Cytokines

Cytokines are small molecules, secreted by cells in response to a stimulus.

- They may have an effect on the cell that produces them and are critical to signaling between cells, with each cytokine often inducing several different biological effects. - Many different cells release cytokines, but each cell type releases only certain of these molecules.

- Cytokines may induce growth, differentiation, chemotaxis, activation, and/or enhanced cytotoxicity.

- Moreover, it is not uncommon for different cytokines to have similar activities and for many cytokines, some with opposing activities, to be released by a particular stimulus. Thus, the resulting biological effect is a factor of the sum of all of these activities.

- To some extent cytokines can be grouped by the cell populations that secrete them. Monokines are cytokines secreted by cells of the myeloid series (monocytes, macrophages) and lymphokines are cytokines secreted primarily by lymphocytes, although some cytokines are produced by both lymphocytes and myeloid cells.

- The term interleukin (IL) is often used to describe cytokines produced by leukocytes, although some interleukins are also produced by other cell populations. - A group of small heparin-binding cytokines, chemokines, direct cell migration, and may also activate cells in response to infectious agents or tissue damage.

- Interferons are produced by a variety of cells in response to viral infection. It is important to note that the same cytokine can be made by several different cell populations. For example, IFNα is made by most if not all nucleated cells in response to viral infection. IFNγ is produced both by Th1 cells and by NK cells.

- IL-1 is produced by macrophages, B cells and non-immune keratinocytes is the predominant cell type in the epidermis, the outermost layer of the skin. Many different cell types make IL-6, several make IL-4, etc.

- Moreover, the same cytokine can induce different functions in different cell types. For example, TNFα can promote the proliferation of B cells but activate killing mechanisms in other cell populations. IFNγ activates macrophages to kill intracellular microbes, induces B cells to switch their antibody class to IgG and induces endothelial cells to increase expression of MHC class II molecules.

Major Histocompatibility Complex

Major histocompatibility complex (MHC) was first detected as the genetic locus encoding the glycoprotein molecules (transplantation antigens) responsible for the rapid rejection of tissue grafts transplanted between genetically no identical individuals. It is now known that MHC molecules bind peptide antigens and present them to T cells. In humans, the MHC is a cluster of extensively studied genes located on chromosome 6. Among the many important genes in the human MHC, also known as HLA (human leukocyte antigens), are those that encode the class I, class II, and class III MHC proteins.

- Class I proteins are encoded by the HLA-A, -B, and -C genes. Class I molecules are to be found on virtually all nucleated cells in the body.
- Class II proteins are encoded by the HLA-D region.
- The class III MHC locus encodes complement proteins and several cytokines.
- The genes of the MHC exhibit a remarkable genetic variability. The MHC is polygenic in that there are several genes for each class of molecule. The MHC is also polymorphic. Thus, a large number of alleles exist in the population for each of the genes. Each individual inherits a restricted set of alleles from its parents. Sets of MHC genes tend to be inherited as a block or haplotype.Allele is one of a number of alternative forms of the same gene or same genetic locus (generally a group of genes). It is the alternative form of a gene for a character producing different effects.

1. Antigens are recognized by the appropriate T cell receptor (TCR) only in the context of the histocompatibility antigens.

2. Exogenous antigens (e.g., bacteria), which would undergo processing by an antigen presenting cell (APC), would be expressed on the surface of the APC in the context of a class II MHC molecule and be recognized by CD4+TH cells.

3. Endogenous antigens (e.g., virally transformed cell proteins) would be expressed on the surface of any cell in the context of a class I MHC molecule and be recognized by a CD8+TC cell.

Human leukocyte antigen : The human leukocyte antigen system (HLA) is the name of the major histocompatibility complex (MHC) in humans. The super locus contains a large number of genes related to immune system function in humans. This group of genes resides on chromosome 6, and encode cell surface antigen-presenting proteins and many other genes. The HLA genes are the human versions of the Major histocompatibility complex (MHC) genes that are found in most vertebrates, and are the most studied of the MHC genes. The proteins encoded by certain genes are also known as antigens, as a result of their historic discovery as factors in organ transplantations. The major HLA antigens are essential elements in immune function. Different classes have different functions. Human MHC class III and IV genes

The major histocompatibility complex (MHC) was initially defined as the genetic locus encoding the Class I and Class II highly polymorphic cell surface antigens that are now known to present antigen to matched sets of T cell receptors. Genes for several diverse complement components, specifically Bf, C2, and C4 were found between the Class I and II genes, in a region later dubbed Class III. More recently, several genes have been described that are encoded in the telomeric end of the Class III region and that appear to be involved in both global and specific inflammatory responses. Due to this commonality of function this gene-rich region was dubbed Class IV, and includes the TNF family, AIF1, and HSP70. The genes of the Class III and Class IV regions are sufficiently divergent in sequence and structure so that clustering is not explicable.