Code : AS-2246

M.Sc. III Semester Biotechnology End Semester Examination, 2013
Model Answer
LBTM: 302 Advanced Immunology

A. Select one correct option for each of the following questions:- 2X10=10

1. (b) spleen 2. Sebum 3.(d)able to kill virus-infected cells without prior sensitization.

4. (c) a signal transduction molecule 5. (d) The antigen must be monovalent

6. (b) Protein A is more potent immunogen than protein B 7. (b) Multiple sclerosis

8. (d) Chromosome 6 9. (a) Adenosine deaminase deficiency 10. (d) Xeno-graft

B. 1. Describe (i) The inflammatory response:-

Tissue damage caused by a wound or by an invading pathogenic microorganism induces a complex sequence of events collectively known as the **inflammatory response.**

The three major events of an inflammatory response:-

1. **Vasodilation**
2. **An increase in capillary permeability**
3. **Influx of phagocytes-** margination, diapedesis or extravasation, and chemotaxis. The accumulation of dead cells, digested material, and fluid forms a substance called pus.(Explain)

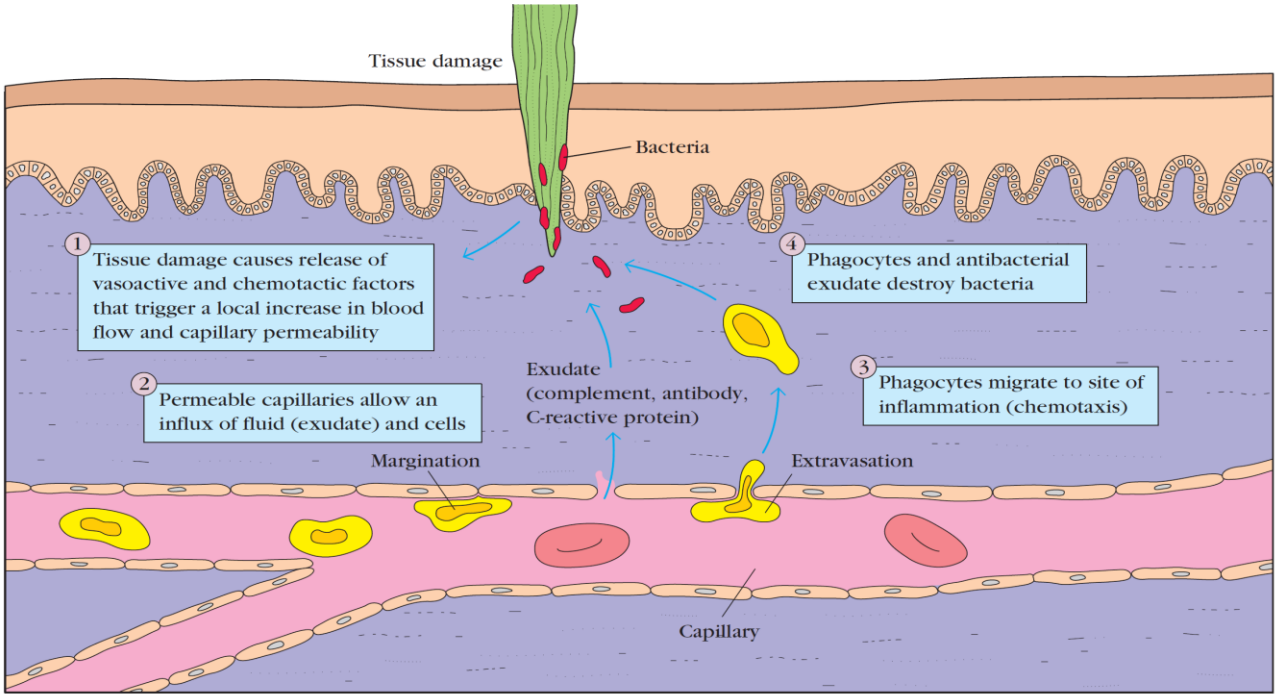


Fig: Inflammatory Response

(ii) phagocytosis process:- One of most important innate defense mechanism is the ingestion of extracellular particulate material by phagocytosis. Phagocytosis is one type of endocytosis, the general term for the uptake by a cell of material from its environment.

(Explain)

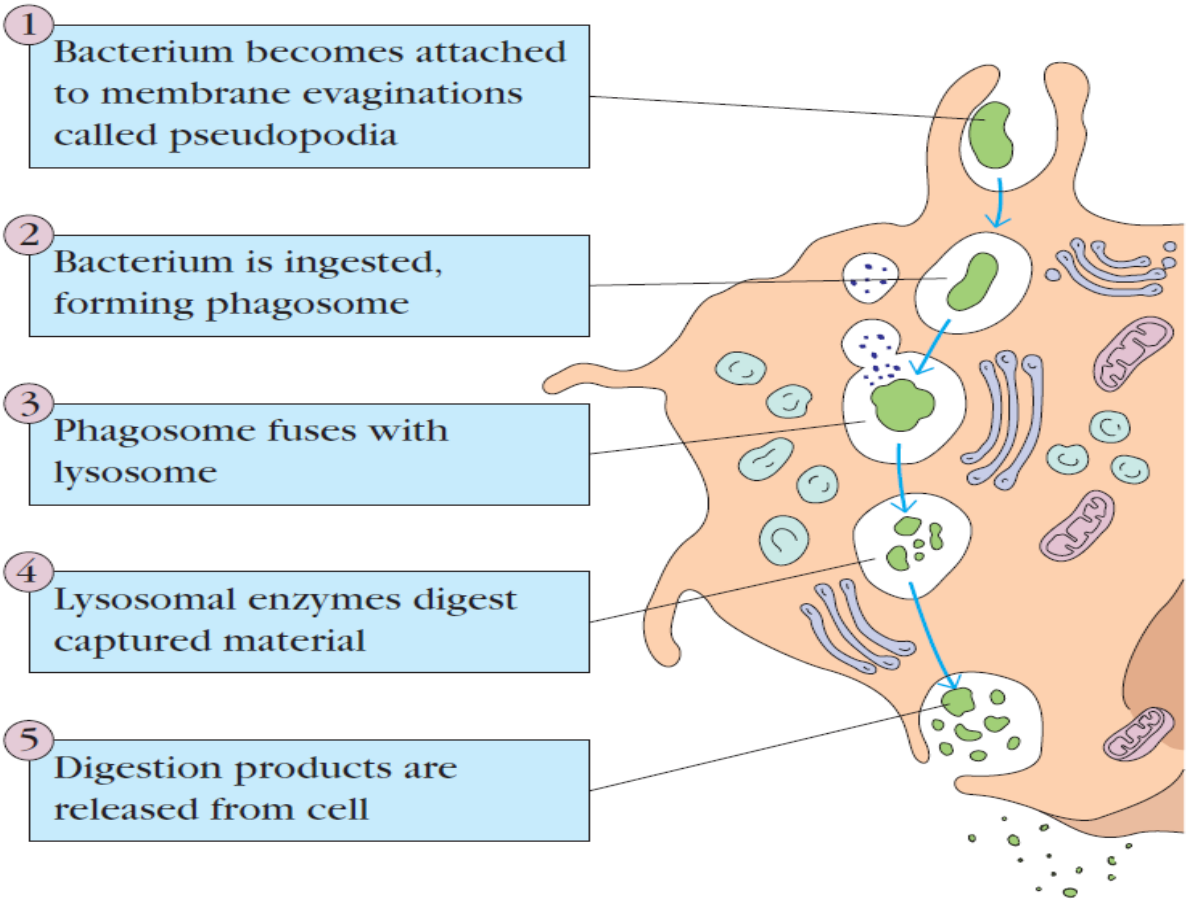


Fig: Phagocytosis Process

2. Describe the development of macrophages.

Ans:- Macrophages are mononuclear phagocytes. The mononuclear phagocytic system consists of monocytes circulating in the blood and macrophages in the tissues.

During hematopoiesis in the bone marrow, granulocyte-monocyte progenitor cells differentiate into promonocytes, which leave the bone marrow and enter the blood, where they further differentiate into mature monocytes.

Monocytes circulate in the bloodstream for about 8 h, during which they enlarge; they then migrate into the tissues and differentiate into specific tissue macrophages or into dendritic cells.

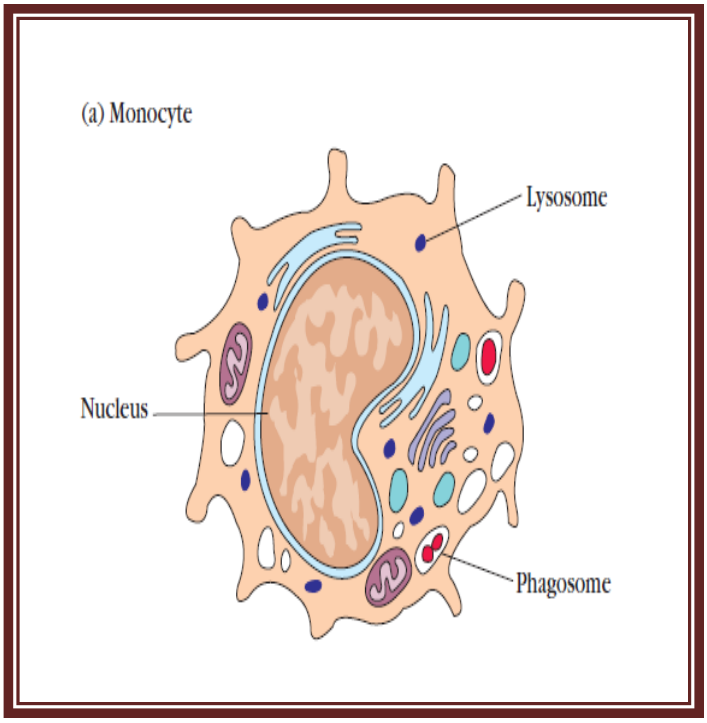
Differentiation of a monocyte into a tissue macrophage involves a number of changes:-

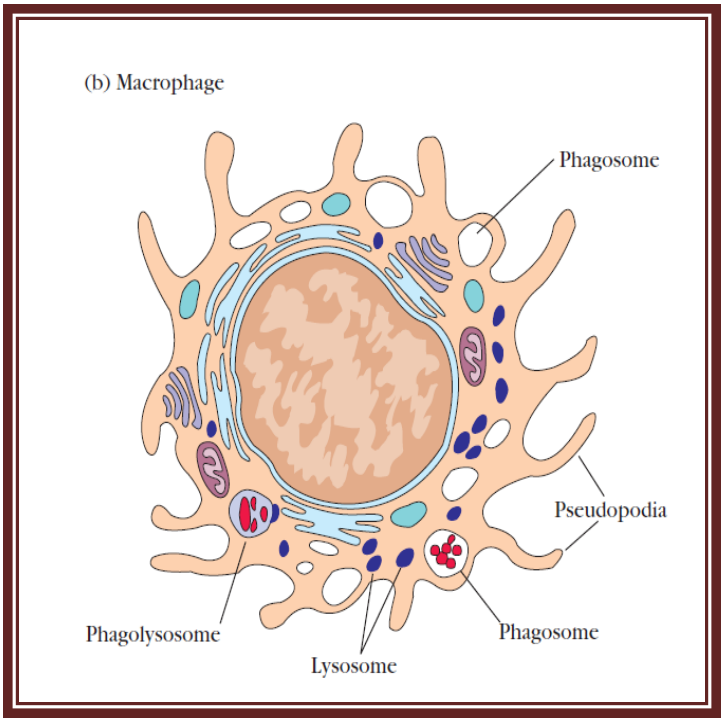
- The cell enlarges five to ten folds.
- Its intracellular organelles increase in both number and complexity.
- It acquires increased phagocytic ability, produces higher levels of hydrolytic enzymes, and begins to secrete a variety of soluble factors.

Macrophages are dispersed throughout the body. Some take up residence in particular tissues, becoming fixed macrophages, whereas others remain motile and are called free, or wandering, macrophages. Free macrophages travel by amoeboid movement throughout the tissues. Macrophage-like cells serve different functions in different tissues and are named according to their tissue location:-

- Alveolar macrophages in the lung
- Histiocytes in connective tissues
- Kupffer cells in the liver
- Mesangial cells in the kidney
- Microglial cells in the brain
- Osteoclasts in bone

Although normally in a resting state, macrophages are activated by a variety of stimuli in the course of an immune response. Phagocytosis of particulate antigens serves as an initial activating stimulus. However, macrophage activity can be further enhanced by cytokines secreted by activated T_H cells, by mediators of the inflammatory response, and by components of bacterial cell walls. One of the most potent activators of macrophages is interferon gamma (IFN-ϒ) secreted by activated T_H cells.





Q. What are APCs? Describe about different type of APC involved in immune system.

Ans**.:- Antigen-presenting cells:-** Activation of both the humoral and cell-mediated branches of the immune system requires cytokines produced by T_H cells. It is essential that activation of T_H cells themselves be carefully regulated, because an inappropriate T-cell response to self-components can have fatal autoimmune consequences. To ensure carefully regulated activation of T_H cells, they can recognize only antigen that is displayed together with class MHC II molecules on the surface of antigen-presenting cells (APCs).

These specialized cells, which include macrophages, B lymphocytes, and dendritic cells, are distinguished by two properties:-

(1) They express class II MHC molecules on their membranes, and

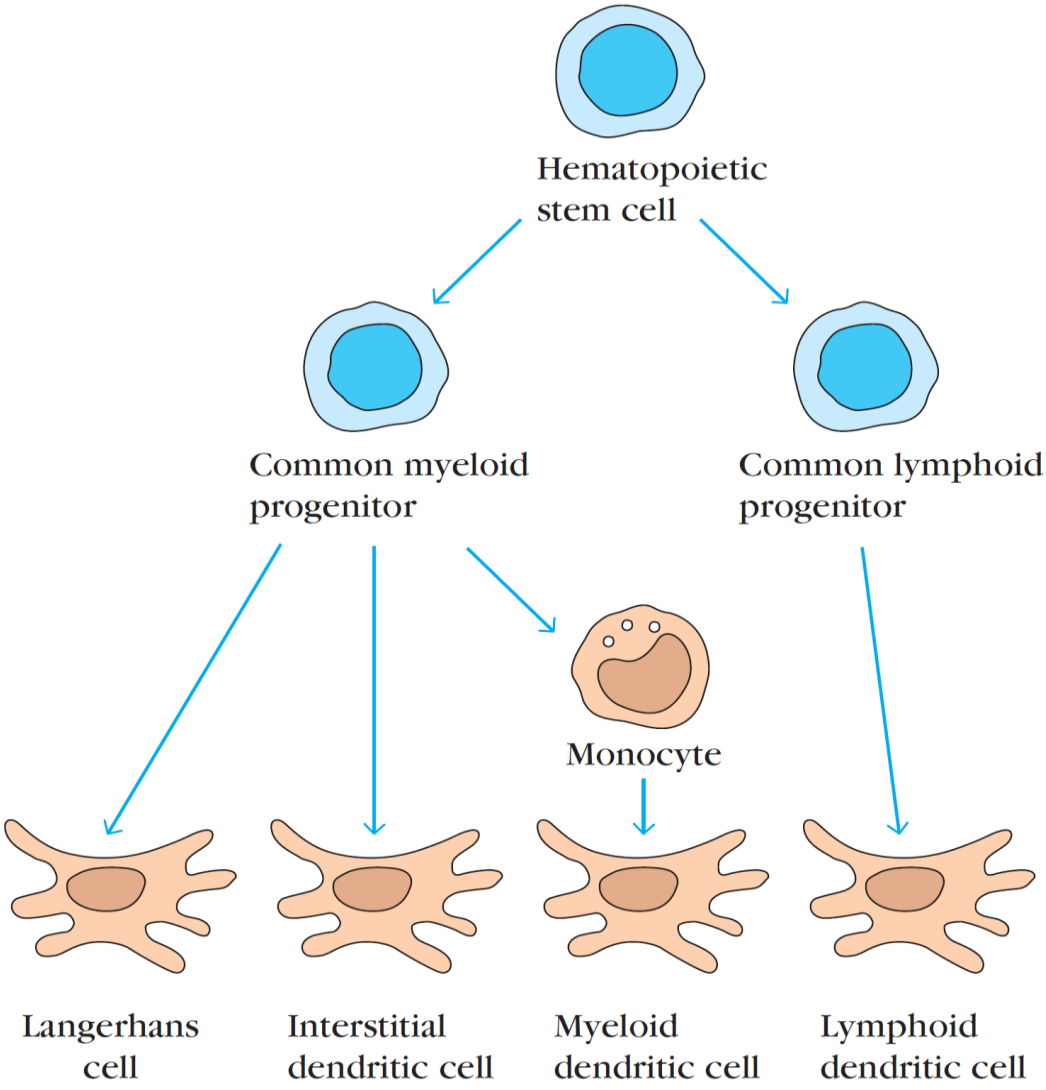
(2) They are able to deliver a co-stimulatory signal that is necessary for T_H-cell activation.

Antigen-presenting cells first internalize antigen, either by phagocytosis or by endocytosis, and then display a part of that antigen on their membrane bound to a class II MHC molecule. The T_H cell recognizes and interacts with the antigen–class II MHC molecule complex on the membrane of the antigen-presenting cell. An additional co-stimulatory signal is then produced by the antigen-presenting cell, leading to activation of the T_H cell.

Different type of APCs:-

Dendritic cells:-The dendritic cell (DC) acquired its name because it is covered with long membrane extensions that resemble the dendrites of nerve cells. Dendritic cells can be difficult to isolate because the conventional procedures for cell isolation tend to damage their long extensions.

There are many types of dendritic cells, although most mature dendritic cells have the same major function, the presentation of antigen to T_H cells. **Four types of dendritic cells are known: Langerhans cells, interstitial dendritic cells, myeloid cells, and lymphoid dendritic cells**. Each arises from hematopoietic stem cells via different pathways and in different locations. They all constitutively express high levels of both class II MHC molecules and members of the co-stimulatory B7 family. For this reason, they are more potent antigen-presenting cells than macrophages and B cells.



Macrophage: - Macrophages are mononuclear phagocytes. Macrophages are dispersed throughout the body. Some take up residence in particular tissues, becoming fixed macrophages, whereas others remain motile and are called free, or wandering, macrophages. Free macrophages travel by amoeboid movement throughout the tissues. Activated macrophages also express higher levels of class II MHC molecules, allowing them to function more effectively as antigen-presenting cells. Macrophages are participating in:-

- Phagocytosis
- Antimicrobial and cytotoxic activities:-

  A number of antimicrobial and cytotoxic substances produced by activated macrophages can destroy phagocytosed microorganisms.

  - ✓ Oxygen-dependent killing mechanisms
  - ✓ Oxygen-independent killing mechanisms
- Antigen processing and presentation
- Secretion of factors

B-Lymphocytes:- B lymphocytes mature within the bone marrow; when they leave it, each expresses a unique antigen-binding receptor on its membrane. This antigen-binding or B-cell receptor is a membrane-bound antibody molecule.

When a naive B cell (one that has not previously encountered antigen) first encounters the antigen that matches its membrane bound antibody, the binding of the antigen to the antibody causes the cell to divide rapidly; its progeny differentiate into **memory B cells and effector B cells called plasma cells**.

Memory B cells have a longer life span than naive cells, and they express the same membrane-bound antibody as their parent B cell.

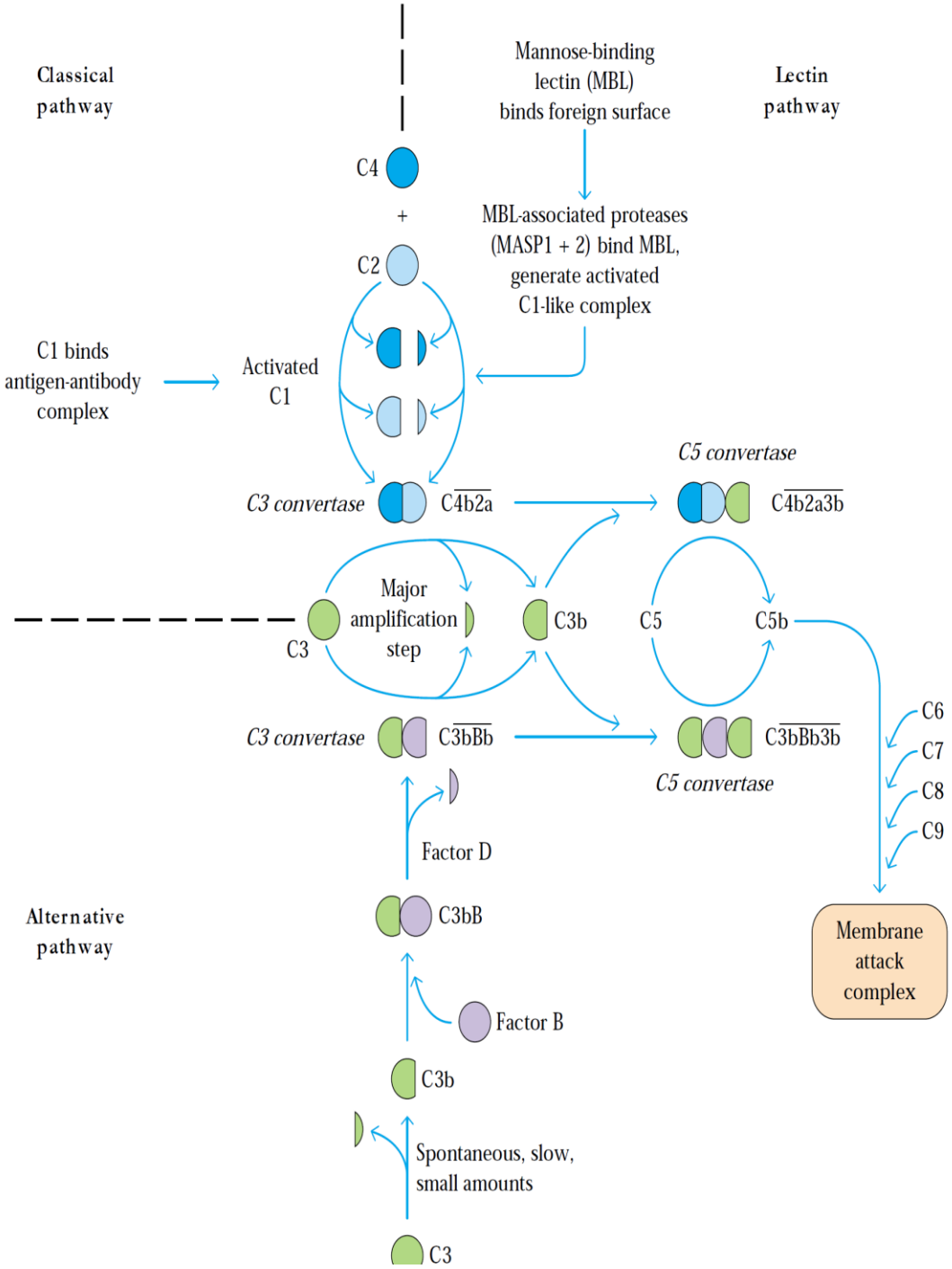
Plasma cells produce the antibody in a form that can be secreted and have little or no membrane-bound antibody. Although plasma cells live for only a few days, they secrete enormous amounts of antibody during this time. The molecules expressed on the membrane of mature B cells are the following:-

- B220 (a form of CD45) , Class II MHC molecules permit the B cell to function as an antigen-presenting cell (APC), CR1 (CD35) and CR2 (CD21), Fc ϒRII (CD32) is a receptor for IgG, a type of antibody, B7-1 (CD80) and B7-2 (CD86), CD40 is a molecule that interacts with CD40 ligand

Q:-Give an overview of the complement activation pathways.

Ans.:- Complement system is a major effector of humoral branch of immune system. This is activated by three pathways:-

- ✓ Classical Pathway
- ✓ Lectin Pathway
- ✓ Alternative Pathway

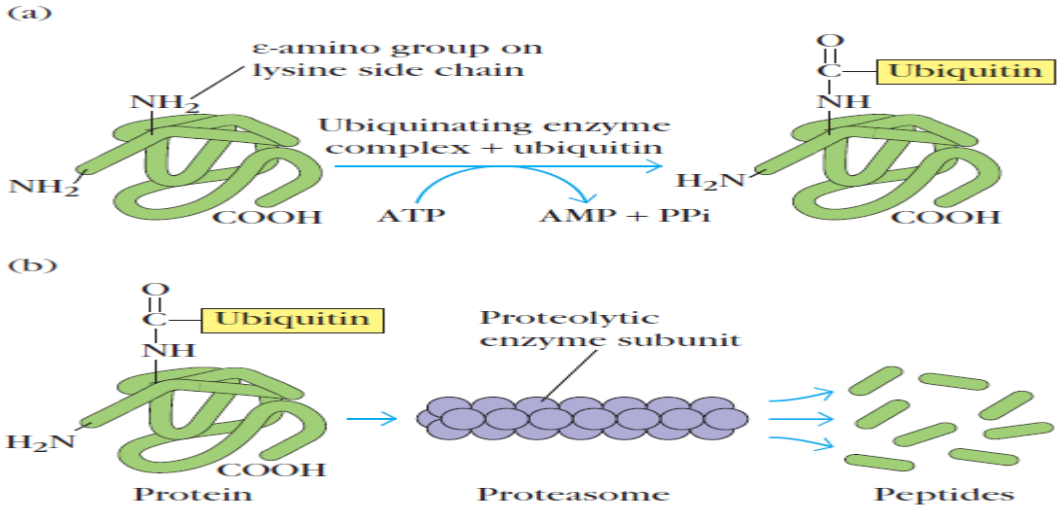


Q. Describe cytosolic and endocytic pathway of antigen processing.

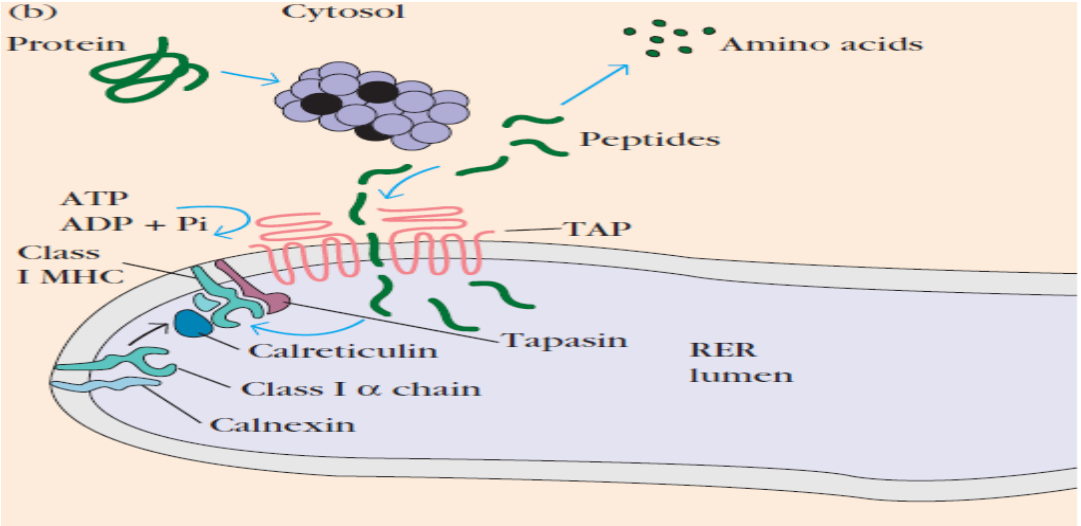
Ans.:-Recognition of foreign protein antigen by T cell requires that peptide derived from the antigen should be displayed in the cleft of MHC molecule on membrane of a cell. The formation of these peptide-MHC complexes requires that a protein antigen be degraded into peptides by a sequence of events called **antigen processing**. The degraded peptides then associate with MHC molecules within the cell interior, and the peptide MHC complexes are transported to the membrane, where they are displayed called antigen **presentation**.

Cytosolic Pathway:- This is for the endogenous antigen and presented through MHC I.

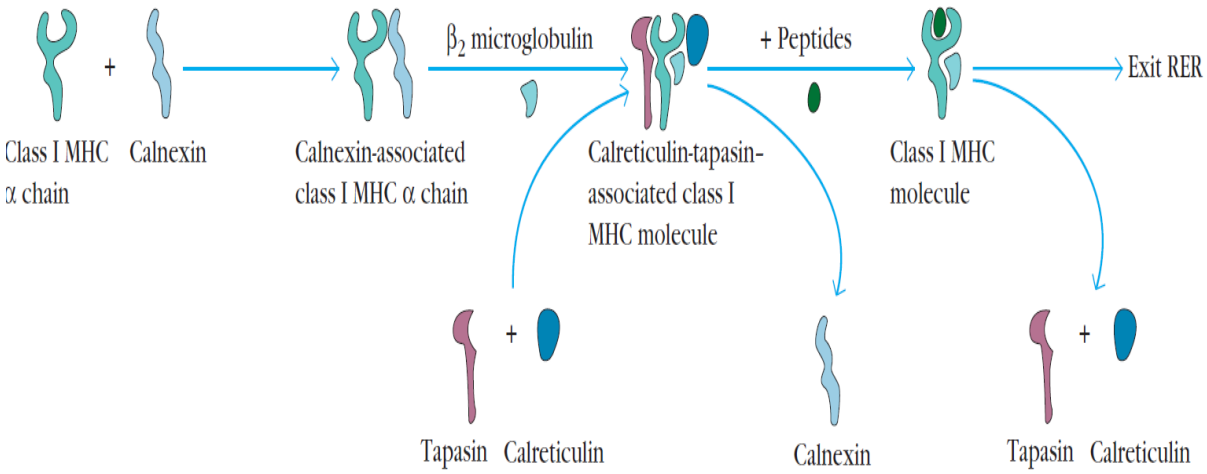
Peptide Generation:-



b.Transpotation of peptide:-

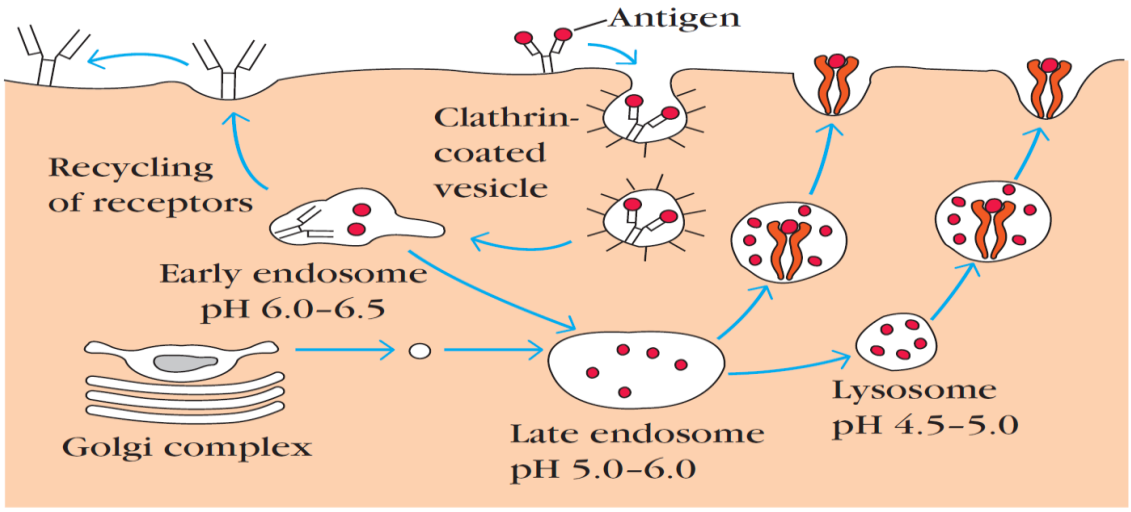


c. Assembly of Peptide with MHC I in ER and presentation:-

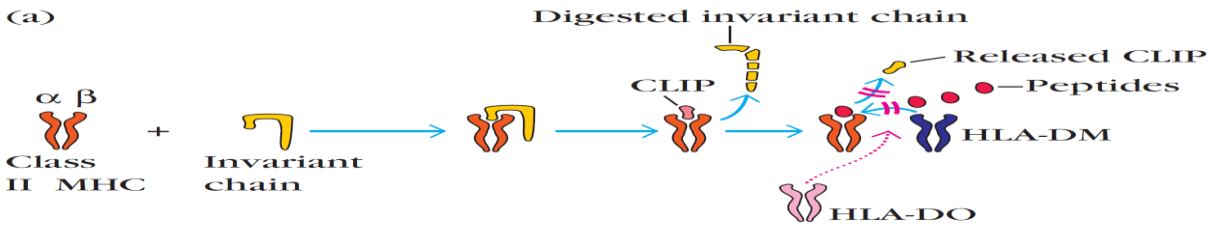


b. **Endocytic Pathway**:- This pathway is for exogenous antigen and through the MHC II Molecule.

Generation of antigenic peptides in the endocytic processing pathway:-



Assembly of MHC II Molecule:-

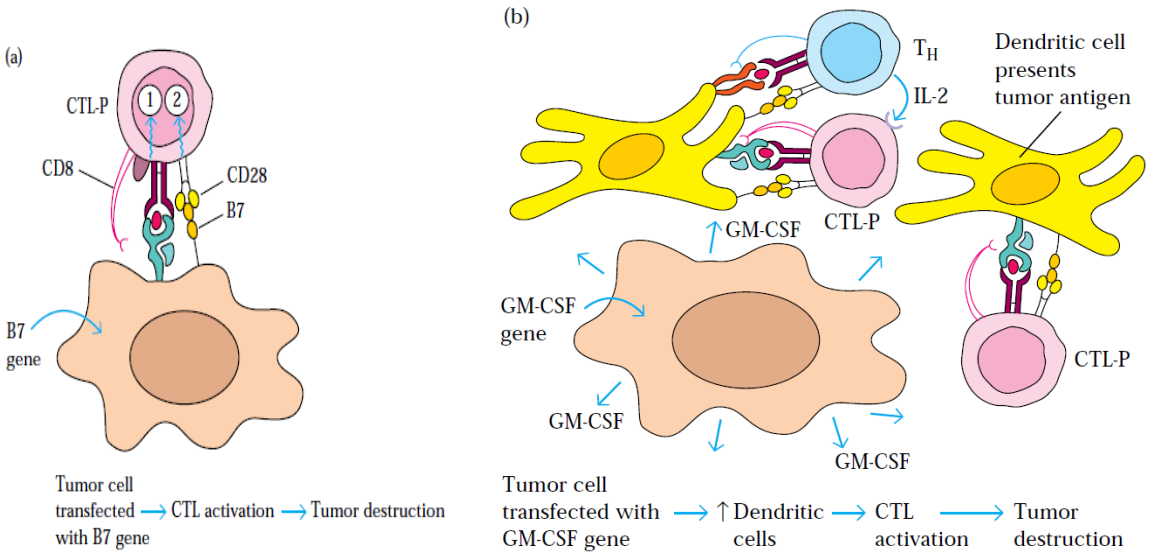


Q. Infusion of transfected melanoma cells into cancer patients is a promising immunotherapy.

a. Which two genes have been transfected into melanoma cells for this purpose? What is the rationale behind use of each of these genes?

b. Why might use of such transfected melanoma cells also be effective in treating other types of cancers?

Ans:- (a)



Use of transfected tumor cells for cancer immunotherapy:-

(a) Tumor cells transfected with the B7 gene express the co-stimulatory B7 molecule, enabling them to provide both activating signal (1) and co-stimulatory signal (2) to CTL-Ps. As a result of the combined signals, the CTL-Ps differentiate into effector CTLs which can mediate tumor destruction. In effect, the transfected tumor cell acts as an antigen-presenting cell.

(b) Transfection of tumor cells with the gene encoding GM-CSF allows the tumor cells to secrete high levels of GM-CSF. This cytokine will activate dendritic cells in the vicinity of the tumor, enabling the dendritic cells to present tumor antigens to both T_H cells and CTL-Ps.

Ans. b.:- Because human melanoma antigens are shared by a number of different human tumors, it might be possible to generate a panel of B7-transfected melanoma cell lines that are typed for tumor-antigen expression and for HLA expression.In this approach, the tumor antigen(s) expressed by a patient's tumor would be determined, and then the patient would be vaccinated with an irradiated B7-transfected cell line that expresses similar tumor antigen(s).

Q. Describe the antigen their features and structure.

Ans. :- The substances that can be recognized by immunoglobulin receptor of B cell and by the T cell complexed with MHC molecule is known as **Antigen**.

Immunogenicity is the ability to induce a humoral and/or cell-mediated immune response.

Antigenicity is the ability to combine specifically with the final products of the above responses (i.e., antibodies and/or cell-surface receptors).

Features of Antigens:-Immunogenicity is determined, in part, by four properties of the immunogen: its foreignness, molecular size, chemical composition and complexity, and ability to be processed and presented with an MHC molecule on the surface of an antigen-presenting cell or altered self-cell.(**Discription)**

The Biological System Contributes to Immunogenicity:-

Genotype of the recipient animal**,** immunogen dosage and route of administration, adjuvants **(Discription)**

Epitopes:-Immune cells do not interact with, or reconize, an entire immunogen molecule; instead, lymphocytes recognize discrete sites on the macromolecule called epitopes, or antigenic determinants. Epitopes are the immunologically active regions of an immunogen that bind to antigen-specific membrane receptors on lymphocytes or to secreted antibodies. Studies with small antigens have revealed that B and T cells recognize different epitopes on the same antigenic molecule.

Comparison of Antigen Recognition by T and B cell

Characteristic	B cells	T cells
Interaction with antigen	Involves binary complex of membrane Ig and Ag	Involves ternary complex of T-cell receptor, Ag, and MHC molecule
Binding of soluble antigen	Yes	No
Involvement of MHC molecules	None required	Required to display processed antigen
Chemical nature of antigens	Protein, polysaccharide, lipid	Mostly proteins, but some lipids and glycolipids presented on MHC-like molecules
Epitope properties	Accessible, hydrophilic, mobile peptides containing sequential or nonsequential amino acids	Internal linear peptides produced by processing of antigen and bound to MHC molecules