BITS PILANI, DUBAI CAMPUS
SECOND SEMESTER 2010-2011
COMPREHENSIVE EXAMINATION (CLOSED BOOK)
MONDAY (8.30AM-11.30 AM)

COURSE TITLE: IMMUNOLOGY — MAXIMUM MARKS: 40
COURSE NO.BIOT C416 — DURATION: 3 HOURS.

- Answer all the questions in the given sequence only with all the parts of a question together
- Draw diagrams wherever necessary

Q1. (a) Differentiate between (i) Tolerance and Autoimmunity

- The number of mechanisms that exist to protect an individual from potentially self reactive lymphocytes are given the general term **Tolerance**.
- Despite the various tolerance mechanisms self- reactive clones of T or B cells are occasionally activated
- generating humoral or cell mediated responses against self antigens.
- Such a response of immune system against self components is termed **Autoimmunity**.

(ii) Central & Peripheral tolerance

Central Tolerance:

- Deletes T or B cell clones before the cells are matured if they possess receptors that recognize self antigens with greater than a low threshold affinity.
- Occurs in primary lymphoid organs, bone marrow, thymus.

Peripheral Tolerance:

- Renders lymphocytes in secondary lymphoid tissues inactive or anergic- unresponsive
- Occurs in Secondary lymphoid Tissues

(iii) Organ specific & systemic autoimmune disease (with 2 examples each)

- In an organ specific autoimmune disease immune response is directed to a target antigen unique to a single organ or gland, so manifestations are largely limited to that organ.

TABLE 14-1 Some autoimmune diseases in humans

Disease	Self antigen	Immune response
ORGAN-SPECIFIC AUTOIMMUNE DISEASES		
Addison's disease	Adrenal cells	Auto-antibodies
Autoimmune hemolytic anemia	RBC membrane proteins	Auto-antibodies
Goodpasture's syndrome	Renal and lung basement membranes	Auto-antibodies
Graves' disease	Thyroid-stimulating hormone receptor	Auto-antibody (stimulating)
Hashimoto's thyroiditis	Thyroid proteins and cells	T_H1 cells; auto-antibodies
Idiopathic thrombocytopenia purpura	Platelet membrane proteins	Auto-antibodies
Insulin-dependent diabetes mellitus	Pancreatic beta cells	T_H1 cells; auto-antibodies
Myasthenia gravis	Acetylcholine receptors	Auto-antibody (blocking)
Myocardial infarction	Heart	Auto-antibodies
Pernicious anemia	Gastric parietal cells; intrinsic factor	Auto-antibody
Poststreptococcal glomerulonephritis	Kidney	Antigen-antibody complexes
Spontaneous infertility	Sperm	Auto-antibodies
SYSTEMIC AUTOIMMUNE DISEASES		
Ankylosing spondylitis	Vertebrae	Immune complexes
Multiple sclerosis	Brain or white matter	T_H1 cells and T_C cells; auto-antibodies
Rheumatoid arthritis	Connective tissue; IgG	Auto-antibodies; immune complexes
Scleroderma	Nuclei, heart, lungs, gastrointestinal tract, kidney	Auto-antibodies
Sjögren's syndrome	Salivary gland, liver, kidney, thyroid	Auto-antibodies
Systemic lupus erythematosus (SLE)	DNA, nuclear protein, RBC and platelet membranes	Auto-antibodies, immune complexes

Table 14-1
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5/30/2011

(1+1+2)

(b) Explain in detail the dominant mechanism that helps to maintain Tolerance

- The dominant mechanism in maintaining tolerance is deletion during early maturation of the lymphocyte clones that may react with self components. (2)

(c)Prove with an example that Cell mediated immunity is very important to the body's defense.
Ans. Thymus absent – no cell mediated immunity (1)

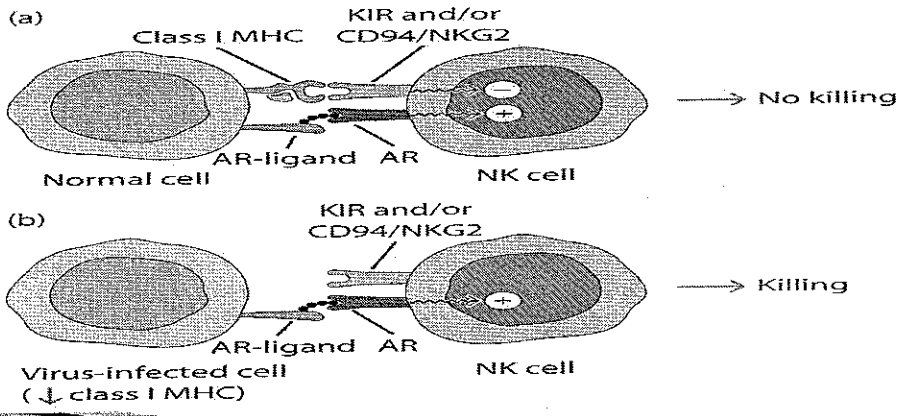
Q2. (a) Natural killer cells do not Express TCR molecules, yet they bind to class I MHC molecules on the potential target cells

(i) Explain how NK cells lacking TCR recognize infected cells (1.5)

Opposing Signal mechanism – target cell contain normal class 1 MHC –receptor on NK induce signal transduction – no killing

Decreased level of MHC-1 - killing

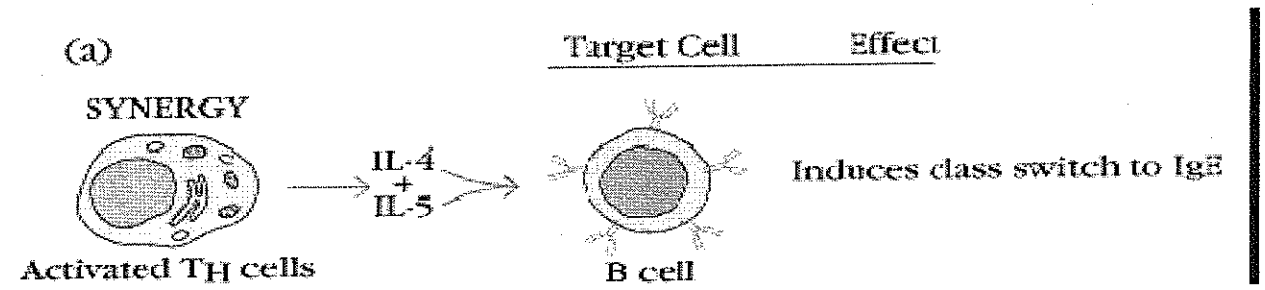
- Balance Between Activating and Inhibiting signals Allows NK Cells To Differentiate Normal cells From Altered
  - C-type lectins – carbohydrate binding protein Are Candidates for AR (have ca dependent carbohydrate recognition domain
    - CD2 (Receptor for adhesion molecule LFA-3)
    - CD16 (FcγRIII, Involved In Antibody Mediated Recognition)
    - NKp30, NKp44 and NKp46
- Inhibitory Receptors
  - MHC Molecules
  - CD94/NKG2 Recognize HLA-E
  - If HLA-E is present –ve signal, no killing
  - No HLA-E (during viral infection), no –ve signal, killing
  - KIRs recognize specific MHC molecules, -ve signal, no killing

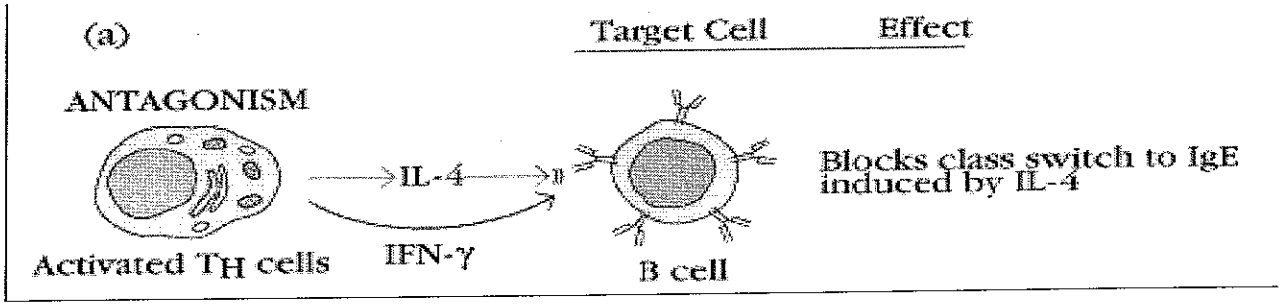


(ii) What is the mechanism used by NK cells to kill target cells. (1.5)
Ans. Similar to that of CTL .NK express fas L and contain granules containing perforins & granzymes , equipping them to induce apoptosis

(b) Biological activity of cytokines exhibit Pleiotropy, Redundancy Synergy& Antagonism, Explain with example. (2)

- ☐ Pleiotropy-different effects (IL-4 produced by activated T cells can act on B cell , Thymocyte & Mast cell - lead to activation , differentiation & proliferation
- ☐ Redundancy –different cytokines , same effect (IL2,4,5- act on B cell and helps proliferation)

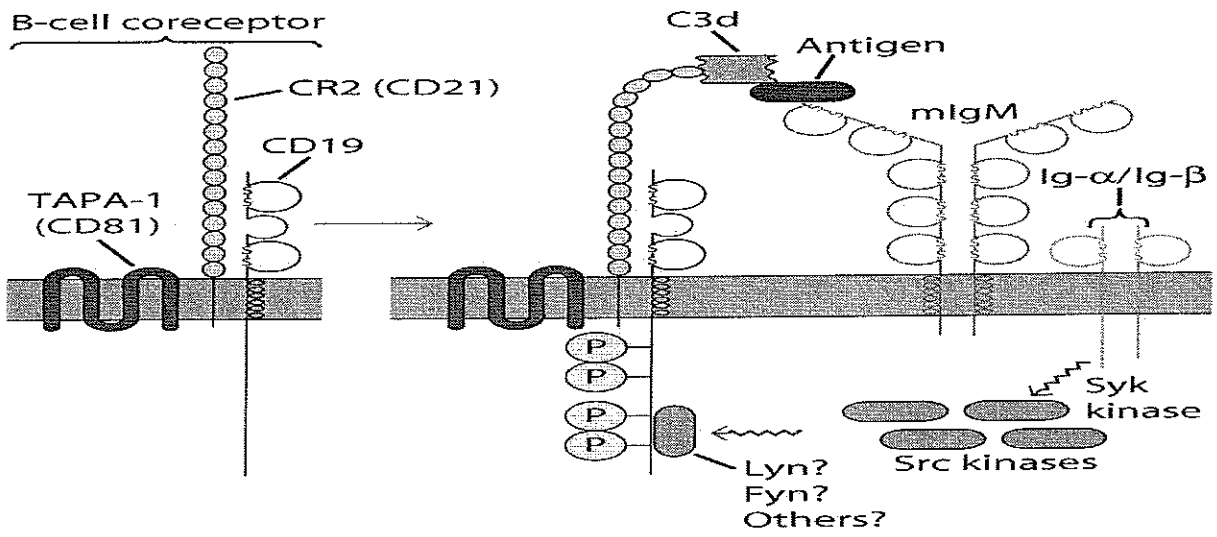




(c) Define the following (i) Clonal anergy - unresponsiveness (1)
Affinity maturation -The progressive increase in average affinity of antibodies produced as response progresses

Q3. (a)Describe the general structure and probable function of B cell Co receptor complex (2)

- ☐ Complex of three proteins
- ☐ CD19,CR2(CD21)&TAPA-1(CD81)
- ☐ CD19- key member , long cytoplasmic tails ,provide docking sites for molecules ,augment signal delivered by BCR
- ☐ Contain 6tyrosinf residues ,major substrate for PTK activity mediated by cross linking of BCR
- ☐ CR2- receptor of C3d (complement product)
- ☐ Also function as receptor for membrane molecule & transmembrane protein TAPA-1



(b) Indicate whether each of the following statement concerning B cell maturation is true or false. (3)

(i) Heavy chain $V_H, D_H J_H$ rearrangements begins in pre B cell stage (F)

(ii) Immature B cells express membrane IgM & IgD (False)Express only IgM

(iii)Enzyme TdT is active in pre B cells (False) Only in Pro B cells

(iv)Surrogate light chain is expressed by pre B cells (True)

(v) Self reactive B cells can be rescued from negative selection by expression of a different light chain(True)

(vi) In order to develop immature B cells, pre B cells must interact directly with BM Stromal cells (False)

(c) Describe the mechanism of positive selection & negative selection during T cell development .what is the outcome/result of these types of selection (2)

Positive selection

- ☐ Results in MHC restriction
- ☐ Take place in cortical regions
- ☐ Involves interaction of immature thymocytes with cortical epithelial cells
- ☐ Mechanism:
  - ■ Immature thymocytes cluster with MHC molecules on the cortical cells of the thymus
    - ☐ If TCR interacts with MHC → *protective signal* results that prevents apoptosis.
    - ☐ If TCR does not interact with MHC → *no protective signal* and apoptosis occurs.

Result? Only reactive thymocytes survive

Negative selection

- ☐ Ensures ***self-tolerance***
- ☐ Weeds out High affinity thymocytes
- ☐ Mechanism:
  - ■ APC's bearing MHC's interact with thymocytes
    - ☐ If avidity is too strong → thymocyte undergoes apoptosis.
    - ☐ Details unknown...
- ☐ Result? Only self-tolerant thymocytes survive.

(d) List out the different receptors used by innate immunity to detect infection (1)

Table 3.3 of TB Kuby

Q4. (a) Describe in detail (Schematically) the mechanism/ Pathway involved in mitochondrial induced cell death/Apoptosis (3)

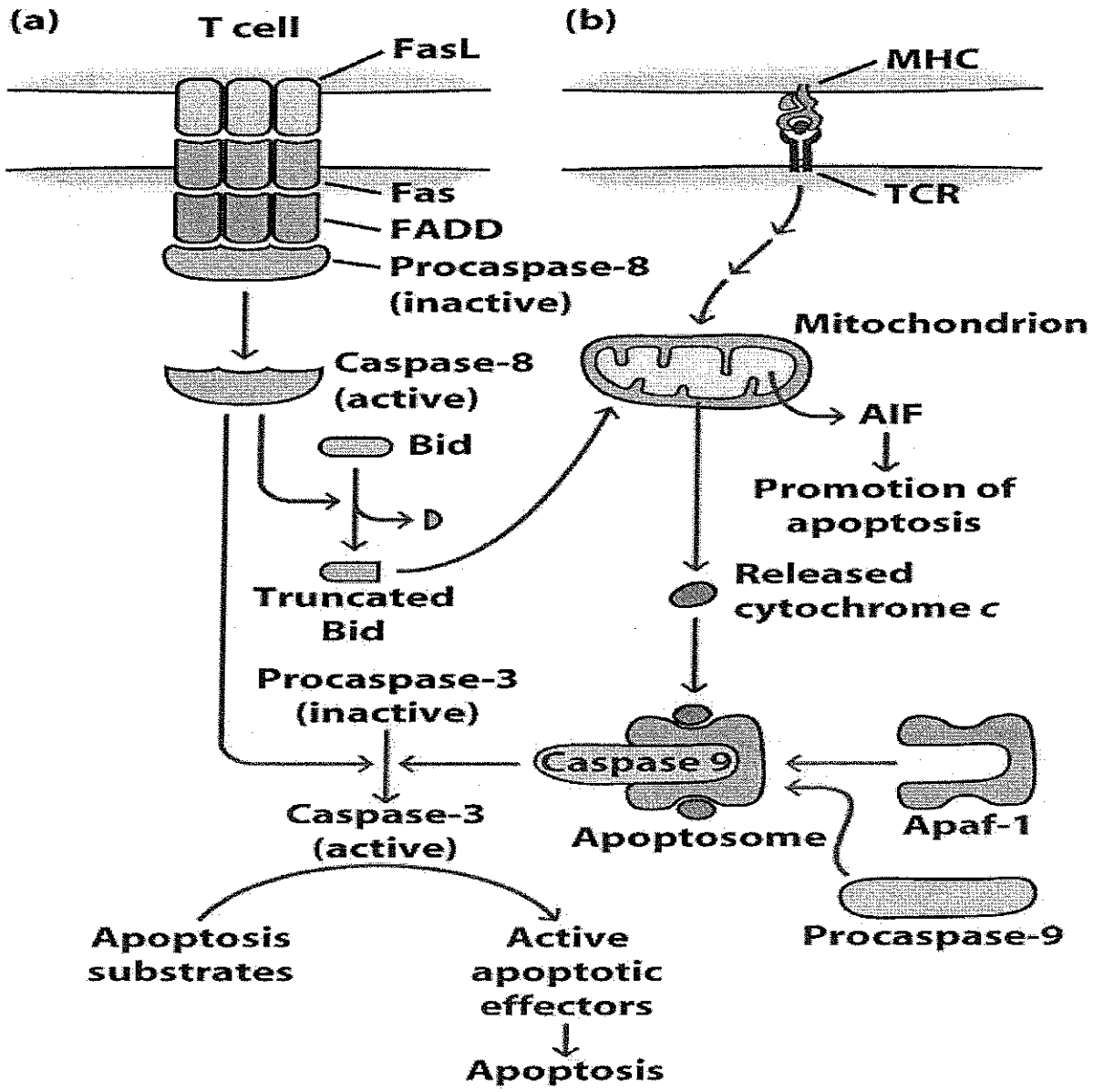


Figure 10-19
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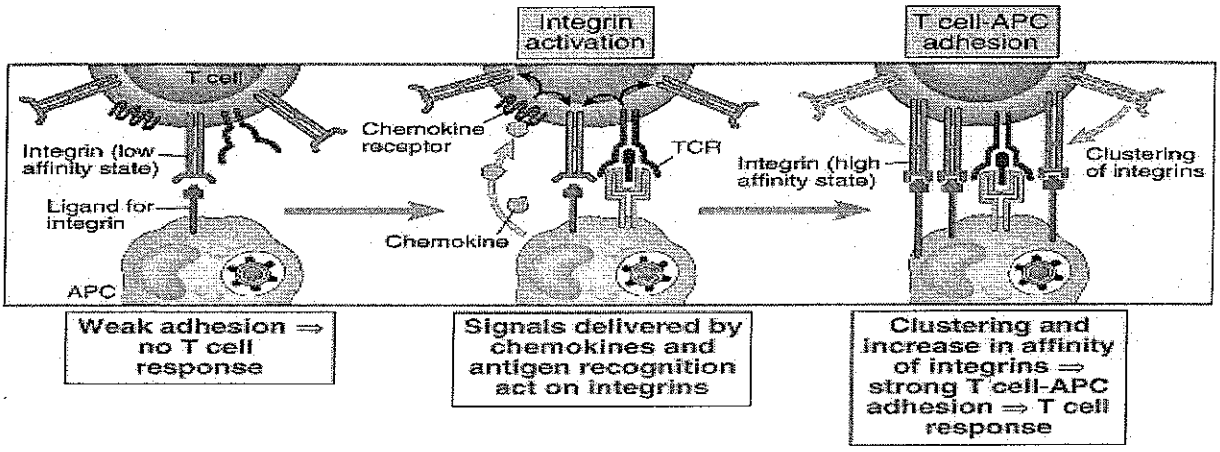
(b) Describe the role of Bcl_2, Bcl-XL in the mitochondrial induced cell death (1)

- ☐ Bcl2 and Bcl-XL, both reside in the mitochondrial membrane.
- ☐ Both of these proteins are strong <u>negative inhibitors of apoptosis.</u>
- ☐ Bcl2 family has three groups.
- ☐ Group 1 are anti-apoptotic and include Bcl2 and Bcl-XL.
- ☐ Group II and group III members are pro-apoptotic and include Bax and Bak in group II and
- ☐ Bid (Bcl2 interacting domain and Bim in group III.

(c) Describe the role of adhesion molecules with an example (1)

- For a productive response ,the binding of T cells to APC must be stabilized for long period that the necessary signaling threshold is achieved
- Done by Adhesion molecules
- ligands are expressed on APC's
- Most important of these belong to family of heterodimer proteins - INTEGRINS .
- Major T cell integrin involved in binding is Leucocyte function associated antigen -1 (LFA-1)
- Ligand on APC is called intracellular adhesion molecules -1 (ICAM-1)



(d) What is the significance of Cross presentation of Antigens. (1)

- Cross-presentation is important because:
- Most viruses infect cells other than APCs, and
- while viral antigens displayed on the surface of any infected cell can serve as **targets** for CYTOTOXIC t CELLS (CTLs),
- the lack of any COSTIMULATORY MOLECULES on the cell surface makes them **poor stimulants** for the development of clones of CTLs in the first place

Q5. (a) Compare the 2 pathways by which antigens are processed & presented (list out the steps involved) (3)

BITS PILANI, DUBAI CAMPUS
SECOND SEMESTER 2010-2011
Test (2) OPEN BOOK

Course Code: BIOT C416 | Date: .15.5.2011
Course Title: Immunology | Max Marks: 20
Duration: 50 minutes | Weightage: 20%

Q1.The T cell & B cell population is maintained at their appropriate levels once the Burst of Antigen induce their proliferation –justify. (3)

Q2.What could be the possible justification& explanation for the statement that all the daughter cells must express the same Antigen specificity? (2)

Q3.Naive T cell Lymphocytes express receptors for antigen but do not perform the function required to eliminate the antigen .Explain the mechanism by which they eliminate the antigens. (2)

Q4.How is it possible to ensure that a population will be able to deal with diversity of microbes and will not succumb to the newly encountered or mutated microbe? (2)

Q5.Would you expect a C1 or C3 complement deficiency to be more serious & why? (3)

Q6.T cell lines & knocked out mice that lacked the Zeta associated proteins show profound defect in TCR induced response, Explain. (3)

Q7.Explain the possible defect or problem involved if MHC II remains bound to CLIP at the surface. (2)

Q8.Explain the mechanism of helper T cell mediated activation of B Lymphocytes. (2)

BITS PILANI, DUBAI CAMPUS
DUBAI INTERNATIONAL ACDEMIC CITY
SECOND SEMESTER 2010-2011
TEST -1 (CLOSED BOOK)

COURSE NO. BIOT C416 27-3-2011 MAXIMUM MARKS: 25
COURSE NAME; IMMUNOLOGY DURATION: 50 Mins

Q1. (i) Why is Human skin resistant to colonization by *E.coli* despite constant exposure to it? (1)

(ii) Where are CDR's located on Antibody molecule? What role do they play? (2)

(iii) Differentiate between:

(a) Immunogenicity & Antigenicity
(b) T dependent & T independent Antigen
(c) Conventional antigen & Super antigen
(d) Mannose receptors & Scavenger receptor
(e) PAMP & PRR
(f) Linear epitope & Conformational Epitope (6)

Q2. (i) Only certain immunoglobulins are able to be transferred to fetus & provide Immunity, justify the statement with example. (2)

(ii) Draw a basic diagram of Antibody molecule and show the major functions related to the specific parts on Ig Molecule. (2)

(iii) How the contribution of immunogen plays a role in influencing the Immunogenicity? Explain briefly. (3)

Q3. (i) Leukocyte extravasation is a highly regulated, multistep process, describe briefly .Explain the mechanism of initiation of Extravasation. (4)

(ii) Describe TLR's briefly, list out the TLR's that identify Bacterial pathogens and viruses . (3)

(iii) Define isotypes, allotypes , idiotypes & Hapten (2)

BITS PILANI, DUBAI CAMPUS
SECOND SEMESTER 2010-2011

Course Code: BIOT C416 | 4th Year | Date: 28.2.2011
Course Title: Immunology | Max Marks: 8
Duration: 20 minutes | Weightage: 8%

Name: Id No: Sec/Prog.

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1) What is the difference between dendritic cells and follicular DC?

2) What is the major difference between death caused by necrosis and apoptosis?

3) List out the major differences between B and T lymphocytes.

4) List out the difference between surface and soluble antibodies.

5) List out the common manifestations of immune dysfunction.

6) List out the genes that promotes or inhibit apoptosis.

7) List out the major steps in signal transaction pathway.

8) List out the primary and secondary lymphoid organs and their function in immune response.

9) List out two primary characteristics that differentiate HSC and progenitor cells.

10) What is DiGeorge's Syndrome?

11) Give two examples of APC's.

12) How the innate system recognize the invader. (0.5X12)

13) Define the following: (2)

a) Leucocytosis b) Opsonization c) ADCC d) Hematopoiesis