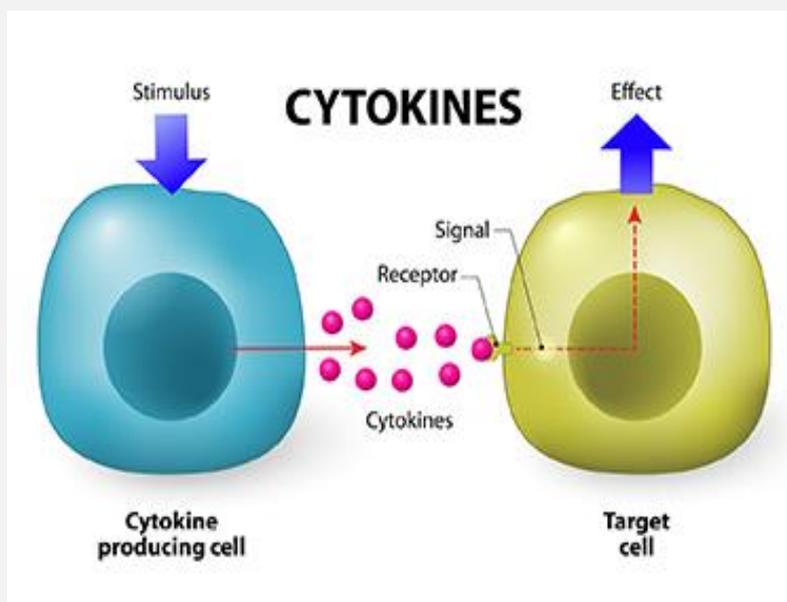
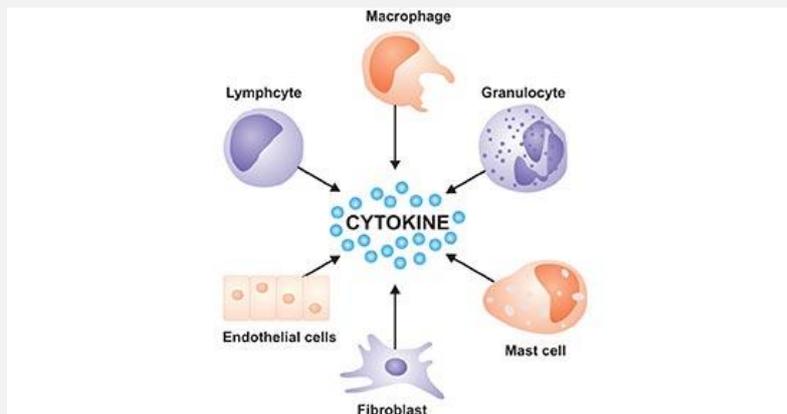


CYTOKINES

- Cytokines are small proteins that act as chemical messengers for cell signaling, particularly within the immune system, regulating the growth and activity of immune and blood cells.
- They are secreted by both immune and non-immune cells to communicate with others, promoting or inhibiting inflammatory responses, cell activation, and proliferation.

1. Definition

- **Cytokines** are **small, soluble proteins or glycoproteins** (~8–30 kDa) secreted mainly by immune cells that **mediate and regulate immunity, inflammation, and hematopoiesis**.
- They act as **intercellular messengers**, allowing communication between cells of the immune system and other tissues.



2. General Characteristics

Property	Description
Molecular Weight	8–30 kDa
Nature	Glycoproteins or polypeptides
Produced by	T cells, macrophages, dendritic cells, NK cells, endothelial cells, fibroblasts, etc.
Receptors	High-affinity membrane receptors; very low concentrations (~pM) are effective
Actions	Autocrine (self), paracrine (neighboring), or endocrine (systemic)
Half-life	Usually short; transiently produced upon activation

3. General Functions

1. **Regulation of immune responses**
 - Activation and differentiation of immune cells.
 - Regulation of antibody production.
2. **Mediation of inflammation**
 - Recruitment and activation of leukocytes.
3. **Cell proliferation and differentiation**
 - In hematopoiesis and immune cell maturation.
4. **Antiviral defense**
 - Via interferons.
5. **Wound healing and tissue repair**
 - Through growth factors and cytokine signaling.

4. Classification of Cytokines

Cytokines are classified based on **function**, **structure**, or **cell of origin**.

A. Based on Function

Category	Examples	Main Functions
Interleukins (ILs)	IL-1 to IL-38	Communication between leukocytes; immune regulation.
Interferons (IFNs)	IFN- α , IFN- β , IFN- γ	Antiviral, immunomodulatory, and anti-tumor actions.
Tumor Necrosis Factors (TNFs)	TNF- α , TNF- β	Inflammation, apoptosis, fever induction.

Colony Stimulating Factors (CSFs)	G-CSF, M-CSF, GM-CSF	Stimulate production of blood cells.
Chemokines	IL-8 (CXCL8), RANTES	Chemotaxis of immune cells.
Transforming Growth Factors (TGFs)	TGF- β	Regulation of proliferation and differentiation, anti-inflammatory.

B. Based on Source/Origin

Source	Major Cytokines Produced
Monocytes/Macrophages	IL-1, IL-6, TNF- α , IL-12
T-helper (Th1) cells	IL-2, IFN- γ , TNF- β
T-helper (Th2) cells	IL-4, IL-5, IL-6, IL-10, IL-13
T-helper (Th17) cells	IL-17, IL-22
NK cells	IFN- γ
Fibroblasts/Endothelial cells	IL-6, IL-8, TGF- β

5. Major Cytokines and Their Actions

Cytokine	Produced by	Major Effects
IL-1	Macrophages	Fever, inflammation, T-cell activation
IL-2	Th1 cells	T & NK cell proliferation
IL-4	Th2 cells	B cell activation, IgE switching
IL-5	Th2 cells	Eosinophil activation
IL-6	Macrophages, Th2	Acute-phase response, B cell differentiation
IL-8 (CXCL8)	Macrophages, endothelial cells	Neutrophil chemotaxis
IL-10	Th2 cells, macrophages	Anti-inflammatory, inhibits Th1
IL-12	Macrophages, dendritic cells	Induces Th1 differentiation
IL-17	Th17 cells	Neutrophil recruitment, inflammation
TNF-α	Macrophages, NK cells	Inflammation, apoptosis, fever
IFN-α / β	Virus-infected cells	Antiviral response
IFN-γ	Th1, NK cells	Macrophage activation, enhances MHC expression

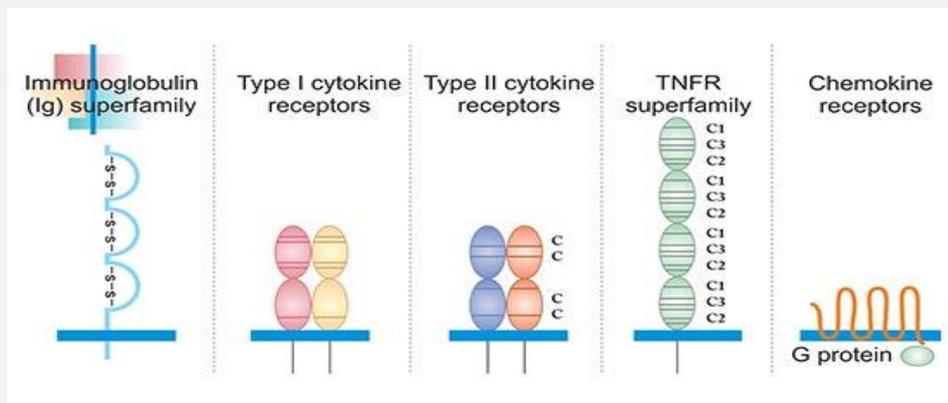
TGF-β	Many cells	Inhibits immune response, promotes wound healing
GM-CSF	T cells, macrophages	Granulocyte & macrophage production

6. Cytokine Receptors

Cytokine receptors are specific and have **high affinity** for their ligands.

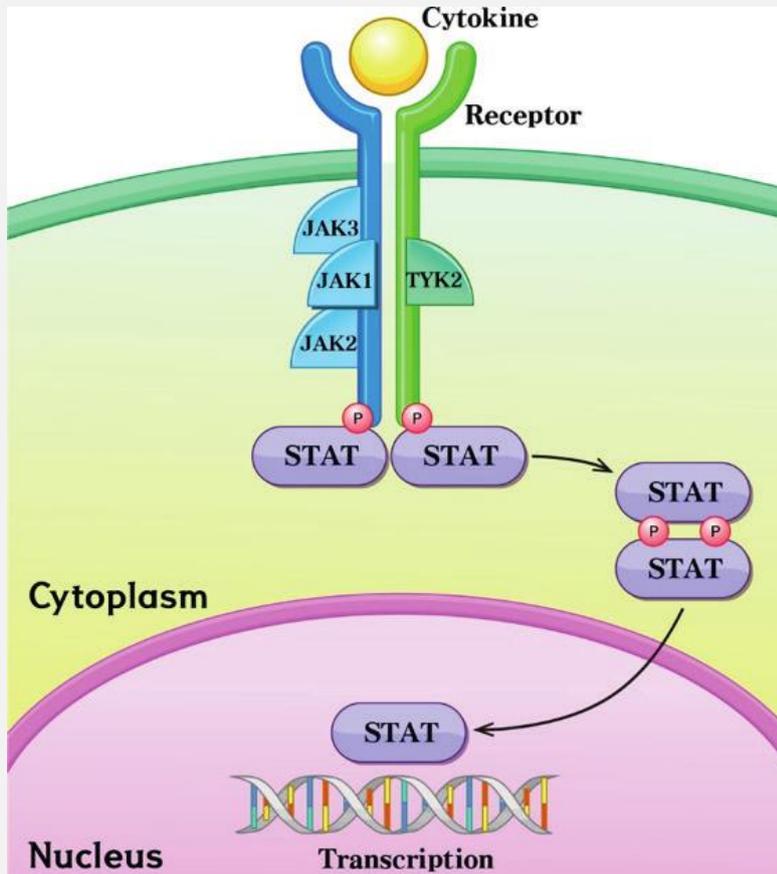
Major Families:

1. **Type I cytokine receptors (hematopoietin receptors)**
 - e.g., IL-2R, IL-4R, IL-6R
2. **Type II cytokine receptors (interferon receptors)**
 - e.g., IFN- α R, IFN- γ R
3. **TNF receptor family**
 - e.g., TNFR1, TNFR2
4. **IL-1 receptor family (Toll/IL-1R superfamily)**
 - e.g., IL-1R, IL-18R
5. **Chemokine receptor family (GPCRs)**
 - e.g., CCR5, CXCR4



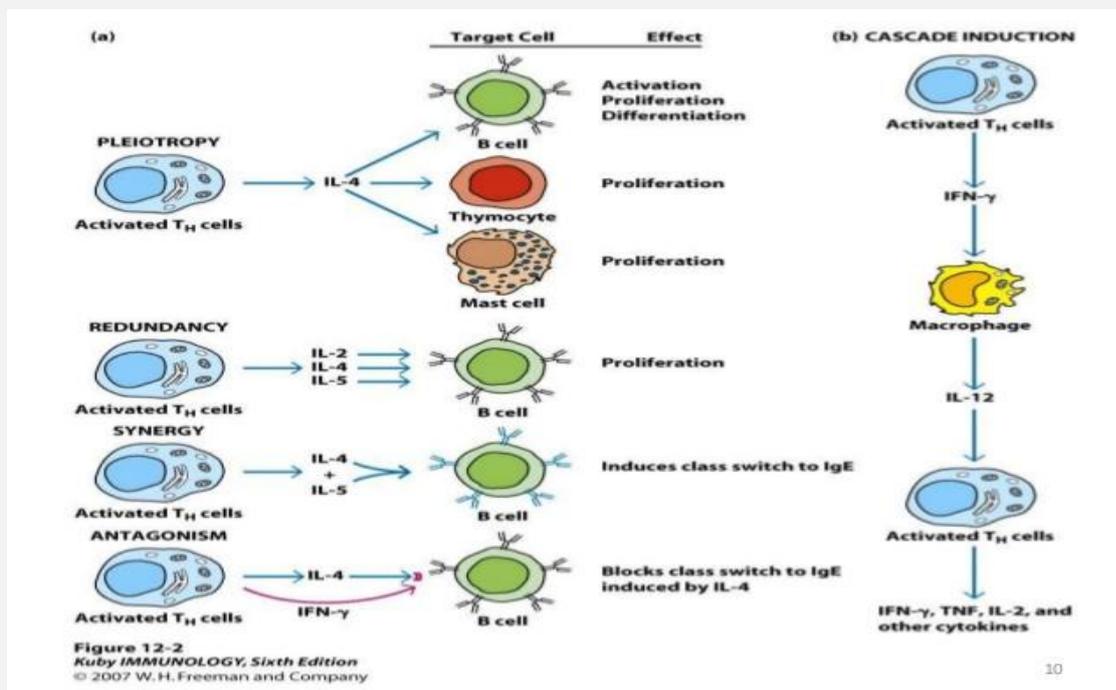
7. Mechanism of Cytokine Signaling

- Binding of cytokine \rightarrow receptor dimerization \rightarrow activation of intracellular kinases (e.g., **JAKs**).
- **JAK-STAT Pathway:**
 1. Cytokine binds receptor.
 2. JAK (Janus kinase) activates and phosphorylates STAT (Signal Transducer and Activator of Transcription).
 3. STAT dimerizes and translocates to the nucleus.
 4. Regulates gene expression \rightarrow cellular response.



8. Cytokine Network and Regulation

- Cytokines act in **networks**, often influencing each other:
 - **Synergistic:** IL-12 + IL-18 → IFN- γ production.
 - **Antagonistic:** IFN- γ (Th1) vs IL-4 (Th2).
 - **Cascade effect:** IL-1 → IL-6 → acute-phase proteins.



9. Cytokines in Disease

Disease / Condition	Cytokines Involved	Effect
Septic Shock	TNF- α , IL-1, IL-6	Fever, hypotension, multi-organ failure
Rheumatoid Arthritis	TNF- α , IL-1, IL-6	Chronic inflammation, joint damage
Asthma / Allergy	IL-4, IL-5, IL-13	IgE production, eosinophilia
Autoimmune Diseases (MS, SLE)	IFN- γ , IL-17	Tissue destruction
Cytokine Storm (e.g. COVID-19)	IL-6, TNF- α , IL-1 β	Hyperinflammation, ARDS
Cancer	IL-10, TGF- β	Immune evasion

10. Therapeutic Uses of Cytokines & Inhibitors

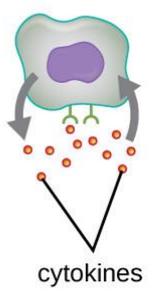
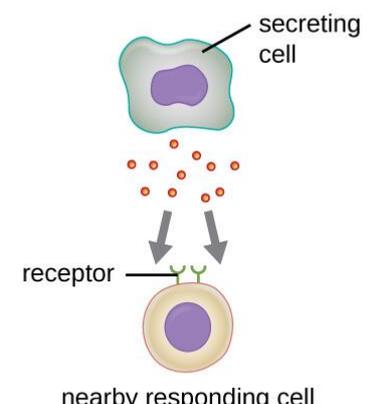
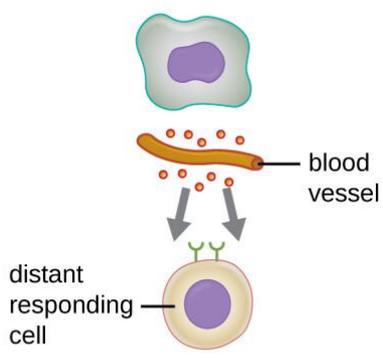
Agent	Type	Clinical Use
IFN- α	Cytokine	Chronic hepatitis B & C, Kaposi's sarcoma
IFN- β	Cytokine	Multiple sclerosis
IL-2	Cytokine	Metastatic melanoma, renal carcinoma
G-CSF (Filgrastim)	Cytokine	Neutropenia after chemotherapy
Erythropoietin (EPO)	Cytokine	Anemia treatment
Anti-TNF- α (Infliximab, Etanercept)	Cytokine inhibitor	Rheumatoid arthritis, Crohn's disease
Tocilizumab (anti-IL-6R)	Cytokine inhibitor	Cytokine storm, RA
Anakinra (IL-1R antagonist)	Cytokine inhibitor	RA, autoinflammatory syndromes

11. Key Takeaways

- Cytokines are **critical immune regulators**.
- They act through **specific receptors and signaling pathways**.

- Dysregulation can cause **autoimmune, inflammatory, or neoplastic diseases**.
- Targeting cytokines therapeutically can **modulate immune responses** beneficially.

12. Cytokine Actions

CYTOKINES: Molecular Messengers		
Autocrine	Paracrine	Endocrine
Same cell secretes and receives cytokine signal.	Cytokine signal secreted to a nearby cell.	Cytokine signal secreted to circulatory system; travels to distant cells.
 <p>cytokines</p>	 <p>secreting cell</p> <p>receptor</p> <p>nearby responding cell</p>	 <p>blood vessel</p> <p>distant responding cell</p>