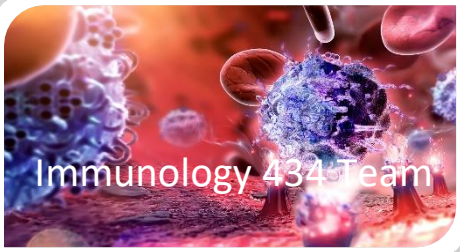

Lecture 3:
Cell Mediated Immunity (CMI)

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 meditated immunity (Chronic Inflammation).

Done by:

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Motivational quote

Our greatest weakness lies in giving up. The most certain way to succeed is always to try just one more time.

Thomas A. Edison

Red = Important Notes Orange = Further Explanation gray = Additional Notes Green = Examples

Navy: boys notes Purple: girls notes

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Adaptive vs. innate Immunity

Check me!!

Innate immunity	Adaptive immunity
➢ Physical barriers; • Skin • Mucosa secretion • Chemical protection ➢ Phagocytic cells. ▪ Neutrophils ▪ Monocytes\Macrophages ▪ Natural killer cells ▪ Other phagocytic cells (Langerhans cells, Dendritic cells ..ect) ➢ Chemical mediators ▪ Cytokines ▪ Chemokine's ▪ Interferon's ➢ Complement system	**Cell Mediated Immunity:** T cell mediated • activation of CD4+ Cells • Activation of CD8+ Cells **Humoral immunity:** B cell mediated • Activation of b cells • Transformation to plasma cells and secretion of antibodies. • Memory cells formation

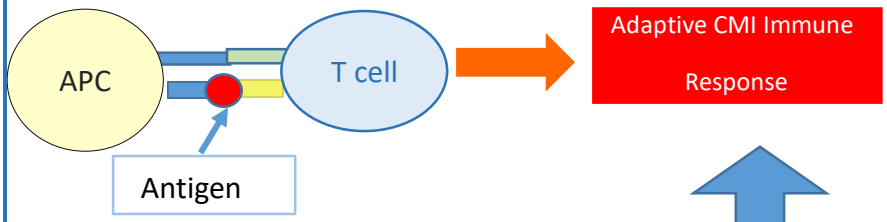
Cell Mediated Immunity (CMI)

It's the immunity that derive form T cells.

Characteris of CMI:

1-Antigenic specificity. 2- Diversity- can recognize > billion different antigens.

3-Immunological memory 4- Self vs nonself recognition

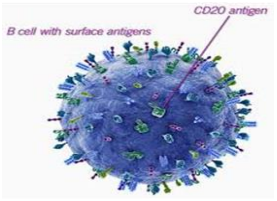


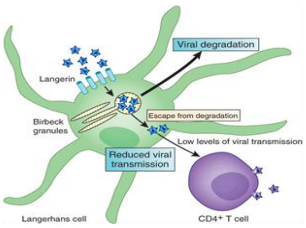
T cells (lymphocytes) bind to the surface of other cells APC (Antigen Presenting Cells) that display the antigen and trigger a response.

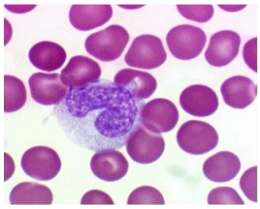
Note:

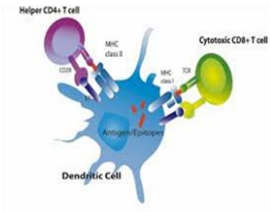
Mononuclear cell inflammatory process usually associated with chronic inflammations

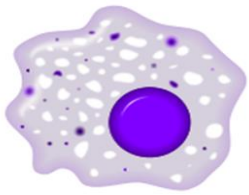
Antigen presenting cells (APC)







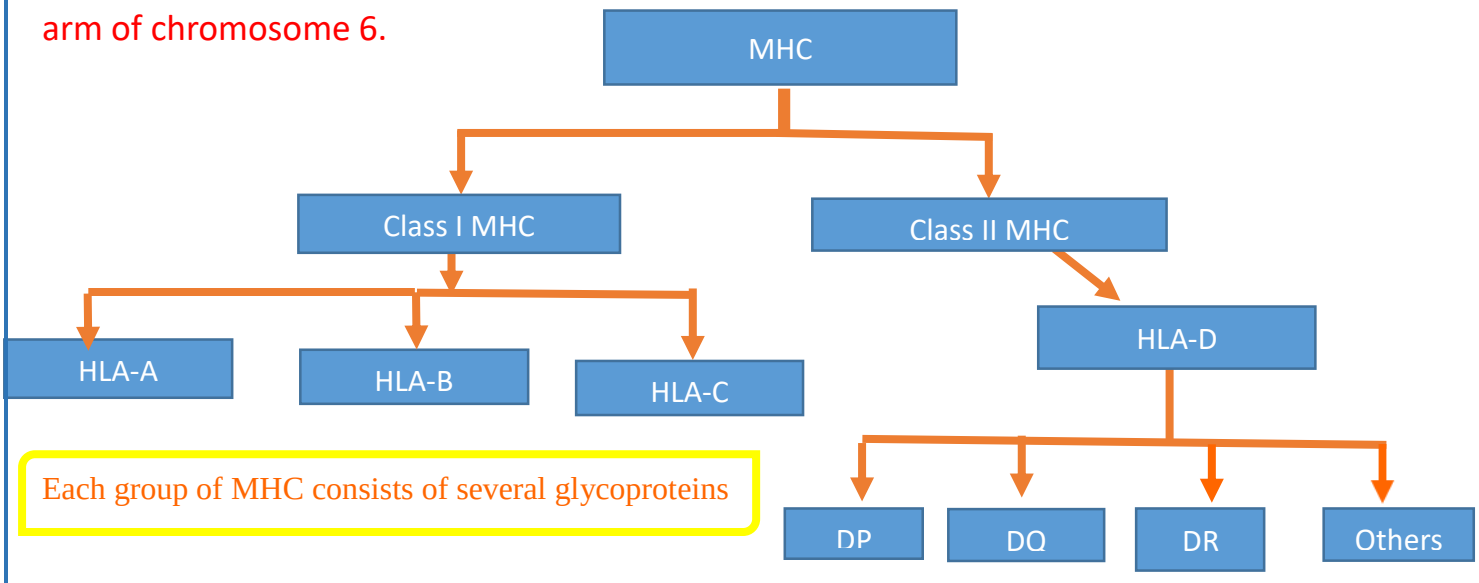




B cell	Langerhans cells	Monocyte	Dendritic cells	Macrophage
Site:	Site:	Site:	Site:	Site:
Lymphoid tissue	**Epidermis**	**Peripheral blood**	**Lymphoid tissues**	**Tissues**
Blood	(nonvascular layer of the skin covering the dermis)			

Major Histocompatibility Complex (MHC)

(MHC) proteins were discovered for the first time with when tissue transplantation started. A success transplantation of organ and tissue depends upon the **match of donor's and recipient's "human leukocyte antigens" (HLA)** encoded by HLA genes which is found in MHC on the short arm of chromosome 6.



Each group of MHC consists of several glycoproteins

- MHC Class I molecule is found on the surface of all nucleated cells.
  - As for Class II MHC is only found on the surface of antigen presenting cells

➢ Each individual has two "haplotypes" two sets of these genes one paternal and one maternal

MHC

Biologic Importance of MHC:

❖ **Antigen recognition**

1. T cytotoxic (CD8) cells kill virus infected cells in association with class I MHC proteins (because viruses are intracellularly proceeded by APC) **endogenous antigens**
2. Helper T (CD4) cells recognize antigen in association with class II MHC proteins (antigens which are extracellularly processed) **exogenous antigens**

- This is called MHC restriction.

❖ **Transplantation**

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

Antigen Presentation:

Check me!!

❖ **Endogenous antigen (Cytoplasm)**

When the antigen is endogenous it's processing starts in the cytoplasm than connect with class I MHC in RER than goes through Golgi to the surface of Antigen presenting cells membrane to present the antigen to CD8 Cytotoxic T cells. Examples of endogenous antigens are viruses, T.B. bacteria.

❖ **Exogenous antigen (Membrane Bound).**

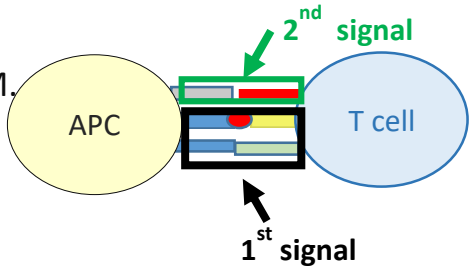
The antigen processing start in the membrane bind to the exogenous antigen than after it phagocytized a part of connect to class II MHC in the endosome than it's travels to the surface of the membrane presenting the antigen to CD4 Helper T cell.

Activation of T cells

- Two signals are required of activation of T cells:

1st is Class II MHC + antigen – TCR + IL-1, LFA-1 with ICAM.

2nd (Costimulatory signal)



B7 on APC interacts with CD28 on lymphocyte

CMI is the action and activation of T lymphocytes

CD 4+ T helper cell enhance CMI and production of antibodies by B cells.

CD8+ cytotoxic T lymphocytes (CTLs) that kill virus-infected and tumor cells.

- T cells CD 4+ activate cells e.g. macrophages, B cell through MHC class II
- T cell CD 8+ recognize the infected cell through MHC class I and kills it

Out come of T helper cell activation

Check me!!

- **Production of IL-2 and its receptor**

  IL-2 is also know as T cell growth factor.

  - Proliferation of antigen specific T cells.
  - Effector and regulatory cells are produced along with “memory” cells.
  - IL-2 also stimulates CD8 cytotoxic cells.

- **Production of Interferon**

  Enhances anti-microbial activity of macrophages.

- **Memory B cells**

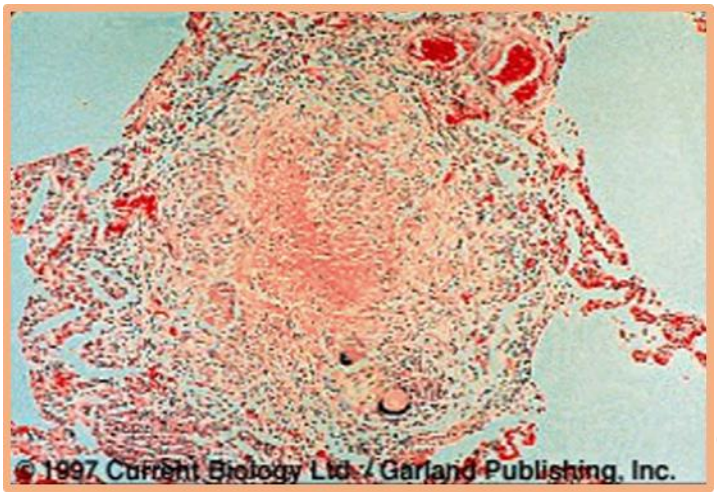
  - Respond rapidly for many years after initial exposure to antigen.
  - A large number of memory cells are produced that is why the secondary response is greater than the primary.
  - Memory cells live for many years and have the capacity to multiply
  - They are activated by smaller amount of antigen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

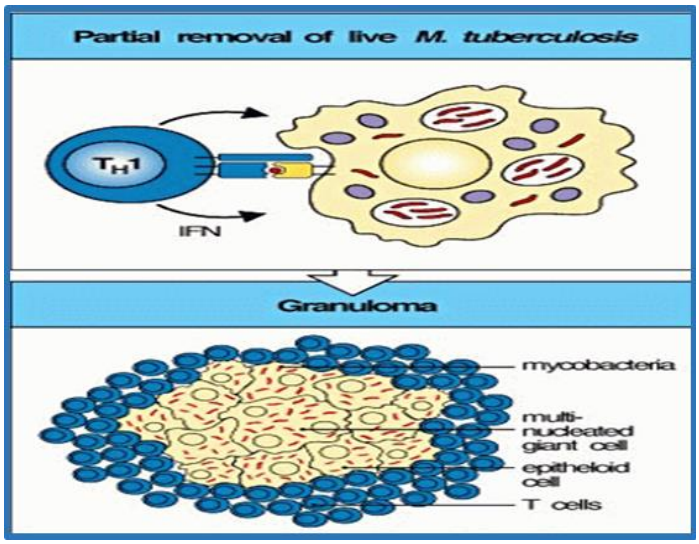
  Note :

  Memory cells available in CMI & Humoral response

Examples of Cell Mediated Immunity

An example of immune system response is Granuloma Formation which is the collection of lymphoid cells forming granules at the site of injure which under goes necrosis it’s a chronic inflammation that happens in T.B. cells involved are giant cells which are fused epitheloid cells, epitheloid cells which are a type of macrophages.





Examples of Cell Mediated Immunity

1. Delayed type of hypersensitivity (DTH) reaction:

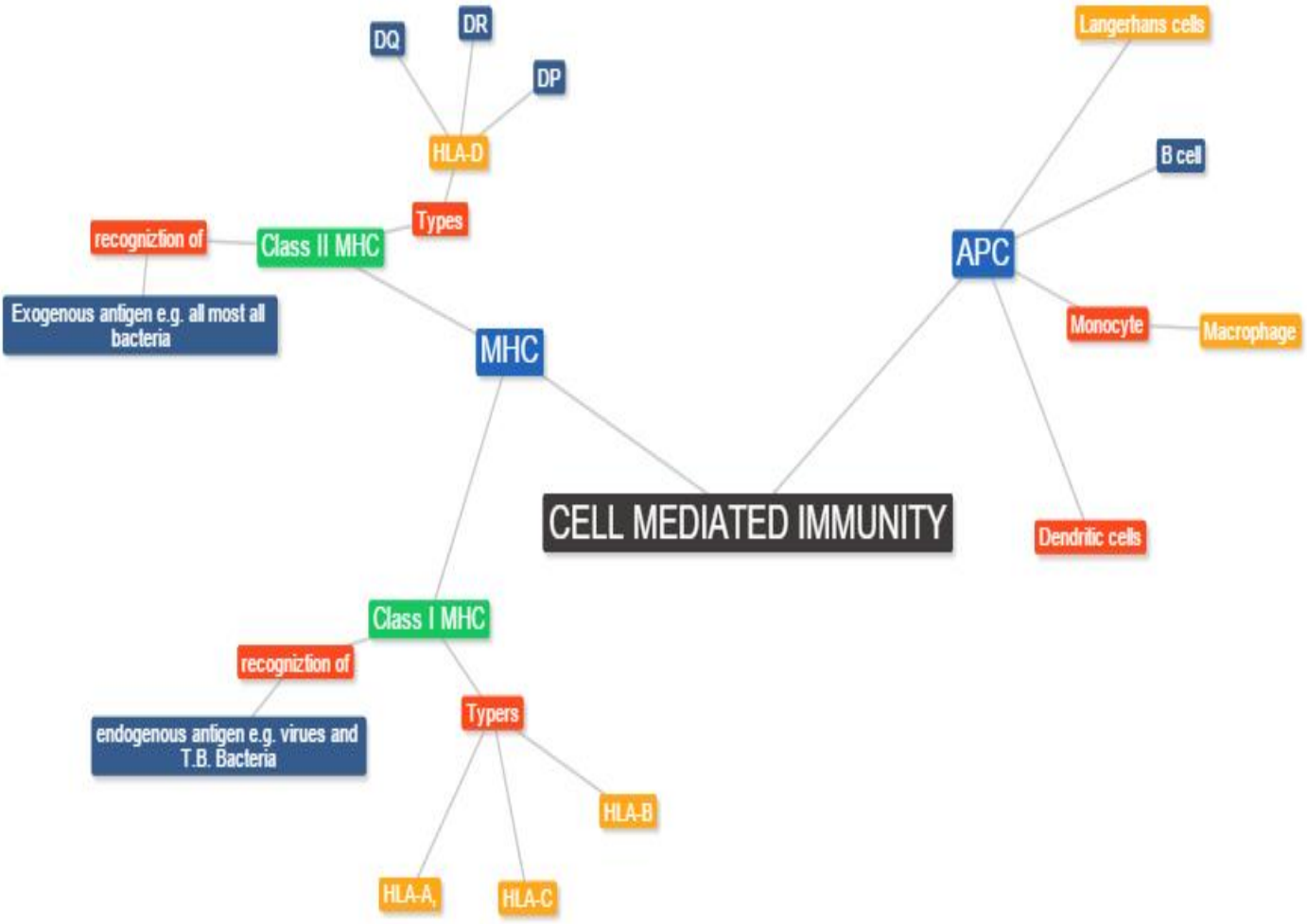
The tuberculin test DTH reaction is mediated by CD4+ T cells and takes about 72 hours to develop

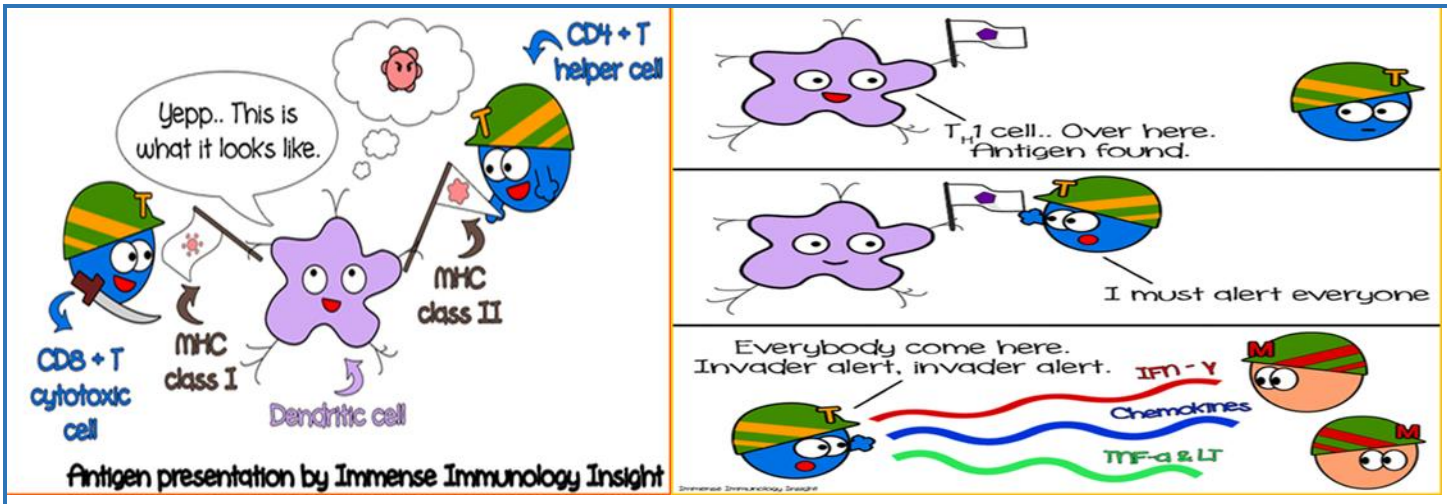
2. Contact Sensitivity:

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.

Mind maps and helping pictures





Picture where taken from http://immense-immunology-insight.tumblr.com/ you should check it!

Summary

- Cell mediated immunity (CMI) is an adaptive, specific immunity that is derive form T cells.
- Antigens presenting cells are (B cell ,Langerhans cells , Monocyte, Dendritic cells, Macrophage)

- It's get activated after the it's get recondition of an antigen
  Antigens are recognized through MHC (Major Histocompatibility Complex) which is a proteins on the surface of cells

- MHC class I is found on the surface of all nucleated cells and the presentation of endogenous antigen happens through it which activities CD8+ cytotoxic T cells
- MHC class II is found on the surface of only antigen presenting cells and the presentation of exogenous antigen happens through it. CD4+ Helper T cells
- Other than MHC the activation of T cells needs other signals.
- When CD8+ cytotoxic T cell gets activated it kills infected cells with the same antigen.
- When CD4+ Helper T cell get activated it start producing Interferon and IL-2 (also called T cells growth factor), also it's stimulates naïve B Cells to become either plasma cells or memory cells (which lives for many years).
- Examples of CMI are (Delayed type of hypersensitivity (DTH) reaction, Contact Sensitivity, Granuloma Formation).

MCQs

Q1) Antigen Presenting cells in the blood

A) Monocytes & Langerhans cells

B) B-cells & Monocytes

C) Dendritic cell

Q2) MHC class I molecules are NOT found on the surfaces of:

A) RBCs

B) B cells

C) Macrophages

Q3) the secondary response according to memory cells is:

A) Less than the primary response

B) More than the primary response

C) Equal to the primary response

Q4) the tuberculin test is mediated by:

A) CD4+

B) CD2+

C) CD28+

Q5) genes code for Class I MHC molecules

A) HLA-A

B) DR

C) DQ

Q6) when the antigen is a virus the recondition is through:

A) MHC class ll

B) MHC class l

C) IL1

D) CD 3

1-B 2-A 3-B 4-A 5-A 6-B