**T-Cell System**

T-Cell Receptors(TCR)and Accessory Molecules Like B cells, Tcells have receptors that bind specifically to their steri ccounterparts on antigen epitopes.

T-cell receptors are associated with their so-called co-receptors—other membrane-enclosed proteins expressed on the Tcell surface—which include

the multiple-chainCD3complex,andCD4orCD8molecules(depending on the specific differentiation of the Tcell).CD stands for “cluster of differentiation”or “cluster determinant” and represents differentiation antigens defined by clusters of monoclonal antibodies.

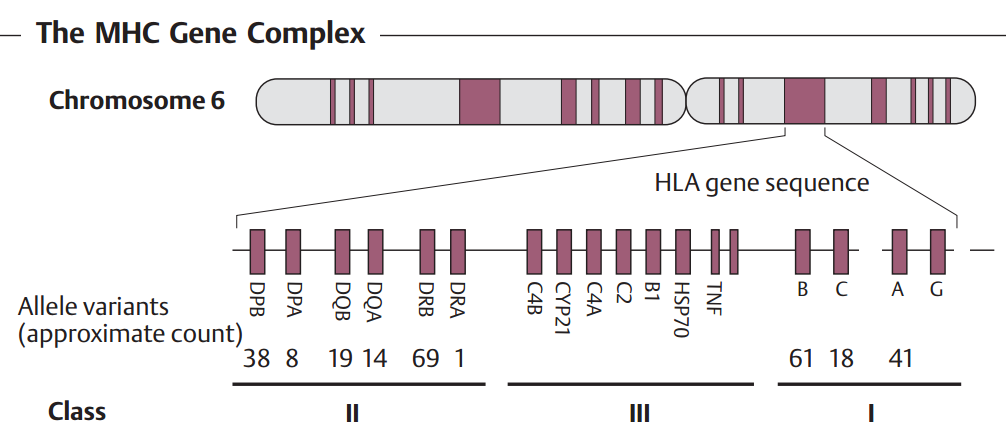
**T-Cell Specificity and the Major Histocompatibility Complex(MHC).**

T-cell receptors are unable to recognize free antigens.Instead theT-cell receptor can only recognizeits specific epitope once the antigen has been Cleaved into shorter peptide fragments by the presenting cell. These fragments must then be embedded with in a specific molecular groove and presented to the T-cell receptor (a process known as MHC-restrictedT-cell recognition or MHCrestriction) .This “binding groove”is located on the MHC molecule. The MHC encodes for the powerful histocompatibility or transplantation antigens (alsoknown in humans as HLA,human leukocyte antigen molecules). The designation “MHC molecule”derivesfrom the initial discoveryof the function of the complex as acell surfaces tructure,responsible for the immunological rejection of cell transfusions or tissue and organ transplants.

Its true function as apeptide-presenting molecule was not discovered until

The seventies.

The resulting conclusion was that a T-cell receptor not only recognizes The corresponding amino acid structure of the presented peptide ,but additionally recognizes certain parts of the MHC structure .It is now known that. This contact between MHC on the APC and the T-cell receptor is stabilized by theco-receptors CD4 and CD8.



MHC classes .Molecules encoded by the MHC can be classified in to three

Groups according to their distribution on somatic cells ,and the types of cells

By which they are recognized::

&MHC class I molecules: These molecules consist of a heavy a chain with

Three Ig-like polymorphic domains (these are encoded by100–1000 alleles,

with the α1and α 2 domains being much more polymorphic than the α 3domain) and a non-membrane-bound(soluble)single-domain β2 microglobulin

.β2 M, which is encoded by a relatively small number of alleles).The a chain

Forms a groove that functions to present antigenic peptides ,Human HLA-A, HLA-B ,and HLA-C molecules are expressed in varying densities on all somatic cells .Additional ,non classical, classI antigens which exhibit a low degree of polymorphism are also present on lympho hematopoietic cells and play a role in cellular differentiation.

& MHC class IImolecules .These are made up by two different polymorphic

Transmembrane chains that consist of two domains each (α1

is highly polymorphic ,whilst β1 is moderately polymorphic ,and β2 is fairly constant).

These chains combine to form the antigen-presenting groove. ClassII molecules are largely restricted to lymphohematopoetic cells, antigen-presenting

cells(APC), macrophages, and soon,In humans ,but not in mice ,they are also found on some epithelial cells ,neuro endocrine cells and Tcells .The product sof the three human gene regions HLA-DP, HLA-DQ and HLA-DR can additionally form molecules representing combinations of two loci—thus providing additional diversity for peptide presentation..

&MHCclass III molecules. These molecules are not MHCantigens in the

Classical sense, but are encoded within the MHC locus. These include complement (C)components C4 and C2, cytokines (IL,TNF), heat shock .hsp70),and other products important for peptide presentation.

