Cell Mediated Immunity

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* Host defenses against extracellular infection are mediated by:
  - Antibody
  - Complement
  - Macrophages

* Intercellular infections are mediates by CMI

* CMI are responsible for:
  - Resistance to intracellular pathogens
  - Resistance to fungal and protozoal infections
  - Resistance to tumors

Cell Mediated Immunity

* CMI may play a role in some harmful conditions:
  - Hypersensitivity reactions type IV (contact dermatitis)
  - Graft rejection
  - Autoimmune diseases

* Cell mediated cytotoxicity mediated by:
  - T-cytotoxic cells cells
  - Natural killer cells
  - Activated macrophages

Characters Of CMI

Cellular immune response is mediated by:

- Subpopulation of T-lymphocytes

- Macrophages and their products

Characters Of CMI

* Macrophages present antigen via their surface MHC to T-cells

* T-cells recognize antigen through their specific receptors (TCR)

* A specific T-cell clone becomes activated and begins to proliferate

* Activated TH lymphocytes becomes effectors cells that secrete cytokines

Characters Of CMI

Cytokines stimulate other effectors cells of CMI and humoral immune response and mediate the following:

- Attract monocytes, macrophages and lymphocytes to the site

- Activate macrophages to kill intracellular microbes

- Promote activity of CD8 CTLs which directly kill virus infected cells, tumour cells, and graft rejection

- They activate NK cells increasing their cytotoxic functions

- Stimulate B-cells to differentiate into plasma cells that secret antibodies

Phases Of CMI

1) Antigen processing and presentation

Protein antigens processed and converted to

peptides then bind to MHC molecules on Antigen Presenting Cell (APCs)

to be presented to T-cells

1) Antigen Processing and Presentation

a- Extracellular proteins are internalized into vesicular compartment of APCs (Dentritic, macrophages,B-cells)

- They are degraded to generate peptides
- These peptides bind into class II MHC molecules
- Peptide-MHC II complex is transported to surface of APCs to be presented to CD4 TH cells (T Helper cell)

Outcome:

Secretion of cytokines by TH cells

1) Antigen Processing and Presentation

b- Endogenously synthesized proteins are degraded to peptides (all nucleated cells e.g virus infected cells)

- They bind to class I MHC in endoplasmic reticulum

- Peptide-MHC I complex is expressed on surface of nucleotide cells to be represented to CD8 cytotoxic cells

Outcome:

Killing of presenting cells by CTLs

2) Activation of T-cells

* Mature CD4 and CD8 cells are activated by two signals:

- First signal is recognition of antigenic peptide-MHC complex on surface of APC by TCR-CD3 complex
- CD4 and CD8 molecules are co-receptors that stabilize the interaction of TH cells and TC-cells respectively with APCs
- CD3,CD4, and CD8 act as signal transduction molecules

- Second co-stimulatory signal is:
  interaction of CD28 on T-cells with CD7 on APCs

2) Activation of T-cells

* TH-cells express IL-2 receptors and secrete cytokines including IL-2
* IL-2 auto activate TH-cells
* APC release IL-I which acts on both APC and TH cell to promote their activation
* All mentioned interactions lead to activation of mature TH-cells
* Mature TH-cells proliferate and differentiate into effectors antigen specific TH-cells releasing cytokines
* Some of them become memory cells which provide secondary immune response
* Cytokine released from activated TH-cells activate macrophages, NK and B-cells

Phases Of CMI

* Activated CD8 TC-cells proliferate and differentiate into a clone of effectors cells CTLs

* Effectors CTLs kill target cells

i.e. nucleated cells (expressing MHC-I) infected with viruses, tumor cells or graft cells

3) Activation of Macrophages and Delayed Type Hypersensitivity (DTH)

* Activated TH cells (TH1) secrete IFN-γ which activates macrophages and increase their ability to kill ingested intracellular pathogens

* The process of activation of macrophages, NK cell and cytotoxic T-cells, infiltration and proliferation of inflammatory cells, stimulated by cytokines released from TH-cells (TH1) is important protective mechanism against intracellular pathogen

3) Activation of Macrophages and Delayed Type Hypersensitivity (DTH)

* Activated macrophages can also kill abnormal host cells (abnormal or tumor cells)

* Its ctotoxicity is non specific and stimulated by TNF, nitric oxid, enzymes and oxygen metabolites

* If infection is not fully resolved, activated macrophages cause tissue injury and fibrosis i.e. DTH reaction