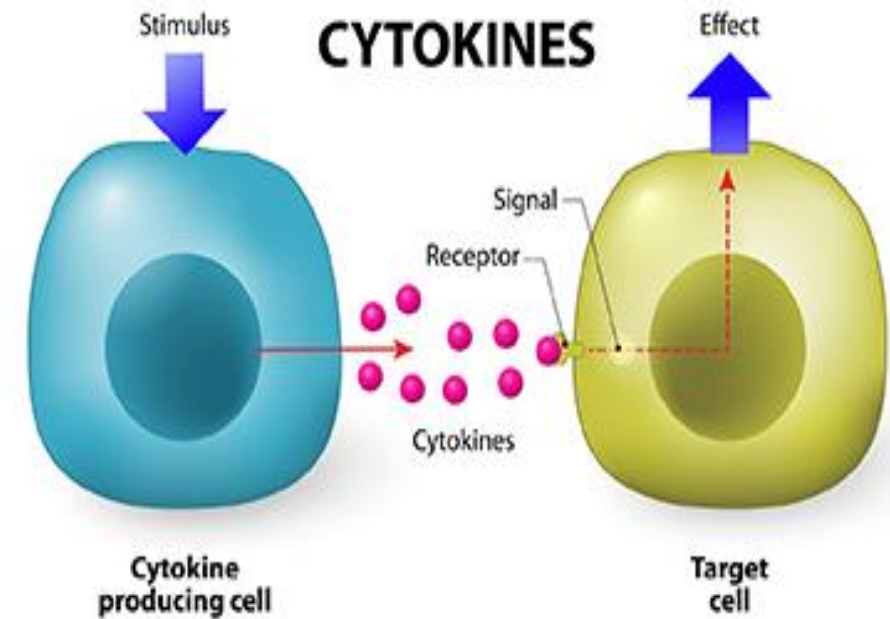
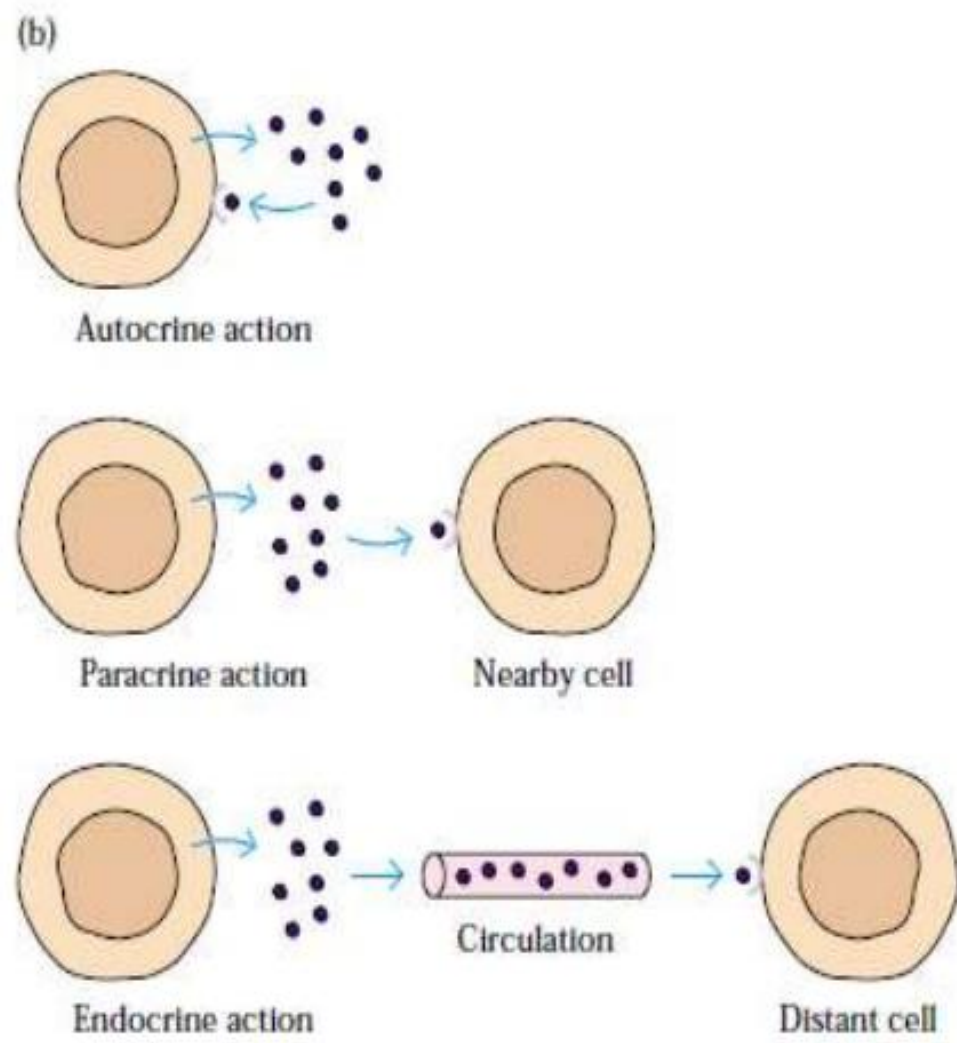
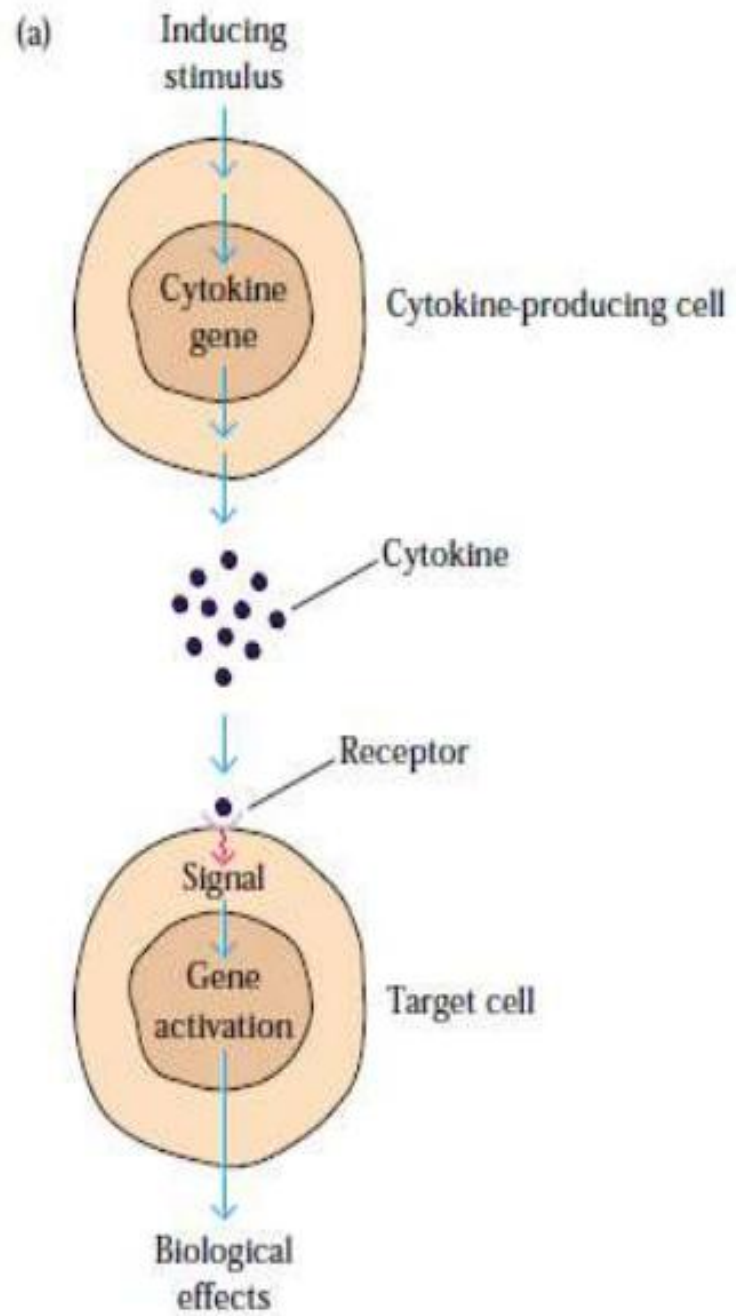


- **Cytokines / immunocytokines**
- Low molecular weight regulatory proteins or glycoproteins. Molecular mass:- less than 30 kDa.
- Secreted by stimulated WBC and other cells.
- Communication between lymphoid cells, inflammatory cells, and hematopoietic cells for effective immune response.



source; integrativepro



TH cells and **macrophages** are the two principal producers of cytokines.

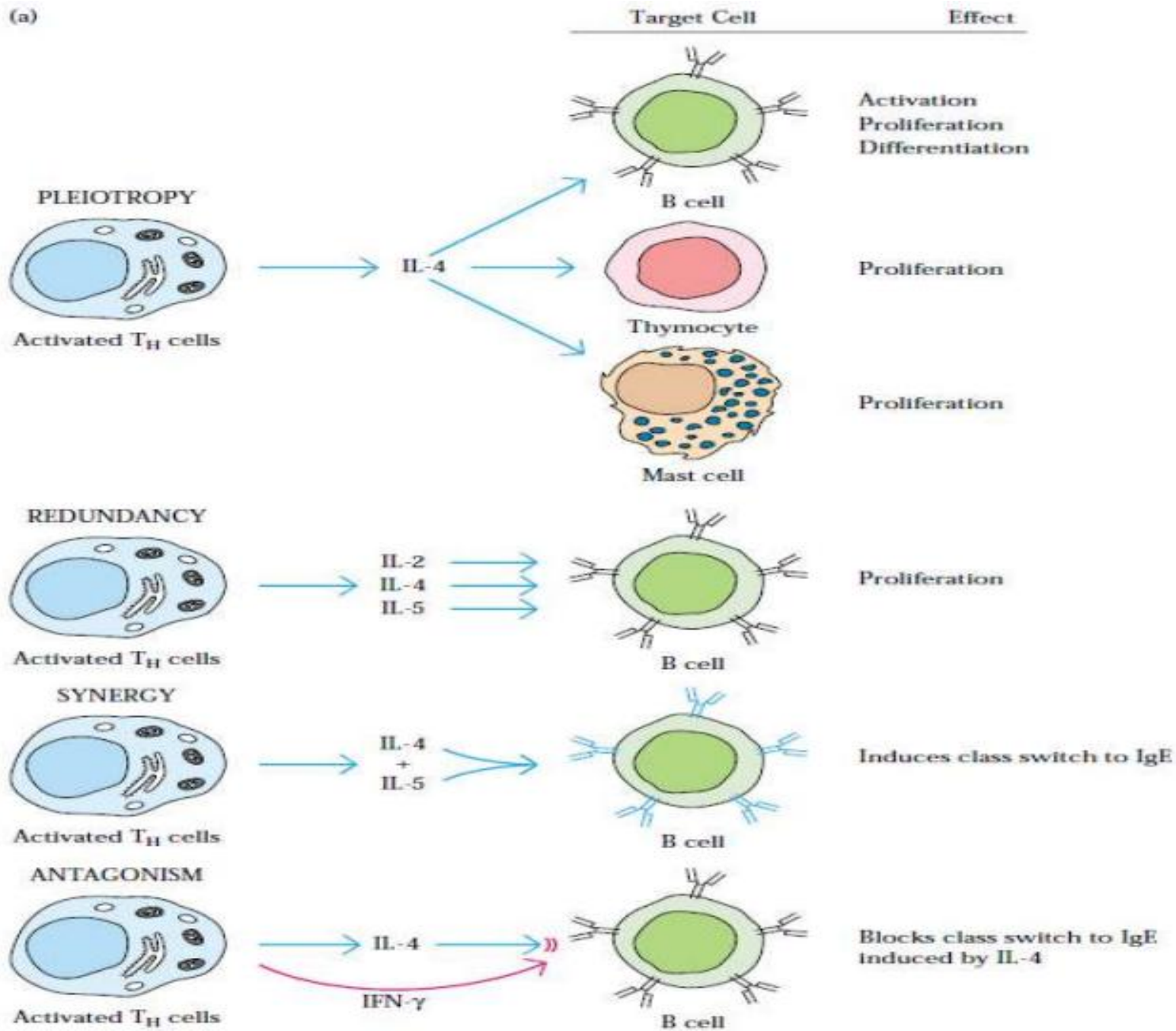
Roles:

- Develop cellular and humoral immune responses,
- induces an inflammatory response,
- Regulate hematopoiesis
- Control cellular proliferation and differentiation
- Heals wound

Properties of cytokines :

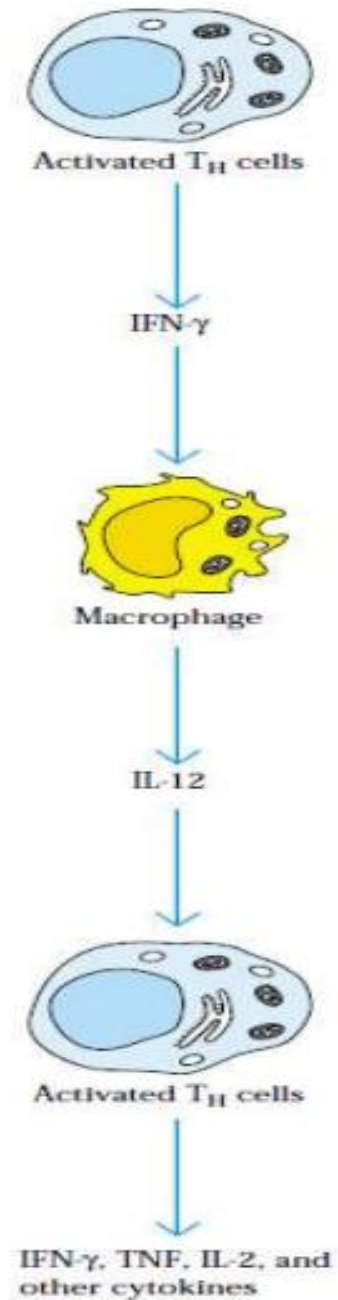
- **Pleiotropic action:** 1 cytokine has different biological effects on different target cells.
- **Redundancy:** two or more cytokines can mediate similar functions.
- **Synergy:** the combined effects of two cytokines is greater than the additive effects of the individual cytokines.
- **Antagonism:** The effects of one cytokine inhibits another cytokine.
- **Cascade induction:** The action of one cytokine induces the production of other cytokines, which in turn induces the production of other cytokines.

(a)



(b)

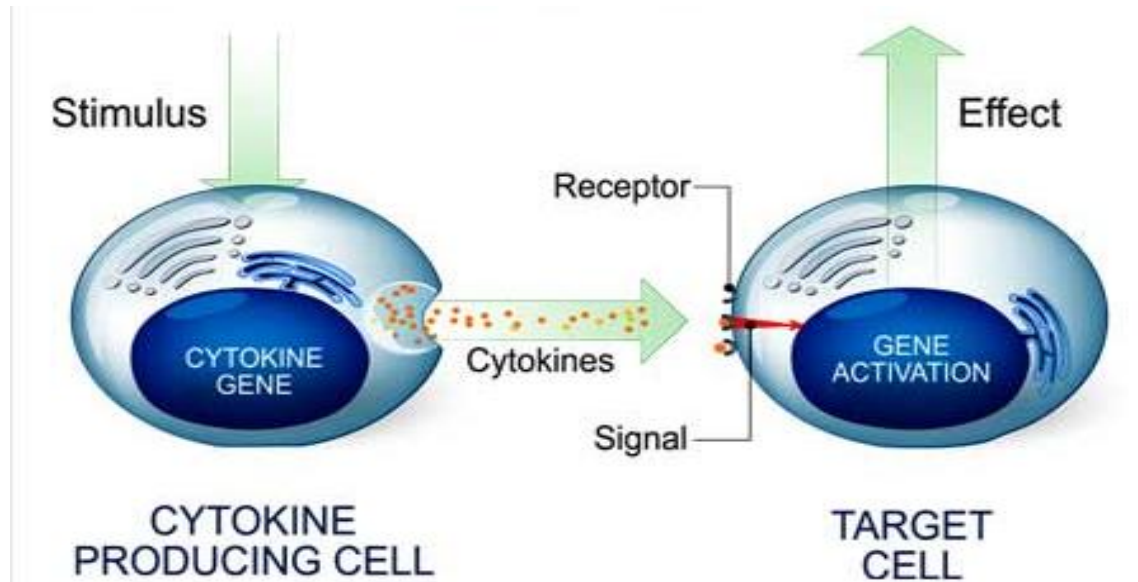
CASCADE INDUCTION



Nomenclature:-

- **Interleukins** - mediators between leukocytes. Mostly produced by T-helper cells.
- **Lymphokines** - produced by lymphocytes.
- **Monokines** - produced by monocytes.
- **Interferons** - involved in antiviral responses.
- **Colony Stimulating Factors** - support the growth of blood cell.
- **Chemokines** - mediate chemoattraction (chemotaxis) between cells.

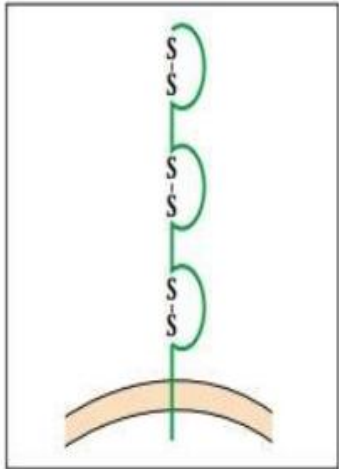
Classification:- depends on their effects on immunocytes.



- ▶ Chemokines
- ▶ Colony-stimulating factors
- ▶ Interferons
- ▶ Interleukins
- ▶ Transforming-growth factor (TGF-Beta)
- ▶ Tumor necrosis factors (TNF)

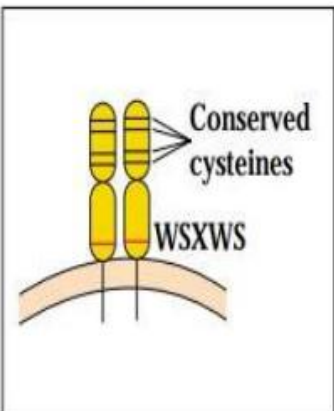
Cytokine receptor: 5 family

(a) Immunoglobulin superfamily receptors



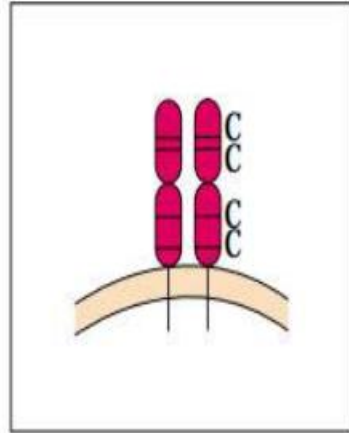
IL-1
M-CSF
C-Kit

(b) Class I cytokine receptors (hematopoietin)



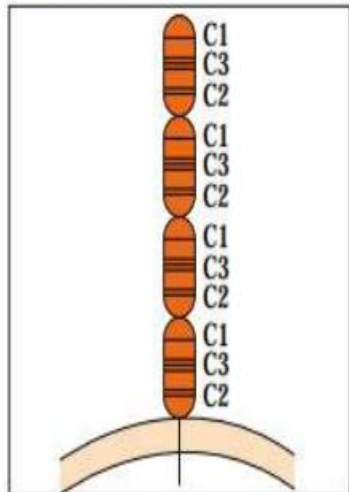
IL-2 IL-13
IL-3 IL-15
IL-4 GM-CSF
IL-5 G-CSF
IL-6 OSM
IL-7 LIF
IL-9 CNTF
IL-11 Growth hormone
IL-12 Prolactin

(c) Class II cytokine receptors (interferon)



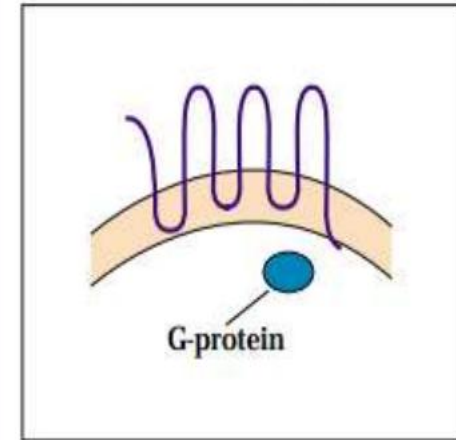
IFN- α
IFN- β
IFN- γ
IL-10

(d) TNF receptors



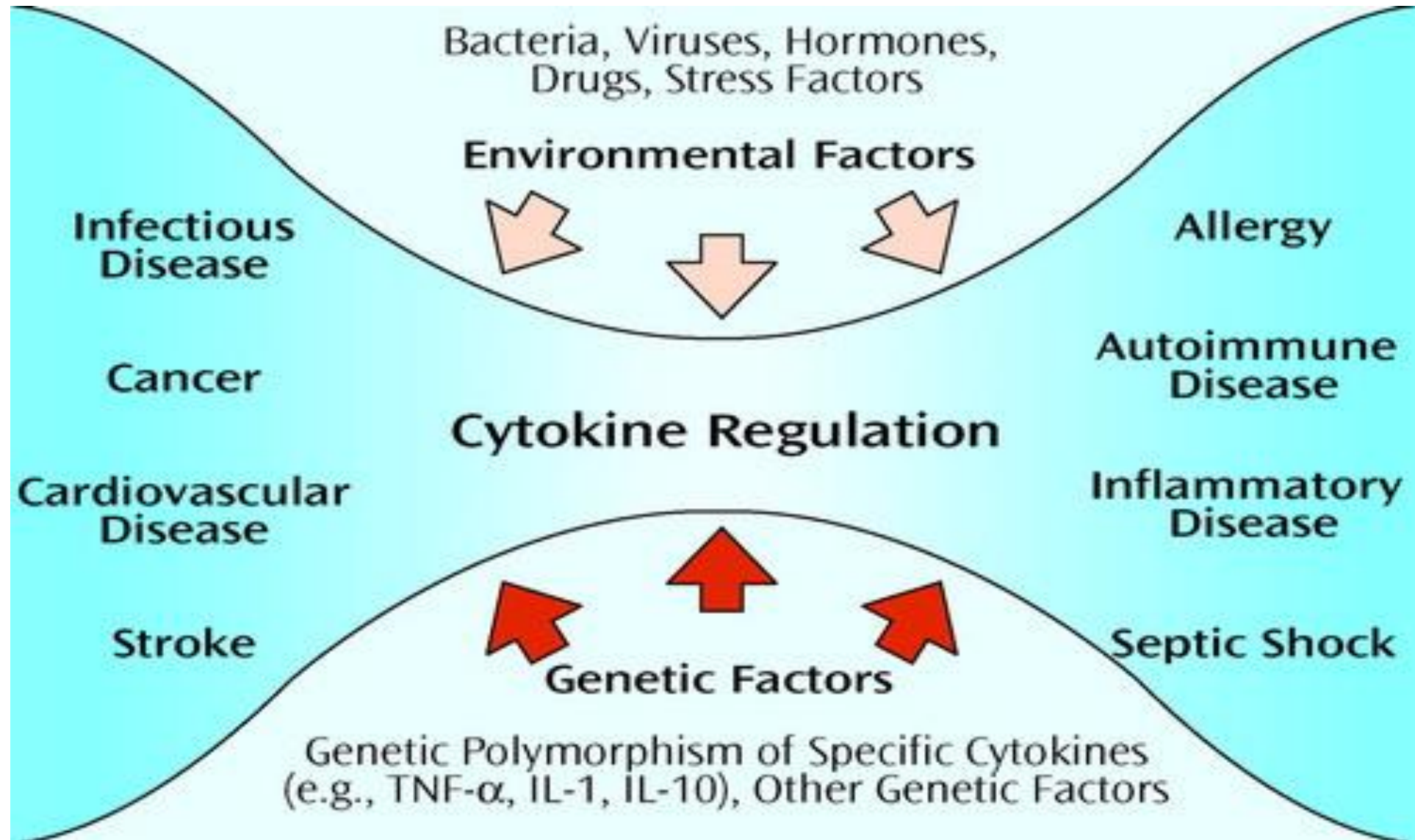
TNF- α
TNF- β
CD40
Nerve growth factor (NGF)
FAS

(e) Chemokine receptors



IL-8
RANTES
MIP-1
PF4
MCAF
NAP-2

Cytokine regulation



Cytokines are secreted by TH1 and TH2 subsets.

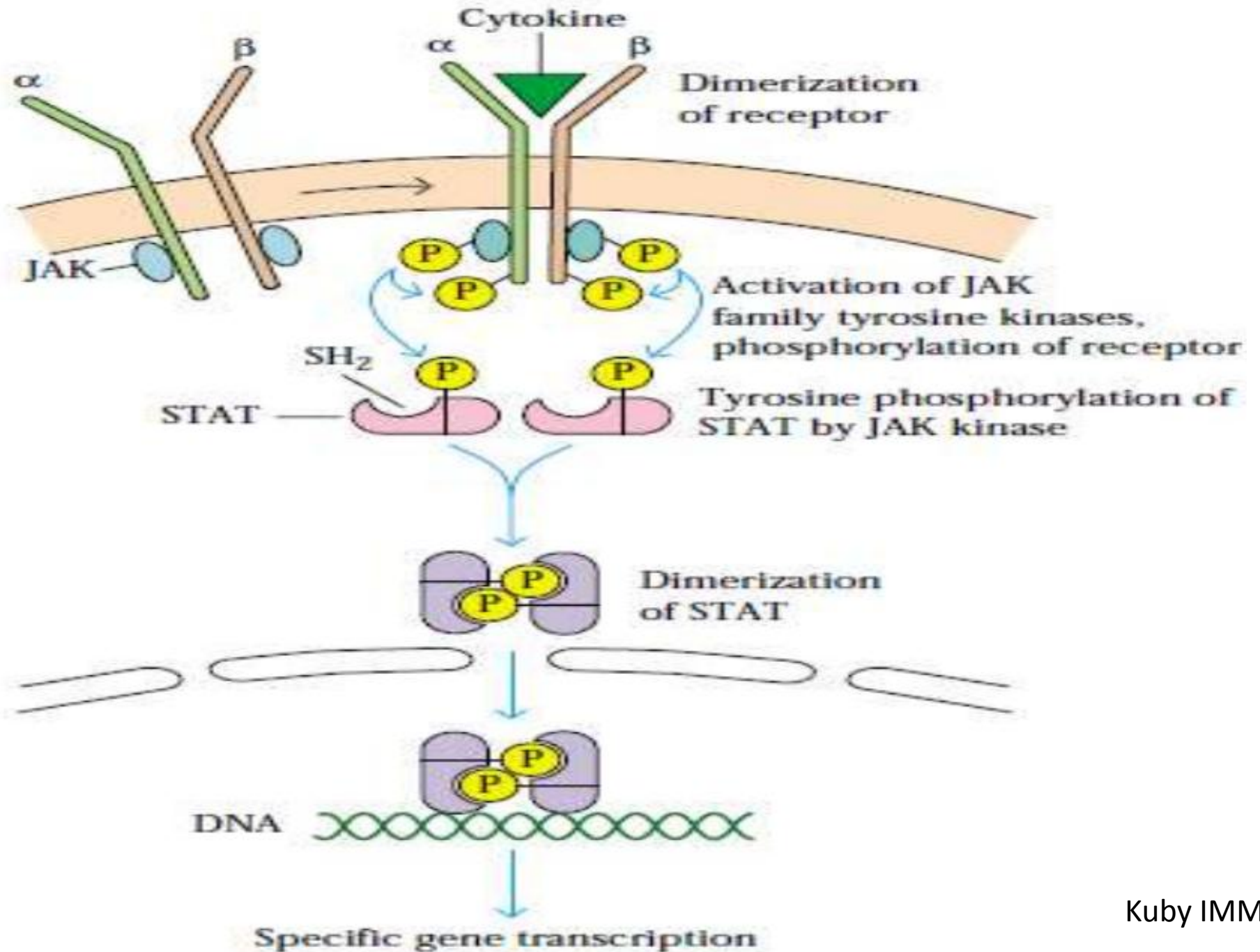
The TH1 subset:- stimulate cell-mediated functions and produce antibodies.

- promotes excessive inflammation.

The TH2 subset:- stimulate Eosinophil activation and differentiation, helps B cells, and promotes the production of IgM, Ig E.

- also support allergic reactions.

Signaling Pathway



Examples of cytokines :

Lymphokines

- They are protein mediators, produced by lymphocytes (typically by T cells).
- Can attract other immune cells, like macrophages and other lymphocytes, towards the site of the infection and activate their immune response.
- Lymphokines aid B cells to produce antibodies.
- **Includes:-** Colony-stimulating factors like GM-CSF, Interferons, Interleukins, Osteoclast-activating factor, Platelet-derived growth factor (PDGF), Transforming growth factor-beta ($\text{tgf}\beta$), $\text{TNF}\alpha$ and $\text{TNF } \beta$

Actions of lymphokines :

- Activates B cells, and inhibits macrophage function: IL-10.
- Activation of neutrophils, eosinophils, and monocyte /macrophages: GM-CSF.
- Bone marrow – growth and differentiation: IL-3
- B cell growth and differentiation: IL-4.
- Co-stimulator of T cells, induces growth in B cells: IL-6
- Inflammation, fever, catabolism, activation of some macrophages: TNF
- Haematopoiesis stimulators :IL-3, IL-7, GM-CSF
- Macrophage-activating activity (MAF) :INF- γ
- Proliferation of activated T and B cells: IL-2
- Inhibits T cell growth, activates macrophages:TNF β

Monokines

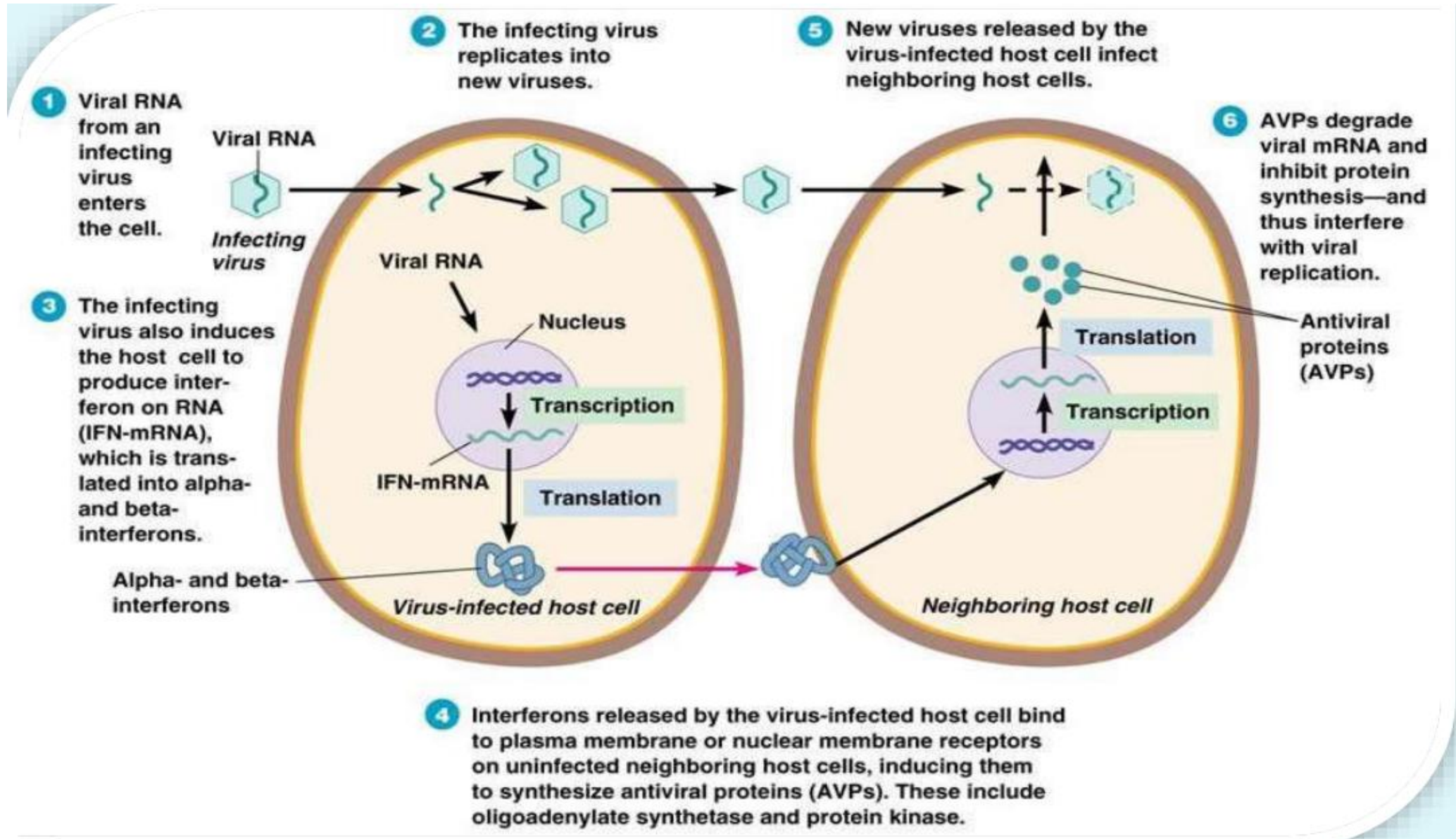
- produced primarily by monocytes and macrophages.
- Examples:- interleukin 1 , TNF -alpha, alpha and beta interferon, and CSF.

Interleukins

- naturally occurring polypeptides (found in small quantities).
- produced by lymphocytes, monocytes and are released by cells in response to antigenic and nonantigenic stimuli. Consist of IL1 to IL37.

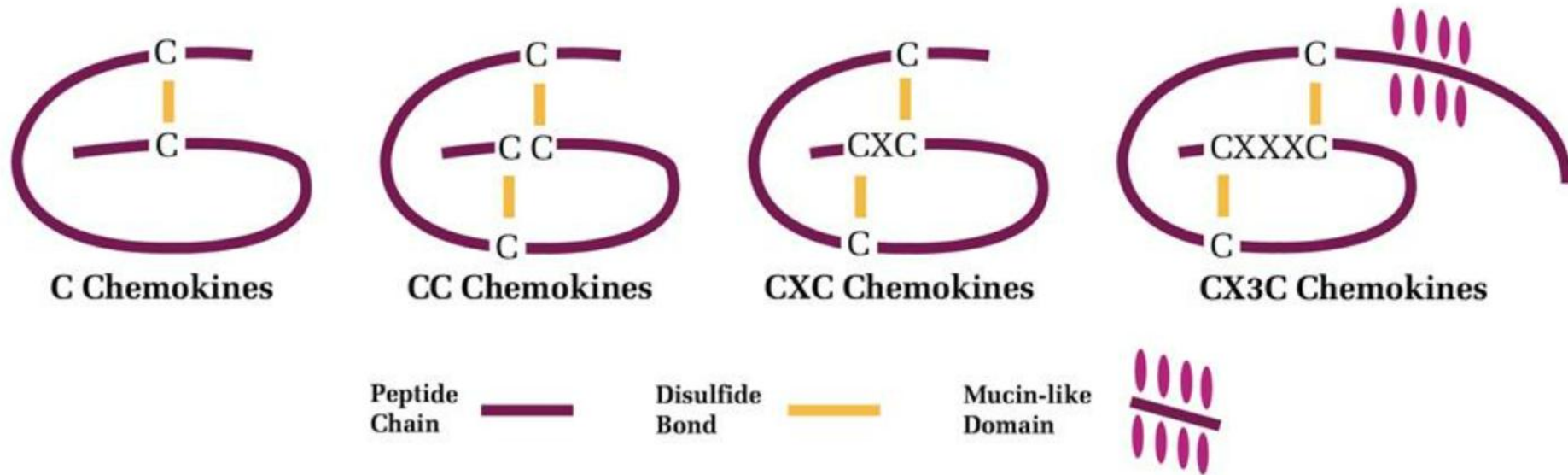
Interferons:- first line of defense against viral infections.

- Resulting in an anti-viral state in target cells.



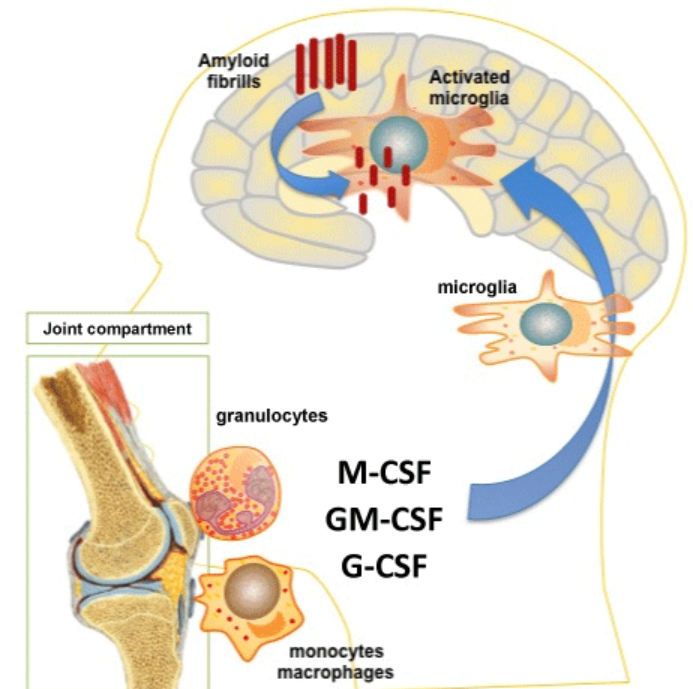
Chemokines

- A family of small cytokines, or Signaling proteins
- induce directed chemotaxis in nearby responsive cells.
- They interact with G protein-linked transmembrane receptors called chemokine receptors, found on the surfaces of target cells.
- 4 main subfamilies :



Colony-stimulating factors (CSFs)

- Secreted glycoproteins.
- Soluble, membrane-bound substances of the hematopoietic microenvironment.
- They transduce by paracrine, endocrine, or autocrine signaling.
- CSF1 - Macrophage colony-stimulating factor(MCSF)
- CSF2 – Granulocyte-macrophage colony-stimulating factors(GMCSF).
- CSF3 - Granulocyte colony-stimulating factors(GCSF)



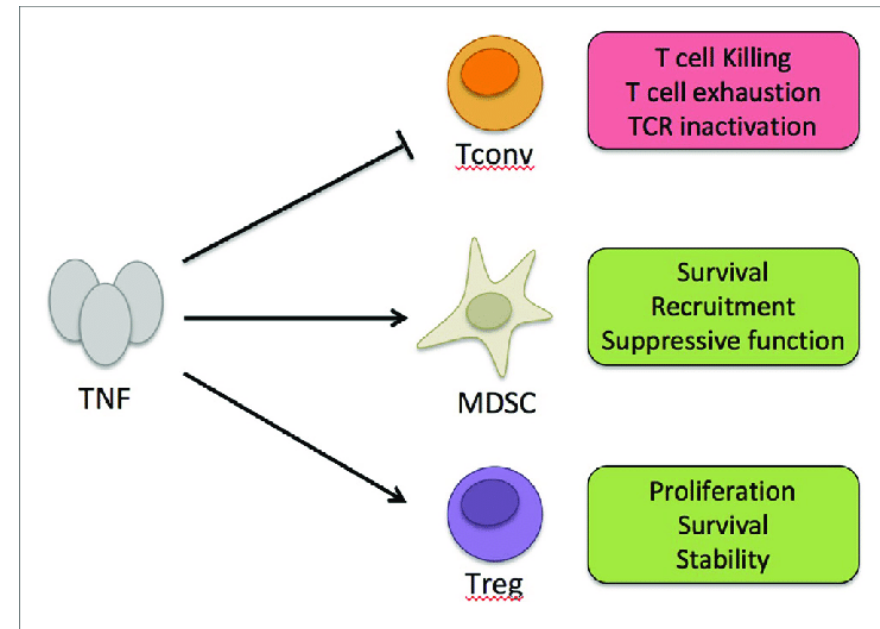
Tumor necrosis factors

- can cause cell death (apoptosis).
- 19 TNFs are reported. They include:

Tumor necrosis factor (TNF), formerly known as TNF α or TNF alpha,

- has been implicated in tumor regression, septic shock.

Lymphotoxin-alpha, lymphotoxin-beta (LT-beta):- produced by lymphocytes. cytotoxic for a wide range of tumor cells.



Immunosuppressive action of TNF

Therapeutic uses of Cytokines

- For inflammation therapy
- Modify responses during organ transplantation,
- For infectious disease
- Allergy.

Cytokine related Diseases:

I. **Bacterial septic shock:** Here bacterial endotoxins can stimulate macrophages to provide more **IL- 1 and TNF –alpha** which causes septic shock.

Symptoms: drop in blood pressure, fever, diarrhea, and blood clotting in various organs.

II. **Lymphoid and Myeloid Cancer:** develop due to overproduction of **IL-6**

III. **Chages diseases:** caused by protozoans Trypanosoma cruzi, caused because of the immune suppression.