

# Cytokines (CKs)

# Objectives

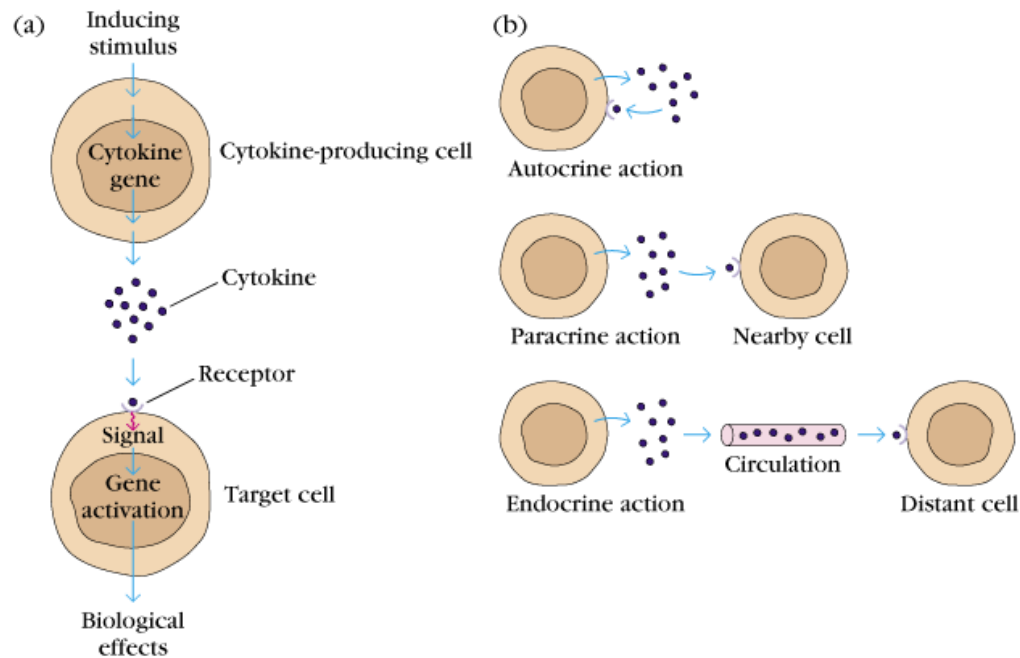
- Definition and general properties of cytokines
- Classification of cytokines
- Cytokine receptor
- Biological functions of cytokines
- Cytokine and disease

# Definition

- 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.
- Cytokine or immunocytokine is a generic name used to describe a diverse group of soluble proteins and peptides which act as humoral regulators at nano- to- picomolar concentrations
- Their major functions are to mediate and regulate immune response and inflammatory reactions.

# General Properties

- Most cytokines are low molecular weight polypeptides or glycoprotein (8~80 KD), and most of them are monomer
- 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.

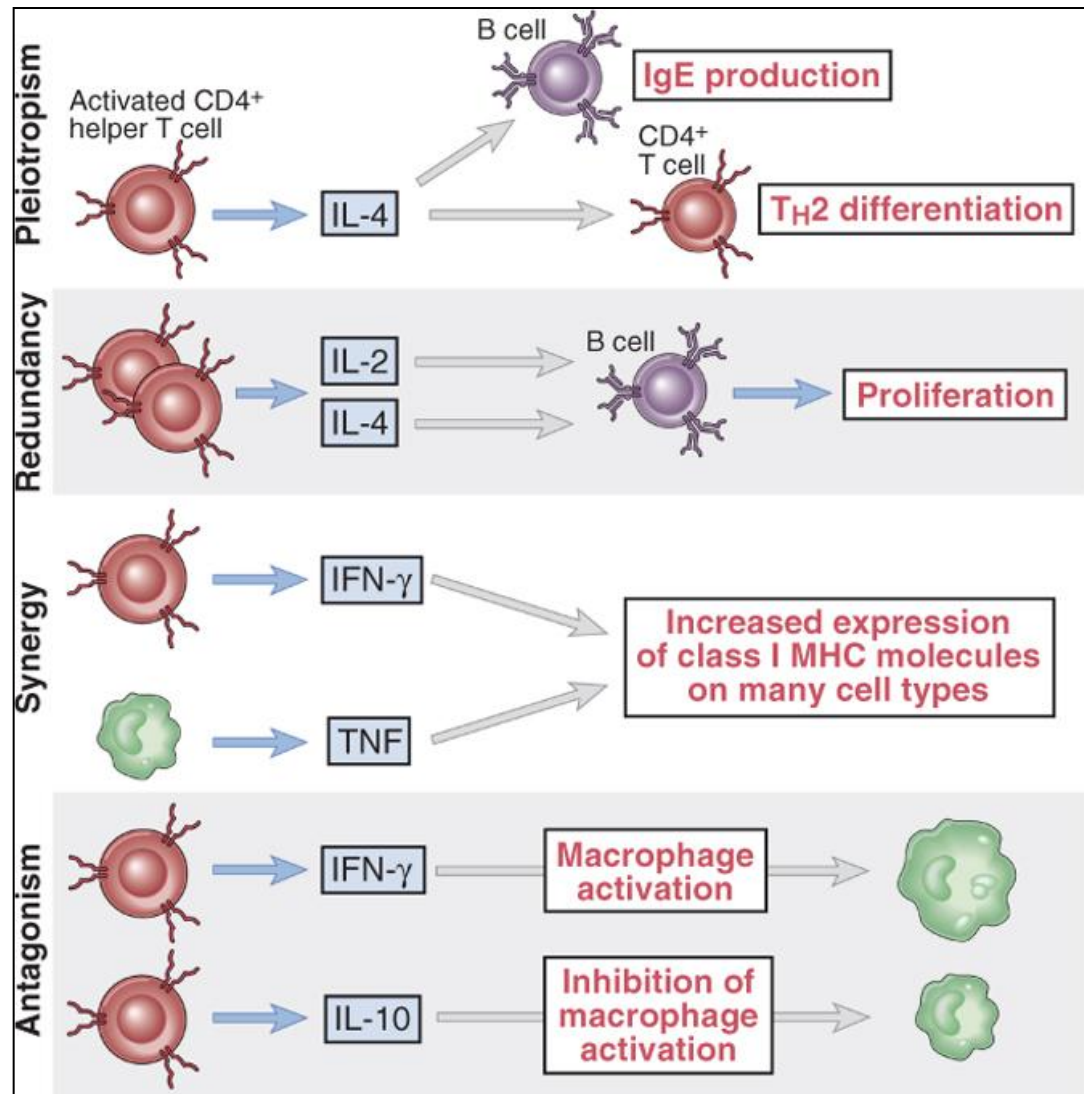


# Cytokine Names

- **Interleukins** - produced exclusively by leukocytes
- **Lymphokines** - produced by lymphocytes
- **Monokines** - produced exclusively by monocytes
- **Interferons** - involved in antiviral responses
- **Colony Stimulating Factors (CSF)** - support the growth of cells in semisolid medias
- **Chemokines** - promote chemotaxis

# 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.



# Cytokine General Actions

- Development of cellular and humoral immune responses
- Induction of inflammation
- Regulation of hematopoiesis
- Control of cellular proliferation and differentiation
- Induction of wound healing
- Chemotaxis

# Classification of cytokines

- Interleukin, IL
- Interferon , IFN
- Tumour necrosis factor, TNF
- Colony stimulating factor (CSF)
- Chemokine
- Transforming growth factor (TGF)

# 1. Interleukin (IL)

- Cytokines secreted by leukocytes that have the ability to act as signal molecules between different population of leukocytes
- IL-1~IL-29
  - Th1: IL-2
  - Th2: IL-4, IL-5
  - Th3/Treg: IL-10
  - Th17: IL-17

# Specific Interleukins Functions

- **IL1:** Play role in inflammation
- **IL2:** Growth factor for B and T cells (clonal expansion)
- **IL3:** Haematopoietic growth factor which stimulates colony formation of blood cells
- **IL4:** Stimulates development of Th2 cells from naïve Th cell. Stimulates Ig class switch from IgG1 to IgE (allergy)
- **IL5:** Produced by Th2 cells and aids in the growth and differentiation of eosinophils
- **IL6:** acute phase response
- **IL10:** **Suppresses** inflammatory responses and inhibits production of IFN- $\gamma$ , IL-2, IL-3, TNF $\alpha$ , GM-CSF

## 2. Interferon (IFN)

- A group of glycoproteins that produced by human or animal cells following the infection of virus and exposure to various inducing agents

	Types	Produced cells	Main functions
IFN- $\alpha$	Type I	leukocyte	anti-virus, immune regulation
IFN- $\beta$	Type I	fibroblast	anti-tumor
IFN- $\gamma$	Type II	Th1, NK	weaker anti-virus effect, stronger immune regulation effect, anti-tumor

### 3. Tumor Necrosis Factor (TNF)

- TNFs were originally thought of as selective antitumour agents, but are now known to have a multiplicity of actions.
- TNF- $\alpha$  is produced mainly by liposaccharide (LPS), activated monocytes and macrophages.
- TNF- $\beta$  is produced mainly by activated Th0 and Th1.

## 4. Colony-Stimulating Factors (CSF)

- Cytokines that stimulate proliferation or differentiation of pluripotent hematopoietic stem cell and different progenitors.
  - Multi-CSF (IL-3)
  - Granulocyte macrophage-CSF (GM-CSF)
  - Monocyte-CSF (M-CSF)
  - Granulocyte-CSF (G-CSF)
  - Stem cell factor (SCF)
  - Erythropoietin (EPO)

# 5. Chemokine

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

# 6. Transforming Growth Factor

- Growth-factor are cytokines which stimulate the growth of their target cells.
- Transforming growth factor- $\beta$  (TGF-  $\beta$ )
- Epithelia growth factor (EGF)
- Vascular endothelia cell growth factor (VEGF)
- Fibroblastic growth factor (FGF)

# CK receptor

- Membrane-binding cytokine receptors:
- The receptor consists of extra-cellular region, trans-membrane region and cytoplasmic region.
- CK receptors can be grouped into five families according to structure and function.

# Cytokines and Clinical Applications

- Cytokines and cytokines inhibitors can be used in many clinical applications and treatments.
  - Advantages: Known ligands, receptors and mechanisms of action
  - Problems with cytokine therapies: Effective dose levels, short half-life, can cause unpredictable side effects
- **Colony stimulating factors (CSFs):** hematological disorders associated with cancer therapy
- **Erythropoietin (EPO):** anemia associated with kidney disease
- **Interferon  $\alpha$ :** antiviral therapy (chronic Hepatitis B and C)
- **IFN- $\beta$ :** multiple sclerosis
- **IFN- $\gamma$ :** chronic granulomatous disease (CGD)
- **IL-2:** kidney cancer, melanoma