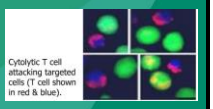
Slide 1

FOUNDATIONS OF PUBLIC HEALTH IMMUNOLOGY



Cytolytic T cell attacking targeted cells (T cell shown in red & blue).

Cell Mediated Immunity: Effector Mechanisms

USF UNIVERSITY OF SOUTH FLORIDA

Slide 2

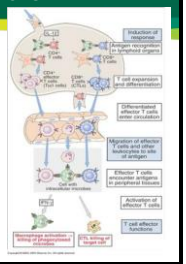
OBJECTIVES

- Describe the process of T cells homing to sites of injury or infection
- Identify effector functions of CD8+ T cells
- Describe how CD4+ helper cells regulate the immune system
- Identify effector functions of Th1 CD4+ cells
- Identify effector functions of Th2 CD4+ cells
- Identify effector functions of Th17 cells
- Identify examples of regulation of the immune response
- Identify examples of cell-mediated immunopathology

Slide 3

EFFECTOR FUNCTIONS

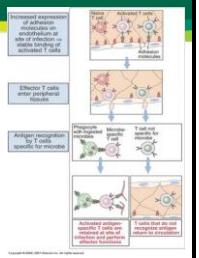
- **Antigen recognition** has occurred in lymphoid organs
- Activated T cells to **expand & differentiate into effector cells**
- Effector cells **migrate into tissues**
- Th1 CD4 cells & CD8 cytotoxic T cells **perform cell-mediated targeting** of the microbes



Slide 4

T CELL HOMING

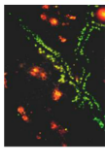
- T cells exit nodes & are attracted to site of infection with **adhesion molecules** (homing)
- Activated **T cells that recognize antigen are retained** to battle the infection
- Other T cells that are **not** Ag specific continue to circulate



Slide 5

FOCUS ON CD8+ CELLS

- CD8 cells primarily respond to **intracellular** pathogens (restricted to MHC I)
- Once activated, CD8 cells proliferate into antigen specific **effector** cells
- Effector cells leave the peripheral lymphoid organs to migrate to the site of infection
- Major effector function: recognize & **kill infected host** cells
- CD8+ cells provide the major cellular response to **viral** infections

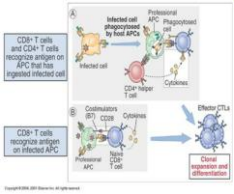


CD8+ T cells in red.

Slide 6

CD8+ T CELLS: DIFFERENTIATION

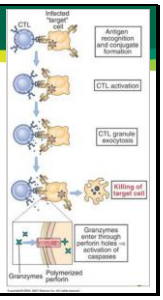
- First signal: **recognize antigen peptide** on surface of host cell displayed by MHC I
- Second signal: need **co-stimulators** (B7 – CD28) to trigger activation
- Differentiation into effector cells leads to **specific targeting of any other cell infected** with same microbe (Ag specificity)



Slide 7

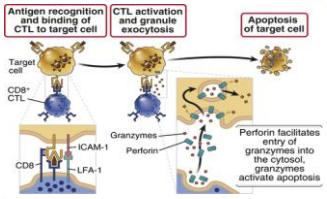
CD8+ T CELLS: DEADLY CONSEQUENCES

- CD8+ cells then **release granules** that kill the organism
  - **Perforin** punches holes through the targeted cell membrane
  - **Granzymes** then enter the cell, activate caspases which induces apoptosis
- Infected cell is killed, CD8 T cell also can produce **IFN γ** to recruit macrophages
- Apoptotic (dead) cells are quickly phagocytosed & removed



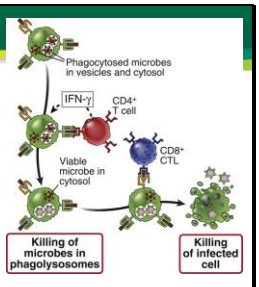
Slide 8

MECHANISM OF KILLING BY CD8+ T CELLS



Slide 9

Cooperation between CD4⁺ and CD8⁺ T cells in eradication of intracellular infections.



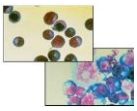
Slide 10

FOCUS ON CD4+ CELLS

- CD4 cells primarily respond to **extracellular** antigens (restricted to MHC II)
- Once activated, CD4 cells differentiate into **effector** cells
- Primarily function to **release cytokines that activate B cells & macrophages**
- Three subsets of CD4 cells:
  - Th1
  - Th2
  - Th17

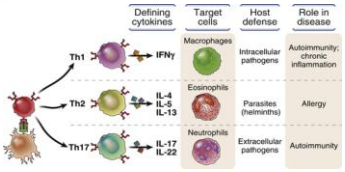
**Also, Th0 (T reg cells – discussed in Block 5)

CD4+ T cells are especially susceptible to infection with HIV. The image on the top are **healthy** T cells, **compared** to those below that have been **infected**.



Slide 11

Characteristics of subsets of CD4+ helper T lymphocytes.



Slide 12

A DELICATE BALANCE

CD4+ Cells Polarize the Immune System

- **Th1 Cells**
- Cytokines: IFN-γ, IL-12, IL-2
- IgG2a antibodies
- Pro-inflammatory
- **Cell mediated Immunity**

- **Th2 cells**
- Cytokines: IL-4, 9, 10, 13
- IgG4 and IgE antibodies
- Anti-inflammatory
- **Humoral Immunity**

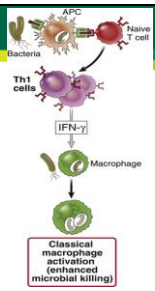
Slide 13

CD4: TYPE 1 HELPER CELLS(TH1)

- Secretes cytokines that influence immune response
- Secretes IFN-γ, a potent activator of macrophages
- Stimulates expression of MHC-II on APCs, which amplifies the T cell response
- Improves cell mediated response
- Pro-inflammatory – result in tissue injury

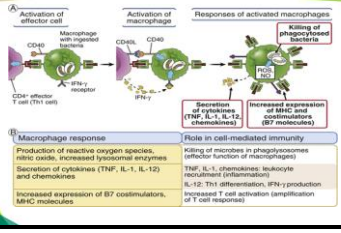
Slide 14

Functions of Th1 cells.



Slide 15

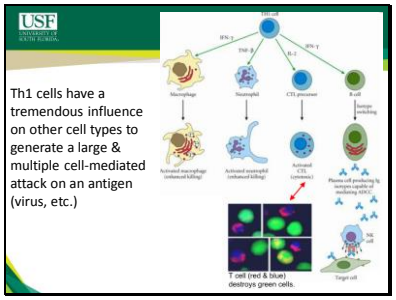
Activation of macrophages by Th1 lymphocytes.



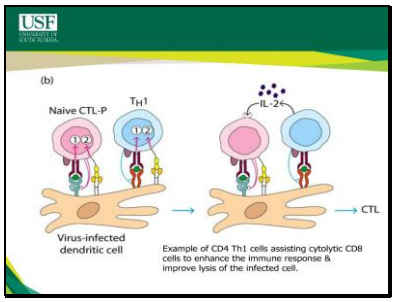
B

Macrophage response	Role in cell-mediated immunity
Production of reactive oxygen species, nitric oxide, increased lysosomal enzymes	Killing of microbes in phagolysosomes (effector function of macrophages)
Secretion of cytokines (TNF, IL-1, IL-12) and chemokines	TNF, IL-1, chemokines: leukocyte recruitment (inflammation) IL-12: Th1 differentiation, IFN-γ production
Increased expression of B7 costimulators, MHC molecules	Increased T cell activation (amplification of T cell response)

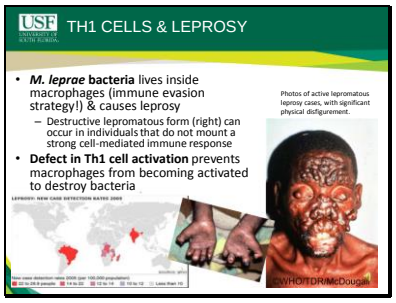
Slide 16



Slide 17



Slide 18



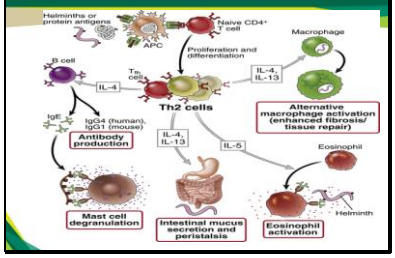
Slide 19

CD4: TYPE 2 HELPER CELLS (TH2)

- Th2 cells secrete IL-4 – stimulates B cell response
- Th2 cells secrete IL-5 – activates eosinophils to defend against parasites via IgE antibodies
- Secretes IL-4 and IL-13- alternate macrophage activation which dampens the Th1 response and limit tissue damage.
- Improves humoral immunity.

Slide 20

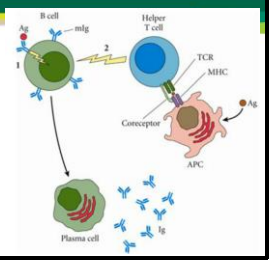
Functions of Th2 cells.



Slide 21

CD4+ Helper (Th2) cells especially promote B cell growth and differentiation to stimulate antibody production.

A B cell will differentiate into a plasma cell after receiving 2 signals:
1) **antigen binding**
2) **T cell help**



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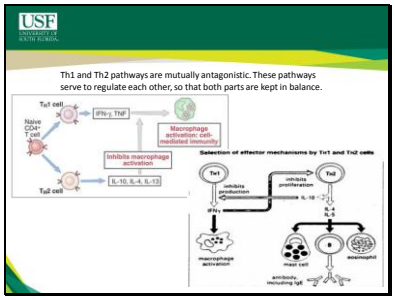

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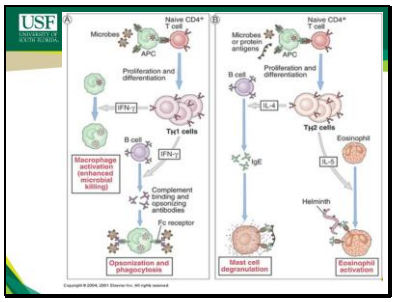

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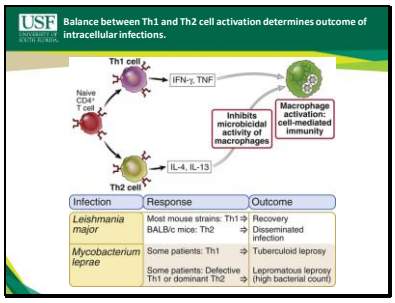


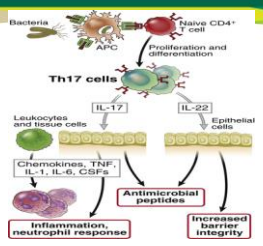
Slide 25

CD4: TYPE 17 HELPER CELLS (TH17)

- Secretes IL-17 which recruitment of neutrophils and monocytes (lesser extent).
- Secretes IL-22 which maintains the integrity of epithelial barriers and promote repair of damaged epithelia.
- Stimulate the production of defensins – antimicrobial peptides.

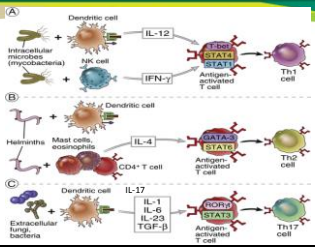
Slide 26

Functions of Th17 cells.

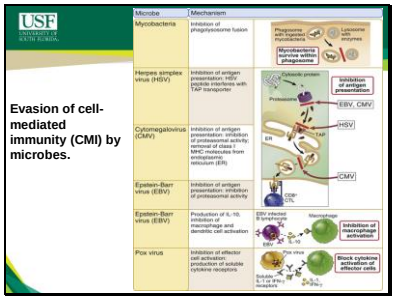


Slide 27

Development of Th1, Th2, and Th17 effector cells.



Slide 28



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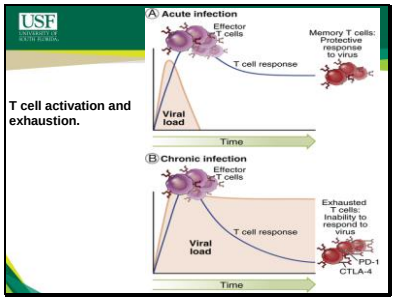

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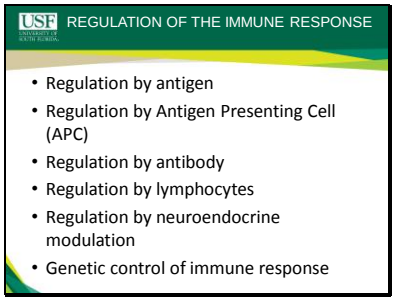

Slide 31

REGULATION BY ANTIGEN

- T & B cells; Antigen receptors, Class 1 & 2 MHC proteins
- Nature of the Antigen: chemical, intracellular or extracellular
- Antigen dose
- Route of administration of antigen (mucosa, skin, blood)

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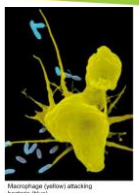
REGULATION BY ANTIGEN PRESENTING CELL (APC)

- Antigen recognition with MHC proteins or tolerance induction
- APC can up-regulate the expression of MHC on surface by cytokine induction



Macrophage (yellow) attacking bacteria (blue).

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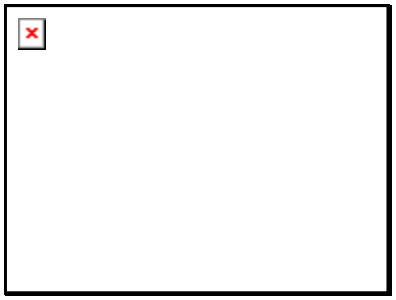
Slide 34



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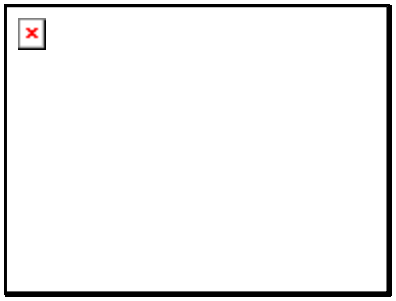

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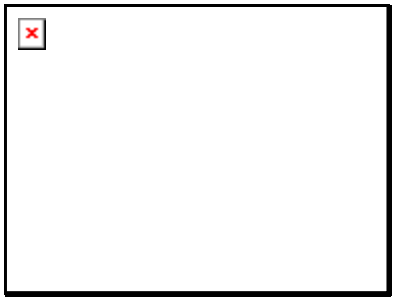

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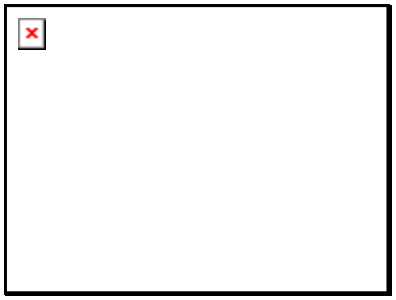
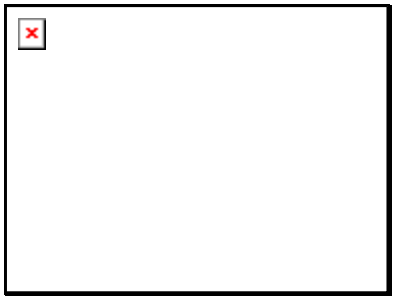


Slide 38

Slide 39

Slide 40



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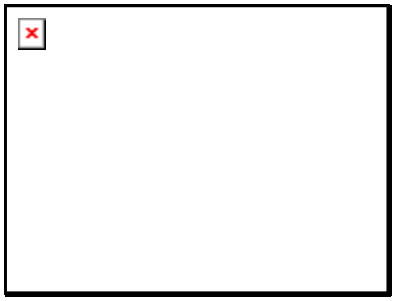

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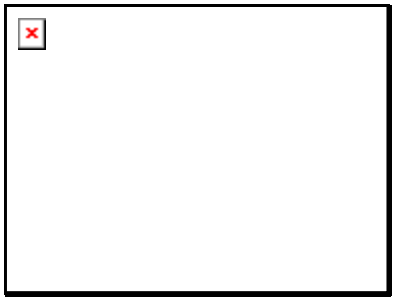

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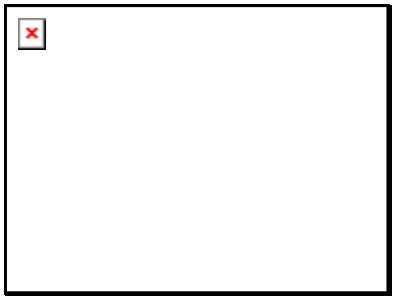

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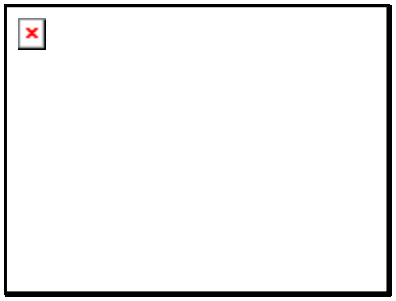

Slide 45