

Cytokines (I)

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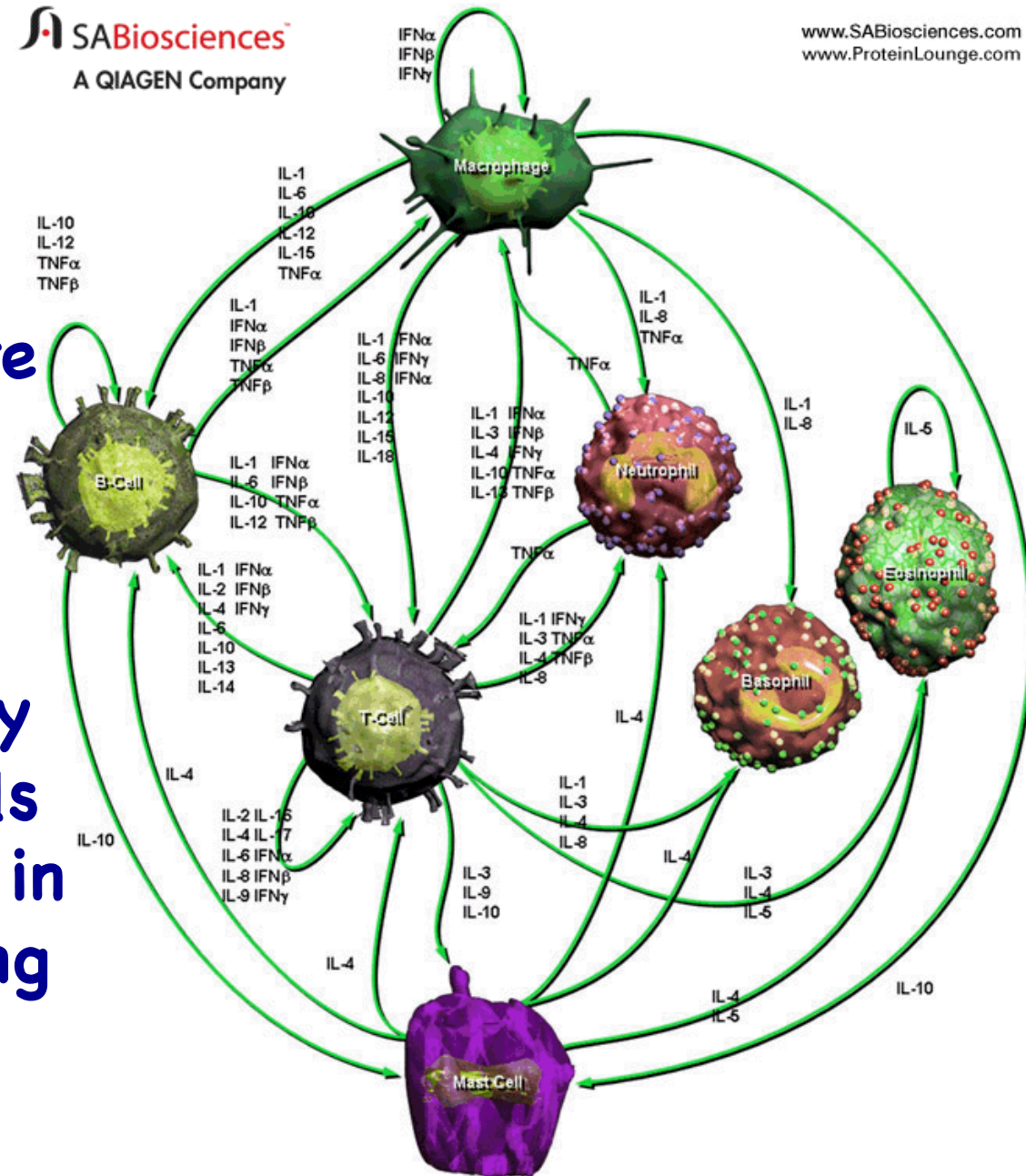
Learning Objectives

By the end of this lecture you will be able to:

- ① Define the term “cytokines”
- ② Describe the patterns of cytokine communication
- ③ Realize the 5 attributes of cytokines
- ④ Recognize the 5 cytokine-receptor families

Cytokines

- A group of small proteins that mediate complex interactions between cells
- They are released by various types of cells in the body, usually in response to activating stimulus



Cytokines

- They bind to specific receptors on the membrane of target cells
- They trigger at pM concentrations signal transduction and alter gene expression leading to biological effects

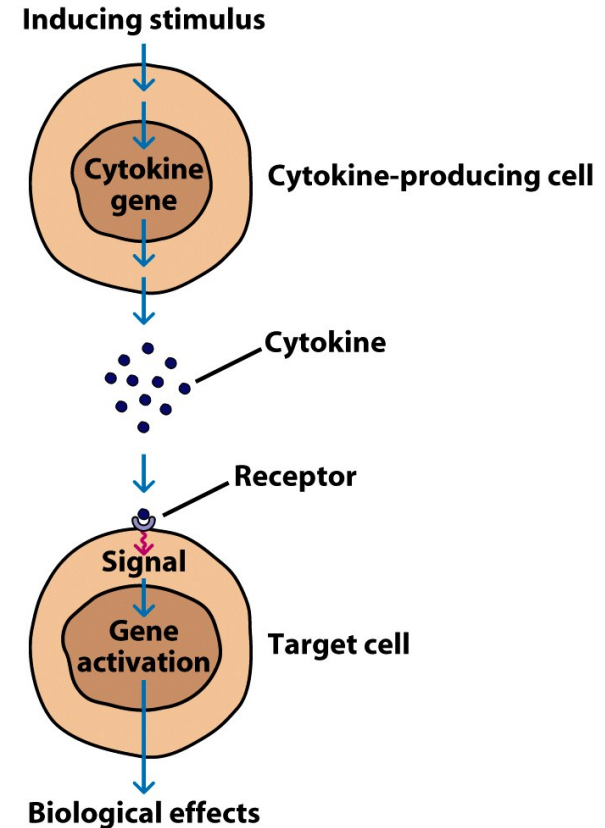


Figure 12-1a
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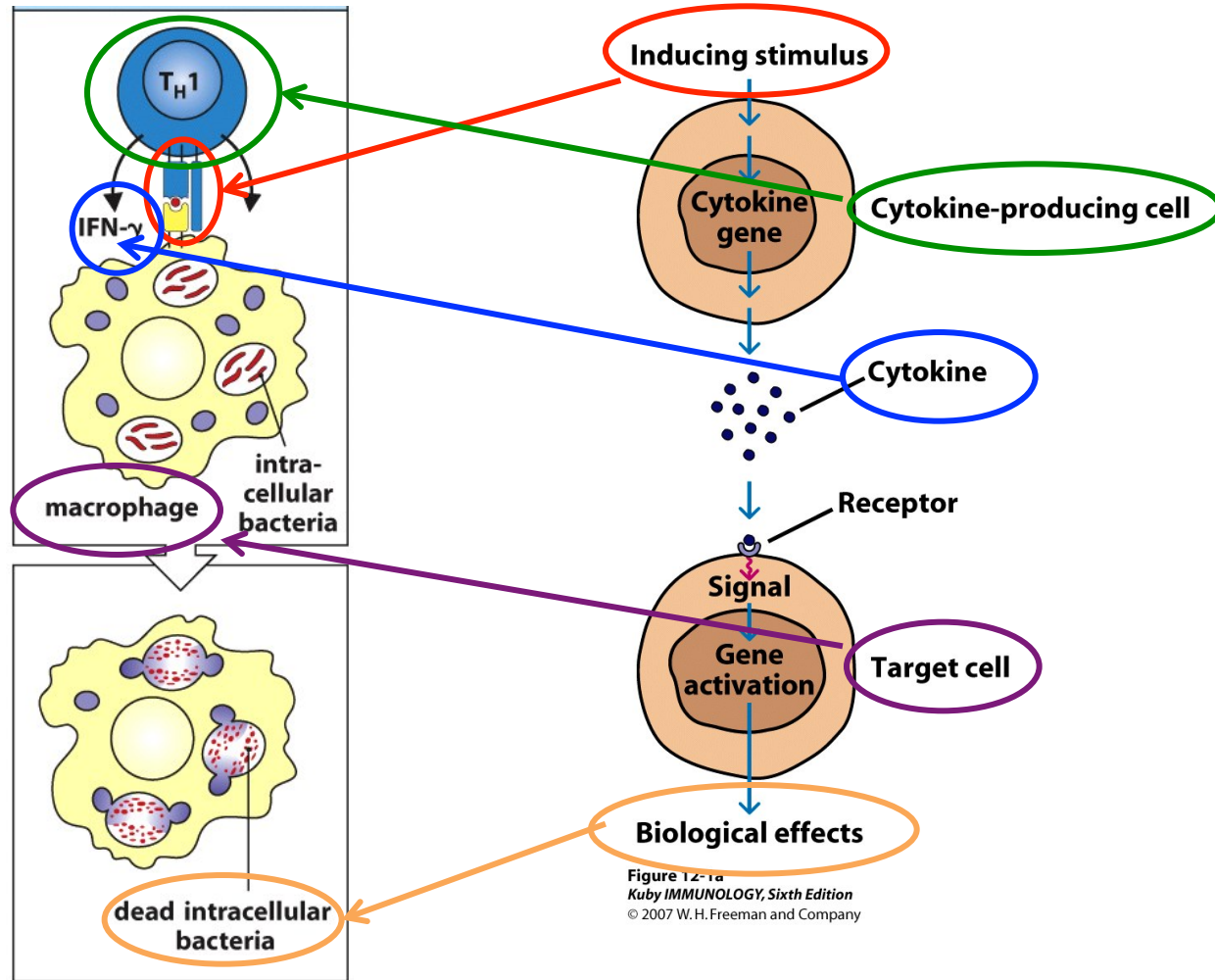
- **Inducing Stimulus:**
Immunological Synapse
(MHC-TCR/CD8/Co-
Stimulatory molecules)

- **Cytokine-producing cell:** T_H1

- **Cytokine:** $IFN-\gamma$

- **Target cell:**
Macrophage

- **Biological effects:**
Bactericidal effect



- **Inducing Stimulus:**
- **Cytokine-producing cell:**
- **Cytokine:**
- **Target cell:**
- **Biological effects:**

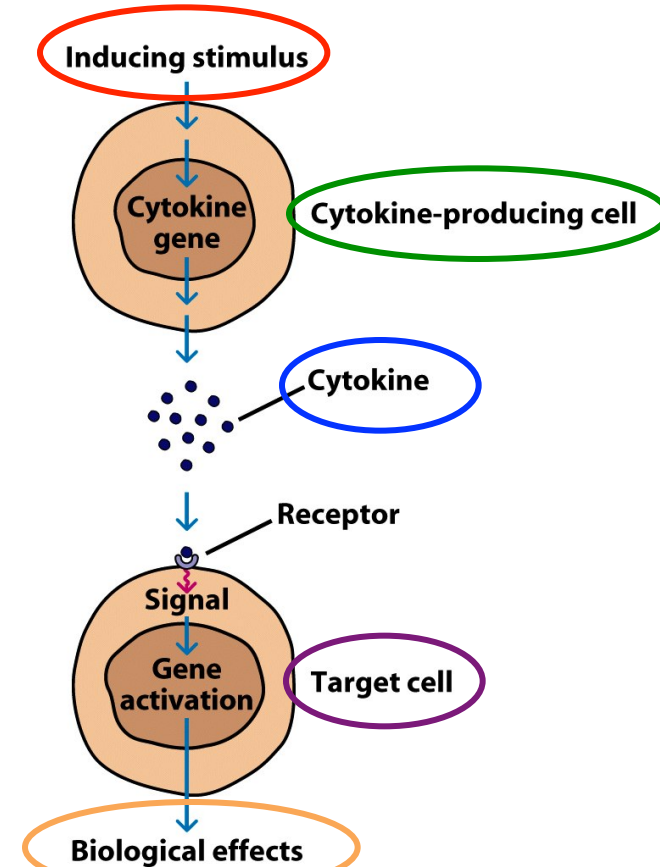
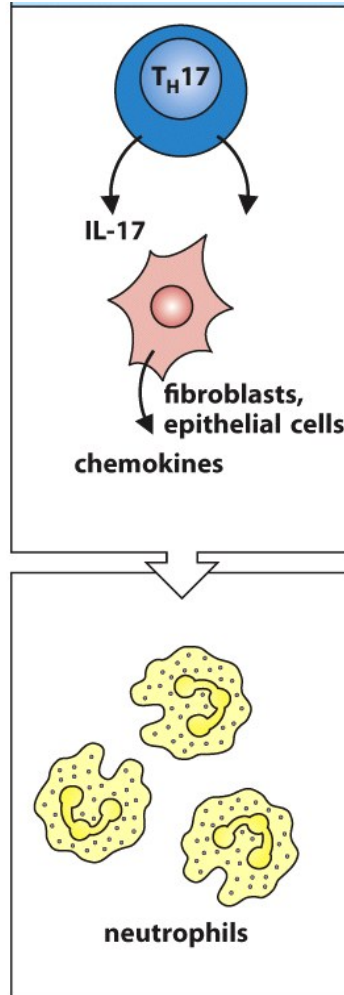
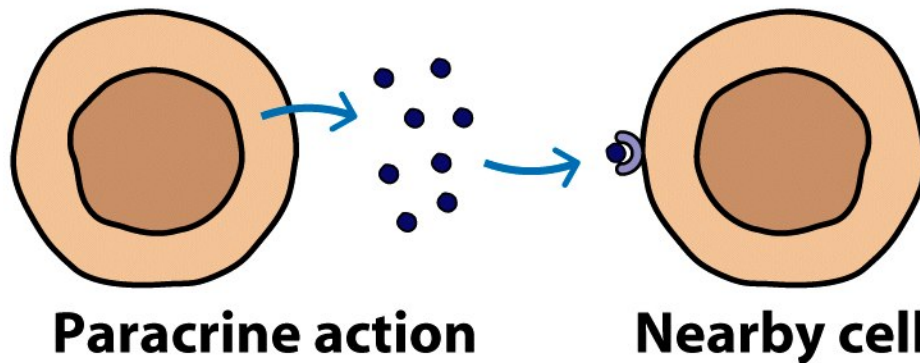


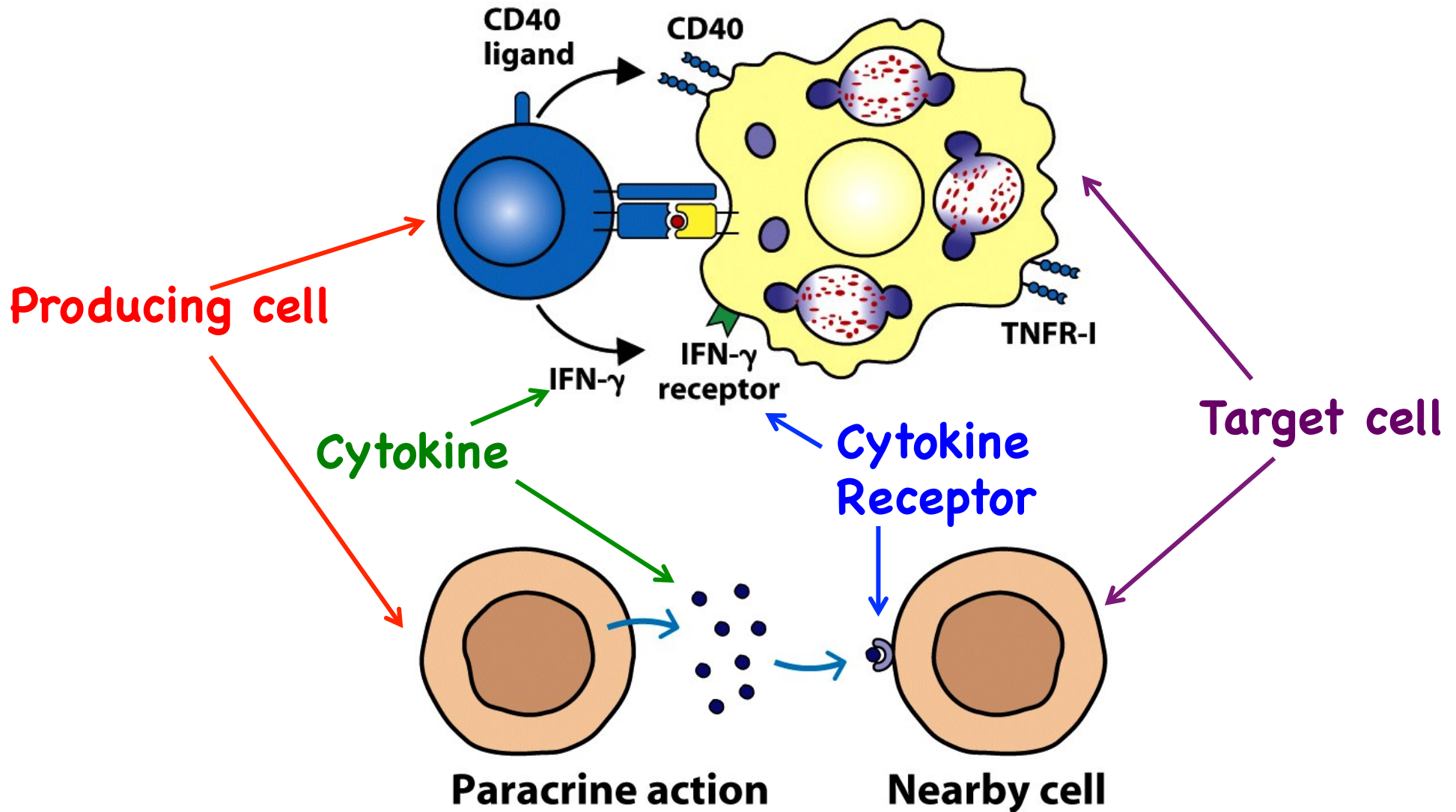
Figure 12-1a
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Cytokines communication

- **Paracrine:** when a cytokine is produced by a cell and binds to a receptor on a **target cell in close proximity** to the producing cell

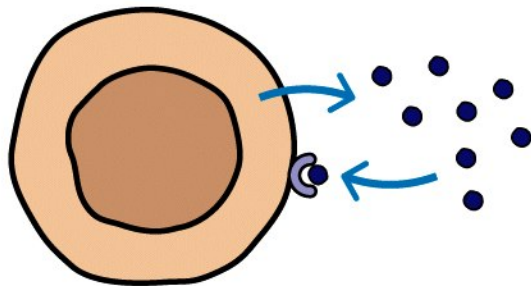


Paracrine action



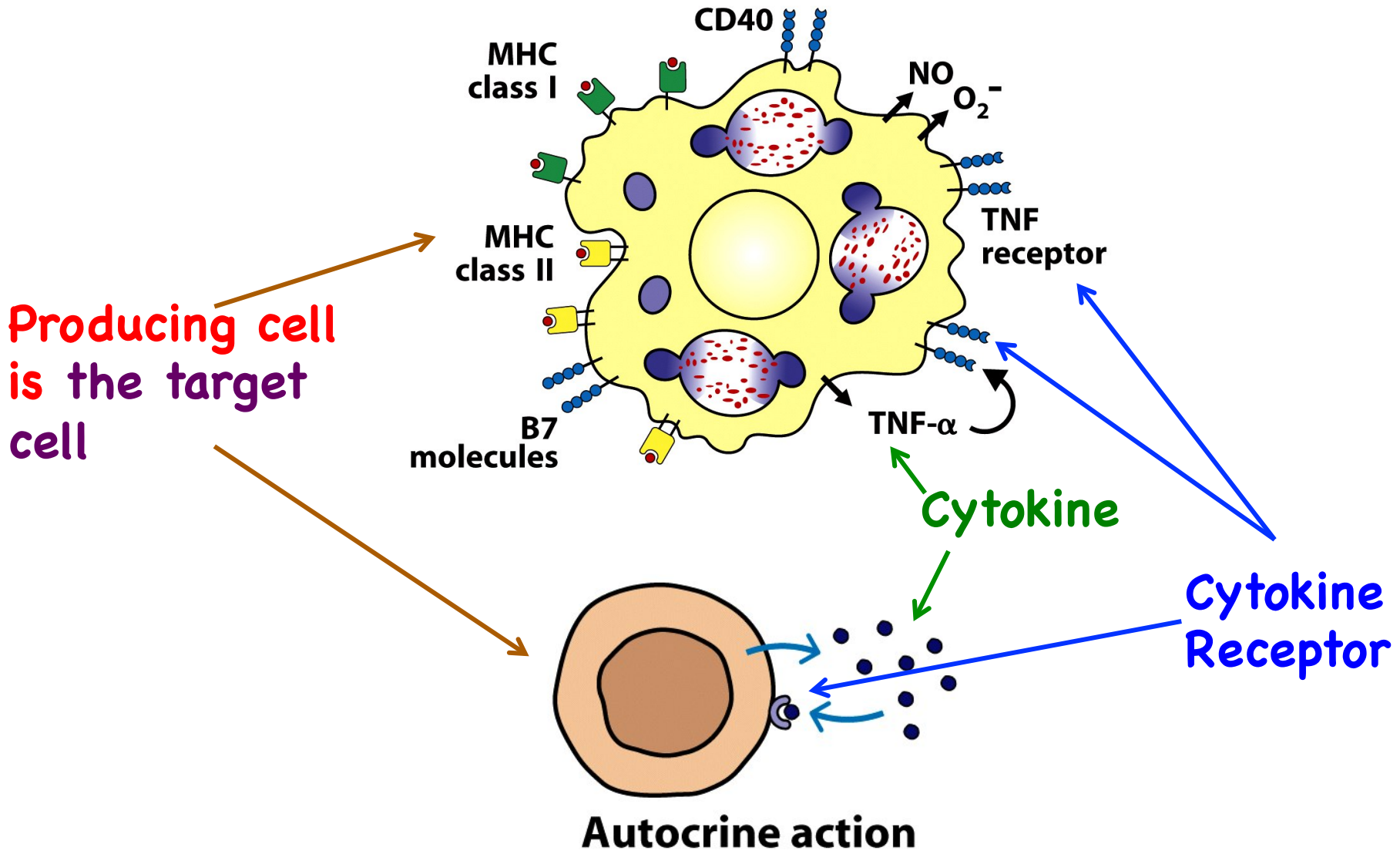
Cytokines communication

- **Autocrine:** when a cytokine is produced by a cell and binds to a receptor on **the same producing cell**

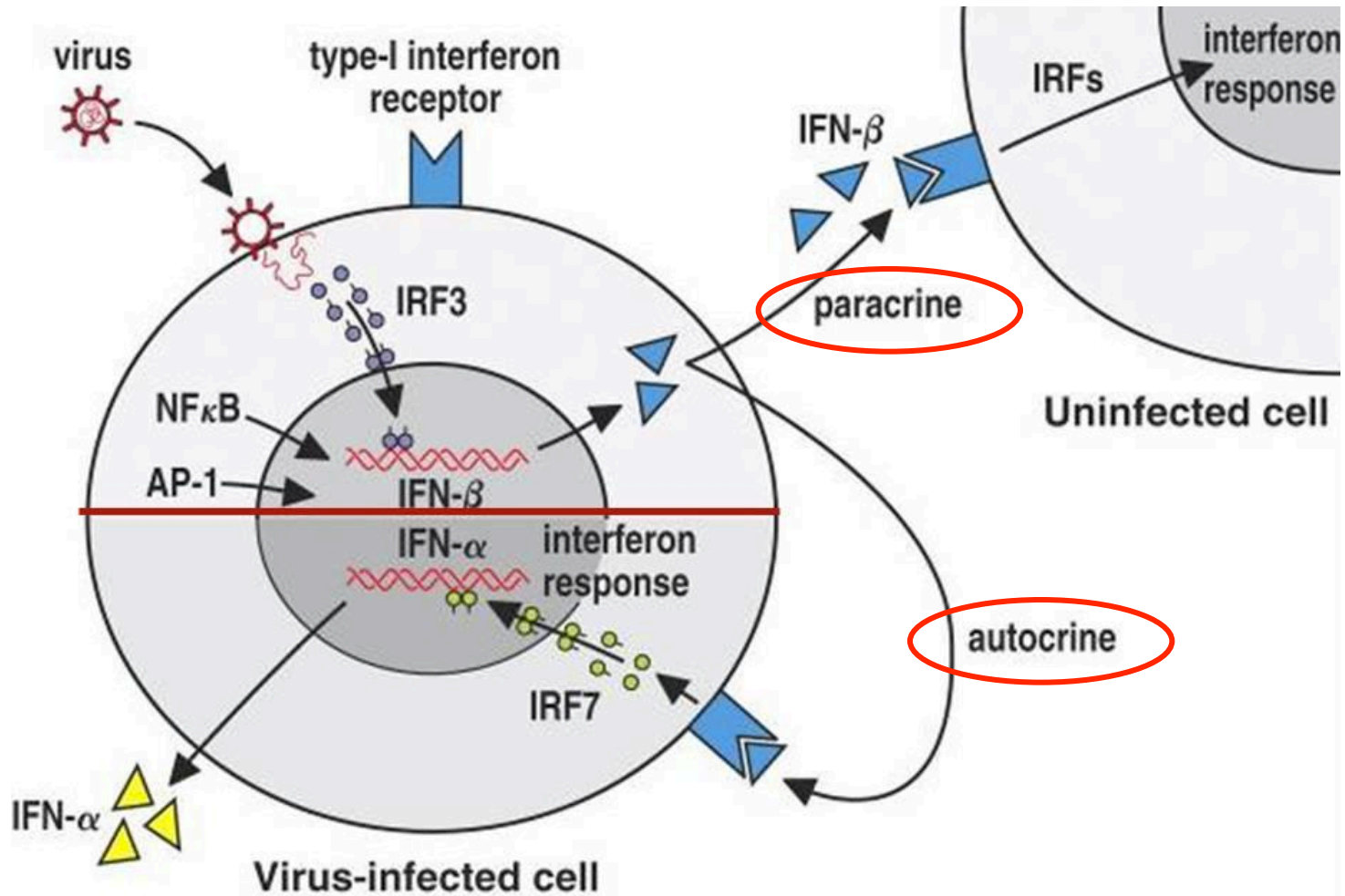


Autocrine action

Autocrine



Paracrine & Autocrine



Mechanism of IFN- α/β

Type I interferon inhibit protein synthesis (needed for virus replication)

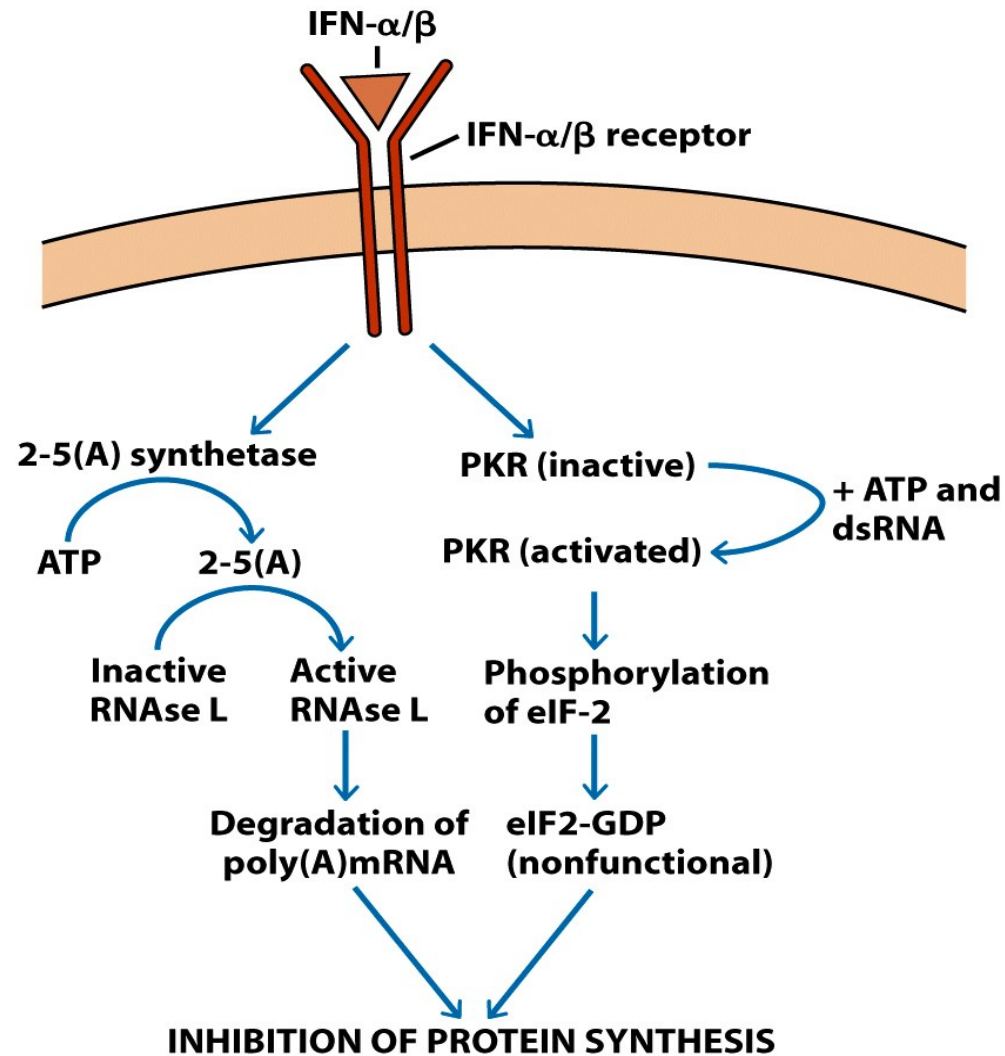
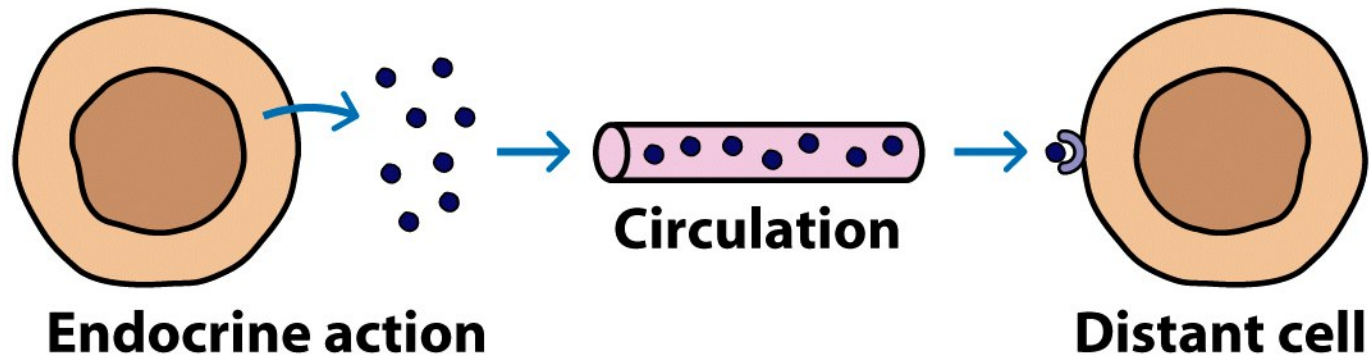


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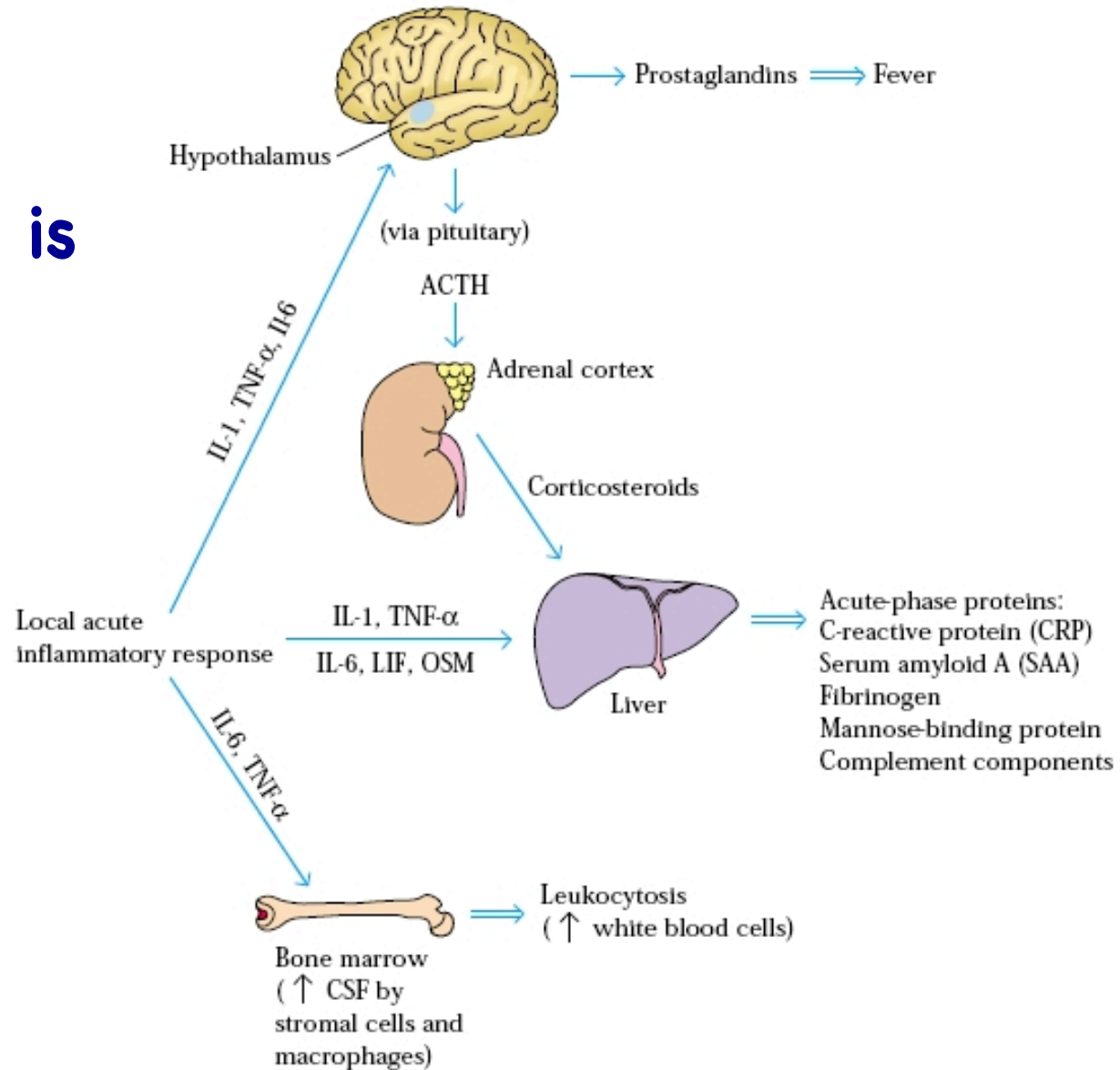
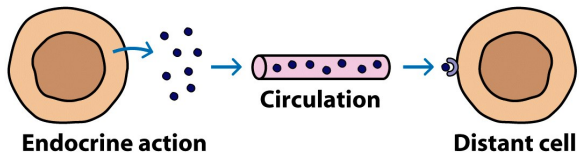
Cytokines communication

- **Endocrine:** when a cytokine is produced by a cell and binds to a receptor on a **target cell in a distant part of the body**



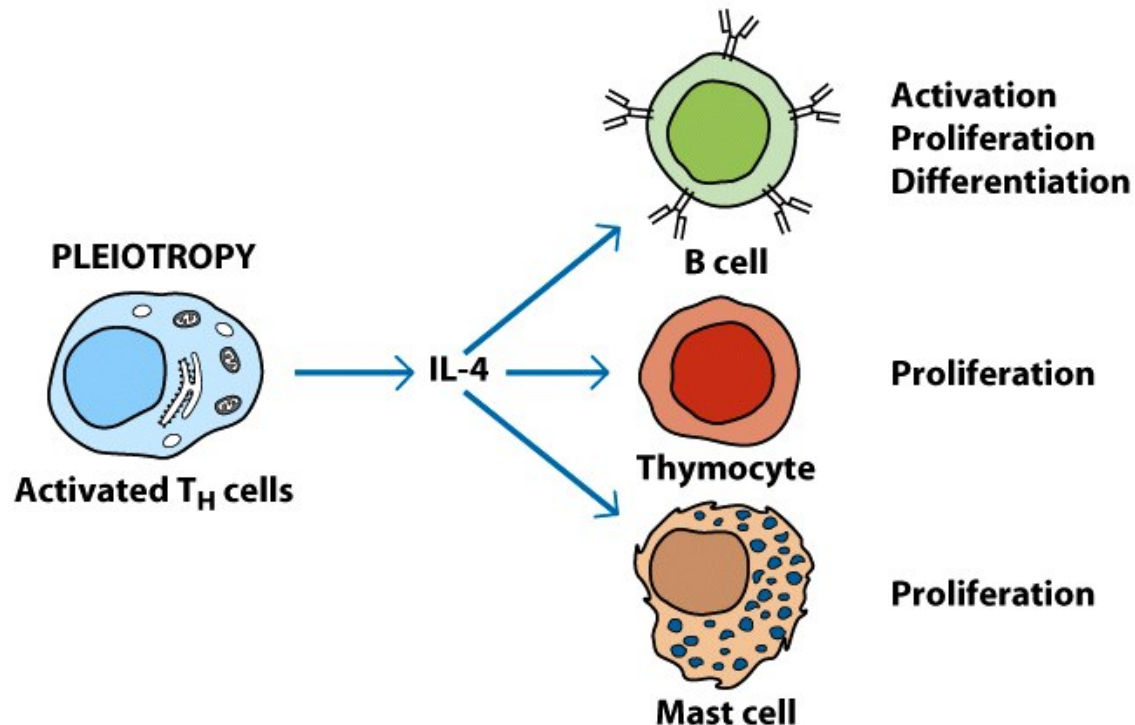
Endocrine

Acute Phase Response is an example of the endocrine action of cytokines



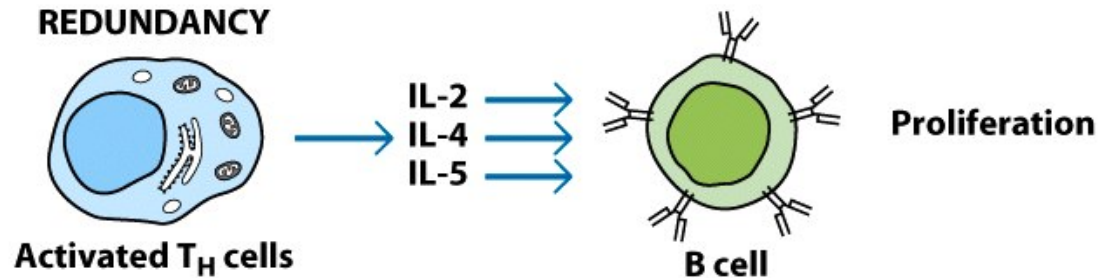
Cytokines attributes

- **Pleiotropy:** when a cytokine has different biological effects or different target cells



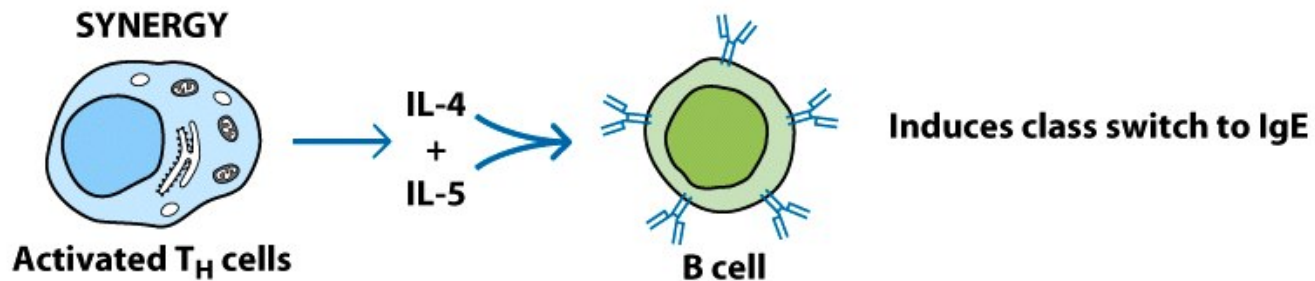
Cytokines attributes

- **Redundancy:** when two or more cytokines have similar biological effect



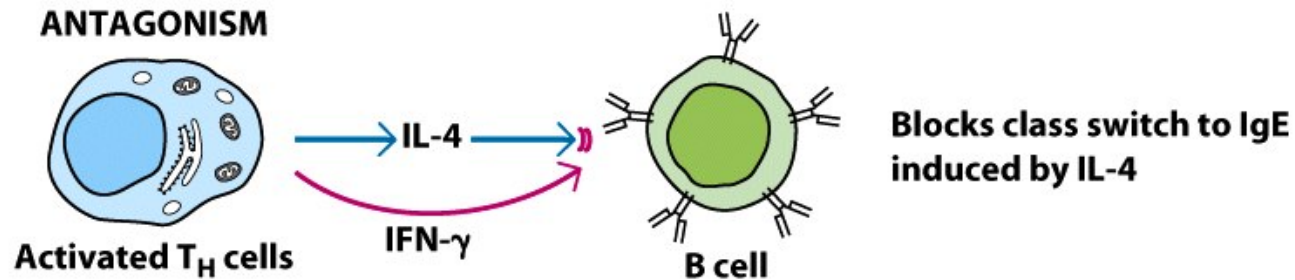
Cytokines attributes

- **Synergy:** when the combined effect of two or more cytokines is greater than the additive effects of the individual cytokines



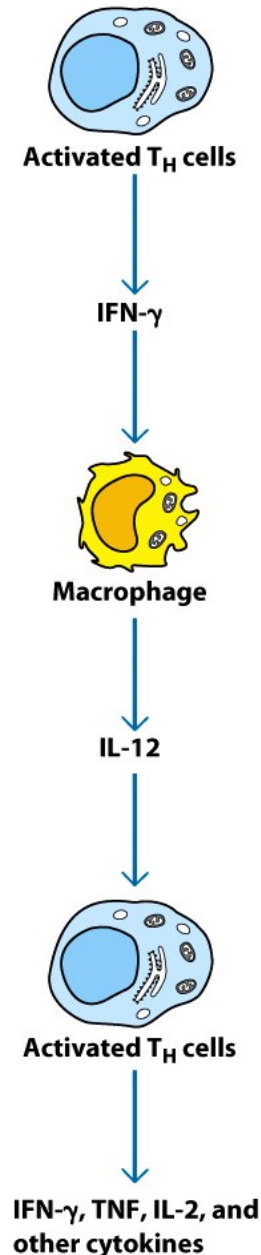
Cytokines attributes

- **Antagonism:** when the effects of one cytokine inhibit or offset the effects of another cytokine



Cytokines attributes

- **Cascade induction:** when the action of once cytokine induces the production of another cytokine that induces the production of another cytokine



Cytokines vs. Hormones

Property	Hormones	Cytokines
Mode of production	Constitutive and induces	Mostly induces
Target location	Mostly distal	Mostly proximal
Producing cells	Specialized glands	Variety of cells

Cytokines Families

- Cytokines can be classified based on their structures into 4 families:
 - Hematopoietin family
 - Interferon family
 - Chemokine family
 - Tumor necrosis family

Cytokines Receptors Families

- Cytokines can be classified based on their structures into 4 families:
 - Immunoglobulin superfamily receptor
 - Class I cytokine receptor family (hematopoietin receptor family)
 - Class II cytokine receptor family (interferon receptor family)
 - Tumor necrosis family
 - Chemokine receptor family

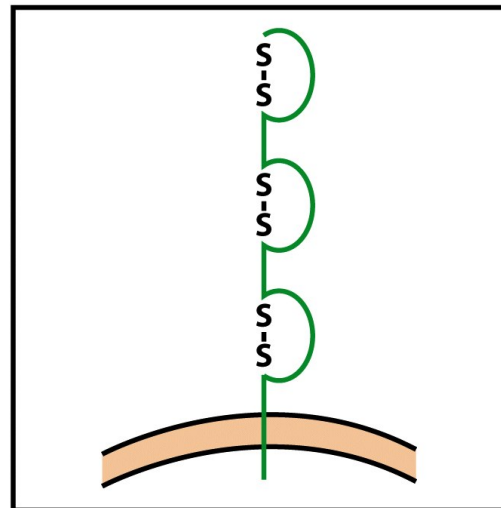
IgSF receptor

- Immunoglobulin Superfamily (IgSF) is a large group of cell surface and soluble proteins possess a structural domain known as the Immunoglobulin (Ig) Domain

RECEPTOR FAMILY

LIGANDS

Immunoglobulin superfamily receptors



IL-1
M-CSF
C-KitL
IL-18

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Class I cytokine receptor family

- Majority of cytokine receptors in the immune system
- Has 3 subfamilies characterized by common signaling subunits

RECEPTOR FAMILY

Class I cytokine receptors
(hematopoietin)

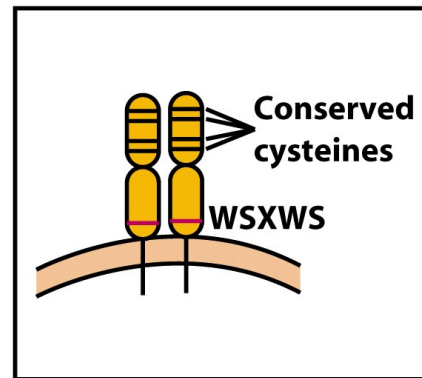
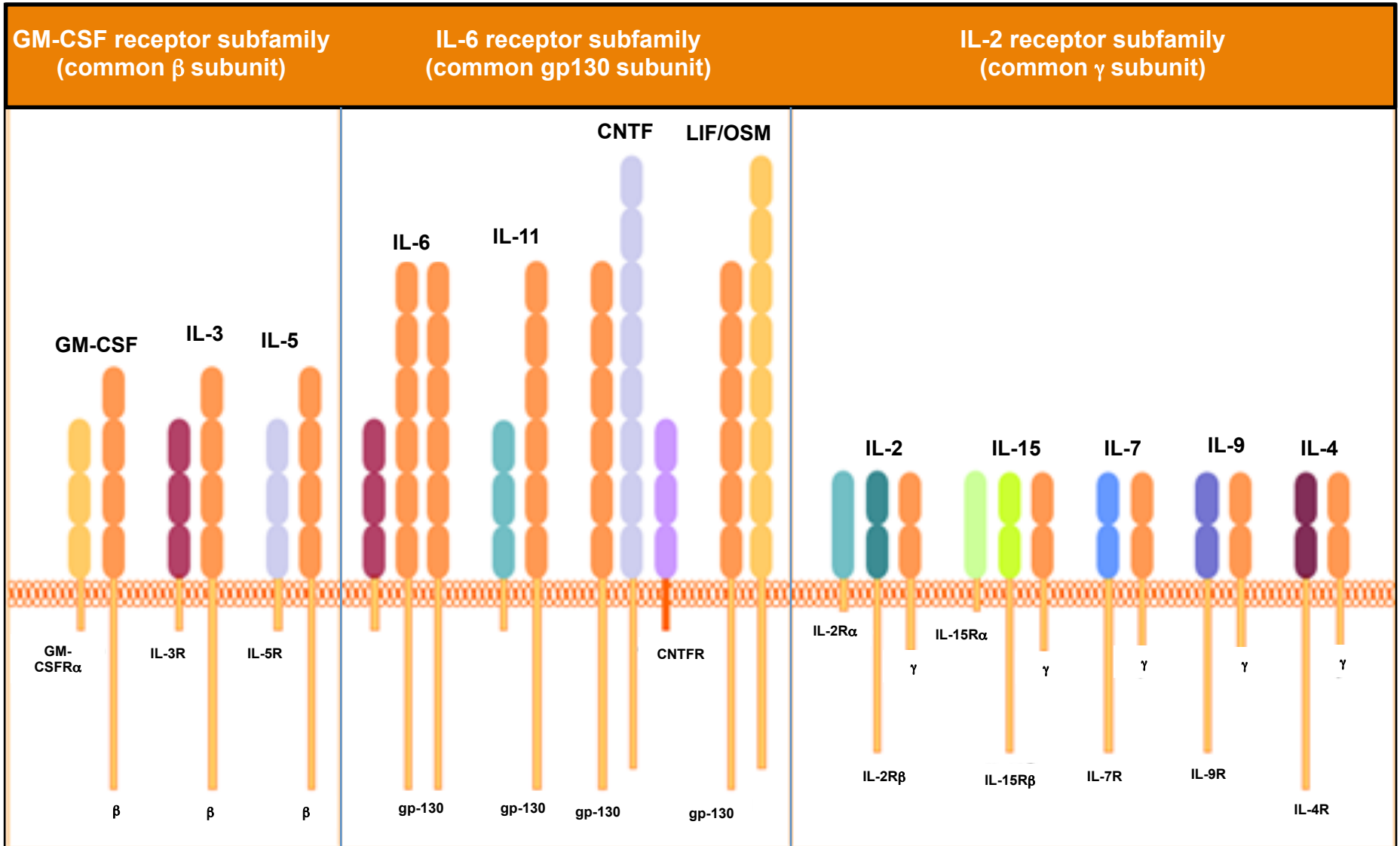


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LIGANDS

IL-2	IL-21
IL-3	IL-23
IL-4	IL-27
IL-5	GM-CSF
IL-6	G-CSF
IL-7	OSM
IL-9	LIF
IL-11	CNTF
IL-12	Growth hormone
IL-13	Prolactin
IL-15	

Class I cytokine receptor family



Class II cytokine receptor family

- Has multiple subunits
- Usually common signaling subunit
- Similar signaling pattern as Class I

RECEPTOR FAMILY

Class II cytokine receptors
(interferon)

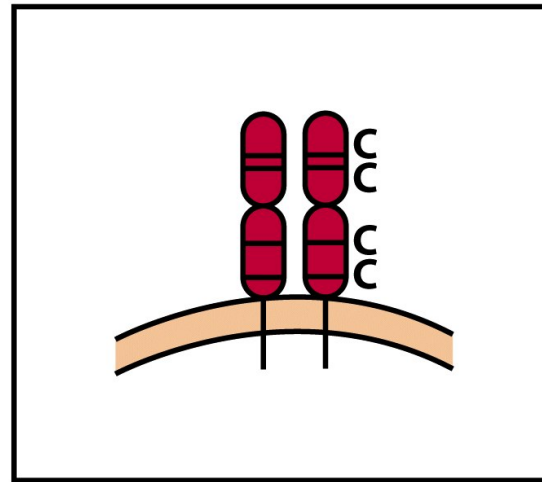


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LIGANDS

IFN- α
IFN- β
IFN- γ
IL-10
IL-19
IL-20
IL-22
IL-24
IL-26
IL-28
IL-29 } IFN- λ

Signaling through class I/II receptor

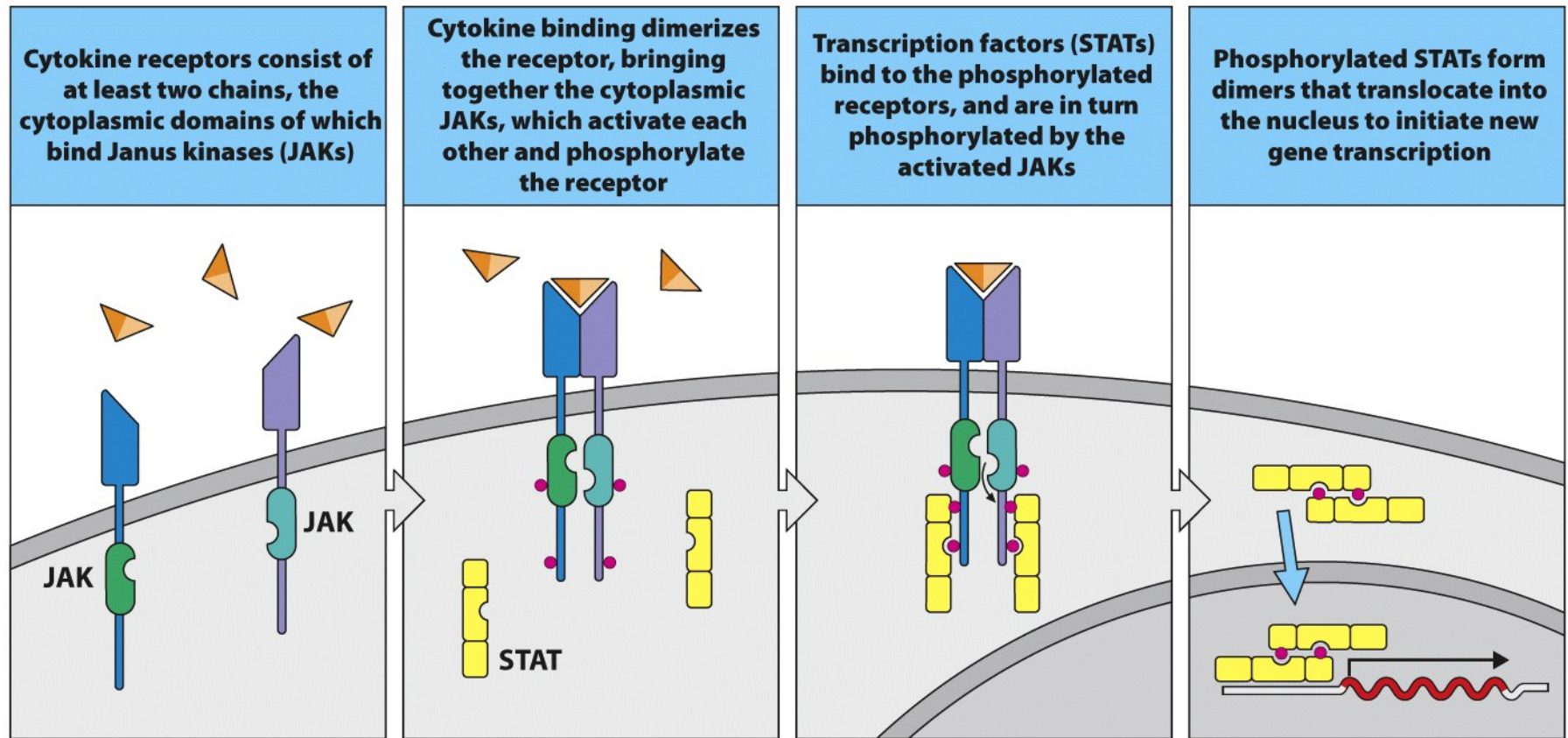
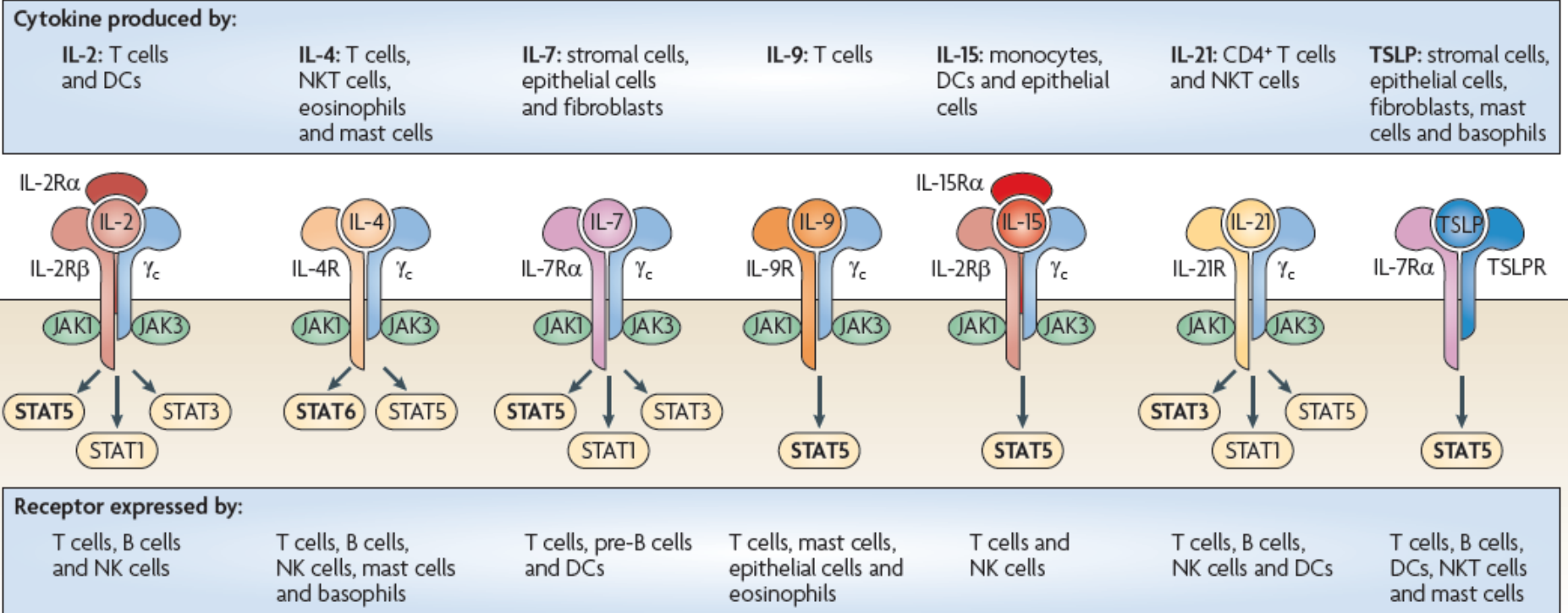


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Signaling pathway dictates cell fate

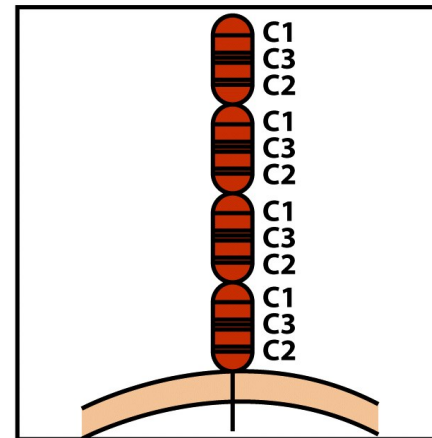


TNF receptor family

- Usually death receptors

RECEPTOR FAMILY

TNF receptors



LIGANDS

TNF- α
TNF- β
CD27L
CD30L
CD40L
Nerve growth factor (NGF)
FASL

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Signaling through TNF receptor family

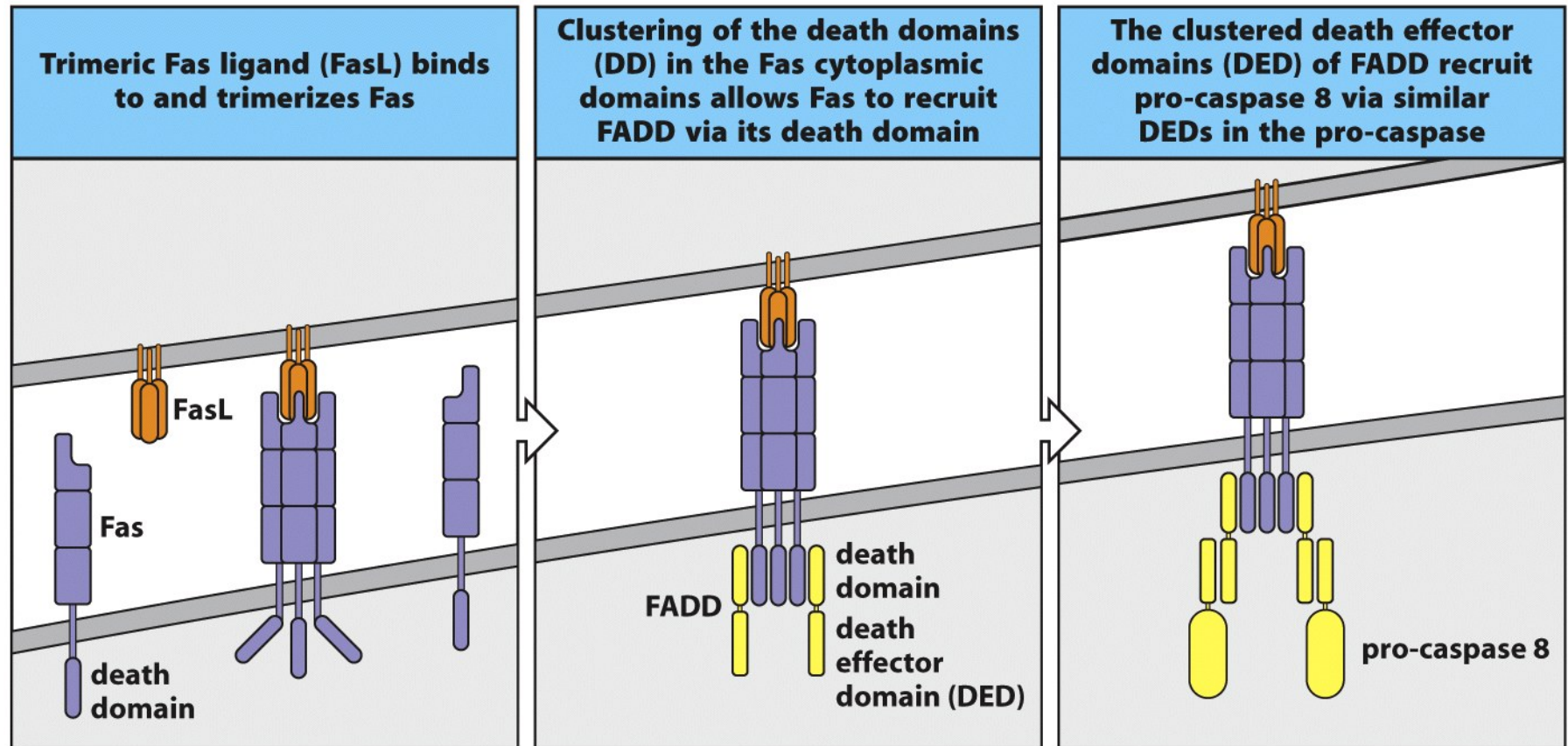


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Chemokine receptor family

- They are structurally distinct from the other cytokine receptors

RECEPTOR FAMILY

Chemokine receptors

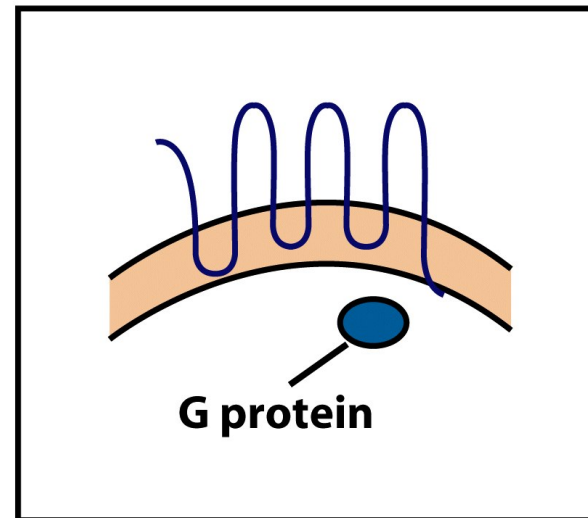


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LIGANDS

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

Chemokine receptor family

- They are structurally distinct from the other cytokine receptors

Chemokines are the major regulators of leukocyte traffic.

They are involved in inflammation, homeostasis, and adherence of leukocytes to endothelial lining

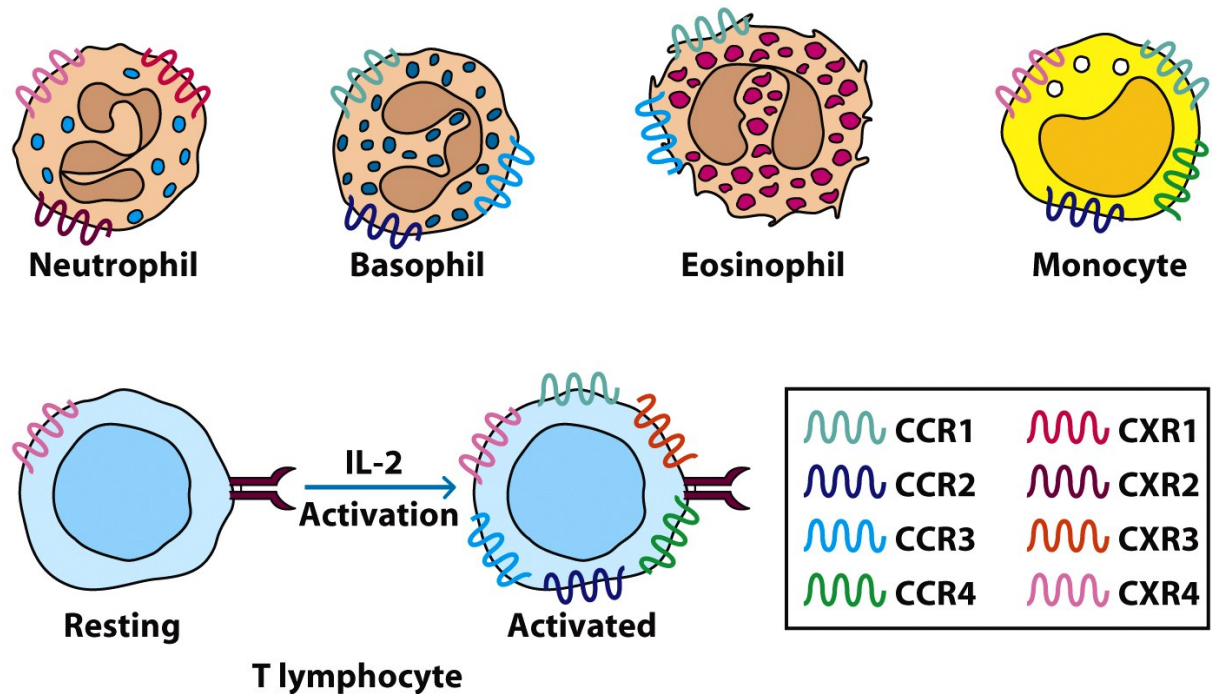


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Signaling through chemokine receptors

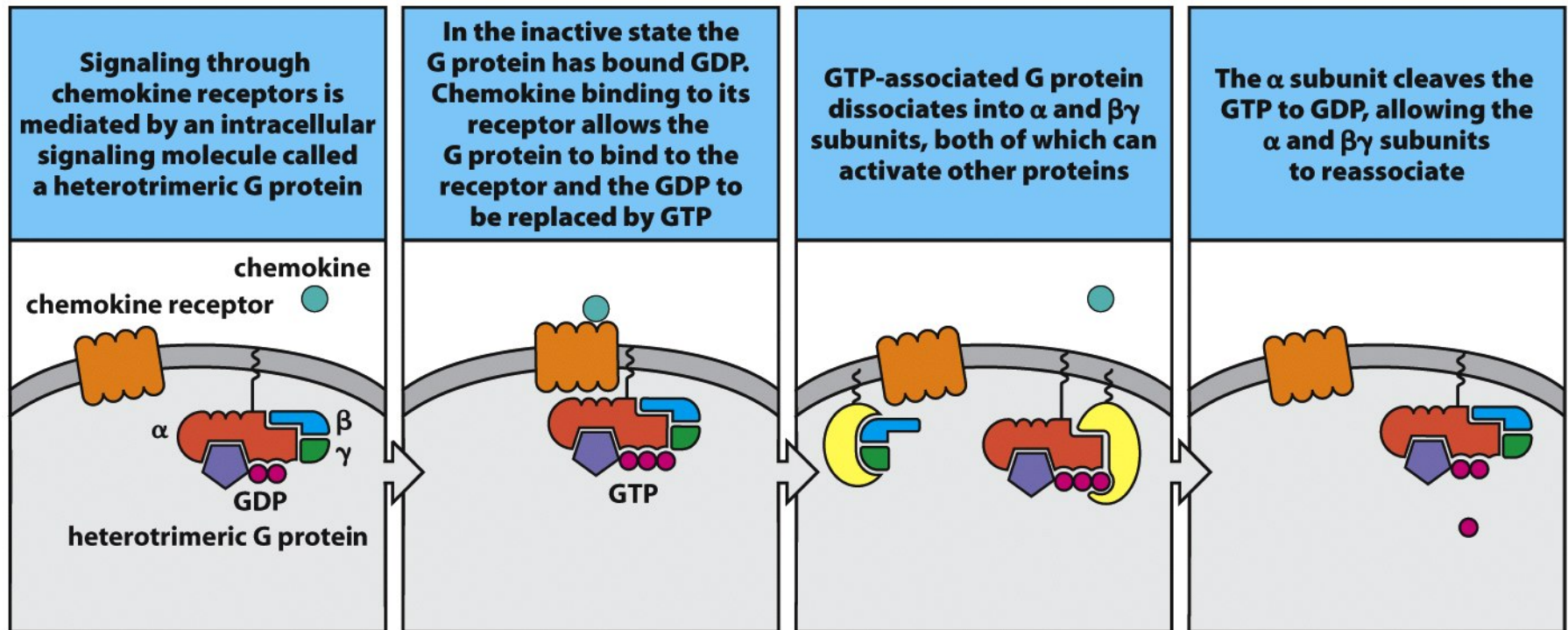


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You are now able to:

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