



٤ Immunomodulatory drugs

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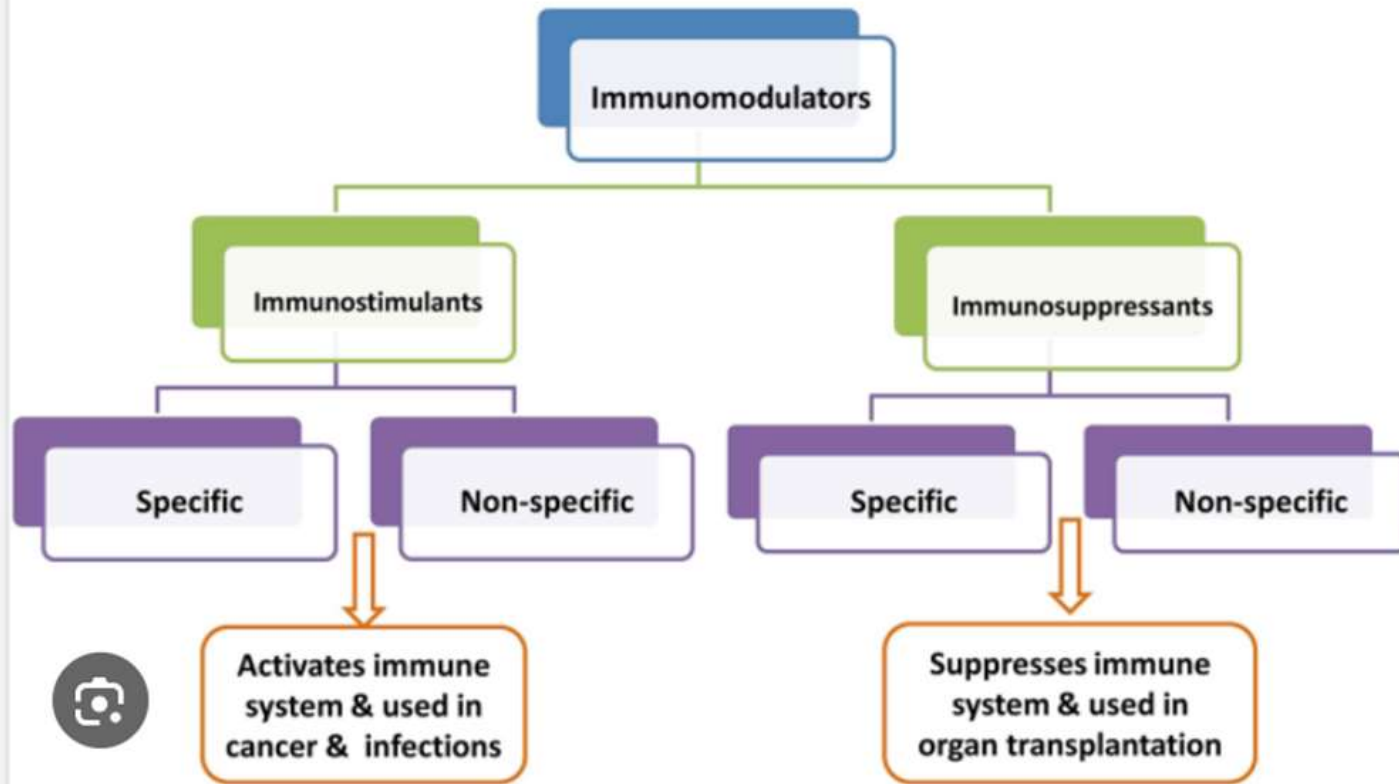


* كُل صَبِّحْ لِهَوَاهِ

مَتَاخِرْ عَنْ صَبِّغَاهِ!

Immunomodulatory drugs

- Drugs that change the immune system so it works more effectively.
- They include treatments that increase or decrease the immune response





Immunosuppressants

What are immunosuppressants?

- Drugs used to ^{inhibit} dampen immune response in ^① organ transplantation and ^② autoimmune diseases.

مهما كان
توقفه الدم والحق
الاحاديث لا فاع

Classification of immunosuppressants

- Glucocorticoids corticosteroid
- Cytostatics stop in anticancer drug
- Drugs acting on immunophilins
- Antibodies
- Others

اهم شي

[I] Glucocorticoids

■ Corticosteroids are the most widely used "front-line" therapy for the treatment of clinical GVHD (**Graft-versus-host disease**)

■ The most commonly utilized corticosteroid is methylprednisolone and dexamethasone.

Immunosuppressive mechanism: 3 mechanism ↓

1. **Inhibition of T-cell function (cell-mediated immune response):** by inhibiting release of cytokines interleukin-1 (IL-1), IL-2, IL-3, IL-4, IL-5, IL-6, IL-8, and TNF-alpha, the most important of which is IL-2.

2. **Inhibition of B-cell function (humoral immunity):** by inhibition of antibody production.

3. **Inhibition of inflammatory events:** cell adhesion, migration, chemotaxis, inflammatory mediators, etc.

الorgan هو الذي يبعد graft

موال الجسم

transplanted tissue

هو الذي يبعد graft للجسم المستقبل

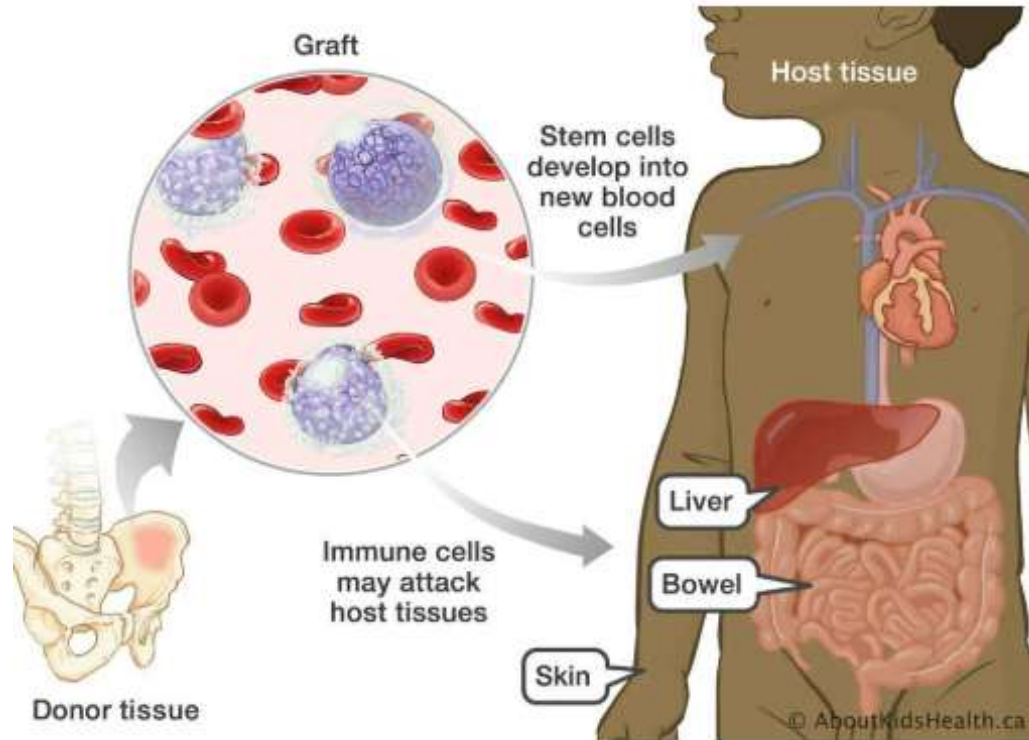
ترتيب العلاجات

recipient

organ transplantation

inhibit

ما في IL-7



GVHD

[I] Glucocorticoids

Clinical uses (as immunosuppressants):

1. Suppression of GVHD.

كل الامراض بنفع استخروفه

2. Treatment of autoimmune disease: such as rheumatoid arthritis, SLE, rheumatic fever, nephrotic syndrome, etc.

اما لو disease كونه يكون بن مرض

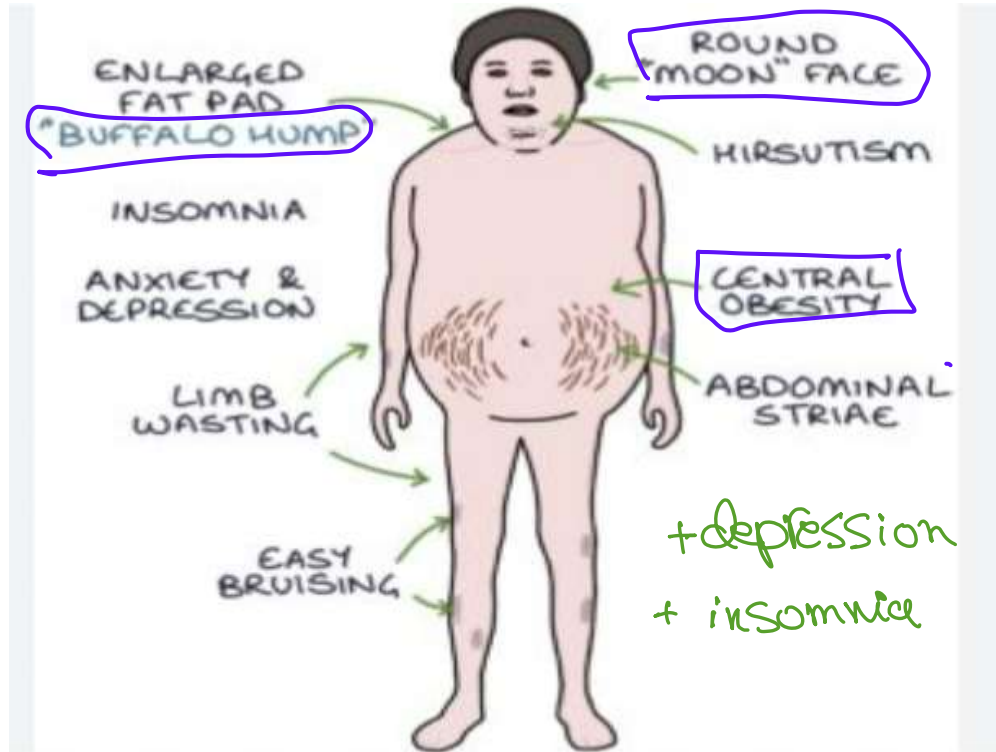
Adverse effects:

Cushing Syndrome الحش

In addition to their immunosuppressive effects, which set the stage for infectious complications, side effects include Cushingoid features, hyperglycemia, salt and water retention, skin and muscle atrophy, osteoporosis and cataract (posterior polar cataract).



Posterior polar cataract



Cushingoid features

[II] ^{cell} ^{stop} Cytostatics

Cytostatics inhibit cell division. They inhibit the proliferation of both T cells and B cells.

In immunotherapy, they are used in smaller doses than in the treatment of malignant diseases.

تستخدم in cancer → large dose

Examples of cytostatic drugs used as immunosuppressants:

■ Alkylating agents: cyclophosphamide

organ transplantation

■ Antimetabolites:

Folic acid antagonists: methotrexate

Purine analogues: azathioprine

بس الاسماء هذه

من دون
تغيير

لقد أخرجنا عنهم

[III] Drugs acting on immunophilins

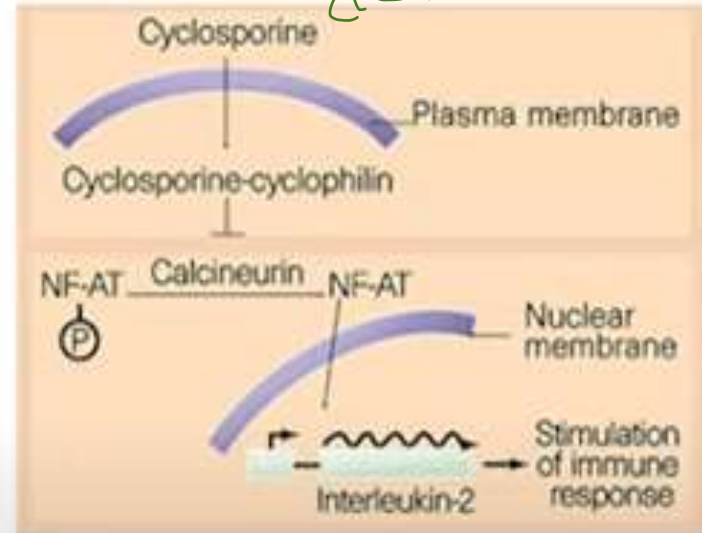
1. Ciclosporin (also spelled cyclosporine and cyclosporin)

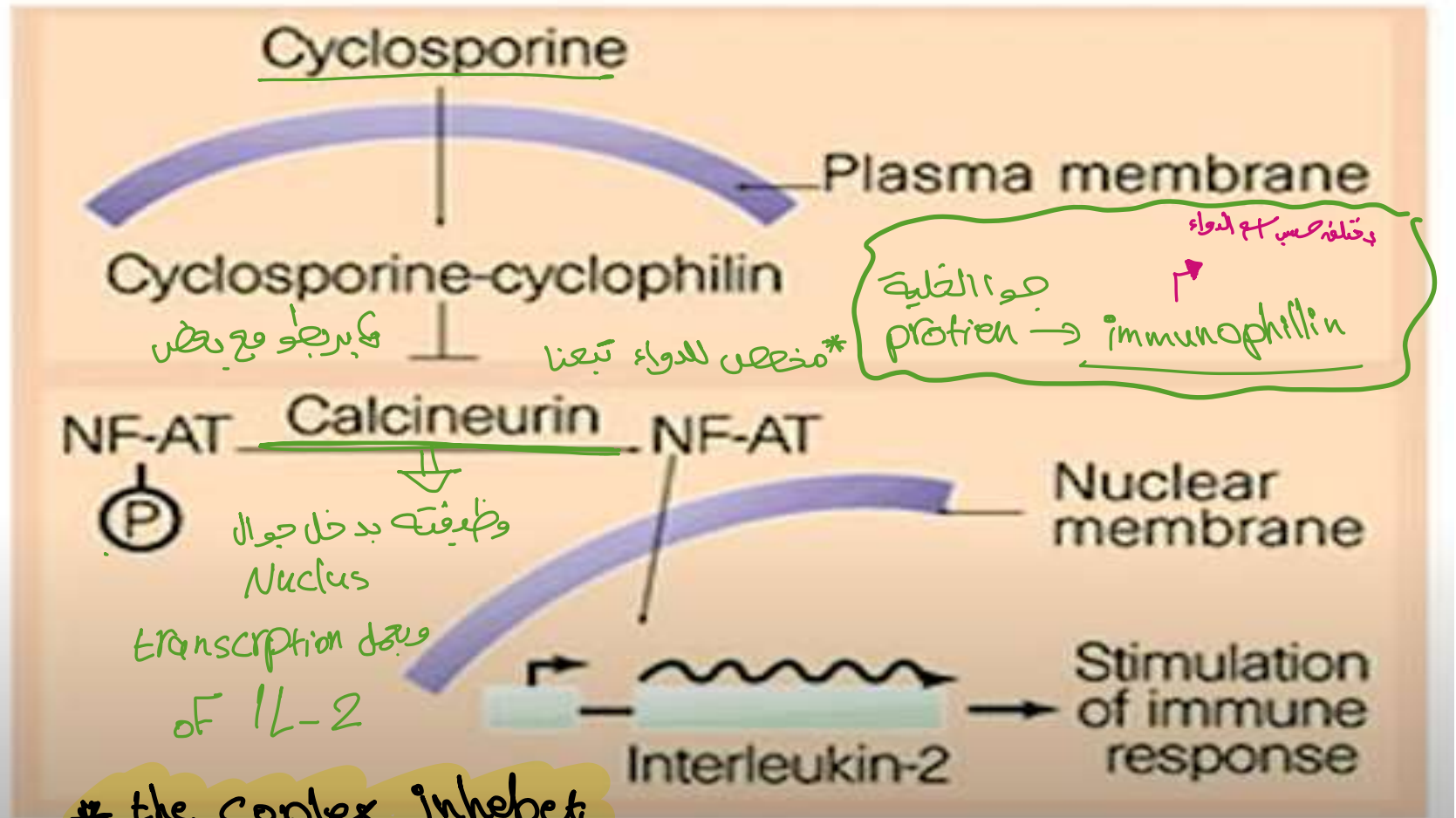
■ It is a natural peptide (11 amino acid) derived from a soil fungus.

■ Discovered in 1970 from new strains of fungi isolated from soil samples taken from Norway.

Mechanism of action

Ciclosporin binds to cytoplasmic protein called **cyclophilin** (immunophilin) of T-lymphocytes ... The ciclosporin-cyclophilin complex then inhibits a transcriptional factor called **calcineurin** which is responsible for transcription of IL-2.





* the complex inhibits calcineurin

[III] Drugs acting on immunophilins

1. Ciclosporin (also spelled cyclosporine and cyclosporin)

Clinical uses

Prevention of GVHD.

Treatment of autoimmune diseases.

Adverse effects

Nephrotoxicity: the most common.

Hypertension

Hyperkalemia

Hypertrichosis (hirsutism) زيادة الشعر

Hyperglycemia

Hyperlipidemia

Hyperuricemia

Gum hyperplasia swelling in Gum → (pain) and (bleeding)

مستقر
دائماً جعل
test
function
بعد الزراعة

↓ Kidney Function

N.B.

In post renal transplant, the 2 most common causes of declining renal function are graft rejection and cyclosporine toxicity.

لو انظر انوفى
يقول واحد من السببين
① cyclosporin
② graft

Everything is increased

زيادة السكر
زيادة الدهون



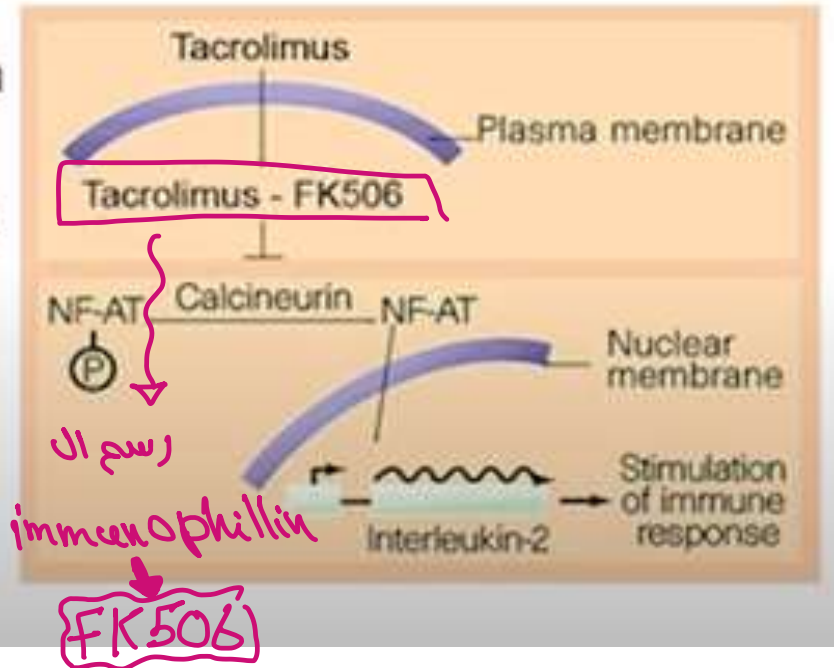
Gum hyperplasia

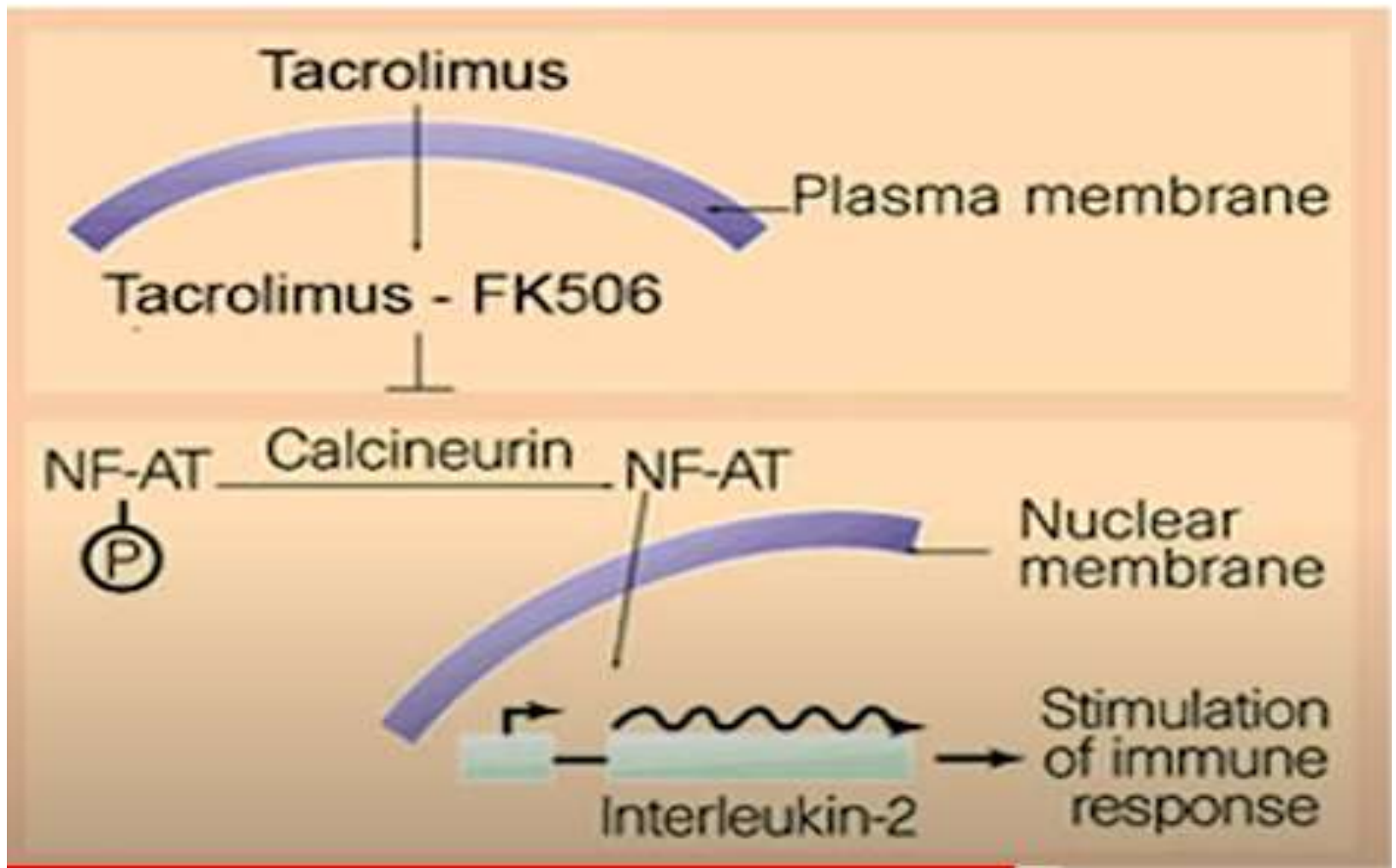
[III] Drugs acting on immunophilins

2. Tacrolimus (also known as FK506)

The mechanism of action, uses, and adverse effects are very similar to ciclosporin except in:

- ① It is macrolide lactone derived from certain species of bacteria.
- It is 200 times more potent than ciclosporin.
- It binds to the cytoplasmic protein caled FK506 in the T-cells, then the complex inhibits calcineurin → inhibition of IL-2 synthesis.





[IV] Antibodies

monoclonal → one type of AB
المونوكلونال ← one type of antibody
AntiBody to Tcell or B الخ
mab ← أجسام

T-cell receptor directed antibodies:

Muromonab-CD3 is monoclonal antibody that prevents T-cell activation and proliferation by binding the T-cell receptor **CD3** present on all differentiated T cells.

↓ proliferation and activation of Tcell

B-cell receptor directed antibodies:

Rituximab is monoclonal antibody that prevents B-cell activation and proliferation by binding the B-cell receptor **CD20**

IL-2 receptor directed antibodies:

Daclizumab is monoclonal antibody that binds to **CD25** the IL-2 receptor of T-cells.

وجود على ال T cell لتستجيب لـ IL-2

TNF binding antibodies:

Infliximab and **adalimumab** are monoclonal antibodies that bind to **TNF-α** preventing it from inducing the synthesis of **IL-1** and **IL-6** by immune cells.

release IL1 & IL-6 in Rheumatoid Fever

related to mouth

المطلوب:
اسم الدواء
في
receptor

Immunostimulants

- Drugs which stimulate the immune system by increasing the activity of any of its components
- Used in immunocompromised patients, cancer and infections

HIV
IDS

- **Specific immunostimulants**: stimulate an immune response to a **specific antigen** (a toxin or other foreign substance: bacteria or virus which induces an immune response in the body) such as **vaccines**.
- **Nonspecific immunostimulants**: act irrespective of antigenic specificity and are used in **immunodeficiency** and **chronic infections**.

↑ immunity in general

[B] Immunostimulating Agents

Types of Immunostimulants

- * ■ Colony stimulating factors
 - Interferons
 - Interleukins
 - Bacterial vaccines
 - Viral vaccines

2

[I] Colony stimulating factors in BM // 5

Stimulates maturation

Granulocyte/macrophage colony stimulating factor (GM-CSF)

مركبة وراثية → recombinant in yeast cell

■ GM-CSF is a recombinant protein expressed in yeasts. Its principal action is to stimulate myelopoiesis in granulocyte-macrophage pathways as well as megakaryocytic and erythroid progenitor cells.

■ It is given I.V. in cases of neutropenia and aplastic anemia, and to stimulate stem cells after bone marrow transplantation.

الذي يصور به ان

→ بي انتط ان BM
العنوع

Granulocyte colony stimulating factor (G-CSF; Filgrastim)

■ G-CSF stimulates maturation of immature neutrophils.

■ Uses: Neutropenia due to cancer chemotherapy.

تباثر اكثر + تسريع
→ rapid divided cell

وعن بعض الخلايا

[II] Interleukins

Aldesleukin (Proleukin)

is a synthetic form of interleukin-2 (IL-2). It is given s.c. to elicit immune response in cases of metastatic renal cell carcinoma and metastatic melanoma (i.e. a type of cancer immunotherapy).

Supcutaneous علاج مناعي للسرطان
السرطانية



Oprelvekin (Neumega)

is a recombinant IL-11 approved for treatment of thrombocytopenia. Interleukin-11 (IL-11) is a protein produced by fibroblasts and stromal cells in the bone marrow. It acts on specific cell receptors to stimulate growth of primitive megakaryocytes to form mature platelets.

↓ علاج thrombocytopenia



References

Lippincott's Illustrated Review

Pharmacology, 8th edition

Lippincott Williams & Wilkins

Katzung by Anthony Trevor, Bertram Katzung, and

Susan Masters . 16th edition McGraw Hill,

Rang & Dale's Pharmacology: by Humphrey P. Rang

; James M. Ritter ; Rod Flower Churchill Livingstone;

10th edition



THANK YOU