

Immunology

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Immunology By of [Word Count] Major Histocompatibility Complex Molecule

Cell surfaces are always covered by many molecules, compounds and atoms, which serve various mechanical, biological and chemical functions. The Major Histocompatibility Complex (MHC) is one such protein. The other name for HMC in humans is Human Leukocyte Antigen (HLA) (Ober, 2007). In essence, the MHC is a protein molecule found on the surface of the cell and it is encoded by a gene family in vertebrates. The main function of this cell surface molecule is to intervene in interactions of leukocytes (the white blood cells). It is the MHC that is used in assessing the compatibility of donor organs and tissues for transplants to recipients (Aderem & Underhill, 1999). Its other function is to assess an individual's susceptibility to autoimmune diseases. The family of genes that encodes MHC is subdivided into class I, II and III subgroups. There are several ways through which the MHC class I and II subgroups present diverse antigens to immune cells. These ways included polygenic encoding of the MHC, polymorphism of MHC genes resulting in many variants and the expression of several MHC genes from both inherited alleles (Kuhara, 2000).

Major Histocompatibility Complex Class I Protein Molecule

The MHC has three main proteins (class I, II and III) as mentioned earlier. A general feature of these proteins is their immunoglobulin-like formation. The MHC class I protein is an α chain made up of three domains namely α 1, α 2, α 3. The α 1 sits on a unit of the non-MHC molecule referred to as β 2 micro-globulin (Haig, 1997). On the other hand, the α 3, trans-membranous subunit, anchors the MHC class I molecule to the cell membrane.

Major Histocompatibility Complex Class II Protein Molecule

The MHC class II molecule is composed of β and α chains each with two domains— β 1 and β 2 and α 1 and α 2 respectively. Notably, each of

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these chains has a trans-membrane domains, $\alpha 2$ and $\beta 2$, respectively.

These trans-membrane domains anchor the MHC class II molecule to the cell membrane (Siddle, 2007). In this molecule of MHC, the peptide-binding groove is formed from the heterodimer of $\alpha 1$ and $\beta 1$. There are five or six isotypes of MHC class II molecules (Lundberg, 2002). These isotypes are the Classic molecules, which present peptides to CD4+ lymphocytes and the non-classic molecules that have intracellular functions since they are not exposed on cell membranes (Castellino, 1997). Although it seems similar to the class I MHC molecule, this class of MHC molecule has its two proteins spanning the membrane. Each of its chains is about kilodaltons and has two globular domains named Alpha-1 (blue-green), Alpha-2 (green), Beta-1 (purple) and Beta-2(magenta) as mentioned earlier (Chaix et al., 2008).

The two furthest regions from the membrane are the alpha-1 and beta-1 chains, which are not associated with covalent bonds. Each of the chains of this protein molecule has immunoglobulin regions adjacent to the cell membrane and has an antigen-binding cleft made up of two alpha-helices on top of a beta-pleated sheet (Boehm & Zufall, 2006). This antigen-binding cleft specifically binds short peptides of fifteen to twenty four residues. The most variable site of the MHC class II protein molecule is the amino acid sequence on the binding site. The role of this site is to specify the antigen-binding properties of the molecule. The differences in the structures of MHC class I and II offer an insightful explanation on the variations in the length requirements for the peptide to be bound. For instance, in the case of MHC class I protein molecule, the ends of the cleft that binds the antigen narrow and get blocked by huge tyrosines, which act by binding the N-terminus of the peptide (Wedekind & Bettens, 2005). In the class II molecule, which lacks

these features of conserved residues, smaller residues such as valine and glycine replace the larger tyrosines in class I MHC molecules. Conclusion Since the class I and II MHC molecules are needed for the presentation of many antigenic peptides for T cell recognition an action, there is need to find a compromise between high affinity and specificity. This problem is addressed by the 3-dimensional structures of the two classes of MHC molecules, via a uniquely structural solution. That is, whereas the peptide's main chain is restricted in movement, the side chains are less restricted, allowing for side chain contacts and variability in conformation to ensure or promote the peptide-MHC complex formation. This complex then presents unique antigenic surface for cell receptors. References Aderem, A., and Underhill, D. M. (1999) Mechanisms of Phagocytosis in Macrophages Annual Review of Immunology, 17: 593. Boehm, T., and Zufall, F. (2006) MHC Peptides and the Sensory Evaluation of Genotype. Trends in Neuroscience, 29 (2): 107. Castellino, F. (1997) Antigen Presentation by MHC Class II Molecules: Invariant Chain Function, Protein Trafficking, and the Molecular Basis of Diverse Determinant Capture. Human Immunology, 54(2): 159. Chaix, R., Chen, C., and Donnelly, P. (2008) Is Mate Choice in Humans MHC-Dependent? PLoS Genetics, 4(9): 233. Haig, D. (1997) Maternal-Fetal Interactions and MHC Polymorphism. Journal of Reproduction Immunology, 35 (2): 101. Kuhara, S. (2000) Changes at the Floor of the Peptide-Binding Groove Induce a Strong Preference for Proline at Position 3 of the Bound Peptide: Molecular Dynamics Simulations of HLA-A*0217. Biopolymers, 54 (5): 318. Lundberg, A. S. (2002) Evolution of Major Histocompatibility Complex Class II Allelic Diversity: Direct Descent in Mice and Humans. Proc Natl Acad Sci U S A, 89(14), 6549. Ober, C. (2007) HLA <https://assignbuster.com/immunology/>

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