Major Histocompatibility Complex

PART-2

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Major Histocompatibility Complex (MHC) genes

- Vertebrate genomes possess tightly linked clusters of genes that constitute the MHC, also known as MHC locus.

- MHC genes are **codominantly** expressed.

- Two types of MHC gene found in the MHC locus i.e., Class I and Class II MHC gene.

- Class I and Class II MHC genes are **highly polymorphic** in the human genome, because every individual has a unique immune system.

- The frequency of crossing over between the MHC genes are very low i.e., once in every 200 meiotic cycles. Thus the individuals inherit all alleles encoded by these MHC gene as a set (Know as linkage disequilibrium). This set of linked alleles is referred to as a **haplotype**.

- As already mentioned in the previous lecture, in humans MHC genes are located in the chromosome no. 6; while in mice, it is located in the chromosome no. 17.

- **In Human-MHC genes are**:-

  - HLA-A
  - HLA-B
  - HLA-C

  } Encode Class I MHC molecule

  - HLA-DP
  - HLA-DQ
  - HLA-DR

  } Encode Class II MHC molecule

- **In Mice-MHC gene are**:-

  - H-2K
  - H-2D
  - H- 2L

  } Encode Class I MHC molecule

  - I-A
  - I-E

  } Encode Class II MHC molecule

Comparison of the organization of the major histocompatibility complex (MHC) in mouse and human

Mouse H-2 complex

Complex	H-2						
MHC class	I	II		III		I	
Region	K	IA	IE	S		D	
Gene products	H-2K	IA αβ	IE αβ	C' proteins	TNF-α Lymphotoxin-α	H-2D	H-2L[a]

[a]Not present in all haplotypes

Human HLA complex

Complex	HLA							
MHC class	II			III		I		
Region	DP	DQ	DR	C4, C2, BF		B	C	A
Gene products	DP αβ	DQ αβ	DR αβ	C' proteins	TNF-α Lymphotoxin-α	HLA-B	HLA-C	HLA-A

Reference: Kuby –Immunology; 7th Edition by Judith A. Owen, Jenni Punt, Sharon A. Stranford and Patricia P. Jones; Chapter-8: The Major Histocompatibility Complex and Antigen Presentation; Page: 268

Human- Class I MHC genes and their products

- ✓ Encode glycoproteins in the form of Class I MHC molecules.
- ✓ All nucleated cell surfaces expressed Class I MHC molecules which are encoded by Class I MHC genes.
- ✓ Class I gene products (Class I MHC molecules) helps in presentation of endogenous antigenic peptides for $CD8^+$ T lymphocyte cells.
- ✓ Class I genes have a 5' leader exon (L) encoding a short **signal peptide** followed by five of six exons encoding the α chain of the class I molecule. Signal peptides guide the nascent α chain and help in insertion in the lumen of the endoplasmic reticulum for further processing.
- ✓ The next three exons encode the extracellular α 1, α 2, and α 3 domains.
- ✓ Another downstream exon encodes the transmembrane (Tm) region of class I MHC molecules.
- ✓ Finally, one or two 3' terminal exons encode the cytoplasmic tail region (C).

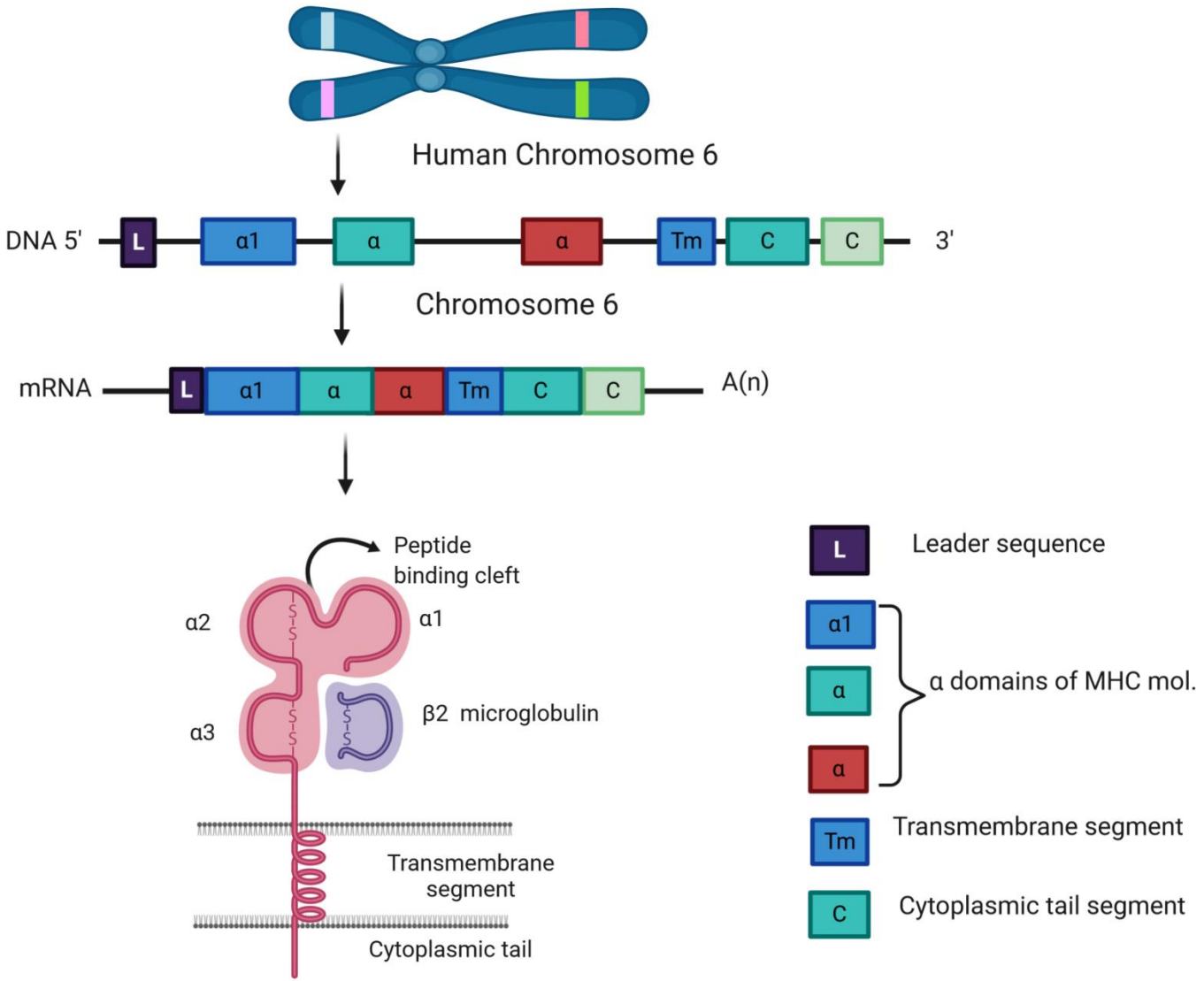

Diagram of Class I MHC chromosome, gene, mRNA transcript and protein mol.

Note:- β2 microglobulin gene located on the other chromosome.

Human- Class II MHC genes and their products

- ✓ The class II MHC genes encode class II MHC molecules.
- ✓ The Class II MHC molecules are expressed on the surface of antigen presenting cells such as B-lymphocyte cells, macrophage cell and dendritic cell.
- ✓ The Class II MHC molecules present exogenous antigen peptide for $CD4^+$ T-lymphocyte cells.
- ✓ The class II MHC genes are also organised into a series of exons and introns representing the domain structure of the α and β chains like class I MHC gene.
- ✓ An α and β gene have a leader exon, an α1 and β1 exon, a transmembrane exon (Tm) and one or more cytoplasmic exons (C).

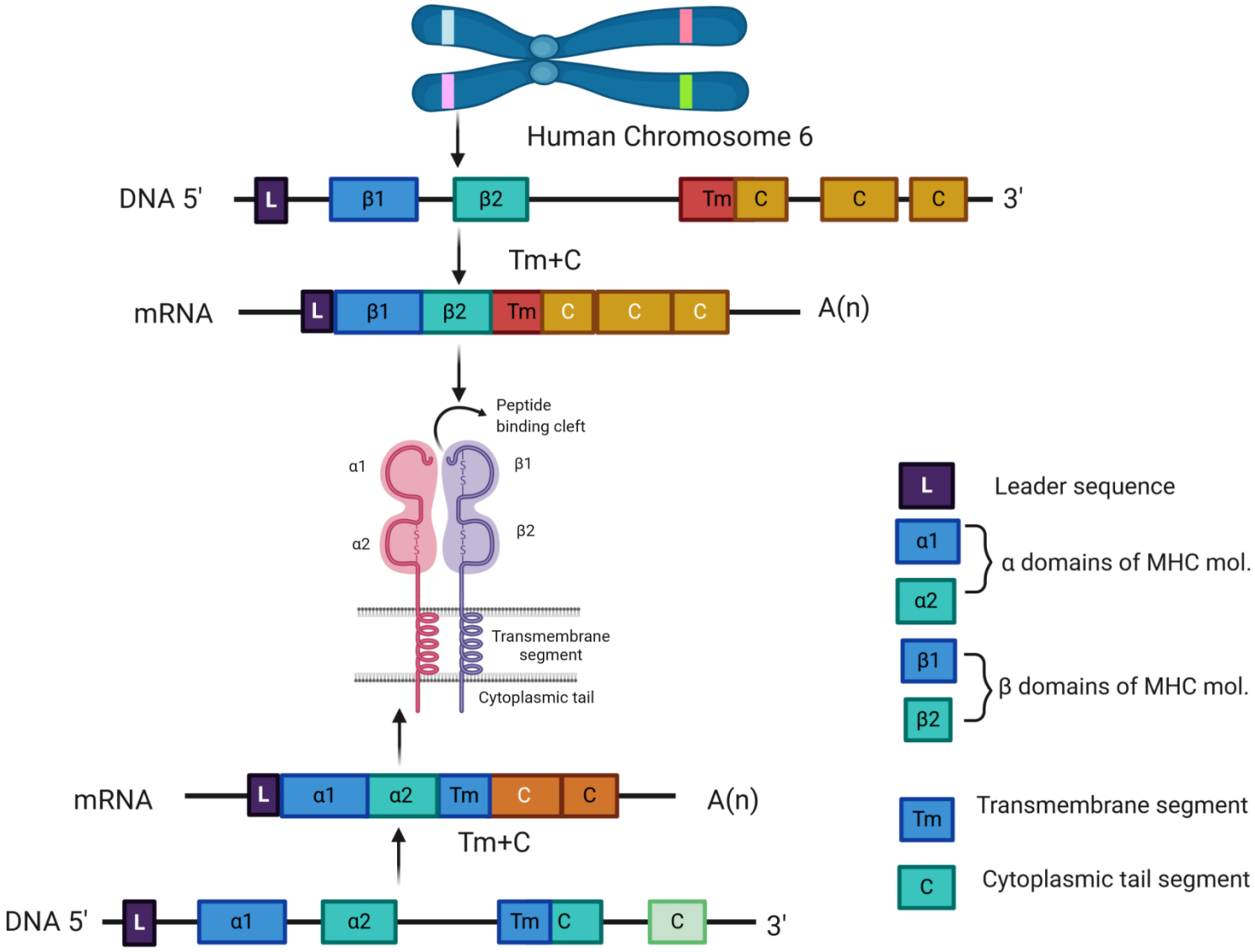

Diagram of Class II MHC chromosome, genes, mRNA transcript and protein mol.

Note:- β2 microglobulin gene located on the other chromosome.

Human- Class III MHC genes and their products

The class III MHC genes encode many complement proteins such as C4, C2 and factor B as well as several cytokines such as TNF- α and TNF- β (tumour necrosis factor protein) helps in inflammatory response.

Thanks