Cytokines :- A group of low molecular weight polypeptides or proteins which are secreted by activated immunocytes or some matrix cells and possess high activity and various functions.

Properties of cytokine

! Natural cytokines are secreted by activated cells such as activated immune cells, matrix cells and tumor cells

! One kind of cytokines can be produced by different cells. One kind of cells can secrete different cytokines

! Cytokines initiate their actions by binding to specific membrane receptors on target cells.

! Cytokines can act on the cells that produce them (autocrine), on other cells in the immediate vicinity (paracrine), or on cells at a distance (endocrine) after being carried in blood or tissue fluids.

Effects of Cytokines

! Pleiotropism refers to the ability of one cytokine having multiple effects on diverse cell types.

! Redundancy refers to the property of multiple cytokines having the same or overlapping functional effects.

! Synergy refers to the property of two or more cytokines having greater than additive effects.

! Antagonism refers to the ability of one cytokine inhibiting the action of another. Regulatory T cells produce many of these suppressor cytokines.

Cytokine General Actions

! Development of cellular and humoral immune responses

! Induction of inflammation ! Regulation of hematopoiesis (by colony stimulating factors)

! Control of cellular proliferation and differentiation

! Induction of wound healing

! Chemotaxis

Cytokine classification

- innate immunity cytokines
- adaptive immunity cytokines
- hematopoietic cytokines
- immunosuppressive cytokines

Innate immunity cytokines

- Secreted by macrophages
- Stimmulated by LPS, nucleic acids, immunocomplexes those are:
- TNF-α, IL-1, IL-12, Ifα, β.
- IL-6, IL-8, IL-18, IL-23, IL-27,…

Other innate immunity cytokines

- **IL-10** Inhibits IL-12 and TNF-α production, as well as MHC –class II (immunosuppression)
- **IL-6** Stimulates acute-phase proteins and lymphocyte T/B growth (adaptive immunity)
- IL-15 Stimulates NK cell proliferation
- IL-8, IL-18, IL-23, IL-27

Adaptive immunity cytokines

- Secreted by T-lymphocytes
- Stimulated by antigens

Those are:

- IL-2, IL-4, IL-5, IF-γ
- IL-6, IL-11, IL-13, IL-17,…

Immunosuppression cytokines

- produced by CD4+T-ly, macrophages
- Suppress macrophages and Th1 Those are:
- TGF-β, IL-10
- IL-4, IL-13,…

TGF-ß

- Inhibits lymphocyte T and macrophages
- Stimulates IgA secretion

- Stimulates production of extracellular
- matrix (healing and reparation)

IL-10

- Inhibits macrophages

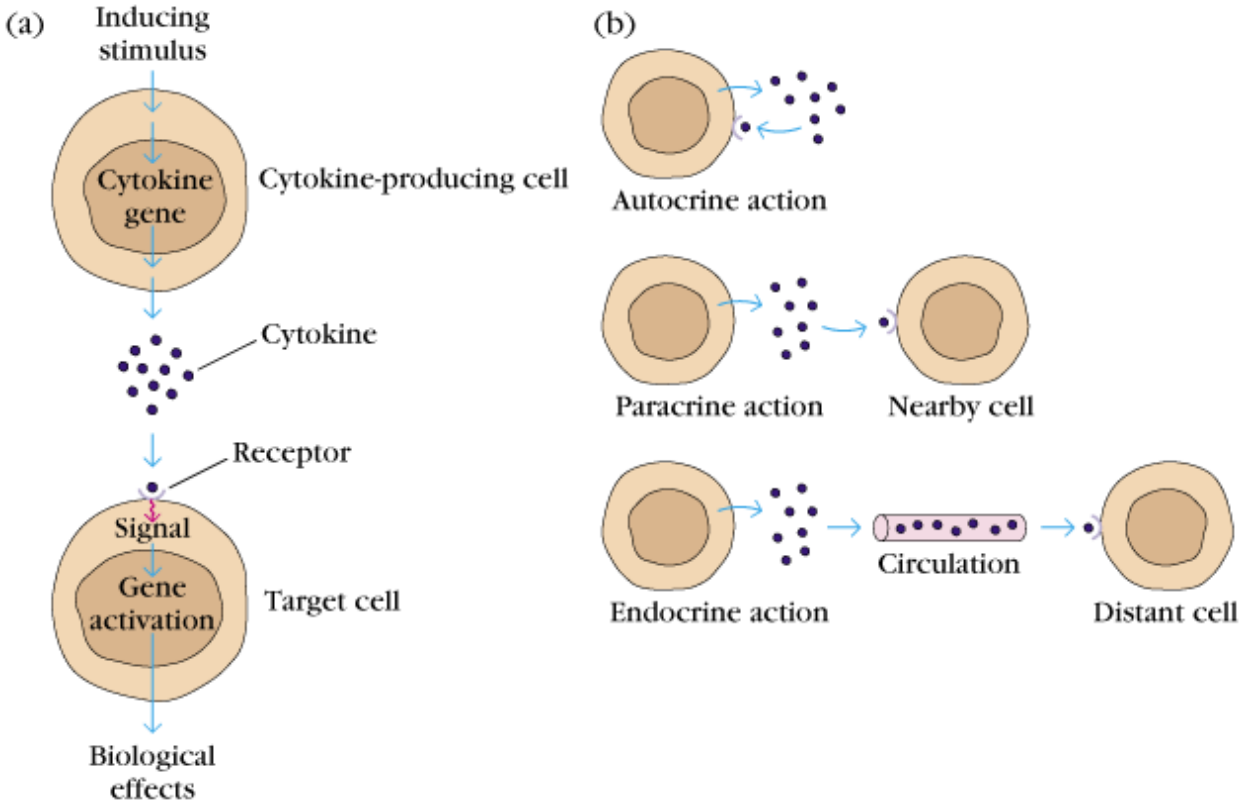
IL-4 and IL-13

- Inhibit cell-mediated and stimulate humoral immunity.

Hematopoietic cytokines

Produced by bone marrow cells and leukocytes Those are:

- CSF
- IL-7
- IL-3 (multi CSF)
- IL-1, IL-5, IL-6, erythropoietin, …


(a)
Inducing stimulus
Cytokine gene
Cytokine-producing cell
Cytokine
Receptor
Signal
Gene activation
Target cell
Biological effects
(b)
Autocrine action
Paracrine action
Nearby cell
Circulation
Endocrine action
Distant cell

Types of IFN

	Types	Produced cells	Main functions
IFN -α	Type I	leukocyte	anti-virus, immune regulation
IFN -β	Type I	fibroblast	anti-tumor
IFN -γ	Type II	Th1, NK	weaker anti-virus effect, stronger immune regulation effect, anti-tumor

Chemokine

Chemokines are cytokines which recruits monocytes, granulocytes and lymphocytes in blood to the sites of inflammation.

CXC chemokines (α subgroup).

CC chemokines (β subgroup)

C chemokines (γ subgroup)

CX_3C chemokines (δ subgroup)

Cytokines and Clinical Applications

1- Cytokines and cytokines inhibitors can be used in many clinical applications and treatments.

2- Advantages: Known ligands, receptors and mechanisms of action

3- Problems with cytokine therapies: Effective dose levels, short half-life, can cause unpredictable side effects

4- Colony stimulating factors (CSFs): hematological disorders associated with cancer therapy

5- Erythropoietin (EPO): anemia associated with kidney disease

6- Interferon α: antiviral therapy (chronic Hepatatis B and C)

7- IFN-β: multiple sclerosis

8- IFN-γ: chronic granulomatous disease (CGD)

9- IL-2: kidney cancer, melanoma