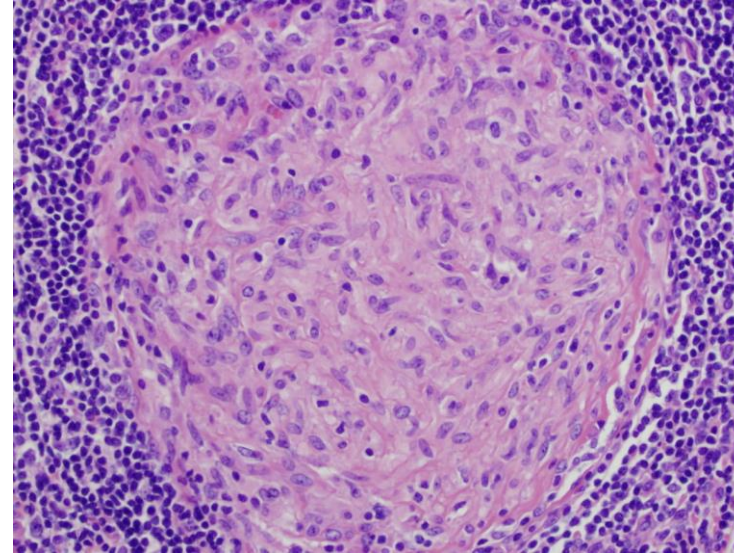
# Granuloma Formation (Chronic Inflammation, e.g. TB)

## What you see is:

A group of macrophages with macrobacteria inside it. Still propping response (inflammation), so it can get populated by Th1 that will form granulomas.

## What is happening:

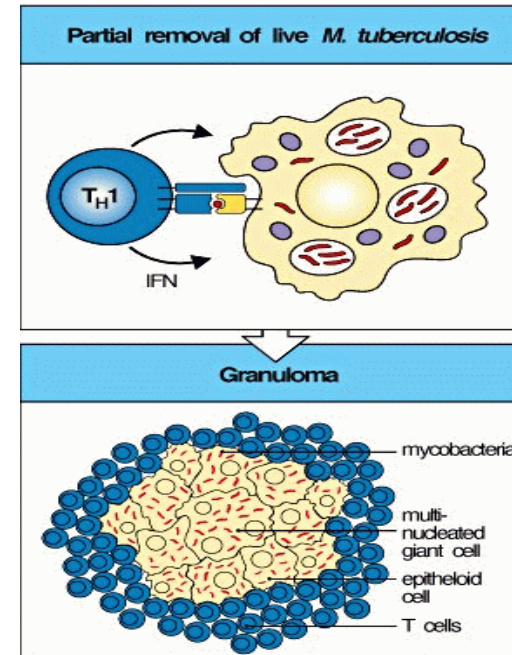
It's an APC in an intracellular organism, and because it's an APC, MHC class II will be exposed, that will lead to activation of T-helper cells (CD4). since it's Intracellular it will do a CMI response (Th1 inflammatory T-helper cell that will mediate chronic inflammation).

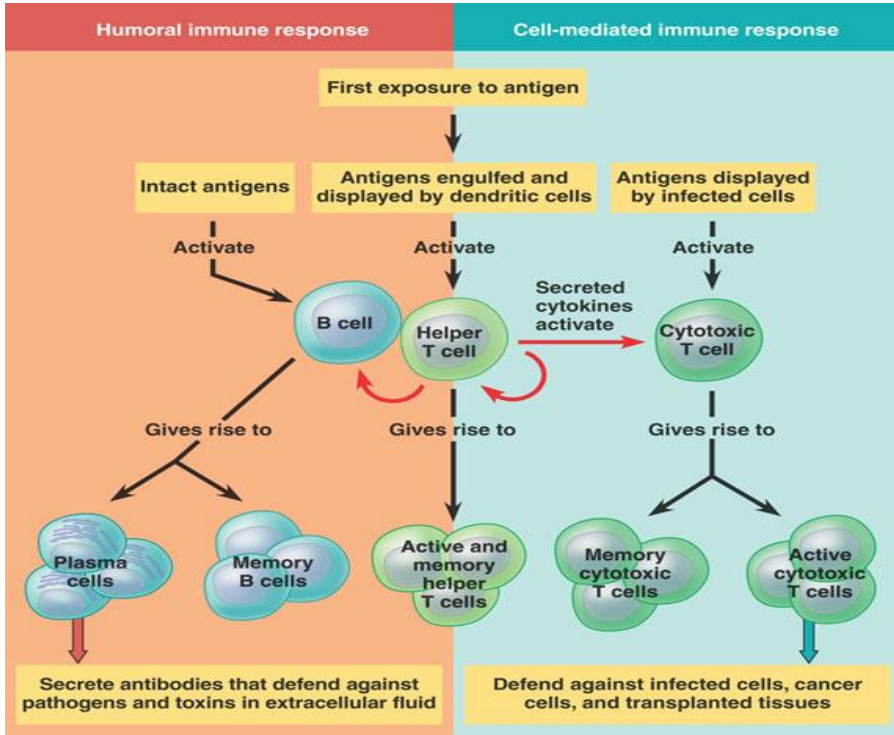


## Outcome of T helper cell activation

### Memory T cells

- Respond **rapidly** for many years after initial exposure to antigen.
- A large number of memory cells are produced so that the **secondary response (future encounter with the same antigen)** is greater than the primary.
- Memory cells **live for many years** and have the capacity to multiply.
- They are activated by **smaller amounts of antigen**.
- They produce greater amounts of interleukins.





Necklace Rash



## • Examples of Cell Mediated Immunity

1. Delayed type of hypersensitivity (DTH) reaction:
  - Ex. the tuberculin test
    - Mediated by CD4+ T cells and takes about 72 hours to develop.
2. Contact hypersensitivity:
  - Many people develop rashes on their skin following contact with certain chemicals such as nickel, certain dyes, and poison ivy plant.
  - The response takes some 24 hours to occur and like DTH, is triggered by CD4+ T cells.

## Take Home Message-SUMMARY

- Cell mediated adaptive immune response is specific and develops after exposure to a pathogen (antigen).
- Initial antigen exposure results in generation of memory cells for a stronger and quicker response against future exposures to the same pathogen.
- It is usually associated with chronic infections.
- Antibodies are not involved.

### Quiz

1-The ..... Enhances anti-microbial activity of macrophages

A.TNS B.IL-2 C .interferon D. B7

2-the process in which B7 on APC interacts with CD28 on lymphocyte is called?

A. First signal B.Costimulatory signal C. the tuberculin test D.MHC restriction

3-Class II MHC interacts with ?

A. Th cell B. Tc cell C.B cell D. Eosinophil

4-An example for Delayed type of hypersensitivity is

A. nickel B. the tuberculin test C. certain dyes D. poison ivy plant

5-you can't find MHC Class I molecules in

A. macrophages B. neurons C. hepatic cells D.RBC

6- MHC complex located on the

A. short arm of chromosome 6  
B. short arm of chromosome 9  
C. long arm of chromosome 6  
D. long arm of chromosome 9

7-the cell that kills virus-infected and tumour cells is

A. CD8+ B.CD4+ C. macrophages. D. B lymphocytes

8- the cell that produces IL-2 is

A. CD8+ B.CD4+ C. macrophages. D. B lymphocytes

9-Cell mediated adaptive immune response is specific and develops after exposure to a/an

A. antibody B. antigen. C. interferon. D.TNS

10- which of the following is not an Antigen Presenting cell

A. Monocytes. B. Dendritic cells. C. B lymphocytes D. Neutrophils

1-C  
2-B  
3-A  
4-B  
5-D  
6-A  
7-A  
8-B  
9-B  
10-D

## Team members

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## Team leaders

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- 3- عبدالله العمر
- 4- عبدالرحمن الطلاسي
- 5- عبدالعزيز الدخيل
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- 7- فيصل السيف
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