Lecture #4

Swarm Intelligence

Dr. Charnon Pattiyanon

Assistant Director of IT, Instructor

Department of Artificial Intelligence and Computer Engineering

CMKL University

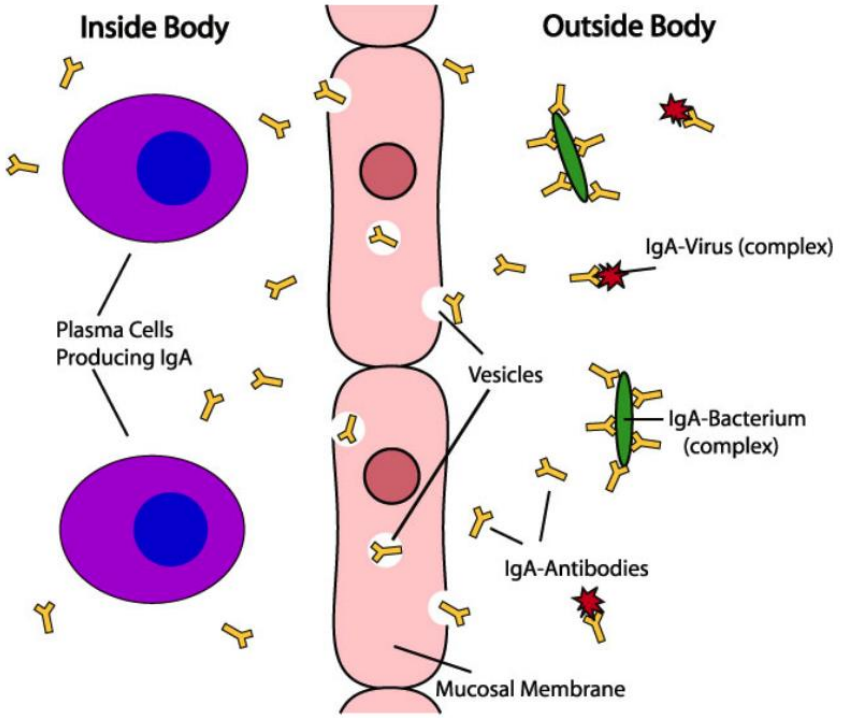
Modified from Companion Slides for "D. Floreano and C. Mattiussi, Bio-Inspired Artificial Intelligence: Theories, Methods, and Technologies, 2008"

Biological Immune Systems

Living organism must **protect themselves** from the attempt of other organisms to exploit their resources.

Homeostasis is the property of a system, either open or closed, that regulates its internal environment and tends to maintain a stable, constant condition.

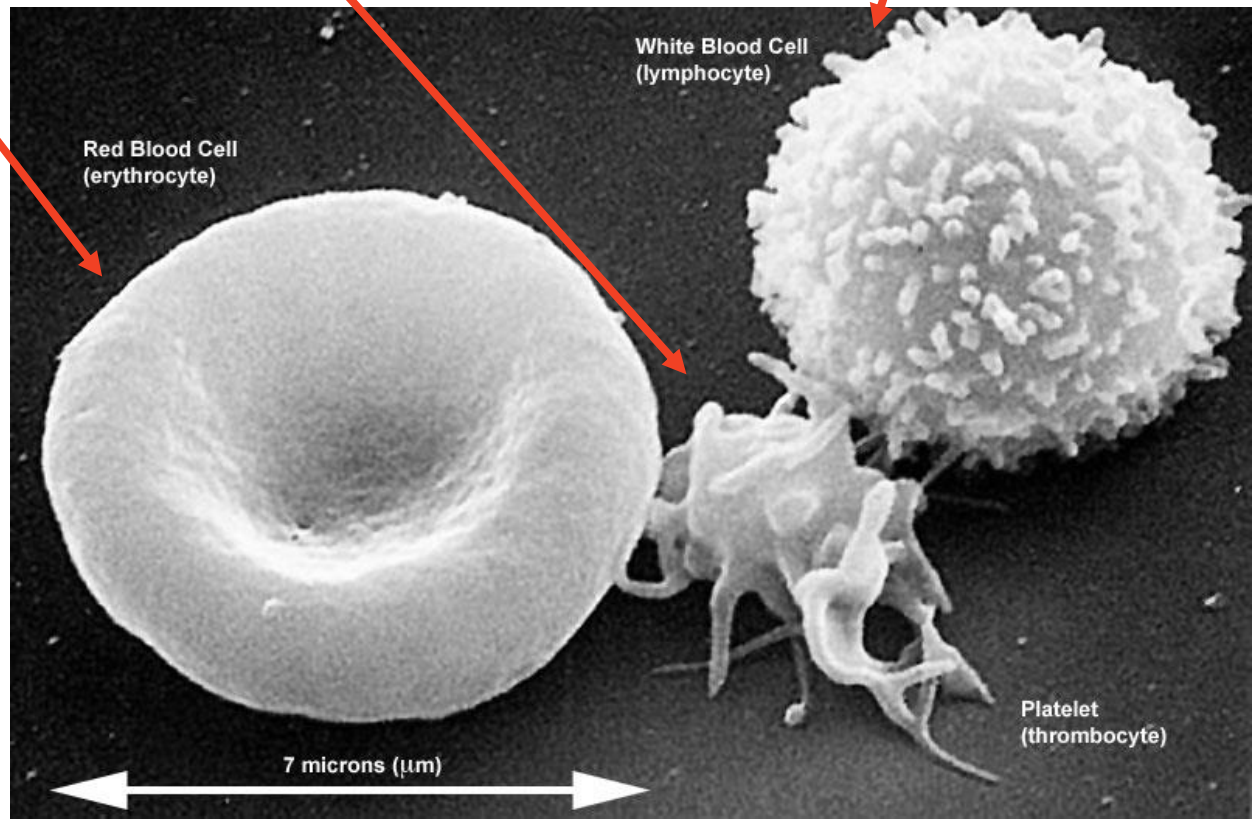
The **pathogen** can reproduce much faster than the typical host and can rapidly evolve new strategies of attack.



A three-dimensional ultra-structural image analysis of

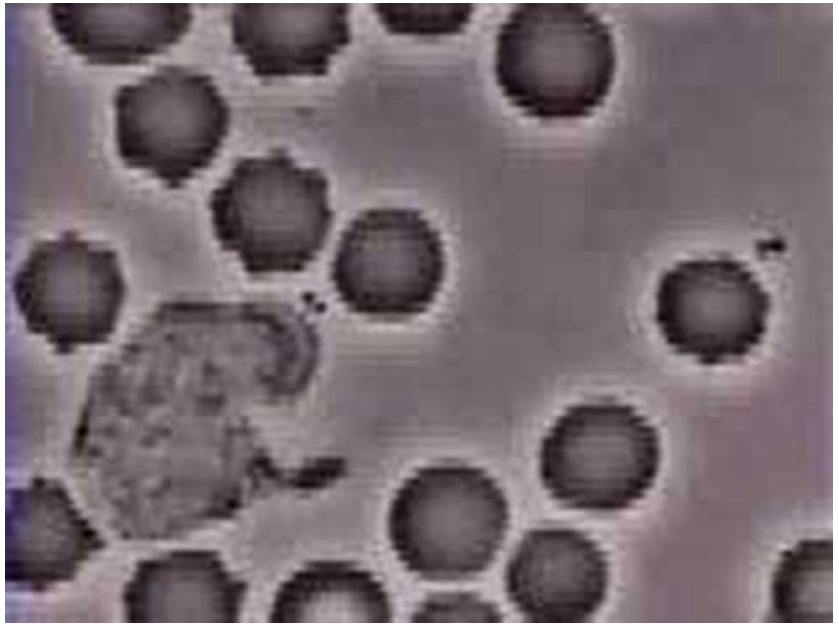
a **red blood cell** (left), **a platelet** (center), and **T-lymphocyte** (right), using a Hitachi

S-570 scanning electron microscope (SEM) equipped with a GW Backscatter Detector.



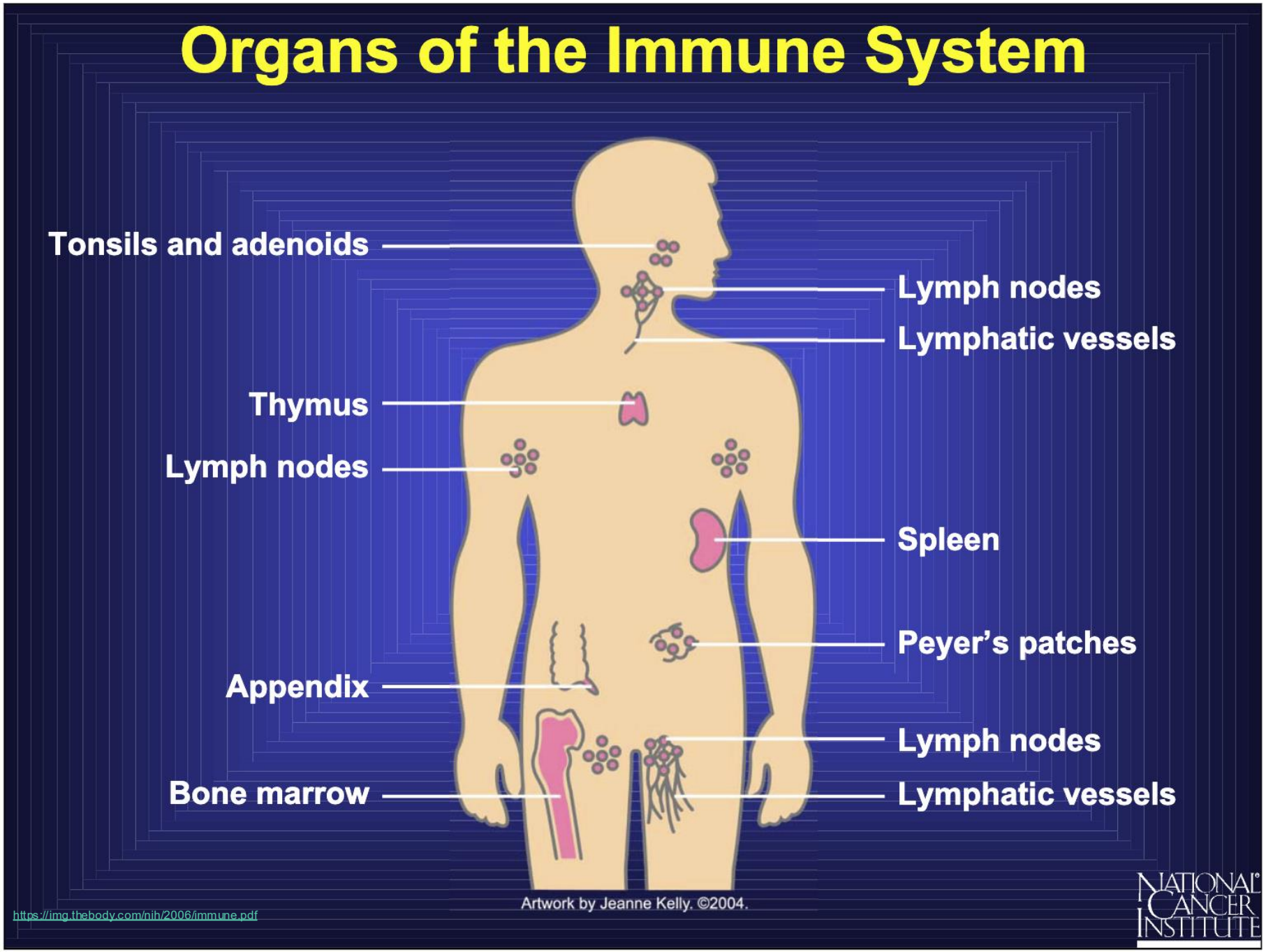
Functions of the Immune Systems

- The immune system must:
  - **Detect** the pathogens once they have entered the host body,
  - **Eliminate** the pathogens with **minimal cost** in terms of resources employed and damage done to the host,
  - **Initiate the repair** of the damages done by the pathogens,
  - **Detect** and **repair** the malfunctioning and failures of individual host cells (e.g., damaged, mutated, and cancerous cells).

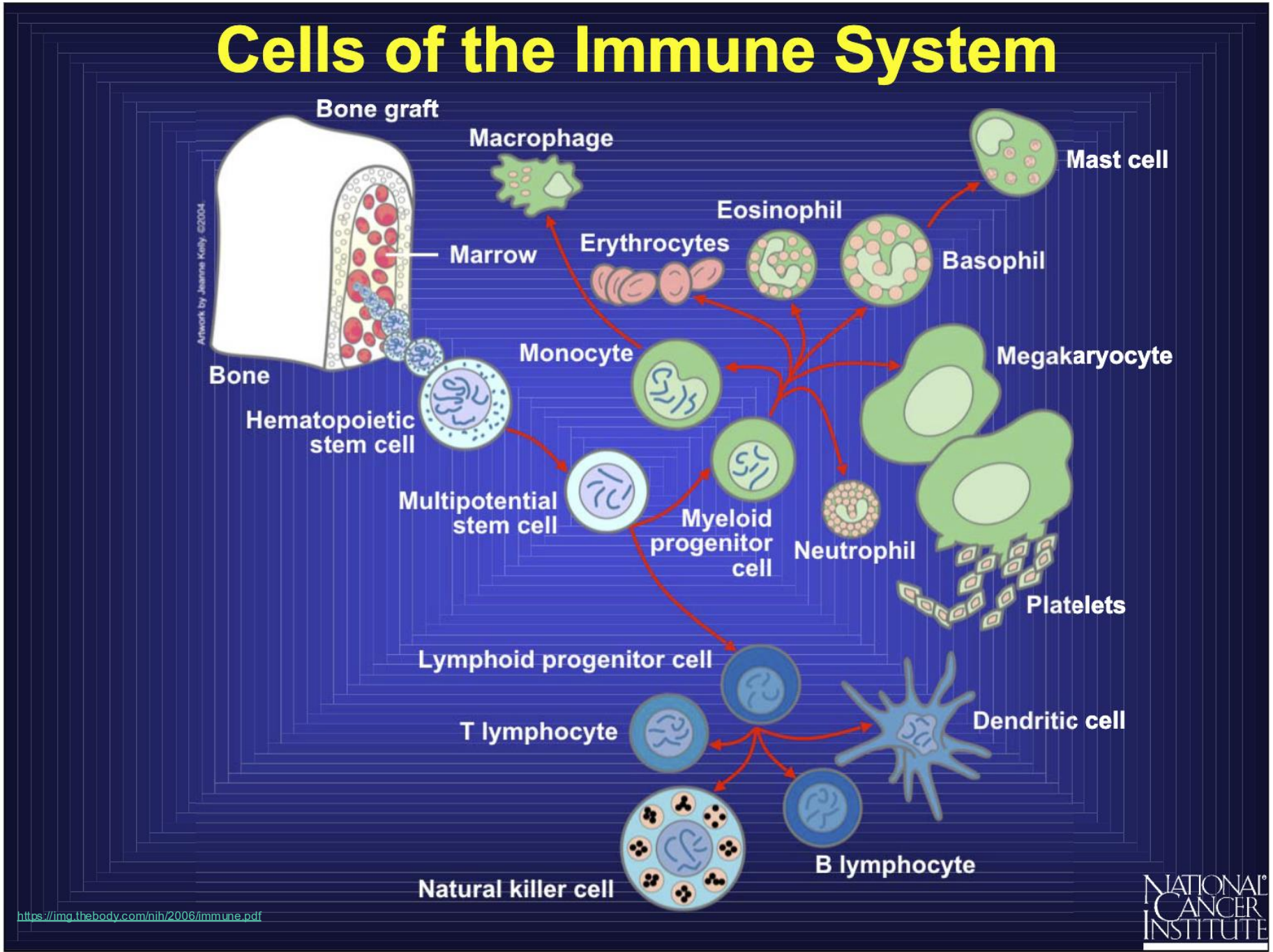


Source: http://www.youtube.com/watch?v=fpOxgAU5fFQ

How do biological immune systems work?



https://img.thebody.com/nih/2006/immune.pdf


Cells of the Immune System
Bone graft
Macrophage
Mast cell
Eosinophil
Erythrocytes
Basophil
Marrow
Monocyte
Megakaryocyte
Bone
Hematopoietic stem cell
Multipotential stem cell
Myeloid progenitor cell
Neutrophil
Platelets
Lymphoid progenitor cell
T lymphocyte
Dendritic cell
B lymphocyte
Natural killer cell
Artwork by Jeanne Kelly. ©2004.
https://img.thebody.com/nih/2006/immune.pdf
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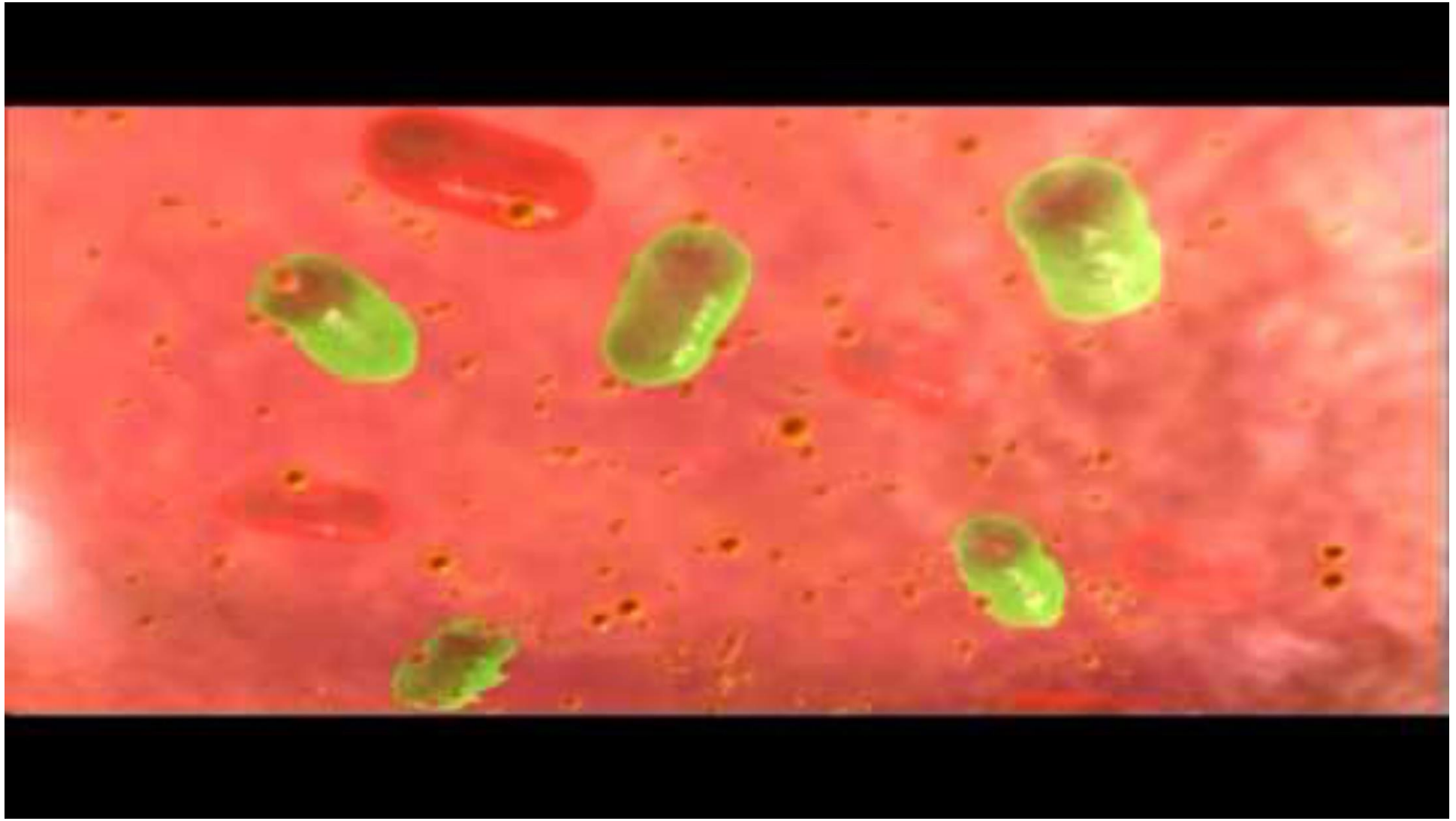
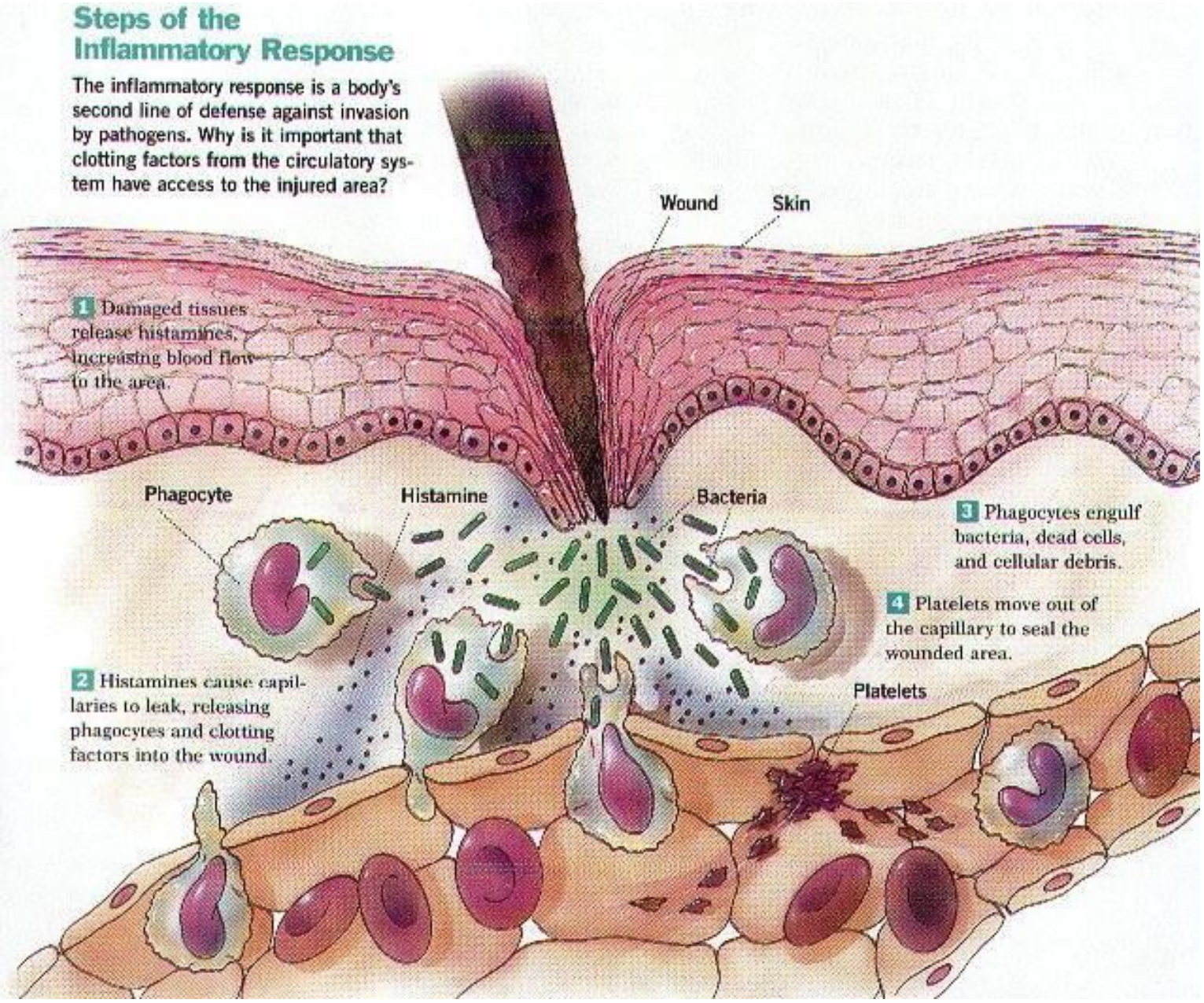
How the Immune System Work



Source: http://www.youtube.com/watch?v=IWMJlMzsEMg



Three Lines of Body Defenses

- Physical and chemical barriers
- Non-specific immunity
- Specific immunity

Physical and Chemical Barriers

- The first line of defense that prevent many pathogens from entering the body.

Skin … Its structure, ability to repair and renew, acidic pH, and antibioitic sweat.

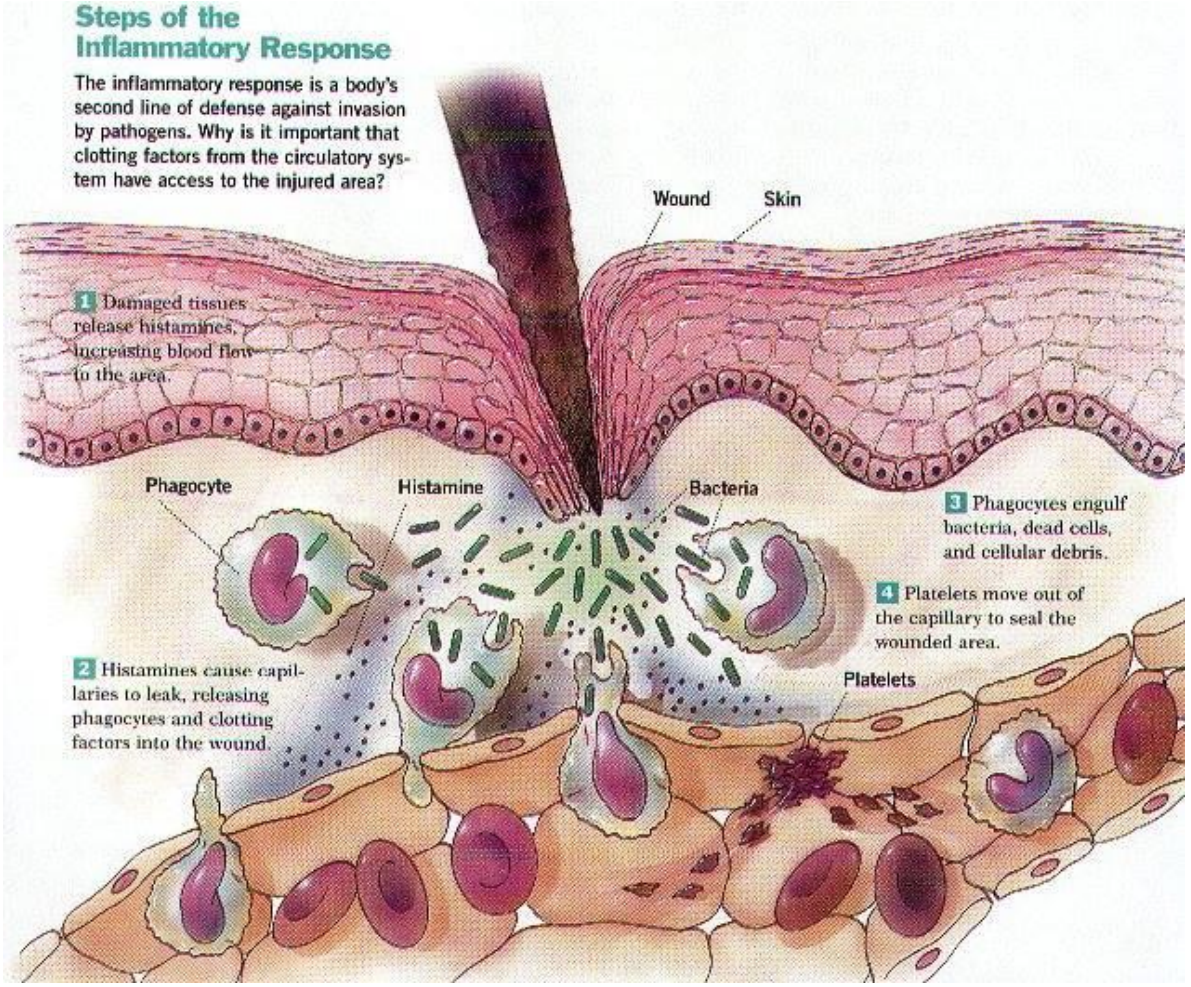
Tears, Saliva, and Earwax … Lubricating, washing away particles, and trapping particles.

Digestive Acids … Strong hydrochloric acid kills nearly all pathogens entering the digestive tract.

Resident Bacteria, i.e., symbiotic bateria … helping control population levels of more harmful organisms by competing against them for food.

Non-Specific Defenses

- If pahogens manage to breach out our physical and chemical barriers and start to kill or damage cells,



Phagocytosis … Phagocytes capture and destroy bacteria.

White blood cells (i.e., neutrophils and macrophages) that destroy foreign cells.

Damage tissues release histamine which increases blood floow to the area.

Histamines cause capillaries to leak, releasing phagocytes and clotting factors into the wound

Phagocytes engulf bacteria dead cells, and cellular debris.

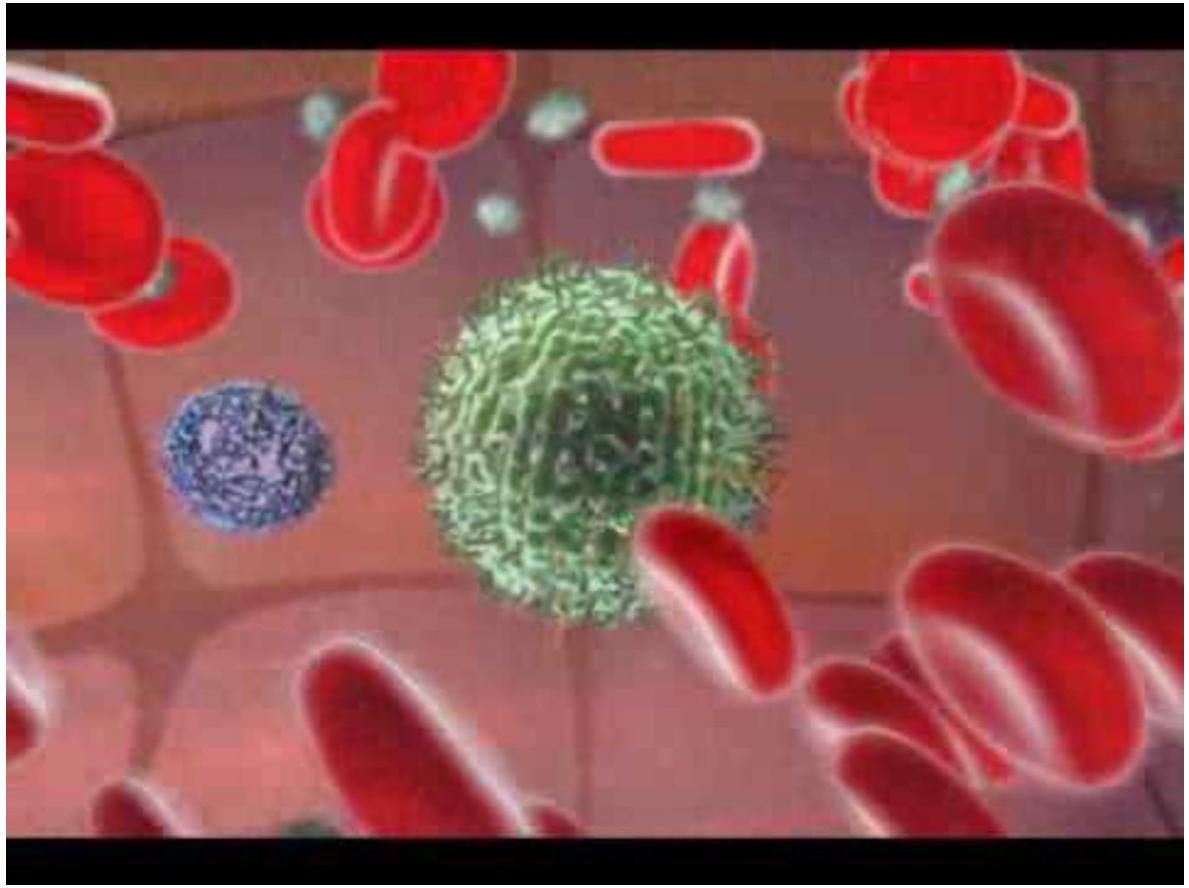
Platelets move out of the capillary to seal the wound area.

Examples for Non-Specific Defenses

Phagocytes

http://www.youtube.com/watch?v=PXUNEJkjQt4

Natural Killer Cells



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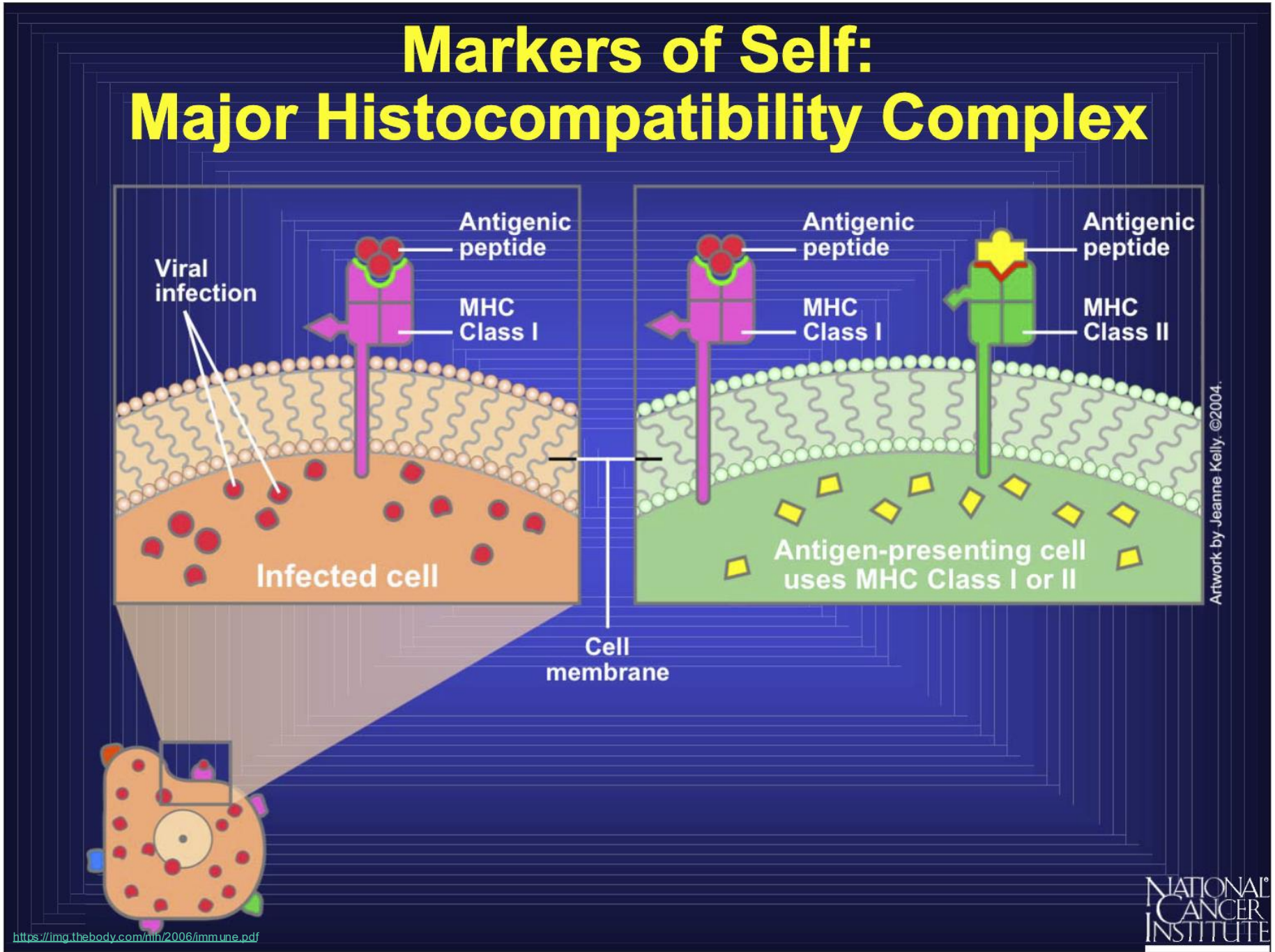
Markers of Self:
Major Histocompatibility Complex
Viral infection
Antigenic peptide
MHC Class I
Infected cell
Cell membrane
Antigenic peptide
MHC Class I
Antigenic peptide
MHC Class II
Antigen-presenting cell uses MHC Class I or II
Artwork by Jeanne Kelly. ©2004.
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https://img.thebody.com/nih/2006/immune.pdf

Specific Defenses

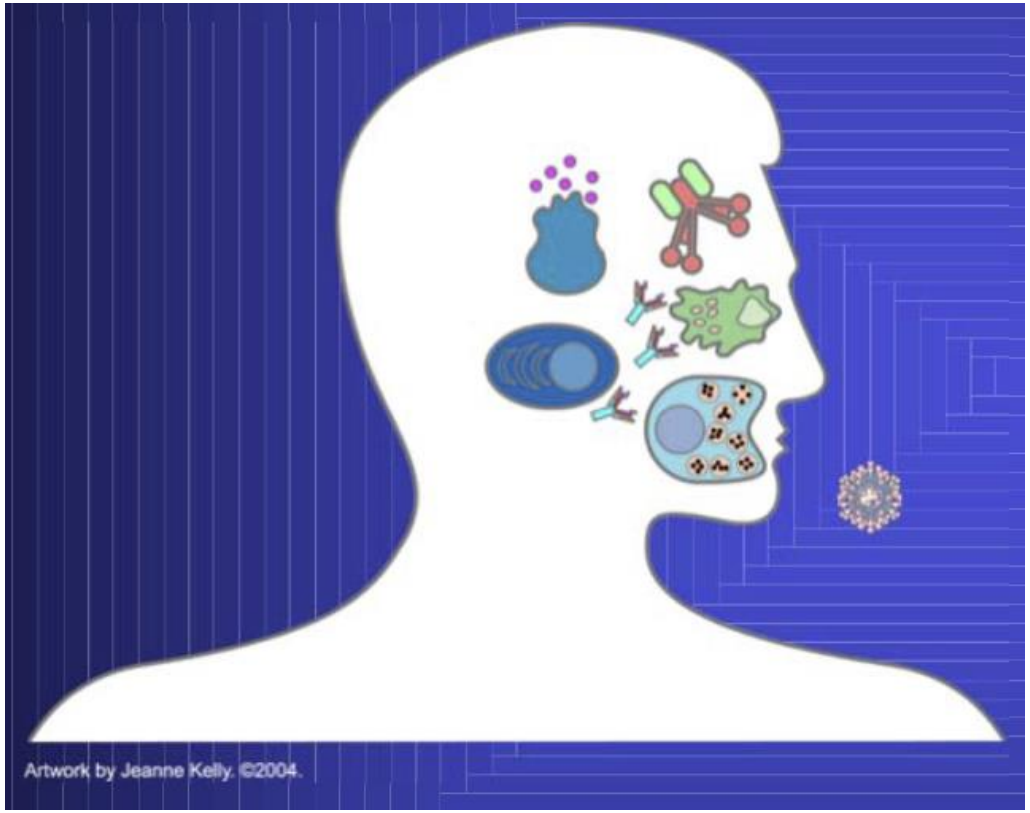
- Specific defense mechanisms exhibit the immune response with **three** characteristics:

1. It recognizes and targets specific pathogens.
2. It has a **memory**, so it can respond more quickly to later invasions by the same pathogen.
3. It protects the entire body (not limited to the site of infection).

The key to specific defenses is the body's ability to distinguish between its own cells and those of foreign invaders.

Self and Non-Self Discrimination

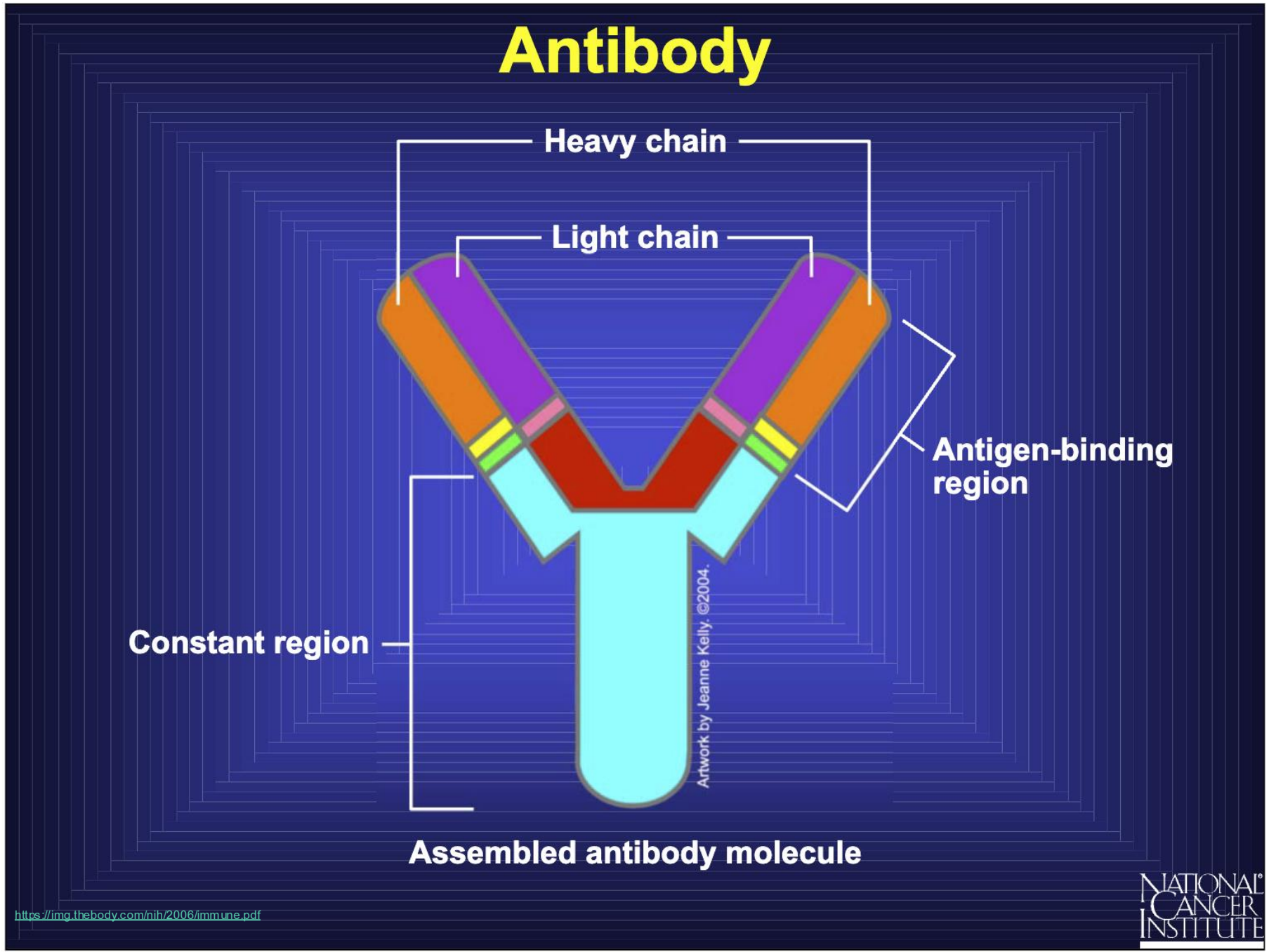
- **Antigen** is any substance that mobilizes the immune system and provokes an immune response.
- Each antigen has **a unique shape** that makes it recognizable.
- Antigens are generally **large protein** or **polysaccaride molecules**.
- Bacteria and viruses all have unique cell surface proteins or polysaccarides (antigens)



Human cells have a unique set of proteins on their surfaces that the immune system uses as **self markers** known as **major histocompatibility complex (MHC)** proteins.

However, the same MHC protein that define your cell as belonging to you would be read as **non-self markers** in another person.

The immune system responds to antigens by producing ANTIBODIES to attack and inactivate the antigens.


Antibody
Heavy chain
Light chain
Antigen-binding region
Constant region
Artwork by Jeanne Kelly. ©2004.
Assembled antibody molecule
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How Antibody Works in Immune Response

https://www.youtube.com/watch?v=IrYlZJiuf18

Cell Mediated Immune Response

https://www.youtube.com/watch?v=1tBOmG0QMbA

Mumoral Mediated Immune Response

https://www.youtube.com/watch?v=hQmaPwP0KRI

Lymphocytes are Central to Specific Defenses

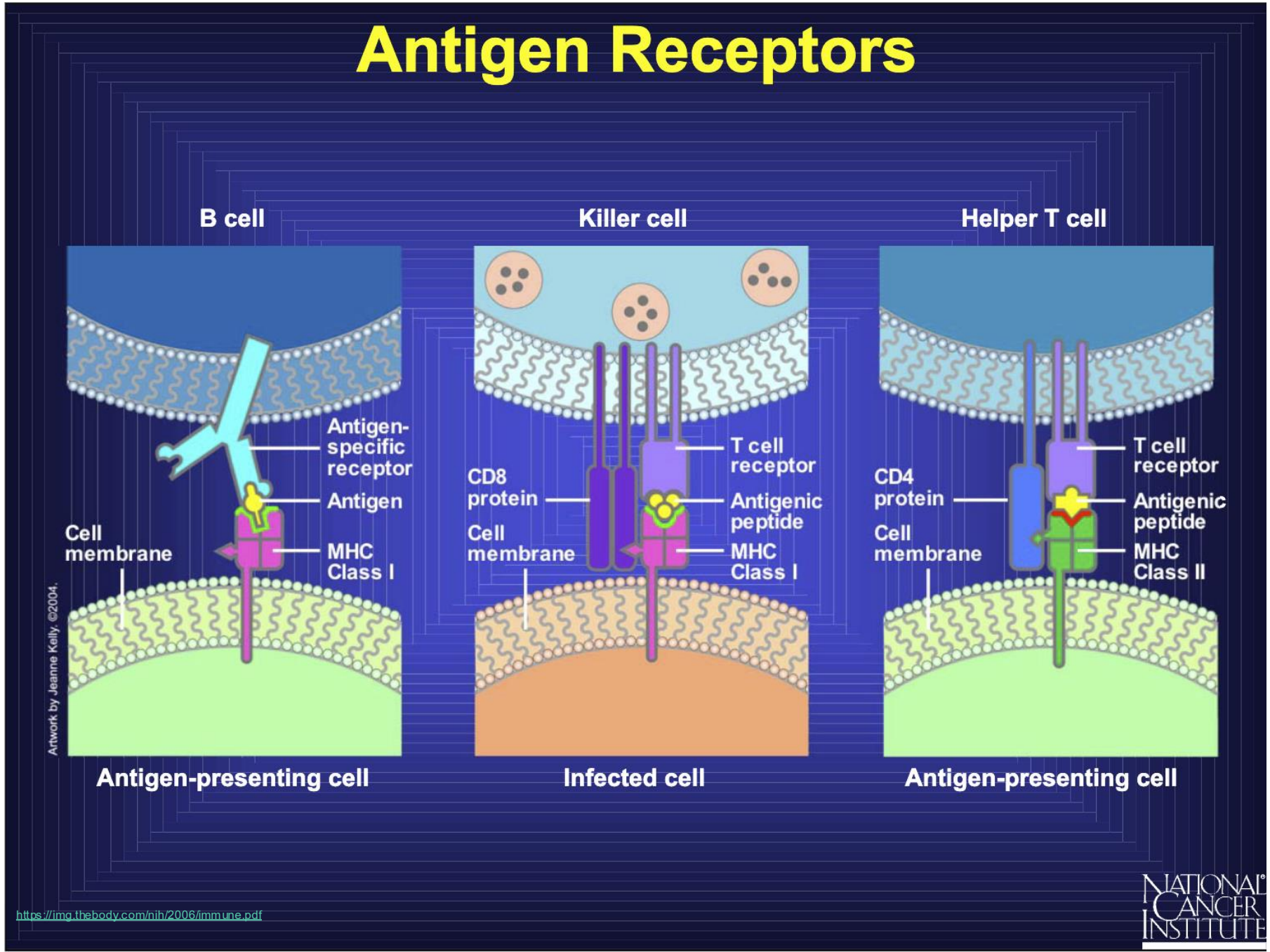
- Lymphocytes are white blood cells originating from stem cells in bone marrow.
- There are two types:
  - T-Lymphocytes or T Cells, maturing in thymus gland
  - B-Lymphocytes or B Cells, maturing in bone marrow
- The both can **recognize and target antigen-bearing cells**, but they perform **in different ways**.

T Cells

- Cell-mediated immunity
- Attack foreign cells that carry antigens directly.
- Release proteins that help coordinate other aspects of the immune response
- Identify and kill infected human cells.

B Cells

- Antibody-mediated immunity
- Produce antibodies
- Release antibodies into bloodstream and lymph.


Antigen Receptors
B cell
Killer cell
Helper T cell
Antigen-specific receptor
Antigen
Cell membrane
MHC Class I
CD8 protein
T cell receptor
Antigenic peptide
MHC Class I
CD4 protein
T cell receptor
Antigenic peptide
MHC Class II
Artwork by Jeanne Kelly. ©2004.
Antigen-presenting cell
Infected cell
Antigen-presenting cell
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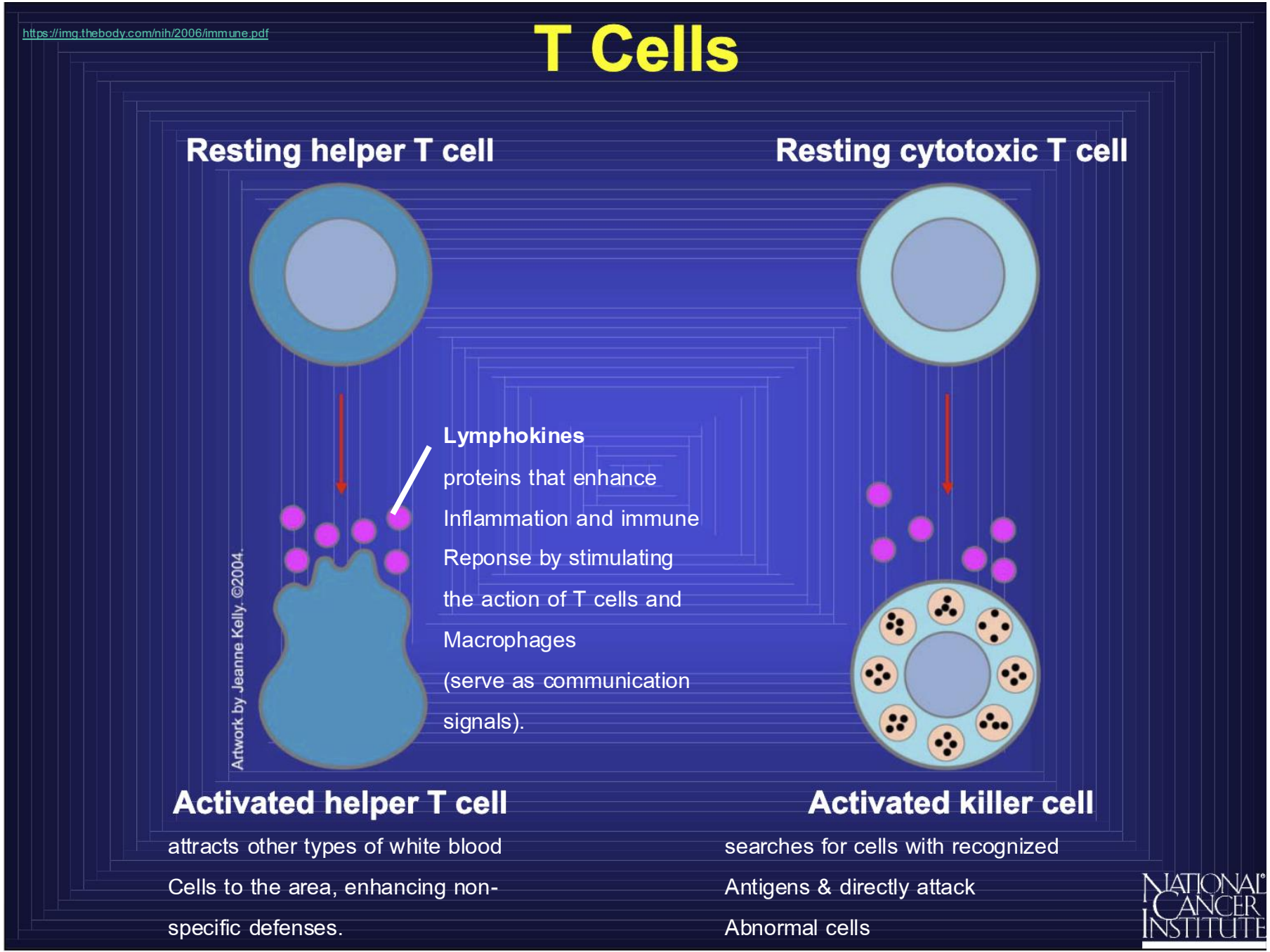
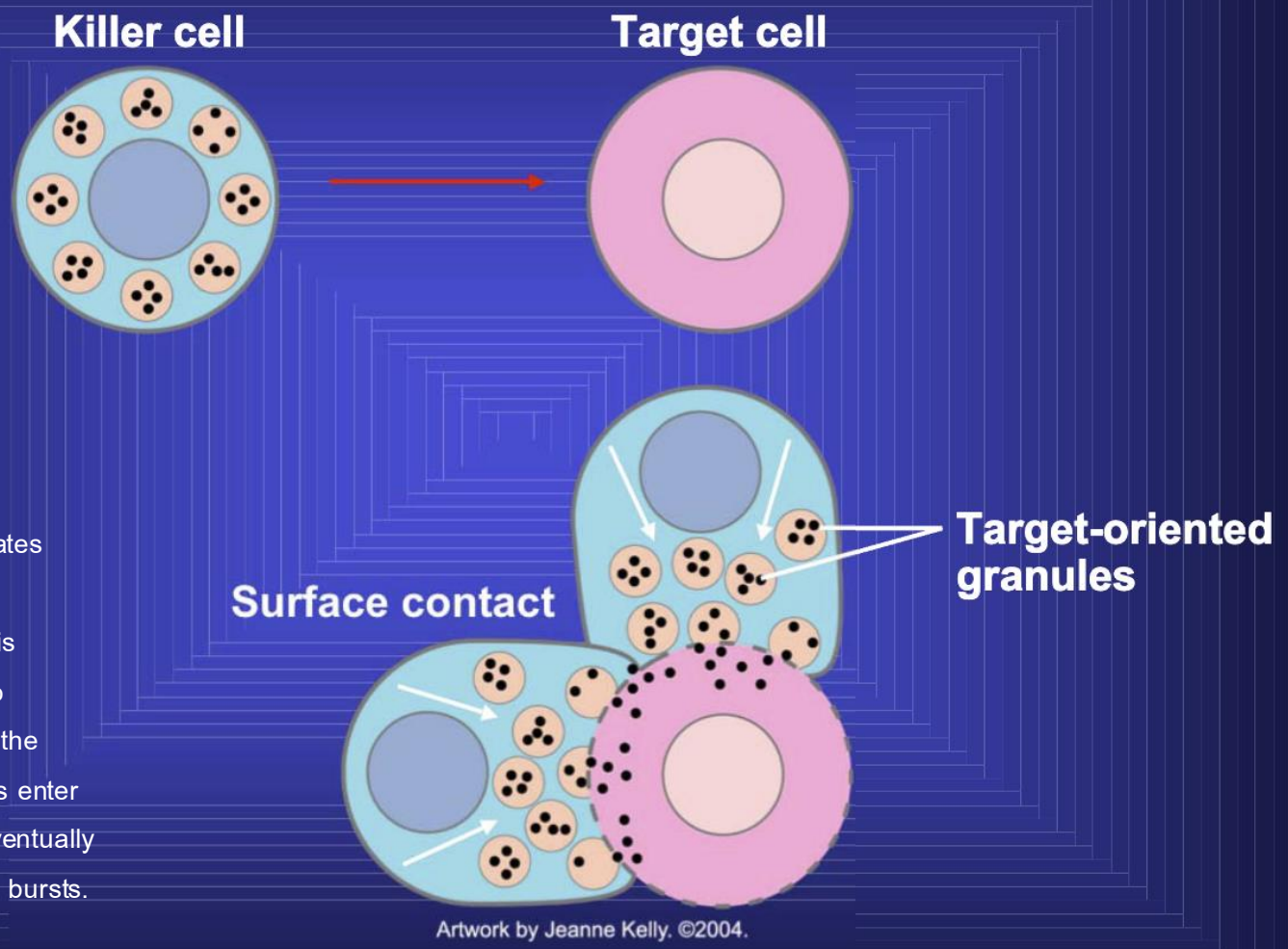
T Cells



Killer Cells: Cytotoxic Ts and NKs



When cytotoxic T cell locates and binds to a target cell, a protein called **perforin** is released and inserted into the plasma membrane of the target cell; water and salts enter Through the holes and eventually The target cell swells and bursts.

https://img.thebody.com/nih/2006/immune.pdf

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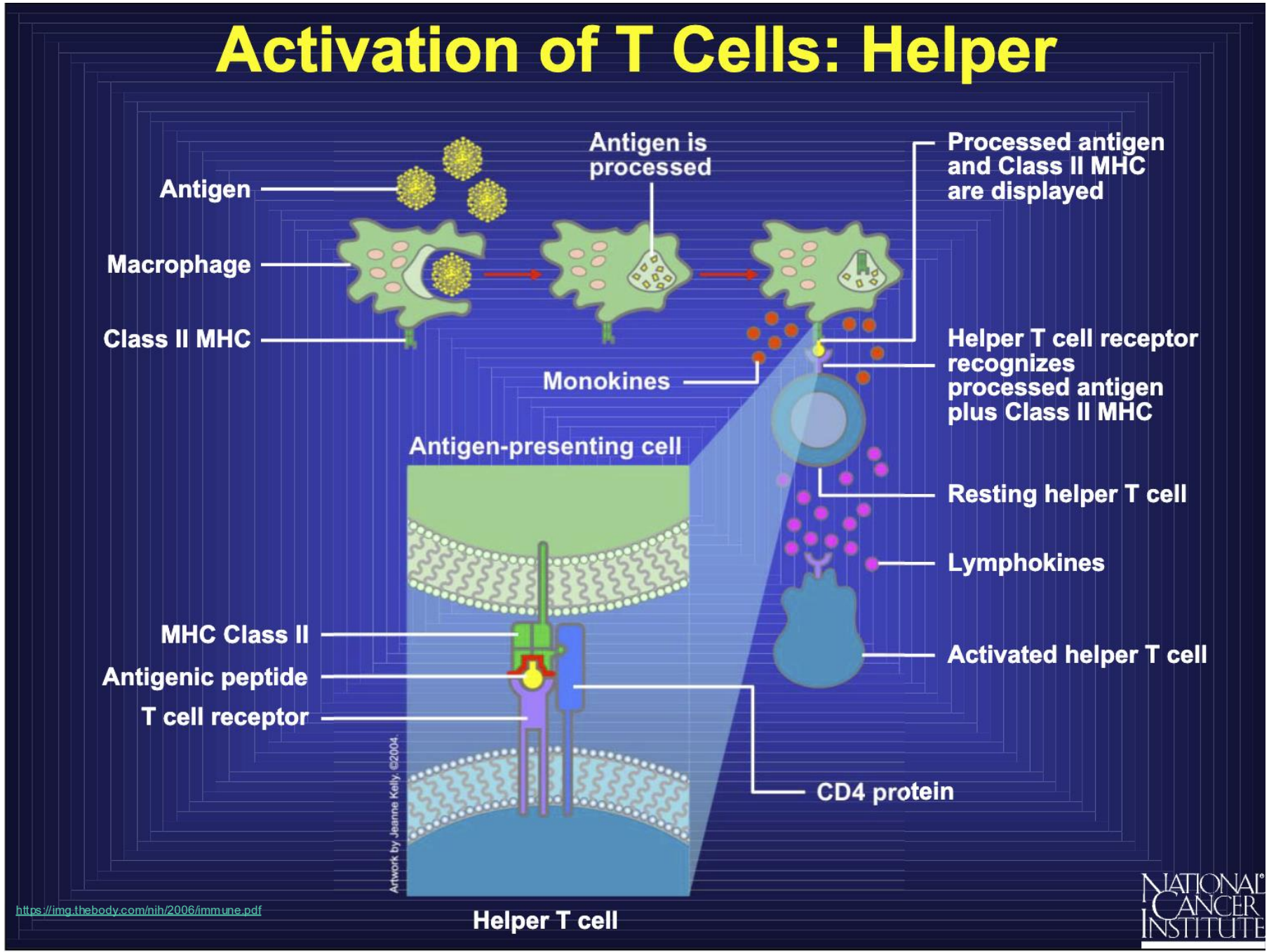
Activation of T Cells: Helper
Antigen
Macrophage
Class II MHC
Antigen is processed
Processed antigen and Class II MHC are displayed
Monokines
Helper T cell receptor recognizes processed antigen plus Class II MHC
Antigen-presenting cell
Resting helper T cell
Lymphokines
Activated helper T cell
MHC Class II
Antigenic peptide
T cell receptor
CD4 protein
Artwork by Jeanne Kelly. ©2004.
Helper T cell
https://img.thebody.com/nih/2006/immune.pdf
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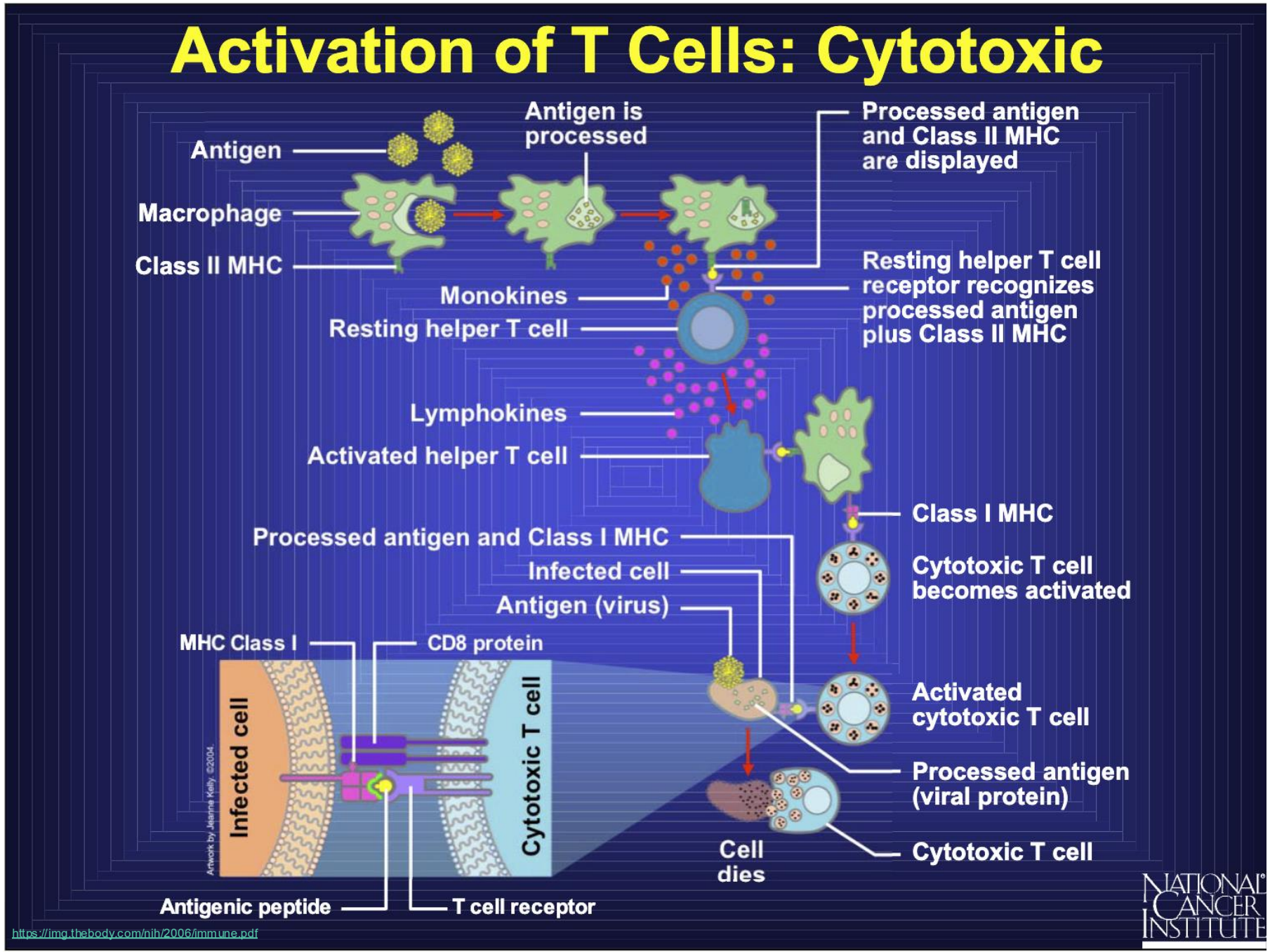

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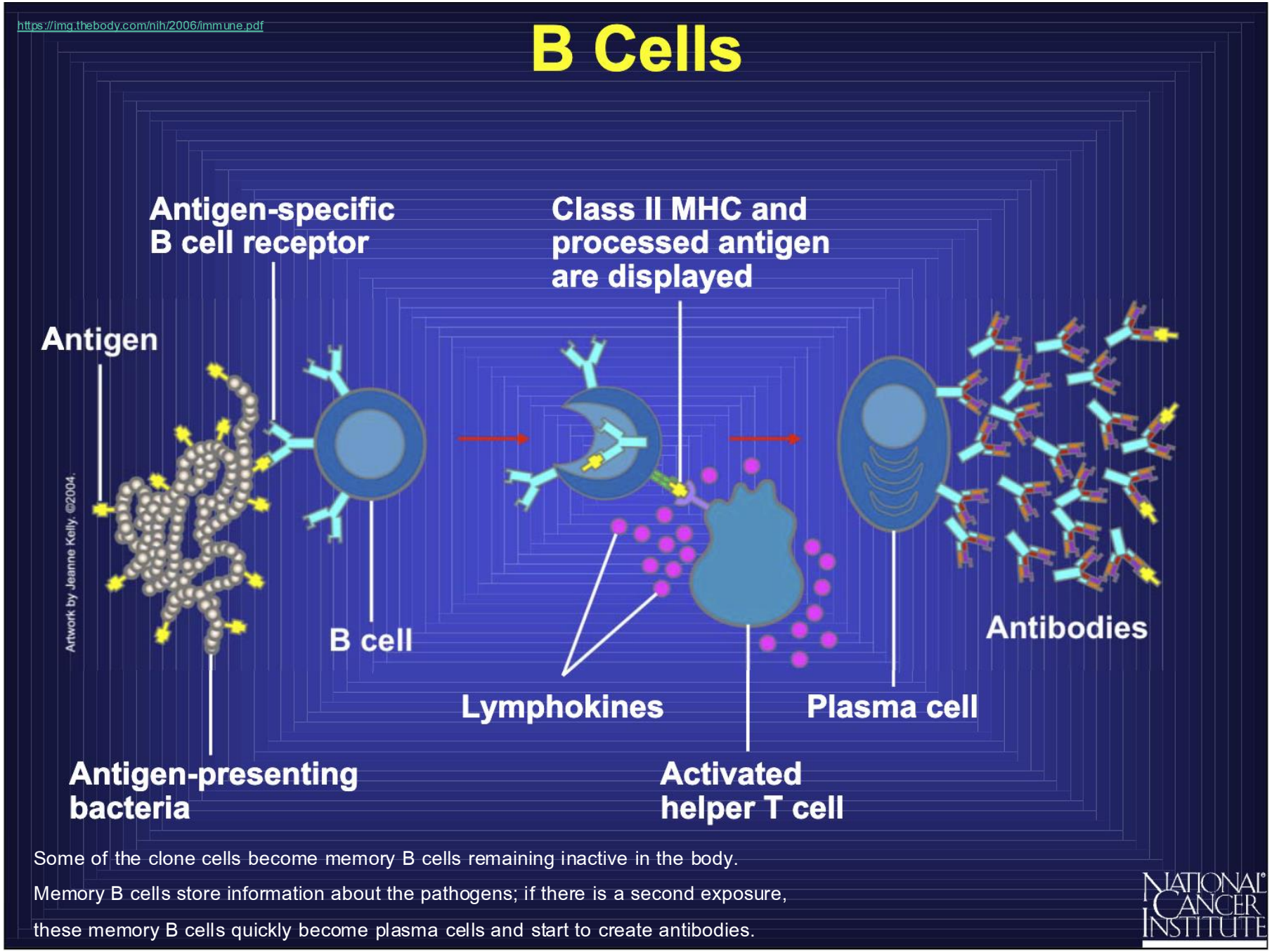
https://img.thebody.com/nih/2006/immune.pdf
B Cells
Antigen-specific
B cell receptor
Class II MHC and
processed antigen
are displayed
Antigen
Artwork by Jeanne Kelly. ©2004.
B cell
Antibodies
Lymphokines
Plasma cell
Antigen-presenting
bacteria
Activated
helper T cell
Some of the clone cells become memory B cells remaining inactive in the body.
Memory B cells store information about the pathogens; if there is a second exposure,
these memory B cells quickly become plasma cells and start to create antibodies.
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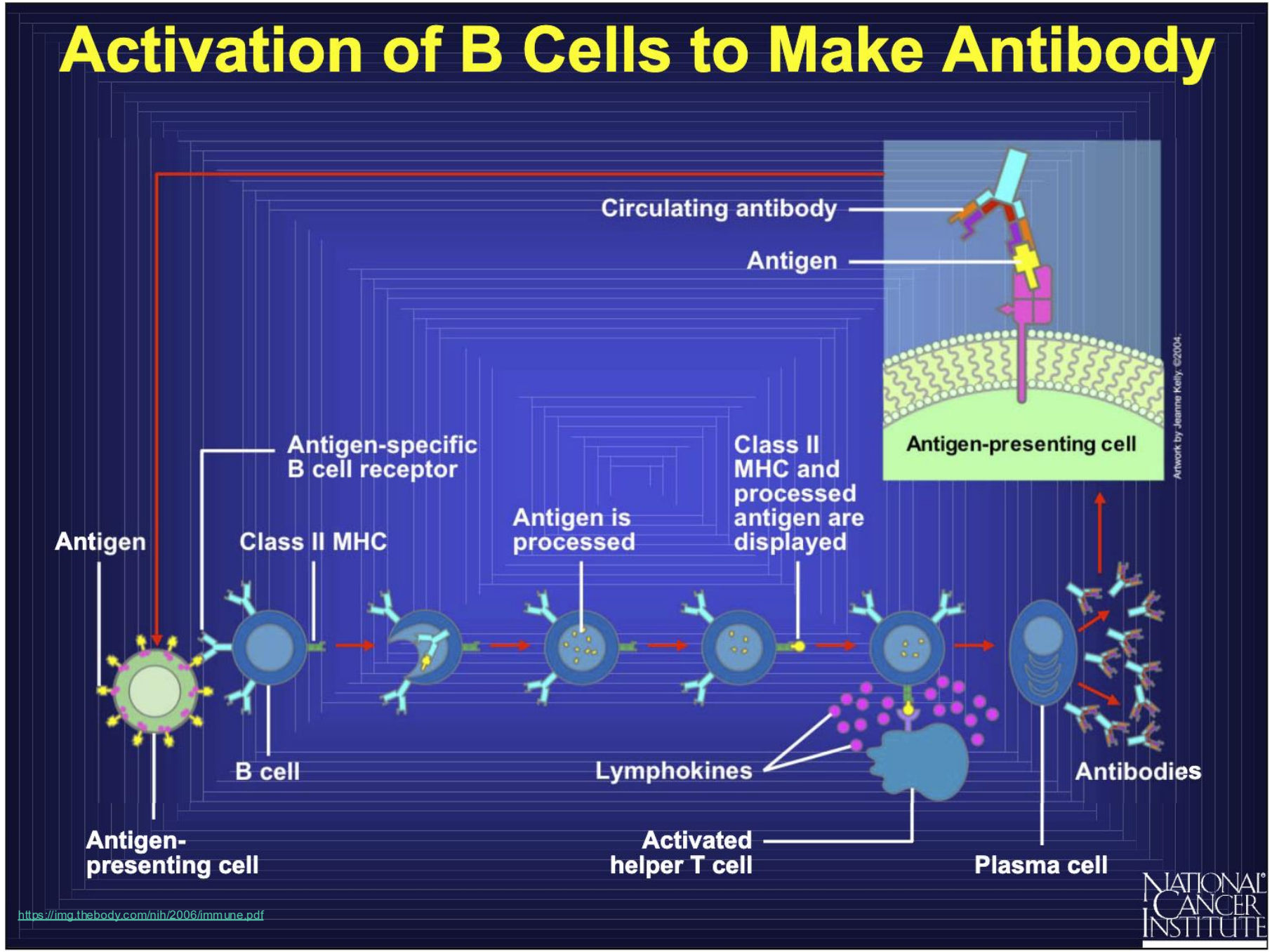
Activation of B Cells to Make Antibody
Circulating antibody
Antigen
Antigen-presenting cell
Artwork by Jeanne Kelly, ©2004.
Antigen-specific B cell receptor
Class II MHC and processed antigen are displayed
Antigen
Class II MHC
Antigen is processed
B cell
Lymphokines
Antibodies
Antigen-presenting cell
Activated helper T cell
Plasma cell
https://img.thebody.com/nih/2006/immune.pdf
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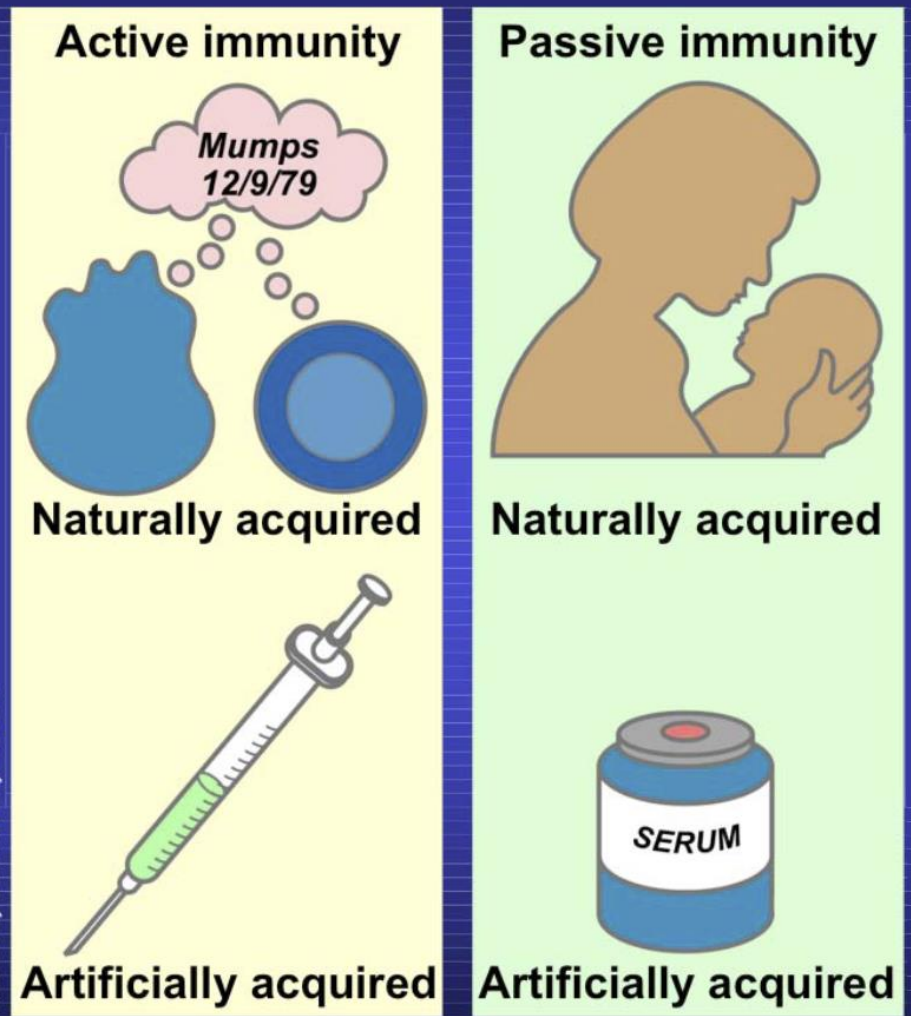
Immunity: Active and Passive

Due to memory-cells, active naturally obtained immunity is permanent. It develops when the body gets infected red blood cells and actively produces antibodies to deactivate the antigens.

Develops when dead organisms or weakened organisms are therapeutically applied. The concept is that special treated organisms keep their antigens without provoking illness-reactions.



It is short-lived since antibodies are continuously broken down without reaction of new antibodies. New antibodies are not created because the antigens did not activate the self immune system.

Obtained when a specific antibody that was produced by another human or animal, is injected into the body for an emergency treatment. Immunity is short-lived, since the immune system is not activated.

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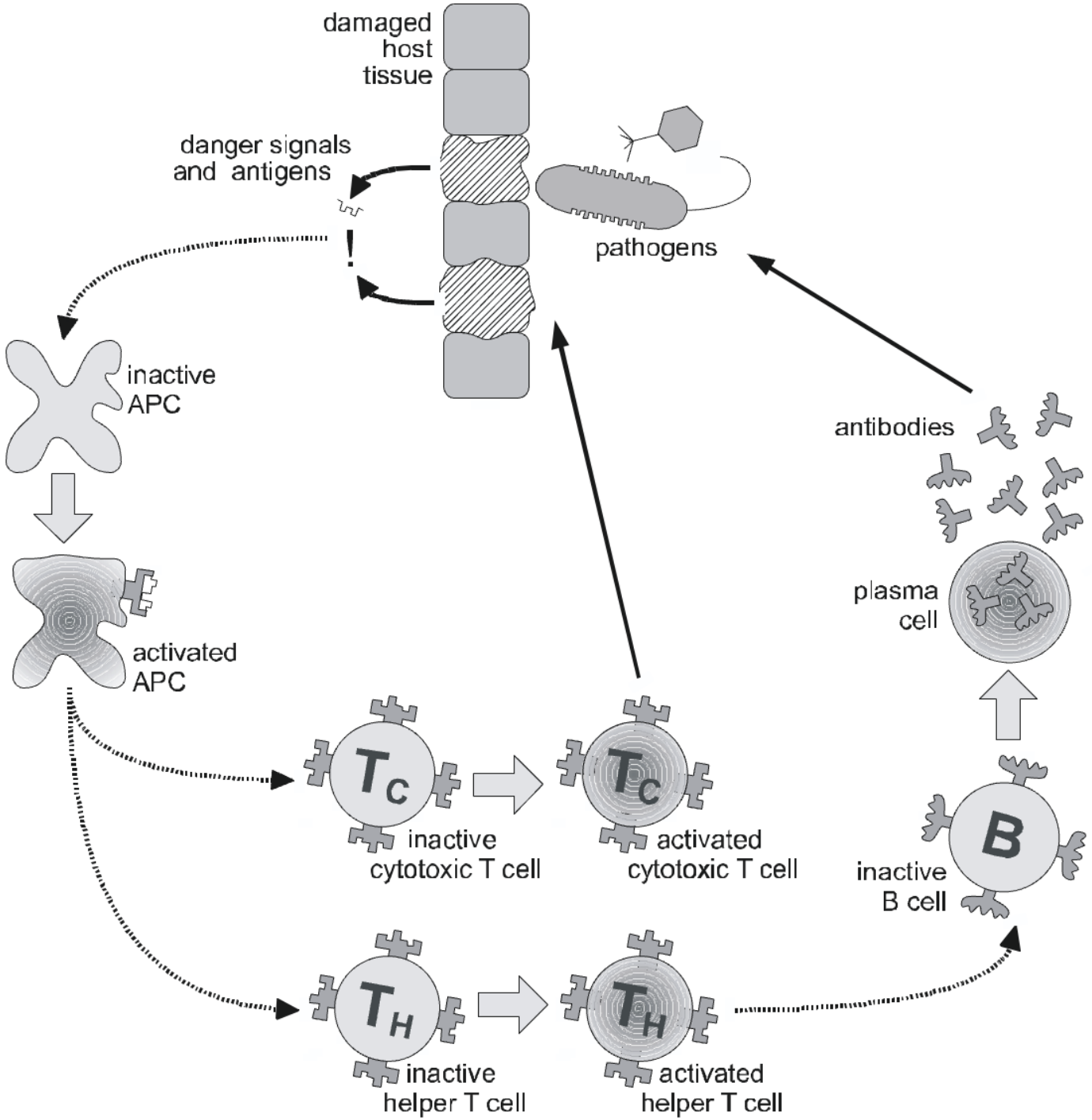
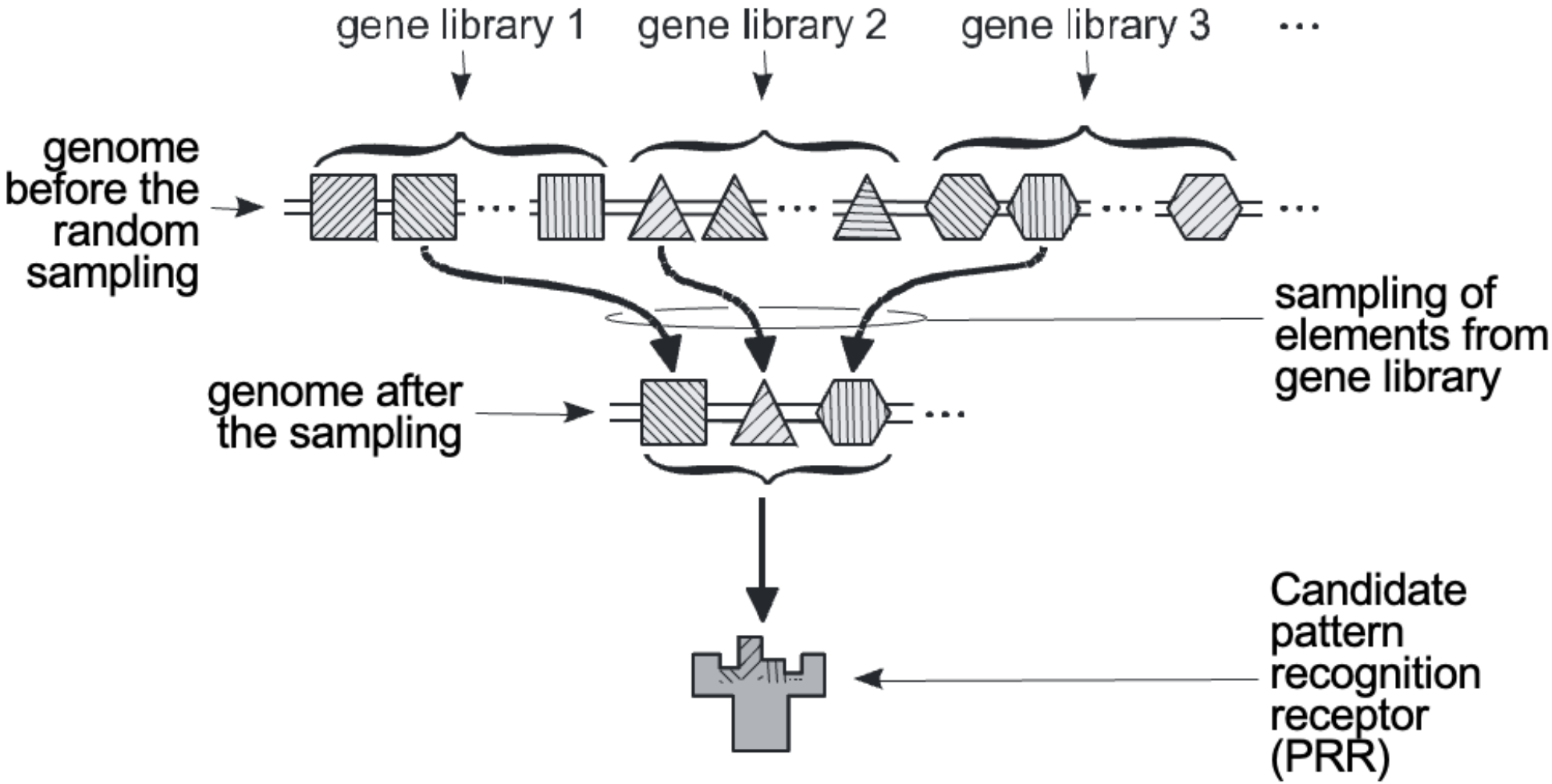
Overview of Adaptive Immunity



Adaptive Immunity

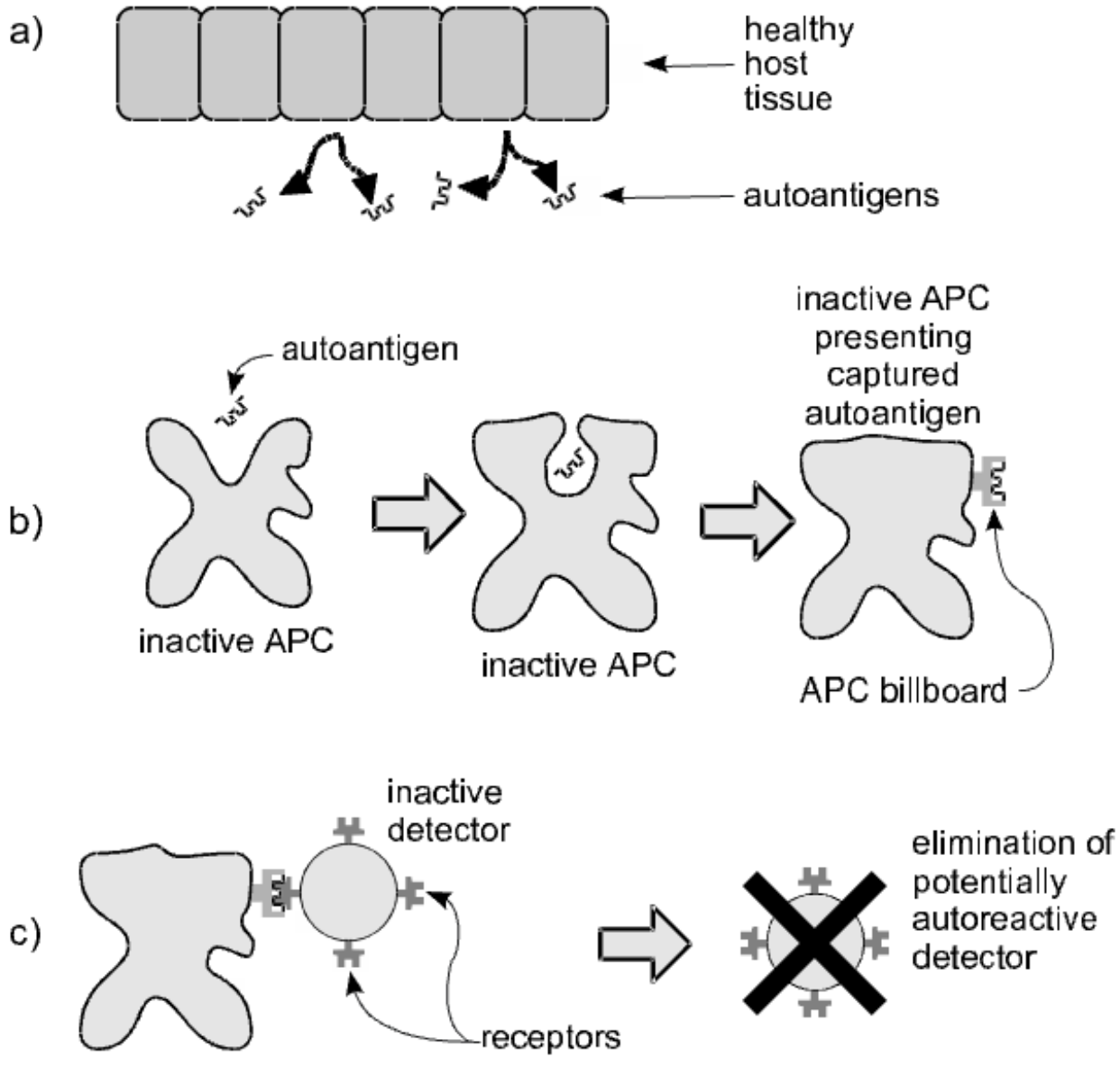
- The adaptive immune system (vertebrates) is also based on a collection of immune detectors and effectors.
- Both **detectors and effectors can change** during the lifetime of the host.
- This requires the definition of a strategy for the generation of detectors and effectors that:
    1. Are effective against pathogens, but
    2. Do not interfere with the normal activity of the host tissues.
- The adaptive immune system uses a multi-stage process.
    1. Generation of inactive elements by random recombination of gene libraries.
    2. Tolerization, i.e., elimination of autoreactive elements by negative selection and of non-reactive elements by limiting their lifespan.
    3. Positive selection of the best non-autoreactive elements
    4. Activation of immune elements according to a notion of context.
    5. Maintenance of a pool of memory elements.

1. Generation via Gene Libraries



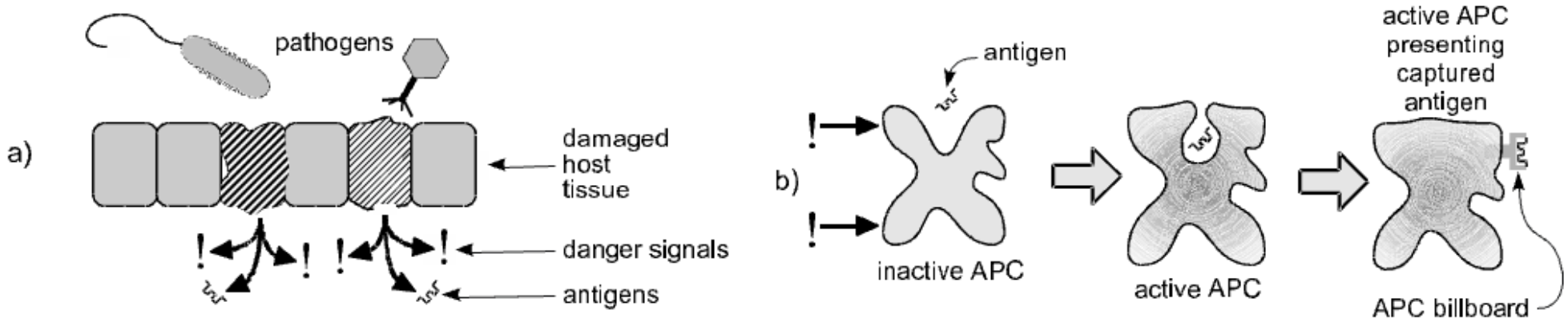
2. Tolerization

- It is based on the activity of antigen presentation of generic cells and of specialized **antigen presenting cells (APCs)**.
- A central tolerization is performed in specialized host regions after the generation of adaptive immune elements.
- Peripheral tolerization is performed while adaptive immune elements criculate in the host body.

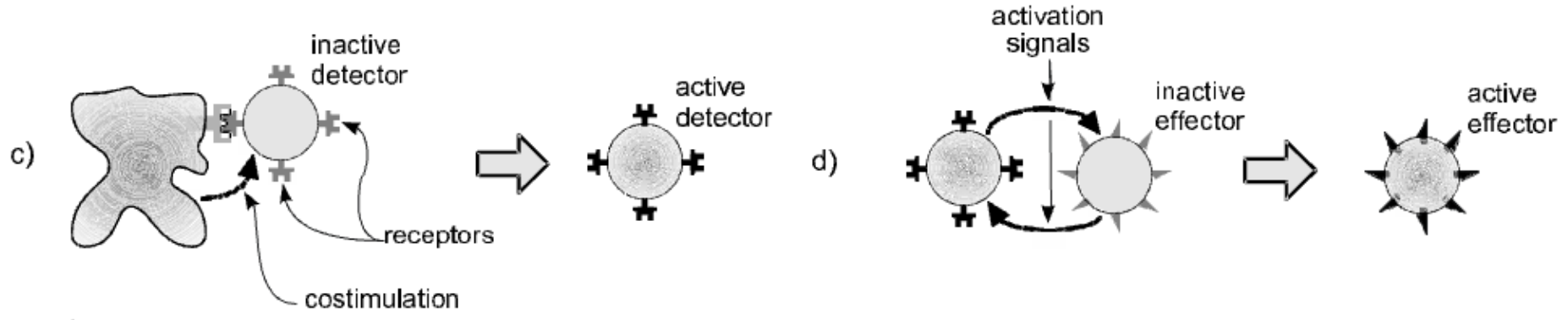


4. Activation of Adaptive Immune Elements

- The damage produced by pathgens results in danger signals which activate the Antigen Presenting Cells (APCs).



- Active APCs activate by costimulation the immune elemens which recognize the antigens presented by the active APC.



Lessons from Biological Immune Systems

1. **Cost:** An adaptive immune system can be expected to be very expensive in term of resources.

2. **Damage and regeneration:** The operation of an immune system can inflict damage to the host; the host must be able to generate new subsystems to replace the ones destroyed.

3. **Design of immunity:** The host is explicitly designed to cooperate with the immune system (e.g., by generating danger signals).

4. **Distributedness, decentralization, self-protection and robustness:** The immune system is a self-organizing distributed system composed by autonomous agents. The control of the immune activity is decentralized. The elements of the immune system can control each other. The immune system is self-protecting and robust to the malfunctioning of individual agents.

5. **Parallel operation and scalability:** scaling to different sizes and complexities of the host requires merely the adaptation of the number of immune elements, not their “reprogramming”.

Lessons from Biological Immune Systems

6. **Mechanisms of adaptation and tolerance:** Mechanism of central tolerance based on a process of positive and negative selection; mechanism of peripheral tolerance based on danger signals.

7. Risk of Autoimmunity

8. **Dynamic allocation of resources and self-limitation:** The resources available to the immune system are dynamically allocated in terms of type of elements and distribution in the host body; the limited lifetime of most immune elements tapers the response when no logner needed.

9. **Mechanisms of generation of diversity:** Recombination of elements of genetically encoded libraries of building blocks rather than random generation of receptors from scratch.

10. **Strategies of detection:** Use of detectors with different modalities of recognition and different specificity; presentation of multiple “views” of the pathogen.

11. **Learning and memory**

Artificial Immune Systems for Computers

- Human-built systems (e.g., a network of computers) must also be protected from attempts to exploit their resources (computational power, data, identity, etc.).
- Some unauthorized operations are executed at a low level in the hierarchy of software levels of the computer system.
  - They do not immediately affect the scale of the computer user or network administrator interface.
  - Strategies of attack can change rapidly.
- Isolation of the computing system is seldom an option.
- **The current solution:** Antivirus and intrusion detection systems designed and updated by specialized firms.
- **A better solution:** A protection system capable of autonomously detecting and opposing attempts at intrusion and exploitation, that is, an artificial immune system (AIS).
- An AIS might also detect and correct (sub)system malfunctioning.

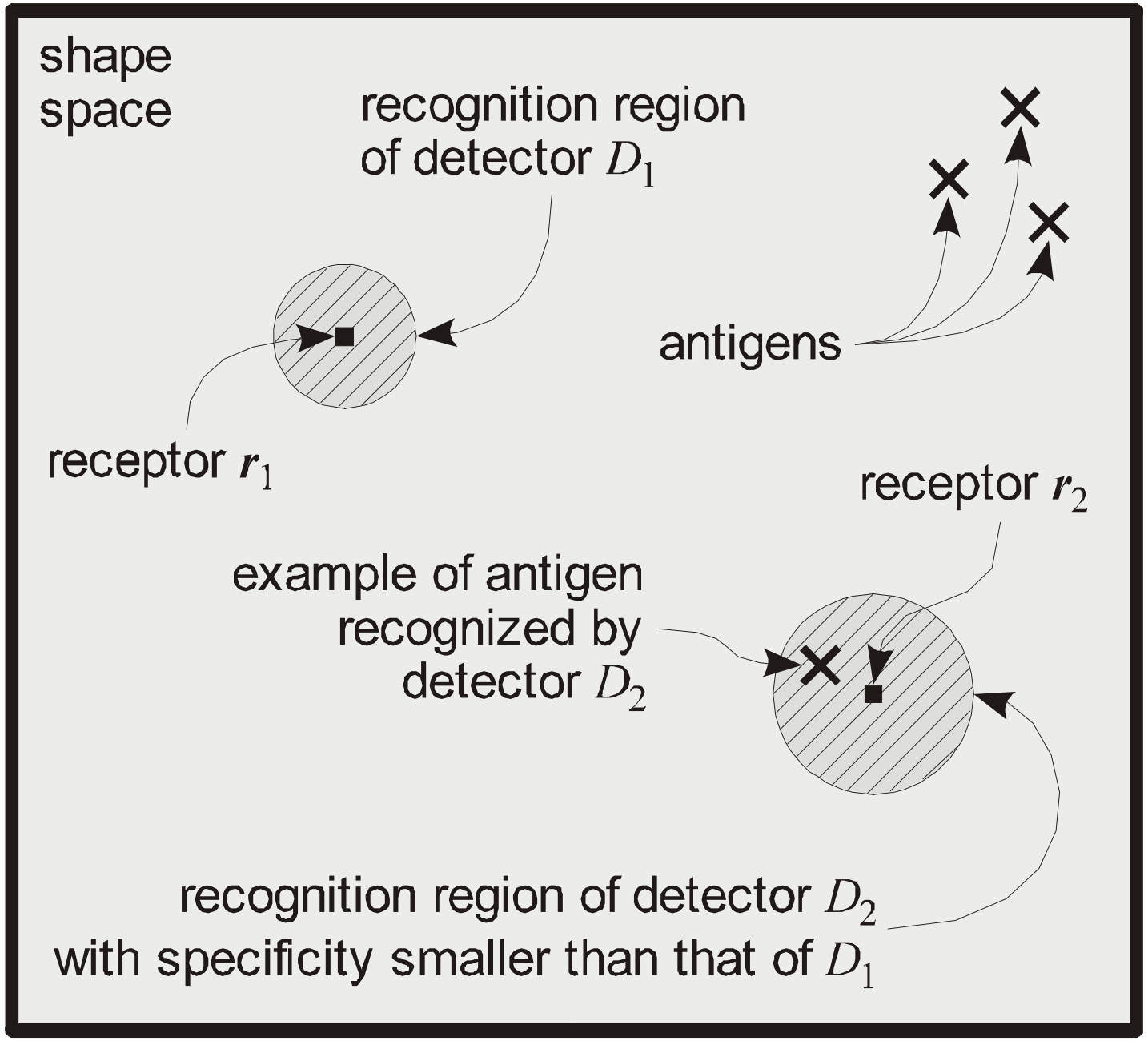
Artificial Immune Systems

- Model the natural immune system's ability to detect cells foreign to the body.
- Powerful pattern recognition abilities
- These models include:
  - **Classical view** of lymphocytes that are used to distinguish between self and non-self,
  - **Clonal selection theory** where stimulated B-cells produce mutated clones,
  - **Danger theory**, which postulates that the AIS has the ability to distinguish between dangerous and safe foreign cells, and
  - **Network theory** where it is assumed that B-cells form a network of detectors.

Shape Space

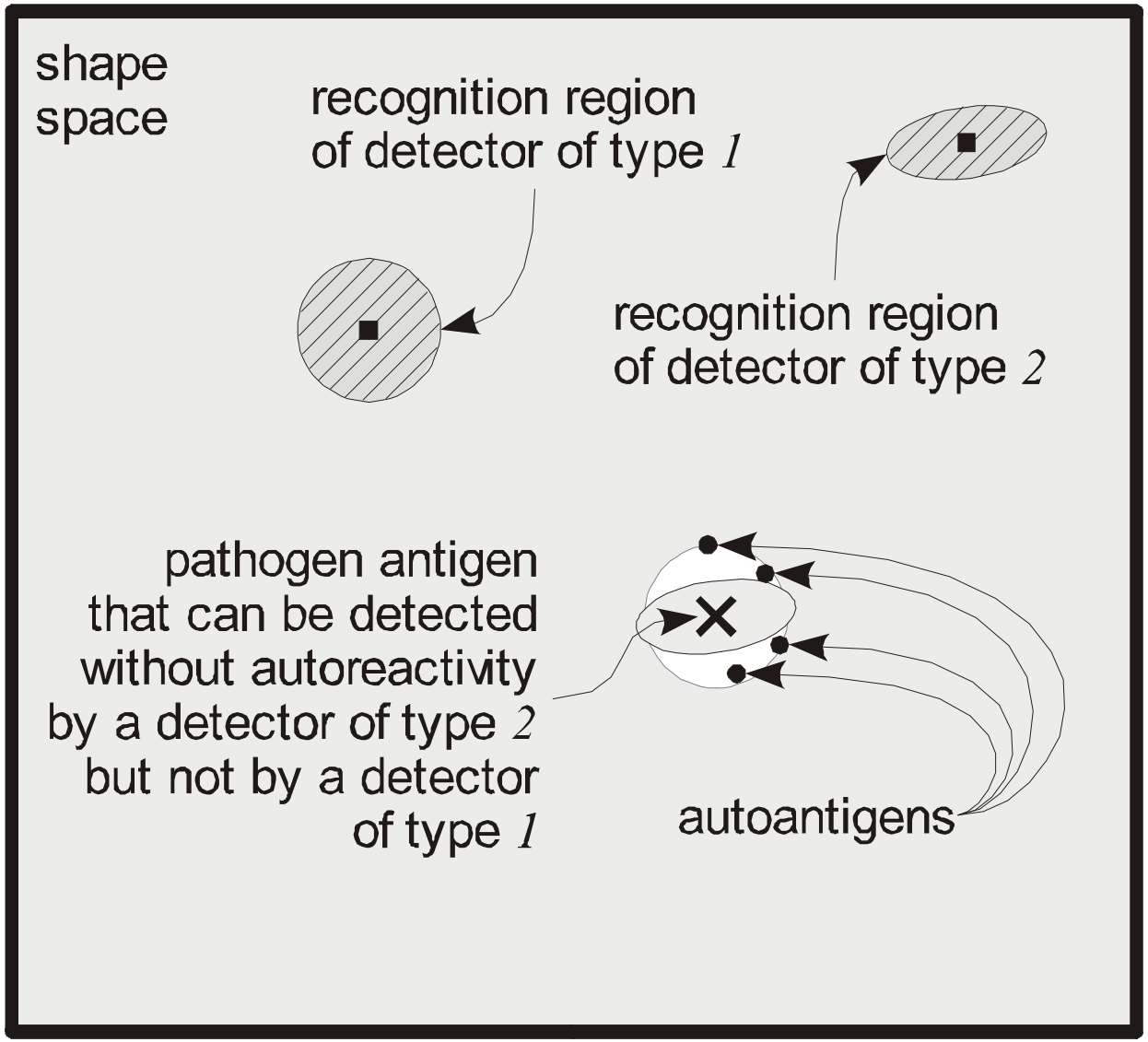
- It is an abstraction that give a geometrical interpretation to the process of recognition of an antigen from the part of an immune detectors.
- The goal is to obtain a simplified model of the action of the immune system to be used in the analysis and design of artificial immune systems.
- The properties of the antigen and of the receptor are represented with a list of l paramenters called **the generalized shape**.
- We specify a measure of the affinity between **the receptor** r and **the antigen** a by defining **a distance** $d(a, r)$ in the shape space (Euclidean distance, Hamming distance, …)
- We say that **a detector** D equipped with receptors of type r recognizes an antigen a if $d(a, r)$ is below a certain **threshold** θ.
  - The value of the threshold determines the specificity of the detector
  - The region of shape space thus defined is the recognition region of D
- The union of the recognition regions of all the detectors of an immune system is called its **immune repertoire**,

Shape Space


shape space
recognition region of detector D_1
antigens
receptor r_1
receptor r_2
example of antigen recognized by detector D_2
recognition region of detector D_2 with specificity smaller than that of D_1

Holes in Immune Repertoire

- Ideally, the immune repertoire should cover all the regions of space that do not correspond to autoantigens.
- If this is not the case, we say that the immune repertoire has **holes** that can be potentially exploited by a pathogen to escape detection.
- A technique reduces the possiblilty of there being holes consists in implementing several distinct distance functions.



Basic AIS Algorithm

Basic AIS Algorithm

Algorithm 19.1 Basic AIS Algorithm

Initialize a set of ALCs as population $\mathcal{C}$;
Determine the antigen patterns as training set D_T;
while *some stopping condition(s) not true* **do**
    for *each antigen pattern* $\mathbf{z}_p \in D_T$ **do**
        Select a subset of ALCs for exposure to $\mathbf{z}_p$, as population $\mathcal{S} \subseteq \mathcal{C}$;
        for *each ALC,* $\mathbf{x}_i \in \mathcal{S}$ **do**
            Calculate the *antigen affinity* between $\mathbf{z}_p$ and $\mathbf{x}_i$;
        end
        Select a subset of ALCs with the highest calculated *antigen affinity* as population $\mathcal{H} \subseteq \mathcal{S}$;
        Adapt the ALCs in $\mathcal{H}$ with some *selection* method, based on the calculated *antigen affinity* and/or the *network affinity* among ALCs in $\mathcal{H}$;
        Update the *stimulation level* of each ALC in $\mathcal{H}$;
    end
end

Basic AIS Algorithm

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    Update the *stimulation level* of each ALC in $\mathcal{H}$;
  end
end

The population C can either be populated with randomly generated artificial lymphocyte (ALC) or with ALCs that are initialized with a cross section of the data set to be learned. If a cross section of the data set is used to initialize the ALCs, the complement of the dataset will determine the training set D_T

Basic AIS Algorithm

Algorithm 19.1 Basic AIS Algorithm

Initialize a set of ALCs as population $\mathcal{C}$;
Determine the antigen patterns as training set D_T;
while *some stopping condition(s) not true* **do**
    for *each antigen pattern* $\mathbf{z}_p \in D_T$ **do**
        Select a subset of ALCs for exposure to $\mathbf{z}_p$, as population $\mathcal{S} \subseteq \mathcal{C}$;
        for *each ALC,* $\mathbf{x}_i \in \mathcal{S}$ **do**
            Calculate the *antigen affinity* between $\mathbf{z}_p$ and $\mathbf{x}_i$;
        end
        Select a subset of ALCs with the highest calculated *antigen affinity* as population $\mathcal{H} \subseteq \mathcal{S}$;
        Adapt the ALCs in $\mathcal{H}$ with some *selection* method, based on the calculated *antigen affinity* and/or the *network affinity* among ALCs in $\mathcal{H}$;
        Update the *stimulation level* of each ALC in $\mathcal{H}$;
    end
end

In most of the discussed AIS models, the stopping criteria condition is based on convergence of the ALC population or a preset number of iterations.

Basic AIS Algorithm

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  for *each antigen pattern* $\mathbf{z}_p \in D_T$ **do**
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      Calculate the *antigen affinity* between $\mathbf{z}_p$ and $\mathbf{x}_i$;
    end
    Select a subset of ALCs with the highest calculated *antigen affinity* as population $\mathcal{H} \subseteq \mathcal{S}$;
    Adapt the ALCs in $\mathcal{H}$ with some *selection* method, based on the calculated *antigen affinity* and/or the *network affinity* among ALCs in $\mathcal{H}$;
    Update the *stimulation level* of each ALC in $\mathcal{H}$;
  end
end

The selected subset S can be the entire set P or a number of randomly selected ALCs from P. Selection of S can also be based on the stimulation level.

Basic AIS Algorithm

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    Adapt the ALCs in $\mathcal{H}$ with some *selection* method, based on the calculated *antigen affinity* and/or the *network affinity* among ALCs in $\mathcal{H}$;
    Update the *stimulation level* of each ALC in $\mathcal{H}$;
  end
end

The antigen affinity is the measurement of similarity or dissimilarity between an ALC and an antigen pattern. The most commonly used measure of affinity in existing AIS models are the Euclidean distance, r-contiguous matching rule, hamming distance and cosine similarity.

Basic AIS Algorithm

Algorithm 19.1 Basic AIS Algorithm

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    Update the *stimulation level* of each ALC in $\mathcal{H}$;
  end
end

In some of the AIS models, the selection of the highest affinity ALCs is based on a preset affinity threshold. Thus, the selected subset H can be the entire set S, depending on the preset affinity threshold.

Basic AIS Algorithm

Algorithm 19.1 Basic AIS Algorithm

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    Update the *stimulation level* of each ALC in $\mathcal{H}$;
  end
end

Adaptation of ALCs can be seen as the maturation process of the ALC, supervised or unsupervised. Some of the selection methods that can be used are negative selection (or positive selection), clonal selection and/or some evolutionary technique with mutation operators. ALCs that form a network can influence each other to adapt to an antigen.

Basic AIS Algorithm

Algorithm 19.1 Basic AIS Algorithm

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    Adapt the ALCs in $\mathcal{H}$ with some *selection* method, based on the calculated *antigen affinity* and/or the *network affinity* among ALCs in $\mathcal{H}$;
    Update the *stimulation level* of each ALC in $\mathcal{H}$;
  end
end

The stimulation level is calculated in different ways in existing AIS models. In some AIS models, the stimulation level is seen as the summation of antigen affinities, which determines the resource level of an ALC. The stimulation level can also be used to determine a selection of ALCs as the memory set. The memory set contains the ALCs that most frequently match an antigen pattern; thus, memory status is given to these ALCs.

Project Assignment 3: Artificial Immune Systems

- Use the problem you formulated and find an optimal solution using one of the following algorithms:
  - **AIS using Negative Selection**
  - **AIS using Clonal Selection**
  - **Immune Network Model**

End of the Lecture

Please don’t hesitate to raise your hand and ask questions if you're curious about anything!