



Immunology

Title : Cytokines (CKs)

Lec no : 10

Done By : Johainah Taha + Nour

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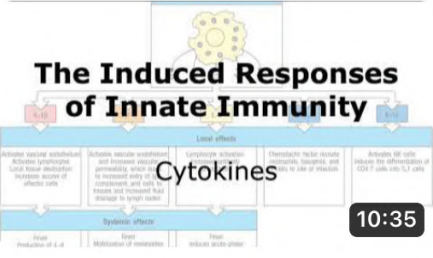
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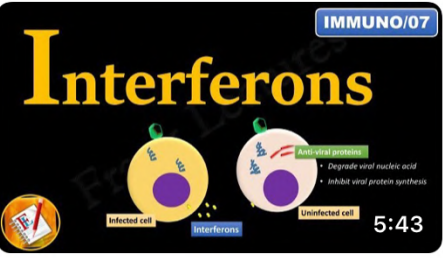
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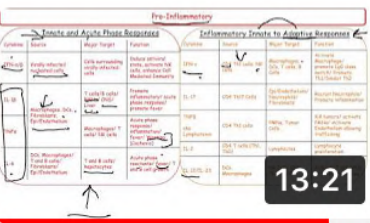
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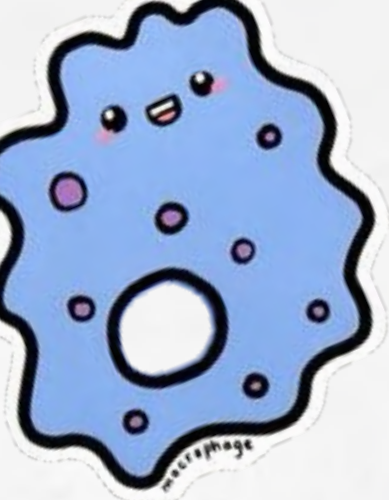
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رسالة اليوم

أفضل استثمار في الوقت الحالي أنك تستثمر في نفسك، اياك أن تنسى نفسك وسط مشاكل الحياة، علم وطور وغير من نفسك للأفضل، لأنك تستحق ذلك

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Definition (what are cytokines?)

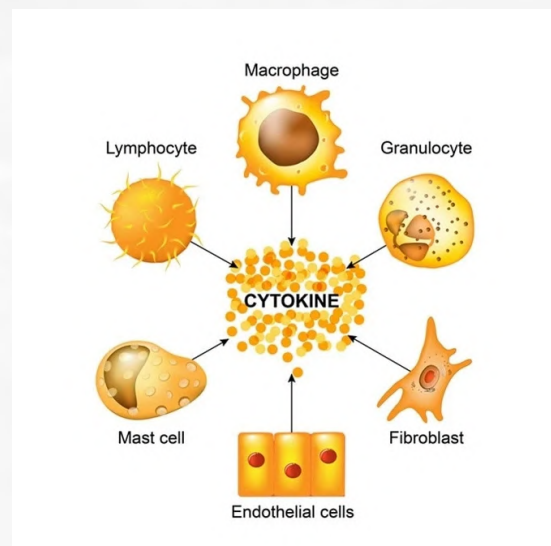
- A group of low molecular weight **polypeptides or proteins** which are secreted by activated immunocytes or some matrix cells and possess high activity and various functions.
- Cytokine or immunocytokine is a generic name used to describe a diverse group of soluble proteins and peptides which act as **humoral regulators** at nano to picomolar concentrations.

They work at minimal concentration

- Their major functions are to mediate and regulate immune response and inflammatory reactions.

Cytokines play role in :

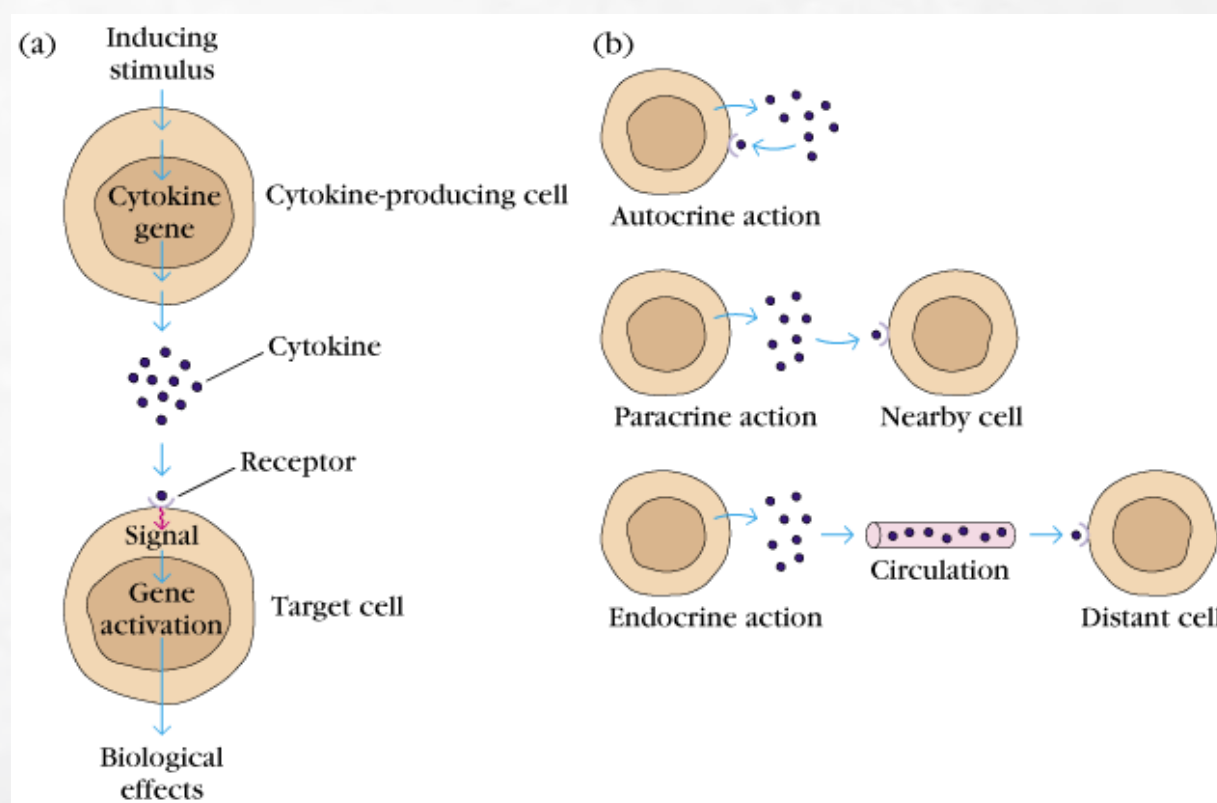
1. Inflammation
2. Chemotaxis
3. Activation of B and T cell



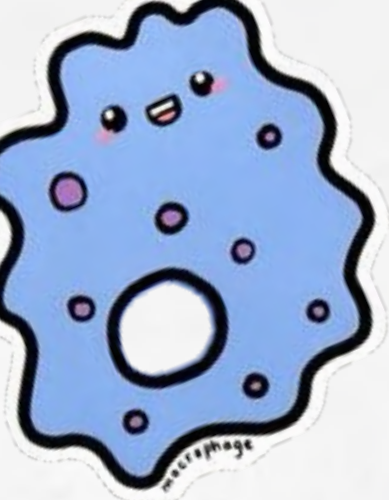
General Properties

- 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.

- Autocrine = produced by the cell to affect itself**
- Paracrine = produced by the cell to affect nearby cells**
- Endocrine = produced by the cell to distant cells**



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Cytokine Names

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

Effects of Cytokines

مهمين ♥

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

يعني ال cytokine الوحدة ممكن تعمل أكثر من وظيفة

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

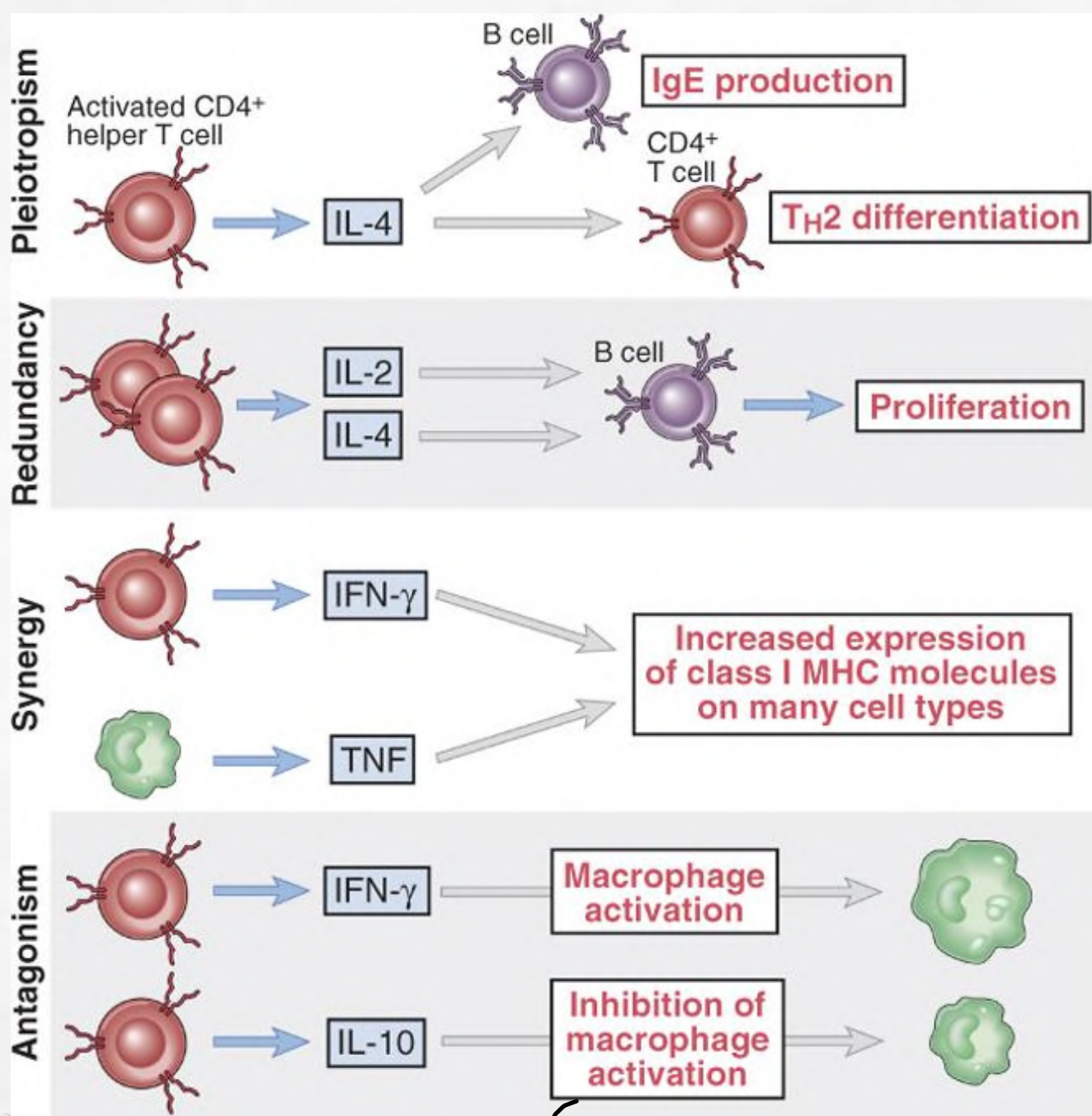
The same cell can be triggered to do the same function by more than one type of cytokine
Ex: IL4 + IL5 + IL12 might have the sam effect on T cells (T cell differentiate into Th2)

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

2 cytokines working on the same cell at the same time, would have synergistic effect

- **Antagonism** refers to the ability of one cytokine inhibiting the action of another.

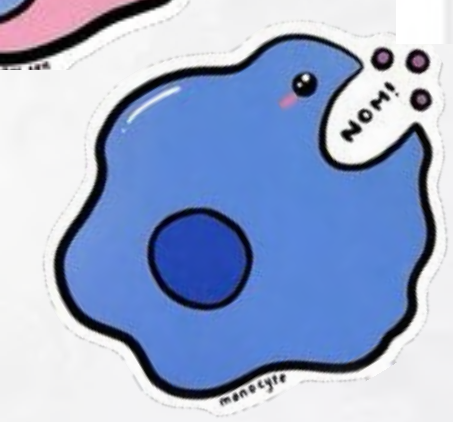
Ex : TNF Beta + IL10 inhibit the immune response

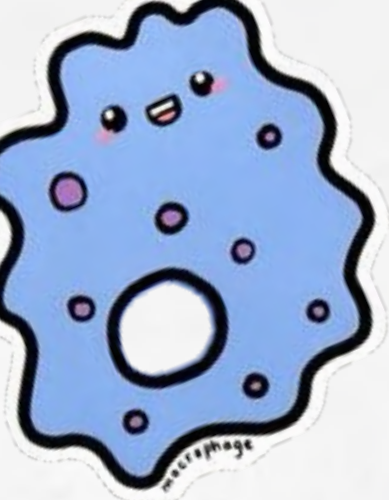


الرسمه مطلوبه، ال effect مع الامثله

At the end of the immune response

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Cytokine General Actions

- Development of cellular and humoral immune responses
- Induction of inflammation -> TNF IL1/IL6/IL8
- Regulation of hematopoiesis -> IL3/IL7/CSF
- Control of cellular proliferation and differentiation -> IL2
- Induction of wound healing
- Chemotaxis

B cell activation? IL1/IL2/IL4
T cell activation? IL2/IL4/IL5

Classification of cytokines

- Interleukin, IL
- Interferon, IFN
- Tumor necrosis factor, TNF
- Colony stimulating factor, CSF
- Chemokine
- Transforming growth factor

حنفصل كل عيلة

حنبدأ نشرح عنهم هسا عيلة عيلة، و حنبدأ نشرح عن ال Interleukin اسمحولي اشرح الكم كم شغلة و معلومة خارجية مني بعدين انتقلوا للسلایدات ♥

IL1 :

1. Are secreted by macrophages.
2. Their functions are :
- Inflammatory response with TNF and IL6, by :

Increase the capillary permeability

Vasodilation

Endothelial cell wall activation

To increase the overall blood flow

To allow the signaling molecules and WBCs to move from the blood into the effected tissues

To express the adhesion molecules to allow WBCs to bind to the endothelium (important step in extravasation)

Soooo! IL1 increased the ability of WBCs to reach the site of the infection

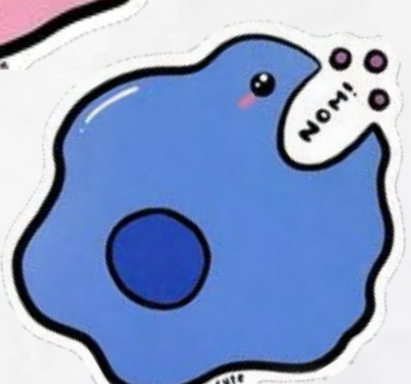
- Causes fever, so it is a PYROGEN.

IL1 goes to the brain to stimulate the production of PGE2 (prostaglandin) from archidonic acid. PGE2 then travel to the anterior hypothalamous, leading to an increase in the set point for temperature -> producing fever

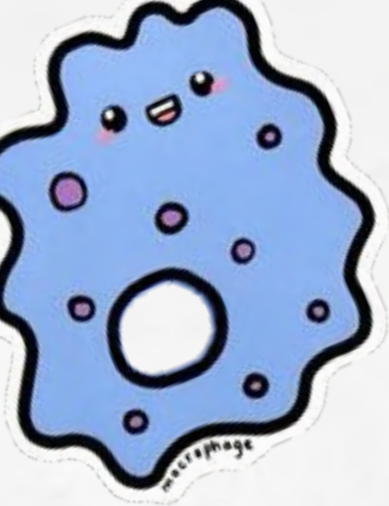
- They promote osteoblast activation which leads to bone resorption (IL1 = Osteoblast activation factor)

**There are 2 important clinical applications:

- 1) IL1 overexpression can lead to weakening of bones, and that is called osteopenia
- 2) Cancer cells can release IL1 generating lytic lesions in bone.



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1. Interleukin 1 (IL-1) Family

The members of this family are : IL1 alpha - IL1 beta - IL18 - IL33

- Typically secreted very early in the immune response by dendritic cells and monocytes or macrophages.
- IL-1 secretion is stimulated by recognition of viral, parasitic, or bacterial antigens by innate immune receptors.
- IL-1 family members are generally pro-inflammatory, (what does that mean)?

حكيانا انه الوظيفتين الاساسيات لل innate immunity هم anti-viral + inflammation
لهيك ال IL1 تعمل مع ال innate immunity و بالتالي هي pro-inflammatory يعني

Its production is going to produce inflammatory reaction in the location of the infection

- they induce an increase in the capillary permeability at the site of cytokine secretion,
- amplification of the level of leukocyte migration into the infected tissues.
- IL-1 has systemic (whole body) effects and signals the liver to produce acute phase (CRP) and IL-6

CRP is an acute marker of inflammation

- These proteins further induce multiple protective effects, including the destruction of viral RNA
- generation of a systemic fever response (which helps to eliminate many temperature-sensitive bacterial strains).

So it has to do with increasing permeability, migration of leukocytes, acute phase reactant, anti-viral effect and fever stimulation

- IL-18 stimulate production of the macrophage-activating cytokine IFN- γ by NK cells and T cells (innate immune response)
- IL-1 also activates both T and B cells at the induction of the (adaptive immune response).
- E.X. IL-1 α and IL-1 β ,IL-18

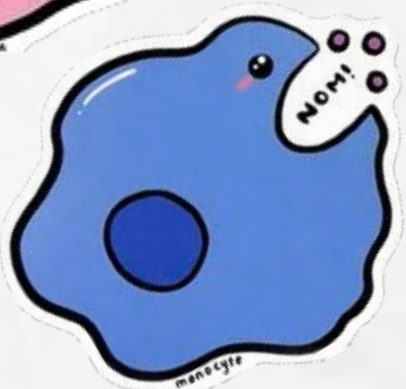
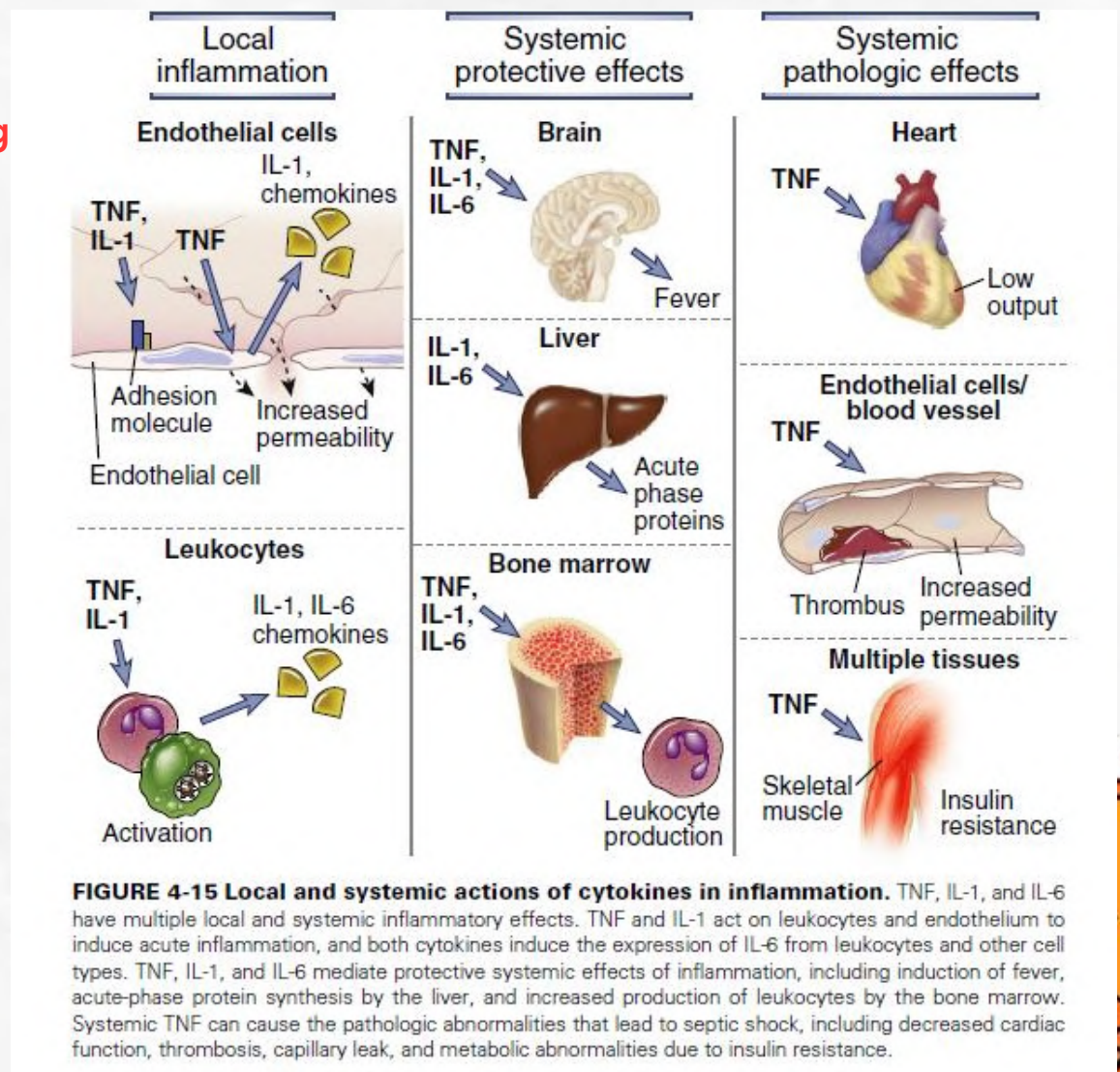
تعليق الدكتور على هاي الرسمة

TNF + IL1 -> adhesion molecule + increasing permeability + activate leukocyte (macrophage + neutrophils) to produce IL1 and IL6

هاد كله متعلق بدورهم بال local inflammation

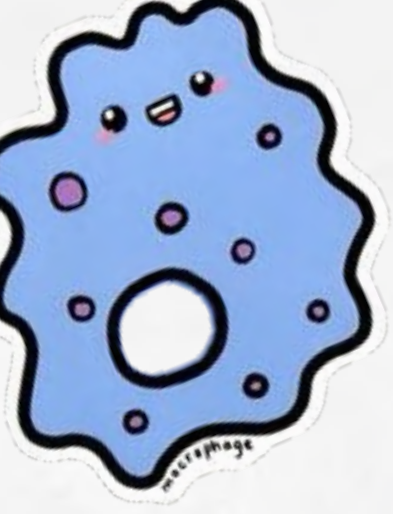
They have also a systemic protective effect, they act on the Brain (fever), Liver (Acute phase proteins), Bone marrow (increase the production of leukocyte)

They have a systemic pathologic effect on the heart on the heart (decreasing the cardiac output), Skeletal muscles (insulin resistance), Endothelial cells (thrombus formation + increasing the permeability)



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• Hematopoietin (Class I) Family:

- Called Class I because earliest to be structurally characterized (not first to be discovered)
- Large family of small cytokine molecules with functional diversity
- Not all involved in hematopoietic functions

Their cellular origins and target cells are as diverse as their ultimate functions, which range from;

- signaling the onset of T- and B-cell proliferation (e.g.,IL-2),

حكيما واحد من ال cytokines الي يتم انتاجه early ليستجيب لل pathogen هو IL2 و الي بي عمل proliferation لل B و T

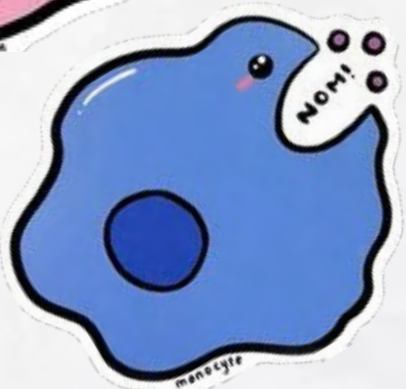
- Signaling the onset of B-cell differentiation to plasma cells and antibody secretion (e.g., IL-6),
- Signaling the differentiation of a T helper cell along one particular differentiation pathway versus another (e.g.,IL-4 vs. IL-12)
- Finally, Initiating the differentiation of particular leukocyte lineages (e.g., granulocyte monocyte-colony stimulating factors GM-CSF, G-CSF).
- E.X. IL-2, IL-4, IL-5, IL-7, IL-9,IL-12, IL-15, IL-21 and GM-CSF

Granulocyte macrophage colony-stimulating factor (GM-CSF) is a cytokine that promotes myeloid cell development and maturation, and dendritic cell differentiation and survival in vitro

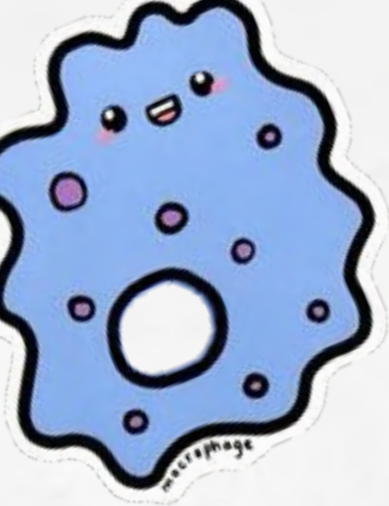
• IL-17 Family

(most recently described cytokines ,proinflammatory cytokine cluster)

- interleukins 17A, 17B, 17C, 17D, and 17F. Signaling through most members of this family culminates in the generation of inflammation.
- IL-17 released by activated T cells and stimulates the production of factors that signal a proinflammatory state, including IL-6, chemokines CXCL8, and (G-CSF).



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2. Interferon (Class II)

First cytokines to be discovered

○ Type I - Secreted by not only macrophages and dendritic cells but also by virus infected cells:

(1) Interferons α . (2) interferon- β .

○ Type II – produced by activate T and NK cells , known as interferon- γ & cytokines include IL-10

	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

The strongest anti-viral effect -> IFN-alpha

The weakest anti-viral effect -> IFN-gamma

• Interferon- γ is used medically to bias the adaptive immune system toward a cytotoxic response in diseases such as leprosy and toxoplasmosis (intracellular pathogens), in which antibody responses are less effective. BY:

Interferone gamma can be used as a treatment against leprosy (الجذام) and toxoplasmosis (an infection with a parasite called *Toxoplasma gondii*)

How ??

– and inducing the activation of macrophages, with subsequent destruction of any intracellular pathogens

– and the differentiation of cytotoxic T cells.

• All three INFs

(increase the expression of MHC complex proteins on the surface of cells, thus enhancing their antigen-presentation

بداخل ال macrophage يكون عنا pathogen مثل الفايروس و لحتى نقتله لازم نعمل antigen presentation و

بالتالي activation لل Cytotoxic T cell

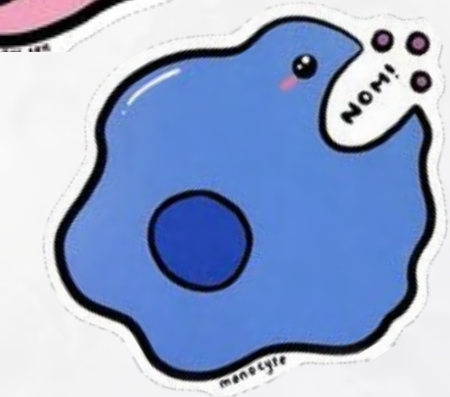
و ال IFN بتساعد على هاي العملية

It activates the production of cytotoxic T cells in order to kill the virus

الدكتور سأل كمان سؤال، كيف الخلية حتحس انه انا هسا لازم افرز cytokines?

الجواب ببساطة عبر ال sensation of Viral RNA

IFNs are going to interfere with the translation of the viral proteins



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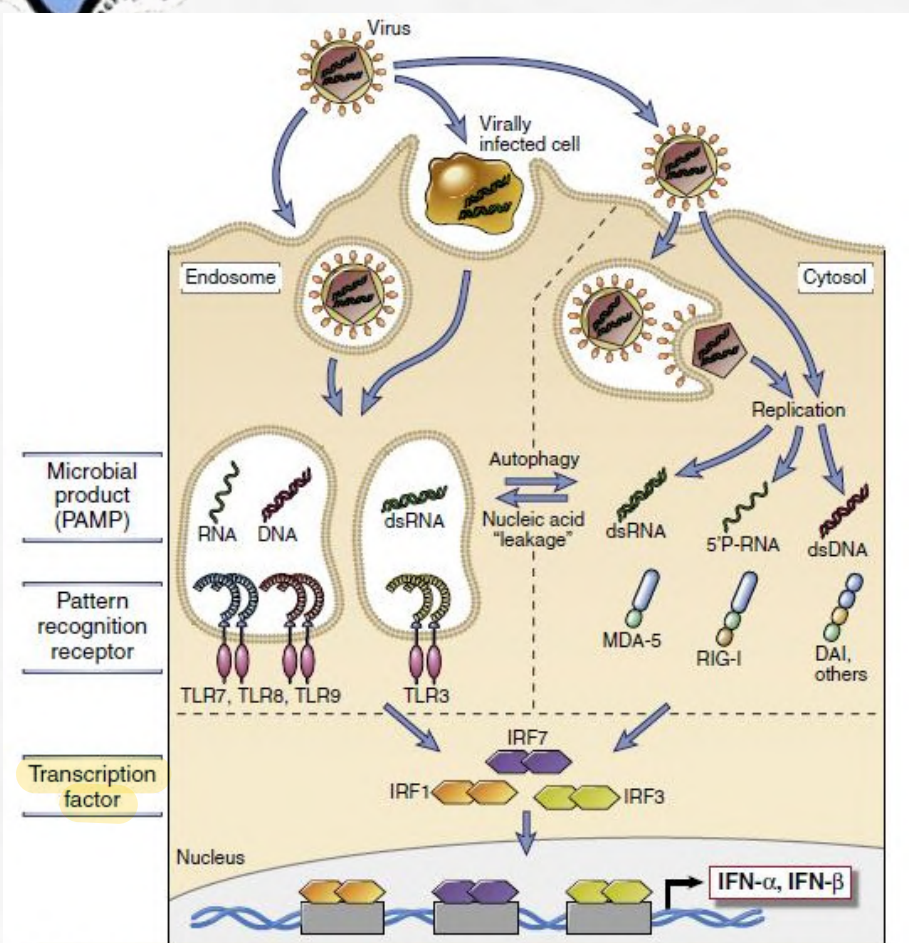
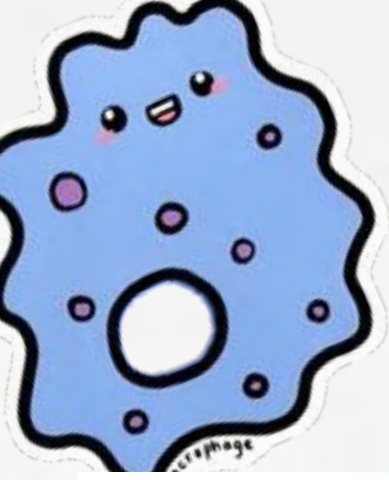


FIGURE 4-16 Mechanisms of induction of type I interferons by viruses. Viral nucleic acids and proteins are recognized by several cellular receptor families (TLRs, the family of cytosolic RIG-like receptors, or RLRs, which include MDA-5, RIG-I, DAI and others, and cytosolic DNA sensors), which activate transcription factors (the IRF proteins) that stimulate the production of

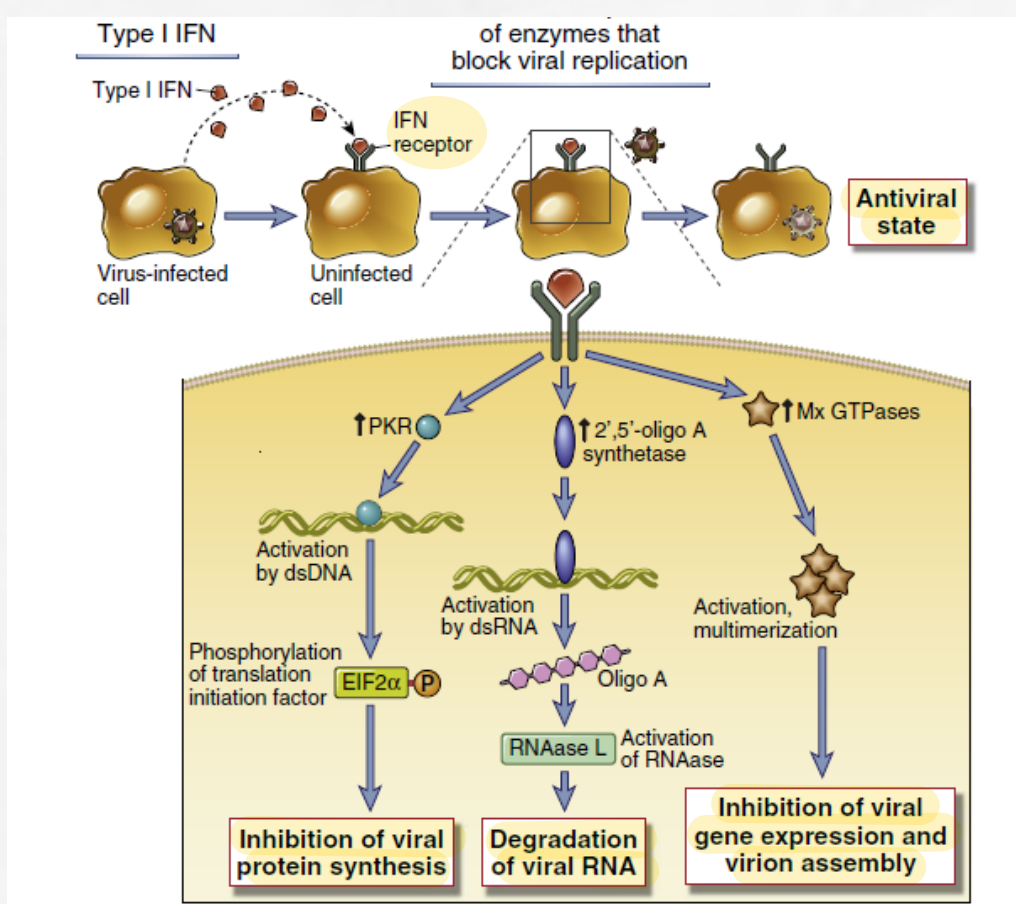


FIGURE 4-17 Biologic actions of type I interferons. Type I interferons (IFN- α , IFN- β) are produced by virus-infected cells in response to intracellular TLR signaling and other sensors of viral RNA. Type I interferons bind to receptors on neighboring uninfected cells and activate JAK-STAT signaling pathways, which induce expression of genes whose products interfere with viral replication. Type I interferons also bind to receptors on infected cells and induce expression of genes whose products enhance the cell's susceptibility to CTL-mediated killing. PKR, double stranded RNA-activated protein kinase.

From the book : Defense against viruses is a special type of host response that involves interferons, NK cells, and other mechanisms, which may occur concomitantly with, but are distinct from, inflammation.

Type I interferons inhibit viral replication and induce an antiviral state, in which cells become resistant to infection. Type I IFNs, which include several forms of IFN- α and one of IFN- β , are secreted by many cell types infected by viruses. A major source of these cytokines is a type of dendritic cell called the plasmacytoid dendritic cell (so named because these cells morphologically resemble plasma cells), which secretes type I IFNs in response to recognition of viral nucleic acids by TLRs and other pattern recognition receptors.

اول شي بدنا نعرفه هو انه الخلية المصابة حتفرز 1 interferon مجرد ما حست بوجود المادة الوراثية تبعت الفايروس

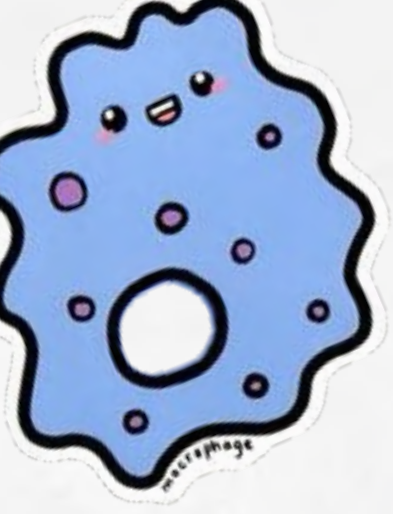
When type I IFNs secreted from dendritic cells or other infected cells bind to the type I IFN receptor on the infected or adjacent uninfected cells, signaling pathways are activated that inhibit viral replication and destroy viral genomes . This action is the basis for the use of IFN- α to treat some forms of chronic viral hepatitis.

هدول ال interferons حيرتبطوا عال receptors تبعونهم على الخلية المصابة و كمان الخلايا المجاورة و حتبدأ عنا pathway هدفها تقتل الفايروس

Virus-infected cells may be destroyed by NK cells, as described earlier. Type I IFNs enhance the ability of NK cells to kill infected cells. Recognition of viral DNA by CDSs also induces autophagy, by which cellular organelles containing viruses are engulfed by lysosomes and proteolytically destroyed . In addition, part of the innate response to viral infections includes increased apoptosis of infected cells, which also helps to eliminate the reservoir of infection



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• How exactly does our innate immune system deal with pathogens that ultimately make their way into our cells such as viruses or intracellular parasites?

• when a cell becomes infected, it responds by releasing proteins called interferons. Interferons will travel to neighboring healthy cells, bind to special receptors on these cells and initiate a response that will prepare them for viral infection. For instance, the cells begin producing anti-viral proteins that function to block viral replication. This way, when the infected cell lyses and releases more viruses, the nearby cells have already mounted a defense.

• These interferons can also bind to, stimulate and recruit specialized leukocytes.

1. Nature Killer Cells

Natural killer cells are mobilized after interacting with interferons. They can seek out and destroy infected cells as well as cancer cells.

2. Macrophages

Interferons recruit these large phagocytic cells that can engulf and break down infected cells. Macrophages themselves can release their own interferons, amplifying the immune response.

• Interferons can also stimulate cell death of the infected host cell.

3. Tumor Necrosis Family (TNF)

• Can signal development, activation, or death of certain cells (homeostasis)

• Which induce apoptosis, or programmed cell death, is a mechanism of cell death in which the cell dies from within and is fragmented into membrane-bound vesicles that can be rapidly phagocytosed by neighboring macrophages.

• There are two members having the same name of the TNF family: TNF- α and TNF- β . Both of these are secreted as soluble proteins.

• There are two members of the TNF family: TNF- α and TNF- β

• TNF- α is a proinflammatory cytokine, produced primarily by activated macrophages, and lymphocytes, in response to infection, or inflammation.

• TNF- β is produced by activated lymphocytes and can deliver a variety of signals. On binding to neutrophils, endothelial cells lead to increased expression of MHC and of adhesion molecules.

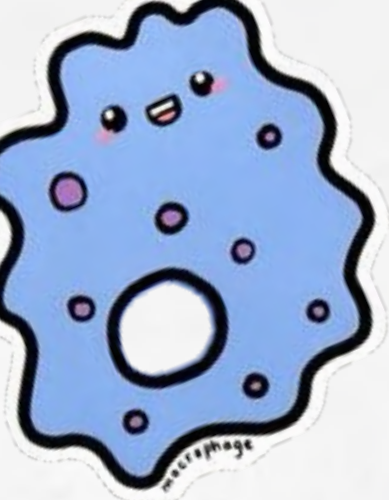
• Fas ligand (FasL), induces apoptosis.

regulate immune system and progression of cancer.

Fas receptor (CD95) is a cell surface protein that belongs to the tumor necrosis factor receptor family, that along with its ligand CD95L, generates a death receptor/death ligand system that mediates apoptosis induction to maintain immune homeostasis.



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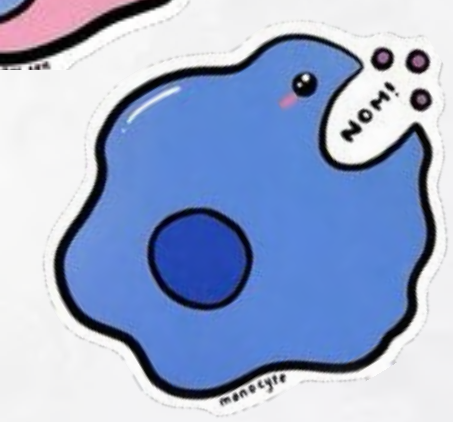
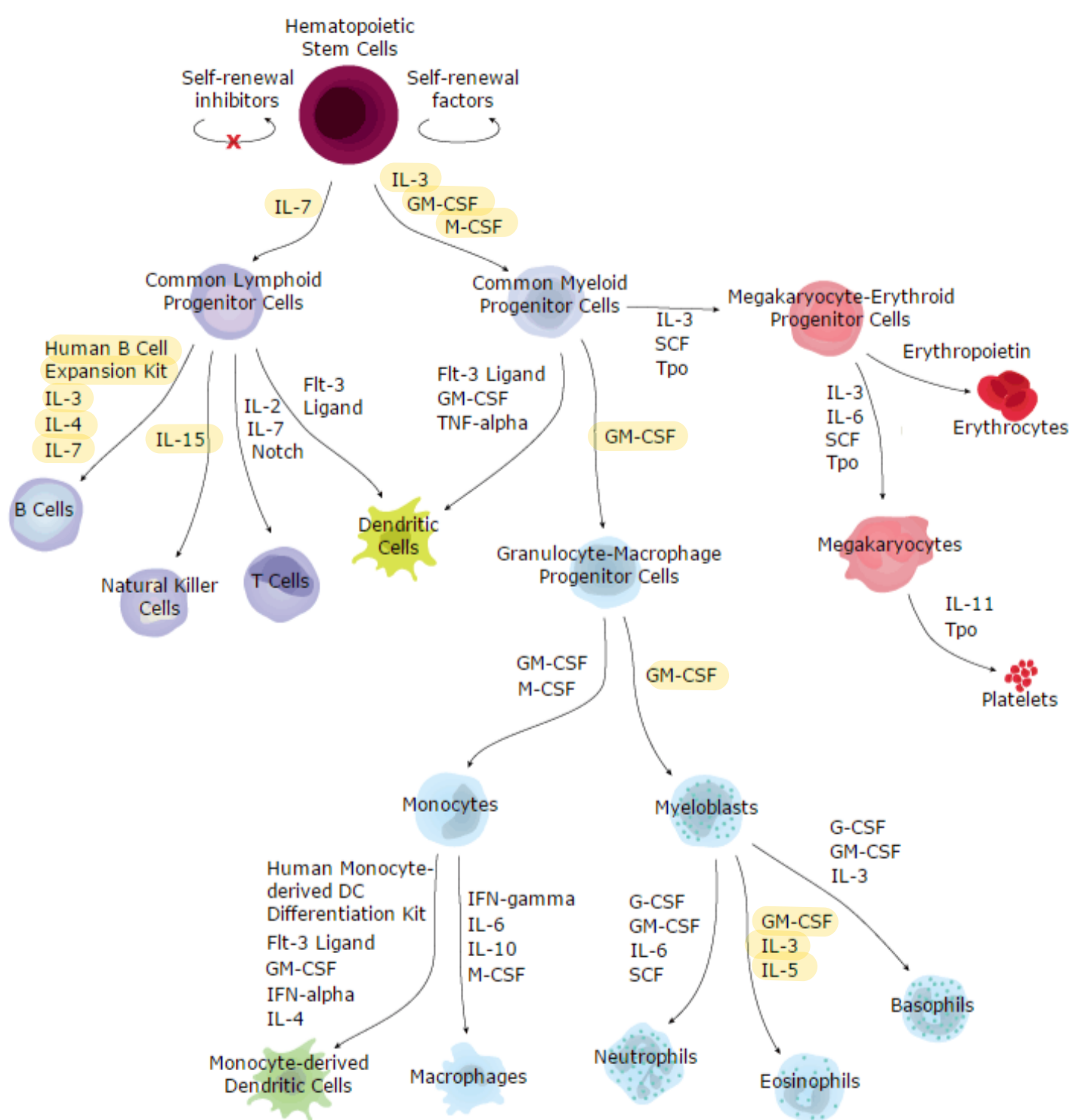
4. Colony-Stimulating Factors (CSF)

- 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) secreted by kidney in response to cellular hypoxia

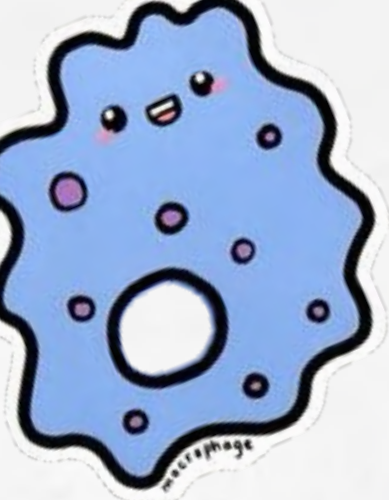
فلو صار عنا bacterial infection ال CSF رح تحفز ال progenitor لتنقسم و تعطينا خلايا مناعية جديدة، حتضل تنقسم لتعمل colony مثل الجيش و بعدها تطلع من bone لدم و من ثم لمكان ال infection

الي عليهم هايلايت الدكتور قرأهم، الفكرة نعرف انه ال cytokines مهمين بعمليات ال hematopoietic cell differentiation

Hematopoietic Stem Cell Differentiation Pathways & Lineage-specific Markers



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5. Chemokines

- Direct the Migration of Leukocytes through the Body
- Are structurally related family of small cytokines that bind to cell-surface receptors and induce the movement of leukocytes up toward the chemokine source.
- This soluble factor-directed cell movement is known as chemotaxis, and molecules that can elicit such movement are referred to as chemoattractants
- located on the surfaces of endothelial cells, enables them to bind to the inner surfaces of blood vessels and directing leukocyte movement
- CXCL group: attract neutrophils
- CCL group: attract monocytes and macrophages (although not neutrophils) to the site of infection.

أهم مثالين على ال chemokines هم CXCL و CCL و حكيما عنهم
بمحاضرة 10 حأط الكم سكرين شوت من التفريغ

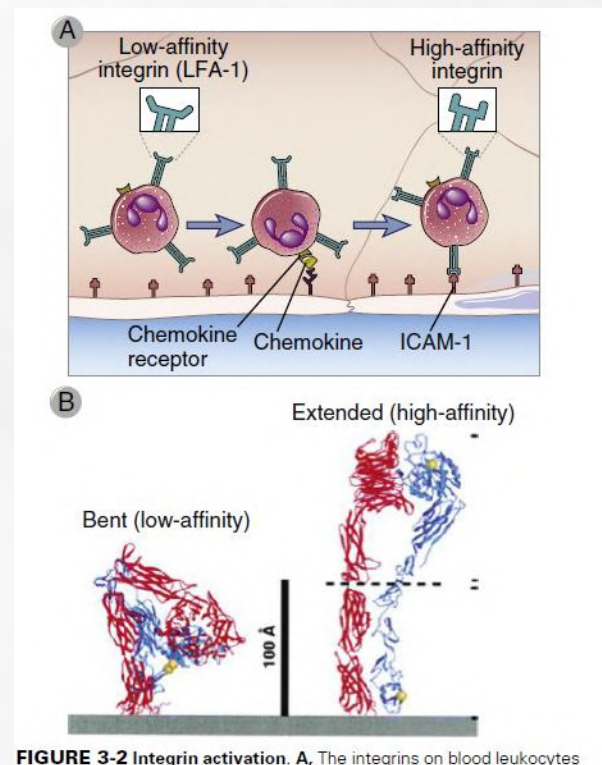


FIGURE 3-2 Integrin activation. A. The integrins on blood leukocytes

- B lymphocytes are activated by antigen in the follicles, as described above, and the activated B cells begin to move out of the follicles toward the T cells. The directed migration of activated B and T cells toward one another depends on changes in the expression of certain chemokine receptors on the activated lymphocytes. Activated T cells reduce expression of the chemokine receptor CCR7, which recognizes chemokines produced in T cell zones, and increase expression of the chemokine receptor CXCR5, which binds a chemokine produced in B cell follicles. Activated B cells undergo precisely the opposite changes, decreasing CXCR5 and increasing CCR7 expression. As a result, antigen-stimulated B and T cells migrate toward one another and meet at the edges of lymphoid follicles or in inter-follicular areas. The next step in their interaction occurs here. Because antigen recognition is required for these changes, the cells that move towards one another are the ones that have been stimulated by antigen. This regulated migration is one mechanism for ensuring that rare antigen-specific lymphocytes can locate one another and interact productively during immune responses to the antigen.

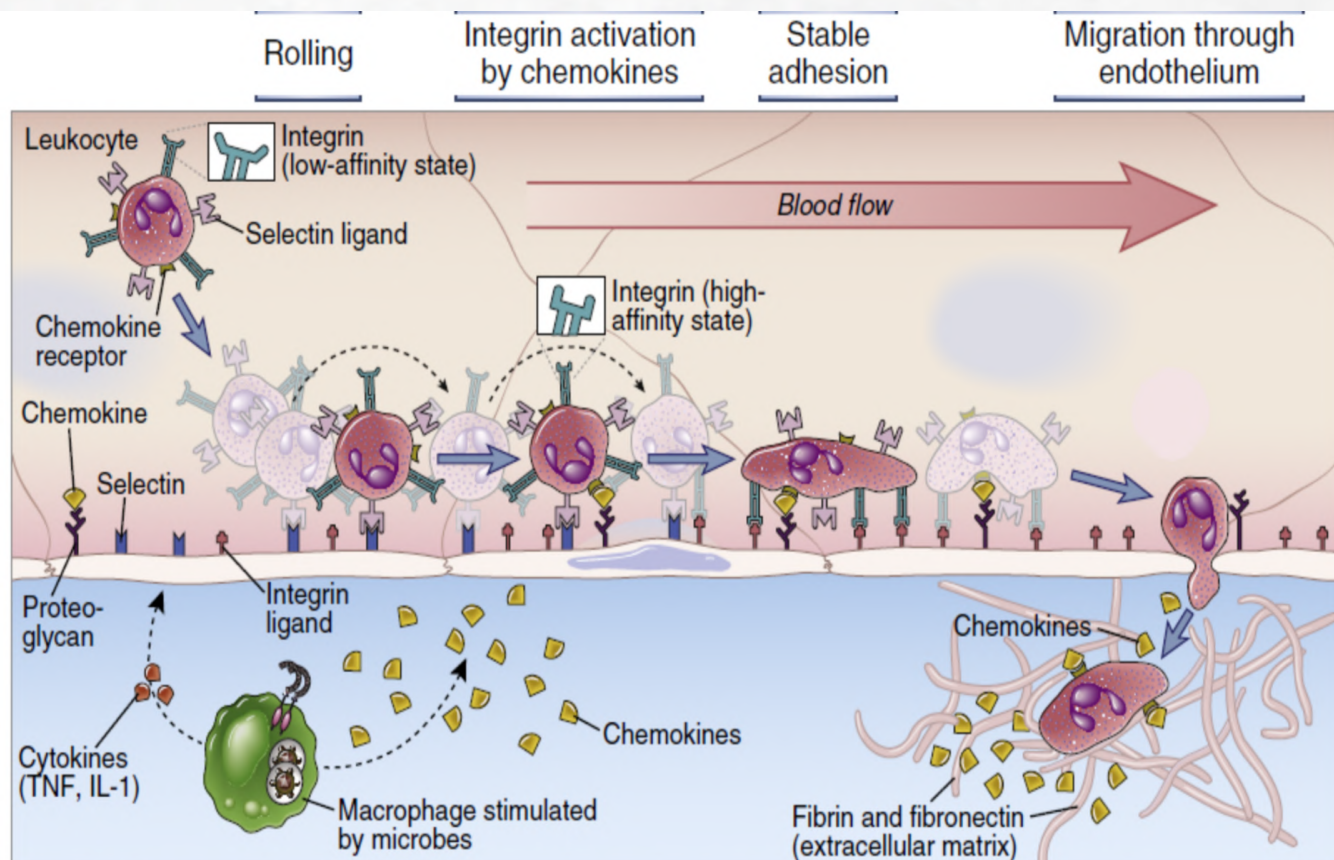
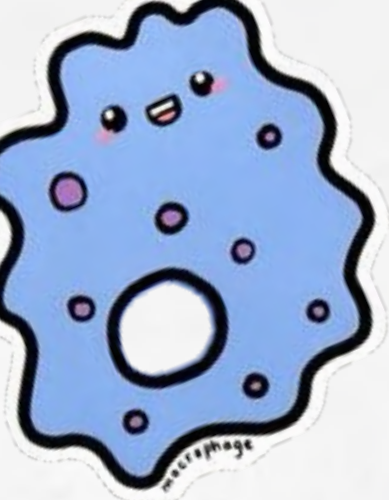


FIGURE 3-3 Multistep leukocyte-endothelial interactions mediating leukocyte recruitment into tissues. At sites of infection, macrophages that have encountered microbes produce cytokines (such as TNF and IL-1) that activate the endothelial cells of nearby venules to produce selectins, ligands for integrins, and chemokines. Selectins mediate weak tethering of blood leukocytes on the endothelium, and the shear force of blood flow causes the leukocytes to roll along the endothelial surface. Chemokines produced in the surrounding infected tissues or by the endothelial cells are displayed on



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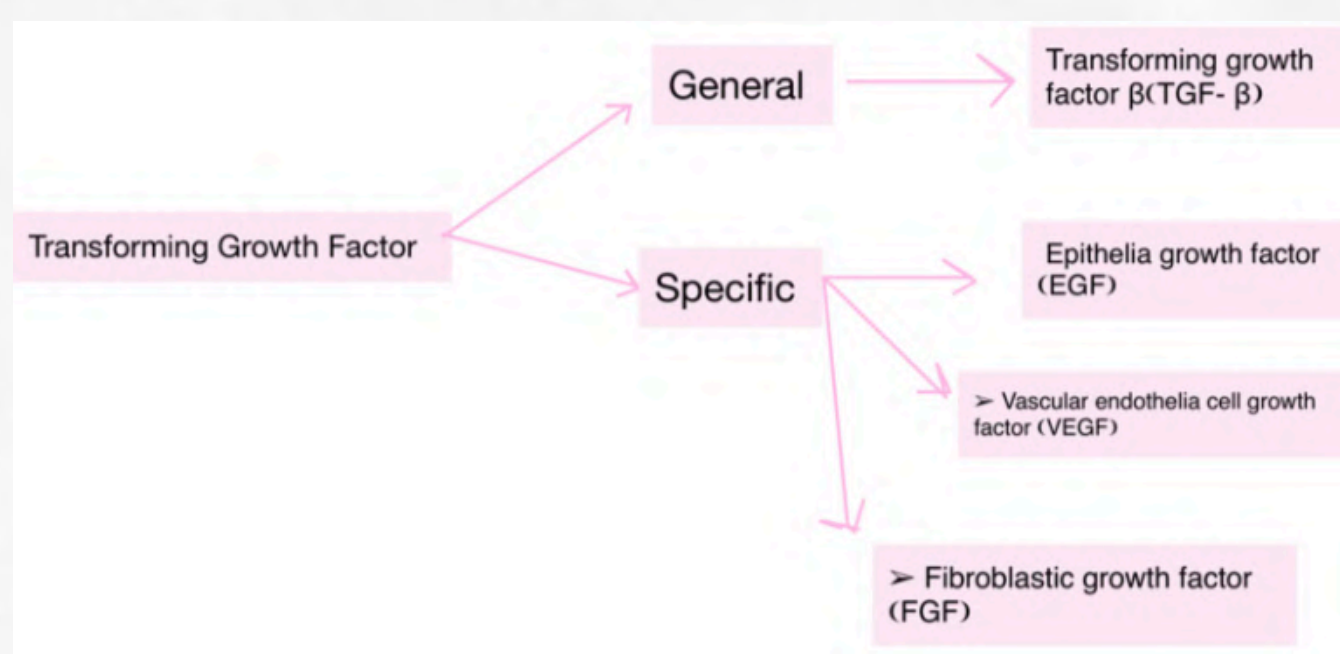


6. Transforming Growth Factor

- Growth-factor are cytokines which stimulate the growth of their target cells.
- Transforming growth factor-Beta (TGF-B)

Which plays an inhibitory rule in immune response to suppress it

- Epithelia growth factor (EGF)
- Vascular endothelia cell growth factor (VEGF)
- Fibroblastic growth factor (FGF)



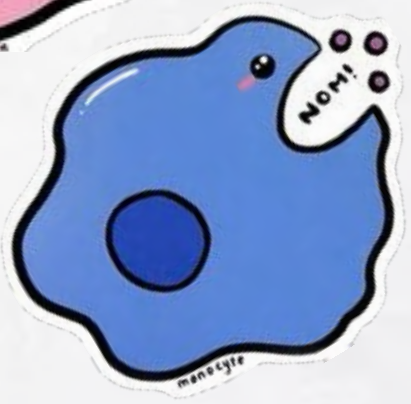
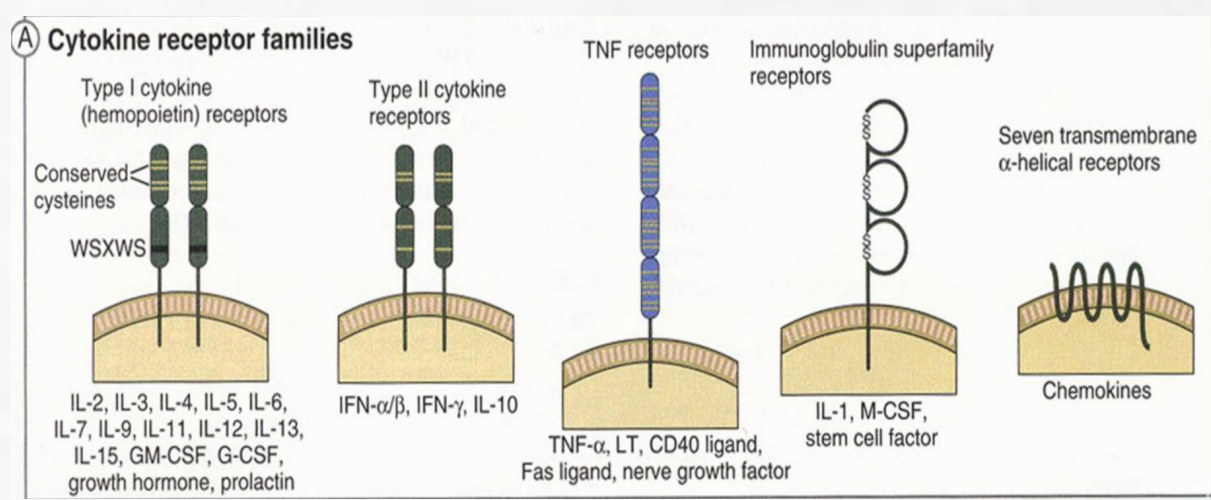
CK receptor

* Membrane-binding cytokine receptors:

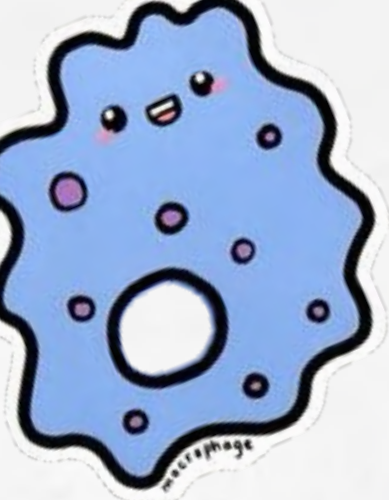
The receptor consists of extra-cellular region, trans-membrane region and cytoplasmic region.

* CK receptors can be grouped into five families according to structure and function:

- * Ig receptor superfamily
- * Type I CK receptor superfamily
- * Type II CK receptor superfamily
- * Type III CK receptor superfamily
- * G-protein linked receptor superfamily



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Functional Categories

- Mediate/regulate innate immunity
 - TNF, IL-1, IL-12, IFN type1, IL-10

- Mediate/regulate adaptive immunity
 - IL-2, IL-4, IFN- γ , TGF- β

- Stimulates hematopoiesis
 - IL-3, IL-7

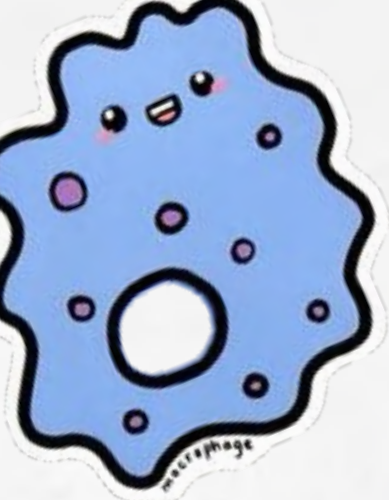
Pro-Inflammatory							
Innate and Acute Phase Responses				Inflammatory Innate to Adaptive Responses			
Cytokine	Source	Major Target	Function	Cytokine	Source	Major Target	Function
IFN- α/β	Virally infected nucleated cells	Cells surrounding virally infected cells	Induce antiviral state, activate NK cells, enhance Cell Mediated Immunity	IFN- γ	CD4 Th1 cells, NK cells	Macrophages, DCs, T cells, B Cells	Activate Macrophage/ promote IgG class switch/ Promote Th1/Inhibit Th2
IL-1 β	Macrophages, DCs, Fibroblasts, Epi/Endothelium	T cells/B cells/ PMNs/ CNS/ Liver	Promote inflammatory/ acute phase response/ promote fever	IL-17	CD4 Th17 Cells	Epi/Endothelium/ Neutrophils/ Fibroblasts	Recruit Neutrophils/ Promote inflammation
TNF α		Macrophages/ T cells/ NK cells	Acute phase response/ inflammation/ fever/ Wasting (Cachexia)	TNF β aka Lymphotoxin	CD4 Th1 cells	PMNs, Tumor Cells	Kill tumors/ activate PMNs/ Activate Endothelium allowing trafficking
IL-6	DCs, Macrophages/ T and B cells/ Fibroblasts/ Epi/Endothelium	T and B cells/ hepatocytes	Acute phase reactants/ fever/ T and B cell growth	IL-2	CD4 T cells (Th1, Th0)	Lymphocytes	Lymphocyte proliferation
				IL-12/IL-23	DCs, Macrophages	Nk Cells, CD4 Th1/TH17	Activate T cell IFN γ or IL-17 Production

Proinflammatory cytokines are produced predominantly by activated macrophages and are involved in the up-regulation of inflammatory reactions

Allergy and Helminth Infections				Immunosuppressive/Anti-inflammatory			
Th2 (Less inflammatory than Th1/Th17)				T regulatory (Tregs)			
Cytokine	Source	Major Target	Function	Cytokine	Source	Major Target	Function
IL-4	CD4 T cells (Th0, Th2, Tfh, ILCs)	B and T cells	T and B cell growth and differentiation/ IgG, IgA, IgE production/ Th2 response/ Allergic responses	IL-10	Treg cells/ Th2	B cells, CD4 Th1/Th17 cells	B cell growth / inhibit Th1 and Th17 responses
IL-5	CD4 Th2	B Cells and Eosinophils (for Helminth infections)		TGF- β	CD4 Tregs	B cells, T cells, Macrophages, DCs	Immunosuppression of all immune responses/ promote oral tolerance/ wound healing
IL-10	CD4 Th2 and Treg	B cells, CD4 Th1/Th17 cells	B cell growth / inhibit Th1 and Th17 responses				



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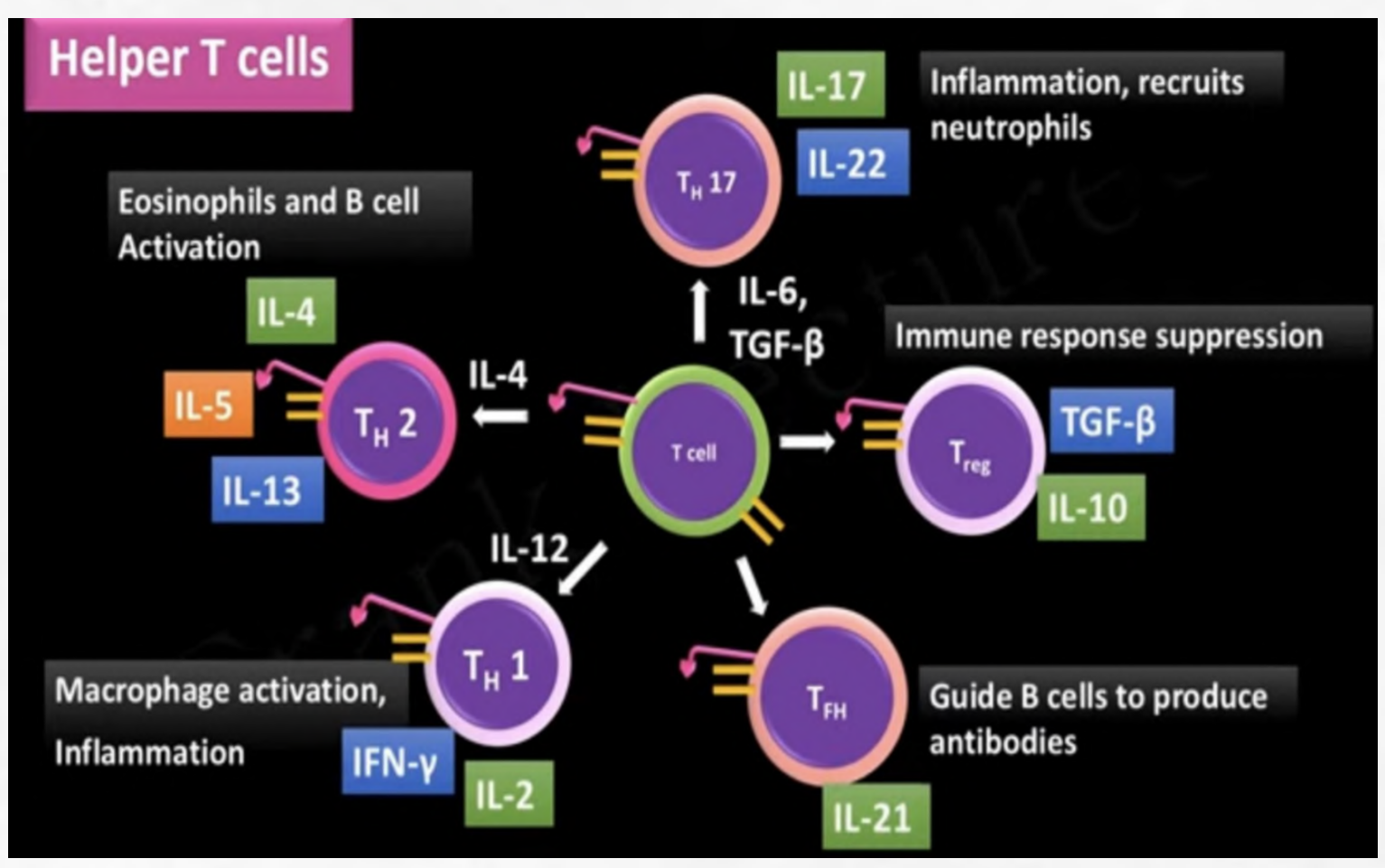


Growth and Differentiation

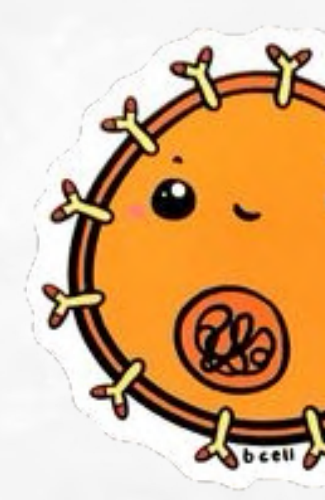
Cytokine	Source	Major Target	Function
GM-CSF & M-CSF	Stromal cells/ T cells	Bone Marrow progenitor cells/ Stem cells/ Precursor cells	Hematopoiesis/ directed growth and differentiation of Monocytes and Granulocytes
IL-3	CD4 T cells/ keritocytes		
IL-7	Bone marrow, stroma		
*IL-2	CD4 T cells	Lymphocytes	Proliferation

Chemotactic Agents

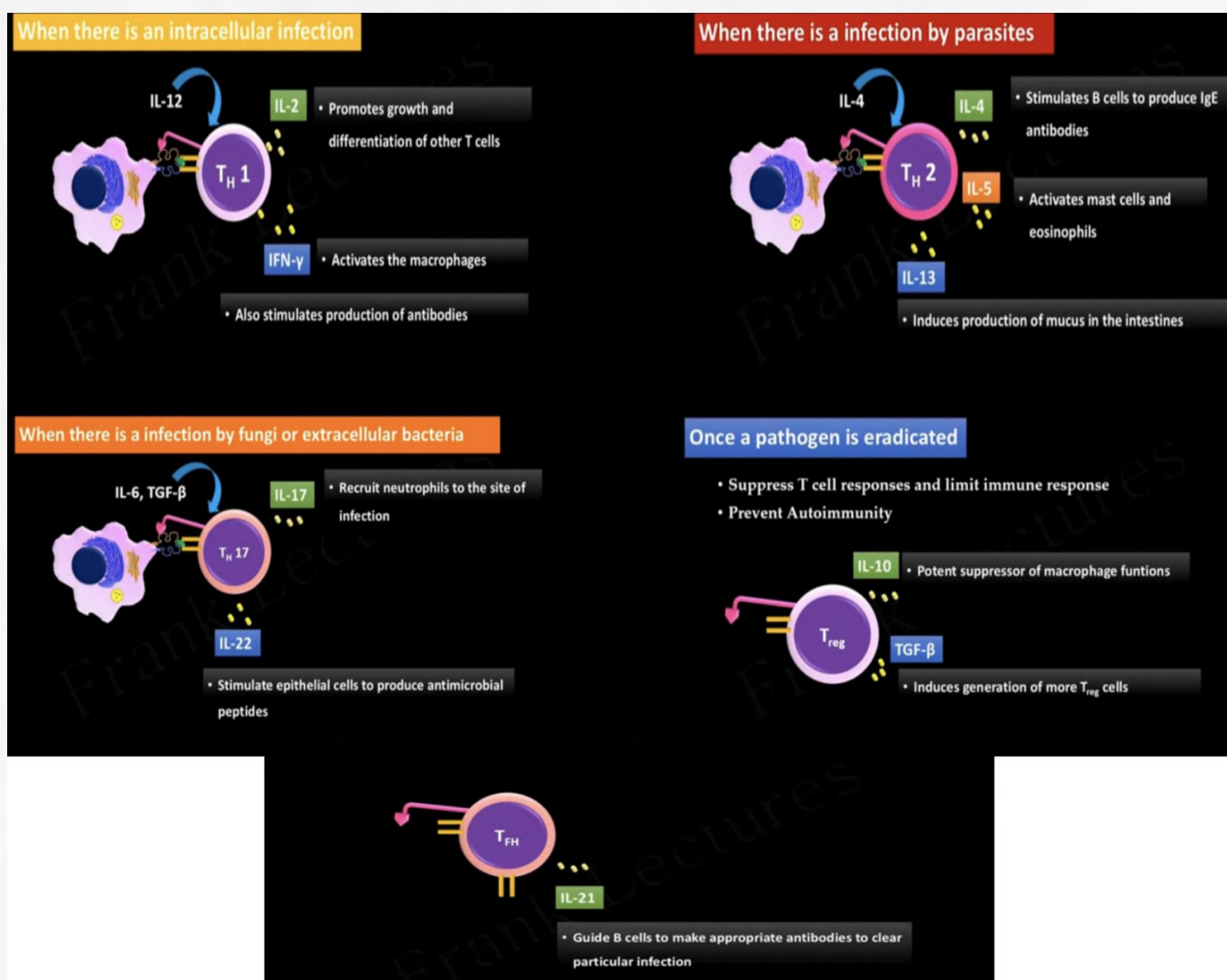
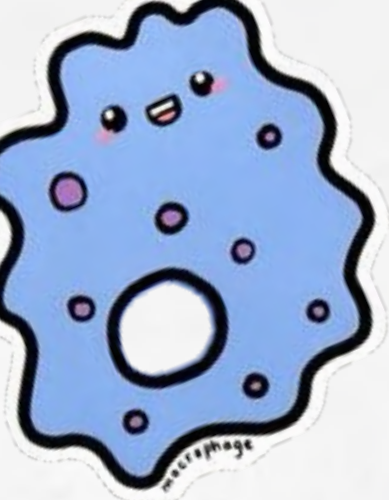
Chemotactic Agent	Source	Major Target	Function
IL-8/CXCL8	Fibroblasts/ Neutrophils/ Macrophages	Phagocytes	Recruit these cells to the site of inflammation
C5a	Complement Cascade		
IL-17	CD4+ Th17		
Over 30 others!	Many cells	Neutrophils, B cells, T cells, Macrophages, DCs, NK cells, Mast Cells etc.	



الدكتور حكي عليها سؤال عالاقل بالامتحان
 مهم تعرفوا اي cytokine بحتاج لحتى احوال ال T cell لنوع اخر
 و هاد النوع شو حيفرن cytokines و شو وظيفتها

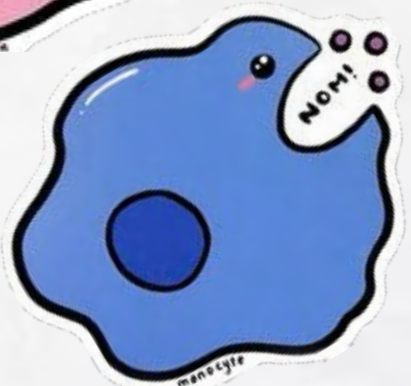


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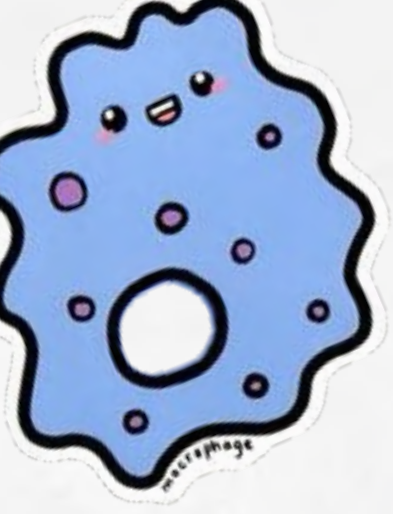


Specific Interleukins Functions

- 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- γ , IL-2, IL-3, TNF α , GM-CSF
- IL-12: is involved in the differentiation of naive T cells into Th1 cells



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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-bata: multiple sclerosis
- IFN-gamma: chronic granulomatous disease (CGD)
- IL-2: kidney cancer, melanoma
- IL-11: thrombocytopenia in cancer patients

Cytokine storm: over production of cytokines due to many causes

Over activation of immune cells من الاسباب هاي هو فيروس كورونا (خاصة ال IL-1/IL-6) طبعا هاد الاشئ مش منيح لانو رح يسوي

هاد رح يقوي ال inflammation بالرئتين ويسوي irreversible damage فيها الي يمكن يسوي ال ARDS الي تعتبر المسبب الاول للموت لمرضى كورونا



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