بنام خدای هستی بخش

By: Dr Maryam Sahebari

Immunology & inflammation In Rheumatology

- Terminology
- Definition of Immunity
- Definition of autoimmunity
- Subtypes for example

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Immunity

Protection /defense

. . . against whatever doesn't belong

Viruses

Other microbes

Bacteria

Tissue irritants

Other pathogens

Toxins

Cancer

Chemicals

Damage/ injury

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Two main strategies . . .

Innate immunity

Adaptive immunity

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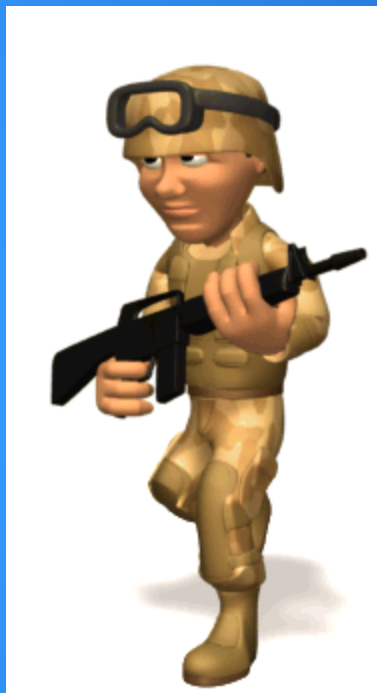
Two main strategies . . .

Innate immunity

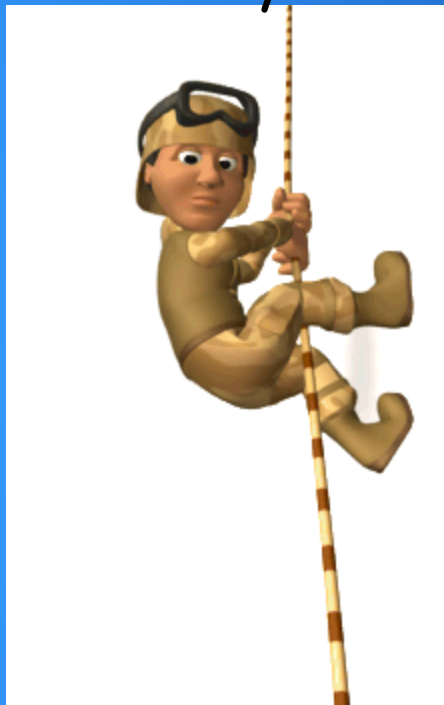
- Mechanisms always "on standby"
  - Can respond rapidly
- Effective against a variety of different "enemies"
- Also called "nonspecific immunity"



Two main strategies . . .

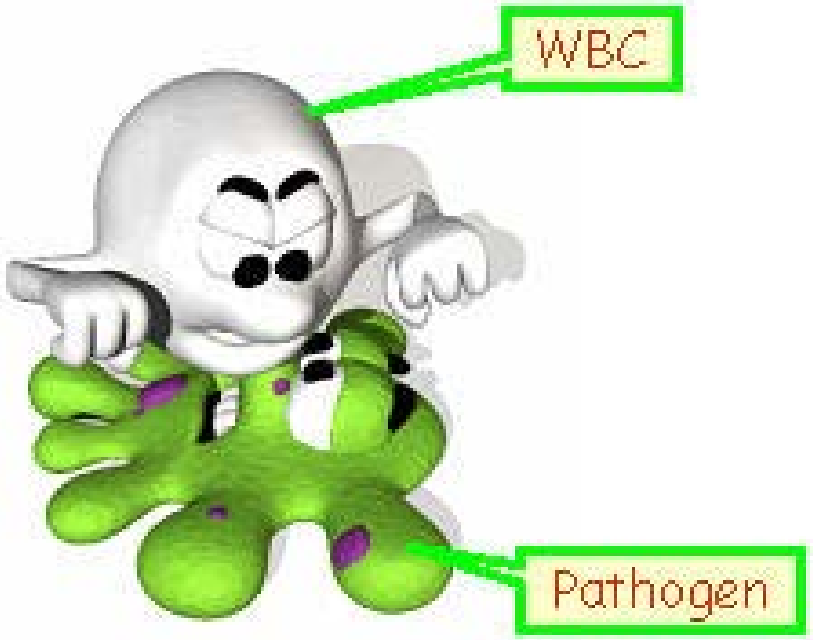
Adaptive immunity

- Mechanisms specialized to fight a particular "enemy"
- Often developed after first exposure,
  then "on standby" for further "attacks"
  - First response is slow, to allow time to prepare
- Also called "specific immunity" or "acquired immunity"

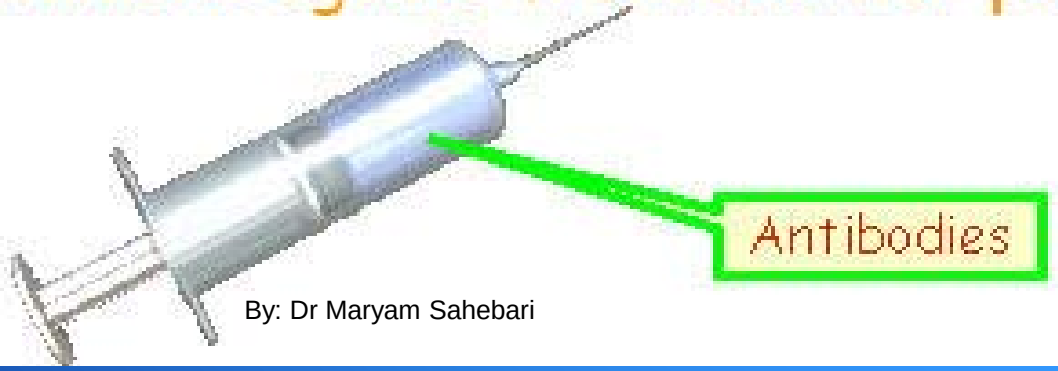


Types of adaptive immunity

- Active
  - reaction of your own system



- Passive
  - borrow immune agents from another person



Innate Immunity cells:

- **Innate immunity: older host defense against primary infection &does not depend on previous exposure to agent**
- Dendritic cells
- Natural killer cells
- Mast cells
- Eosinophils
- Eosinophils
- Basophils

Innate immunity

- Pattern Recognition Receptors(PRR):
- Toll like receptors(TLR): TLR13 : Leprosy, atherosclerosis, asthma, IBD
- Node like receptors (NLR): IBD, FMF, Pseudogout
- Rig like receptors (RLR): increased susceptibility to RNA virus

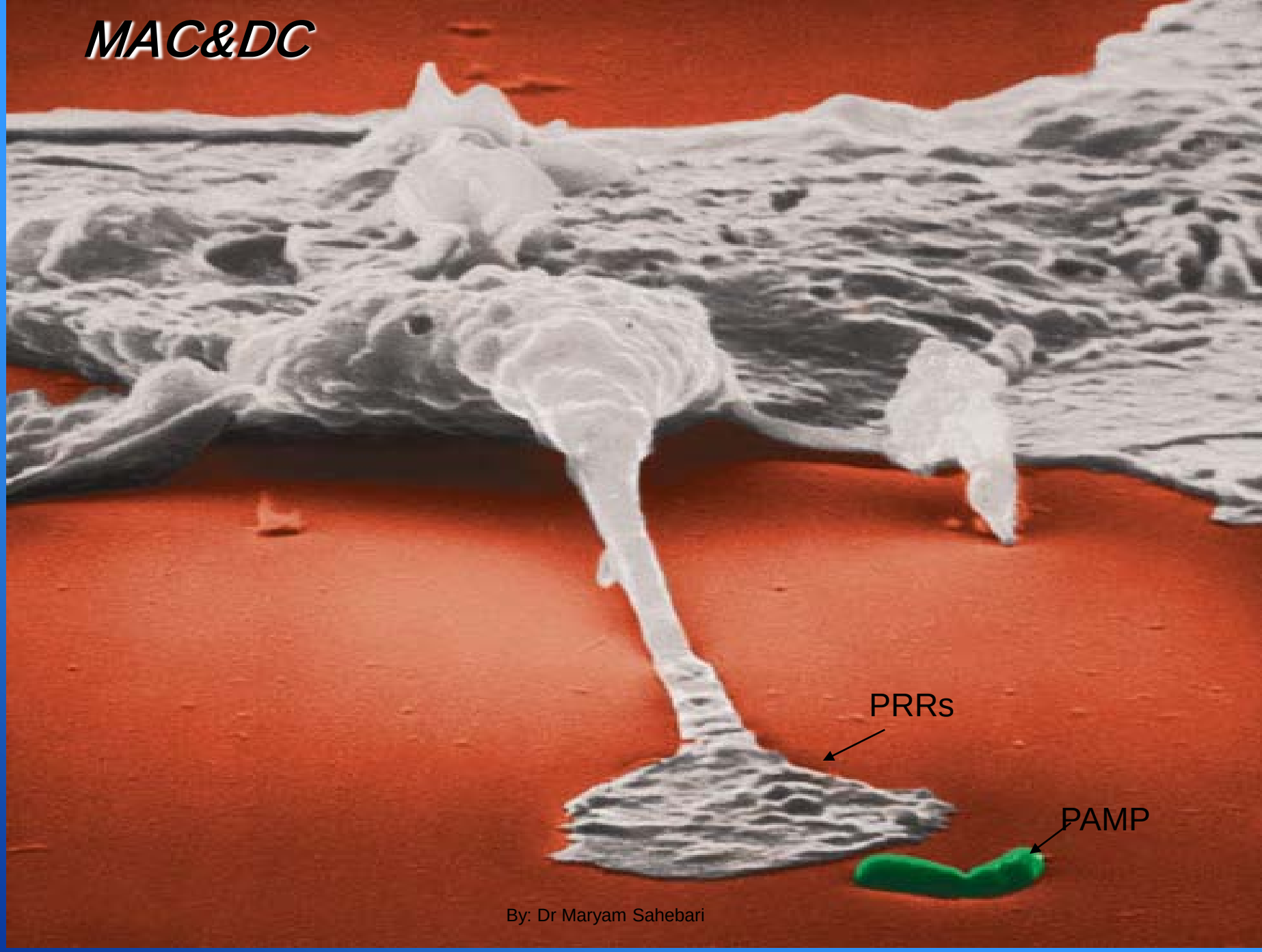
Innate immune cells: Dendritic cells

- The release of pro-inflammatory cytokines activates the innate and adaptive immune system, DC are the key to this connection.
- DC activation → migration to lymph node and spleen → presentation of the antigens to T cells
- Adjuvants in vaccines increase the antigenicity of vaccines through the activation of DCs and other phagocytes.

Innate immune cells: Dendritic cells

- DCs is the main source of INFs type 1 in the body, SLE is a disease of over production of INFs
- NK cells : They produce INF gamma, they play a role in the development of T cells
- Eosinophils: secretion of cytokines which regulate T and B cells
- Basophils and mast cells : IgE receptors, secret histamine, Bas: activation of T and B cells
- Mast cells : important in arthritis

MAC&DC



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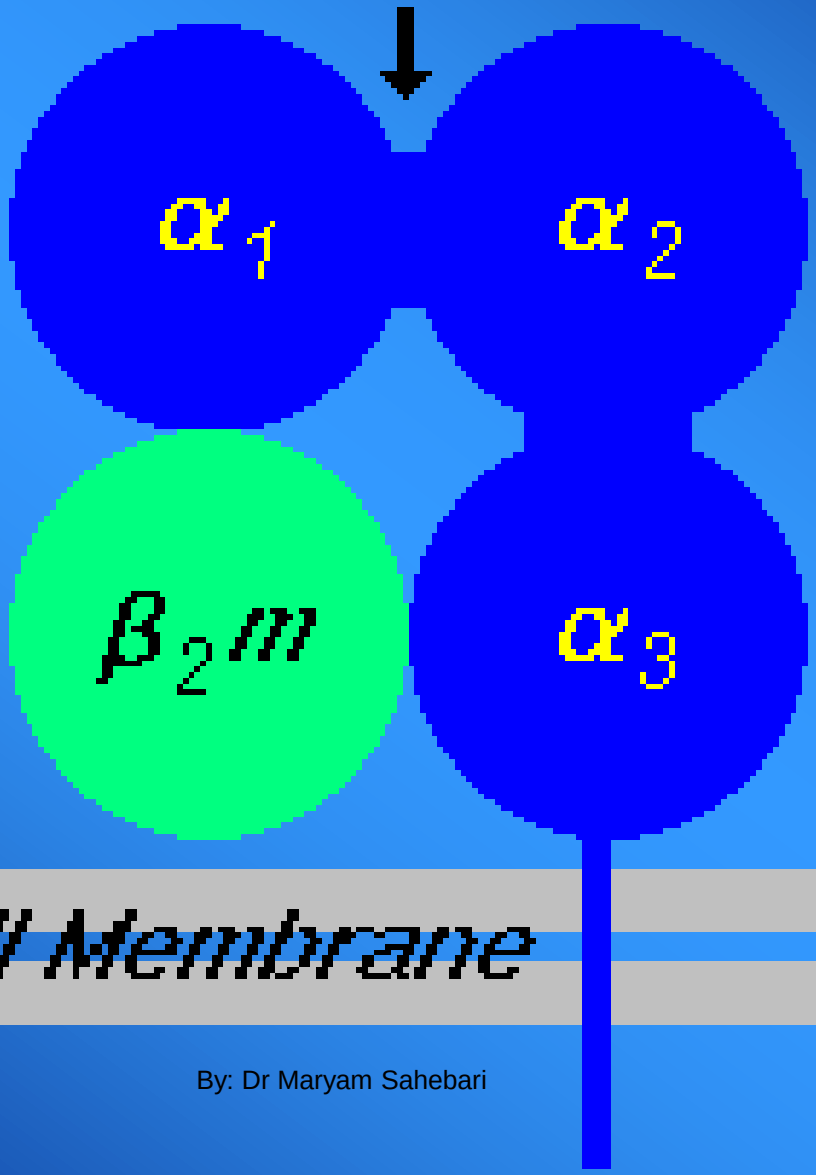
MHC I

Peptide Binding



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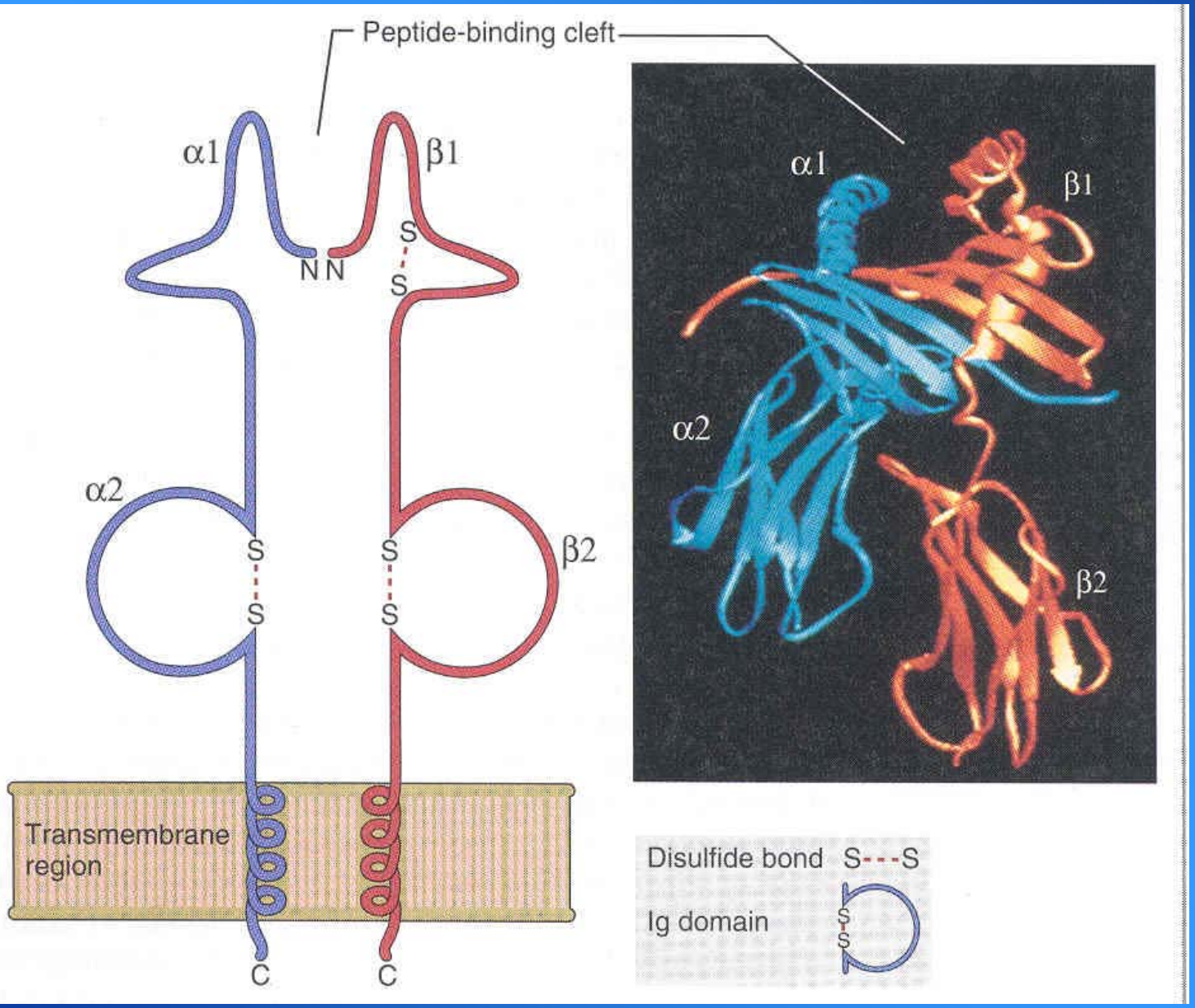

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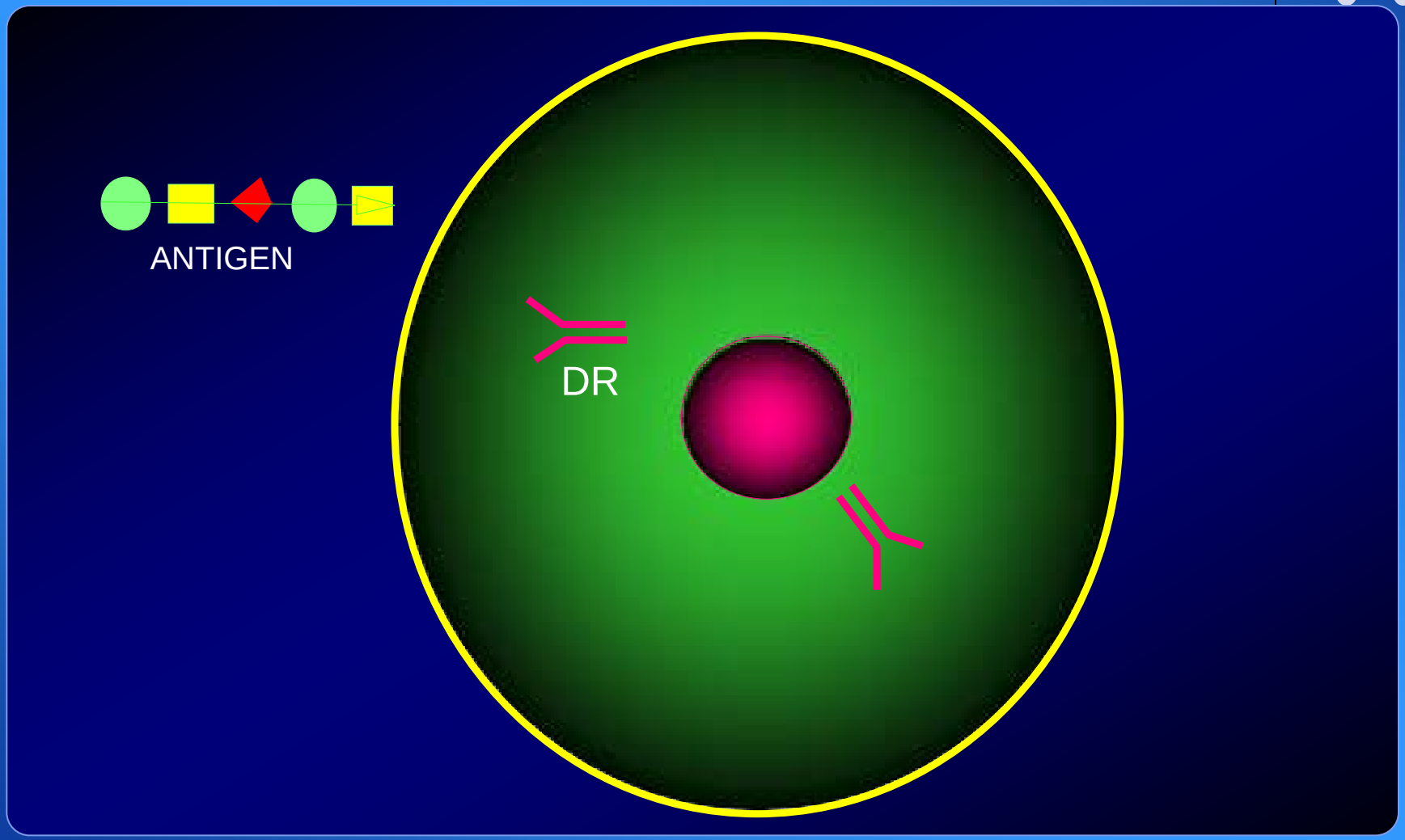
ANTIGEN PROCESSING



MACROPHAGE

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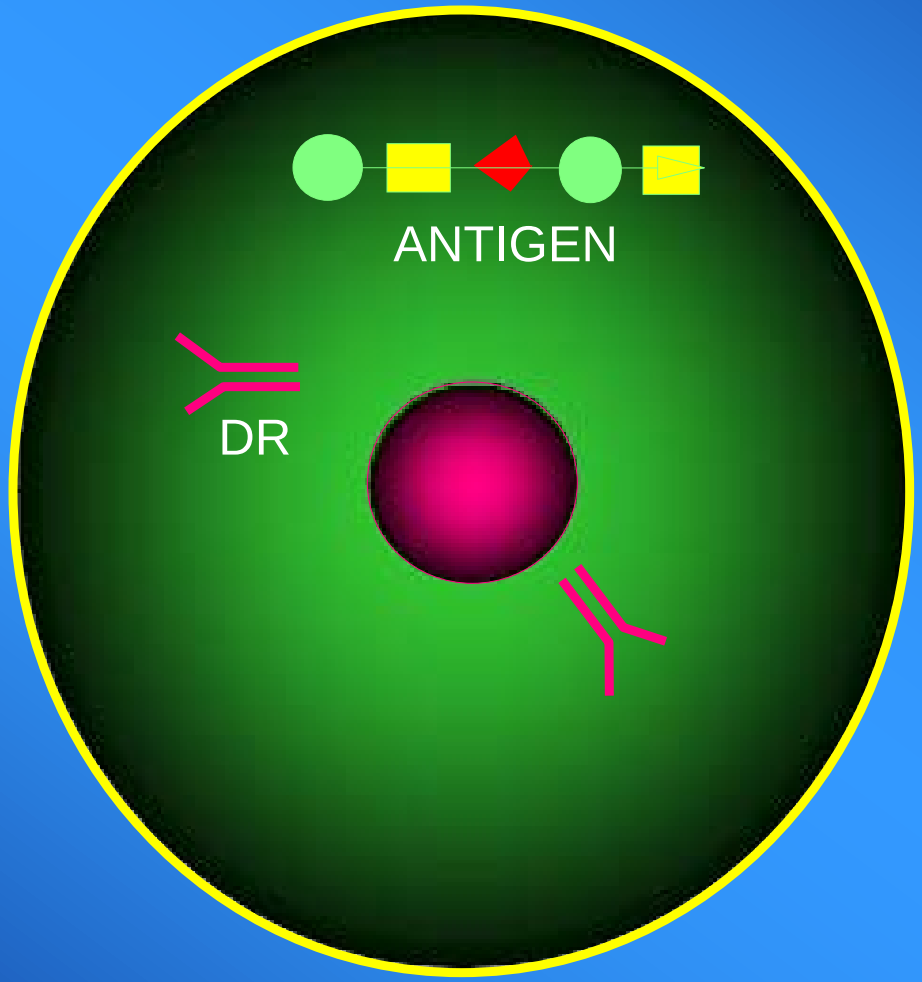
ANTIGEN PROCESSING



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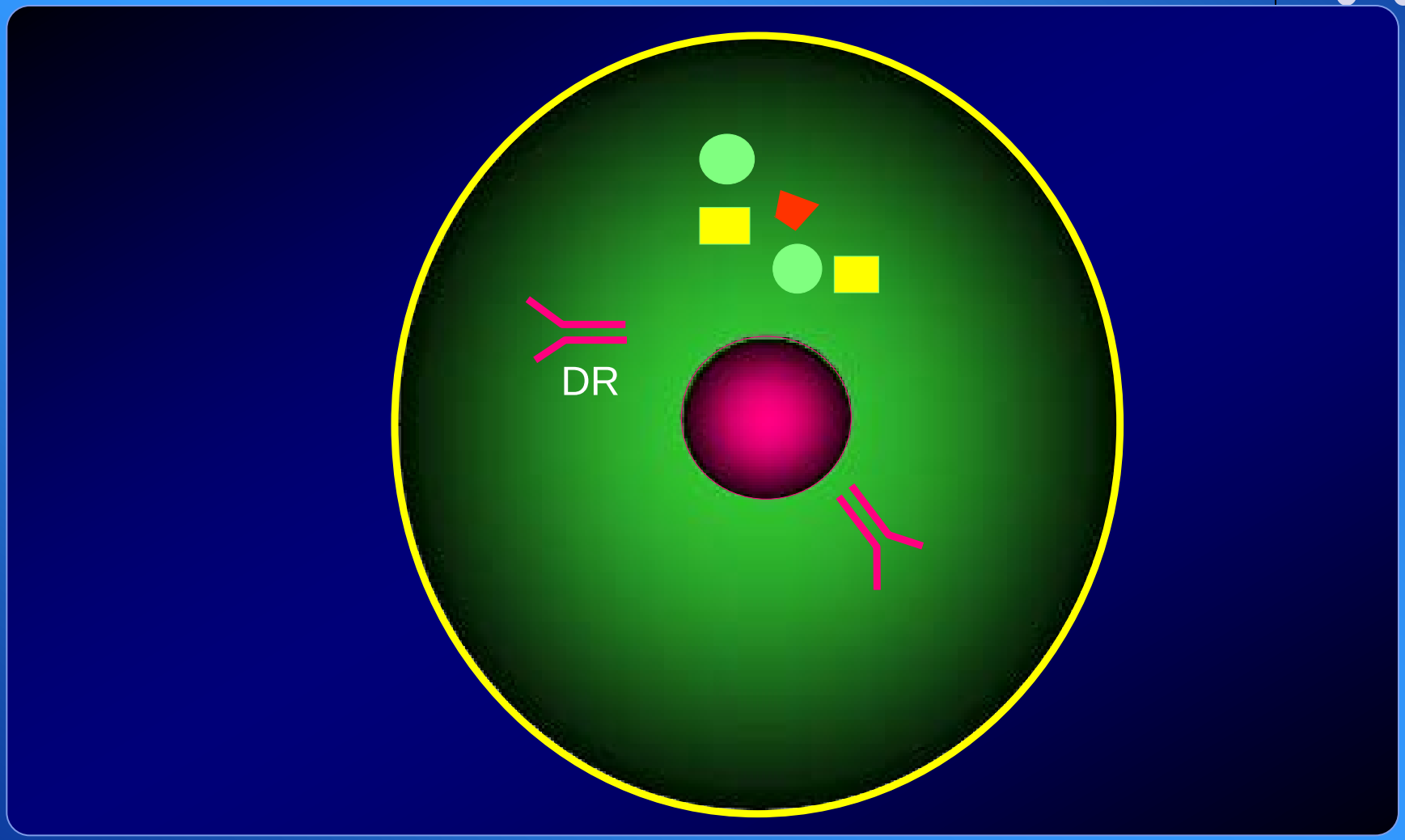
ANTIGEN PROCESSING



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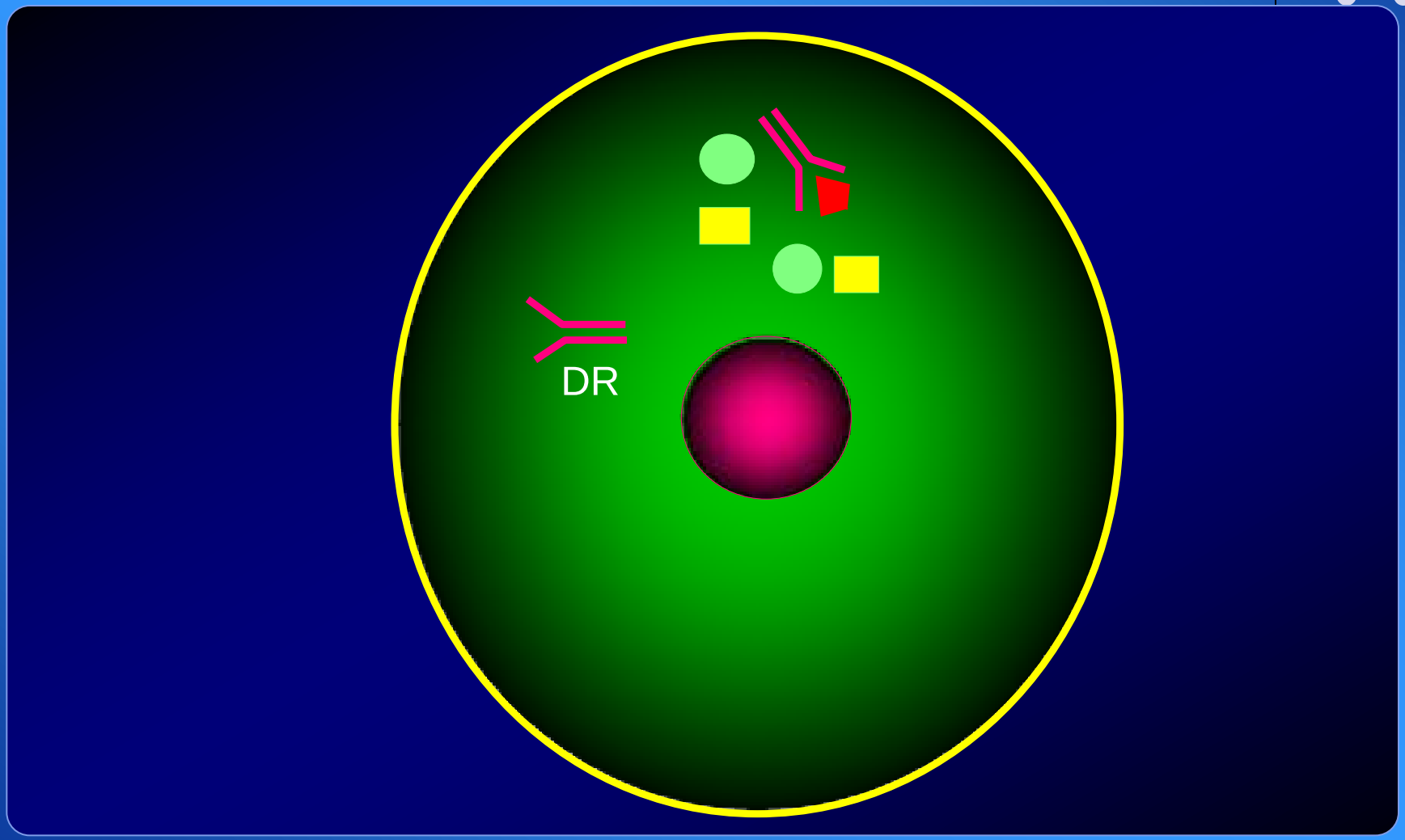

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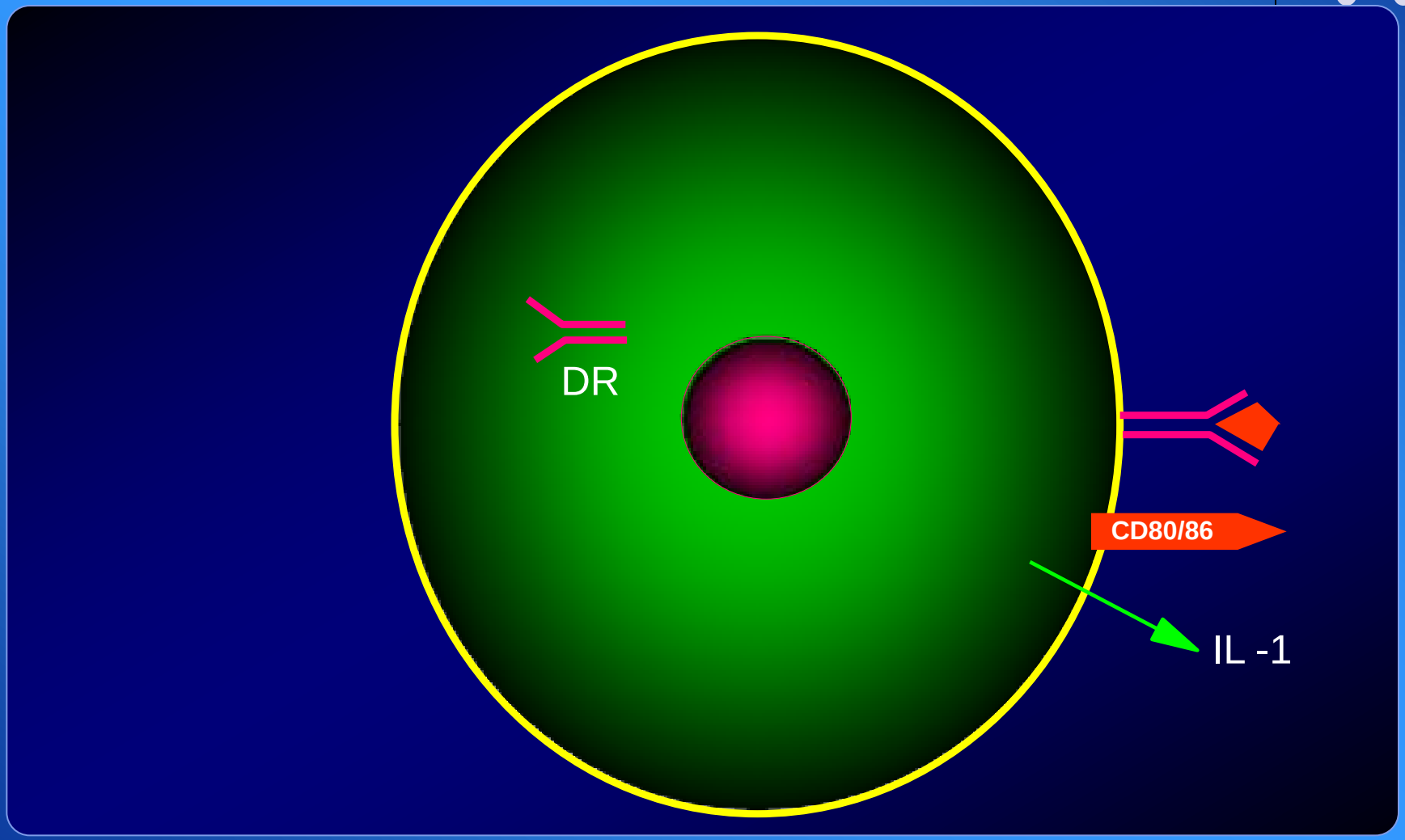

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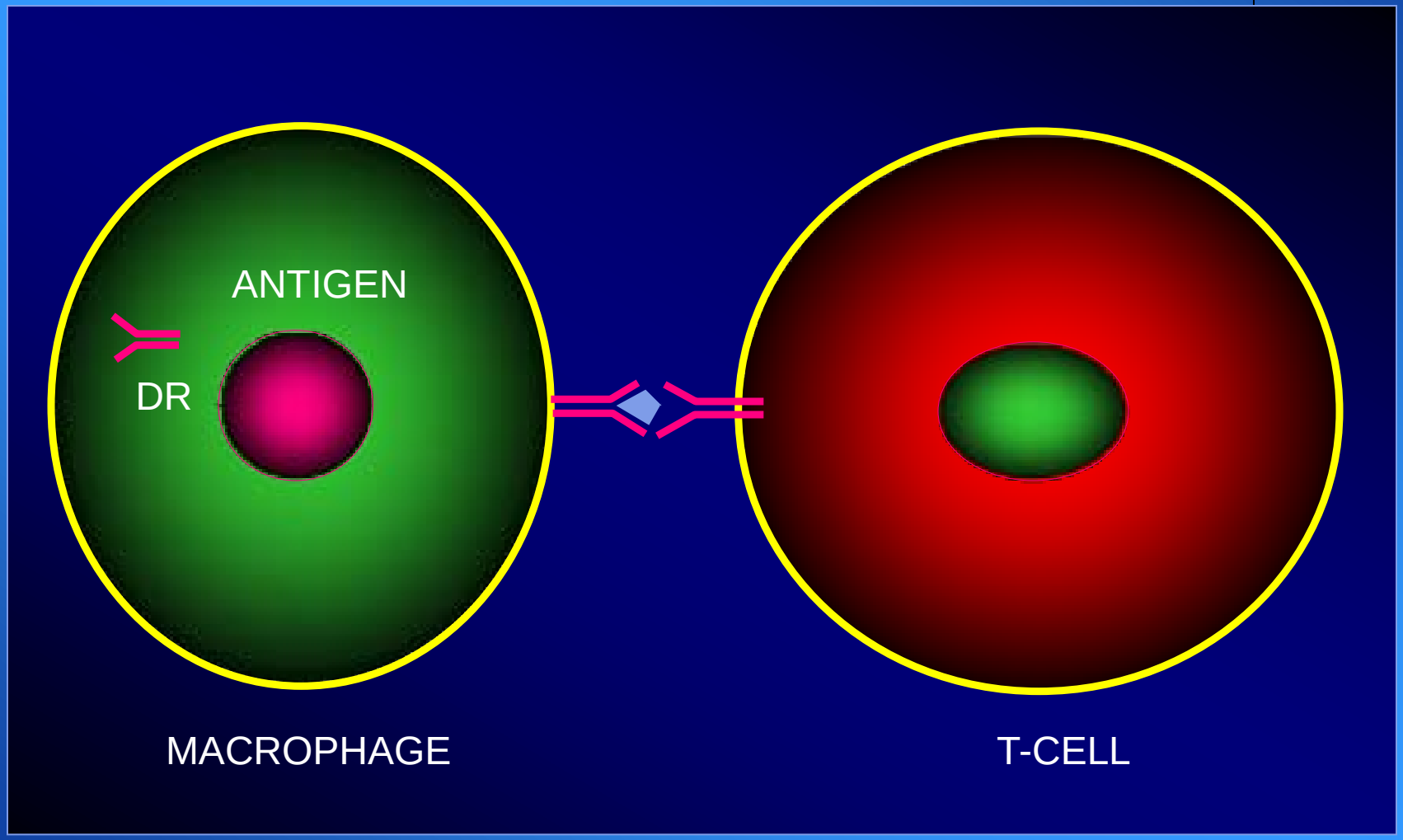
ANTIGEN RECOGNITION



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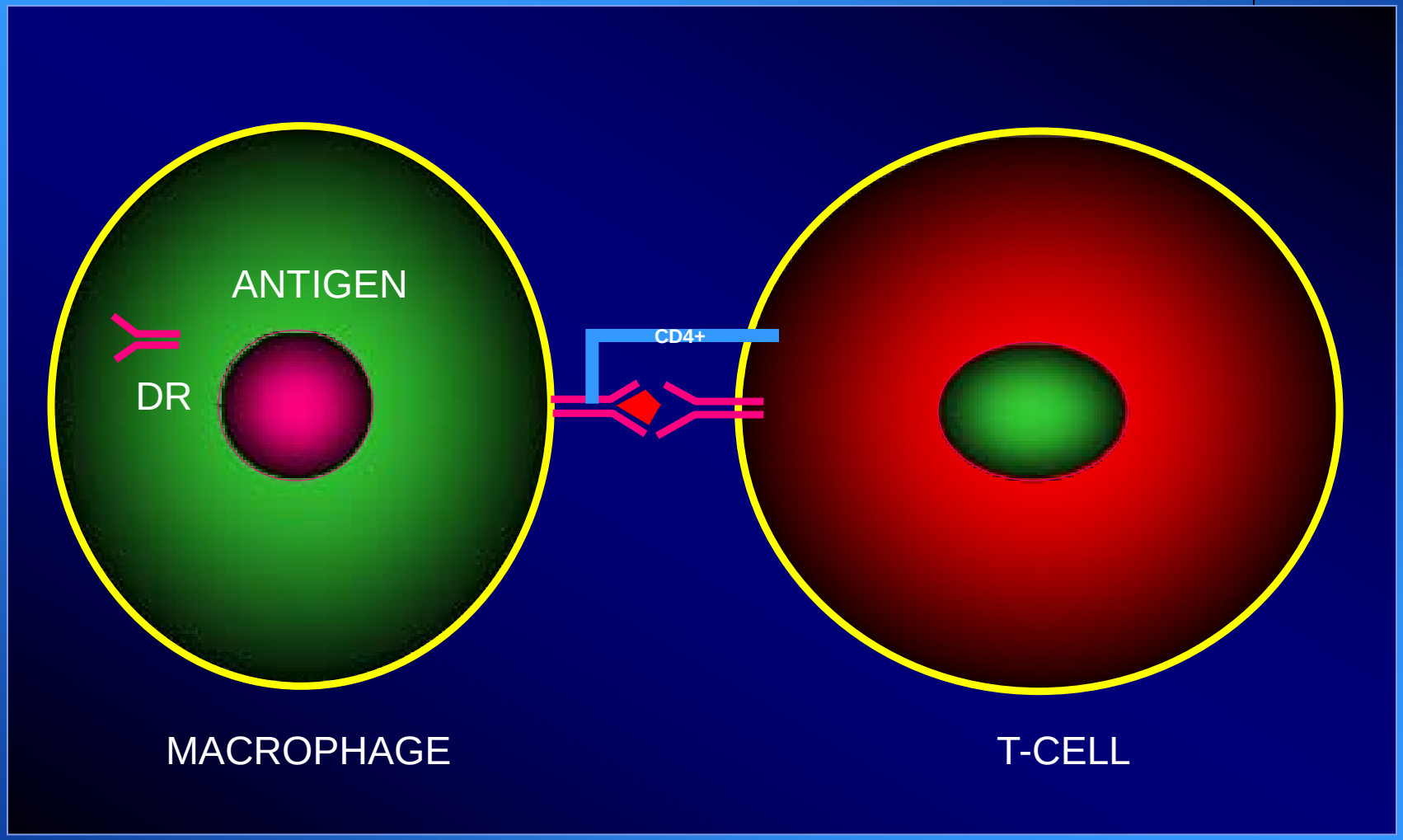

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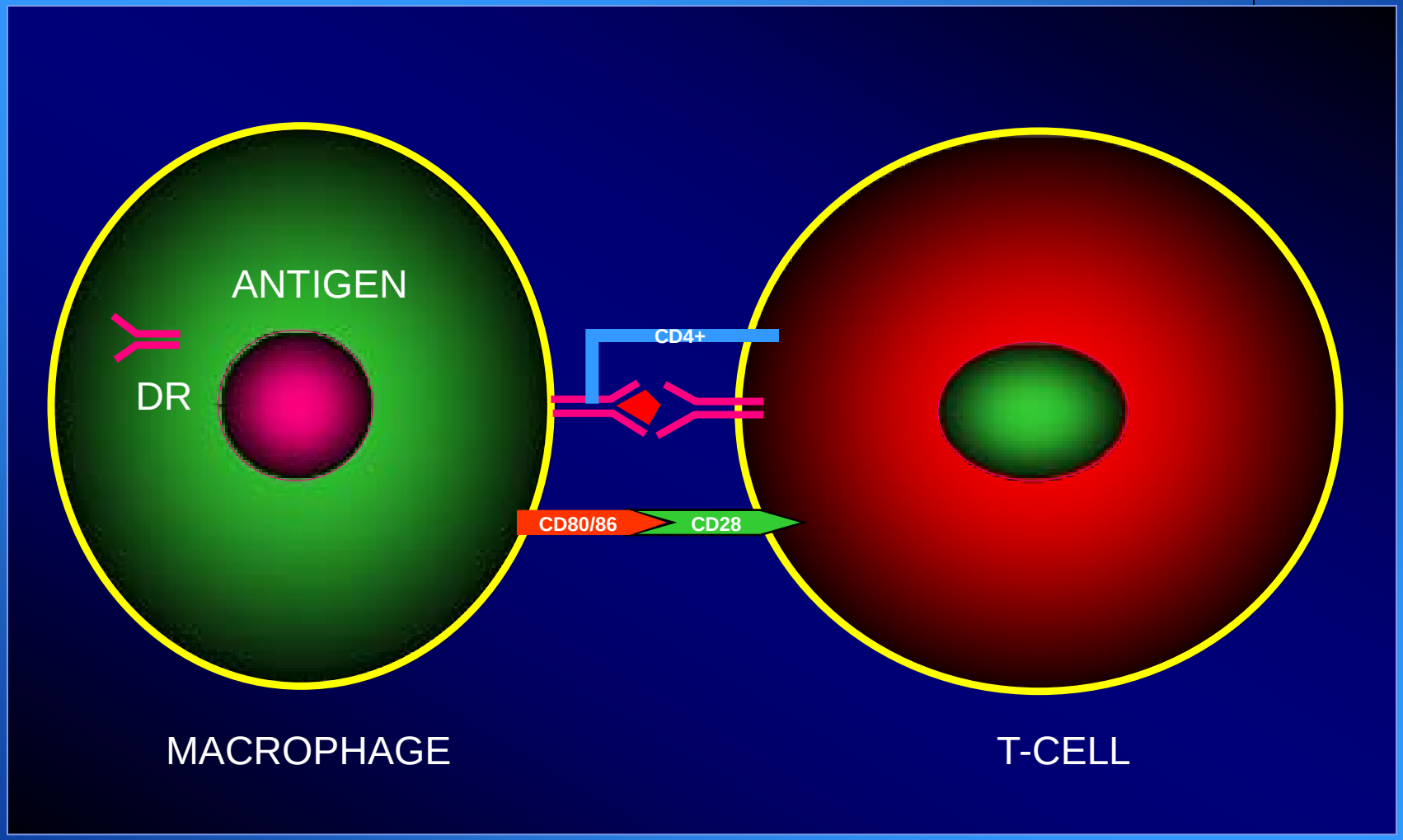

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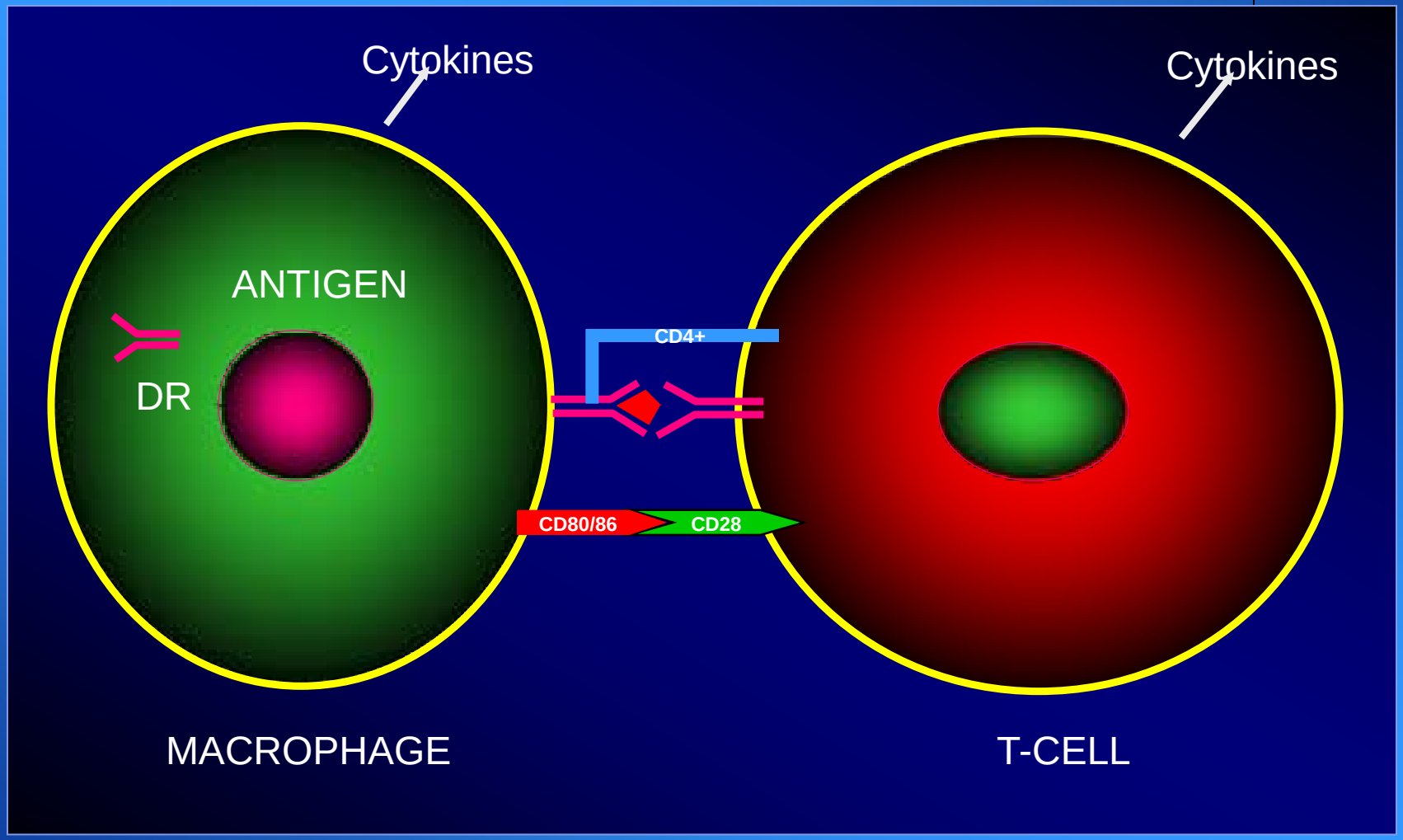

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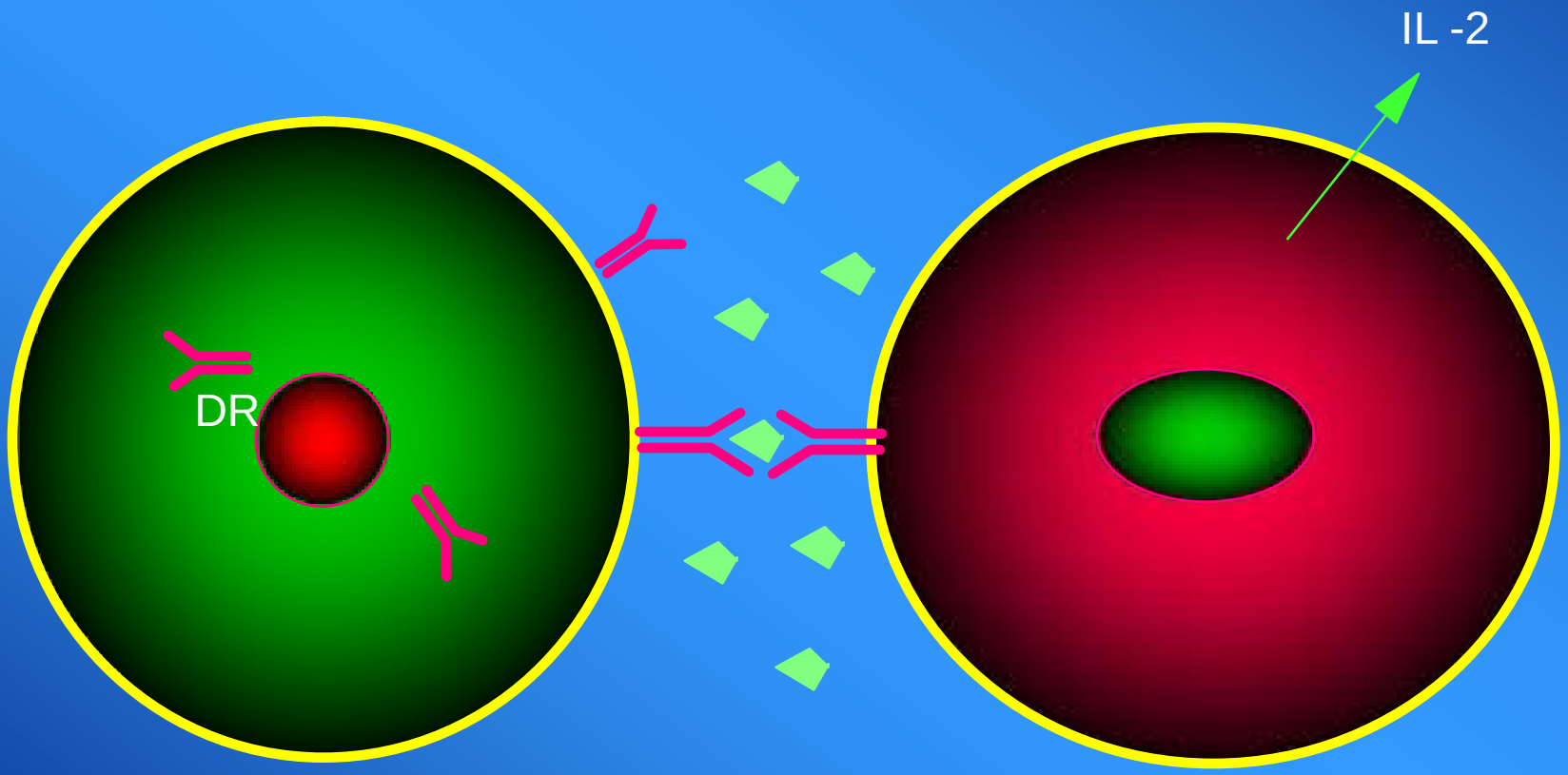
SUPER ANTIGEN



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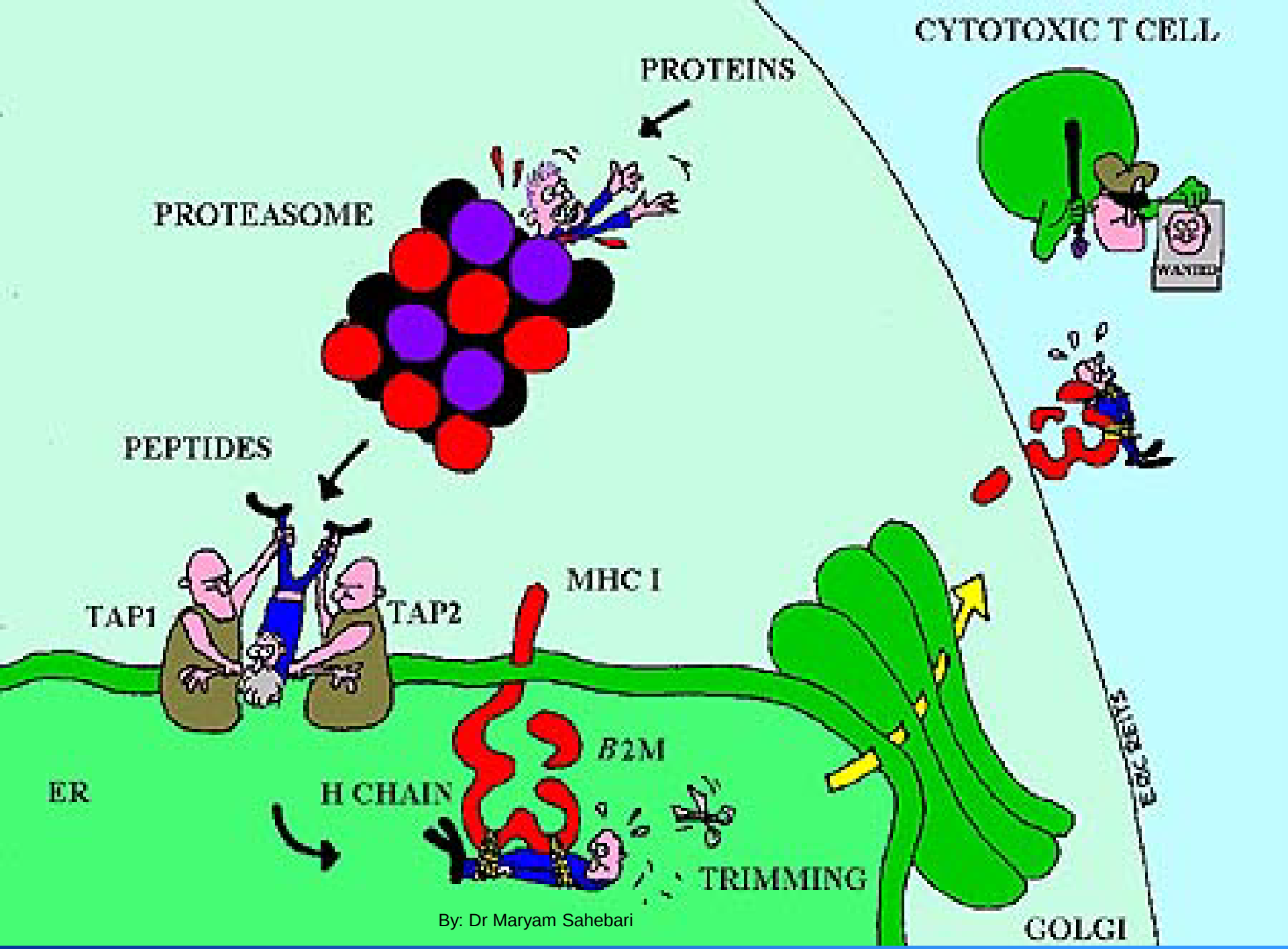
MHC: (major histocompatibility complex)

MHC protein: → Ag presentation to T cell

→ Recognition ligand

MHC class I → **Ag presentation to T cell** **CD8**

MHC class II → Ag presentation to T cell CD4



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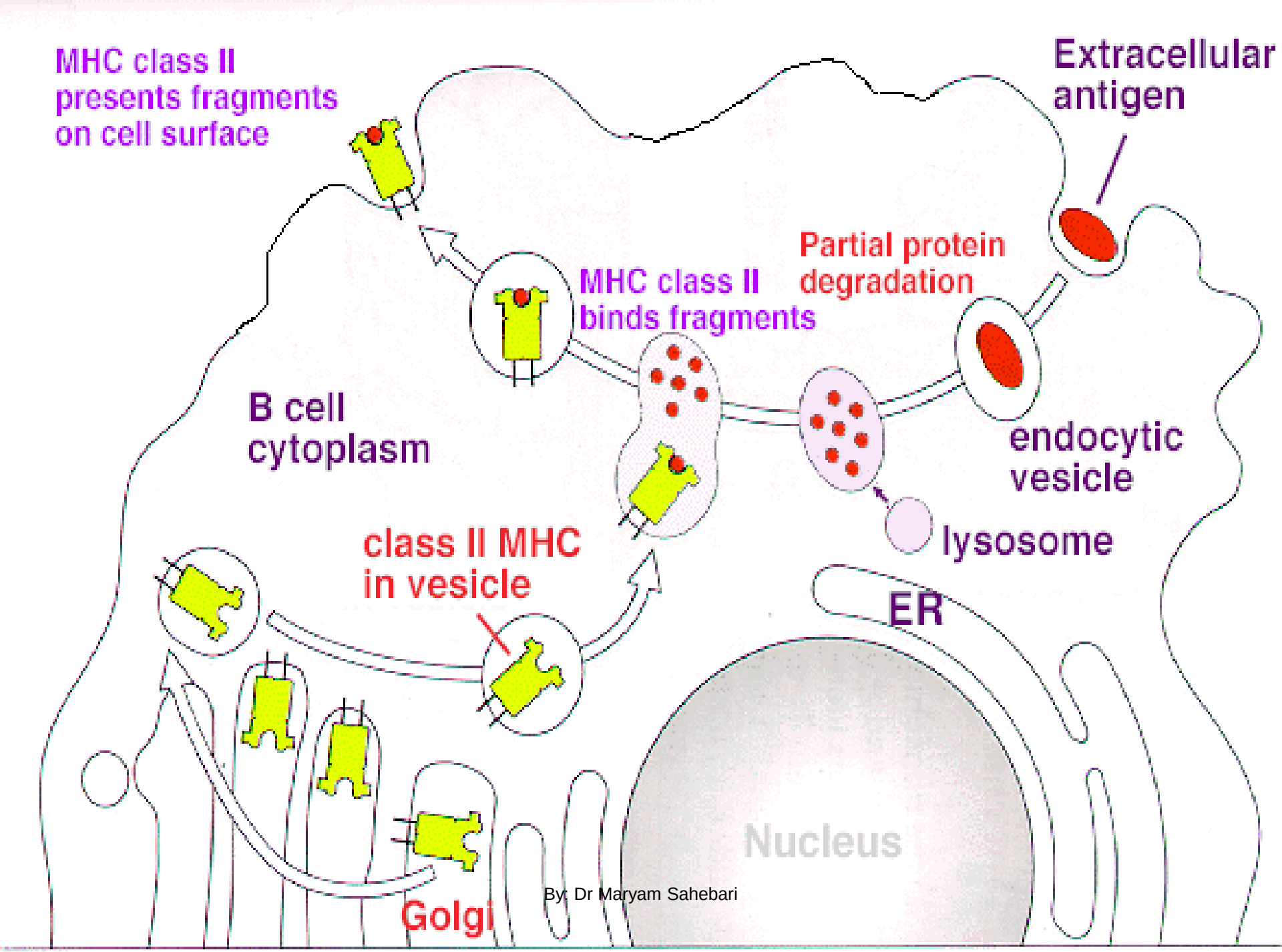
MHC class II
presents fragments
on cell surface
Extracellular
antigen
Partial protein
degradation
MHC class II
binds fragments
B cell
cytoplasm
endocytic
vesicle
lysosome
class II MHC
in vesicle
ER
Nucleus
Golgi
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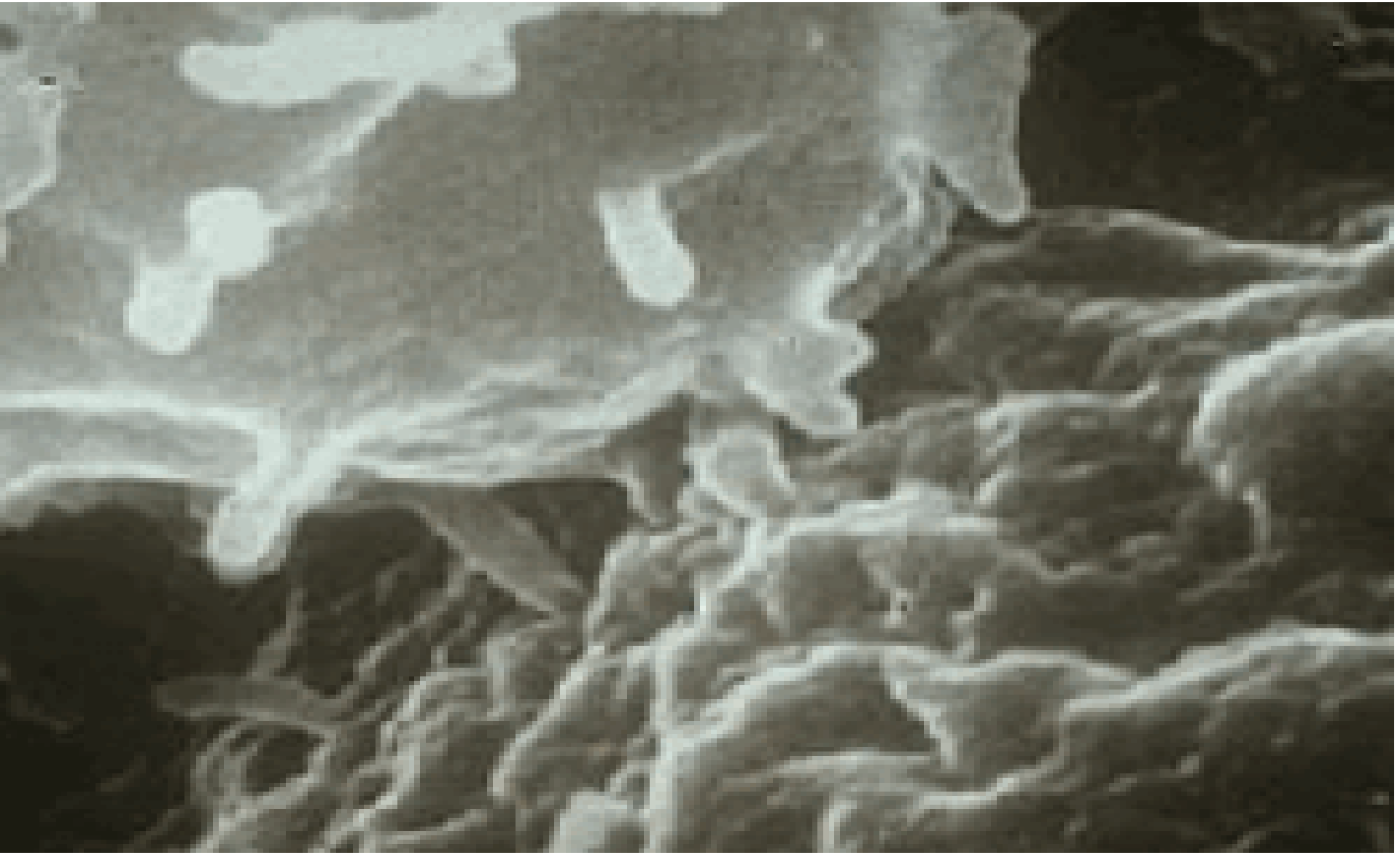
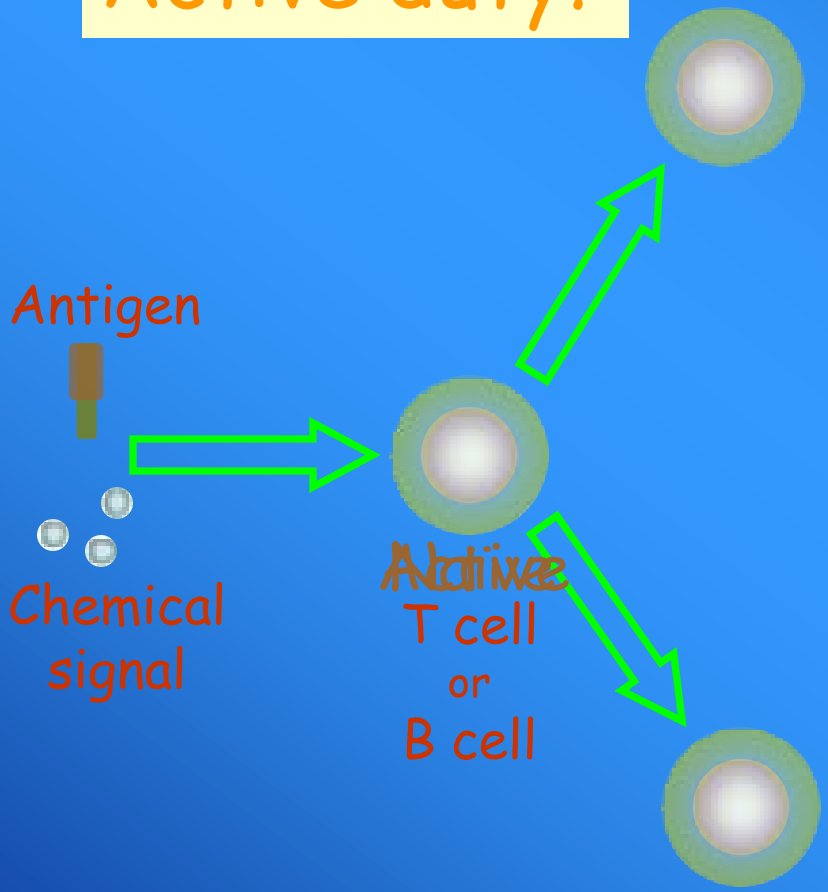
Cytotoxic Lymphocyte (top) recognizing a tumor cell.



Source: Oakland University

Active duty?



Reserves?

Effector cells

- "Active-duty" cells
- Die off during or just after "battle"

clone

family of cells descended from one ancestor cell

Memory cells

- "Reserve" cells
- "Called up to the front" for later battles

CYTOKINES AND CYTOKINE RECEPTORS

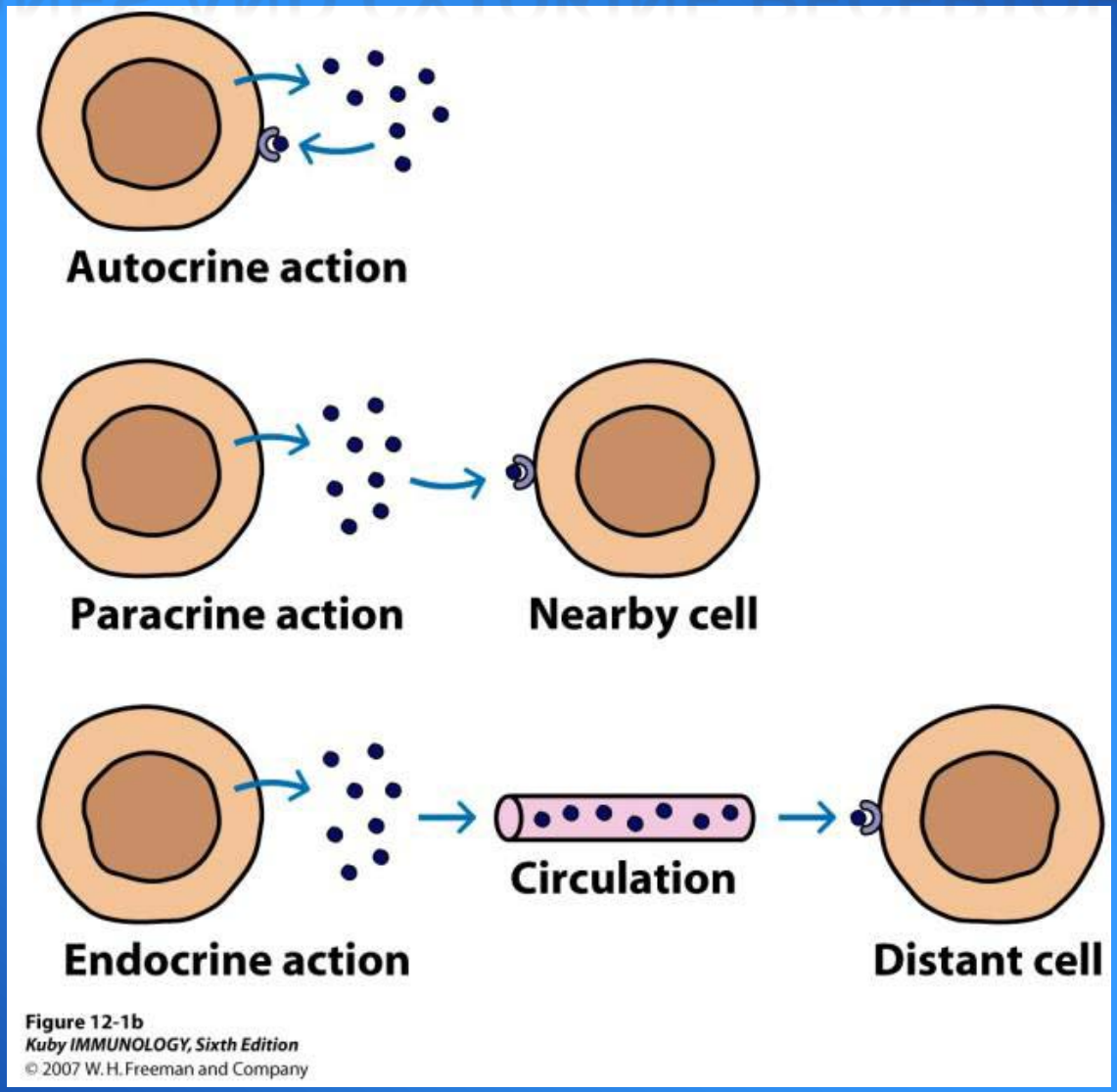


Figure 12-1b
Kuby IMMUNOLOGY, Sixth Edition

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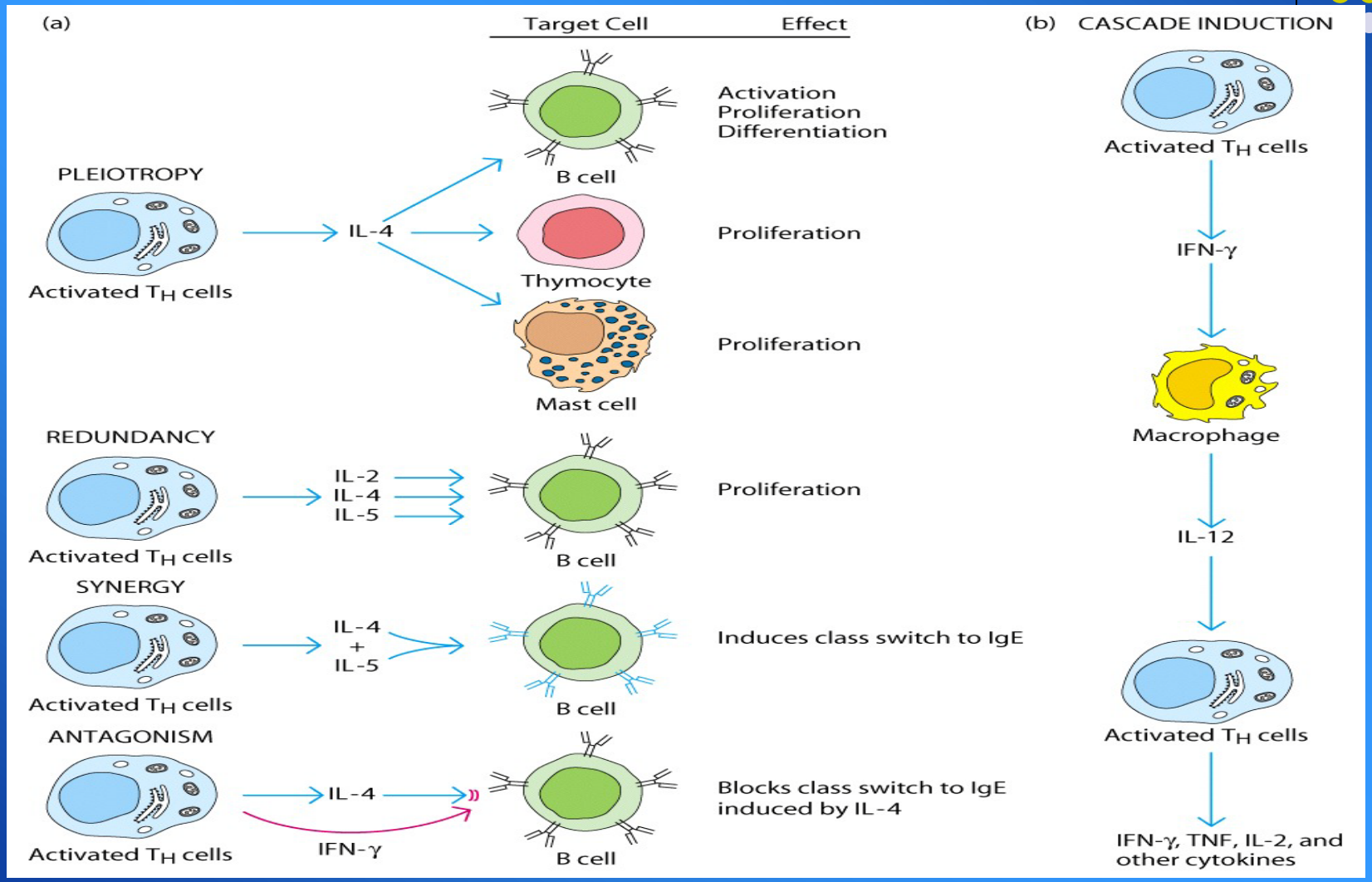
CYTOKINES AND CYTOKINE RECEPTORS



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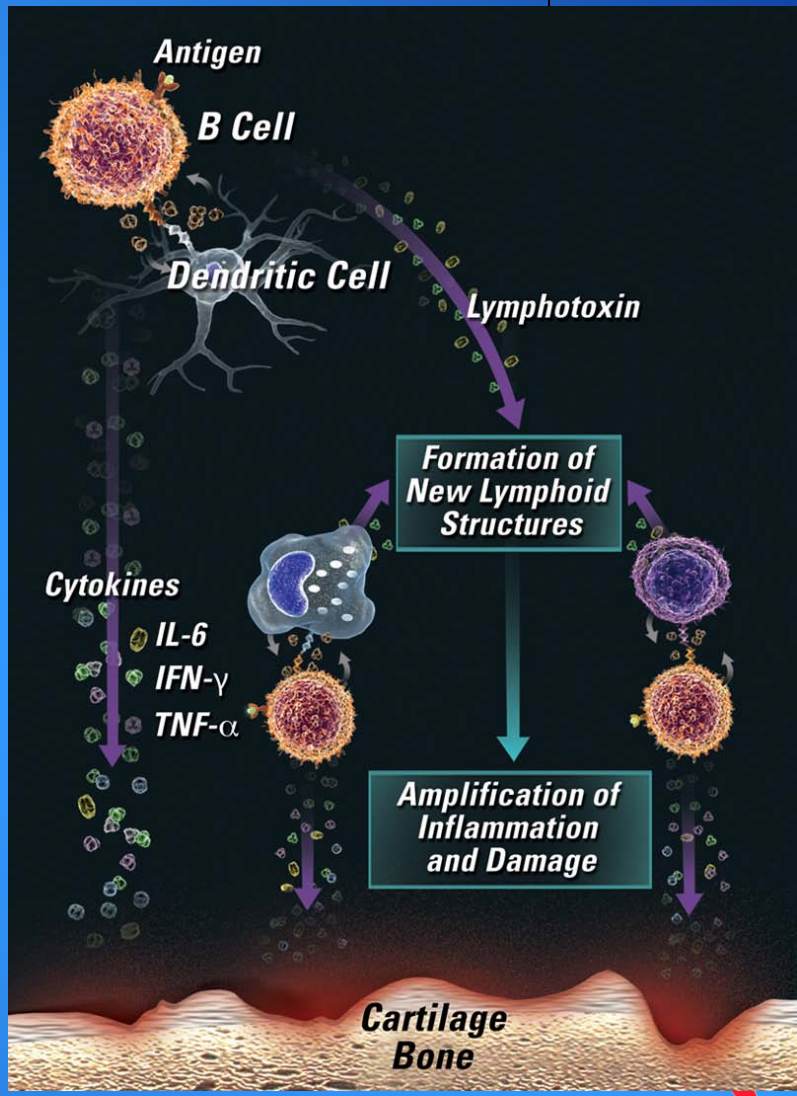
Role of B cells

(Cytokine production)



Duddy et al. J Immunol 2004;172:3422–3427
Lund et al. Curr Dir Autoimmun 2005;8:25–54

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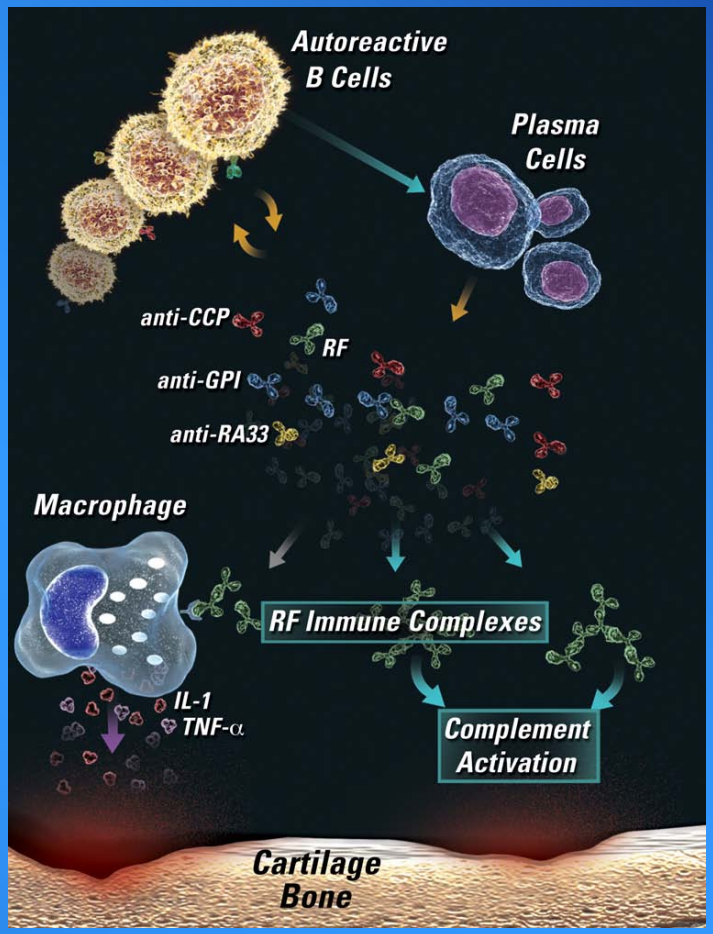
Role of

(Autoantibody production)



Abrahams et al. Arthritis Rheum 2000;43:608–616
Silverman et al. Arthritis Res Ther 2003;5(Suppl 4):S1–S6
Sutton et al. Immunol Today 2000;21:177–183

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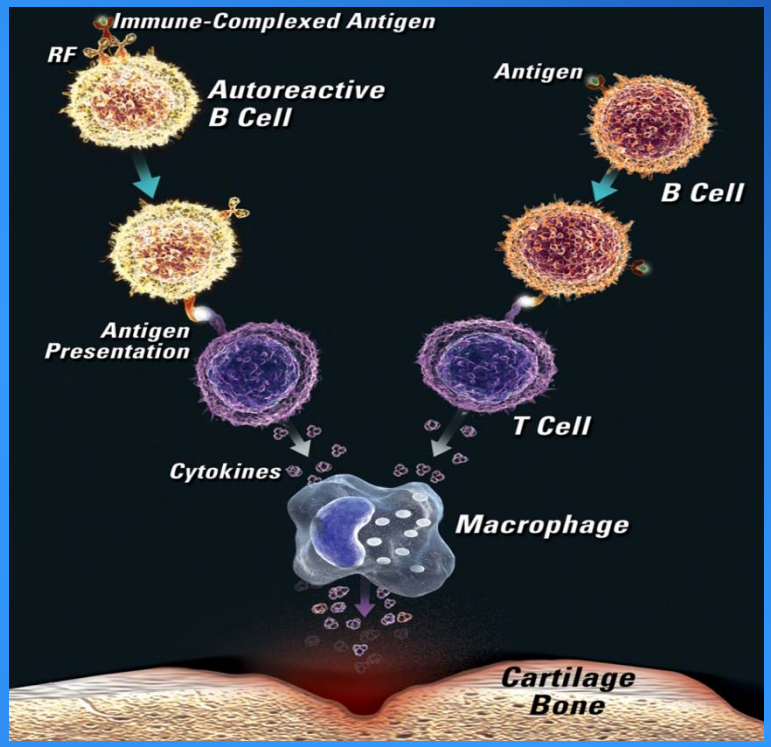
Role of B cells

(Antigen presentation and T cell activation)



Lanzavecchia. Annu Rev Immunol 1990;8:773–793; Lund et al. Curr Dir Autoimmun 2005;8:25–54; O'Neill et al. J Immunol 2005;174:3781–3788; Roosnek et al. J Exp Med 1991;173:487–489; Silverman et al. Arthritis Res Ther 2003;5(Suppl. 4):S1–S6

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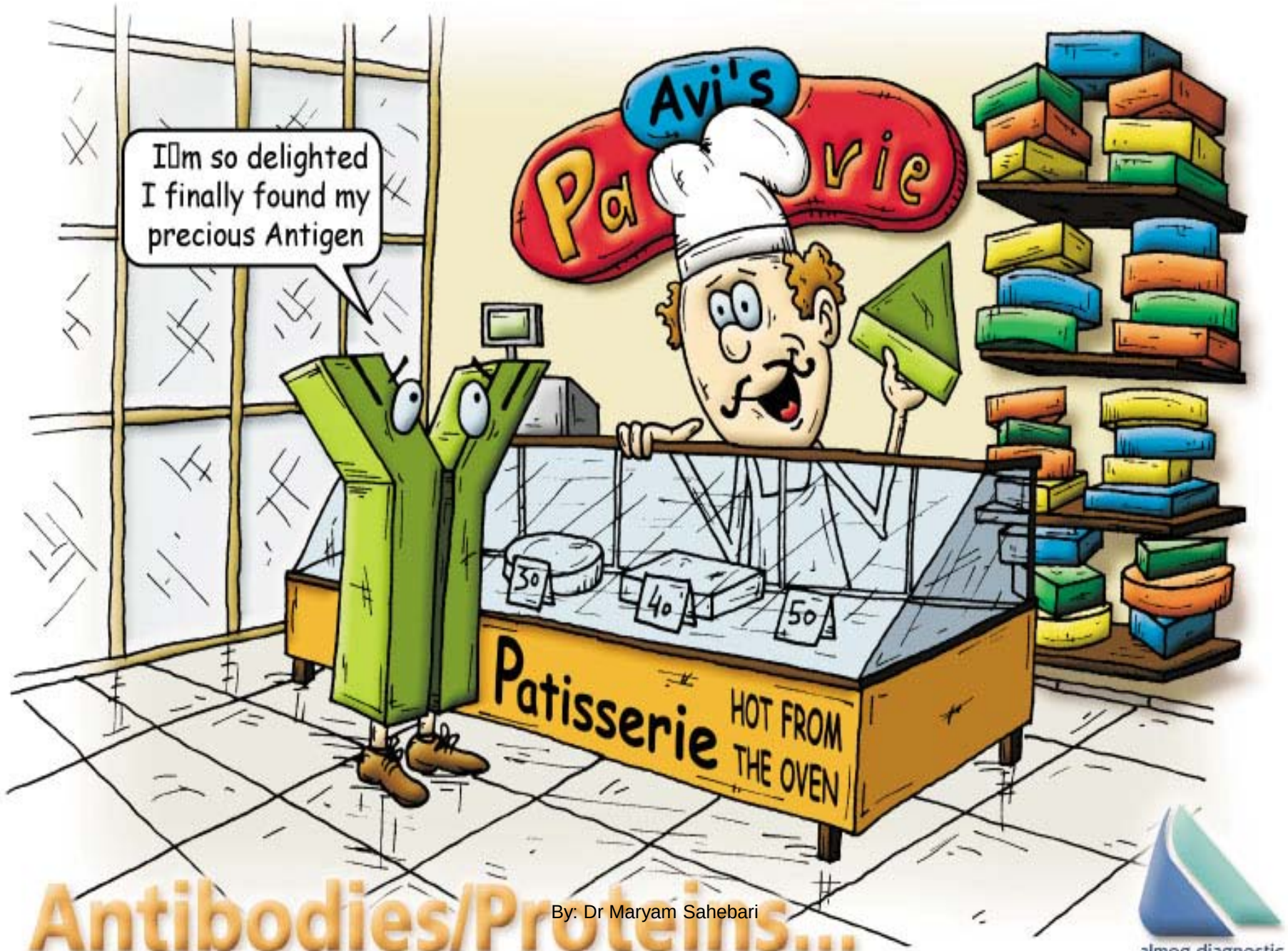
I'm so delighted I finally found my precious Antigen
Avi's
Patisserie
30
40
50
Patisserie
HOT FROM THE OVEN
Antibodies/Proteins...
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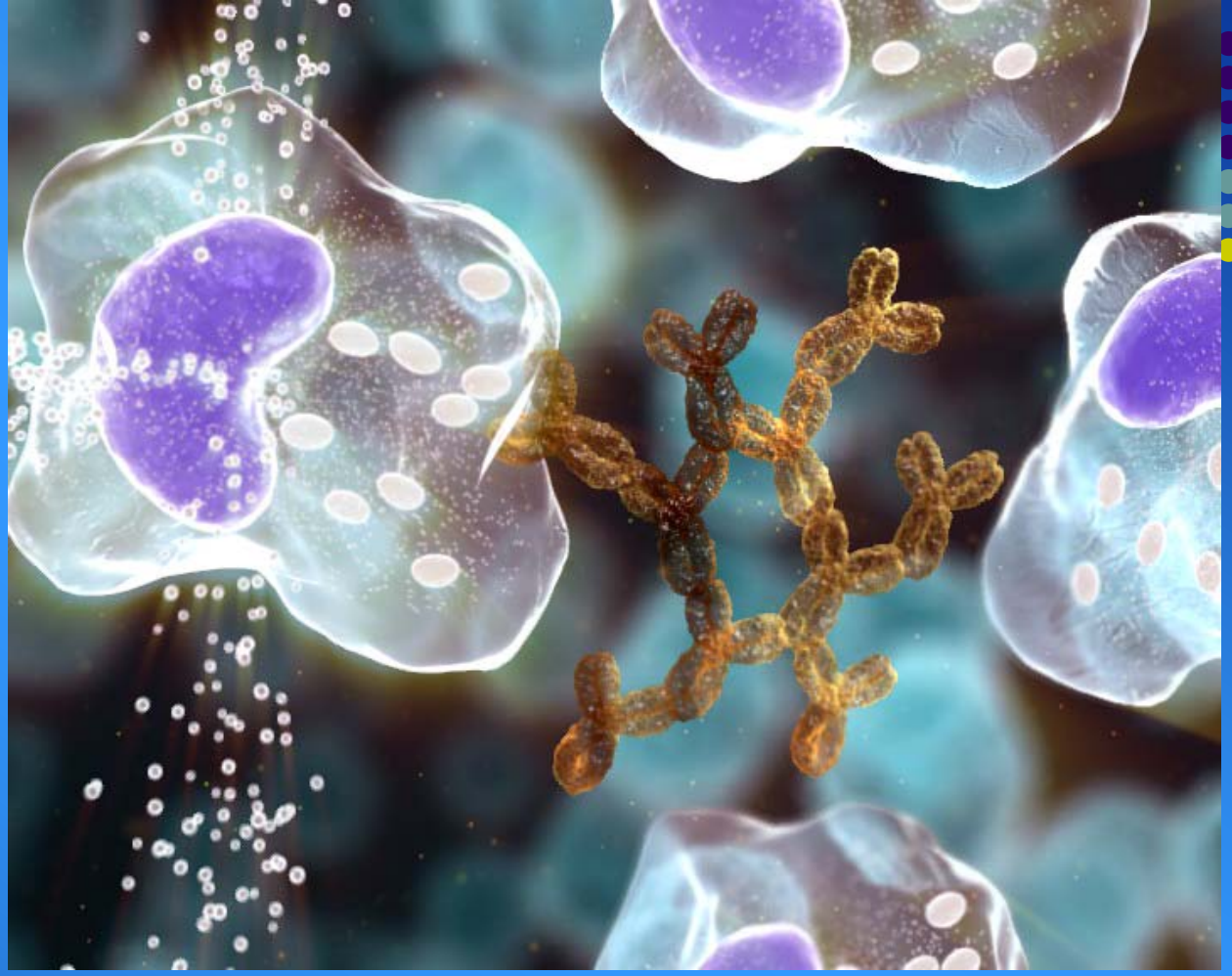
almog diagnostic



Immune complexes activate destructive processes

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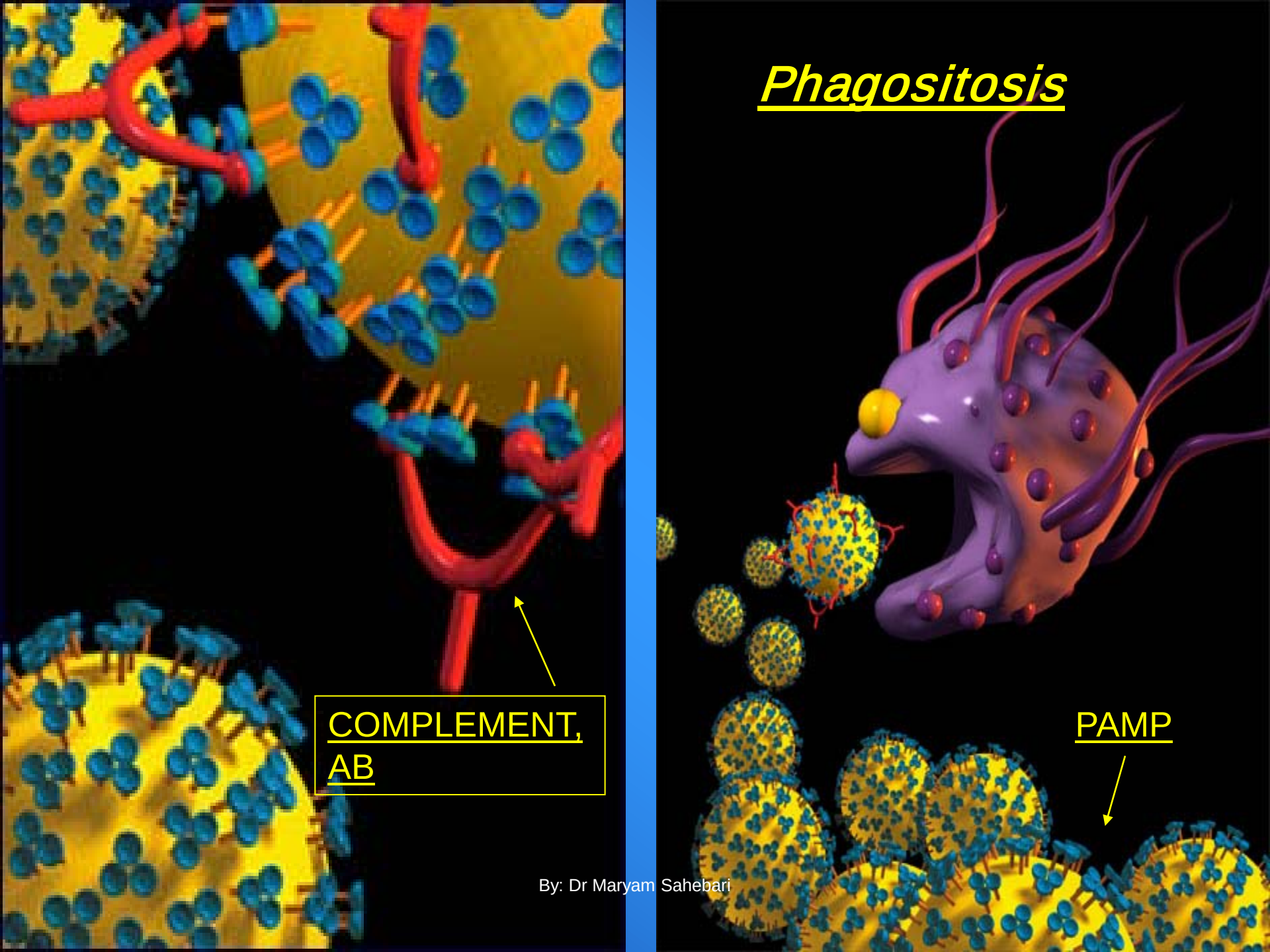
Complement system

- **Complement proteins exist in blood serum. They coat pathogens and form pores on pathogen membranes, causing lysis of pathogens with the help of antibodies.**
- **Fragments of complements make anaphylatoxins that cane activate inflammatory cells and induce inflammation**

Complement system

- C4 deficiency→ SLE
- H deficiency→ HUS
- C1 inhibitor deficiency→ hereditary angioedema

Phagositosis



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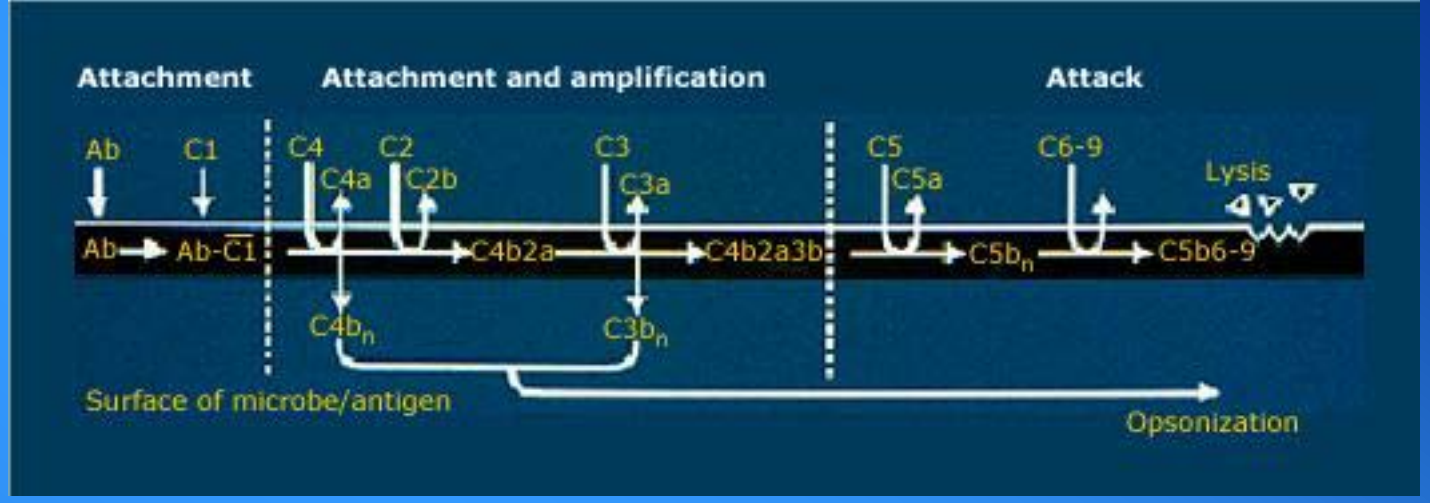

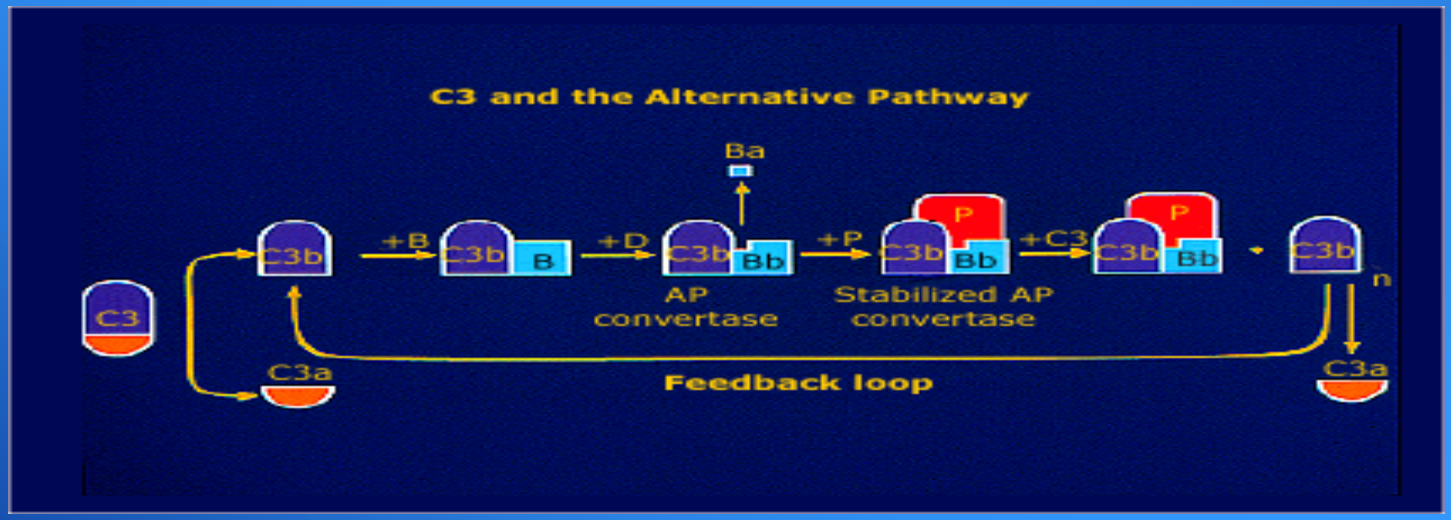

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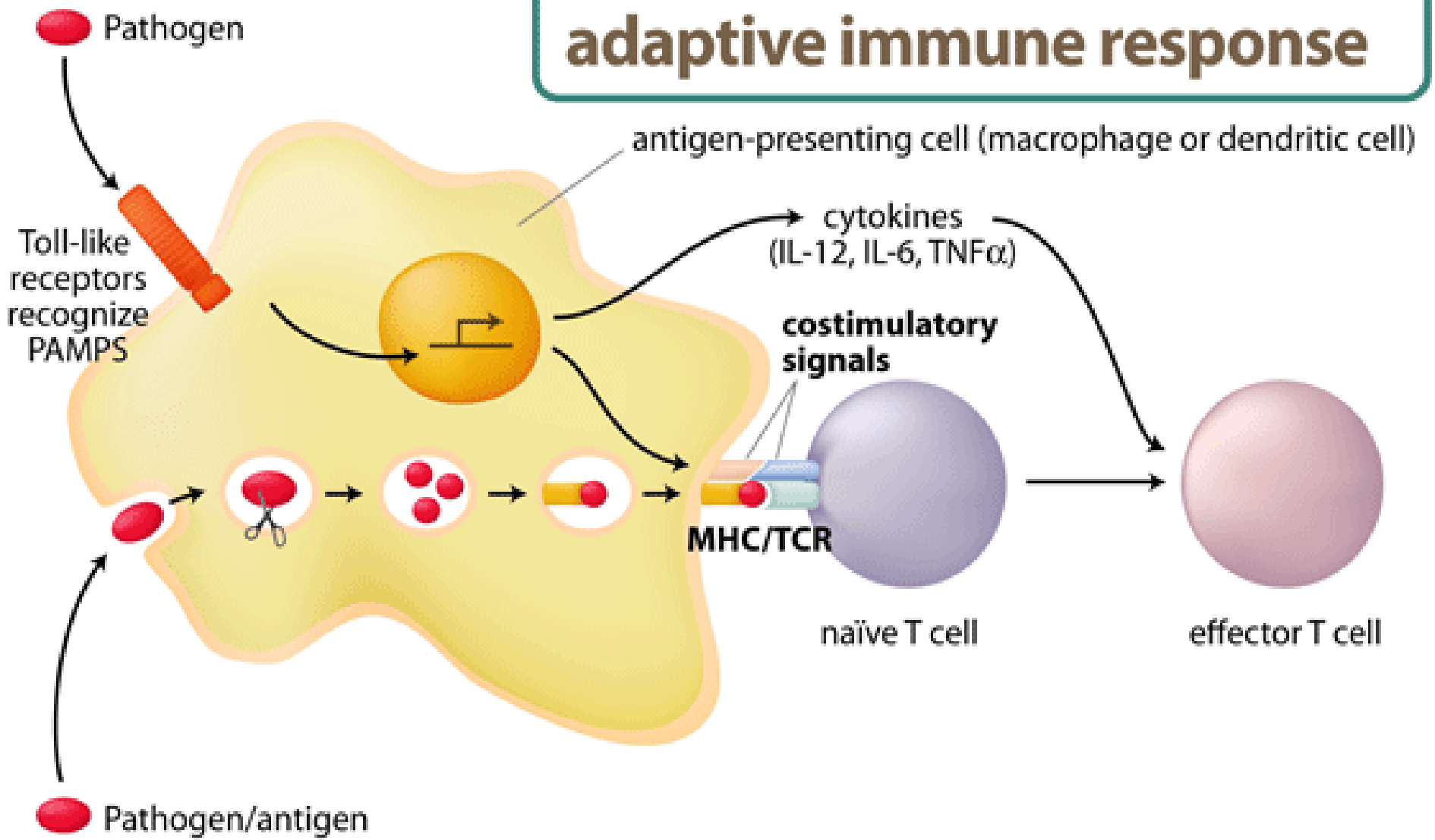
Innate immunity is critical to adaptive immune response



Innate Immunity **Adaptive Immunity**

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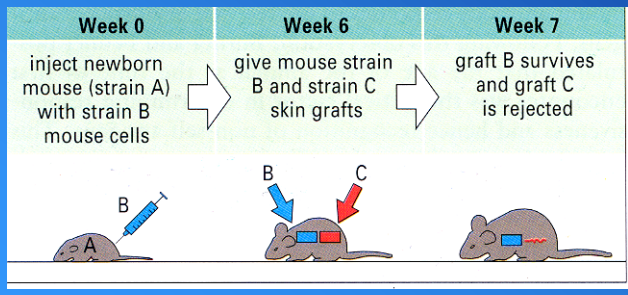
IMMUNOLOGIC TOLERANCE:

A state of unresponsiveness for a particular antigen ; induced by prior exposure to that Ag



A process for elimination or neutralization of auto reactive cells

Tolerance to self antigen
or to innocuous non self antigen

Impaired tolerance causes autoimmunity

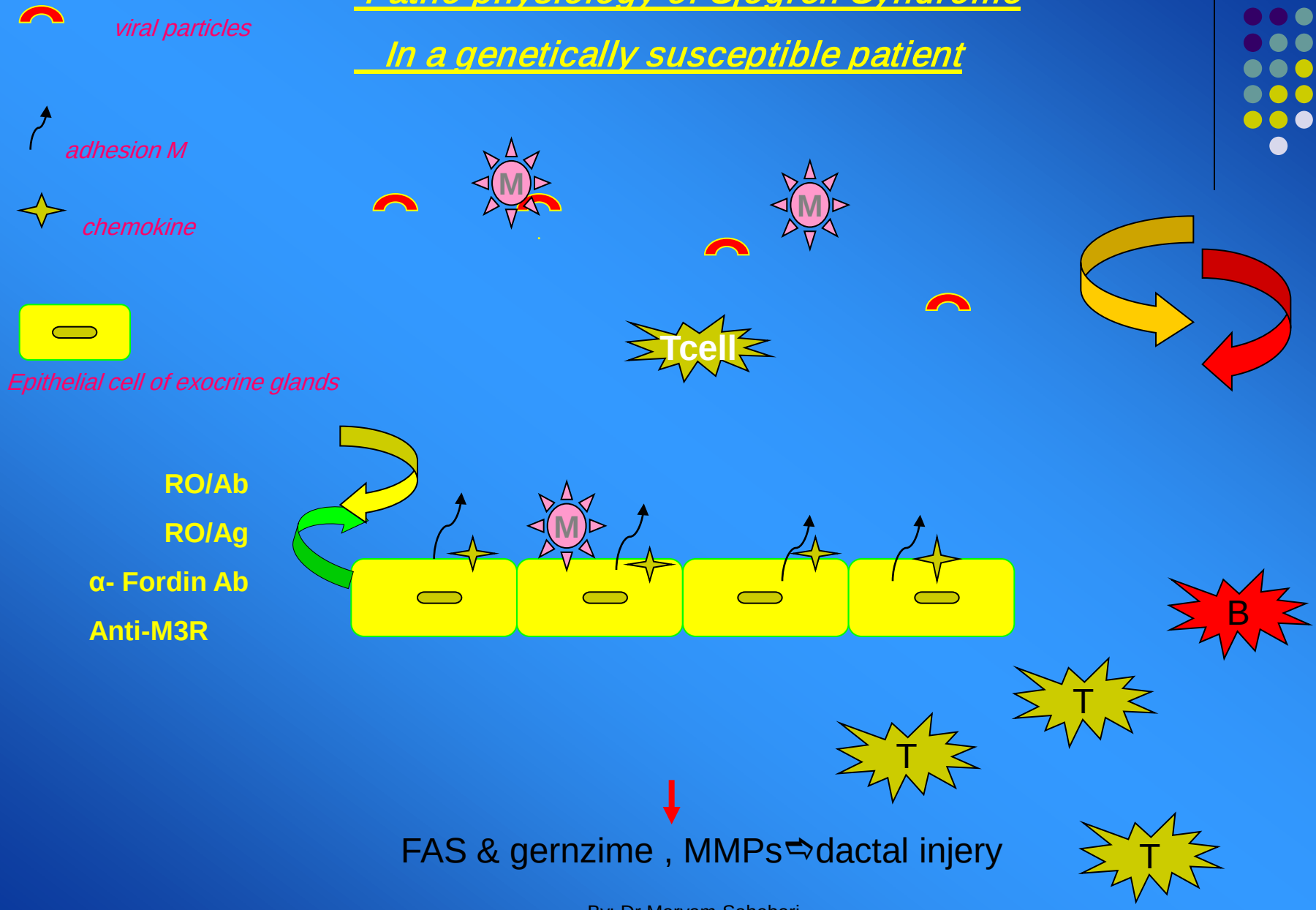
Factors of immunogenicity and tolerogenicity of Ag

Factor	Factors That Favor Stimulation of Immune Responses	Factors That Favor Tolerance
Amount	Optimal doses that vary for different antigens	High doses
Persistence	Short lived (eliminated by immune response)	Prolonged (repeated T cell stimulation induces apoptosis)
Portal of entry; location	Subcutaneous, intradermal; absence from generative organs	Intravenous, oral; presence in generative organs
Presence of adjuvants	Antigens with adjuvants: stimulate helper T cells	Antigens without adjuvants: nonimmunogenic or tolerogenic
Properties of antigen-presenting cells	High levels of costimulators, secretion of cytokines (e.g., IL-12)	Low levels of costimulators and cytokines

Abbreviation: IL-12, interleukin-12.

Patho physiology of Sjogren Syndrome

In a genetically susceptible patient



FAS & gernzime , MMPs⇨dactal injery

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