

## Cytokines (Interleukins) and its classification

The lymphocytes and other cells secrete certain glycoproteins in response to stimulus and infection. These glycoproteins are referred as interleukins which promote cellular growth of immune component cells. The interleukins are named as IL-1, IL-2 to IL-15 as per their order of discovery.

Alic Isaacs and Team Lindemann identified the first cytokine in 1957 while working on viral interference by anti viral agents. They isolated anti viral protein and called it ~~inter~~ interferon. The interferon (IFN) is secreted by T cells. Certain cytokines possess anti tumor activities and one called tumor necrosis factor- $\alpha$  (TNF- $\alpha$ )

The term cytokines and lymphokines refer to glycoproteins secreted by lymphocytes. Monocytes and macrophages produce interleukin called as Monokines. The study of cytokines can be done as follows -

1) Structure of cytokines - The cytokines belong to hematopoietin family its about 30K Da mol wt. The IL-2 and IL-4 are four polypeptide chain structure contain 2  $\alpha$ -helical proteins and  $\beta$  pleated sheets. These polypeptides are connected by loops.

2) Production of cytokines -  
The Production and classification of Key immune cytokines are shown in the table in next page.

Table showing a profile of activities of key immune cytokine

Cytokine	Producing cell	Target cell	function.
GM-CSF	TH <sup>1</sup> cells	Progenitor cells	Production of monocytes
IL-1 $\alpha$	Macrophages		
IL-1 $\beta$	B cells dendritic cells	NK cells	Inflammation, fever
IL-2	TH <sup>1</sup> cells	Activated T cells	Growth
		B cells and NK cells	Proliferation
IL-3	<del>TH<sup>1</sup> cells and</del> <sup>Stem cells</sup> mast cells	Stem cells & mast cells	Growth and differentiation
	TH <sup>1</sup> cells and NK cells		
IL-4	TH <sup>2</sup> cells	Activated B cells macrophages T cells	Differentiation Ig G <sup>1</sup> and Ig E Synthesis MHC-II, activation of B cells.
IL-5	TH <sup>2</sup> cells monocytes	Activated B cells	Proliferation and differentiation of B cells. Ig A synthesis
IL-6	Macrophages Stromal cells TH <sup>2</sup> cells	Plasma cells stem cells	Antibody secretion
IL-7	Marrow stroma Thymus stroma	Stem cells	Differentiation of progenitor B and T cells.
IL-8	Macrophages endothelial cells	Neutrophils	Chemotaxis
IL-10	TH <sup>2</sup> cells	Macrophages B cells	Inhibition of cytokine production
IL-12	Macrophages B cells	Activated T cells	Differentiation into CTL, inhibition of viral replication

11. IFN- $\alpha$	Leukocytes	various	Increase, MHC class II expression and inhibition of viral replication
IFN- $\beta$	Fibroblasts	various	

12. IFN- $\gamma$	Fibroblast TH <sup>1</sup> cells, Tc cells NK cells	Macrophages Activated B cells TH2 cells Macrophages	MHC expression Ig class Switch to IgG2a Inhibition of Proliferation Pathogen elimination
-------------------	---	--	--

13 MIP-1 $\alpha$	Macrophages	Monocytes - T cells	chemotaxis
MIP-1 $\beta$	Lymphocytes	Monocytes - T cells	

TGF $\beta$  - T cells monocytes Activated Macrophages IL-1 synthesis

TNF- $\alpha$  - Macrophages, mast cells, NK cells Macrophages Tumor cells CAM and cytokine expression cell death.

TNF $\beta$  - TH<sup>1</sup> cells and Tc cells Phagocytes Tumor cells Phagocytosis nitric oxide production cell death.

CTL - Cytotoxic T lymphocyte GM-CSF Granulocyte monocyte colony stimulating factor IFN - Interferon, IL - interleukin, MIP - Macrophage inflammatory protein TGF - Tumor growth factor, TNF Tumor necrosis factor.  
Tc - Cytotoxic T cell.

Properties of cytokines -  
1/ Cytokines are small secreted protein produced in response to an immune stimulus  
2/ cytokines act at a very low concentration

and mediate and regulate immunity, inflammation and hematopoiesis.

3/ They normally act over short distances via binding to specific membrane receptors.

4) They act via second messengers, such as tyrosine Kinase, to alter its behaviour via ~~binding~~ altered gene expression.

5) cytokines may act on the cells that secrete them (autocrine) or nearby cells (paracrine) or distant cells (endocrine)

6/ Cytokines are often produced in a cascade as one cytokine stimulates its target cells to express additional cytokines, it can also act synergistically in which two or more cytokines act together or antagonistically in which cytokines cause opposite activities.

7/ The Properties of cytokines depend upon cytokine function and cytokine receptors.