MAJOR HISTOCOMPATIBILITY COMPLEX

Q.What is major histocompatibility complex?

i)Every mammal's species possesses a tightly linked cluster of genes, the major histocompatibility complex (MHC), whose products play roles in intercellular recognition and in discrimination between self and nonself.

ii)The MHC participates in the development of both humoral and cell mediated immune responses.

iii)While antibodies may react with antigens alone, most T cells recognize antigen only when it is combined with an MHC molecule.

iv)The particular set of MHC molecules expressed by an individual influences the repertoire of antigens to which that individual's T_H and T_C cells can respond.

v)The major histocompatibility complex is a collection of genes arrayed within a long continuous stretch of DNA **on chromosome 6** in humans and **on chromosome 17** in mice.

vi)The MHC is referred to **as the HLA complex** in humans and as **the H-2 complex** in mice.

Q.State the role of MHC genes./ Q.How MHC I differs from MHC II?

i)Class I MHC genes encode glycoproteins expressed on the surface of nearly all nucleated cells.

ii)The major function of the class I gene products is presentation of peptide antigens to T_C cells.

iii)Class II MHC genes encode glycoproteins expressed primarily on antigen-presenting cells (**macrophages, dendritic cells, and B cells**), where they present processed antigenic peptides to T_H cells.

iv)Class III MHC genes encode, in addition to other products, *various secreted proteins that have immune functions, including components of the complement system* and molecules involved in **inflammation**.

The loci constituting the MHC are highly polymorphic, that is, many alternative forms of the gene, or alleles, exist at each locus among the population.

Class I and class II MHC molecules are membrane-bound glycoproteins that are closely related in both structure and function. Both types of membrane glycoproteins function as highly specialized antigen-presenting molecules that form unusually stable complexes with antigenic peptides, displaying them on the cell surface for recognition by T cells. In contrast, class III MHC molecules are a group of unrelated proteins that do not share structural similarity and common function with class I and II molecules.

Q.Give a comparative analysis between MHC I and MHC II./ Q.Give characteristic features of MHC I/ Q.Give characteristic features of MHC II.

i)Structural analyses have revealed that the α chain of class I MHC molecules is organized into three external domains (α1, α2, and α3), each containing approximately **90 amino acids**.

ii)A transmembrane domain of about 25 hydrophobic amino acids followed by a short stretch of charged (hydrophilic) amino acids and a cytoplasmic anchor segment of 30 amino acids.

iii)**The β-microglobulin** is similar in size and organization to the α3 domain; it does not contain a transmembrane region and is noncovalently bound to the class I glycoprotein.

iv)Sequence data reveal homology between the α3 domain , β2-microglobulin, and the constant-region domains in immunoglobulins.

v)**The α1 and α2 domains** interact to form a platform of eight antiparallel β- strands spanned by two long αhelical regions.

vi)The structure forms a deep groove, or cleft with the long α helices as sides and the β strands of the β sheet as the bottom (**Figure1**). This peptide-binding cleft is located on the top surface of the *class I MHC molecule,* and it is large enough to bind a peptide of 8–10 amino acids.

vii)Processed antigen and self-peptides bound to the α1 and α2 domains in this deep groove. The α3 domain and β_2-microglobulin are organized into Two β pleated sheets each formed by antiparallel β strands of amino acids.

viii)The α3 domain appears to be highly conserved among class I MHC molecules and contains a sequence that interacts with the **CD8 membrane molecule** present on T_C cells.