

Major Histocompatibility Complex

In humans proteins coded by the genes of the major histocompatibility complex (MHC) include human leukocyte antigen (HLA) as well as other proteins. HLA proteins are present on the surface of most of the body's cells and are important in helping the immune system distinguish self from non self molecules, cells and others. MHC molecule is a cell surface glycoprotein receptor present in APCs and acts as antigen presenting structure. It plays a vital role in immune recognition, including interaction between T cells and other cell types.

In humans the MHC is located on the short arm of chromosome 6, in mice it is found on chromosome 17. HLA is the human version of the major histocompatibility complex (MHC), a gene group that occurs in many species. In humans, the MHC complex consists of more than 200 genes located close together on [chromosome 6](#). Genes in this complex are categorized into three basic groups: class I, class II, and class III.

Humans have three main MHC class I genes, known as [HLA-A](#), [HLA-B](#), and [HLA-C](#). The proteins produced from these genes are present on the surface of almost all cells. On the cell surface, these proteins are bound to protein fragments (peptides) that have been exported from within the cell. MHC class I proteins display these peptides to the immune system. If the immune system recognizes the peptides as foreign (such as viral or bacterial peptides), it responds by triggering the infected cell to self-destruct.

There are six main MHC class II genes in humans: HLA-DPA1, [HLA-DPB1](#), [HLA-DQA1](#), [HLA-DQB1](#), [HLA-DRA](#), and [HLA-DRB1](#). MHC class II genes provide instructions for making proteins that are present almost exclusively on the surface of certain immune system cells. Like MHC class I proteins, these proteins display peptides to the immune system.

MHC class-I:

- Class-I MHC gene encodes glycoprotein molecule which is expressed on the surface of all nucleated cells and platelets.
- MHC-I molecule contains a 45KDa α -chain associated non-covalently with a 12KDa β 2 microglobulin molecule.
- Association of α -chain and β 2 microglobulin is required for expression of class-I MHC molecule on cell membrane.

- The α -chain is a transmembrane glycoprotein encoded by polymorphic gene within A, B and C region of Human HLA complex
- The α -chain is anchored in the plasma membrane by its hydrophobic trans-membrane segment and hydrophilic cytoplasmic tail.
- α -chain is made up of 3 domains (α_1, α_2 and α_3). Each domain containing approximately 90 aminoacids, a transmembrane domain of about 25 hydrophobic aminoacids followed by short stretch of charged (hydrophilic) aminoacids of cytoplasmic tails of 30 aminoacids.
- The folding of alpha 1 and alpha 2 domains creates a long cleft or groove on the top which is a **peptide binding cleft**. It can binds antigen of 8-10 aminoacids long and are presented to CD 8 lymphocyte.

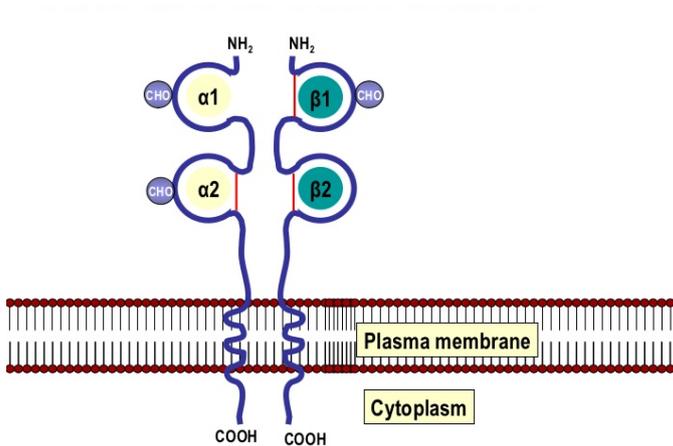
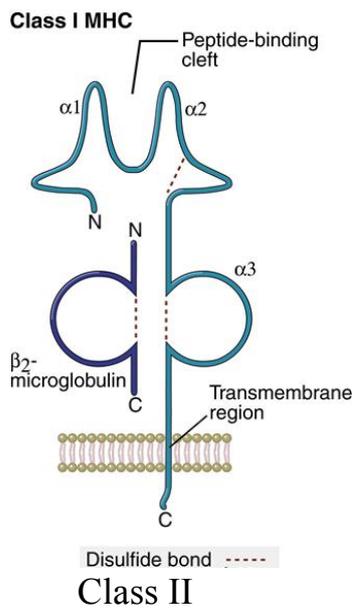
β_2 microglobulin of MHC-I:

β_2 microglobulin is similar in size and organization to α_3 domain.

β_2 microglobulin does not contain transmembrane region and is non-covalently linked with α -chain and is encoded on chromosome 15. The α_1 and α_2 domains fold together into a single structure consisting of two segmented alpha helices lying on a sheet of eight antiparallel b strands.

Functions of MHC class I:

- Major function of MHC-I is to bind peptide antigens and present to CD8+ T cells (T helper cells)
- CD8 T cells are specific for MHC-I antigen
- MHC-I binds endogenous antigen and present to T helper cells.
- MHC-I molecules are found on surface of all nucleated cells.



- Class-II MHC is the glycoprotein molecule expressed primarily on antigen presenting cells such as macrophages, dendritic cells and B-cells.
- MHC-II molecules contains two different polypeptide chains, 1 33 KDa α -chain and 28KDa β -chain which are associated by non-covalent interactions.

α -chain and β -chain of MHC-II:

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- MHC-II molecules contains two different polypeptide chains, 1 33 KDa α -chain and 28KDa β -chain which are associated by non-covalent interactions.

α -chain and β -chain of MHC-II:

- α -chain and β -chain of MHC-II is a membrane bound glycoprotein that contains external domains, a transmembrane segment and a cytoplasmic tail.
- α -chain and β -chain are made up of two domains (α 1 and α 2) and (β 1 and β 2) respectively.
- The peptide binding cleft is an open ended groove formed between α -chain and β -chain at proximal end. The cleft can bind antigenic peptide of 13-18 aminoacids long.

Functions of MHC class II:

- Major function of MHC-II is to bind peptide antigen and present to CD4 T cells.
- MHC-II are found on surface of Antigen presenting cells (APCs).
- CD4+T-cells are specific for MHC-II
- Activates B cells for antibody production