

CYTOKINES SUMMARIZATION



- Cytokines are **pleiotropic**, **redundant**, and **multifunctional**.
- Cytokines classified into 3 categories :
 1. Cytokines that produced by innate immune responses,
 2. Cytokines that produced by adaptive Immune responses, and
 3. Cytokines that stimulate hematopoiesis.

Cytokines that produced by innate immune responses :

CYTOKINES	SECRETED BY	TARGET(S)	FUNCTION(S)
IL-1 & TNF-α	M Φ & Neutrophil	M Φ , hypothalamus & liver.	1) Stimulate the synthesis of adhesion factors. 2) Activates macrophages to secrete chemokines. 3) Stimulate hypothalamus to increase prostaglandin syn. causing fever . 4) Stimulate the production of acute phase proteins from liver.
IL-12	M Φ & DC	CD8, NK & TH1.	1) Responses to intracellular microbes. 2) Inducer CD8 T cells , and NK cells . 3) TH1 cells differentiation. 4) It also stimulates IFN-γ production from these cells.
Type I INF (INF-α & INF-β)	INF- α ; M Φ INF- β ; viral infected cells & fibroblast cells.	Uninfected cells & viral infected cells.	1) Inhibits viral replication (paracrine & autocrine). 2) Increase expression of IL-12 (CD4 \rightarrow TH1). 3) Activation of CD8 \rightarrow Killing virus infected cells. 4) Activation NK \rightarrow Act against virus.
IL-6	M Φ & TH2	B cells.	1) Stimulate the liver to produce acute phase proteins. 2) differentiation & growth of B-Cells (from TH1). 3) CD4 \rightarrow TH17 (IF TGF- β present).
IL-10 (regulatory cytokine)	Treg & TH2	M Φ & DC	1) Inhibit activation of M Φ & DC \rightarrow Inhibit production of IL-12 & Co-stimulator molecules. 2) Regulates innate and cell-mediated immunity.
Chemokines CXC, CC, CCR7, IL-8, CCL2.	Leucocytes	Neutrophils, monocyte & lymphocyte	1) Recruitment of neutrophils (CXC). 2) Recruitment of monocyte (CC). 3) Recruitment of lymphocyte (CXC & CC). 4) Migration of immune cells from sites of infection into draining lymph nodes (CCR7). 5) Neutrophil migration into tissues (IL-8 by tissue resident macrophages). 6) Monocyte recruitment (CCL2).

NOTES :

- 1) Pro-inflammatory cytokines : **IL-1, TNF- α , IL6 & Lymphotoxin (LT, adaptive immunity).**
- 2) The most powerful stimulus for **INF-I** is the **first immune reaction** against viral infection.
- 3) **IL-12** : is a **primary mediator** of early innate immune responses to **intracellular microbes** (as: listeria, mycobacteria and viruses).

Cytokines that produced by adaptive Immune responses:

CYTOKINES	SECRETED BY	TARGET(S)	FUNCTION(S)
IL-2 (GF)	DC & TH1	T-cell, B-cell & CD8.	1) Growth factor for T-cell upon activation (3 rd signal) , it activates B cells (by DC). 2) Activate CD8 cells (By TH1).
IL-4	TH2 & Mast cell & UNKNOWN CELLS	B-cell & TH2.	1) Production of IgE in B cells. 2) Development of Th2 cells in allergy. 3) Inhibits cell-mediated immunity (antagonism to IFN- γ).
IL-5	TH2	Eosinophil & B-cell.	1) A growth and activating factor for eosinophils as a defense against helminths . 2) proliferation and differentiation of antigen-activated B-cells and the production of IgA .
IFN-γ (Type II INF)	TH1, NK & CH8	M Φ , TH2 & B-cell.	1) Activating macrophages (principal cytokine). 2) It also promote cell-mediated immunity . 3) Inhibits the proliferation of Th2 cells. 4) Stimulates the production of IgG that activate the complement pathway and promote opsonization .
TGF-β (regulatory cytokine)	Treg	T-cell, B-cell & M Φ .	1) Inhibit the proliferation and effector function of T-cell. 2) Inhibit the proliferation of B-cell. 3) Inhibit macrophage function.
Lymphotoxin (LT)	T-cell	Neutrophils	1) Recruitment and activation of neutrophils . 2) in lymphoid organogenesis .
IL-17	TH17	Neutrophils & M Φ .	1) Recruiting neutrophils and M Φ to site of infection. 2) Inducing inflammation .

Cytokines that stimulate hematopoiesis:

CYTOKINES	SECRETED BY	TARGET(S)	FUNCTION(S)
GM-CSF G-CSF M-CSF	bone marrow, stromal cells	Bone marrow	The various CSFs are produced by T-lymphocytes, macrophages, and other cells.
Stem cell factor		Stem cell	Makes stem cells in the bone marrow more responsive to the various CSFs.
IL-3 & IL-7		-	Supports the growth of multilineage bone marrow stem cells.

Cytokine Receptors :

- 5 Major Families
- 1) Immunoglobulin Superfamily.
 - 2) Hematopoietin Receptor Family (Class I).
 - 3) Interferon Receptor Family (Class II).
 - 4) TNF Receptor Family.
 - 5) Chemokine Receptor Family.
- *Class I and II (Majority Of Receptors).

Cytokines and Ab differentiation :

