

- For MHC class II, the β polypeptide chain is far more variable than the α chain.

MHC genes are co-dominantly expressed so that the variant of for example *HLA-A* inherited from both parents will both be expressed. Therefore, a given individual might express HLA-A2 and HLA-A74, HLA-B8 and HLA-B27 and HLA-C1 and HLA-C6, one set inherited from their mother and the other from their father. The same co-dominant expression is seen with the MHC class II molecules.

Structure of MHC molecules

MHC class I

- The MHC class I molecule is a heterodimer.
- It is comprised of a highly polymorphic α polypeptide chain of 44kDa. This α chain is organized into three globular domains (α_1 , α_2 and α_3) that protrudes from the cell surface; a hydrophobic section anchors the molecule in the membrane and it also have a short cytoplasmic N-terminal tail.
- This α chain is linked to the smaller, non-polymorphic, 12kDa polypeptide called β -microglobulin. This β -microglobulin ensures correct folding of the MHC class I molecule and is not involved in peptide binding.
- The β -microglobulin and α_3 regions of the MHC class I molecule form into what resemble an immunoglobulin domain.
- The α_1 and α_2 , which are most distal to the membrane, form two extended α helices above a β -pleated sheet, forming the peptide-binding groove.
- The peptide-binding groove of MHC class I molecules is closed at both ends, thereby allowing it to occupy smaller peptides.

MHC class II

- The MHC class II molecule is also a heterodimer.
- It is comprised of a 34kDa α polypeptide organized into two globular domains (α_1 and α_2) and a 29kDa β polypeptide chain, also organized into two globular domains (β_1 and β_2).
- α_2 and β_2 (nearest to surface) fold into immunoglobulin domains.
- α_1 and β_1 (distal to surface) form two extended helices above a β -pleated sheet, similar to the α_1 and α_2 of MHC class I. Again, this forms the peptide-binding groove.
- The peptide-binding groove of MHC class II molecules is open at both ends, thereby allowing it to occupy larger peptides.

Peptide-binding to MHC

To MHC class I

- MHC class I molecules present peptides of 8-10 amino acids in length.
- The peptides that bind to MHC class I are derived from endogenous antigens.
- The forces involved in peptide binding to MHC are non-covalent.