



COVID-19 & The Immune System

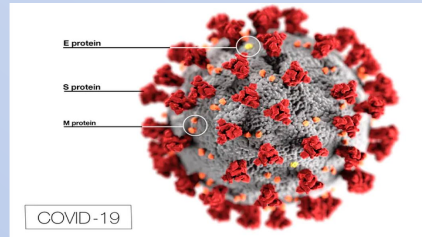
Part 2: The Adaptive Immune Response

Gillian S. Backus, Ph.D.

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<https://vaccinemakers.org/resources/videos-animations>

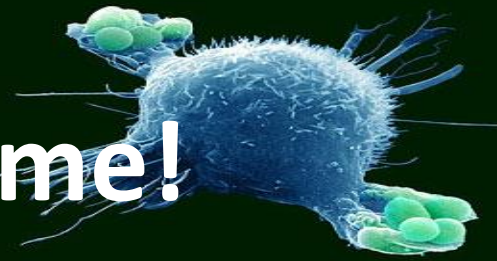
What you will learn today



1. Recognizing what belongs
2. Sounding the alarm (call 911!)
3. Launching the Battle
 1. Training the Troops (B-cell method, T-cell method)
 2. Eliminating the ones who fail.
4. Learning from the Battle
 1. Memory – immunization



Send it to me!



Draw a multi-panel cartoon depicting the adaptive immune response as your body fights COVID-19.

Remember: COVID-19 is a VIRUS. It hides out inside cells, but also breaks out of cells in search of other cells to infect.

How the adaptive immune response attack viruses while inside infected cells or inside macrophages?

How does the adaptive immune response attack viruses when they are released from cells?

Draw both methods as they happen!



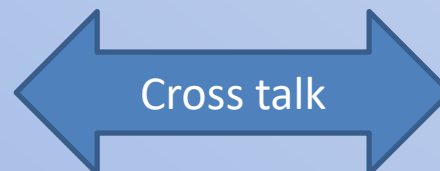
The two arms of the immune response

Innate Immune Response

- Fast-acting
- Non-specific
- No memory
- Requires cells (macrophages NK cells)
- Cytokine Storm!!!
- Generates inflammation and fever

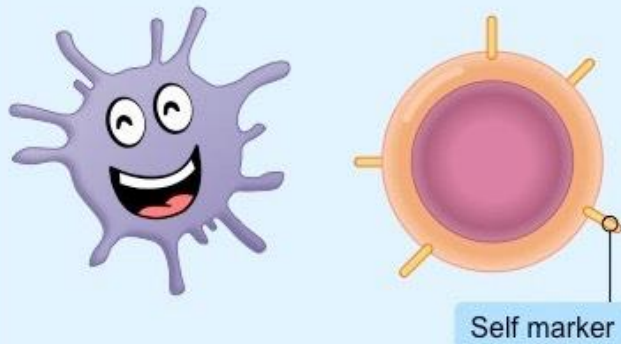
Adaptive Immune Response

- Slower-acting
- Specific
- Memory produced
- Requires cells (lymphocytes)
 - B-cells (make antibodies)
 - T-cells (cytotoxic T cells)



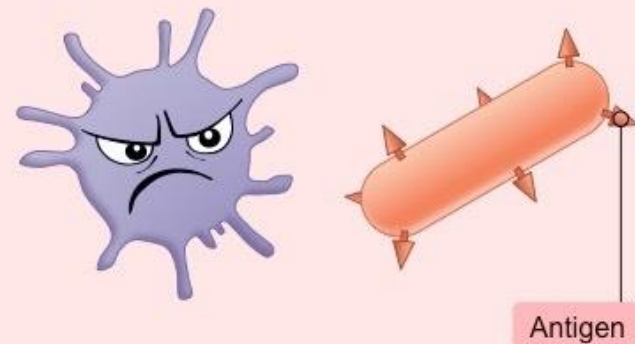


IDENTIFYING SELF



A **self marker** (MHC) labels the body's cells as a *'friend'* and are tolerated by the immune system.

IDENTIFYING NON-SELF



An **antigen** is a molecule that the immune system recognises as foreign (non-self) and treats as a *'foe'*.

ADAPTIVE IMMUNE RESPONSE



Our cells



Our immune cells



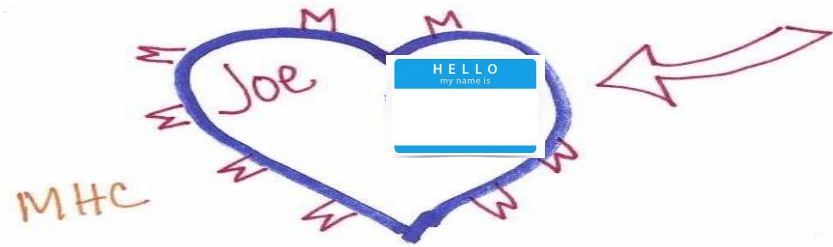
Foreign cells

Viruses and bacteria

Awareness of what belongs and what doesn't. Alerting the authorities.

OUR CELLULAR NAMETAGS

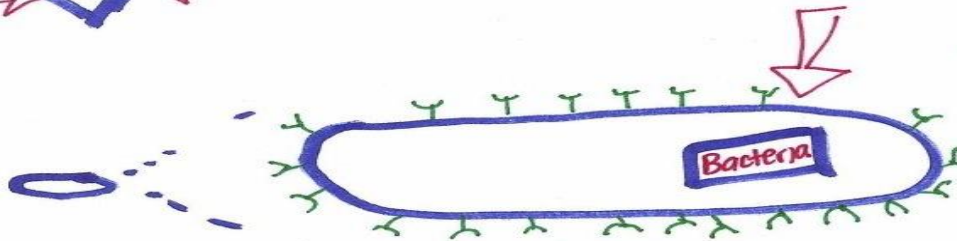
CONCEPT: SELF VS. NON-SELF



MHC

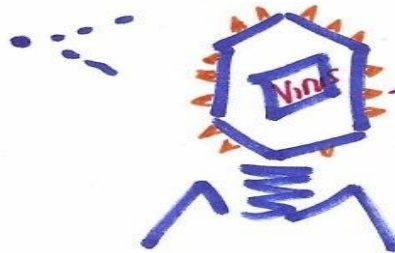
All cells - foreign or not - wear Nametags.

antigen

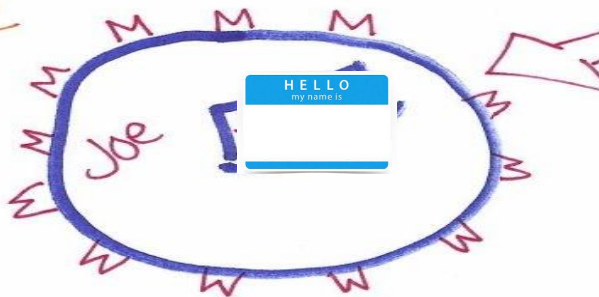


Nametags = antigens (if on foreign molecules)

antigen



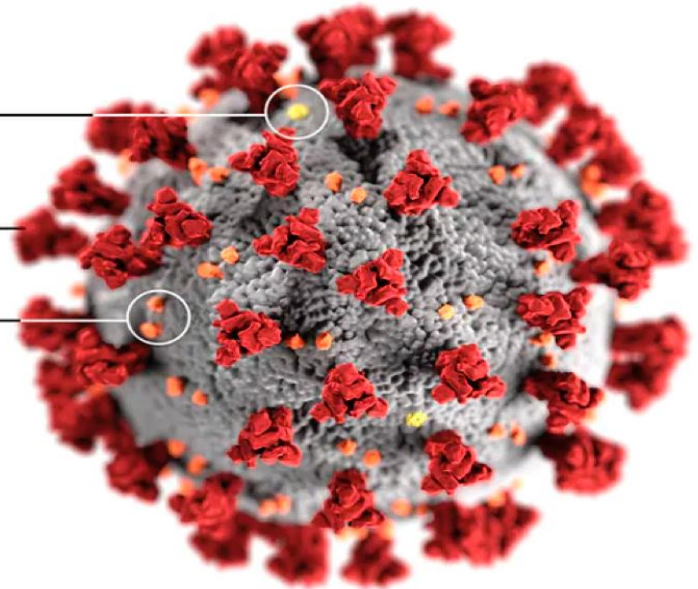
MHC



E protein

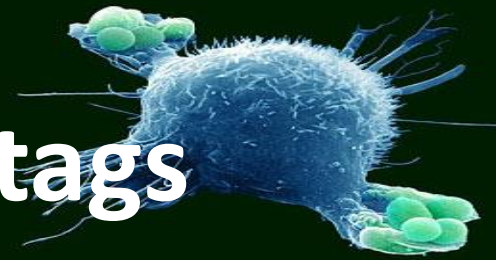
S protein

M protein



COVID-19

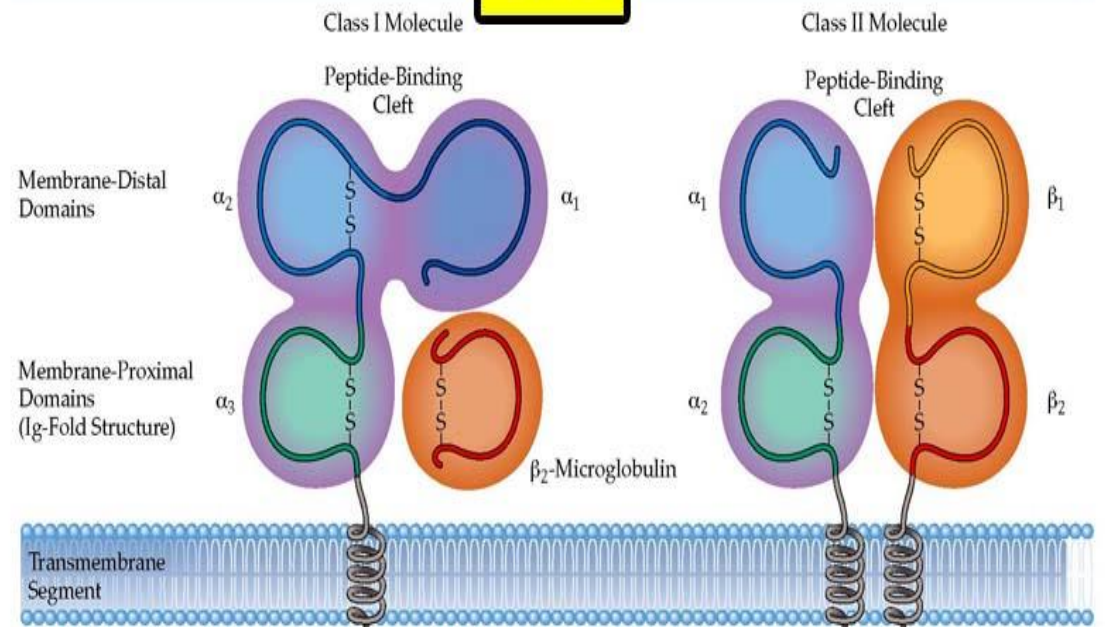
Our nametags



HELLO
my name is

Gillian's cell (liver)

MHC Class I vs MHC Class II



MHC = Major Histocompatibility Complex Antigens
(also known as HLA (Human Leukocyte Antigens))

[How a virus breaks in \(1:43\)](#)

Macrophages become APCs



Antigen Processing + MHC



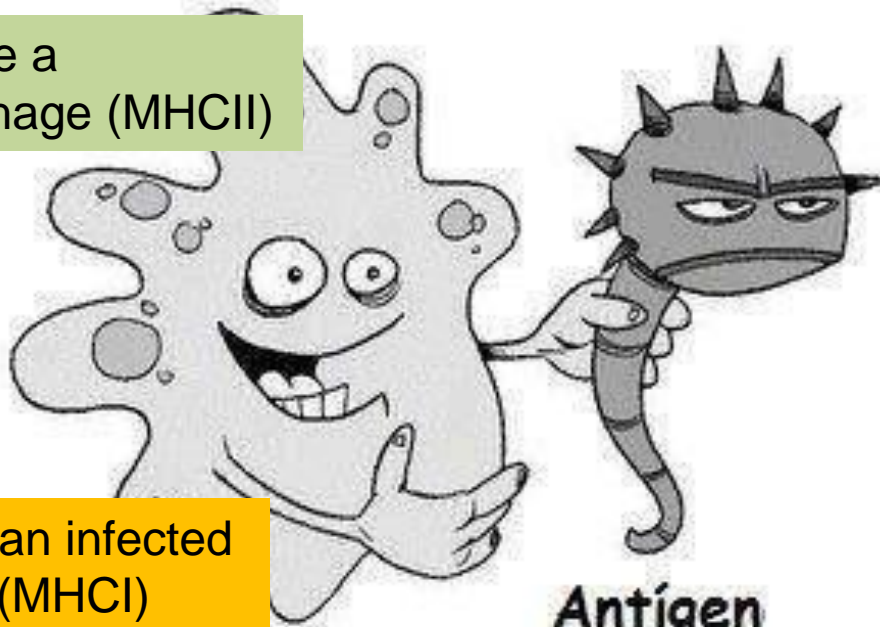
Macrophages digest **exogenous** antigens, and display what they have “eaten” on their MHC

Antigen presentation



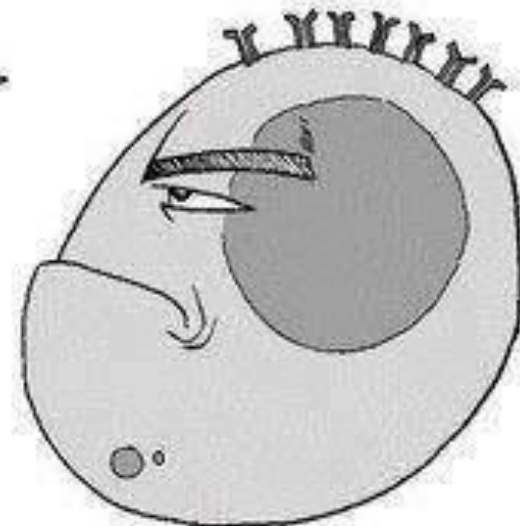
- Display what “infected” you!

Could be a
macrophage (MHCII)



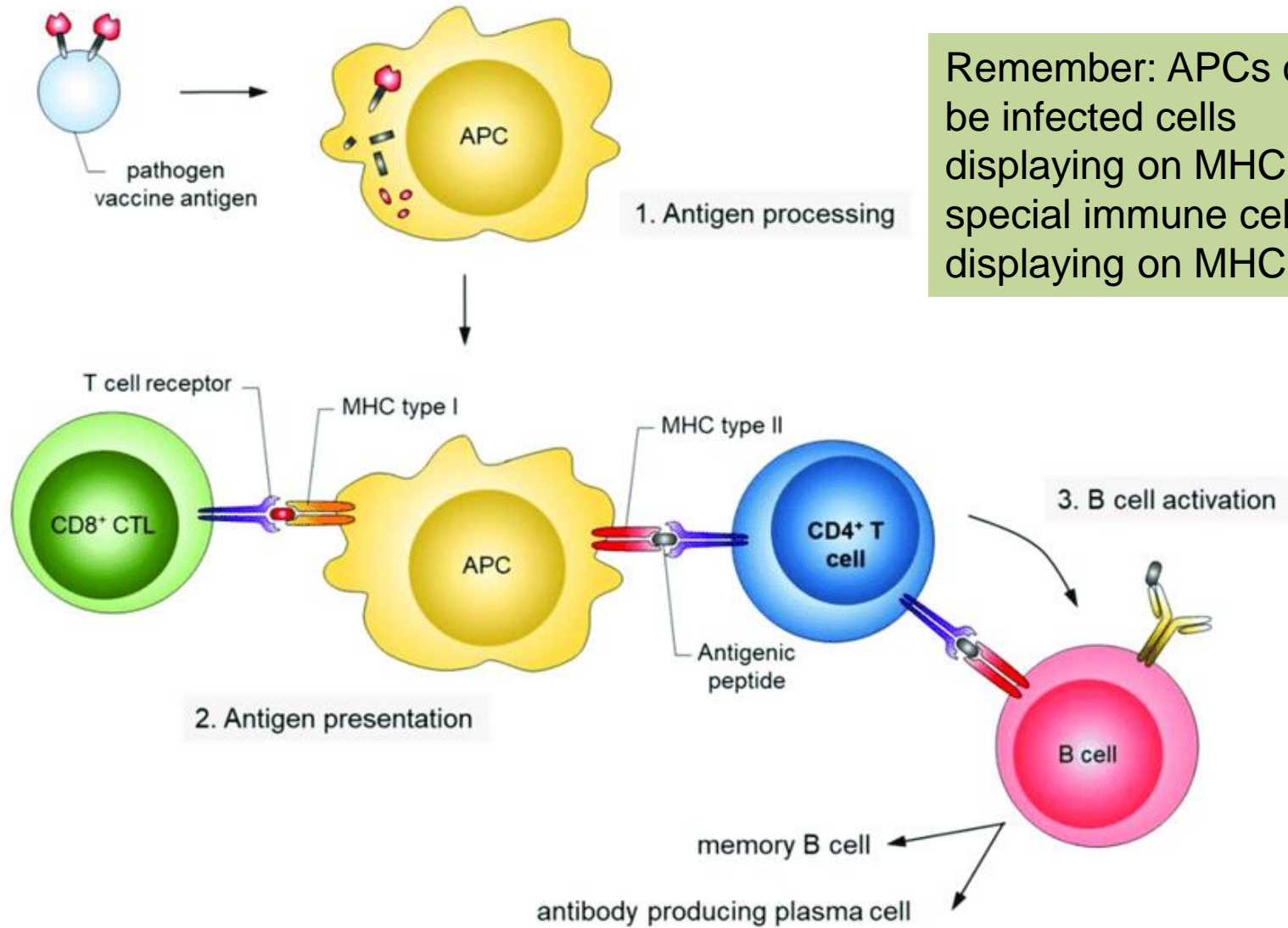
Antigen Presenting
cell

Could be an infected
body cell (MHCI)



Helper T Cell

Antigen Presentation



Remember: APCs can be infected cells displaying on MHC I or special immune cells displaying on MHC II

Two main concepts



1. All cells “wear” nametags (antigens, HLA, MHC I or MHC II)...to identify as “self”
2. Cells “display” what is inside them...ON their nametags

(They are now called Antigen Presenting Cells (APCs))

1. Macrophages digest **exogenous** antigens, or
2. Body cells are infected with **endogenous** antigens (viruses) by displaying epitopes (antigenic determinants) on their MHC I complexes

Why are APCs so important?

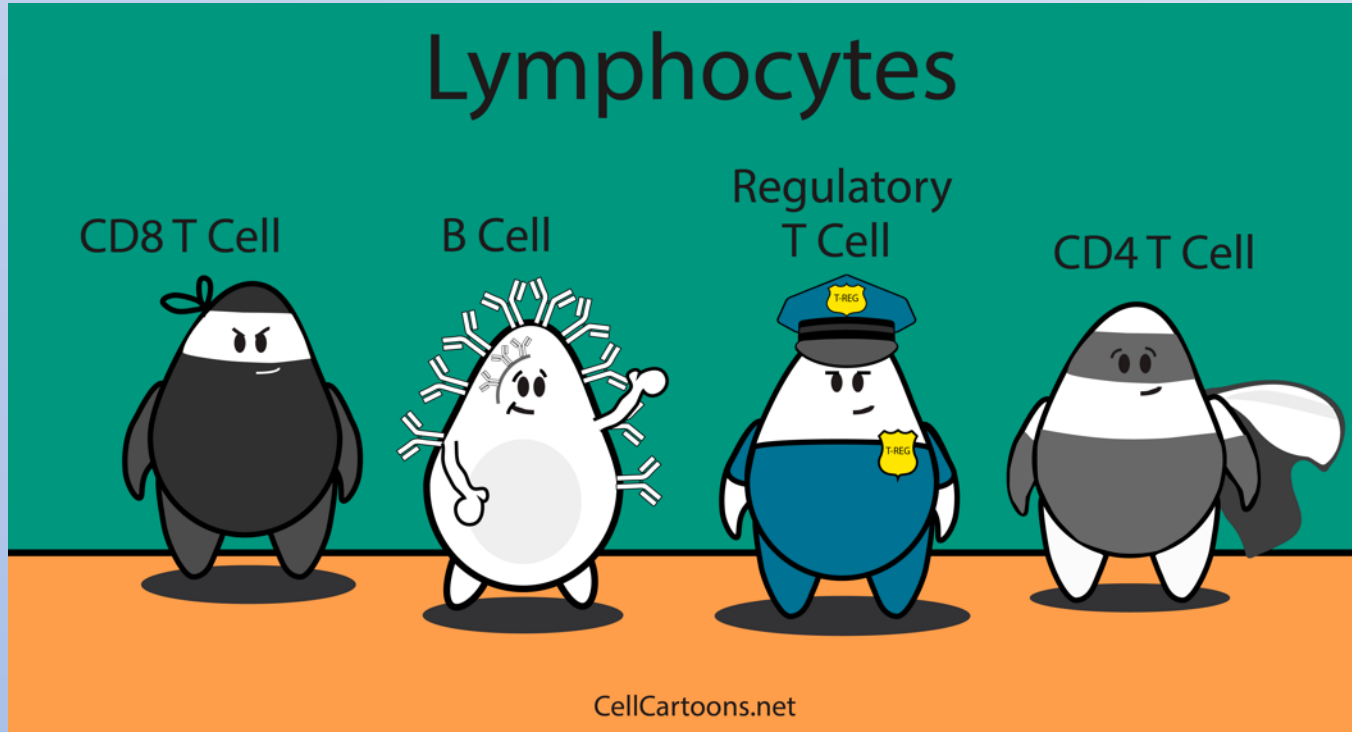


- Triggers the adaptive immune response!
- By binding to cells of the Adaptive Immune Response (B- and T-lymphocytes) and activating them!
- (as do all those inflammatory chemicals from the innate immune response)



FACT OF THE DAY

The immune system uses cytokines to "sound the alarm."



B-cell antibody formation and T-cell activation

**ONCE THE ADAPTIVE IMMUNE
SYSTEM HAS BEEN ALERTED...**

Cells of the Adaptive Immune Response:

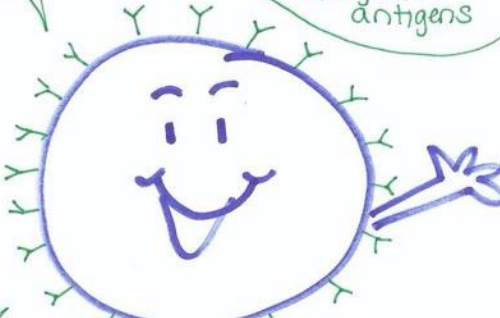


Lymphocytes

B-cells

Hi! I come from + mature in the BONE MARROW!

My B-cell receptors resemble antibodies. I bind to exogenous antigens

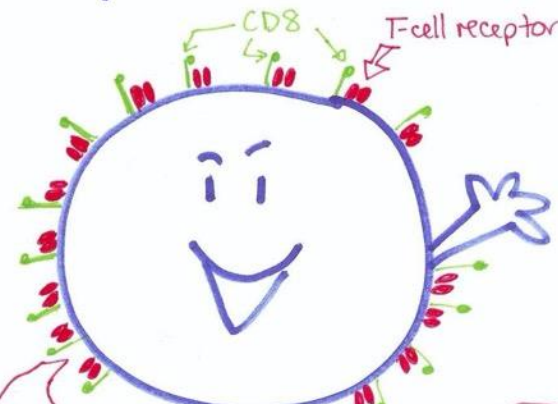


There are 2 types of B-cells

- plasma cells
- memory B-cells

Antibody-Mediated

T-cells



CD8

T-cell receptor

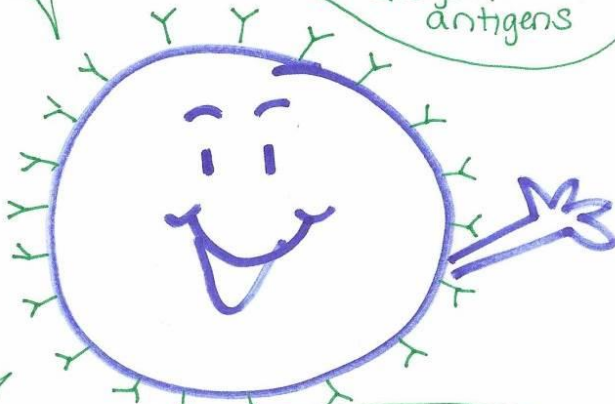
- Hi! I am born in BONE MARROW but receive most of my training + maturation in the THYMUS gland!
- There are 4 types of T-cells
 - Cytotoxic T-cells (CD8+)
 - Helper T-cells (CD4+)
 - Memory T-cells
 - Suppressor T-cells
- My T-cell receptor (TCR) recognizes infected cells (APCs)

Who makes the Antibodies?



B-cells

Hi! I come from + mature in the BONE MARROW!
My B-cell receptors resemble antibodies. I bind to exogenous antigens

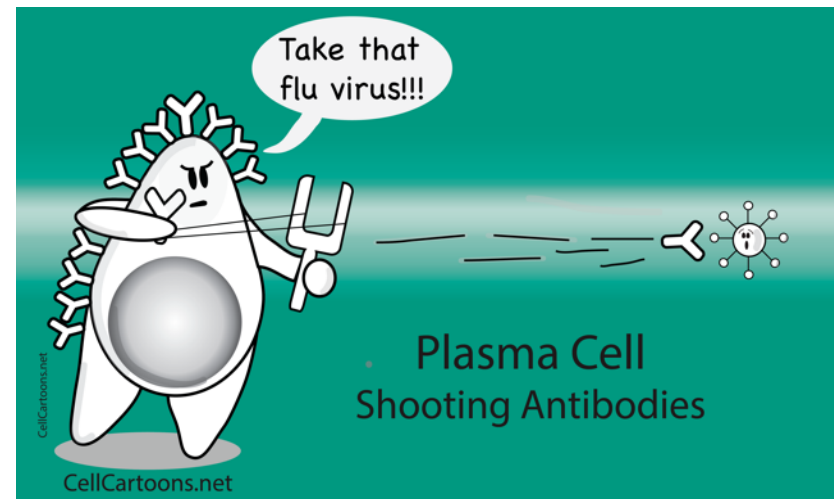


There are 2 types of B-cells

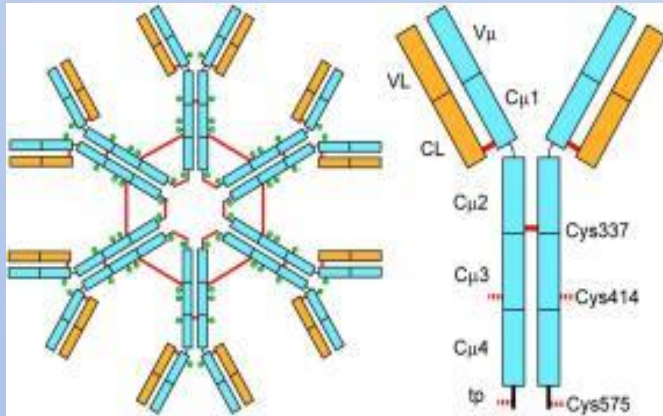
- plasma cells
- memory B-cells

Antibody-Mediated

How do antibodies work?



An overview of Antibodies:



IgM

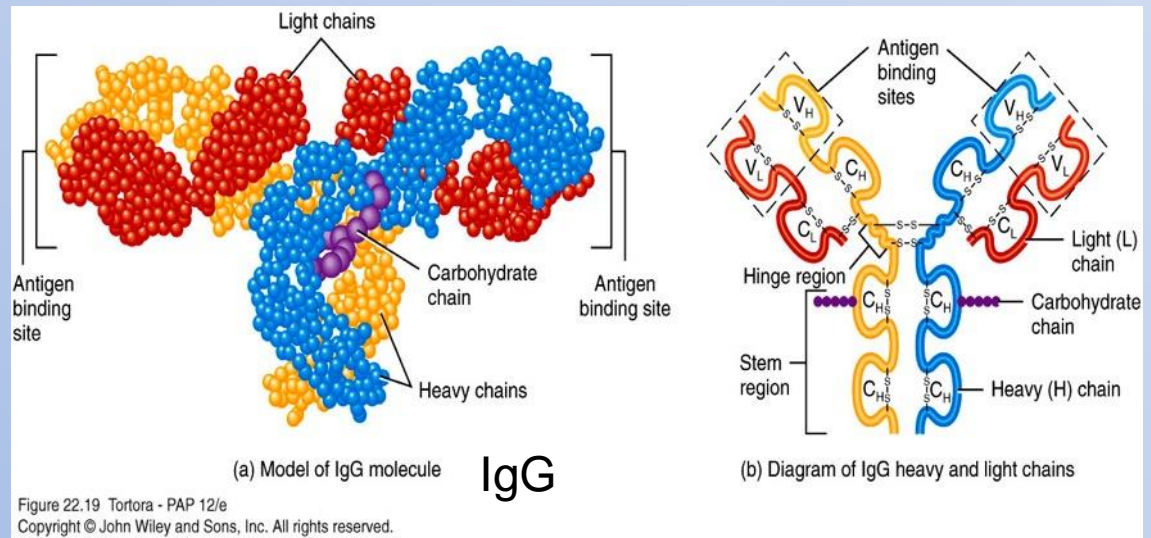
Antibodies are produced by plasma cells (a type of B cell)

Antibodies are specific!

Antibodies = Immunoglobulin (Ig)

All are “Y” shaped plasma proteins

Five Classes: IgG, IgM, IgE, IgD, IgA

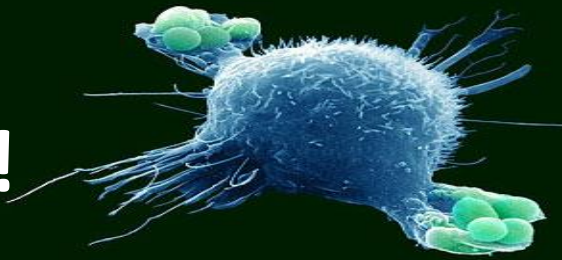


(a) Model of IgG molecule **IgG**

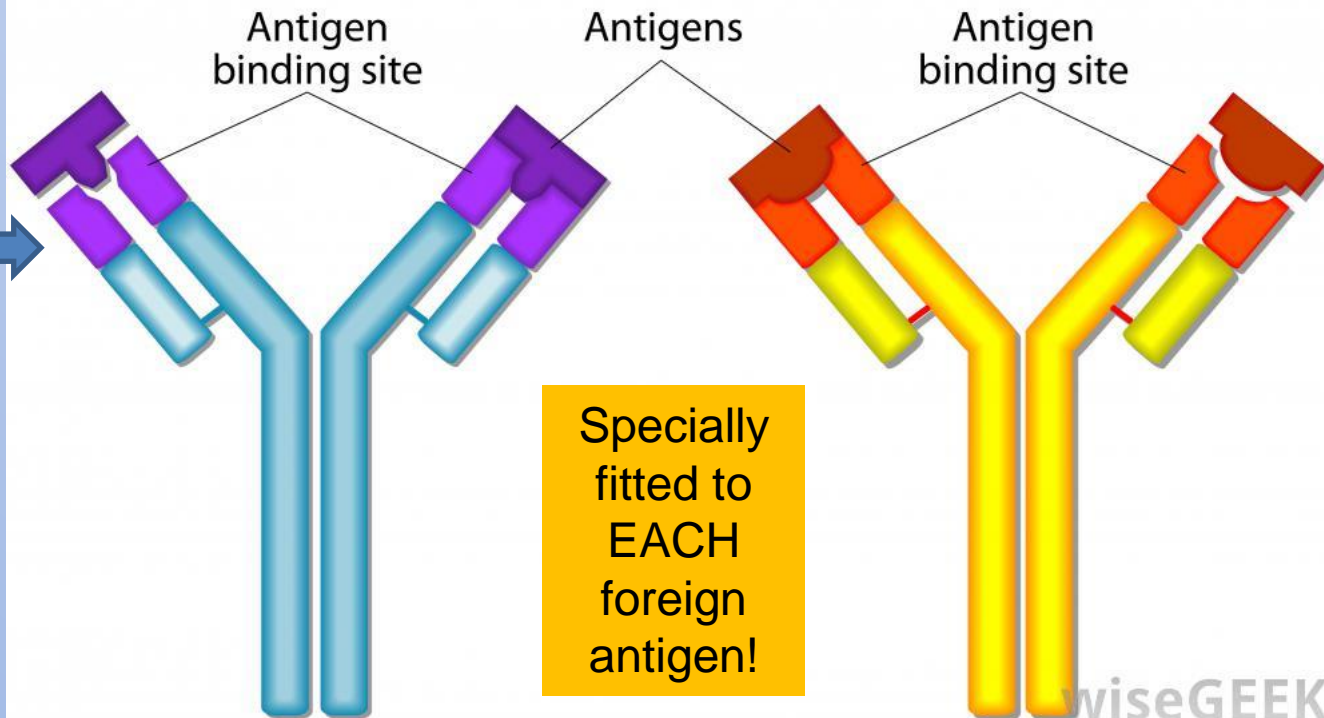
(b) Diagram of IgG heavy and light chains

Figure 22.19 Tortora - PAP 12/e
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Antibodies to the rescue!



ANTIBODY



What type is made in response to COVID-19?



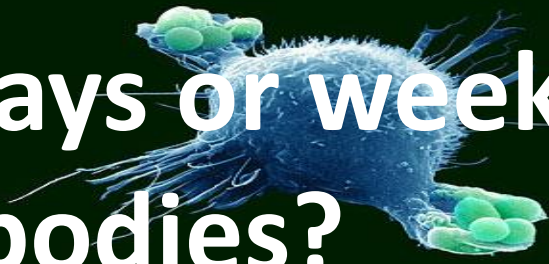
- IgG and IgM
 - Most abundant circulating antibody, (80% of the total Abs)
 - Synthesized in response to an infection
 - Can pass through the wall of small blood vessels to access antigens present in the extracellular spaces.
 - Crosses the placenta in humans

What is the COVID-19 Antibody test?

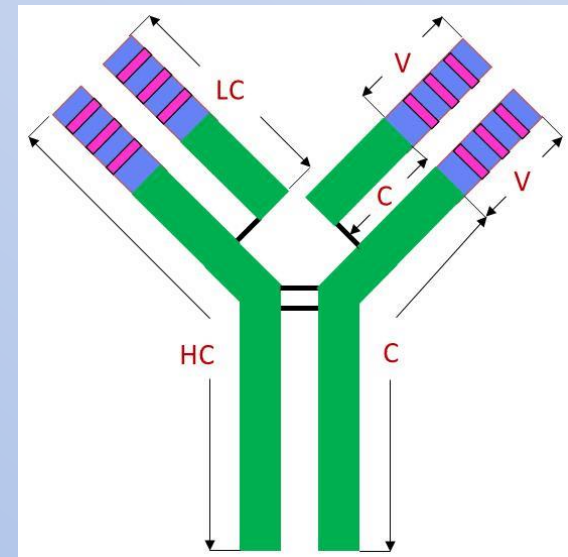


- An antibody test → antibodies that are made by the immune system in response to a threat, such as a specific virus.
- May **take several days or weeks** to develop after infection and may stay in your blood for several weeks after recovery.
- Because of this, antibody tests should not be used to diagnose an active coronavirus infection.

Why does it take days or weeks to make antibodies?



B-cells must figure out the exact right fit of antibody to antigen



Do antibodies make you immune to COVID-19?



- Having antibodies to the virus that causes COVID-19 may provide protection from getting infected with the virus again.
- But even if it does, we do not know how much protection the antibodies may provide or how long this protection may last.

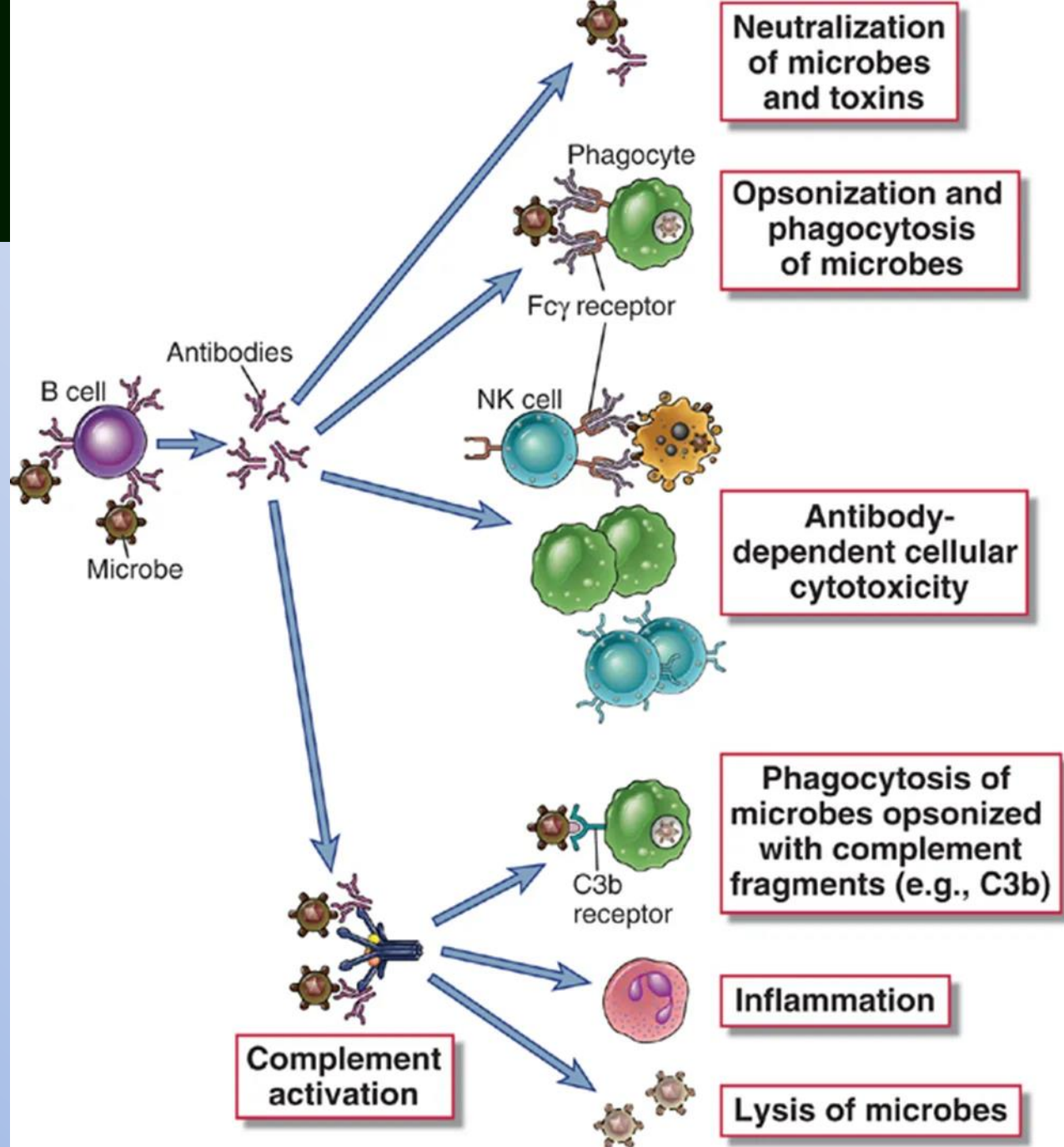
Other Ig Classes



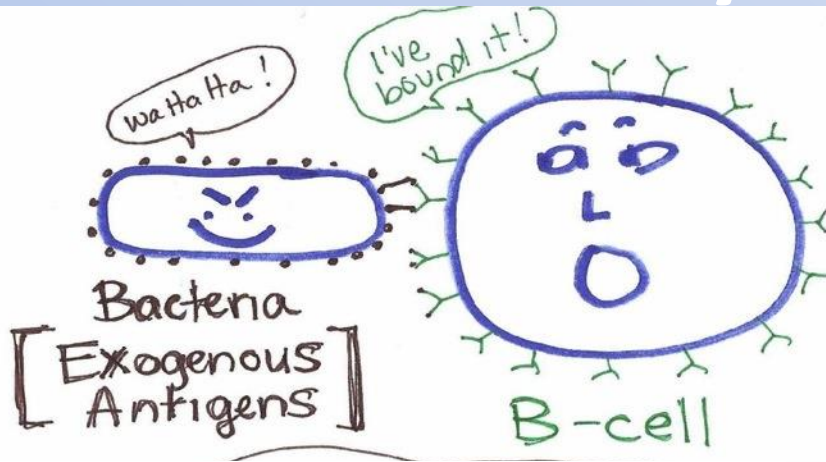
- **IgM** = largest antibody
 - Found on surface of B cells
- **IgA** in serum, mucus, saliva, tears, sweat and milk.
 - IgA in breast milk interferes with the colonization of the GI tract by harmful microorganisms in the first few months of life.
- **IgD** = on B-cells
- **IgE** = Allergic inflammation, in response to eosinophilic activation, mast cells. 0.002% of Ig in serum.

How do antibodies help?

- Neutralize antigen
- Immobilize pathogen
- Agglutinate pathogen
- Make it easier to phagocytose the clump.
- Activate **complement**



Antibody-mediated immunity



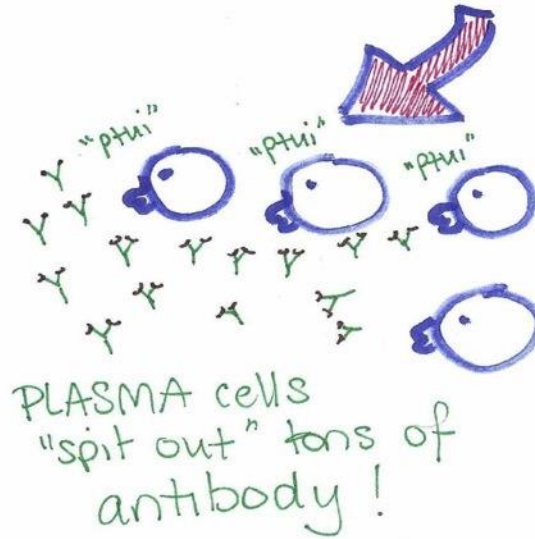
Clonal
Expansion



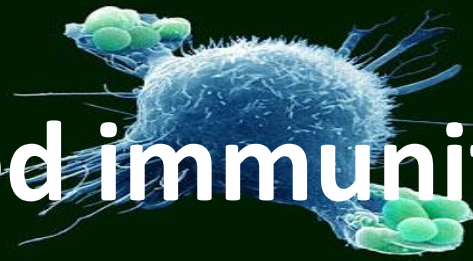
B-cells spend 7-10 days "sampling" and puzzling the proper antibody shape

Once they get the right shape, they go into overdrive, clonally expanding

The resulting plasma cells make JUST that antibody....the war is on!



Antibody-mediated immunity



- A type of Adaptive immunity
- Requires B-cells
- B-cells generate Antibodies (one of five classes)
- Takes 7-10 days to “puzzle” it out
- Generates memory B-cells....that last for days/months/years
- This is ACTIVE IMMUNITY
- Vaccines generate ACTIVE IMMUNITY

You get your COVID-19 vaccination...

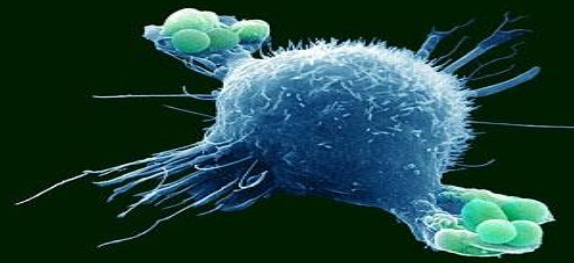


- What is happening in your body to generate immunity?
 - Discuss role and activities of B-cells
 - Discuss how B-cells make antibodies
 - Discuss how memory is formed.



Can vaccinated people have no symptoms and still spread the virus to the unvaccinated?

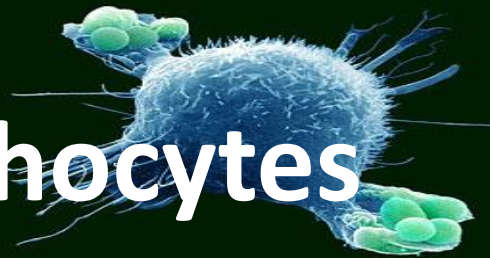
- Studies are unclear on this. The data available so far indicate that vaccination [significantly curbs infection](#) in people who show no symptoms. In Moderna's [phase 3 clinical trial](#), a diagnostic test before the second dose of the vaccine showed 89.6 percent of asymptomatic and symptomatic cases were prevented by the first dose. (National Geographic.com)



How long after being vaccinated does 'full' immunity kick in?

- It takes one to two weeks after the second shot to achieve the maximum level of protection from [COVID-19](#). In clinical trials, these vaccines are each about 95 percent effective in preventing [cases of COVID-19](#). (National Geographic.com)
- At this point, it is unknown how long immunity will last after a person is fully vaccinated, and only time will reveal the answer. The COVID-19 vaccine could become a yearly shot, similar to the flu shot; its benefits could last for a shorter time, or longer. (National Geographic.com)

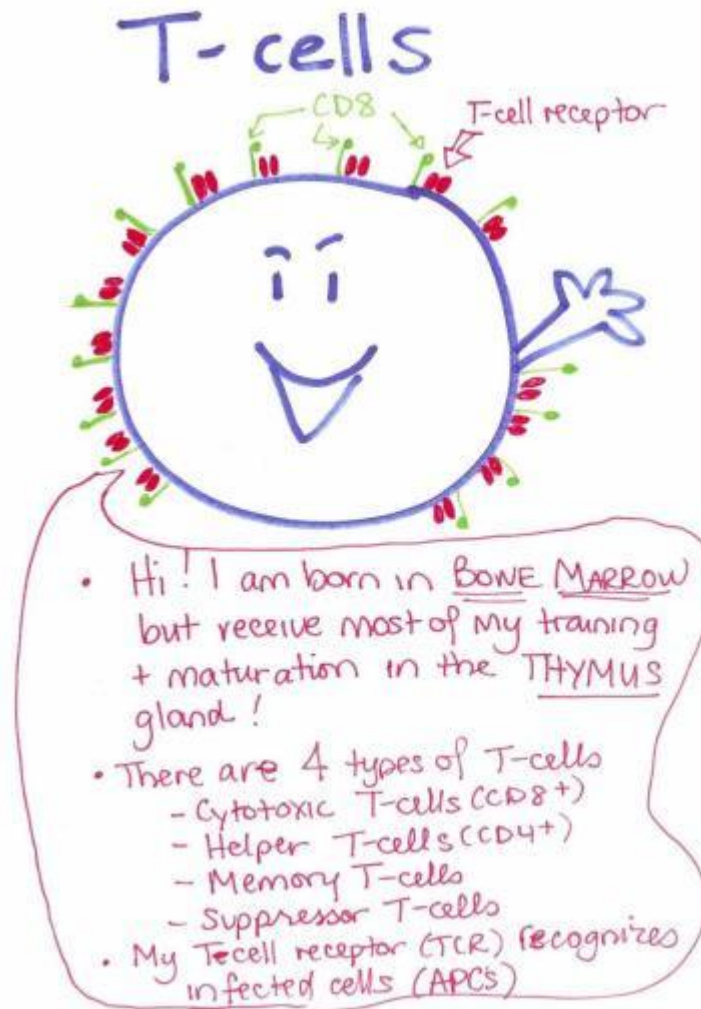
Now....T lymphocytes



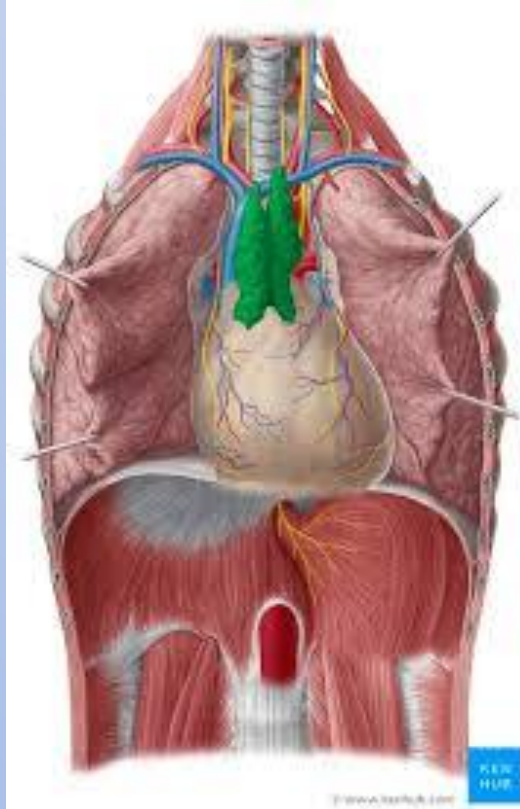
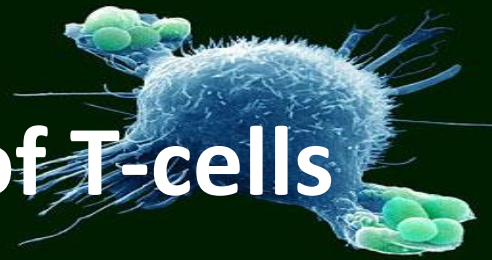
T-lymphocytes, over 7-10 days, learn to recognize infected cells. They are killer cells...killing by causing lysis of infected cells.

They attack Antigen Presenting Cells (APCs)

As such, they better be SURE they are attacking an infected cell not a normal body cell.



The Schooling of T-cells



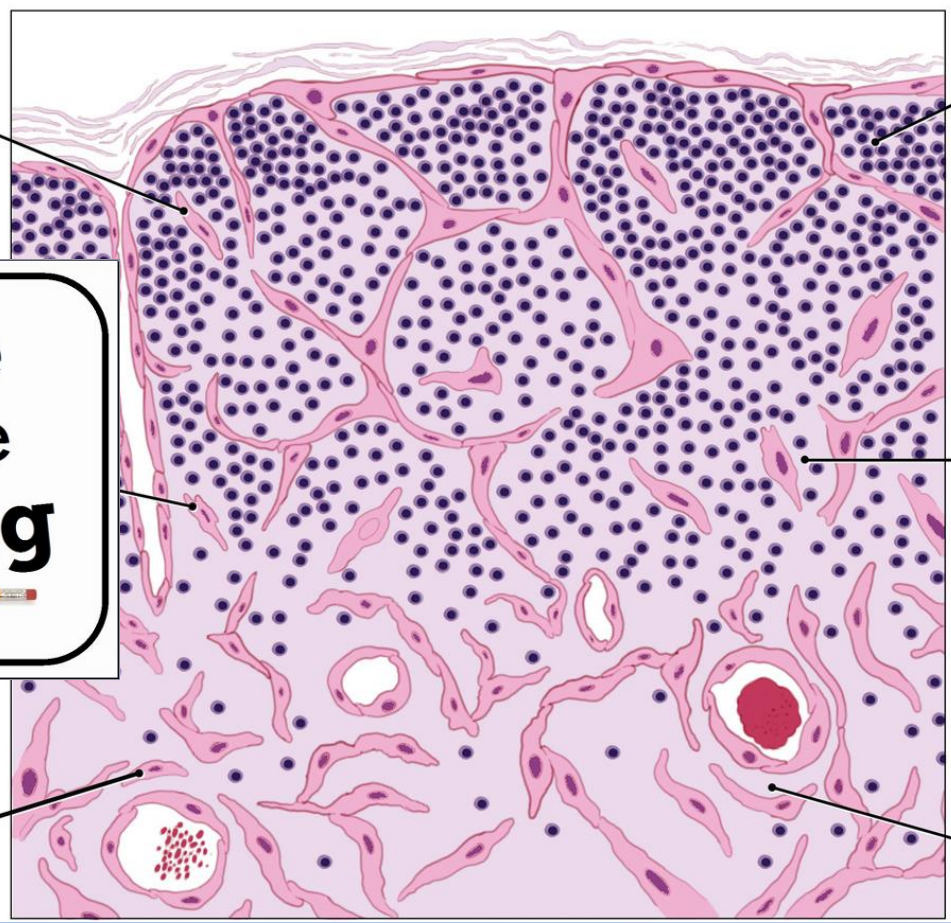
1. Thou shalt recognize APC and ONLY APCs
2. Thou shalt NOT attack thine own MHC molecules
3. Thou shalt attack APCs without mercy, causing lysis

Thymus University

How do the thymus and lymph nodes work?

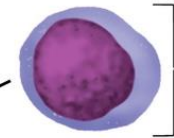


il Cells
ocytes)



Thymocytes

Subcapsular



CD4⊖
CD3⊖
CD8⊖

Cortical



CD3⊕
CD4⊕
CD8⊕

Medullary



Single⊕ CD4
CD8 Immunocompetent
Activated T-cell

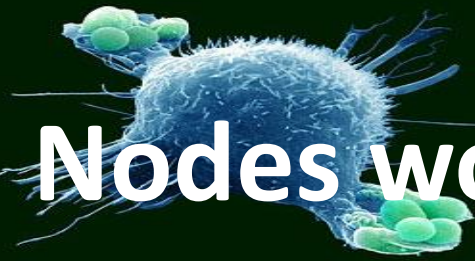
PLEASE DO NOT DISTURB!

We Are **Testing**

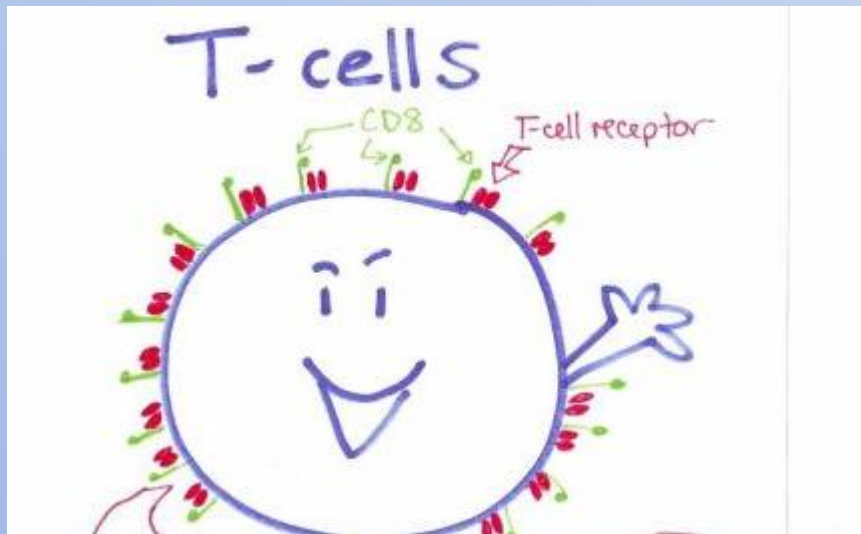
Thank you!

Medullary
(types 4-5)

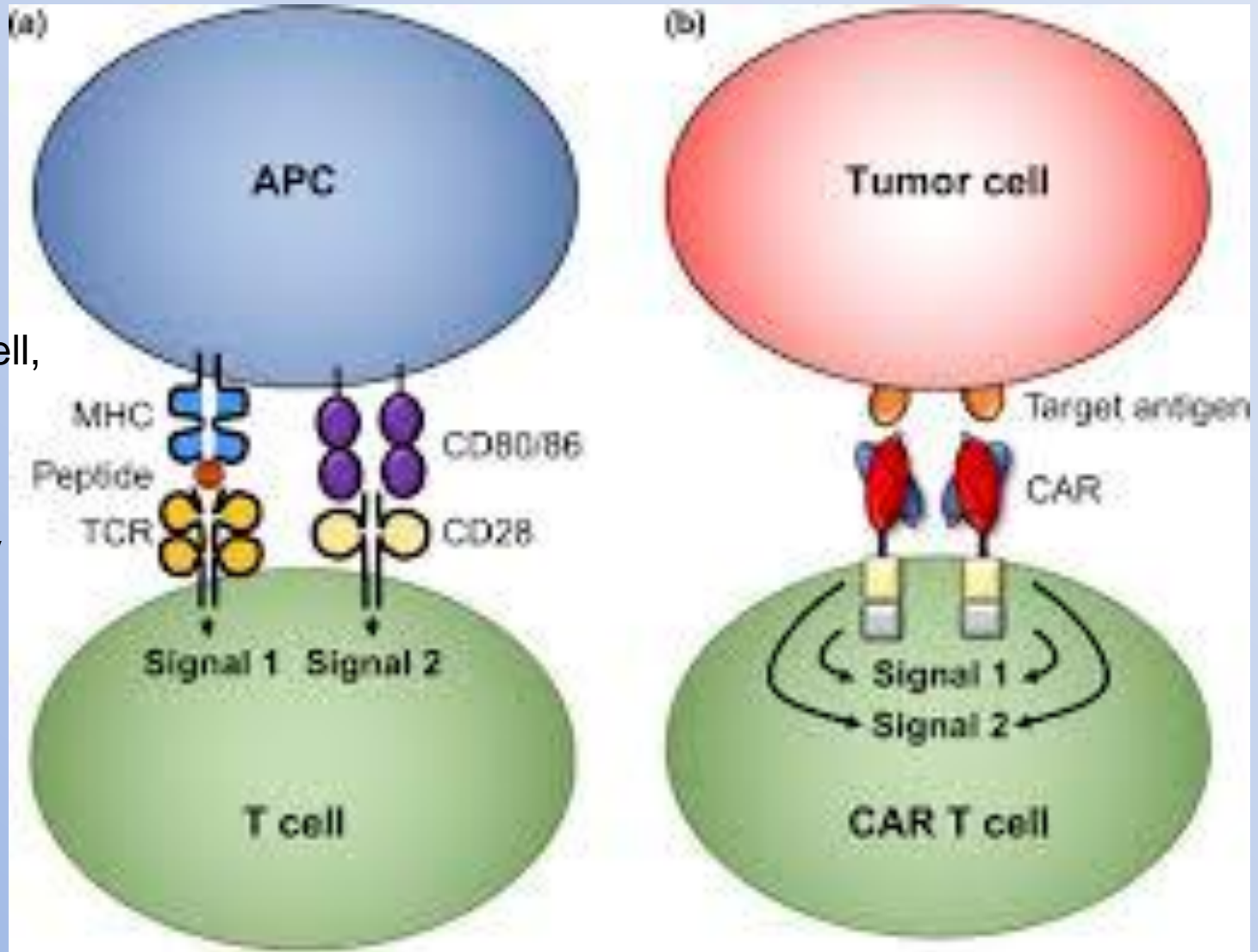
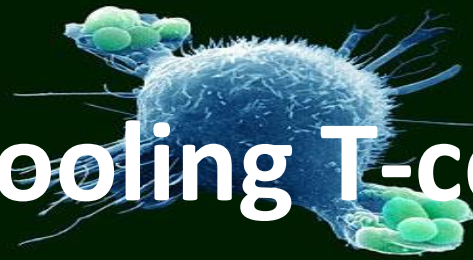
Thymus and Lymph Nodes work



- How the adaptive immune system works
(1:27)



Co-stimulation: schooling T-cells



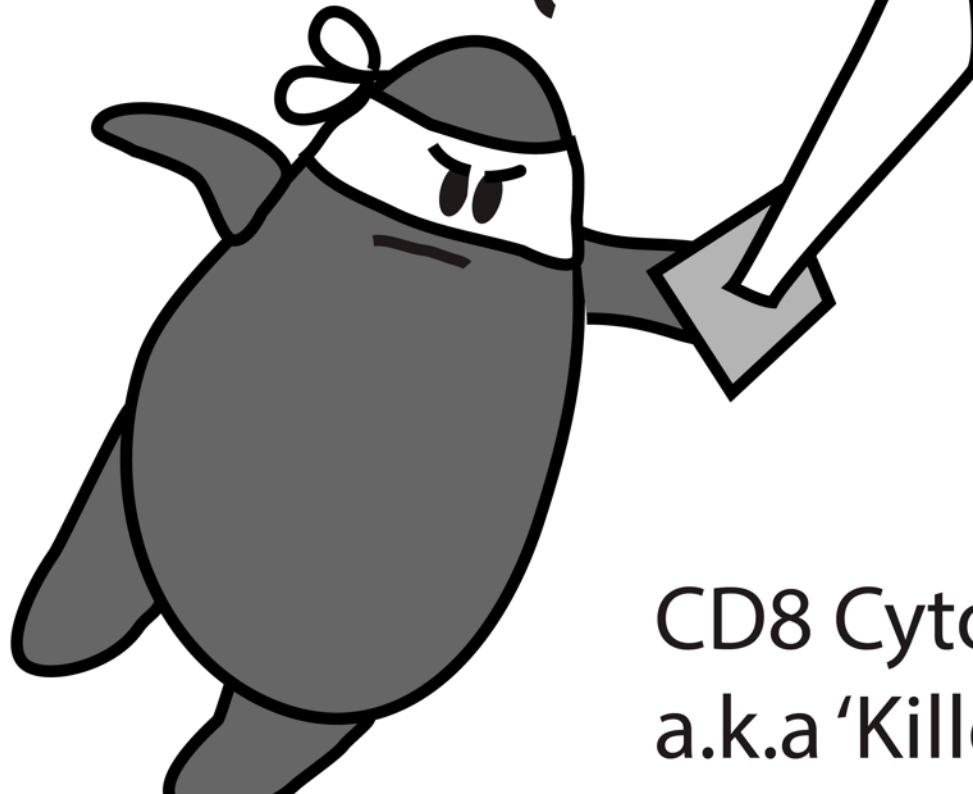
To activate a T-cell,
need 2 signals

1. APC signal
2. Costimulatory signal

CD8 Cytotoxic “Killer” T cell



I'M READY TO FIND AND
KILL THOSE INFECTED CELLS!

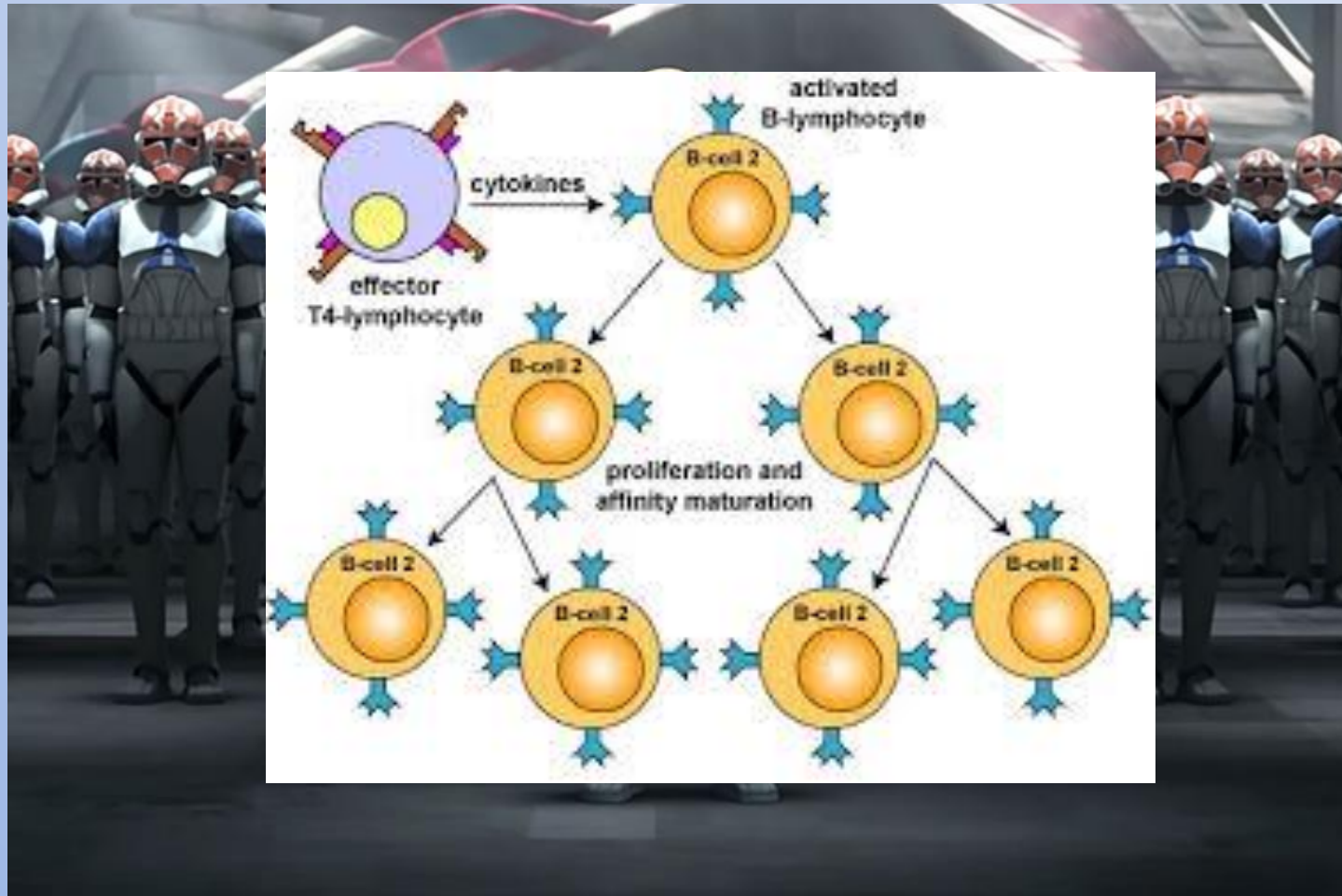


CD8 Cytotoxic T Cell
a.k.a 'Killer T cell'

Once one cell learns...it makes an army of clones!



Both B- and T-cells can undergo clonal expansion



Summa Cum laude graduates of Thymus University



Memory is created!

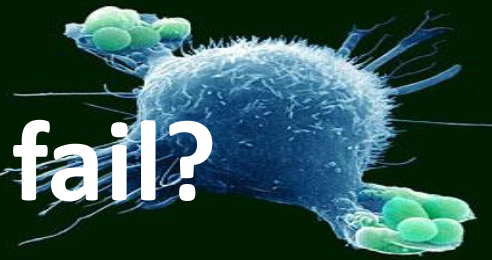


- B- and T-cells require TIME to create specific, activated cells (7-10 days, of puzzle-piecing)
- Both B- and T-cells are able to **SPECIFICALLY** target the pathogen, in ways innate immune cells cannot
- Memory B- and Memory T-cells will remember these antigens **FOREVER.**

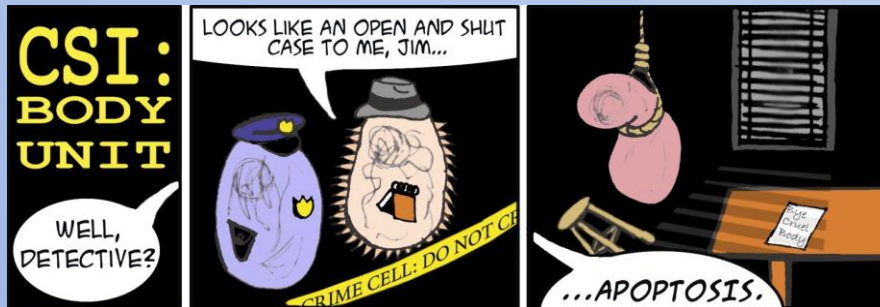
This is
true
immunity!



Can T-cells fail?



- Yes. overreactive & underreactive T-cells are deactivated...they do not graduate from thymus university.

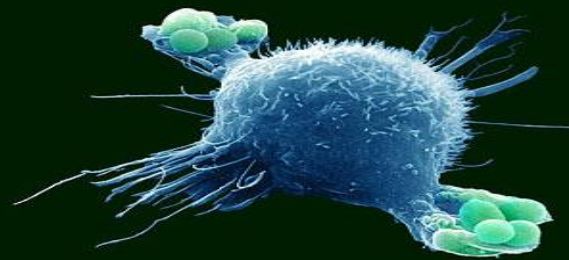


Deletion – undergo apoptosis



Anergic T-cells – remain alive but are unresponsive

Autoimmune disorders



- When trigger-happy CD8 T-cells attack YOUR tissue...even when it isn't infected.
- Autoimmune disorders attack "self" as foreign.

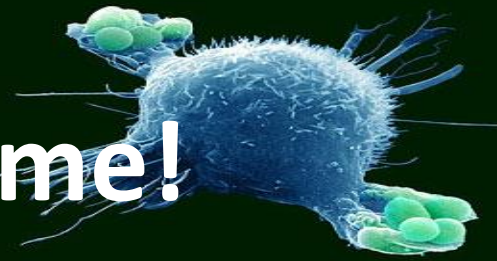


Let's Wrap up with History....



- [The Influenza epidemic \(8:21\)](#)
 - Why doesn't one vaccine work?
 - Why was there never an influenza vaccine?
 - Disaster averted: 1957 Asian Flu pandemic

Send it to me!



Draw a multi-panel cartoon depicting the adaptive immune response as your body fights COVID-19.

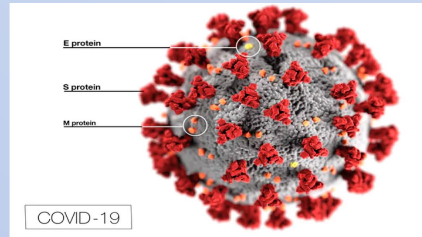
Remember: COVID-19 is a VIRUS. It hides out inside cells, but also breaks out of cells in search of other cells to infect.

How the adaptive immune response attack viruses while inside infected cells or inside macrophages?

How does the adaptive immune response attack viruses when they are released from cells?

Draw both methods as they happen!

What you learned today



1. Recognizing what belongs
2. Sounding the alarm (call 911!)
3. Launching the Battle
 1. Training the Troops (B-cell method, T-cell method)
 2. Eliminating the ones who fail.
4. Learning from the Battle
 1. Memory – immunization

