MAJOR HISTOCOMPATABILITY COMPLEX - GENETICS

A. INDUMATHI
Assistant Professor
PG & Research Department of Biotechnology
Bon Secours College for Women, Thanjavur

Introduction

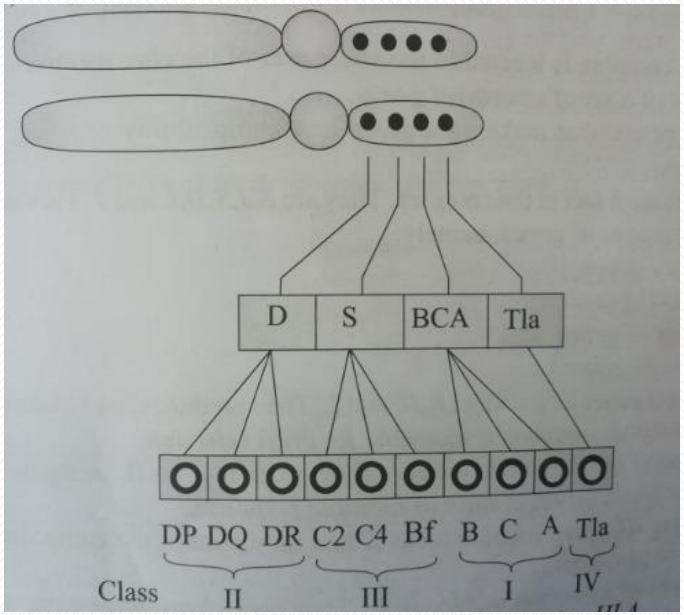
❖ The MHC system in humans was subsequently discovered in early 1950s.

❖ The MHC has genes (including the HLA) that form part of the normal function of the immune system.

❖ The MHC is an extreme gene-dense region of the genome, and it can be divided into three sub-regions; the class I, the class and the class III regions. All encoded by a gene complex located on the short arm of 6.

Introduction

- The complex genes has **SIX loci** and they are named as **B, C, A, D, S** and **Tla.**
- **BCA** produces **class I MHC molecules.**
- **D** produces **class II MHC molecules.**
- **S** produces **class III MHC molecules.**
- **Tla** produces **class IV MHC molecules.**



- The **locus D** is further divided into **3 loci, DR, DQ & DP**
- **Tla** is located adjacent to **A**
- **S** is located between **B** & **D**
- The **locus S** is further divided into **3 loci, C2, C4 & Bf (factor B)**

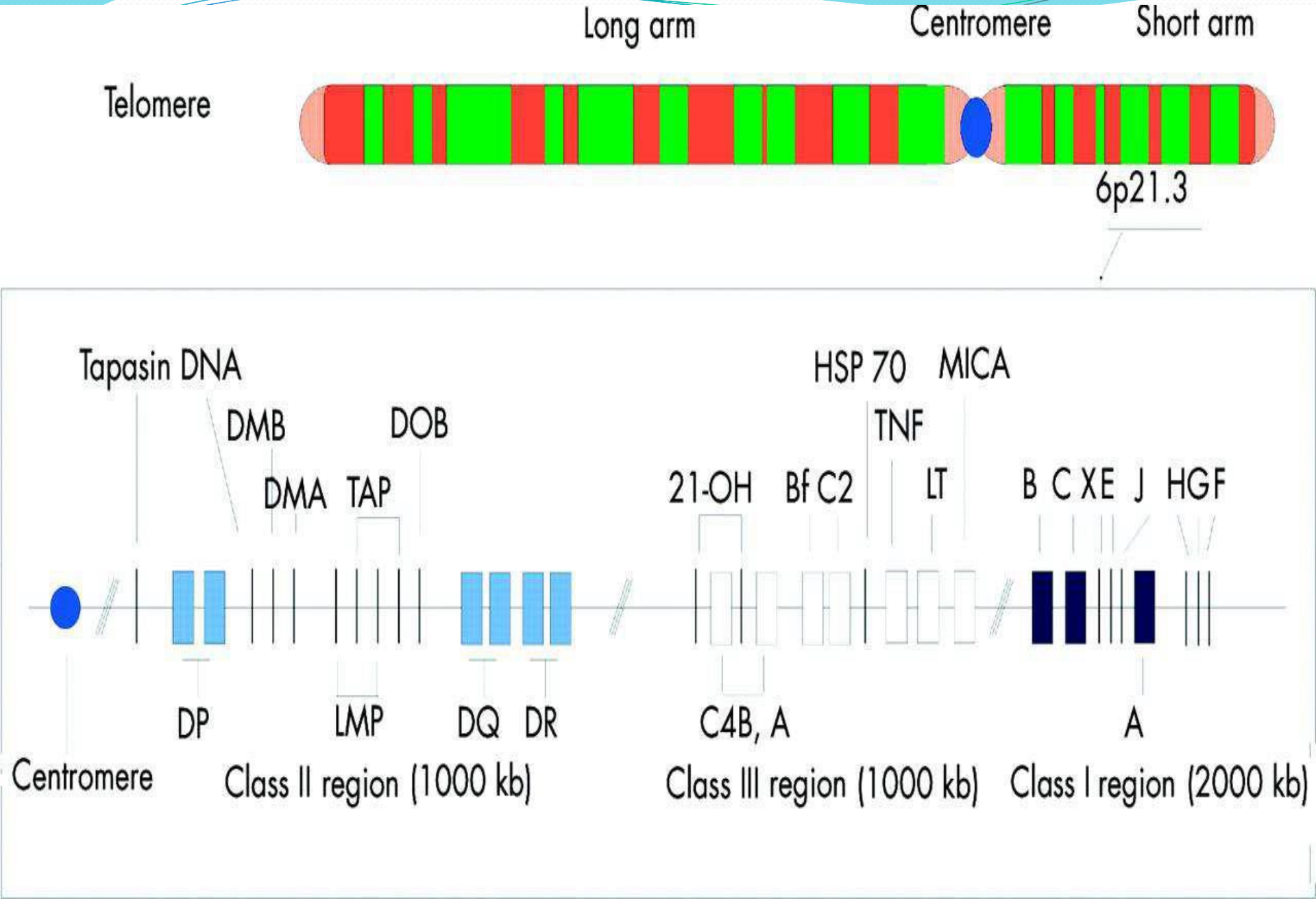
Major Histocompatability complex- Genes

❖**The class I region** of approximately 2000 kilobases include; the polymorphic HLA-A, B, C loci; non classical class HLA E,F, G,..

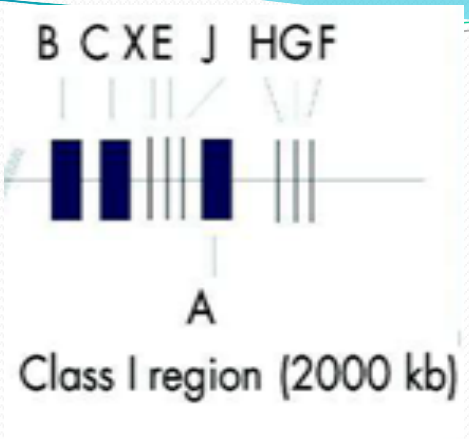
❖**The class II region** of approximately 1000 kilobases include; HLA-DR, DQ an DP loci, ...and non classical class HLA class II HLA-DM, DO,.

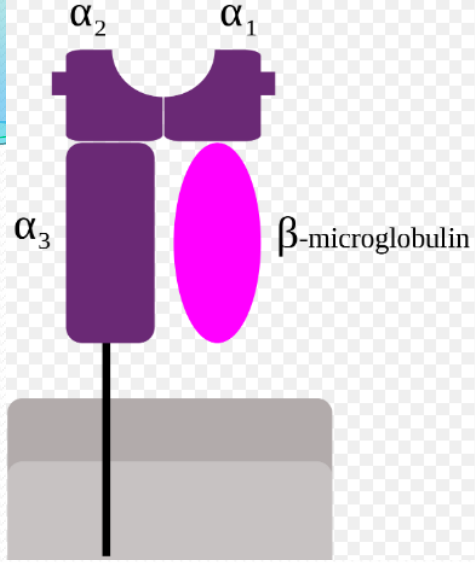
❖ **The class III region** of approximately 1000 kilobases encode genes with diverse functions and does not contain any HLA

❖genes. Contain loci responsible for the complement, hormones,...


Long arm
Centromere
Short arm
Telomere
6p21.3
Tapasin DNA
DMB
DOB
DMA
TAP
HSP 70
MICA
TNF
21-OH
Bf C2
LT
B C XE J HGF
DP
LMP
DQ
DR
C4B, A
A
Centromere
Class II region (1000 kb)
Class III region (1000 kb)
Class I region (2000 kb)

CLASS I REGION MHC GENES





❖Encoded by A,B,C etc loci.

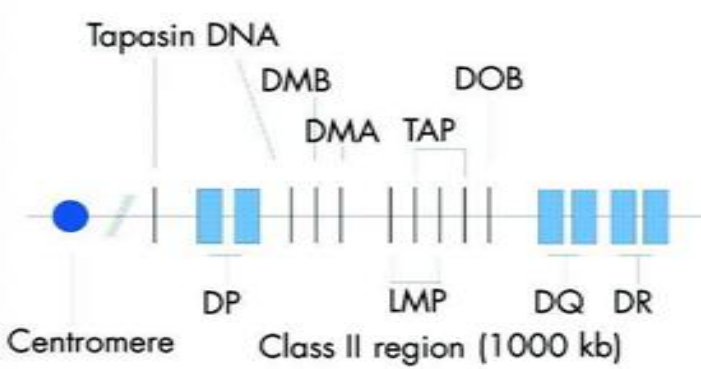
❖Expressed on all nucleated cells and platelets.

❖ Present antigenic peptides from within the cells (endogenous) to CD8 + T cell.

❖ MHC restriction of cell mediated cytotoxicity , the acceptance and rejection of grafts.

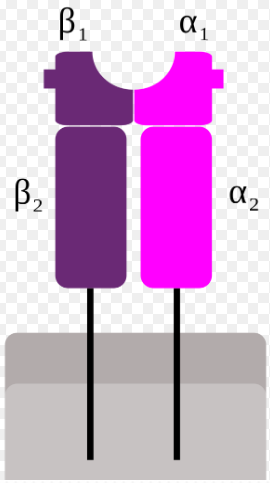
❖ These antigens also function as complement of hormone.

CLASS II MHC GENES



D region –DR, DQ & DP loci

- Protein that regulate the immune response.
- These are found only on the cell of immune system such as macrophage, dendritic cell activated T cell and B cell.
- These are the heterodimer consists of an alpha and beta chains.
- Each chain has two domain – a proximal constant region and a distal variable region.
- The distal region constitute the antigen-binding site for reorganization by CD4 Lymphocyte.
- The immune response genes, which control immunological response to specific antigen, are situated in this class 2 antigen.
- These are responsible for the graft versus host response and mixed leucocytes reaction (MLR).



CLASS III MHC GENES

complement region---

❖This group contains genes for C2 and C4 of classical pathway, properdin factor of alternative, heat shock protein, and tumor necrosis factor.

❖These are important component of complement system and are responsible for various cellular activities.

❖HLA loci are multiallelic, that is the genes occupying the locus can be any one of the of several alternative forms (alleles).

❖As each allele determines a distinct product (antigen),the HLA system is very **pleomorphic .**

❖For examples, at least 24 distinct allele have been identified at HLA locus A and 50 at B.

Expression of MHC Genes

MHC Region	Gene Product	Tissue location	Function
HLA-class I	HLA-A-B-C	Nucleated cells	Recognition of tumor and virus infected cells by CD8+ T lymphocytes
HLA-class II	HLA-DR-DQ-DP	Antigen presenting cells. B lymphocyte, Macrophage, Dendritic cells and Endothelial cells	Recognition of foreign antigens cells by CD4+ T lymphocytes
HLA-class III	Complement C2,C4,B	Plasma	Lysis of extracellular pathogens

References

Immunology –by – Janis Kuby

Essential immunology ---Ivan M. Roitt

https://www.slideshare.net/drnisha22/hla-92546736